Supporting information

A General Strategy to Synthesize ADP-7-Azido-Heptose and ADP-Azido-Mannoses and Their Heptosyltransferase Binding Properties

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I. Materials and Methods

All reactions were carried out under an argon atmosphere. Yields refer to chromatographically and spectroscopically homogeneous materials. Reagents and chemicals were purchased from Sigma-Aldrich or Acros at ACS grade and were used without purification. All reactions were performed using purified and dried solvents: tetrahydrofuran (THF) was refluxed over sodium-benzophenone, dichloromethane (DCM), triethylamine (Et_3N), and pyridine were refluxed over calcium hydride (CaH_2). All reactions were monitored by thin-layer chromatography (TLC) carried out on Merck aluminum roll silica gel 60-F254 using UV light and a molybdate-sufuric acid solution as revelator. Merck silica gel (60, particle size 40-63 μm) was employed for flash column chromatography and preparative thin layer chromatography using technically solvent distilled prior to use as eluting solvents. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a JEOL ECX 400 with solvent peaks as reference. Chemical shifts (δ ppm) and coupling constants (Hz) are reported in standard fashion with reference to either internal standard tetramethylsilane (TMS) (δ H = 0.00 ppm), $CHCl_3$ (δ H = 7.25 ppm), CD_3OD (δ H = 3.31 ppm) or D_2O (δ H = 4.79 ppm). ^{13}C NMR spectra were recorded on 100 MHz spectrometer at 25 °C in $CDCl_3$, CD_3OD or D_2O; chemical shifts (δ ppm) are reported relative to $CHCl_3$ [δ C = 77.00 ppm (central line of triplet)] or CD_3OD [δ C = 49.00 ppm (central line of quartet)]. All compounds were characterized by ^{1}H and ^{13}C NMR as well as by ^{1}H-^{1}H and ^{1}H-^{13}C correlation experiments when necessary. The following abbreviations are used to describe the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Aromatic, benzyl and methyl (carbons and protons) are respectively labeled with "Arom.", "CH_2Ph", quaternary carbons are indicated with a "q" superscript. Chemical shifts (δ) are reported in ppm and referenced indirectly to residual solvent signals. Molecules **6**[1,3], **7**[1,3], **8**[1,3], **9**[1,3,4], **3c**[2], **3d**[2], **3e**[2], **14e**[2], **17e**[2] and **2e**[2] have been already described in the literature.

Nucleotide-sugars were purified by HPLC on Waters 600 systems. Analyses of reactionnal crude were realized on analytical system:

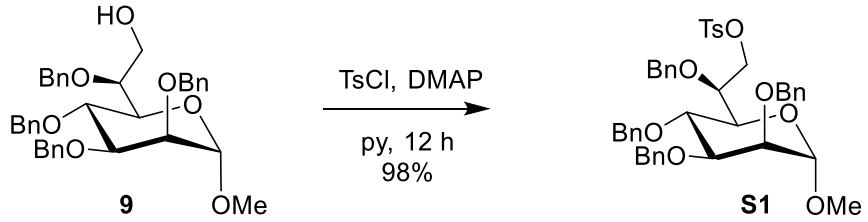
- Column : Agilent Zorbax SB-C_{18} 4.6 x 250 mm 5 µM;
- Flow = 1.0 mL/min;
- Detection: UV 254 & 262 nm (Waters 2996 PDA detector).
- Volume injection = 5-10 µL.

Purifications were realized on a semi-preparative HPLC Waters 600 system:

- Column = Agilent Zorbax SB-C_{18} 21.2x250mm 7µM;
- Flow = 21.0 mL/min;
- Detection: UV 254 & 262nm (Waters 2486 Dual λ Absorbance detector).
- Volume injection = 1 – 5 mL.

II. Procedures and Characterizations

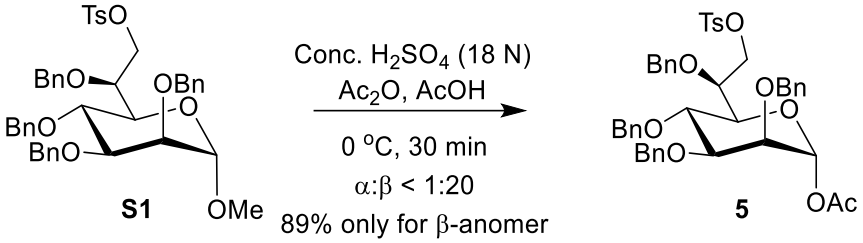
Methyl-2,3,4,6-tetra-*O*-benzyl-7-*O*-tosyl-L-*glycero*-α-D-*manno*-heptopyranoside (S1)



A solution of **9** (8.0 g, 1.0 equiv., 13.7 mmol) and DMAP (175 mg, 0.1 equiv., 1.4 mmol) in dry pyridine (50 mL), was stirred at 0 ºC in an ice bath. A solution of *p*-toluensulfonyl chloride (7.8 g, 3.0 equiv., 40.9 mmol) in dry pyridine (30 mL) was then added dropwise by syringe pump at 0 °C. The reaction was warmed to room temperature and stirred overnight. The solvent was then removed in vacuo to afford yellow syrup. The crude material was purified by flash chromatography over silica gel (cyclohexane/ethyl acetate 70:30) to obtain compound **S1** (9.9 g, 98%). **$[\alpha]_D^{20}$** = +25.5 (c 0.9, CH_3Cl). **^{1}H-NMR (400 MHz, $CDCl_3$)**: δ 7.77 (d, *J* = 8.2 Hz, 2H, H-Ar), 7.39-7.19 (m, 22H, H-Ar), 4.92 (d, *J* = 11.2 Hz, 1H, CH_2Ph), 4.79 (d, J =1.7 Hz, 1H, H-1), 4.73 (s, 2H, CH_2Ph), 4.66 (d, *J* = 11.7 Hz, 1H, CH_2Ph), 4.57 (q, *J* = 11.7 Hz, 2H, CH_2Ph), 4.44 (d, *J* = 11.7 Hz, 1H, CH_2Ph), 4.31 (d, *J* = 7.8 Hz, 1H, CH_2Ph), 4.28 (m, 2H, H-7), 4.16 (t, *J* = 9.4 Hz, 1H, H-4), 4.11 (m, 1H, H-6), 3.92 (dd, *J* = 3.0 Hz and 9.4 Hz, 1H, H-3), 3.79 (t, *J* = 2.8 Hz, 1H, H-2), 3.69 (d, *J* = 9.6 Hz, 1H, H-5), 3.26 (s, 3H, -OCH_3), 2.45 (s, 3H, CH_3-Ts). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 145.1 (Cq-Ar), 138.7 (Cq-Ar), 138.33 (Cq-Ar), 138.3 (Cq-Ar), 137.9 (Cq-Ar), 132.8 (Cq-Ar), 130.0 (-CH=), 128.5 (-CH=), 128.47 (-CH=), 128.4 (-CH=), 128.1 (-CH=), 127.9 (-CH=), 127.86

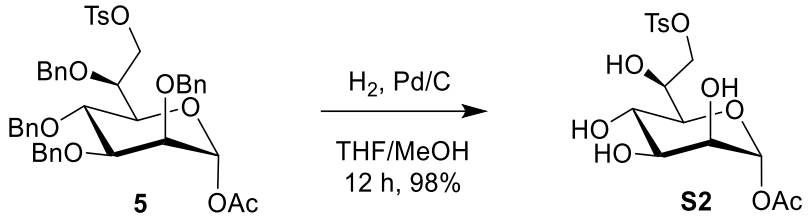
(-CH=), 127.8 (-CH=), 127.77 (-CH=), 127.7 (-CH=), 127.69 (-CH=), 127.6 (-CH=), 127.58 (-CH=), 99.3 (C-1), 80.6 (C-3), 74.5 (CH_2Ph), 74.2 (C-4 and C-6), 73.9 (C-2), 73.2 (CH_2Ph), 72.7 (CH_2Ph), 72.1 (CH_2Ph), 71.0 (C-5), 69.0 (C-7), 21.8 (CH_3-Ts). **HRMS (APCI)**: calc. for $C_{43}H_{50}NO_9S$ $[M+NH_4]^+$: 756.3202; found: 756.3201.

1-*O*- Acetyl-2,3,4,6-tetra-*O*-benzyl-7-*O*-tosyl-L-*glycero*-α-D-*manno*-heptopyranoside (5)



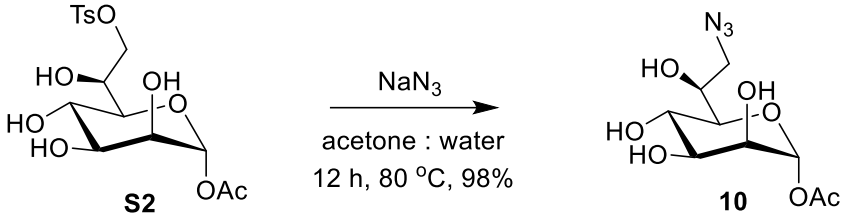
To a solution of **S1** (10.0 g, 1.0 equiv., 13.4 mmol) in AcOH (36 mL, 46.0 equiv., 616.0 mmol) was added acetic anhydride (11.0 mL, 9.0 equiv., 121.0 mmol) under argon at 0 °C. Concentrated H_2SO_4 (18 N, 0.7 mL) was added dropwise at 0 °C. The reaction was stirred for 30 min. The reaction mixture was poured into ice water (100 mL) and the aqueous phase was extracted with ethyl acetate (200 mL × 3). The combined organic phases were washed with water (100 mL × 2), sat. aq. $NaHCO_3$ (100 mL × 2) and dried over $MgSO_4$, filtered, concentrated to give a colorless solid. The residue was purified by silica gel flash column chromatography (cyclohexane/ethyl acetate 70:30) to afford compound **5** (9.2 g, 89%, only one isomer was isolated after purification) as a colorless syrup. **$[\alpha]_D^{20}$** = +15.4 (c 1.0, CH_3Cl). **^{1}H-NMR (400 MHz, $CDCl_3$)**: δ 7.72 (d, *J* = 8.2 Hz, 2H, H-Ar), 7.38-7.19 (m, 22H, H-Ar), 6.18 (d, $J_{1\text{-}2}$ = 1.2 Hz, 1H, H-1), 4.93 (d, *J* = 11.0 Hz, 1H, CH_2Ph), 4.79 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.70 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.64 (d, *J* = 11.7 Hz, 1H, CH_2Ph), 4.54 (s, 2H, CH_2Ph), 4.43 (d, *J* = 11.0 Hz, 1H, CH_2Ph), 4.34 (d, *J* = 11.0 Hz, 1H, CH_2Ph), 4.23-4.13 (m, 4H, H-4, H-6 and H-7), 3.90 (dd, *J* = 3.2 Hz and 9.6 Hz, 1H, H-3), 3.84 (dd, *J* = 1.2 Hz and 9.6 Hz, 1H, H-2), 3.70 (dd, *J* = 2.1 Hz and 4.0 Hz, 1H, H-5), 2.42 (s, 3H, $\underline{CH_3}$-Ts), 2.04 (s, 3H, $\underline{CH_3}$COO). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 169.0 (Cq), 145.0 (Cq-Ar), 138.4 (Cq-Ar), 137.9 (Cq-Ar), 137.8 (Cq-Ar), 137.75 (Cq-Ar), 132.6 (Cq-Ar), 130.0 (-CH=), 128.5 (-CH=), 128.46 (-CH=), 128.1 (-CH=), 127.9 (-CH=), 127.8 (-CH=), 127.75 (-CH=), 127.6 (-CH=), 91.4 (C-1), 79.7 (C-3), 74.8 (CH_2Ph), 73.9 (C-4 and C-2), 73.4 (C-6), 73.1 (CH_2Ph), 73.0 (CH_2Ph), 72.4 (CH_2Ph), 72.1 (C-5), 68.9 (C-7), 21.8 ($\underline{CH_3}$-Ts), 21.1 ($\underline{CH_3}$COO). **HRMS (APCI)**: calc. for $C_{44}H_{50}NO_{10}S$ $[M+NH_4]^+$: 784.3165; found:784.3168.

1-*O*-Acetyl-2,3,4,6-penta-*O*-benzyl-7-*O*-tosyl-L-*glycero*-α-D-manno-heptopyranoside (S2)



To a solution of **5** (9.0 g, 1.0 equiv., 11.7 mmol) in THF/MeOH (1/1, 40 mL/40 mL) was hydrogenated in the presence of Pd/C (10% wt, 900 mg) for overnight under H_2 atmospheric pressure. The catalyst was removed by filtration through a pad of Celite and washed with MeOH (45 mL). The combined filtrates were concentrated to obtain compound **S2** (5.2 g, 98%). **^{1}H-NMR (400 MHz, CD_3OD)**: δ 7.78 (d, *J* = 8.5 Hz, 2H, H-Ar), 7.45 (d, *J* = 8.5 Hz, 1H, H-2), 5.95 (d, *J* = 1.6 Hz, 1H, H-1), 4.09 (ddd, *J* = 1.4 Hz and 6.9 Hz, 1H, H-6), 4.0 (dd, *J* = 1.4 Hz and 6.9 Hz, 1H, H-7a), 3.91 (dd, *J* = 6.6 Hz and 9.4 Hz, 1H, H-7b), 3.87 (d, *J* = 9.6 Hz, 1H, H-4), 3.79 (m, 1H, H-2), 3.71 (dd, *J* = 3.4 Hz and 9.6 Hz, 1H, H-3), 3.60 (dd, *J* = 1.1 Hz and 9.9 Hz, 1H, H-5), 2.45 (s, 3H, CH_3-Ts), 2.09 (s, 3H, $\underline{CH_3}COO$). **^{13}C-NMR (100 MHz, CD_3OD)**: δ 170.7 (Cq), 146.6 (Cq-Ar), 134.2 (Cq-Ar), 131.1 (-CH=), 129.0 (-CH=), 95.1 (C-1), 74.2 (C-5), 72.5 (C-3), 71.1 (C-7), 71.0 (C-2), 67.4 (C-6), 66.9 (C-4), 21.6 (CH_3-Ts), 20.9 ($\underline{CH_3}COO$). **HRMS (ESI+)**: calc. for $C_{16}H_{22}NaO_{10}S$ $[M+Na]^+$: 429.0826; found: 429.0835.

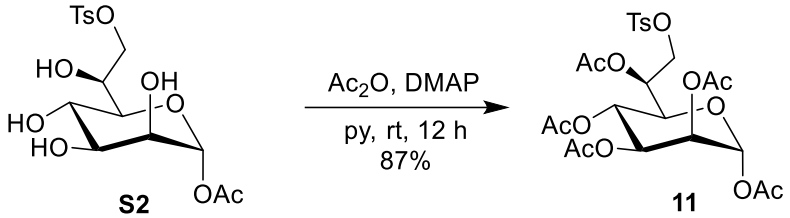
1-*O*-Acetyl-7-azido-7-deoxy-L-*glycero*-α-D-*manno*-heptopyranoside (10)



To a solution of NaN_3 (5.1 g, 7.0 equiv., 77.7 mmol) in water (20 mL), was added a solution of compound **S2** (4.5 g, 1.0 equiv., 11.1 mmol) in 20 mL acetone. The reaction was warmed to 80 °C in a heating mantle with stirring behind a blast shield overnight. Upon cooling to r.t., the solvent was removed under vacuum. The solid was dissolved in 100 mL DCM. The white precipitate was removed by filtration through a plug of celite under suction and the solvent was evaporated under vacuum. This crude **10** (98%, 3.0 g) was directly used for the next step without further purification. **^{1}H-NMR (400 MHz, $CDCl_3$)**: δ 6.00 (d, *J* = 1.8 Hz, 1H, H-1), 4.01 (ddd, *J* = 1.6 Hz and 3.4 Hz,

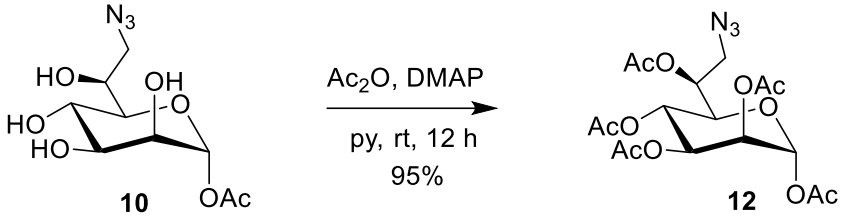
1H, H-6), 3.92 (t, *J* = 9.6 Hz, 1H, H-4), 3.81 (m, 1H, H-2), 3.73 (dd, *J* = 3.4 Hz and 9.4 Hz, 1H, H-3), 3.55 (dd, *J* = 1.6 Hz and 9.9 Hz, 1H, H-5), 3.41 (dd, *J* = 7.3 Hz, 12.1 Hz, 1H, H-7a), 3.28 (dd, *J* = 7.3 Hz and 12.1 Hz, 1H H-7b), 2.1 (s, 3H, C*H*$_3$COO). **^{13}C-NMR (100 MHz, CDCl$_3$)**: δ 170.7 (CH$_3$COO), 95.4 (C-1), 75.3 (C-5), 69.1 (C-3), 67.2 (C-6), 54.5 (C-4), 54.5 (C-7), 20.8 (CH$_3$COO). **HRMS (ESI+)**: calc. for $C_9H_{15}N_3NaO_7$ $[M+Na]^+$: 300.0802; found: 300.0812.

1,2,3,4,6-Penta-*O*-acetyl-7-*O*-tosyl-L-*glycero*-α-D-*manno*-heptopyranoside (11)



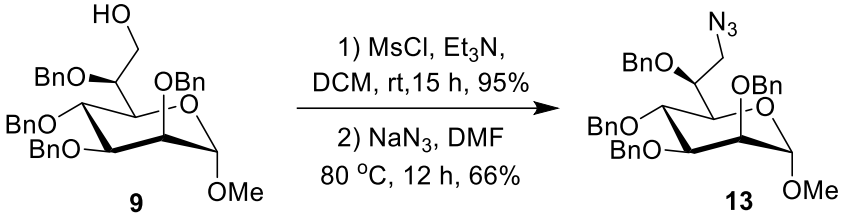
To a solution of **S2** (2.3 g, 1.0 equiv., 5.7 mmol) in distilled and anhydrous pyridine (12 mL) were added DMAP (75 mg, 0.1 equiv., 0.6 mmol) and acetic anhydride (3.4 mL, 8.0 equiv., 45.6 mmol) at 0 °C, under argon. Then the reaction was warmed to room temperature and stirred overnight. The mixture was diluted in 100 mL of ethyl acetate, the organic phase was washed with sat. aq. $NaHCO_3$ soln. (50 mL × 2), HCl (1 M, 50 mL × 2) and brine (75 mL), dried over $MgSO_4$, filtered and concentrated. The residue was purified by silica-gel column chromatography (cyclohexane/ethyl acetate = 7:3 to 1:1) to give compound **11** as a colorless syrup (2.83g, 87%). **^{1}H-NMR (400 MHz, CDCl$_3$)**: δ 7.75 (d, *J* = 8.4 Hz, 2H, H-Ar), δ 7.35 (d, *J* = 8.4 Hz, 2H, H-Ar), 6.10 (d, *J* = 1.8 Hz, 1H, H-1), 5.33 (dd, *J* = 3.9 Hz and 9.9 Hz, 1H, H-3), 5.31 (d, *J* = 9.6 Hz, 1H, H-2), 5.27 (m, 1H, H-4), 5.16 (ddd, *J* = 1.9 Hz and 7.9 Hz, 1H, H-7a), 4.20 (dd, *J* = 1.8 Hz and 9.7 Hz, 1H, H-7b), 4.10 (m, 1H, H-6), 3.96 (dd, *J* = 6.1 Hz and 9.4 Hz, 1H, H-5), 2.44 (s, 3H, CH$_3$-Ts), 2.20 (s, 3H, CH$_3$COO), 2.17 (s, 3H, CH$_3$COO), 2.07 (s, 3H, CH$_3$COO), 2.02 (s, 3H, CH$_3$COO), 1.99 (s, 3H, CH$_3$COO). **^{13}C-NMR (100 MHz, CDCl$_3$)**: δ170.0, 169.98, 169.9, 169.7, 168.3, 145.4, 132.3, 130.2, 128.2, 90.4, 69.4, 69.2, 68.6, 66.4, 65.3, 64.4, 21.8, 20.95, 20.9, 20.74, 20.7, 20.66. **HRMS (ESI+)**: calc. for $C_{24}H_{30}NaO_{14}S$ $[M+Na]^+$: 597.1256; found: 597.1258.

1,2,3,4,6-Penta-*O*-acetyl-7-azido-7-deoxy-L-*glycero*-α-D-*manno*-heptopyranoside (12)



Compound **10** (5 g, 1.0 equiv., 18.1 mol) was dissolved in anhydrous pyridine (40 mL) at 0 °C under argon. DMAP (219 mg, 0.1 equiv., 1.8 mmol) and acetic anhydride (13.6 mL, 8.0 equiv., 181 mmol) was subsequently added at 0 °C. The reaction mixture was warmed to room temperature and stirred overnight. The solution was diluted with 200 mL CH_2Cl_2, the organic phase was washed with sat. aq. $NaHCO_3$ soln. (150 mL × 2), HCl (1 M,150 mL × 2) and brine (250 mL), dried over $MgSO_4$, filtered and concentrated. The residue was purified by silica-gel column chromatography (cyclohexane/ethyl acetate = 7:3 to 1:1) to give compound **12** as a colorless syrup (7.7 g, 95%). **$[\alpha]_D^{20}$** = +34. 4 (c 1.2, CH_3Cl). **^{1}H-NMR (400 MHz, $CDCl_3$)**: δ 6.11 (d, *J* = 1.84 Hz, 1H, H-1), 5.34 (d, *J* = 2.5 Hz, 1H, H-4), 5.32 (d, *J* = 3.9 Hz, 1H, H-3), 5.27 (t, *J* = 1.9 Hz, 1H, H-2), 5.05 (ddd, *J* = 1.8 Hz, 7.6 Hz and 14.6 Hz, 1H, H-6), 4.10 (m, 2H, H-7), 3.49 (m, 1H, H-5), 2.19 (s, 3H, $\underline{CH_3}COO$), 2.16 (s, 3H, $\underline{CH_3}COO$), 2.13 (s, 3H, $\underline{CH_3}COO$), 2.03 (s, 3H, $\underline{CH_3}COO$), 1.99 (s, 3H, $\underline{CH_3}COO$). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 170.2 (Cq), 170.0 (Cq), 169.8 (Cq), 169.6 (Cq), 168.1 (Cq), 90.8 (C-1), 70.1 (C-5), 69.1 (C-4), 68.5 (C-2), 67.5 (C-6), 54.5 (C-2), 49.2 (C-7), 20.9 ($\underline{CH_3}COO$), 20.86 ($\underline{CH_3}COO$), 20.8 ($\underline{CH_3}COO$), 20.78 ($\underline{CH_3}COO$), 20.7 ($\underline{CH_3}COO$). **HRMS (ESI+)**: calc. for $C_{17}H_{23}N_3NaO_{11}$ $[M+Na]^+$: 468.1226; found: 468.1225.

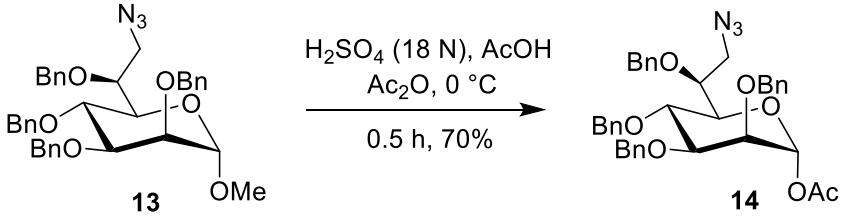
1-*O*-Methyl-7-azido-7-deoxy-2,3,4,6-tetra-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranoside (13)



A solution of **9** (5.28 g, 1.0 equiv., 9.0 mmol) and DMAP (110.4 mg, 0.1 equiv., 0.9 mmol) in dry DCM (50 mL), was stirred at 0 °C in an ice bath. A solution of methylsulfonyl chloride (3.09 g, 3.0 equiv., 27.0 mmol) in dry DCM (10 mL) was added dropwise by syringe pump, then

followed a slow addition of Et_3N (5.6 mL, 4.5 eq., 40.5 mmol) at 0 °C. The reaction was warmed to room temperature and stirred overnight. The solvent was then removed in vacuo to afford a yellow syrup. The crude material was purified by flash chromatography over silica gel (cyclohexane/ethyl acetate 80:20) to obtain the desired mesylation compound (5.66 g, 95%). To the intermediate mesylate (1.0 eq, 8.55 mmol) in 45 mL DMF, was then added NaN_3 (3.89 g, 7.0 eq., 59.9 mmol) at room temperature. The reaction mixture was warmed to 80 °C in an oil bath overnight. After cooling down, the solution was diluted with 200 mL EtOAc, the organic phase was washed with water (150 mL × 2) and brine (300 mL), dried over $MgSO_4$ and concentrated. The residue was purified by silica-gel column chromatography (cyclohexane/ethyl acetate = 8:2 to1:1) to give compound **13** as a colorless syrup (3.43 g, 66%). **^{1}H-NMR (400 MHz, $CDCl_3$)**: δ 7.39-7.19 (m, 20H, Ar-H), 4.93 (d, *J* = 11.0 Hz, 1H, CH_2Ph), 4.84 (d, *J* = 2.4 Hz, 1H, H-1), 4.77-4.73 (m, 2H, CH_2Ph), 4.58 (m, 2H, CH_2Ph), 4.52 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.37 (s, d, *J* = 12.4 Hz, CH_2Ph), 4.16 (t, *J* = 8.4 Hz, 1H, H-4), 3.98 (ddd, *J* = 3.2 Hz and 9.4 Hz, 1H, H-6), 3.90 (dd, *J* = 1.1 Hz and 9.6 Hz, 1H, H-3), 3.72-3.65 (m, 2H, H-5 and H-7a), 3.49 (dd, *J* = 8.0 Hz and 12.4 Hz, 1H, H-7b), 3.32 (s, 3H, -OCH_3). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 138.7 (Cq-Ar), 138.4 (Cq-Ar), 138.35 (Cq-Ar), 138.0 (Cq-Ar), 128.5 (-CH=), 128.4 (-CH=), 128.39 (-CH=), 127.9 (-CH=), 127.87 (-CH=), 127.8 (-CH=), 127.77 (-CH=), 127.7 (-CH=), 127.6 (-CH=), 127.61 (-CH=), 99.6 (C-1), 80.7 (C-3), 75.3 (C-6), 74.6 (CH_2Ph), 74.3 (C-4), 74.2 (C-2), 73.1 (CH_2Ph), 72.6 (CH_2Ph), 72.0 (CH_2Ph), 71.3 (C-5), 55.1 (OCH_3), 51.3 (C-7). **HRMS (ESI+)**: calc. for $C_{36}H_{39}N_3NaO_6$ $[M+Na]^+$: 632.2731; found: 632.2732.

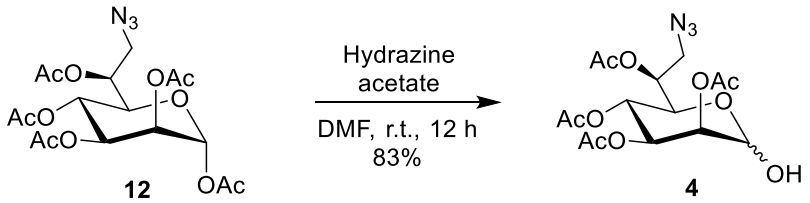
1-*O*-Acetyl-7-azido-7-deoxy-2,3,4,6-tetra-*O*-benzyl-L-*glycero*-α-D-*manno*-heptopyranoside (14)



To a solution of **13** (2.0 g, 1.0 equiv., 3.28 mmol) in AcOH (8.9 mL, 46.0 equiv., 150.9 mmol) was added acetic anhydride (2.7 mL, 9.0 equiv., 29.5 mmol) under argon at 0 °C. Concentrated H_2SO_4 (18 N, 0.3 mL) was added dropwise at 0 °C. The reaction was stirred for 30 min at 0 °C. The reaction mixture was poured into ice water (100 mL) and the aqueous phase was extracted

with ethyl acetate (200 mL × 3). The combined organic phases were washed with water (100 mL × 2), sat. aq. $NaHCO_3$ (100 mL × 2) and dried over $MgSO_4$, filtered, concentrated to give a colorless solid. The residue was purified by silica gel flash column chromatography (cyclohexane/ethyl acetate 70:30) to afford compound **14** (1.47 g, 70%) as a colorless syrup. **^{1}H-NMR (400 MHz, $CDCl_3$)**: δ 7.41-7.20 (m, 20H, Ar-H), 6.26 (d, *J* = 2.4 Hz, 1H, H-1), 4.93 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.80 (d, *J* = 12.4 Hz, 1H, CH_2Ph), 4.70 (d, *J* = 12.4 Hz, 2H, CH_2Ph), 4.55-4.49 (m, 2H, CH_2Ph), 4.40 (d, *J* = 12.2 Hz, 1H, CH_2Ph), 4.22 (t, *J* = 8.4 Hz, 1H, H-4), 3.94-3.88 (m, 2H, H-6 and H-3), 3.80 (dd, *J* = 3.6 and 8.4 Hz, 1H, H-5), 3.75 (t, *J* = 2.4 Hz, 1H, H-2), 3.53-3.49 (m, 2H, H-7), 2.03 (s, 3H, OMe). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 169.0 (Cq-Ac), 138.5 (Cq-Ar), 138.0 (Cq-Ar), 137.9 (Cq-Ar), 137.85 (Cq-Ar), 128.6 (-CH=), 128.5 (-CH=), 128.4 (-CH=), 128.1 (-CH=), 128.0 (-CH=), 127.9 (-CH=), 127.8 (-CH=), 127.77 (-CH=), 91.7 (C-1), 79.8 (C-6), 75.2 (CH_2Ph), 74.9 (C-3), 73.7 (C-4), 73.3 (C-5), 73.2 (C-2), 72.8 (CH_2Ph), 72.5 (CH_2Ph), 72.1 (CH_2Ph), 50.5 (C-7), 21.1(CH_3). **HRMS (ESI+)**: calc. for $C_{37}H_{39}N_3NaO_7$ $[M+Na]^+$: 660.2684; found: 660.2685.

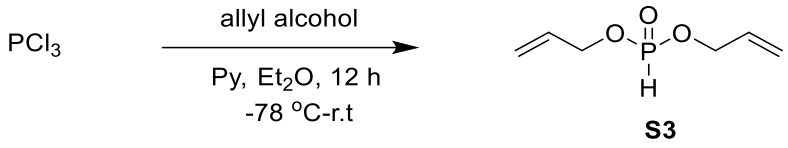
1,2,3,4,6-Penta-*O*-acetyl-7-azido-7-deoxy-*L-glycero*-α-D-*manno*-heptopyranose (4)



To a solution of **12** (6.0 g, 1.0 equiv., 13.5 mmol) in 30 mL of dry DMF was added solid hydrazine acetate (1.4 g, 1.1 equiv., 14.9 mmol) under argon. The reaction mixture was stirred for overnight at room temperature, diluted with ethyl acetate (100 mL), washed with HCl (1 M, 75 mL × 3) and brine (100 mL × 3), dried over $MgSO_4$ and concentrated. The residue was purifed by silica-gel column chromatography (cyclohexane/ethyl acetate = 7:3 to 4:6) to give compound **4** (4.5 g, 83%) as a colorless syrup. **^{1}H-NMR (400 MHz, $CDCl_3$)**: δ 5.40 (dd, *J* = 3.0 Hz and 10.1 Hz, 1H, H-3), 5.30 (m, 3H, H-1, H-2 and H-4), 5.13 (ddd, *J* = 2.1 Hz, 7.1 Hz and 14.6 Hz, 1H, H-6), 4.31 (dd, *J* = 2.1 Hz and 10.1 Hz, 1H, H-5), 3.49 (m, 2H, H-7), 2.17 (s, 3H, $\underline{CH_3}COO$), 2.14 (s, 3H, $\underline{CH_3}COO$), 2.03 (s, 3H, $\underline{CH_3}COO$), 1.99 (s, 3H, $\underline{CH_3}COO$). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 170.4 (Cq), 170.3 (Cq), 170.1 (Cq), 169.9 (Cq), 92.8 (C-1), 70.6 (C-5), 69.1 (C-4), 68.4 (C-2), 68.1 (C-6), 65.2 (C-4), 49.7 (C-7), 21.1 ($\underline{CH_3}COO$), 20.9 ($\underline{CH_3}COO$), 20.8 ($\underline{CH_3}COO$ × 2). **HRMS**

(ESI+): calc. for $C_{15}H_{21}N_3NaO_{10}$ $[M+Na]^+$: 426.1098; found: 426.1119.

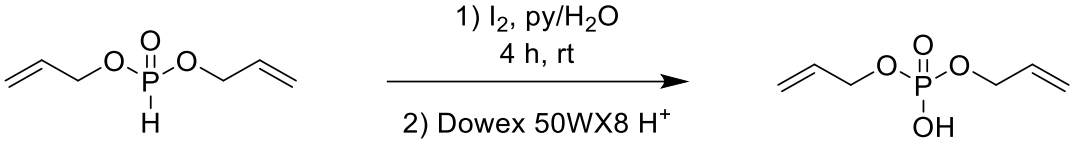
Diallylphosphite (S3)



S3

To a solution of PCl_3 (30.0 mL, 1.0 equiv., 343.6 mmol) in anhydrous ether (1200 mL) at -78 °C, allyl alcohol (46.9 mL, 2.0 equiv. 687.4 mmol) was added under argon. A solution of pyridine (56.0 mL, 2.0 equiv., 687.4 mmol) in 300 mL anhydrous ether was added dropwise to the mixture at -78 °C. After addition, the reaction was allowed to warm to room temperature for overnight. The reaction was quenched with 20 mL water at -78 °C. The aqueous phase was extracted with ethyl acetate (150 mL × 2). The combined organic phases were washed with brine (300 mL × 3), dried over $MgSO_4$, filtered, and concentrated to give a colorless liquid. The residue was purified by silica gel flash column chromatography (cyclohexane/ethyl acetate 80:20 to 50:50) to afford compound **S3** (44.0 g, 79%) as a colorless liquid. This compound is known and its characterization data are in accordance with the reference report.[2] **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.87 (d, $J_{H\text{-}P}$ = 701.4 Hz, 1H, H-P), 5.90 (m, 2H, H-2'), 5.38 (m, 1H, H-3'), 5.34 (m, 1H, H-3'), 5.26 (m, 1H, H-3'), 5.24 (m, 1H, H-3'), 4.56 (m, 4H, H-1'). **^{31}P NMR (162 MHz, $CDCl_3$):** δ 8.3 (s, 1P). **HRMS (ESI+)**: calc. for $C_6H_{11}NaO_3P$ $[M+Na]^+$: 185.0338, found: 185.0369

Diallylphosphate (S4)

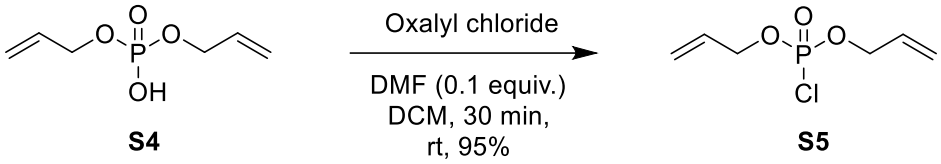


S3 **S4**

To a solution of diallyl phosphite **S3** (1.0 g, 1.0 equiv., 6.2 mmol) in pyridine (27 mL) at 0 °C, iodine (4.7 g, 3.0 equiv., 18.6 mmol) and water (3 mL) were slowly added, sequentially, under argon. The reaction mixture was warmed to room temperature and stirred for 6 h. The reaction was stopped by adding a saturated solution of sodium sulfite (25 mL) at 0 °C until the dark red solution turned pale yellow. The aqueous phase was acidified to pH = 1 with aq. HCl (5 M) and extracted with ethyl acetate (3 × 50 mL). The combined organic phases were dried over $MgSO_4$, filtered, concentrated to give a colorless liquid. The residue was passed through a Dowex® resin (50-WX8,

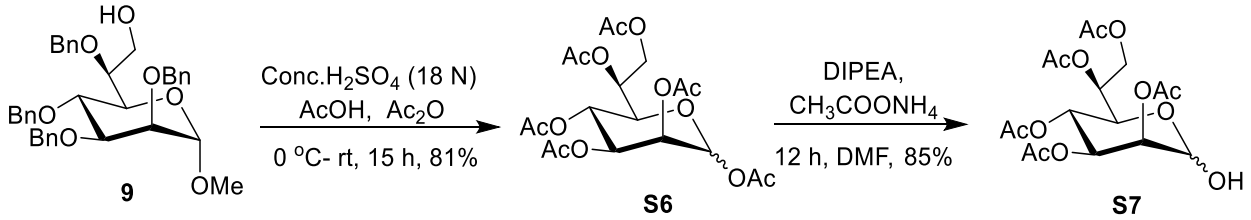
H^+ form) to afford diallyl phosphate **S4** (893 mg, 81%) as a yellow oil. This compound is known and its characterization data are in accordance with the reference report.[2] **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.92 (m, 2H, H-2), 5.38 (m, 1H, H-3), 5.34 (m, 1H, H-3), 5.25 (m, 1H, H-3), 5.22 (m, 1H, H-3), 4.51 (m, 4H, H-1). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 132.4 (d, $J_{2\text{-P}}$ = 6.7 Hz, 2C, C-2), 118.5 (2C, C-3), 68.3 (d, $J_{1\text{-P}}$ = 4.8 Hz, 2C, C-1). **^{31}P NMR (162 MHz, $CDCl_3$):** δ 1.3. **HRMS (ESI+):** calc. for $C_6H_{11}N_8O_4P$ $[M\text{-}H]^-$: 177.0322; found:177.0324.

Diallyl chlorophosphate (S5)



To a solution of oxalyl chloride (290 µL, 3.0 equiv., 3.4 mmol) in anhydrous DCM (5 mL) at 0 °C, was added DMF (12 µL, 0.1 equiv., 0.15 mmol) under argon. The solution mixture was warmed to room temperature and stirred for 10 min. To this mixture was added a solution of diallyl phosphate **S4** (203 mg, 1.0 equiv., 1.13 mmol) in DCM (5 mL) during 5 min. The reaction was complete after 20 min as indicated by the ^{31}P-NMR spectrum of an aliquot of the crude material that indicated percentage conversion of 95% in the desired diallyl chlorophosphate. The solution was concentrated under reduced pressure at room temperature. Then, the residue was dried in high vacuum (oil pump), at least during 15 min, to afford diallyl chlorophosphate **S5** as a colorless oil. This product was directly employed in the phosphorylation step without any further purification. This compound is known and its characterization data are in accordance with the reference report.[2] **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.96 (m, J = 5.7 Hz, 2H, H-2), 5.44 (m, 1H, H-3), 5.40 (m, 1H, H-3), 5.34 (m, 1H, H-3), 5.31 (m, 1H, H-3), 4.67 (m, 4H, H-1). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 131.1 (d, $J_{2\text{-P}}$ = 7.7 Hz, 2C, C-2), 119.8 (2C, C-3), 70.0 (d, $J_{1\text{-P}}$ = 6.7 Hz, 2C, C-1). **^{31}P NMR (162 MHz, $CDCl_3$):** δ 5.5.

2,3,4,6,7-Penta-*O*-acetyl-L-*glycero*-α/β-D-*manno*-heptopyranoside (S7)

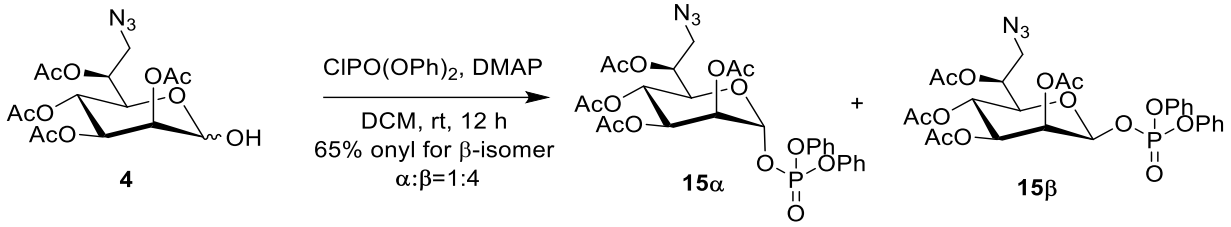


To a solution of **9** (5.0 g, 1.0 equiv., 8.55 mmol) in AcOH (16.1 mL, 21 equiv., 179.6 mmol) /Ac_2O (75 mL) at 0 °C, was added concentrated H_2SO_4 (18 N, 4.0 mL, 3.0 equiv.) over 30 min. The reaction was then allowed to warm to room temperature and the stirring was continued overnight. After 15 hours the reaction mixture was poured into ice water (100 mL) and the aqueous phase was extracted with ethyl acetate (150 mL × 3). The combined organic phases were washed with water (150 mL × 2), sat. aq. $NaHCO_3$ (150 mL × 2) and dried over $MgSO_4$, filtered, concentrated to give a white solid. The residue was purified by silica gel flash column chromatography (cyclohexane/ethyl acetate 60:40) to afford compound **S6** (3.2 g, 81%) as a colorless syrup. This compound is known and its characterization data are in accordance with the reference report.[3] **$[\alpha]_D^{20}$** = +22.8 (c 1, CH_3Cl). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 6.08 (d, $J_{1\text{-}2}$ = 1.6 Hz, 1H, H-1), 5.36 (m, 2H, H-3 and H-4), 5.29 -5.21(m, 2H, H-2 and H-6), 4.26 (dd, $J_{7a\text{-}6}$ = 7.3 Hz, $J_{7a\text{-}7b}$ =11.7 Hz, 1H, H-7a), 4.17 (dd, $J_{7b\text{-}6}$ = 7.3 Hz and $J_{7b\text{-}7a}$ =11.7 Hz, 1H, H-7b), 4.10 (m, 1H, H-5), 2.19 (s, 3H, $\underline{CH_3}COO$), 2.16 (s, 3H, $\underline{CH_3}COO$), 2.13 (s, 3H, $\underline{CH_3}COO$), 2.02 (s, 6H, 2 × $\underline{CH_3}COO$), 1.99 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170.5 (Cq), 170.3 (Cq), 170.0 (Cq), 169.8 (Cq), 169.5 (Cq), 167.9 (Cq), 91.8 (C-1), 70.9, 69.0, 68.4, 66.9, 64.4, 62.4, 62.41, 62.2, 20.9 ($\underline{CH_3}COO$), 20.8 ($\underline{CH_3}COO$), 20.76 ($\underline{CH_3}COO$), 20.7 ($\underline{CH_3}COO$), 20.67 ($\underline{CH_3}COO$), 20.6 ($\underline{CH_3}COO$). **HRMS (ESI+):** calcd. for $C_{19}H_{26}O_{13}Na$ $[M+Na]^+$: 485.1266, found: 485.1250.

A solution of **S6** (2.5 g, 1.0 equiv., 5.4 mmol) in a mixture of dry DMF (25 mL) and *N, N*-diisopropylethylamine (2.7 mL, 5.0 equiv., 27.1 mmol) was stirred with ammonium acetate (1.7 g, 4.0 equiv., 21.6 mmol, which was prewashed with dry ether and dried over high vacuum pump for 12 h at 40 °C) overnight. The reaction mixture was filtered to remove the undissolved crystrals of ammonium acetate, then diluted by CH_2Cl_2 (100 mL) and washed with HCl (1 M, 100 mL × 2), sat. aq. $NaHCO_3$ soln. (100 mL × 2), and brine (100 mL), dried over $MgSO_4$ and concentrated under diminished pressure. The residue was purified by silica-gel column chromatography (cyclohexane/ethyl acetate 70:30 to 40:60) to give compound **S7** (1.9 g, 85%) as a white solid. This compound is known and its characterization data are in accordance with the reference report.[3] **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.39 (dd, *J* = 3.4 Hz, 10.3 Hz, 1H), 5.32-5.26 (m, 3H), 5.22 (ddd, *J* =2.1 Hz, 5.5 Hz, 7.1 Hz, 1H), 4.04 (dd, *J* = 5.7 Hz, 11.5 Hz, 1H, H-7a), 4.25 (dd, *J* = 2.1 Hz, 10.1 Hz, 1H), 4.15 (dd, *J* = 6.9 Hz, 11.5 Hz, 1H, 7b), 2.17 (s, 3H, $\underline{CH_3}COO$), 2.14 (s, 3H, $\underline{CH_3}COO$), 2.06 (s, 3H, $\underline{CH_3}COO$), 2.02 (s, 3H, $\underline{CH_3}COO$), 1.99 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 171.4 (Cq), 170.4 (Cq), 170.37 (Cq), 170.1 (Cq), 169.8 (Cq), 92.6 (C-1), 70.2 (C-5),

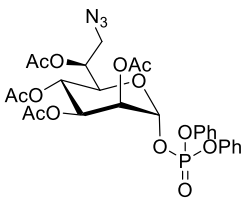
69.2 (C-4), 68.5 (C-2), 67.2 (C-6), 65.1 (C-3), 62.6 (C-7), 21.1 (<u>CH</u>$_3$COO), 20.9 (<u>CH</u>$_3$COO), 20.8 (<u>CH</u>$_3$COO), 20.76 (<u>CH</u>$_3$COO), 20.7 (<u>CH</u>$_3$COO). **HRMS (ESI+):** calc. for $C_{17}H_{24}NaO_{12}$ $[M+Na]^+$: 443.1160; found: 443.1145.

Diphenyl(2,3,4,6-tetra-*O*-acetyl-7-deoxy-7-azido-L-*glycero*-α/β-D-*manno*-heptopyranosyl) phosphate (15α and 15β)



In a 50 mL round bottom two-neck flask, a solution of **4** (100 mg, 1.0 equiv., 0.25 mmol) and DMAP (305.5 mg, 10.0 equiv., 2.5 mmol) in anhydrous DCM (10 mL) was stirred under argon at room temperature. After 15 min, a solution of diphenyl chlorophosphate (400 µL, 7.5 equiv., 1.93 mmol) in anhydrous DCM (20 mL, C = 0.2 M) was added with a syringe pump (0.7 mL/h) at room temperature. After 12 h, 8.4 mL of the solution of diphenyl chlorophosphate was added (corresponding to 0.82 mmol diphenyl chlorophosphate). The solution was diluted with a saturated sodium bicarbonate solution (30 mL) and extracted with DCM (25 mL × 3). Combined organic phases were dried over $MgSO_4$, filtered, concentrated to obtain a colorless solid. The ratio of α-phosphate/β-phosphate was 1:4 from the crude ^{31}P-NMR. The crude material was purified by flash chromatography using cyclohexane/ethyl acetate 90:10 to 60:40 as a gradient eluent to afford α-phosphate **15α** (26 mg, 16%) and β-phosphate **15β** (102 mg, 65%) as colorless syrup.

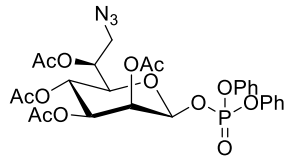
Diphenyl(2,3,4,6-tetra-*O*-acetyl-7-azido-7-deoxy-L-*glycero*-α-D-*manno*-heptopyranosyl) phosphate (15α)



^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 5H, H-Ar), 7.22 (m, 5H, H-Ar), 5.86 (dd, *J* = 1.6 Hz and 6.4 Hz, 1H, H-1), 5.32 (m, 3H, H-2, H-3 and H-4), 5.15 (m, 1H, H-6), 5.13 (dd, *J* = 1.6 Hz and 9.9 Hz, 1H, H-5), 3.45 (dd, *J* = 4.6 Hz and 13.2 Hz, 1H, H-7a), 3.15 (dd, *J* = 4.6 Hz and 13.2 Hz, 1H, H-7b), 2.17 (s, 3H, <u>CH</u>$_3$COO), 2.13 (s, 3H, <u>CH</u>$_3$COO), 2.03 (s, 3H, <u>CH</u>$_3$COO), 1.99 (s, 3H, <u>CH</u>$_3$COO). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 170.2 (Cq), 169.8 (Cq), 169.6 (Cq), 169.5 (Cq), 150.2 (d, *J* = 7.6 Hz, 1C, Cq-Ar), 150.0 (d, *Jc-p* = 7.6 Hz, 1C, Cq-Ar), 130.2

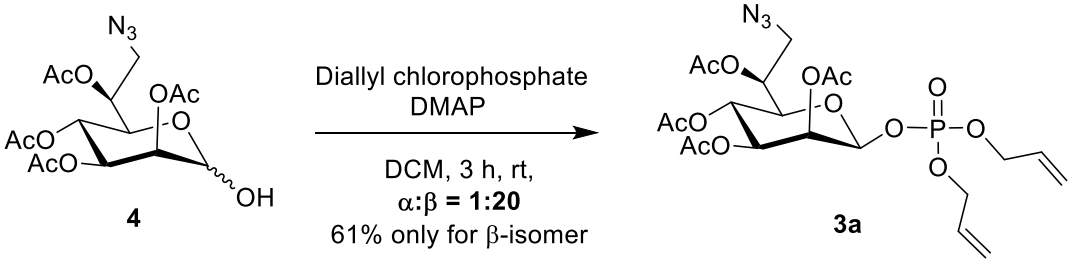
(CH-Ar), 126.1 (CH-Ar), 120.2-120.0 (CH-Ar), 96.2 (d, J = 5.8 Hz, 1C, C-1), 71.4 (C-3), 68.8 (d, J = 10.5 Hz, 1C, C-2), 68.5 (C-5), 67.2 (C-6), 64.5 (C-4), 50.5 (C-7), 20.8 ($\underline{CH_3}COO$), 20.7 ($\underline{CH_3}COO$ × 2), 20.68 ($\underline{CH_3}COO$). **^{31}P-NMR (162 MHz, $CDCl_3$)**: δ -13.2. **HRMS (ESI+):** calc. for $C_{27}H_{30}N_3NaO_{13}P$ $[M+Na]^+$: 658.1408; found: 658.1409.

Diphenyl(2,3,4,6-tetra-*O*-acetyl-7-azido-7-deoxy-L-*glycero*-β-D-*manno*-heptopyranosyl) phosphate (15β)



^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.38-7.14 (m, 10H, 5.53 (d, $J_{1\text{-}p}$ = 7.1 Hz, 1H, H-1), 5.50 (d, J = 3.2 Hz,1H, H-2), 5.26 (t, J = 9.6 Hz, 1H, H-4), 5.10 (ddd, J = 2.1 Hz, 6.2 Hz and 13.7 Hz, 1H, H-6), 5.04 (dd, J = 3.2 Hz and 10.1 Hz, 1H, H-3), 3.74 (dd, J = 3.0 Hz and 9.9 Hz, 1H, H-5), 3.35 (dd, J = 6.2 Hz and 12.6 Hz, 1H, H-7a), 3.30 (dd, J = 6.2 Hz and 12.6 Hz, 1H, H-7b), 2.14 (s, 3H, $\underline{CH_3}COO$), 2.12 (s, 3H, $\underline{CH_3}COO$), 2.03 (s, 3H, $\underline{CH_3}COO$), 2.02 (s, 3H, $\underline{CH_3}COO$). **^{13}C-NMR (100 MHz, $CDCl_3$)**: δ 170.2 (Cq), 169.9 (Cq), 169.8 (Cq), 169.5 (Cq), 150.3 (d, J = 7.7 Hz, 1C, Cq-Ar), 150.0 (d, J = 7.7 Hz, 1C, Cq-Ar), 130.0 (CH-Ar), 129.9 (CH-Ar), 126.0 (CH-Ar), 125.9 (CH-Ar), 120.6 (CH-Ar), 120.5 (CH-Ar), 120.3 (CH-Ar), 95.4 (d, J = 4.8 Hz, 1C, C-1), 73.3 (C-5), 70.6 (C-3), 68.3 (d, J = 8.6 Hz, 1C, C-2), 67.3 (C-6), 64.1 (C-4), 49.8 (C-7), 20.8 ($\underline{CH_3}COO$), 20.7 ($\underline{CH_3}COO$), 20.67 ($\underline{CH_3}COO$), 20.5 ($\underline{CH_3}COO$). **^{31}P-NMR (162 MHz, $CDCl_3$)**: δ -13.4. **HRMS (ESI+)**: calc. for $C_{27}H_{30}N_3NaO_{13}P$ $[M+Na]^+$: 658.1408; found: 658.1416.

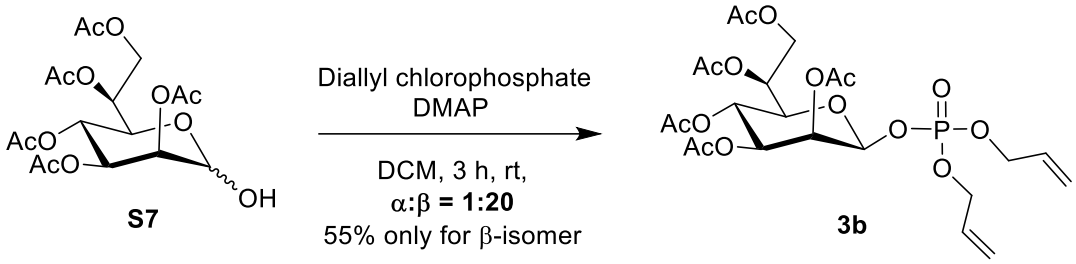
Diallyl(2,3,4,6,-tetra-*O*-acetyl-7-azido-7-deoxy-L-*glycero*-β-D-*manno*-heptopyranosyl) phosphate (3a)



In a two-neck round bottom flask, DMAP (166.2 mg, 10.0 equiv., 1.36 mmol) was added under argon at room temperature to a solution of **4** (55 mg, 1.0 equiv., 0.14 mmol) in anhydrous DCM (5 mL) was stirred under argon at room temperature. After 15 min, a solution of diallyl chlorophosphate **S5** (7.5 equiv., 1.0 mmol) in anhydrous DCM (5 mL, C = 0.2 M) was added with a syringe pump (injection rate 1.6 mL/h in a 12 mL syringe) at room temperature. After 3 hours the reaction mixture was diluted with sat. $NaHCO_3$ (15 mL) and extracted with DCM (3 × 10 mL).

The combined organic phases were dried over $MgSO_4$, filtered, concentrated to give a colorless solid. The residue was purified by silica gel flash column chromatography (cyclohexane/ethyl acetate 90:10 to 40:60) to afford compound **3a** (47 mg, 61%) as a colorless syrup. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.91 (m, 2H, H-2'), 5.52 (d, $J_{2\text{-}3}$ = 3.4 Hz, 1H, H-2), 5.44 (dd, $J_{1\text{-}2}$ = 0.9 Hz, $J_{1\text{-}P}$ =7.6 Hz, 1H, H-1), 5.40 (m, 2H, H-3'), 5.37 (m, 1H, H-3'), 5.36 (m, 1H, H-3'), 5.33 (m, 1H, H-3'), 5.27 (t, $J_{4\text{-}3}$ = $J_{4\text{-}5}$ =10.1 Hz, 1H, H-4), 5.24 (m, 1H, H-3'), 5.14 (ddd, $J_{6\text{-}5}$ = 2.3 Hz, 8.5 Hz, 1H, H-6), 5.06 (dd, $J_{3\text{-}2}$ = 3.4 Hz, $J_{3\text{-}4}$ = 10.1 Hz, 1H, H-3), 4.56 (m, 4H, H-1'), 3.74 (dd, $J_{5\text{-}6}$ = 2.3 Hz, $J_{5\text{-}4}$ = 10.1 Hz, 1H, H-5), 3.58 (dd, $J_{7a\text{-}6}$ = 7.2 Hz, $J_{7a\text{-}7b}$ = 12.4 Hz, 1H, H-7a), 4.17 (dd, $J_{7b\text{-}6}$ = 7.2 Hz, $J_{7b\text{-}7a}$ = 12.4 Hz, 1H, H-7b), 2.20 (s, 3H, $\underline{CH_3}COO$), 2.13 (s, 3H, $\underline{CH_3}COO$), 2.02 (s, 3H, $\underline{CH_3}COO$), 1.97 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170. 3 (Cq), 170.1 (Cq), 169.9 (Cq), 169.6 (Cq), 132.0 (d, $J_{2'\text{-}P}$ = 7.7 Hz, 1C, C-2'), 131.9 (d, $J_{2'\text{-}P}$ = 7.7 Hz, 1C, C-2'), 119.0 (C-3'), 118.9 (C-3'), 94.7 (d, $J_{1\text{-}P}$ = 3.8 Hz, 1C, C-1), 73.2 (C-5), 70.8 (C-3), 68.9 (d, $J_{1'\text{-}P}$ = 5.8 Hz, 1C, C-1'), 68.85 (d, $J_{1'\text{-}P}$ = 5.8 Hz, 1C, C-1'), 68.6 (d, $J_{2\text{-}P}$ = 8.6 Hz, 1C, C-2), 67.3 (C-6), 64.1 (C-4), 49.8 (C-7), 20.84 ($\underline{CH_3}COO$), 20.8 ($\underline{CH_3}COO$), 20.7 ($\underline{CH_3}COO$), 20.6 ($\underline{CH_3}COO$).**^{31}P NMR (162 MHz, $CDCl_3$):** δ -2.3. **HRMS (ESI+):** calc. for $C_{21}H_{30}N_3NaO_{13}P$ $[M+Na]^+$: 586.1408; found: 586.1416.

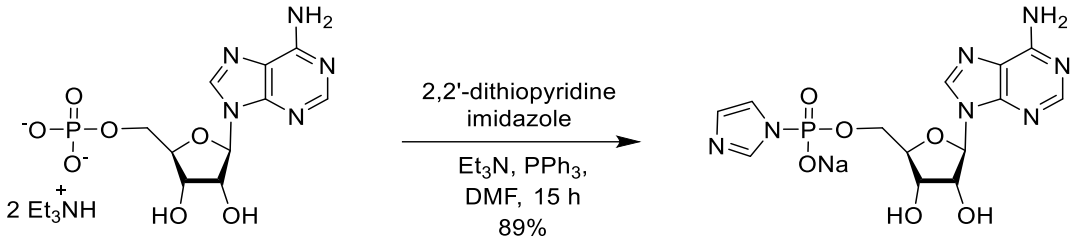
Diallyl(2,3,4,6,7-penta-*O*-acetyl-L-*glycero*-β-D-*manno*-heptopyranosyl) phosphate (3b)



In a two-neck round bottom flask, DMAP (231.8 mg, 10.0 equiv., 1.9 mmol) was added under argon at room temperature to a solution of **S7** (80 mg, 1.0 equiv., 0.19 mmol) in anhydrous DCM (5 mL) was stirred under argon at room temperature. After 15 min, a solution of diallyl chlorophosphite **S5** (7.5 equiv., 1.4 mmol) in anhydrous DCM (5 mL, C = 0.2 M) was added with a syringe pump (injection rate 1.6 mL/h with a 12 mL syringe) at room temperature. After 3 h the reaction mixture was diluted with sat. $NaHCO_3$ (15 mL) and extracted with DCM (3 × 10 mL). The combined organic phases were dried over $MgSO_4$, filtered, concentrated to give a colorless solid. The residue was purified by silica gel flash column chromatography (cyclohexane/ethyl

acetate 90:10 to 40:60) to afford compound **3b** (61 mg, 55%) as a colorless syrup. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 5.91 (m, 2H, H-2'), 5.52 (d, $J_{2\text{-}3}$ = 3.0 Hz, 1H, H-2), 5.44 (dd, $J_{1\text{-}2}$ = 0.9 Hz, $J_{1\text{-}P}$ =7.6 Hz, 1H, H-1), 5.40 (m, 2H, H-3'), 5.37 (m, 1H, H-3'), 5.36 (m, 1H, H-3'), 5.33 (m, 1H, H-3'), 5.27 (t, $J_{4\text{-}3}$ = $J_{4\text{-}5}$ =10.1 Hz, 1H, H-4), 5.24 (m, 1H, H-3'), 5.14 (ddd, $J_{6\text{-}5}$ = 2.3 Hz, 8.5 Hz, 1H, H-6), 5.06 (dd, $J_{3\text{-}2}$ = 3.4 Hz, $J_{3\text{-}4}$ = 10.1 Hz, 1H, H-3), 4.56 (m, 4H, H-1'), 3.74 (dd, $J_{5\text{-}6}$ = 2.3 Hz, $J_{5\text{-}4}$ = 10.1 Hz, 1H, H-5), 3.58 (dd, $J_{7a\text{-}6}$ = 7.8 Hz, $J_{7a\text{-}7b}$ = 12.6 Hz, 1H, H-7a), 4.17 (dd, $J_{7b\text{-}6}$ = 6.2 Hz, $J_{7b\text{-}7a}$ = 12.4 Hz, 1H, H-7b), 2.20 (s, 3H, $\underline{CH_3}COO$), 2.13 (s, 3H, $\underline{CH_3}COO$), 2.02 (s, 3H, $\underline{CH_3}COO$), 1.97 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, $CDCl_3$):** δ 170. 3 (Cq), 170.1 (Cq), 169.9 (Cq), 169.6 (Cq), 132.0 (d, $J_{2'\text{-}P}$ = 7.7 Hz, 1C, C-2'), 131.9 (d, $J_{2'\text{-}P}$ = 7.7 Hz, 1C, C-2'), 119.0 (C-3'), 118.9 (C-3'), 94.7 (d, $J_{1\text{-}P}$ = 3.8 Hz, 1C, C-1), 73.2 (C-5), 70.8 (C-3), 68.9 (d, $J_{1'\text{-}P}$ = 5.8 Hz, 1C, C-1'), 68.85 (d, $J_{1'\text{-}P}$ = 5.8 Hz, 1C, C-1'), 68.6 (d, $J_{2\text{-}P}$ = 8.6 Hz, 1C, C-2), 67.3 (C-6), 64.1 (C-4), 49.8 (C-7), 20.84 ($\underline{CH_3}COO$), 20.8 ($\underline{CH_3}COO$), 20.7 ($\underline{CH_3}COO$), 20.6 ($\underline{CH_3}COO$). **^{31}P NMR (162 MHz, $CDCl_3$):** δ -2.3. **HRMS (ESI+):** calc. for $C_{23}H_{33}KO_{15}P$ $[M+K]^+$: 619.1189; found: 619.1189.

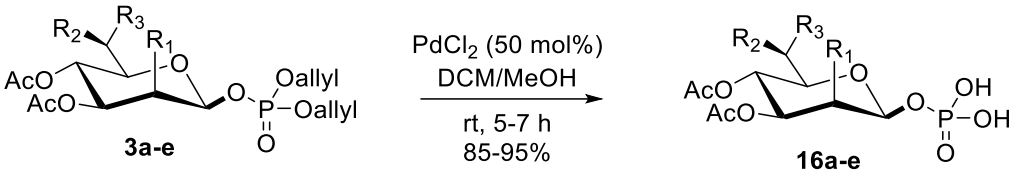
Adenosine 5'-phosphorimidazolide (S9)



To obtain Adenosine Mono Phosphate (AMP) triethylammonium salt **S8**, AMP (free acid) was suspended in a water/ethanol mixture and neutralized to pH 7 by a stepwise addition of triethylamine under vigorous stirring. The residue was lyophilized and dried under vacuum (in a dessicator containing P_4O_{10}), to give the triethylammonium salt as a white solid. To a solution of AMP triethylamonium salt **S8** (500 mg, 1.0 equiv., 1.4 mmol), 2,2'-dithiopyridine (952 mg, 3.0 equiv., 4.3 mmol), and imidazole (980.4 mg, 10.0 equiv., 14.4 mmol) in anhydrous DMF (4 mL), was added triethylamine (0.8 mL, 4.0 equiv., 5.8 mmol) and triphenylphosphine (1.1 g, 3.0 equiv., 4.3 mmol) at room temperature under argon. The reaction was stirred for 15 hours. The product was precipitated from the reaction mixture by the addition of an anhydrous solution of $NaClO_4$ (1.5 g, 8.0 equiv., 1.5 mmol) in dry acetone (80 mL). The heterogeneous mixture was cooled at 0 °C under argon. The precipitate was filtered, washed repeatedly with cold, dry acetone, and dried

in vacuo over P_4O_{10}, to yield **S9** (520 mg, 89%) as a white solid. This compound is known and its characterization data are in accordance with the reference report.[8] **^{1}H NMR (400 MHz, D_2O):** δ 7.90 (s, 1H), 7.64 (dd, *J* = 4.0 Hz and 8.0 Hz, 1H), 7.27 (s, 1H), 7.09 (s, 1H), 5.88 (dd, *J* = 4.0 Hz and 8.0 Hz, 1H), 5.84 (dd, *J* = 2.3 Hz and 4.6 Hz, 1H, H-1^{Rib}), 4.26 (m, 1H, H-2^{Rib}), 4.15-4.09 (m, 3H, H-3^{Rib}, H-4^{Rib} and H-5^{Rib}), 4.01 (m, 1H, H-5^{Rib}) **^{31}P NMR (162 MHz, D_2O):** δ -7.4. **HRMS (ESI-):** calc. for $C_{13}H_{16}N_7O_6P$ $[M-H]^-$: 396.0827; found: 396.0843

General procedure for the deallylation (general procedure A)

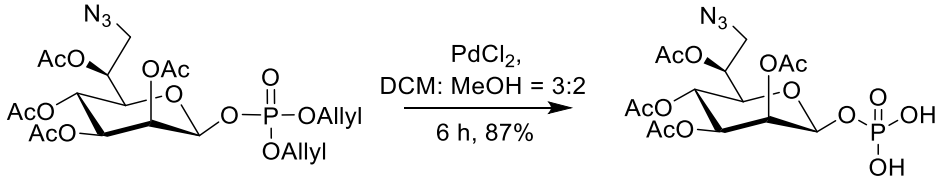


R_1, R_2 = OAc, N_3
R_3 = H, CH_2OAc, CH_2N_3

R_1, R_2 = OAc, N_3
R_3 = H, CH_2OAc, CH_2N_3

To a solution of **3a-e** (1.0 equiv., 0.24 mmol) in DCM/MeOH (3/2, 1.5 mL/1.0 mL) was added $PdCl_2$ (0.5 equiv., 0.12 mmol) under argon. The reaction was stirred for 5-7 hours at room temperature. The solvents were removed under vacuum and the residue was purified by silica gel flash column chromatography (chloroform/methanol 7:3 to 1:2, all eluents contained 2% v/v of triethylamine) to afford compound **16a-e** as a yellow solid. In order to remove the trace of palladium, a solution of phosphate **16a-e** in MeOH (5 mL) was stirred with a palladium scavenger (Quadra Pure^{TM}, 50 mg) during 2 hours until the solution became colorless. The solution was filtered and concentrated to give compound **16a-e** (85-95%).

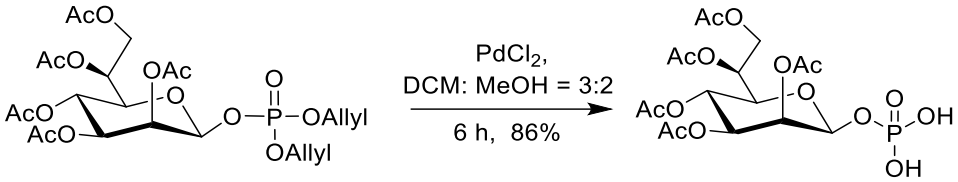
7-Azido-1-*O*-phosphoryl-2,3,4,6-tetra-*O*-acetyl-7-deoxy-L-*glycero*-β-D-*manno*-heptopyranoside (16a)



Following the general procedure A, a solution of **3a** (70.6 mg, 1.0 equiv., 0.13 mmol) in DCM/MeOH (3/2, 1.5 mL/1.0 mL) was added $PdCl_2$ (11.7 mg, 0.5 equiv., 66 μmol) under argon. The reaction was stirred for 6 hours at room temperature. After purification, the reaction gave the desired product **16a** (55.3 mg, 87%) as a colorless syrup. **^{1}H NMR (400 MHz, CD_3OD)**: δ 5.48

(m, 1H, H-2), 5.45 (d, $J_{1\text{-p}}$ = 7.8 Hz, 1H, H-1), 5.20 (m, 3H, H-3, H-4, and H-6), 3.94 (m, 1H, H-5), 3.62 (dd, $J_{7\text{a-5}}$ = 5.0 Hz, $J_{6\text{a-6b}}$ = 13.1 Hz, 1H, H-7a), 3.56 (dd, $J_{7\text{b-5}}$ = 5.0 Hz, $J_{6\text{a-6b}}$ = 13.1 Hz, 1H, H-7b), 2.17 (s, 3H, $\underline{CH_3}COO$), 2.09 (s, 3H, $\underline{CH_3}COO$), 2.00 (s, 3H, $\underline{CH_3}COO$), 1.94 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, CD_3OD)**: δ 171.9 (Cq × 2), 171.4 (Cq), 171.3 (Cq), 95.3 (d, *J* = 5.7 Hz, 1C. C-1), 74.1 (C-5), 72.5 (C-3), 70.8 (d, *J* = 6.7 Hz, 1C, C-2), 69.2 (C-4), 65.8 (C-6), 57.7 (C-7), 20.8 ($\underline{CH_3}COO$), 20.7 ($\underline{CH_3}COO$ × 2), 20.5 ($\underline{CH_3}COO$). **^{31}P NMR (162 MHz, D_2O):** δ -1.6. **HRMS (ESI-):** calc. for $C_{15}H_{22}N_3O_{13}P$ $[M-H]^-$: 482.0817; found: 482.0824.

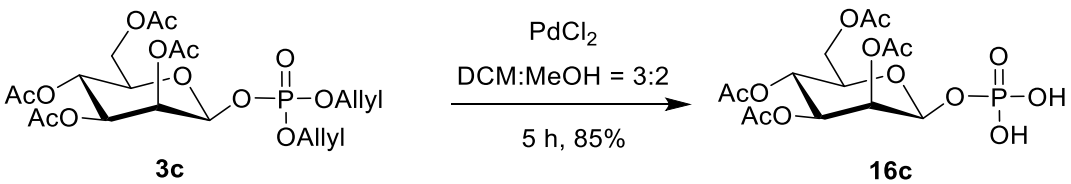
1-*O*-Phosphoryl-2,3,4,6,7-penta-O-acetyl-L-*glycero*-β-D-*manno*-heptopyranoside (16b)



3b **16b**

Following the general procedure A, a solution of **3b** (139.5 mg, 1.0 equiv., 0.24 mmol) in DCM/MeOH (3/2, 1.5 mL/1.0 mL) was added $PdCl_2$ (21.3 mg, 0.5 equiv., 0.12 mmol) under argon. The reaction was stirred for 6 hours at room temperature. After purification, the reaction gave the desired product **16b** (103.2 mg, 86%). This compound is known and its characterization data are in accordance with the reference report.[5] **^{1}H-NMR** (400 MHz, CD_3OD): δ 5.73 (d, *J* = 2.5 Hz, 1H, H-2), 5.58 (d, *J* = 9.2 Hz, 1H, H-1), 5.46 (dd, *J* = 2.3 Hz and 10.1 Hz, 1H, H-4), 5.42 (dd, *J* = 2.8 Hz and 10.3 Hz, 1H, H-3), 4.73 (dd, *J* = 3.4 Hz and 12.1 Hz, 1H, H-7a), 4.51 (dd, *J* = 3.4 Hz and 12.1 Hz, 1H, H-7b), 4.18 (dd, *J* = 2.3 Hz and 9.4 Hz, 1H, H-5), 2.39 (s, 3H, $\underline{CH_3}COO$), 2.30 (s, 3H, $\underline{CH_3}COO$), 2.22 (s, 6H, 2$\underline{CH_3}COO$), 2.17 (s, 3H, $\underline{CH_3}COO$). **^{31}P-NMR (162 MHz, CD_3OD)**: δ -1.5. **HRMS (ESI-)**: calc. for $C_{17}H_{24}O_{15}P$ $[M-H]^-$: 499.0858; found: 499.0860.

1-O-Phosphoryl-2,3,4,6-penta-O-acetyl-β-mannopyranoside (16c)

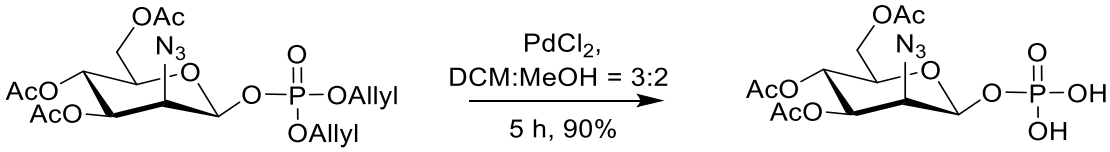


3c **16c**

Following the general procedure A, a solution of **3c** (100 mg, 1.0 equiv., 0.17 mmol) in DCM/MeOH (3/2, 1.5 mL/1.0 mL) was added $PdCl_2$ (15.1 mg, 0.5 equiv., 85 μmol) under argon.

The reaction was stirred for 5 hours at room temperature. After purification, the reaction gave the desired product **16c** (62 mg, 85%). **^{1}H NMR (400 MHz, CD_3OD)**: δ 5.50 (m, 1H, H-2), 5.47 (dd, $J_{1\text{-}2}$ =1.4 Hz, $J_{1\text{-}p}$ = 8.9 Hz, 1H, H-1), 5.23 -5.15 (m, 2H, H-3 and H-4), 4.32 (dd, $J_{6a\text{-}5}$ = 4.8 Hz, $J_{6a\text{-}6b}$ = 12.4 Hz, 1H, H-6a), 3.35 (dd, $J_{6b\text{-}5}$ = 2.5 Hz, $J_{6a\text{-}6b}$ = 12.4 Hz, 1H, H-6b), 3.91 (m, 1H. H-5), 2.16 (s, 3H, $\underline{CH_3}COO$), 2.05 (s, 3H, $\underline{CH_3}COO$), 2.03 (s, 3H, $\underline{CH_3}COO$), 1.95 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, CD_3OD)**: δ 172.3 (Cq), 171.7 (Cq), 171.3 (Cq), 171.2 (Cq), 95.0 (d, J = 5.6 Hz, 1C. C-1), 73.7 (C-5), 72.1 (C-3), 70.4 (d, J = 6.7 Hz, 1C, C-2), 66.7 (C-4), 63.1 (C-6), 20.67 ($\underline{CH_3}COO$), 20.6 ($\underline{CH_3}COO$), 20.64 ($\underline{CH_3}COO$), 20.6 ($\underline{CH_3}COO$), 20.5 ($\underline{CH_3}COO$). **^{31}P NMR (162 MHz, D_2O):** δ -1.45.

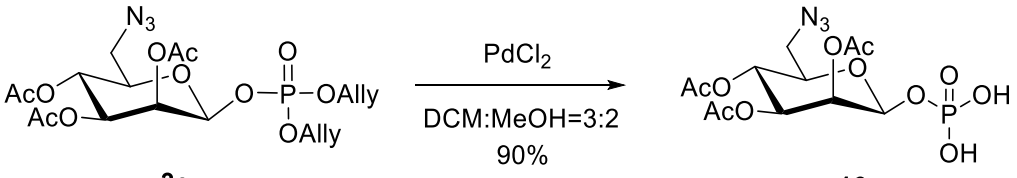
2-Azido-1-O-phosphoryl-3,4,6-tri-O-acetyl-2-deoxy-β-mannopyranoside (16d)



3d **16d**

Following the general procedure A, a solution of **3d** (70 mg, 1.0 equiv., 0.14 mmol) in DCM/MeOH (3/2, 1.5 mL/1.0 mL) was added $PdCl_2$ (12.6 mg, 0.5 equiv., 71 μmol) under argon. The reaction was stirred for 5 hours at room temperature. After purification, the reaction gave the desired product **16d** (53 mg, 90%). **^{1}H NMR (400 MHz, CD_3OD)**: δ 5.50 (dd, $J_{1\text{-}2}$ = 0.9 Hz, $J_{1\text{-}p}$ = 7.6 Hz,1H, H-1), 5.23 (d, $J_{3\text{-}2}$ = 3.7 Hz, $J_{3\text{-}4}$ = 9.9 Hz, 1H, H-3), 5.17 (t, J = 9.6 Hz, 1H, H-4), 5.03 (m, 1H, H-2), 4.24 (dd, $J_{6a\text{-}5}$ = 2.3 Hz, $J_{6a\text{-}6b}$ = 12.4 Hz, 1H, H-6a), 4.11 (dd, $J_{6b\text{-}5}$ = 2.3 Hz, $J_{6a\text{-}6b}$ = 12.4 Hz, 1H, H-6b), 3.82 (m, 1H, H-5), 2.06 (s, 3H, $\underline{CH_3}COO$), 2.04 (s, 3H, $\underline{CH_3}COO$), 2.01 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, CD_3OD):** δ 171.2 (Cq), 170.2 (Cq), 170.0 (Cq), 94.6 (d, J = 2.9 Hz, 1C, C-1), 72.4 (C-5), 71.8 (C-4), 65.5 (C-3), 62.9 (d, J = 6.7 Hz, 1C, C-2^{Mann}), 61.8 (C-6^{Mann}), 19.4 ($\underline{CH_3}COO$ × 2), 19.2 ($\underline{CH_3}COO$). **^{31}P NMR (162 MHz, CD_3OD):** δ 0.7**. HRMS (ESI-):** calc. for $C_{12}H_{17}N_3O_{11}P$ $[M\text{-}H]^-$: 410. 0588; found: 410.0606.

6-Azido-1-*O*-phosphoryl-2,3,4-tri-O-acetyl-6-deoxy-β-mannopyranoside (16e)

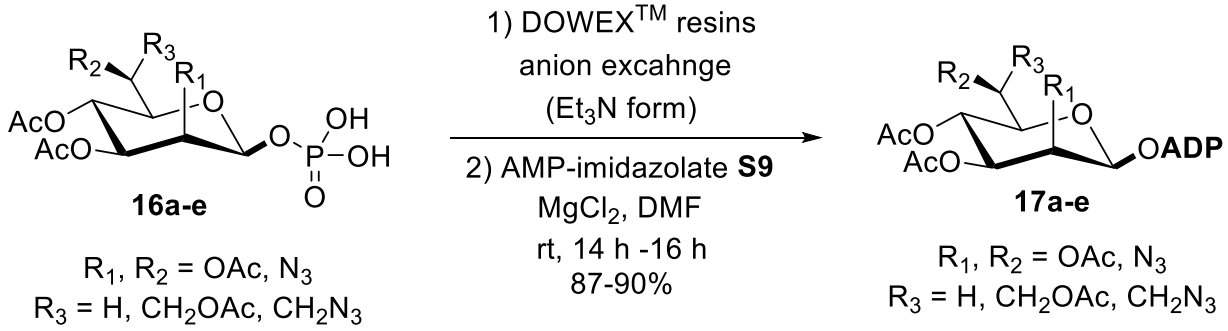


3e **16e**

Following the general procedure A, a solution of **3e** (50 mg, 1.0 equiv., 0.1 mmol) in

DCM/MeOH (3/2, 0.6 mL/0.4 mL) was added $PdCl_2$ (5 mg, 0.5 equiv., 51 μmol) under argon. The reaction was stirred for 5 hours at room temperature. After purification, the reaction gave the desired product **16e** (38 mg, 90%). **^{1}H NMR (400 MHz, CD_3OD)**: δ 5.49 (m, 1H, H-2), 5.38 (d, $J_{1\text{-p}}$ = 9.2 Hz, 1H, H-1), 5.32 (t, J = 9.6 Hz, 1H, H-4), 5.15 (dd, $J_{3\text{-}2}$ = 3.2 Hz, $J_{3\text{-}4}$ = 10.1 Hz, 1H, H-3), 3.80 (ddd, $J_{5\text{-}6a}$ = 3.0 Hz, $J_{5\text{-}6b}$ = 7.8 Hz, $J_{5\text{-}4}$ = 9.6 Hz, 1H. H-5), 3.57 (dd, $J_{6a\text{-}5}$ = 3.0 Hz, $J_{6a\text{-}6b}$ = 13.5 Hz, 1H, H-6a), 3.35 (dd, $J_{6b\text{-}5}$ = 4.6 Hz, $J_{6a\text{-}6b}$ = 13.5 Hz, 1H, H-6b), 2.15 (s, 3H, $\underline{CH_3}COO$), 2.04 (s, 3H, $\underline{CH_3}COO$), 1.96 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, CD_3OD)**: δ 172.1 (Cq), 171.5 (Cq), 171.3, 94.8 (d, J = 5.7 Hz, 1C. C-1), 74.5 (C-5), 72.8 (C-3), 71.5 (d, J = 6.7 Hz, 1C, C-2), 67.7 (C-4), 54.8 (C-6), 20.7 ($\underline{CH_3}COO$), 20.68 ($\underline{CH_3}COO$), 20.6 ($\underline{CH_3}COO$). **^{31}P NMR (162 MHz, CD_3OD):** δ -0.85. **HRMS (ESI-):** calc. for $C_{12}H_{17}N_3O_{11}P$ $[M\text{-}H]^-$: 410. 0588; found: 410.0606.

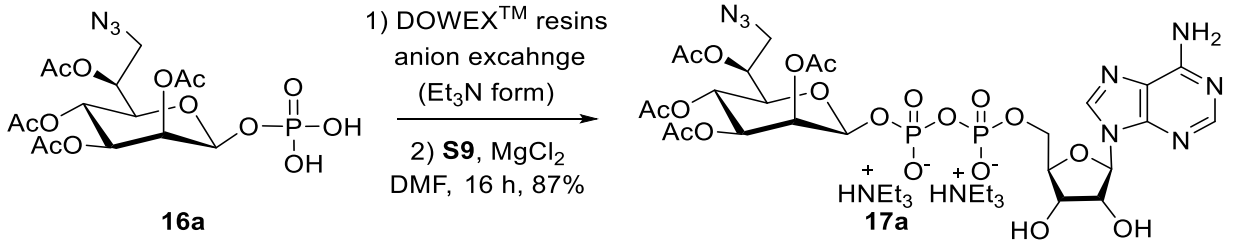
General procedure for the synthesis of protected nucleotide sugars (general procedure B):



Phosphate **16a-e** were transformed into the corresponding triethylammonium salt by DOWEX™ resins, and the triethylammonium salts were lyophilized and dried in vacuo over P_4O_{10}, to yield the monophosphate triethylammonium salts as a white solid. The dry phosphate **16a-e** triethylammonium salts (1.0 equiv.) and $MgCl_2$ (2.0 equiv.) were vigorously stirred in DMF (1.5 mL) until a clear solution was obtained (approximately 10 min). To this mixture was then added a solution of S9 (1.5 equiv.) in anhydrous DMF (1.5 mL) under argon. This reaction mixture was stirred for 16 h at room temperature, and the reaction progress was monitored by reverse-phase HPLC (Zorbax SB-C18: 4.6 × 250 mm, 5 Micron, 5% acetonitrile in 50 mM triethylammonium acetate). The reaction was quenched by the addition of water (10 mL, HPLC grade) and lyophilized to give the crude products. The crude products were purified through a G-15 Sephadex column (50 mM triethylammonium acetate). The fractions containing 17a were collected and freeze-dried, then purified by HPLC (Zorbax SB-C18: 21.8 × 150 mm, 5 μM, 50 mM triethylammonium acetate)

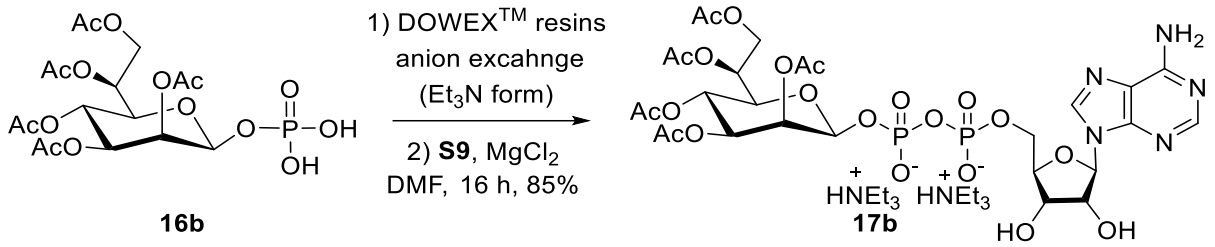
as eluent. The fractions were lyophilized to afford pure protected nucleotide sugars (triethylammonium salt) as a colorless syrup.

Adenosine 5'-diphospho-2,3,4,6-tetra-*O*-acetyl-7-azido-7-deoxy-L-*glycero*-β-D-*manno*-heptopyranoside (17a)



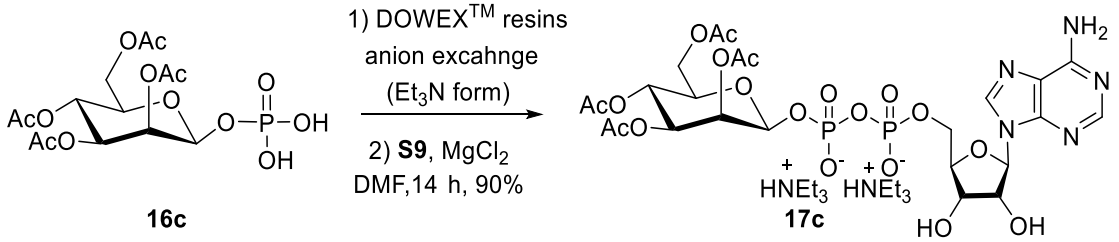
Following the general procedure for the synthesis of protected nucleotide sugars, phosphate **16a** triethylammonium salt (55.3 mg, 1.0 equiv., 0.12 mmol) and $MgCl_2$ (21.9 mg, 2.0 equiv., 0.23 mmol) were vigorously stirred in DMF (1.5 mL) until a clear solution was obtained (approximately 10 min). To this mixture was then added a solution of **S9** (72.3 mg, 1.5 equiv., 0.17 mmol) in anhydrous DMF (1.5 mL) under argon. The fractions were lyophilized to afford pure **17a** (102 mg, 2.0 equiv. triethylammonium salt, 87%) as a colorless syrup. **^{1}H NMR (400 MHz, D_2O):** δ 8.61 (s, 1H, H-8^{Ade}), 8.34 (s, 1H, H-2^{Ade}), 6.22 (d, $J_{1\text{-}2}$ = 6.0 Hz, 1H, H-1^{Rib}), 5.61 (d, $J_{2\text{-}3}$ = 3.0 Hz, 1H, H-2^{Hept}), 5.53 (d, $J_{1\text{-}P}$ = 9.4 Hz, 1H, H-1^{Hept}), 5.21 (m, 1H, H-6^{Hept}), 5.16 (dd, $J_{3\text{-}2}$ = 3.2 Hz, $J_{3\text{-}4}$ = 9.9 Hz, 1H, H-3^{Hept}), 5.11 (t, $J_{4\text{-}3}$ = $J_{4\text{-}5}$ = 9.9 Hz, 1H, H-4^{Hept}), 4.81 (t, $J_{2\text{-}1}$ = $J_{2\text{-}3}$ = 6.0 Hz, 1H, H-2^{Rib}), 4.56 (dd, $J_{3\text{-}4}$ = 3.7 Hz, $J_{3\text{-}2}$ = 6.0 Hz, 1H, H-3^{Rib}), 4.46 (m, 1H, H-4^{Rib}), 4.29 (m, 2H, H-5^{Rib}), 3.81 (dd, $J_{5\text{-}6}$ = 1.6 Hz, $J_{5\text{-}4}$ = 9.9 Hz, 1H, H-5^{Hept}), 3.71 (dd, $J_{7a\text{-}6}$ = 8.9 Hz, $J_{7a\text{-}7b}$ = 13.5 Hz, 1H, H-7a^{Hept}), 3.68 (dd, $J_{7a\text{-}6}$ = 4.1 Hz, $J_{7a\text{-}7b}$ = 13.5 Hz, 1H, H-7b^{Hept}), 2.28 (s, 3H, $\underline{CH_3}$COO), 2.23 (s, 3H, $\underline{CH_3}$COO), 2.13 (s, 3H, $\underline{CH_3}$COO), 2.04 (s, 3H, $\underline{CH_3}$COO). **^{13}C NMR (100 MHz, D_2O):** δ 171.7 (Cq), 171.5 (Cq × 2), 170.8 (Cq), 154.1 (C-6^{Ade}), 151.5 (C-2^{Ade}), 147.6 (C-4^{Ade}), 138.5 (C-8^{Ade}), 117.0 (C-5^{Ade}), 92.4 (d, J = 3.8 Hz, 1C, C-1^{Hept}), 85.4 (C-1^{Rib}), 82.4 (d, J = 9.5 Hz, 1C,C-4^{Rib}), 72.8 (C-2^{Rib}), 71.0 (C-5^{Hept}), 69.6 (C-4^{Hept}), 68.9 (C-3^{Rib}), 68.3 (d, J = 6.7 Hz, 1C, C-2^{Hept}), 66.9 (C-3^{Hept}), 64.1 (d, J = 4.8 Hz, 1C, C-5^{Rib}), 63.4 (C-6^{Hept}), 49.2 (C-7^{Hept}), 18.8 ($\underline{CH_3}$COO), 18.7 ($\underline{CH_3}$COO × 2), 18.5 ($\underline{CH_3}$COO). **^{31}P NMR (162 MHz, D_2O):** δ -8.2 (d, J = 19.8 Hz, 1P), -11.1 (d, J = 19.8 Hz, 1P). **HRMS (ESI-):** calc. for $C_{25}H_{34}N_8O_{19}P_2$ [M-H]$^-$: 811.1343; found: 811.1352.

Adenosine 5'-diphospho-2,3,4,6,7-penta-*O*-acetyl-L-*glycero*-β-D-*manno*-heptopyranoside, bis triethylammonium salt (17b)



Following the general procedure for the synthesis of protected nucleotide sugars, phosphate **16b** triethylammonium salt (56.4 mg, 1.0 equiv., 0.12 mmol) and $MgCl_2$ (22.9 mg, 2.0 equiv., 0.24 mmol) were stirred vigorously in DMF (1.5 mL) until a clear solution or homogeneous suspension was obtained (approximately 10 min). A solution of **S9** (73.1 mg, 1.5 equiv., 0.17 mmol) in anhydrous DMF (1.5 mL) was added under argon. This reaction mixture was stirred for 16 hours at room temperature. The fractions containing **17b** (108 mg, triethylammonium salt, 85%) were lyophilized. This compound is known and its characterization data are in accordance with the reference report.[5-6] **^{1}H-NMR (400 MHz, D_2O)**:δ 8.49 (s, 1H, H-8^{Ade}), 8.22 (s, 1H, H-2^{Ade}), 6.10 (d, *J* = 6.0 Hz, 1H, H-1^{Rib}), 5.50 (d, *J* = 2.1 Hz, 1H, H-2^{Hep}), 5.42 (d, *J* = 9.4 Hz, 1H, H-1^{Hep}), 5.14 (d, *J* = 4.2 Hz and 8.5 Hz, 1H, H-6^{Hep}), 5.08 (dd, *J* = 3.2 Hz and 10.3 Hz, 1H, H-3^{Hep}), 5.00 (dd, *J* = 10.1 Hz, 1H, H^{Hep}), 4.68 (t, *J* = 5.5 Hz, 1H, H-2^{Rib}), 4.45 (t, *J* = 3.9 Hz, 1H, H-3^{Rib}), 4.34 (m, 1H, H-4^{Rib}), 4.31 (dd, *J* = 8.7 Hz and 12.1 Hz, 1H, H-7a), 4.22 (dd, *J* = 8.7 Hz and 12.1 Hz, 1H, H-7b), 4.17 (m, 2H, H-5^{Rib}), 3.77 (d, *J* = 9.2 Hz, 1H, H-5^{Mann}), 3.16 ($CH_3\underline{CH_2}N$), 2.17 (s, 3H, $\underline{CH_3}COO$), 2.09 (s, 3H, $\underline{CH_3}COO$), 1.99 (s, 3H, $\underline{CH_3}COO$), 1.95 (s, 3H, $\underline{CH_3}COO$), 1.87 (s, 3H, $\underline{CH_3}COO$), 1.23 ($\underline{CH_3}CH_2N$). **^{31}P-NMR (162 MHz, D_2O)**: δ -10.7 (d, *J* = 19.8 Hz, 1P), -13.7 (d, *J* = 19.8 Hz, 1P). **HRMS (ESI-)**: calc. for $C_{27}H_{37}N_5O_{21}P_2$ $[M-H]^-$: 828.1383; found: 828.1353.

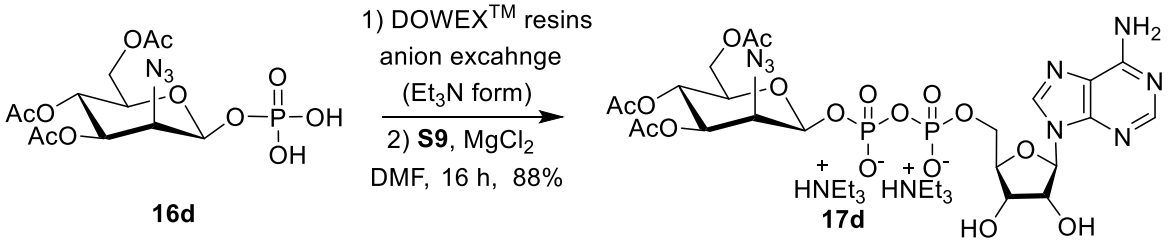
Adenosine 5'-diphospho-2,3,4,6-tetra-*O*-acetyl-β-D-mannopyranose, bis triethylammonium salt (17c)



Following the general procedure for the synthesis of protected nucleotide sugars, phosphate

16c triethylammonium salt (64 mg, 1.0 equiv., 0.15 mmol) and $MgCl_2$ (28.6 mg, 2.0 equiv., 0.30 mmol) were vigorously stirred in DMF (1.5 mL) until a clear solution was obtained (approximately 10 min). To this mixture was then added a solution of **S9** (94.4 mg, 1.5 equiv., 0.23 mmol) in anhydrous DMF (1.5 mL) under argon. This reaction mixture was stirred for 14 hours at room temperature. The fractions were lyophilized to afford pure **17c** (122.7 mg, 1.5 equiv. triethylammonium salt, 90%) as a colorless syrup. **^{1}H NMR (400 MHz, D_2O):** δ 8.56 (s, 1H, H-8^{Ade}), 8.26 (s, 1H, H-2^{Ade}), 6.15 (d, $J_{1\text{-}2}$ = 6.0 Hz, 1H, H-1^{Rib}), 5.58 (br, 1H, H-2^{Man}), 5.53 (d, $J_{1\text{-}P}$ = 9.6 Hz, 1H, H-1^{Man}), 5.18 (m, 2H, H-3^{Man} and H-4^{Man}), 4.78 (t, $J_{2\text{-}1} = J_{2\text{-}3}$ = 5.5 Hz, 1H, H-2^{Rib}), 4.54 (dd, $J_{3\text{-}4}$ = 3.7 Hz, $J_{3\text{-}2}$ = 5.5 Hz, 1H, H-3^{Rib}), 4.40 (m, 1H, H-4^{Rib}), 4.35 (dd, $J_{6a\text{-}5}$ = 3.0 Hz, $J_{6a\text{-}6b}$ = 12.8 Hz, 1H, H-$6a^{Man}$), 4.24 (m, 2H, H-5^{Rib}), 4.10 (dd, $J_{6a\text{-}5}$ = 3.0 Hz, $J_{6a\text{-}6b}$ = 12.8 Hz, 1H, H-$6b^{Man}$), 3.79(m, 1H , H-5^{Man}), 2.25 (s, 3H, CH_3COO), 2.17 (s, 3H, CH_3COO), 2.09 (s, 3H, CH_3COO), 2.02 (CH_3COO). **^{13}C NMR (100 MHz, D_2O):** δ 174.0 (Cq), 173.6 (Cq), 173.2 (Cq), 172.4 (Cq), 155.5 (C-6^{Ade}), 152.9 (C-2^{Ade}), 149.1 (C-4^{Ade}), 139.9 (C-8^{Ade}), 118.5 (C-5^{Ade}), 93.6 (d, J = 2.9 Hz, 1C, C-1^{Man}), 86.9 (C-1^{Rib}), 83.8 (d, J = 9.5 Hz, C-4^{Rib}), 74.3 (C-2^{Rib}), 71.8 (C-5^{Man}), 71.1 (C-4^{Man}), 70.5 (C-3^{Rib}), 69.8 (d, J = 6.7 Hz, 1C, C-2^{Man}), 65.4 (d, J = 6.7 Hz, 1C, C-5^{Rib}), 65.3 (C-3^{Man}), 61.6 (C-6^{Man}), 20.1 ($\underline{CH_3}COO$ × 2), 20.0 ($\underline{CH_3}COO$ × 2). **^{31}P NMR (162 MHz, D_2O):** δ -10.9 (d, J = 19.8 Hz, 1P), -13.6 (d, J = 19.8 Hz, 1P). **HRMS (ESI-):** calc. for $C_{24}H_{33}N_5O_{19}P_2$ [M-H]$^-$: 756.1172; found: 756.1173.

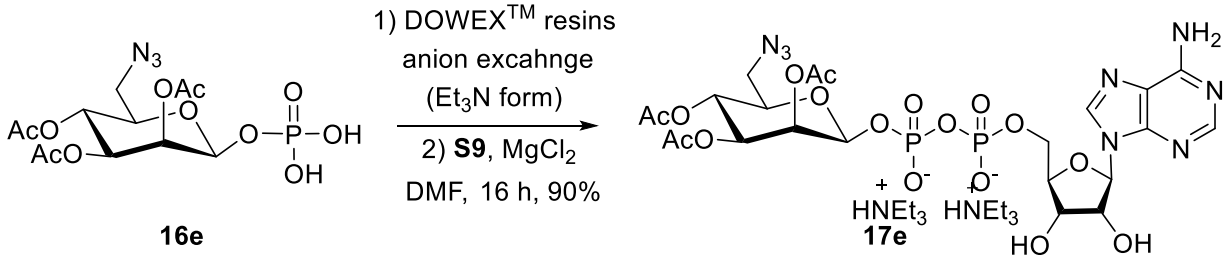
Adenosine 5'-diphospho-3,4,6-tri-*O*-acetyl-2-azido-2-deoxy-β-D-mannopyranose, bis triethylammonium salt (17d)



Following the general procedure for the synthesis of protected nucleotide sugars, phosphate **16d** triethylammonium salt (53 mg, 1.0 equiv., 0.13 mmol) and $MgCl_2$ (24.8 mg, 2.0 equiv., 0.26 mmol) were vigorously stirred in DMF (1.5 mL) until a clear solution was obtained (approximately 10 min). To this mixture was then added a solution of **S9** (86.0 mg, 1.5 equiv., 0.20 mmol) in anhydrous DMF (1.5 mL) under argon. This reaction mixture was stirred for 16 hours at room temperature. The fractions were lyophilized to afford pure **17d** (141 mg, 4.1 equiv. triethylammonium salt, 88%) as a colorless syrup. **^{1}H NMR (400 MHz, D_2O):** δ 8.57 (s, 1H, H-

8^{Ade}), 8.27 (s, 1H, H-2^{Ade}), 6.16 (d, $J_{1\text{-}2}$ = 5.7 Hz, 1H, H-1^{Rib}), 5.53 (d, $J_{1\text{-}P}$ = 9.2 Hz, 1H, H-1^{Man}), 5.19 (dd, $J_{3\text{-}2}$ = 3.4 Hz, $J_{3\text{-}4}$ = 10.1 Hz, 1H, H-3^{Man}), 5.08 (t, $J_{4\text{-}3}$ = $J_{4\text{-}5}$ = 10.1 Hz, 1H, H-4^{Man}), 4.78 (t, $J_{2\text{-}1}$ = $J_{2\text{-}3}$ = 5.5 Hz, 1H, H-2^{Rib}), 4.55 (dd, $J_{3\text{-}4}$ = 3.7 Hz, $J_{3\text{-}2}$ = 5.5 Hz, 1H, H-3^{Rib}), 4.46 (d, $J_{2\text{-}3}$ = 3.4 Hz, 1H, H-2^{Man}), 4.43 (m, 1H, H-4^{Rib}), 4.29 (m, 3H, H-5^{Rib} and H-6a^{Man}), 4.04 (dd, $J_{6a\text{-}5}$ = 1.8 Hz, $J_{6a\text{-}6b}$ = 14.4 Hz, 1H, H-6b^{Man}), 3.65 (m, 1H , H-5^{Man}), 2.13 (s, 3H, C*H*$_3$COO), 2.10 (s, 3H, C*H*$_3$COO), 2.07 (s, 3H, C*H*$_3$COO). **^{13}C NMR (100 MHz, D$_2$O):** δ 173.5 (Cq), 172.9 (Cq), 172.2 (Cq), 155.3 (C-6^{Ade}), 152.5 (C-2^{Ade}), 149.5 (C-4^{Ade}), 140.0 (C-8^{Ade}), 118.2 (C-5^{Ade}), 94.8 (d, *J* = 2.9 Hz, 1C, C-1^{Man}), 87.0 (C-1^{Rib}), 83.8 (d, *J* = 9.5 Hz, C-4^{Rib}), 74.3 (C-2^{Rib}), 71.8 (C-5^{Man}), 71.2 (C-4^{Man}), 70.3 (C-3^{Rib}), 65.5 (d, *J* = 6.7 Hz, 1C, C-5^{Rib}), 65.3 (C-3^{Man}), 62.2 (d, *J* = 6.7 Hz, 1C, C-2^{Man}), 61.5 (C-6^{Man}), 20.1 (2 × CH$_3$COO), 20.0 (CH$_3$COO). **^{31}P NMR (162 MHz, D$_2$O):** δ -11.0 (d, *J* = 19.8 Hz, 1P), -13.9 (d, *J* = 19.8 Hz, 1P). **HRMS (ESI-):** calc. for $C_{22}H_{30}N_8O_{17}P_2$ [M-H]$^-$: 739.1131; found: 739.1145.

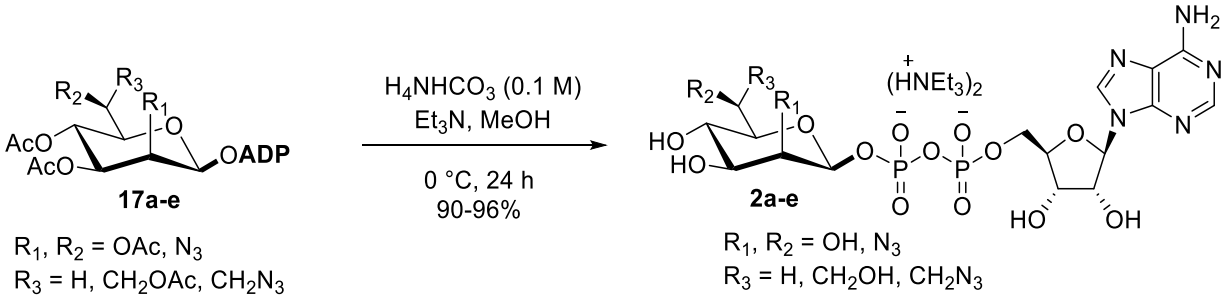
Adenosine 5'-diphospho-2,3,4-tri-*O*-acetyl-6-azido-6-deoxy-β-D-mannopyranoside, bis triethylammonium salt (17e)



Following the general procedure for the synthesis of protected nucleotide sugars, phosphate **16e** triethylammonium salt (56.4 mg, 1.0 equiv., 0.12 mmol) and $MgCl_2$ (22.9 mg, 2.0 equiv., 0.24 mmol) were vigorously stirred in DMF (1.5 mL) until a clear solution was obtained (approximately 10 min). To this mixture was then added a solution of **S9** (73.1 mg, 1.5 equiv., 0.17 mmol) in anhydrous DMF (1.5 mL) under argon. This reaction mixture was stirred for 16 hours at room temperature. The fractions were lyophilized to afford pure **17e** (120 mg, 3.6 equiv. triethylammonium salt, 90%) as a colorless syrup. **^{1}H NMR (400 MHz, D$_2$O):** δ 8.60 (s, 1H, H-8^{Ade}), 8.32 (s, 1H, H-2^{Ade}), 6.21 (d, $J_{1\text{-}2}$ = 6.0 Hz, 1H, H-1^{Rib}), 5.59 (d, $J_{2\text{-}3}$ = 3.2 Hz, 1H, H-2^{Man}), 5.53 (d, $J_{1\text{-}P}$ = 9.4 Hz, 1H, H-1^{Man}), 5.21 (t, $J_{4\text{-}3}$ = $J_{4\text{-}5}$ =9.6 Hz, 1H, H-4^{Man}), 5.16 (dd, $J_{3\text{-}2}$ = 3.2 Hz, $J_{3\text{-}4}$ = 9.6 Hz, 1H, H-3^{Man}), 4.80 (t, $J_{2\text{-}1}$ = $J_{2\text{-}3}$ = 6.0 Hz, 1H, H-2^{Rib}), 4.57 (dd, $J_{3\text{-}4}$ = 3.7 Hz, $J_{3\text{-}2}$ = 6.0 Hz, 1H, H-3^{Rib}), 4.45 (m, 1H, H-4^{Rib}), 4.27 (m, 2H, H-5^{Rib}), 3.68 (m, 1H, H-5^{Man}), 3.68 (dd, $J_{6a\text{-}5}$ = 2.8 Hz, $J_{6a\text{-}6b}$ = 14.4 Hz, 1H, H-6a^{Man}), 3.48 (dd, $J_{6b\text{-}5}$ = 5.0 Hz, $J_{6b\text{-}6a}$ = 14.4 Hz, 1H , H-

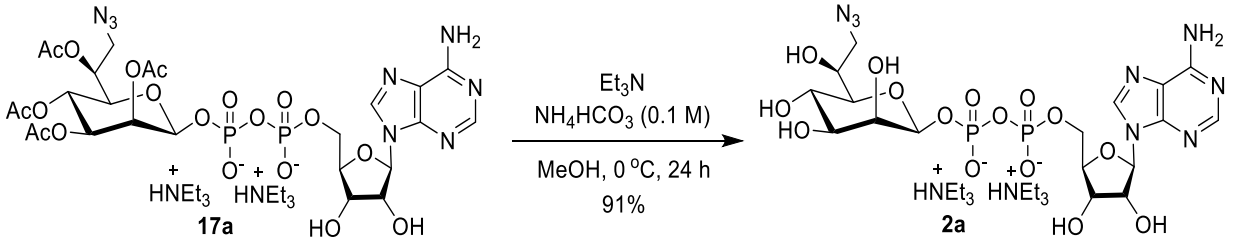
6b^{Man}), 2.27 (s, 3H, $\underline{CH_3}COO$), 2.14 (s, 3H, $\underline{CH_3}COO$), 2.05 (s, 3H, $\underline{CH_3}COO$). **^{13}C NMR (100 MHz, D_2O):** δ 172.9 (Cq), 172.8 (Cq), 172.2 (Cq), 155.4 (C-6^{Ade}), 152.7 (C-2^{Ade}), 149.2 (C-4^{Ade}), 139.9 (C-8^{Ade}), 118.1 (C-5^{Ade}), 93.4 (d, *J* = 2.9 Hz, 1C, C-1^{Man}), 86.8 (C-1^{Rib}), 83.8 (C-4^{Rib}), 74.3 (C-2^{Rib}), 72.3 (C-5^{Man}), 71.2 (C-4^{Man}), 70.4 (C-3^{Rib}), 69.8 (d, *J* = 10.5 Hz, 1C, C-2^{Man}), 66.2 (C-3^{Man}), 65.4 (d, *J* = 6.7 Hz, 1C, C-5^{Rib}), 50.0 (C-6^{Man}), 20.1 (2 × $\underline{CH_3}COO$), 20.0 ($\underline{CH_3}COO$). **^{31}P NMR (162 MHz, D_2O):** δ -10.8 (d, *J* = 19.8 Hz, 1P), -13.7 (d, *J* = 19.8 Hz, 1P). **HRMS (ESI):** calc. for $C_{22}H_{29}N_8O_{17}P_2$ $[M-H]^-$: 739.1129; found: 739.1131.

General procedure for the deacetylation of nucleotide sugars (general procedure C)



To a solution of **17a-e** (1.0 equiv.) and NH_4HCO_3 (9.5 equiv.) in water (0.65 mL) at 0 °C was added dropwise a solution of Et_3N (27.0 equiv.). The reaction was kept at 0 °C for 24 h. The reaction mixture was diluted with cool water (15 mL), the pH was then adjusted to 7 by addition of a Dowex® resin (50-WX8, H^+ form) at 0 °C. The resin was filtrated off, washed with water (15 mL) and the combined filtrates were lyophilized. The residue was purified by HPLC (Zorbax SB-C18: 3% acetonitrile in 50 mM triethylammonium acetate, retention time) to give **2a-e** (triethylammonium salt, 90-96%).

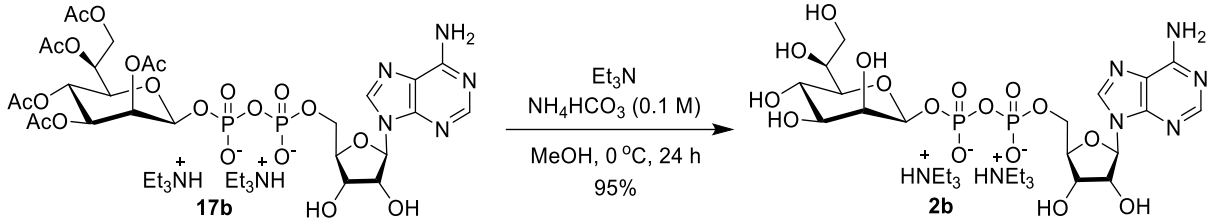
Adenosine 5'-diphospho-7-azido-7-deoxy-L-*glycero*-β-D-*manno*-heptopyranoside (triethylammonium salt) (2a)



Following the general procedure for the deacetylation of nucleotide sugars, a solution of **17a** (7.0 mg, 1.0 equiv., 5.3 μmol) and NH_4HCO_3 (4.0 mg, 9.5 equiv., 50.4 μmol) in water (0.65 mL)

at 0 °C was added dropwise a solution of Et_3N (20.2 µL, 27.0 equiv., 143.5 µmol). The crude product was purified by HPLC ((Zorbax SB-C18, 3% acetonitrile in 50 mM triethylammonium acetate, retention time: 18 min) to give **2a** (4.2 mg, 2.3 equiv. triethylammonium salt, 91%). **^{1}H NMR (400 MHz, D_2O):** δ 8.61 (s, 1H, H-8^{Ade}), 8.34 (s, 1H, H-2^{Ade}), 6.22 (d, $J_{1\text{-}2}$ = 6.0 Hz, 1H, H-1^{Rib}), 5.61 (d, $J_{2\text{-}3}$ = 3.0 Hz, 1H, H-2^{Hept}), 5.30 (d, $J_{1\text{-}P}$ = 9.4 Hz, 1H, H-1^{Hept}), 4.89 (m, 1H, H-2^{Rib}), 4.61 (t, $J_{3\text{-}4}$ = 3.9 Hz, 1H, H-3^{Rib}), 4.48 (m, 1H, H-4^{Rib}), 4.16 (d, d, $J_{2\text{-}3}$ = 3.0 Hz, 1H, H-2^{Hept}), 4.10 (m, 1H, H-6^{Hept}), 3.87 ((t, $J_{4\text{-}3}$ = $J_{4\text{-}5}$ = 9.9 Hz, 1H, H-4^{Hept}), 3.75 (dd, $J_{3\text{-}2}$ = 3.2 Hz, $J_{3\text{-}4}$ = 9.9 Hz, 1H, H-3^{Hept}), 3.68 (dd, $J_{7a\text{-}6}$ = 8.9 Hz, $J_{7a\text{-}7b}$ = 13.5 Hz, 1H, H-7a^{Hept}), 3.48 (dd, $J_{7a\text{-}6}$ = 8.9 Hz, $J_{7a\text{-}7b}$ = 13.5 Hz, 1H, H-7b^{Hept}), 3.34 (dd, $J_{5\text{-}6}$ = 1.6 Hz, $J_{5\text{-}4}$ = 9.9 Hz, 1H, H-5^{Hept}). **^{13}C NMR (100 MHz, D_2O):** δ 154.2 (C-6^{Ade}), 151.5 (C-2^{Ade}), 147.7 (C-4^{Ade}), 138.4 (C-8^{Ade}), 117.2 (C-5^{Ade}), 94.4 (d, J = 3.8 Hz, 1C, C-1^{Hept}), 85.4 (C-1^{Rib}), 82.6 (d, J = 9.5 Hz, 1C, C-4^{Rib}), 74.4 (C-2^{Rib}), 73.1 (C-5^{Hept}), 71.2 (C-3^{Hept}), 69.3 (d, J = 6.7 Hz, 1C, C-2^{Hept}), 69.1 (C-3^{Rib}), 66.7 (C-3^{Hept}), 63.3 (C-6^{Hept}), 63.9 (d, J = 4.8 Hz, 1C, C-5^{Rib}), 52.2 (C-7^{Hept}). **^{31}P NMR (162 MHz, D_2O):** δ -10.8 (d, J = 19.8 Hz, 1P), -12.9 (d, J = 19.8 Hz, 1P). **HRMS (ESI-):** calc. for $C_{17}H_{26}N_8O_{15}P_2$ $[M\text{-}H]^-$: 643.0920; found: 643.0932.

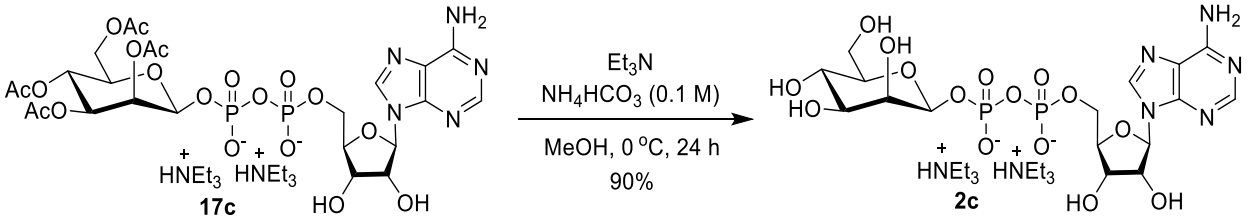
Adenosine 5'-diphospho-L-glycero-β-D-manno-heptopyranose (triethylammonium salt) (2b)



Following the general procedure for the deacetylation of nucleotide sugars, a solution of **17b** (7.0 mg, 1.0 equiv., 6.7 µmol) and NH_4HCO_3 (5.0 mg, 9.5 equiv., 63.9 µmol) in water (0.65 mL) at 0 °C was added dropwise a solution of Et_3N (27 µL, 27.0 equiv., 181.7 umol). The reaction was kept at 0 °C for 24 h. The crude product was purified by HPLC (Zorbax SB-C18:, 3% acetonitrile in 50 mM triethylammonium acetate retention time: 16 min) to obtain **2b** (4.0 mg, 95%). This compound is known and its characterization data are in accordance with the reference report.[5] **^{1}H-NMR (400 MHz, D_2O)**: δ 8.49 (s, 1H, H-8^{Ade}), 8.23 (s, 1H, H-2^{Ade}), 6.11 (d, $J_{1\text{-}2}$ = 6.0 Hz, 1H, H-1^{Rib}), 5.19 (d, $J_{2\text{-}p}$ = 8.2 Hz, 1H, H-2^{Hep}), 4.50 (dd, J = 3.4 Hz and 4.8 Hz, 1H), 4.38 (q, J = 3.0 Hz, 1H), 4.20 (dd, J = 3.0 Hz and 4.8 Hz, 2H), 4.04 (d, J = 3.2 Hz, 1H), 3.90 (ddd, J = 0.2 Hz, 6.6 Hz and 7.3 Hz, 1H), 3.78 (t, J = 9.9 Hz, 1H), 3.70 (dd, J = 6.4 Hz and 8.9 Hz, 1H), 3.65 (dd, J =

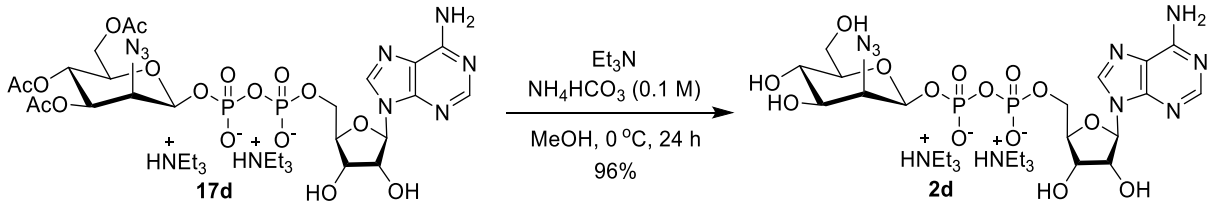
4.1 Hz and 5.0 Hz, 1H), 3.62 (dd, J = 1.4 Hz and 4.1 Hz, 1H), 3.16 (CH_3CH_2N), 1.24 (CH_3CH_2N). **^{31}P-NMR (162 MHz, CD_3OD)**: δ -8.3 (d, J = 19.8 Hz, 1P), -10.2 (d, J = 19.8 Hz, 1P). **MS (ESI-)**: calc. for $C_{17}H_{27}N_5O_{16}P_2$ $(M-H)^-$: 618.36; found: 618.63.

Adenosine 5'-diphospho-β-D-mannopyranose (triethylammonium salt) (2c)



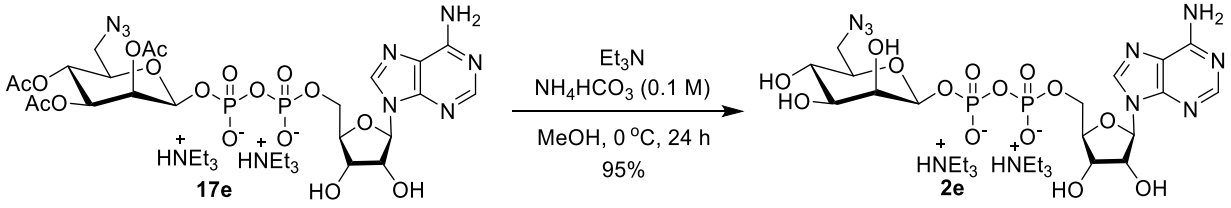
Following the general procedure for the deacetylation of nucleotide sugars, a solution of **17c** (6.8 mg, 1.0 equiv., 7.5 μmol) and NH_4HCO_3 (5.6 mg, 9.5 equiv., 70.8 μmol) in water (0.65 mL) at 0 °C was added dropwise a solution of Et_3N (28 μL, 27.0 equiv., 201.2 μmol). The reaction was kept at 0 °C for 24 h. The crude product was purified by HPLC (Zorbax SB-C18: 3% acetonitrile in 50 mM triethylammonium acetate, retention time: 21 min) to give **2c** (5.0 mg, 1.5 equiv. triethylammonium salt, 90%). This compound is known and its characterization data are in accordance with the reference report.[7] **^{1}H NMR (400 MHz, D_2O):** δ 8.60 (s, 1H, H-8^{Ade}), 8.35 (s, 1H, H-2^{Ade}), 6.23 (d, $J_{1\text{-}2}$ = 6.0 Hz, 1H, H-1^{Rib}), 5.33 (d, $J_{1\text{-}p}$ = 8.9 Hz, 1H, H-1^{Man}), 4.85 (m, 1H, H-2^{Rib}), 4.62 (dd, $J_{3\text{-}2}$ = 3.4 Hz, $J_{3\text{-}4}$ = 8.7 Hz, 1H, H-3^{Rib}), 4.49 (m, 1H, H-4^{Rib}), 4.31 (m, 2H, H-5^{Rib}), 4.17 (d, $J_{2\text{-}1}$ = 3.2 Hz, 1H, H-2^{Man}), 3.97 (dd, $J_{4\text{-}5}$ = 2.1 Hz, $J_{4\text{-}3}$ = 12.4 Hz, 1H, H-4^{Man}), 3.79 (dd, $J_{3\text{-}2}$ = 2.1 Hz, $J_{3\text{-}4}$ = 12.4 Hz, 1H, H-4^{Man}), 3.75 (dd, $J_{6a\text{-}5}$ = 3.2 Hz, $J_{6a\text{-}6b}$ = 9.9 Hz, 1H, H-6a^{Man}), 3.64 (t, $J_{5\text{-}6}$ = 9.6 Hz, 1H, H-5 ^{Man}), 3.48 (dd, $J_{6b\text{-}5}$ = 3.2 Hz, $J_{6b\text{-}6a}$ = 9.9 Hz, 1H, H-6b^{Man}). **^{13}C NMR (100 MHz, D_2O):** δ 155.6 (C-6^{Ade}), 152.9 (C-2^{Ade}), 149.1 (C-4^{Ade}), 139.8 (C-8^{Ade}), 118.6 (C-5^{Ade}), 95.6 (d, J = 3.8 Hz, 1C, C-1^{Man}), 86.8 (C-1^{Rib}), 84.0 (d, $J_{4\text{-}p}$ = 9.6 Hz, 1C, C-4^{Rib}), 76.9 (C-5^{Man}), 74.3 (C-2^{Rib}), 72.4 (C-3^{Man}), 70.7 (d, J = 9.6 Hz, 1C, C-2^{Man}), 70.5 (C-3^{Rib}), 66.4 (C-4^{Man}), 65.3 (d, J = 6.7 Hz, 1C, C-5^{Rib}), 61.1 (C-6^{Man}), **^{31}P NMR (162 MHz, D_2O):** δ -10.9 (d, J = 19.8 Hz, 1P), -12.7 (d, J = 19.8 Hz, 1P). **HRMS (ESI-):** calc. for $C_{16}H_{25}N_5O_{15}P_2$ $[M-H]^-$: 588.0750; found: 588.0769.

Adenosine 5'-diphospho-2-azido-2-deoxy-β-D-mannopyranose (triethylammonium salt) (2d)



Following the general procedure for the deacetylation of nucleotide sugars, a solution of **17d** (7.0 mg, 1.0 equiv., 7.1 μmol) and NH_4HCO_3 (5.3 mg, 9.5 equiv., 67.5 μmol) in water (0.65 mL) at 0 °C was added dropwise a solution of Et_3N (27 μL, 27.0 equiv., 191.7 μmol). The crude product was purified by HPLC (Zorbax SB-C18: 3% acetonitrile in 50 mM triethylammonium acetate, retention time: 21 min) to give **2d** (5.1 mg, 1.5 equiv. triethylammonium salt, 96%). **^{1}H NMR (400 MHz, D_2O):** δ 8.62 (s, 1H, H-8^{Ade}), 8.36 (s, 1H, H-2^{Ade}), 6.25 (d, $J_{1\text{-}2}$ = 6.0 Hz, 1H, H-1^{Rib}), 5.50 (d, $J_{1\text{-}P}$ = 8.7 Hz, 1H, H-1^{Man}), 4.89 (t, $J_{2\text{-}1}$ = $J_{2\text{-}3}$ = 5.5 Hz, 1H, H-2^{Rib}), 4.64 (dd, $J_{3\text{-}4}$ = 3.7 Hz, $J_{3\text{-}2}$ = 5.5 Hz, 1H, H-3^{Rib}), 4.50 (m, 1H, H-4^{Rib}), 4.34 (m, 2H, H-5^{Rib}), 4.30 (d, $J_{2\text{-}3}$ = 3.4 Hz, 1H, H-2^{Man}), 3.96 (dd, $J_{3\text{-}2}$ = 3.4 Hz, $J_{3\text{-}4}$ = 10.1 Hz, 1H, H-3^{Man}), 3.91 (dd, $J_{6a\text{-}5}$ = 3.6 Hz, $J_{6a\text{-}6b}$ = 12.4 Hz, 1H, H-6a^{Man}), 3.78 (dd, $J_{6b\text{-}5}$ = 3.6 Hz, $J_{6a\text{-}6b}$ = 12.4 Hz, 1H, H-6b^{Man}), 3.57 (t, $J_{4\text{-}3}$ = $J_{4\text{-}5}$ = 10.1 Hz, 1H, H-4^{Man}), 3.48 (m, 1H , H-5^{Man}). **^{31}P NMR (162 MHz, D_2O):** δ -10.9 (d, J = 19.8 Hz, 1P), -13.3 (d, J = 19.8 Hz, 1P). **HRMS (ESI-):** calc. for $C_{16}H_{24}N_8O_{14}P_2$ [M-H]$^-$: 613.0814; found: 613.0817.

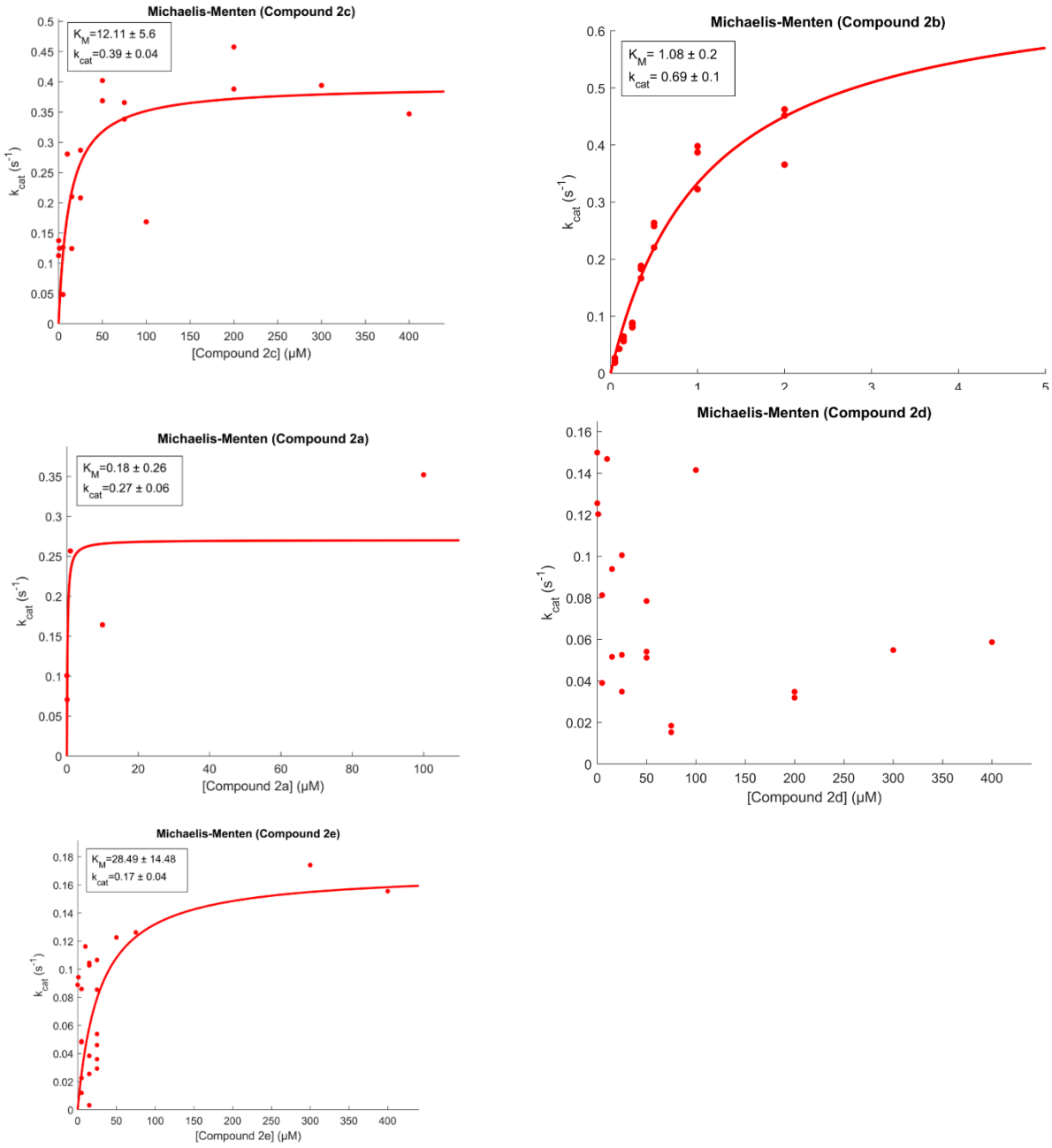
Adenosine 5'-diphospho-6-azido-6-deoxy-β-D-mannopyranoside (triethylammonium salt) (2e)



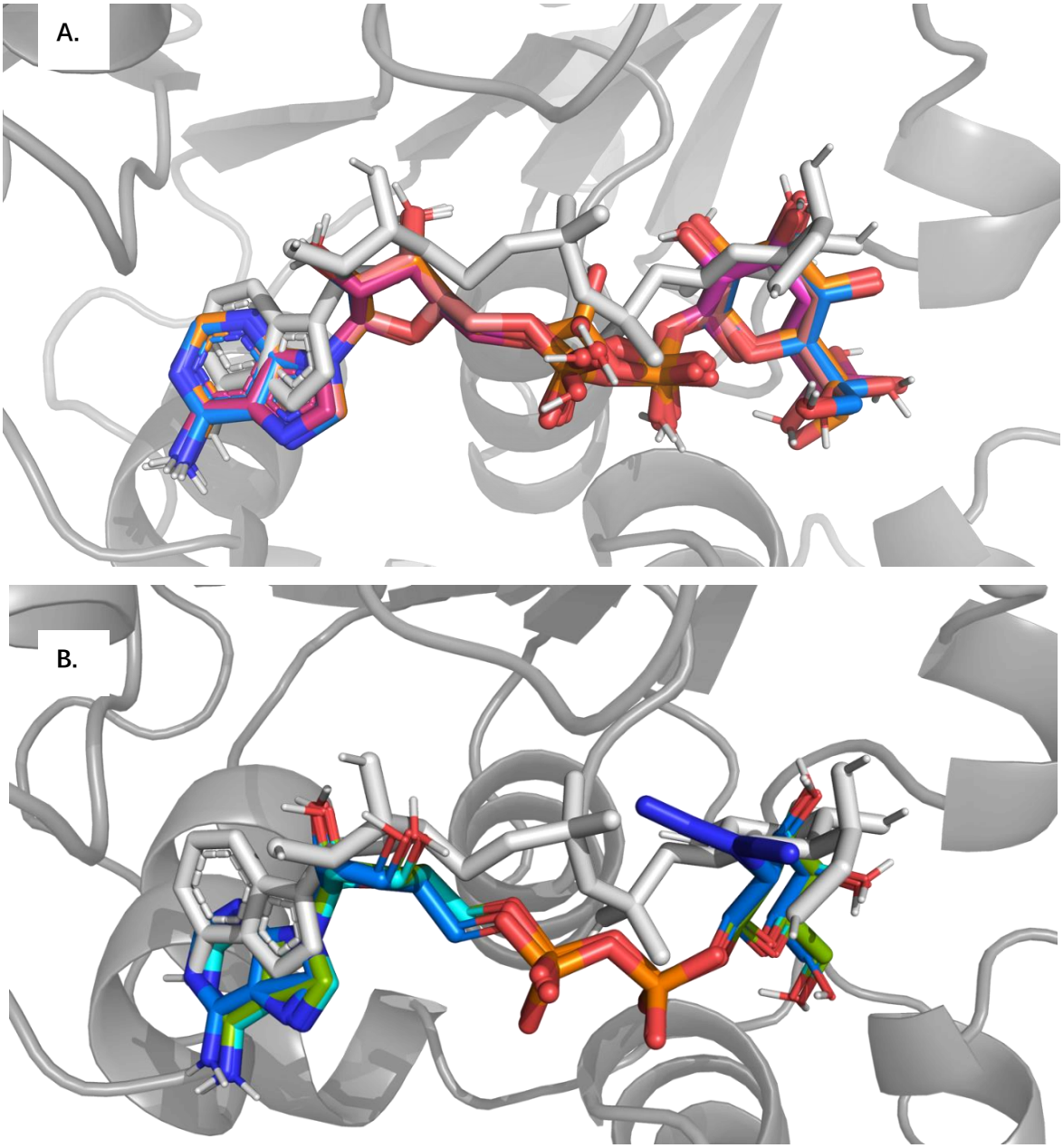
Following the general procedure for the deacetylation of nucleotide sugars, a solution of **17e** (7 mg, 1.0 equiv., 6.7 μmol) and NH_4HCO_3 (5 mg, 9.5 equiv., 63.9 μmol) in water (0.65 mL) at 0 °C was added dropwise a solution of Et_3N (27 μL, 27.0 equiv., 181.7 μmol). The crude product was purified by HPLC (Zorbax SB-C18: 3% acetonitrile in 50 mM triethylammonium acetate, retention time: 19 min) to give **2e** (4.8 mg, 1.5 equiv. triethylammonium salt, 95%). This compound is known and its characterization data are in accordance with the reference report.[2] **^{1}H**

NMR (400 MHz, D_2O): δ 8.65 (s, 1H, H-8^{Ade}), 8.40 (s, 1H, H-2^{Ade}), 6.27 (d, $J_{1\text{-}2}$ = 6.0 Hz, 1H, H-1^{Rib}), 5.37 (d, $J_{1\text{-}p}$ = 8.9 Hz, 1H, H-1^{Man}), 4.88 (m, 1H, H-2^{Rib}), 4.66 (t, $J_{3\text{-}4}$ = 3.9 Hz, 1H, H-3^{Rib}), 4.52 (m, 1H, H-4^{Rib}), 4.35 (m, 2H, H-5^{Rib}), 4.23 (d, $J_{2\text{-}3}$ = 2.5 Hz, 1H, H-2^{Man}), 3.81-3.74 (m, 3H, H-3^{Man}, H-4^{Man}, H-6a^{Man}), 3.67 (dd, $J_{6a\text{-}5}$ = 6.0 Hz, $J_{6a\text{-}6b}$ = 13.3 Hz, 1H, H-6a^{Man}), 3.58 (m, 1H, H-5^{Man}). **^{13}C NMR (100 MHz, D_2O):** δ 155.6 (C-6^{Ade}), 152.9 (C-2^{Ade}), 149.1 (C-4^{Ade}), 139.9 (C-8^{Ade}), 118.6 (C-5^{Ade}), 95.7 (d, J = 3.8 Hz, 1C, C-1^{Man}), 86.8 (C-1^{Rib}), 83.9 (d, $J_{4\text{-}p}$ = 9.6 Hz, 1C, C-4^{Rib}), 74.9 (C-2^{Rib}), 74.3 (C-5^{Man}), 72.2 (C-3^{Man}), 70.6 (d, J = 9.6 Hz, 1C, C-2^{Man}), 70.5 (C-3^{Rib}), 66.9 (C-4^{Man}), 65.3 (d, J = 6.7 Hz, 1C, C-5^{Rib}), 50.9 (C-6^{Man}), 46.7 ($CH_3\underline{CH_2}N$), 8.2 ($\underline{CH_3}CH_2N$). **^{31}P NMR (162 MHz, D_2O):** δ -10.7 (d, J = 19.8 Hz, 1P), -13.1 (d, J = 19.8 Hz, 1P). **HRMS (ESI-):** calc. for $C_{16}H_{23}N_8O_{14}P_2$ $[M\text{-}H]^-$: 613.0809; found: 613.0787.

III. Enzymatic assays



Supplemental Figure 1. Kinetic data for compounds **2a-e**. Note **2d** was unable to be fit to the Michaelis-Menten equation or rate equations the consider substrate inhibition.



Supplemental Figure 2. (A) Representative examples of ADP-heptose (**2b)** docking poses as compared to the crystal structure conformation of ADPH (solid white) with HepI (gray); (B) Representative examples of **2d** docking poses overlaid on HepI (gray) crystal structure (PDB ID: 2H1H), with ADP-heptose (solid white) bound

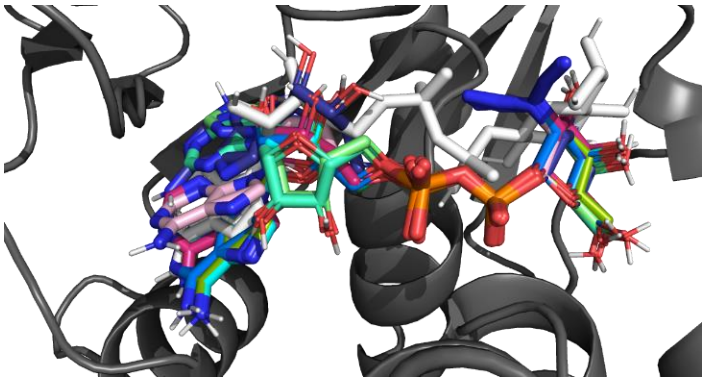


Figure S3. Representative examples of **2d** docking poses overlaid on HepI (dark gray) crystal structure (PDB ID: 2H1H), with ADP-heptose (solid white) bound.

Kinetic Analysis of 2a-e with Heptosyltransferase I

Table 4. Kinetics and binding energies of azido-ADP-Heptose analogues

Compound	Average binding energy (kcal/mol)	# of Conformations in binding site	Kinetics Result
2a	-7.798	154	**Substrate** K_M = 0.2±0.3 μM k_{cat} = 0.27±0.06 s^{-1}
2b	-7.595	158	**Native Substrate** K_M = 1.1±0.2 μM k_{cat} = 0.7±0.1 s^{-1}
2c	-7.733	135	**Substrate** K_M = 12±6 μM k_{cat} = 0.39±0.04 s^{-1}
2d	-7.528	157	**Non-substrate**
2e	-8.047	169	**Substrate** K_M = 28±14 μM k_{cat} = 0.17±0.04 s^{-1}

Materials and Equipment

E. coli strains DH5α and BL-21-AI were obtained from Invitrogen (Carlsbad, CA). Isopropyl β-D-1-thiogalactopyranoside (IPTG) was obtained from Gold Bio Technologies (St. Louis, MO). EDTA free protease inhibitor tablets, Amicon Ultra-15 (30KDa, 10KDa and 3KDa Molecular Weight Cut-Off (MWCO)) centrifugal concentrators, Sartorius Vivaspin 20 (10 KDa MWCO)

centrifugal concentrators, tryptone and yeast extract were obtained from ThermoFisher Scientific (Pittsburg, PA). Sodium chloride, sodium hydroxide, ampicillin (Amp), tetracycline (Tet), tobramycin (Tob), streptomycin (Strp), HEPES, imidazole, ethylenediaminetetraacetic acid (EDTA), cobalt sulfate, and L-arabinose were acquired from Sigma (St. Louis, MO). Bio-Scale Mini Bio-Gel P-6 desalting cartridge was obtained from Bio-Rad (Hercules, CA). All UV-Vis measurements were taken using Cary 100 Bio UV-Vis from Agilent (Santa Clara, CA). All cells were lysed using a EmulsiFlex-C5 homogenizer manufactured by Avestin Inc. (Ottawa, ON). Toyopearl AF-Chelate-640 resin was obtained from Tosoh Biosciences (Grove City, OH). All ESI-MS spectra were collected using a Thermo Scientific (Waltham, MA) ESI spectrometer.

Substrate Preparation

ADPH and Kdo_2-Lipid A were isolated from *E. coli* WBB06 cells (HepI and HepII knockout E. coli strain), in methods analogous to previously published protocols.[9, 10] Overnight cultures were started by inoculating 10 mL of LB-Tet with WBB06 cells from a glycerol stock stored at -80 °C. LB-Tet media (8 L) was inoculated (1 mL of overnight growth per 2L of media) and allowed to grow at 37 °C to an OD600 of 1 (approximately 12 hrs), then centrifuged for 10 min at 5,000 rpm to pellet the cells. ADPH was extracted by adding 80 mL of 50% ethanol to the pellet and stirred on ice for a minimum of 30 min and a maximum of 2 hrs. In 30 mL Nalgene tubes, cells were centrifuged for 10 min at 10,000 rpm and supernatant was saved and the ethanol was removed by vacuum. The crude extract was filtered successively using Amicon Ultra-15 30KDa, 10KDa and 3KDa centrifugal filters to remove proteins and other large nucleotide species. Finally, the flow through was place over a 64 mL DEAE column using a triethylamine bicarbonate (pH=8) gradient from 1-500 mM to purify (yield is ~20 mg), ADPH and water were also brought to a pH of 8. Approximately 500 μL of each fraction were lyophilized and ESI-mass spectrometry was used to determine fractions that contained pure ADPH by observation of a peak at (m/z-1 =619) in a 50:50 acetonitrile:water solution. Fractions confirmed to contain ADPH were pooled and lyophilized successively to remove traces of triethylamine.

Kdo_2-Lipid A was extracted from 8 L of frozen or fresh WBB06 cells grown as described for ADPH extraction. The cells were resuspended in 80 mL of water and the mixture was divided into 30mL Kimble glass tubes (10 mL per tube) and centrifuged for 10 mins at 5,000 rpm. The supernatant was discarded and cells were washed with 160 mL ethanol followed by 160 mL of acetone twice and finally 160 mL of diethyl ether by cellular resuspension in each of the solvents and centrifugation to discard the supernatant before the next wash. Cells were then left to dry in the hood at room temperature 1hr-overnight in a large weigh boat. Kdo_2-Lipid A was then extracted from the dried down cells by pulverizing the cells into a fine powder and adding 20 mL of a solution per tube of 2:5:8 phenol, chloroform, and petroleum ether to 1 gram of cells per 30 mL tube. The mixture was vortexed for 3-5 mins, left on a nutator for 10 mins, then centrifuged for 5,000 rpm for 10 min. Supernatant was gravity filtered through filter paper and the extraction was repeated. The

diethyl ether and chloroform was removed in vacuo from the supernatant which reduces the volume by half approximately. A mixture of 75 mL acetone, 15 mL diethyl ether and 5 drops of water was added to the solution and left to sit for 45 mins-overnight to precipitate the Kdo_2-Lipid A. The solution was centrifuged at 5,000 rpm for 10 min in 30 mL glass tubes and supernatant was discarded. Pellets were washed a minimum of 3 times with ~1 mL 80% phenol and diethyl ether each separately; solutions were centrifuged in between washes and supernatant was removed prior to next wash. The pellets will dramatically diminish over the course of the washes and become more colorless. The dried pellets were then dissolved in 0.5% triethylamine aqueous solution and flash frozen for lyophilization (yield ~50 mg).

Synthesis of ODLA has previously been reported. O-deacylation of Kdo_2-Lipid A was done by refluxing a mixture of 5 mL hydrazine to 50 mg of extracted Kdo_2-Lipid A for 1 hour at 37 °C in a round-bottom flask with stirring (1 mL of hydrazine for every 10 mg of Kdo_2-Lipid A). The solution was then placed on ice and 10 mL cold acetone was added slowly for every 1 mL hydrazine to precipitate ODLA followed by centrifugation for 30 min at 11,000 rpm. The pellet was washed twice with cold acetone and once with diethyl ether, no centrifugation is required, solvent was carefully decanted. After allowing the diethyl ether that remained after decanting to evaporate ~5 min on its side under the fume hood, the pellets were dissolved in water and pooled together, flash frozen and lyophilized. Deacylation was confirmed by ESI-mass spectroscopy in 50:50 acetonitrile:water by observation of the half mass (m/z-2= 695).

HepI Expression and Purification

HepI cloned from the *E. coli* K12 strain MB1760 (*Escherichia coli* ATCC 19215) was expressed in *E. coli* One Shot BL21-AI as described previously with some changes.[10] Two liters of LB-Amp media was inoculated with 10 mL of an overnight culture and allowed to grow at 37 °C, 200 rpm until an OD600 of 04-0.8 was reached (approximately 3-5 hrs). The cells were induced to a final concentration of 1 mM IPTG and 0.002% L-arabinose at 30 °C and expressed for 24 h. Cells were harvested by centrifugation for 10 min at 5,000 rpm. Supernatant was discarded and cell pellets were resuspended in 20 mL of binding buffer (20 mM HEPES, 1 mM imidazole and 500 mM NaCl, pH 7.4) for every liter of grown culture, to which ~1 mg of lysozyme was also added to aid in the lysing of cells. Cells were incubated on ice while mixing for 30 min, followed by homogenization at 18,000 psi for 5-10 cycles. The lysate was clarified by centrifugation at 13,000 rpm for 1 hr and the supernatant was loaded on to a Toyopearl AF-chelate-640 column attached to an ÄKTA purifier stored at 4 °C. The purification method charges the column with 500 μM cobalt sulfate, equilibrates with binding buffer, then protein is loaded and washed again with binding buffer. To remove any unbound protein, the column was washed with wash buffer (20 mM HEPES, 40 mM imidazole and 500 mM NaCl, pH 7.4). Finally, HepI is eluted with strip buffer (50 mM ethylenediaminetetraacetic acid (EDTA) and 500 mM NaCl, pH 6.8).

In order to determine which samples contained HepI, SDS-PAGE gels stained with Coomassie

blue were used to determine which fractions contain the 37 kDa protein (HepI). HepI consistently is co-eluted in the strip buffer with cobalt; fractions were pooled together and concentrated using a 10,000 MWCO Vivaspin Ultra centrifugal concentrator. Concentrated (~ 5 mL) HepI was then placed over Bio-Scale Mini Bio-Gel P-6 desalting cartridge to buffer exchange into HepI Storage buffer (100 mM HEPES, 1 M KCl, pH 7.5), column was also attached to an Äkta purifier at 4 °C. Again, fractions that contained purified protein were combined and concentrated using a 10,000 MWCO Vivaspin Ultra centrifugal concentrator.

Protein was then stored in an amber glass vials as a 50% ammonium sulfate precipitate at 4 °C. Protein remains stable for a few months after purification. To use for desired assay, precipitate was centrifuged at 4 °C for 6 min at 13,000 rpm, supernatant was removed and pellet was dissolved in desired buffer depending on experiment(s) to be carried out. Concentration was determined via nanodrop using the absorbance at 280 nm (using a 1:10 diluted protein), and Beer's law was employed to determine concentration given the extinction coefficient of HepI 55,928 M^{-1} cm^{-1}.

Enzymatic Assay

Kinetic characterization was performed as previously reported.[11] In brief, an ADP/NADH coupled assay was used to monitor HepI activity by monitoring the absorbance change at 340 nm at 37 °C on a Cary Bio 100 UV-Vis Spectrometer. Under normal conditions, the assay buffer was composed of 50 mM HEPES, 50 mM KCl, 10 mM $MgCl_2$, pH 7.5. The coupled enzyme reaction additionally contained 100 μM phosphoenolpyruvate, 100 μM NADH, 100 μM dithiothreitol (DTT) and 0.05 U/μL of both pyruvate kinase and lactate dehydrogenase. 100 μM ADPH was used when ODLA concentration was varied and 100 μM ODLA was used when ADPH was varied. Once a stable baseline was established the reaction was initiated by addition of HepI to a final concentration of 50 nM or 100 nM (for high and lower substrate concentrations respectively) and all reported reaction rates are after background subtraction. For these data, ADPH was replaced with compounds 2a,c-e to examine their behavior as a substrate. Data was fit to the following equation: $v = vmax[S]$ using Kaleidagraph 4.1.3.

Computational Docking Experiments

The structure of HepI (PDB 2GT1, 1.90 Å) was used as a template for docking experiments. From this dimeric structure, only one of the two chains was used for docking. Using the program AutoDock Tools, a PDBQT file of HepI was generated for docking with the following specifications: no bonds repaired, hydrogens added, gasteiger charges added, non-polar hydrogens and lone pairs removed, waters removed, and charges merged.

Using ChemDraw 3D, four azido-analogues of ADPH, **2a** and **2c-e**, and the native substrate ADPH, were prepared for docking as MDL MOLfiles. Using the program OpenBabel, the analogues were optimized by adding the appropriate hydrogens found at pH 7.5. Then, 3D dimensional coordinates for each analogue were generated, and the results were output as PDB files. Using OpenBabel's obminimize program, low-energy conformers of each ligand with optimal geometry were generated. The MOLfiles were then converted to PDBQT files for docking experiments.

Docking experiments were performed within a grid box that included both the ADPH and FDLA binding sites. The parameters were as follows: size in x-direction = 60, size in y-direction = 72, size in z-direction = 88, center in x-direction = 41.89, center in y-direction = 2.69, center in z-direction = -1.85.

Docking was performed using AutoDock Vina on the Wesleyan University High-Performance Computing Cluster. The azido-analogues were docked to the protein within the grid box described above. The exhaustiveness was set to 20, and the number of conformations generated for each analogue was set to 200.

After docking, the AutoDock Tools script, process_VinaResult.py, was used to separate each conformation of each azido-analogue into its own file, as well as to process the binding energy and which protein residues were contacted by each conformation of each azido-analogue. Scripts written by Zarek Siegel were used to extract the binding data from these result PDBQT files as a CSV file. The results of docking and analysis were visualized using PyMol.

A binding site analysis was done to determine if the analogues were binding to a similar area of HepI as ADPH. From the structure of HepI with ADPH bound (PDB 2H1H, 2.40 Å), a binding site was defined with all residues within 2 Å of the native substrate, ADPH. For each conformation of each azido-analogue, if at least 10% of the residues in this binding site were contacted, that conformation was considered “in” the ADPH binding site.

Summarized results of the docking are included in Table 4.

IV. Reference

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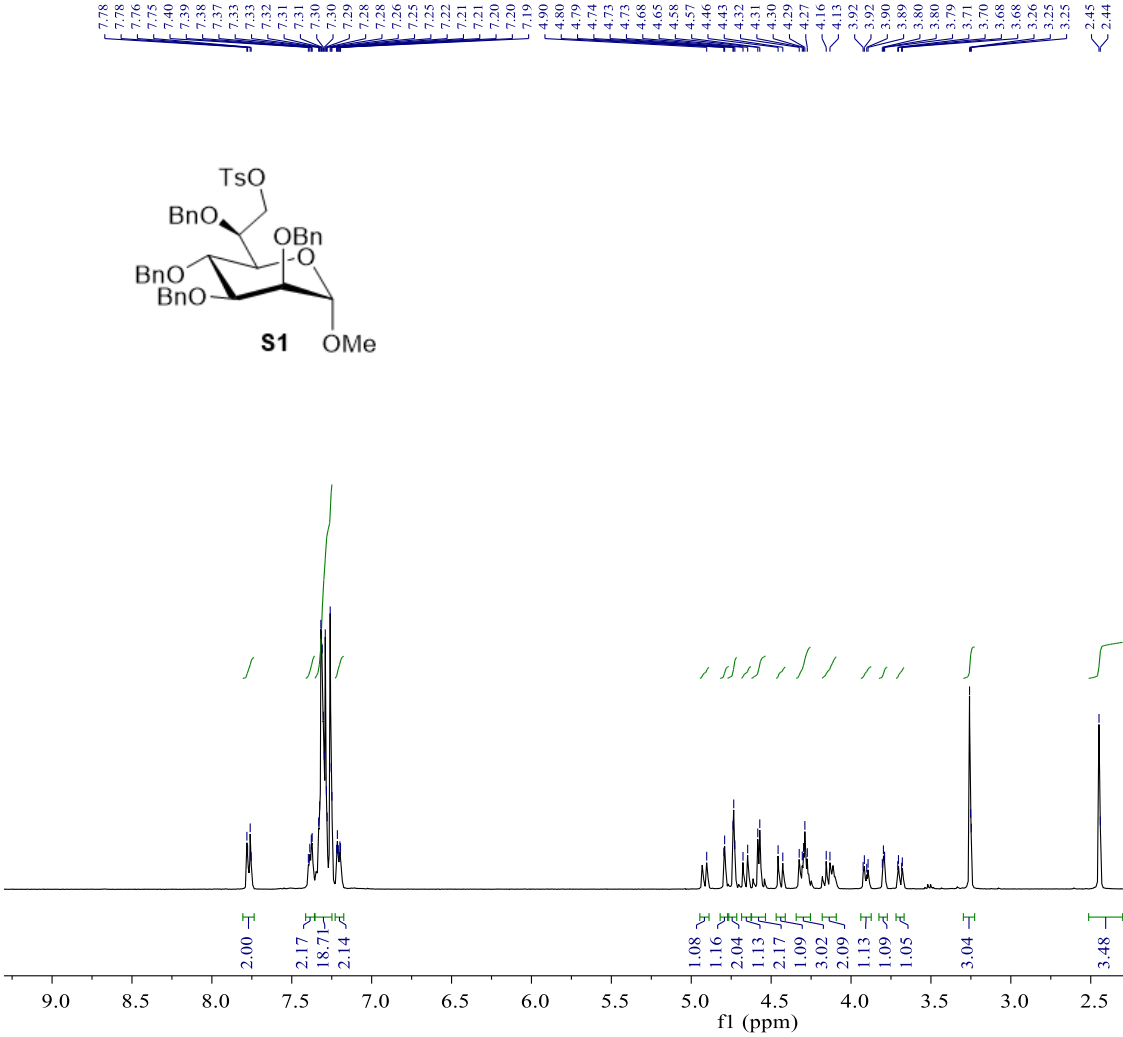
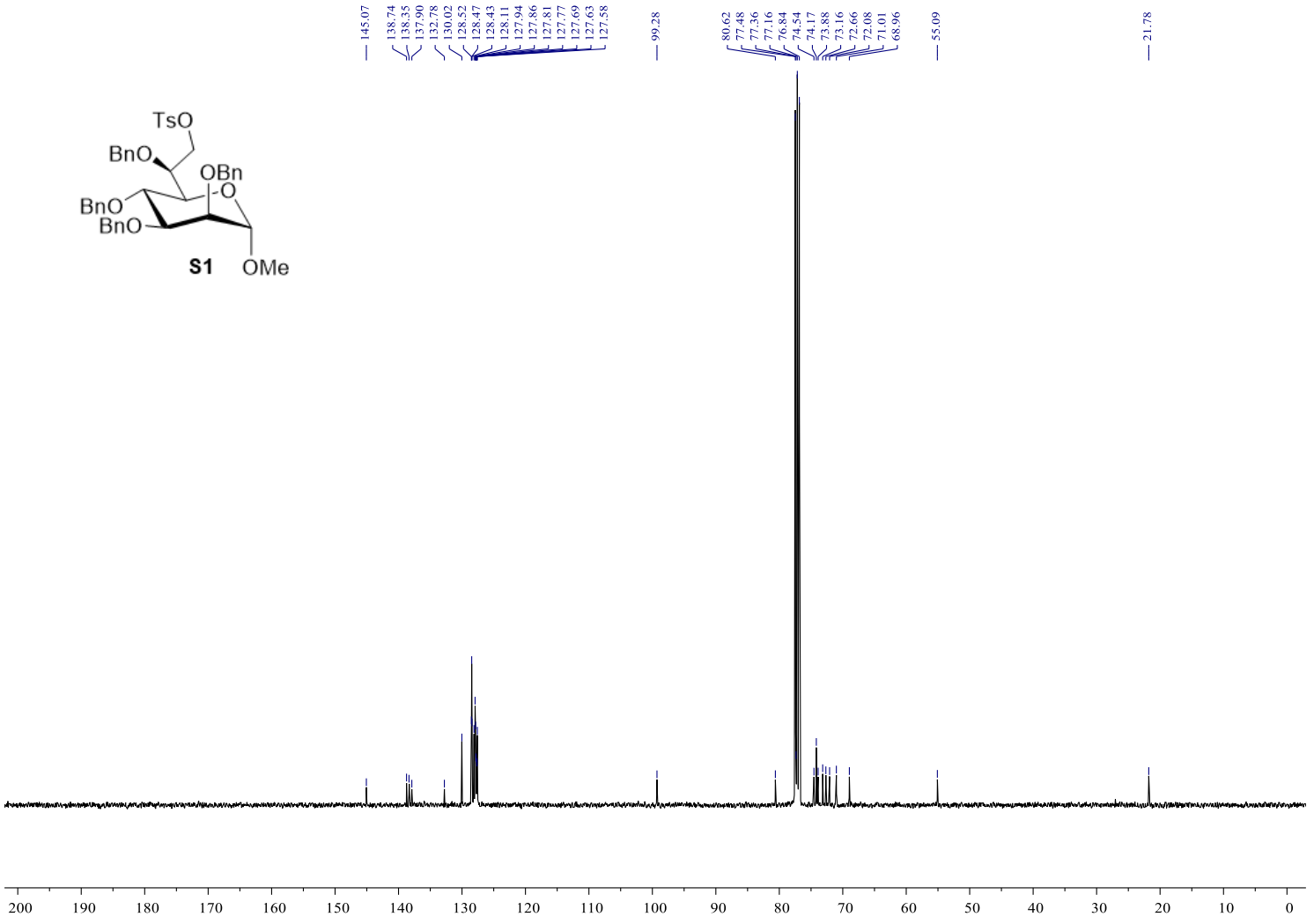
V. NMR spectra

[1]H-NMR (400 MHz, Chloroform-*d*)



^{13}C-NMR (100 MHz, Chloroform-*d*)



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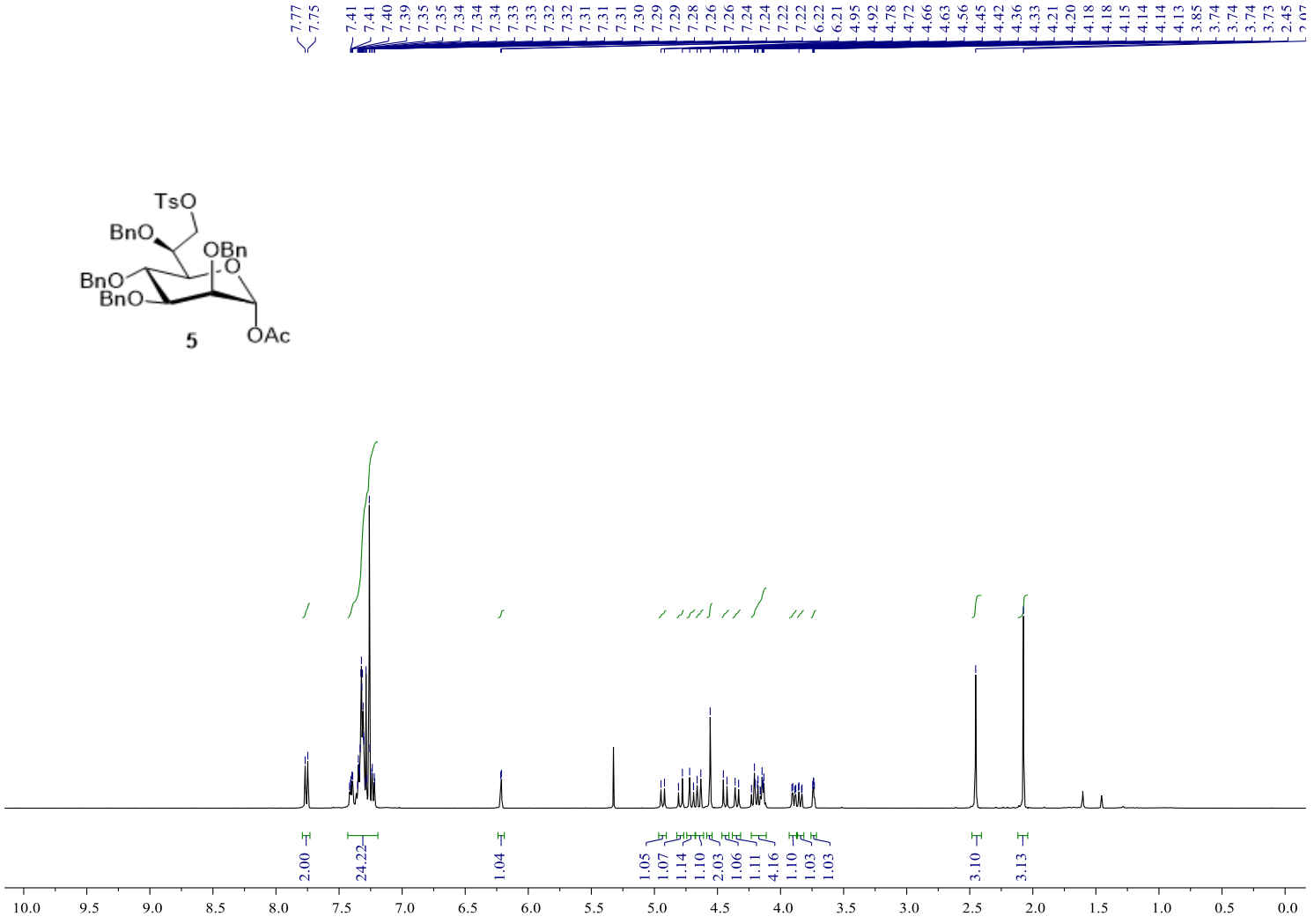

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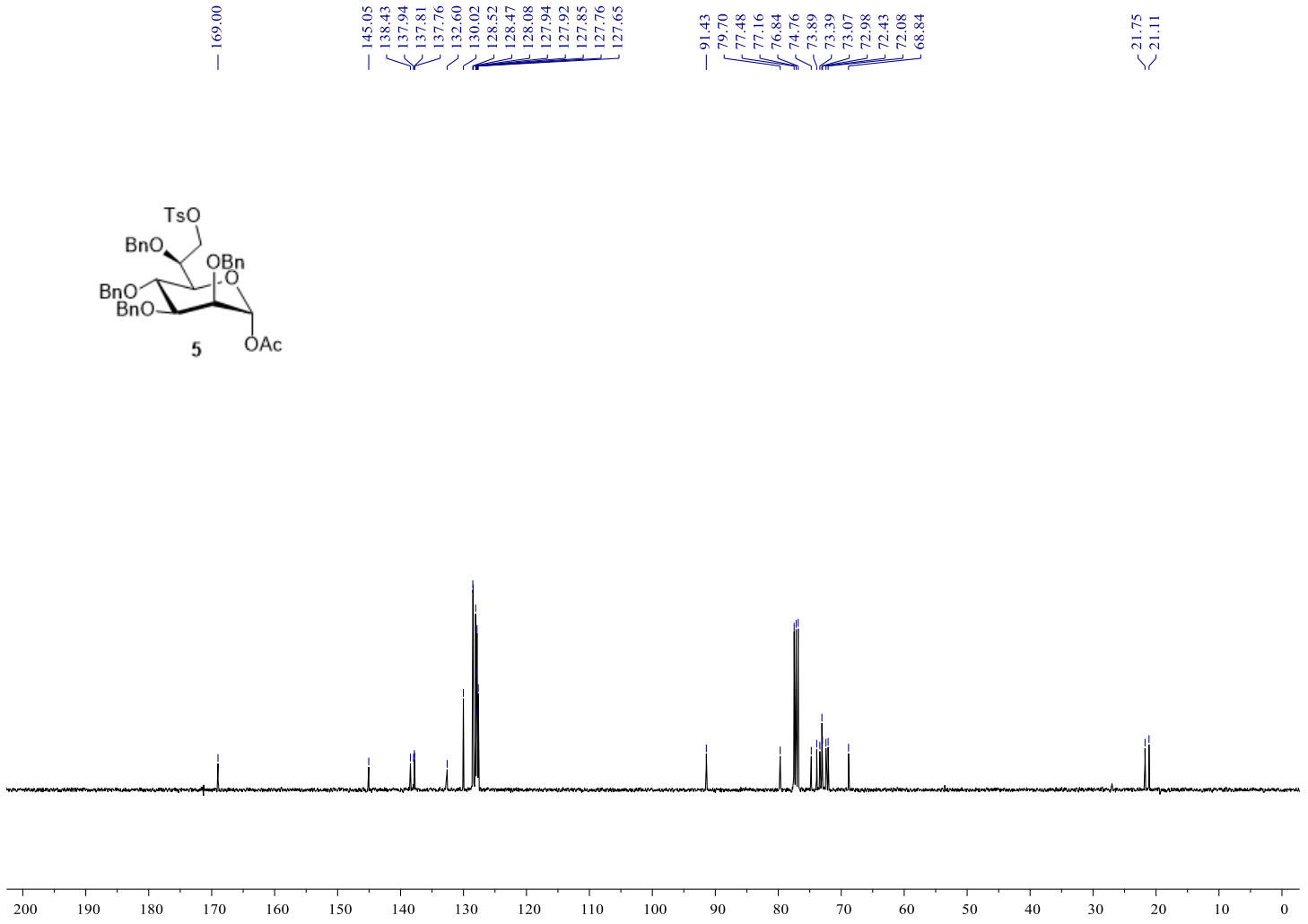
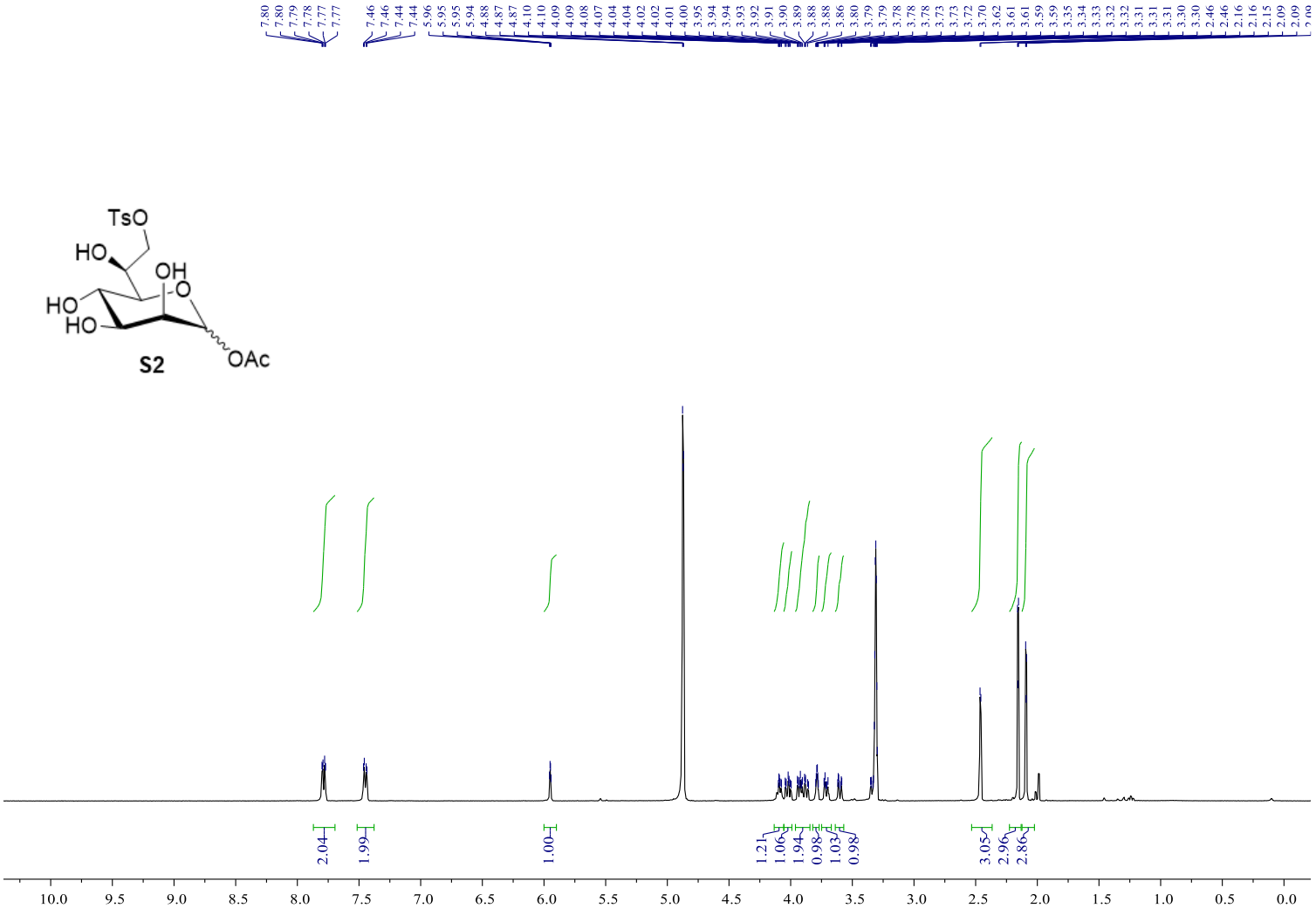


^{1}H-NMR (400 MHz, Methanol-*d*)



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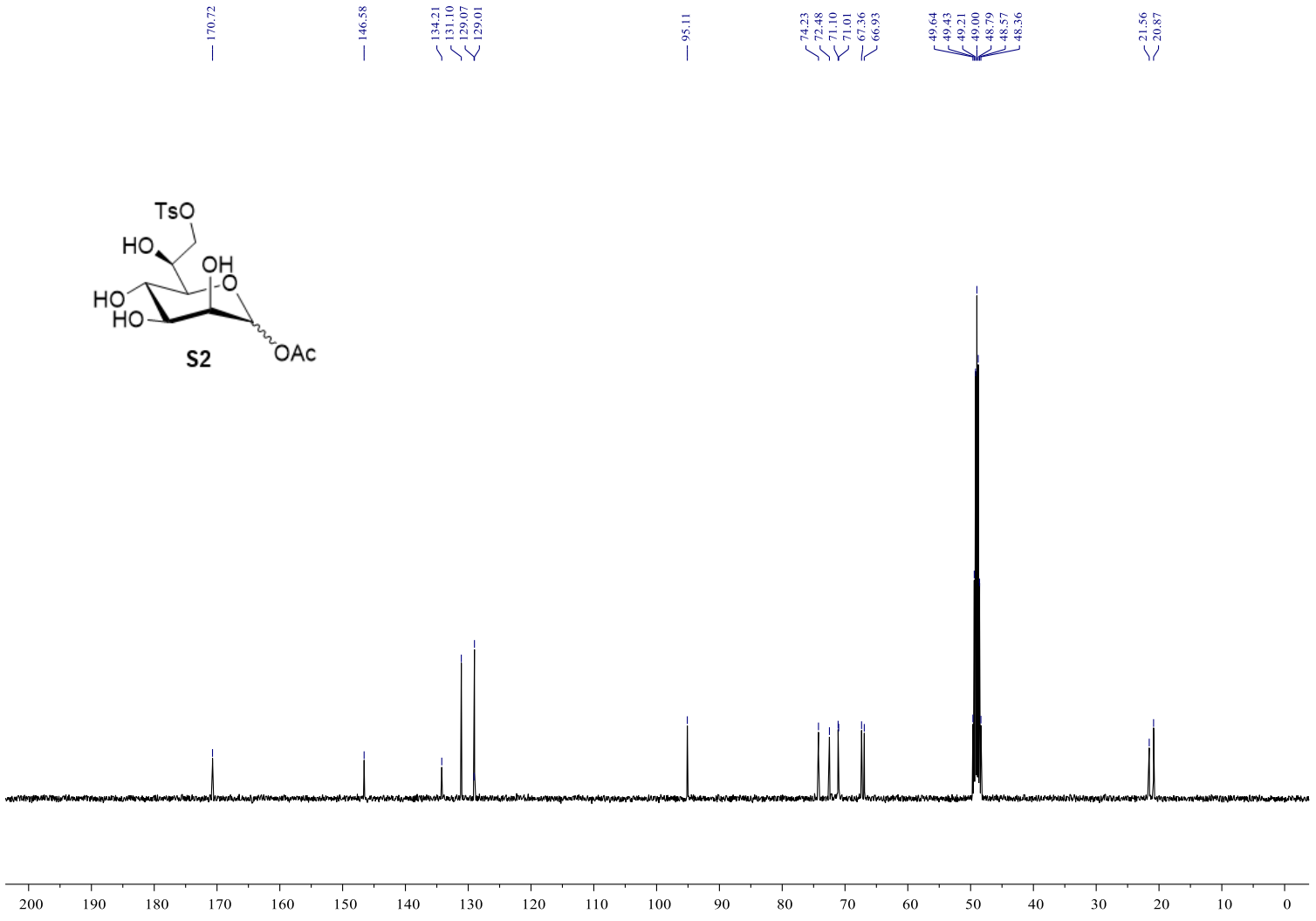

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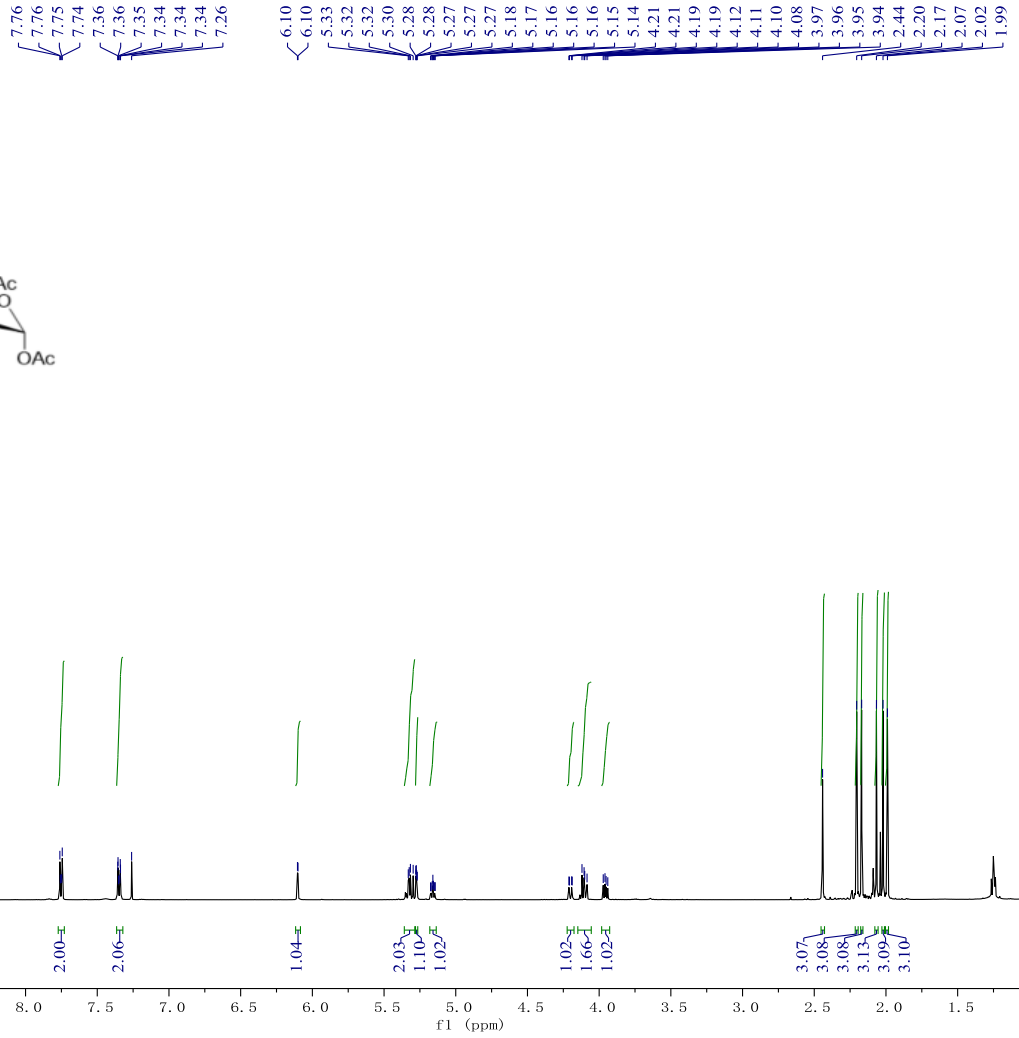

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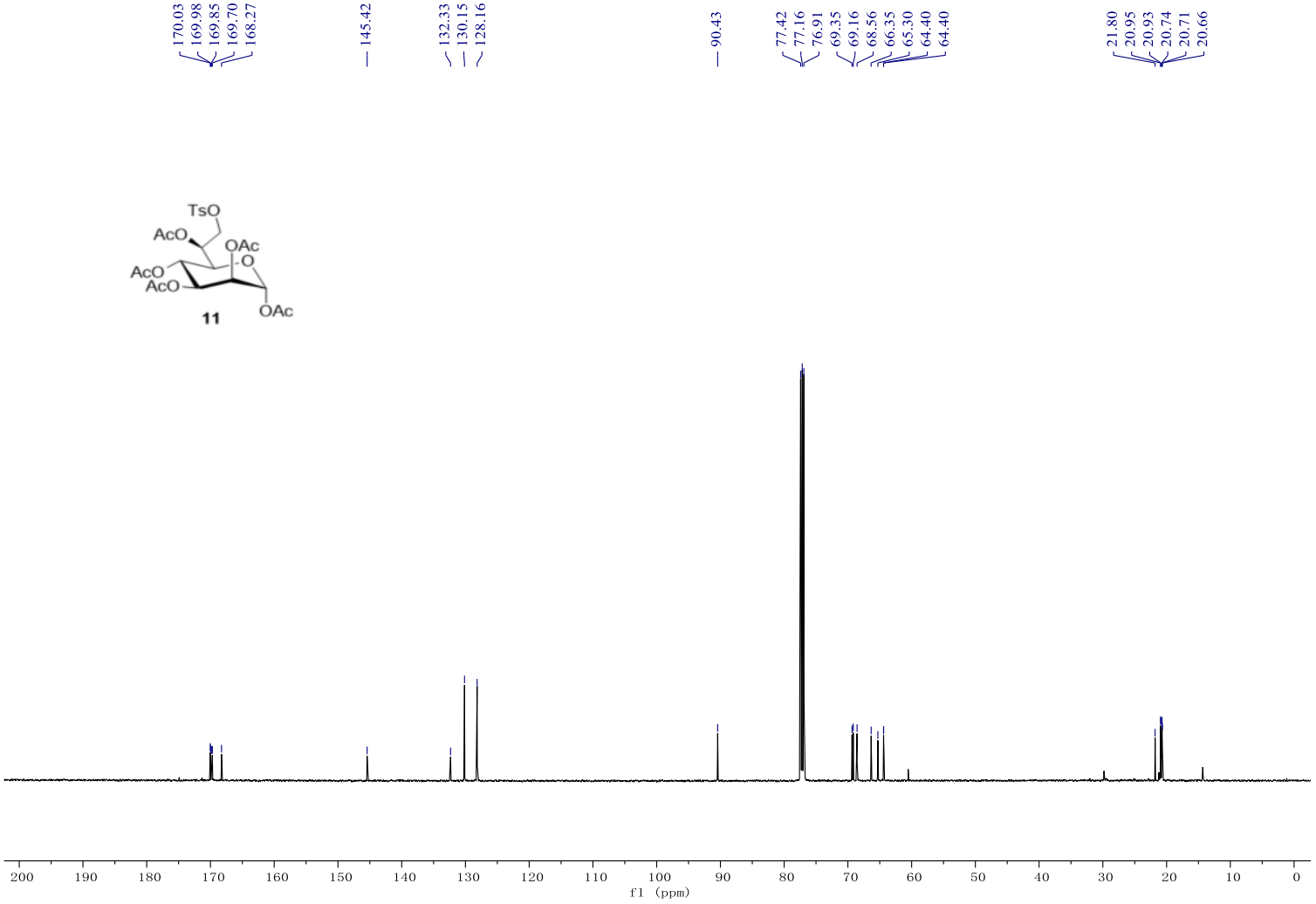

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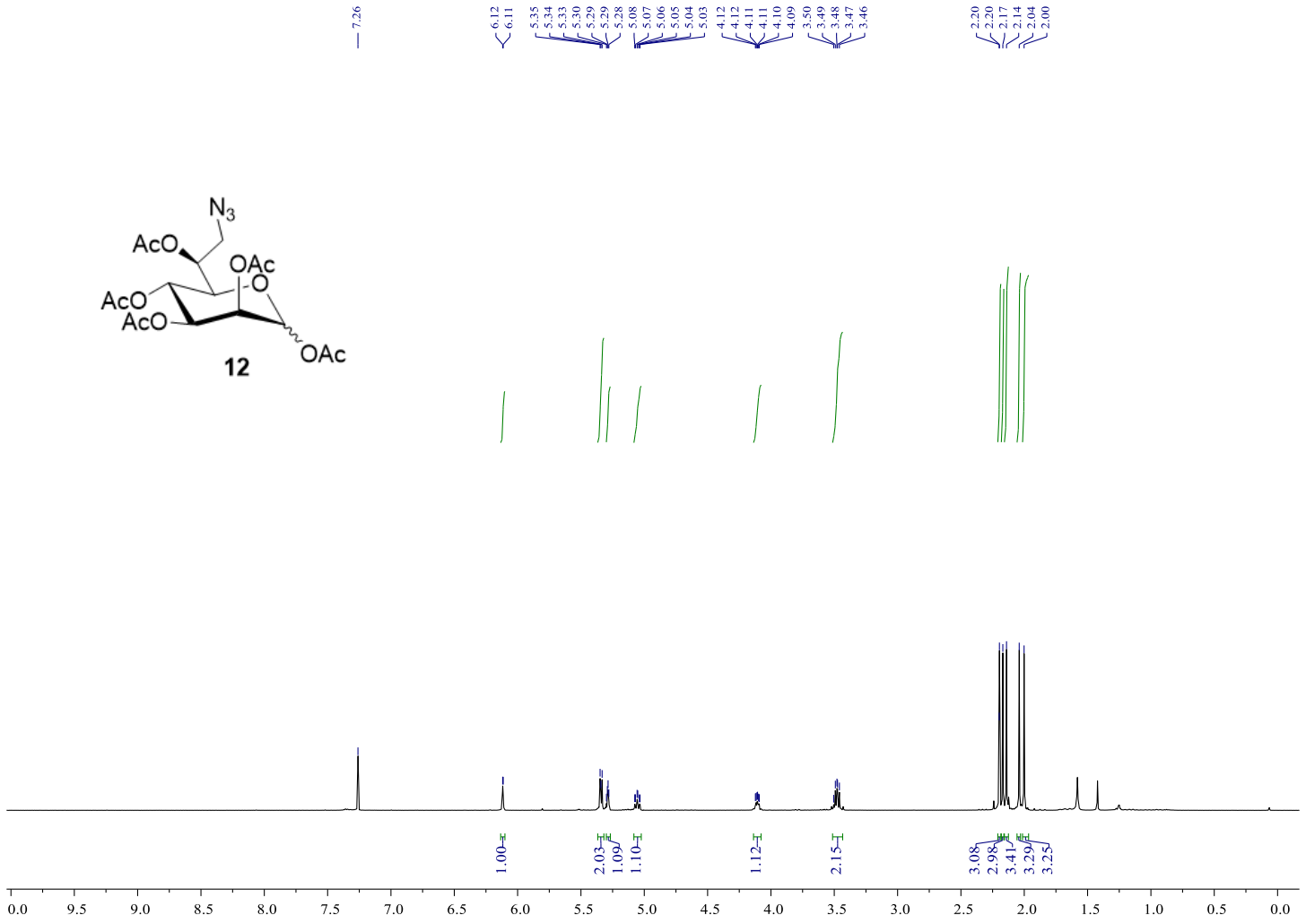

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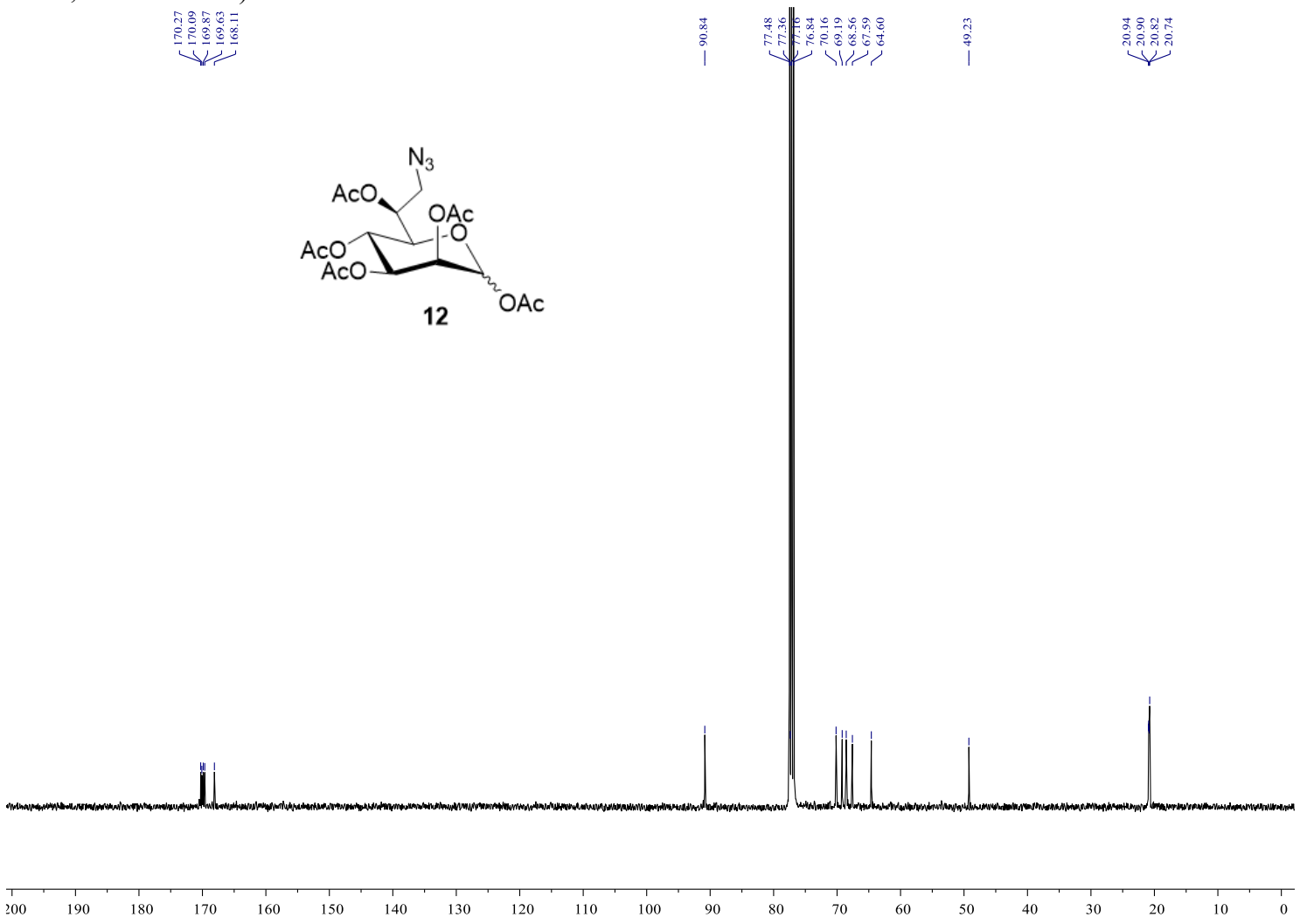

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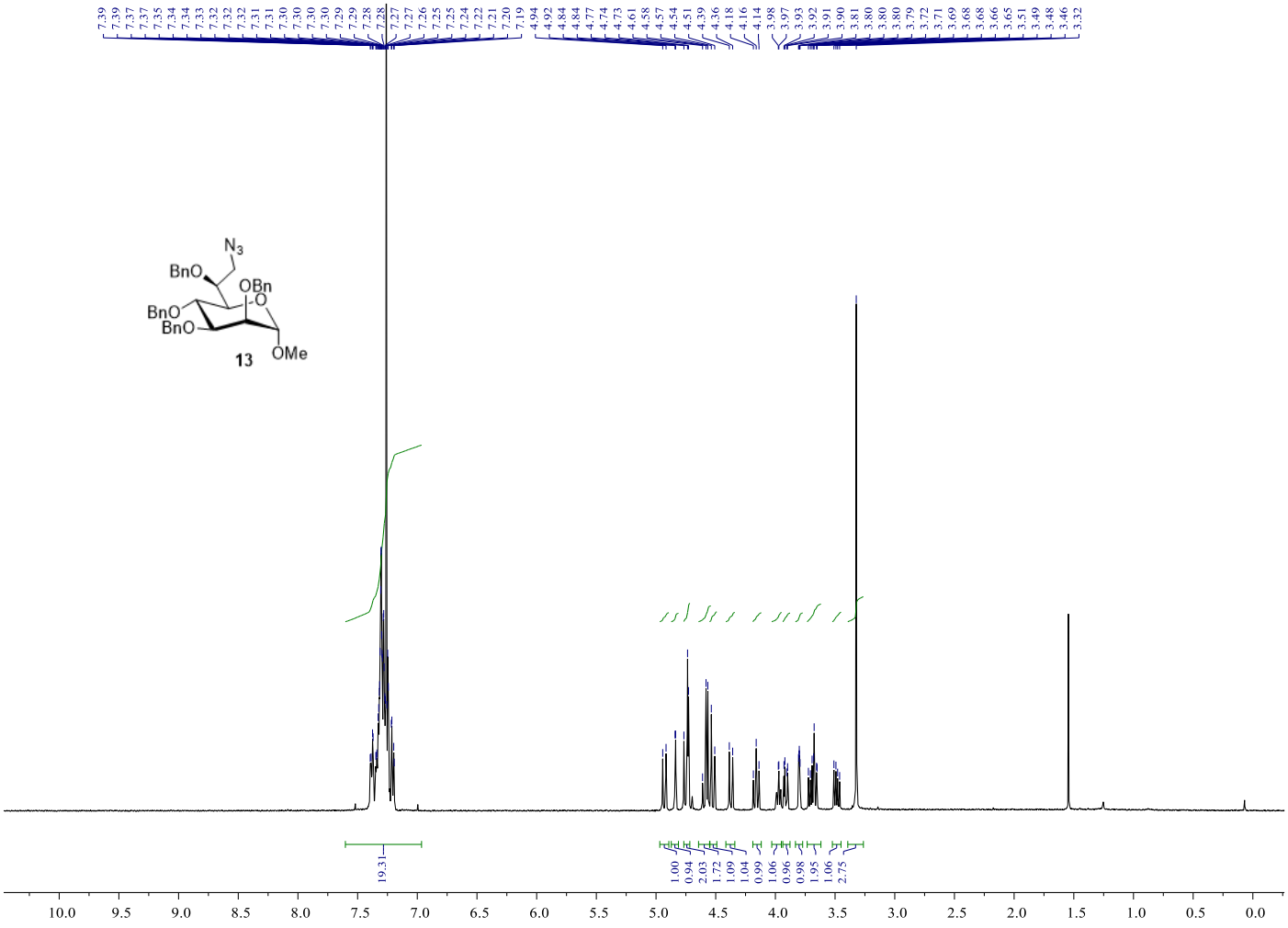

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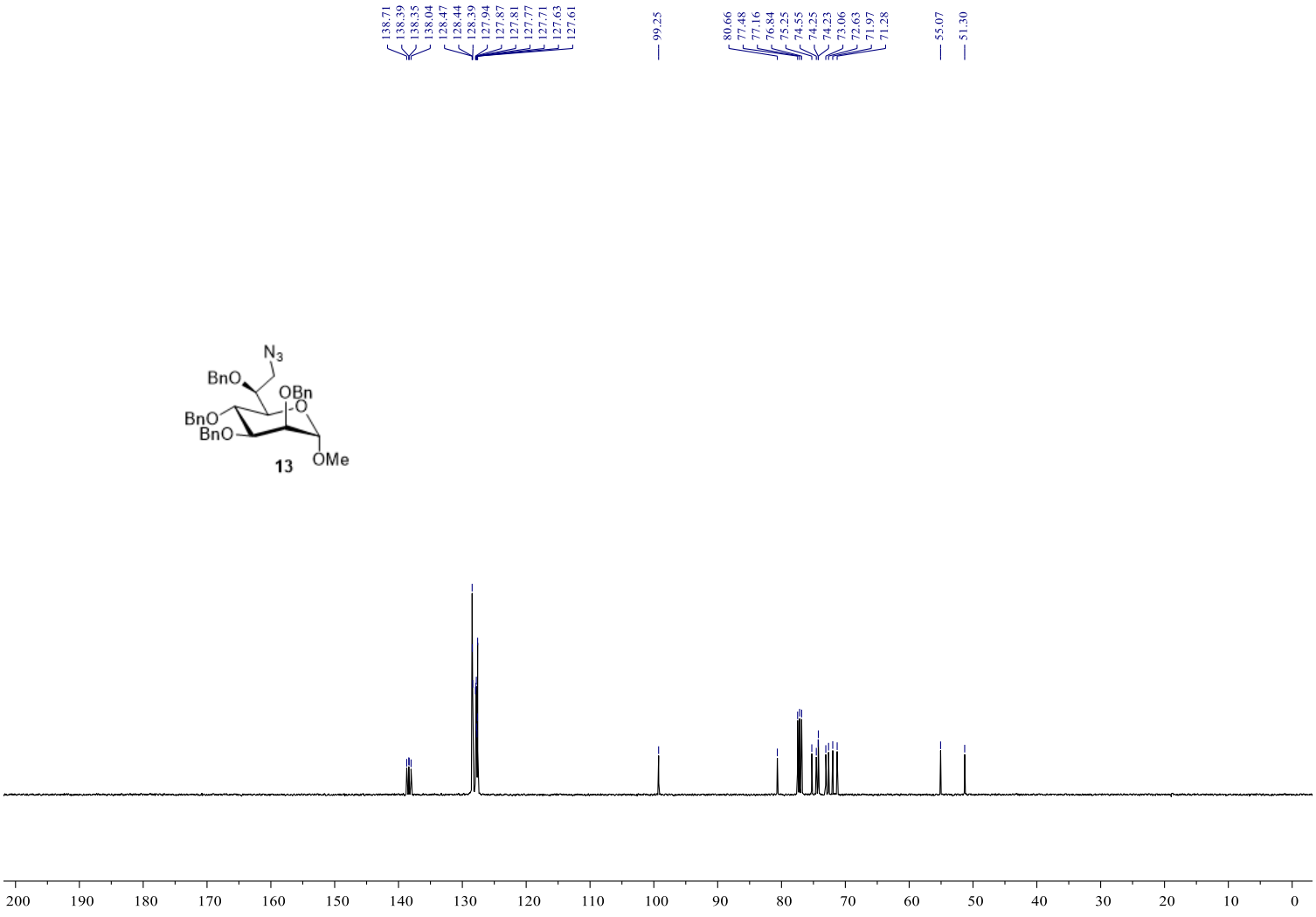

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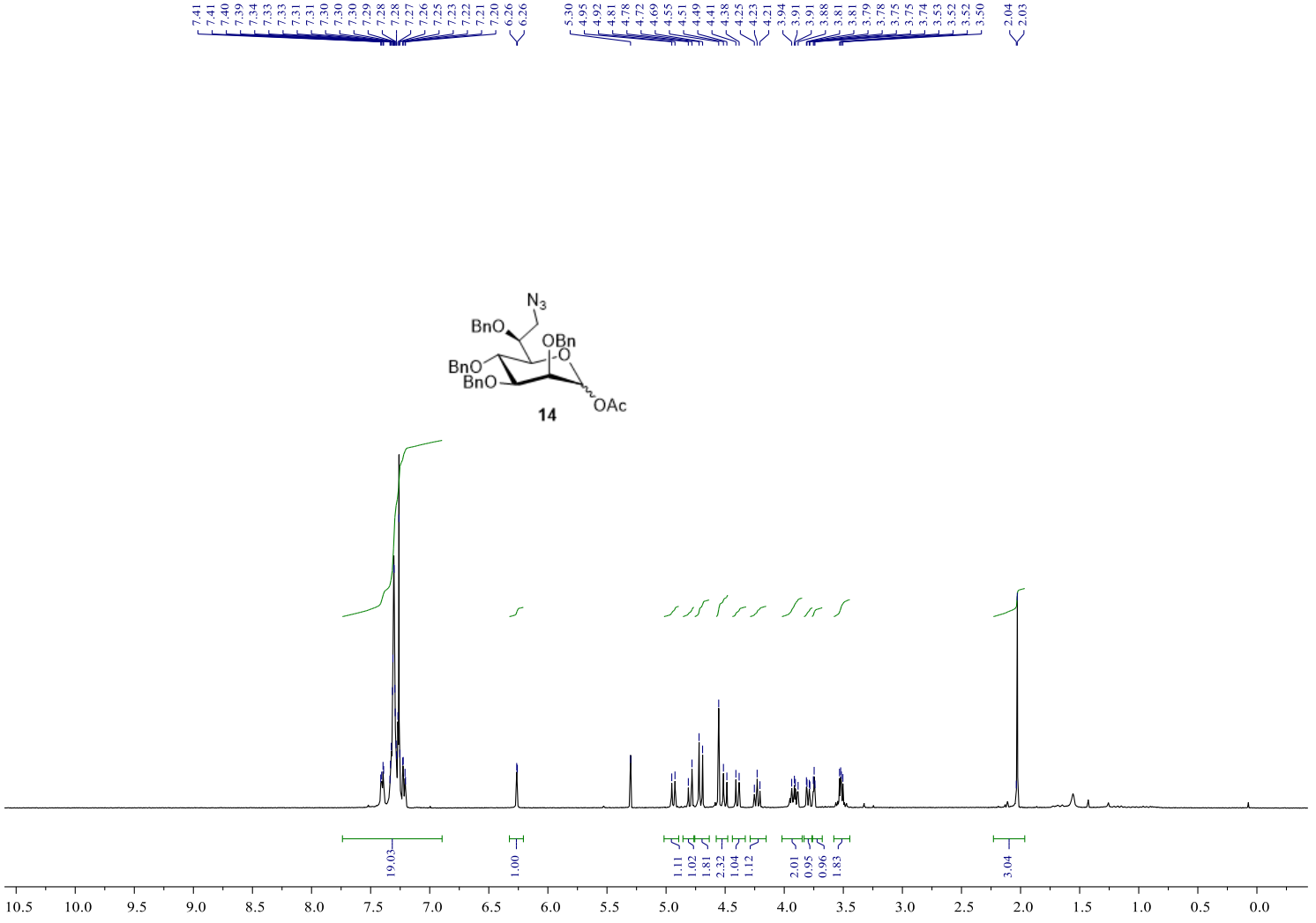

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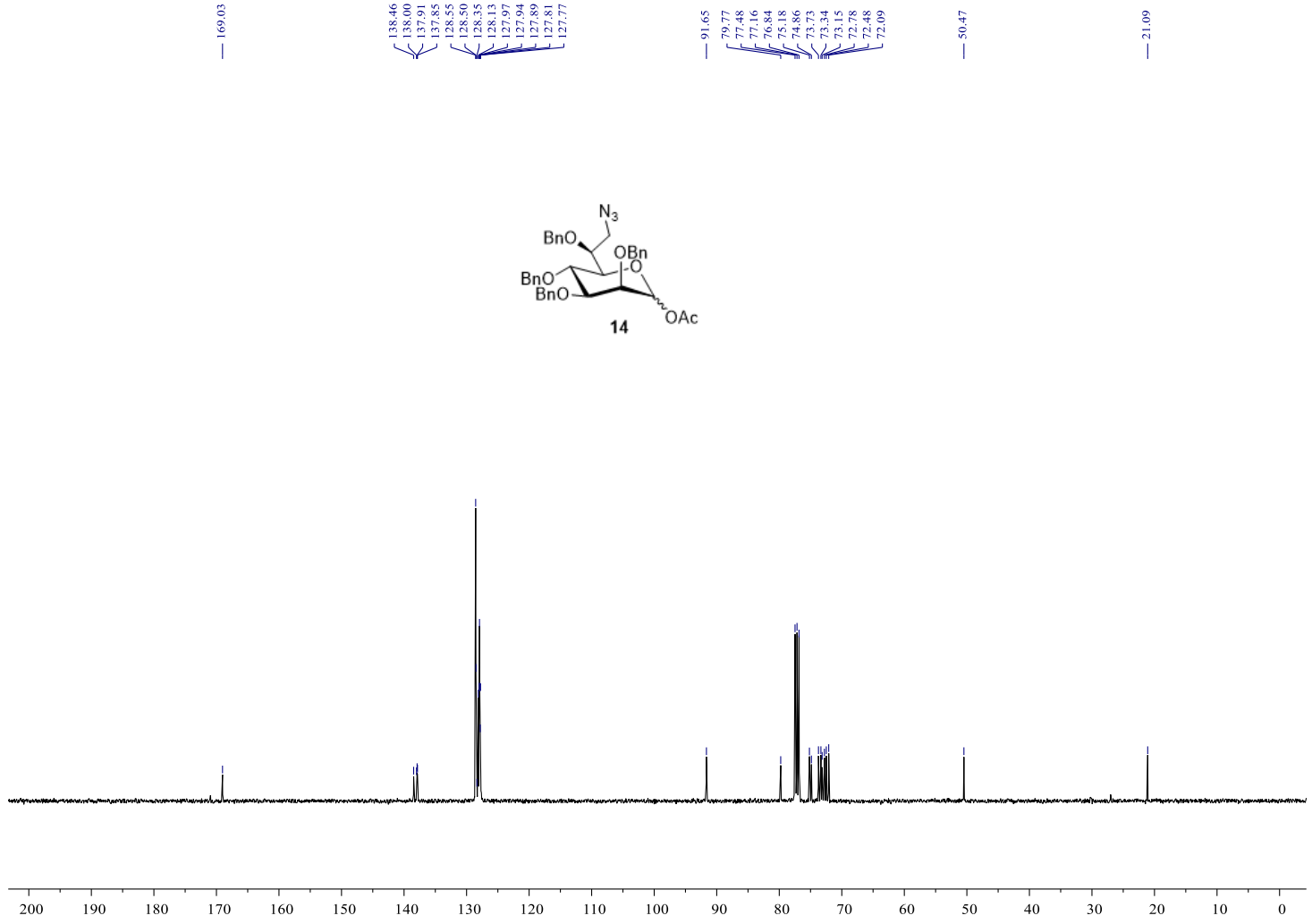

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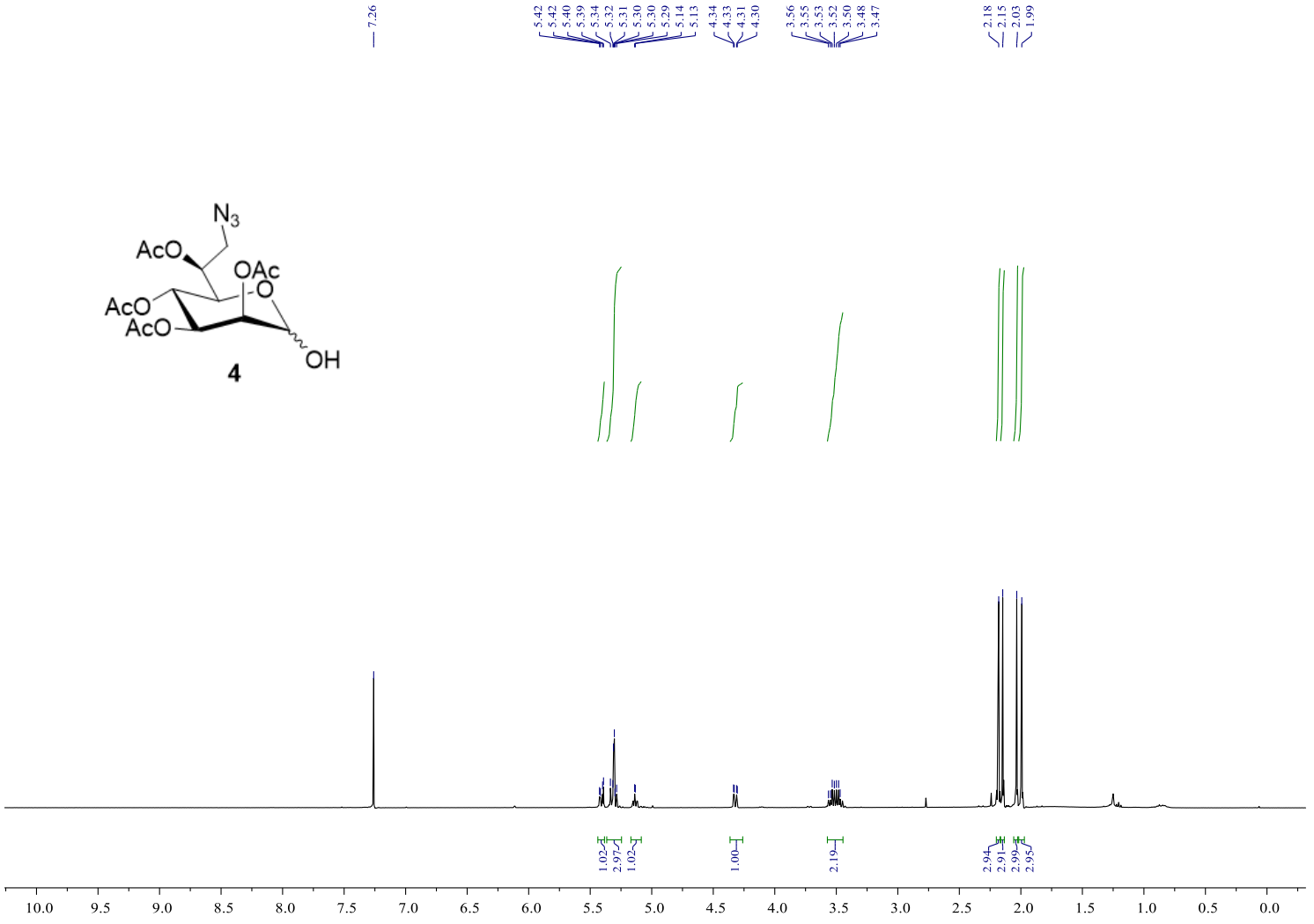

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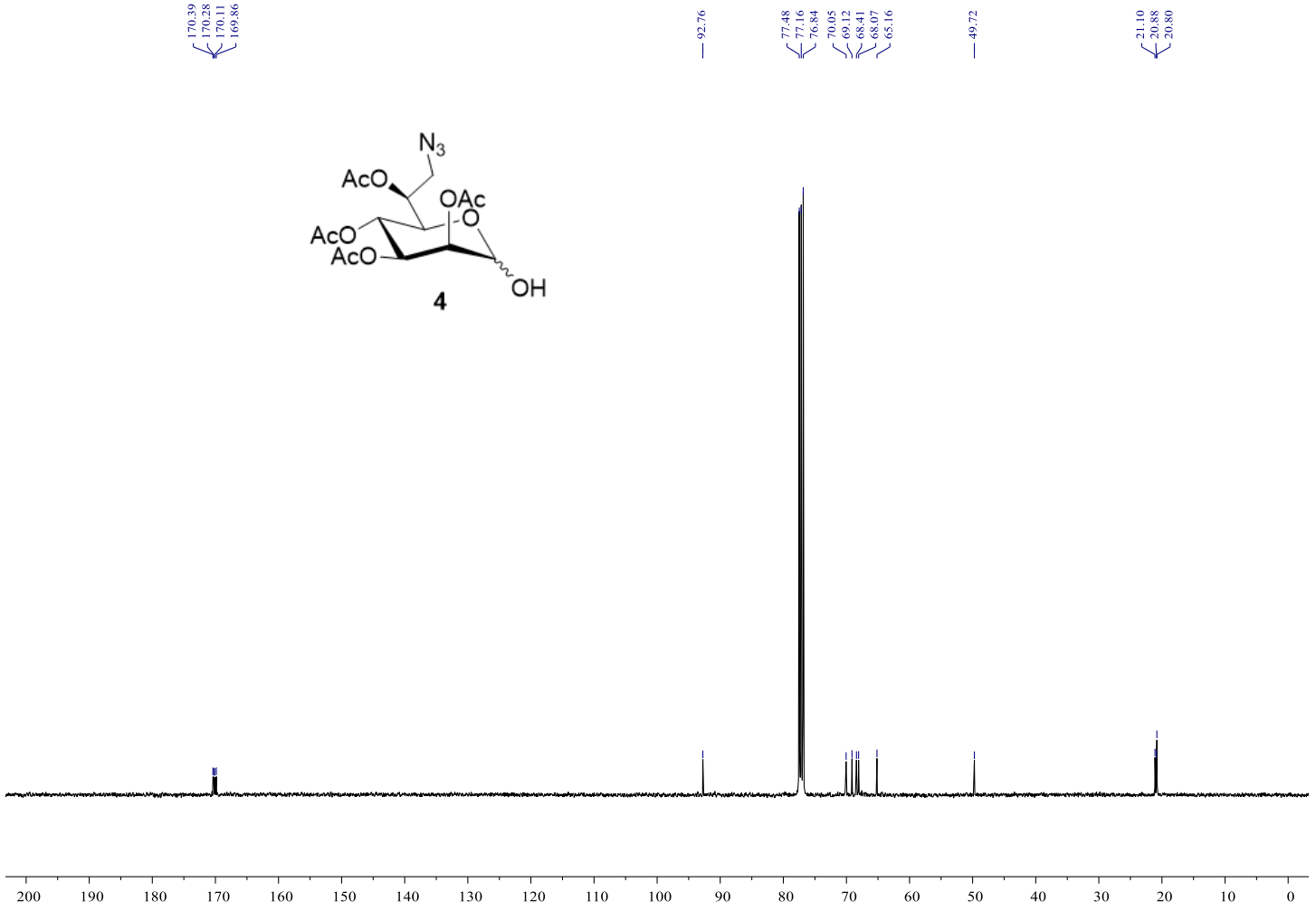

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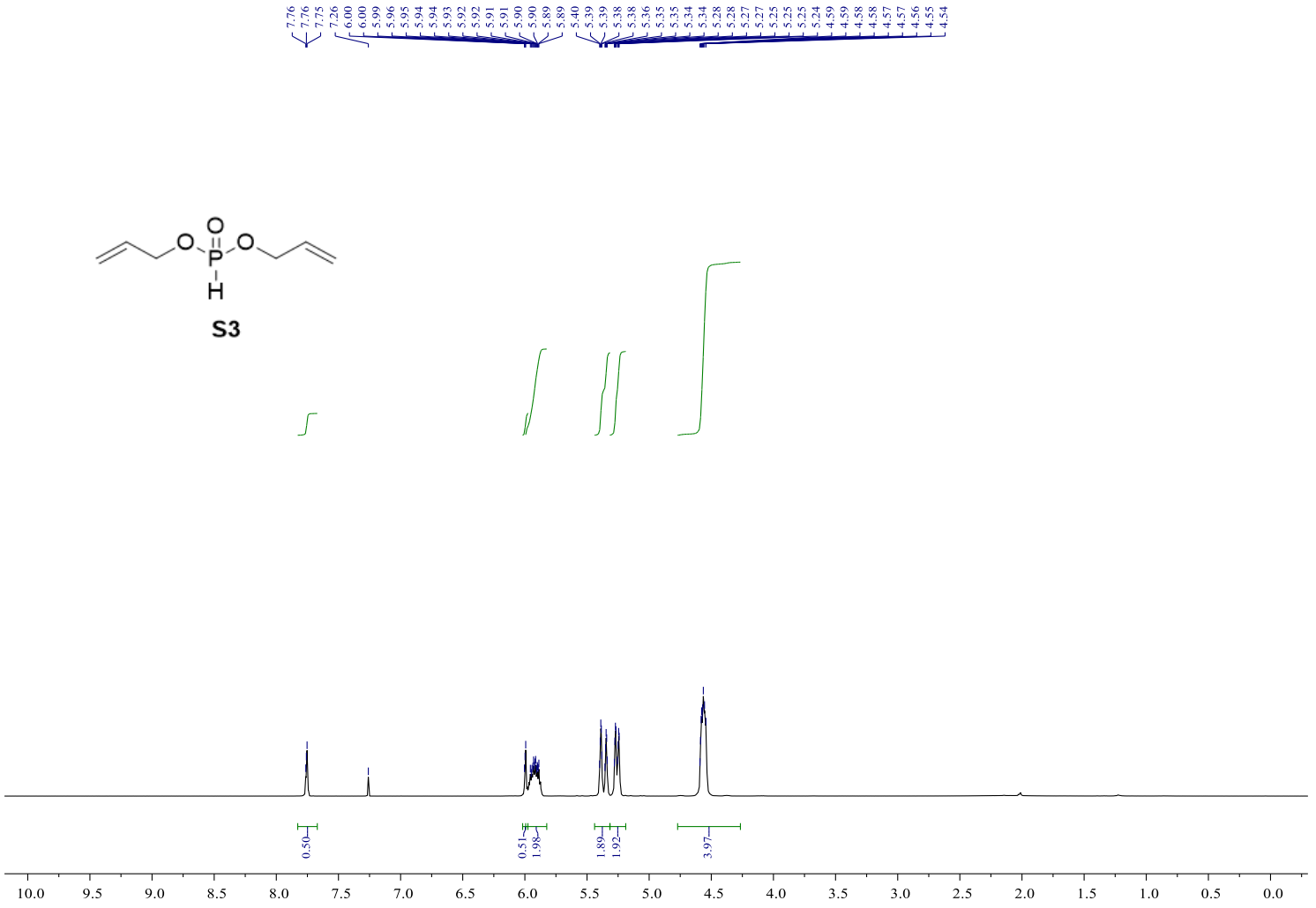
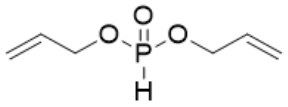
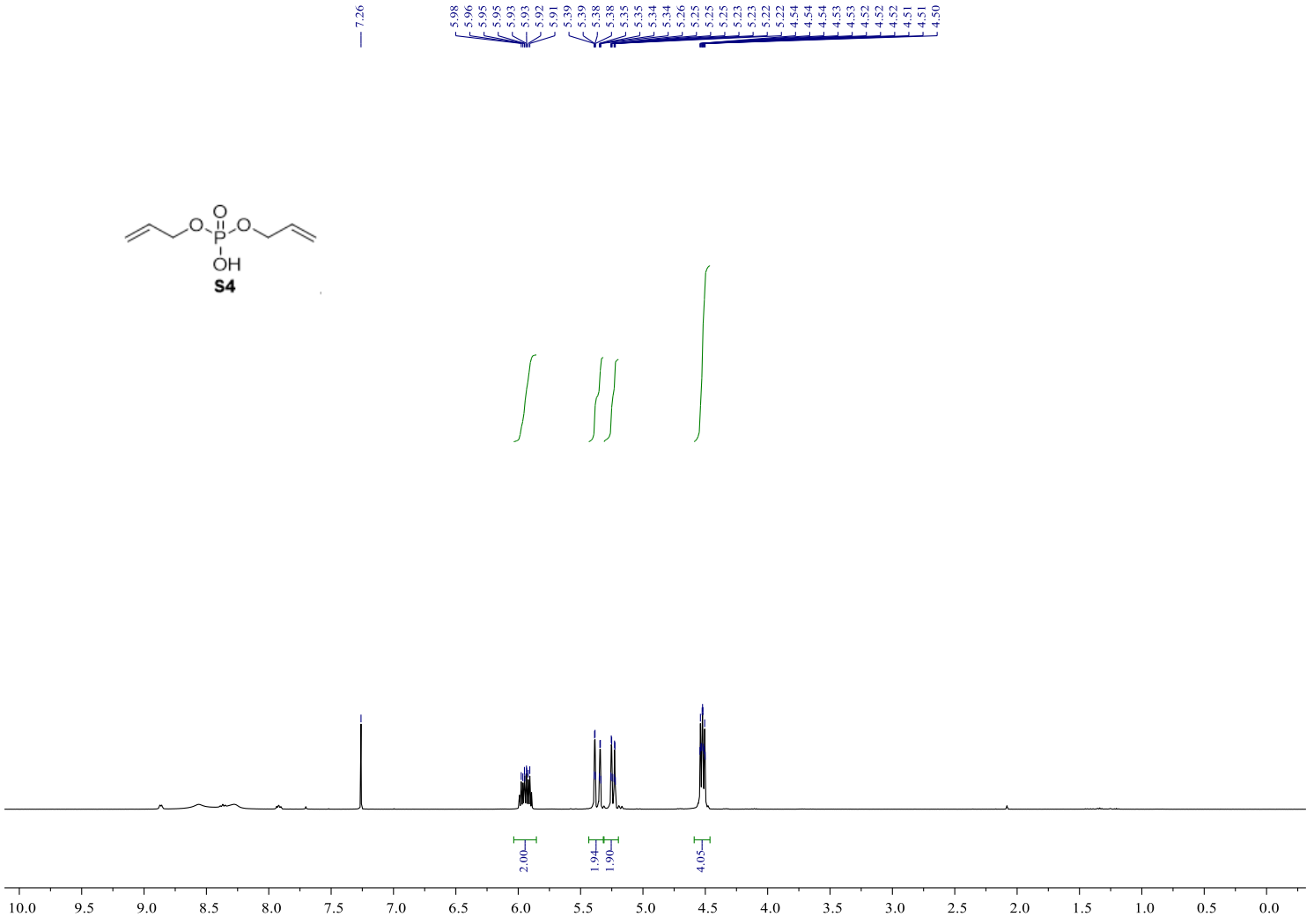


^{31}P-NMR (162 MHz, Chloroform-*d*)



S3

^{1}H-NMR (400 MHz, Chloroform-*d*)



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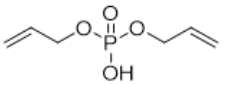

S4

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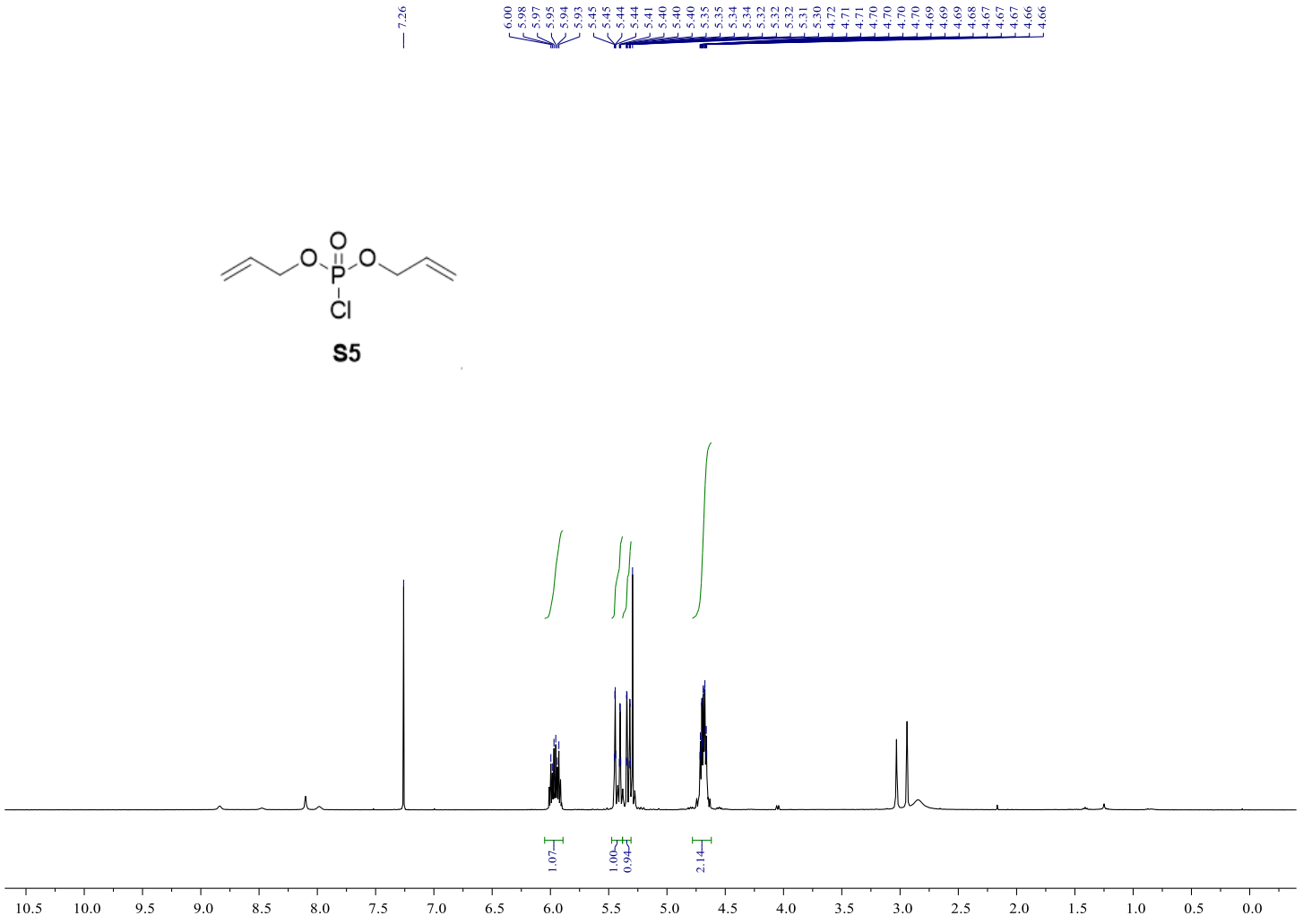

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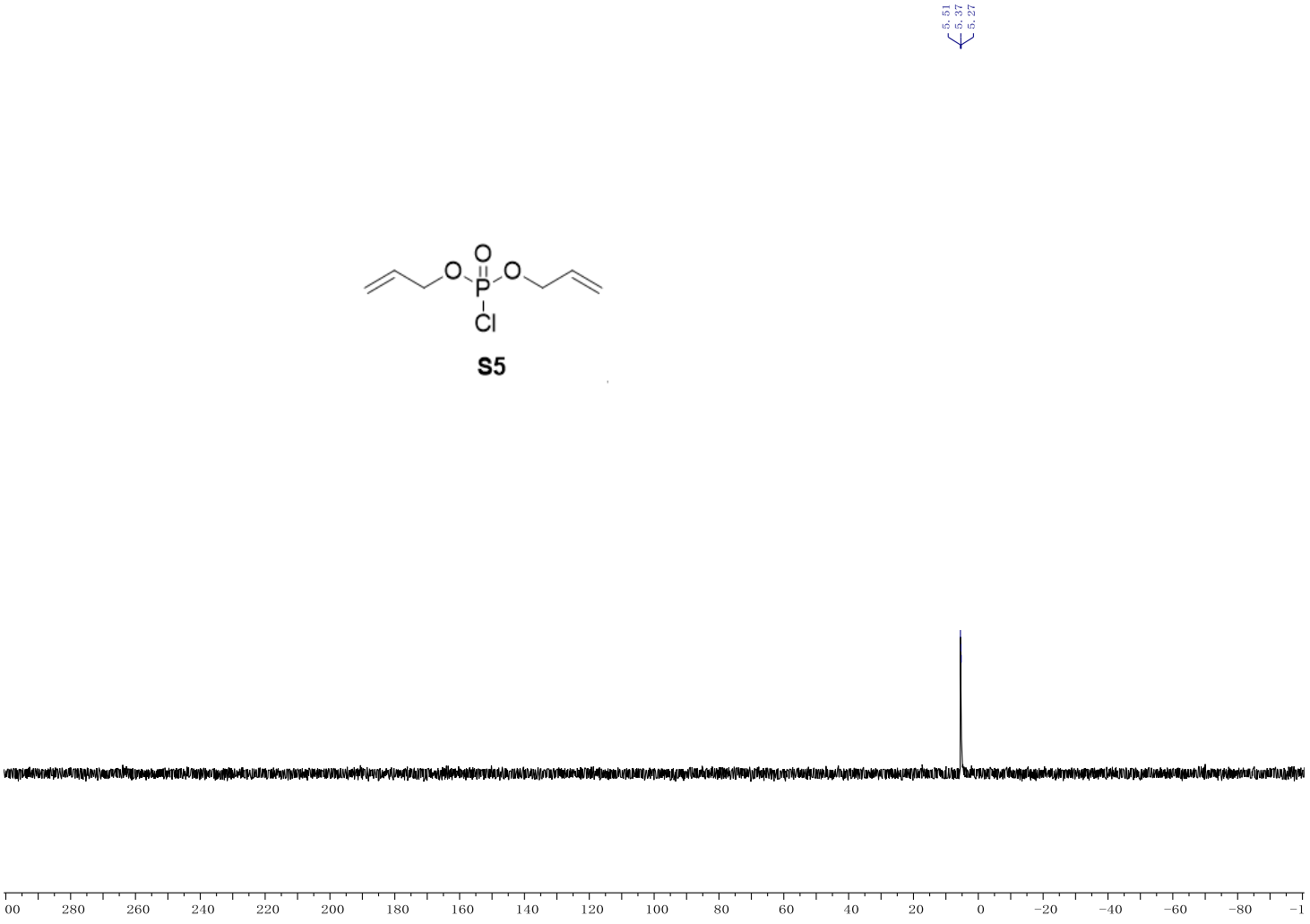
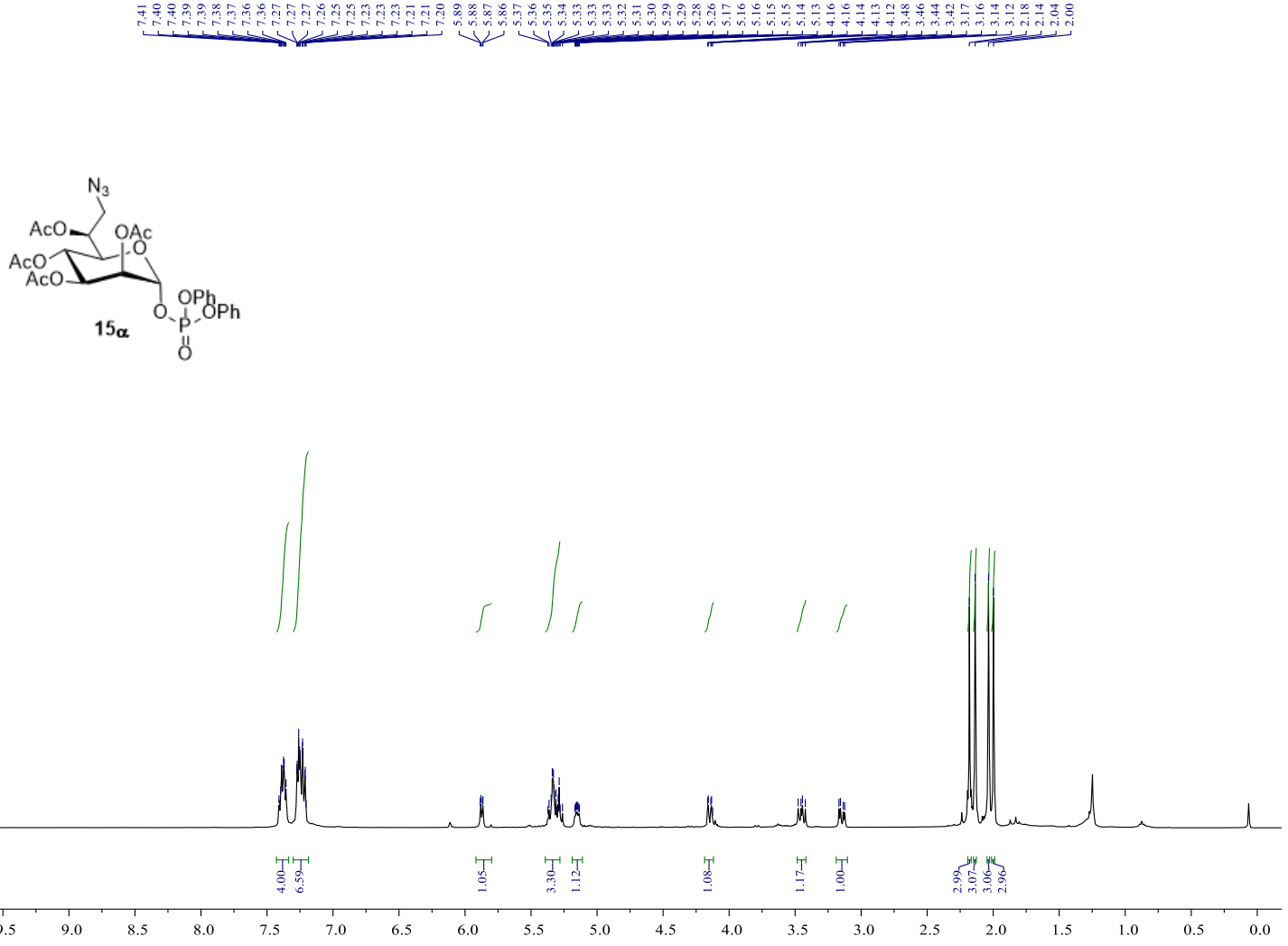


S5

^{1}H-NMR (400 MHz, Chloroform-*d*)



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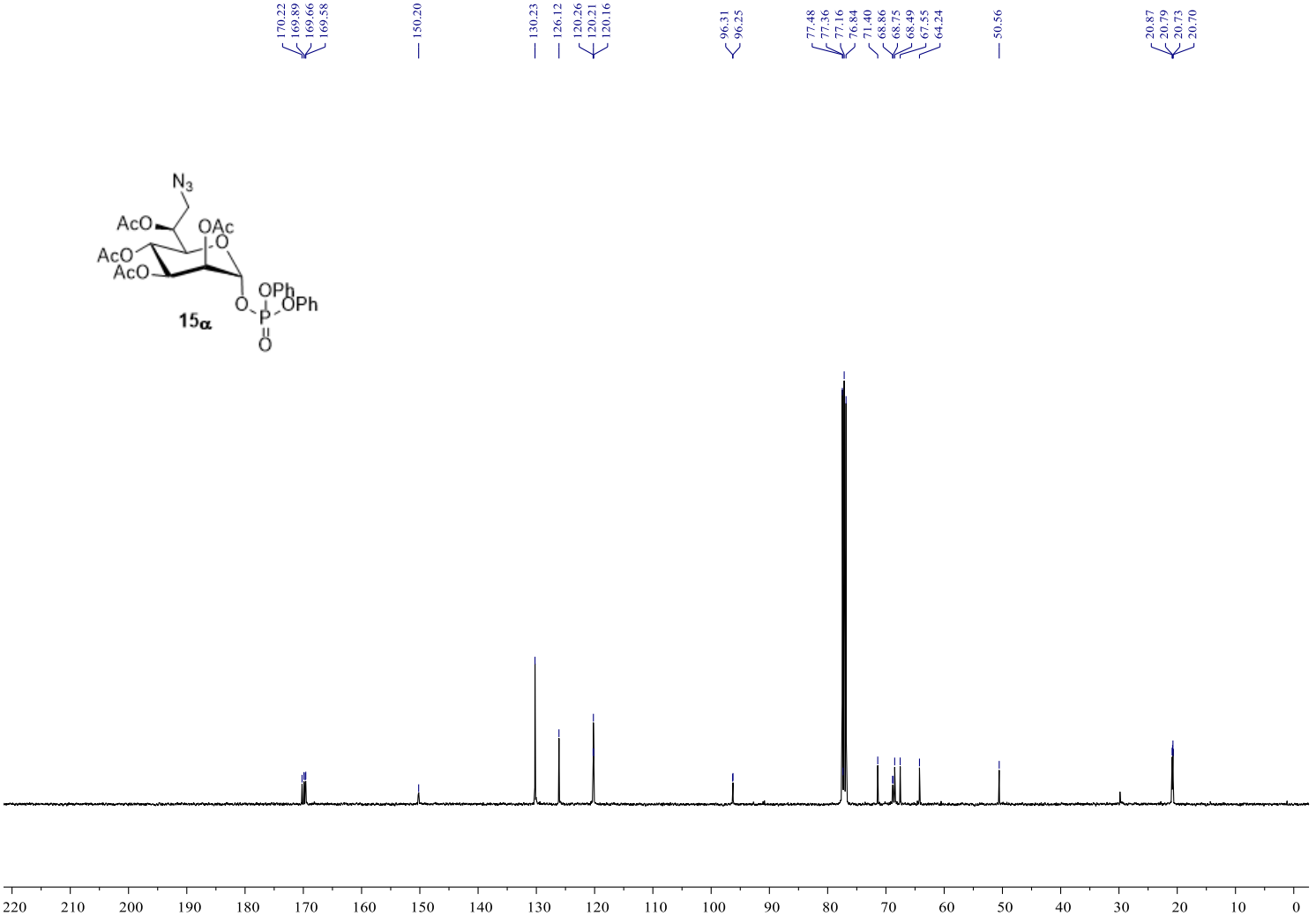
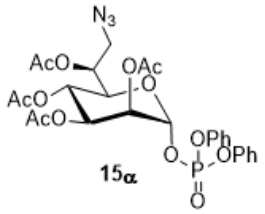
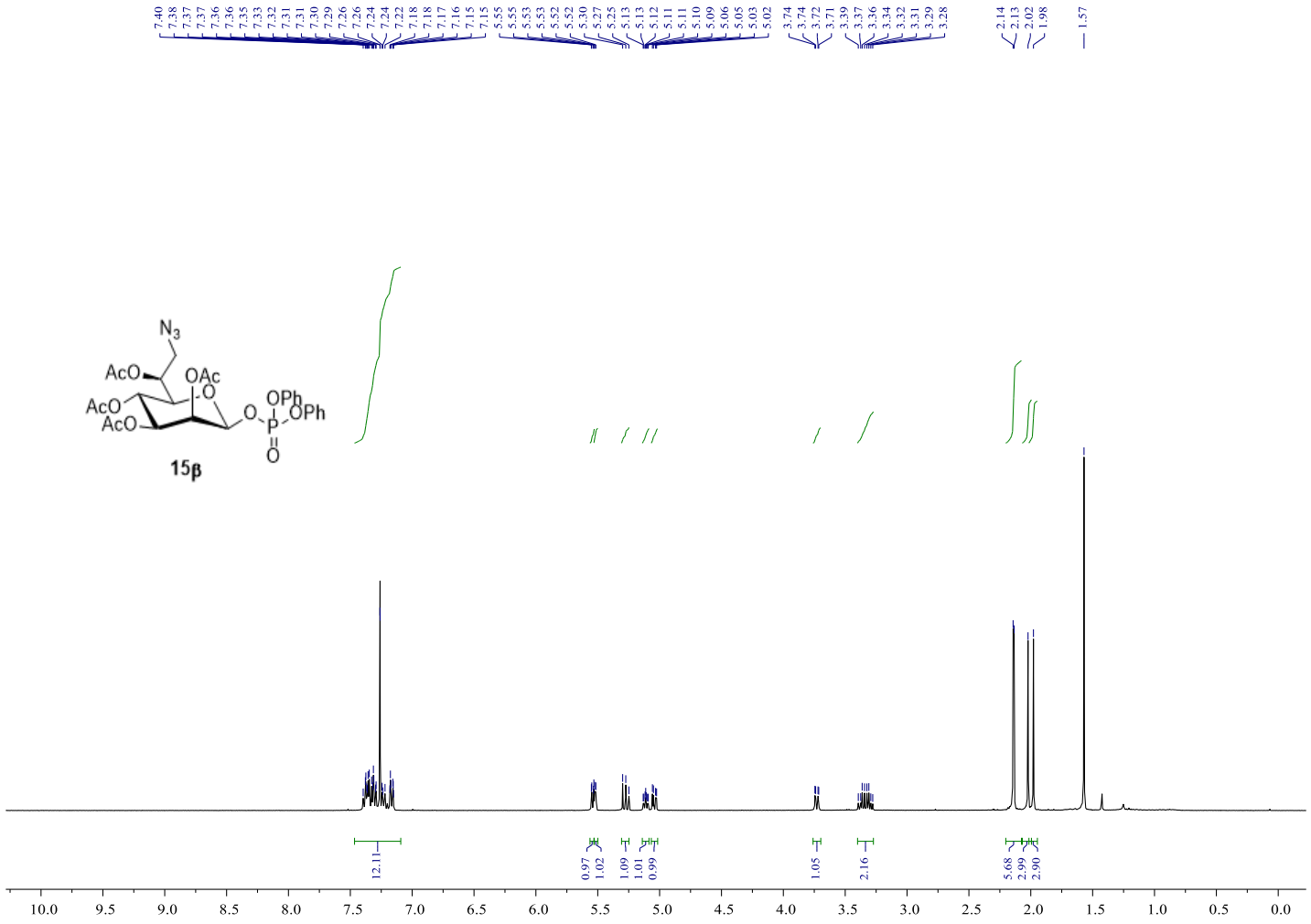


^{31}P-NMR (162 MHz, Chloroform-*d*)



15α

^{1}H-NMR (400 MHz, Chloroform-*d*)



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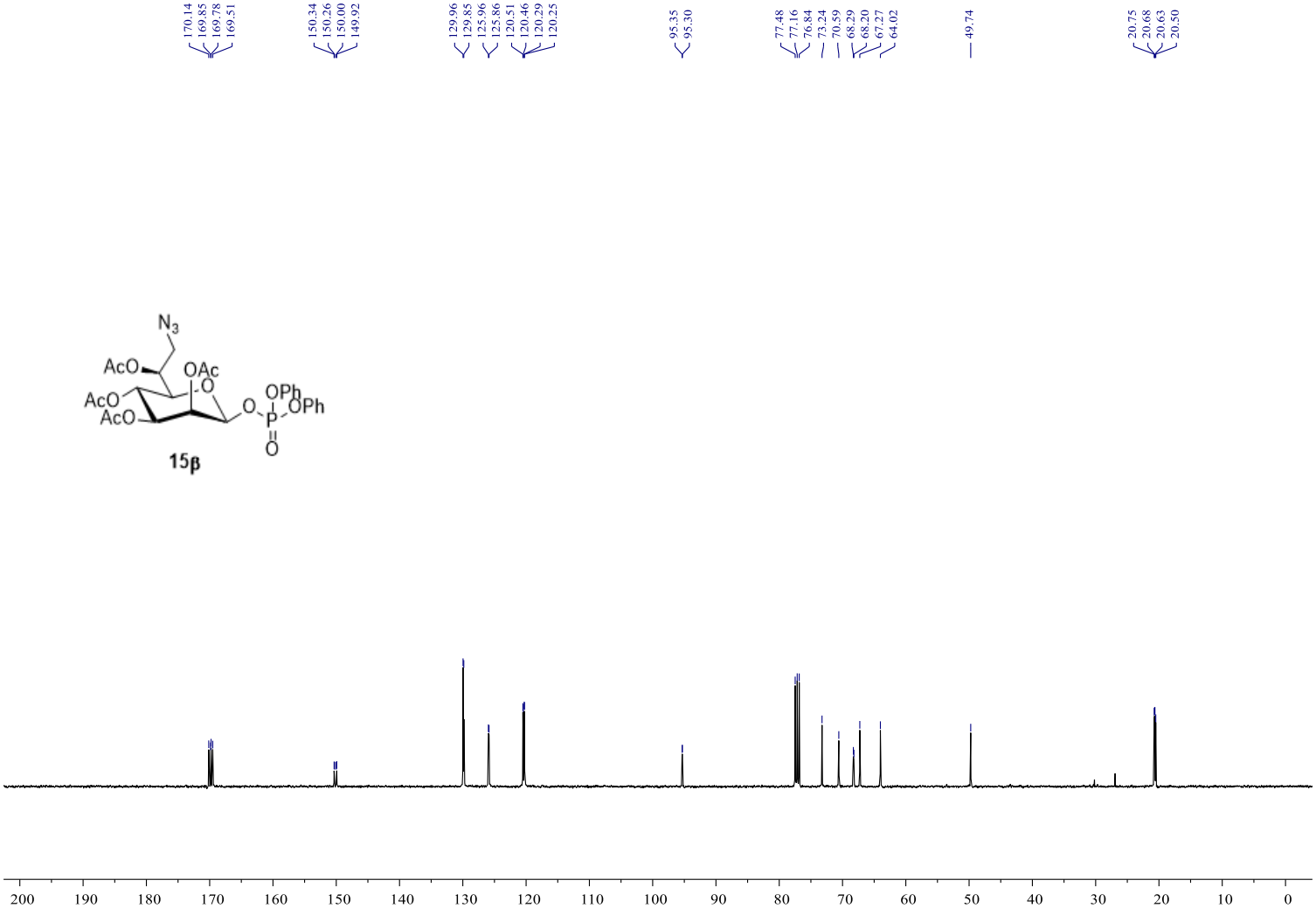

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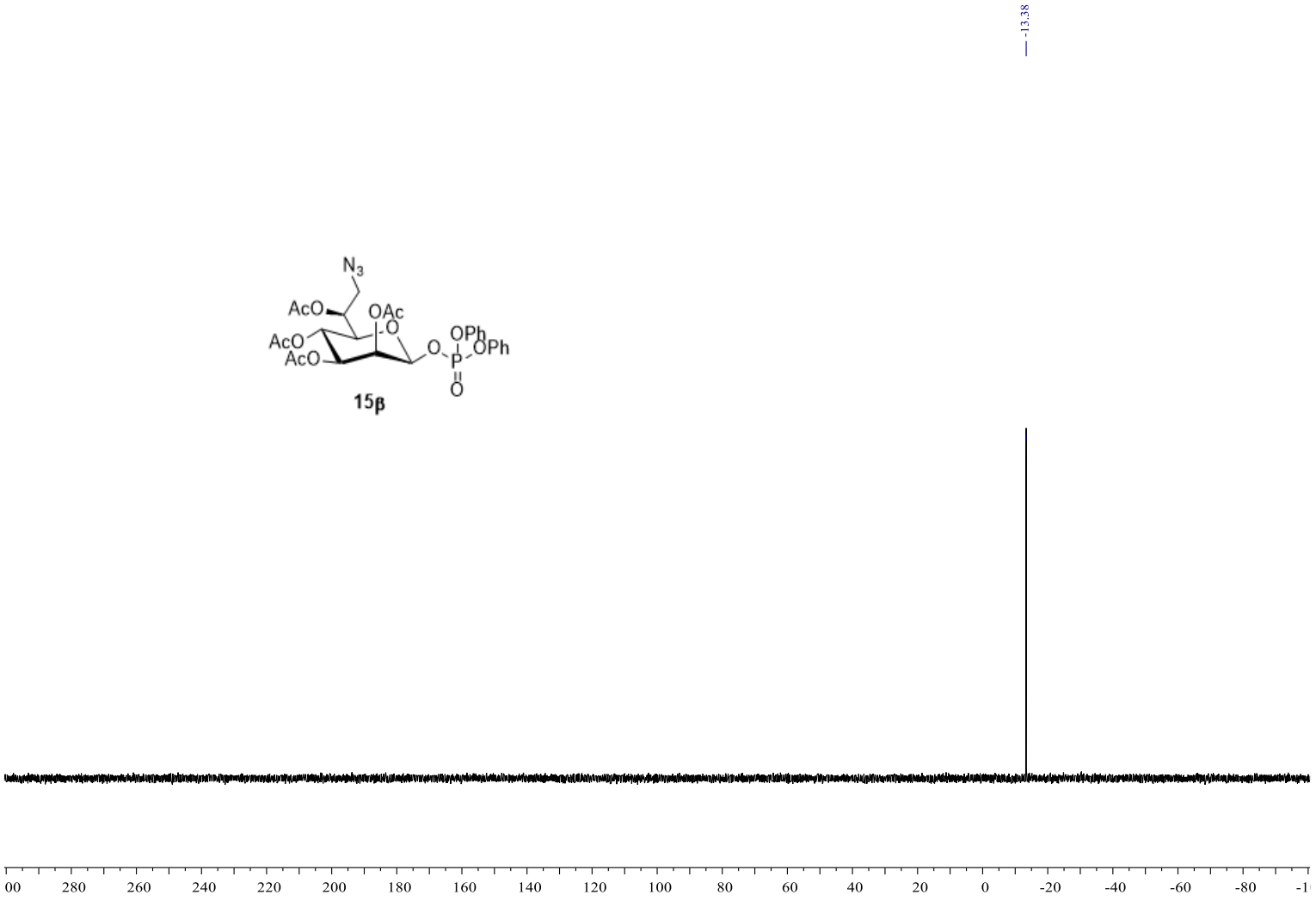

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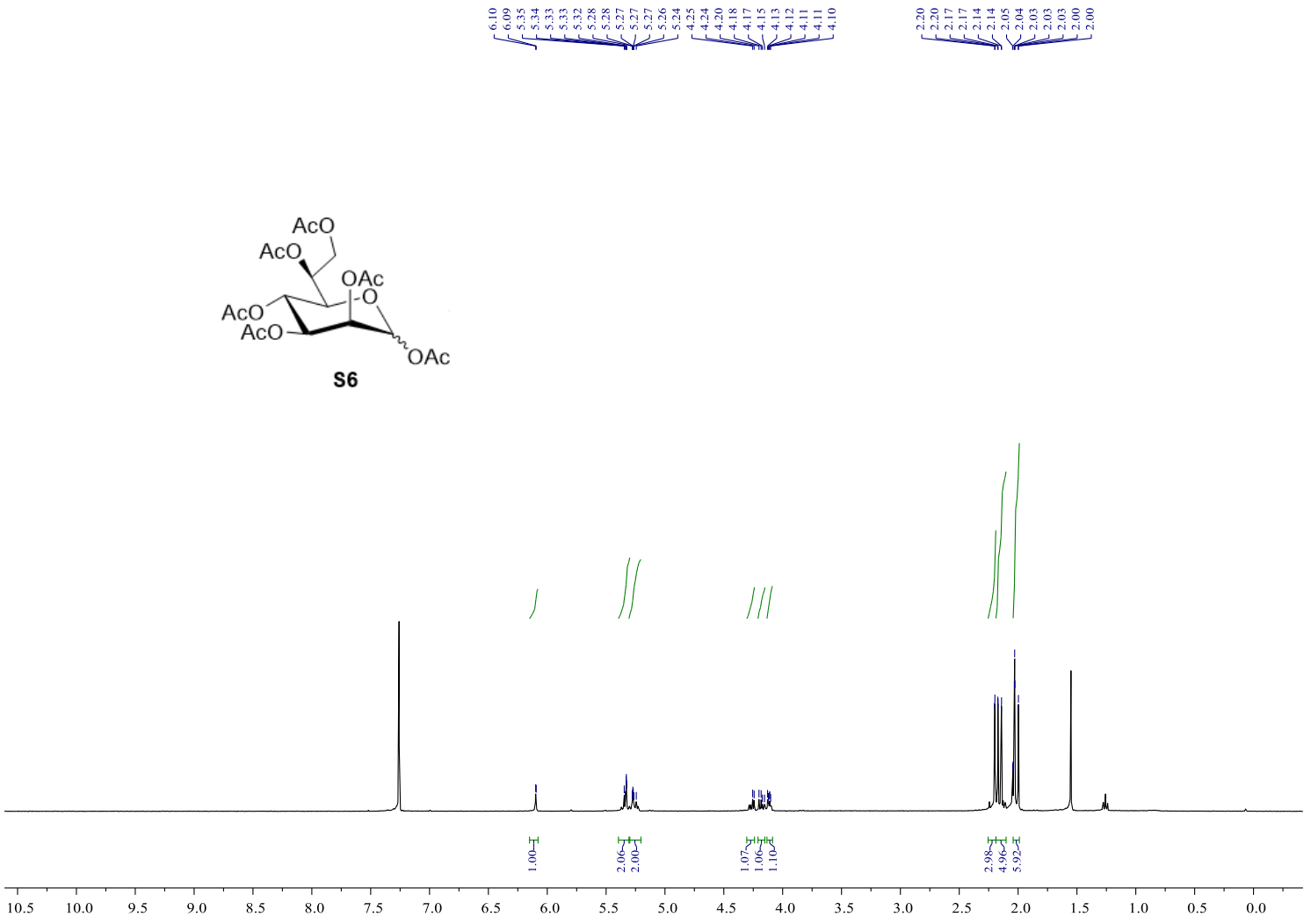

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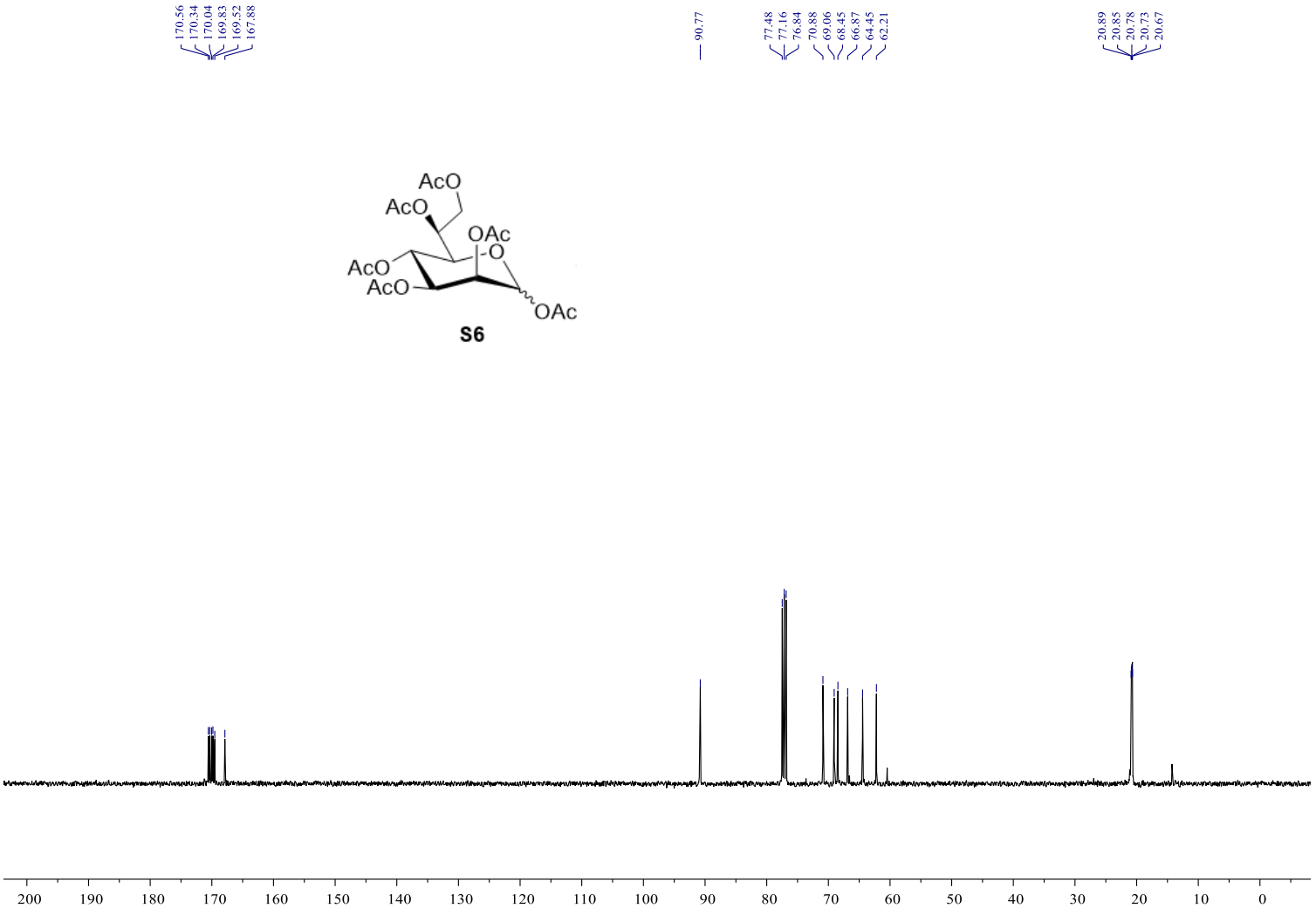

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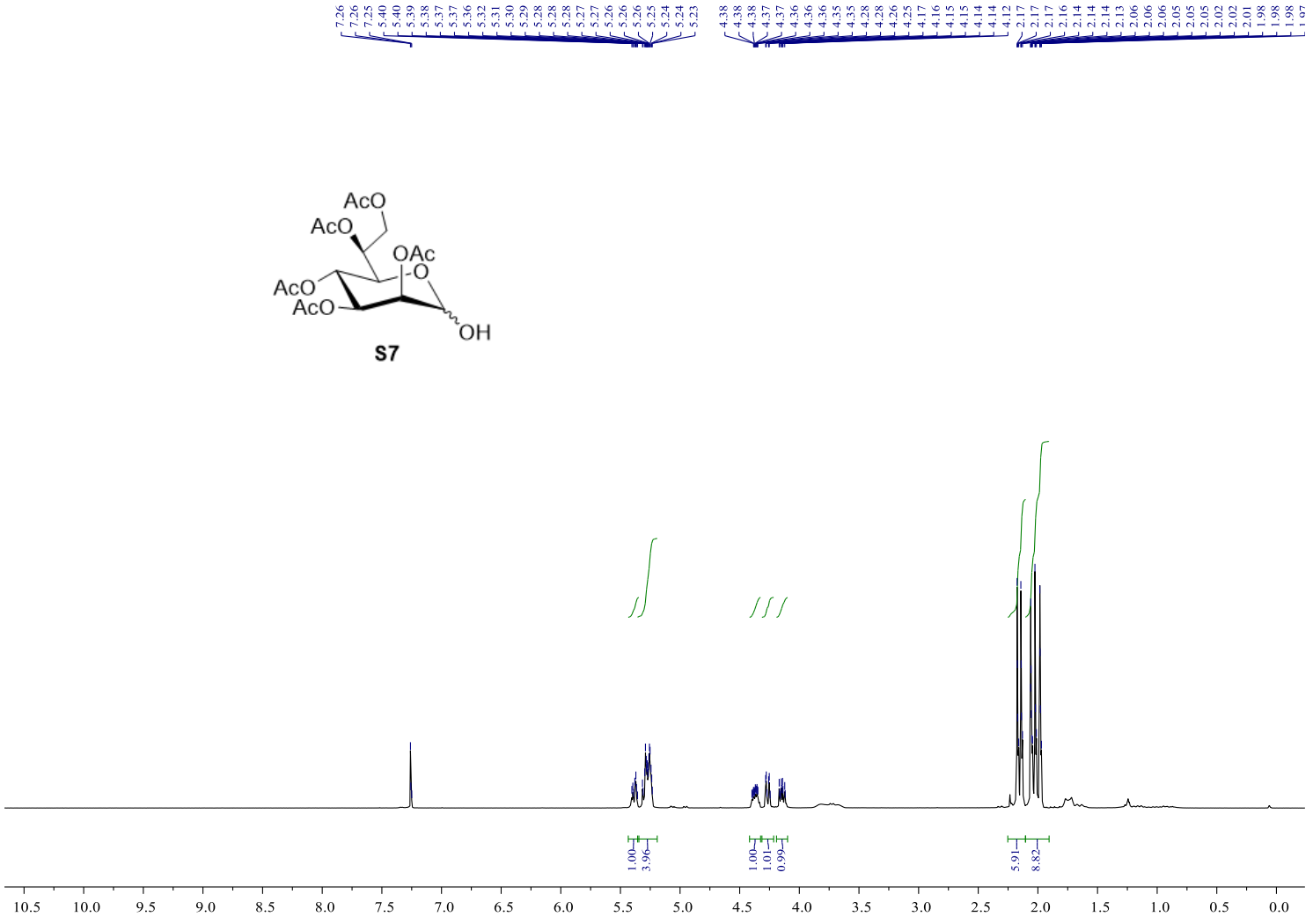

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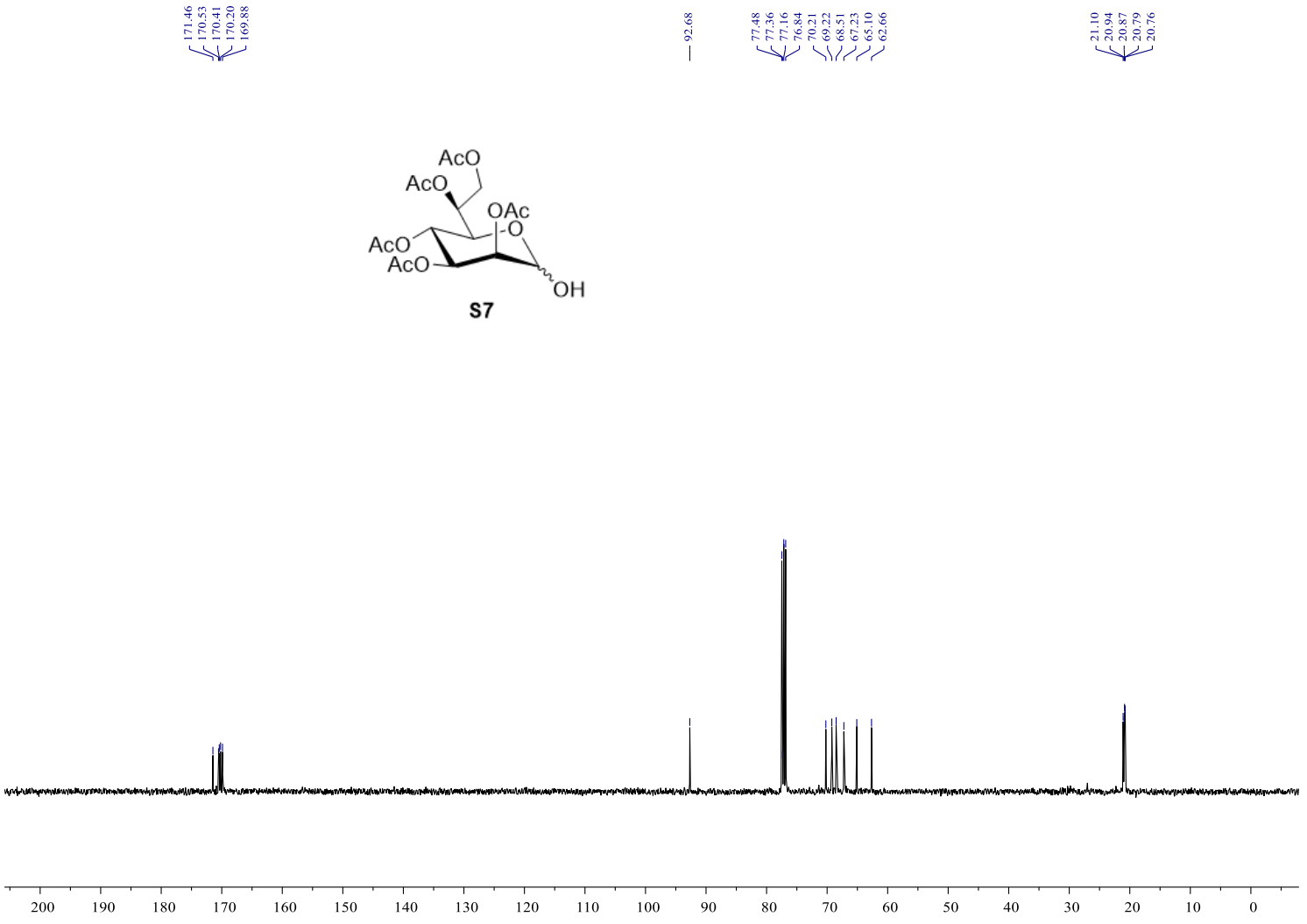

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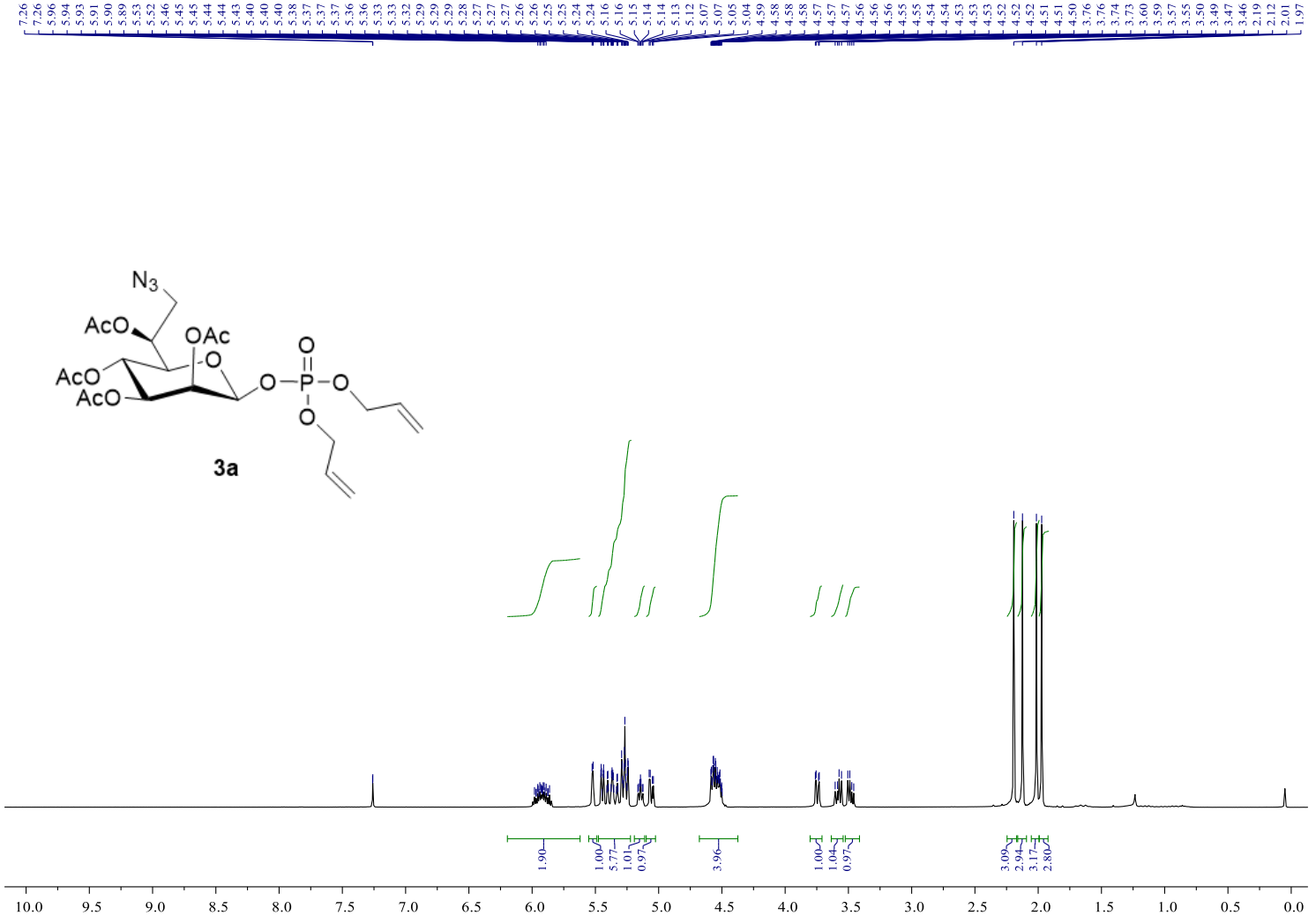

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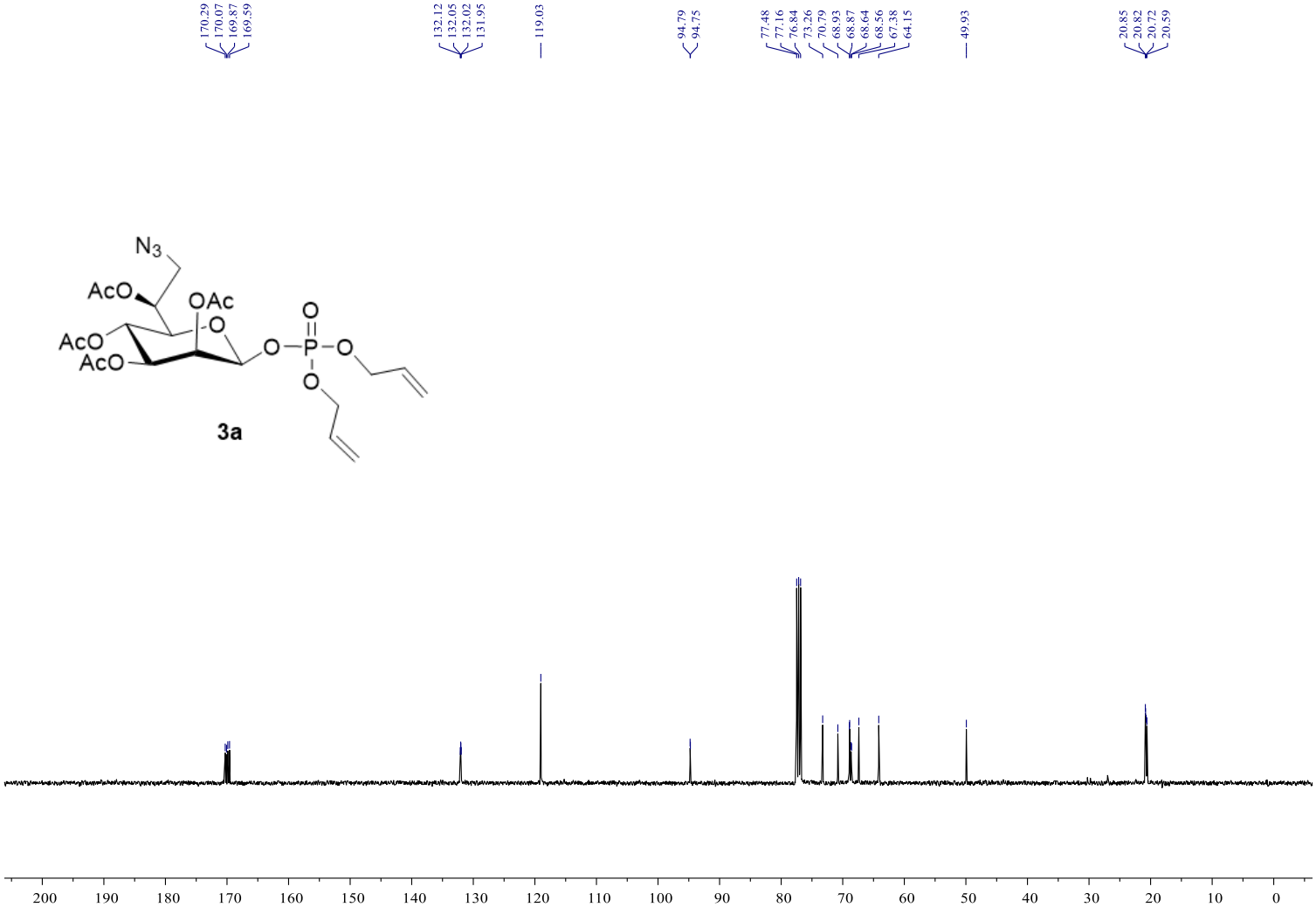
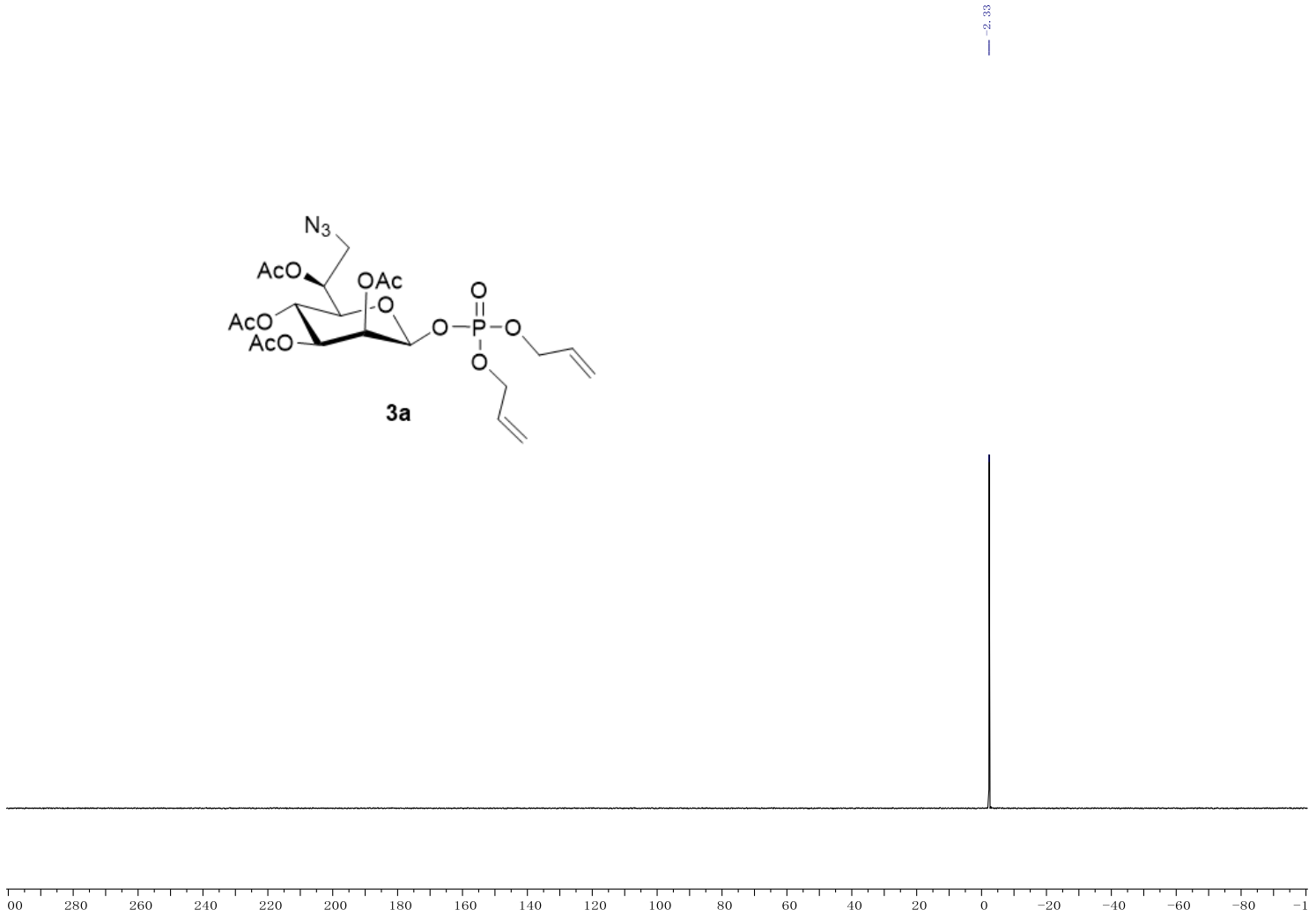


^{31}P-NMR (162 MHz, Chloroform-*d*)



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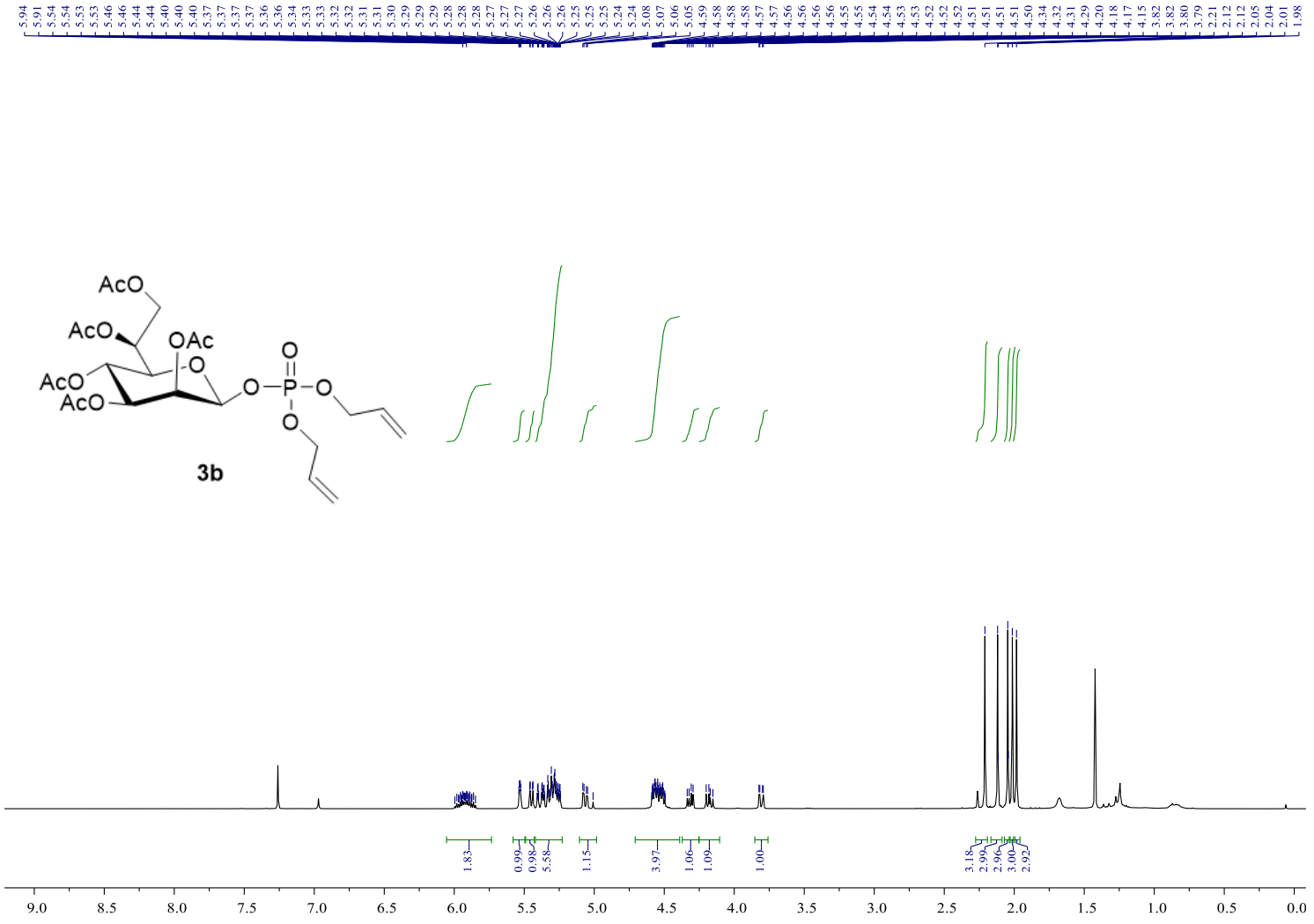

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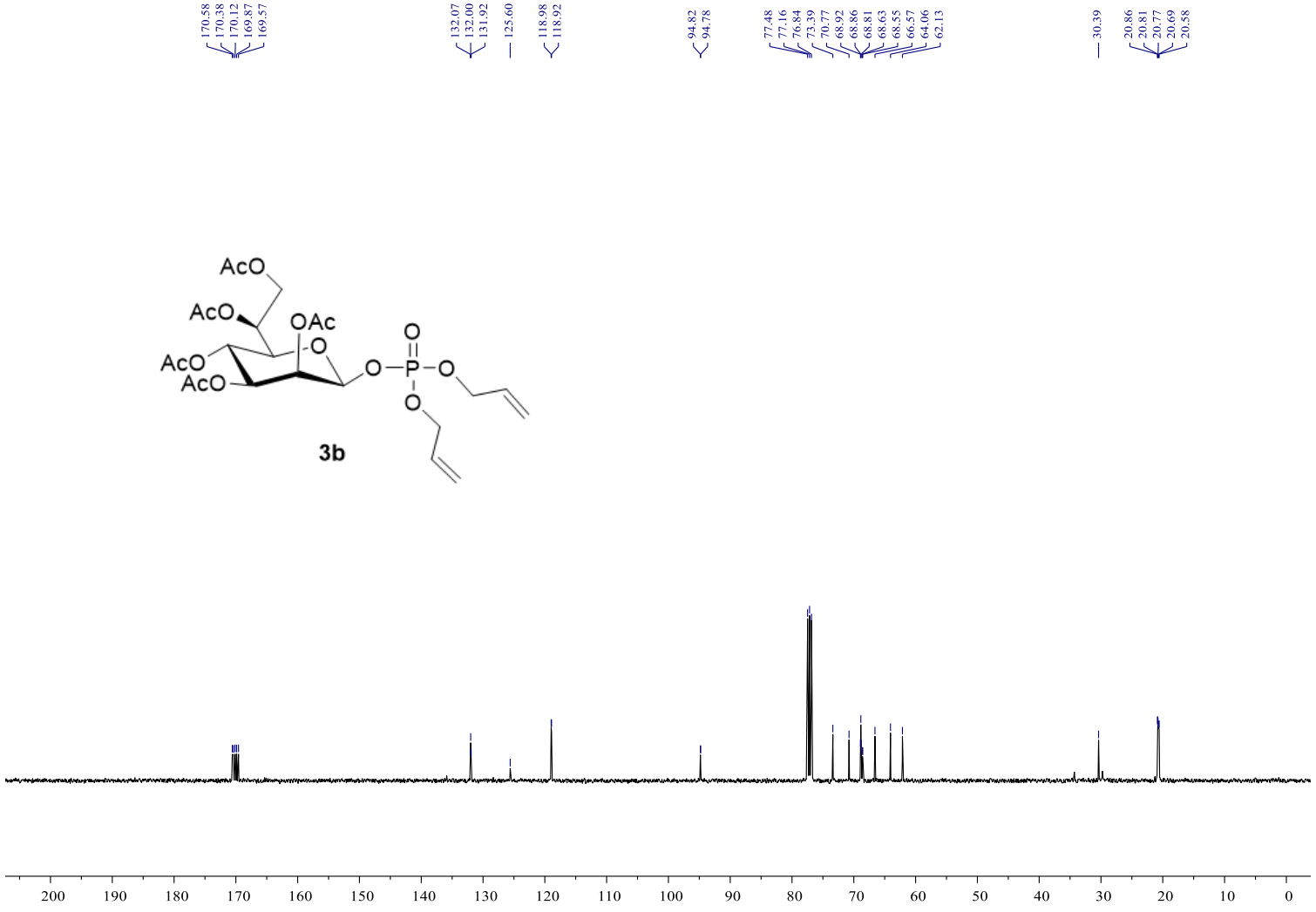
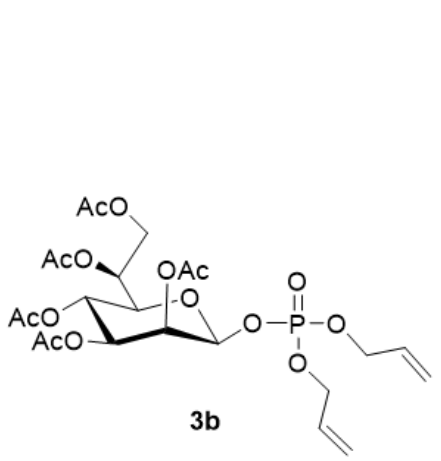
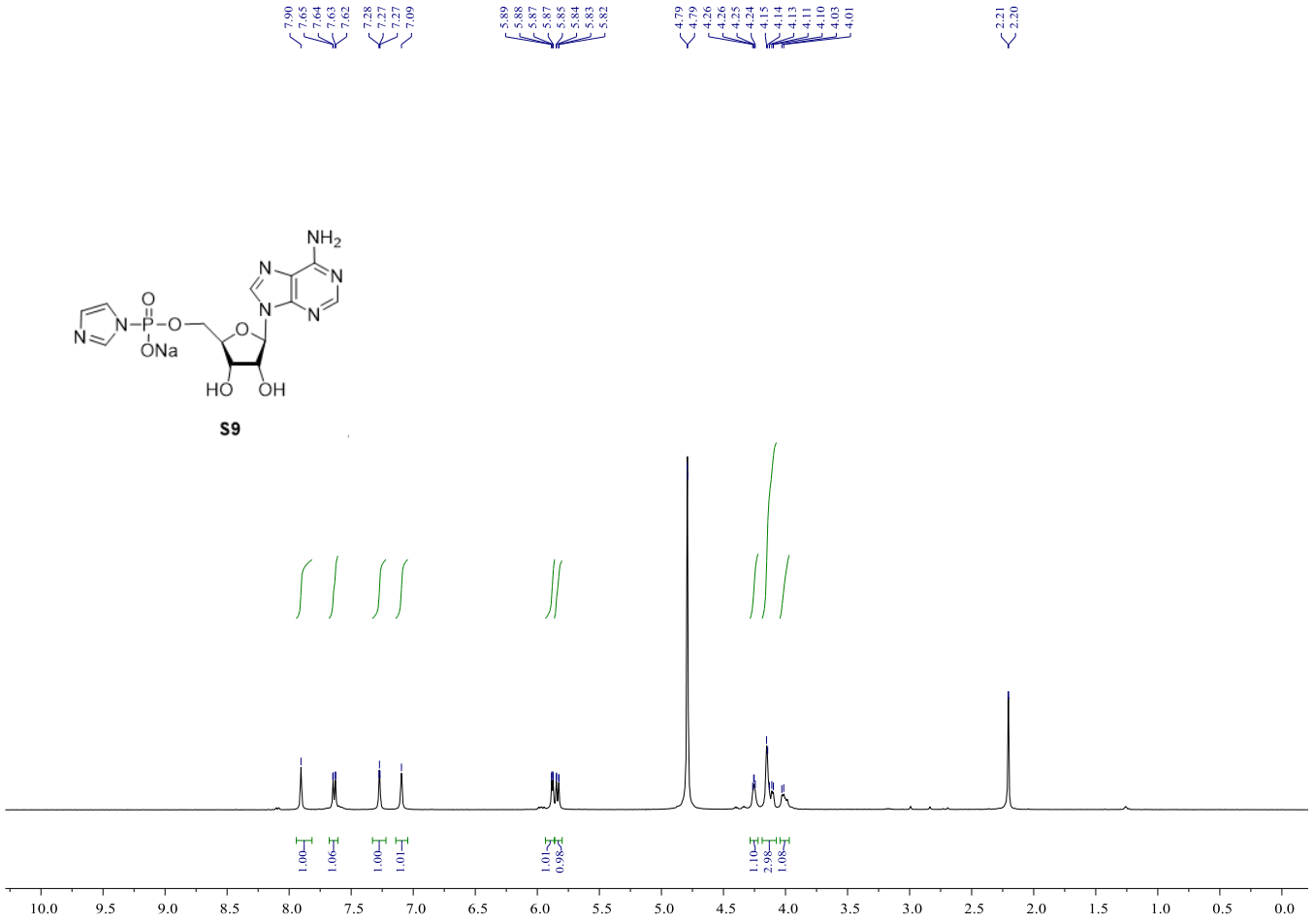


^{31}P-NMR (162 MHz, Chloroform-*d*)



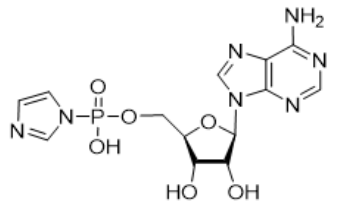
3b

^{1}H-NMR (400 MHz, DMSO-*d*)



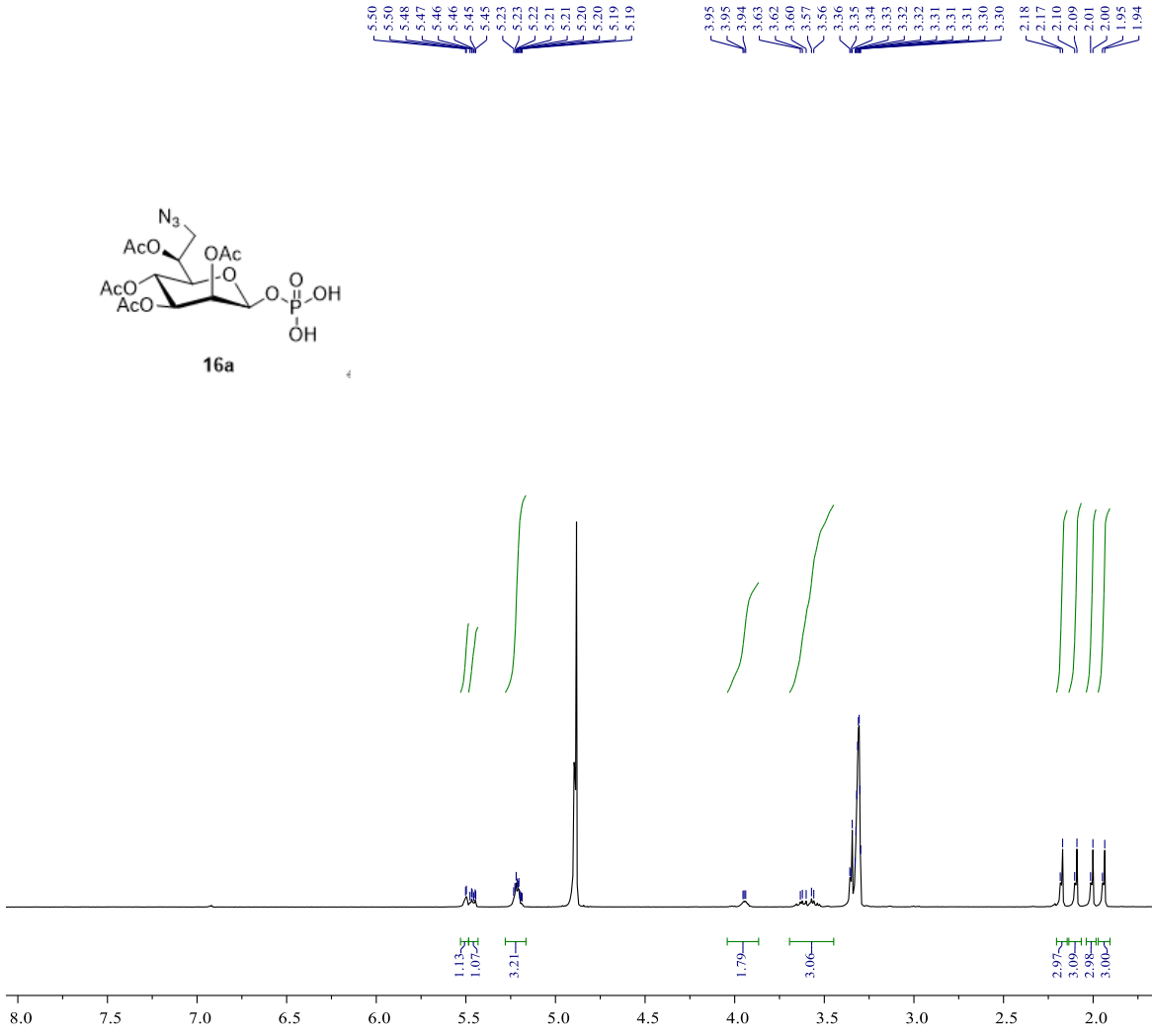
S9

^{31}P-NMR (162 MHz, DMSO-*d*)

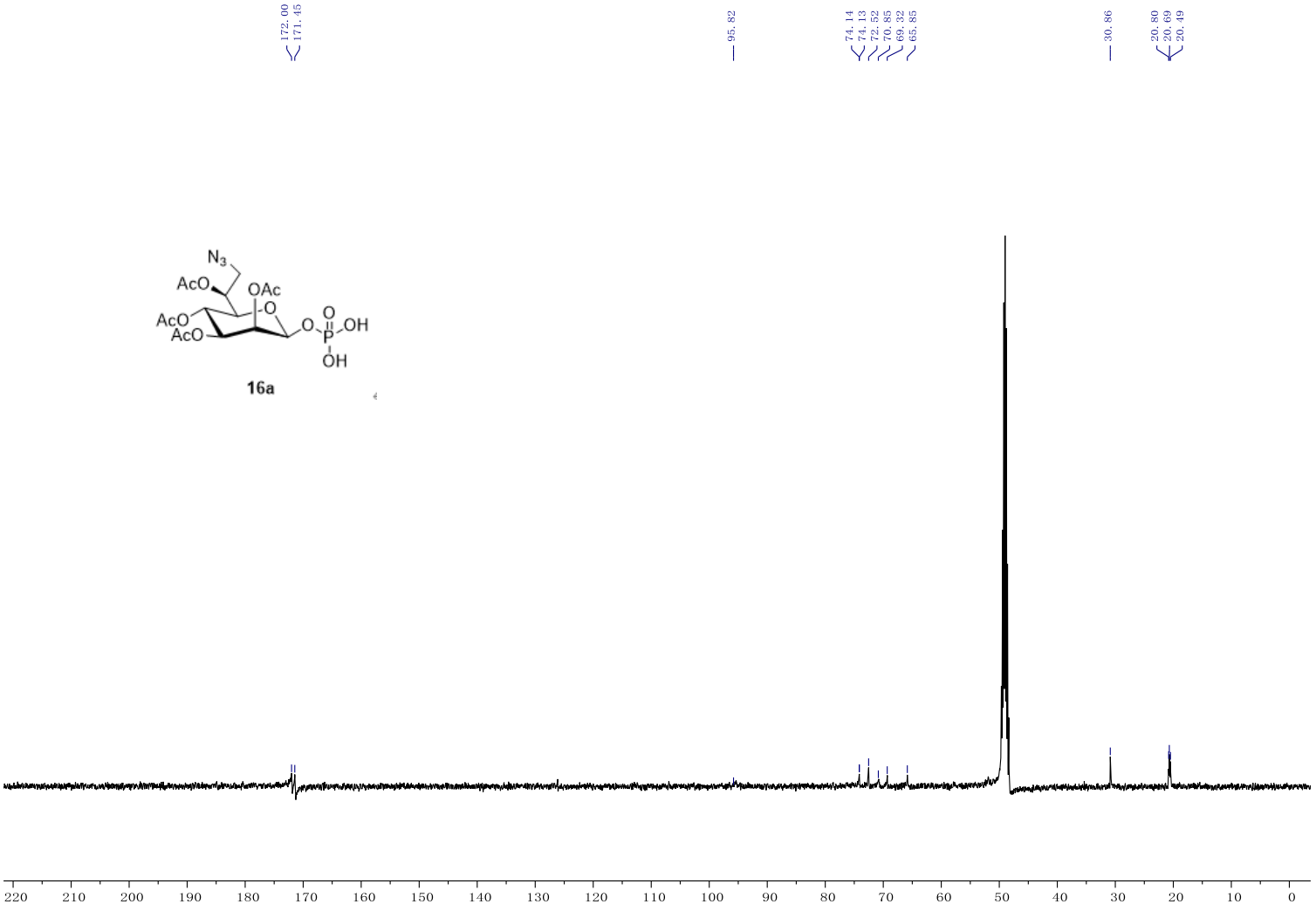


S9

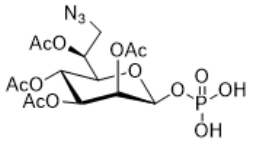
[1]H-NMR (400 MHz, Methanol-*d*)



^{13}C-NMR (100 MHz, Methanol-*d*)



^{31}P-NMR (162 MHz,Methanol-*d*)



16a

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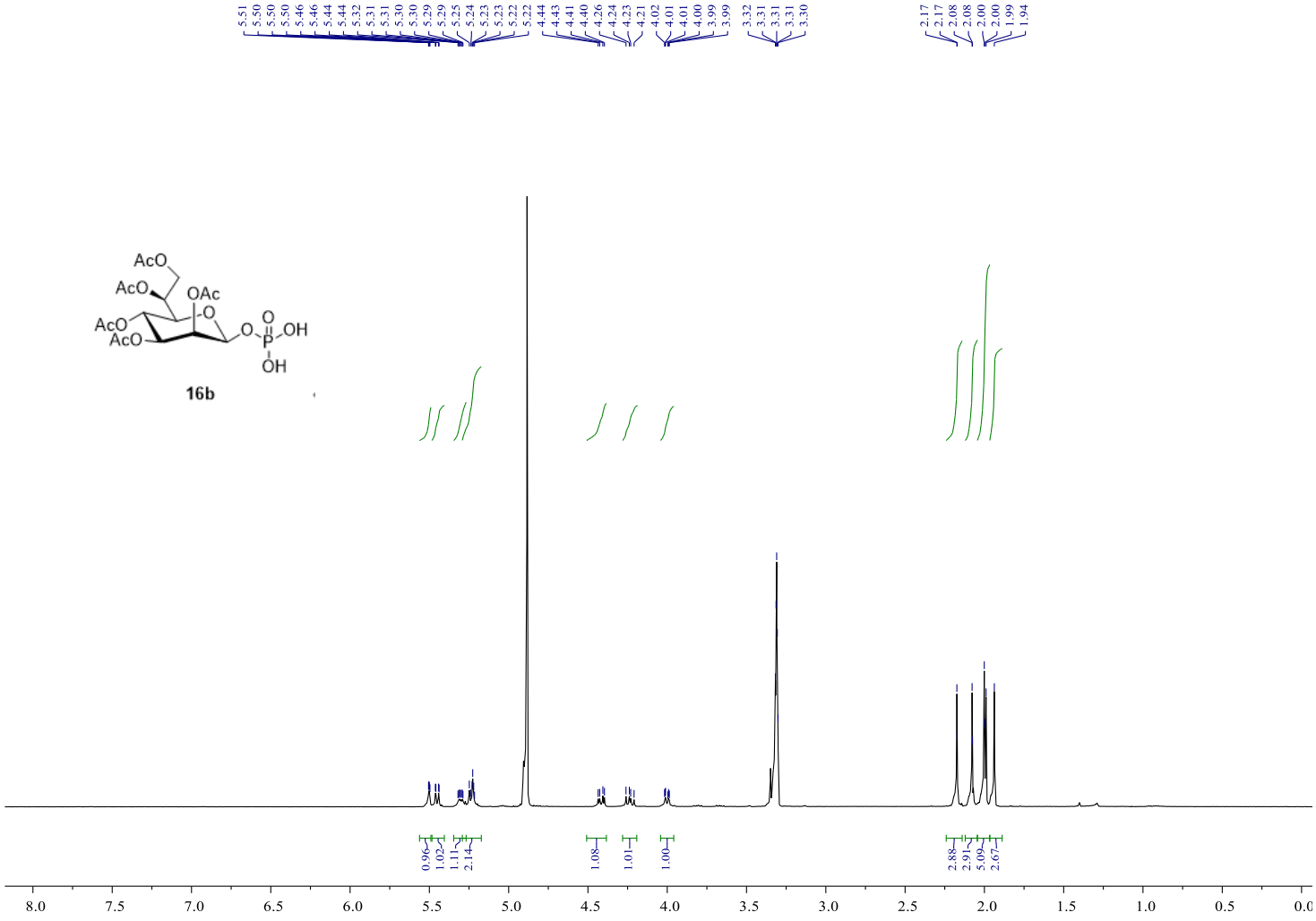

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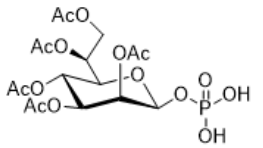
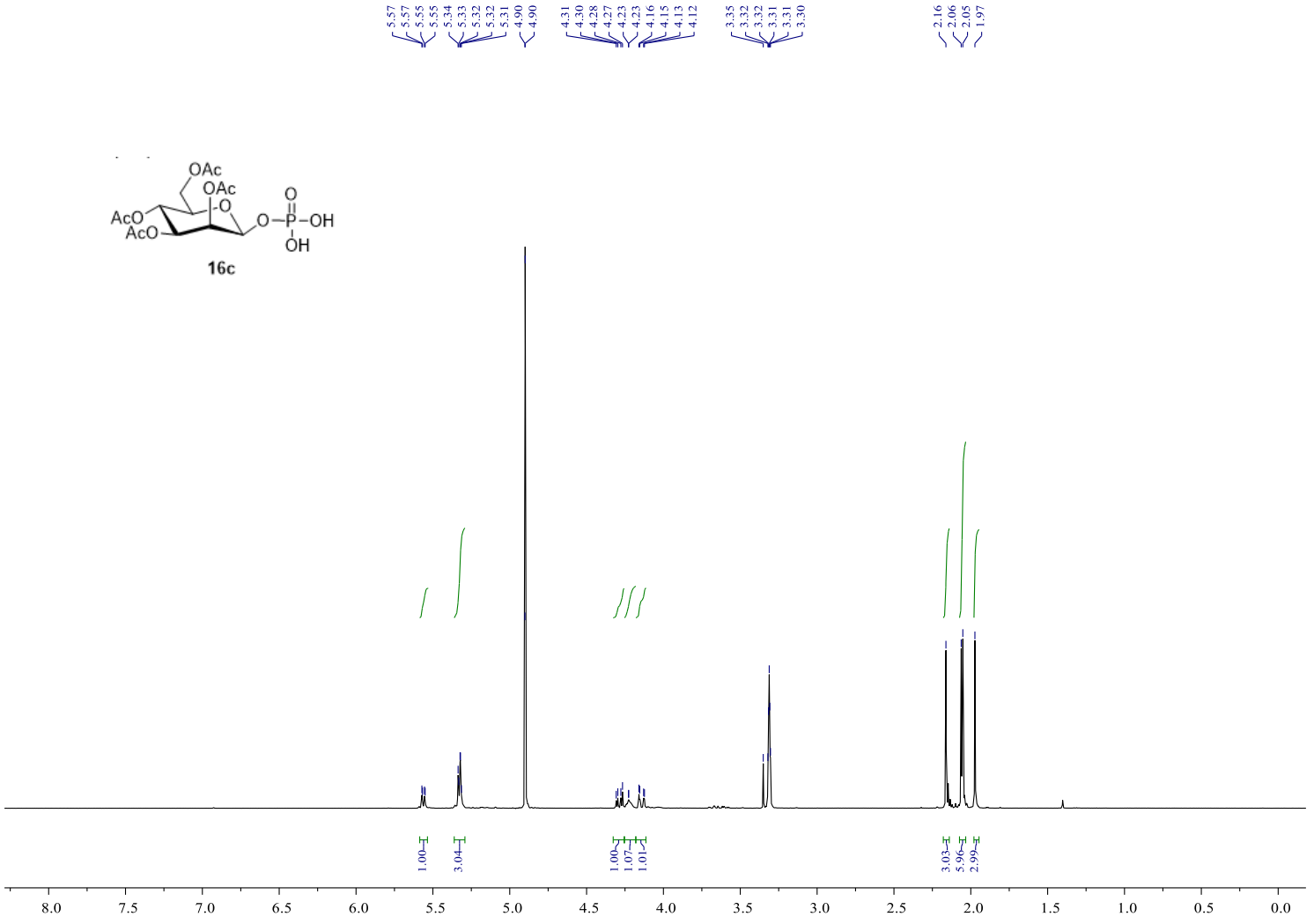
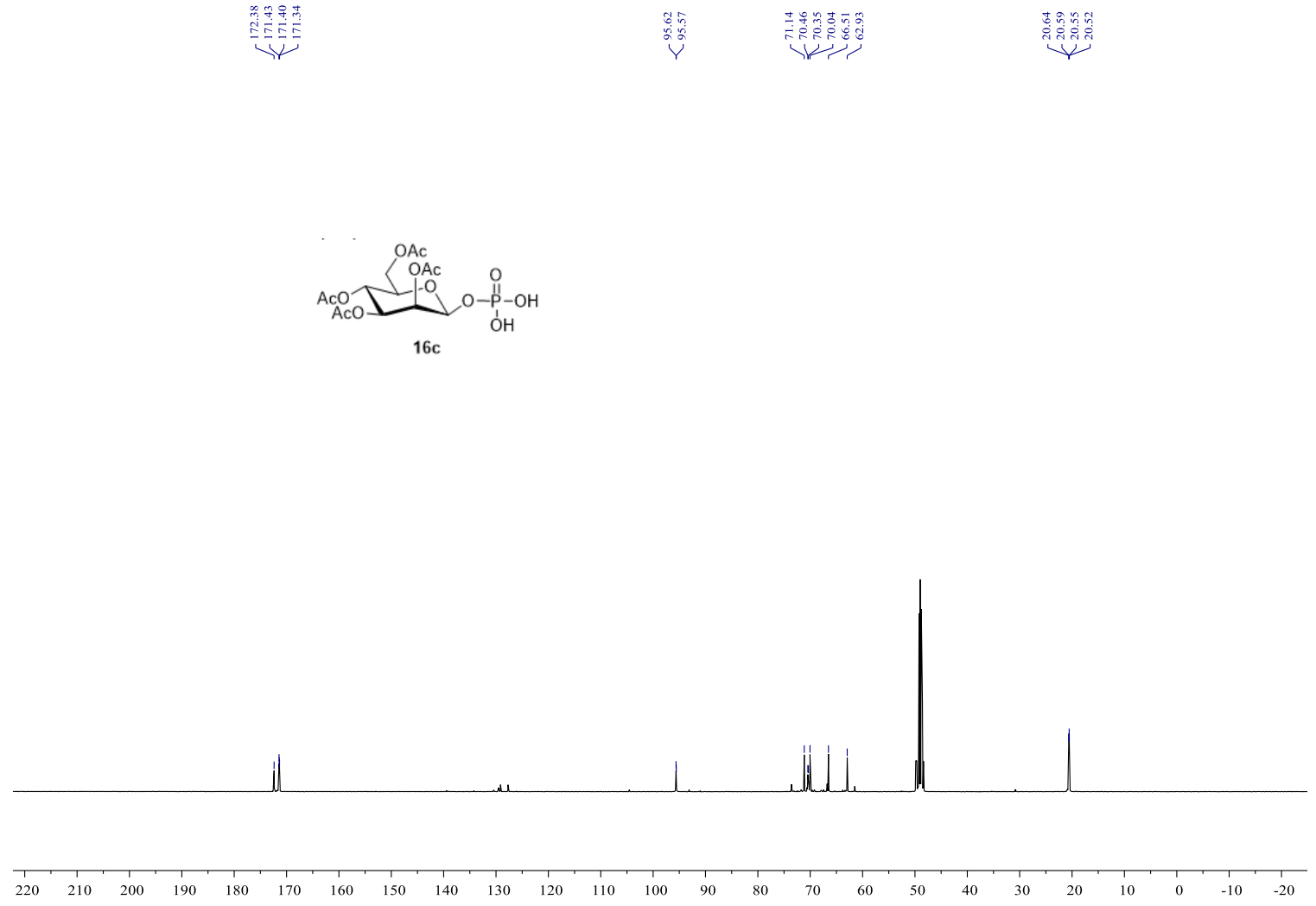


16b

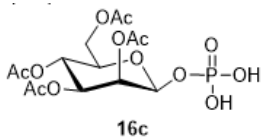
[1]H-NMR (400 MHz, Methanol-*d*)



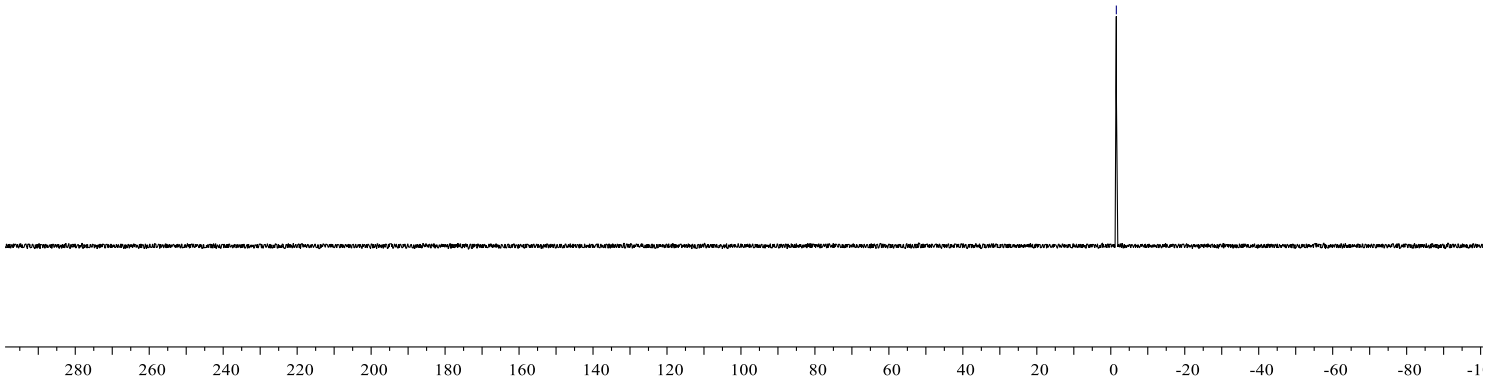
^{13}C-NMR (100 MHz, Methanol-*d*)



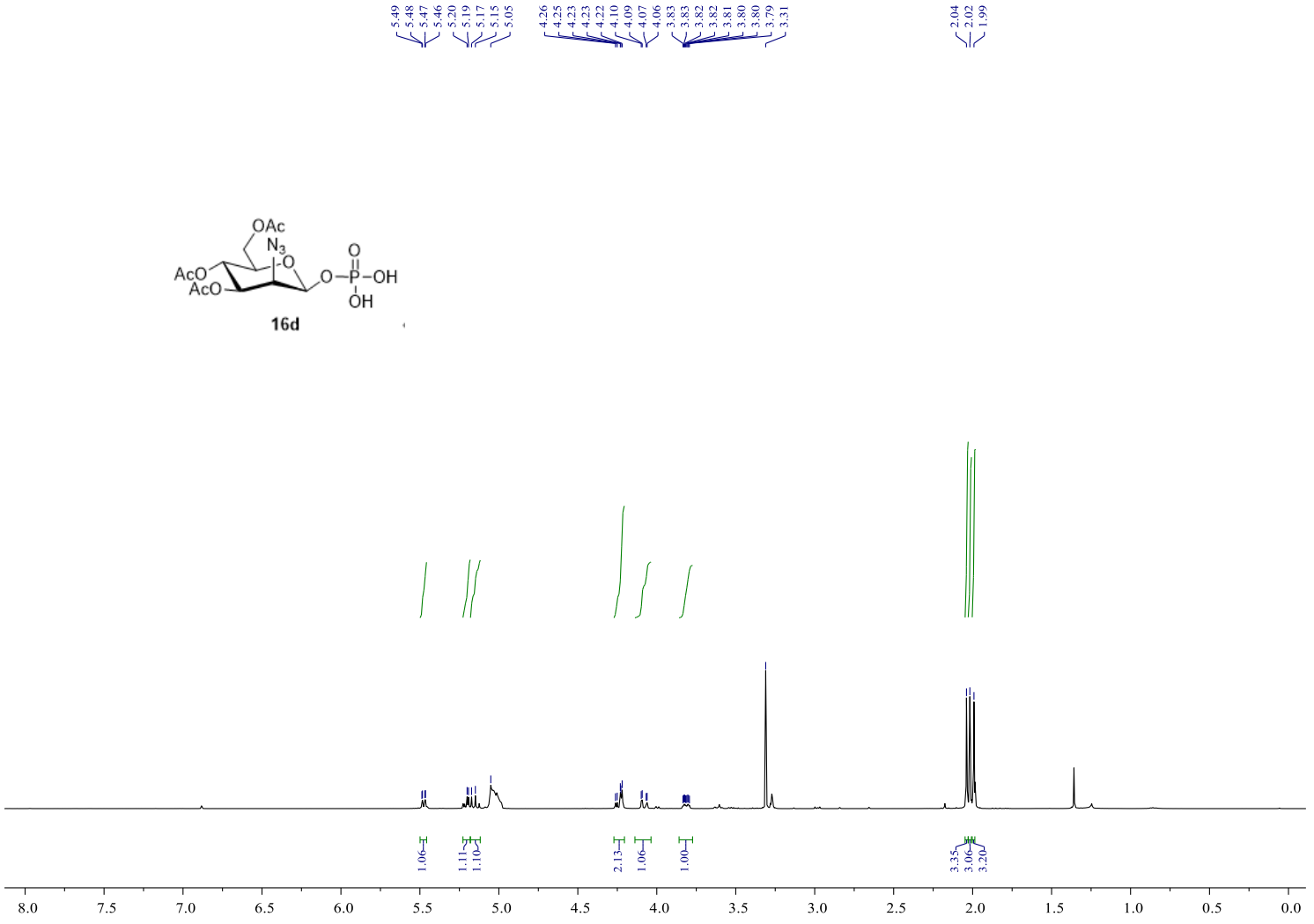
^{31}P-NMR (162 MHz, Methanol-*d*)



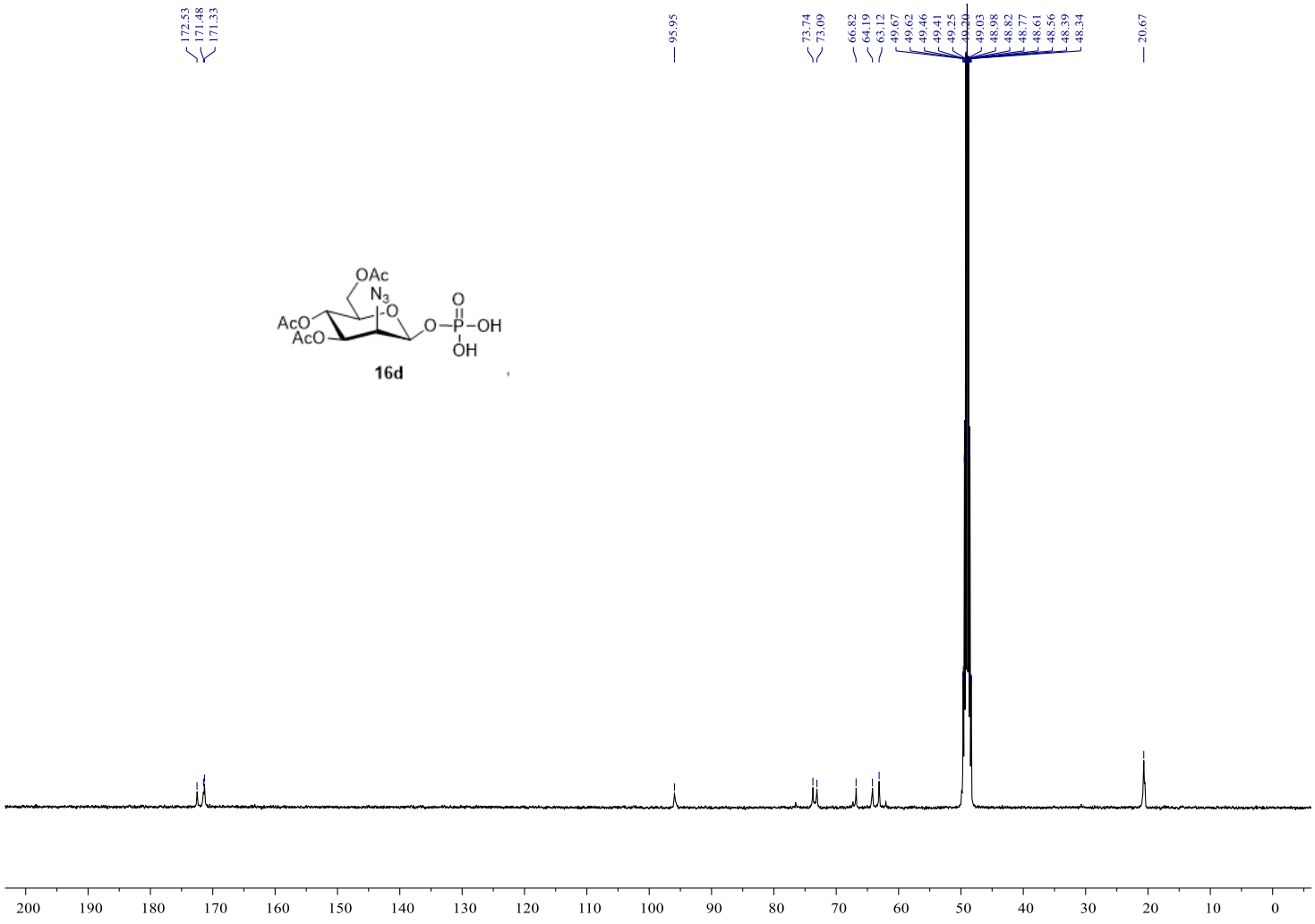
16c



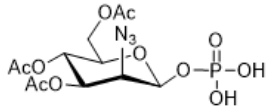
^{1}H-NMR (400 MHz, Methanol-*d*)



^{13}C-NMR (100 MHz, Methanol-*d*)

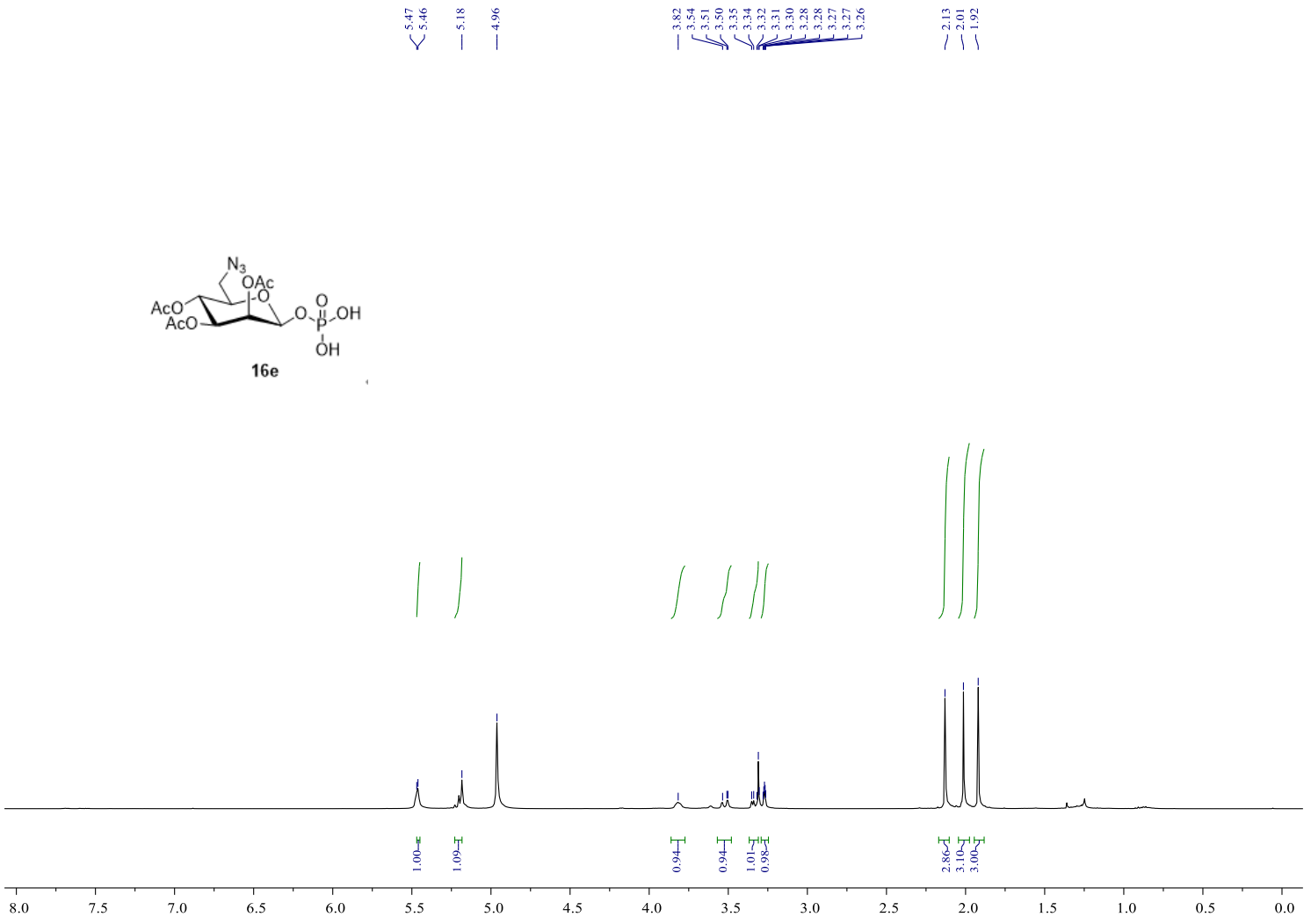


^{31}P-NMR (162 MHz, Methanol-*d*)

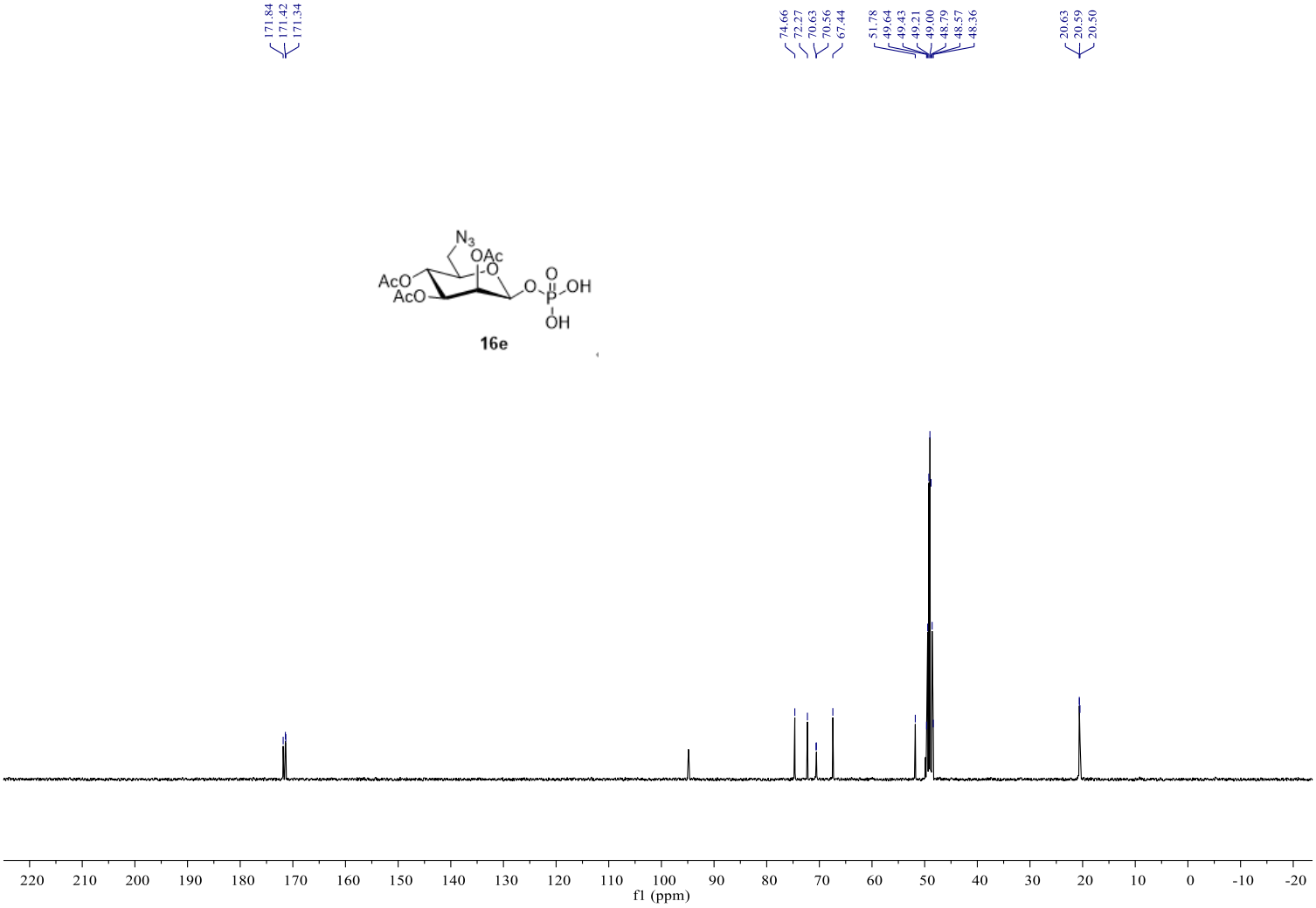


16d

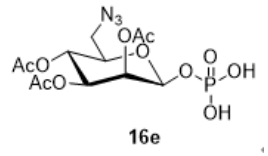
^{1}H-NMR (400 MHz, Methnaol-*d*)



^{13}C-NMR (100 MHz, Methanol-*d*)

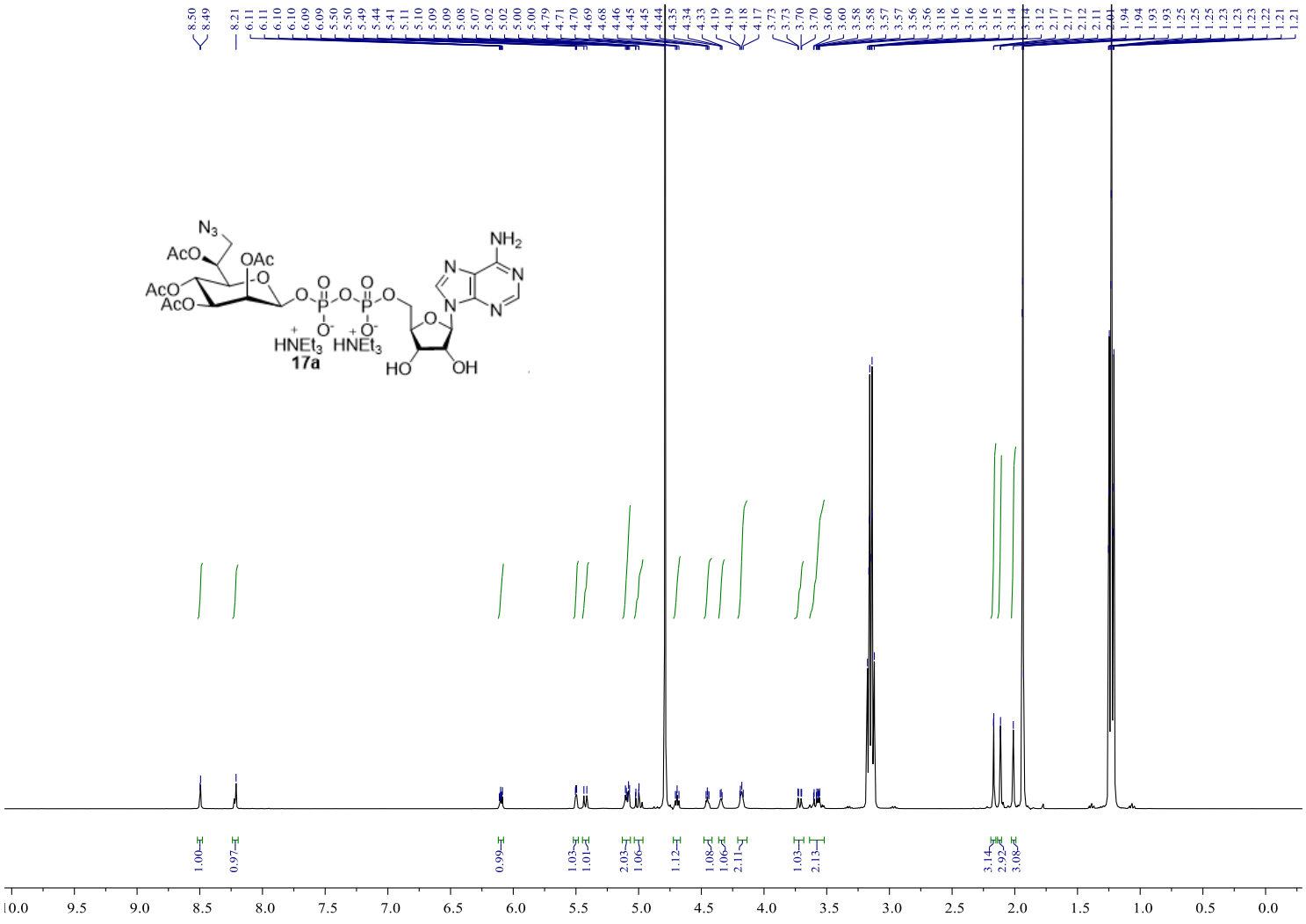


^{31}P-NMR (162 MHz, Methanol-*d*)

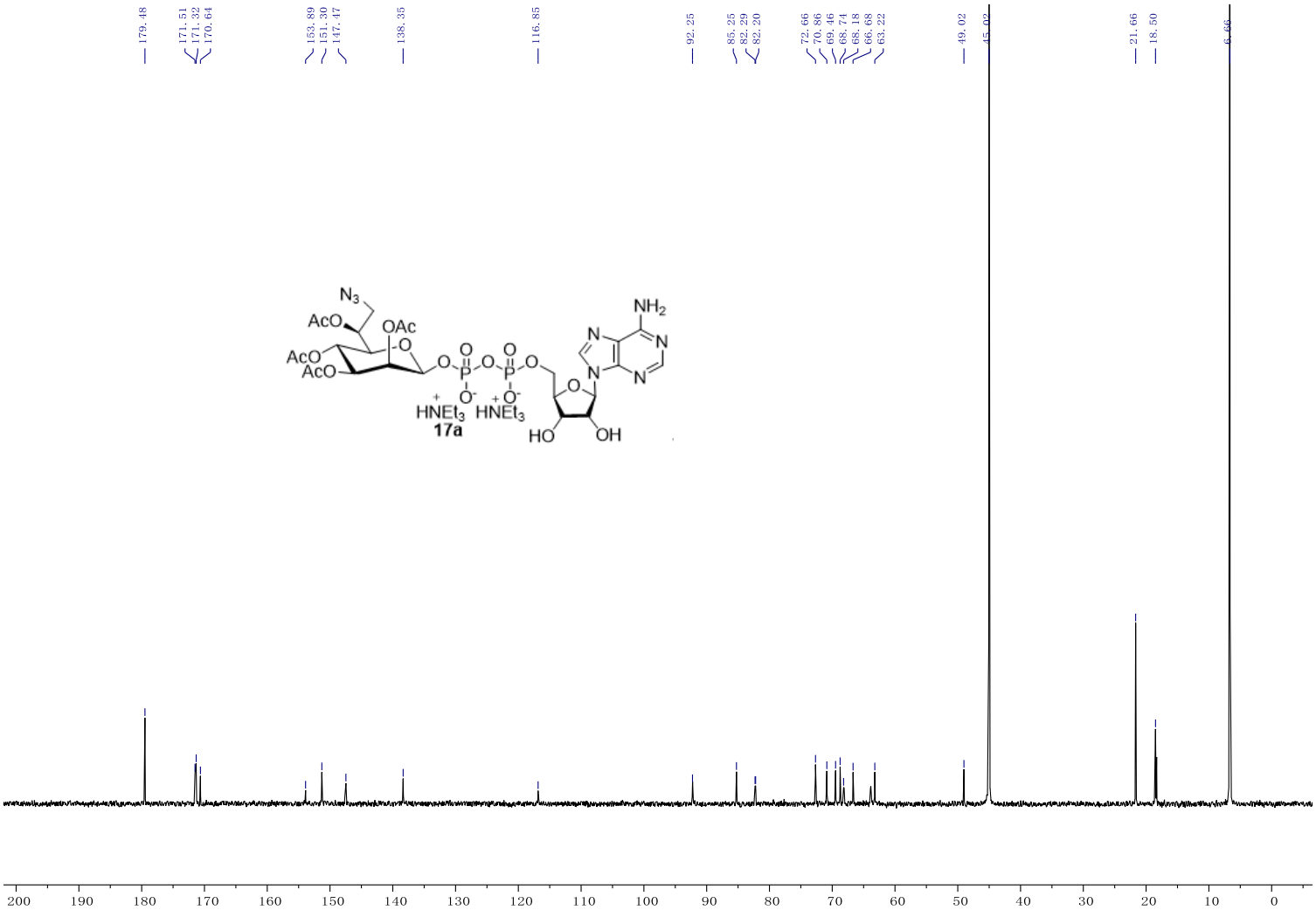


16e

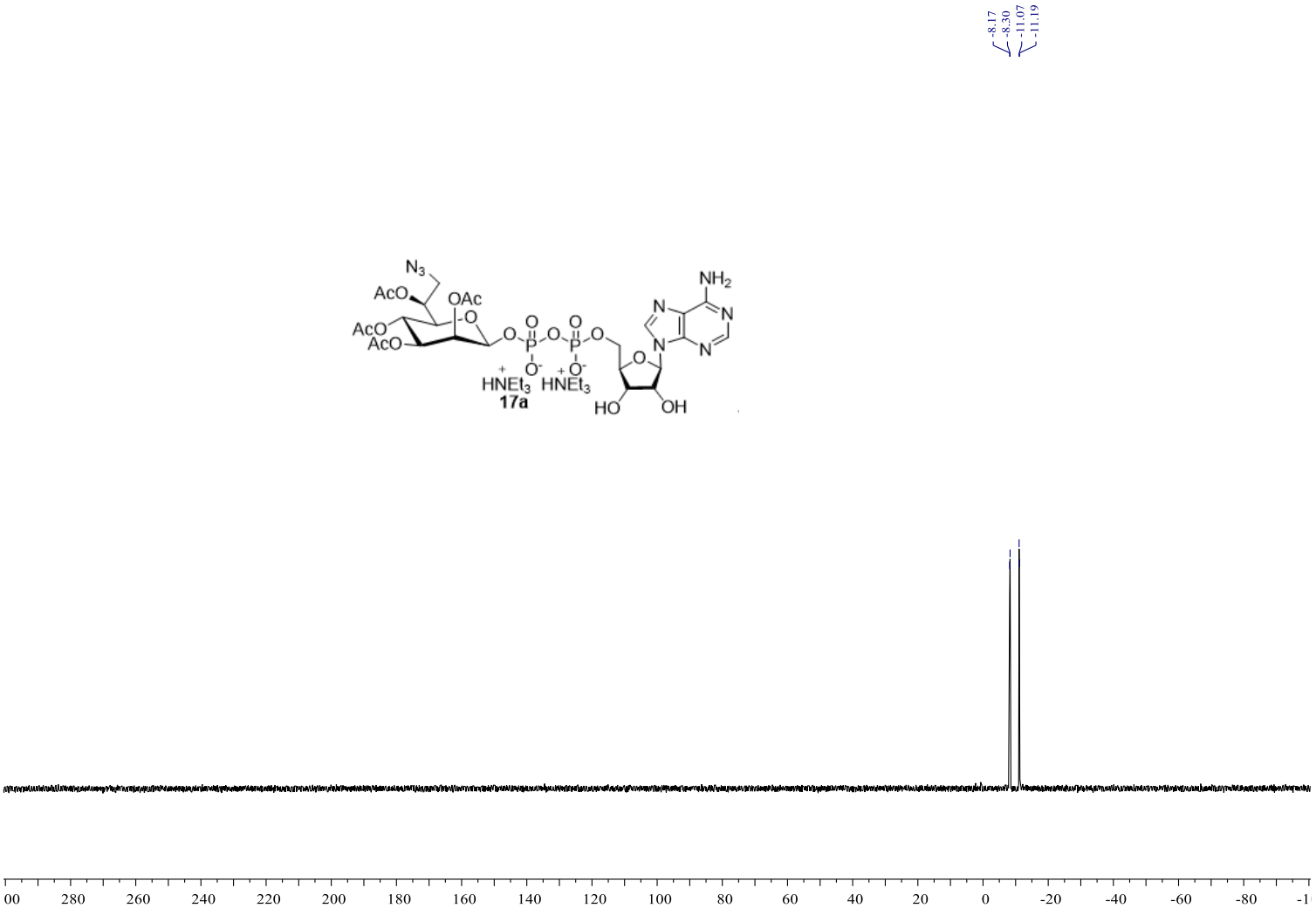
^{1}H-NMR (400 MHz, D_2O-*d*)



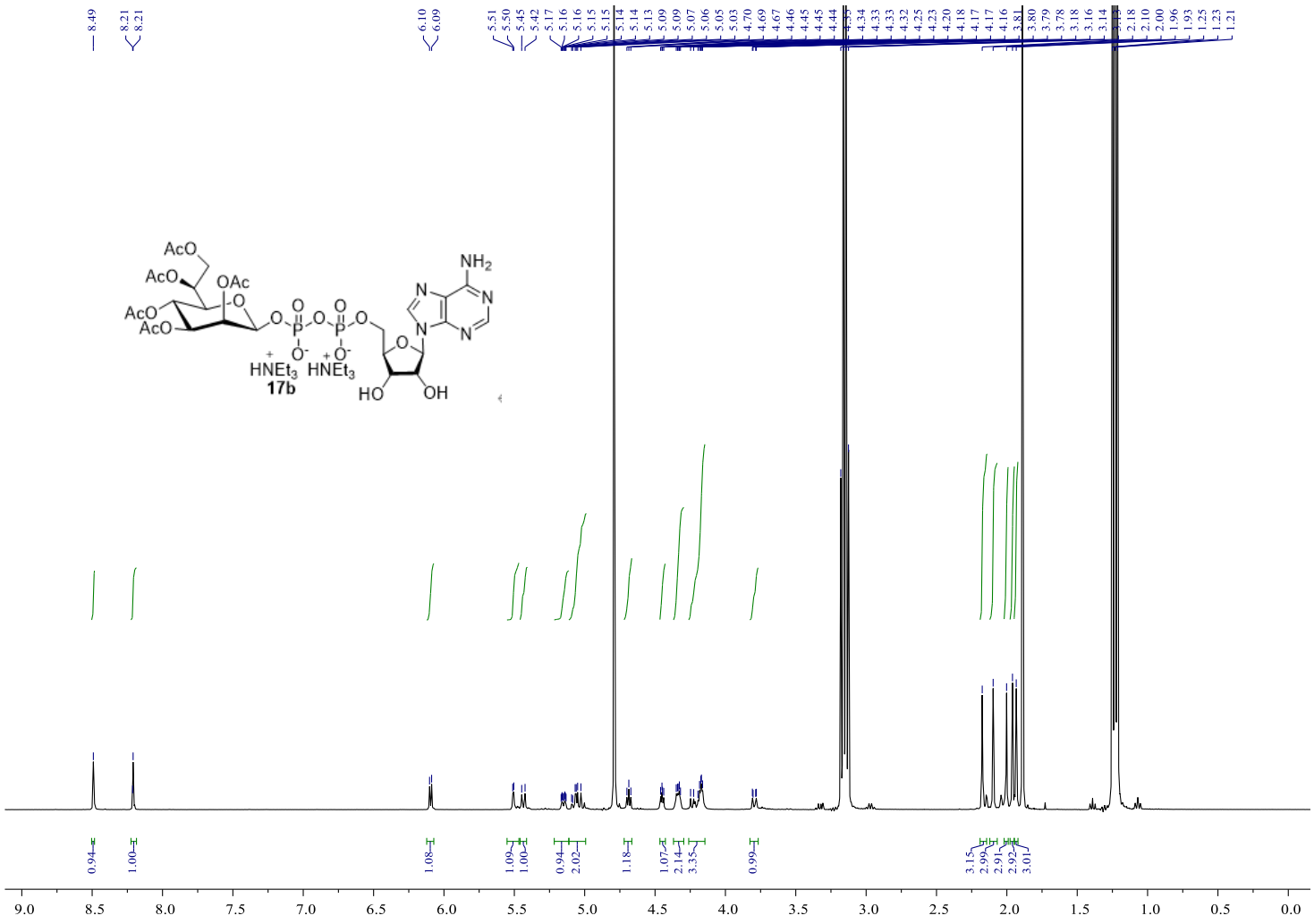
^{13}C-NMR (100 MHz, D_2O-*d*)



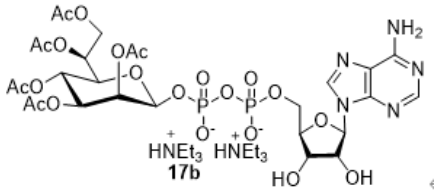
^{31}P-NMR (162 MHz, D_2O-*d*)



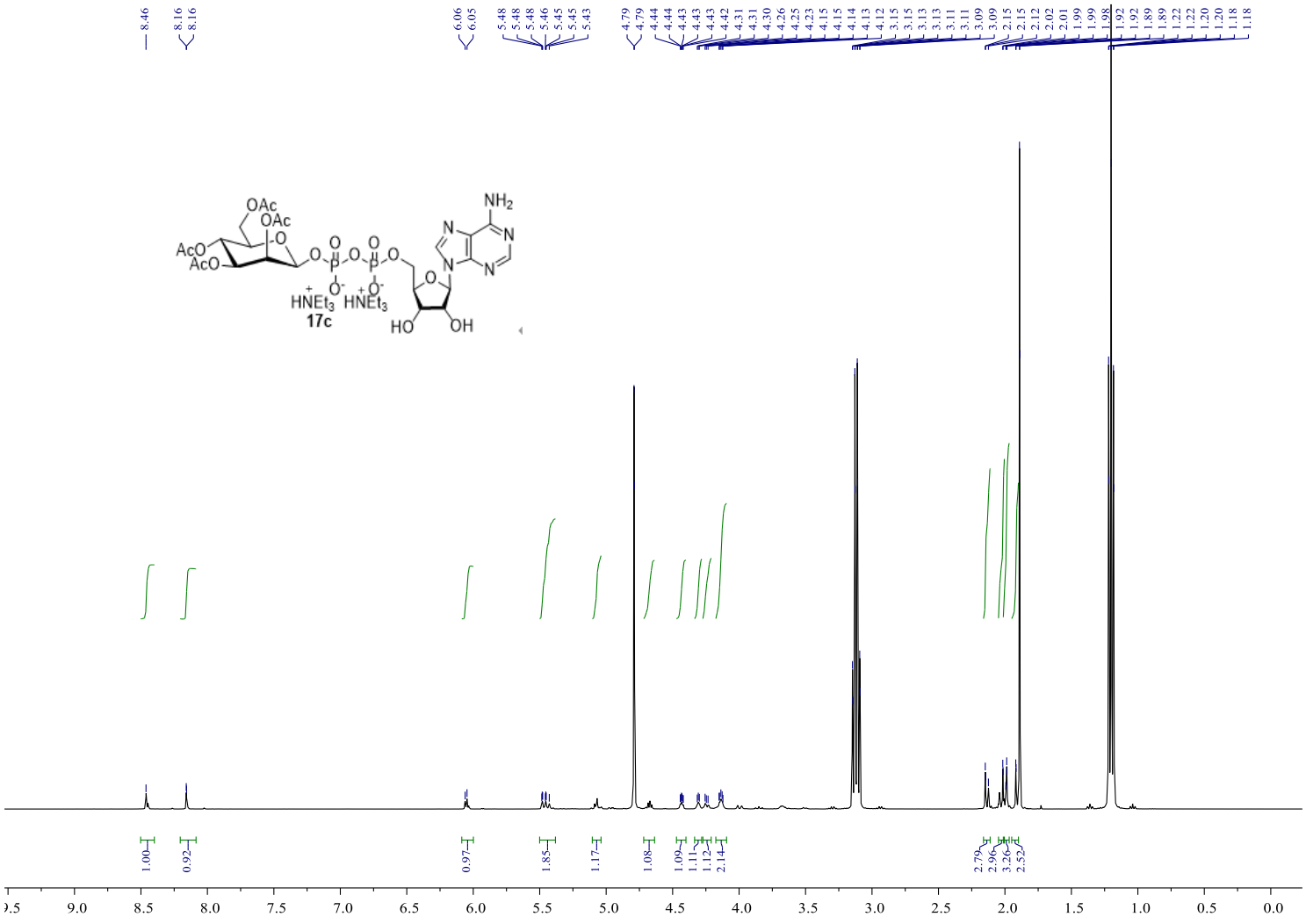
^{1}H-NMR (400 MHz, D_2O-*d*)



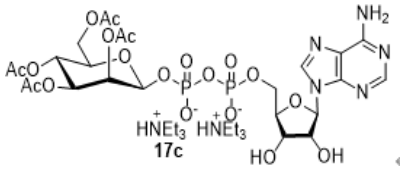
^{31}P-NMR (162 MHz, D_2O-*d*)



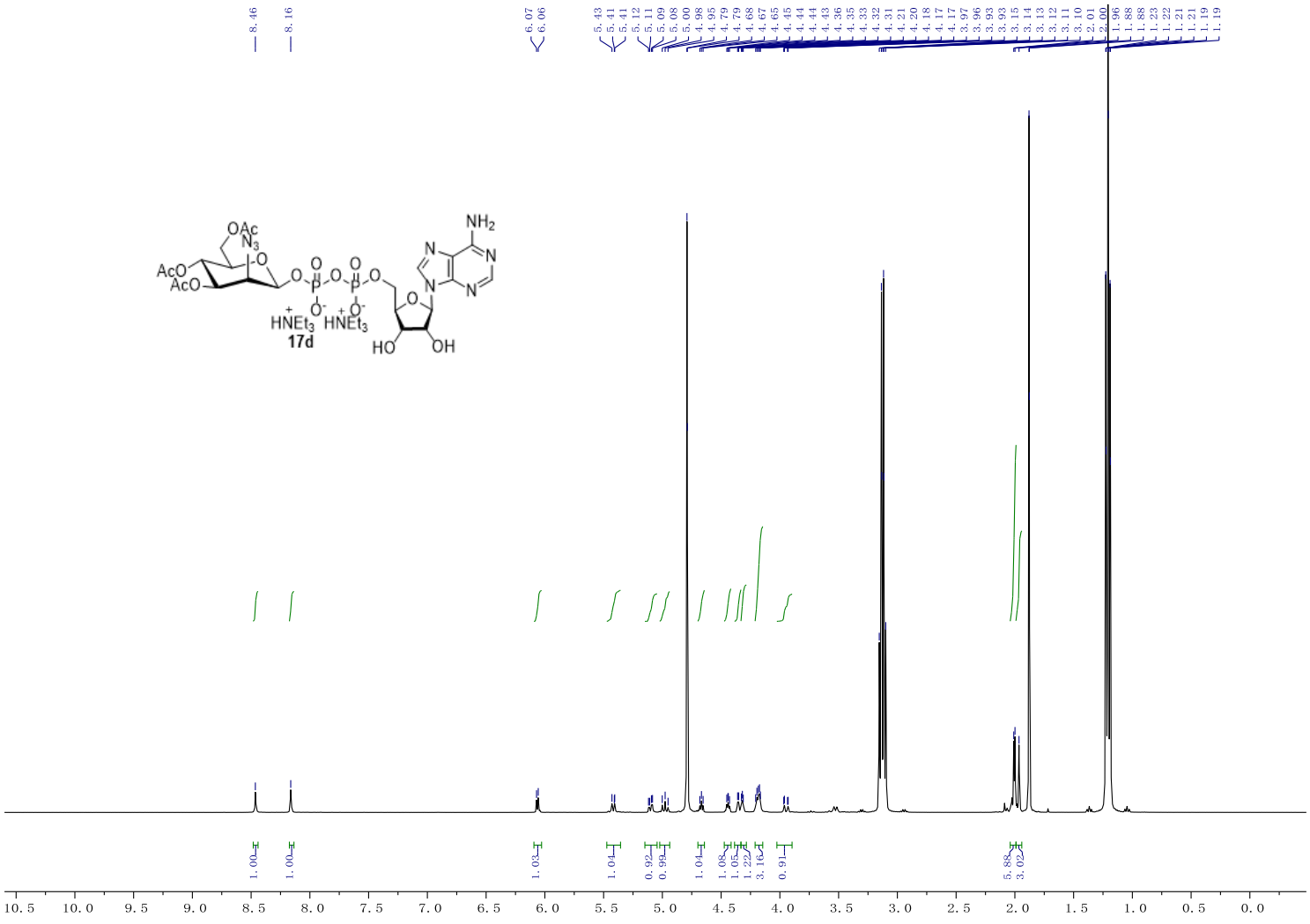
^{1}H-NMR (400 MHz, D_2O-*d*)



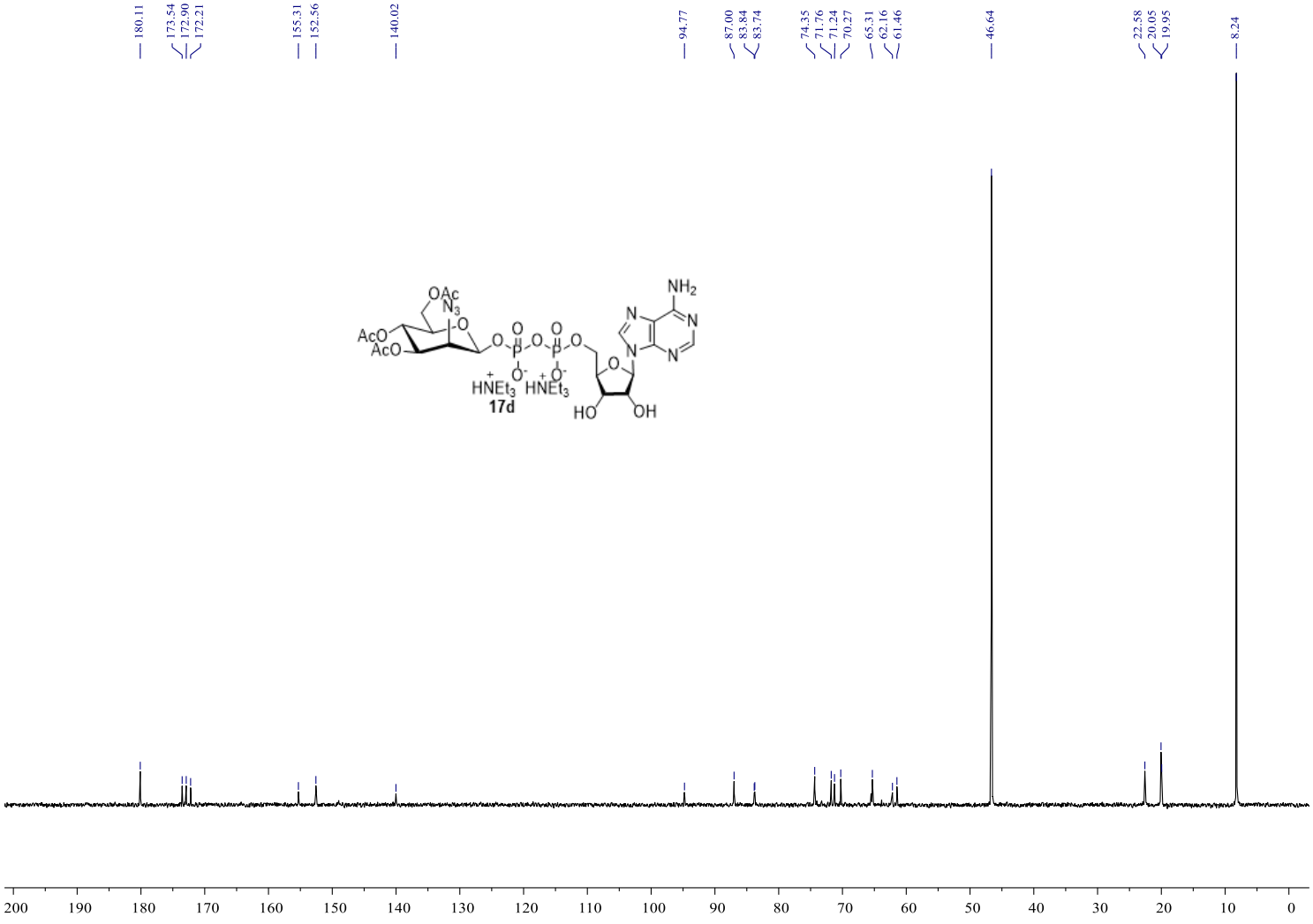
^{31}P-NMR (162 MHz, D_2O-*d*)



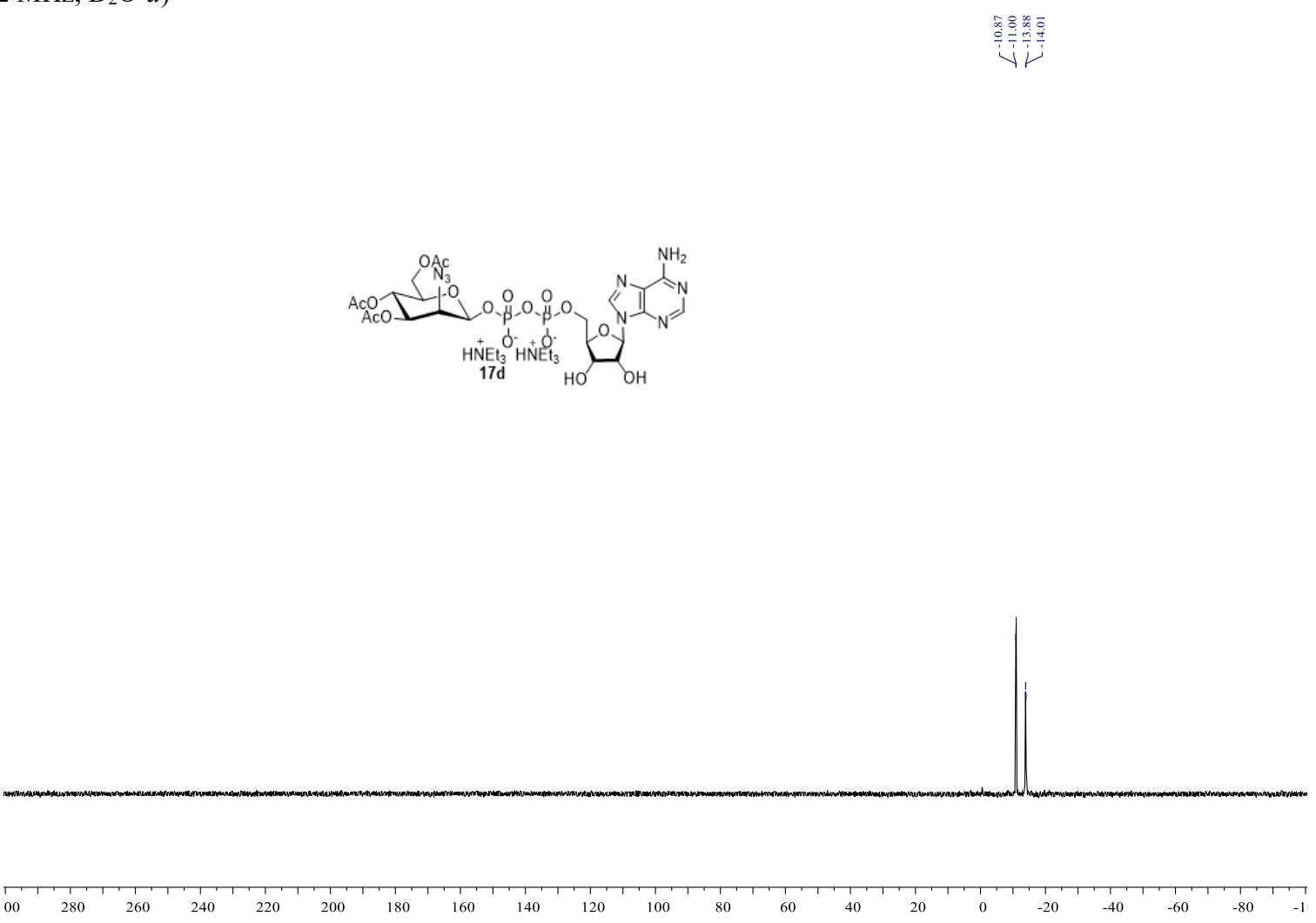
^{1}H-NMR (400 MHz, D_2O-*d*)



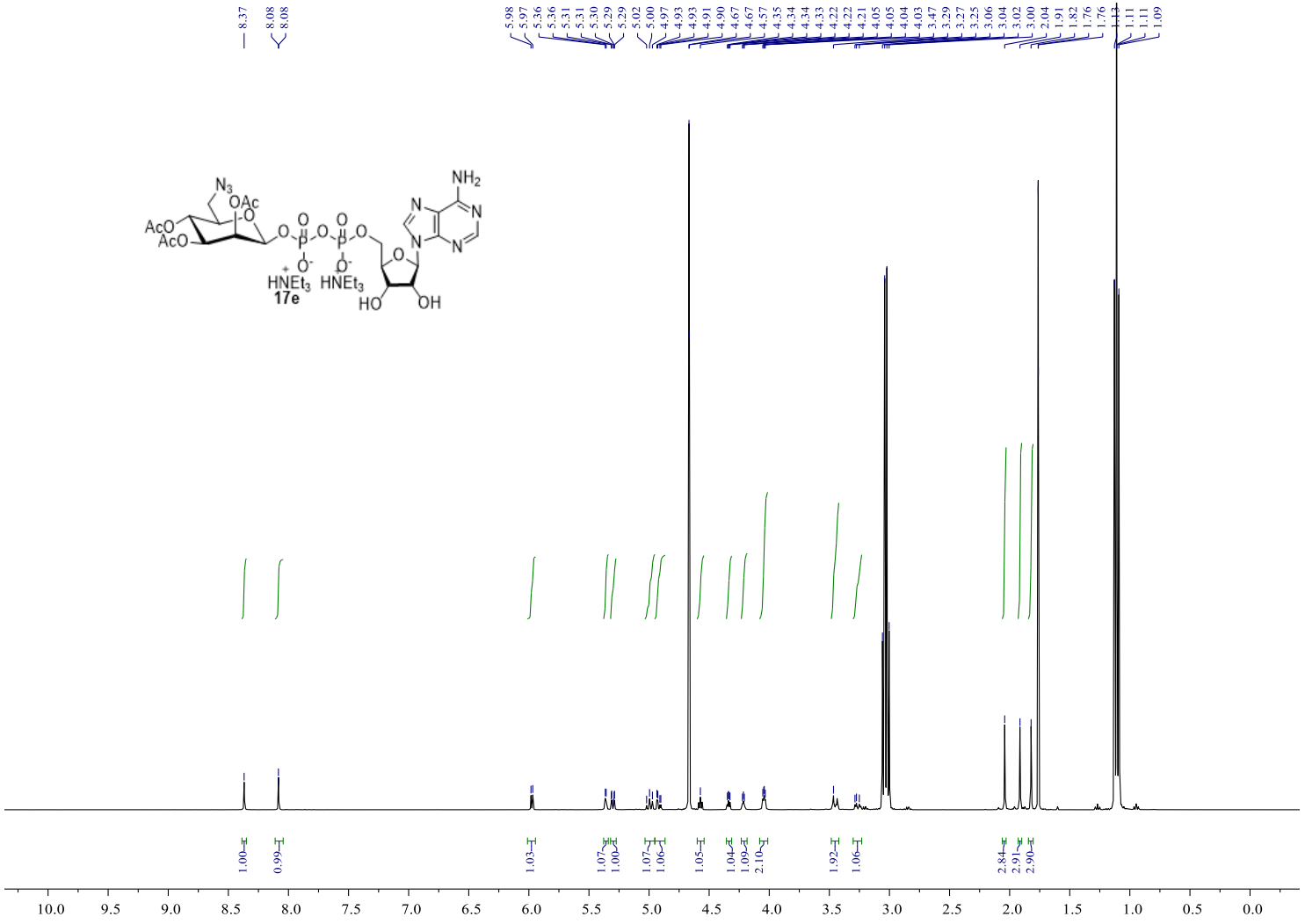
^{13}C-NMR (100 MHz, D_2O-*d*)



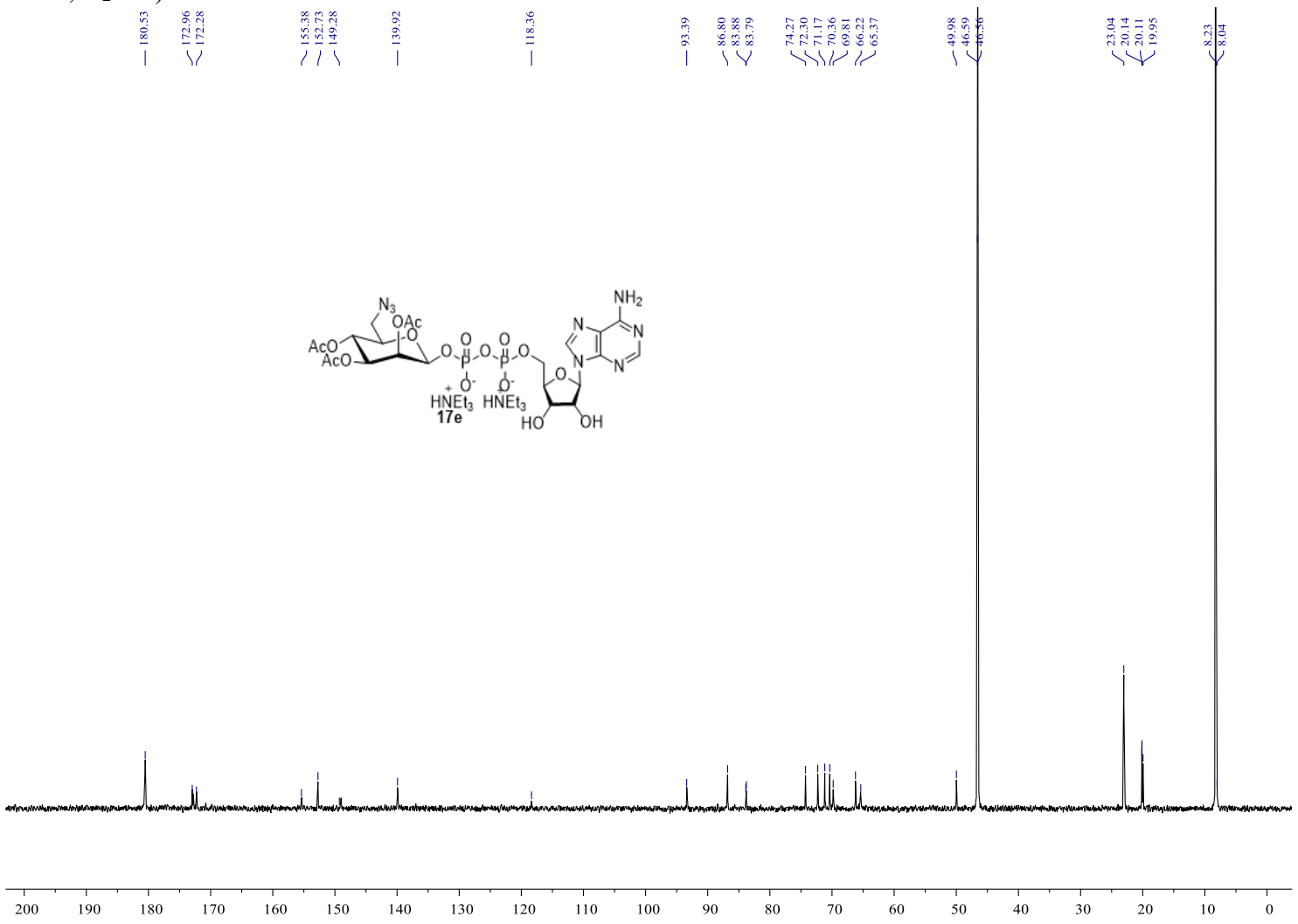
^{31}P-NMR (162 MHz, D_2O-*d*)



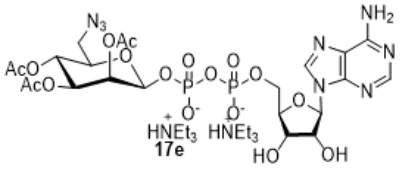
^{1}H-NMR (400 MHz, D_2O-*d*)



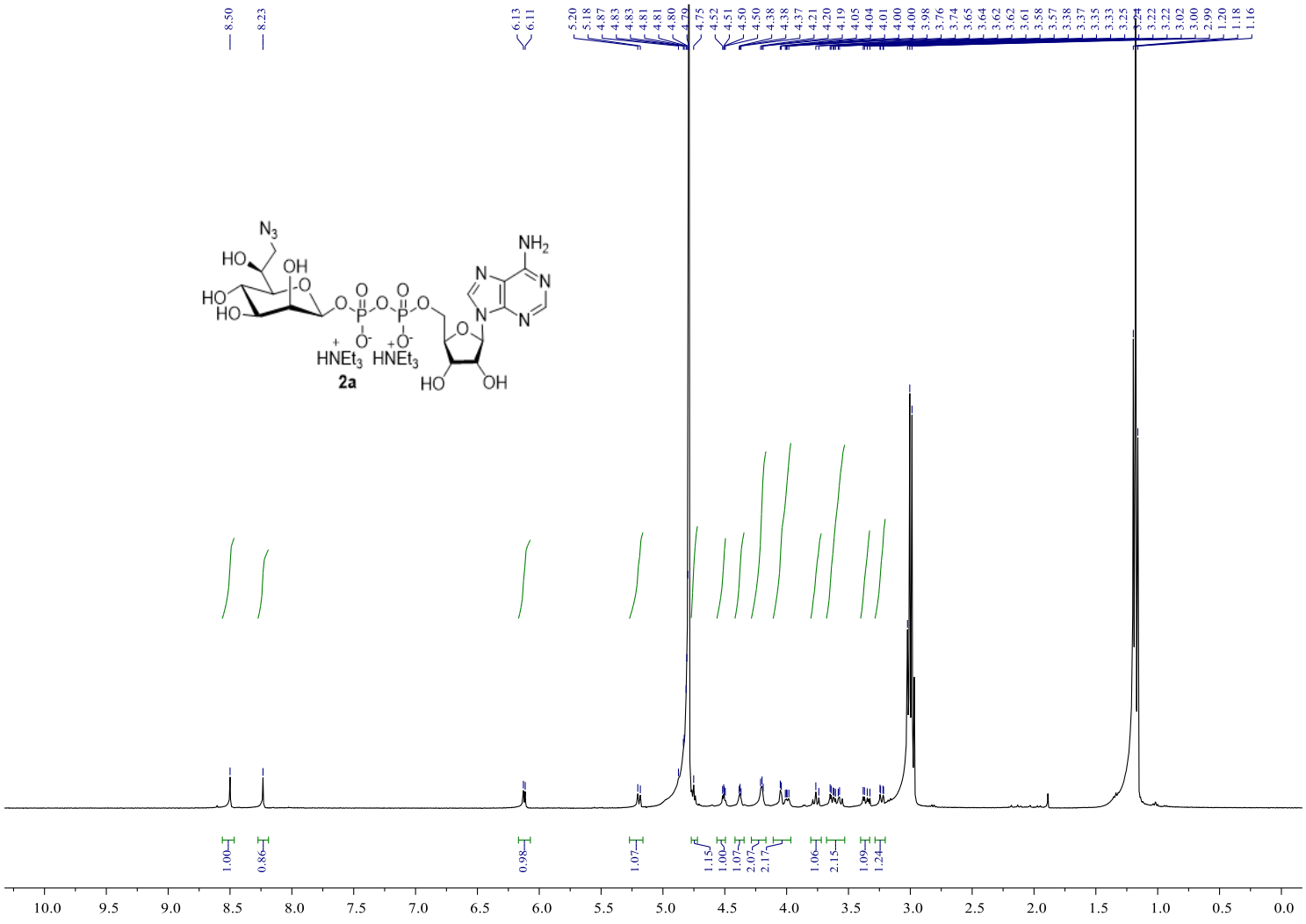
^{13}C-NMR (100 MHz, D_2O-*d*)



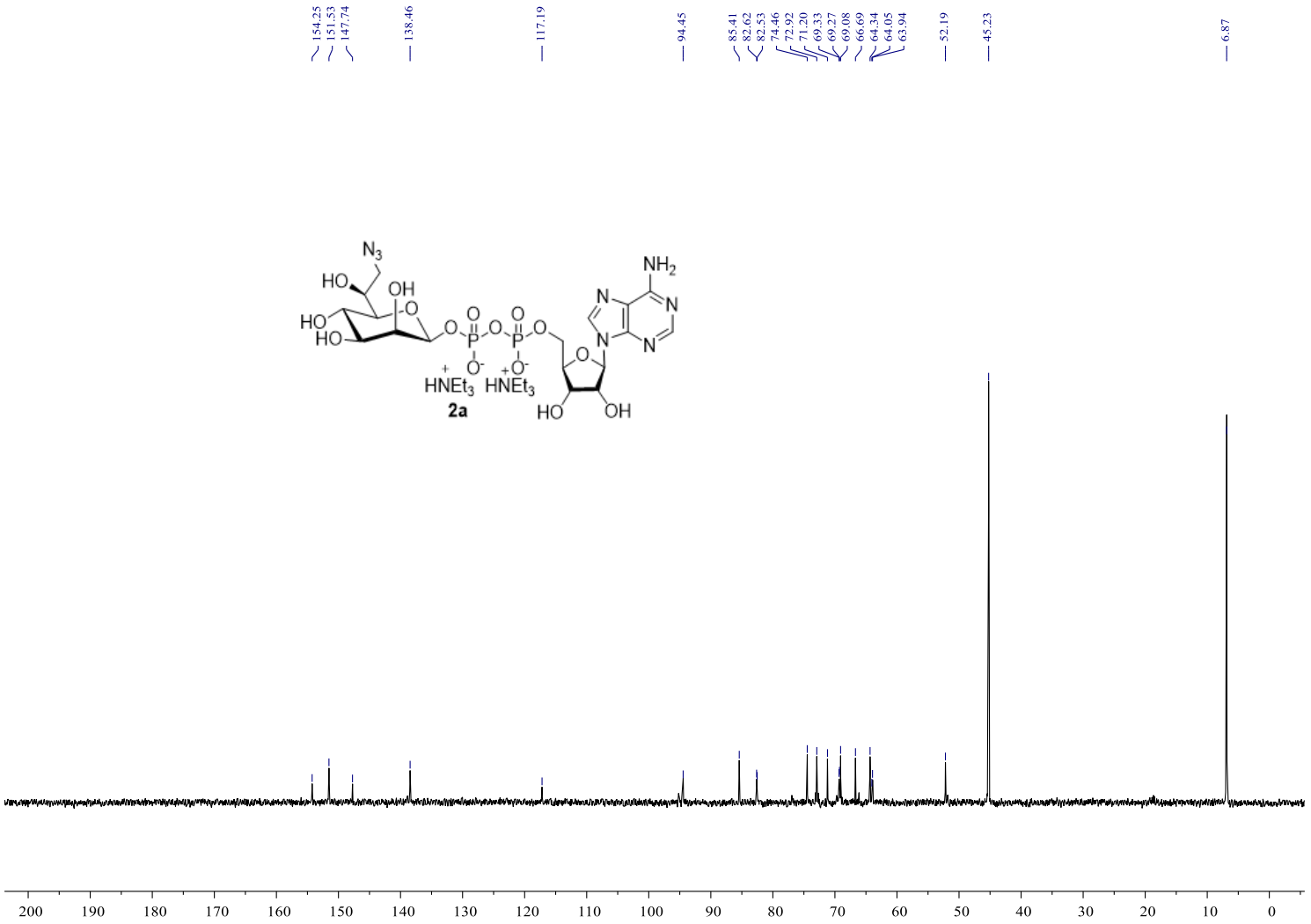
^{31}P-NMR (162 MHz, D_2O-*d*)



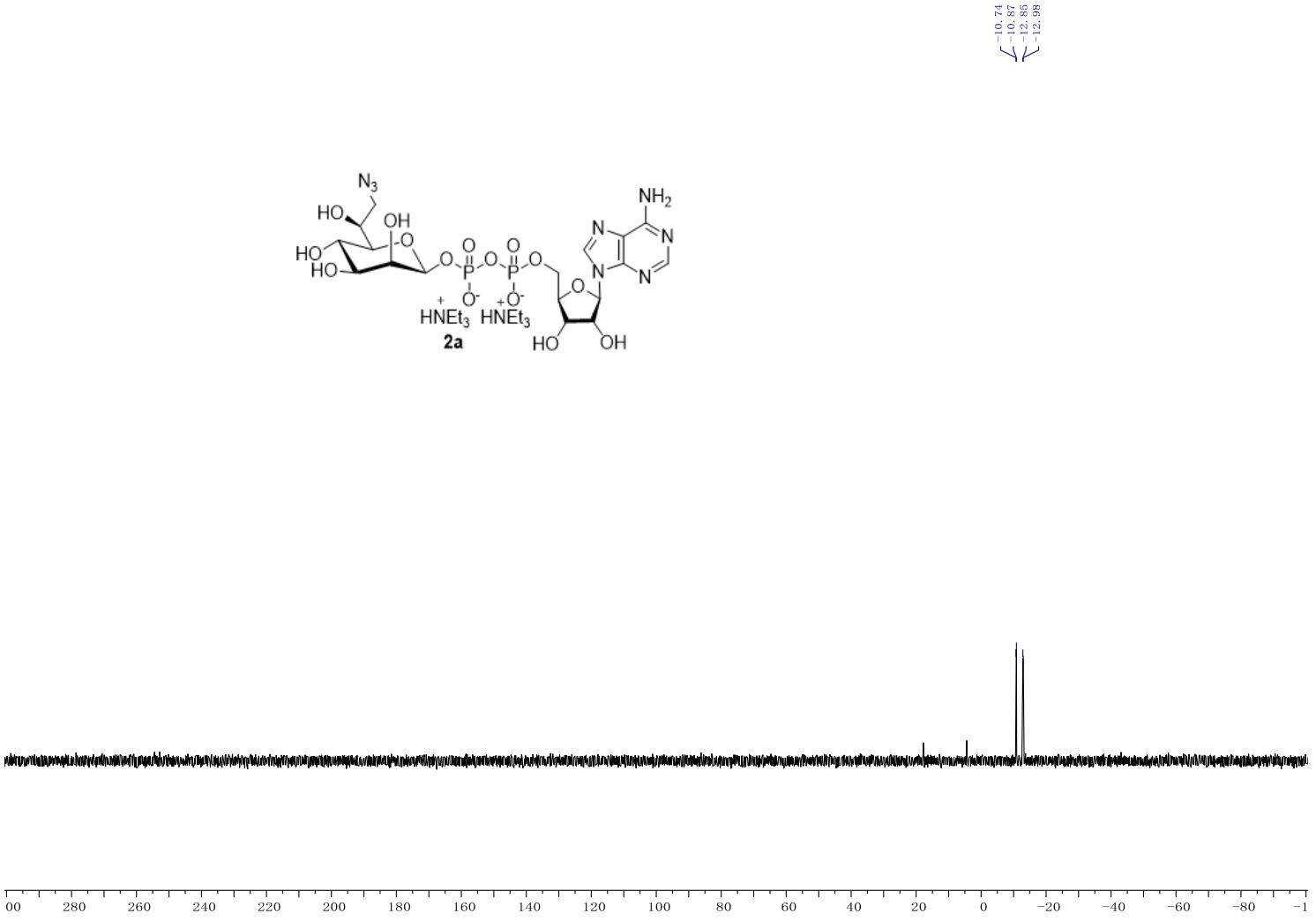
^{1}H-NMR (400 MHz, D_2O-*d*)



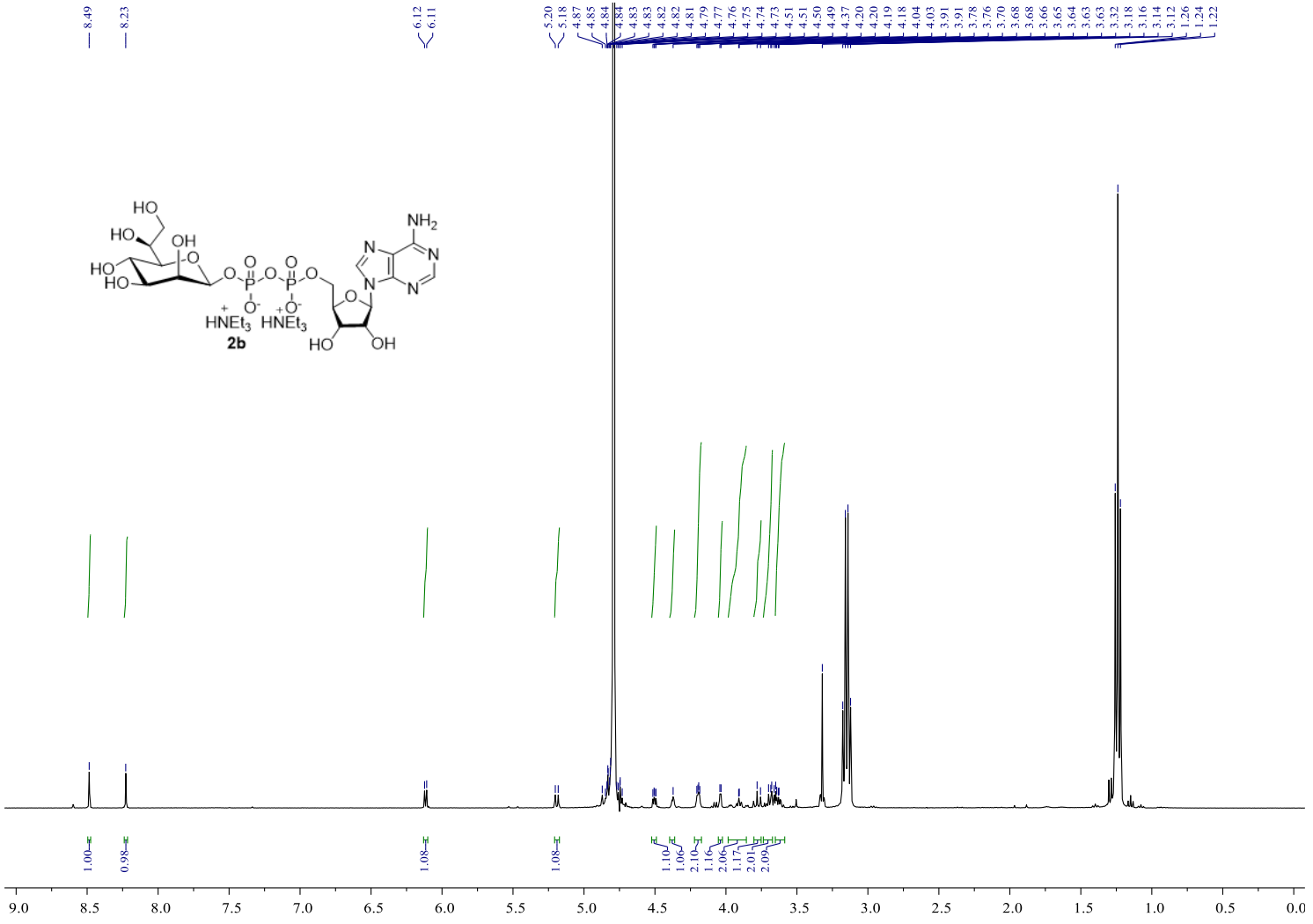
^{13}C-NMR (100 MHz, D_2O-*d*)



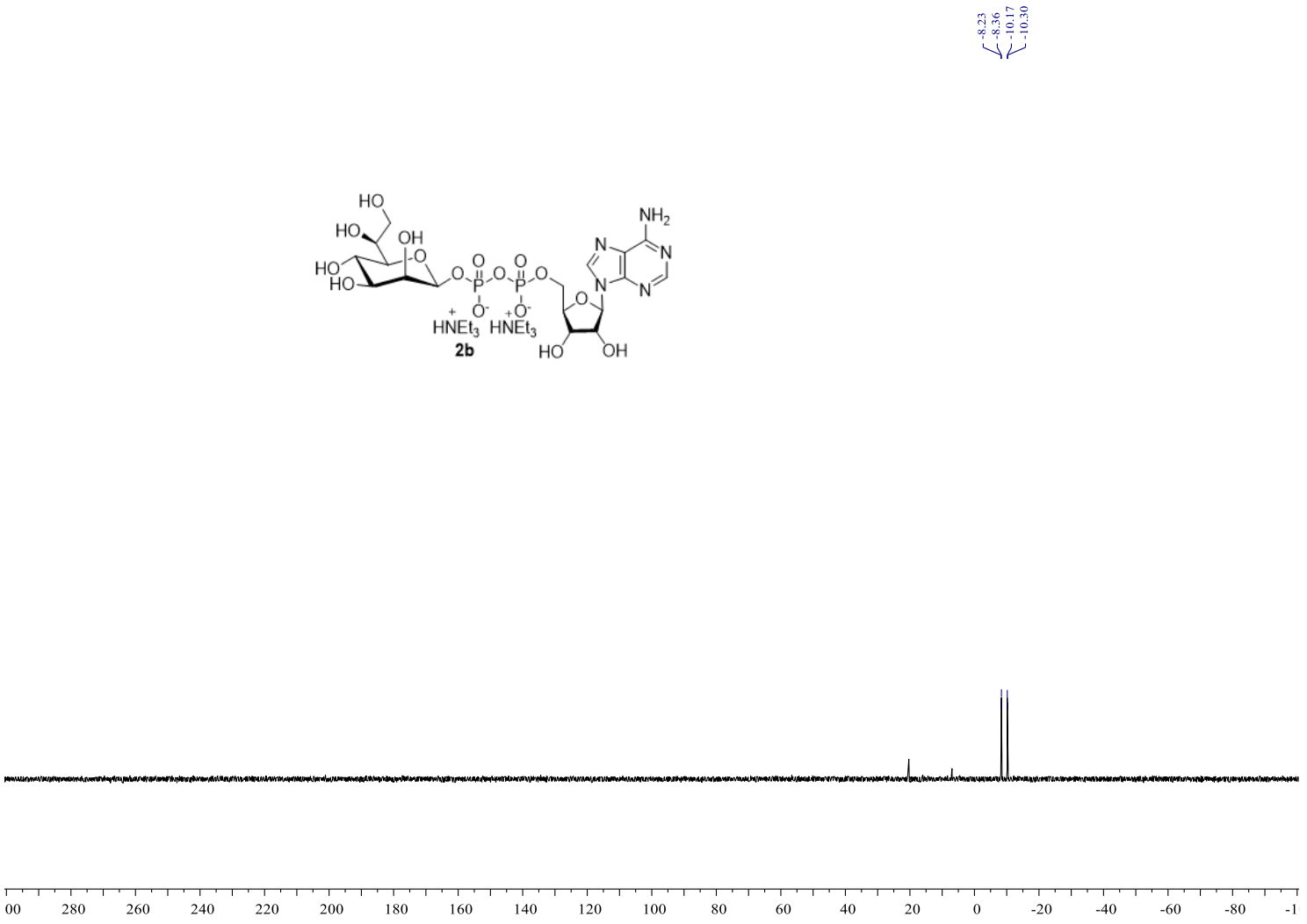
^{31}P-NMR (162 MHz, D_2O-*d*)



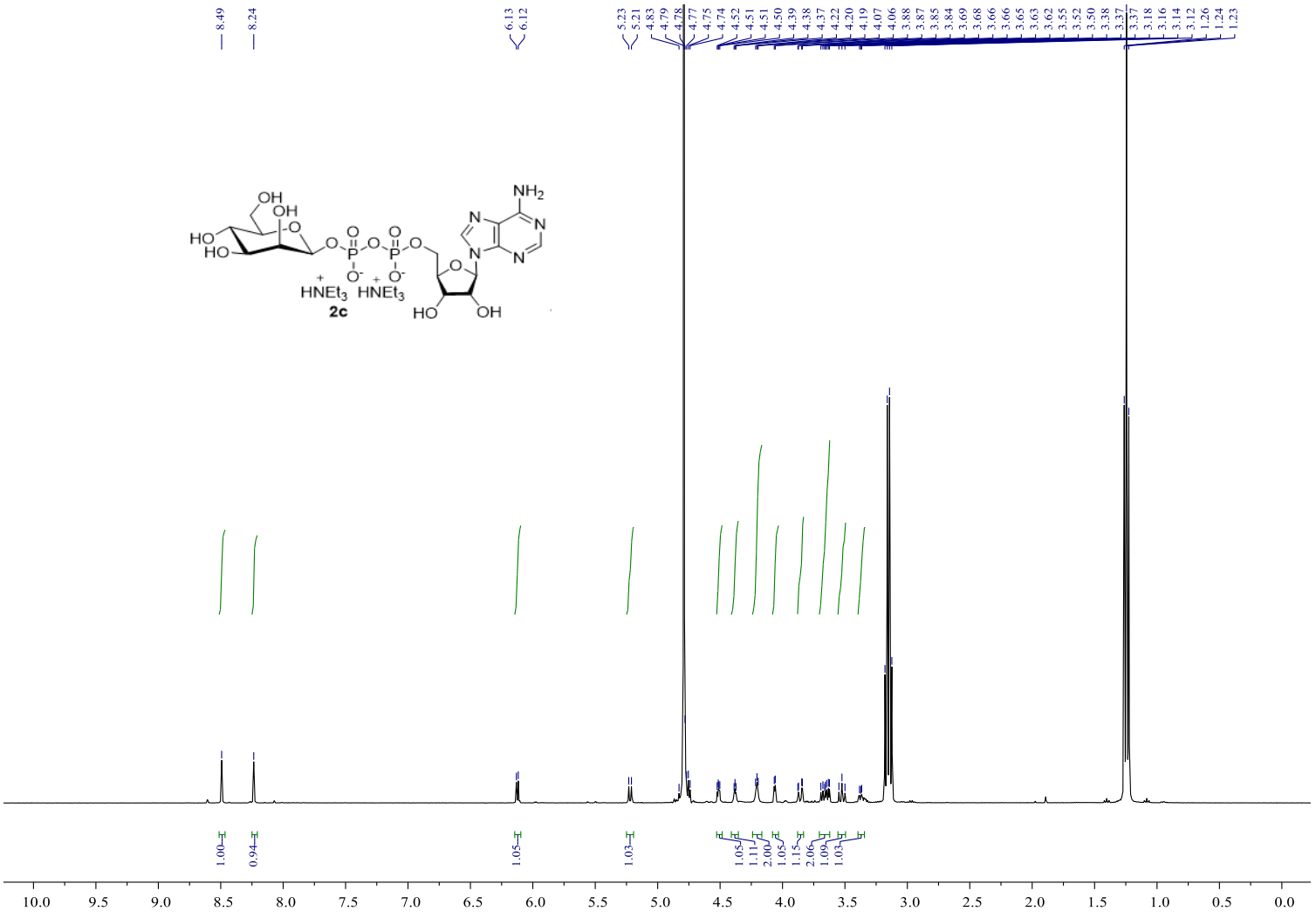
^{1}H-NMR (400 MHz, D_2O-*d*)



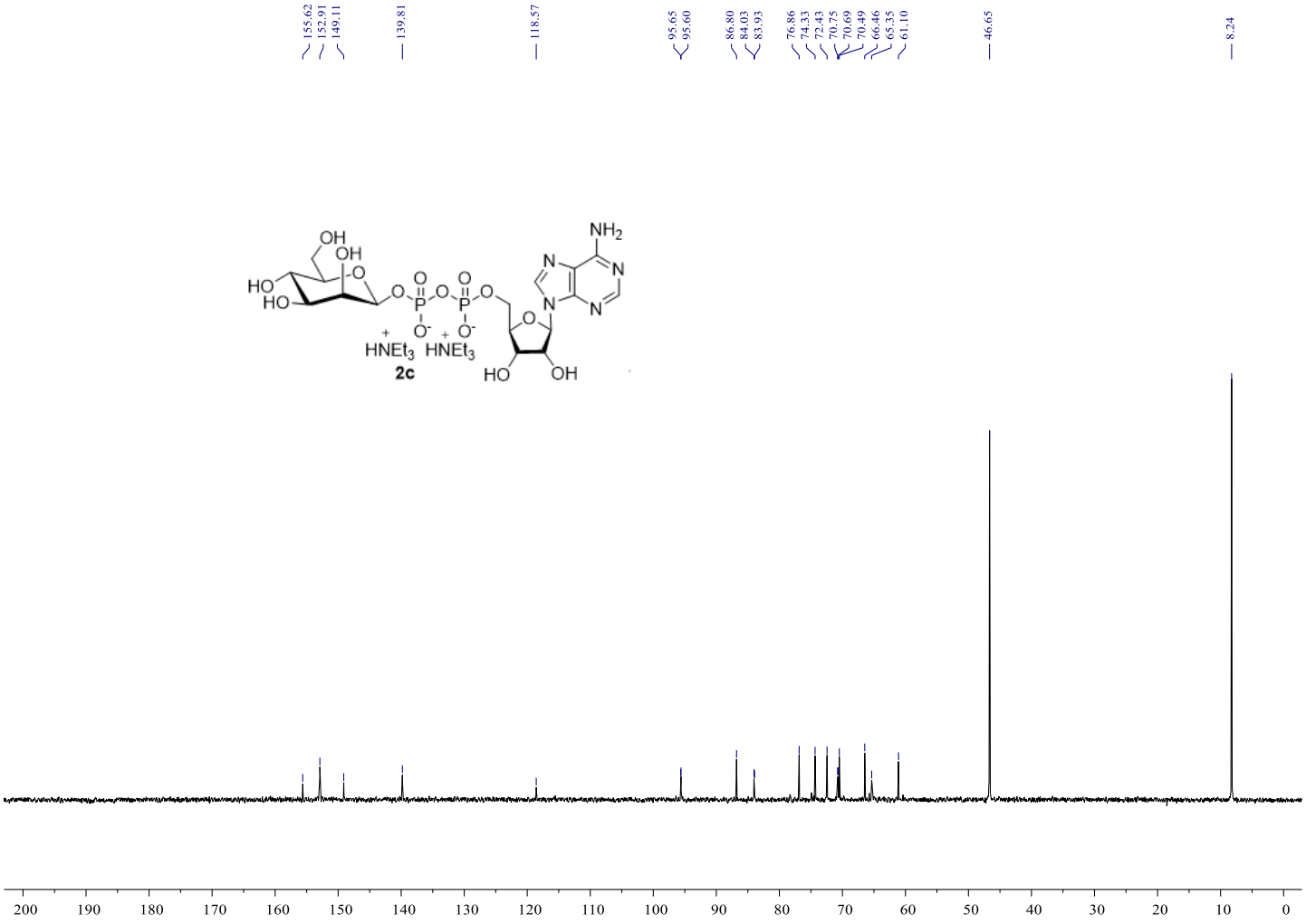
^{31}P-NMR (162 MHz, D_2O-*d*)



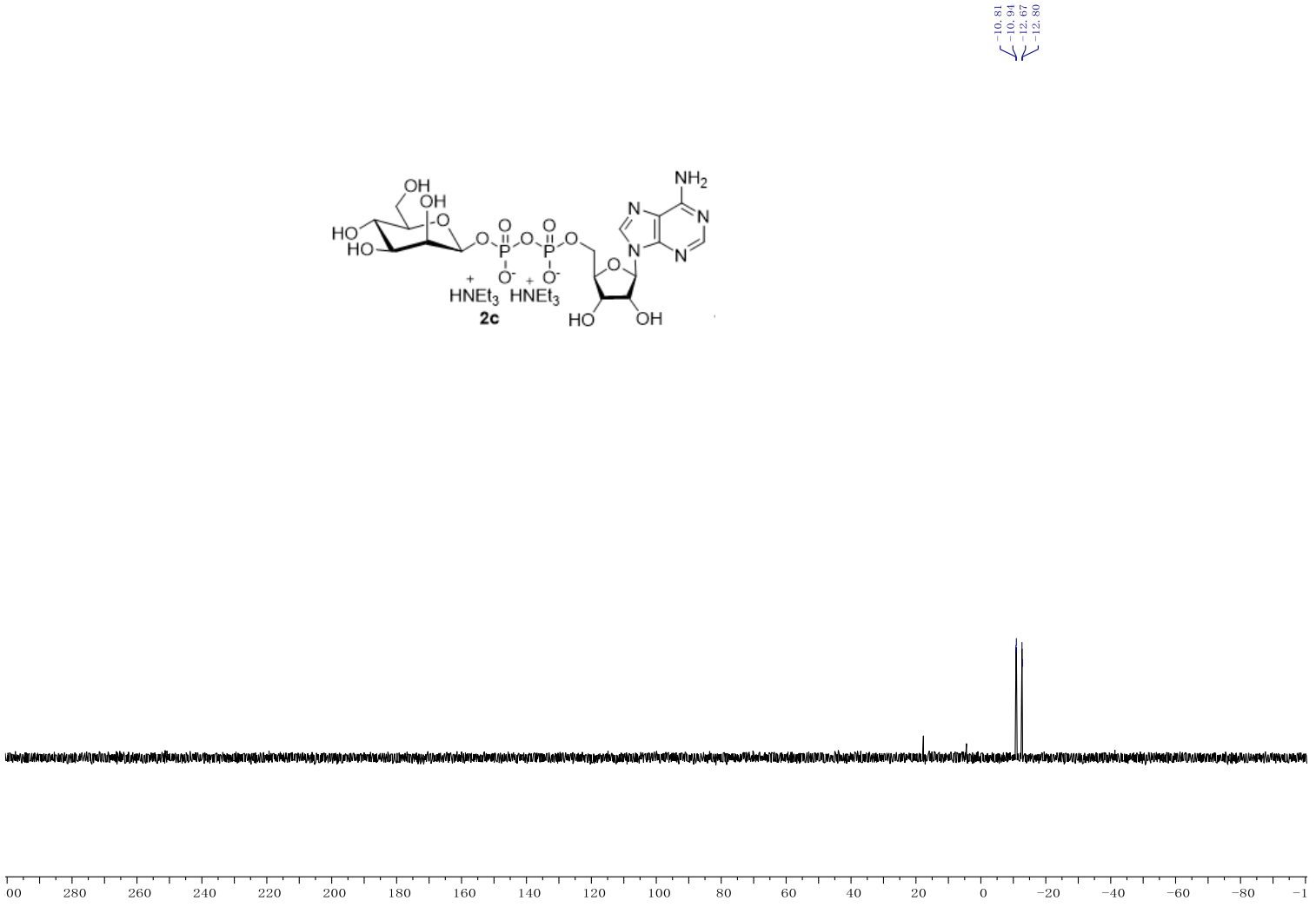
^{1}H-NMR (400 MHz, D_2O-*d*)



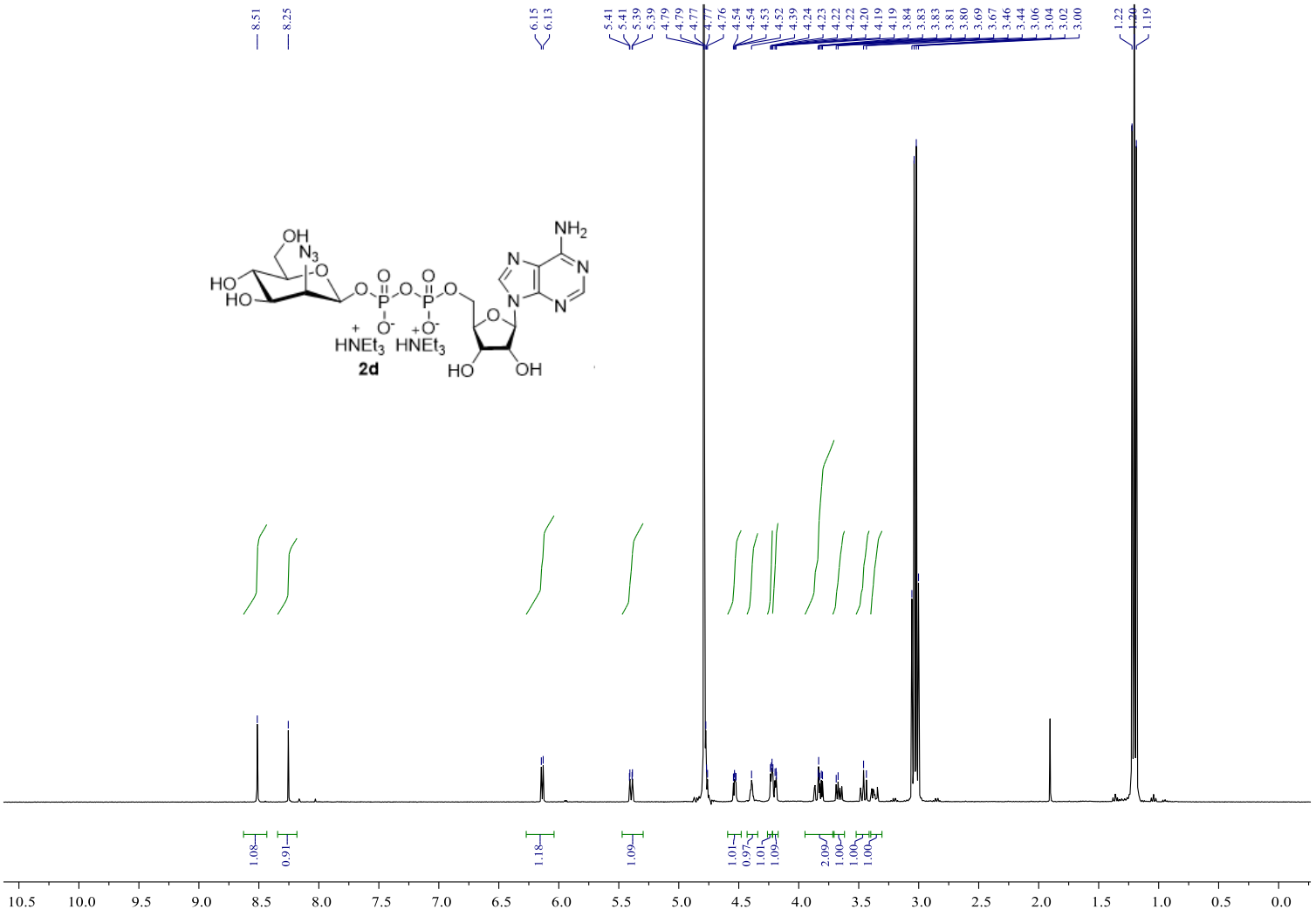
^{13}C-NMR (100 MHz, D_2O-*d*)



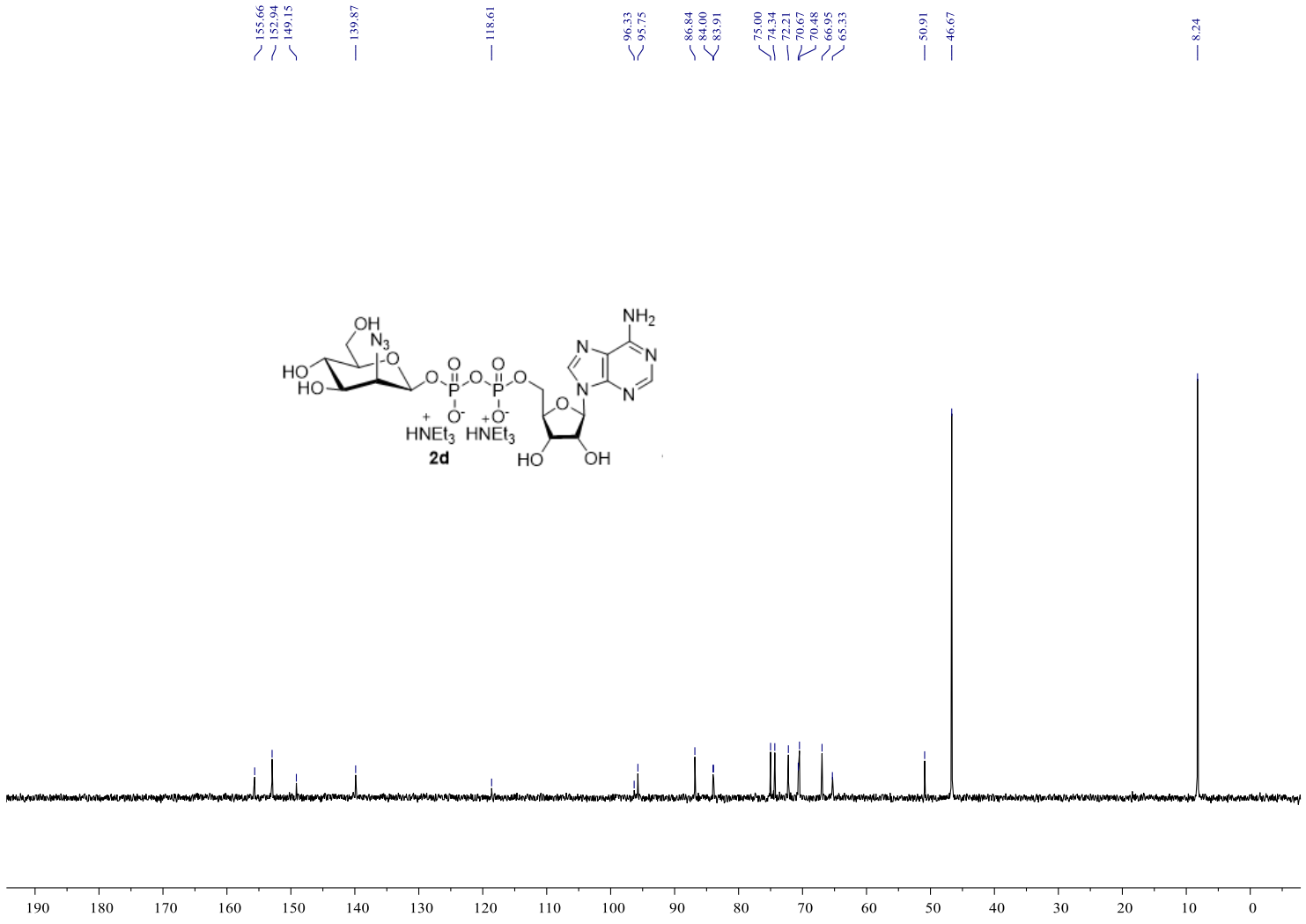
^{31}P-NMR (162 MHz, D_2O-*d*)



^{1}H-NMR (400 MHz, D_2O-*d*)



^{13}C-NMR (100 MHz, D_2O-*d*)



^{31}P-NMR (162 MHz, D_2O-*d*)