

Supporting information for

Synthesis of C-glycosyl phosphonate derivatives of 4-amino-4-deoxy- α -L-arabinose

Lukáš Kerner and Paul Kosma*

University of Natural Resources and Life Sciences-Vienna, Department of Chemistry,
Muthgasse 18, A-1190 Vienna, Austria

Email: paul.kosma@boku.ac.at

* Corresponding author

Experimental procedures, characterization data of new compounds and ^1H , ^{13}C and ^{31}P NMR spectra of compounds 4, 6, 8-17.

Contents

General Methods	S2
Experimental procedures and physico-chemical characterization	S2
References for Supporting Information	S11
^1H , ^{13}C and ^{31}P NMR spectra	S12

General Methods

Solvents and reagents were purchased from commercial suppliers and used as provided without further purification unless stated otherwise. Solvents (THF, CH₂Cl₂, DMF) were dried over activated 4 Å molecular sieves. Cation exchange resin DOWEX 50 H⁺ was regenerated by consecutive washing with HCl (3 M), water and dry MeOH. If not indicated otherwise, concentration of organic solutions was performed under reduced pressure at < 40 °C. Optical rotation was measured with an Anton Paar MCP100 Polarimeter at 20 °C. Reactions were followed by thin layer chromatography using Merck plates: generally on 5 x 10 cm, layer thickness 0.25 mm, Silica Gel 60F₂₅₄; alternatively on HPTLC plates with 2.5 cm concentration zone (Merck). Spots were visualized with UV (254 nm) and/or anisaldehyde-H₂SO₄ staining. Preparative chromatography was performed using silica gel (0.040 – 0.063 mm) or a flash-purification system (Interchim, PuriFlash 4125). NMR spectra were recorded with a Bruker Avance III 600 instrument (¹H at 600 MHz, ¹³C at 151 MHz and ³¹P at 243 MHz) using standard Bruker NMR software. Chemical shifts are given in ppm down-field from SiMe₄ using the residual peak of CDCl₃ (7.26 for ¹H and 77.00 for ¹³C), CD₃OD (3.31 for ¹H and 49.86 for ¹³C) or D₂O (0.00 for ¹H, external calibration to 2,2-dimethyl-2-silapentane-5-sulfonic acid), 67.40 for ¹³C (external calibration to 1,4-dioxane in D₂O), and orthophosphoric acid (δ = 0) for ³¹P. Assignments for octyl signals are labeled with '. Numbering of phosphonate compounds was based on the nomenclature as hexit-1-yl derivatives. HR MS ESI-TOF data were obtained on a Waters Micromass Q-TOF Ultima Global instrument.

*General conditions for hydrogenation of **9**, **13** and **15**:*

Hydrogenation was carried out in a ThalesNano H-Cube® reactor under the following conditions: flowrate 0.5 mL/min, cartridge length 30 mm, catalyst 20% Pd(OH)₂/C, temperature 50 °C, nominal H₂ pressure 50 bar. The starting material (typically 10 mg) was dissolved in 5-10 mL of a 1:1 MeOH-AcOH mixture and was run in loop for 2-3 h. After this time, the crude mixture was concentrated *in vacuo*, filtered over a syringe filter (0.45 µm, MeOH) and concentrated to dryness. All products were purified on a semi-preparative Merck SeQuant® ZIC®-HILIC (250x10 mm) HPLC column (MeCN → 1:1 MeCN-H₂O, 8 mL/min).

Methyl 4-azido-2,3-di-O-benzyl-4-deoxy-α-L-arabinopyranoside (2)

NaH (60% in mineral oil, 444 mg, 11.1 mmol, 2.1 eq.) was suspended in dry DMF (10 mL) and the mixture was cooled to 0 °C. A solution of **1**¹ (1 g, 5.29 mmol) in dry DMF (20 mL) was added dropwise under an inert atmosphere and stirring was continued at 0 °C for 30 min. Next, benzyl bromide (1.32 mL, 11.1 mmol, 2.1 eq.) was added dropwise, the reaction mixture was allowed to reach rt and stirring was continued for 22 h. The reaction was quenched by adding H₂O (20 mL) under cooling, which was followed by extraction with EtOAc (3 x 20 mL). Combined organic phases were washed with H₂O (20 mL), brine (20 mL), dried (MgSO₄) and concentrated *in vacuo*. The crude material was flash-chromatographed on silica gel (MePh → 1:1 MePh-EtOAc) to give 1.536 g (79 %) of **2** as colorless oil, which solidified upon cooling. Physical and spectroscopic data were in agreement with literature.²

Oxidation of 4-azido-2,3-di-O-benzyl-4-deoxy-L-arabinopyranose (3)

Methyl glycoside **2** (100 mg, 0.27 mmol) was dissolved in a solution of SrCl₂·6H₂O (5 mg, 0.02 mmol, 0.07 eq.) in 1 mL of glacial AcOH and the mixture was warmed to 70 °C. Diluted aq HCl (5 M, 0.16 mL, 0.81 mmol) was added dropwise and the resulting solution was stirred at 70 °C for 3 h and then for 70 h at rt. The reaction mixture was made neutral by adding a satd aq solution of NaHCO₃ (3 mL) and extracted with EtOAc (3 x 3 mL). Combined organic phases were dried (MgSO₄), concentrated *in vacuo* and flash-chromatographed on silica gel (4:1 MePh-EtOAc → EtOAc) to afford **3** as an oil which solidified upon standing. Yield: 58 mg (60 %). NMR data matched published data.² The anomeric mixture was directly used without further separation. Lactol **3** (1.22 g, 3.43 mmol) was dissolved in DMSO (10 mL) followed by dropwise addition of acetic anhydride (8 mL, 85 mmol) under an inert atmosphere. The solution was stirred at rt overnight (22 h) and concentrated *in vacuo* at 50 °C. DMSO was removed by lyophilization and drying under high vacuum (<1 mbar) to give **4** (4-azido-2,3-di-O-benzyl-4-deoxy-L-arabinonic acid 1,5-lactone) as unstable brownish oil. Yield: 1.11 g (92%). R_f = 0.67 (4:1 MePh-EtOAc); [α]_D²⁰ +87 (c 1.0, CHCl₃); ¹H NMR (CDCl₃): δ 7.34-7.29 (m, 10 H, H-Ar), 5.05 (d, 1 H, J = 11.2 Hz) and 4.68 (d, 1 H, J = 11.2 Hz, CH₂Ph), 4.74 (d, 1 H, J = 11.8 Hz) and 4.70 (d, 1 H, CH₂Ph), 4.33 4 (dd, 1 H, J_{5a,5b} = 11.9 Hz, J_{5a,4} = 5.2 Hz, H-5a), 4.25 (d, 1 H, J_{2,3} = 7.4 Hz, H-2), 4.21 (dd, 1 H, J_{5a,5b} = 11.9, J_{5b,4} = 3.4 Hz Hz, H-5b), 4.04 (dt, 1 H, H-4), 3.99 (dd, 1 H, J_{3,4} = 3.1, J_{3,2} = 7.3 Hz, H-3); ¹³C NMR (CDCl₃): δ 168.52 (C-1), 136.94 (d.i., Cq, C-Ar), 128.59 (d.i.), 128.48 (d.i.), 128.40 (d.i.), 128.20, 128.16 and 127.85 (d.i., C-Ar), 77.58

(C-3), 76.16 (C-2), 74.67 (CH₂Ph), 73.11 (CH₂Ph), 66.86 (C-5) and 56.47 (C-4). HRMS (ESI) m/z [M+H]⁺ calcd for C₁₉H₁₉N₃O₄: 354.1448, found 354.1444.

Dimethyl (2,6-anhydro-5-azido-3,4-di-O-benzyl-1,5-dideoxy-β-L-arabino-hexulopyranosyl)phosphonate (6)

Dimethyl methyl phosphonate **5** (0.40 mL, 3.68 mmol, 1.3 eq.) was dissolved under an inert atmosphere in dry THF (5 mL) in a flame-pre-dried Schlenk flask and then cooled to -70 °C. Subsequently, 1.6 M solution of *n*-BuLi in hexanes (2.30 mL, 3.68 mmol, 1.3 eq.) was added dropwise into the flask and stirred for 30 min at -70 °C. A pre-cooled solution of lactone **4** (1.0 g, 2.83 mmol) in dry THF (5 mL) was added dropwise during 20 min, the resulting mixture was stirred at -70 °C for 1 h and then left to reach rt overnight (17 h). The reaction was quenched by adding MeOH (2 mL) and the solution was concentrated *in vacuo*. The crude residue was flash-chromatographed on silica gel (2:1 MePh-EtOAc → EtOAc) to give 773 mg (57 %) of **6** as off-yellow syrup. R_f = 0.15 (2:1 MePh-EtOAc); [α]_D²⁰ -14 (c 1.5, CHCl₃); ¹H NMR (CDCl₃): δ 7.41-7.29 (m, 10 H, H-Ar), 5.80 (br, s, 1 H, OH), 4.98 (d, 1 H, J = 11.6 Hz) and 4.66 (d, 1 H, J = 11.6 Hz, CH₂Ph), 4.76 (d, 2 H, CH₂Ph), 4.17 (dd, 1 H, $J_{4,5}$ = 3.7 Hz, $J_{3,4}$ = 9.5 Hz, H-4), 4.06 (dd, 1 H, $J_{6a,5}$ = 1.7 Hz, $J_{6a,6b}$ = 12.5 Hz, H-6a), 3.91 (ddd, 1 H, H-5), 3.71 (d, 3 H, $J_{Me,P}$ = 11.2 Hz, POCH₃), 3.64 (d, 3 H, $J_{Me,P}$ = 11.1 Hz, POCH₃), 3.59 (dd, 1 H, $J_{6b,5}$ = 1.7 Hz, $J_{6a,6b}$ = 12.5 Hz, H-6b), 3.56 (d, 1 H, $J_{4,3}$ = 9.5 Hz, H-3), 2.35 (dd, 1 H, $J_{CH2a,P}$ = 17.5 Hz, $J_{CH2a,CH2b}$ = 15.2 Hz, PCH_{2a}) and 1.71 (dd, 1 H, $J_{CH2b,P}$ = 18.6 Hz, $J_{CH2a,CH2b}$ = 15.2 Hz, PCH_{2b}); ¹³C NMR (CDCl₃): δ 137.86 and 137.74 (C_q, C-Ar), 128.74 (d.i.), 128.54 (d.i.), 128.46 (d.i.), 128.00, 127.96 and 127.93 (d.i., C-Ar), 97.41 (d, $J_{C,P}$ = 8.6 Hz, C-2), 78.92 (d, $J_{C,P}$ = 14.1 Hz, C-3), 78.49 (d, $J_{C,P}$ = 4.4 Hz, C-4), 75.36 (CH₂Ph), 72.76 (CH₂Ph), 61.21 (C-6), 60.44 (C-5), 53.30 (d, $J_{C,P}$ = 5.5 Hz, POCH₃), 51.88 (d, $J_{C,P}$ = 6.5 Hz, POCH₃), 32.31 (d, $J_{C,P}$ = 134.5 Hz, C-1); ³¹P NMR (CDCl₃): δ 31.27. HRMS (ESI) m/z [M+H]⁺ calcd for C₂₂H₂₈N₃O₇P: 478.1738, found 478.1735.

Dimethyl (2,6-anhydro-5-azido-3,4-di-O-benzyl-1,5-dideoxy-L-arabino-hex-1-enit-1-yl)phosphonate (8)

A solution of **6** (400 mg, 0.84 mmol) in dry DCM (15 mL) was cooled to 0 °C. Dry pyridine (3.38 mL, 41.88 mmol) was added dropwise under an inert atmosphere, followed by addition of methyl oxalyl chloride (0.77 mL, 8.38 mmol, 10 eq.), which

resulted in immediate formation of a white precipitate. The suspension was stirred for 1 h at 0-5 °C, and then at rt for 23 h. The reaction mixture was diluted with DCM (15 mL) and treated with satd aq NaHCO₃ solution (20 mL) under cooling. The phases were separated and the aqueous portion was extracted with DCM (2 x 15 mL). The combined organic phases were dried (MgSO₄) and concentrated. The residue was purified by flash-chromatography on silica gel (1:1 MePh-EtOAc → EtOAc) to afford **8** as light brown oil. Yield: 286 mg (74 %); R_f = 0.11 (1:1 MePh-EtOAc); [α]_D²⁰ +54 (c 1.0, CHCl₃); ¹H NMR (CDCl₃): δ 7.35-7.29 (m, 10 H, H-Ar), 5.19 (dd, 1 H, J_{=CH,2} = 0.8 Hz, J_{=CH,P} = 12.6 Hz, =CH), 4.72 and 4.69 (2 d, each 1 H, J = 11.9 Hz, CH₂Ph), 4.69 and 4.61 (d, each 1 H, J = 11.5 Hz, CH₂Ph), 4.17 (dd, 1 H, J_{6a,5} = 5.6 Hz, J_{6a,6b} = 11.2 Hz, H-6a), 4.10 (br d, 1 H, J_{4,3} = 7.1 Hz, H-3), 3.98 (dt, 1 H, J_{4,5} = 3.2 Hz, H-5), 3.95 (dd, 1 H, J_{6b,5} = 3.3 Hz, J_{6a,6b} = 11.3 Hz, H-6b), 3.87 (dd, 1 H, J_{4,3} = 7.1 Hz, J_{5,4} = 3.2 Hz, H-4), 3.72 (d, 3 H, J_{Me,P} = 3.5 Hz, POCH₃) and 3.70 (d, 3 H, J_{Me,P} = 3.4 Hz, POCH₃); ¹³C NMR (CDCl₃): δ 165.91 (d, J_{C,P} = 1.6 Hz, =CH), 137.14 and 137.02 (Cq, C-Ar), 128.55 (d.i.), 128.17, 128.07, 127.93 (d.i.) and 127.87 (d.i., Ar-C), 97.37 (d, J_{C,P} = 189.5 Hz, C-2), 78.46 (C-4), 75.90 (d, J_{C,P} = 14.1 Hz, C-3), 73.15 (CH₂Ph), 73.04 (CH₂Ph), 67.91 (C-6), 56.93 (C-5), 52.48 (d, J_{C,P} = 5.5 Hz, POCH₃), 52.15 (d, J_{C,P} = 5.5 Hz, POCH₃); ³¹P NMR (CDCl₃): δ 19.05. HRMS (ESI) *m/z* [M+H]⁺ calcd for C₂₂H₂₆N₃O₆P: 460.1632, found 460.1639.

Alternatively, **8** was prepared using TFAA:

Compound **6** (58 mg, 0.12 mmol) was dissolved in dry THF (1.5 mL) and cooled to 0°C. Dry pyridine (98 μL, 1.21 mmol) was added dropwise under an inert atmosphere, followed by trifluoroacetic anhydride (0.51 mL, 3.64 mmol, 30 eq.). After stirring at 0-5°C for 90 min, the reaction mixture was allowed to reach rt and kept at this temperature for 27 h. Satd aq NaHCO₃ (5 mL) was added under cooling, which was followed by extraction with EtOAc (3 x 5 mL). Combined organic phases were dried (MgSO₄), concentrated and purified as described above to give 36 mg (57 %) of **8** as turbid colorless oil.

Methyl (2,6-anhydro-5-azido-3,4-di-O-benzyl-1,5-dideoxy-L-arabino-hex-1-enit-1-yl)phosphonate (9)

Exo-glycal **8** (312 mg, 0.68 mmol) and NaI (204 mg, 1.36 mmol, 2 eq.) were mixed with dry acetone (5 mL). Under atmospheric pressure, the solution was concentrated at 70 °C to such an extent that stirring was still effective (~1 h). The reaction vessel

was then equipped with a septum and a balloon filled with Ar and the thick slurry was stirred at 60 °C overnight. The suspension was concentrated *in vacuo* and the residue was flash-chromatographed on silica gel (MePh-MeOH 2:1 → 1:2) to furnish **9** as yellow amorphous solid. Yield: 298 mg (98%), $R_f = 0.39$ (1:1 MePh-MeOH). $[\alpha]_D^{20} +32$ (c 1.0, CHCl₃); ¹H NMR (CD₃OD): δ 7.37-7.26 (m, 10 H, H-Ar), 5.29 (d, 1 H, $J_{=CH,P} = 10.1$ Hz, =CH), 4.74 and 4.62 (2 d, each 1 H, $J = 11.5$ Hz, CH₂Ph), 4.69 (d, 2 H, $J = 11.7$ Hz, CH₂Ph), 4.14-4.11 (m, 2 H, H-5, H-3), 4.09 (dd, 1 H, $J_{6a,5} = 5.6$ Hz, $J_{6a,6b} = 11.5$ Hz, H-6a), 3.91 (dd, 1 H, $J_{3,4} = 7.1$ Hz, $J_{5,4} = 3.3$ Hz H-4), 3.90 (dd, 1 H, $J_{6b,5} = 3.0$ Hz, H-6b), 3.51 (d, 3 H, $J_{Me,P} = 11.2$ Hz, POCH₃); ¹³C NMR (CD₃OD): δ 163.01 (=CH), 140.11 and 140.08 (C_q, C-Ar), 130.27 and 130.26 (3 C), 129.92, 129.86 (d.i.), 129.73, and 129.66 (Ar-C), 105.55 (d, $J_{C,P} = 176.3$ Hz, C-2), 81.35 (C-4), 78.41 (d, $J_{C,P} = 12.9$ Hz, C-3), 74.75 (CH₂Ph), 74.38 (CH₂Ph), 69.59 (C-6), 59.56 (C-5), 52.82 (d, $J_{C,P} = 5.1$ Hz, POCH₃); ³¹P NMR (CD₃OD): δ 10.95. HRMS (ESI) m/z [M+H]⁺ calcd for C₂₁H₂₄N₃O₆P: 446.1475, found 446.1482.

Methyl (2,6-anhydro-5-azido-3,4-di-O-benzyl-1,5-dideoxy-L-erythro-hex-2-enit-1-yl)phosphonate (10)

Exo-glycal **9** (50 mg, 0.11 mmol) was dissolved in MeOH (2 mL) and mixed with 1 M aq. NaOH solution (~5.5 mL). The resulting suspension was stirred at 60-70°C for 75 h. The reaction mixture was then concentrated *in vacuo*, filtered over Celite (CHCl₃) and the filtrate was concentrated. Yield: 40 mg (80 %, crude) of **10** as brownish syrup. $R_f = 0.28$ (2:1 CHCl₃-MeOH). The crude material was repeatedly purified on silica gel (CHCl₃-MeOH = 2:1 → 1:1). $[\alpha]_D^{20} -48$ (c 0.4, MeOH); ¹H NMR (CD₃OD): δ 7.38-7.24 (m, 10 H, H-Ar), 4.83 and 4.74 (2 d, each 1 H, $J = 11.5$ Hz, CH₂Ph), 4.73 (s, 2 H, CH₂Ph), 4.45 (app t, 1 H, $J_{5,4} = 3.8$ Hz, H-4), 4.03 (ddd, 1 H, $J_{6a,4} = 1.0$ Hz, $J_{6a,5} = 3.5$ Hz, $J_{6a,6b} = 10.4$ Hz, H-6a), 3.96 (t, 1 H, $J_{6b,5} = J_{6a,6b} = 10.3$ Hz, H-6b), 3.83 (dt, 1 H, H-5), 3.55 (d, 3 H, $J_{Me,P} = 10.7$ Hz, POCH₃), 2.72 (dd, 1 H, $J = 15.4$ Hz, $J = 20.2$ Hz, H-1a), 2.55 (dd, 1 H, $J = 14.8$ Hz, $J = 20.5$ Hz, H-1b); ¹³C NMR (CD₃OD): δ 146.48 (d, $J_{C,P} = 12.5$ Hz, C-2), 140.55 and 140.00 (C_q, C-Ar), 133.95 (d, $J_{C,P} = 10.6$ Hz, C-3), 130.24 (d.i.), 130.22 (d.i.), 130.19 (d.i.), 130.08 (d.i.), 129.76 and 129.59 (Ar-C), 76.15 (CH₂Ph), 74.94 (CH₂Ph), 73.00 (C-4), 65.34 (C-6), 58.85 (C-5), 53.28 (d, $J_{C,P} = 5.9$ Hz, POCH₃), 29.11 (d, $J_{C,P} = 134.2$ Hz, C-1); ³¹P NMR (CD₃OD): δ 17.97. HRMS (ESI) m/z [M+H]⁺ calcd for C₂₁H₂₄N₃O₆P: 446.1475, found 446.1474.

Methyl (2,6-anhydro-5-amino-1,5-dideoxy-L-mannit-1-yl) phosphonic acid (11)

Hydrogenation of **9** (30 mg, 0.067 mmol) was carried out as described under general conditions to give 2.5 mg (15%) of **11** as colorless oil after HILIC purification; $[\alpha]_D^{20} +32$ (c 0.25, MeOH); $^1\text{H NMR}$ (D_2O): δ 3.87 (dd, 1 H, $J_{6a,5} = 1.1$ Hz, $J_{6a,6b} = 13.6$ Hz, H-6a), 3.77 (dd, 1 H, $J_{3,4} = 9.5$ Hz, $J_{5,4} = 4.7$ Hz, H-4), 3.62 (dd, 1 H, $J_{6b,5} = 1.2$ Hz, $J_{6a,6b} = 13.6$ Hz, H-6b), 3.51 (br d, 1 H, H-5), 3.395 (d, 3 H, $J_{\text{Me,P}} = 10.4$ Hz, POCH_3), 3.325 (ddd, 1 H, $J_{2,3} = 9.7$ Hz, $J_{2,1a} = 1.5$ Hz, H-2) 3.25 (t, 1 H, $J_{2,3} = J_{4,3} = 9.5$ Hz, H-3), 2.02 (ddd, 1 H, $J_{1a,P} = 18.4$ Hz, $J_{1a,1b} = 15.6$ Hz, $J_{1a,12} = 2.5$ Hz, H-1a), 1.68 (dt, 1 H, $J_{1b,P} = 15.5$ Hz, $J_{1b,2} = 9.7$ Hz, H-1b); $^{13}\text{C NMR}$ (D_2O): δ 77.92 (d, $J_{\text{C,P}} = 5.6$ Hz, C-2), 71.96 (d, $J_{\text{C,P}} = 13.4$ Hz, C-3), 70.69 (C-4), 66.62 (C-6), 53.19 (C-5), 52.04 (d, $J_{\text{C,P}} = 5.5$ Hz, POCH_3), and 29.17 (d, $J_{\text{C,P}} = 135.3$ Hz, CH_2P); $^{31}\text{P NMR}$ (D_2O): δ 24.81. HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_7\text{H}_{16}\text{NO}_6\text{P}$: 242.0788, found 242.0786.

Methyl, octyl (2,6-anhydro-5-azido-3,4-di-O-benzyl-1,5-dideoxy-L-arabino-hex-1-enit-1-yl)phosphonate (12) and Methyl, octyl (2,6-anhydro-5-azido-3,4-di-O-benzyl-1,5-dideoxy-L-erythro-hex-2-enit-1-yl)phosphonate (14)

Method A

Phosphonate **9** (85 mg, 0.19 mmol) and Cs_2CO_3 (373 mg, 1.15 mmol) were suspended in dry DMF (2 mL) and warmed to 80°C under an inert atmosphere. Then octyl bromide (99 μL , 0.57 mmol, 3 eq) was added dropwise and the suspension was stirred for 2 h at 80°C : The crude mixture was allowed to cool down and was concentrated under reduced pressure. The residue was suspended in MeOH, mixed with silica gel (~2 g), concentrated *in vacuo* (40°C) and the solid material was placed on top of a silica gel column and eluted with MePh \rightarrow EtOAc, which gave 59 mg (55 %) of **14** and 33 mg (31 %) of **12** as yellow oils.

Method B

Phosphonate **9** (100 mg, 0.225 mmol) and Cs_2CO_3 (439 mg, 1.374 mmol, 6 eq.) were suspended in dry DMF (2.8 mL) and reacted with octyl bromide (116 μL , 0.674 mmol) as described above. The mixture was brought to rt, concentrated under reduced pressure and directly flash-chromatographed on silica gel (MePh \rightarrow EtOAc) to afford 21 mg (17 %) of **14** and 76 mg (61 %) of **12** as off-yellow syrups. Resolution of diastereomers of **12** and **14** was achieved on a semi-preparative YMC Pack Sil 06 (250 x 20 mm) HPLC column (MePh \rightarrow EtOAc, 25 mL/min) to give **14a** as transparent oil, $R_f = 0.60$ (EtOAc); $[\alpha]_D^{20} -50$ (c 0.95, CHCl_3) followed by **14b** as

transparent oil, $R_f = 0.56$ (EtOAc); $[\alpha]_D^{20} -450$ (c 1.16, CHCl_3); $^1\text{H NMR}$ (CDCl_3): δ 7.38-7.27 (m, 10 H, H-Ar), 4.845 and 4.75 (2 d, each 1 H, $J = 11.5$ Hz, CH_2Ph), 4.72 and 4.68 (2 d, each 1 H, $J = 11.1$ Hz, CH_2Ph), 4.28 (app t, 1 H, $J_{5,4} = 3.9$ Hz, H-4), 4.05 (d, 2 H, H-6a, H-6b), 4.01 (q, 2 H, $J = 7.0$ Hz, H-1'a, H-1'b of **14a**), 4.00 (q, 2 H, $J = 7.0$ Hz, H-1'a, H-1'b of **14b**), 3.73 (d, 3 H, $J_{\text{Me,P}} = 11.0$ Hz, POCH_3 of **14b**), 3.70 (d, 3 H, $J_{\text{Me,P}} = 11.0$ Hz, POCH_3 of **14a**), 3.69 (ddd, 1 H, $J_{5,4} = 3.9$ Hz, H-5), 2.915 (dd, 1 H, $J = 15.1$ Hz, $J = 21.3$ Hz, H-1a), 2.71 (dd, 1 H, $J = 15.1$ Hz, $J = 21.2$ Hz, H-1b), 1.66-1.60 (m, 2 H, $J = 6.7$ Hz, H-2'a, H-2'b), 1.34-1.26 (m, 10 H, octyl signals H-3', H-4', H-5', H-6', H-7') and 0.88 (t, 3 H, $J = 6.9$ Hz, H-8'); $^{13}\text{C NMR}$ (CDCl_3) for **14a**: δ 141.16 (d, $J_{\text{C,P}} = 12.9$ Hz, C-2), 137.86 and 137.23 (Cq, C-Ar), 133.26 (d, $J_{\text{C,P}} = 11.7$ Hz, C-3), 128.47 (d.i.), 128.41 (d.i.), 128.03 (d.i.), 128.01, 127.92 (d.i.) and 127.83 (Ar-C), 74.51 (d, $J_{\text{C,P}} = 3.1$ Hz, 2-OCH₂Ph), 73.21 (CH₂Ph), 70.48 (C-4), 66.36 (d, $J_{\text{C,P}} = 6.5$ Hz, C-1'), 63.23 (C-6), 56.82 (C-5), 52.52 (d, $J_{\text{C,P}} = 6.5$ Hz, POCH_3), 31.76 (C-6'), 30.51 (d, $J_{\text{C,P}} = 6.4$ Hz, C-2'), 29.18 and 29.12 (C-4', C-5'), 26.22 (d, $J_{\text{C,P}} = 139.6$ Hz, C-1), 25.46 (C-3'), 22.61 (C-7') and 14.05 (C-8'); $^{13}\text{C NMR}$ (CDCl_3) for **14b**: δ 141.13 (d, $J_{\text{C,P}} = 13.0$ Hz, C-2), 137.86 and 137.22 (Cq, C-Ar), 133.30 (d, $J_{\text{C,P}} = 11.9$ Hz, C-3), 128.46 (d.i.), 128.41 (d.i.), 128.03 (d.i.), 128.02, 127.93 (d.i.) and 127.83 (Ar-C), 74.49 (d, $J_{\text{C,P}} = 3.1$ Hz, 2-OCH₂Ph), 73.20 (CH₂Ph), 70.41 (C-4), 66.21 (d, $J_{\text{C,P}} = 6.6$ Hz, C-1'), 63.25 (C-6), 56.80 (C-5), 52.70 (d, $J_{\text{C,P}} = 6.5$ Hz, POCH_3), 31.76 (C-6'), 30.48 (d, $J_{\text{C,P}} = 5.8$ Hz, C-2'), 29.16 and 29.12 (C-4', C-5'), 26.26 (d, $J_{\text{C,P}} = 139.6$ Hz, C-1), 25.45 (C-3'), 22.61 (C-7') and 14.06 (C-8'); $^{31}\text{P NMR}$ (CDCl_3): δ 25.65 (**14b**) and 25.62 (**14a**). HRMS (ESI) m/z $[\text{M}+\text{H}^+]^+$ calcd for $\text{C}_{29}\text{H}_{40}\text{N}_3\text{O}_6\text{P}$: 558.2727, found 558.2734 for **14a**; found 558.2740 for **14b**.

Continued elution of the column afforded **12a** as transparent oil, $R_f = 0.34$ (EtOAc); $[\alpha]_D^{20} +40$ (c 1.12, CHCl_3) and **12b** $R_f = 0.34$ (EtOAc); $[\alpha]_D^{20} +42$ (c 1.20, CHCl_3); $^1\text{H NMR}$ (CDCl_3): δ 7.36-7.29 (m, 10 H, H-Ar), 5.20 (d, 1 H, $J_{=\text{CH,P}} = 12.5$ Hz, =CH of **12b**), 5.19 (d, 1 H, $J_{=\text{CH,P}} = 12.4$ Hz, =CH of **12b**), 4.70 (br s, 2 H, CH_2Ph), 4.69 and 4.59 (2 d, each 1 H, $J = 11.5$ Hz, CH_2Ph), 4.15 (dd, 1 H, $J_{6a,5} = 5.7$ Hz, $J_{6a,6b} = 11.1$ Hz, H-6a), 4.09 (br d, 1 H, $J_{3,4} = 7.0$ Hz, H-3), 4.01-3.97 (m, 3 H, H-4, H-1'a, H-1'b), 3.95 (dd, 1 H, $J_{6b,5} = 3.4$ Hz, $J_{6a,6b} = 11.1$ Hz, H-6b of **12a**), 3.93 (dd, 1 H, $J_{6b,5} = 3.5$ Hz, $J_{6a,6b} = 11.4$ Hz, H-6b of **12b**), 3.87 (dd, 1 H, $J_{4,3} = 7.0$ Hz, $J_{5,4} = 3.1$ Hz, H-4 of **12a**), 3.86 (dd, 1 H, $J_{4,3} = 7.1$ Hz, $J_{5,4} = 3.3$ Hz, H-4 of **12b**), 3.71 (d, 3 H, $J_{\text{Me,P}} = 11.4$ Hz, POCH_3 of **12a**), 3.70 (d, 3 H, $J_{\text{Me,P}} = 11.3$ Hz, POCH_3 of **12b**), 1.64 (dt, 2 H, $J = 6.8$ Hz, H-2'a, H-2'b), 1.36-1.24 (m, 10 H, octyl signals H-3', H-4', H-5', H-6', H-7')

and 0.88 (t, 3 H, $J = 7.1$ Hz, H-8'); ^{13}C NMR (CDCl_3) for **12a**: δ 165.40 (=CH), 137.17 and 137.07 (Cq, C-Ar), 128.56 (d.i.), 128.17, 128.07, 127.93 (d.i.) and 127.87 (d.i., Ar-C), 98.78 (d, $J_{\text{C,P}} = 188.7$ Hz, C-2), 78.41 (C-4), 75.95 (d, $J_{\text{C,P}} = 14.7$ Hz, C-3), 73.04 (CH_2Ph), 73.03 (CH_2Ph), 67.78 (C-6), 65.72 (d, $J_{\text{C,P}} = 5.7$ Hz, C-1') 56.86 (C-5), 52.39 (d, $J_{\text{C,P}} = 5.8$ Hz, POCH_3), 31.77 (C-6'), 30.50 (d, $J_{\text{C,P}} = 6.3$ Hz, C-3'), 29.18 and 29.15 (C-4', C-5'), 25.55 (C-3'), 22.62 (C-7') and 14.06 (C-8'); ^{13}C NMR (CDCl_3) for **12b**: δ 165.47 (=CH), 137.18 and 137.07 (Cq, C-Ar), 128.56, 128.55, 128.16, 128.07, 127.93 (d.i.) and 127.88 (d.i., Ar-C), 98.16 (d, $J_{\text{C,P}} = 188.9$ Hz, C-2), 78.49 (C-4), 75.89 (d, $J_{\text{C,P}} = 14.1$ Hz, C-3), 73.11 (CH_2Ph), 73.04 (CH_2Ph), 67.83 (C-6), 65.99 (d, $J_{\text{C,P}} = 6.1$ Hz, C-1') 56.96 (C-5), 52.07 (d, $J_{\text{C,P}} = 5.5$ Hz, POCH_3), 31.77 (C-6'), 30.51 (d, $J_{\text{C,P}} = 6.6$ Hz, C-3'), 29.18 and 29.15 (C-4', C-5'), 25.55 (C-3'), 22.62 (C-7') and 14.06 (C-8'); ^{31}P NMR (CDCl_3): δ 17.53 (**12b**) and 17.52 (**12a**). HRMS (ESI) m/z $[\text{M}+\text{H}^+]^+$ calcd for $\text{C}_{29}\text{H}_{40}\text{N}_3\text{O}_6\text{P}$: 558.2727, found 558.2739 for **12a**; found 558.2740 for **12b**.

Octyl (2,6-anhydro-5-azido-3,4-di-O-benzyl-1,5-dideoxy-L-arabino-hex-1-enit-1-yl)phosphonate (**13**)

Dry acetone (2 mL) was added to *exo*-glycal **12** (75 mg, 0.13 mmol) and NaI (81 mg, 0.54 mmol, 4 eq.). The suspension was concentrated at 70 °C at atmospheric pressure to such an extent that stirring was still effective (~30 min). The reaction vessel was then equipped with a septum and a balloon filled with Ar and the thick slurry was stirred at 55 °C overnight (19 h). Then another portion of NaI was added (40 mg, 0.27 mmol, 2 eq.) and stirring was continued for additional 47 h. The suspension was concentrated *in vacuo* and subjected to flash-chromatography on silica gel (CHCl_3 -MeOH 9:1 \rightarrow 1:1) to give 60 mg (82 %) of **13** as yellow oil. $R_f = 0.17$ (EtOAc); $[\alpha]_{\text{D}}^{20} +31$ (c 1.2, MeOH); ^1H NMR (CD_3OD): δ 7.36-7.26 (m, 10 H, H-Ar), 5.29 (d, 1 H, $J_{=\text{CH,P}} = 10.0$ Hz, =CH), 4.73 and 4.69 (2 d, each 1 H, $J = 11.6$ Hz, CH_2Ph), 4.68 and 4.61 (2 d, each 1 H, $J = 11.5$ Hz, CH_2Ph), 4.13-4.11 (m, 2 H, H-5, H-3), 4.08 (dd, 1 H, $J_{6\text{a},5} = 5.9$ Hz, $J_{6\text{a},6\text{b}} = 11.2$ Hz, H-6a), 3.93 (dd, 1 H, $J_{3,4} = 7.1$ Hz, $J_{5,4} = 3.2$ Hz, H-4), 3.91 (dd, 1 H, $J_{6\text{b},5} = 3.1$ Hz, H-6b), 3.77 (dt, $J = 6.5$ Hz, H-1'a, H-1'b), 1.55 (m, 2 H, $J = 6.7$ Hz, H-2'a, H-2'b), 1.35-1.24 (m, 10 H, octyl signals H-3', H-4', H-5', H-6', H-7') and 0.88 (t, 3 H, $J = 6.9$ Hz, H-8'); ^{13}C NMR (CD_3OD): δ 162.70 (by HMBC, C-2), 140.11 and 140.06 (Cq, C-Ar), 130.28 and 130.26 (3 C), 129.94 (d.i.), 129.83 (d.i.), 129.75, and 129.67 (Ar-C), 105.9 (by HMBC, C-1), 81.18 (C-4),

78.40 (d, $J_{C,P} = 12.8$ Hz, C-3), 74.60 (CH₂Ph), 74.39 (CH₂Ph), 69.42 (C-6), 66.41 (C-1'), 59.30 (C-5), 33.87 (C-6'), 32.91 (C-2'), 31.35 and 31.31 (C-4', C-5'), 27.89 (C-3'), 24.58 (C-7') and 15.28 (C-8'); ³¹P NMR (CD₃OD): δ 9.06. HRMS (ESI) m/z [M+H]⁺ calcd for C₂₈H₃₈N₃O₆P: 544.2571, found 544.2577.

Octyl (2,6-anhydro-5-azido-3,4-di-O-benzyl-1,5-dideoxy-L-erythro-hex-2-enit-1-yl)phosphonate (15)

Dry acetone (1 mL) was added to *endo*-glycal **14** (22 mg, 0.039 mmol) and NaI (24 mg, 0.158 mmol, 4 eq.). The suspension was concentrated at atmospheric pressure so that stirring was still effective and the resulting slurry was stirred at 60 °C overnight (16 h) under Ar. Then another portion of NaI was added (24 mg, 0.158 mmol, 4 eq.) and stirring was continued for additional 28 h. The reaction mixture was concentrated *in vacuo* and flash-chromatographed on silica gel (CHCl₃-MeOH = 9:1 → 1:1) to afford **15** as off-yellow syrup. Yield: 16 mg (75 %); R_f = 0.25 (EtOAc); [α]_D²⁰ -50 (c 0.44, CHCl₃); ¹H NMR (CDCl₃): δ 7.38-7.24 (m, 10 H, H-Ar), 4.85 and 4.75 (2 d, each 1 H, $J = 11.5$ Hz, CH₂Ph), 4.73 and 4.70 (2 d, each 1 H, $J = 11.1$ Hz, CH₂Ph), 4.28 (br t, 1 H, H-4), 4.02 (dd, 1 H, $J_{6a,5} = 3.2$ Hz, $J_{6a,6b} = 10.4$ Hz, H-6a), 3.96 (t, 1 H, $J_{6b,5} = J_{6a,6b} = 10.2$ Hz, H-6b), 3.85-3.81 (m, 3 H, H-5, H-1'a, H-1'b), 1.68-1.58 (m, 2 H, $J = 6.7$ Hz, H-2'a, H-2'b), 1.33-1.22 (m, 10 H, octyl signals H-3', H-4', H-5', H-6', H-7') and 0.88 (t, 3 H, $J = 7.2$ Hz, H-8'); ¹³C NMR (CDCl₃): δ 146.53 (d, $J_{C,P} = 11.0$ Hz, C-2), 140.56 and 139.94 (Cq, C-Ar), 133.96 (d, $J_{C,P} = 9.6$ Hz, C-3), 130.25 (d.i.), 130.20 (d.i.), 130.19 (d.i.), 130.03 (d.i.), 129.80 and 129.59 (Ar-C), 76.13 (CH₂Ph), 74.96 (CH₂Ph), 73.01 (C-4), 66.84 (C-1'), 65.36 (C-6), 58.90 (C-5), 33.87 (C-6'), 32.97 (d, $J_{C,P} = 6.6$ Hz, C-2'), 31.38 and 31.32 (C-4', C-5'), 29.6 (C-1 by HSQC), 27.84 (C-3'), 24.58 (C-7'), 15.29 (C-8'); ³¹P NMR (CDCl₃): δ 16.19. HRMS (ESI) m/z [M+H]⁺ calcd for C₂₈H₃₈N₃O₆P: 544.2571, found 544.2579.

Octyl (2,6-anhydro-5-amino-1,5-dideoxy-L-mannit-1-yl) phosphonic acid (16)

Hydrogenation of **13** (13 mg, 0.024 mmol) was carried out as described under general conditions to give 3.1 mg (38%) of **16** as colorless oil after HILIC purification; [α]_D²⁰ +27 (c 0.3, MeOH); ¹H NMR (CD₃OD): δ 3.88 (dd, 1 H, $J_{6a,5} = 1.6$ Hz, $J_{6a,6b} = 13.0$ Hz, H-6a), 3.85 (q, 2 H, $J = 6.5$ Hz, POCH₂), 3.77-3.64 (m, 2 H, H-6b, H-4), 3.45-3.39 (m, 2 H, H-2, H-3), 3.28 (br, d, 1 H, $J_{5,4} = 4.4$ Hz, H-5), 2.09 (ddd, 1 H, $J_{1a,P} = 17.6$ Hz, $J_{1a,1b} = 15.3$ Hz, $J_{1a,2} = 4.8$ Hz, H-1a), 1.91 (ddd, 1 H, $J_{1b,P} = 17.3$ Hz, $J_{1b,2}$

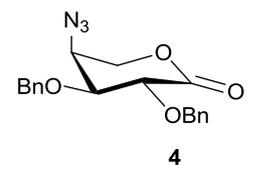
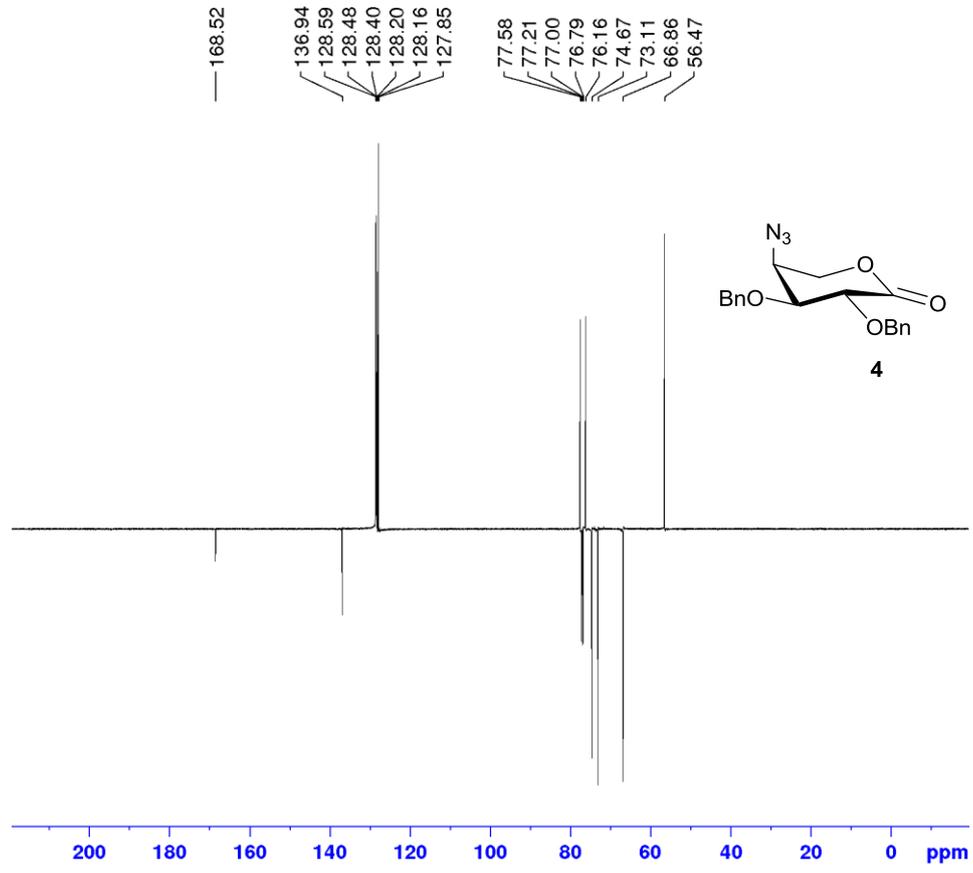
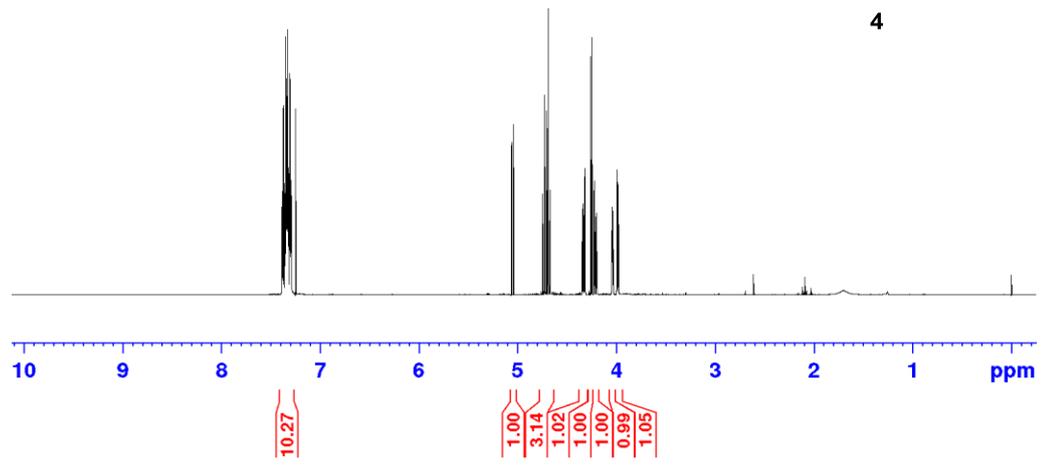
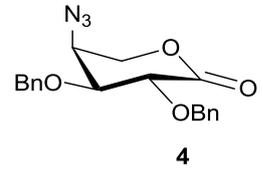
= 6.0 Hz, $J_{1a,1b} = 15.2$ Hz, H-1b), 1.64-1.59 (m, 2 H, $J = 6.7$ Hz, H-2'a, H-2'b), 1.41-1.28 (m, 10 H, octyl signals H-3', H-4', H-5', H-6', H-7') and 0.90 (t, 3 H, $J = 7.0$ Hz, H-8'); ^{13}C NMR (CD_3OD): δ 79.74 (d, $J_{\text{C,P}} = 2.8$ Hz, C-2), 74.30 (d, $J_{\text{C,P}} = 7.8$ Hz, C-3), 73.86 (C-4), 69.09 (C-6), 66.13 (d, $J_{\text{C,P}} = 5.6$ Hz, C-1'), 54.49 (C-5), 33.87 (C-6'), 32.76 (d, $J_{\text{C,P}} = 134.0$ Hz, C-1), 33.04 and 33.00 (C-4', C-5'), 27.86 (C-3'), 24.57 (C-7') and 15.26 (C-8'); ^{31}P NMR (CD_3OD): δ 21.56. HRMS (ESI) m/z $[\text{M}+\text{H}^+]^+$ calcd for $\text{C}_{14}\text{H}_{30}\text{NO}_6\text{P}$: 340.1884, found 340.1887.

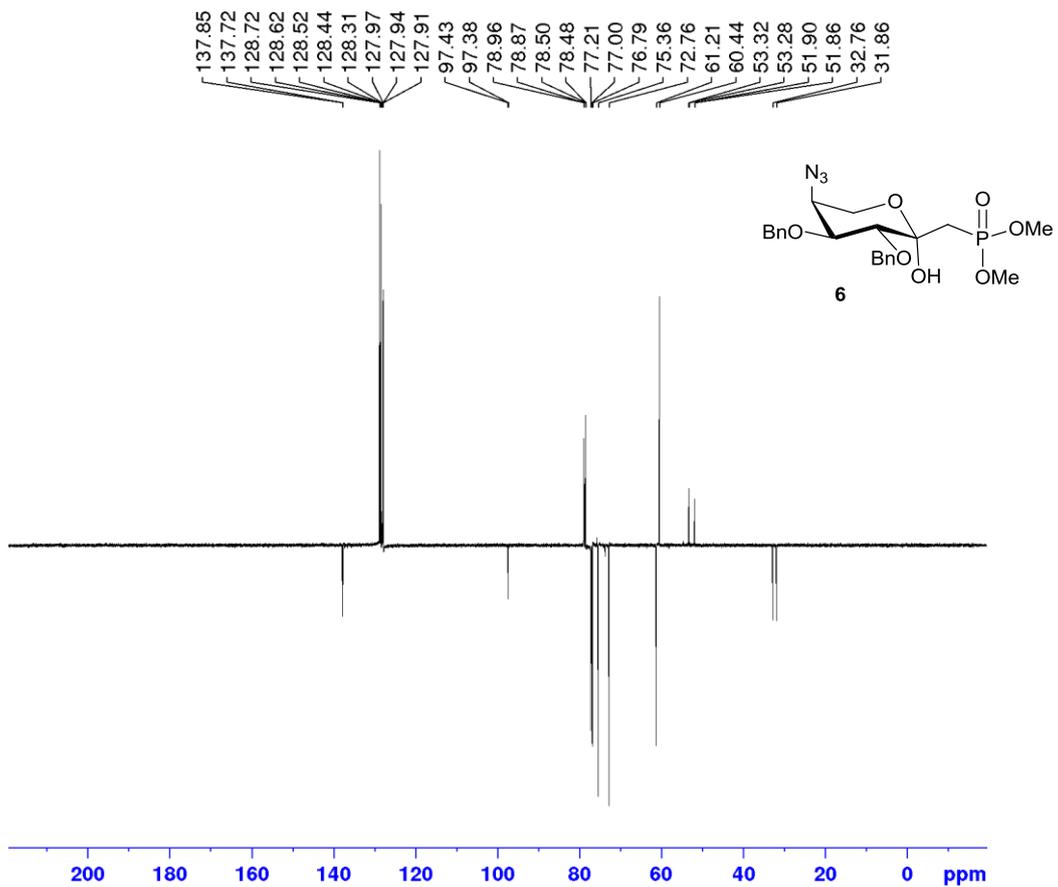
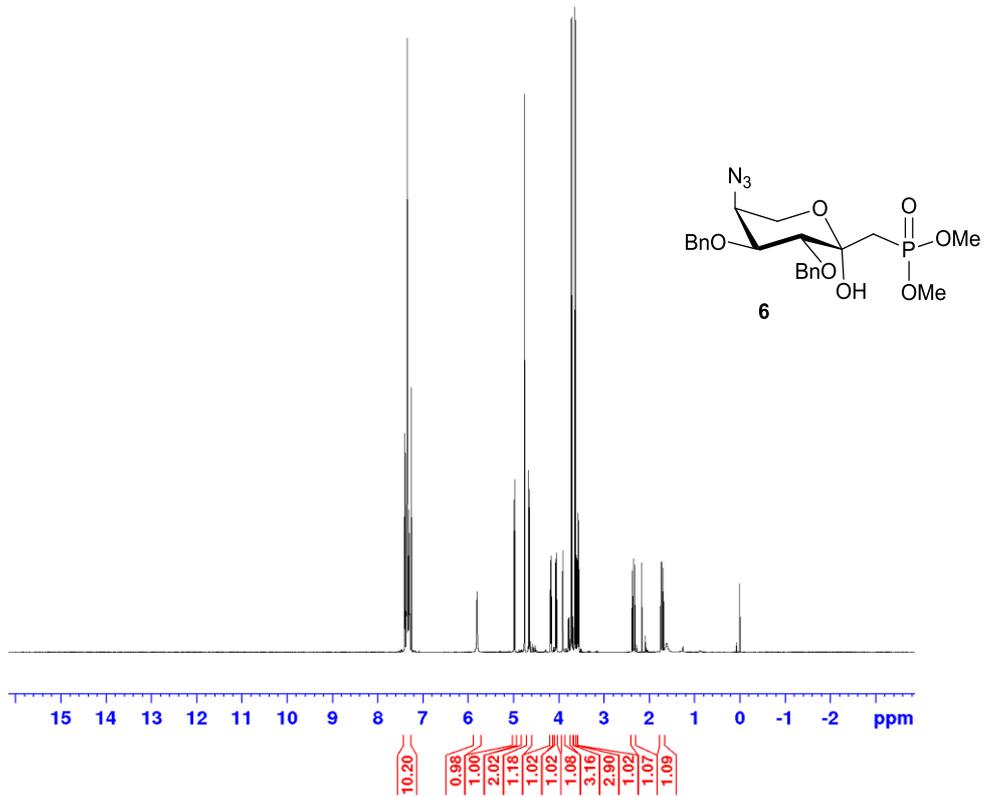
Octyl (2,6-anhydro-5-amino-1,5-dideoxy-L-altrit-1-yl) phosphonic acid (17)

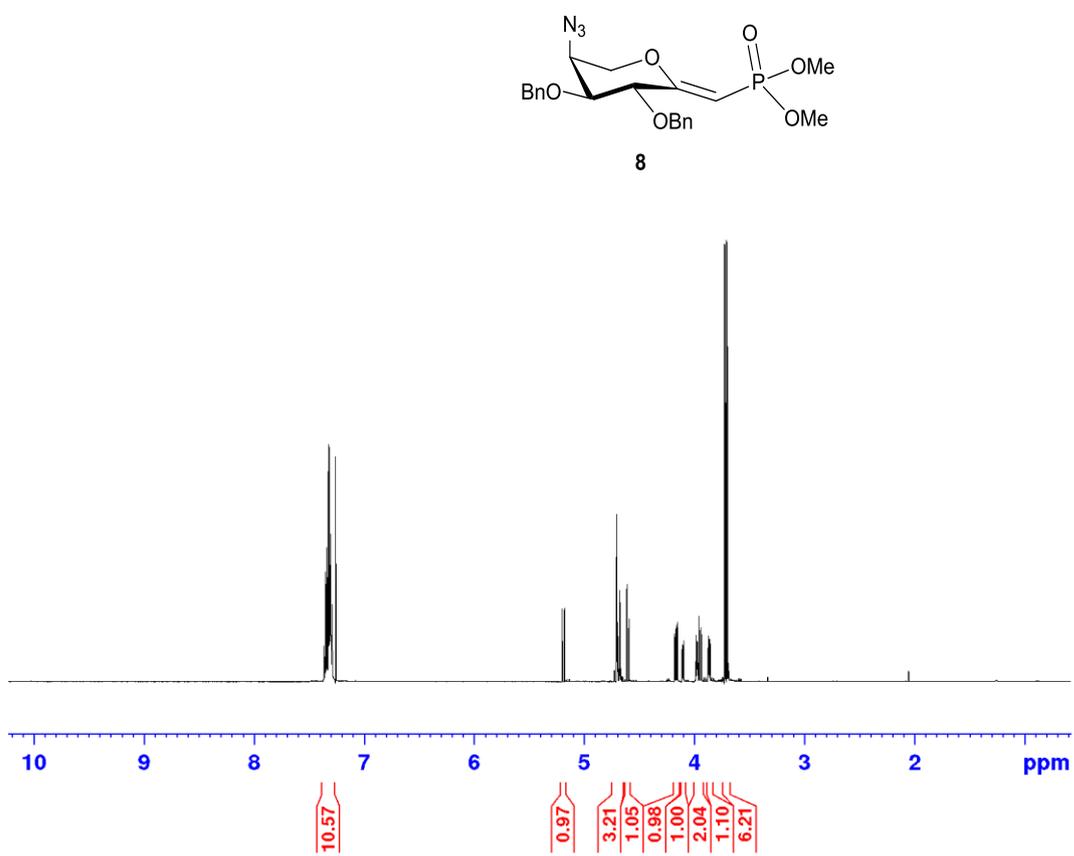
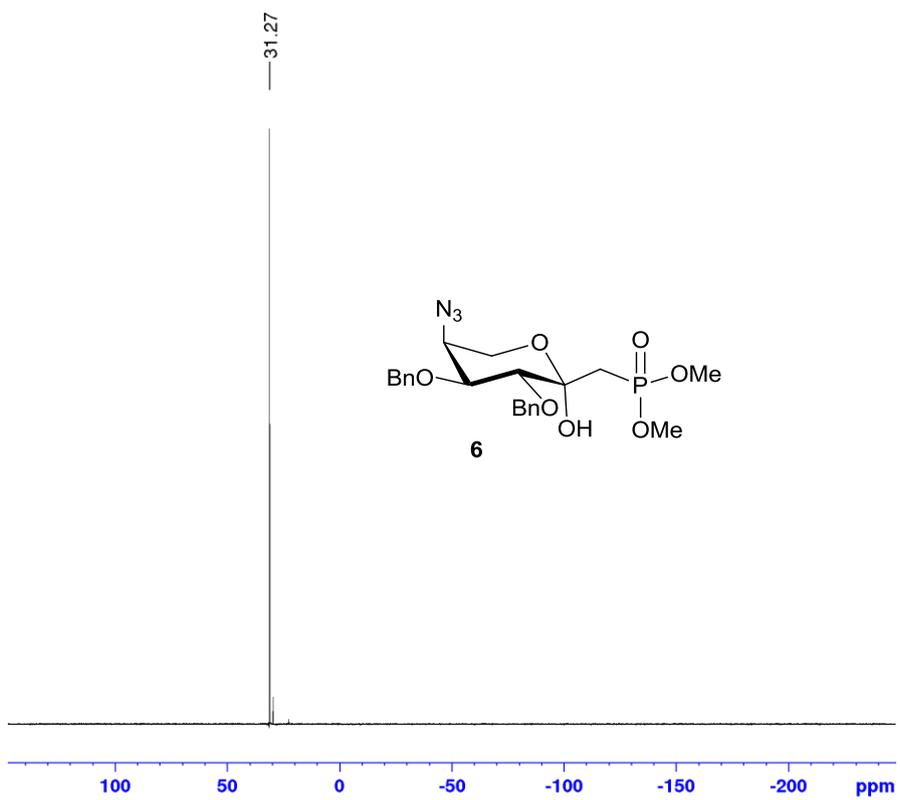
Hydrogenation of **15** (9 mg, 0.017 mmol) was carried out as described under general conditions to give 2.3 mg (41%) of **17** as white solid after HILIC purification; $[\alpha]_{\text{D}}^{20} +43$ (c 0.2, MeOH); ^1H NMR (CD_3OD): δ 4.02 (br d, 1 H, H-3), 4.01 (br d, 1 H, $J_{6a,5} = 1.4$ Hz, $J_{6a,6b} = 13.4$ Hz, H-6a), 3.84 (m, 3 H, $J = 8.6$ Hz, POCH_2 , H-4), 3.71 (br d, 1 H, $J_{6a,6b} = 13.5$ Hz, H-6b), 3.68 (ddd, 1 H, $J_{2,\text{P}} = 5.6$ Hz, $J_{2,1a} = 8.3$ Hz, $J_{2,1b} = 5.3$ Hz, H-2), 3.32 (br d, 1 H, $J = 2.5$ Hz, H-5), 2.05 (ddd, 1 H, $J_{1a,\text{P}} = 16.9$ Hz, $J_{1a,1b} = 14.9$ Hz, $J_{1a,2} = 8.2$ Hz, H-1a), 1.93 (ddd, 1 H, $J_{1b,\text{P}} = 18.4$ Hz, $J_{1b,2} = 5.3$ Hz, H-1b), 1.64-1.59 (m, 2 H, $J = 6.7$ Hz, H-2'a, H-2'b), 1.40-1.30 (m, 10 H, octyl signals H-3', H-4', H-5', H-6', H-7') and 0.90 (t, 3 H, $J = 7.1$ Hz, H-8'); ^{13}C NMR (CD_3OD): δ 78.44 (C-2), 72.44 (d, $J_{\text{C,P}} = 4.95$ Hz, C-3), 68.67 (C-4), 68.62 (C-6), 66.03 (d, $J_{\text{C,P}} = 6.1$ Hz, C-1'), 53.76 (C-5), 33.86 (C-6'), 33.01 (d, $J_{\text{C,P}} = 6.6$ Hz, C-2'), 31.40 (d, $J_{\text{C,P}} = 133.1$ Hz, CH_2P), 31.34 and 31.29 (C-4', C-5'), 27.85 (C-3'), 24.56 (C-7'), 15.26 (C-8'); ^{31}P NMR (CD_3OD): δ 20.56. HRMS (ESI) m/z $[\text{M}+\text{H}^+]^+$ calcd for $\text{C}_{14}\text{H}_{30}\text{NO}_6\text{P}$: 340.1884, found 340.1887.

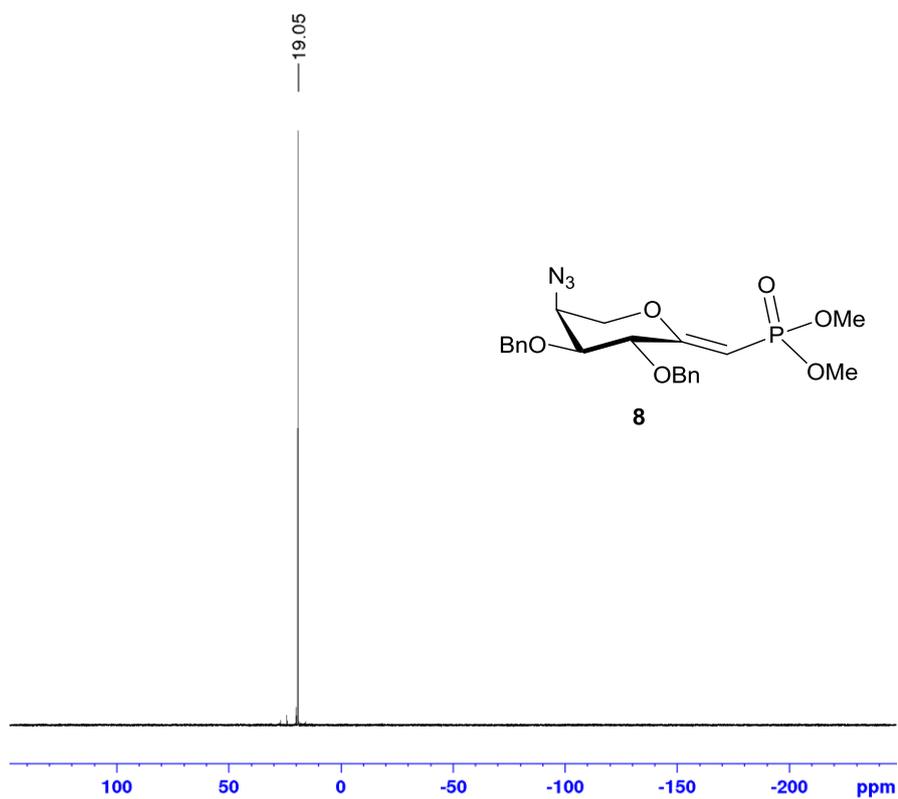
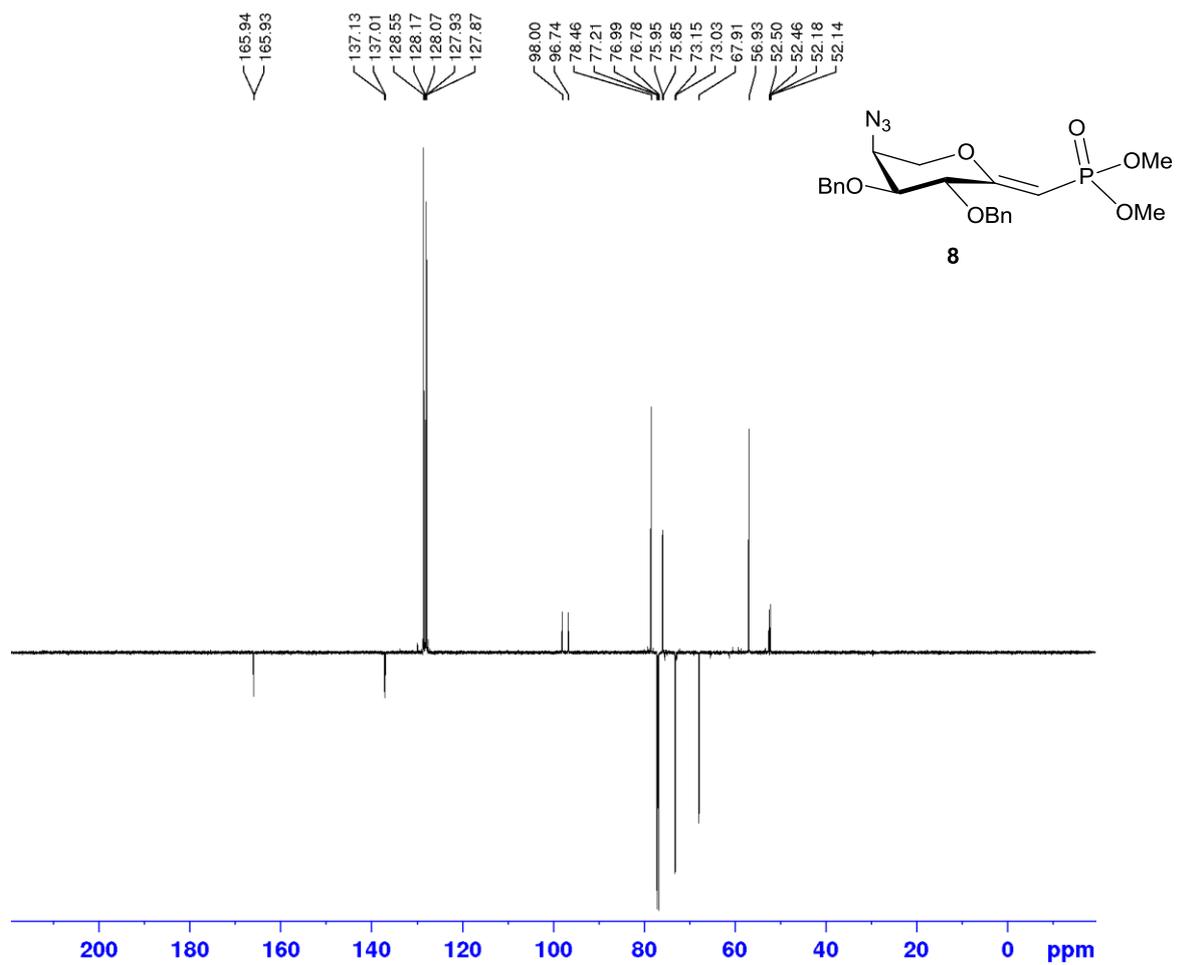
References for Supporting information

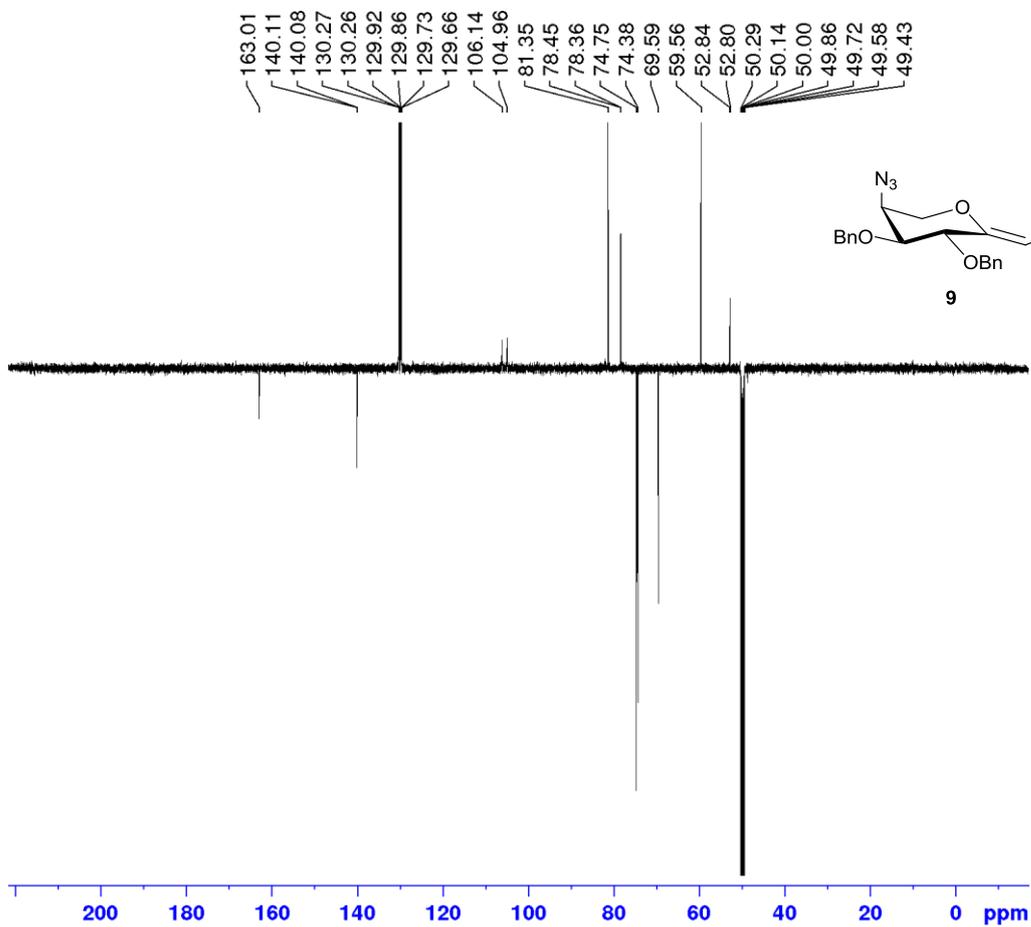
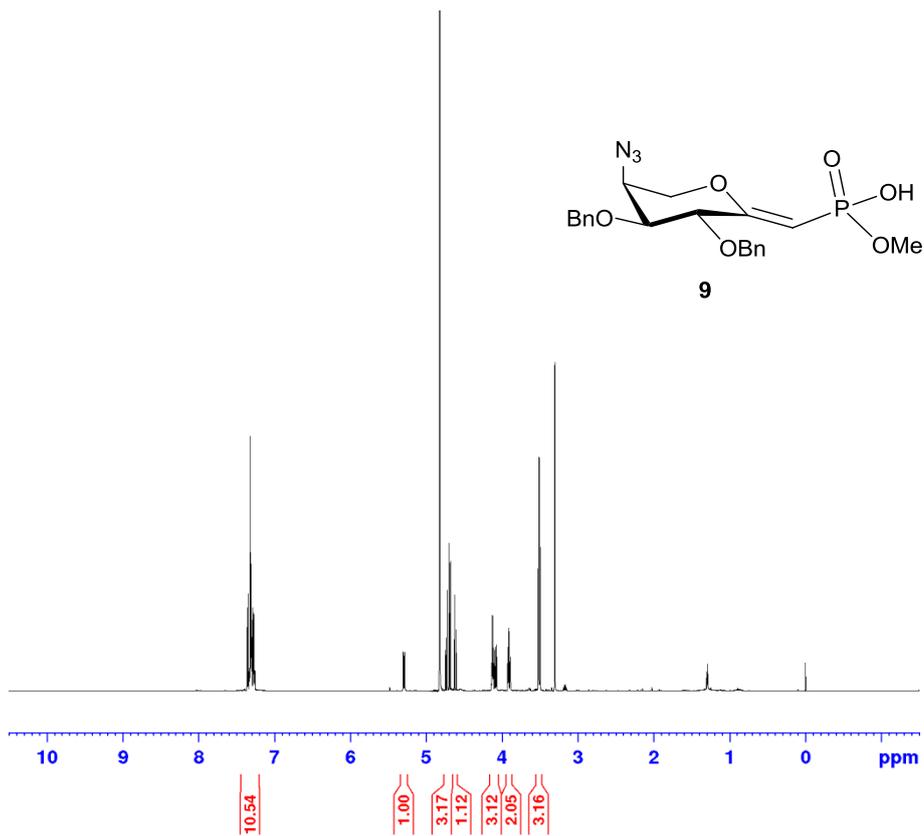
1. B. Müller, M. Blaukopf, A. Hofinger, A. Zamyatina, H. Brade, P. Kosma, *Synthesis* **2010**, 3134-3151.
2. M. Blaukopf, B. Müller, A. Hofinger, P. Kosma, *Eur. J. Org. Chem.* **2012**, 119-131.



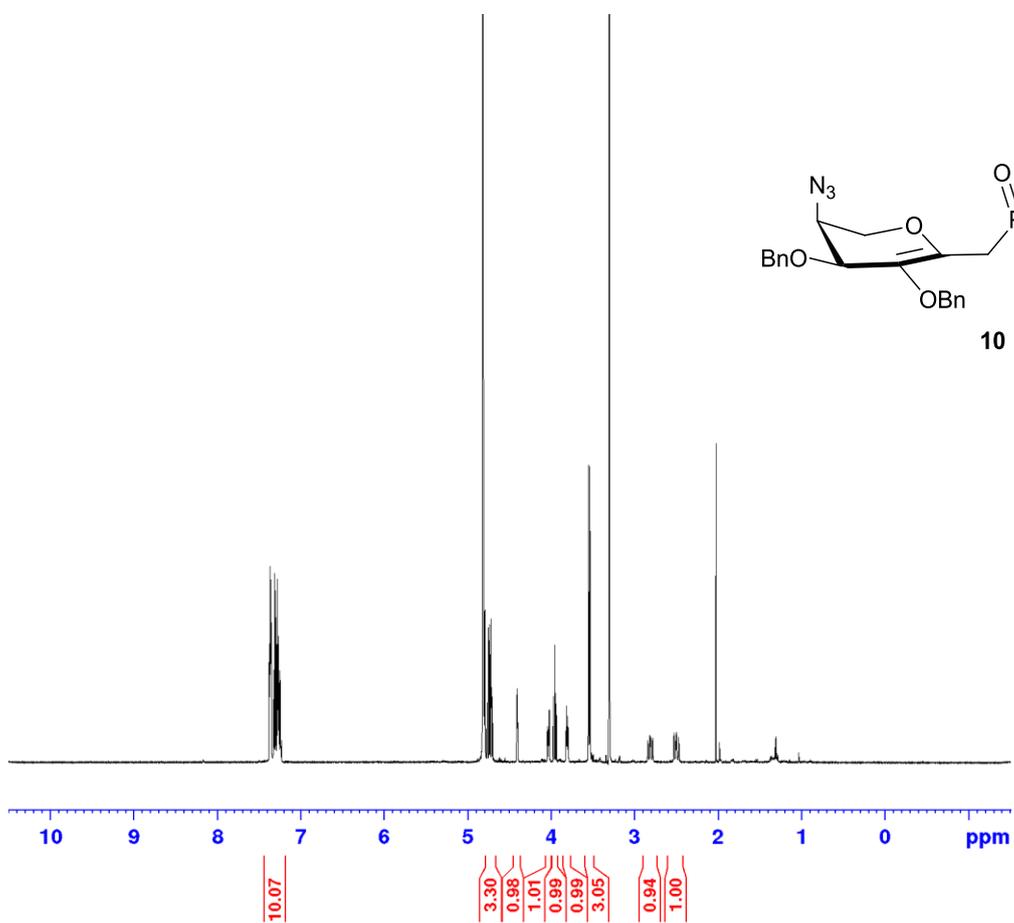
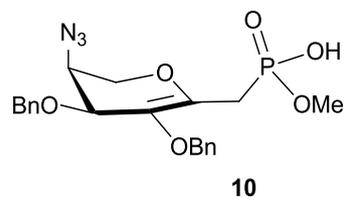
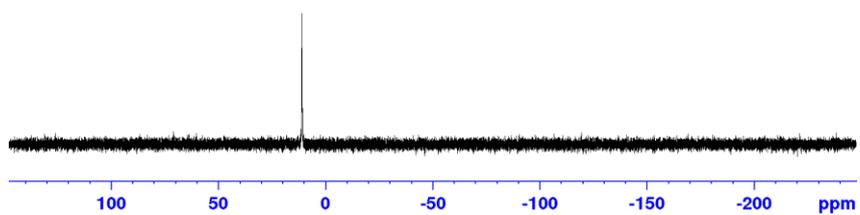
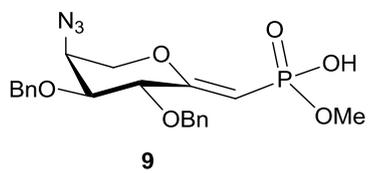


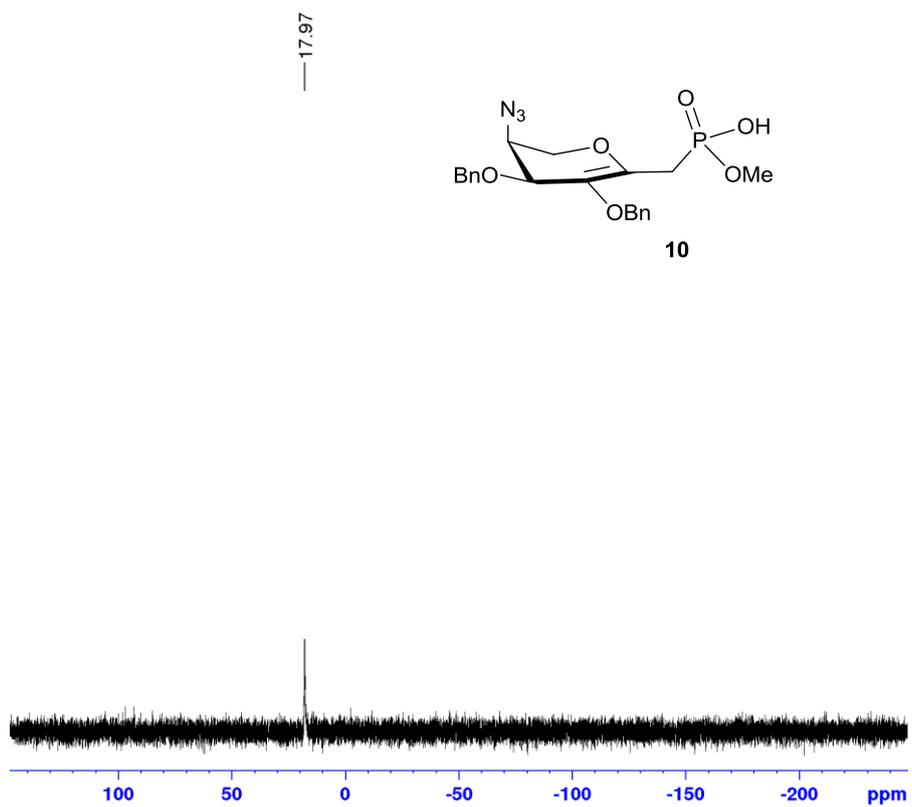
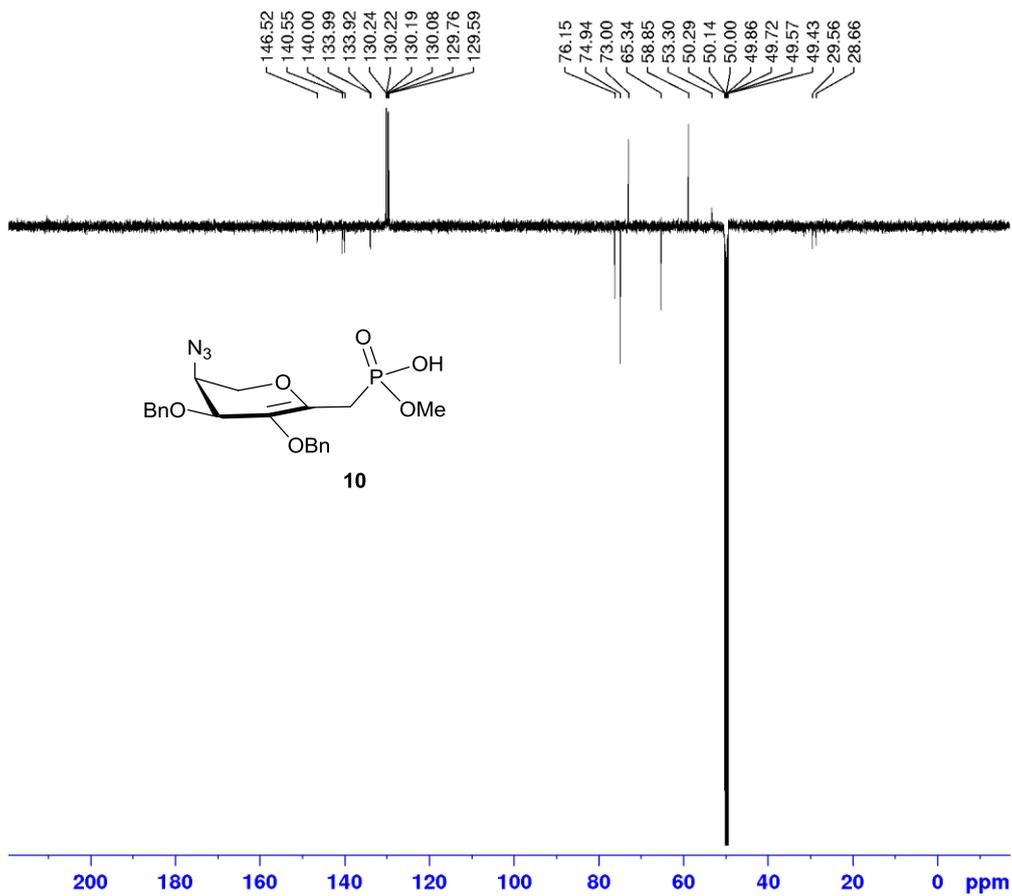


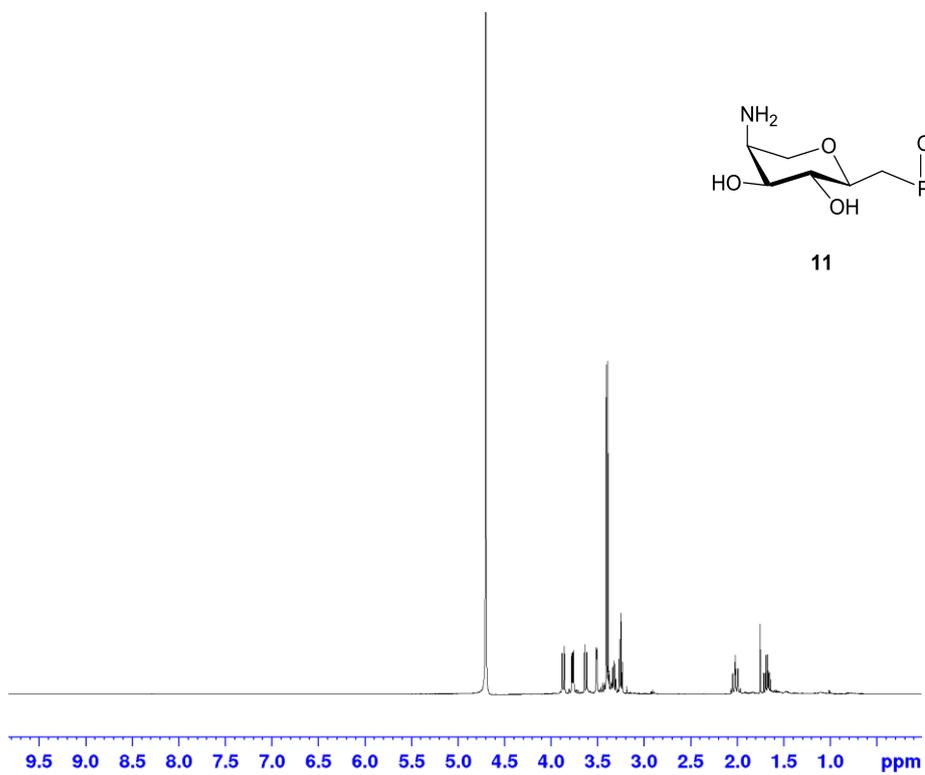




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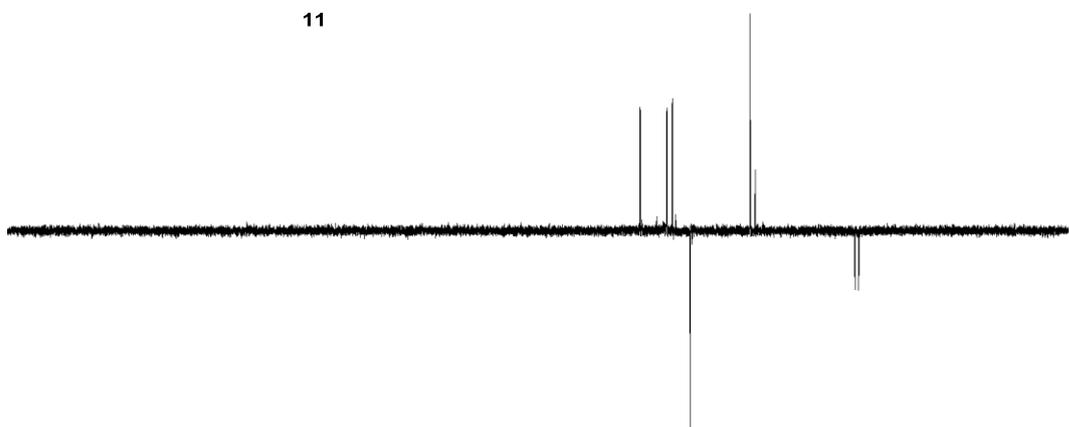
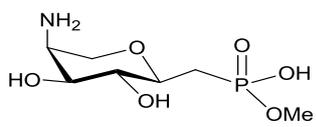


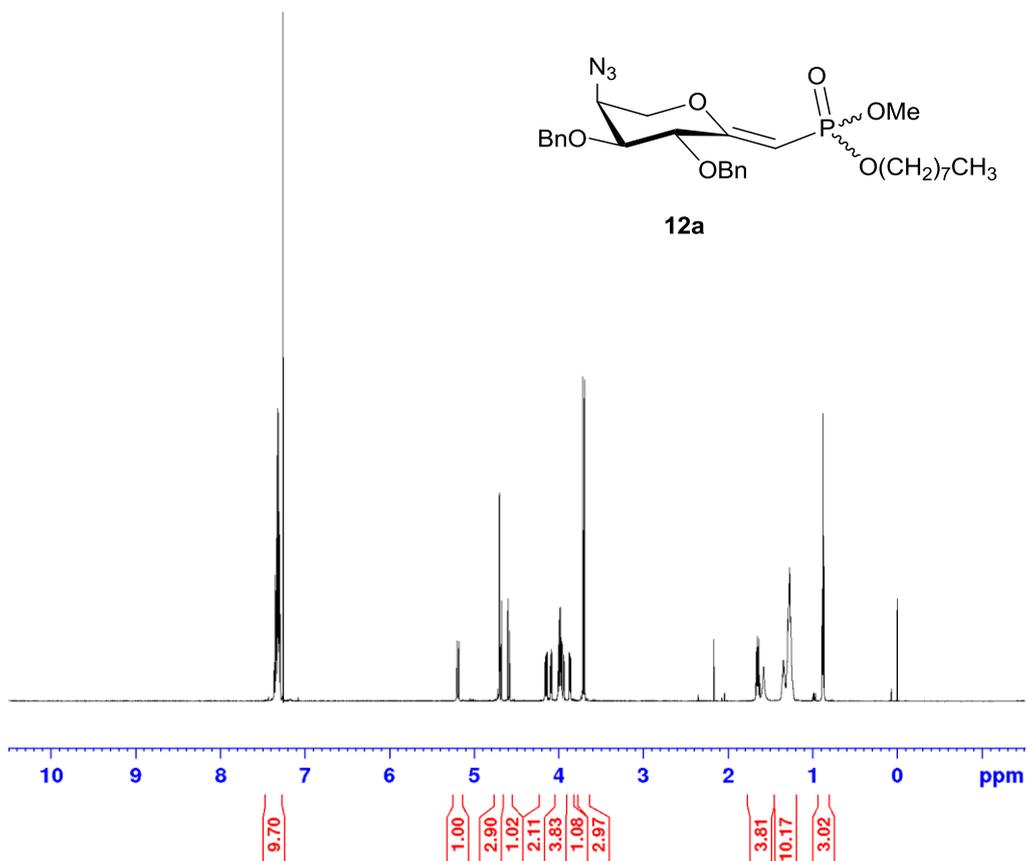
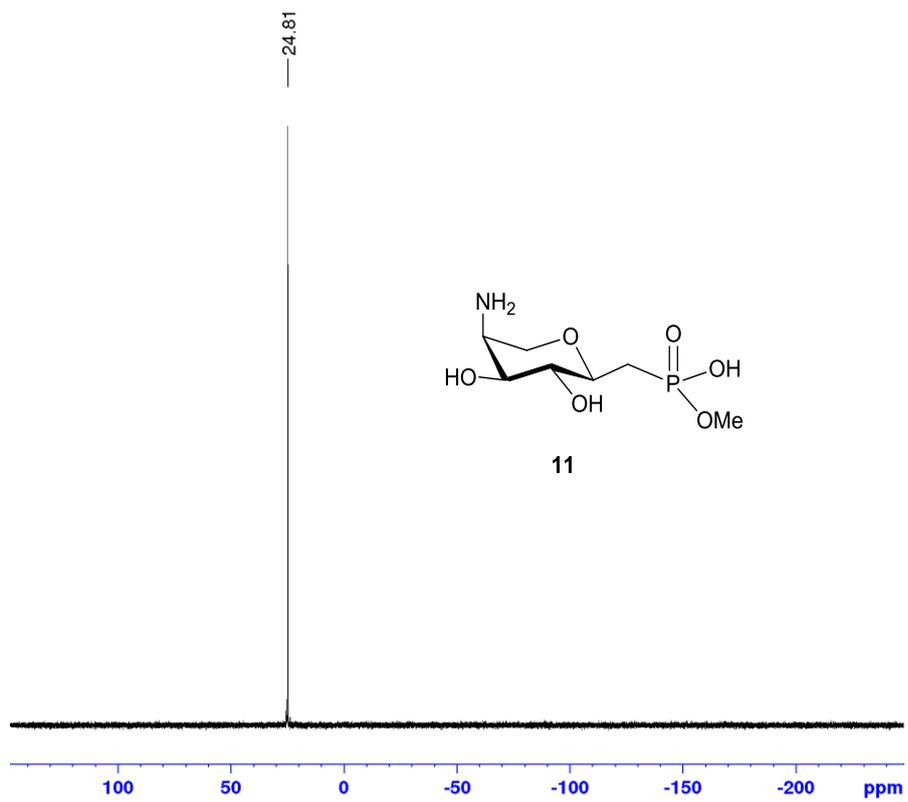


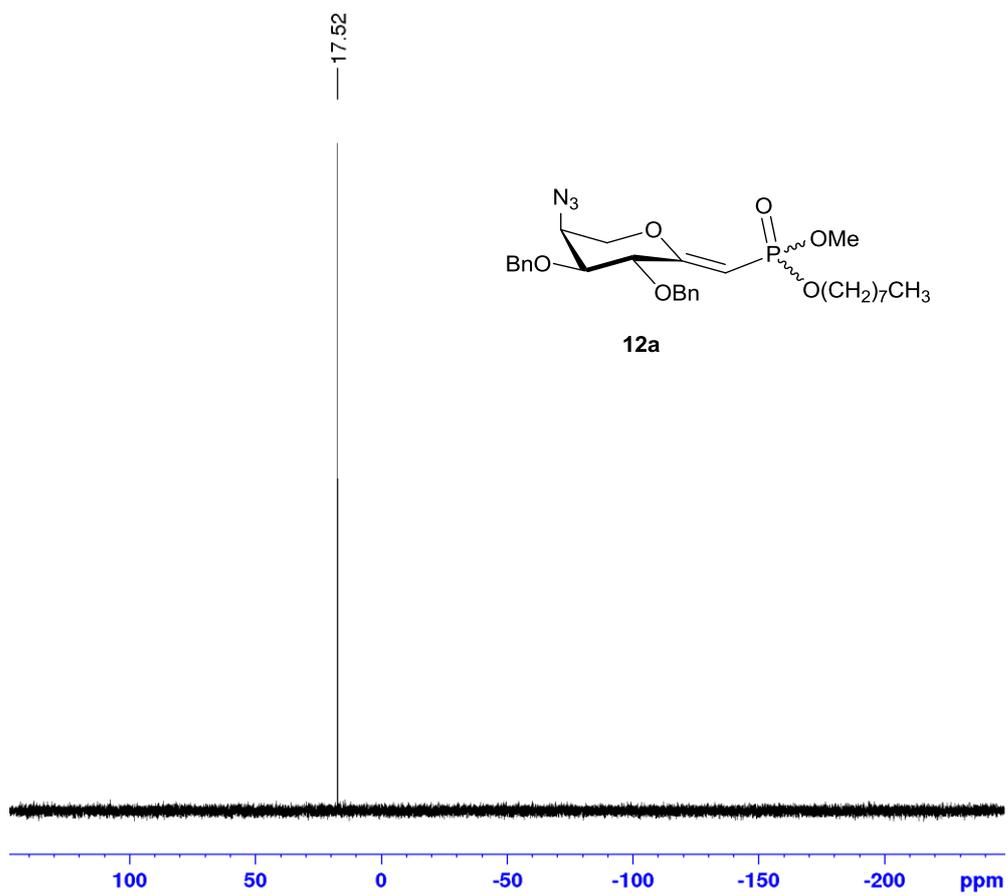
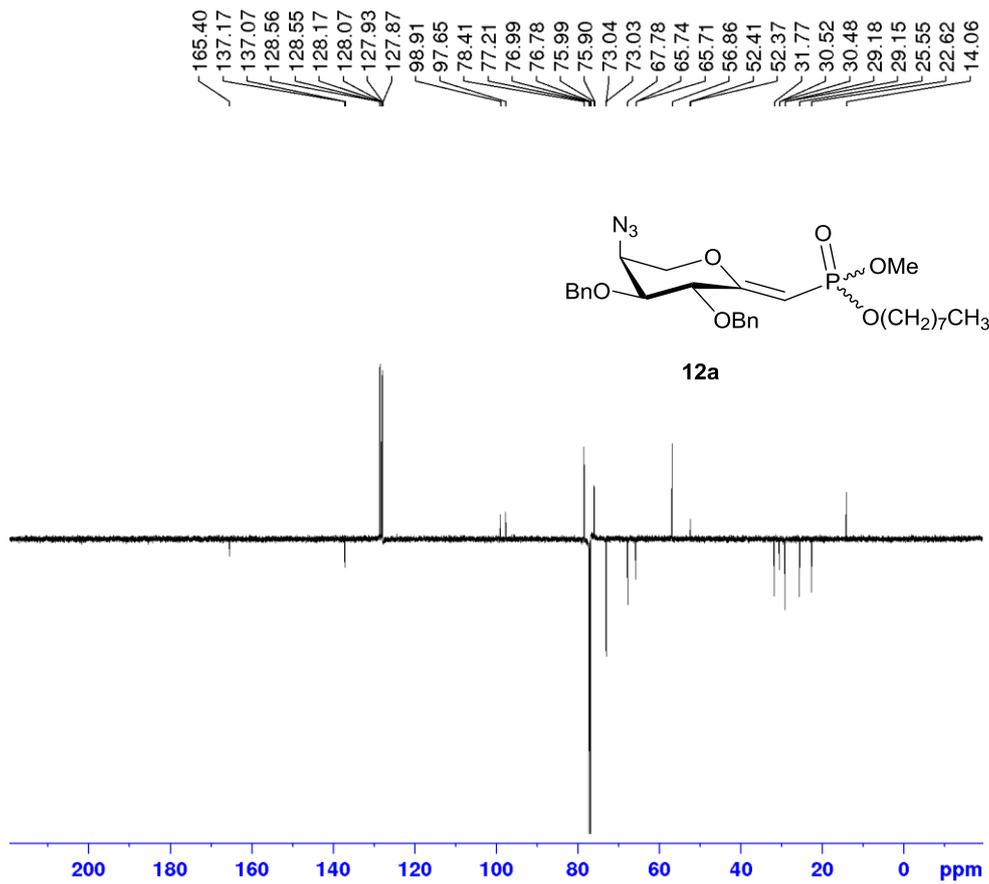
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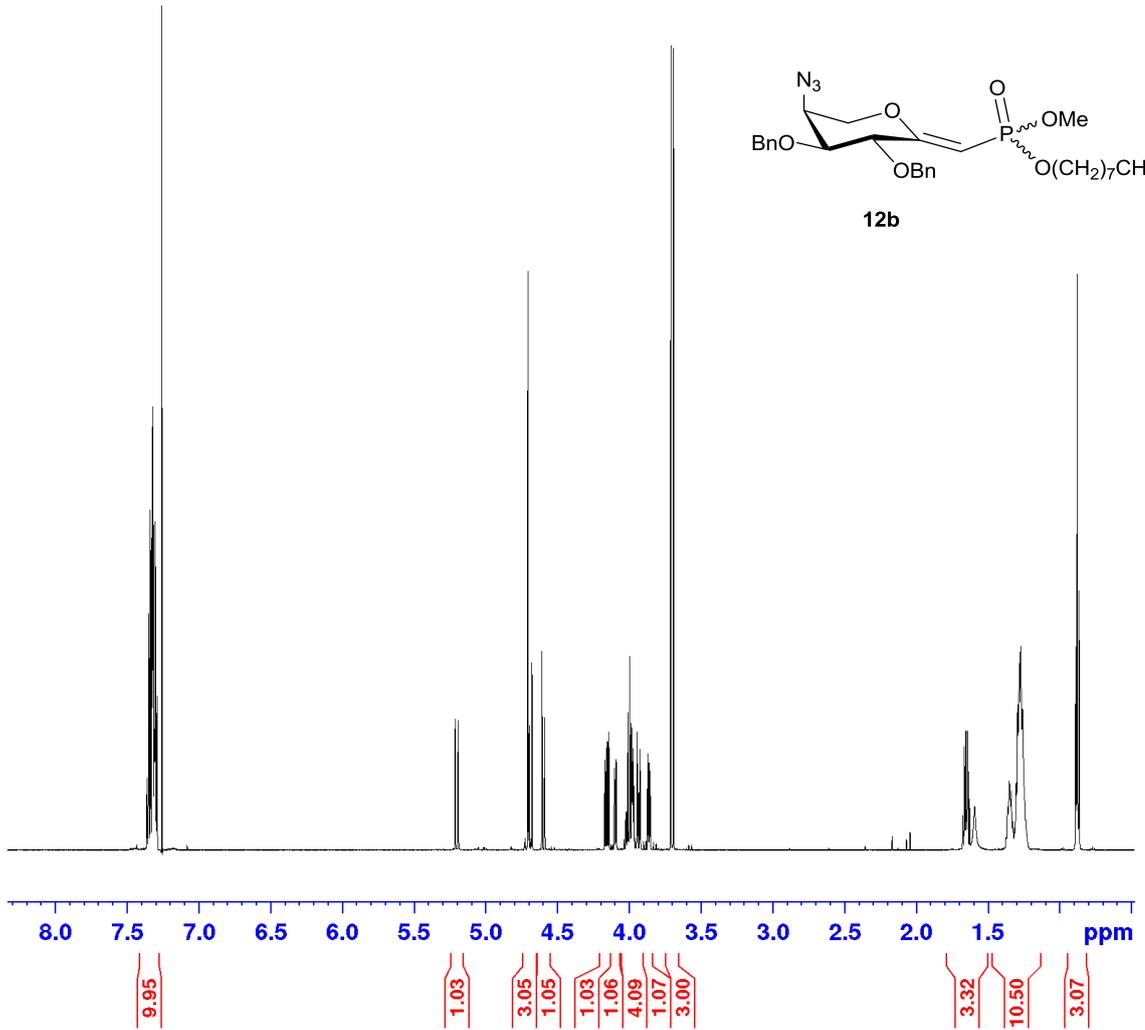
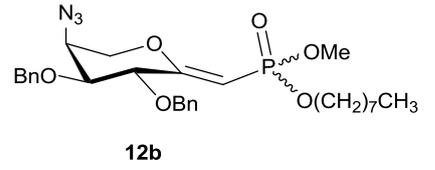
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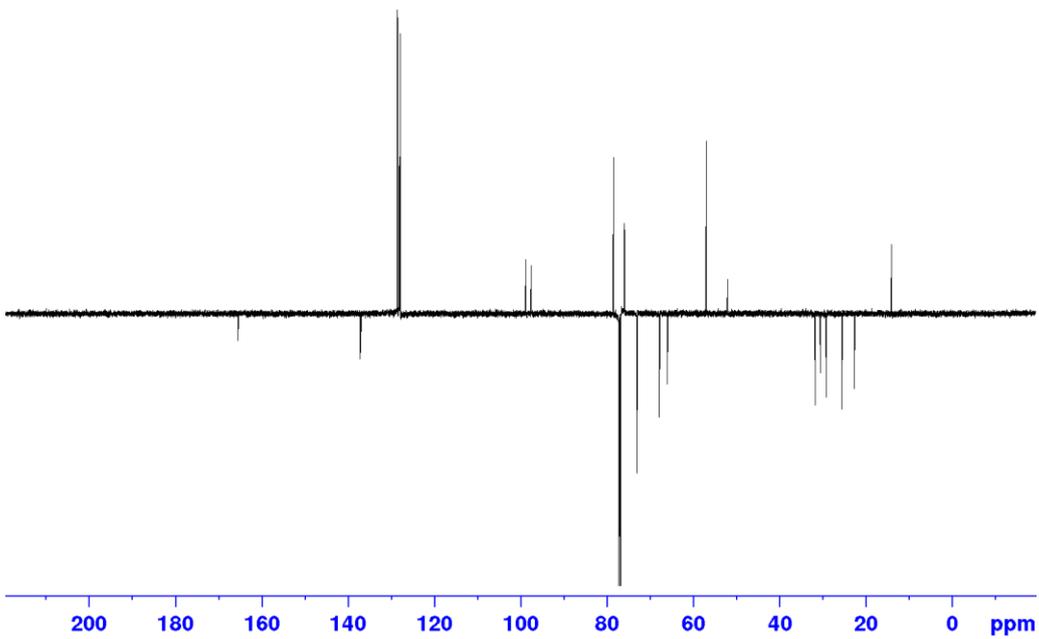
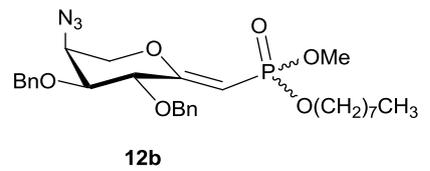


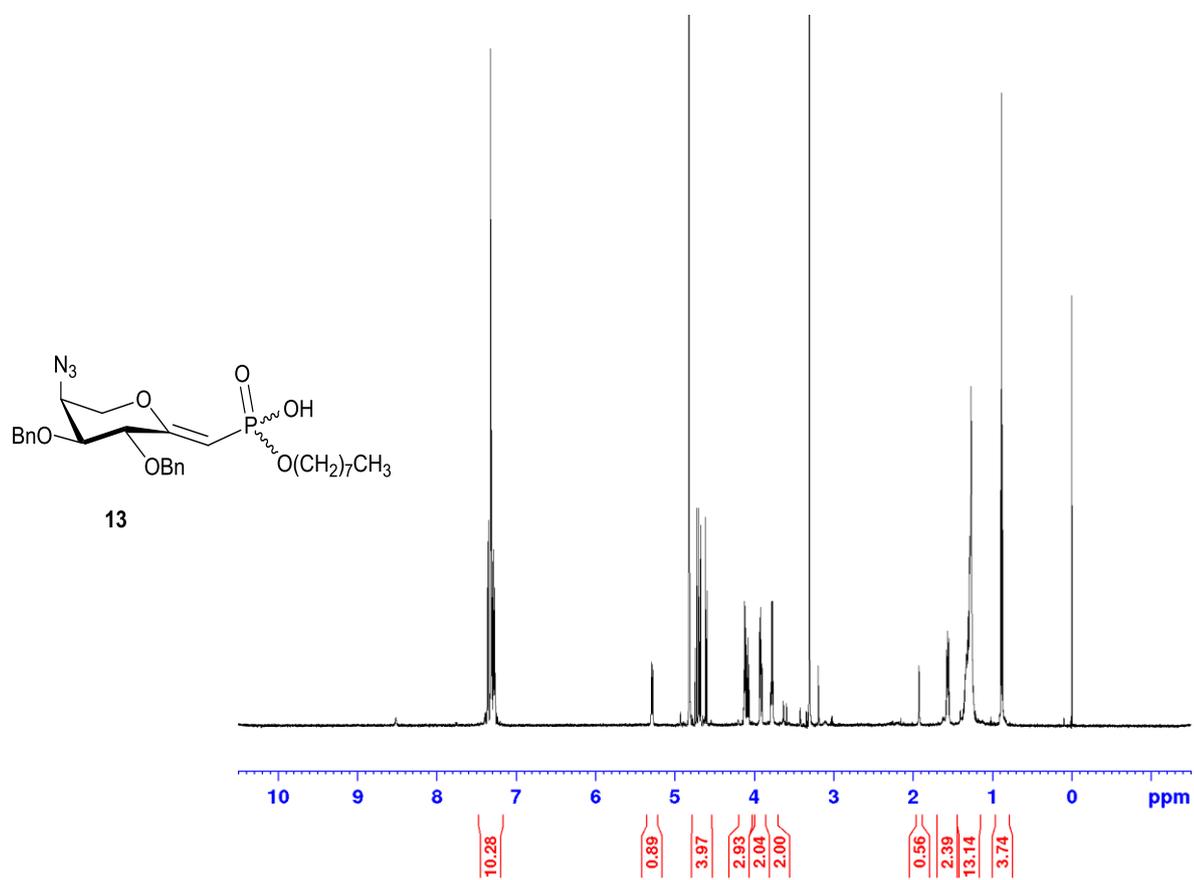
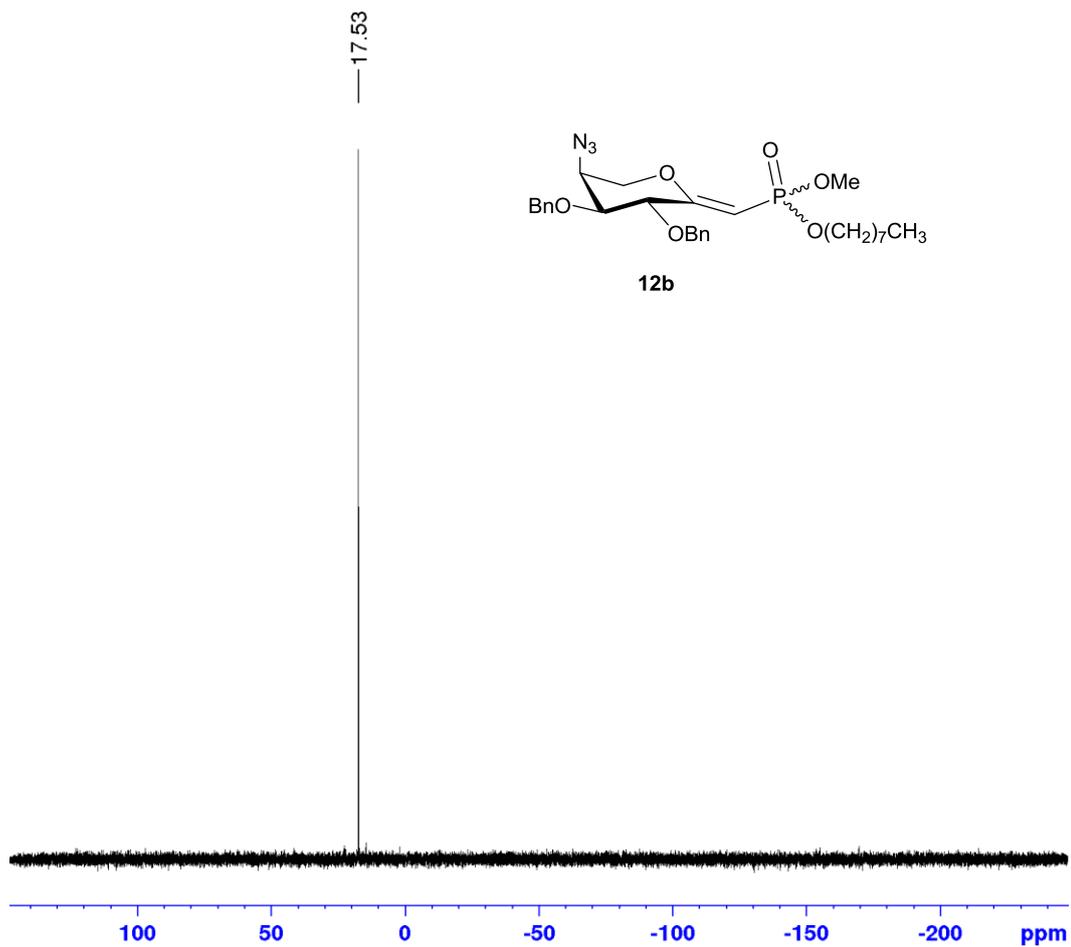


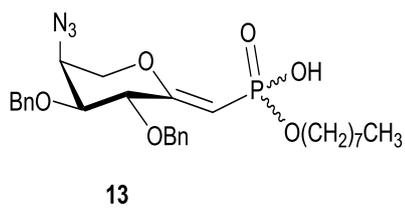
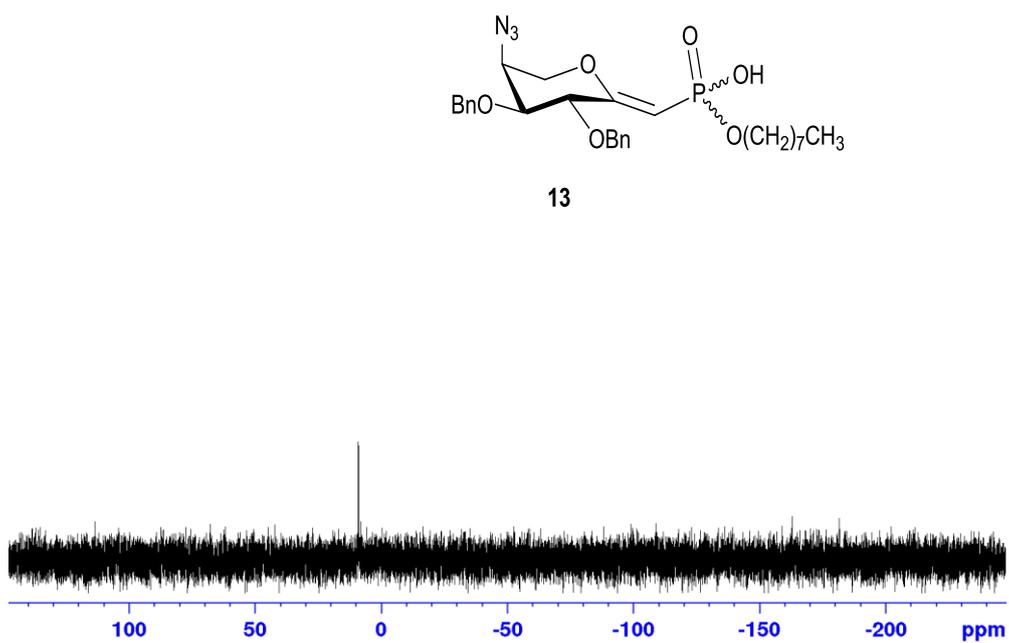
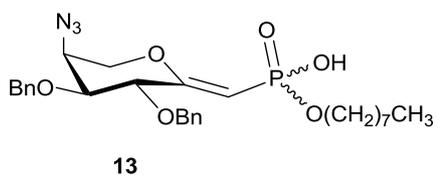
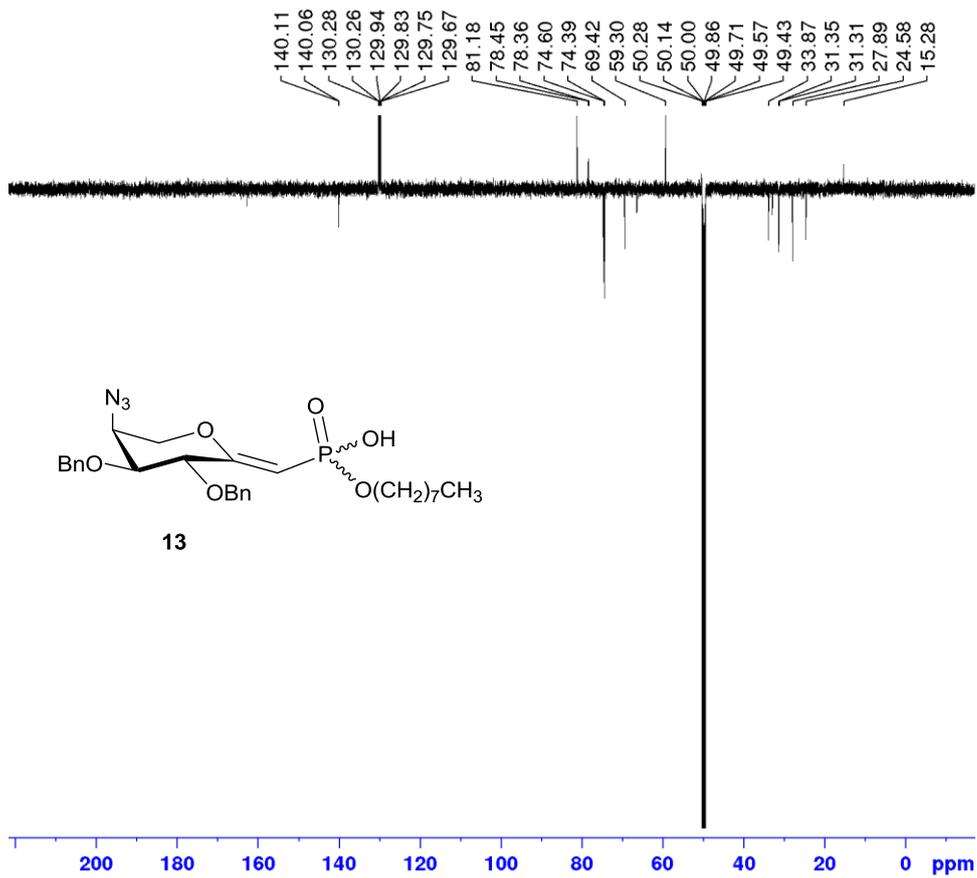


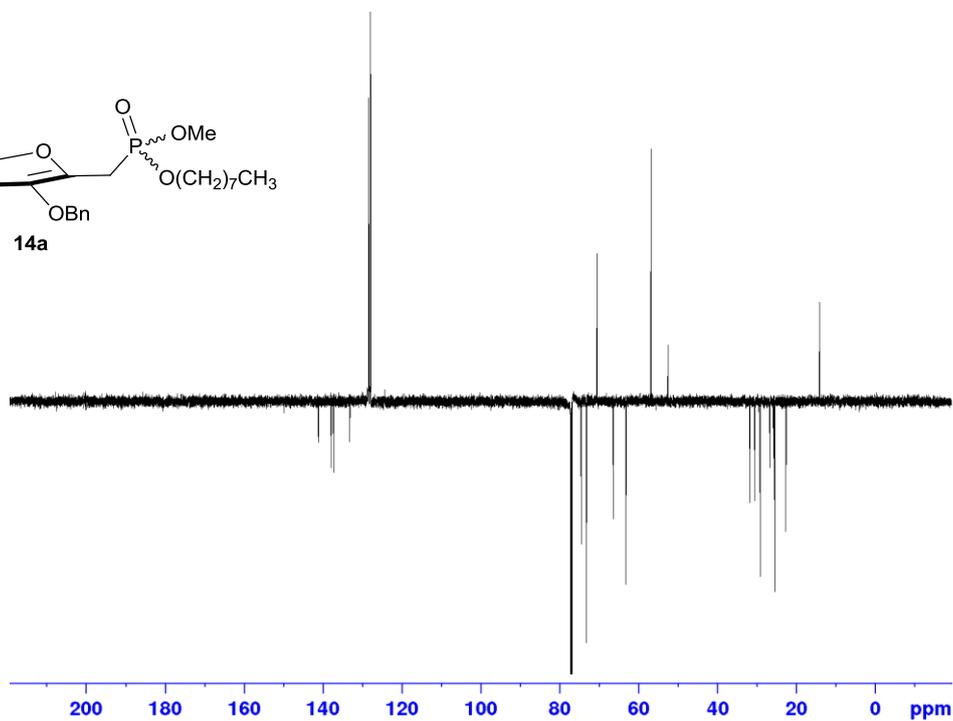
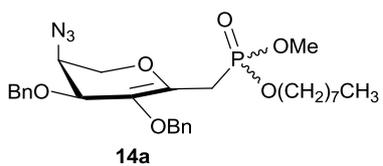
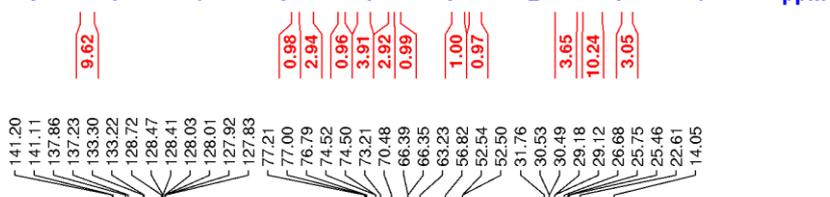
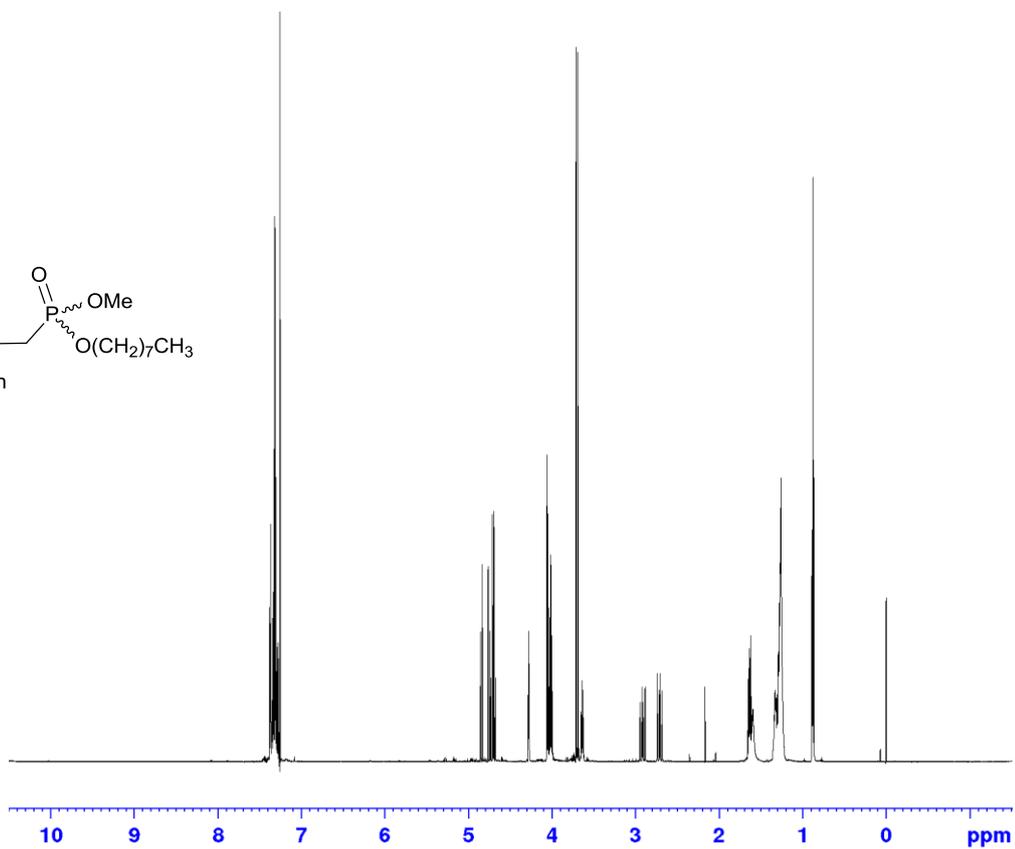
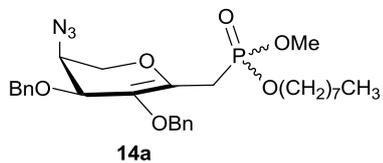


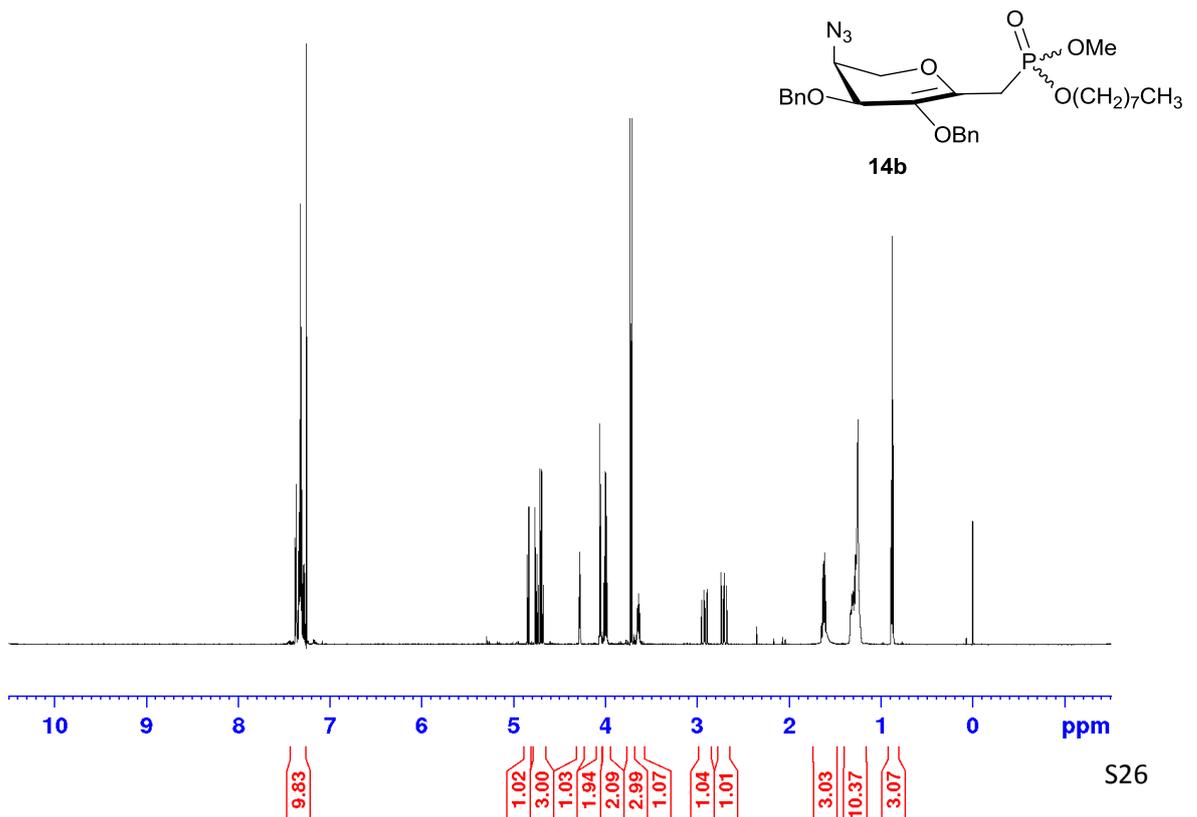
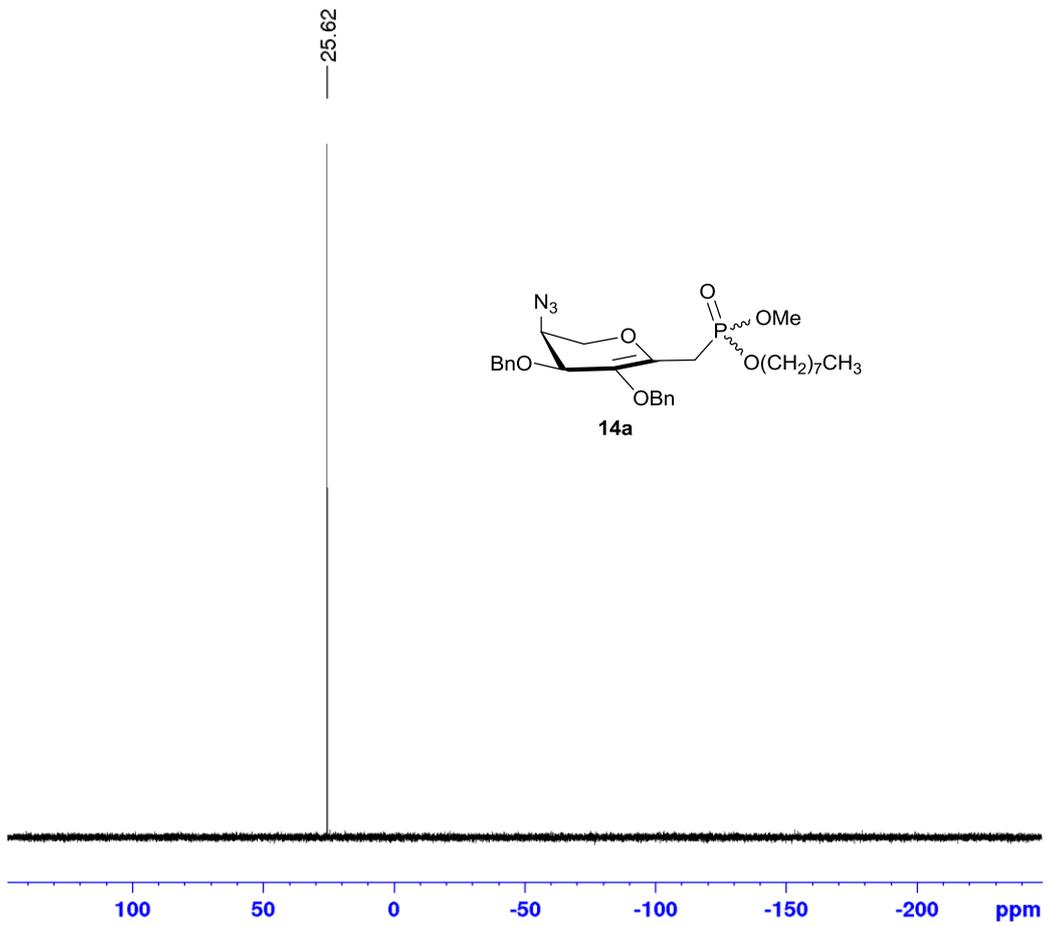
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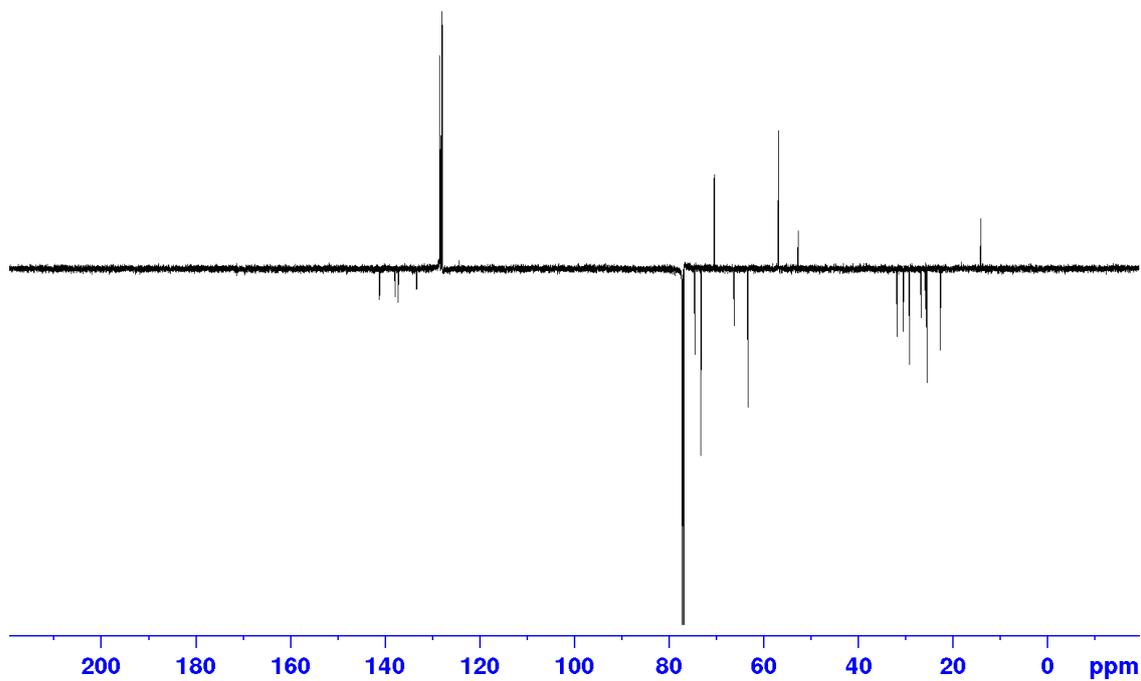
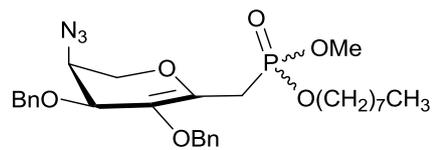




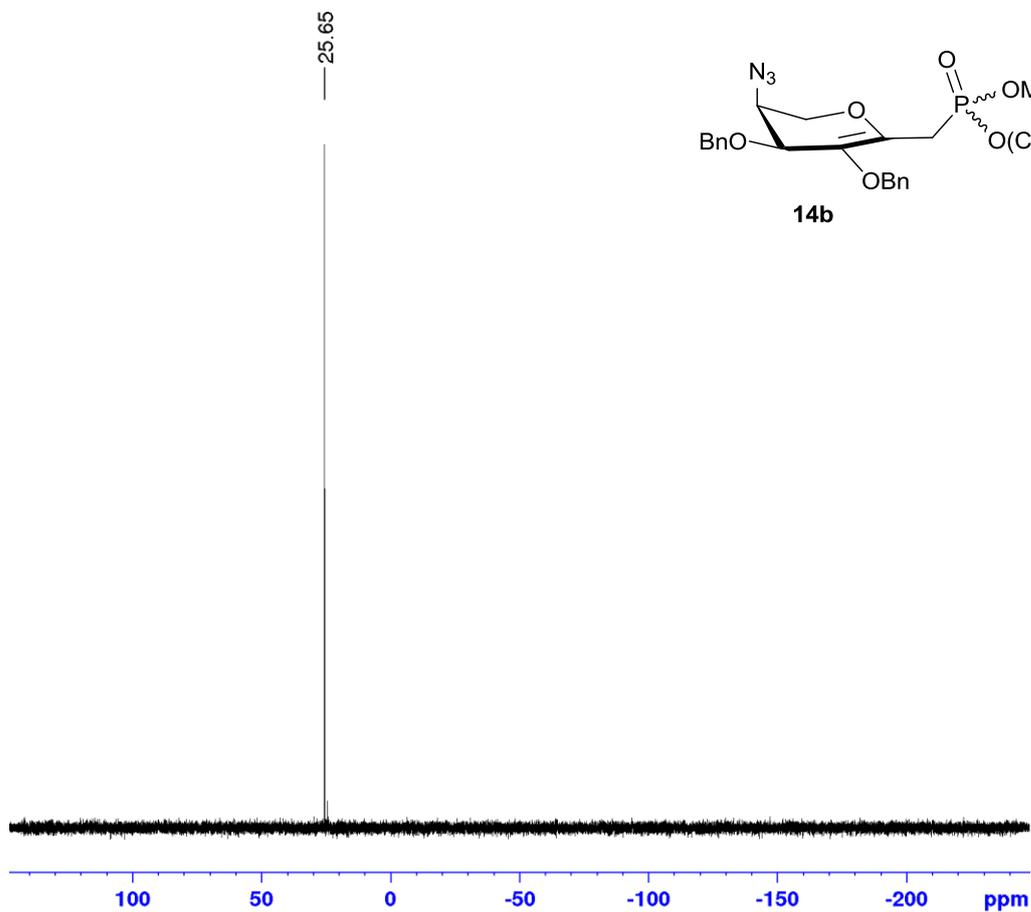
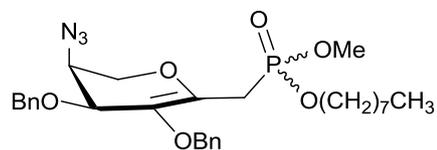


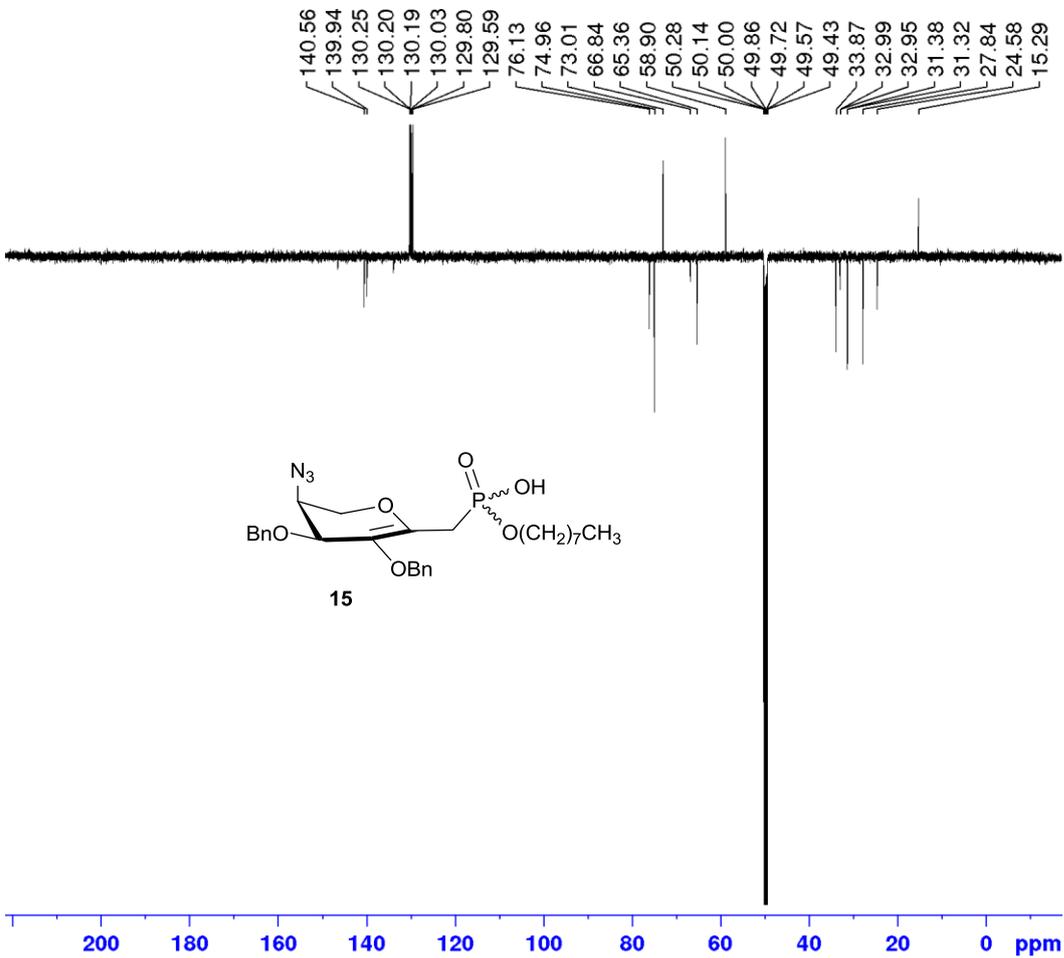
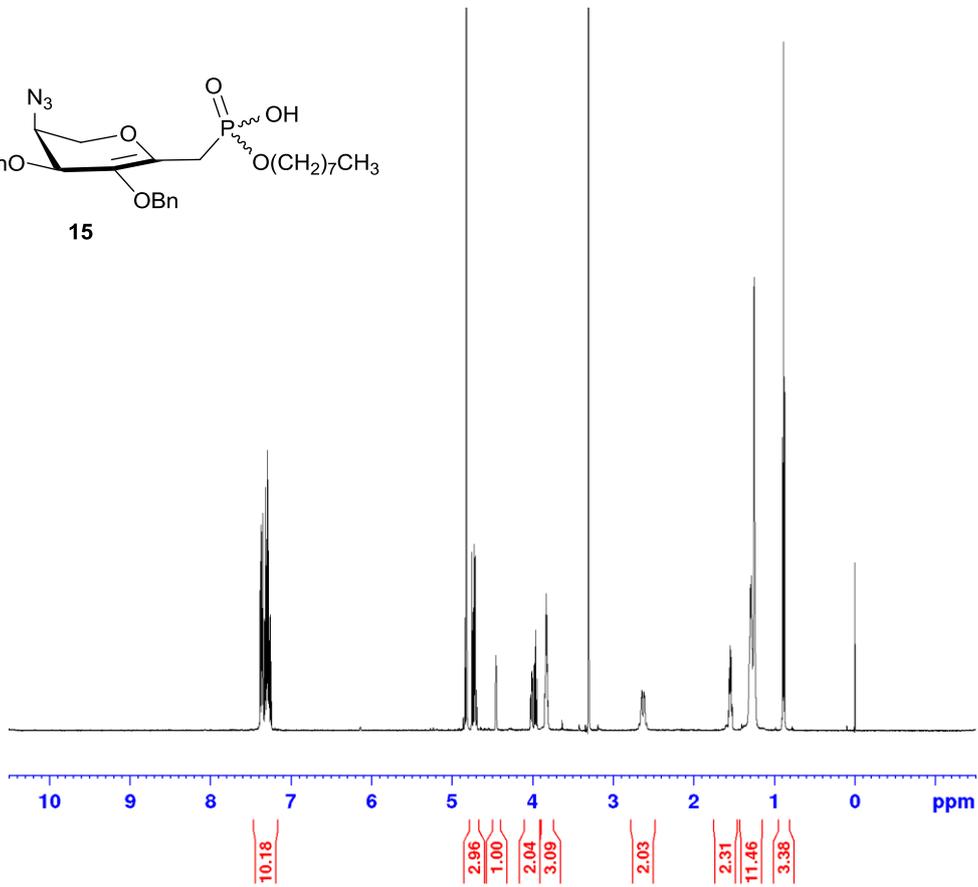
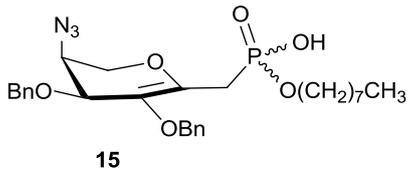


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25.65





—16.19

