Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
This journal is © The Royal Society of Chemistry 2014

Electronic Supplementary Information

Stereoselective Synthesis of Fluorinated Aminoglycosyl Phosphonates

Sanne Bouwman, Romano V. A. Orru, and Eelco Ruijter*

Department of Chemistry & Pharmaceutical Sciences and Amsterdam Institute for Molecules, Medicines and Systems (AIMMS), VU University Amsterdam, De Boelelaan 1083, 1081 HV Amsterdam, The Netherlands

*E-Mail: e.ruijter@vu.nl

Contents:

General information

All reactions were carried out in flame-dried glassware under an inert atmosphere of dry nitrogen. Solvents were dried and distilled from appropriate drying agents prior to use and stored under nitrogen. Commercially available reagents were used as received, unless stated otherwise. The 2-nitroglycals **1a-j** were prepared according to the procedures developed by Vankar.[1] Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 500 (125.78 MHz for ^{13}C), Bruker Avance 400 (100.62 MHz for ^{13}C, 161.97 MHz for ^{31}P) or Bruker Avance 250 (62.90 MHz for ^{13}C, 101.26 MHz for ^{31}P, 235.33 MHz for ^{19}F) using the residual solvent as internal standard (^{1}H: δ 7.26 ppm, ^{13}C{^{1}H}: δ 77.00 ppm for $CDCl_3$, ^{1}H: δ 2.50 ppm, ^{13}C{^{1}H}: δ 39.43 ppm for DMSO-d_6 and ^{1}H: δ 3.31 ppm, ^{13}C{^{1}H}: δ 49.05 ppm for MeOD-d_4) or 85 % H_3PO_4 (^{31}P) and $CFCl_3$ (^{19}F) as external standards. Chemical shifts (δ) are given in ppm and coupling constants (*J*) are reported in hertz (Hz). Peak multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), br s (broad singlet) and m (multiplet) or combinations thereof. The numbers of protons (*n*) for a given resonance is indicated as *n*H, and is based on spectral integration values. Electrospray Ionization (ESI) high-resolution mass spectrometry was carried out using a Bruker micrOTOF-Q instrument in positive or negative ion mode (capillary potential of 4500 V). Optical rotations were measured with a polarimeter (589 nm) and reported as follows: $[\alpha]_D^{20}$ (*c* = g/100 mL, solvent). Flash chromatography was performed on Silicycle Silia-P Flash Silica Gel (particle size 40-63 µm, pore diameter 60 Å) using the indicated eluent. Thin Layer Chromatography (TLC) was performed using TLC plates from Merck (SiO2, Kieselgel 60 F254 neutral, on aluminium with fluorescence indicator) and compounds were visualized by UV detection (254 nm), and/or by charring at ~150 °C after dipping into a solution of cerium molybdate, 5% H_2SO_4 in ethanol, or $KMnO_4$.

Experimental procedures and characterization data

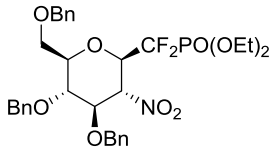
General procedure for the synthesis 2-deoxy-2-nitro-CF_2-glycosyl phosphonates

A solution of *n*-BuLi (960 µL, 1.6 M, 0.6 mmol) in THF was added dropwise to a stirred solution of *i*-Pr_2NH (84 µL, 0.6 mmol) in THF (3 mL) at –40 °C. The reaction mixture was warmed up to 0 °C, stirred for 20 min, and cooled down again to –78 °C. The difluoromethylphosphonate (0.6 mmol) was added, followed by stirring at this temperature for 30 min. Subsequently, a solution of the nitroglycal (0.5 mmol) in THF (5 mL) was added dropwise and stirred for 30 min at –78 °C. Then, the resulting mixture was quenched with a saturated aqueous NH_4Cl solution and extracted three times with EtOAc (10 mL). The combined organic extracts were washed with water (10 mL), brine (10 mL) and dried over Na_2SO_4. The crude product was purified by flash chromatography using the eluent specified below.

Note: α,α,α-trifluorotoluene (61 µL, 0.5 mmol) was added as internal standard to determine the yield and diastereomeric ratio of the product by ^{19}F NMR.

Note: In some cases the reaction gave inseparable diastereoisomers, resulting in the isolation of the major isomer contaminated with the other isomer(s).

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (2a):



According to the general procedure, the reaction of 3,4,6-tri-*O*-benzyl-2-nitro-D-glucal **1a** with diethyl lithiodifluoromethanephosphonate afforded the corresponding 2-deoxy-2-nitro-CF_2-glycosyl phosphonates as a 89:7:3:1 diastereomeric mixture in 83% yield. Flash chromotagraphy using *c*-hex/EtOAc (2:1) afforded the major isomer **2a** as a colorless oil.

R_F: 0.22 (*c*-hex/EtOAc, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.36-7.29 (m, 11H), 7.26-7.23 (m, 2H), 7.21-7.18 (m, 2H), 5.06 (t, *J* = 10.0 Hz, 1H), 4.80 (dd, *J* = 10.8, 5.6 Hz, 2H), 4.63-4.45 (m, 5H), 4.34-4.20 (m, 5H), 3.81-3.66 (m, 4H), 1.31 (dt, *J* = 7.1, 3.6 Hz, 6H).

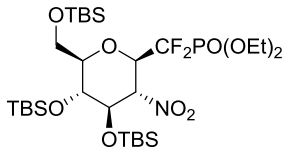
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 137.4 (C), 137.3 (C), 136.8 (C), 128.4 (CH), 128.4 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 117.0 (ddd, J_{CF} = 273.3 Hz, J_{CF} = 262.7 Hz, J_{CP} = 208.0 Hz, C), 83.5 (br s, CH), 82.7 (CH), 79.6 (CH), 76.7 (CH), 76.7-76.1 (m, CH), 75.8 (CH_2), 75.1 (CH_2), 73.4 (CH_2), 67.9 (CH_2), 65.1 (d, J_{CP} = 6.7 Hz, CH_2), 64.9 (d, J_{CP} = 6.5 Hz, CH_2), 16.2 (d, J_{CP} = 5.7 Hz, CH_3).

^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –115.6 (ddd, J_{FF} = 317.7, J_{FP} = 94.8 Hz, J_{FH} = 4.9 Hz), –125.4 (ddd, J_{FF} = 317.7, J_{FP} = 95.6 Hz, J_{FH} = 16.0 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 4.71 (t, J_{PF} = 95.3 Hz).

HRMS (ESI+): *m/z* calculated for $C_{32}H_{39}F_2NO_9P$ $[M+H]^+$ 650.2325, found 650.2292.

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranosyl)phosphonate (2b):



According to the general procedure, the reaction of 3,4,6-tri-*O*-TBS-2-nitro-D-glucal **1b** with diethyl lithiodifluoromethanephosphonate afforded the corresponding 2-deoxy-2-nitro-CF_2-glycosyl phosphonates as a 90:10 diastereomeric mixture in 42% yield. Flash chromotagraphy using *c*-hex/EtOAc (9:1) afforded the major isomer **2b** as a colorless oil.

R_F: 0.31 (*c*-hex/EtOAc, 9:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.22-5.09 (m, 1H), 4.89-4.78 (m, 1H), 4.55-4.46 (m, 1H), 4.37-4.19 (m, 4H), 4.08-4.00 (m, 1H), 3.90-3.81 (m, 1H), 3.80-3.66 (m, 2H), 1.44-1.31 (m, 6H), 0.92 (s, 9H), 0.89 (s, 9H), 0.84 (s, 9H), 0.31-0.12 (m, 6H), 0.12-0.00 (m, 12H).

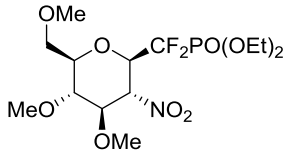
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 117.1 (ddd, J_{CF} = 270.9 Hz, J_{CF} = 263.2 Hz, J_{CP} = 209.9 Hz, C), 82.6 (CH), 81.2 (br s, CH), 74.4 (CH), 71.4 (ddd, J_{CF} = 28.3 Hz, J_{CF} = 21.9 Hz, J_{CP} = 14.3 Hz, CH), 69.1 (CH), 64.8-64.7 (m, CH_2), 63.7 (CH_2), 25.9 (CH_3), 25.7 (CH_3), 25.5 (CH_3), 18.4 (C), 17.9 (C), 17.8 (C), 16.3 (dd, J_{CP} = 5.8, J_{CP} = 3.2 Hz, CH_3), –4.7 (CH_3), –4.9 (CH_3), –5.0 (CH_3), –5.2 (CH_3), –5.4 (CH_3), –5.4 (CH_3).

^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –118.3 (ddd, J_{FF} = 315.5, J_{FP} = 96.1 Hz, J_{FH} = 5.5 Hz), –125.9 (ddd, J_{FF} = 315.5, J_{FP} = 100.2 Hz, J_{FH} = 16.6 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 4.91 (dd, J_{PF} = 100.1, J_{PF} = 96.3 Hz).

HRMS (ESI+): *m/z* calculated for $C_{29}H_{62}F_2NNaO_9PSi_3$ $[M+Na]^+$ 744.3330, found 744.3375.

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-methyl-β-D-glucopyranosyl)phosphonate (2c):



According to the general procedure, the reaction of 3,4,6-tri-*O*-methyl-2-nitro-D-glucal **1c** with diethyl lithiodifluoromethanephosphonate afforded the corresponding 2-deoxy-2-nitro-CF_2-glycosyl phosphonates as a 86:3:11 diastereomeric mixture in 86% yield. Flash chromotagraphy using *c*-hex/EtOAc (1:1) afforded the major isomer **2c** as a colorless oil.

R_F: 0.50 (*c*-hex/EtOAc, 1:2).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.84 (t, *J* = 10.0 Hz, 1H), 4.38 (ddd, *J* = 15.4, 10.0, 5.0 Hz, 1H), 4.33-4.18 (m, 4H), 3.90 (t, *J* = 9.5 Hz, 1H), 3.65-3.57 (m, 2H), 3.54 (s, 3H), 3.53 (s, 3H), 3.51-3.34 (m, 4H), 3.34 (t, *J* = 9.5 Hz, 1H), 1.35 (t, *J* = 7.2 Hz, 6H).

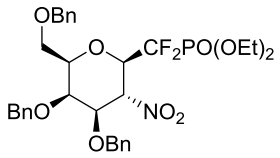
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 117.0 (ddd, J_{CF} = 274.2 Hz, J_{CF} = 262.2 Hz, J_{CP} = 208.1 Hz, C), 84.7 (CH), 83.3 (t, J_{CF} = 3.4 Hz, CH), 79.5 (CH), 78.4 (CH), 76.3 (ddd, J_{CF} = 29.9 Hz, J_{CF} = 23.4 Hz, J_{CP} = 13.4 Hz, CH), 70.2 (CH_2), 65.1 (d, J_{CP} = 6.3 Hz, CH_2), 64.9 (d, J_{CP} = 6.5 Hz, CH_2), 61.3 (CH), 60.6 (CH), 59.0 (CH), 16.3 (t, J_{CP} = 5.9 Hz, CH_3).

^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –115.9 (ddd, J_{FF} = 317.4, J_{FP} = 94.3 Hz, J_{FH} = 4.5 Hz), –125.5 (ddd, J_{FF} = 317.4, J_{FP} = 94.4 Hz, J_{FH} = 16.1 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 3.70 (t, J_{PF} = 94.5 Hz).

HRMS (ESI+): *m/z* calculated for $C_{14}H_{27}F_2NO_9P$ $[M+H]^+$ 422.1386, found 422.1382.

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)phosphonate (2e):



According to the general procedure, the reaction of 3,4,6-tri-*O*-benzyl-2-nitro-D-galactal **1e** with diethyl lithiodifluoromethanephosphonate afforded the corresponding 2-deoxy-2-nitro-CF_2-glycosyl phosphonates as a >98:2 diastereomeric mixture in 70% yield. Flash chromotagraphy using *c*-hex/EtOAc (3:1) afforded major isomer **2e** as a colorless oil.

R_F: 0.24 (*c*-hex/EtOAc, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.41-7.25 (m, 15H), 5.17-5.05 (m, 2H), 4.75-4.57 (m, 5H), 4.54-4.43 (m, 2H), 4.36-4.20 (m, 5H), 3.99 (dd, *J* = 11.5, 7.9 Hz, 1H), 3.85 (dd, *J* = 5.2, 2.1 Hz, 1H), 3.82 (dd, *J* = 11.6, 3.1 Hz, 1H), 1.34 (dt, *J* = 23.2, 7.1 Hz, 6H).

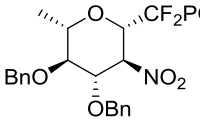
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 138.0 (C), 137.2 (C), 136.7 (C), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 127.6 (CH), 118.3 (ddd, J_{CF} = 270.9 Hz, J_{CF} = 268.1 Hz, J_{CP} = 209.7 Hz, C), 78.4 (br s, CH), 75.4 (CH), 74.8 (CH), 74.6 (CH_2), 74.3 (CH), 73.3 (CH_2), 72.6 (CH_2), 68.3 (ddd, J_{CF} = 28.4 Hz, J_{CF} = 22.4 Hz, J_{CP} = 13.2 Hz, CH) 66.1 (CH_2), 65.0 (d, J_{CP} = 6.4 Hz, CH_2), 16.3 (d, J_{CP} = 5.5 Hz, CH_3).

^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –113.8 - –115.0 (m), –122.4 (ddd, J_{FF} = 310.8, J_{FP} = 97.5 Hz, J_{FH} = 14.3 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 4.83 (dd, J_{PF} = 97.7, J_{PF} = 94.4 Hz).

HRMS (ESI+): *m/z* calculated for $C_{32}H_{39}F_2NO_9P$ $[M+H]^+$ 650.2325, found 650.2295.

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4-di-*O*-benzyl-6-deoxy-β-L-glucopyranosyl)phosphonate (2f):



According to the general procedure, the reaction of 3,4-di-*O*-benzyl-2-nitro-L-rhamnal **1f** with diethyl lithiodifluoromethanephosphonate afforded the corresponding 2-deoxy-2-nitro-CF_2-glycosyl phosphonates as a 75:12:12:1 diastereomeric mixture in 98% yield. Flash chromotagraphy using *c*-hex/EtOAc (3:1) afforded the major isomer **2f** as a colorless oil.

R_F: 0.36 (*c*-hex/EtOAc, 2:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.41-7.22 (m, 10H), 4.99 (t, *J* = 10.1 Hz, 1H), 4.87-4.55 (m, 4H), 4.49-4.40 (m, 1H), 4.35-4.19 (m, 5H), 3.64 (dq, *J* = 12.3, 6.1 Hz, 1H), 3.27 (t, *J* = 9.2 Hz, 1H), 138-1.31 (m, 9H).

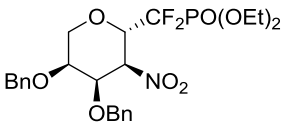
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ (ppm): 137.2 (C), 136.7 (C), 128.5 (CH), 128.4 (CH), 128.1 (CH), 128.1 (CH), 128.1 (CH), 127.9 (CH), 117.0 (ddd, J_{CF} = 273.9 Hz, J_{CF} = 262.0 Hz, J_{CP} = 209.0 Hz, C), 83.7 (t, J_{CF} = 3.4 Hz, CH), 82.7 (br s, CH), 82.2 (CH), 76.5 (CH), 76.4-75.9 (m, CH), 75.9 (CH_2), 75.5 (CH_2), 65.0 (d, J_{CP} = 6.8 Hz, CH_2), 64.8 (d, J_{CP} = 6.5 Hz, CH_2), 17.4 (CH_3), 16.3 (d, J_{CP} = 5.7 Hz, CH_3), 16.3 (d, J_{CP} = 5.7 Hz, CH_3).

^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –116.2 (ddd, J_{FF} = 317.0, J_{FP} = 94.7 Hz, J_{FH} = 4.6 Hz), –125.9 (ddd, J_{FF} = 317.0, J_{FP} = 95.0 Hz, J_{FH} = 16.4 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 6.37 (t, J_{PF} = 94.9 Hz).

HRMS (ESI+): *m/z* calculated for $C_{25}H_{33}F_2NO_8P$ $[M+H]^+$ 544.1906, found 544.1883.

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4-di-*O*-benzyl-β-L-ribopyranosyl)phosphonate (2g):



According to the general procedure, the reaction of 3,4-di-*O*-benzyl-2-nitro-L-arabinal **1g** with diethyl lithiodifluoromethanephosphonate afforded the corresponding 2-deoxy-2-nitro-CF_2-glycosyl phosphonates as a >98:2 diastereomeric mixture in 98% yield. Flash chromotagraphy using *c*-hex/EtOAc 2:1) afforded major isomer **2g** as a colorless oil.

R_F: 0.24 (*c*-hex/EtOAc, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.40-7.27 (m, 10H), 5.01 (dd, *J* = 10.2, 3.2 Hz, 1H), 4.92-4.82 (m, 2H), 4.66-4.55 (m, 4H), 4.30-4.16 (m, 4H), 3.94-3.85 (m, 2H), 3.68 (ddd, *J* = 10.4, 4.9, 2.1 Hz, 1H), 1.35 (dt, *J* = 7.1, 1.3 Hz, 6H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 137.2 (C), 137.0 (C), 128.6 (CH), 128.3 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.4 (CH), 117.8 (ddd, J_{CF} = 268.6 Hz, J_{CF} = 268.5 Hz, J_{CP} = 210.0 Hz, C), 79.7 (br s, CH), 75.4 (CH_2), 74.9 (CH), 74.5 (CH), 72.1 (ddd, J_{CF} = 28.2 Hz, J_{CF} = 23.3 Hz, J_{CP} = 12.6 Hz, CH), 71.8 (CH_2), 64.8 (d, J_{CP} = 6.4 Hz, CH_2), 64.8 (d, J_{CP} = 6.4 Hz, CH_2), 63.2 (CH_2), 16.2 (d, J_{CP} = 5.6 Hz, CH_3).

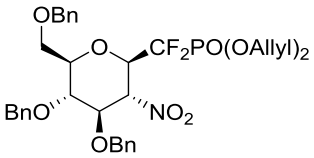
^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –112.6 (ddd, J_{FF} = 314.1, J_{FP} = 94.9 Hz, J_{FH} = 7.0 Hz), –121.7 (ddd, J_{FF} = 314.1, J_{FP} = 99.7 Hz, J_{FH} = 11.1 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 4.77 (dd, J_{PF} = 99.6, J_{PF} = 95.0 Hz).

$[\alpha]_D^{20}$ –18.0 (*c* 2.0, EtOH).

HRMS (ESI+): *m/z* calculated for $C_{24}H_{31}F_2NO_8P$ $[M+H]^+$ 530.1750, found 520.1727.

Diallyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (2h):



According to the general procedure, the reaction of 3,4,6-tri-*O*-benzyl-2-nitro-D-glucal **1a** with diallyl lithiodifluoromethanephosphonate afforded the corresponding 2-deoxy-2-nitro-CF_2-glycosyl phosphonates as a 98:2 diastereomeric mixture in 17% yield. Flash chromotagraphy using *c*-hex/EtOAc (4:1) afforded the major isomer **2h** as a colorless oil.

R_F: 0.48 (*c*-hex/EtOAc, 2:1).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.28-7.18 (m, 11H), 7.16-7.13 (m, 2H), 7.11-7.08 (m, 2H), 5.84-5.73 (m, 2H), 5.28-5.22 (m, 2H), 5.18-5.13 (m, 2H), 4.96 (t, *J* = 10.0 Hz, 1H), 4.71 (dd, *J* = 10.8, 4.8 Hz, 2H), 4.64-4.53 (m, 4H), 4.50 (dd, *J* = 10.8, 5.1 Hz, 2H), 4.45-4.35 (m, 3H), 4.22 (t, *J* = 9.5 Hz, 1H), 3.70-3.64 (m, 3H), 3.61-3.58 (m, 1H).

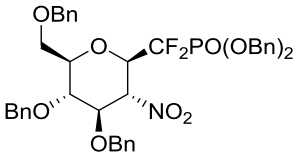
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 137.5 (C), 137.3 (C), 136.8 (C), 128.4 (CH), 132.0 (t, *J* = 5.9 Hz, CH), 128.5 (CH), 128.5 (CH), 128.1 (CH), 128.1 (CH), 128.0 (CH), 127.8 (CH), 127.7 (CH), 118.8 (d, *J* = 6.0 Hz, CH_2), 117.0 (ddd, J_{CF} = 273.6 Hz, J_{CF} = 263.1 Hz, J_{CP} = 209.5 Hz, C), 83.5 (br s, CH), 82.8 (CH), 79.7 (CH), 76.7 (CH), 76.6-76.2 (m, CH), 75.9 (CH_2), 75.2 (CH_2), 73.5 (CH_2), 69.0 (d, J_{CP} = 6.2 Hz, CH_2), 68.9 (d, J_{CP} = 6.2 Hz, CH_2), 68.0 (CH_2).

^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –114.2 (ddd, J_{FF} = 317.8, J_{FP} = 94.9 Hz, J_{FH} = 4.7 Hz), –123.9 (ddd, J_{FF} = 317.7, J_{FP} = 96.3 Hz, J_{FH} = 15.5 Hz).

^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 3.90 (t, J_{PF} = 95.6 Hz).

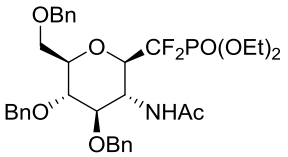
HRMS (ESI+): *m/z* calculated for $C_{34}H_{38}F_2NNaO_9P$ $[M+Na]^+$ 696.2144, found 696.2175.

Dibenzyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (2i):



According to the general procedure, the reaction of 3,4,6-tri-*O*-benzyl-2-nitro-D-glucal **1a** with 1.5 equiv. dibenzyl lithiodifluoromethanephosphonate afforded the corresponding 2-deoxy-2-nitro-CF_2-glycosyl phosphonates as a 90:8 diastereomeric mixture in 52% yield. Due to instability of the product, the product could not be isolated.

Diethyl 2,2-difluoro-2-(2-acetylamino-2-deoxy-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (3):



Compound **2a** (106 mg, 0.16 mmol) was dissolved in a mixture of THF (10 mL), H_2O (4.5 mL), AcOH (4.5 mL), concentrated HCl (0.46 mL) and cooled to 0 °C. Zinc dust (250 mg, 3.82 mmol) was added portionwise. After stirring for 2 h at 0 °C the solids were filtered off and the reaction mixture was diluted with CH_2Cl_2, washed with water (10 mL), saturated aqeuous $NaHCO_3$, brine (10 mL) and dried over Na_2SO_4. Evaporation of the solvents gave the crude amine which subsequently was treated with pyridine (2mL) and acetic anhydride (2mL) and stirred for 1 h. Removal of the volatiles and flash chromatography purification (*c*-hex/EtOAc (1:1 → 1:2)) afforded acetamide **3** as a colorless oil (71 % yield).

R_F: 0.24 (*c*-hex/EtOAc, 1:2).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37-7.23 (m, 13H), 7.21-7.16 (m, 2H), 5.72 (d, *J* = 7.2 Hz, 1H), 4.86-4.78 (m, 2H), 4.70-4.57 (m, 2H), 4.55-4.44 (m, 2H), 4.44-4.33 (m, 1H), 4.33-4.16 (m, 5H), 3.93-

3.78 (m, 1H), 3.75-3.72 (m, 2H), 3.69-3.59 (m, 2H), 1.84 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.0 Hz, 3H).

^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 170.6 (C), 138.4 (C), 138.0 (C), 137.9 (C), 128.4 (CH), 128.4 (CH), 128.3 (CH), 127.8 (CH), 127.8 (CH), 127.7 (CH), 127.7 (CH), 127.7 (CH), 118.4 (ddd, J_{CF} = 269.9 Hz, J_{CF} = 265.0 Hz, J_{CP} = 208.1 Hz, C), 81.4 (CH), 79.4 (CH), 78.2 (CH), 77.4 (CH), 75.4-74.8 (m, CH), 75.1 (CH_2), 74.7 (CH_2), 73.3 (CH_2), 68.7 (CH_2), 64.9 (d, J_{CP} = 6.8 Hz, CH_2), 64.7 (d, J_{CP} = 6.7 Hz, CH_2), 23.5 (CH_3), 16.3 (d, J_{CP} = 6.0 Hz, CH_3), 16.3 (d, J_{CP} = 6.1 Hz, CH_3).

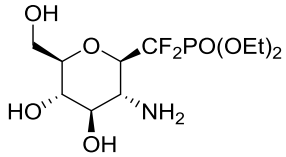
^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –112.5 - –114.7 (m), –120.6 - –123.0 (m).

^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 4.81 (t, J_{PF} = 99.0 Hz).

$[\alpha]_D^{20}$ +10.0 (*c* 1.0, EtOH).

HRMS (ESI+): *m/z* calculated for $C_{34}H_{43}F_2NO_8P$ $[M+H]^+$ 662.2689, found 662.2657.

Diethyl 2,2-difluoro-2-(2-amino-2-deoxy-β-D-glucopyranosyl)phosphonate (4):



10% $Pd(OH)_2/C$ (12 mg) was added to a solution of compound **2a** (202 mg, 0.31 mmol) in EtOH (10 mL). The mixture was stirred for 20 h under a balloon atmosphere of hydrogen whereafter the mixture was filtered over Celite and concentrated *in vacuo*. Debenzylated glycosyl phosphonate **4** was obtained in 96% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 5.17 (br s, 1H), 5.03 (br s, 1H), 4.36 (br s, 1H), 4.27-4.12 (m, 4H), 3.74-3.65 (m, 1H), 3.62-3.52 (m, 1H), 3.49-3.41 (m, 1H), 3.21-3.14 (m, 1H), 3.13-3.06 (m, 2H), 2.87-2.79 (m, 1H), 2.45-1.92 (br s, 2H), 1.28-1.23 (m, 6H).

^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6) δ (ppm): 119.1 (ddd, J_{CF} = 269.9 Hz, J_{CF} = 262.9 Hz, J_{CP} = 208.8 Hz, C), 81.6 (CH), 78.5 (ddd, J_{CF} = 23.5 Hz, J_{CF} = 23.4 Hz, J_{CP} = 11.2 Hz, CH), 77.2 (br s, CH), 69.3 (CH), 64.0 (d, J_{CP} = 6.2 Hz, CH_2), 63.9 (d, J_{CP} = 6.6 Hz, CH_2), 60.8 (CH_2), 52.2 (br s), 16.2 (d, J_{CP} = 5.4 Hz, CH_3), 16.2 (d, J_{CP} = 5.5 Hz, CH_3).

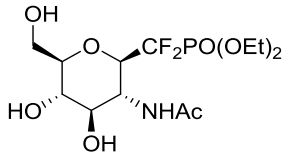
^{19}F NMR (235 MHz, DMSO-d_6) δ (ppm): –112.8 (ddd, J_{FF} = 312.1, J_{FP} = 96.6 Hz, J_{FH} = 6.1 Hz), –126.0 (ddd, J_{FF} = 312.1, J_{FP} = 106.6 Hz, J_{FH} = 19.0 Hz).

^{31}P NMR (162 MHz, DMSO-d_6) δ (ppm): 6.34 (dd, J_{PF} = 99.9, J_{PF} = 96.3 Hz).

$[\alpha]_D^{20}$ +2.0 (*c* 1.0, EtOH).

HRMS (ESI+): *m/z* calculated for $C_{11}H_{23}F_2NO_7P$ $[M+H]^+$ 350.1175, found 350.1172.

Diethyl 2,2-difluoro-2-(2-acetylamino-2-deoxy-β-D-glucopyranosyl)phosphonate (5):

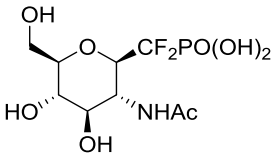


10% $Pd(OH)_2/C$ (6 mg) was added to a solution of compound **3** (60 mg, 0.091 mmol) in EtOH (3 mL). The mixture was stirred for 10 h under a balloon atmosphere of hydrogen whereafter the mixture was filtered over Celite and purified by flash chromotagraphy using CH_2Cl_2/MeOH (9:1). Debenzylated glycosyl phosphonate **5** was obtained quantitatively. **R_F:** 0.16 (*c*-hex/EtOAc, 9:1).

^{1}H NMR (500 MHz, DMSO-d_6) δ (ppm): 7.70 (d, J = 9.1 Hz, 1H), 5.11 (d, J = 5.1 Hz, 1H), 5.07 (d, J = 5.4 Hz, 1H), 4.38 (t, J = 5.3 Hz, 1H), 4.27-4.10 (m, 4H), 3.94-3.84 (m, 1H), 3.78 (q, J = 9.7 Hz, 1H), 3.74-3.68 (m, 1H), 3.49-3.43 (m, 1H), 3.43-3.36 (m, 1H), 3.17-3.06 (m, 2H), 1.76 (s, 3H), 1.24 (q, J = 7.0 Hz, 6H).

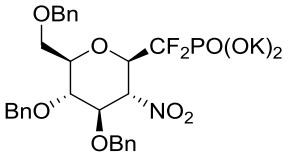
$^{13}C\{^1H\}$ NMR (126 MHz, DMSO-d_6) δ (ppm): 168.6 (C), 118.5 (ddd, J_{CF} = 274.7 Hz, J_{CF} = 260.8 Hz, J_{CP} = 209.5 Hz, C), 81.7 (CH), 75.3-74.8 (m, CH), 74.8 (CH), 69.9 (CH), 64.0 (d, J_{CP} = 6.1 Hz, CH_2), 63.7 (d, J_{CP} = 6.7 Hz, CH_2), 60.8 (CH_2), 49.5 (br s), 23.0 (CH_3), 16.2 (d, J_{CP} = 5.4 Hz, CH_3), 16.2 (d, J_{CP} = 5.4 Hz, CH_3).
^{19}F NMR (235 MHz, DMSO-d_6) δ (ppm): –117.5 (dd, J_{FF} = 310.4, J_{FP} = 95.4 Hz), –128.3 (ddd, J_{FF} = 310.0, J_{FP} = 99.6 Hz, J_{FH} = 21.1 Hz).
^{31}P NMR (162 MHz, DMSO-d_6) δ (ppm): 9.55 (dd, J_{PF} = 99.7, J_{PF} = 95.4 Hz).
HRMS (ESI+): *m/z* calculated for $C_{13}H_{25}F_2NO_8P$ $[M+H]^+$ 392.1280, found 392.1284.

2,2-Difluoro-2-(2-acetylamino-2-deoxy-β-D-glucopyranosyl)phosphonate (6):



Fully protected compound **3** (43 mg, 65.1 µmol) was dissolved in CH_2Cl_2 (2 mL) and cooled to 0 °C before TMSI (463 µL, 3.26 mmol) was added dropwise. The ice bath was removed, and the reaction was allowed to stir at room temperature for 5 h. Then, methanol (4 mL) was added and the mixture was stirred for another 20 min before being concentrated *in vacuo*. The crude mixture was dissolved in water (10 mL) and extracted with diethyl ether (8 × 10 mL). The aqueous layer was concentrated with methanol (3 × 10 mL) before being taken up in water (2 mL) and passed though an C18 column (eluent: MeCN/H_2O, 1:9 with 1% TFA). Lyophilization provided 19 mg of **6** (55.3 mmol, 87%).
^1H NMR (400 MHz, MeOD-d_4) δ (ppm): 2.43-2.26 (m, 2H), 2.24-2.16 (m, 1H), 2.03-1.96 (m, 1H), 1.88 (t, *J* = 8.2 Hz, 1H), 1.71-1.62 (m, 2H), 0.35 (s, 3H).
$^{13}C\{^1H\}$ NMR (126 MHz, DMSO-d_6) δ (ppm): 168.9 (C), 80.6 (CH), 75.4 (CH), 70.8 (CH), 61.5 (CH_2), 50.2 (CH), 22.9 (CH_3).
^{19}F NMR (235 MHz, MeOD-d_4) δ (ppm): –115.5 (dd, J_{FF} = 310.6, J_{FP} = 95.4 Hz), –127.4 (ddd, J_{FF} = 311.8, J_{FP} = 102.6 Hz, J_{FH} = 17.9 Hz).
^{31}P NMR (162 MHz, MeOD-d_4) δ (ppm): 2.65 (t, J_{PF} = 98.8).
HRMS (ESI–): *m/z* calculated for $C_9H_{15}F_2NO_8P$ $[M-H]^-$ 334.0509, found 334.0518.

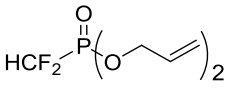
Potassium 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (7):



A solution of **2h** (14 mg, 0.021 mmol), potassium 2-ethylhexanoate (73 mg, 0.040 mmol), and $Pd(PPh_3)_4$ (3 mg, 3 µmol)) in CH_2Cl_2 (0.5 mL) was stirred in the dark for 10 h. The solvent was evaporated and the residue was dissolved in 50% H_2O/MeOH (2 ml) and extracted with Et_2O (2 x 2 mL). Evaporation of the aqueous layer, followed by thorough drying *in vacuo* provided the potassium salt **7** in a reasonable purity (+/- 80% by ^1H NMR). Yield determined by ^{19}F NMR: 91%.
^1H NMR (500 MHz, MeOD-d_4) δ (ppm): 7.32-7.18 (m, 10H), 7.12-7.10 (m, 2H), 7.02-6.99 (m, 2H), 4.68-4.58 (m, 3H), 4.50-4.40 (m, 3H), 4.34-4.21 (m, 2H), 3.83-3.81 (m, 1H), 3.68-3.58 (m, 3H).
$^{13}C\{^1H\}$ NMR (126 MHz, MeOD-d_4) δ (ppm): 139.2 (C), 138.9 (C), 138.7 (C), 130.1 (CH), 130.0 (CH), 129.8 (CH), 129.7 (CH), 129.4 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.8 (CH), 121.5 (ddd, J_{CF} = 272.3 Hz, J_{CF} = 263.0 Hz, J_{CP} = 173.4 Hz, C), 84.7 (CH), 80.0 (CH), 79.1-78.6 (m, CH), 78.3 (CH), 76.7 (CH_2), 75.9 (CH_2), 74.3 (CH_2), 68.4 (CH_2), 52.5 (CH).
^{19}F NMR (235 MHz, MeOD-d_4) δ (ppm): –113.7 (dd, J_{FF} = 304.6, J_{FP} = 76.3 Hz), –125.9 (ddd, J_{FF} = 304.3, J_{FP} = 80.1 Hz, J_{FH} = 19.7 Hz).

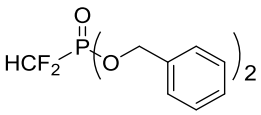
^{31}P NMR (162 MHz, MeOD-d_4) δ (ppm): 6.26 (t, J_{PF} = 75.8).
HRMS (ESI–): *m/z* calculated for $C_{28}H_{29}F_2NO_9P$ $[M\text{-H}]^-$ 592.1553, found 592.1569.

Diallyl (α-α-difluoromethyl)phosphonate



To a solution of diallyl phosphite (1.00, 6.17 mmol) in THF (3 mL) was added sodium bis(trimethylsilyl)amide (6.9 mL of a 1M solution in THF, 6.85 mmol). The reaction mixture was stirred for 1 h. Excess chlorodifluoromethane was bubbled into the solution for 30 min, and the reaction mixture was stirred for an additional 16 h under a balloon atmosphere of HCF_2Cl. Subsequently, precipitated NaCl was removed by filtration over Celite. The filtrate was purified by flash chromatography with *c*-hex/EtOAc (9:1) as eluent to obtain diallyl (α-α-difluoromethyl)phosphonate as a colorless liquid in 54% yield. (stored at –20 °C).
R_F: 0.48 (*c*-hex/EtOAc, 9:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.03 – 5.78 (m, 3H), 5.37 (d, *J* = 17.1 Hz, 2H), 5.27 (d, *J* = 10.4 Hz, 2H), 4.67-4.64 (m, 4H).
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 131.7 (d, J_{CP} = 5.5 Hz, CH), 119.2 (CH_2), 111.2 (dt, J_{CF} = 258.3 Hz, J_{CP} = 214.0 Hz, CH), 68.4 (d, J_{CP} = 6.3 Hz, CH_2).
^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –141.0 (dd, J_{FP} = 90.8 Hz, J_{FH} = 48.3 Hz).
^{31}P NMR (101 MHz, $CDCl_3$) δ (ppm): 5.53 (t, J_{PF} = 92.3 Hz).
HRMS (ESI+): *m/z* calculated for $C_7H_{12}F_2O_3P$ $[M\text{+H}]^+$ 213.0487, found 213.0482.

Dibenzyl (α-α-difluoromethyl)phosphonate



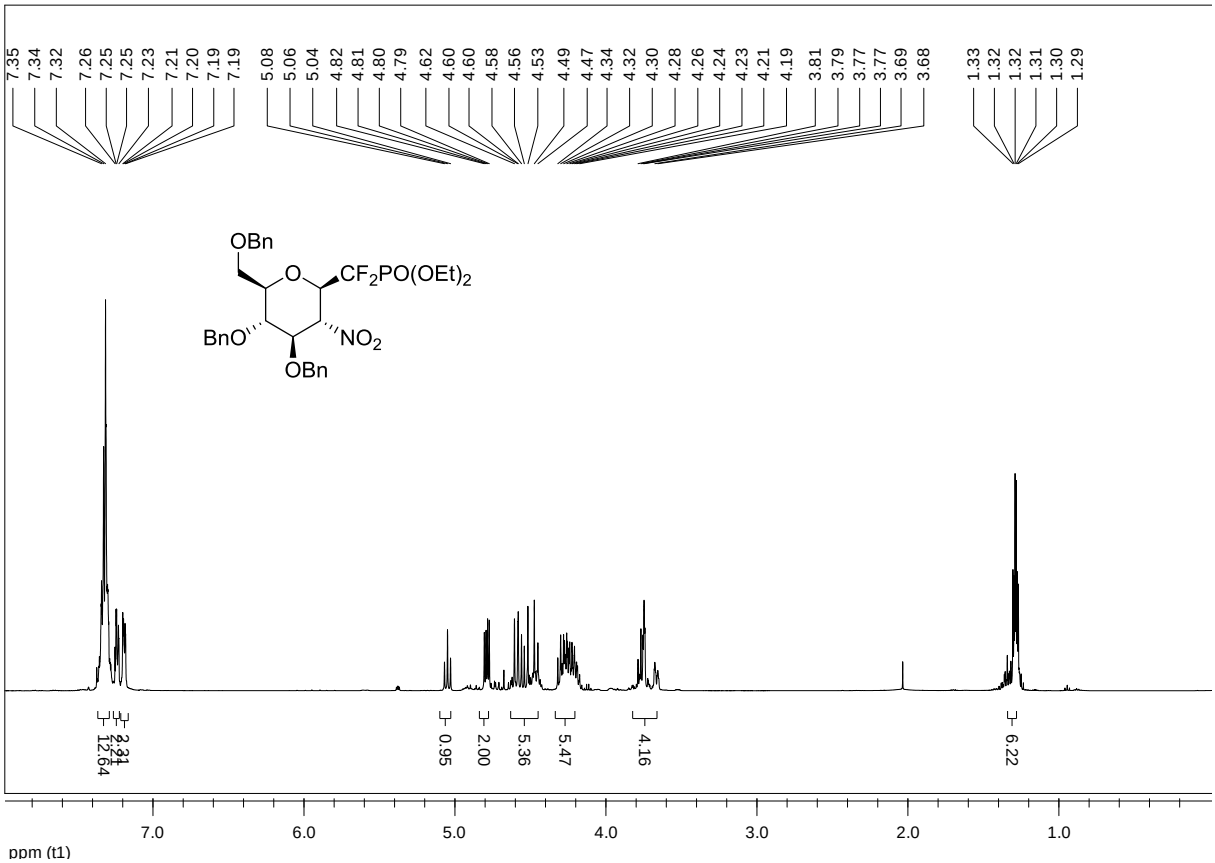
Prepared from dibenzyl phosphite (3.79 mL, 17.16 mmol) using the same procedure as for diallyl (α-α-difluoromethyl)phosphonate. Purification: flash chromatography *c*-hex/EtOAc (4:1). Isolated as a colorless liquid in 51% yield. (stored at –20 °C). **R_F:** 0.13 (*c*-hex/EtOAc, 9:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.40 – 7.32 (m, 10H), 5.84 (dt, *J* = 48.7, 27.9 Hz, 1H), 5.16 (d, *J* = 8.6 Hz, 4H).
^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ (ppm): 135.0 (d, J_{CP} = 5.5 Hz, C), 129.0 (CH), 128.7 (CH), 128.2 (CH), 111.4 (dt, J_{CF} = 258.6 Hz, J_{CP} = 214.0 Hz, CH), 69.6 (d, J_{CP} = 6.5 Hz, CH_2).
^{19}F NMR (235 MHz, $CDCl_3$) δ (ppm): –135.1 (dd, J_{FP} = 92.5 Hz, J_{FH} = 48.7 Hz).
^{31}P NMR (162 MHz, $CDCl_3$) δ (ppm): 5.70 (t, J_{PF} = 92.4 Hz).
HRMS (ESI+): *m/z* calculated for $C_{15}H_{15}F_2NaO_3P$ $[M\text{+Na}]^+$ 335.0625, found 335.0638.

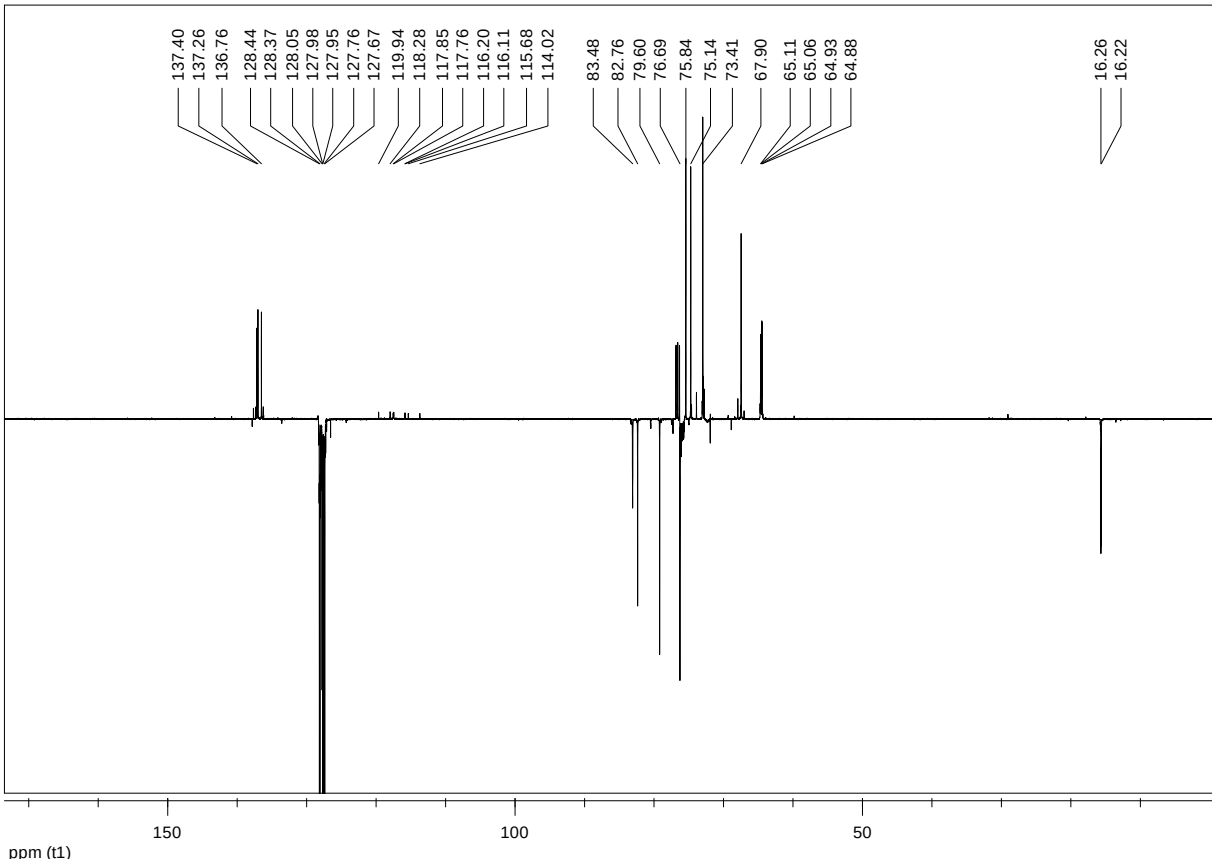
References

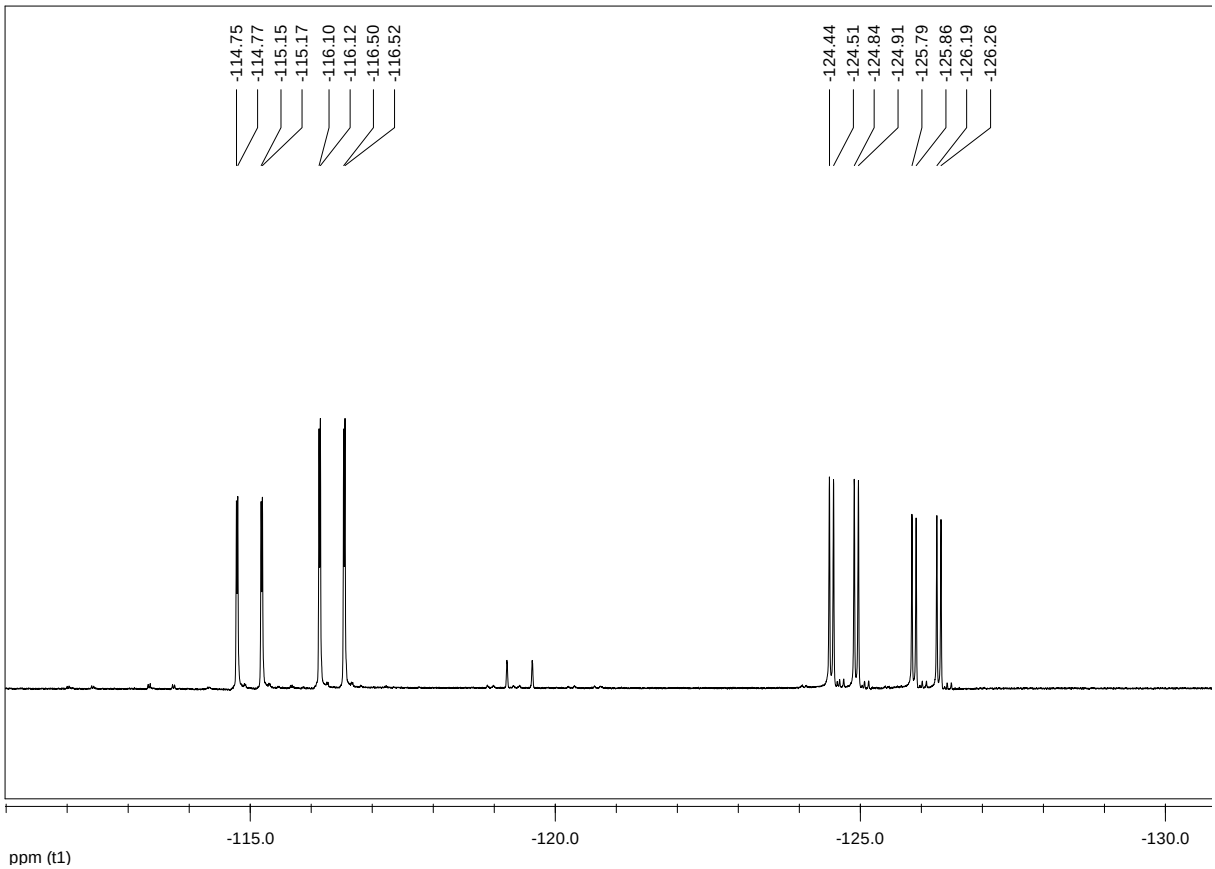
[1] a) Schmidt, R. R.; Vankar, Y. D. *Acc. Chem. Res.* **2008**, 41, 1059. b) Kancharla, P. K.; Reddy, Y. S.; Dharuman, S.; Vankar, Y. D. *J. Org. Chem*. **2011**, 76, 5832.

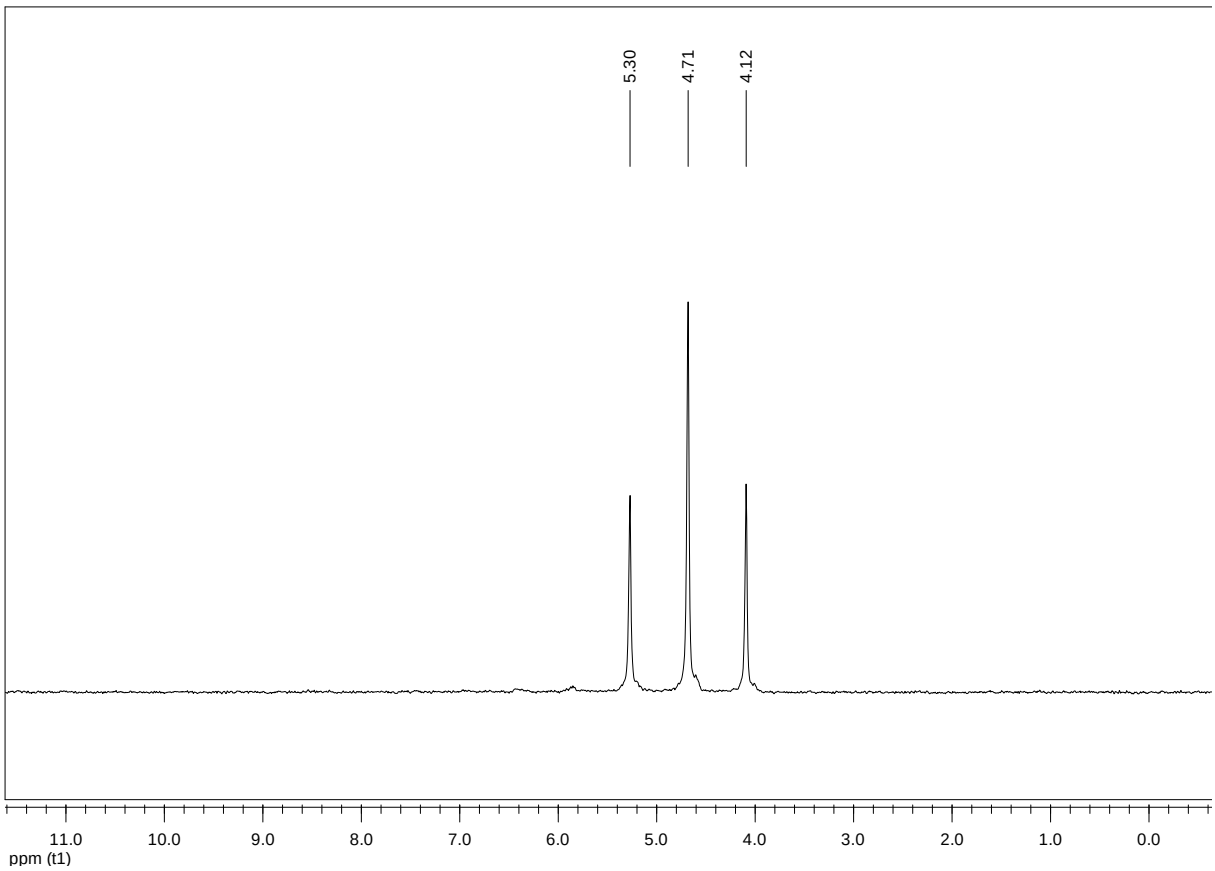
Copies of NMR spectra

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (2a):

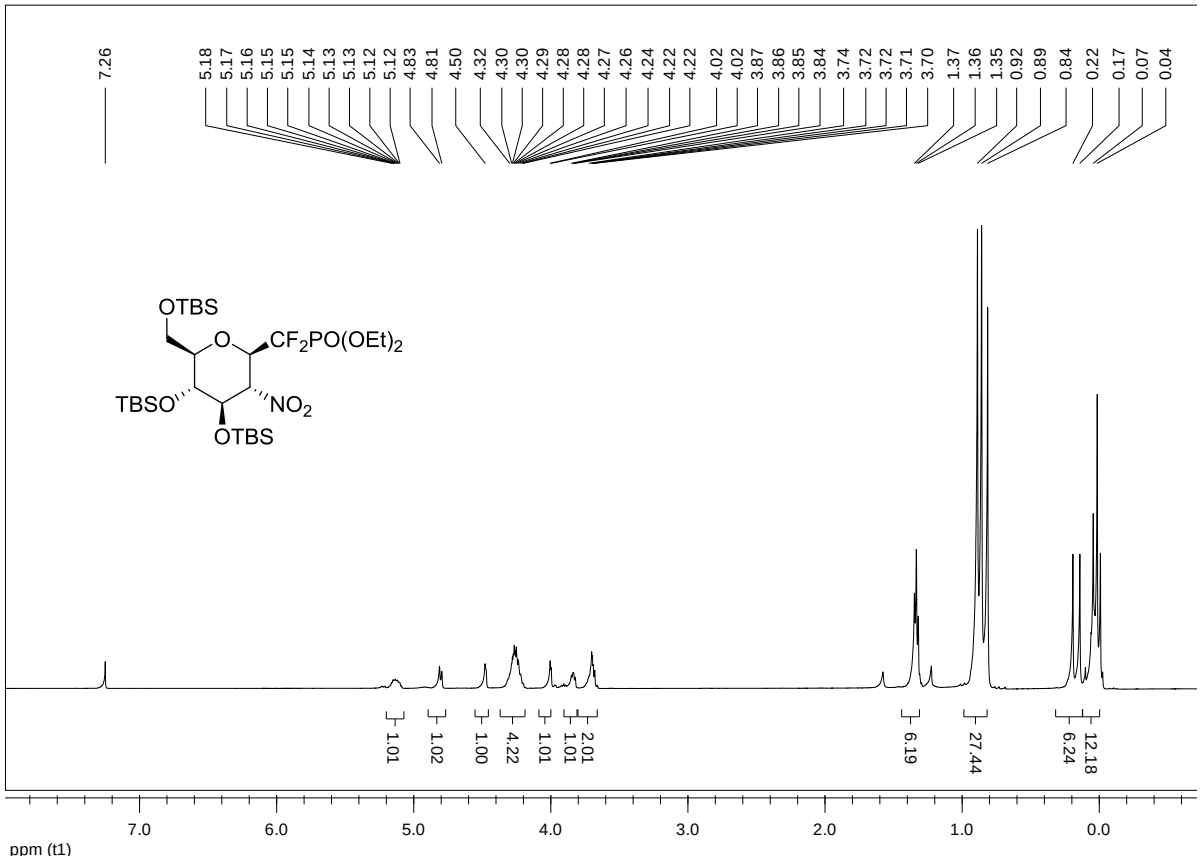


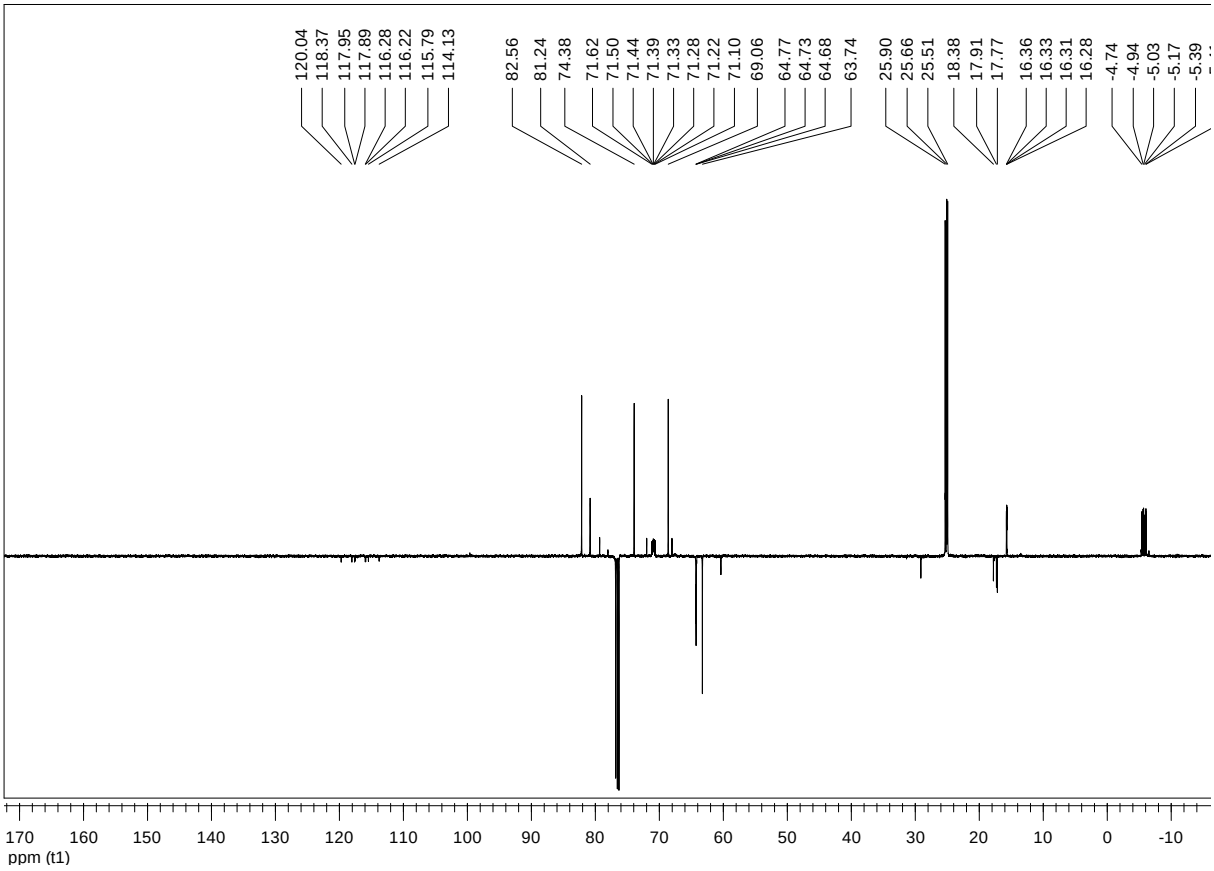


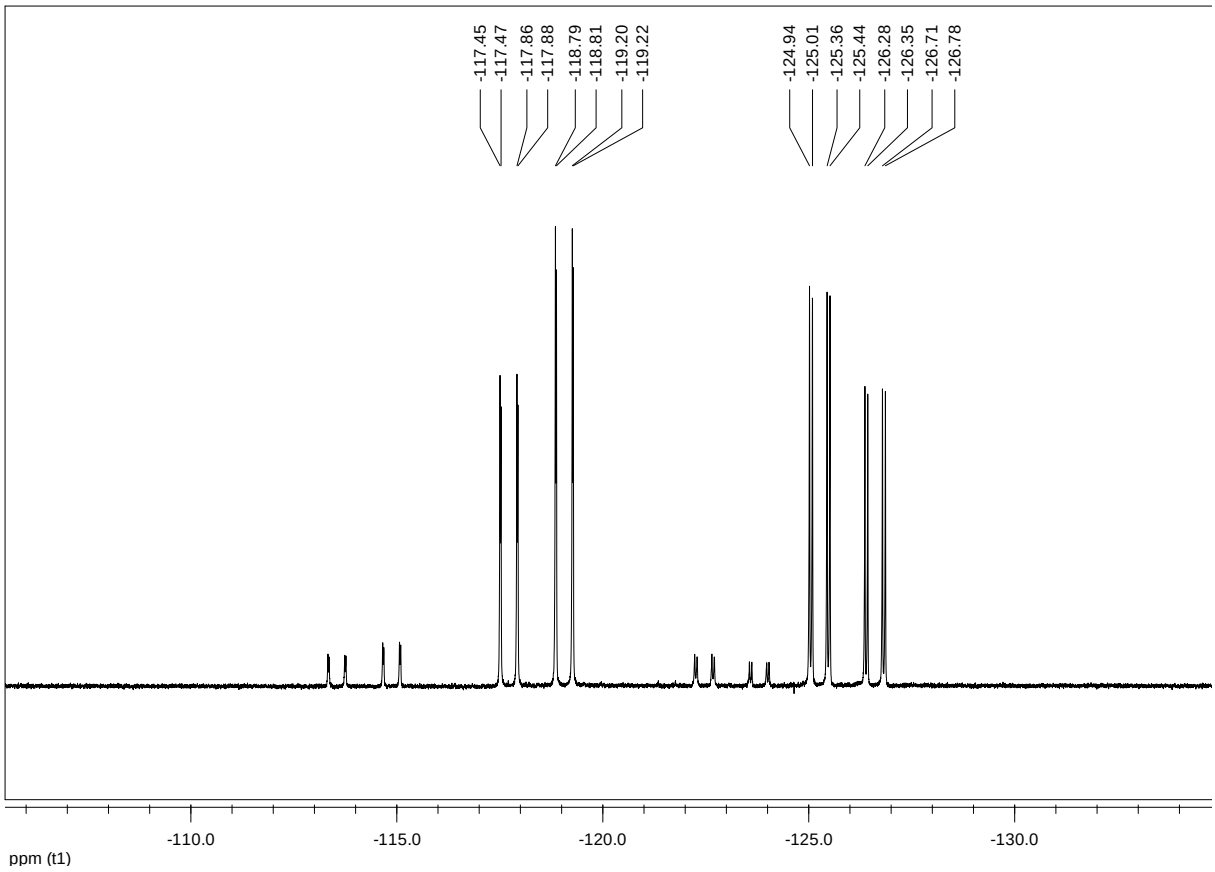

-114.75
-114.77
-115.15
-115.17
-116.10
-116.12
-116.50
-116.52
-124.44
-124.51
-124.84
-124.91
-125.79
-125.86
-126.19
-126.26
-115.0
-120.0
-125.0
-130.0
ppm (t1)

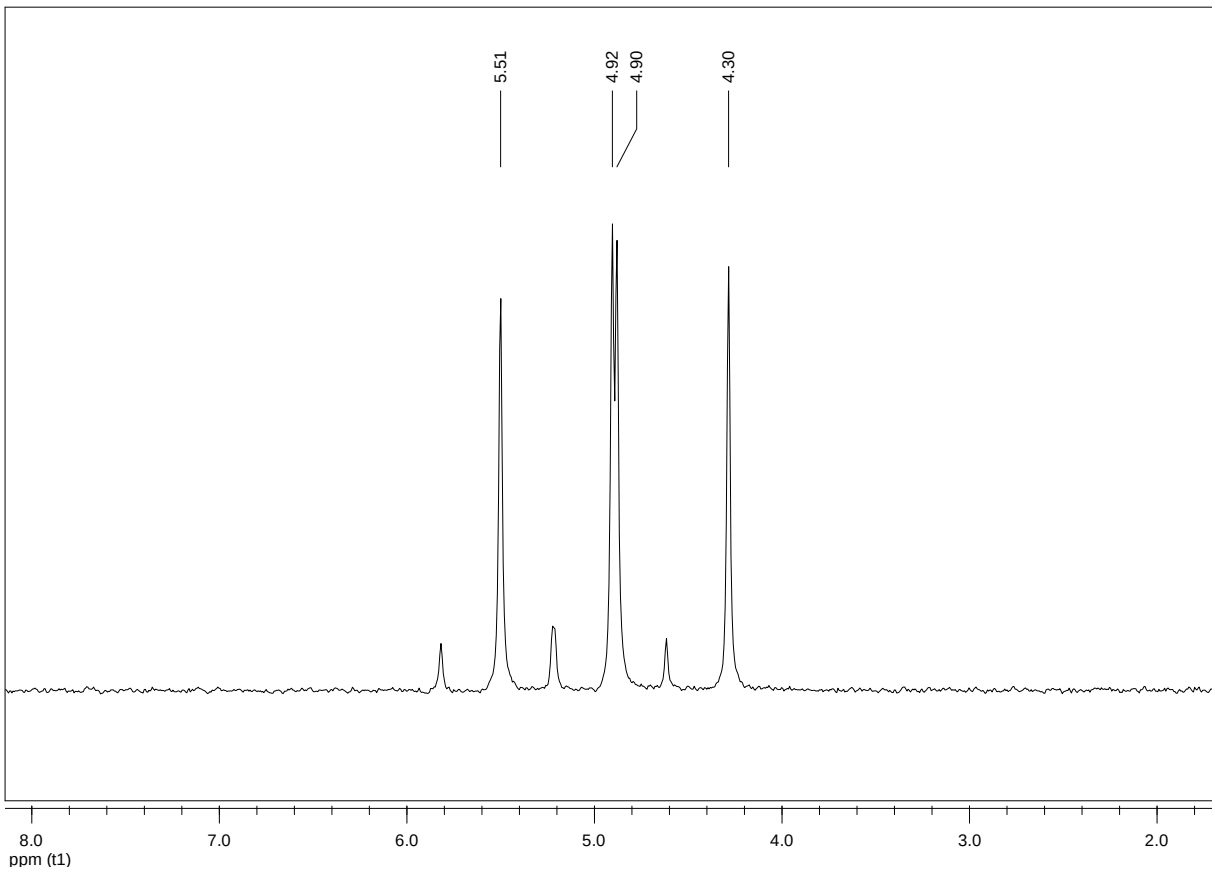

5.30
4.71
4.12
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O-tert*-butyldimethylsilyl-β-D-glucopyranosyl)phosphonate (2b):

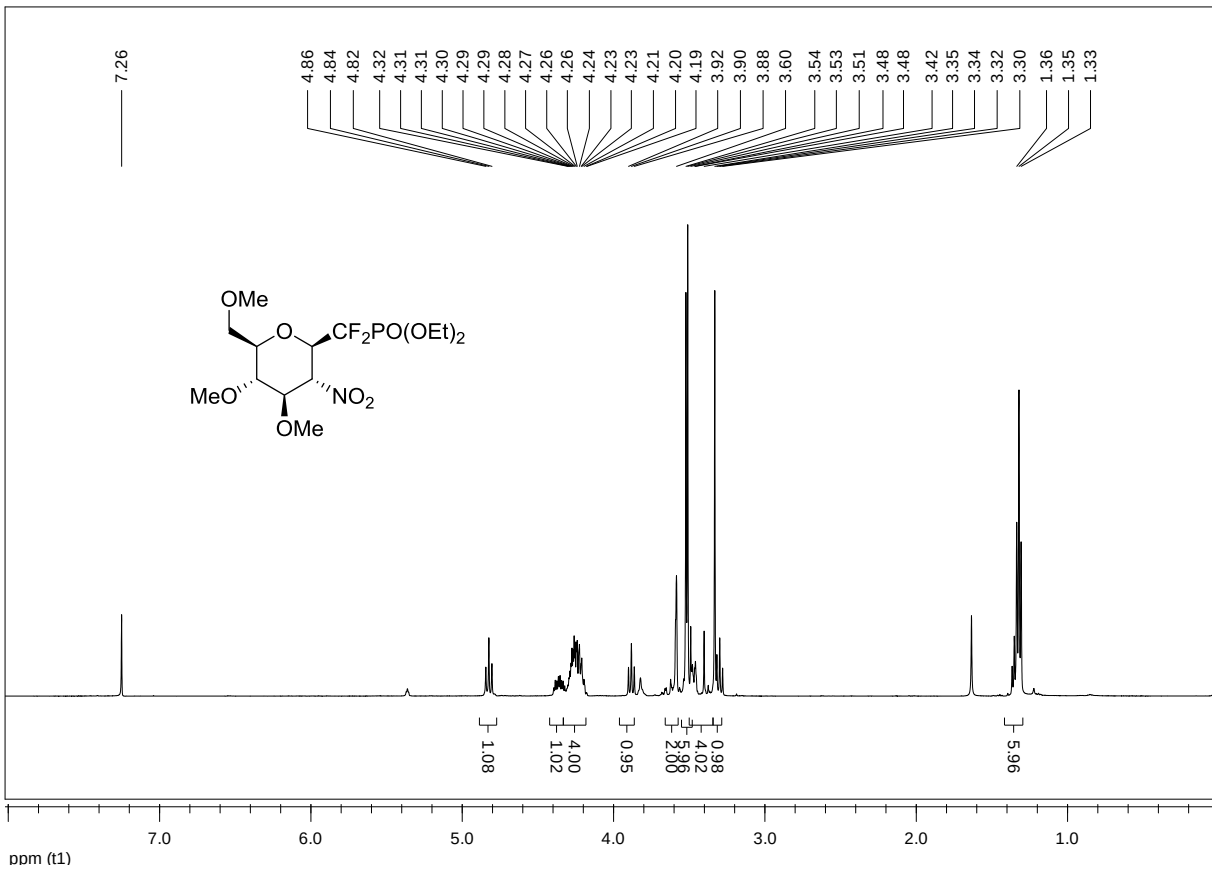


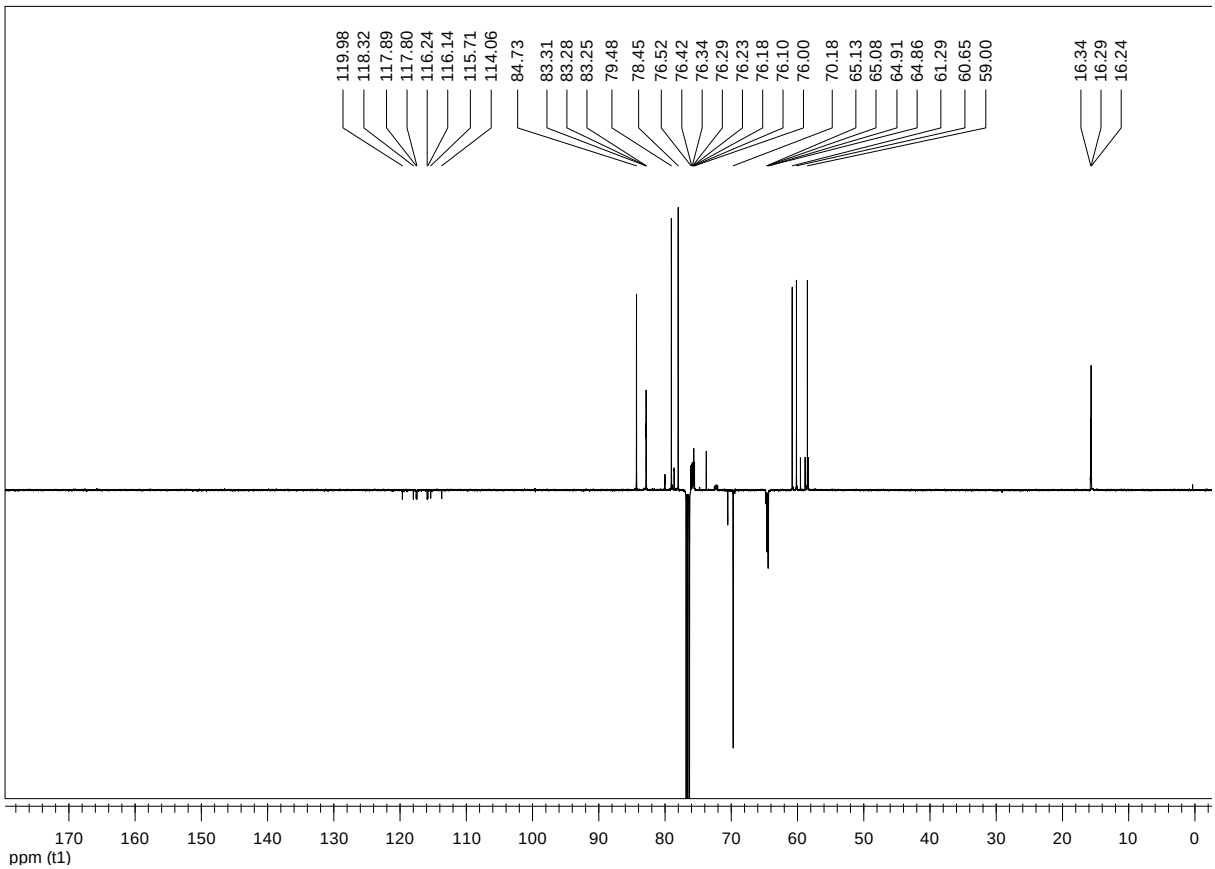


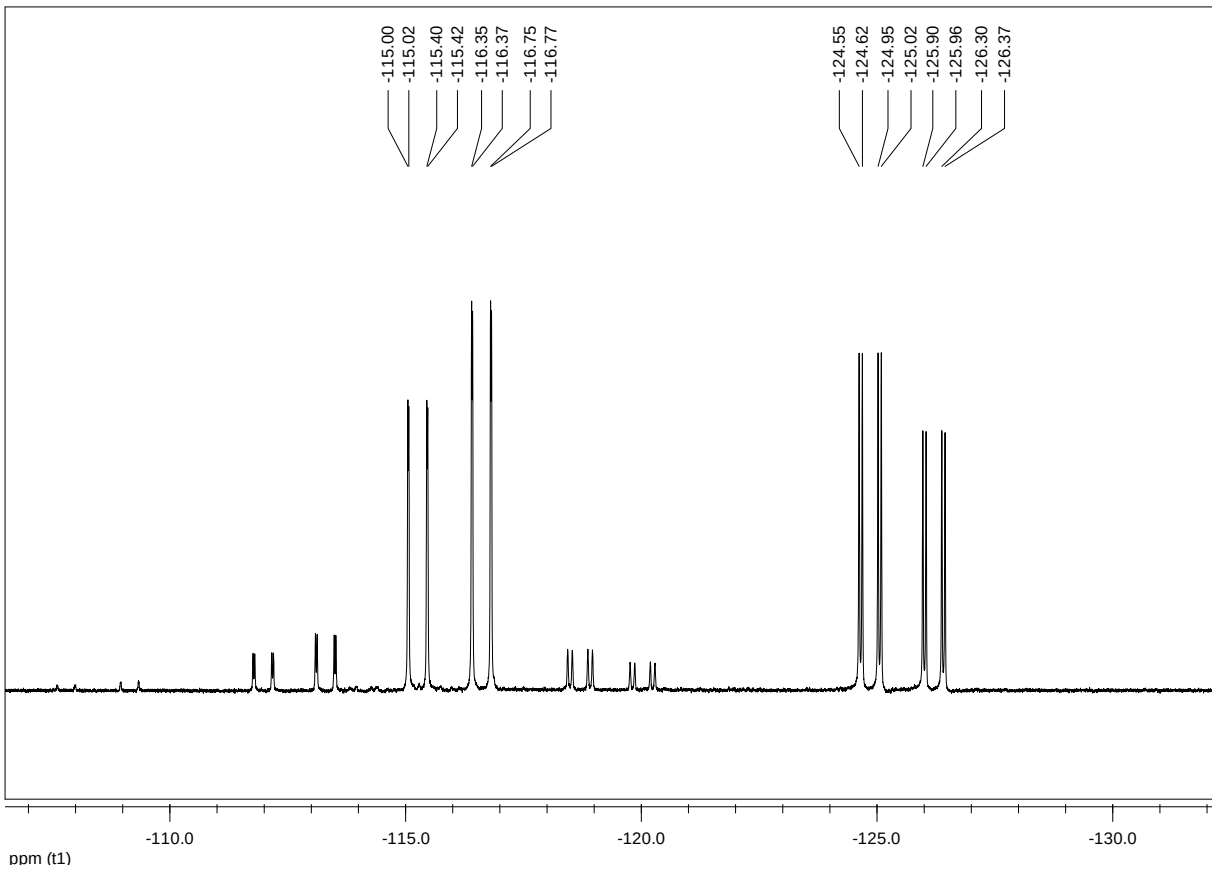

-117.45
-117.47
-117.86
-117.88
-118.79
-118.81
-119.20
-119.22
-124.94
-125.01
-125.36
-125.44
-126.28
-126.35
-126.71
-126.78
-110.0
-115.0
-120.0
-125.0
-130.0
ppm (t1)

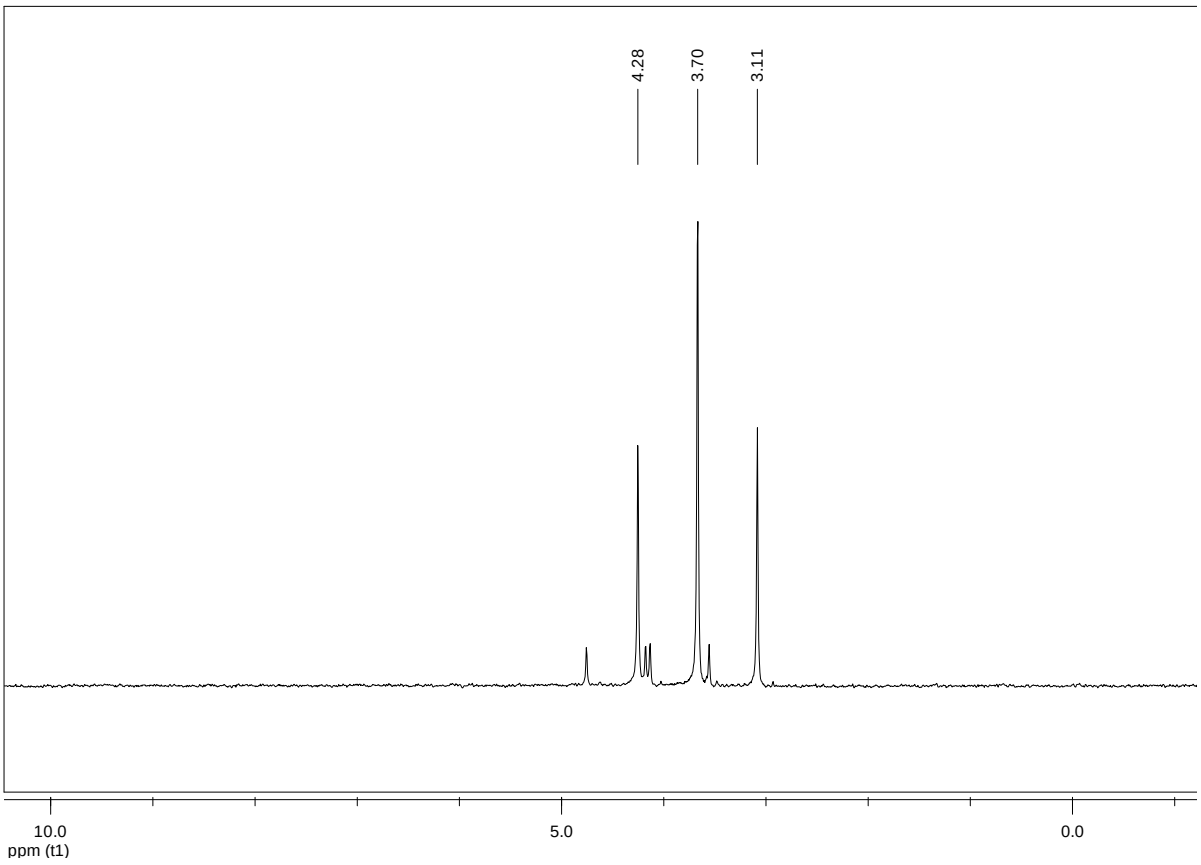

5.51
4.92
4.90
4.30
8.0
7.0
6.0
5.0
4.0
3.0
2.0
ppm (t1)

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-methyl-β-D-glucopyranosyl)phosphonate (2c):

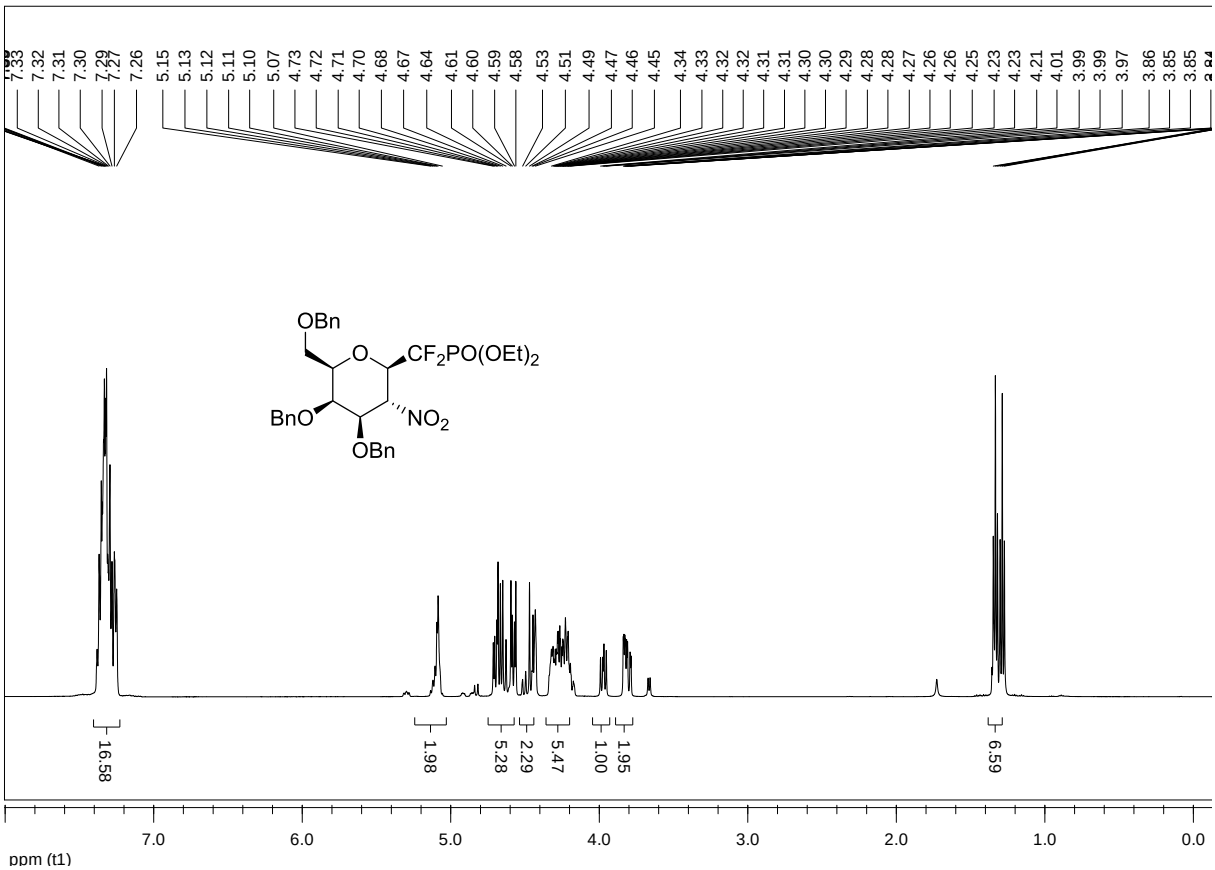


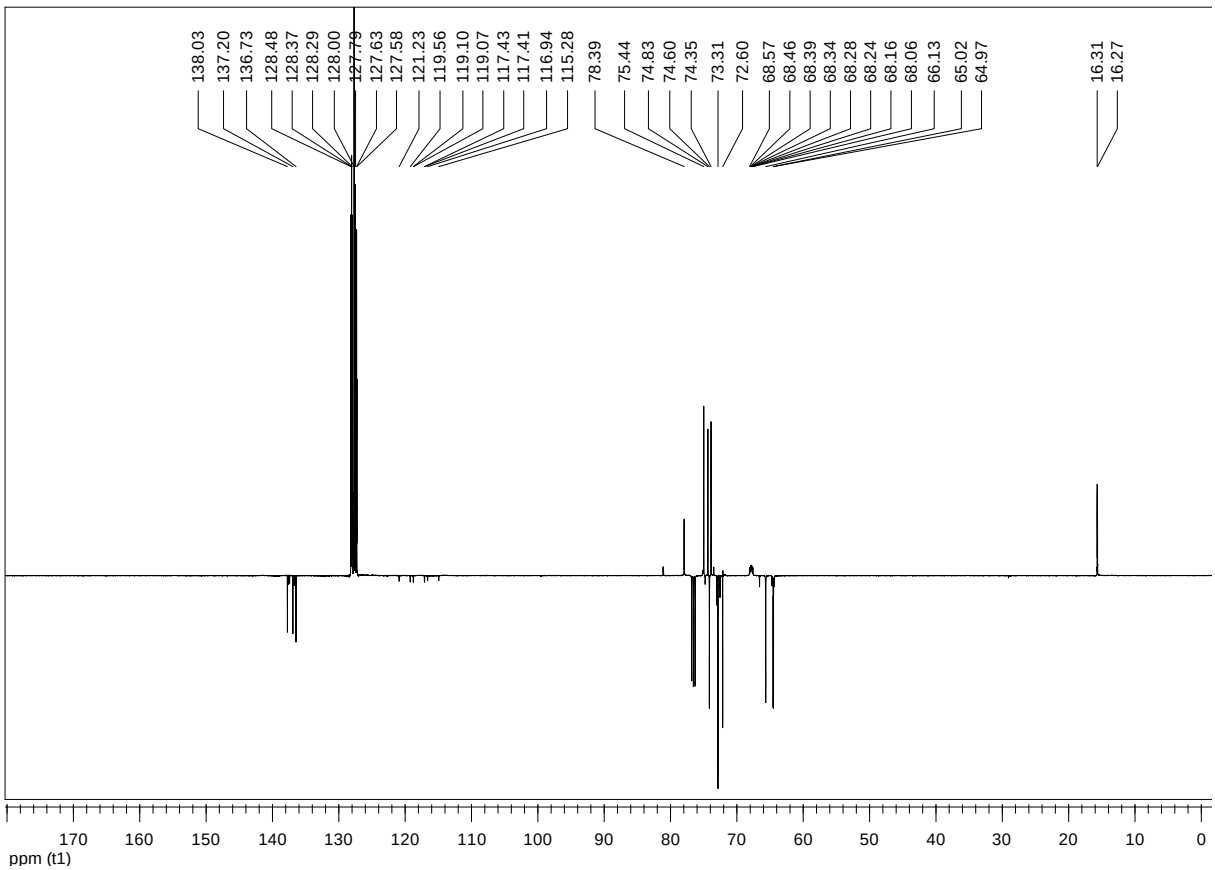


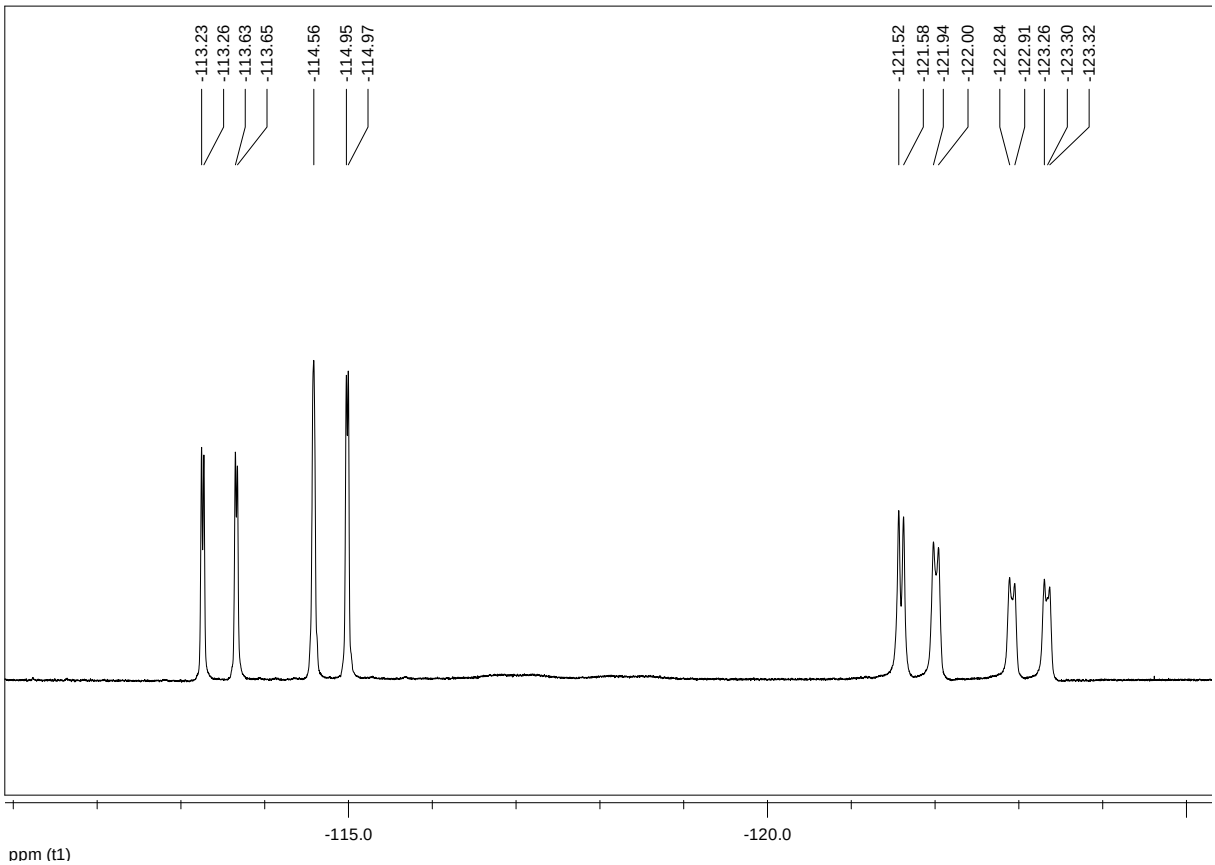

-115.00
-115.02
-115.40
-115.42
-116.35
-116.37
-116.75
-116.77
-124.55
-124.62
-124.95
-125.02
-125.90
-125.96
-126.30
-126.37
-110.0
-115.0
-120.0
-125.0
-130.0
ppm (t1)

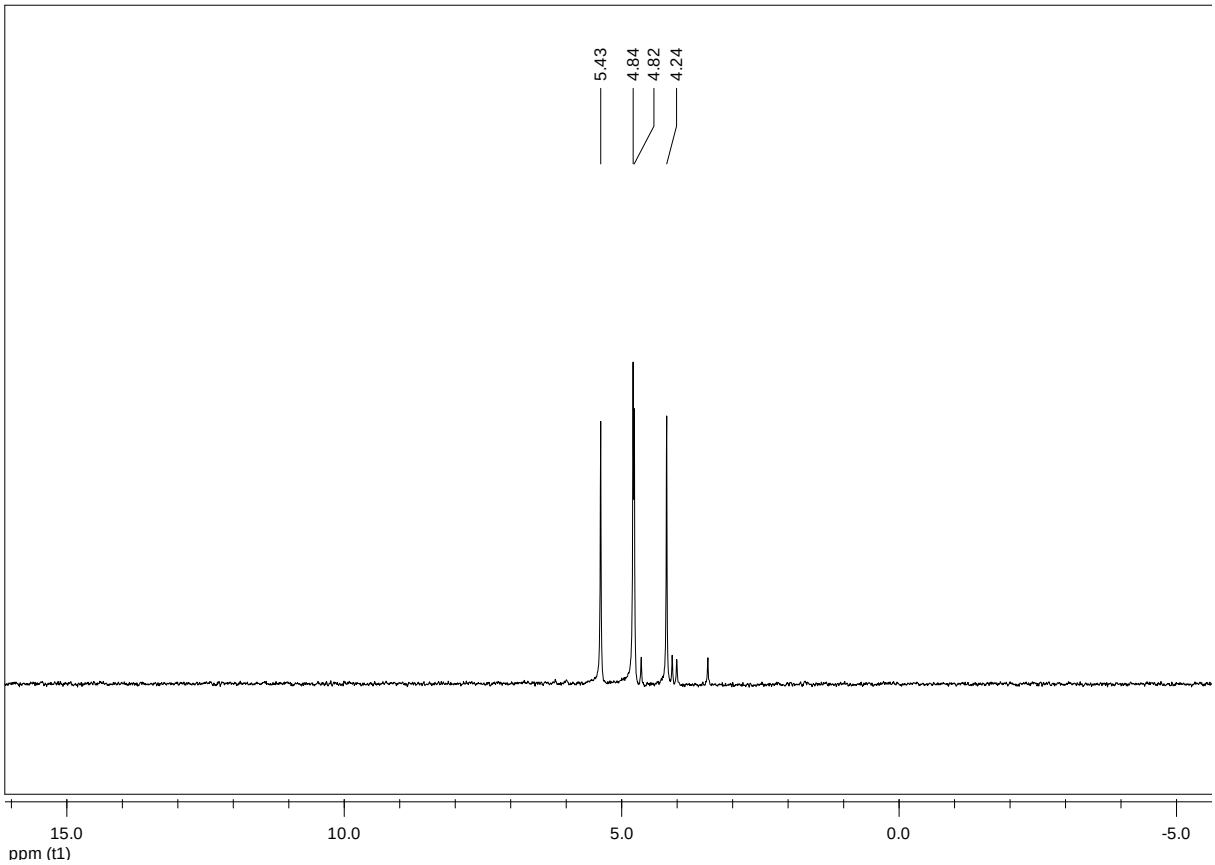

4.28
3.70
3.11
10.0
5.0
0.0
ppm (t1)

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)phosphonate (2e):

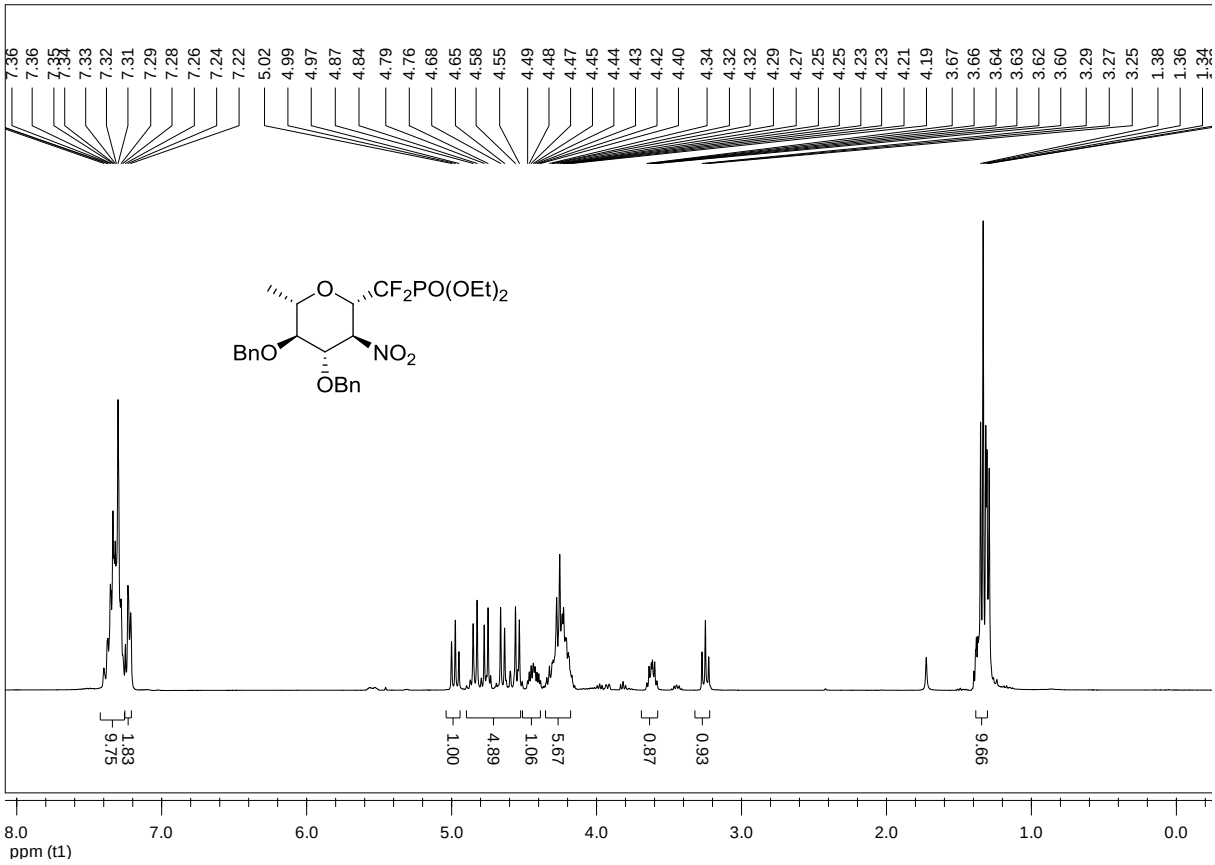


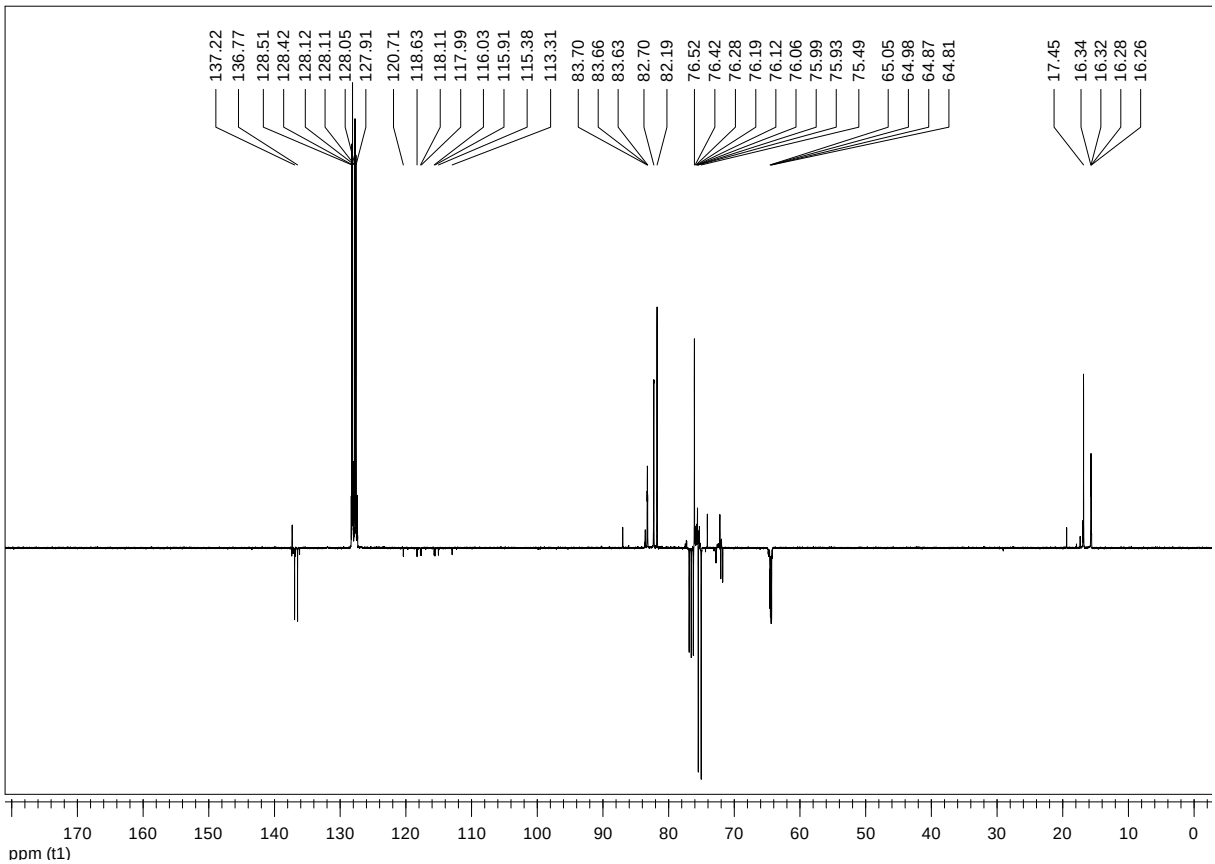


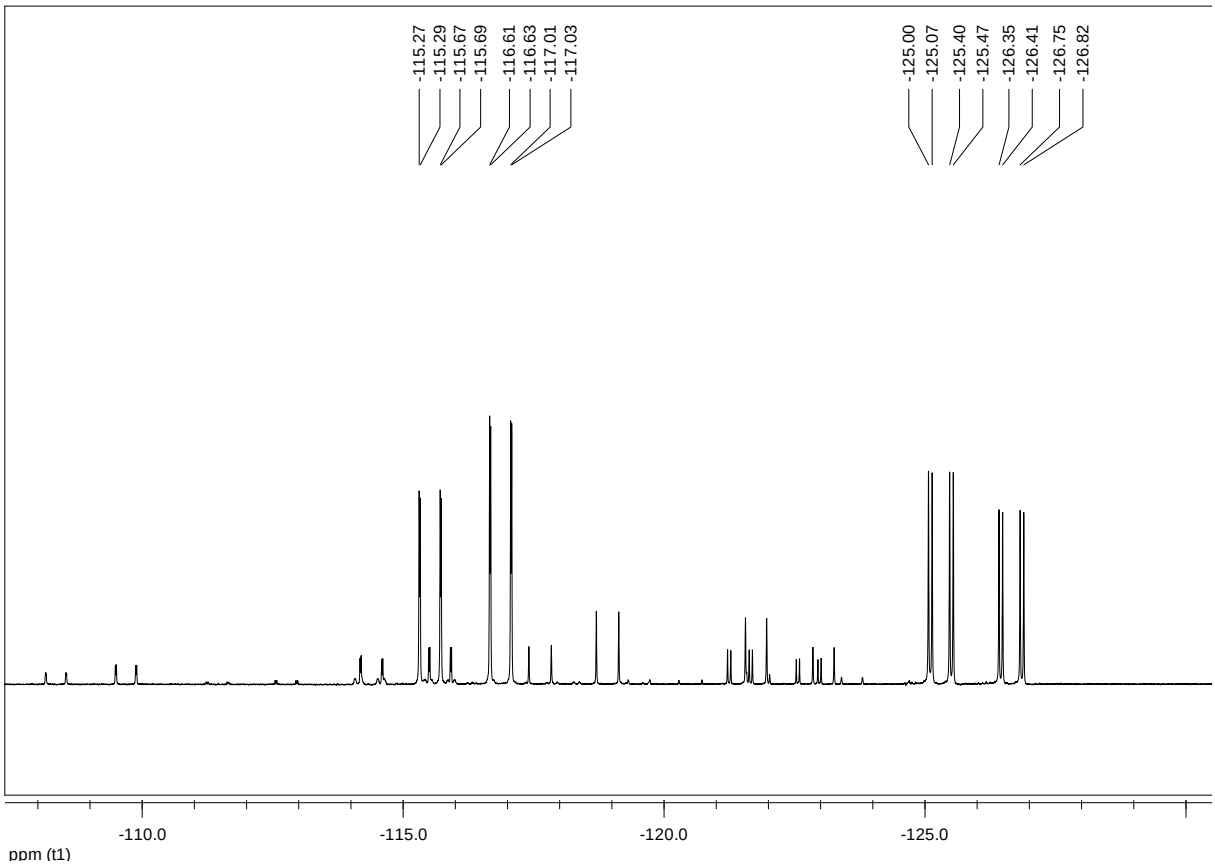

-113.23
-113.26
-113.63
-113.65
-114.56
-114.95
-114.97
-121.52
-121.58
-121.94
-122.00
-122.84
-122.91
-123.26
-123.30
-123.32
-115.0
-120.0
ppm (t1)

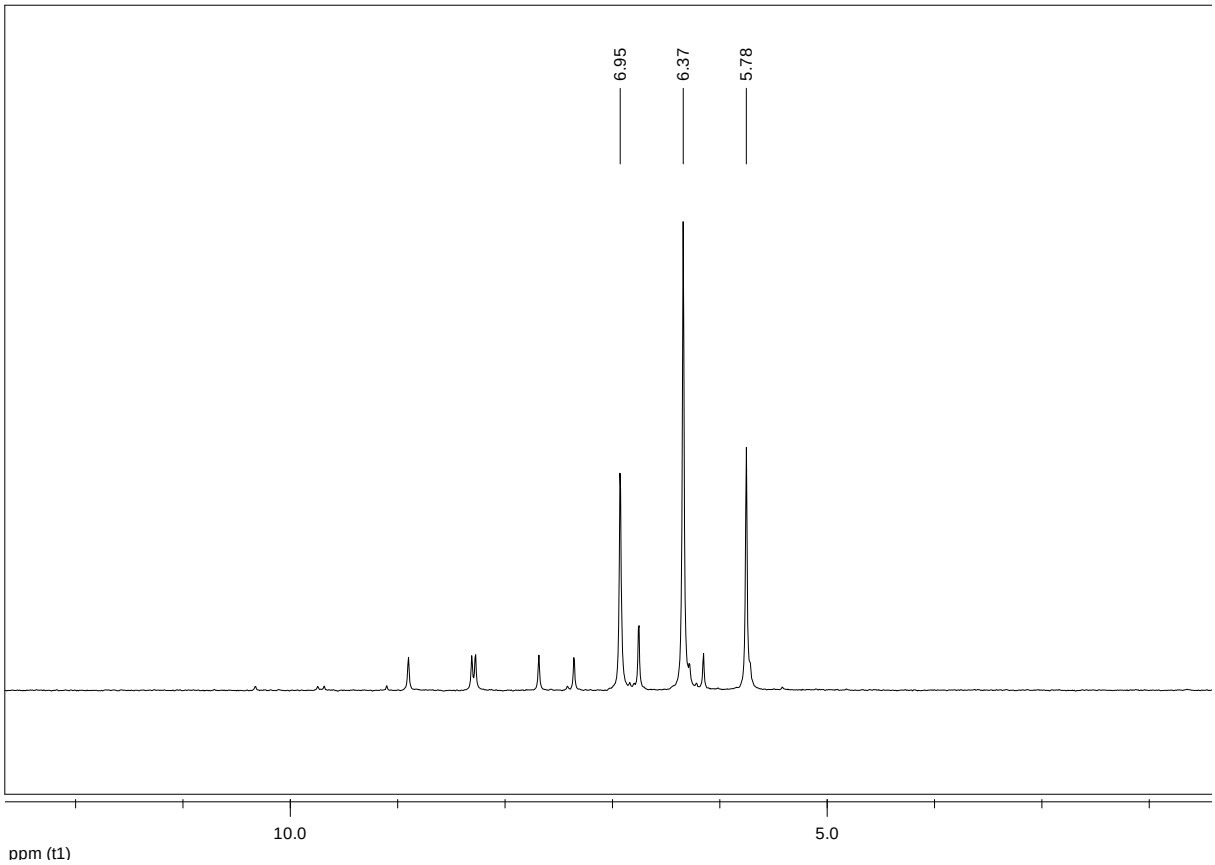

5.43
4.84
4.82
4.24
15.0
10.0
5.0
0.0
-5.0
ppm (t1)

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4-di-*O*-benzyl-6-deoxy-β-L-glucopyranosyl)phosphonate (2f):

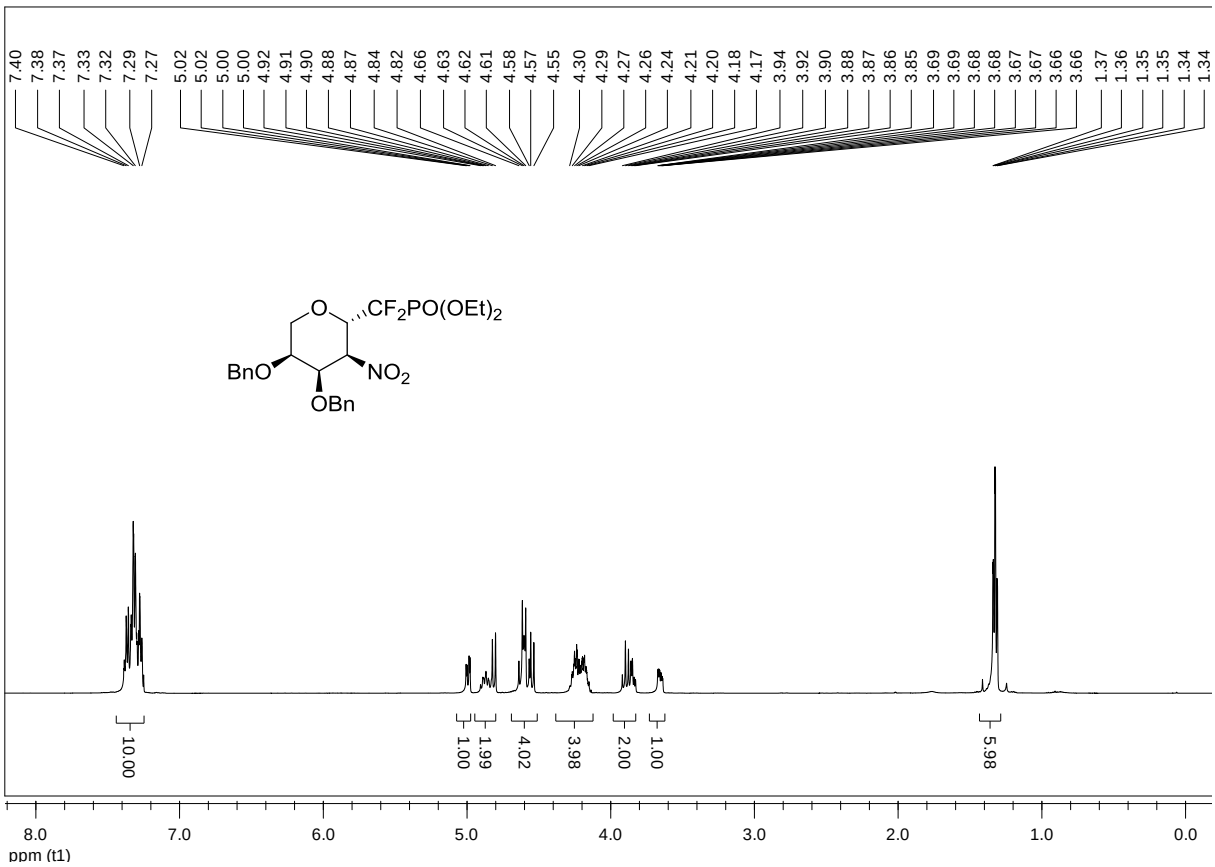


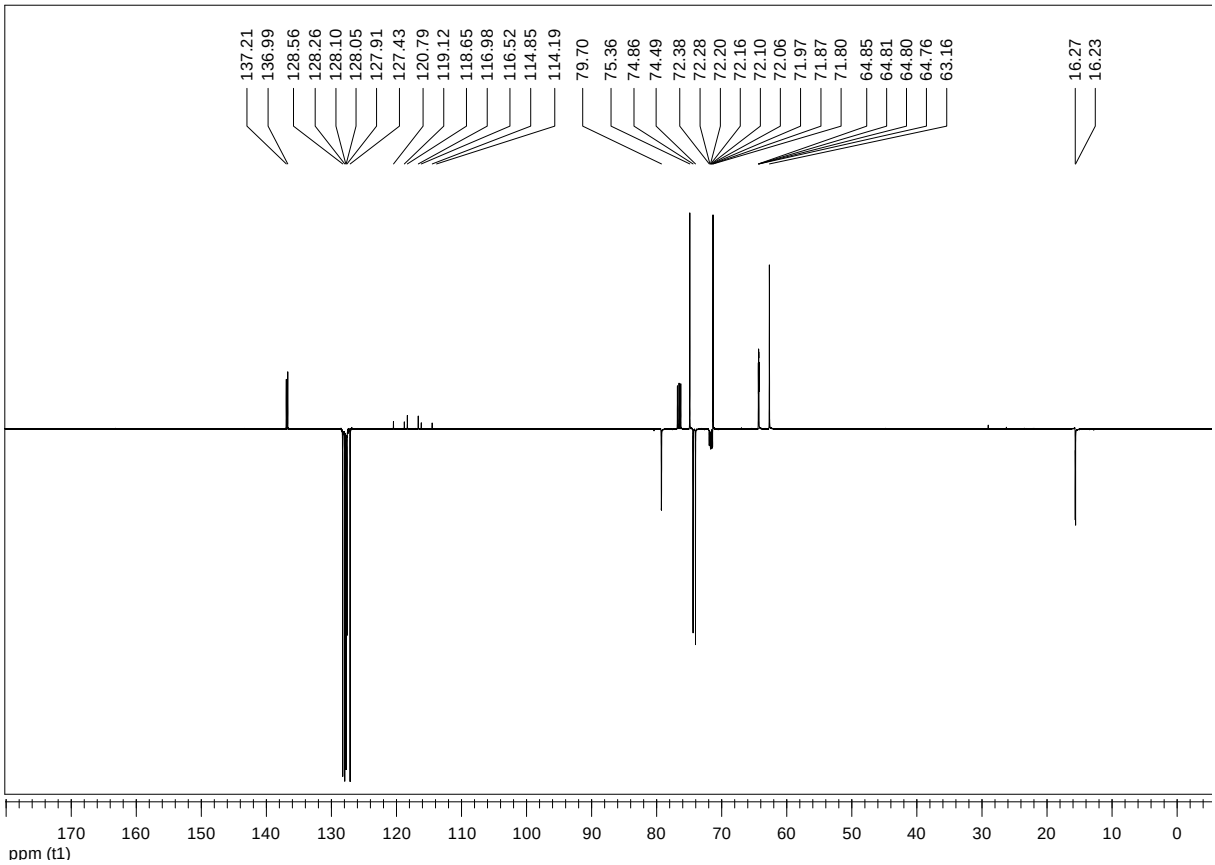


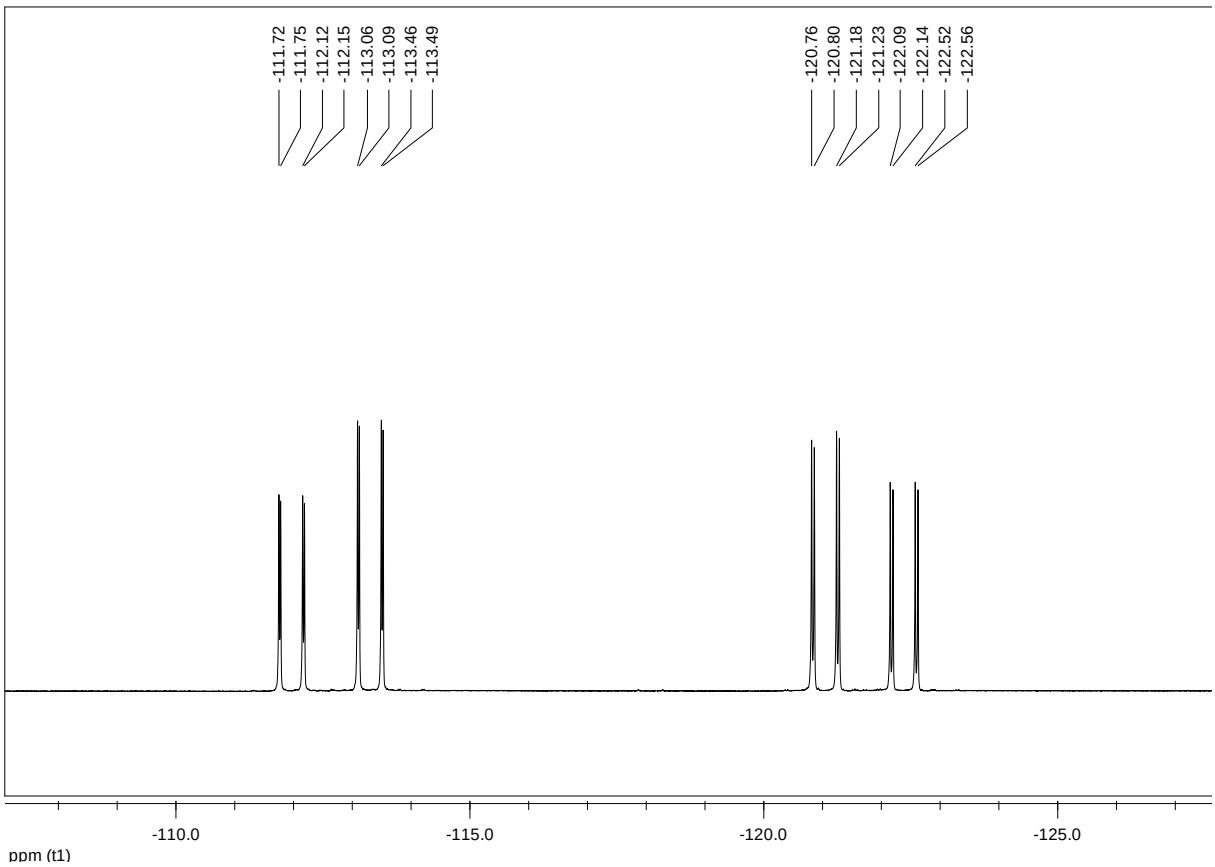

-115.27
-115.29
-115.67
-115.69
-116.61
-116.63
-117.01
-117.03
-125.00
-125.07
-125.40
-125.47
-126.35
-126.41
-126.75
-126.82
-110.0
-115.0
-120.0
-125.0
ppm (t1)

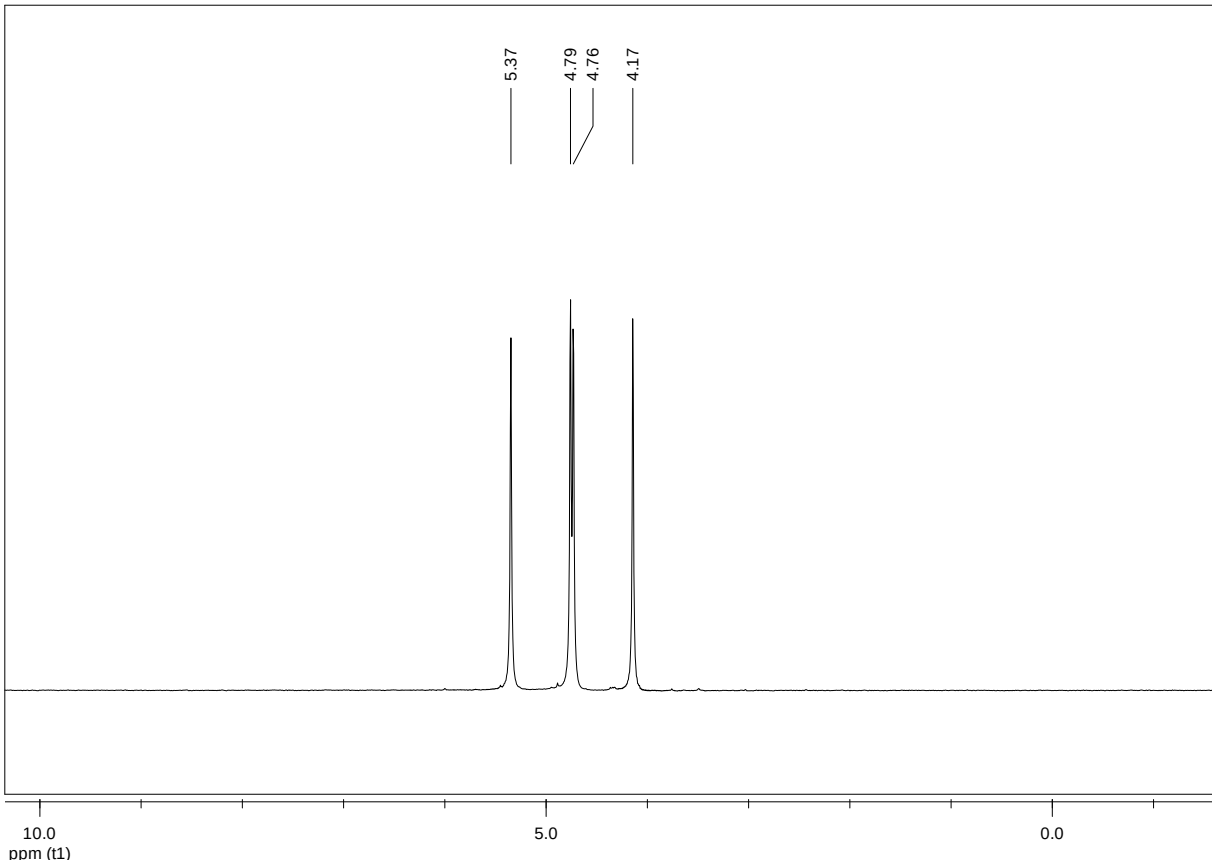

6.95
6.37
5.78
10.0
5.0
ppm (t1)

Diethyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4-di-*O*-benzyl-β-L-ribopyranosyl)phosphonate (2g):

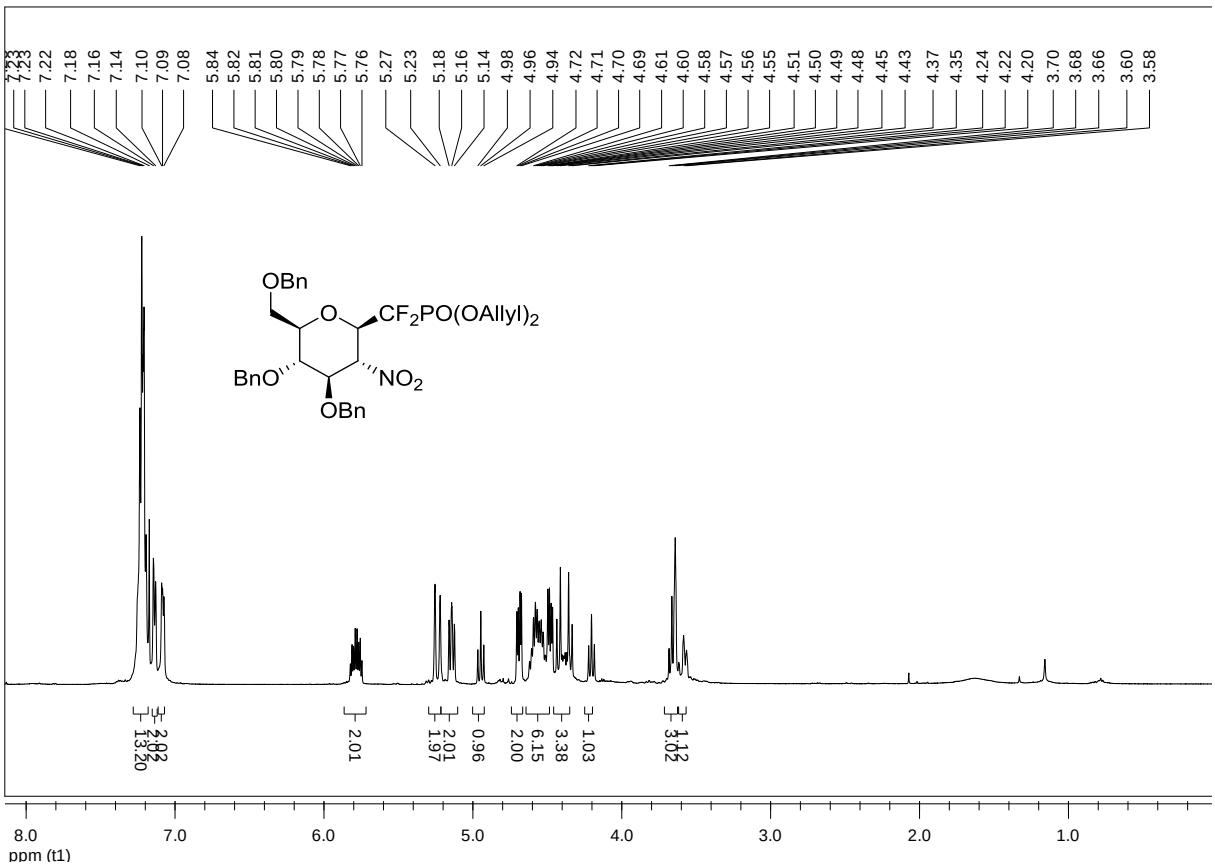


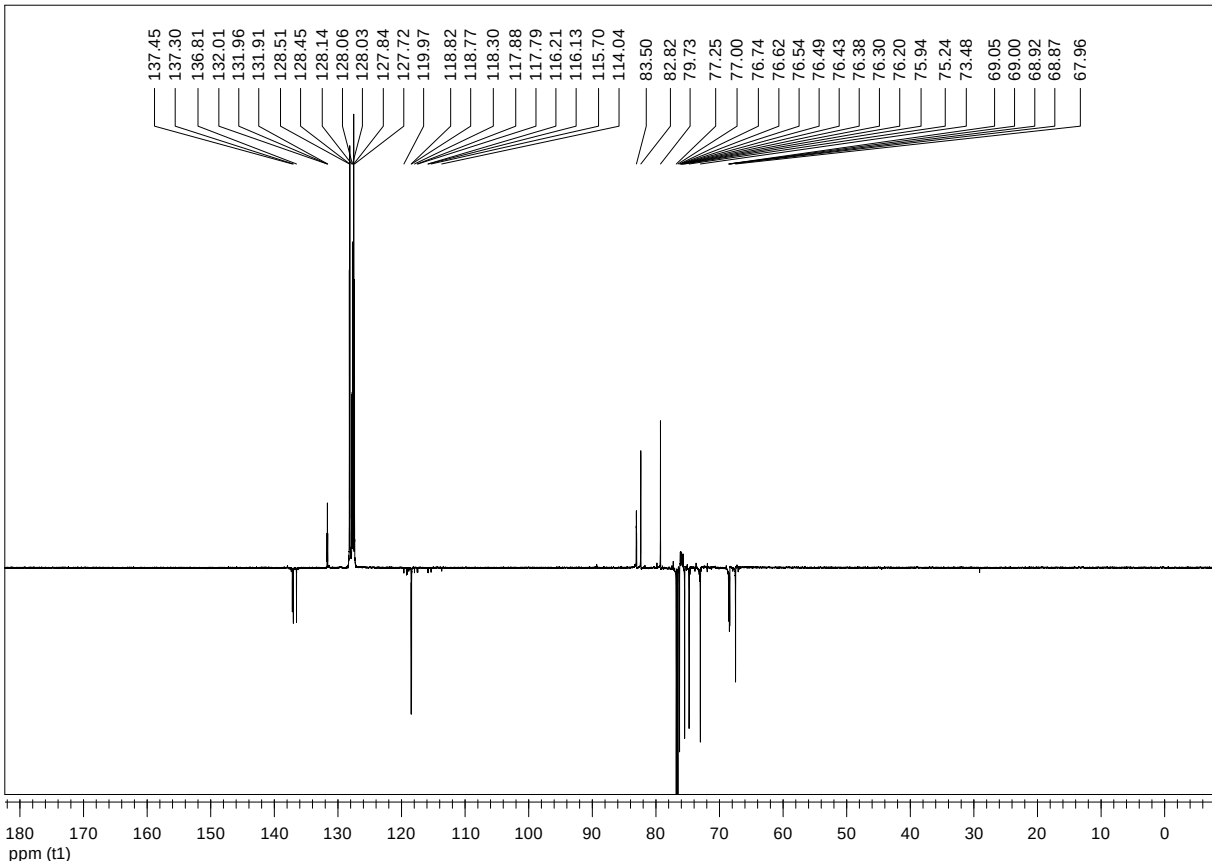


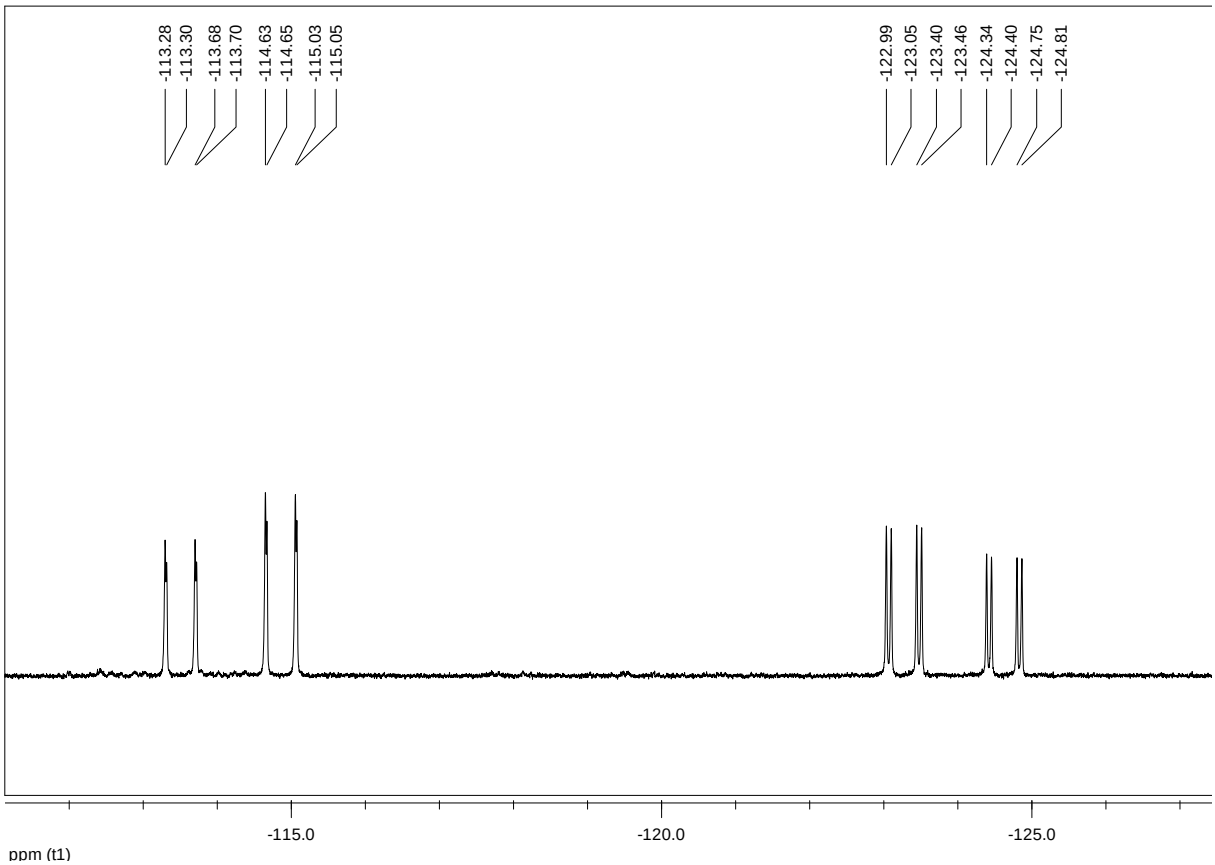

-111.72
-111.75
-112.12
-112.15
-113.06
-113.09
-113.46
-113.49
-120.76
-120.80
-121.18
-121.23
-122.09
-122.14
-122.52
-122.56
-110.0
-115.0
-120.0
-125.0
ppm (t1)

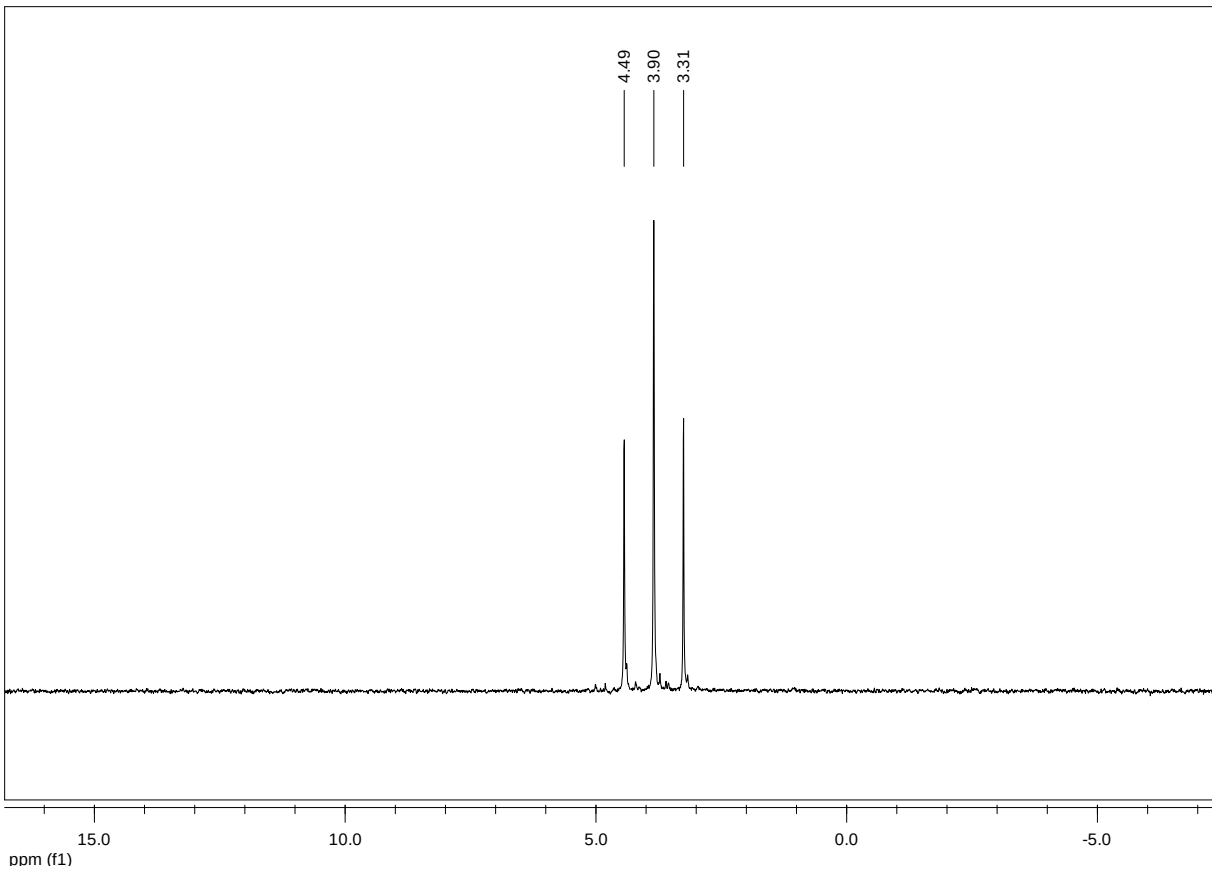

5.37
4.79
4.76
4.17
10.0
5.0
0.0
ppm (t1)

Diallyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (2h):

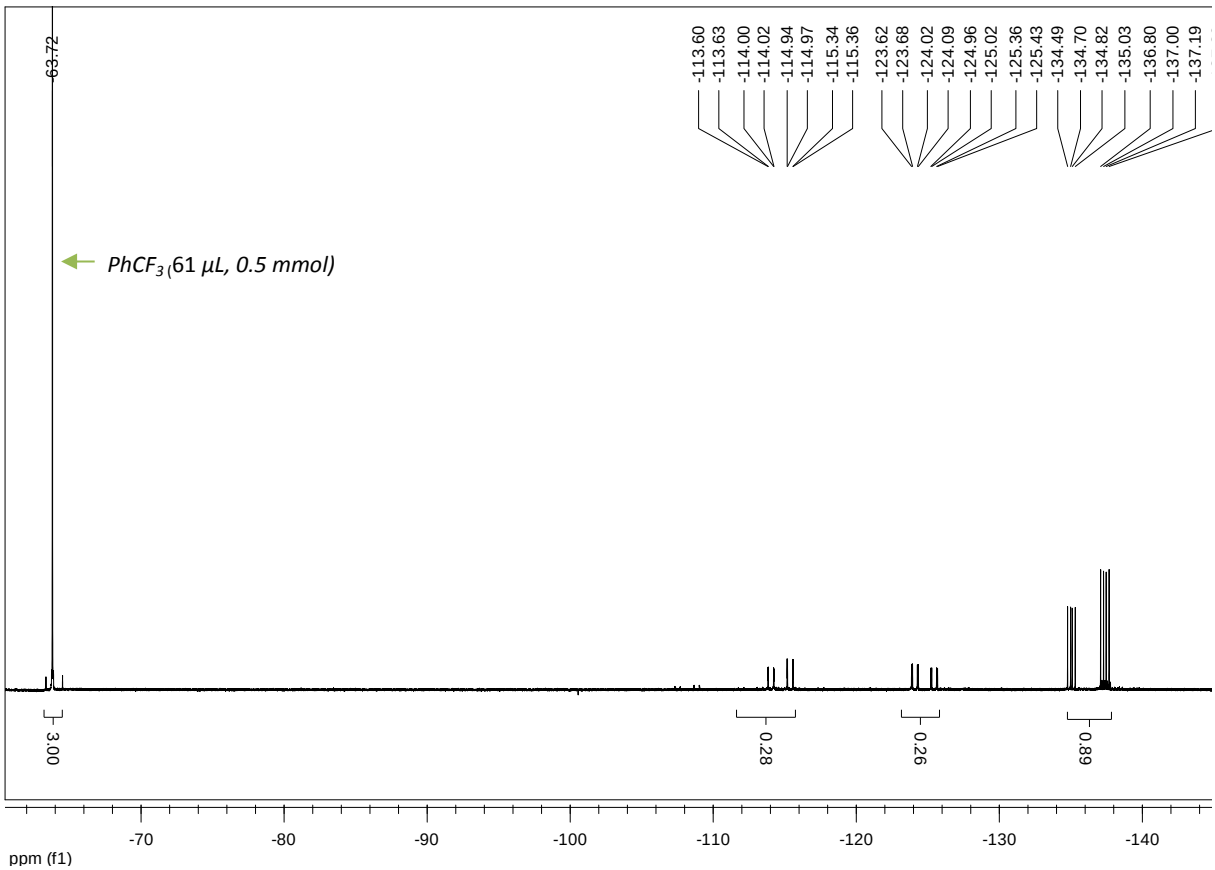




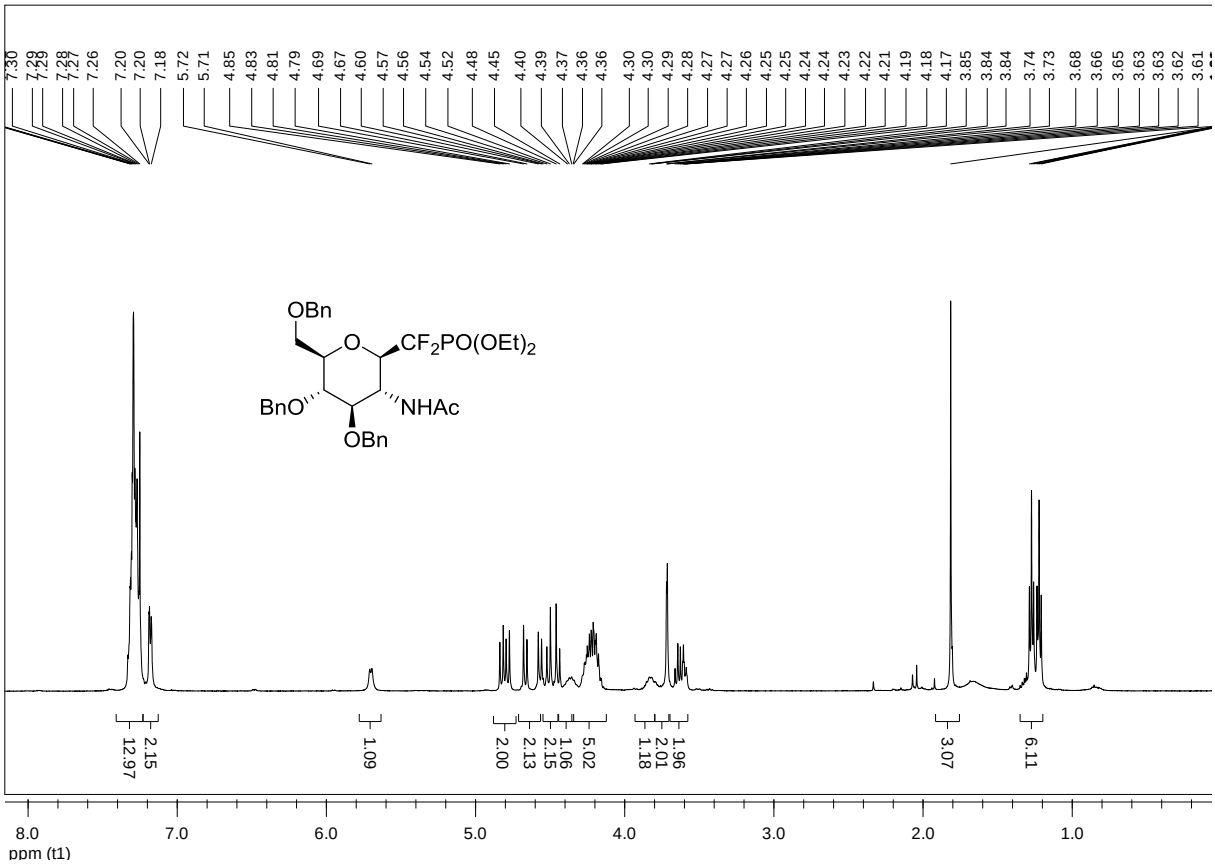

-113.28
-113.30
-113.68
-113.70
-114.63
-114.65
-115.03
-115.05
-122.99
-123.05
-123.40
-123.46
-124.34
-124.40
-124.75
-124.81
-115.0
-120.0
-125.0
ppm (t1)

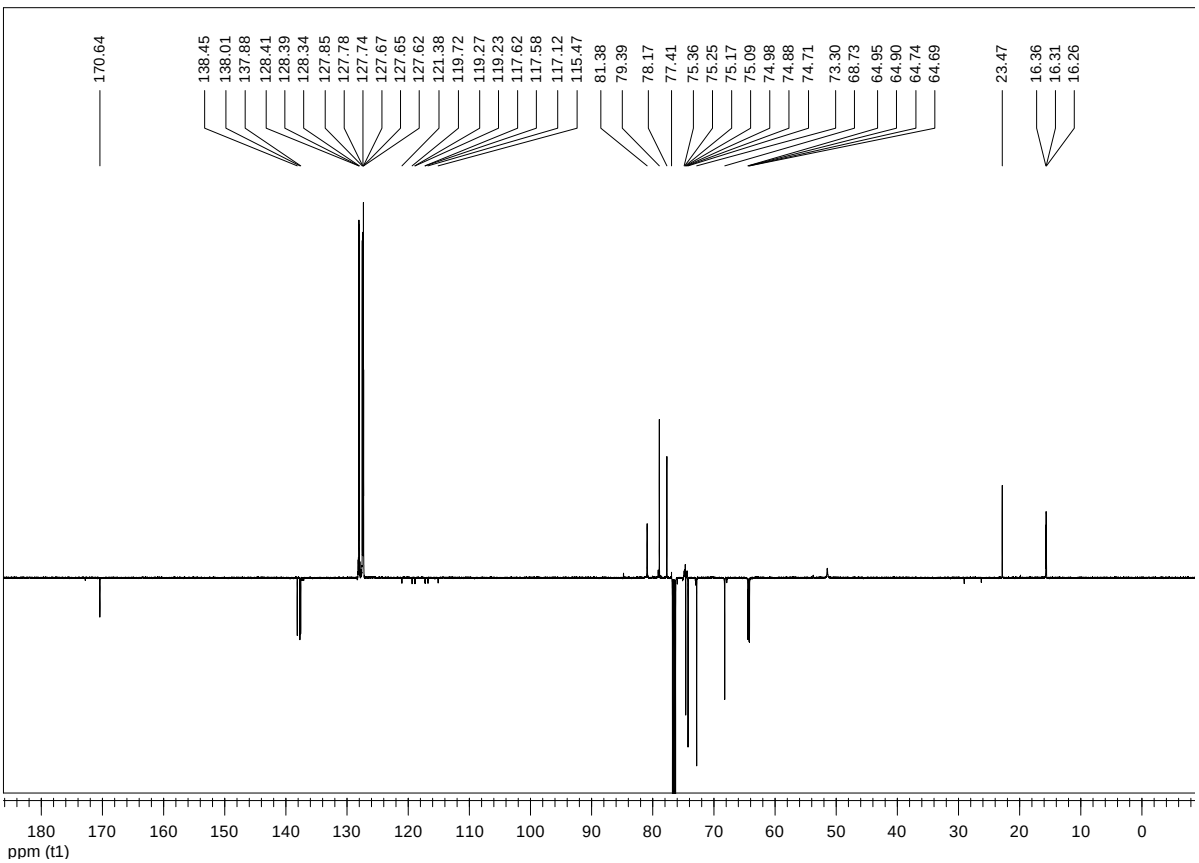

4.49
3.90
3.31
15.0
10.0
5.0
0.0
-5.0
ppm (f1)

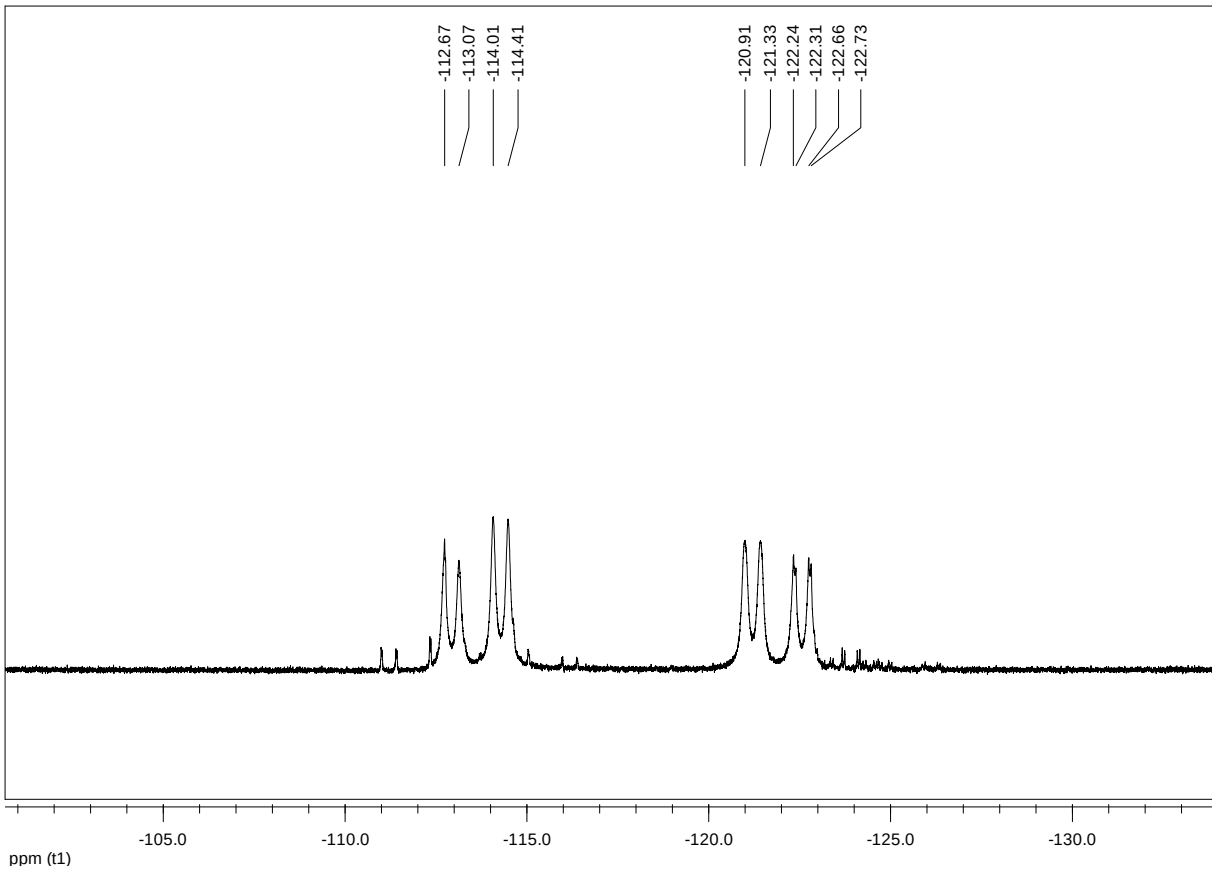
Dibenzyl 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (2i):

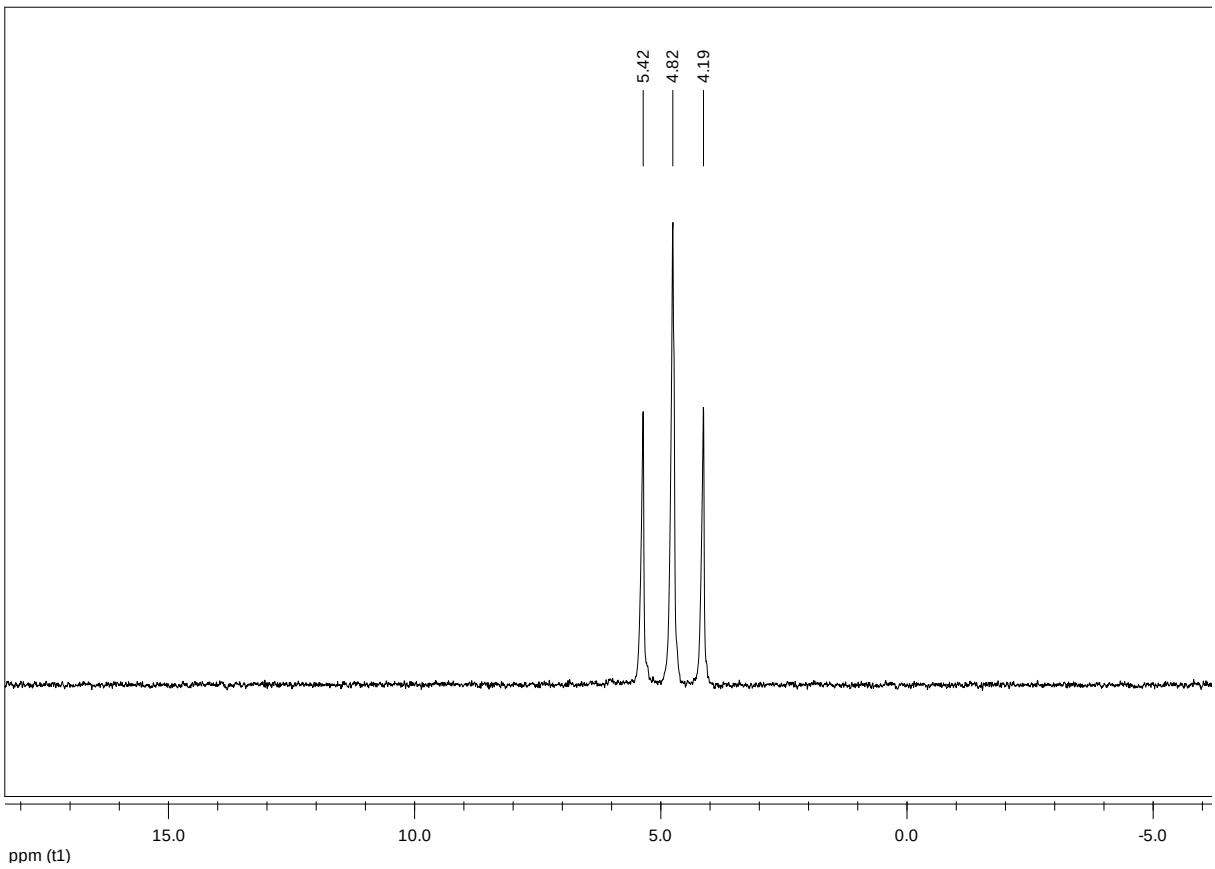


Diethyl 2,2-difluoro-2-(2-acetylamino-2-deoxy-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (3):

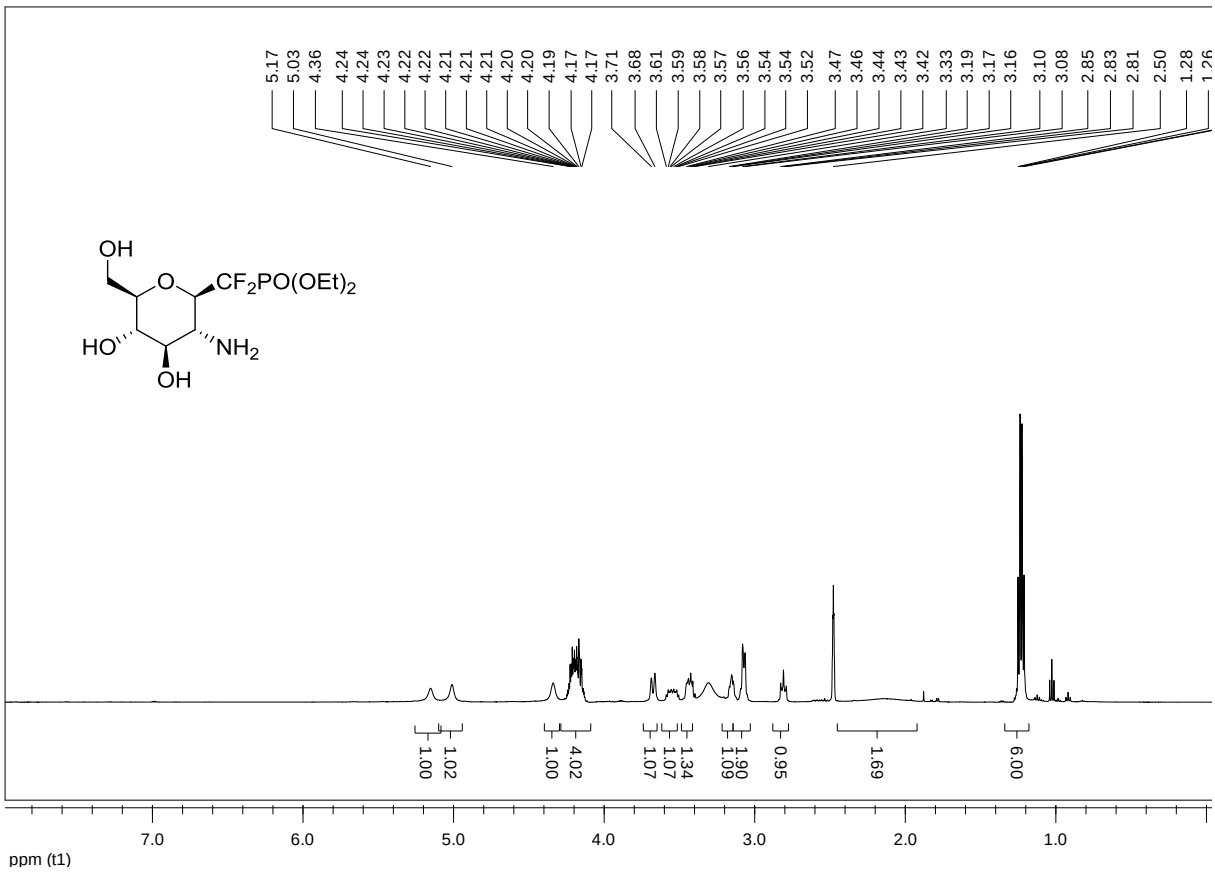


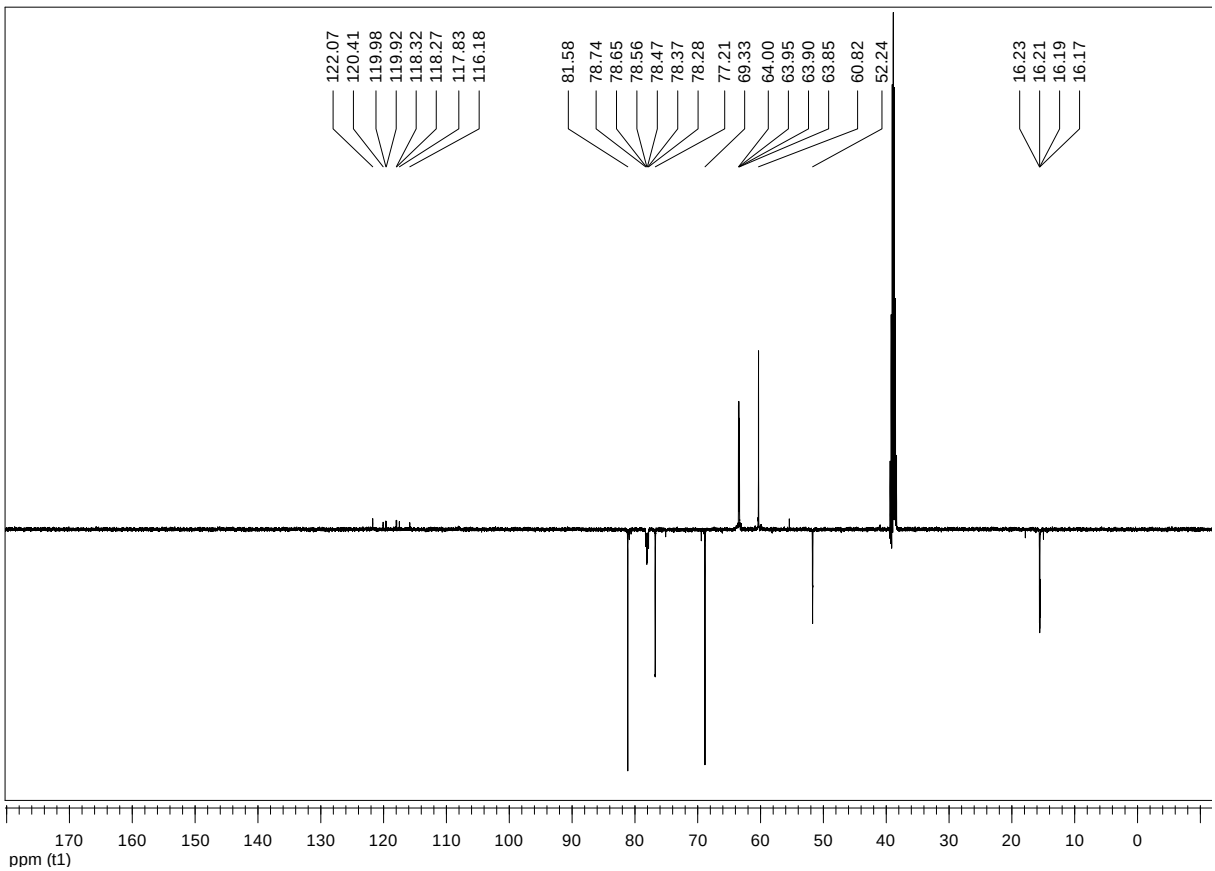


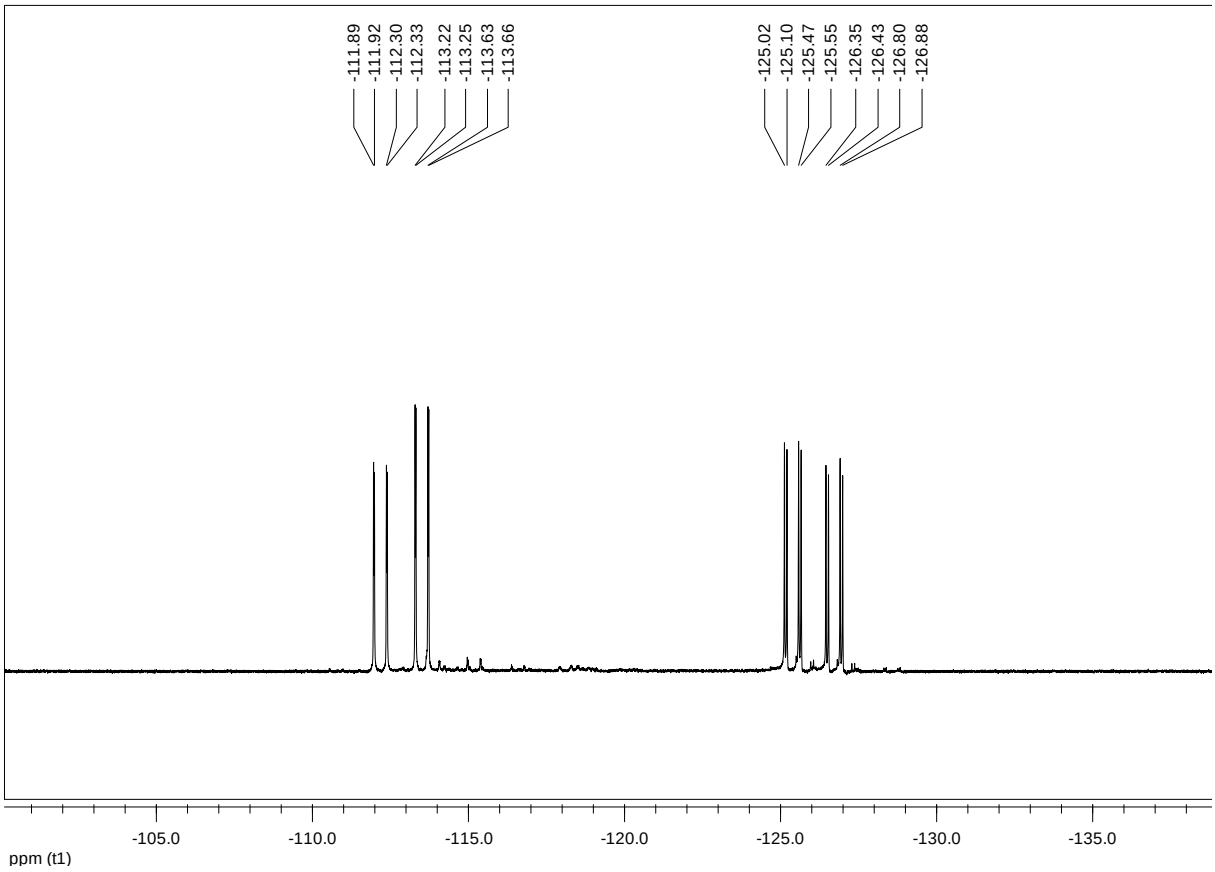

-112.67
-113.07
-114.01
-114.41
-120.91
-121.33
-122.24
-122.31
-122.66
-122.73
-105.0
-110.0
-115.0
-120.0
-125.0
-130.0
ppm (t1)

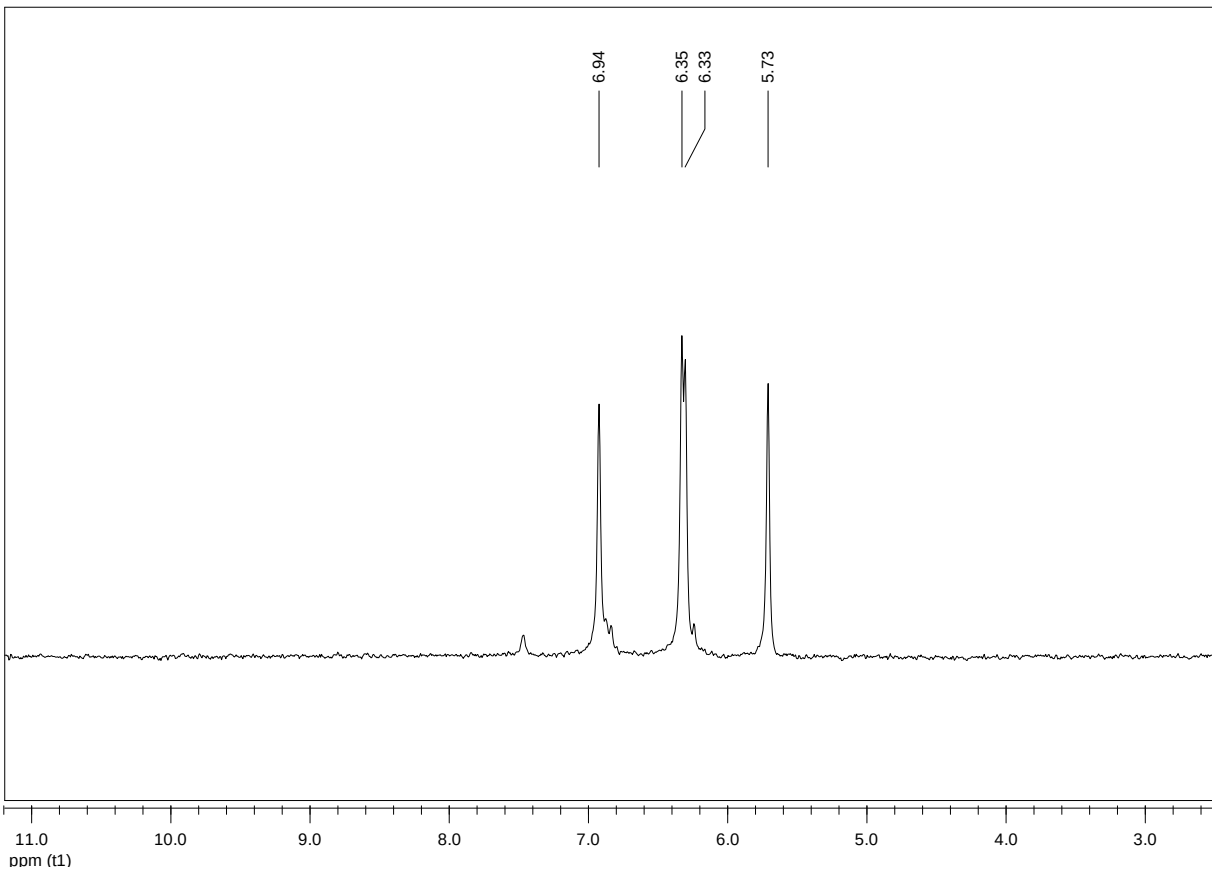

5.42
4.82
4.19
15.0
10.0
5.0
0.0
-5.0
ppm (t1)

Diethyl 2,2-difluoro-2-(2-amino-2-deoxy-β-D-glucopyranosyl)phosphonate (4):

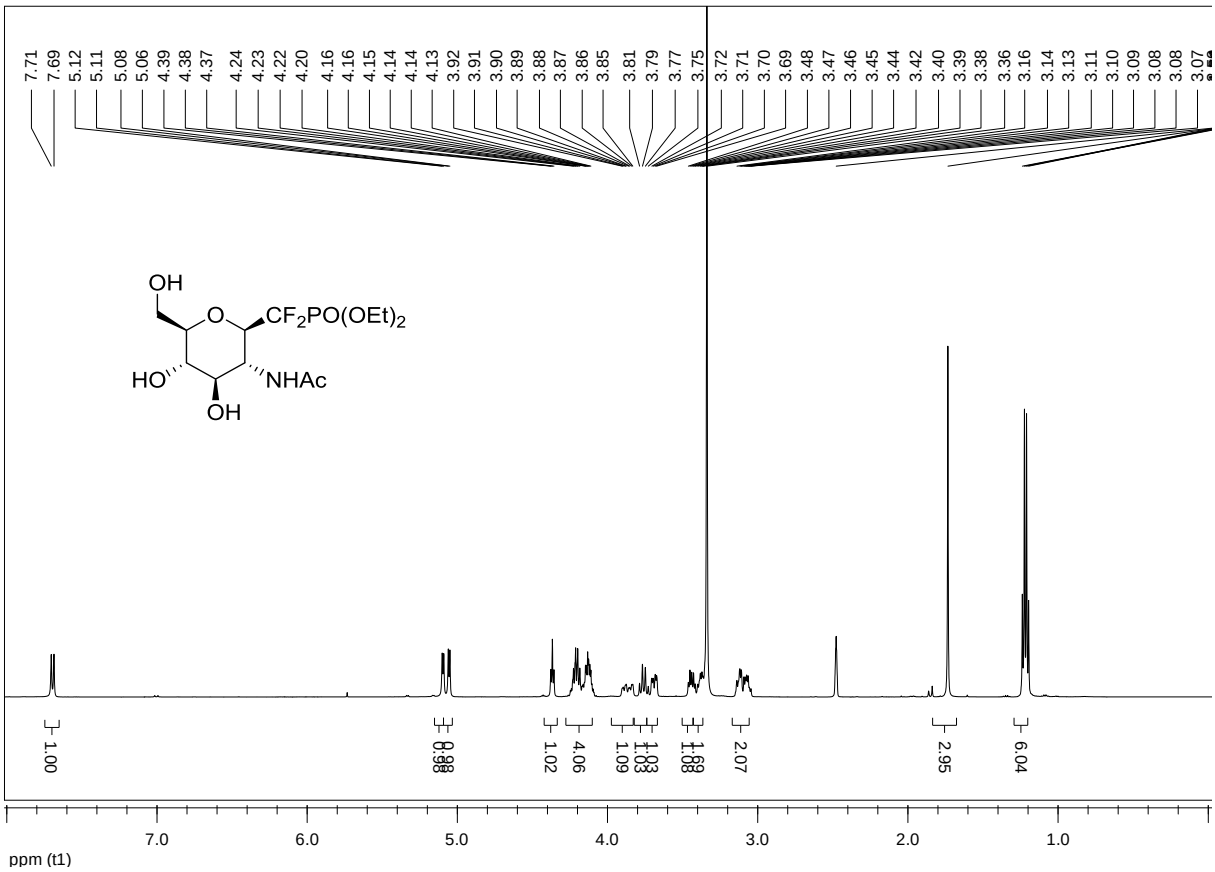


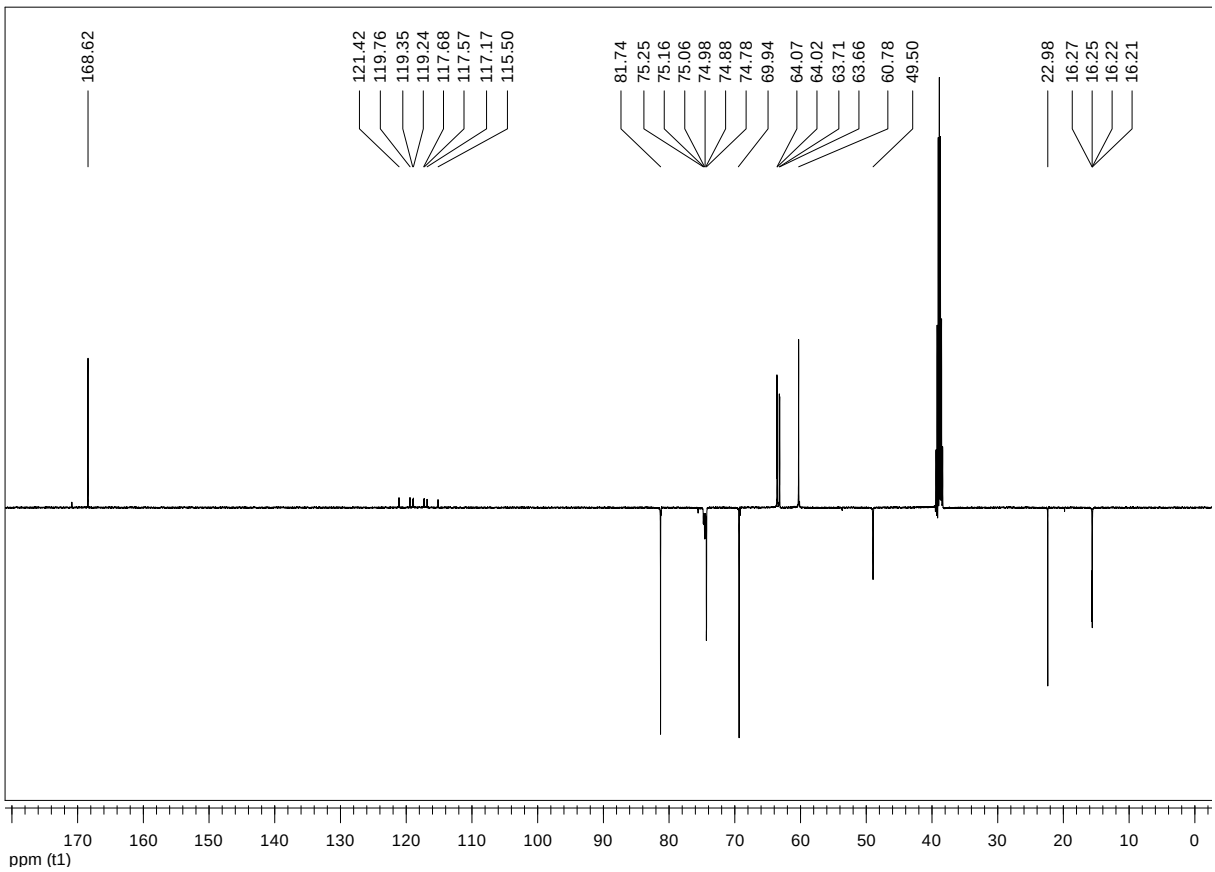


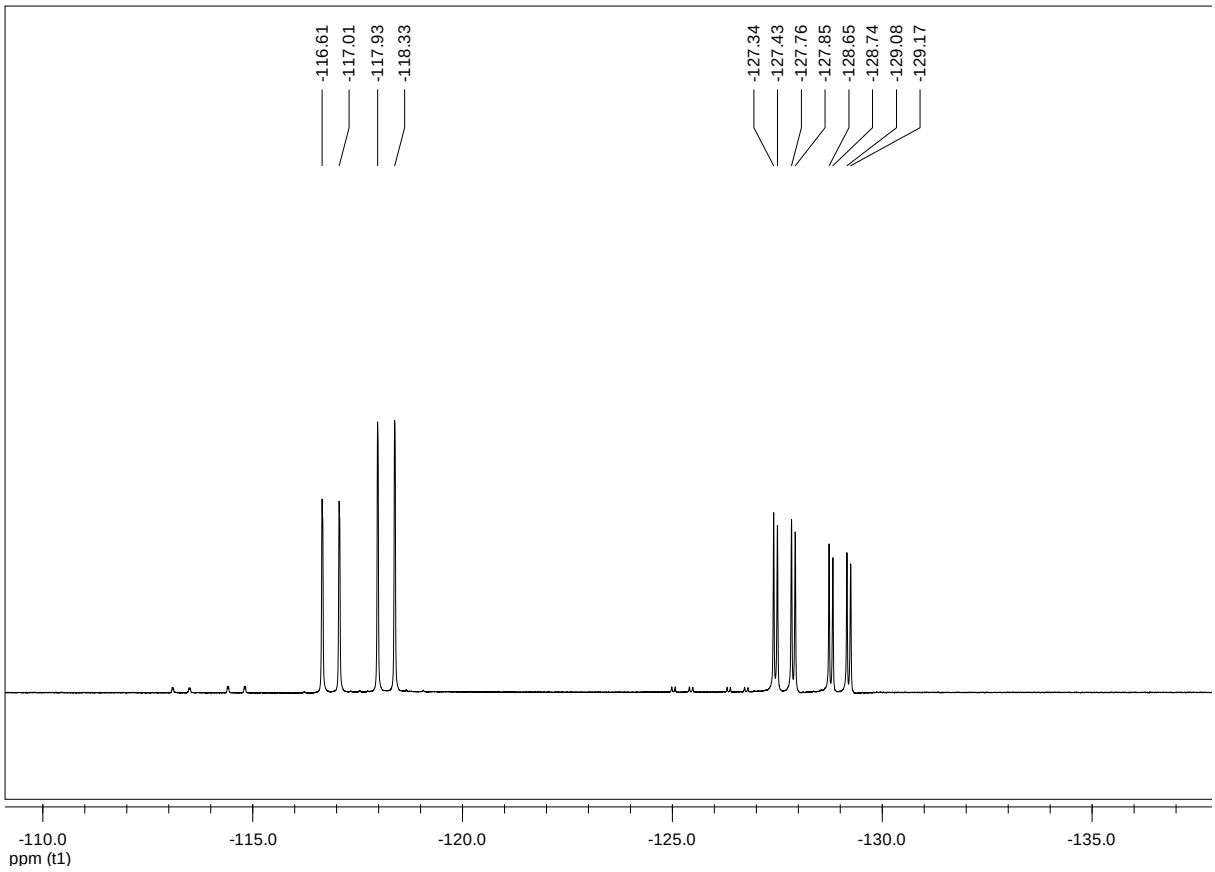

-111.89
-111.92
-112.30
-112.33
-113.22
-113.25
-113.63
-113.66
-125.02
-125.10
-125.47
-125.55
-126.35
-126.43
-126.80
-126.88
-105.0
-110.0
-115.0
-120.0
-125.0
-130.0
-135.0
ppm (t1)

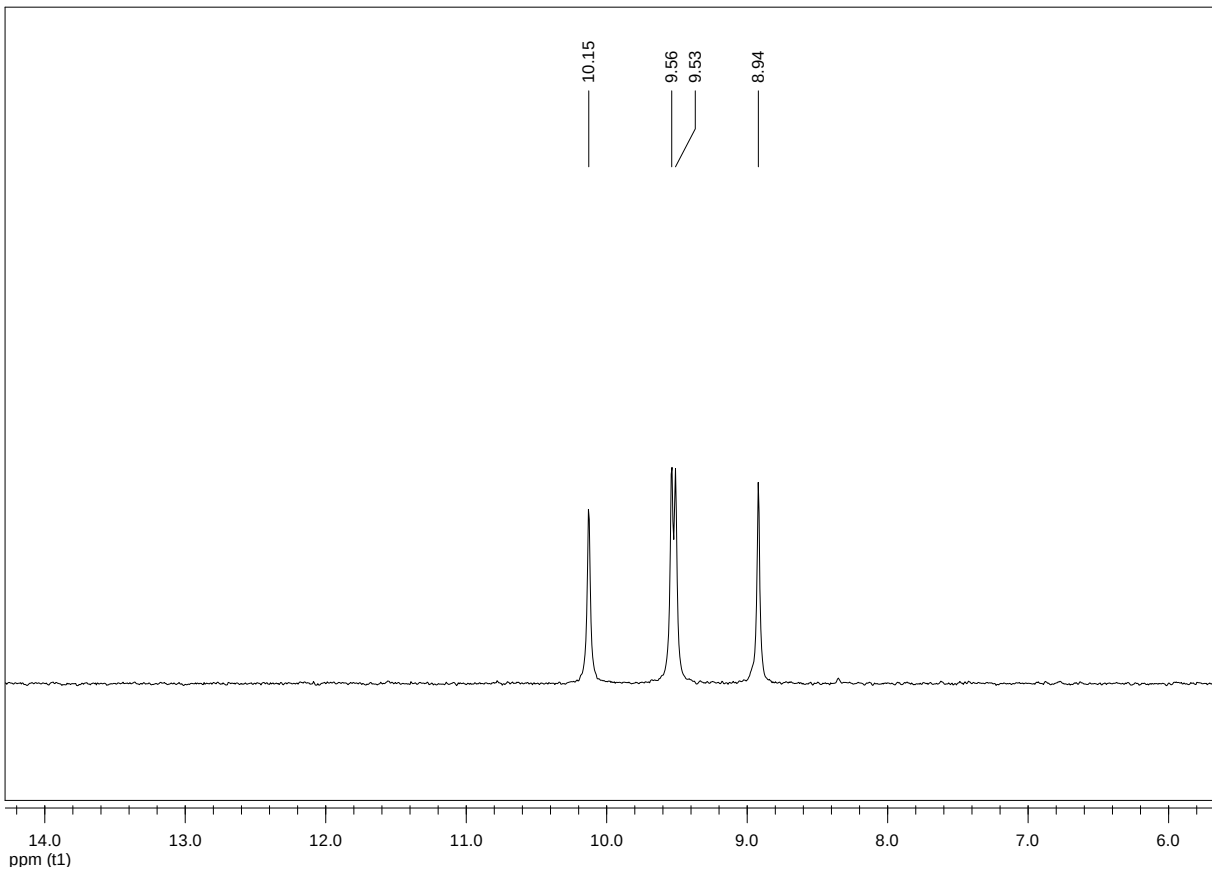

6.94
6.35
6.33
5.73
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
ppm (t1)

Diethyl 2,2-difluoro-2-(2-acetylamino-2-deoxy-β-D-glucopyranosyl)phosphonate (5):

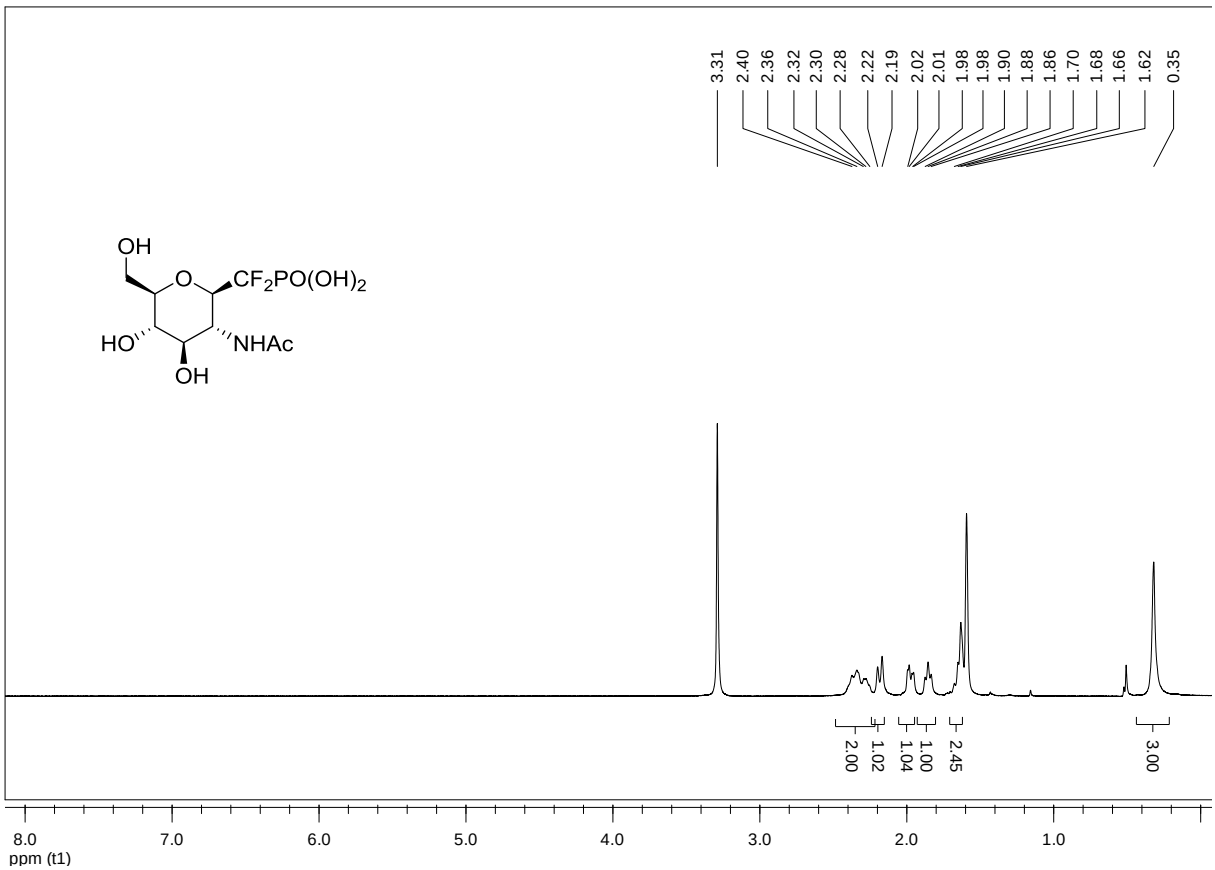


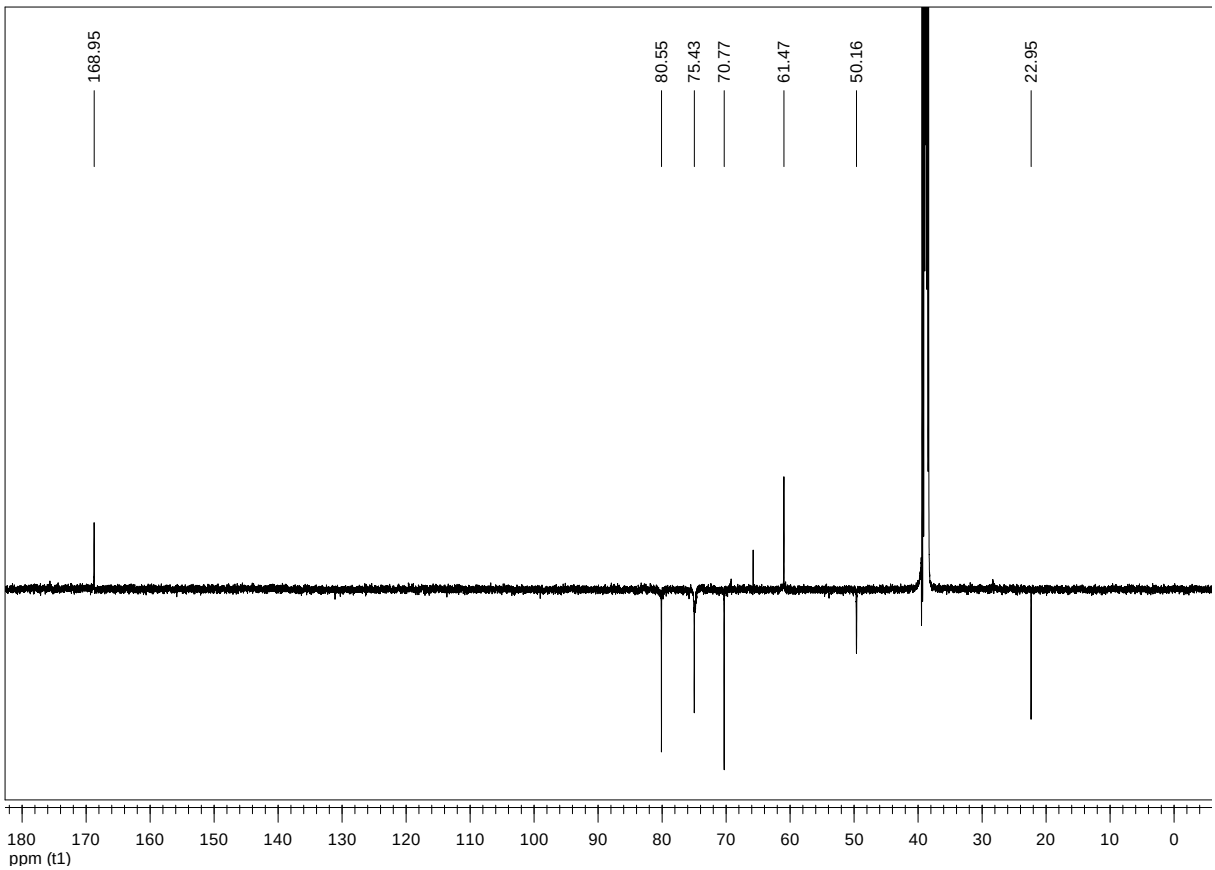


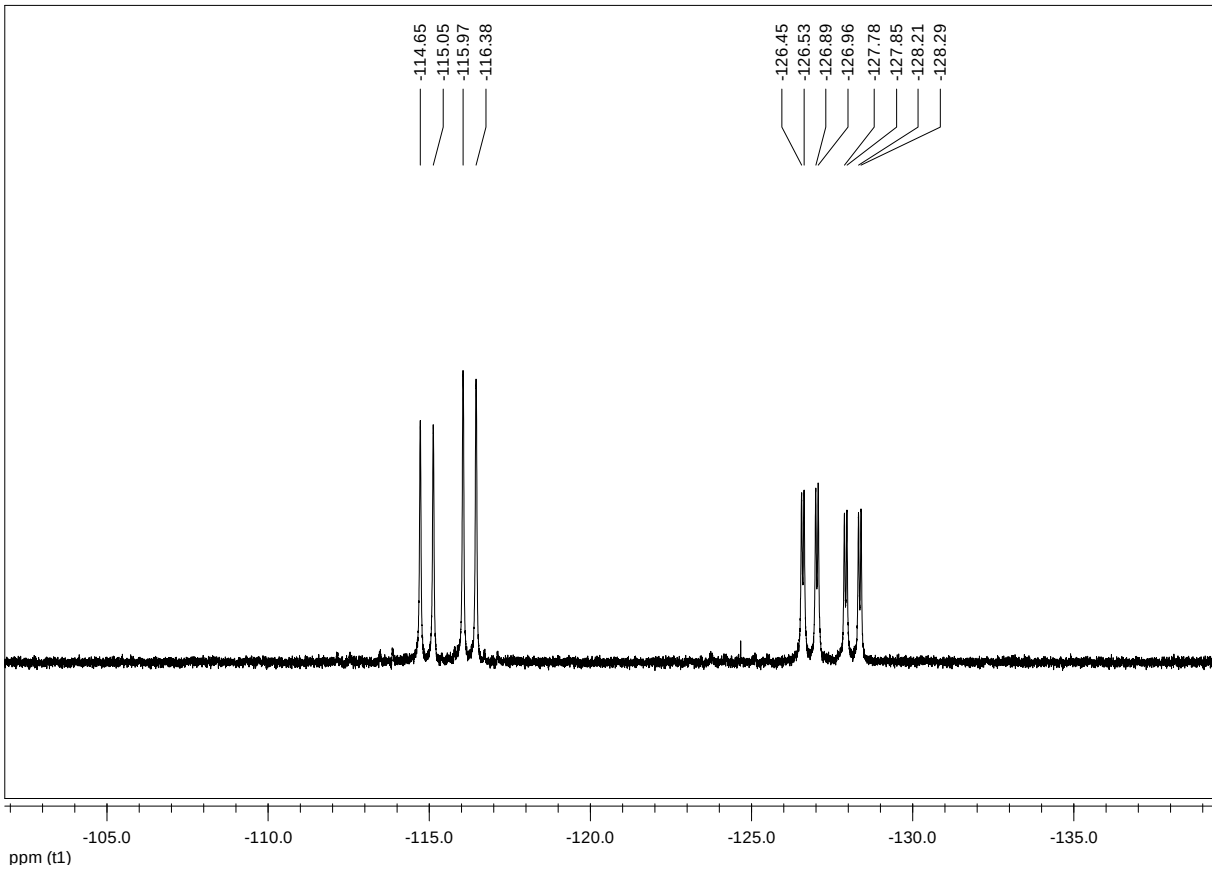

-116.61
-117.01
-117.93
-118.33
-127.34
-127.43
-127.76
-127.85
-128.65
-128.74
-129.08
-129.17
-110.0
-115.0
-120.0
-125.0
-130.0
-135.0
ppm (t1)

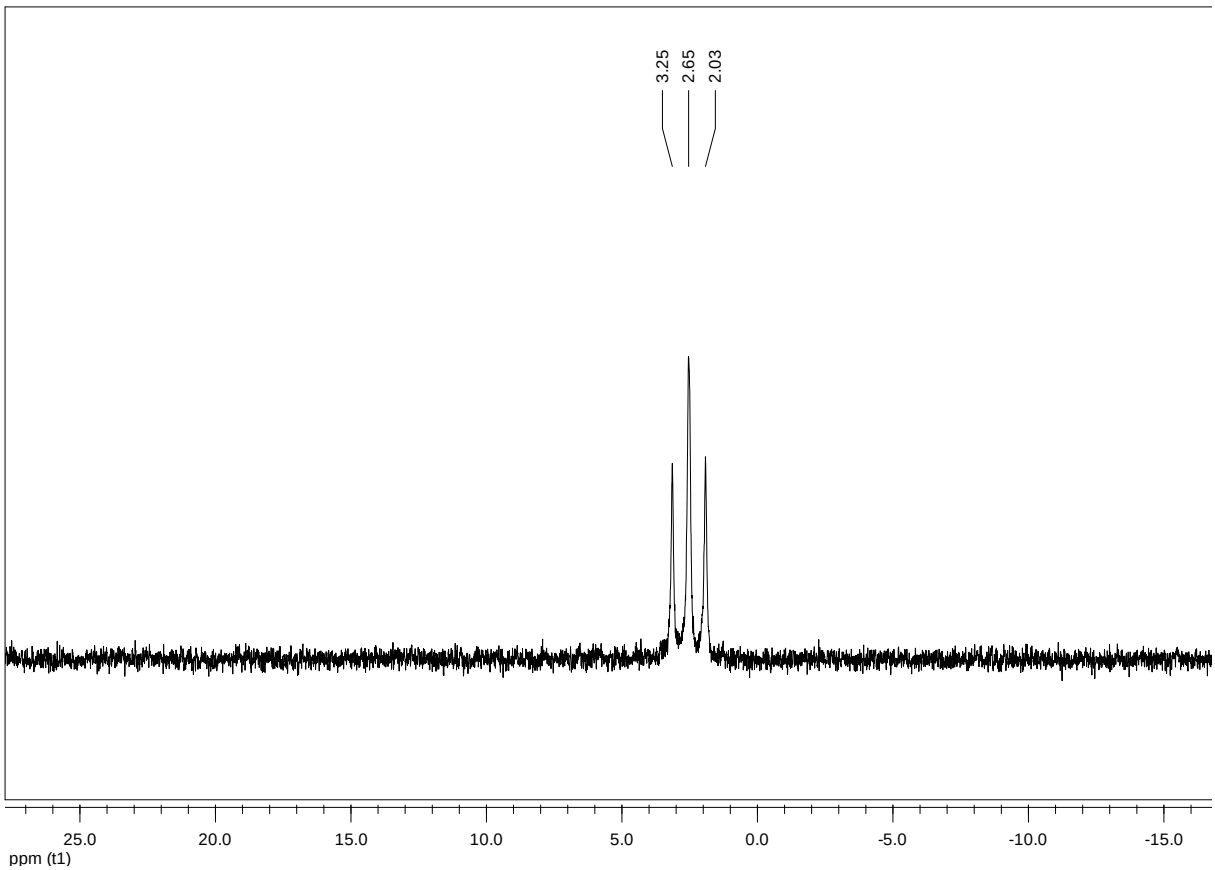

10.15
9.56
9.53
8.94
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
ppm (t1)

2,2-Difluoro-2-(2-acetylamino-2-deoxy-β-D-glucopyranosyl)phosphonate (6):

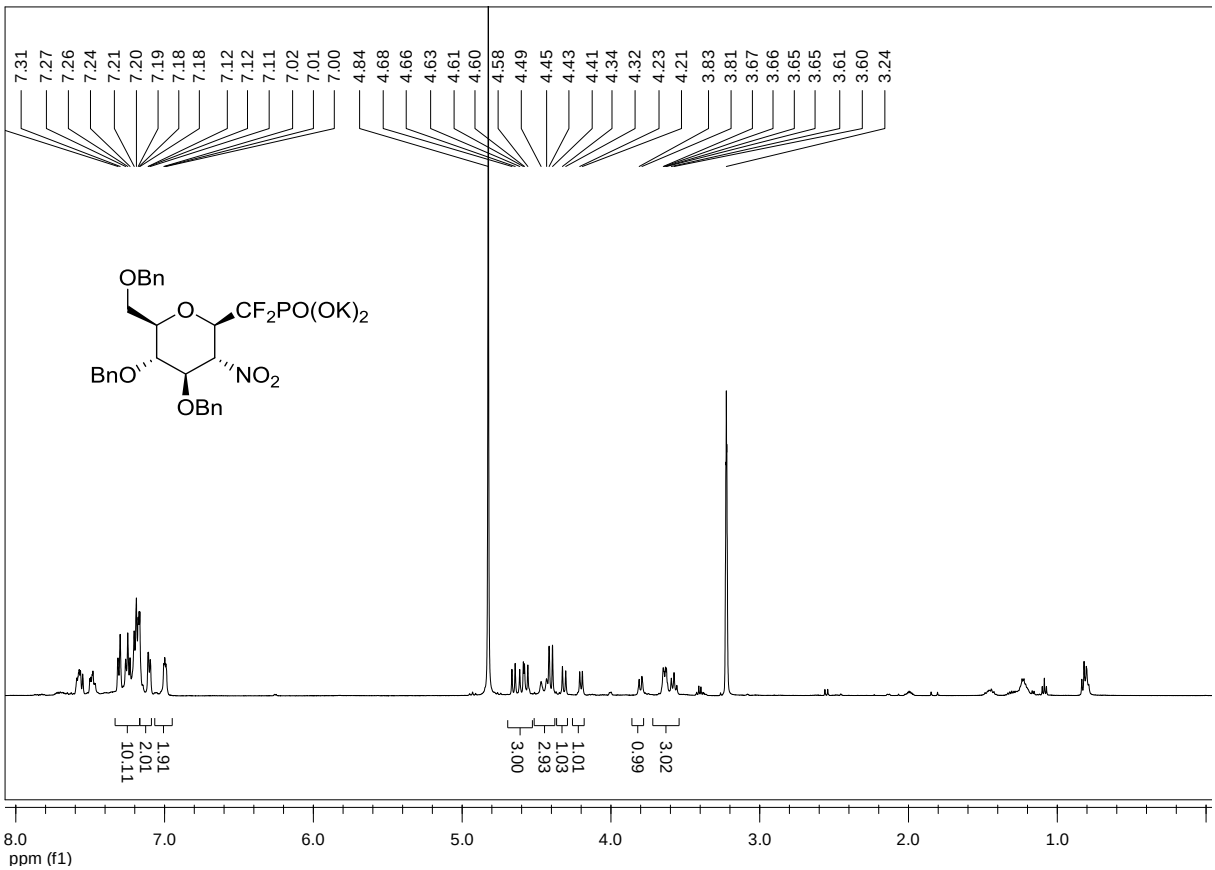


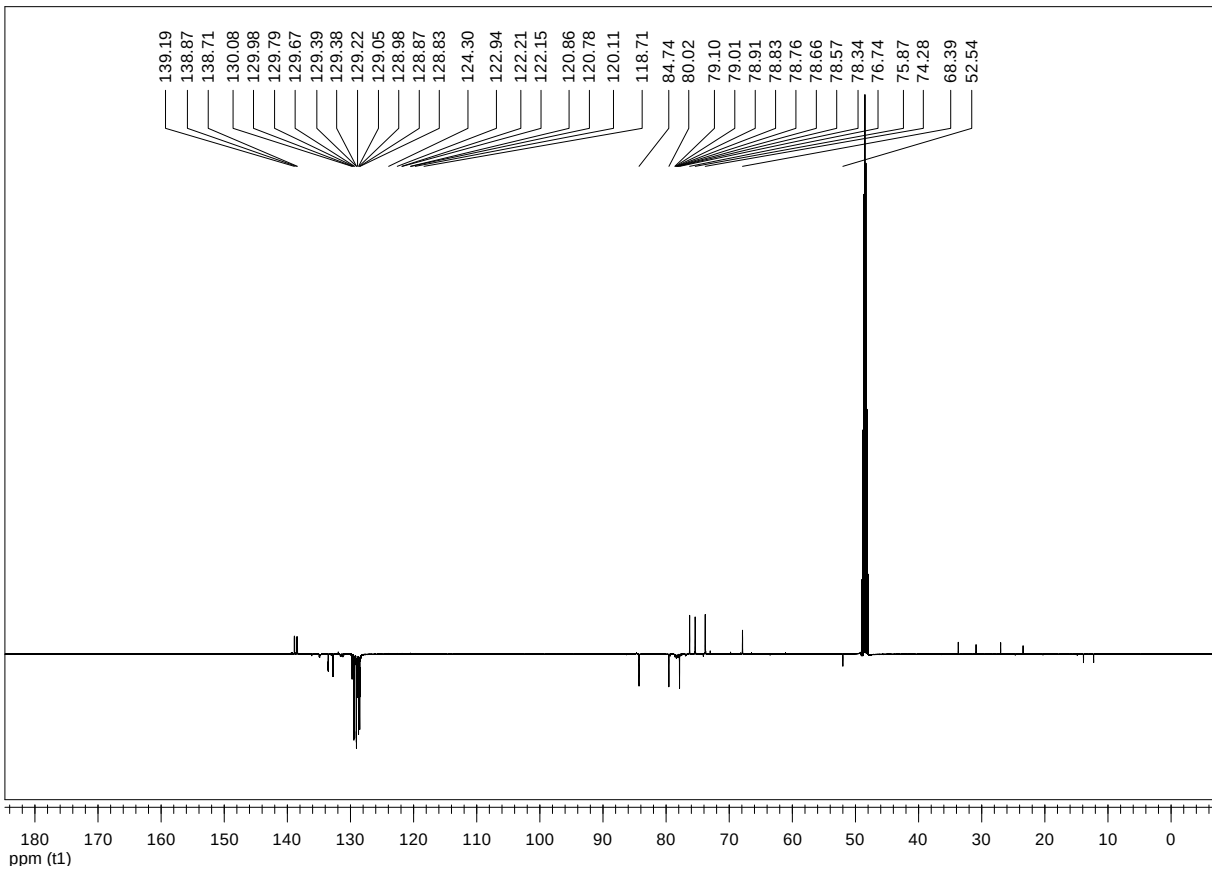


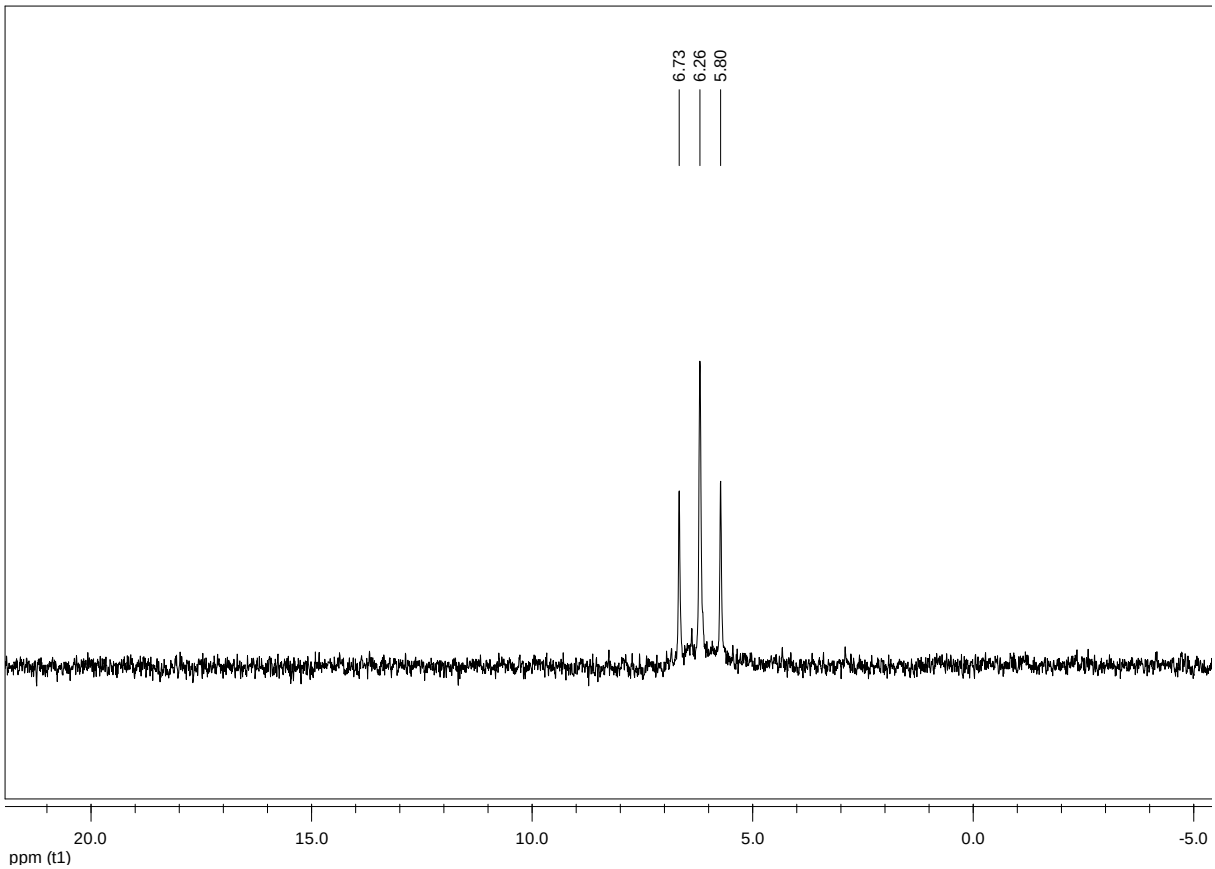

-114.65
-115.05
-115.97
-116.38
-126.45
-126.53
-126.89
-126.96
-127.78
-127.85
-128.21
-128.29
-105.0
-110.0
-115.0
-120.0
-125.0
-130.0
-135.0
ppm (t1)

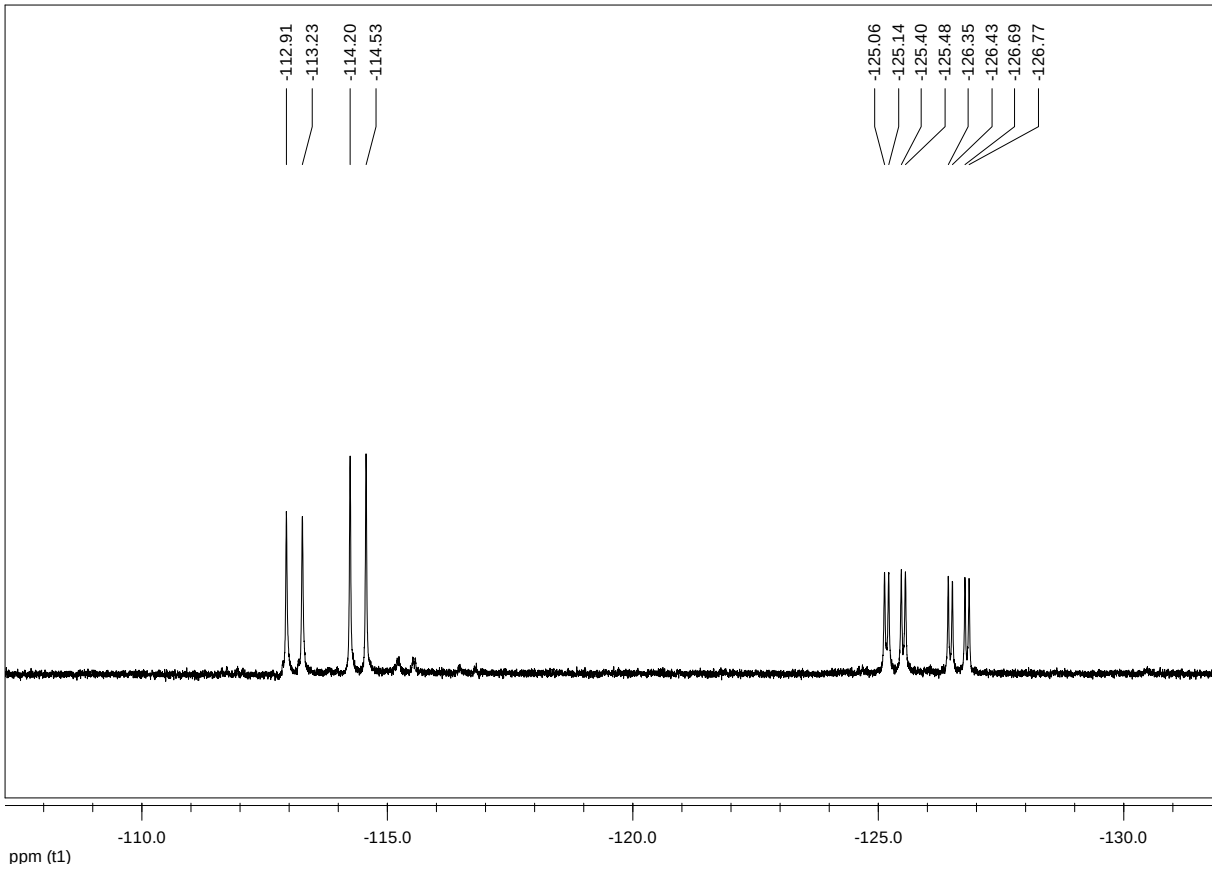

3.25
2.65
2.03
25.0
20.0
15.0
10.0
5.0
0.0
-5.0
-10.0
-15.0
ppm (t1)

Potassium 2,2-difluoro-2-(2-deoxy-2-nitro-3,4,6-tri-*O*-benzyl-β-D-glucopyranosyl)phosphonate (7):

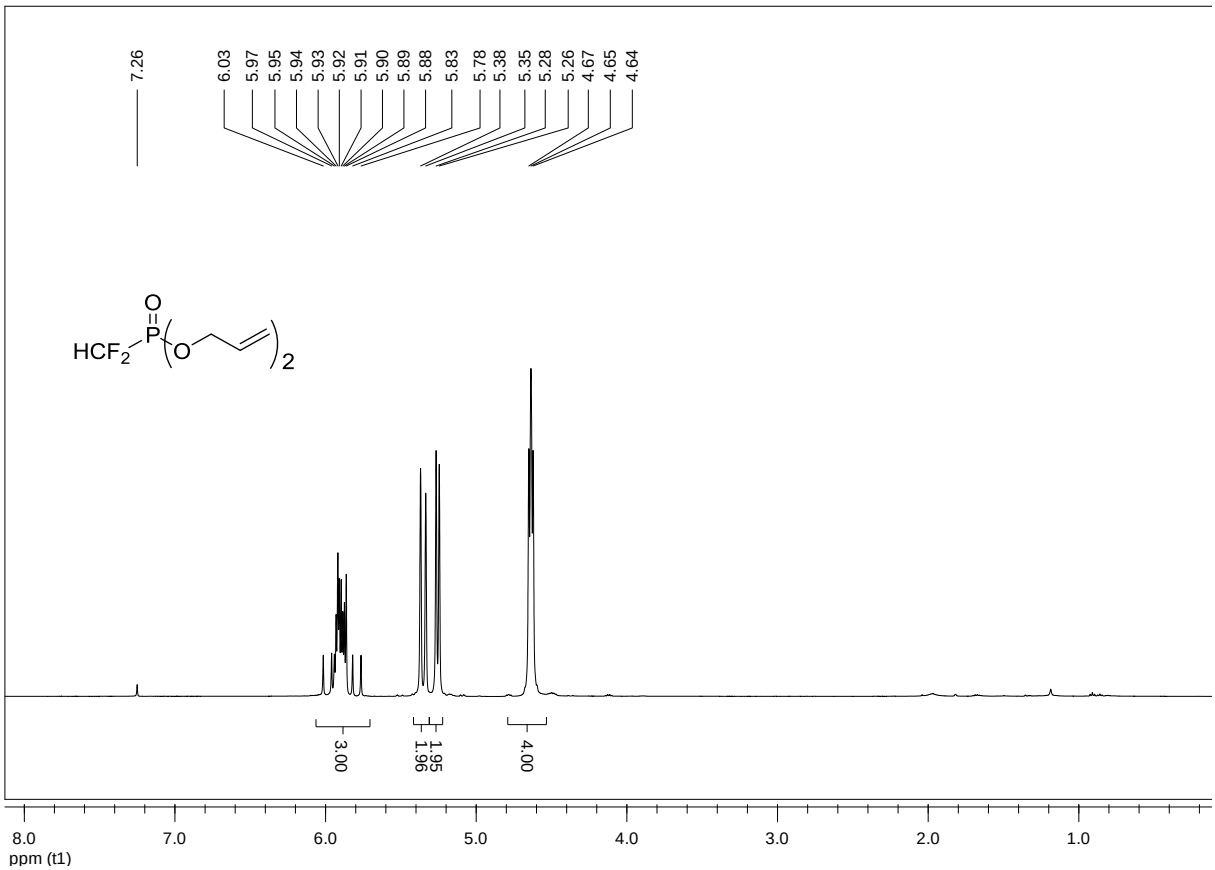


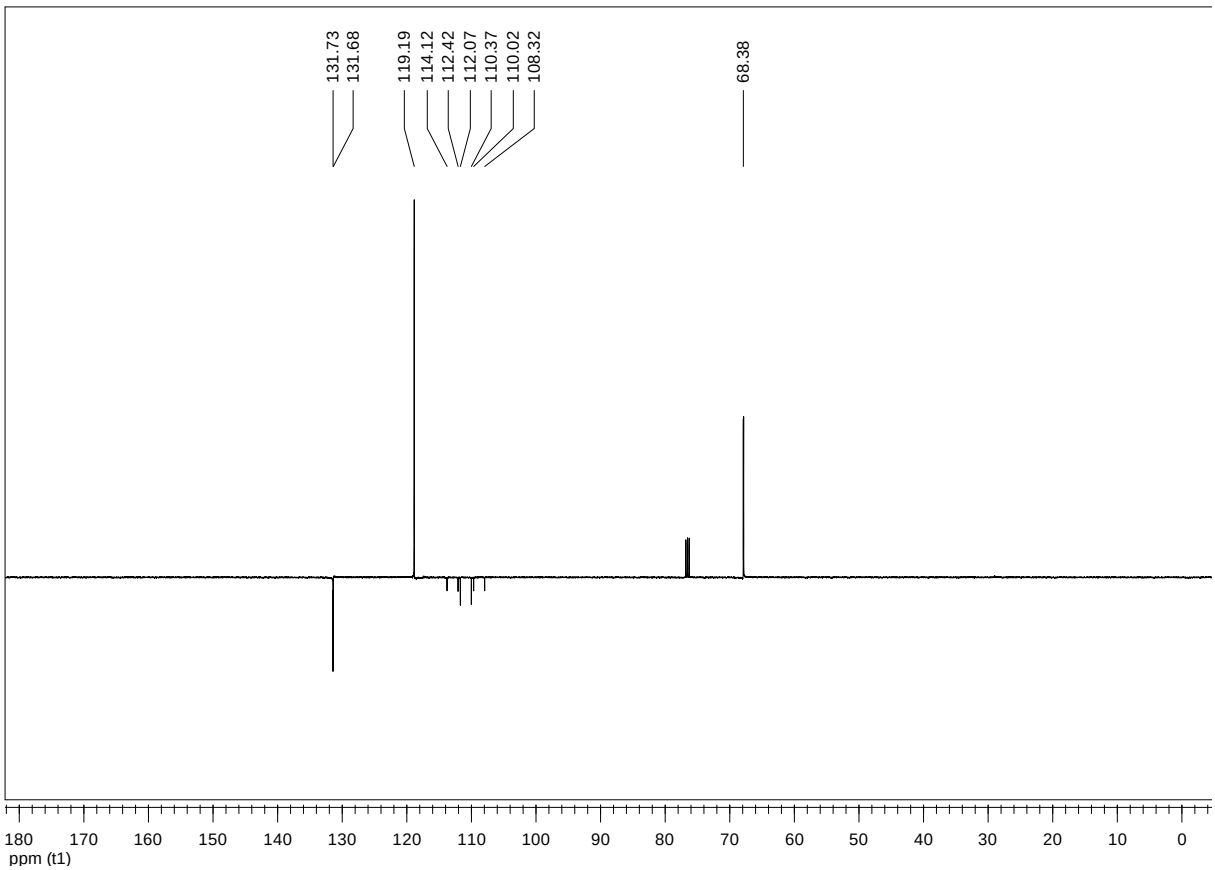


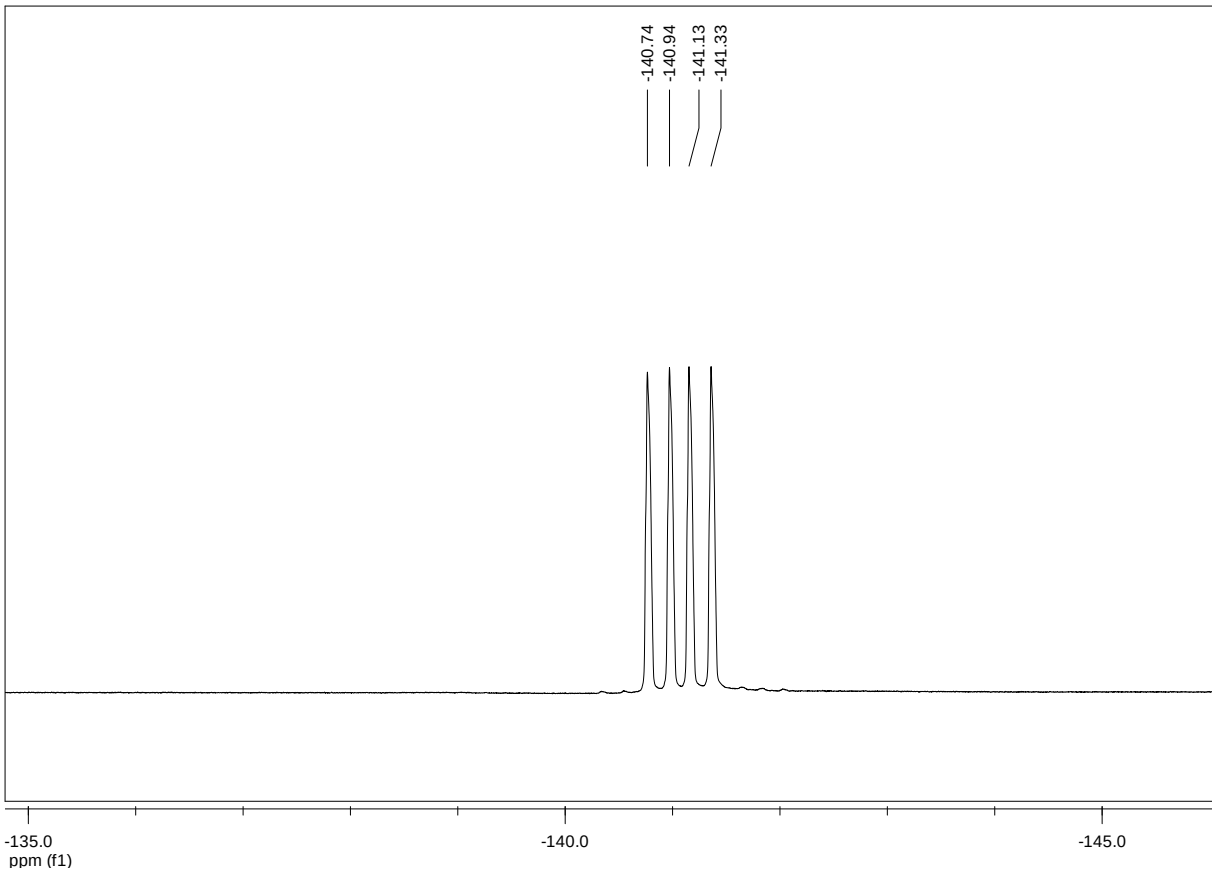

6.73
6.26
5.80
20.0
15.0
10.0
5.0
0.0
-5.0
ppm (t1)

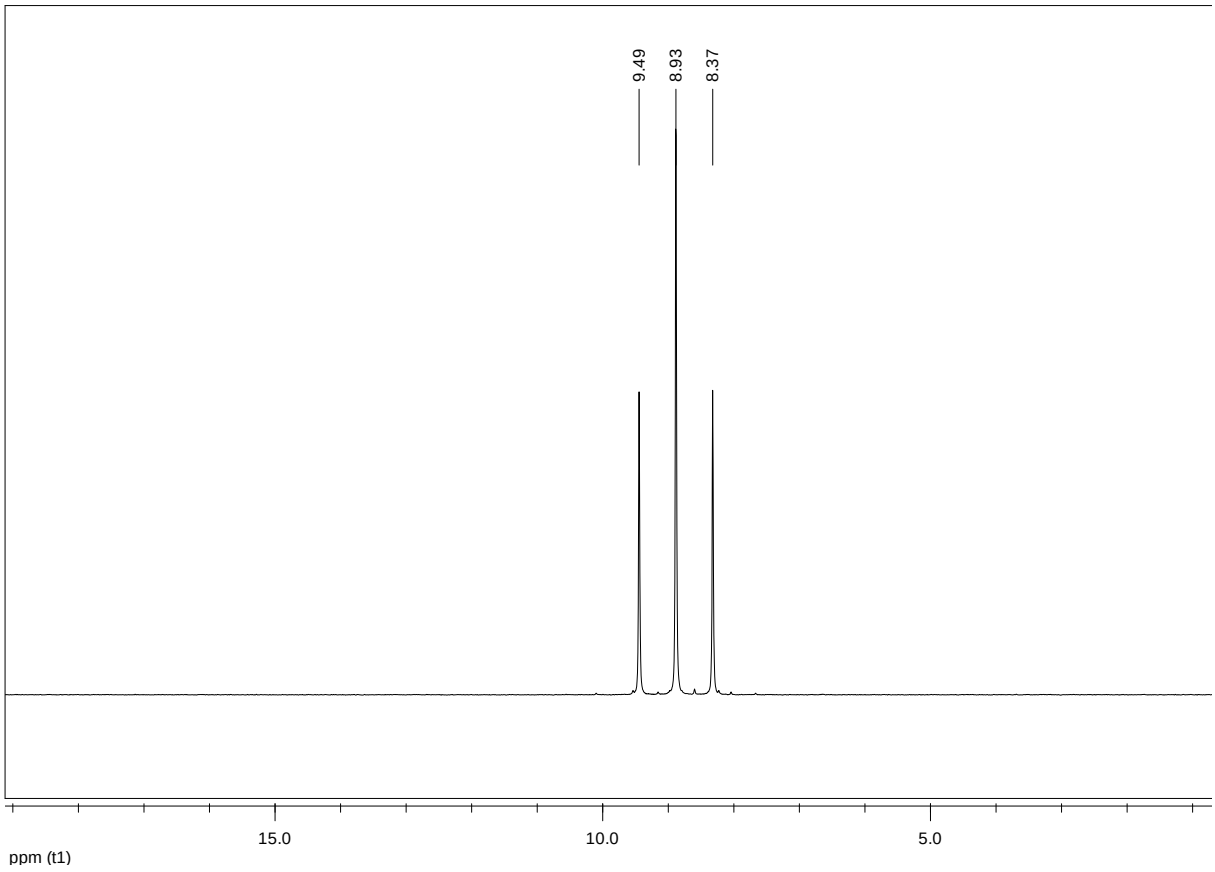

-112.91
-113.23
-114.20
-114.53
-125.06
-125.14
-125.40
-125.48
-126.35
-126.43
-126.69
-126.77
-110.0
-115.0
-120.0
-125.0
-130.0
ppm (t1)

Diallyl (α-α-difluoromethyl)phosphonate

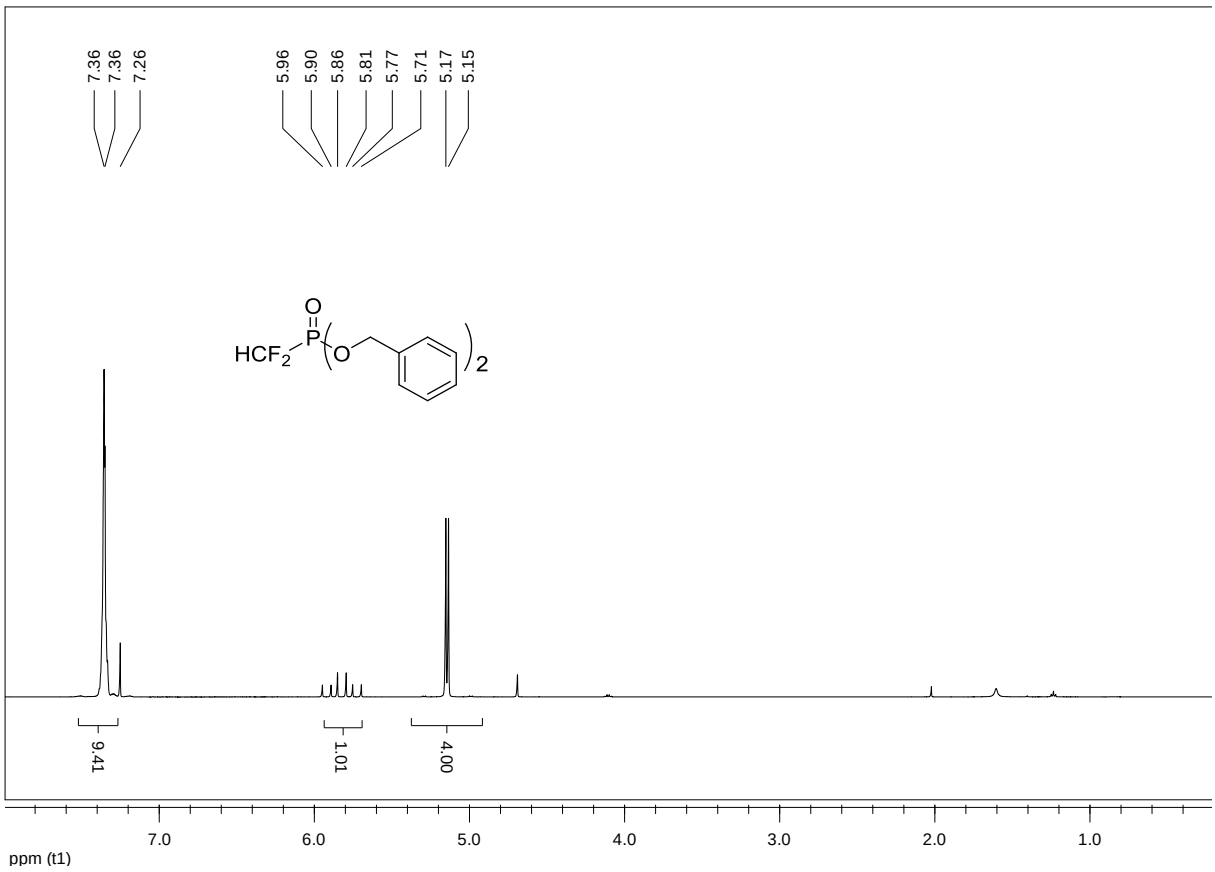


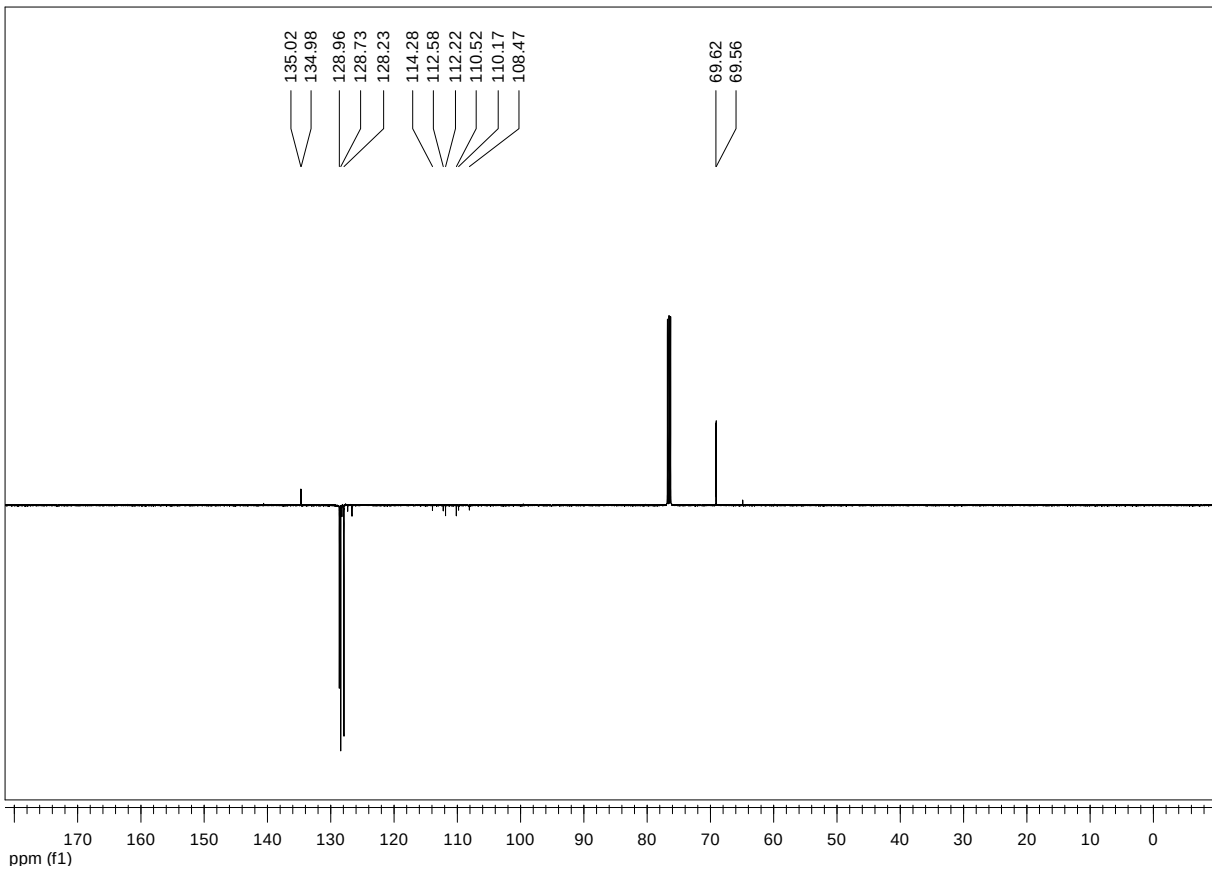


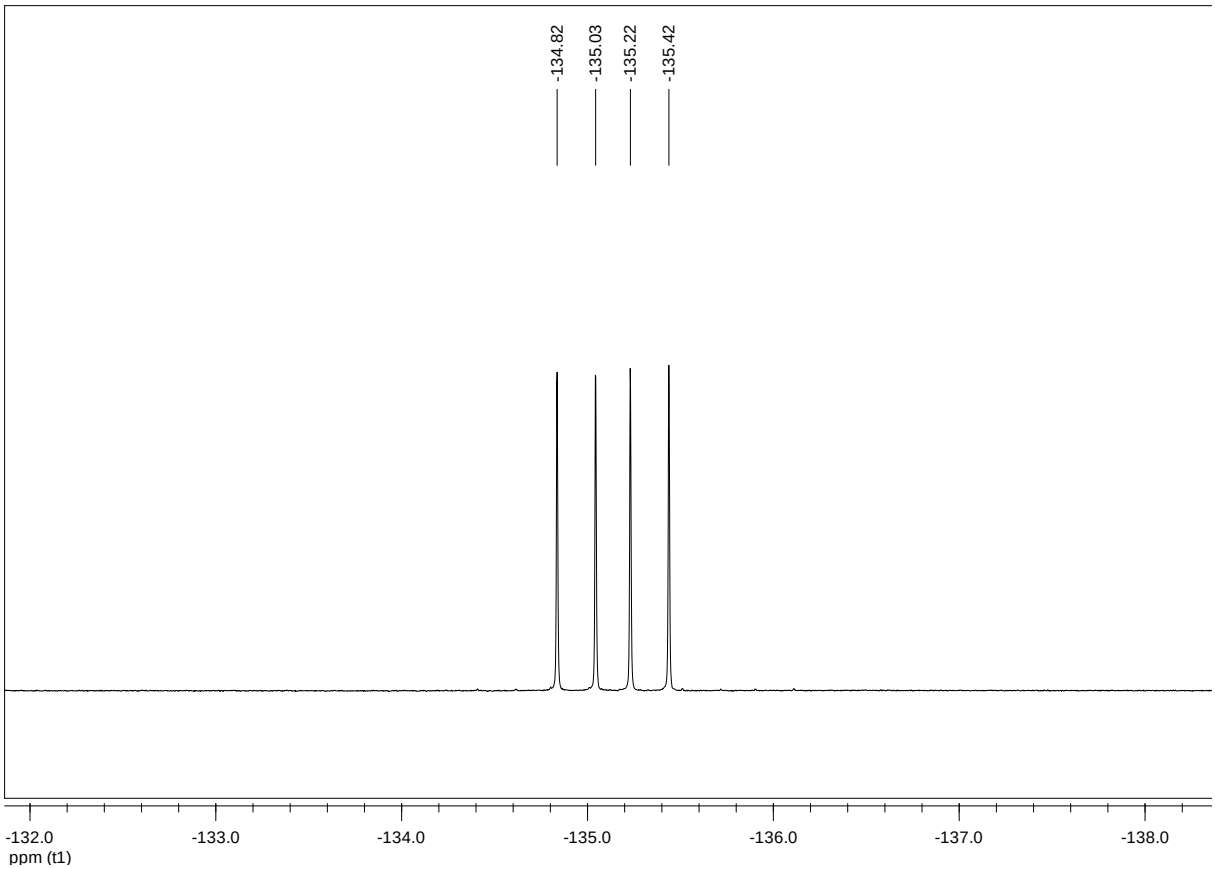

-140.74
-140.94
-141.13
-141.33
-135.0
-140.0
-145.0
ppm (f1)

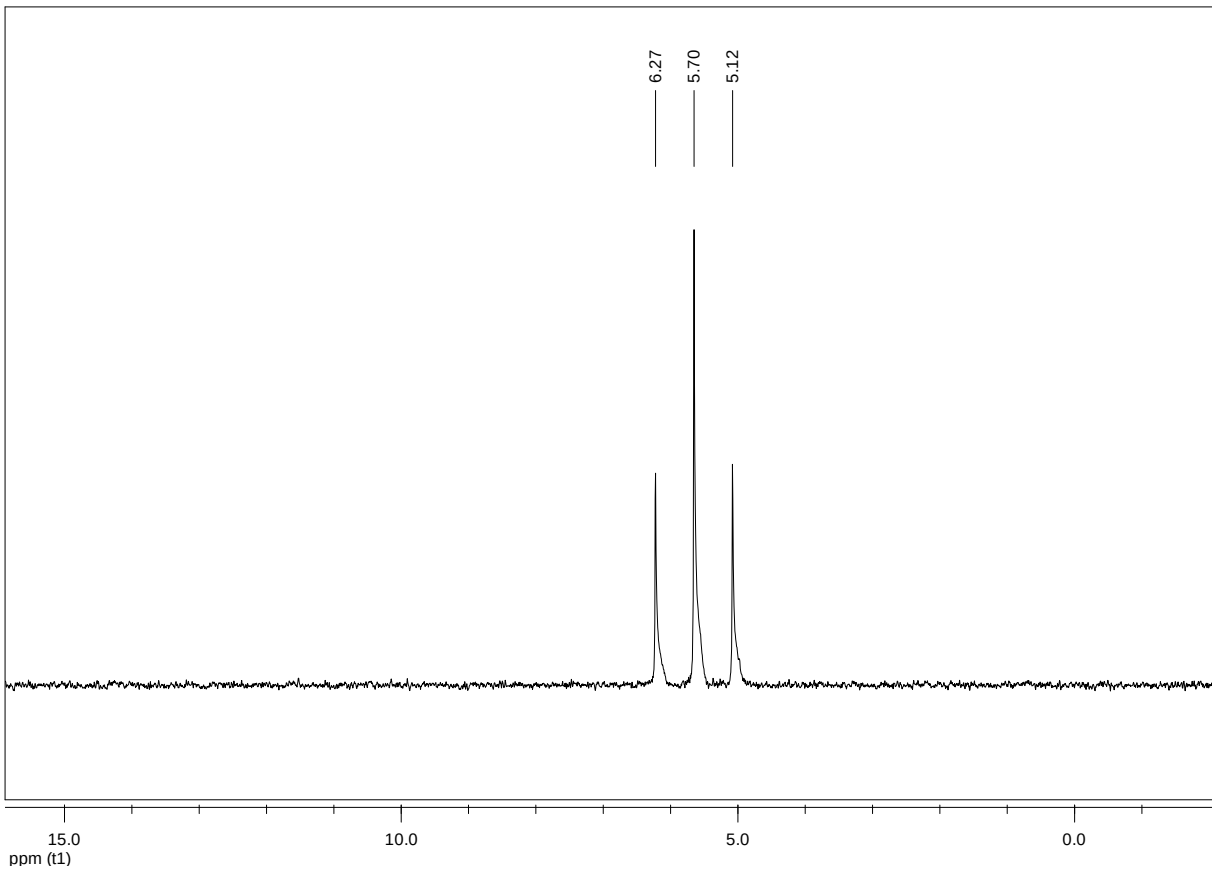

9.49
8.93
8.37
15.0
10.0
5.0
ppm (t1)

Dibenzyl (α-α-difluoromethyl)phosphonate






-134.82
-135.03
-135.22
-135.42
-132.0
-133.0
-134.0
-135.0
-136.0
-137.0
-138.0
ppm (t1)


6.27
5.70
5.12
15.0
10.0
5.0
0.0
ppm (t1)