Supporting Information

Synthesis of Dimeric ADP-Ribose and its Structure with Human Poly(ADP-Ribose) Glycohydrolase

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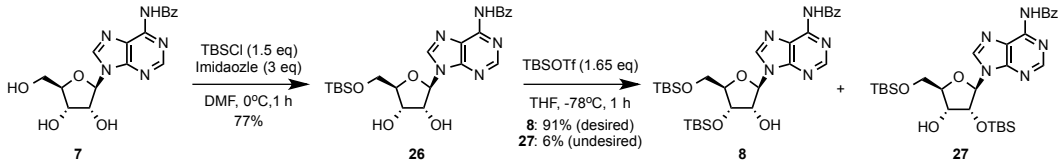
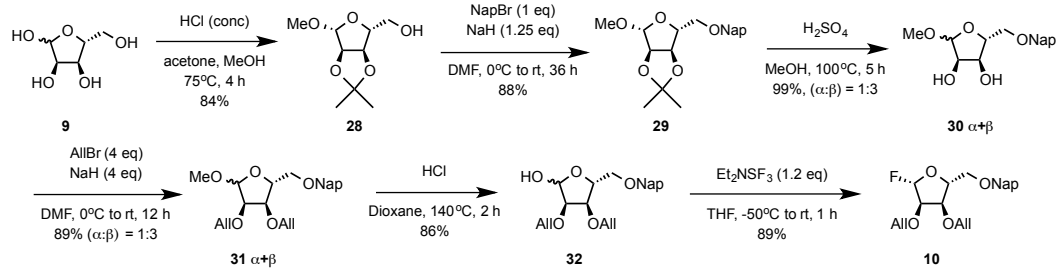
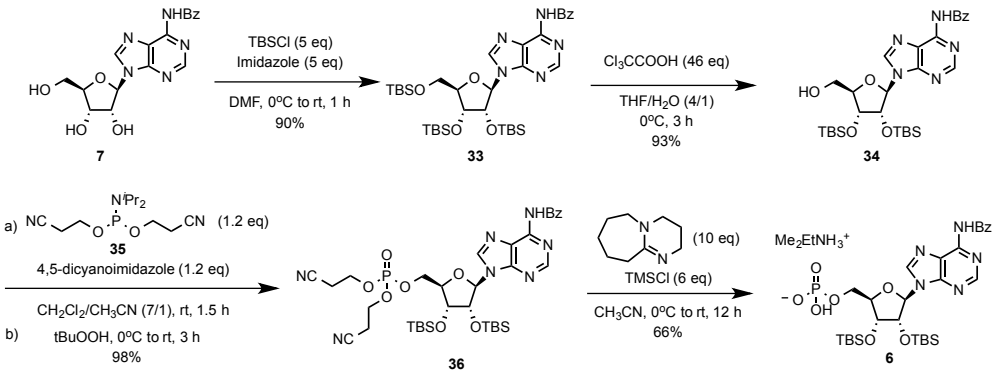


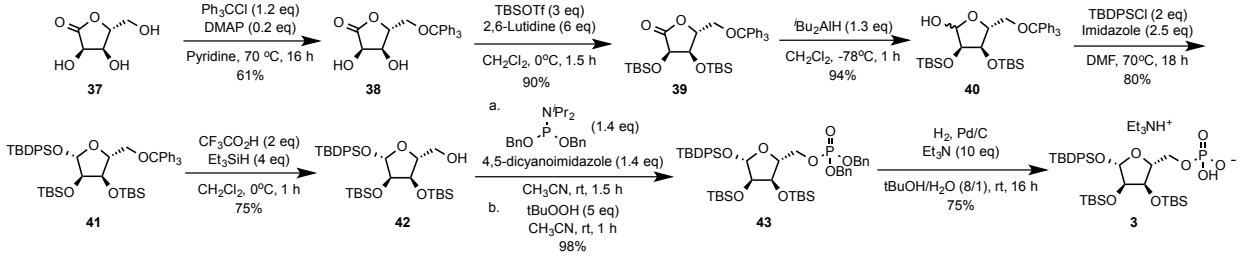
Supplementary Figure 1: Synthesis of Glycosyl Acceptor



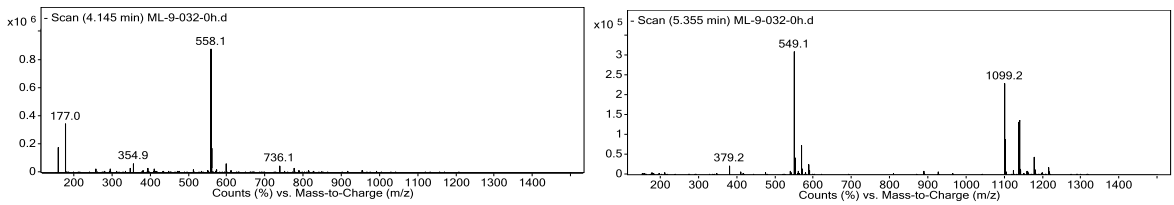
Supplementary Figure 2: Synthesis of Glycosyl Donor



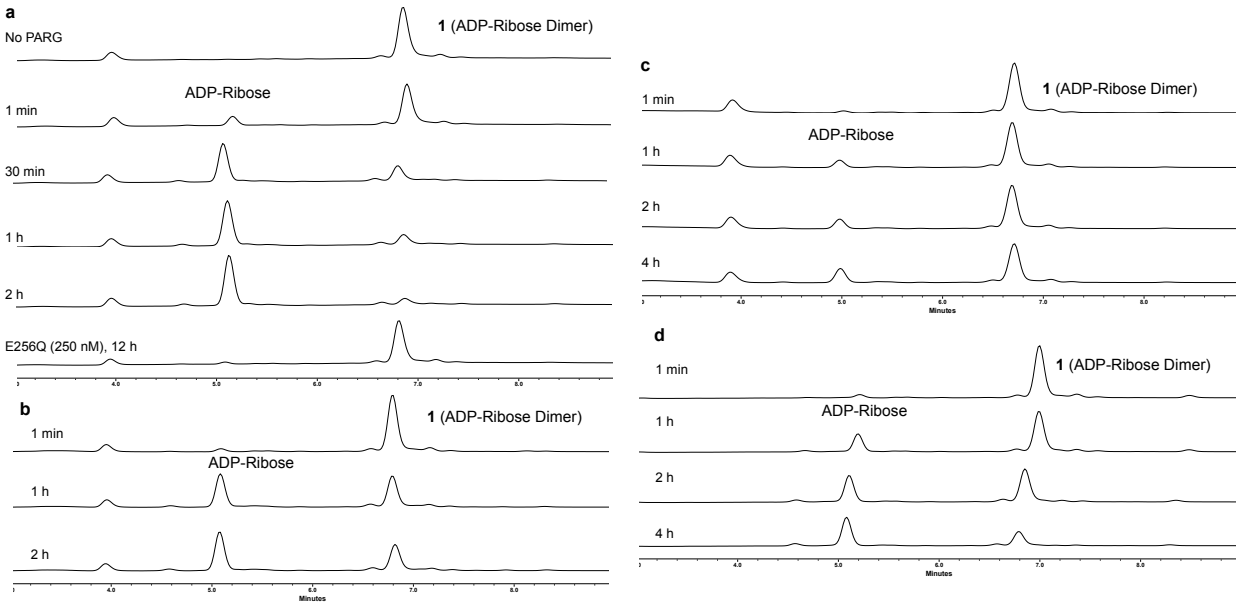
Supplementary Figure 3: Synthesis of Adenosine Monophosphate Initiator



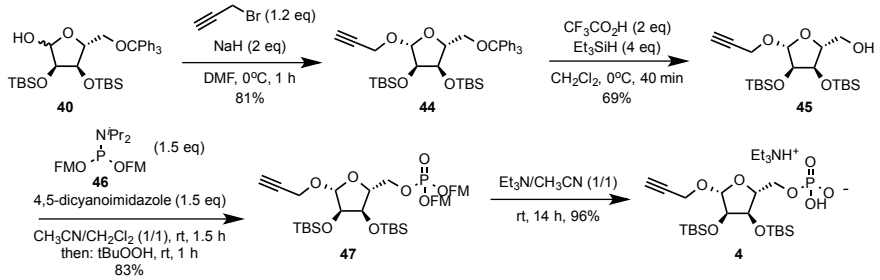
Supplementary Figure 4: Synthesis of Ribose Monophosphate Terminator



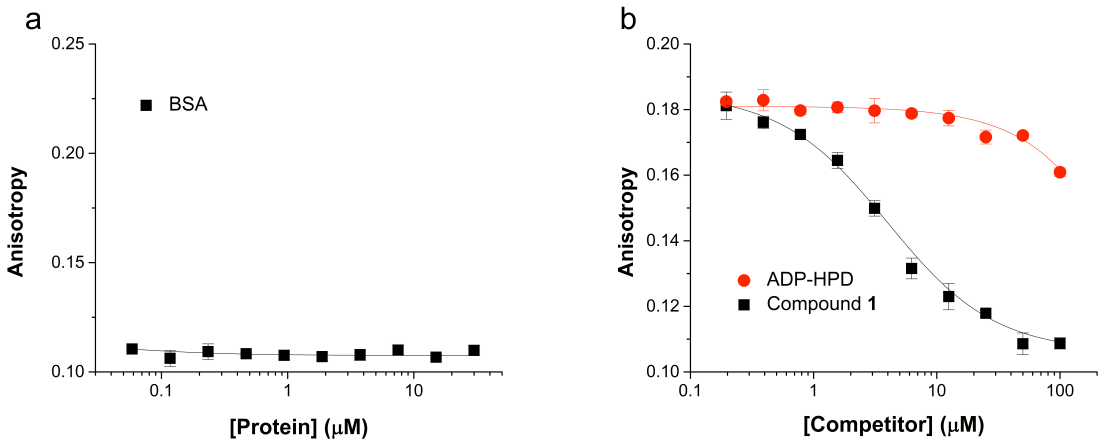
Supplementary Figure 5: Mass spectra at 4.15 min, 5.36 min for Human PARG processing of ADP-Ribose Dimer (**1**) by LCMS. ADP Ribose (m/z = 558.1) is shown at left and the ADP-Ribose Dimer (m/z=1099.2, m/2z=549.1) is shown on the right.



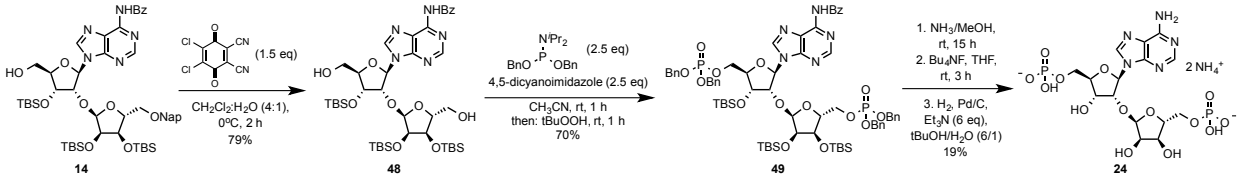
Supplementary Figure 6: HPLC analysis of PARG or ARH3 Processing of ADP-Ribose Dimer (**1**) (a) 25 nM *T. thermophilia* PARG without enzyme, at 1 min, 30 min, 1 h, 2 h and with 250 nM E256Q *T. thermophilia* at 12 h. (b) 5 nM *B. taurus* PARG at 1 min, 1 h, 2 h. (c) 250 nM *T. curvata* PARG at 1 min, 1 h, 2 h and 4 h and (d) 250 nM Human ARH3 at 1 min, 1 h, 2 h, 4 h. The peak near 4 min in panels (a), (b) and (d) is found in all traces of the PARG assay buffer.



Supplementary Figure 7: Synthesis of alkyne phosphate **4**



Supplementary Figure 8: (a) BSA does not bind compound compound **22** at high concentrations of protein. (b) Compound **1** but not ADP-HPD displaces compound **22** from E755N PARG.



Supplementary Figure 9: Synthesis of bisphosphate **24**

Crystallographic Data and Model Refinement Parameters

Data collection	
Space group	$P2_12_12_1$
Cell dimensions	
a, b, c (Å)	67.5, 91.3, 96.12
α, β, γ (°)	90, 90, 90
Resolution	55.22-1.95 (2.00-1.95)
R_{merge} (%)	10.5 (58.1)
I/sigma	21.4 (4.9)
Completeness	99.9 (99.8)
Multiplicity	13.2 (12.1)
Refinement	
Resolution	55.22-1.95
No. unique reflections	44991
R_{work}/R_{free}	13.7 / 17.9
No of atoms	
Protein	4202
Ligand/ion	205
Water	421
r.m.s. deviations	
Bond lengths (Å)	0.019
Bond angles (°)	1.55
B factors (Å^2)	
Protein	23.025
Ligand/ion	43.813
Water	35.080

Methods

Plasmids and proteins

T. thermophila PARG (TTHERM_00294690) and human PARG (a.a. 448–976 [K616A, Q617A, K618A, E688A, K689A, K690A]) proteins were expressed and purified as described previously[1,2] with the following changes. 6His-TEV-tagged catalytic mutant human PARG was obtained by introducing the E756N mutation using the QuickChange II site-directed mutagenesis kit (Stratagene). The human PARG proteins were purified from the clarified lysate by immobilised metal affinity chromatography (IMAC) using a 5 mL His-TRAP HP column (GE Healthcare). Pooled fractions enriched for 6His-TEV-PARG were incubated with 6-His-tagged TEV protease whilst being dialysed for 24 hours at 4ºC. Cleaved protein was separated from uncleaved material, free 6-His tags and TEV protease by subtractive IMAC. The cleaved protein was concentrated before loading on a Superdex 200 pg (16/600) column (GE Healthcare) for size exclusion chromatography. Pooled fractions containing human PARG were concentrated to 7.5 mg/mL for crystallisation studies. IMAC and size exclusion chromatography were performed on an ÄKTA PURE FPLC system (GE Healthcare).

Crystallization and structure solution

Crystals were grown at 293K by sitting-drop vapour diffusion by mixing 350 nL purified protein (at 7.5 mg/mL in 50mM HEPES, pH 7.0, 150 mM NaCl, 2mM DTT) briefly pre-incubated with 1mM of **1** dimer with 150 nL of seed stock and 500 nL of mother liquor consisting of 18-23%

PEG-3350, 0.2 M ammonium sulphate, 0.1 M PCTP pH 7.5. Seed stock was prepared using a Seed Bead™ (Hampton Research) from a co-crystal of mutant human PARG with ADP-ribose. The co-crystal mother liquor (19% PEG-3350, 0.2 M ammonium sulphate, 0.1 M PCTP pH 7.5) was used as the stabilising solution for the seed stock. Crystals appeared over 48 hours and continued to grow for a further week and were then cryoprotected in a solution of 20% glycerol in mother liquor prior to being flash-cooled in liquid nitrogen. The diffraction data were collected at the Diamond Light Source (UK), with the automatic processing carried out by *Xia2*. The structure was solved by molecular replacement using using *Phaser* and the previously reported human PARG structure, by iterative rounds of manual building in *Coot* and crystallographic refinement in *REFMAC5*. Crystallographic figures were generated using PyMOL (http://www.pymol.org).

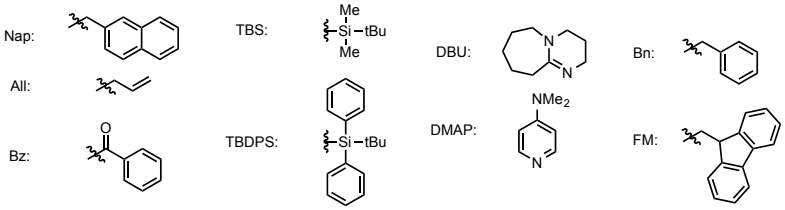
General Chemistry Experimental

All reactions were run in flame or oven dried glassware under an atmosphere of dry nitrogen unless otherwise noted. Acetonitrile, tetrahydrofuran, methanol and methylene chloride used in reactions were obtained from a solvent dispensing system. Diethyl ether was distilled from sodium metal. 4 Å molecular sieves were dried at 200 ^{o}C on high vacuum overnight. Pyridine and Diazabicyclo[5.4.0]undec-7-ene were distilled from CaH_2 and stored on 4 Å molecular sieves. 1,2-Dichloroethane and d_3-acetonitrile were dried over 4 Å molecular sieves. All other reagents were of standard commercial purity and were used as received. Tetrakis(triphenylphosphine)palladium(0) was prepared using the procedure of Malpass, *et al.*[3] and was packaged in a glove-bag under nitrogen.

Analytical thin-layer chromatography was performed on EMD Merck silica gel plates with F254 indicator. Plates were visualized with UV light (254 nm) or staining with p-anisaldehyde. Silica gel for column chromatography was purchased from Sorbent Technologies (40-75 μm particle size).

Unless otherwise indicated, ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra were recorded at 500, 125, 470 and 203 MHz, respectively. ^{1}H and ^{13}C NMR spectra were referenced to tetramethylsilane or the residual solvent peak as reported by Fulmer *et al*.[4] ^{13}C Spectra taken in D_2O contain 0.05% EtOH (17.47, 58.05 ppm) as an internal standard for referencing. ^{19}F NMR spectra were referenced using C_6F_6 as an internal standard (-164.9 ppm). ^{31}P NMR spectra were externally referenced to 85% H_3PO_4 (0.00 ppm) in water. Chemical shifts are reported in ppm and multiplicities are reported as s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), hep (heptet), m (multiplet), and br (broad). Mass spectrometry analysis was performed by the University of Illinois Mass Spectrometry Center or by direct injection on an Agilent 6230 LC/MS TOF for samples run in negative ion mode. The LC/MS assay was performed on the Agilent 6230 LC/MS TOF system with a 1.8 μm, 2.1x50 mm Agilent ZORBAX Eclipse Plus C18 column and is described in more detail below. Analytical HPLC analysis was performed on a Waters e2695 separations module with a Waters 2489 UV detector using a 5 μm, 4.6x150 mm Waters XBridge BEH130 HPLC column and is described in more detail below. Other preparative C18 chromatography was performed using a Teledyne Isco CombiFlash Rf system with CombiFlash Gold columns using a gradient of H_2O/CH_3CN beginning with 95% H_2O:5% CH_3CN, ramping to 65% H_2O:35% CH_3CN over 6 min, ramping to 100% CH_3CN for 3 min, and holding 100% CH_3CN for 5 min. Optical rotations were measured using a Jasco DIP-360 digital polarimeter in either EtOH or $CHCl_3$ with concentrations reported in g/dL. Infrared spectra were recorded on a Mattson Galaxy 5020 spectrophotometer with NaCl cells. Peaks are reported in cm^{-1}.

Summary of Abbreviations Used



PARG Catalyzed Degradation LC/MS Assay (Scheme 2)

Concentrated PARG stock solutions were diluted to the appropriate concentration in PARG activity buffer (50 mM K_2HPO_4, 50 mM KCl, 9 mM β-mercaptoethanol, pH = 7.5). Next, to a 0.5 mL tube was added 80 μL of PARG/ARH3 activity buffer, 10 μL of a 1 mM solution of synthetic ADP-Ribose Dimer, and 10 μL of the diluted PARG/ARH3. The tube was vortexed and transferred to a 384-well plate. The sample was analyzed by LC/MS (10 μL injections) at the appropriate time points. The HPLC method (98% 5 mM pentylamine:HOAc (pH=6.5) with 2% CH_3CN to 75% 6 mM pentylamine:HOAc (pH=6.5) with 25% CH_3CN over 5 min, then hold 75% 6 mM pentylamine:HOAc (pH=6.5) with 25% CH_3CN for 3 min) results in elution of ADP-Ribose at 4 min and PAR dimer at 5.2 min.

PARG or ARH3 Catalyzed Degradation HPLC Assay (Supplementary Figure 6)

Concentrated PARG/ARH3 stock solutions were diluted to the appropriate concentration in PARG activity buffer (50 mM K_2HPO_4, 50 mM KCl, 9 mM β-mercaptoethanol, pH = 7.5) or ARH3 activity buffer (50 mM PBS, 10 mM $MgCl_2$, 5 mM TCEP, pH = 7.1). Next, to a 0.5 mL tube was added 42.5 μL of PARG/ARH3 activity buffer, 5 μL of a 1 mM solution of synthetic ADP-Ribose Dimer, and 2.5 μL of the diluted PARG/ARH3. The tube was vortexed and transferred to an HPLC vial with a small volume insert. The sample was analyzed by HPLC (10 μL injections) at the appropriate time points. The HPLC method (99% 8 mM Et_3NHOAc/1% CH_3CN to 90% 8 mM Et_3NHOAc/10% CH_3CN) results in elution of ADP-Ribose at 5.1 min and PAR dimer at 6.9 min.

For assessment of the glycohydrolase product by mass spectrometry, the entire 50 μL sample was injected on the HPLC at the 2 h time point and the effluent from 4.9-5.2 min was collected. The collected solution was desalted using a G-10 size exclusion column and analyzed by mass spectrometry.

Fluorescence Polarization Assays

E755N and E756N PARG dilutions (final concentrations of 5 μM to 0 μM) were made in PARG binding buffer (50 mM KCl, 50 mM K_2HPO_4, 0.05% Trition X-100, pH = 7.5) and compound **22** was added to a final concentration of 7.5 nM. The solutions were transferred to a black 384 well plate incubated at room temperature for 30 min and read using an Analyst HT (excitation at 530 ± 25 nm and emission at 570 ± 10 nm). Polarization data was converted to anisotropy, plotted and fit to the following equation[5,6] using Origin Lab:

$$A_{OBS} = A_F + \frac{(A_B - A_F)\left(K_D + L_{ST} + R_T - \sqrt{((K_D + L_{ST} + R_T)^2 + 4L_{ST}R_T)}\right)}{2L_{ST}}$$

where A_{OBS} is the observed anisotropy, A_F is the anisotropy of the free probe, A_B is the anisotropy of the bound probe K_D is the dissociation constant of the protein-ligand (fluorescently labeled compound) interaction, L_{ST} is the total concentration of the labeled ligand

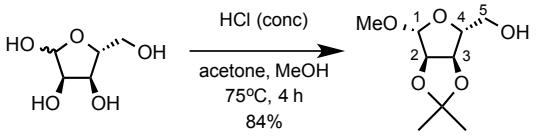
in the assay, and R_T is the total receptor (protein) concentration. The error of the reported K_D values corresponds to the error in the curve fitting.

For competition binding experiments, unlabeled compound **1** or ADP-HPD was diluted to the appropriate concentrations and protein in binding buffer was added to final concentrations for E755N and E756N of 500 nM and 250 nM, respectively. The solutions were incubated for 30 min at room temperature at which point compound **22** was added at a final concentration of 7.5 nM. The solutions were transferred to a 384 well black plate incubated an additional 30 min and read using the conditions described above. Polarization data was converted to anisotropy, plotted and fit to the following equation using Origin Lab:

$$A = A_F + \frac{A_B - A_F}{1 + 10^{log(L_T - IC_{50})}}$$

where L_T is the concentration of unlabeled competitor and IC_{50} is the concentration of unlabeled competitor necessary to produce 50% decrease in binding of the labeled probe.

Procedures for Chemical Synthesis



D-ribose (**9**) **28**

Compound 28: A modified version of the procedure of Paquette *et al*.[7] was followed. Specifically, to a 250 mL round bottom flask was added D-ribose (**9**) (10.0 g, 66.1 mmol, 1 eq), methanol (40 mL), and acetone (40 mL). Next, concentrated HCl (1 mL) was added at room temperature, the flask was sealed, and the reaction was heated to 75 °C for 4 h. The solution was cooled to room temperature and quenched with pyridine (10 mL). The solution was concentrated, diluted with EtOAc, and poured into a saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted ten times with EtOAc, the combined organic layers were dried over Na_2SO_4, concentrated, and purified by distillation under high vacuum (bp 110 °C at 1 torr, R_f 0.34, 50:50 hexanes:ethyl acetate). Compound **28** was obtained as a colorless oil (11.3 g, 84%).

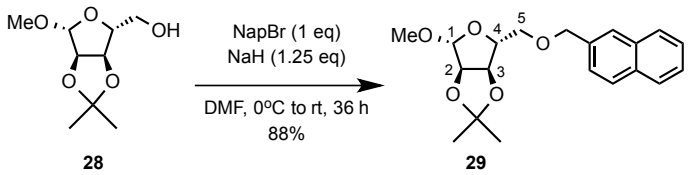
^{1}H NMR (499 MHz, $CDCl_3$) δ 4.97 (s, 1H, H-1), 4.84 (d, *J* = 5.9 Hz, 1H, H-2), 4.59 (d, *J* = 5.9 Hz, 1H, H-3), 4.43 (bs, 1H, H-4), 3.70 (ddd, *J* = 12.6, 2.4, 2.7 Hz, 1H, H-5a), 3.65-3.57 (m, 1H, H-5b), 3.44 (s, 3H, -OCH_3), 3.21 (dd, *J* = 10.7, 2.7 Hz, 1H,-OH), 1.49 (s, 3H, -CH_3), 1.32 (s, 3H, -CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 112.3, 110.3, 88.6, 86.0, 81.7, 64.2, 55.6, 26.6, 25.0.

HRMS (ESI) m/*z* calcd for $C_9H_{16}O_5Na$ ($[M+Na]^+$) 227.0895, found 227.0896.

IR (neat) ν 3457, 2986, 2934, 2836, 1455, 1380, 1276, 1208, 1162, 1097, 1045, 1009, 963, 869 cm^{-1}.

$[\alpha]_D^{21}$ -73.5 (*c* = 2.71, $CHCl_3$)



Compound 29: To a 500 mL round bottom flask was added DMF (180 mL) and compound **28** (10.0 g, 49.0 mmol, 1.1 eq). The reaction was cooled to 0 °C. Next, NaH (1.34 g, 55.6 mmol, 1.25 eq) was added in one portion and stirred for 15 min at 0 °C. Lastly, 2-bromomethyl-naphthalene (9.84 g, 44.5 mmol, 1 eq) was added portionwise and slowly warmed to room temperature. The reaction was stirred at room temperature for 36 h. The reaction was then cooled to 0 °C, quenched with saturated aqueous NH_4Cl, extracted with EtOAc twice, the organic layer was dried over Na_2SO_4, concentrated and purified by silica gel chromatography. Compound **29** was obtained as a white solid (13.54 g, 88%).

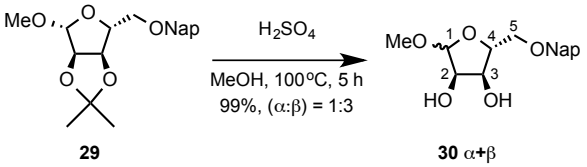
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.80 (m, 3H, Nap), 7.78 (s, 1H, Nap), 7.51 – 7.44 (m, 3H, Nap), 4.97 (s, 1H, H-1), 4.72 (s, 2H, -OC*H*$_2$Nap), 4.70 (d, *J* = 6.1 Hz, 1H, H-2), 4.57 (d, *J* = 6.0 Hz, 1H, H-3), 4.41 (ddd, *J* = 7.7, 6.5, 1.1 Hz, 1H, H-4), 3.56 (dd, *J* = 9.7, 6.4 Hz, 1H, H-5a), 3.50 (dd, *J* = 9.7, 8.1 Hz, 1H, H-5b), 3.29 (s, 3H, -OCH_3), 1.49 (s, 3H, -CH_3), 1.32 (s, 3H, -CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.6, 133.3, 133.1, 128.3, 128.0, 127.8, 126.5, 126.2, 126.0, 125.8, 112.5, 109.4, 85.3, 85.3, 82.3, 73.4, 71.2, 54.9, 26.6, 25.1.

HRMS (ESI) m/*z* calcd for $C_{20}H_{25}O_5$ ($[M+H]^+$) 345.1702, found 345.1695.

IR (neat) ν 3052, 2996, 2938, 1601, 1510, 1458, 1372, 1271, 1243, 1210, 1107, 1059, 1018, 966, 870, 818, 753 cm^{-1}.

$[\alpha]_D^{22}$ -41.0 (*c* = 10.0, $CHCl_3$)



Compound 30: To a 1 L round bottom flask was added compound **29** (12.16 g, 35.3 mmol, 1 eq) and MeOH (500 mL). The flask was placed in an oil bath at 114 °C and equipped with a distillation head. While the solution was warming to the bath temperature, concentrated H_2SO_4 (4.6 mL) was added slowly over 5 minutes. The solution was heated to a vigorous boil and the distillate was collected. Fresh anhydrous methanol was slowly added to the solution to replenish the methanol that was lost. After 5 h the solution was cooled to room temperature. The reaction was quenched with solid $NaHCO_3$ (20 g), the solution was decanted and concentrated. The organic slurry was diluted with CH_2Cl_2, filtered, and the filtrate was once again concentrated. The crude oil was purified by silica gel chromatography to furnish compound **30** as a white solid (10.68 g, 99%, α:β = ~1:3).

α-anomer (R_f 0.23, 75:25 ethyl acetate:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.80 (m, 3H, Nap), 7.75 (s, 1H, Nap), 7.53 – 7.40 (m, 3H, Nap), 4.96 (d, *J* = 4.5 Hz, 1H, H-1), 4.74 (d, *J* = 12.1 Hz, 1H, C*H*$_2$Nap), 4.69 (d, *J* = 12.2 Hz, 1H, C*H*$_2$Nap), 4.21 – 4.12 (m, 2H, H-2 + H-3), 3.98 (ddd, *J* = 7.7, 6.1, 3.1 Hz, 1H, H-4), 3.65 (dd, *J* = 10.5, 3.4 Hz, 1H, H-5a), 3.62 (dd, *J* = 10.5, 4.3 Hz, 1H, H-5b), 3.49 (s, 3H, -OCH_3), 2.92 (d, *J* = 9.1 Hz, 1H, -OH), 2.66 (d, *J* = 8.1 Hz, 1H, -OH).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.4, 133.3, 133.1, 128.4, 128.0, 127.8, 126.7, 126.3, 126.1, 125.8, 103.0, 84.0, 73.8, 71.7, 71.5, 70.2, 55.8.

HRMS (ESI) m/*z* calcd for $C_{17}H_{20}O_5Na$ ([M+Na]$^+$) 327.1208, found 327.1210.

IR (neat) ν 3410, 3059, 2926, 2850, 1635, 1507, 1465, 1448, 1403, 1372, 1347, 1271, 1188, 1125, 1094, 1039, 955, 896, 855, 817, 758 cm^{-1}.

$[\alpha]_D^{22}$ + 72.5 (*c* = 1.9, $CHCl_3$)

β-anomer (R_f 0.34, 75:25 ethyl acetae:hexanes)

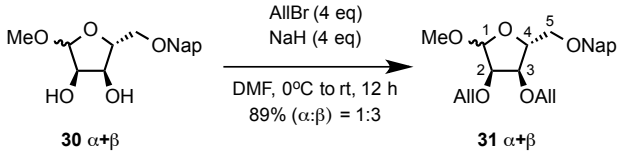
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (td, *J* = 6.0, 5.5, 3.3 Hz, 3H, Nap), 7.77 (s, 1H, Nap), 7.51 – 7.44 (m, 3H, Nap), 4.83 (s, 1H, H-1), 4.72 (d, *J* = 12.3 Hz, 1H, C*H*$_2$Nap), 4.69 (d, *J* = 12.3 Hz, 1H, C*H*$_2$Nap), 4.23 – 4.09 (m, 3H, H-2 + H-3 + H-4), 3.99 (d, *J* = 4.6 Hz, 1H, -OH), 3.93 (s, 1H, -OH), 3.65 (dd, *J* = 10.3, 4.0 Hz, 1H, H-5a), 3.55 (dd, *J* = 10.3, 6.5 Hz, 1H, H-5b), 3.29 (s, 3H, -OCH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.3, 133.2, 133.0, 128.2, 127.9, 127.7, 126.6, 126.1, 125.9, 125.8, 108.2, 81.9, 74.8, 73.5, 72.5, 72.1, 55.1.

HRMS (ESI) m/*z* calcd for $C_{17}H_{20}O_5Na$ ([M+Na]$^+$) 327.1208, found 327.1199.

IR (neat) ν 3390, 3045, 1639, 1604, 1503, 1451, 1354, 1264, 1188, 1113, 1063, 1028, 976, 945, 886, 858, 817, 752 cm^{-1}.

$[\alpha]_D^{22}$ -32.5 (*c* = 4.55, $CHCl_3$)



30 α+β **31** α+β

Compound 31: To a flame dried 500 mL round bottom flask was added NaH (3.37 g, 140.0 mmol, 4 eq) followed by DMF (80 mL) and the mixture was cooled to 0 ^{o}C. Then, compound **30** (10.68 g, 35.1 mmol, 1 eq) was added dropwise as a solution in DMF (80 mL). After 30 min at 0 ^{o}C, allyl bromide (11.9 mL, 140.0 mmol, 4 eq) was added, the reaction was slowly warmed to room temperature and was stirred for 12 h. The reaction was cooled to 0 ^{o}C, quenched with a saturated aqueous NH_4Cl solution, diluted with H_2O and extracted with EtOAc three times. The organic layer was dried over Na_2SO_4, concentrated, and purified by silica gel chromatography. Compound **31** was obtained as a slightly yellow oil (11.985 g, 89%, α:β = ~1:3).

α-anomer (R_f 0.21, 30:70 ethyl acetate:hexanes)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.78 (m, 3H, Nap), 7.76 (s, 1H, Nap), 7.51 – 7.43 (m, 3H, Nap), 5.97 (ddt, *J* = 17.2, 10.3, 5.9 Hz, 1H, -CH_2CH=CH_2), 5.87 (ddt, *J* = 17.3, 10.3, 5.9 Hz, 1H, -CH_2CH=CH_2), 5.28 (dd, *J* = 17.2, 1.6 Hz, 1H, -CH_2CH=CH_2), 5.22 – 5.13 (m, 2H, -CH_2CH=CH_2), 5.09 (dd, *J* = 10.3, 1.7 Hz, 1H, -CH_2CH=CH_2), 4.97 (d, *J* = 4.3 Hz, 1H, H-1), 4.77 (d, *J* = 12.3 Hz, 1H, -CH_2Nap), 4.69 (d, *J* = 12.3 Hz, 1H, -CH_2Nap), 4.26 (appq, *J* = 4.0 Hz, 1H, H-4), 4.17 – 4.10 (m, 3H, -CH_2CH=CH_2), 4.06 (dd, *J* = 13.2, 5.9 Hz, 1H, -CH_2CH=CH_2), 3.89 (dd, *J* = 6.7, 2.9 Hz, 1H, H-3), 3.84 (dd, *J* = 6.8, 4.3 Hz, 1H, H-2), 3.60 (d, *J* = 4.0 Hz, 2H, H-5a + H-5b), 3.46 (s, 3H, -OCH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.5, 135.0, 134.7, 133.3, 133.1, 128.3, 127.9, 127.8, 126.6, 126.3, 126.0, 125.7, 117.9, 117.6, 102.5, 82.2, 78.2, 75.5, 73.7, 72.0, 71.9, 70.3, 55.5.

HRMS (ESI) m/*z* calcd for $C_{23}H_{28}O_5Na$ ([M+Na]$^+$) 407.1834, found 407.1830

IR (neat) ν 2912, 1642, 1594, 1509, 1346, 1275, 1108, 1040, 910, 856, 818, 753 cm^{-1}**.**

[α]$_D^{22}$ + 60.1 (*c* = 5.8, $CHCl_3$)

β-anomer (R_f 0.58, 30:70 ethyl acetate:hexanes)

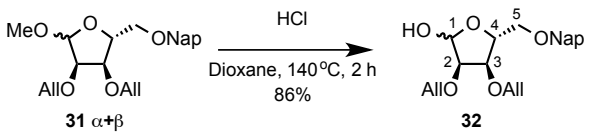
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.75 (m, 4H, Nap), 7.52 – 7.41 (m, 3H, Nap), 5.99 – 5.83 (m, 2H, -CH_2CH=CH_2), 5.31 (dd, *J* = 17.2, 1.6 Hz, 1H, -CH_2CH=CH_2), 5.25 (dd, *J* = 17.2, 1.6 Hz, 1H, -CH_2CH=CH_2), 5.20 (dd, *J* = 10.4, 1.5 Hz, 1H, -CH_2CH=CH_2), 5.16 (dd, *J* = 10.4, 1.5 Hz, 1H, -CH_2CH=CH_2), 4.92 (s, 1H, H-1), 4.78 (d, *J* = 12.6 Hz, 1H, -CH_2Nap), 4.74 (d, *J* = 12.2 Hz, 1H, -CH_2Nap), 4.32 (ddd, 7.07, 5.85, 3.59 Hz, 1H, H-4), 4.19 – 4.04 (m, 3H, -CH_2CH=CH_2), 4.03 – 3.97 (m, 2H, -CH_2CH=CH_2 + H-3), 3.83 (d, *J* = 4.6 Hz, 1H, H-2), 3.69 (dd, *J* = 10.6, 3.6 Hz, 1H, H-5a), 3.59 (dd, *J* = 10.6, 5.9 Hz, 1H, H-5b), 3.35 (s, 3H, -OCH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 135.9, 134.5, 134.4, 133.3, 133.0, 128.1, 127.9, 127.8, 126.3, 126.1, 125.9, 125.7, 117.7, 117.6, 106.5, 80.5, 79.7, 78.4, 73.3, 71.6, 71.5, 71.5, 55.2.

HRMS (ESI) m/*z* calcd for $C_{23}H_{28}O_5Na$ ([M+Na]$^+$) 407.1834, found 407.1839.

IR (neat) ν 3059, 2916, 2850, 1639, 1507, 1458, 1354, 1254, 1106, 1066, 1039, 983, 935, 818, 754 cm^{-1}.

[α]$_D^{21}$ + 7.3 (*c* = 4.97, $CHCl_3$)



31 α+β **32**

Compound 32: To a 1 L round bottom flask was added compound **31** (11.95 g, 31.1 mmol, 1 eq) and 1,4-dioxane (150 mL). The flask was fitted with an air condenser and a rubber septum without positive pressure of nitrogen and heated in an oil bath. While the solution was warming, 1 M HCl (150 mL) was added in portions over 5 min. The solution was heated at 140 °C for 2 h.

The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc three times. The organic layer was dried over $NaSO_4$, concentrated, and purified by silica gel chromatography (R_f=0.6 in 50:50 hexanes:ethyl acetate) to provide compound **32** as a yellow oil (9.91 g, 86%, 1.6:1 anomeric mixture).

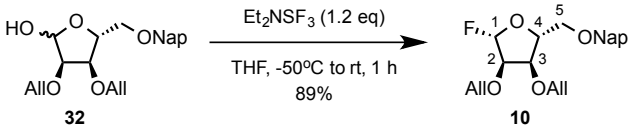
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 –7.71 (m, 4H major, 4H minor, Nap), 7.51 – 7.39 (m, 3H major, 3H minor, Nap), 5.99 – 5.80 (m, 2H major, 2H minor, -CH_2CH=CH_2), 5.34 – 5.12 (m, 5H major, 5H minor, H-1 + -CH_2CH=CH_2), 4.83 – 4.62 (m, 2H major, 2H minor, -CH_2Nap), 4.33 (ddd, *J* = 4.0, 3.9, 2.4 Hz, 1H major, H-4), 4.26 (ddd, *J* = 6.6, 3.2, 3.2 Hz, 1H minor, H-4), 4.21 – 3.90 (m, 6H major, 5H minor, H-3 (major + minor), H-2 (major), -CH_2CH=CH_2), 3.83 (d, *J* = 4.7 Hz, 1H minor, H-2), 3.72 (dd, *J* = 10.4, 2.9 Hz, 1H minor, H-5a), 3.61 (dd, *J* = 10.4, 3.5 Hz, 1H minor, H-5b), 3.57 (dd, *J* = 10.5, 3.7 Hz, 1H major, H-5a), 3.53 (dd, *J* = 10.5, 4.4 Hz, 1H major, H-5b).

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4 (major), 135.0 (minor), 134.4 (minor), 134.4 (minor), 134.2 (major), 134.1 (major), 133.3 (minor), 133.3 (major), 133.1 (minor), 133.1 (major), 128.4 (minor), 128.3 (major), 127.9 (minor), 127.9 (major), 127.8 (major), 127.8 (minor), 126.8 (minor), 126.5 (major), 126.3 (major), 126.3 (minor), 126.1 (minor), 126.0 (major), 125.8 (minor), 125.6 (major), 117.8 (major), 117.7 (minor), 117.7 (minor), 117.6 (major), 100.5 (minor, C-1), 96.2 (major, C-1), 80.9 (minor, C-4), 80.7 (major, C-4), 77.9 (minor, C-2), 77.7 (major), 77.5 (minor), 77.4 (minor, C-3), 73.7 (major), 73.6 (minor), 71.9 (major), 71.7 (major), 71.6 (minor), 71.5 (minor), 70.1 (major), 70.0 (minor).

HRMS (ESI) m/*z* calcd for $C_{22}H_{26}O_5Na$ ($[M+Na]^+$) 393.1678, found 393.1674

IR (neat) ν 3421, 3045, 2912, 2863, 1646, 1509, 1455, 1427, 1344, 1271, 1089, 1032, 924, 856, 817, 753 cm^{-1}.

$[\alpha]_D^{21}$ +37.5 (*c* = 8.5, $CHCl_3$)



Compound 10: To a 25 mL round-bottomed flask was added compound **32** (5.0 g, 13.5 mmol, 1 eq) and THF (65 mL). The solution was cooled to -50 °C and diethylaminosulfur trifluoride (2.1 mL, 16.2 mmol, 1.2 eq) was added slowly over 2 min. The solution was immediately warmed to room temperature and stirred for 1 h. The solution was cooled to -50 °C and quenched with saturated aqueous $NaHCO_3$ (20 mL). The solution was warmed to room temperature, the organic layer was extracted with EtOAc three times, dried over Na_2SO_4, concentrated, and purified by silica gel chromatography to give compound **10** as a pale yellow oil (4.48 g, 89%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.77 (m, 4H, Nap), 7.51 – 7.44 (m, 3H, Nap), 5.99 – 5.81 (m, 2H, -CH_2CH=CH_2), 5.73 (d, *J* = 63.4 Hz, 1H, H-1), 5.37 – 5.15 (m, 4H, -CH_2CH=CH_2), 4.81 (d, *J* = 12.3 Hz, 1H, CH_2Nap), 4.75 (d, *J* = 12.3 Hz, 1H, CH_2Nap), 4.39 (dddd, *J* = 8.2, 8.2, 5.3, 3.2 Hz, 1H, H-4), 4.18 (appdt, *J* = 5.7, 1.4 Hz, 1H, H-3), 4.14 – 3.97 (m, 5H, -CH_2CH=CH_2, + H-2), 3.77 (dd, *J* = 11.1, 3.2 Hz, 1H, H-5a), 3.67 (dd, *J* = 11.0, 5.4 Hz, 1H, H-5b).

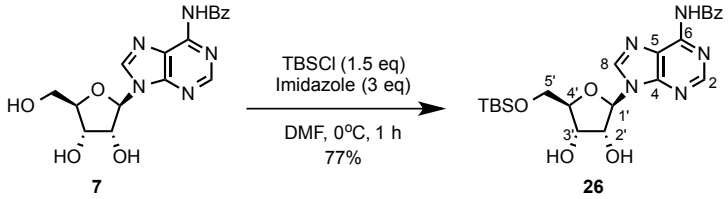
^{13}C NMR (125 MHz, $CDCl_3$) δ 135.7, 134.2, 134.1, 133.4, 133.1, 128.3, 128.0, 127.8, 126.5, 126.2, 126.0, 125.8, 118.3, 118.0, 112.8 (d, *J* = 224.4 Hz), 82.5 (d, *J* = 2.6 Hz), 79.1 (d, *J* = 29.9 Hz), 77.1, 73.6, 72.1, 72.0, 70.4.

^{19}F NMR (470 MHz, $CDCl_3$) δ -118.4 (d, *J* = 63.6 Hz).

HRMS (ESI) m/*z* calcd for $C_{22}H_{25}O_4NaF$ ($[M+Na]^+$) 395.1635, found 395.1638

IR (neat) ν 3052, 2919, 2862, 1646, 1601, 1510, 1469, 1420, 1347, 1271, 1101, 994, 948, 855, 818, 747 cm^{-1}.

$[a]_D^{21}$ +46.6 (c = 4.8, $CHCl_3$)



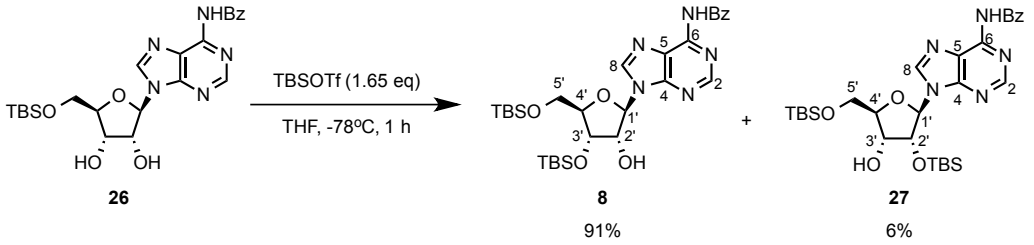
7 26

Compound 26: To a 0 °C solution of *N*-Benzoyladenosine (**7**) (10.0 g, 26.9 mmol, 1 eq) in DMF (150 mL) was added imidazole (5.5 g, 80.8 mmol, 3 eq). Next, TBSCl (6.09 g, 40.4 mmol, 1.5 eq) was added in DMF (20 mL) and the reaction was stirred at 0°C for 1 h. The reaction was poured into saturated aqueous NH_4Cl, extracted three times with EtOAc, washed twice with saturated aqueous NH_4Cl, dried through Na_2SO_4, and concentrated. Water was added to precipitate the product and the solid was washed twice with water. The solid was collected; EtOH was added and evaporated to remove residual water. The product was purified by silica column chromatography (R_f=0.31 in 25:75 Hexanes:EtOAc) to isolate compound **26** as a white foam (10.1 g, 77%). Compounds **8** (822 mg, 5%) and **27** (872 mg, 5%) were also isolated as minor products. Detailed characterization data for **8** and **27** is provided below.

^{1}H NMR (500 MHz, CD_3OD) δ 8.72 (s, 1H, H-8), 8.67 (s, 1H, H-2), 8.09 (d, *J* = 7.4 Hz, 2H, Bz), 7.66 (t, *J* = 7.4 Hz, 1H, Bz), 7.57 (t, *J* = 7.7 Hz, 2H, Bz), 6.19 (d, J = 4.3 Hz, 1H, H-1'), 4.66 (dd, *J* = 4.9, 4.2 Hz, 1H, H-2'), 4.41 (dd, *J* = 5.2, 4.9 Hz, 1H, H-3'), 4.16 (ddd, *J* = 5.2, 3.1, 3.1 Hz, 1H, H-4'), 4.04 (dd, *J* = 11.6, 3.1 Hz, 1H, H-5'a), 3.91 (dd, *J* = 11.6, 3.1 Hz, 1H, H-5'b), 0.94 (s, 9H, -tBu), 0.13 (s, 6H, $-CH_3$).

^{13}C NMR (125 MHz, CD_3OD) δ 167.9, 153.2, 153.0, 151.0, 143.8, 134.9, 133.8, 129.7, 129.4, 124.9, 90.3, 86.4, 76.3, 71.2, 63.8, 26.5, 19.3, -5.3, -5.3.

HRMS (ESI) m/*z* calcd for $C_{23}H_{32}N_5O_5Si$ ($[M+H]^+$) 486.2173, found 486.2173.



Compound 8: To a 250 mL round bottomed flask containing compound **26** (1.70 g, 3.5 mmol, 1 eq) was added THF (35 mL), and the solution was cooled to -78°C. Next, TBSOTf (0.88 mL, 3.85 mmol, 1.1 eq) was added and the solution was stirred at -78°C for 30 min. After 30 min, additional TBSOTf (0.44 mL, 1.92 mmol, 0.55 eq) was added and stirred for 30 min at -78°C. The reaction was quenched at -78°C with saturated aqueous $NaHCO_3$ and slowly warmed to room temperature. The aqueous layer was extracted once with ethyl acetate, once with methylene chloride and once with chloroform. The combined organic layers were dried though Na_2SO_4, concentrated and purified by silica column chromatography to give known[8] compounds **8** (1.92 g, 91%) **27** as a minor byproduct (0.12 g, 6%) as white foams.

Compound 27 (R_f 0.30 in 50:50 hexanes:ethyl acetate)

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.10 (s, 1H, NHBz), 8.80 (s, 1H, H-8), 8.41 (s, 1H, H-2), 8.01 (d, *J* = 7.7 Hz, 2H, Bz), 7.62 – 7.55 (m, 1H, Bz), 7.51 (t, *J* = 7.9 Hz, 2H, Bz), 6.18 (d, *J* = 5.0 Hz, 1H, H-1'), 4.64 (appt, *J* = 5.0 Hz, 1H, H-2'), 4.28 (appq, *J* = 4.1 Hz, 1H, H-3'), 4.22 (appq, *J* = 2.5 Hz, 1H, H-4'), 4.01 (dd, *J* = 11.5, 2.5 Hz, 1H, H-5'a), 3.86 (dd, *J* = 11.5, 2.4 Hz, 1H, H-5'b), 2.79 (d, *J* = 4.2 Hz, 1H, -OH), 0.94 (s, 9H, -tBu), 0.83 (s, 9H, -tBu), 0.14 (s, 3H, $-CH_3$), 0.13 (s, 3H, $-CH_3$), -0.06 (s, 3H, $-CH_3$), -0.15 (s, 3H, $-CH_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 153.0, 151.8, 149.6, 141.4, 133.9, 132.8, 129.0, 127.9, 123.1, 88.3, 85.5, 77.2, 71.4, 63.2, 26.2, 25.7, 18.6, 18.0, -4.9, -5.1, -5.2, -5.3.

HRMS (ESI) m/*z* calcd for $C_{29}H_{46}N_5O_5Si_2$ ($[M+H]^+$) 600.3038, found 600.3039

IR (neat) ν 3365, 2947, 2926, 2850, 1701, 1611, 1580, 1455, 1247, 1136, 1063, 837, 782, 706 cm^{-1}.

$[\alpha]_D^{23}$ -35.0 (*c* = 0.88, $CHCl_3$)

Compound 8 (R_f 0.16 in 50:50 hexanes:ethyl acetate)

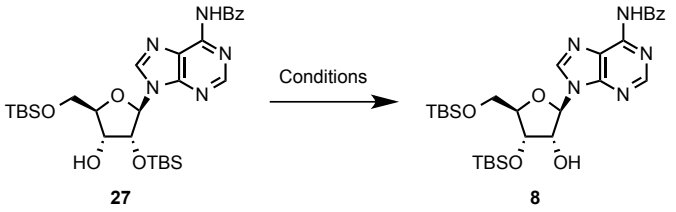
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.08 (s, 1H, NHBz), 8.78 (s, 1H, H-8), 8.27 (s, 1H, H-2), 8.01 (d, *J* = 7.3 Hz, 2H, Bz), 7.59 (t, *J* = 7.4 Hz, 1H, Bz), 7.50 (t, *J* = 7.7 Hz, 2H, Bz), 6.09 (d, *J* = 4.7 Hz, 1H, H-1'), 4.63 – 4.54 (m, 2H, H-2'+H-3'), 4.13 (appq, *J* = 3.3 Hz, 1H, H-4'), 3.93 (dd, *J* = 11.4, 3.5 Hz, 1H, H-5'a), 3.78 (dd, *J* = 11.4, 2.9 Hz, 1H, H-5'b), 3.21 (d, *J* = 6.6 Hz, 1H, -OH), 0.95 (s, 9H, -tBu), 0.89 (s, 9H, -tBu), 0.17 (s, 6H, $-CH_3$), 0.08 (s, 3H, $-CH_3$), 0.05 (s, 3H, $-CH_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 152.8, 151.8, 149.6, 141.7, 133.9, 132.9, 129.0, 128.0, 123.5, 89.1, 85.7, 75.3, 71.8, 62.5, 26.1, 25.9, 18.5, 18.2, -4.5, -4.7, -5.3, -5.4.

HRMS (ESI) m/*z* calcd for $C_{29}H_{46}N_5O_5Si_2$ ($[M+H]^+$) 600.3038, found 600.3032

IR (neat) ν 3310, 2928, 2864, 1704, 1613, 1580, 1461, 1253, 1073, 836, 775, 702 cm^{-1}.

$[\alpha]_D^{23}$ -20.5 (*c* = 1.13, $CHCl_3$)



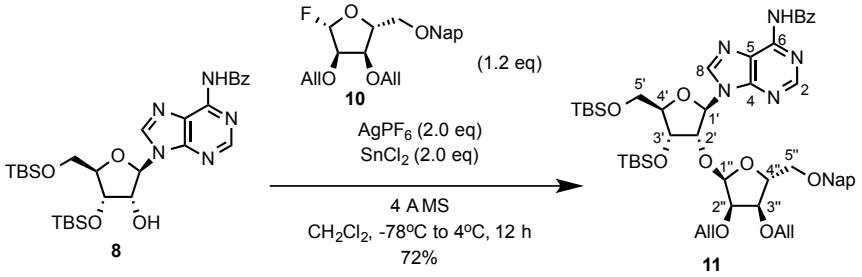
27 **8**

Isomerization of compound **27** to **8**

To a 7 mL reaction vial was added compound **27** (100 mg, 0.17 mmol, 1 eq) and MeOH or EtOH (1 mL). The solution was stirred at 30 °C for 48 h, concentrated and purified by silica column chromatography to yield compound **8** (45 mg, 45% for MeOH treatment or 40 mg, 40% for EtOH treatment).

Alternatively, compound **27** (100 mg, 0.17 mmol, 1 eq) was added to a 7 mL scintillation vial, followed by imidazole (22.8 mg, 0.33 mmol, 2 eq) and DMF (2 mL). The reaction was stirred at 30 °C for 48 h, at which point a saturated aqueous NH_4Cl solution was added. The reaction was extracted three times with EtOAc, dried through Na_2SO_4, concentrated, and purified by silica column chromatography to yield compound **8** (50.4 mg, 50%).

Compound **27** could be recovered in nearly equal quantities as the desired compound (**8**) in all of the above treatments.



8 **10** **11**

Compound 11: To a 250 mL schlenk flask was added $SnCl_2$ (3.39 g, 17.9 mmol, 2.0 eq) and freshly dried powdered 4 Å molecular sieves (6.0 g). Dried $AgPF_6$ (4.53 g, 17.90 mmol, 2.0 eq), contained in a 7 mL vial, was added to the flask keeping the $AgPF_6$ and $SnCl_2$ segregated. The flask was dried overnight under high vacuum. To the flask was added CH_2Cl_2 (60 mL) and the reaction was cooled to -78 °C. Lastly, compound **10** (4.0 g, 10.7 mmol, 1.2 eq) and compound **8** (5.37 g, 8.95 mmol, 1 eq) were added in CH_2Cl_2 (40 mL). Compounds **10** and **8** had been previously dried by azeotropic removal of water with dry CH_3CN three times on a rotary evaporator filled with dry nitrogen and dried over P_2O_5 under high vacuum for 5 h. The solution was stirred for 30 min at -78 °C and then stirred at 4 °C for 15 h. The solution was quenched with a 0°C saturated aqueous $NaHCO_3$ solution stirred for 3 h, after which point the biphasic mixture was filtered through celite washing with CH_2Cl_2. The organic layer was dried over Na_2SO_4, concentrated, and purified by silica gel chromatography (R_f 0.5 in 50:50 hexanes:ethyl acetate) to give compound **11** as a pale yellow foam (6.04 g, 72%).

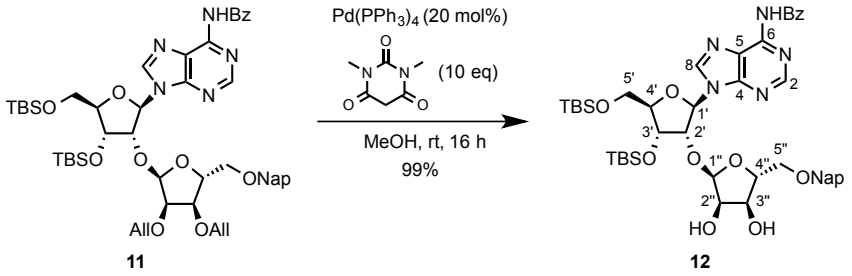
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (s, 1H, N*H*Bz), 8.81 (s, 1H, H-8), 8.39 (s, 1H, H-2), 8.00 (d, *J* = 7.0 Hz, 2H, Bz), 7.86 – 7.75 (m, 3H, Nap), 7.71 (s, 1H, Nap), 7.61 (t, *J* = 7.5 Hz, 1H, Bz), 7.52 (t, *J* = 7.5 Hz, 2H, Bz), 7.48 – 7.42 (m, 2H, Nap), 7.39 (dd, *J* = 8.5, 1.7 Hz, 1H, Nap), 6.33 (d, *J* = 5.0 Hz, 1H, H-1'), 5.89-5.78 (m, 2H, -CH_2CH=CH_2), 5.23 – 5.10 (m, 5H, -CH_2CH=CH_2 + H-1''), 4.84 (appt, *J* = 4.8 Hz, 1H, H-2'), 4.69 (d, *J* = 12.3 Hz, 1H, -CH_2Nap), 4.61 (d, *J* = 12.3 Hz, 1H, -CH_2Nap), 4.53 (appt, *J* = 4.4 Hz, 1H, H-3'), 4.23-4.17 (m, 2H, H-4' + H-4''), 4.13 – 4.02 (m, 2H, - CH_2CH=CH_2), 4.02 – 3.91 (m, 3H, -CH_2CH=CH_2 + H-5'a), 3.85 (dd, *J* = 6.4, 4.4 Hz, 1H, H-3''), 3.81 – 3.72 (m, 2H, H-2''+ H-5'b), 3.52 (d, *J* = 3.7 Hz, 2H, H-5''a + H-5''b) 0.93 (s, 9H, -tBu), 0.91 (s, 9H, -tBu), 0.16 (s, 3H, -CH_3), 0.14 (s, 3H, -CH_3), 0.10 (s, 3H, -CH_3), 0.10 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) d 164.7, 152.8, 151.6, 149.5, 142.3, 135.6, 134.9, 134.6, 133.9, 133.3, 133.1, 132.8, 129.0, 128.3, 127.9, 127.9, 127.8, 126.5, 126.3, 126.0, 125.7, 123.3, 117.6, 117.5, 101.5, 87.0, 85.6, 81.9, 79.6, 77.8, 75.6, 73.7, 72.0, 71.6, 71.2, 69.9, 62.3, 26.2, 26.0, 18.6, 18.3, -4.4, -5.0, -5.3, -5.3.

HRMS (ESI) m/*z* calcd for $C_{51}H_{70}N_5O_9Si_2$ ($[M+H]^+$) 952.4712, found 952.4711.

IR (neat) ν 2933, 2857, 1698, 1611, 1580, 1455, 1250, 1084, 1039, 834, 782 cm^{-1}.

$[\alpha]_D^{21}$ +2.7 (c = 2.41, $CHCl_3$)



11 **12**

Compound 12: To a 125 mL round bottomed flask containing compound **11** (1.0 g, 1.05 mmol, 1 eq) was added $Pd(PPh_3)_4$ (240 mg, 0.21 mmol, 0.2 eq) and 1,3-Dimethylbarbituric acid (1.62 g, 10.3 mmol, 10 eq). Methanol (30 mL) was added and the reaction was stirred at room temperature for 16 h. The reaction was quenched at 0°C with an aqueous Na_2CO_3 solution and stirred for 2 h at room temperature. The reaction mixture was extracted three times with ethyl acetate and three times with chloroform, filtered through Na_2SO_4, and concentrated. The product was purified by silica gel chromatography (R_f 0.53 in 40:60 hexanes:ethyl acetate) to yield compound **12** as a bright yellow foam (917 mg, 99%).

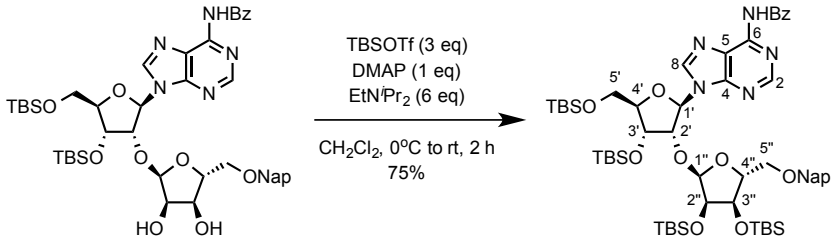
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.92 (s, 1H, N*H*Bz), 8.62 (s, 1H, H-8), 8.40 (s, 1H, H-2), 8.02 (dd, J=7.0 Hz, 1.5 Hz, 2 H, -Bz), 7.83-7.80 (m, 3H, -Nap), 7.69-7.44 (m, 7H, -Nap+Bz), 6.25 (d, *J* = 2.7 Hz, 1H, H-1'), 5.37 (d, *J* = 4.2 Hz, 1H, H-1''), 4.73-4.63 (m, 4H, CH_2Nap + H-2' + H-3;), 4.26-4.25 (m, 1H, H-4''), 4.21 (ddd, *J* = 9.8, 5.7, 4.1 Hz, 1H, H-2''), 4.13 (dd, *J* = 6.0, 2.8 Hz, 1H, H-4'), 4.09-3.98 (m, 2H, H-5'a, H-3''), 3.81 (dd, *J* = 11.7, 2.4 Hz, 1H, H-5'b), 3.62 (dd, *J* = 10.6, 3.8 Hz, 1H, H-5''a), 3.58 (dd, J = 10.6, 3.6 Hz, 1H, H-5''b), 3.06 (d, *J* = 9.8 Hz, 1H, -OH), 2.94 (d, *J* = 10.7 Hz, 1H, -OH), 0.94 (s, 9H, -tBu), 0.92 (s, 9H, -tBu), 0.151 (s, 6H, -CH_3), 0.11 (s, 3H, -CH_3), 0.10 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 152.9, 151.2, 149.6, 141.4, 135.3, 133.8, 133.3, 133.1, 132.9, 129.0, 128.4, 128.0, 127.9, 127.8, 126.6, 126.3, 126.1, 125.7, 123.4, 101.5, 87.3, 85.1, 84.6, 79.5, 73.8, 72.0, 72.0, 67.0, 69.8, 61.3, 26.2, 26.0, 18.6, 18.3, -4.1, -4.7, -5.2, -5.3.

HRMS m/z calcd for $C_{45}H_{62}N_5O_9Si_2$ ($[M+H]^+$) 872.4086, found 872.4077

IR (neat) ν 3344, 2926, 2850, 1698, 1608, 1576, 1458, 1438, 1254, 1119, 830 cm^{-1}.

$[\alpha_D]^{21}$ +15.3 (c = 15.3, $CHCl_3$)



12 **13**

Compound 13: A 7 mL reaction vial containing compound **12** (910 mg, 1.043 mmol, 1 eq) and 4-dimethylaminopyridine (127 mg, 1.043 mmol, 1 eq) was evacuated and backfilled three times with dry nitrogen. Methylene chloride (10 mL) was added and the vial was cooled to 0 °C. Next, EtN^{i}Pr$_2$ (1.09 mL, 6.26 mmol, 6 eq) and TBSOTf (0.72 mL, 3.13 mmol, 3 eq) were added and the reaction was allowed to warm to room temperature. A saturated aqueous NH_4Cl solution was added after 2 h, and the reaction was stirred vigorously for 1 h. The product was purified by silica gel chromatography (R_f 0.68 in 60:40 hexanes:ethyl acetate) to yield compound **13** (862 mg, 75%) as a white foam.

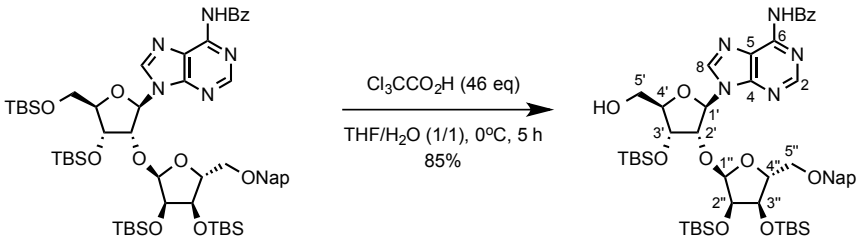
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.93 (s, 1H, N*H*Bz), 8.78 (s, 1H, H-8), 8.39 (s, 1H, H-2), 8.01 (d, J=7.1 Hz, 2H, -Bz), 7.85 – 7.76 (m, 3H, -Nap), 7.74 (s, 1H, -Nap), 7.61 (t, J=7.6 Hz, 1H, -Bz), 7.53 (t, *J* = 7.6 Hz, 2H, -Bz), 7.49 – 7.45 (m, 2H, Nap), 7.42 (dd, *J* = 8.4, 1.7 Hz, 1H, -Nap), 6.23 (d, *J* = 3.2 Hz, 1H, H-1'), 5.28 (d, *J* = 3.7 Hz, 1H, H-1''), 4.76 – 4.62 (m, 3H, -C*H*$_2$Nap + H-2'), 4.55 (dd, *J* = 6.1, 4.5 Hz, 1H, H-3'), 4.24-4.18 (m, 2H, H-4' + H-4''), 4.05-3.99 (m, 3H, H-2'' + H-3'' + H-5'a), 3.78 (dd, *J* = 11.5, 2.5 Hz, 1H, H-5'b), 3.62 (dd, *J* = 10.7, 3.0 Hz, 1H, H-5''a), 3.57 (dd, *J* = 10.8, 3.8 Hz, 1H, H-5''b), 0.91 (s, 18H, -tBu), 0.86 (s, 9H, -tBu), 0.85 (s, 9H, -tBu), 0.13 (s, 3H, -CH_3), 0.10 (s, 6H, -CH_3), 0.09 (s, 3H, -CH_3), 0.03 (s, 6H, -CH_3), 0.00 (s, 3H, -CH_3), -0.01 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 152.8, 151.3, 149.4, 142.1, 135.8, 134.0, 133.4, 133.1, 132.8, 129.0, 128.2, 127.9, 127.9, 127.8, 126.4, 126.2, 126.0, 125.7, 123.4, 103.2, 87.9, 84.6, 83.6, 81.0, 73.7, 73.6, 71.5, 70.0, 69.7, 61.7, 26.2, 26.2, 26.1, 26.0, 18.6, 18.5, 18.3, 18.3, -4.2, -4.3, -4.4, -4.5, -4.6, -4.8, -5.2, -5.2.

HRMS m/z calcd for $C_{57}H_{90}N_5O_9Si_4$ ($[M+H]^+$) 1100.5816, found 1100.5829

IR (neat) ν 2928, 2857, 1701, 1610, 1576, 1455, 1252, 1070, 836, 778 cm^{-1}

$[\alpha_D]^{23}$ + 10.1 (c = 1.04, $CHCl_3$)



13 **14**

Compound 14: To a 100 mL round bottomed flask was added compound **13 (**530 mg, 0.48 mmol, 1 eq) and THF (12 mL). The solution was cooled to 0 ^{o}C. A cold solution of trichloroacetic acid (3.5 g, 21.7 mmol, 45 eq) in water (12 mL) was added dropwise at 0 ^{o}C over 30 min. The reaction was stirred at 0 ^{o}C for 5 h, at which point it was quenched by pouring into a 0 ^{o}C solution of saturated aqueous $NaHCO_3$. The quenched reaction was extracted three times with EtOAc, dried through Na_2SO_4 and concentrated. Silica gel chromatography (R_f=0.46 in 60:40 hexanes:ethyl acetate) yielded compound **14** as a white foam (403 mg, 85%).

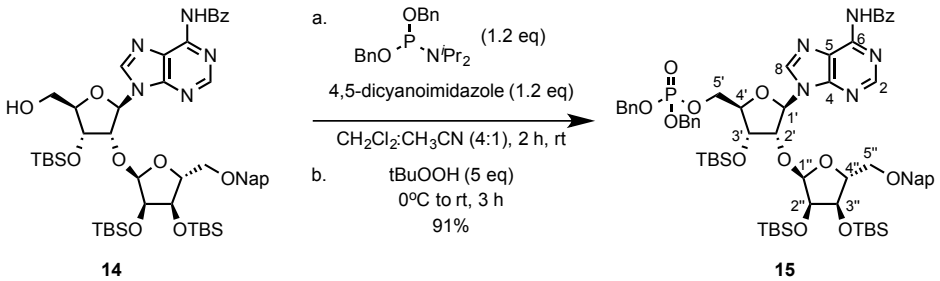
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.19 (s, 1H, -N*H*Bz), 8.78 (s, 1H, H-8), 8.07 (s, 1H, H-2), 8.00 (d, J=7.6 Hz, 2H, -Bz), 7.84 – 7.78 (m, 3H, -Nap), 7.75 (s, 1H, -Nap), 7.59 (t, *J* = 7.6 Hz, 1H, -Bz), 7.51-7.41 (m, 5H, -Nap + -Bz), 6.07 (d, *J* = 7.5 Hz, 1H, H-1'), 5.84 (bd, J=10.6 Hz, 1H, -OH), 4.99 (dd, *J* = 7.5, 4.4 Hz, 1H, H-2'), 4.89 (d, *J* = 3.6 Hz, 1H, H-1''), 4.67 (d, *J* = 3.5 Hz, 2H, -CH_2Nap), 4.62 (dd, *J* = 4.5, 1.3 Hz, 1H, H-3'), 4.24 – 4.16 (m, 2H, H-4' + H-4''), 4.02 – 3.92 (m, 2H, H-5'a + H-3''), 3.85 (dd, *J* = 4.9, 3.6 Hz, 1H, H-2''), 3.76 (ddd, *J* = 12.9, 11.1, 1.9 Hz, 1H, H-5'b), 3.59 (dd, *J* = 10.8, 3.0 Hz, 1H, H-5''a), 3.53 (dd, *J* = 10.8, 3.6 Hz, 1H, H-5''b), 0.93 (s, 9H, -tBu), 0.86 (s, 9H, -tBu), 0.75 (s, 9H, -tBu), 0.14 (s, 3H, -CH_3), 0.10 (s, 3H, -CH_3), -0.01 (s, 3H, -CH_3), -0.02 (s, 3H, -CH_3), -0.09 (s, 3H, -CH_3), -0.12 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 152.2, 150.6, 150.3, 143.7, 135.7, 133.6, 133.3, 133.0, 132.9, 129.0, 128.2, 127.9, 127.9, 127.7, 126.4, 126.1, 125.9, 125.8, 124.5, 104.1, 89.3, 89.2, 83.0, 81.4, 73.6, 73.6, 73.0, 71.4, 69.4, 62.7, 26.1, 26.1, 26.1, 18.5, 18.2, 18.2, -4.2, -4.3, -4.4, -4.5, -4.6, -4.7.

HRMS (ESI) m/z calcd for $C_{51}H_{76}N_5O_9Si_3$ ($[M+H]^+$) 986.4951, found 986.4959

IR (neat) ν 3254, 2919, 2857, 1705, 1611, 1580, 1458, 1251, 1153, 1108, 834, 775 cm^{-1}

$[\alpha_D]^{23}$ +3.0 (*c* = 1.08, $CHCl_3$)



14 **15**

Compound 15: To a dry 20 mL reaction vial was added compound **14** (520 mg, 0.47 mmol, 1 eq) and dibenzyl N,N-diisopropylphosphoramidite (195 mg, 0.56 mmol, 1.2 eq). The compounds were co-evaporated three times on a N_2-filled rotary evaporator with dry CH_3CN

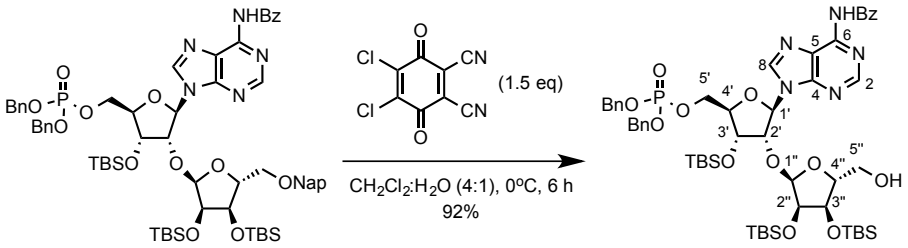
and then dried over P_2O_5 overnight. Separately, 4,5-dicyanoimidazole (66.6 mg, 0.56 mmol, 1.2 eq) was evaporated and dried in a similar manner. To compound **14** and the phosphoramidite was added dry CH_2Cl_2 (4.7 mL), followed by a solution of the 4,5-dicyanoimidazole in CH_3CN (1.5 mL) at room temperature. After 2 h, the reaction was cooled to 0 °C and a solution of t-butyl peroxide (0.39 mL of a 5.5 M solution in decane, 2.35 mmol, 5 eq) was added. The reaction was warmed to room temperature and stirred for 3 h. Next, the reaction was poured into a saturated aqueous $NaHCO_3$ solution, extracted three times with ethyl acetate, dried through Na_2SO_4, and concentrated. The product was purified by silica gel chromatography (R_f 0.29 in 50:50 hexanes:ethyl acetate) to give compound **15** as a colorless oil (533 mg, 91%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.07 (s, 1H, -N*H*Bz), 8.74 (s, 1H, H-8), 8.27 (s, 1H, H-2), 8.01 (d, *J* = 7.0 Hz, 2H, -Bz), 7.86 – 7.77 (m, 3H, -Nap), 7.75 (s, 1H, -Nap), 7.60 (t, *J* = 7.4 Hz, 1H, -Bz), 7.55 – 7.39 (m, 5H, -Nap + -Bz), 7.33 – 7.27 (m, 10H), 6.18 (d, *J* = 3.1 Hz, 1H, H-1'), 5.26 (d, *J* = 3.8 Hz, 1H, H-1''), 5.00 (appt, *J* = 8.1 Hz, 4H, -C*H*$_2$Bn), 4.83 (dd, J = 4.4, 3.5 Hz, 1H, H-2'), 4.72 (d, *J* = 12.0 Hz, 1H, -C*H*$_2$Nap), 4.66 (d, *J* = 12.2 Hz, 1H, -C*H*$_2$Nap), 4.55 (dd, *J* = 6.2, 4.5 Hz, 1H, H-3'), 4.40 (ddd, *J* = 11.2, 5.6, 3.6 Hz, 1H, H-5'a), 4.35 – 4.28 (m, 1H, H-4'), 4.25 (appq, *J* = 3.6 Hz, 1H, H-4''), 4.19 (ddd, *J* = 11.2, 5.2, 3.7 Hz, 1H, H-5'b), 4.03 (dd, J = 5.3, 4.3 Hz, 1H, H-3''), 4.00 (dd, *J* = 5.3, 3.9 Hz, 1H, H-2''), 3.63 (dd, *J* = 10.8, 3.1 Hz, 1H, H-5''a), 3.58 (dd, *J* = 10.8, 3.7 Hz, 1H, H-5''b), 0.91 (s, 9H, -tBu), 0.88 (s, 9H, -tBu), 0.83 (s, 9H, -tBu), 0.13 (s, 3H, -CH_3), 0.09 (s, 3H, -CH_3), 0.04 (s, 3H, -CH_3), -0.00 (s, 6H, -CH_3), -0.02 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 152.7, 151.2, 149.6, 142.2, 135.7, 135.6, 133.8, 133.3, 133.1, 132.8, 128.9, 128.6, 128.6, 128.2, 128.0, 128.0, 128.0, 127.8, 127.8, 126.4, 126.2, 125.9, 125.7, 123.7, 103.5, 88.5, 83.9, 82.3 (d, *J* = 8.7 Hz), 80.3, 73.6, 71.5, 70.4, 69.7, 69.5 (appt, *J* = 4.9 Hz), 65.5 (d, *J* = 3.9 Hz), 26.1, 26.1, 25.9, 18.4, 18.2, 18.2, -4.3, -4.4, -4.5, -4.6, -4.6, -4.9.

^{31}P NMR (202 MHz, $CDCl_3$) δ 0.030

HRMS (ESI) m/z calcd for $C_{65}H_{89}N_5O_{12}Si_3P$ ($[M+H]^+$) 1246.5553, found 1246.5544



15 50

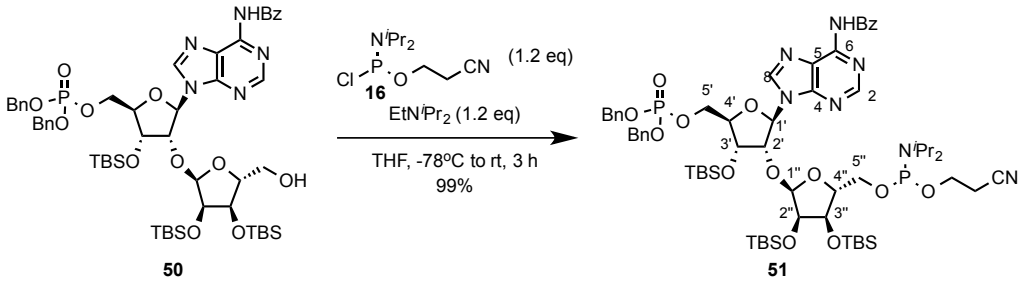
Compound 50: To a 20 mL reaction vial was added compound **15** (308 mg, 0.247 mmol, 1 eq), methylene chloride (5.3 mL) and deionized water (1.2 mL). The solution was cooled to 0 °C and 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (84.1 mg, 0.371 mmol, 1.5 eq) was added. The reaction was stirred at 0 °C for 2 h. After 2 h, the reaction was poured into a saturated aqueous $Na_2S_2O_3$ solution, extracted three times with ethyl acetate, dried through Na_2SO_4, and concentrated. The product was purified by silica column chromatography (R_f 0.69 in 30:70 hexanes:ethyl acetate) to yield compound **50** as a colorless oil (251 mg, 92%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.97 (s, 1H, -N*H*Bz), 8.77 (s, 1H, H-8), 8.25 (s, 1H, H-2), 8.01 (d, *J* = 7.4, 2H, -Bz), 7.62 (t, *J* = 7.4 Hz, 1H, -Bz), 7.54 (t, *J* = 7.7 Hz, 2H, -Bz), 7.31-7.29 (m, 10H, -Bn), 6.16 (d, *J* = 4.1 Hz, 1H, H-1'), 5.19 (d, *J* = 3.5 Hz, 1H, H-1''), 5.03 - 4.99 (m, 4H, -CH_2Bn), 4.90 (appt, *J* = 4.4 Hz, 1H, H-2'), 4.52 (appt, *J* = 4.8 Hz, 1H, H-3'), 4.39 (ddd, *J* = 10.7, 6.0, 4.2 Hz, 1H, H-5'a), 4.31 – 4.23 (m, 1H, H-4'), 4.21 – 4.08 (m, 2H, H-5'b + H-4''), 4.00 (appt, J = 6.0 Hz, 1H, H-3''), 3.92 (dd, *J* = 5.0, 3.5 Hz, 1H, H-2''), 3.78 (d, *J* = 12.1 Hz, 1H, H-5''a), 3.60-3.54 (m, 1H, H-5''b), 0.90 (s, 9H, -tBu), 0.90 (s, 9H, -tBu), 0.85 (s, 9H, -tBu), 0.11 (s, 3H, -CH_3), 0.08 (s, 3H, -CH_3), 0.07 (s, 3H, -CH_3), 0.06 (s, 3H, -CH_3), -0.00 (d, 3H, -CH_3), -0.02 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 152.8, 151.5, 149.6, 142.6, 135.7, 135.6, 133.2, 129.1, 128.9, 128.8, 128.2, 128.1, 123.7, 103.5, 88.1, 83.5, 82.9, 80.2, 77.5, 73.8, 70.8, 69.8, 65.9, 61.4, 26.2, 26.2, 26.0, 18.6, 18.3, 18.3, -4.0, -4.2, -4.3, -4.5, -4.5, -4.8.

^{31}P NMR (202 MHz, $CDCl_3$) δ 0.06

HRMS (ESI) m/*z* calcd for $C_{54}H_{81}N_5O_{12}Si_3P$ ($[M+H]^+$) 1106.4927, found 1106.4918.



Compound 51: To a -78°C solution of compound **50** (250 mg, 0.23 mmol, 1 eq) in THF (2 mL) was added diisopropylethylamine (0.047 mL, 0.27 mmol, 1.2 eq) followed by 2-Cyanoethyl N,N-diisopropylchlorophosphoramidite (**16**) (64 mg, 0.27 mmol, 1.2 eq). The -78°C bath was removed and the reaction was allowed to warm to room temperature and stirred for 3 h. The reaction mixture was filtered through celite, concentrated. The product was purified by silica column chromatography (0.67 in 50:50 hexanes:ethyl acetate with 1% triethylamine) to give compound **51** (310 mg, 99%) as a mixture of 2 diastereomers at the phosphoramidite.

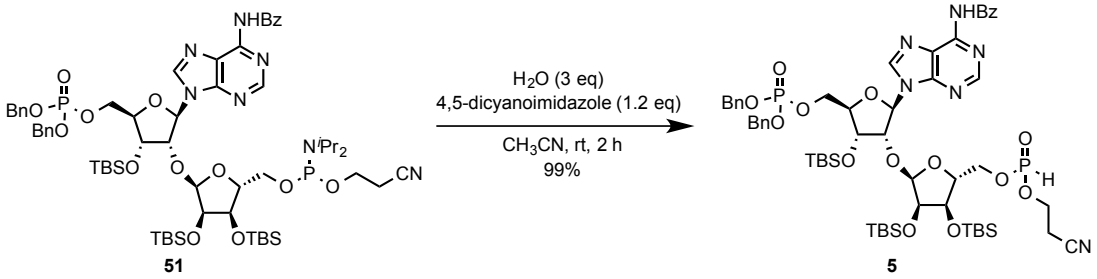
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.91 (s, 2H, -N*H*Bz), 8.75 (s, 1H, H-8), 8.75 (s, 1H, H-8), 8.27 (s, 1H, H-2), 8.24 (s, 1H, H-2), 8.03 – 7.98 (m, 4H, -Bz), 7.66 – 7.58 (m, 2H, -Bz), 7.57 – 7.50 (m, 4H, -Bz), 7.31-7.28 (m, 20H, -Bn), 6.16 (d, *J* = 3.0 Hz, 1H, H-1'), 6.15 (d, *J* = 3.1 Hz, 1H, H-1'), 5.22 (d, *J* = 3.9 Hz, 1H, H-1''), 5.21 (d, *J* = 3.8 Hz, 1H, H-1''), 5.02 – 4.94 (m, 8H, -CH_2Bn), 4.81 – 4.74 (m, 2H, H-2'), 4.55 – 4.48 (m, 2H, H-3'), 4.43 – 4.34 (m, 2H, H-5'a), 4.32 – 4.25 (m, 2H, H-4'), 4.22 – 4.14 (m, 4H, H-5'b + H-4''), 4.07 – 3.99 (m, 2H, H-3''), 3.99 – 3.91 (m, 2H, H-2''), 3.87 - 3.52 (m, 12H, H-5''a+b + -CH_2CH_2CN + -CH(CH_3)$_2$), 2.59 (appq, *J* = 6.1 Hz, 4H, -CH_2CH_2CN), 1.20 – 1.12 (m, 24H, -CH(CH_3)$_2$), 0.90 (s, 9H, -tBu), 0.90 (s, 9H, -tBu), 0.89 (s, 9H, -tBu), 0.89 (s, 9H, -tBu), 0.83 (s, 9H, -tBu), 0.83 (s, 9H, -tBu), 0.12 (s, 3H, -CH_3), 0.12 (s, 3H, -CH_3), 0.08 (s, 3H, -CH_3), 0.08 (s, 3H, -CH_3), 0.06 (s, 3H, -CH_3), 0.06 (s, 3H, -CH_3), 0.06 (s, 3H, -CH_3), 0.06 (s, 3H, -CH_3) 0.01 (s, 3H, -CH_3), 0.00 (s, 3H, -CH_3), -0.01 (s, 3H, -CH_3), -0.01 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5, 152.8, 151.3, 151.2, 149.6, 149.6, 142.4, 142.3, 135.8, 135.8, 133.9, 133.0, 133.0, 129.1, 128.8, 128.2, 128.2, 128.0, 123.8, 123.7, 117.8, 117.7, 103.6, 103.5, 88.7, 88.7, 84.6, 84.5, 84.2, 84.1, 80.5, 80.4, 73.8, 71.3, 71.1, 70.5, 70.4, 69.7,

69.6, 69.6, 69.6, 65.6, 65.6, 63.2, 63.2, 63.1, 63.0, 58.7, 58.6, 58.5, 58.4, 43.4, 43.3, 43.3, 43.2, 26.2, 26.2, 26.2, 26.0, 26.0, 25.0, 24.9, 24.9, 24.8, 24.8, 20.6, 20.6, 20.6, 20.6, 18.6, 18.5, 18.3, -4.1, -4.2, -4.2, -4.2, -4.3, -4.3, -4.4, -4.4, -4.5, -4.8, -4.8.

^{31}P NMR (202 MHz, $CDCl_3$) δ 149.67, 0.15, 0.12

Compound **51** hydrolyzed when subjected to ESI-MS.



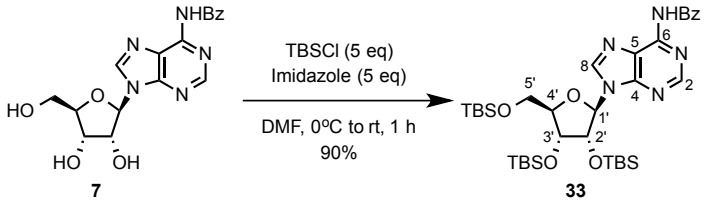
Compound 5: To a 7 mL reaction vial was added compound **51** (170 mg, 0.13 mmol, 1 eq) and CH_3CN (1 mL). Next, 4,5-dicyanoimidazole (18.4 mg, 0.16 mmol, 1.2 eq) and deionized water (7.0 mg, 0.39 mmol, 3 eq) were added and the reaction was stirred at room temperature for 2 h. The reaction mixture was poured into saturated aqueous $NaHCO_3$, extracted three times with EtOAc, dried through Na_2SO_4, and concentrated to give compound **5** (158 mg, 99%) as a brown oil and a mixture of diastereomers at the H-phosphonate. The compound was of sufficient purity to be used in the next step without further purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.91 (s, 1H, -N*H*Bz), 8.90 (s, 1H, N*H*Bz), 8.78 (s, 1H, H-8), 8.77 (s, 1H, H-8), 8.29 (s, 1H, H-2), 8.26 (s, 1H, H-2), 8.01 (d, *J* = 6.7 Hz, 4H, -Bz), 7.67-7.60 (m, 2H, -Bz) 7.57 – 7.50 (m, 4H, -Bz), 7.33-7.29 (m, 20H, -Bn), 6.93 (d, J = 729 Hz, 1H, -PH), 6.93 (d, J = 707 Hz, 1H, -PH), 6.16 (d, *J* = 3.8 Hz, 2H, H-1'), 5.28 (d, *J* = 3.2 Hz, 1H, H-1''), 5.25 (d, *J* = 3.3 Hz, 1H, H-1''), 5.04-4.97 (m, 8H, -Bn), 4.88 (appt, *J* = 4.2 Hz, 1H, H-2'), 4.84 (appt, *J* = 4.2 Hz, 1H, H-2'), 4.56 – 4.45 (m, 2H, H-3'), 4.42 - 3.93 (m, 20H), 2.77 – 2.67 (m, 4H), 0.90 (s, 9H), 0.90 (s, 9H), 0.90 (s, 9H), 0.90 (s, 9H), 0.86 (s, 9H), 0.86 (s, 9H), 0.12 (s, 3H), 0.11 (s, 3H), 0.08 (s, 3H), 0.08 (s, 3H), 0.08 (s, 3H), 0.08 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.02 (s, 3H), 0.02 (s, 3H), -0.01 (s, 3H), -0.01 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.6, 164.6, 152.7, 152.6, 151.3, 151.3, 149.7, 149.6, 142.2, 142.1, 135.7, 135.6, 133.8, 132.9, 129.0, 128.7, 128.7, 128.1, 128.1, 128.0, 127.9, 123.8, 103.4, 103.2, 88.0, 87.9, 82.8, 82.7, 80.5, 80.3, 73.3, 70.8, 70.6, 70.5, 69.6, 65.6, 64.9, 64.8, 60.1, 59.9, 47.0, 46.2, 22.7, 22.5, 20.1, 20.0, 19.2, 18.5, 18.5, 18.2, 18.2, 18.2, -4.0, -4.1, -4.3, -4.3, -4.4, -4.4, -4.5, -4.6, -4.6, -4.7, -4.9, -4.9.

^{31}P NMR (202 MHz, $CDCl_3$) δ 9.40, 9.28, -0.17, -0.18

HRMS (ESI) m/*z* calcd for $C_{57}H_{85}N_6O_{14}Si_3P_2$ ($[M+H]^+$) 1223.4907, found 1223.4899.



Compound 33: A modified version of the procedure of Aritomo *et al.*[9] was followed. To a 20 mL scintillation vial was added N-Benzoyladenosine (**7**) (500 mg, 1.35 mmol, 1 eq) and imidazole (458 mg, 6.73 mmol, 5 eq). Next, DMF (5 mL) was added followed by TBSCl (1.01 g, 6.73 mmol, 5 eq) and the reaction was stirred at room temperature for 14 h. The reaction was concentrated and purified by silica column chromatography (R_f 0.32 in 70:30 hexanes:ethyl acetate) to yield compound **33** as a yellow oil (866 mg, 90%).

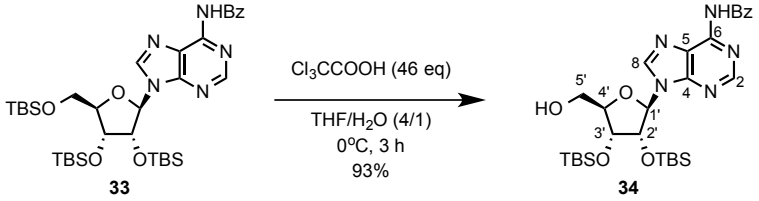
^{1}H NMR (500 MHz, $CDCl_3$) δ 9.50 (s, 1H, NHBz), 8.82 (s, 1H, H-8), 8.35 (s, 1H, H-2), 8.05 (d, J = 7.5 Hz, 2H, Bz), 7.59 (t, J = 7.4 Hz, 1H, Bz), 7.51 (dd, *J* =7.6 Hz, 2H, Bz), 6.12 (d, *J* = 5.3 Hz, 1H, H-1'), 4.68 (t, J = 4.8 Hz, 1H, H-2'), 4.30 (appt, J = 3.9 Hz, 1H, H-3'), 4.15 (q, *J* = 3.4 Hz, 1H, H-4'), 4.03 (dd, *J* = 11.4, 3.9 Hz, 1H, H-5'a), 3.80 (dd, *J* = 11.4, 2.8 Hz, 1H, H-5'b), 0.96 (s, 9H, -tBu), 0.93 (s, 9H, -tBu), 0.78 (s, 9H, -tBu), 0.15 (s, 3H, $-CH_3$), 0.14 (s, 3H, $-CH_3$), 0.10 (s, 3H, $-CH_3$), 0.05 (s, 3H, $-CH_3$), -0.05 (s, 3H, $-CH_3$), -0.27 (s, 3H, $-CH_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.9, 152.9, 151.7, 149.8, 141.8, 134.1, 132.8, 128.9, 128.1, 123.0, 88.5, 86.0, 76.1, 72.2, 62.7, 26.2, 26.0, 25.8, 18.7, 18.2, 18.0, -3.5, -4.3, -4.5, -4.6, -4.9, -5.2.

HRMS (ESI) m/*z* calcd for $C_{35}H_{60}N_5O_5Si_3$ ($[M+H]^+$) 714.3902, found 714.3909.

IR (neat) ν 2929, 2857, 1698, 1611, 1580, 1454, 1254, 1072, 837, 776 cm^{-1}.

$[\alpha]_D^{23}$ -35.9 (*c* = 1.23, $CHCl_3$)



Compound 34: A modified version of the procedure of Zhu *et al.*[1,2,10] was followed. To a 250 mL round bottom flask was added compound **33** (3.0 g, 4.2 mmol, 1 eq) and THF (60 mL). The solution was cooled to 0 °C. Next, a 0 °C solution of trichloroacetic acid (32 g, 193 mmol, 46 eq) in water (15 mL) was added slowly dropwise by cannula. The reaction was stirred at 0 °C for 3 h and then quenched by dropwise addition of a 0 °C solution of saturated sodium bicarbonate. The reaction was extracted three times with CH_2Cl_2, dried through Na_2SO_4, concentrated and purified by silica column chromatography (R_f 0.10 in 50:50 hexanes:ethyl acetate) to yield compound **34** as a white solid (2.02 g, 93%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.04 (s, 1H, -N*H*Bz), 8.83 (s, 1H, H-8), 8.06 – 8.01 (m, 3H, H-2 + -Bz), 7.63 (t, *J* = 7.4 Hz, 1H, -Bz), 7.54 (t, *J* = 7.6 Hz, 2H, -Bz), 6.13 (dd, *J* = 12.0, 2.0 Hz, 1H, -OH), 5.86 (d, *J* = 7.9 Hz, 1H, H-1'), 5.06 (dd, *J* = 7.9, 4.5 Hz, 1H, H-2'), 4.35 (d, *J* = 4.5 Hz, 1H,

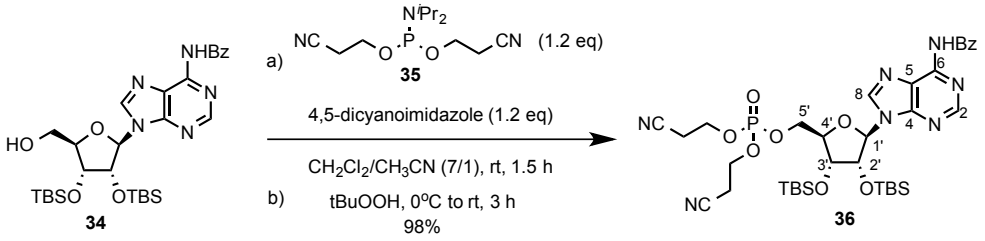
H-3'), 4.21-4.18 (m, 1H, H-4'), 3.98 (appdt, *J* = 13.1, 2.0 Hz, 1H, H-5'a), 3.74 (ddd, *J* = 13.3, 12.1, 1.6 Hz, 1H, H-5'b), 0.96 (s, 9H, -tBu), 0.75 (s, 9H, -tBu), 0.14 (s, 3H, $-CH_3$), 0.13 (s, 3H, $-CH_3$), -0.13 (s, 3H, $-CH_3$), -0.64 (s, 3H, $-CH_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 152.4, 150.6, 150.5, 143.4, 133.7, 133.1, 129.1, 128.0, 124.5, 91.4, 89.8, 74.2, 74.0, 63.1, 25.9, 25.8, 18.2, 17.9, -4.4, -4.4, -4.5, -5.7.

HRMS (ESI) m/*z* calcd for $C_{29}H_{46}N_5O_5Si_2$ ($[M+H]^+$) 600.3038, found 600.3030.

IR (neat) ν 3268, 2929, 2850, 1702, 1611, 1510, 1459, 1252, 1157, 1098, 1063, 836, 777 cm^{-1}.

$[\alpha]_D^{23}$ -46.1 (*c* = 1.1, $CHCl_3$)



Compound 36: To a 25 mL round-bottomed flask was added compound **34** (500 mg, 0.83 mmol, 1 eq) and phosphoramidite **35** (301 mg, 1.0 mmol, 1.2 eq). The compounds were co-evaporated three times on a N_2-filled rotary evaporator with dry CH_3CN and then dried over P_2O_5 overnight. Separately, 4,5-dicyanoimidazole (118 mg, 1.0 mmol, 1.2 eq) was evaporated and dried in a similar manner. To compounds **34** and **35** was added dry CH_2Cl_2 (7 mL), followed by a solution of the 4,5-dicyanoimidazole in CH_3CN (1 mL). After 1.5 h, the reaction was cooled to 0 °C and a solution of t-butyl peroxide (1.0 mL of a 5.5 M solution in decane, 5.5 mmol, 5.5 eq) was added. The reaction was warmed to room temperature and stirred for 3 h. Next, the reaction was poured into a saturated aqueous $NaHCO_3$ solution, extracted three times with EtOAc, dried through Na_2SO_4 and concentrated. The product was purified by silica gel chromatography (R_f=0.11 in 100% EtOAc) to give compound **36** as a white foam (640 mg, 98%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (s, 1H, -N*H*Bz), 8.82 (s, 1H, H-8), 8.25 (s, 1H, H-2), 8.02 (d, *J* = 8.2 Hz, 2H, -Bz), 7.63 (t, *J* = 7.4 Hz, 1H, -Bz), 7.54 (t, *J* = 7.6 Hz, 2H, -Bz), 6.00 (d, *J* = 4.0 Hz, 1H, H-1'), 4.92 (appt, *J* = 4.1 Hz, 1H, H-2'), 4.51 (dd, *J* = 10.6, 4.3 Hz, 1H, H-5'a), 4.43 – 4.35 (m, 2H, H-3' + H-5'), 4.35 – 4.21 (m, 5H, H-4' + $-CH_2CH_2CN$), 2.81 – 2.73 (m, 4H, $-CH_2CH_2CN$), 0.94 (s, 9H, -tBu), 0.85 (s, 9H, -tBu), 0.14 (s, 3H, $-CH_3$), 0.12 (s, 3H, $-CH_3$), 0.03 (s, 3H, $-CH_3$), -0.12 (s, 3H, $-CH_3$).

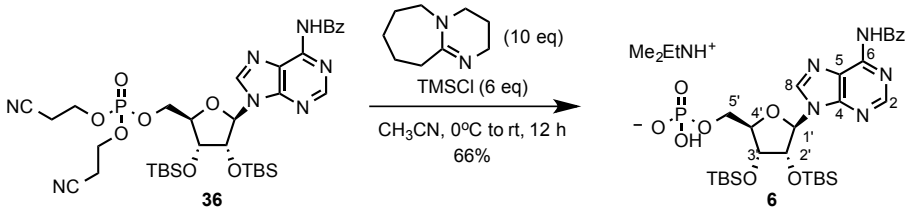
^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 152.9, 151.7, 149.9, 142.5, 133.8, 133.1, 129.1, 128.1, 116.5, 90.1, 82.6 (d, J = 8.5 Hz), 74.8, 71.6, 67.0 (d, J = 5.0 Hz), 62.7 (t, J = 4.8 Hz), 26.0, 26.0, 19.9 (d, J = 7.3 Hz), 18.3, 18.1, -4.1, -4.4, -4.6, -4.6.

^{31}P NMR (202 MHz, $CDCl_3$) δ -0.97

HRMS (ESI) m/z calcd for $C_{35}H_{53}N_7O_8PSi_2$ ($[M+H]^+$) 786.3232, found 786.3225

IR (neat) ν 2954, 2919, 2857, 1701, 1611, 1576, 1458, 1250, 1036, 997, 884, 782 cm^{-1}

$[\alpha]_D^{23}$ -6.7 (*c* = 1.05, $CHCl_3$)



Compound 6: To a 25 mL round-bottomed flask was added compound **36** (500 mg, 0.64 mmol, 1 eq), followed by CH_3CN (7 mL). The solution was cooled to 0 ^oC, and 1,8-Diazabicyclo[5.4.0]undec-7-ene (974 mg, 6.4 mmol, 10 eq) was added dropwise. Finally, TMSCl (413 mg, 3.8 mmol, 6 eq) was added. After 5 min, the reaction was removed from the 0 ^oC bath, allowed to warm to room temperature, and stirred for 12 h. The reaction was concentrated and applied to a Dowex 50W-X8 cation exchange resin (Me_2EtNH^+ form) and eluted with MeOH. The product was purified by C-18 chromatography to yield compound **6** as the dimethyl ethyl ammonium salt (316 mg, 66%) as a white foam.

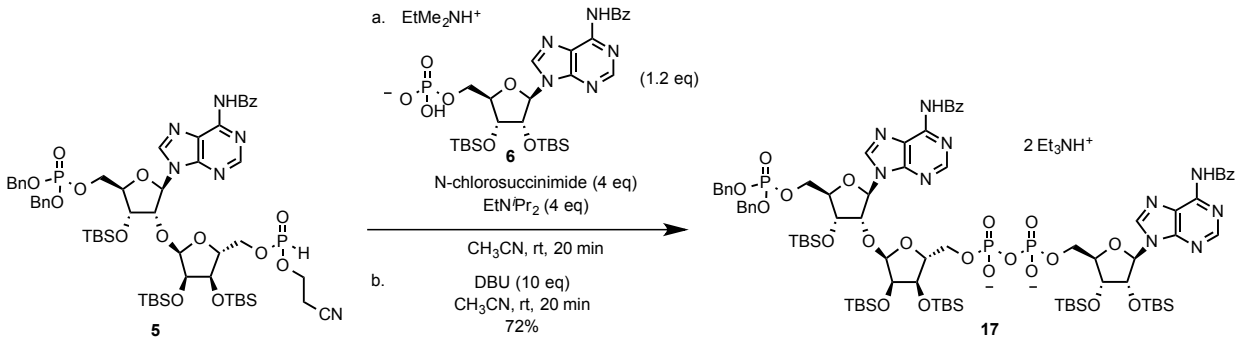
^{1}H NMR (500 MHz, CD_3OD) δ 8.90 (s, 1H, H-8), 8.75 (s, 1H, H-2), 8.11 (d, J=7.0, 2H, -Bz), 7.67 (t, J=7.5 Hz, 1H, -Bz), 7.58 (t, J=7.5 Hz, 2H, -Bz), 6.26 (d, *J* = 6.8 Hz, 1H, H-1'), 4.99 – 4.85 (m, 1H, H-2'), 4.49 (dd, *J* = 4.4, 1.8 Hz, 1H, H-3'), 4.32 – 4.24 (m, 1H, H-4'), 4.24 – 4.18 (m, 1H, H-5'a), 4.13 (ddd, *J* = 11.3, 5.0, 3.2 Hz, 1H, H-5'b), 3.16 (q, *J* = 7.3 Hz, 2H, $CH_3CH_2N(CH_3)_2$), 2.85 (s, 6H, $CH_3CH_2N(CH_3)_2$), 1.33 (t, J = 7.3 Hz, 3H, $CH_3CH_2N(CH_3)_2$), 1.01 (s, 9H, -tBu), 0.77 (s, 9H, -tBu), 0.22 (s, 3H, $-CH_3$), 0.19 (s, 3H, $-CH_3$), 0.03 (s, 3H, $-CH_3$), -0.31 (s, 3H, $-CH_3$)

^{13}C NMR (125 MHz, CD_3OD) δ 168.1, 153.8, 153.3, 151.2, 144.7, 135.1, 133.8, 129.8, 129.4, 124.8, 88.8, 87.5 (d, J=9.0 Hz), 77.6, 74.7, 65.7 (d, J=5.8 Hz), 53.9, 42.8, 26.4, 26.2, 18.9, 18.7, 10.0, -4.2, -4.3, -4.3, -5.1.

^{31}P NMR (202 MHz, CD_3OD) δ 1.93

HRMS (ESI) m/z calcd for $C_{29}H_{47}N_5O_8PSi_2$ ($[M+H]^+$) 680.2701, found 680.2706

$[\alpha]_D^{22}$ -46.1 (*c* = 1.2, EtOH)



Compound 17: To a 7 mL reaction vial was added compound **5** (68 mg, 0.056 mmol, 1 eq) and compound **6** (50 mg, 0.067 mmol, 1.2 eq). The mixture was co-evaporated three times with dry CH_3CN and dried over P_2O_5 overnight. Compounds **5** and **6** were dissolved in dry CH_3CN (0.5 mL) containing N,N-diisopropylethylamine (29 mg, 0.22 mmol, 4 eq) and N-chlorosuccinimide (30 mg, 0.22 mmol, 4 eq) was added and the reaction was stirred for 20 min at room temperature. Diazabicyclo[5.4.0]undec-7-ene (84 mg, 0.556 mmol, 10 eq) was added and the reaction was stirred for 20 min at room temperature. The solution was concentrated and purified by reverse phase chromatography. The purified compound was passed through a short column of Dowex 50W-X8 (Et_3NH^+ form) to yield compound **17** as the triethylammonium salt as a pale yellow foam (82 mg, 72%).

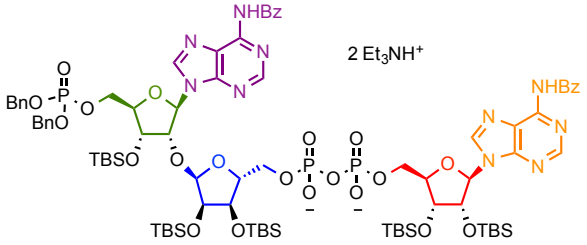
^{1}H NMR (500 MHz, CD_3OD) δ 8.96 (s, 1H), 8.71 (s, 1H), 8.66 (s, 1H), 8.45 (s, 1H), 8.12 – 8.00 (m, 4H), 7.71 – 7.60 (m, 2H), 7.59 – 7.48 (m, 4H), 7.37 – 7.19 (m, 10H), 6.27 (d, *J* = 2.7 Hz, 1H), 6.25 (d, *J* = 6.9 Hz, 1H), 5.20 (d, *J* = 4.3 Hz, 1H), 4.99 – 4.88 (m, 6H), 4.78 – 4.71 (m, 1H), 4.46 (dd, *J* = 4.3, 1.5 Hz, 1H), 4.40 – 4.29 (m, 3H), 4.28 – 4.13 (m, 6H), 4.12 – 4.03 (m, 2H), 3.16 (q, *J* = 7.3 Hz, 12H), 1.28 (t, *J* = 7.3 Hz, 18H), 0.98 (s, 9H), 0.92 (s, 9H), 0.91 (s, 9H), 0.81 (s, 9H), 0.73 (s, 9H), 0.19 (s, 3H), 0.17 (s, 3H), 0.16 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.04 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), -0.36 (s, 3H).

^{13}C NMR (125 MHz, CD_3OD) δ 168.0, 168.0, 153.9, 153.4, 153.3, 152.9, 151.4, 151.3, 144.9, 144.5, 137.0, 137.0, 135.3, 135.1, 134.0, 134.0, 129.9, 129.8, 129.8, 129.6, 129.6, 129.2, 125.4, 124.8, 104.8, 90.1, 88.7, 87.4 (d, *J* = 8.9 Hz), 86.4 (d, *J* = 9.7 Hz), 83.5 (d, *J* = 8.0 Hz), 81.5, 77.6, 75.0, 74.7, 72.5, 71.8, 71.0, 71.0, 67.3 (d, *J* = 5.7 Hz), 66.7 (d, J_P = 5.8 Hz), 66.6 (d, J_P = 5.4 Hz), 47.4, 27.0, 26.8, 26.7, 26.7, 26.4, 19.3, 19.2, 19.2, 19.1, 18.8, 9.3, -3.6, -3.7, -3.9, -3.9, -4.0, -4.0, -4.1, -4.1, -4.5, -4.9.

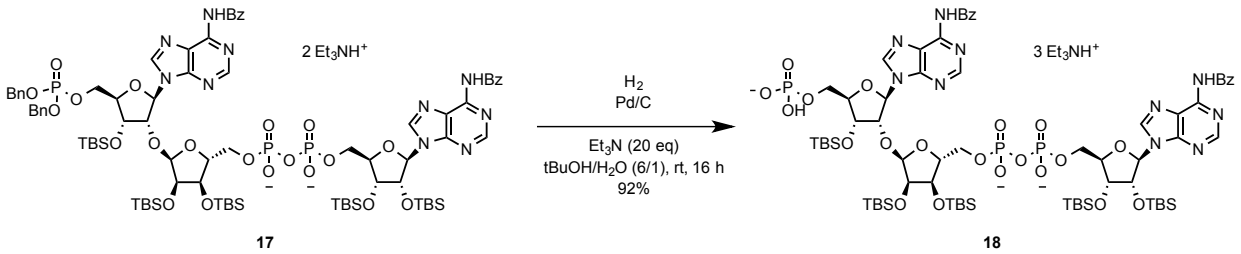
^{31}P NMR (202 MHz, CD_3OD) δ -0.09, -10.01 (d, *J* = 19.9 Hz), -10.34 (d, *J* = 19.8 Hz).

HRMS (ESI) m/z calcd for $C_{83}H_{124}N_{10}O_{22}P_3Si_5$ ($[M-H]^-$) 1845.6956, found 1845.6959

	^{1}H	^{13}C	^{31}P	^{1}H-^{1}H COSY	^{1}H-^{13}C HMBC
I-Ado 1’	6.25 (d, *J* = 6.9 Hz)	88.69		4.89	74.73, 77.60, 87.43, 144.92, 153.89
I-Ado 2’	4.90 (dd, 6.9, 4.4 Hz)	77.60		4.47, 6.25	74.73, 88.69
I-Ado 3’	4.47 (d, *J* = 3.6 Hz)	74.73		4.25, 4.90	66.63, 77.60, 87.43, 88.69
I-Ado 4’	4.25	87.43 (d, J_P = 8.9 Hz)			
I-Ado 5’a	4.24	66.63	-10.34	4.35	
I-Ado 5’b	4.35	(d, J_P = 5.4 Hz)	(d, *J* = 19.8 Hz)	4.24	
I-Ade 2	8.71	153.39		-	124.81, 151.27, 153.89
I-Ade 4	-	153.89		-	-
I-Ade 5	-	124.81		-	-
I-Ade 6	-	151.27		-	-
I-Ade 8	8.95	144.92		-	124, 81, 153.89
a- Rib 1’’	5.20 (d, *J* = 4.2 Hz).	104.78		4.09	72.52, 75.03, 81.47, 86.40
a- Rib 2’’	4.09 (dd, *J* = 5.8, 4.2 Hz)	75.03		4.18, 5.20	104.78
a- Rib 3’’	4.18 (dd, *J* = 5.8, 3.1 Hz)	72.52		4.09	66.67, 75.03, 86.40
a- Rib 4’’	4.25	86.40 (d, J_P = 9.7 Hz).		4.07	75.03
a- Rib 5’’a	4.07	66.67	-10.01	4.25	72.52, 86.40
a- Rib 5’’b	4.07	(d, J_P = 5.8 Hz).	(d, *J* = 19.8 Hz)	4.25	72.52, 86.40
D-Ado 1’	6.27 (d, *J* = 2.6 Hz),	90.11		4.89	71.83, 81.47, 83.46, 144.53, 152.87
D-Ado 2’	4.90	81.47		4.74, 6.27	71.83, 83.46, 104.78
D-Ado 3’	4.74 (dd, *J* = 6.7, 4.5 Hz)	71.83		4.33, 4.90	67.25, 81.47, 83.46, 90.11
D-Ado 4’	4.33	83.46 (d, J_P = 8.0 Hz)			
D-Ado 5’a	4.20	67.25	-0.09	4.37	
D-Ado 5’b	4.37	(d, J_P = 5.7 Hz)		4.20	
D-Ade 2	8.66	153.32		-	125.37, 151.39, 152.87
D-Ade 4	-	152.87		-	-
D-Ade 5	-	125.37		-	-
D-Ade 6	-	151.39		-	-
D-Ade 8	8.44	144.53		-	125.37, 152.87



17



17 18

Compound 18: To a 20 mL vial was added compound **17** (51 mg, 0.025 mmol, 1 eq) and 10% palladium on activated charcoal (50 mg). Next, t-butanol (2.4 mL) and deionized water (0.4 mL) were added followed by Et_3N (0.070 mL, 0.498 mmol, 20 eq). Lastly, the vial was fitted with a balloon of hydrogen gas and purged for 1 min. The reaction was stirred under an atmosphere of hydrogen gas at room temperature for 16 h. The reaction was filtered through celite and the product was purified by reverse phase chromatography to yield compound **18** as a white foam (45 mg, 92%).

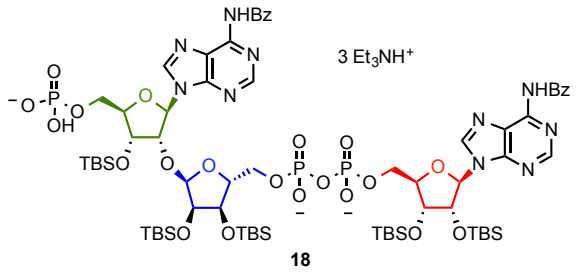
^{1}H NMR (600 MHz, CD_3OD) δ 9.00 (s, 1H), 8.84 (s, 1H), 8.71 (s, 1H), 8.70 (s, 1H), 8.12 – 8.03 (m, 4H), 7.67 – 7.62 (m, 2H), 7.60 – 7.52 (m, 4H), 6.34 (d, *J* = 3.6 Hz, 1H), 6.25 (d, *J* = 6.7 Hz, 1H), 5.26 (d, *J* = 4.1 Hz, 1H), 4.88 (dd, *J* = 6.8, 4.4 Hz, 1H), 4.67 (appt, *J* = 4.1 Hz, 1H), 4.61 (appt, *J* = 5.0 Hz, 1H), 4.46 (dd, *J* = 4.4, 1.7 Hz, 1H), 4.36-4.30 (m, 2H), 4.29 – 4.22 (m, 4H), 4.17 (dd, *J* = 5.7, 3.1 Hz, 1H), 4.11 – 4.02 (m, 4H), 3.18 (q, *J* = 7.3 Hz, 18H), 1.29 (t, *J* = 7.3 Hz, 27H), 0.98 (s, 9H), 0.93 (s, 9H), 0.91 (s, 9H), 0.82 (s, 9H), 0.74 (s, 9H), 0.19 (s, 3H), 0.17 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.08 (s, 3H), 0.08 (s, 3H), 0.03 (s, 3H), 0.03 (s, 3H), 0.02 (s, 3H), -0.33 (s, 3H).

^{13}C NMR (125 MHz, CD_3OD) δ 168.1, 168.1, 153.8, 153.8, 153.2, 153.2, 153.1, 153.1, 151.1, 151.0, 144.9, 144.3, 135.1, 133.8, 133.8, 129.7, 129.7, 129.4, 129.4, 125.0, 124.7, 104.9, 89.0, 88.7, 87.2 (d, *J* = 9.2 Hz), 85.9 (d, *J* = 9.8 Hz) 85.2 (d, *J* = 9.3 Hz) 82.8, 77.6, 74.7, 74.5, 72.3, 72.1, 66.5 (d, *J* = 5.5 Hz), 66.4 (d, *J* = 5.0 Hz), 64.6 (d, *J* = 4.6 Hz), 47.4, 26.9, 26.7, 26.7, 26.5, 26.3, 19.1, 19.1, 19.1, 18.9, 18.7, 9.2, -3.7, -3.8, -4.1, -4.1, -4.2, -4.2, -4.3, -4.3 -4.4, -5.0.

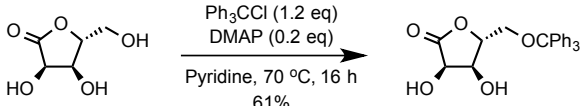
^{31}P NMR (202 MHz, CD_3OD) δ 1.86, -9.66 (d, *J* = 19.3 Hz), -10.06 (d, *J* = 19.1 Hz).

HRMS (ESI) m/z calcd for $C_{69}H_{112}N_{10}O_{22}P_3Si_5$ ($[M-H]^-$) 1665.6017, found 1665.6018

	^{1}H	^{13}C	^{31}P	^{1}H-^{1}H COSY
I-Ado 1'	6.25 (d, J = 6.7 Hz)	88.7		4.88
I-Ado 2'	4.88 (dd, J = 6.8, 4.4 Hz)	77.6		6.25, 4.46
I-Ado 3'	4.46 (dd, J =4.4, 1.7 Hz)	74.5		4.88, 4.25
I-Ado 4'	4.25	87.2 (d, J_P = 9.2 Hz)		4.46, 4.43, 4.25
I-Ado 5'a	4.25	66.4 (d, J_P = 5.0 Hz)	-10.06 (d, J = 19.1 Hz)	4.33, 4.25
I-Ado 5'b	4.33			4.25, 4.25
a- Rib 1''	5.26 (d, J = 4.1 Hz)	104.9		4.04
a- Rib 2''	4.04	74.7		5.26, 4.17
a- Rib 3''	4.17	72.3		4.23,4.04
a- Rib 4''	4.23	85.9 (d, J_P = 9.8 Hz)		4.23, 4.06, 4.06
a- Rib 5''a	4.06	66.5 (d, J_P = 5.5 Hz)	-9.66 (d, J = 19.3 Hz)	4.23, 4.06
a- Rib 5''b	4.06			4.23, 4.06
D-Ado 1'	6.34 (d, J = 3.6 Hz)	89.0		4.67
D-Ado 2'	4.67 (appt, J = 4.1 Hz)	82.8		6.34, 4.61
D-Ado 3'	4.61 (appt, J = 5.0 Hz)	72.1		4.67, 4.32
D-Ado 4'	4.32	85.2 (d, J_P = 9.3 Hz)		4.61, 4.26, 4.05
D-Ado 5'a	4.26	64.6 (d, J_P = 4.6 Hz)	1.86	4.32, 4.05
D-Ado 5'b	4.05			4.32, 4.26



18



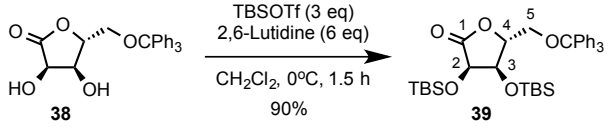
37 38

Compound 38: A modified version of the procedure of Ireland *et al.*[3,11] was followed. To a 20 mL reaction vial was added compound D-ribonolactone (**37**) (500 mg, 3.38 mmol, 1 eq) and pyridine (10 mL). Next, triphenylmethyl chloride (1.13 g, 4.05 mmol, 1.2 eq) was added followed by and 4-dimethylaminopyridine (82 mg, 0.675 mmol, 0.2 eq). The reaction was stirred at 70°C for 16 h at which point it was concentrated and purified by silica column chromatography to yield compound **37** (800 mg, 61%) as a white solid.

^{1}H NMR (500 MHz, Acetone-*d*$_6$) δ 7.46 -7.26 (m, 15H, -CPh_3), 4.76 (d, *J* = 5.4 Hz, 1H, H-2), 4.47 (apptd, *J* = 3.4, 1.0 Hz, 1H, H-4), 4.27 (d, *J* = 5.3 Hz, 1H, H-3), 3.55 (dd, *J* = 10.9, 3.4 Hz, 1H, H-5a), 3.28 (dd, *J* = 10.9, 3.3 Hz, 1H, H-5b).

^{13}C NMR (125 MHz, Acetone-d$_6$) δ 176.2, 144.4, 129.4, 128.8, 128.2, 88.2, 84.3, 70.9, 69.8, 64.1.

HRMS (ESI) m/z calcd for $C_{24}H_{22}O_5Na$ ([M+Na]$^+$) 413.1365, found 413.1361



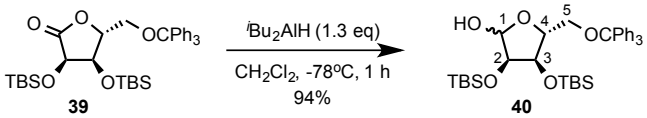
38 **39**

Compound 39: To a 20 mL reaction vial was added compound **38** (370 mg, 0.95 mmol, 1 eq) and CH_2Cl_2 (10 mL). The vial was cooled to 0^{o}C and 2,6-Lutidine (0.66 mL, 5.7 mmol, 6 eq) was added. Finally, TBSOTf (0.65 mL, 2.9 mmol, 3 eq) was added over 30 min. The reaction was stirred for 1 h at 0^{o}C at which point a saturated aqueous $NaHCO_3$ solution. The mixture was extracted three times with $CHCl_3$, dried through Na_2SO_4, concentrated and purified by silica column chromatography to yield known[4,12] compound **39** (527 mg, 90%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 6H, -CPh_3), 7.38 – 7.31 (m, 6H, -CPh_3), 7.31 – 7.25 (m, 3H, -CPh_3), 4.72 (d, *J* = 5.2 Hz, 1H, H-2), 4.33 (ddd, *J* = 3.6, 2.7, 1.1 Hz, 1H, H-4), 3.99 (dd, *J* = 5.1 Hz, 1.1 Hz, 1H, H-3), 3.66 (dd, *J* = 11.0, 3.6 Hz, 1H, H-5a), 3.25 (dd, *J* = 11.0, 2.8 Hz, 1H, H-5b), 0.97 (s, 9H, -tBu), 0.84 (s, 9H, -tBu), 0.23 (s, 3H, -CH_3), 0.15 (s, 3H, -CH_3), 0.05 (s, 3H, -CH_3), -0.02 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 175.2, 143.2, 128.6, 128.2, 127.5, 87.7, 84.7, 72.2, 70.4, 62.4, 26.0, 25.8, 18.5, 18.2, -4.5, -4.5, -4.7, -5.0.

HRMS (ESI) m/z calcd for $C_{36}H_{50}NaO_5Si_2$ ([M+Na]$^+$) 641.3089, found 641.3064.



39 **40**

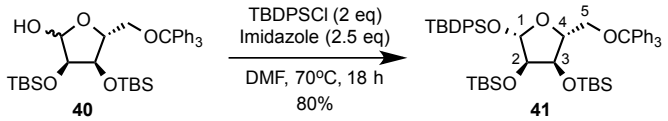
Compound 40: To a -78^{o}C solution of compound **39** (200 mg, 0.32 mmol, 1 eq) in CH_2Cl_2 (3.5 mL) was added diisobutylaluminum hydride (0.42 mL of 1 M solution in hexanes, 0.42 mmol, 1.3 eq). The reaction was stirred at -78^{o}C for 1 h, at which point the reaction was slowly quenched with MeOH. The reaction mixture was poured into a saturated aqueous solution of potassium sodium tartrate, extracted three times with EtOAc and CH_2Cl_2, dried through Na_2SO_4, concentrated and purified by silica column chromatography to give compound **40** as a white solid (187 mg, 94%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 – 7.41 (m, 6H major and minor, -CPh_3), 7.38 – 7.29 (m, 6H, major and minor, -CPh_3), 7.29 – 7.21 (m, 3H major and minor, -CPh_3), 5.22 (dd, *J* = 4.4, 1.1 Hz, 1H minor, H-1β), 5.16 (dd, *J* = 11.3, 4.2 Hz, 1H major, H-1α), 4.42 (dd, *J* = 7.3, 4.0 Hz, 1H, H-3β minor), 4.26 (d, *J* = 11.3 Hz, 1H major, -OHα), 4.23 (appt, *J*= 4.0 Hz, 1H major, H-4α), 4.19 (appt, *J* = 4.5 Hz, 1H major, H-2α), 4.10 (ddd, *J* = 6.9, 3.8, 2.8 Hz, 1H minor, H-4β), 3.99 (d, *J* = 4.0 Hz, 1H minor, H-2β), 3.95 (d, *J* = 4.6 Hz, 1H major, H-3α), 3.51 (dd, *J* = 10.3, 2.7 Hz, 1H minor, H-5β), 3.30 (dd, *J* = 10.3, 5.0 Hz, 1H major, H-5α), 3.14 (dd, *J* = 10.3, 3.3 Hz, 1H major, H-5α'), 3.14-3.11 (m, 1H, minor, H-5β') 2.79 (d, *J* = 4.6 Hz, 1H minor, -OHβ), 0.96 (s, 9H

major, -tBu), 0.94 (s, 9H minor, -tBu), 0.88 (s, 9H major, -tBu), 0.78 (s, 9H minor, -tBu), 0.16 (s, 3H major, $-CH_3$), 0.14 (s, 3H minor, $-CH_3$), 0.13 (s, 3H major, $-CH_3$), 0.12 (s, 3H minor, $-CH_3$), 0.07 (s, 3H major, $-CH_3$), 0.01 (s, 3H major, $-CH_3$), 0.00 (s, 3H minor, $-CH_3$), -0.16 (s, 3H minor, $-CH_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8 (major), 143.8 (minor), 129.0 (minor), 128.8 (major), 128.0 (major), 127.9 (minor), 127.3 (major), 127.2 (minor), 102.2 (minor), 97.9 (major), 87.1 (major), 87.0 (minor), 84.4 (major), 81.8 (minor), 74.6 (major and minor), 72.6 (major), 71.8 (major), 63.8 (major), 63.4 (minor), 26.0 (major), 26.0 (minor), 25.9 (minor), 25.9 (major), 18.4 (major), 18.3 (minor), 18.1 (major and minor), -4.1 (minor), -4.3 (minor), -4.4 (minor), -4.5 (major), -4.6 (major), -4.7 (major), -4.9 (major), -4.9 (minor).

HRMS (ESI) m/z calcd for $C_{36}H_{52}O_5Si_2Na$ ($[M+Na]^+$) 643.3251, found 643.3259.

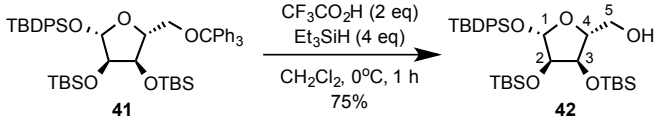


Compound 41: To a 7 mL reaction vial was added compound **40** (100 mg, 0.16 mmol, 1 eq) and DMF (1 mL). Imidazole (27 mg, 0.4 mmol, 2.5 eq) was added, followed by tert-Butyl(chloro)diphenylsilane (0.083 mL, 0.32 mmol, 2 eq) and the reaction was heated to 70°C for 18 h. The reaction was quenched with a saturated aqueous NH_4Cl solution, extracted three times with CH_2Cl_2, dried through Na_2SO_4, concentrated and purified by silica column chromatography to yield compound **41** as a white foam (110 mg, 80%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 – 7.78 (m, 2H, -TBDPS), 7.73 – 7.66 (m, 2H, -TBDPS), 7.63 – 7.53 (m, 6H, $-CPh_3$), 7.49 – 7.36 (m, 6H, -TBDPS), 7.30 – 7.24 (m, 6H, $-CPh_3$), 7.24 – 7.17 (m, 3H, $-CPh_3$), 5.17 (s, 1H, H-1), 4.40 (dd, *J* = 8.5, 3.6 Hz, 1H, H-3), 4.18 (ddd, *J* = 8.4, 6.2, 2.0 Hz, 1H, H-4), 3.79 (d, *J* = 3.6 Hz, 1H, H-2), 3.44 (dd, *J* = 10.1, 2.0 Hz, 1H, H-5a), 3.15 (dd, *J* = 10.2, 6.2 Hz, 1H, H-5b), 1.03 (s, 9H, -tBu), 0.77 (s, 9H, -tBu), 0.76 (s, 9H, -tBu), -0.02 (s, 3H, $-CH_3$), -0.12 (s, 3H, $-CH_3$), -0.14 (s, 3H, $-CH_3$), -0.39 (s, 3H, $-CH_3$).

^{13}C NMR (125 MHz, $CDCl_3$) δ 144.3, 135.9, 135.7, 134.1, 132.9, 130.0, 130.0, 129.1, 128.0, 128.0, 127.8, 126.9, 102.1, 86.6, 80.6, 77.8, 72.1, 65.3, 27.0, 26.0, 25.9, 19.3, 18.3, 18.1, -4.0, -4.7, -4.9, -5.0.

HRMS (ESI) m/z calcd for $C_{52}H_{70}O_5Si_3Na$ ($[M+Na]^+$) 881.4429, found 881.4441.



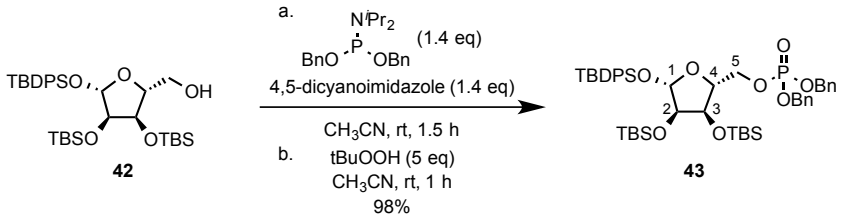
Compound 42: To a 7 mL reaction vial was added compound **41** (90 mg, 0.105 mmol, 1 eq) and CH_2Cl_2 (1 mL). The solution was cooled to 0°C and Et_3SiH (0.067 mL, 0.419 mmol, 4 eq) was added. Finally, CF_3CO_2H (0.016 mL, 0.209 mmol, 2 eq) was added in a solution of CH_2Cl_2 (0.1 mL) and the reaction was stirred at 0°C for 1 h. The reaction was quenched with a solution of saturated aqueous $NaHCO_3$, extracted three times with CH_2Cl_2, dried through Na_2SO_4,

concentrated, and purified by silica column chromatography to give compound **42** (44 mg, 75%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 – 7.69 (m, 2H, -TBDPS), 7.66 – 7.62 (m, 2H, -TBDPS), 7.48 – 7.36 (m, 6H, -TBDPS), 5.05 (s, 1H, H-1), 4.60 (dd, *J* = 8.3, 3.6 Hz, 1H, H-3), 4.04 (ddd, *J* = 8.3, 2.6, 2.5 Hz, 1H, H-4), 3.86 (dd, *J* = 12.0, 2.5 Hz, 1H, H-5a), 3.78 (d, *J* = 3.6 Hz, 1H, H-2), 3.60 (dd, *J* = 12.2, 2.6 Hz, 1H, H-5b), 2.01 (bs, 1H, -OH), 1.07 (s, 9H, -tBu), 0.92 (s, 9H, -tBu), 0.76 (s, 9H, -tBu), 0.15 (s, 3H, -CH_3), 0.11 (s, 3H, -CH_3), -0.10 (s, 3H, -CH_3), -0.34 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 133.3, 132.7, 130.3, 130.2, 128.1, 101.8, 82.0, 78.2, 70.3, 60.8, 26.9, 26.1, 25.8, 19.2, 18.3, 18.1, -4.1, -4.7, -4.8, -4.8.

HRMS (ESI) m/z calcd for $C_{33}H_{56}O_5NaSi_3$ ($[M+Na]^+$) 639.3333, found 639.3342.



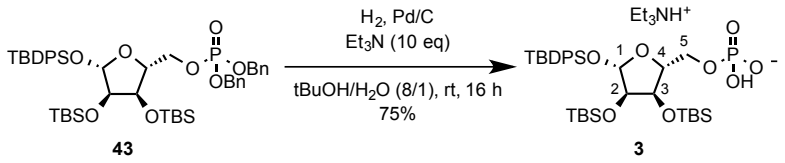
Compound 43: A 7 mL vial containing compound **42** (35 mg, 0.057 mmol, 1 eq) was azeotroped twice in a nitrogen filled rotary evaporator with dry CH_3CN and dried on a high vacuum for 20 min. To compound **42** was added dibenzyl N,N-diisopropylphosphoramidite (28 mg, 0.080 mmol, 1.4 eq) in a solution of CH_3CN (0.4 mL). Next, dicyanoimidazole (9.4 mg, 0.080 mmol, 1.4 eq) was added in a solution of CH_3CN (0.1 mL), the reaction was stirred at room temperature for 1.5 h at which point tBuOOH (0.052 mL of a 5.5 M solution in decane, 0.285 mmol, 5 eq) was added. The reaction stirred an additional 1 h at room temperature at which point it was quenched with saturated aqueous $NaHCO_3$, extracted three times with CH_2Cl_2, dried through Na_2SO_4, and concentrated. The reaction was purified by silica column chromatography to give compound **43** (49 mg, 98%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.69 (m, 2H, -TBDPS), 7.66 – 7.60 (m, 2H, -TBDPS), 7.47 – 7.28 (m, 16H, -TBDPS + -Bn), 5.10 – 4.96 (m, 5H, H-1 + CH_2Ph), 4.40 (dd, *J* = 8.0, 3.6 Hz, 1H, H-3), 4.35 – 4.29 (m, 1H, H-5a), 4.20 – 4.09 (m, 2H, H-4 + H-5b), 3.83 (d, *J* = 3.6 Hz, 1H, H-2), 1.05 (s, 9H, -tBu), 0.91 (s, 9H, -tBu), 0.77 (s, 9H, -tBu), 0.12 (s, 3H, -CH_3), 0.10 (s, 3H, -CH_3), -0.08 (s, 3H, -CH_3), -0.32 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 135.7, 133.6, 132.9, 130.1, 129.9, 128.6, 128.5, 128.0, 128.0, 128.0, 127.9, 101.9, 79.6 (d, *J* = 8.5 Hz), 77.8, 72.0, 69.3 (d, *J* = 5.6 Hz), 69.2 (d, *J* = 5.6 Hz), 68.6 (d, *J* = 5.6 Hz), 26.9, 26.0, 25.8, 19.2, 18.2, 18.0, -4.1, -4.6, -4.8.

^{31}P NMR (202 MHz, $CDCl_3$) δ -0.29

HRMS (ESI) m/z calcd for $C_{47}H_{69}O_8PSi_3Na$ ($[M+Na]^+$) 899.3936, found 899.3935.



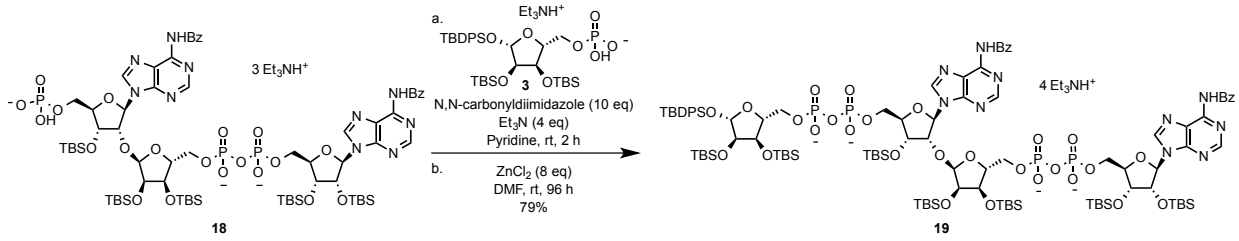
Compound 3: To a 20 mL vial containing compound **43** (48 mg, 0.055 mmol, 1 eq) was added 10% Palladium on activated charcoal (50 mg). Next, tBuOH (4 mL) and deionized water (0.5 mL) were added, followed by Et_3N (0.075 mL, 0.55 mmol, 10 eq). The reaction was fitted with a ballon of hydrogen gas, purged for 1 min and stirred at room temperature for 16 h. After 16 h, the reaction was filtered through celite, concentrated, and purified by reverse phase chromatography to give compound **3** as a pale yellow oil (32 mg, 75%).

^{1}H NMR (500 MHz, CD_3OD) δ 7.79 – 7.71 (m, 2H, -TBDPS), 7.68 – 7.61 (m, 2H, -TBDPS), 7.52 – 7.35 (m, 6H, -TBDPS), 5.03 (s, 1H, H-1), 4.34 (dd, *J* = 7.9, 3.6 Hz, 1H, H-3), 4.24 (ddd, *J* = 10.5, 6.1, 2.7 Hz, 1H, H-5a), 4.12 (apptd, *J* = 8.1, 2.7 Hz, 1H, H-4), 3.99 (ddd, *J* = 10.5, 8.3, 5.0 Hz, 1H, H-5b), 3.89 (d, *J* = 3.6 Hz, 1H, H-2), 3.15 (q, *J* = 7.3 Hz, 6H, -(CH_3CH_2)$_3$N), 1.28 (t, *J* = 7.3 Hz, 9H, -(CH_3CH_2)$_3$N), 1.06 (s, 9H, -tBu), 0.94 (s, 9H, -tBu), 0.78 (s, 9H, -tBu), 0.18 (s, 3H, -CH_3), 0.15 (s, 3H, -CH_3), -0.06 (s, 3H, -CH_3), -0.28 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, CD_3OD) δ 137.0, 136.8, 134.5, 133.9, 131.2, 131.0, 129.0, 128.9, 103.0, 82.4 (d, *J* = 8.8 Hz), 79.08, 74.34, 69.2 (d, *J* = 5.4 Hz), 47.4, 27.3, 26.6, 26.2, 19.9, 19.0, 18.8, 9.1, -4.0, -4.3, -4.4, -4.5.

^{31}P NMR (202 MHz, CD_3OD) δ 2.11

HRMS (ESI) m/z calcd for $C_{33}H_{58}O_8Si_3P$ ($[M+H]^+$) 697.3177, found 697.3192.



Compound 19: To a 7 mL vial was added compound **18** (10 mg, 5.7 μmol, 1 eq). This material was azeotropically dried three times with anhydrous CH_3CN. To a separate 7 mL vial was added compound **3** (8.1 mg, 10.1 μmol, 2 eq) and carbonyldiimidazole (8.3 mg, 51.1 μmol, 10 eq). A solution of triethylamine (2.1 mg, 20.7 μmol, 4 eq) in pyridine (0.2 mL) was added and the reaction was stirred at room temperature for 2 h. The reaction was quenched with MeOH containing 10% Et_3N (v/v). After 30 min, the solution was concentrated to dryness and azeotropically dried with anhydrous CH_3CN (three times). Compound **18** was added in methanol to the crude imidazolide, the solution was concentrated to dryness and azeotropically dried with anhydrous CH_3CN (three times). The solid residue was dried under high vacuum over P_2O_5 for 16 h. A solution of freshly dried $ZnCl_2$ (5.5 mg, 40.4 μmol, 8 eq) in DMF (0.3 mL) was added and the reaction was stirred at room temperature for 96 h. The reaction was quenched by addition of a methanol solution containing the triethylammonium salt of EDTA (1

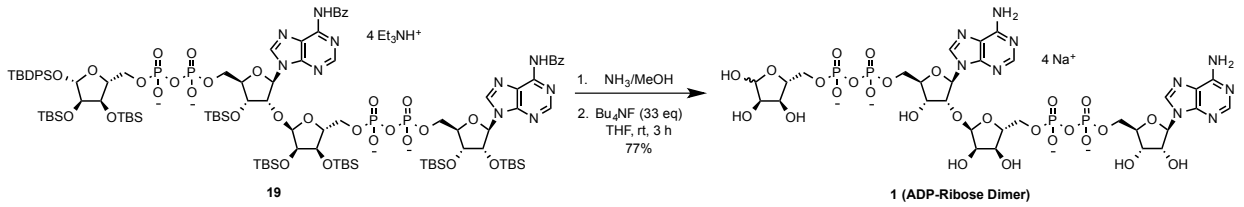
mL of methanol, 100 mg of EDTA (0.342 mmol, 67 eq, tetraacid), and 0.2 mL of triethylamine) and stirred for 30 min. The reaction was concentrated and purified by C18 chromatography to give compound **19** as the triethylammonium salt (11.0 mg, 79%).

^{1}H NMR (600 MHz, CD_3OD) δ 9.01 (s, 1H), 8.97 (s, 1H), 8.71 (s, 1H), 8.70 (s, 1H), 8.10-8.05 (m, 4H), 7.76 – 7.69 (m, 2H), 7.68 – 7.61 (m, 4H), 7.56 – 7.52 (m, 4H), 7.47 – 7.35 (m, 6H), 6.33 (d, *J* = 3.7 Hz, 1H), 6.25 (d, *J* = 6.8 Hz, 1H), 5.23 (bs, 1H), 5.01 (s, 1H), 4.87 (m, 1H) 4.64 (bs, 1H), 4.59 (appt, *J* = 4.9 Hz, 1H), 4.46 (dd, *J* = 4.4, 1.6 Hz, 1H), 4.43-4.38 (m, 1H), 4.34-4.27 (m, 4H), 4.26 – 4.03 (m, 10H), 3.89 – 3.86 (m, 1H), 3.17 (q, *J* = 7.3 Hz, 24H), 1.28 (t, *J* = 7.3 Hz, 36H), 1.01 (s, 9H), 0.97 (s, 9H), 0.91 (s, 9H), 0.90 (s, 9H), 0.90 (s, 9H) 0.79 (s, 9H), 0.76 (s, 9H), 0.74 (s, 9H), 0.18 (s, 3H), 0.18 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.07 (s, 3H), 0.07 (s, 3H), 0.01 (s, 3H), -0.08 (s, 3H), -0.29 (s, 3H), -0.34 (s, 3H).

^{13}C NMR (125 MHz, CD_3OD) δ 168.1, 168.0, 153.8, 153.2, 153.2, 153.1, 151.1, 151.0, 144.9, 144.4, 137.0, 136.8, 135.7, 135.2, 135.1, 134.6, 133.9, 133.8, 131.2, 131.0, 129.8, 129.4, 129.0, 129.0, 128.9, 128.9, 124.9, 124.6, 105.0, 102.9, 88.8, 88.6, 87.3, 87.2, 86.2, 85.2, 83.1, 82.2, 79.2, 77.7, 74.8, 74.6, 74.5, 72.3, 69.8, 66.6, 66.4, 65.3, 47.3, 27.4, 27.0, 26.8, 26.7, 26.7, 26.5, 26.3, 26.3, 19.9, 19.1, 19.1, 19.1, 18.9, 18.8, 18.8, 18.7, 9.2, -3.7, -3.8, -3.9, -4.0, -4.1, -4.2, -4.2, -4.2, -4.2, -4.2, -4.3, -4.3, -4.4, -5.0.

^{31}P NMR (243 MHz, CD_3OD) δ -10.84 (d, *J* = 18.5 Hz), -11.01 (d, *J* = 19.5 Hz), -11.39 (d, *J* = 19.3 Hz), -11.44 (*d*, J = 18.3 Hz).

HRMS (ESI) m/z calcd for $C_{102}H_{167}O_{29}Si_8P_4$ ([M-H]$^-$) 2343.9011, found 2343.9024.



Compound 1: To a 4 mL reaction vial was added compound **19** (9.0 mg, 3.27 μmol, 1 eq) and 7M ammonia in methanol (1.5 mL). The reaction was at room temperature for 20 h at which point the solution was concentrated to dryness. The residue was dissolved in methanol containing 10% triethylamine (v/v) and concentrated to dryness (twice). The solution was then azeotropically dried with CH_3CN (three times), and dried over P_2O_5 under high vacuum for 2 h. Next, THF (0.22 mL) was added followed by tetrabutylammonium fluoride (0.1 mL of a 1 M solution in THF, 0.11 mmol, 33 eq). The reaction was stirred for 3 h at room temperature. The reaction was concentrated to a total volume of ~0.1 mL, 0.1 mL of a 3M aqueous NaOAc solution was added, and the solution was stirred for 0.5 h. The solution was transferred in 0.1 mL aliquots to 1.7 mL centrifuge tubes and 0.95 mL of ethanol was added to each tube. The tubes were cooled to -78^{o}C for 0.5 h and were centrifuged at 4^{o}C for 20 min at 14,000 rcf. The supernatant was discarded and the pellet was resuspended in 1 mL of fresh ethanol. The tubes were again cooled at -78^{o}C and centrifuged as described above. The pellet was dissolved in 1 mL of water and purified by reverse phase chromatography (99% 8 mM Et_3NHOAc/1% CH_3CN to 90% 8 mM Et_3NHOAc/10% CH_3CN over 12 min). The fractions containing the product were concentrated to dryness followed by repeated lyophillization with H_2O and exchange for the

sodium salt (Dowex 50W-X8 Na^+ form) to produce compound **1** (3.0 mg, 77%) as the sodium salt.

Note: NMR Data for compound **1** was obtained before exchange for the Na^+ ion and contains ~10 eq of Et_3NHOAc. It was observed that removal of the buffer beyond this point caused dramatic suppression of the NMR signal, which we believe is due to a compound aggregation phenomenon. Addition of a solution containing ~10 eq Et_3NHOAc in D_2O to buffer-free samples of **1** restored its NMR signal.

^{1}H NMR (600 MHz, D_2O) δ 8.47 (bs, 2H), 8.24 (bs, 2H), 6.22 (d, *J* = 3.1 Hz, 1H), 6.03 (d, *J* = 5.6 Hz, 1H), 5.35 (d, *J* = 4.1 Hz, 1H), 5.33 (d, *J* = 4.3 Hz, 1H), 5.23 (d, J = 2.2 Hz, 1H), 4.71 (appt, *J* = 5.7 Hz, 1H), 4.65-4.61 (m, 1H), 4.60 – 4.56 (m, 1H), 4.52 – 4.49 (m, 1H), 4.43 – 4.38 (m, 1H), 4.38 – 4.33 (m, 3H), 4.33 – 4.30 (m, 1H), 4.29 – 4.17 (m, 7H), 4.13 – 4.01 (m, 9H).

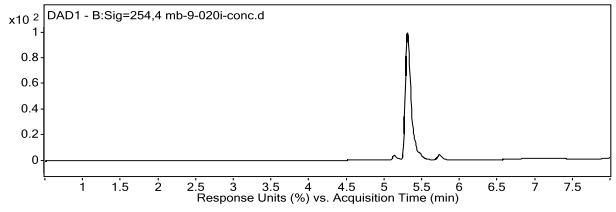
^{13}C NMR (125 MHz, D_2O) δ See table; assignments and shifts from HSQC/HMBC.

^{31}P NMR (243 MHz, D_2O) δ -9.65 - -11.98 (m, 4P)

HRMS (ESI) m/z calcd for $C_{30}H_{43}N_{10}O_{27}P_4$ ($[M-H]^-$) 1099.1255 found 1099.1221.

LCMS:

tR = 5.3 min, 98% 5 mM pentylamine:HOAc (pH=6.5) with 2% CH_3CN to 75% 6 mM pentylamine:HOAc (pH=6.5) with 25% CH_3CN over 5 min, then hold 75% 6 mM pentylamine:HOAc (pH=6.5) with 25% CH_3CN for 3 min



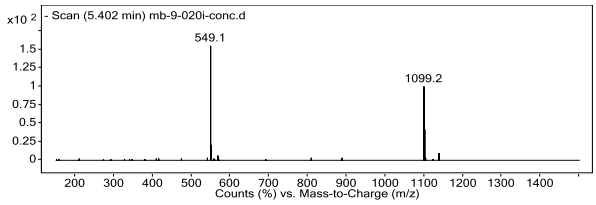
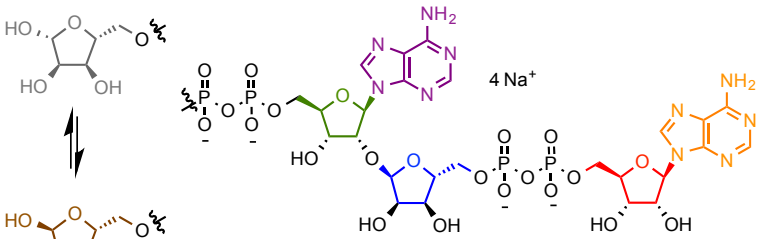
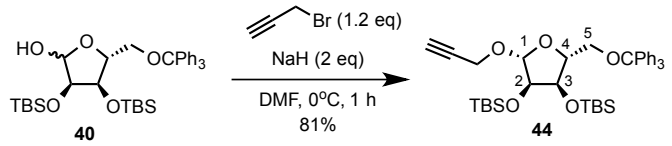


Table of NMR Data:

	^{1}H	^{13}C	^{1}H-^{1}H COSY	^{1}H-^{13}C HMBC
I-Ado 1'	6.03 (d, *J* = 5.9 Hz)	87.23	4.71	74.63, 140.45, 148.3
I-Ado 2'	4.71 (at, 5.4 Hz)	74.63	6.03, 4.51	84.02, 87.23
I-Ado 3'	4.51 (dd, *J* = 4.9, 3.3 Hz)	70.63	4.71, 4.37	65.01, 87.25
I-Ado 4'	4.36	84.02	4.51	65.01
I-Ado 5'a	4.22	65.01		
I-Ado 5'b	4.22			
I-Ade 2	8.25	150.45	-	118.24, 148.33, 153.81
I-Ade 4	-	148.33	-	-
I-Ade 5	-	118.24	-	-
I-Ade 6	-	153.81	-	-
I-Ade 8	8.47	140.45	-	118.49, 148.36
D-Rib 1''	5.33 (d, *J* = 4.3 Hz)	101.42		69.88, 71.67, 78.92, 84.31,
D-Rib 2''	4.27	71.48		84.52
D-Rib 3''	4.23	69.94		84.31, 65.67
D-Rib 4''	4.36	84.31		
D-Rib 5''a	4.07	65.8		
D-Rib 5''b	4.07			
D-Ado 1'	6.22 (d, *J* = 3.1 Hz)	87.04	4.63	140.45
D-Ado 2'	4.63 (m)	78.94	6.22, 4.58	101.34, 83.21
D-Ado 3'	4.58 (m)	68.94	4.63, 4.40	64.52, 86.94
D-Ado 4'	4.40	83.15	4.58	
D-Ado 5'a	4.35	64.49		68.94
D-Ado 5'b	4.25*			
D-Ade 2	8.25	150.45	-	118.24, 148.33, 153.81
D-Ade 4	-	148.33	-	-
D-Ade 5	-	118.24	-	-
D-Ade 6	-	153.81	-	-
D-Ade 8	8.47	140.45	-	118.49, 148.36
α Rib 1''	5.35 (d, *J* = 4.1 Hz)	96.40	4.13	70.09, 81.87
α Rib 2''	4.14	70.81		
α Rib 3''	4.19	70.11		96.36, 65.67
α Rib 4''	4.24	81.92		
α Rib 5''a	4.07	65.8		
α Rib 5''b	4.04			
β Rib 1''	5.23 (d, *J* = 2.2 Hz)	101.23	4.03	70.72, 81.26
β Rib 2''	4.03	75.22	4.32, 5.23	81.16
β Rib 3''	4.32	70.55	4.03	66.38, 101.28
β Rib 4''	4.10	81.19		
β Rib 5''a	4.13	66.41		
β Rib 5''b	4.07			



1 (ADP-Ribose Dimer)

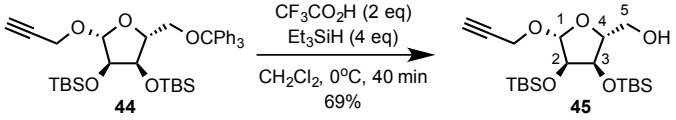


Compound 44: To a 0°C solution of compound **40** (90 mg, 0.145 mmol, 1 eq) in DMF (1 mL) was added sodium hydride (60% dispersion in mineral oil, 12.8 mg, 0.322 mmol, 2.2 eq) followed by propargyl bromide (0.027 mL, 0.242 mmol, 1.7 eq). The solution was stirred at 0°C for 1 h at which time it was poured into saturated aqueous NH_4Cl and extracted three times with diethyl ether. The combined ether extracts were washed three times with water, dried through Na_2SO_4, concentrated and purified by silica column chromatography to afford compound **44** (80 mg, 81%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 – 7.49 (m, 6H, -CPh_3), 7.33 – 7.27 (m, 6H, -CPh_3), 7.26 – 7.20 (m, 3H), 5.12 (s, 1H, H-1), 4.33 (dd, *J* = 2.4, 1.6 Hz, 2H, -C*H*$_2$CCH), 4.24 – 4.17 (m, 2H, H-3, H-4), 3.98 (d, *J* = 2.8 Hz, 1H, H-2), 3.37 (dd, *J* = 10.2, 1.7 Hz, 1H, H-5a), 3.09 – 3.00 (m, 1H, H-5b), 2.44 (t, *J* = 2.4 Hz, 1H, -CH_2CC*H*), 0.93 (s, 9H, -tBu), 0.72 (s, 9H, -tBu), 0.13 (s, 3H, -CH_3), 0.09 (s, 3H-CH_3), -0.05 (s, 3H-CH_3), -0.25 (s, 3H-CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 144.1, 128.9, 127.9, 127.0, 105.3, 86.4, 81.5, 79.4, 76.3, 74.6, 71.9, 64.0, 54.5, 25.9, 25.9, 18.2, 18.0, -4.1, -4.3, -4.6, -5.1.

HRMS (ESI) m/z calcd for $C_{39}H_{54}O_5Si_2Na$ ([M+Na]$^+$) 681.3408, found 681.3408.

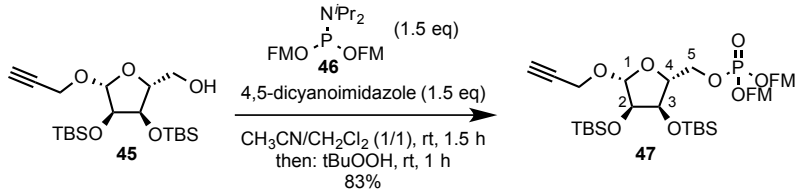


Compound 45: To a 0°C solution of compound **44** (80 mg, 0.121 mmol, 1 eq) in CH_2Cl_2 (1 mL) was added triethylsilane (0.077 mL, 0.486 mmol, 1 eq) followed by a solution of trifluoroacetic acid (28 mg, 0.243 mmol, 2 eq) in CH_2Cl_2 (0.1 mL) and the reaction was stirred at 0°C for 40 min. The reaction was quenched with saturated aqueous $NaHCO_3$ (1 mL), extracted three times with chloroform, dried through Na_2SO_4, concentrated and purified by silica column chromatography to afford compound **45** (35 mg, 69%) as a white foam.

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.95 (s, 1H, H-1), 4.33 – 4.18 (m, 3H, -C*H*$_2$CCH, H-3), 4.10 – 4.03 (m, 1H, H-4), 3.95 (d, *J* = 4.0 Hz, 1H, H-2), 3.85 (dd, *J* = 12.2, 2.5 Hz, 1H, H-5a), 3.57 (dd, *J* = 12.2, 3.5 Hz, 1H, H-5b), 2.46 (t, *J* = 2.4 Hz, 1H, -CH_2CC*H*), 1.88 (bs, 1H, -OH), 0.91 (s, 9H, -tBu), 0.89 (s, 9H, -tBu), 0.10 (s, 6H, -CH_3), 0.09 (s, 3H, -CH_3), 0.08 (s, 3H, -CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 106.6, 82.8, 79.7, 76.7, 74.7, 70.6, 61.5, 55.4, 26.0, 25.9, 18.2, 18.2, -4.1, -4.4, -4.5, -4.9.

HRMS (ESI) m/z calcd for $C_{20}H_{41}O_5Si_2$ ([M+H]$^+$) 417.2493, found 417.2489.



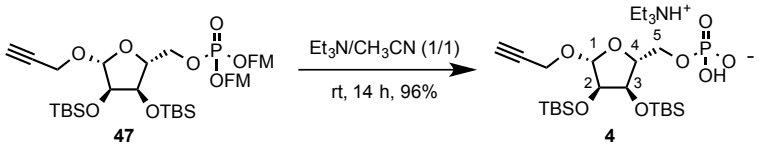
Compound 47: To a room temperature solution of compound **45** (10 mg, 0.024 mmol, 1 eq) in CH_2Cl_2 (0.3 mL) was added phosphoramidite **46** (18.8 mg, 0.036 mmol, 1.5 eq) in CH_2Cl_2 (0.1 mL) followed by 4,5-dicyanoimidazole (4.2 mg, 0.036 mmol, 1.5 eq) in CH_3CN (0.4 mL). The reaction was stirred at room temperature for 1.5 h, at which point tBuOOH (0.021 mL of 5.5 M solution, 0.12 mmol, 5 eq) was added and the reaction was stirred for an additional 1 h. The reaction was poured into saturated aqueous $NaHCO_3$, extracted three times with chloroform, dried through Na_2SO_4, concentrated and purified by silica column chromatography to give compound **47** (17 mg, 83%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.67 (m, 4H, -FM), 7.60 – 7.48 (m, 4H, -FM), 7.43 – 7.31 (m, 4H, -FM), 7.30 – 7.20 (m, 4H, -FM), 4.95 (s, 1H, H-1), 4.32-4.24 (m, 4H, -C*H*$_2$CHAryl), 4.22 – 4.03 (m, 7H, -CH_2C*H*Aryl + H-4 + H-5a + H-3, -C*H*$_2$CCH), 3.96 (appdt, *J* = 10.6, 5.1 Hz, 1H, H-5b), 3.92 (d, *J* = 3.8 Hz, 1H, H-2), 2.28 (t, *J* = 2.4 Hz, 1H, -CH_2CC*H*), 0.89 (s, 9H, -tBu), 0.86 (s, 9H, -tBu), 0.09 (s, 3H, -CH_3), 0.08 (s, 3H, -CH_3), 0.03 (s, 3H, -CH_3), 0.00 (s, 3H, -CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3, 141.5, 128.0, 127.2, 125.3, 120.1, 104.9, 80.4 (d, *J* = 7.8 Hz), 79.2, 76.3, 74.7, 71.4, 69.5 (appt, *J* = 6.3 Hz), 67.2 (d, *J* = 5.2 Hz), 54.1, 48.1 (d, *J* = 8.1 Hz), 25.9, 25.9, 18.2, 18.1, -4.1, -4.4, -4.5, -5.0.

^{31}P NMR (202 MHz, CD_3OD) δ -0.80

HRMS (ESI) m/z calcd for $C_{48}H_{62}O_8PSi_2$ ([M+H]$^+$) 853.3721, found 853.3718.



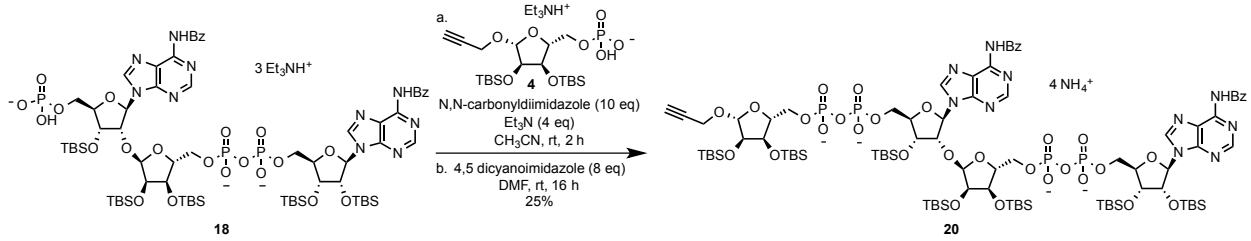
Compound 4: To a room temperature solution of compound **47** (17 mg, 0.020 mmol, 1 eq) in CH_3CN (0.4 mL) was added Et_3N (0.2 mL). The solution was stirred for 14 h at which point it was evaporated and purified by C-18 chromatography to give compound **4** (11.5 mg, 96%).

^{1}H NMR (500 MHz, CD_3OD) δ 5.05 (d, *J* = 1.3 Hz, 1H, H-1), 4.34 (dd, *J* = 16.1, 2.4 Hz, 1H, -C*H*$_2$CCH), 4.28 – 4.20 (m, 2H, -C*H*$_2$CCH + H-3), 4.10 – 4.02 (m, 2H, H-4 + H-5a), 3.98 (dd, *J* = 4.1, 1.3 Hz, 1H, H-2), 3.81 (ddd, *J* = 11.3, 6.7, 4.2 Hz, 1H, H-5b), 3.19 (q, *J* = 7.3 Hz, 6H, (CH_3C*H*$_2$)$_3$N), 2.81 (appt, *J* = 2.4 Hz, 1H, -CH_2CC*H*), 1.31 (t, *J* = 7.3 Hz, 9H(C*H*$_3$CH$_2$)$_3$N), 0.93 (s, 9H, -tBu), 0.92 (s, 9H, -tBu), 0.14 (s, 3H, -CH_3), 0.13 (s, 3H, -CH_3), 0.12 (s, 3H, -CH_3), 0.11 (s, 3H, -CH_3).

^{13}C NMR (126 MHz, CD_3OD) δ 105.5, 83.5 (d, *J* = 9.0 Hz), 80.2, 77.8, 75.7, 73.5, 66.5 (d, *J* = 5.6 Hz) 54.7, 47.8, 26.5, 26.4, 19.0, 18.9, 9.2, -4.1, -4.3, -4.3, -4.6.

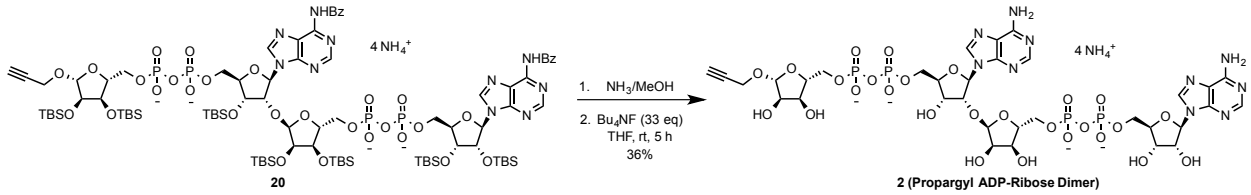
^{31}P NMR (202 MHz, CD_3OD) δ 2.11

HRMS (ESI) m/z calcd for $C_{20}H_{40}O_8PSi_2$ ([M-H]$^-$) 495.2005, found 495.1999.



Compound 20: To a 4 mL reaction vial was added compound **4** (4.3 mg, 7.2 μmol, 2 eq) and the compound was azeotroped three times with CH_3CN and dried under high vacuum. Compound **4** was dissolved in CH_3CN (0.2 mL) and Et_3N (1.5 mg, 14.4 μmol, 4 eq). N,N-carbonyldiimidazole (5.8 mg, 36 μmol, 10 eq) was added and the reaction stirred for 2 h at room temperature. Excess carbonydiimidazole was quenched using 10% Et_3N in methanol (0.2 mL) and the crude reaction was concentrated to dryness. Compound **18** (7.0 mg, 3.6 μmol, 1 eq) was added and the solution was azeotroped three times with CH_3CN and dried under high vacuum. The coupling reaction was initiated by addition of of 4,5-dicyanoimidazole (3.4 mg, 29 μmol, 8 eq) in DMF (0.2 mL) and was stirred for 16 h at room temperature. The crude reaction was applied to a column of silica and eluted using a gradient of 90:0:10 iPrOH:H_2O:NH_4OH to 70:20:10 iPrOH:H_2O:NH_4OH to give compound **20** as the ammonium salt (2.0 mg, 25%) and an inseparable by-product resulting from dimerization of compound **4**.

HRMS (ESI) m/z calcd for $C_{89}H_{152}N_{10}O_{29}P_4Si_7$ ([M-H]$^-$) 2144.8012, found 2144.7959.



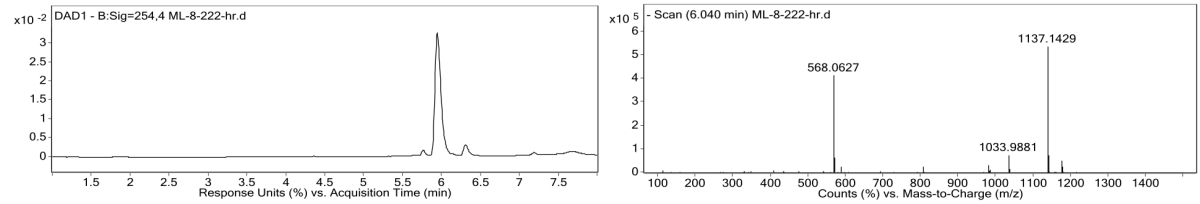
Compound 2: To a 4 mL reaction vial was added compound **20** (2.0 mg, 0.903 μmol, 1 eq) and NH_3/MeOH (0.2 mL of a 7M solution). The solution was stirred for 14 h, the solvent was evaporated and 0.5 mL of 40% Et_3N in MeOH was added and subsequently evaporated. A solution of Bu_4NF (0.2 mL of 1M solution in THF) was added and the reaction was stirred for 5 h at room temperature. To the solution was added 0.2 mL of a 3M aqueous NaOAc solution and the solution stirred for 20 min. Ethanol (0.5 mL) was added, the solution was aliquoted into centrifuge tubes and put into a -80^{o}C freezer. The tubes were centrifuged for 5 min at 14,000 rcf, the supernatant was discarded, ethanol was again added and the tubes were again centrifuged. The pellet was dissolved in water and purified by preparative HPLC (99% 8 mM Et_3NHOAc/1% CH_3CN to 90% 8 mM Et_3NHOAc/10% CH_3CN over 12 min). The fractions containing the product were concentrated to dryness followed by repeated lyophillization with H_2O and exchange for the ammonium salt (Dowex 50W-X8 NH_4^+ form) to produce compound **2** (0.4 mg, 36%) as the ammonium salt.

^{1}H NMR (600 MHz, D_2O) δ 8.41 (s, 1H), 8.39 (s, 1H), 8.17 (s, 1H), 8.16 (s, 1H), 6.19 (d, *J* = 3.3 Hz, 1H), 6.02 (d, *J* = 6.0 Hz, 1H), 5.31 (d, *J* = 4.2 Hz, 1H), 5.10 (s, 1H), 4.68 (appt, *J* = 5.6 Hz, 1H), 4.65 (q, *J* = 2.5 Hz, 1H), 4.61 (appt, *J* = 5.7 Hz, 1H), 4.52 – 4.48 (m, 1H), 4.42 – 4.17 (m, 13H), 4.17-4.06 (m, 3H), 4.03 (d, *J* = 4.6 Hz, 1H), 4.00-3.94 (m, 1H), 2.82 (s, 1H).

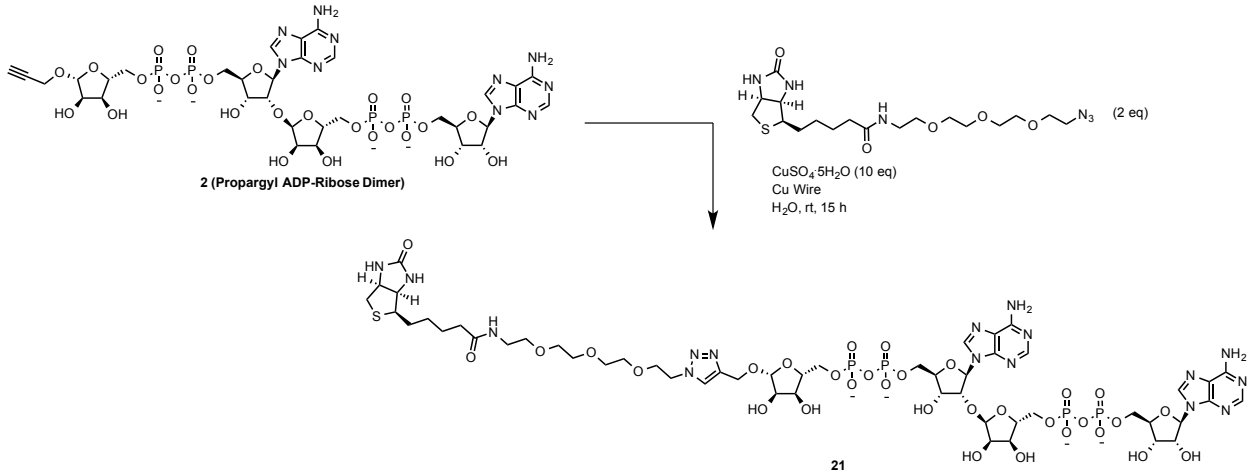
^{31}P NMR (243 MHz, D_2O) δ -10.55 – -11.90 (m, 4P).

HRMS (ESI) m/z calcd for $C_{33}H_{46}N_{10}O_{27}P_4$ ([M-H]$^-$) 1137.1412, found 1137.1423.

LCMS:
tR = 6.0 min, 98% 5 mM pentylamine:HOAc (pH=6.5) with 2% CH_3CN to 75% 6 mM pentylamine:HOAc (pH=6.5) with 25% CH_3CN over 5 min, then hold 75% 6 mM pentylamine:HOAc (pH=6.5) with 25% CH_3CN for 3 min



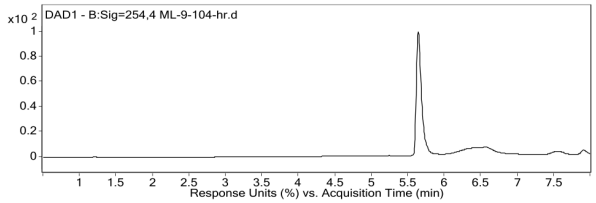
Note: m/z = 1033.9 corresponds to a component of the reference mixture

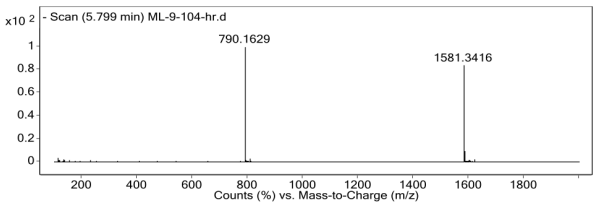


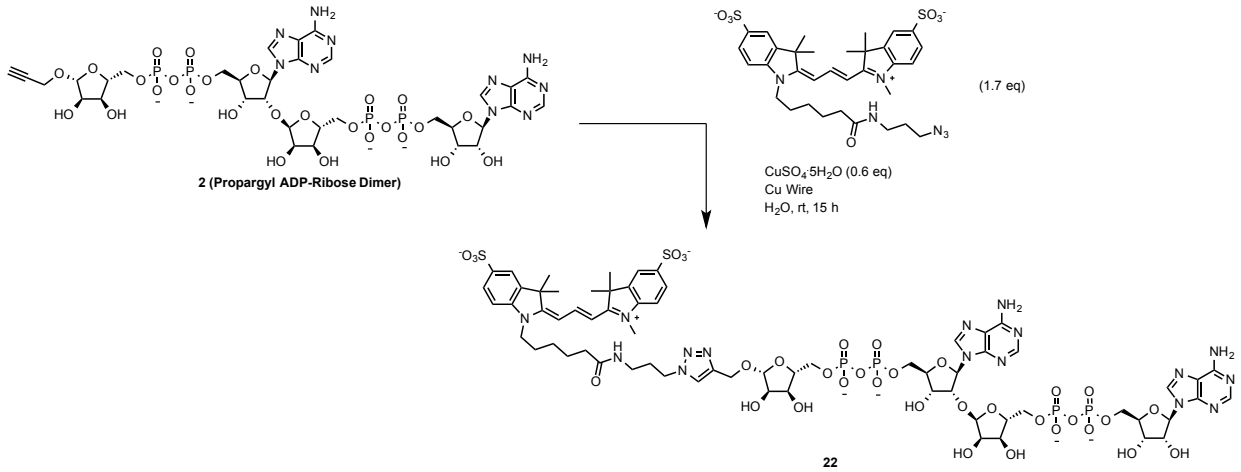
Compound 21: To a well of a 384 well plate was added a solution of compound **2** (10 μL of a 2 mM aqueous solution, 0.002 μmol, 1 eq), a solution of Peg_3-biotin-N_3 (10 μL of a 4 mM aqueous solution, 0.004 μmol, 2 eq), a solution of $CuSO_4 \cdot 5H_2O$ (10 μL of a 20 mM aqueous solution) and copper wire (3.2 mg). The solution was diluted to a final volume of 50 μL and incubated at room temperature overnight. The solution was purified by reverse phase HPLC (99% 8 mM Et_3NHOAc/1% CH_3CN to 70% 8 mM Et_3NHOAc/30% CH_3CN over 12 min) to give compound **21**. Compound **21** was >95% pure by LC/MS analysis when background absorbance was subtracted.

HRMS (ESI) m/z calcd for $C_{51}H_{78}N_{16}O_{32}P_4S$ ([M-H]$^-$) 1581.3566, found 1581.3615.

LCMS: tR = 5.80 min, 98% 5 mM pentylamine:HOAc (pH=6.5) with 2% CH_3CN to 65% 6 mM pentylamine:HOAc (pH=6.5) with 35% CH_3CN over 5 min, then hold 65% 6 mM pentylamine:HOAc (pH=6.5) with 35% CH_3CN for 3 min



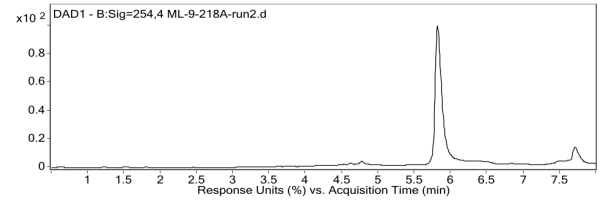


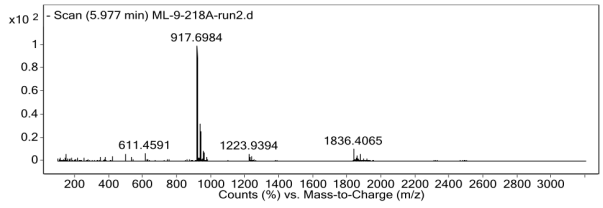


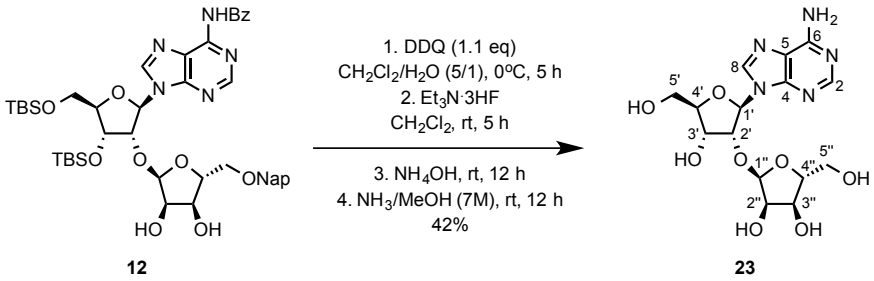
Compound 22: To a 500 μL eppendorf tube was added copper wire (2 mg). A solution of compound **2** (50 μL of a 3.1 mM solution, 0.16 μmol, 1 eq), a solution of sulfoCy3-N_3 (20 μL of a 10 mg/mL solution, 0.27 μmol, 1.7 eq) and a solution of $CuSO_4 \cdot 5H_2O$ (50 μL of a 0.5 mg/mL solution, 0.1 μmol, 0.6 eq). The reaction was incubated at room temperature for 15 h and purified by HPLC (99% 8 mM Et_3NHOAc/1% CH_3CN to 70% 8 mM Et_3NHOAc/30% CH_3CN over 12 min) to give compound **22**. Compound **22** was >95% pure by LC/MS analysis when background absorbance was subtracted.

HRMS (ESI) m/z calcd for $C_{66}H_{89}N_{16}O_{34}P_4S_2$ ($[M-H]^-$) 1836.4046, found 1836.4058.
m/z calcd for $C_{66}H_{89}N_{16}O_{34}P_4S_2$ ($[M-2H]^2$) 917.6987, found 917.6983.

LCMS:
tR = 5.97 min, 98% 5 mM pentylamine:HOAc (pH=6.5) with 2% CH_3CN to 65% 6 mM pentylamine:HOAc (pH=6.5) with 35% CH_3CN over 5 min, then hold 65% 6 mM pentylamine:HOAc (pH=6.5) with 35% CH_3CN for 3 min







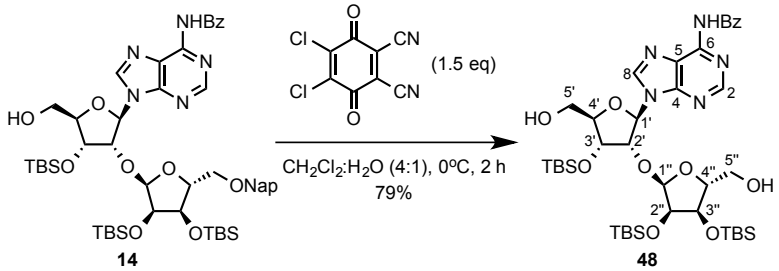
12 23

Compound 23: To a 4 mL reaction vial was added compound **12** (50 mg, 0.057 mmol, 1 eq), CH_2Cl_2 (1.3 mL), and H_2O (0.26 mL). The solution was cooled to 0 ^oC, and 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (14.3 mg, 0.063 mmol, 1.1 eq) was added. The reaction was stirred at 0 ^oC for 3 h, at which point an additional 1.1 eq of 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone was added and the reaction stirred for 1 h. The reaction was quenched with a saturated aqueous $Na_2S_2O_3$ solution, extracted three times with EtOAc, filtered through Na_2SO_4 and concentrated. The crude reaction mixture was dissolved in CH_2Cl_2 (0.2 mL), $Et_3N{\cdot}3HF$ (46 μL, 0.285 mmol, 5 eq) was added, and the reaction stirred at room temperature for 5 h. Next, NH_4OH (0.16 mL of a 25% solution) was added and the reaction stirred for 12 h. The crude reaction was poured into CH_2Cl_2, extracted three times with water and concentrated. Silica column chromatography was performed revealing two compounds (Rf = 0.38 and 0.15 in 80:20 CH_2Cl_2:MeOH). The mixture was treated with NH_3/MeOH (0.3 mL of a 7 M solution) for 12 h. Next, Dowex 50W-X8 (Na^+ form) was added and stirred for 15 min. The mixture was filtered through a cotton plug, concentrated and purified by silica column chromatography (R_f 0.15 in 80:20 CH_2Cl_2:MeOH) to furnish compound **23** as a yellow oil (9.5 mg, 42%).

^{1}H NMR (500 MHz, D_2O) δ 8.33 (s, 1H, H-2), 8.20 (s, 1H, H-8), 6.19 (d, *J* = 6.2 Hz, 1H, H-1'), 5.07 (d, *J* = 4.1 Hz, 1H, H-1''), 4.88 (dd, *J* = 6.3, 5.2 Hz, 1H, H-2'), 4.54 (dd, *J* = 5.2, 3.0 Hz, 1H, H-3'), 4.32 (appq, *J* = 3.1 Hz, 1H, H-4'), 4.20 (appdt, *J* = 4.9, 3.4 Hz, 1H, H-4''), 4.10 – 4.02 (m, 2H, H-2'' + H-3''), 3.92 (dd, *J* = 12.9, 2.7 Hz, 1H, H-5'a), 3.84 (dd, *J* = 12.9, 3.5 Hz, 1H, H-5'b), 3.68 (dd, *J* = 12.5, 3.6 Hz, 1H, H-5''a), 3.61 (dd, *J* = 12.5, 4.8 Hz, 1H, H-5''b).

^{13}C NMR (125 MHz, D_2O) δ 156.3, 153.2, 149.0, 141.4, 119.8, 102.6, 87.7, 86.9, 86.1, 79.8, 72.2, 71.6, 70.4, 62.2, 62.1.

HRMS (ESI) m/z calcd for $C_{15}H_{22}N_5O_8$ ($[M+H]^+$) 400.1477, found 400.1468.



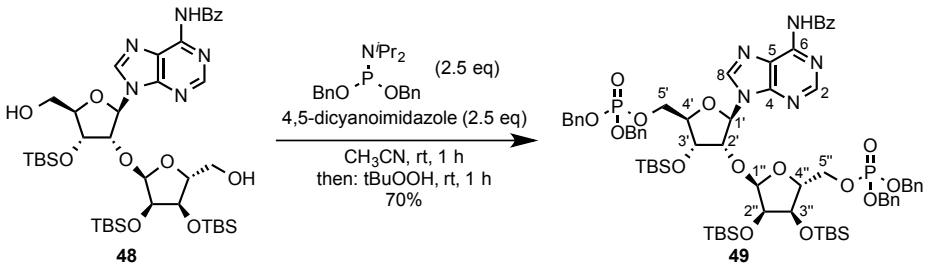
14 48

Compound 48: To a 0°C solution of compound **14** (50 mg, 0.051 mmol, 1 eq) in CH_2Cl_2 (0.9 mL) and H_2O (0.2 mL) was added 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (17.3 mg, 0.076 mmol, 1.5 eq). The solution was stirred at 0°C for 2 h, poured into saturated aqueous $Na_2S_2O_3$, extracted three times with ethyl acetate, dried through Na_2SO_4, concentrated and purified by silica column chromatography to afford compound **48** (34 mg, 79%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.19 (s, 1H, -N*H*Bz), 8.79 (s, 1H, H-8), 8.09 (s, 1H, H-2), 8.02 (d, J = 7.7 Hz, 2H, -Bz), 7.62 (t, J = 7.5 Hz, 1H, -Bz), 7.53 (t, J = 7.7 Hz, 2H, -Bz), 6.07 (d, J = 7.6 Hz, 1H, H-1'), 5.02 (dd, J = 7.7, 4.3 Hz, 1H, H-2'), 4.82 (d, J = 3.1 Hz, 1H, H-1''), 4.59 (d, J = 4.3 Hz, 1H, H-3'), 4.21 (s, 1H, H-4'), 4.10 (d, J = 6.7 Hz, 1H, H-3''), 4.02 – 3.91 (m, 2H, H-4'' + 5'a), 3.87 – 3.69 (m, 3H, 2'' + 5'b + 5''a), 3.53 (d, J = 12.1 Hz, 1H, H-5''b), 0.94 (s, 9H, -tBu), 0.88 (s, 9H, -tBu), 0.85 (s, 9H, -tBu), 0.16 (s, 3H, -CH_3), 0.13 (s, 3H, -CH_3), 0.03 (s, 3H, -CH_3), 0.01 (s, 3H, -CH_3), -0.00 (s, 3H, -CH_3), -0.05 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 152.4, 150.8, 150.5, 143.9, 133.7, 133.2, 129.2, 128.1, 124.7, 104.9, 89.7, 89.1, 82.8, 81.9, 73.9, 73.5, 70.6, 63.0, 60.9, 26.3, 26.2, 26.2, 18.8, 18.4, 18.4, -3.9, -4.0, -4.1, -4.4, -4.7.

HRMS (ESI) m/z calcd for $C_{40}H_{68}N_5O_9Si_3$ ($[M+H]^+$) 846.4325, found 846.4318.



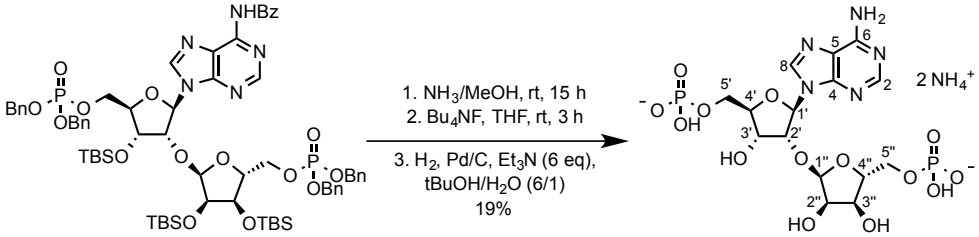
Compound 49: To a dry 4 mL reaction vial was added compound **48** (19.0 mg, 0.0225 mmol, 1 eq) and dibenzyl N,N-diisopropylphosphoramidite (19.4 mg, 0.562 mmol, 2.5 eq). The compounds were co-evaporated three times on a N_2-filled rotary evaporator with dry CH_3CN and then dried over P_2O_5 overnight. Separately, 4,5-dicyanoimidazole (6.6 mg, 0.0562 mmol, 2.5 eq) was evaporated and dried in a similar manner. To compound **48** and the phosphoramidite was added dry CH_3CN (0.1 mL), followed by a solution of the 4,5-dicyanoimidazole in CH_3CN (0.1 mL) at room temperature. The reaction was stirred for 1 h at which point tBuOOH (0.041 mL of a 5.5 M solution, 0.225 mmol, 10 eq) was added and the reaction stirred an additional hour. The reaction was quenched with saturated aqueous $NaHCO_3$, extracted three times with ethyl acetate, dried through Na_2SO_4, and purified by silica column chromatography to give compound **49** (21.5 mg, 70%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.96 (bs, 1H, -N*H*Bz) 8.69 (s, 1H, H-8), 8.24 (s, 1H, H-2), 7.98 (d, *J* = 7.5 Hz, 2H, -Bz), 7.63 – 7.56 (m, 1H, -Bz), 7.51 (t, *J* = 7.7 Hz, 2H, -Bz), 7.37 – 7.25 (m, 20H, -Bn), 6.11 (d, *J* = 2.8 Hz, 1H, H-1'), 5.19 (d, *J* = 3.7 Hz, 1H, H-1''), 5.03 – 4.88 (m, 8H, -C*H*$_2$Ph), 4.71 (dd, *J* = 4.5, 2.9 Hz, 1H, H-2'), 4.46 (dd, *J* = 6.6, 4.5 Hz, 1H, H-3'), 4.35 (ddd, *J* = 11.4, 5.7, 3.4 Hz, 1H, H-5'a), 4.28 – 4.23 (m, 1H, H-4''), 4.18 (dd, *J* = 4.5, 2.7 Hz, 1H, H-4'), 4.15 – 4.05 (m, 2H, H-5'b, H-5''a), 3.97 (ddd, *J* = 11.2, 5.8, 3.6 Hz, 1H, H-5''b), 3.93 (appt, *J* = 4.9 Hz, 1H, H-3''), 3.89 (dd, *J* = 5.3, 3.7 Hz, 1H, H-2''), 0.84 (s, 18H, -tBu), 0.79 (s, 9H, -tBu), 0.05 (s, 3H, -CH_3), 0.03 (s, 3H, -CH_3), 0.00 (s, 3H, -CH_3), -0.02 (s, 3H, -CH_3), -0.04 (s, 3H, -CH_3), -0.06 (s, 3H, -CH_3).

^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 152.8, 151.2, 149.6, 142.2, 136.01 – 135.87 (m), 135.80 (d, *J* = 6.7 Hz), 133.0, 129.1, 128.8, 128.1, 120.2, 103.5, 88.7, 82.87 (d, *J* = 8.0 Hz), 82.26 (d, *J* = 8.3 Hz), 80.7, 73.6, 71.0, 70.3, 69.79 – 69.55 (m), 69.7 – 69.4 (m), 66.8 (d, *J* = 5.4 Hz), 65.5 (d, *J* = 5.3 Hz), 26.2, 26.0, 18.5, 18.3, 18.3, -4.1, -4.3, -4.4, -4.4, -4.5, -4.8.

^{31}P NMR (202 MHz, $CDCl_3$) δ 0.17, 0.05

HRMS (ESI) m/z calcd for $C_{66}H_{95}N_5O_{15}Si_3P_2Na$ ($[M+Na]^+$) 1366.5506, found 1366.5494.



49 **24**

Compound 24: To a 7 mL reaction vial containing compound **49** (24 mg, 0.0176 mmol, 1 eq) was added ammonia solution (0.5 mL of a 7M solution in MeOH) and the reaction was stirred at room temperature for 15 h. The reaction was evaporated and THF (0.2 mL) and tetrabutylammonium fluoride (0.11 mL of a 1M solution in THF, 0.11 mmol, 6 eq) was added and the reaction was stirred at room temperature for 3 h at which time the solution was concentrated and run through a short column of silica. The eluent was collected, concentrated and transferred to a 7 mL reaction vial. Palladium on carbon (10 mg) was added followed by tBuOH (0.2 mL), water (0.03 mL) and triethylamine (11 mg, 0.109 mmol, 6 eq). A balloon filled with hydrogen was fitted to the flask and stirred at room temperature for 16 h. The solution was filtered through celite, concentrated and purified by preparative HPLC (gradient of 99% 8 mM Et_3NHOAc/1% CH_3CN to 90% 8 mM Et_3NHOAc/10% CH_3CN). The fractions containing product were combined, concentrated and exchanged for the NH_4^+ cation using a Dowex 50W-X8 cation exchange column to give compound **24** (2.0 mg, 19%).

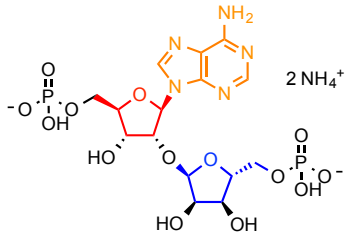
^{1}H NMR (500 MHz, D_2O) δ 8.57 (s, 1H, H-8), 8.27 (s, 1H, H-2), 6.29 (d, *J* = 5.6 Hz, 1H, H-1'), 5.22 (d, *J* = 4.1 Hz, 1H, H-1''), 4.86 (dd, *J* = 5.5, 5.2 Hz, 1H, H-2'), 4.62 (dd, *J* = 5.2, 3.6 Hz, 1H, H-3'), 4.45 – 4.39 (m, 1H, H-4'), 4.34 (appdt, *J* = 4.1, 2.2 Hz, 1H, H-4''), 4.18-4.16 (m, 2H, H-2'' + H-3''), 4.13 – 4.02 (m, 2H, H-5'a + H-5'b), 3.90 (ddd, *J* = 11.5, 5.9, 4.0 Hz, 1H, H-5''a), 3.84 (dt, *J* = 11.4, 4.3 Hz, 1H, H-5''b).

^{13}C NMR (125 MHz, D_2O) δ ^{13}C shifts determined from HSQC/HMBC, see table.

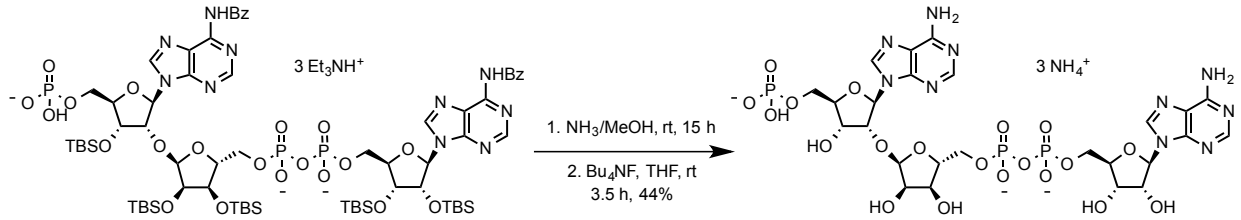
^{31}P NMR (242 MHz, D_2O) δ 2.12-1.92 (m, 2P)

HRMS (ESI) m/z calcd for $C_{15}H_{22}N_5O_{14}P_2$ ($[M-H]^-$) 558.0644, found 558.0637.

	^{1}H	^{13}C	^{31}P
Ado 1'	6.29 (d, *J* = 5.6 Hz)	86.1	
Ado 2'	4.86 (dd, *J* = 5.6, 5.2 Hz)	80.2	
Ado 3'	4.62 (dd, *J* = 4.9, 3.3 Hz)	70.8	
Ado 4'	4.42	84.9	
Ado 5'a	4.18	64.3	2.05
Ado 5'b	4.16		
Ade 2	8.27	152.6	
Ade 4	-	148.8	
Ade 5	-	118.5	
Ade 6	-	155.6	
Ade 8	8.57	140.3	
Rib 1''	5.22 (d, *J* = 4.1 Hz)	102.1	
Rib 2''	4.17	70.2	
Rib 3''	4.17	71.5	
Rib 4''	4.34	84.7	
Rib 5''a	3.90	64.5	2.05
Rib 5''b	3.84		



Compound 24



18 **25**

Compound 25: To a 7 mL vial containing compound **18** (5.7 mg, 2.9 μmol, 1 eq), was added NH_3/MeOH (0.5 mL of a 7M solution) and the reaction was stirred for 15 h. The solution was evaporated and Bu_4NF solution was added (0.2 mL of a 1 M solution in THF) and the reaction was stirred for 3.5 h. The reaction was quenched by addition of 3M aqueous NaOAc (0.2 mL) and stirred for 30 min. The solution was transferred to four 1.5 mL centrifuge tubes, EtOH (0.5 mL) was added to each tube, and the tubes were centrifuged for 5 min at 4°C and 14,000 rcf. The supernatant was discarded and the pellet was washed with EtOH (0.5 mL) and again centrifuged. The pellet was suspended in H_2O (1 mL) and purified by preparative HPLC (gradient of 99% 8 mM Et_3NHOAc/1% CH_3CN to 90% 8 mM Et_3NHOAc/10% CH_3CN). Compound **25** was obtained as the ammonium salt (1.1 mg, 44%) of the product was obtained after concentration and cation exchange (Dowex 50W-X8, NH_4^+ form).

^{1}H NMR (500 MHz, D_2O) δ 8.51 (s, 1H), 8.35 (s, 1H), 8.14 (s, 1H), 8.11 (s, 1H), 6.17 (d, *J* = 4.0 Hz, 1H), 6.00 (d, *J* = 5.9 Hz, 1H), 5.24 (d, *J* = 4.2 Hz, 1H), 4.69-4.64 (m, 2H), 4.58 (appt, *J* =

5.3 Hz, 1H), 4.47 (dd, *J* = 5.2, 3.5 Hz, 1H), 4.39 – 4.31 (m, 3H), 4.27 – 4.15 (m, 4H), 4.12 – 3.95 (m, 4H).

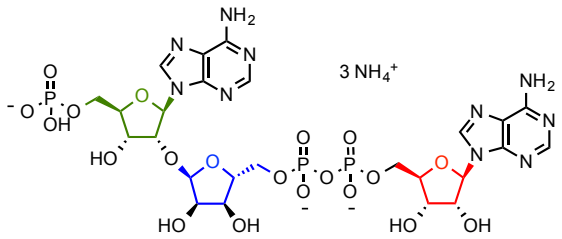
^{13}C NMR (125 MHz, D_2O) δ 155.6, 155.4, 153.0, 152.8, 148.9, 148.9, 140.1, 139.9, 118.6, 118.5, 101.7, 87.3, 86.6, 84.5, 84.5, 84.5, 79.7, 74.7, 74.6, 70.7, 70.2, 70.0, 65.8, 65.5, 64.9

Note: ^{13}C shifts determined from HSQC/HMBC

^{31}P NMR (242 MHz, D_2O) δ 3.71, -11.14 (d, *J* = 23.2 Hz), -11.27 (d, *J* = 22.1 Hz).

HRMS (ESI) m/z calcd for $C_{25}H_{35}N_{10}O_{20}P_3$ ($[M-H]^-$) 887.1169, found 887.1175.

	^{1}H	^{13}C	^{31}P
I-Ado 1'	6.00 (d, J = 5.9 Hz)	87.3	
I-Ado 2'	4.67	74.7	
I-Ado 3'	4.47 (dd, J =5.2, 3.5 Hz)	70.7	
I-Ado 4'	4.38	84.5	
I-Ado 5'a	4.22	65.5	-11.27 (d, J = 22.1 Hz)
I-Ado 5'b	4.22		
a- Rib 1''	5.24 (d, J = 4.2 Hz)	101.7	
a- Rib 2''	4.20	70.2	
a- Rib 3''	4.20	71.6	
a- Rib 4''	4.38	84.5	
a- Rib 5''a	4.09	64.9	-11.14 (d, J = 23.2 Hz)
a- Rib 5''b	4.03		
D-Ado 1'	6.17 (d, J = 4.0 Hz)	86.6	
D-Ado 2'	4.67	79.7	
D-Ado 3'	4.58 (appt, J = 5.3 Hz)	70.0	
D-Ado 4'	4.38	84.5	
D-Ado 5'a	4.09	65.8	3.71
D-Ado 5'b	4.03		



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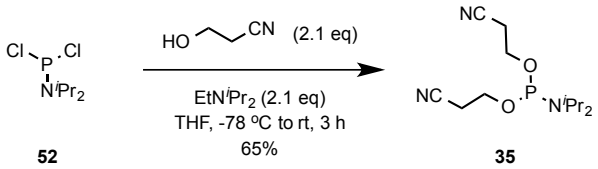


52 **35**

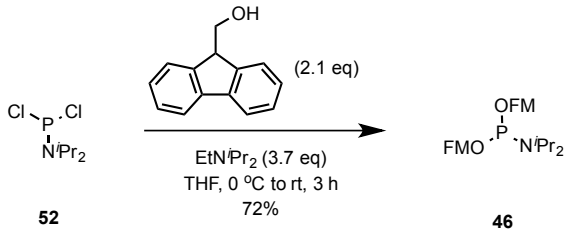
Compound 35: A modified version of the procedure of Imoto *et al.*[7,13] was followed. To a 100 mL round bottomed flask was added diisopropylphosphoramidous dichloride (**52**) (1.0 g, 4.9 mmol, 1 eq) and THF (50 mL). The solution was cooled to -78 °C, and diisopropylethylamine (1.34 g, 10.3 mmol, 2.1 eq) was added. Finally, 3-hydroxypropionitrile (735 mg, 10.3 mmol, 2.1 eq) was added dropwise at -78 °C over 10 min, and then allowed to warm to room temperature. The reaction was stirred at room temperature for 3 h. The reaction was filtered, concentrated, and purified by silica column chromatography (80:20 hexanes:ethyl aceate with 1% triethylamine) to give compound **35** (867 mg, 65%).

^{1}H NMR (500 MHz, CDCl$_3$) δ 3.95 – 3.75 (m, 4H), 3.62 (dp, *J* = 10.7, 6.8 Hz, 2H), 2.66 (t, *J* = 6.3 Hz, 4H), 1.19 (d, *J* = 6.9 Hz, 12H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 123.0, 58.8, 58.6, 43.6, 43.5, 24.9, 24.8, 20.7, 20.6.

^{31}P NMR (202 MHz, CDCl$_3$) δ 150.1

Compound **35** hydrolyzed when subjected to ESI-MS



52 **46**

Compound 46: To a 0°C solution of compound **52** (1.0 g, 4.95 mmol, 1 eq) in THF (11 mL) was added Hunig's base (3.2 mL, 18.3 mmol, 3.7 eq) and 9-fluorenemethanol (1.94 g, 9.9 mmol, 2 eq). The solution was allowed to slowly warm to room temperature, and was stirred at room temperature for 3 h. The solution was filtered through celite, concentrated and purified by silica column chromatography (hexane/ethyl acetate gradient with 2% dimethylethylamine) to give compound **46** (1.87 g, 72%) as a yellow oil.

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.79 – 7.72 (m, 4H), 7.65 (ddd, *J* = 11.9, 7.5, 1.1 Hz, 4H), 7.43 – 7.34 (m, 4H), 7.33 – 7.24 (m, 4H), 4.19 (t, *J* = 7.1 Hz, 2H), 4.01 (dt, *J* = 9.9, 6.7 Hz, 2H), 3.81 (dt, *J* = 10.0, 7.2 Hz, 2H), 3.66 (dp, *J* = 10.0, 6.8 Hz, 2H), 1.17 (s, 6H), 1.16 (s, 6H).

^{13}C NMR (126 MHz, CDCl$_3$) δ 145.2, 144.9, 141.6, 141.5, 127.6, 127.6, 127.1, 127.0, 125.7, 125.4, 120.1, 120.0, 66.2, 66.1, 49.5, 49.4, 43.3, 43.2, 24.9, 24.8.

^{31}P NMR (202 MHz, CDCl$_3$) δ 146.8

Compound **46** hydrolyzed when subjected to ESI-MS

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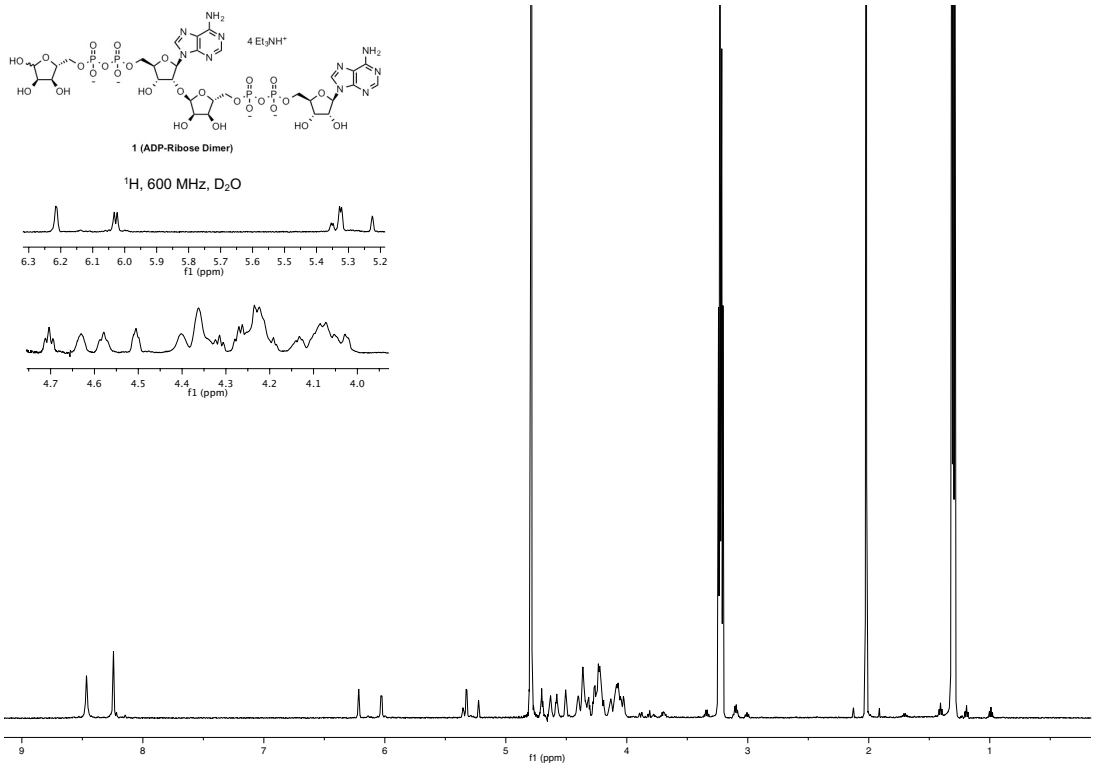
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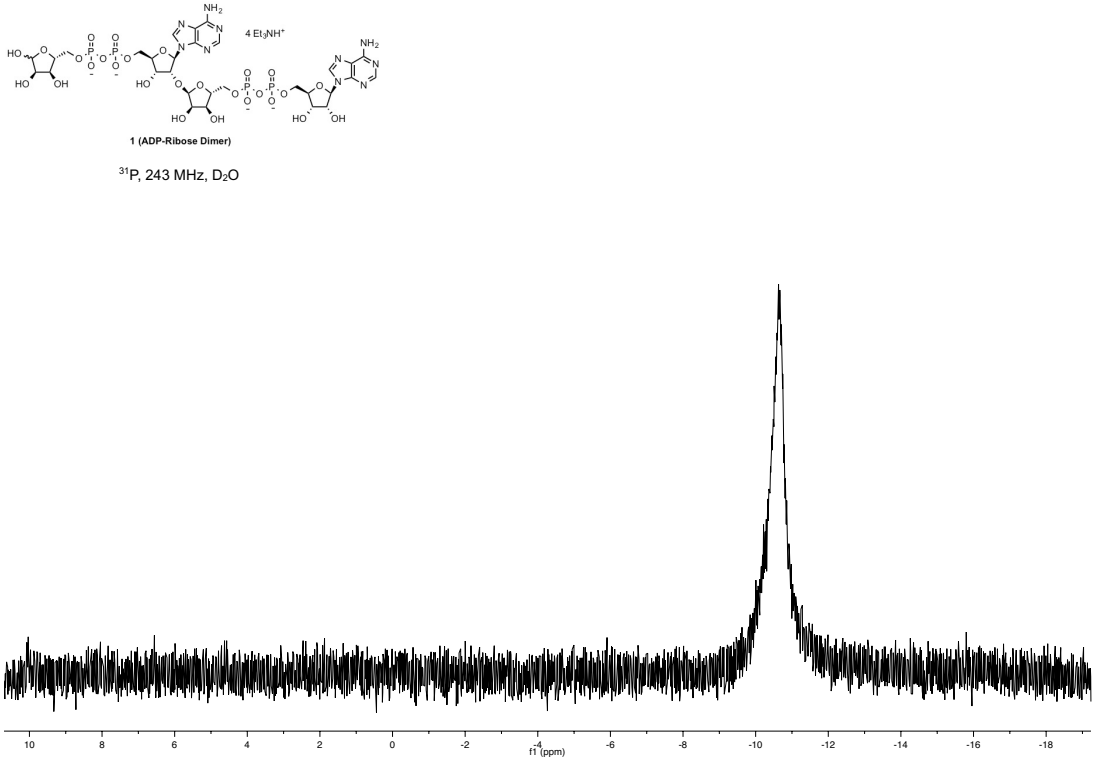
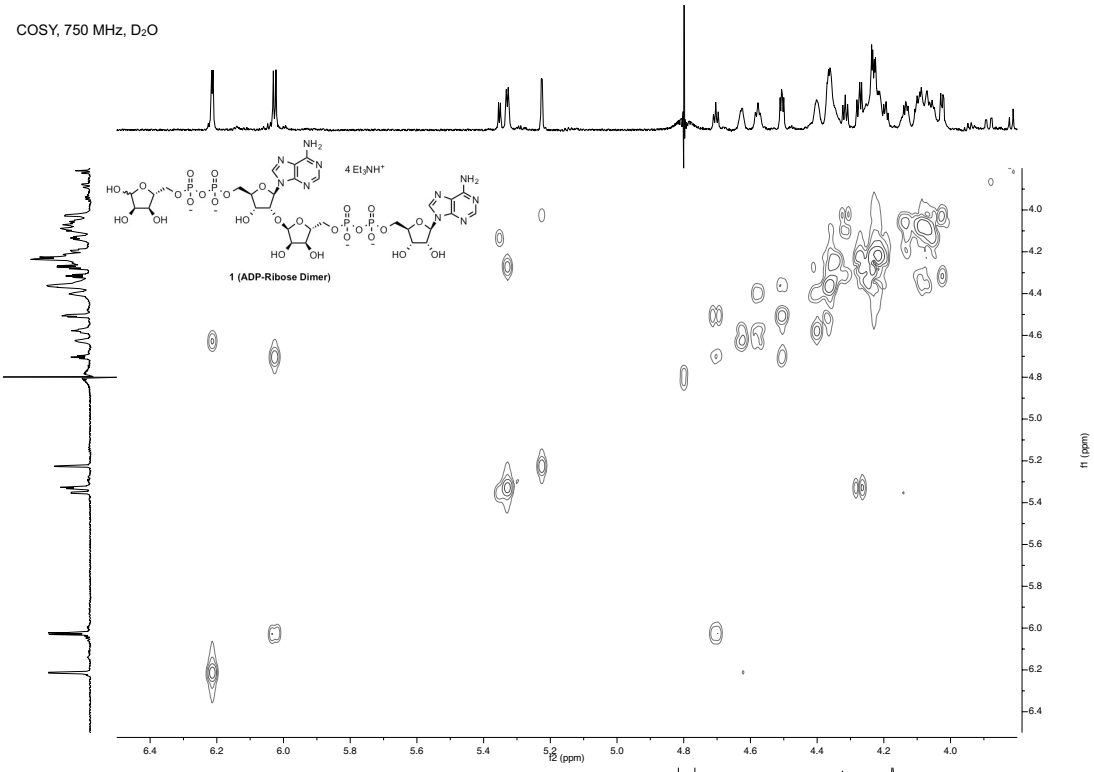
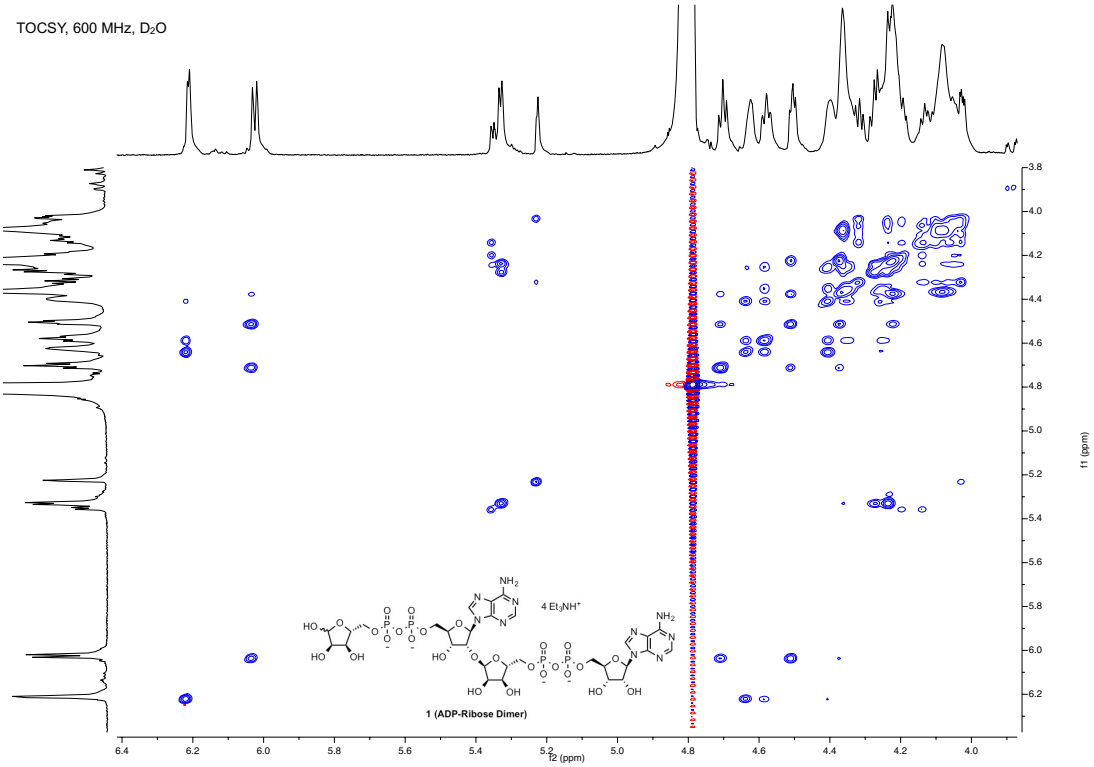
1 (ADP-Ribose Dimer)
1H, 600 MHz, D2O
f1 (ppm)

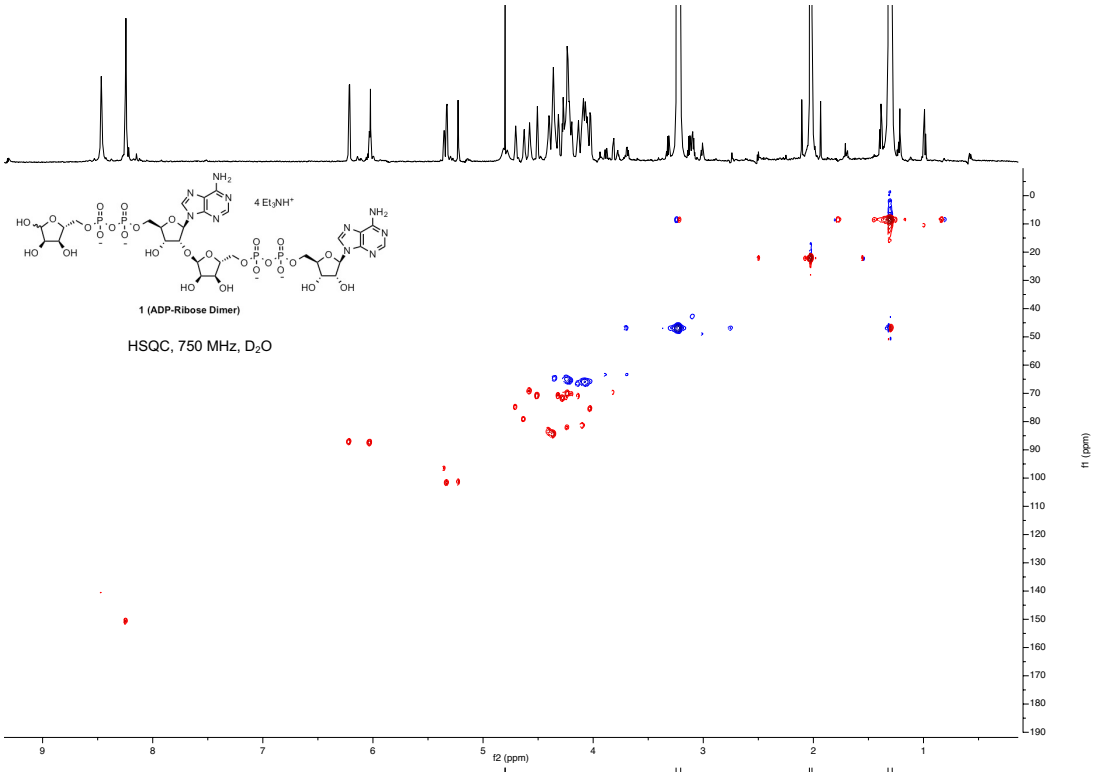

4 Et3NH+
1 (ADP-Ribose Dimer)
31P, 243 MHz, D2O
f1 (ppm)

COSY, 750 MHz, D_2O



TOCSY, 600 MHz, D_2O

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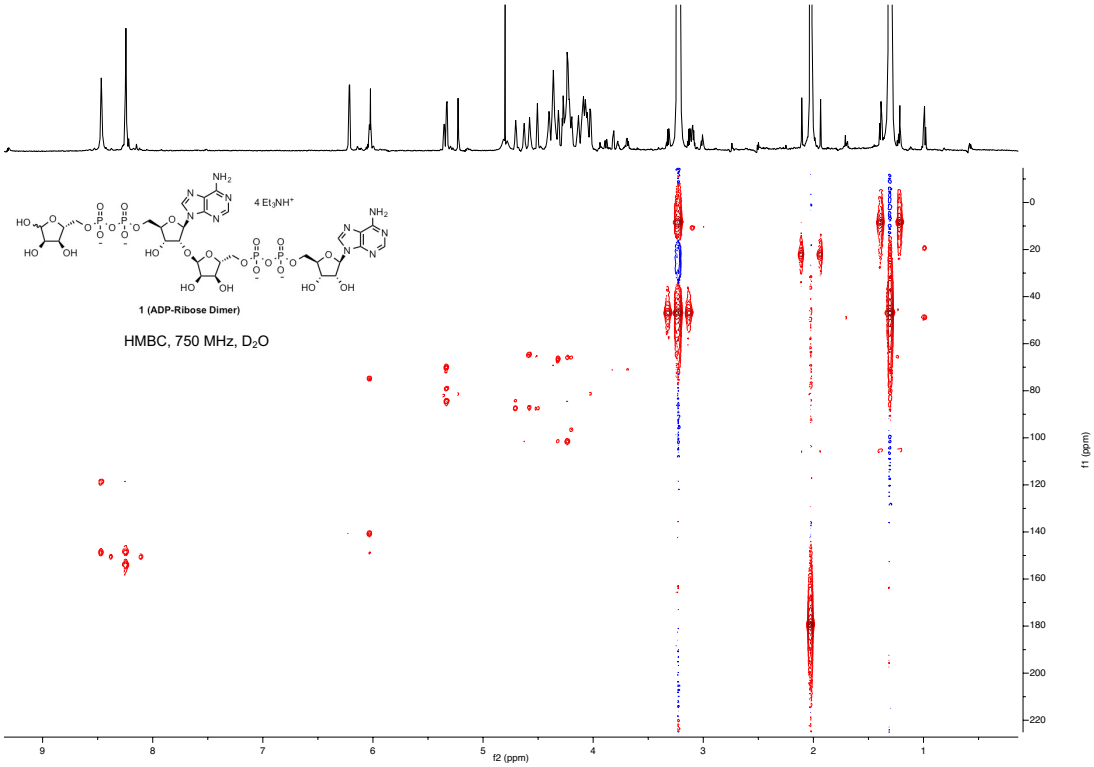
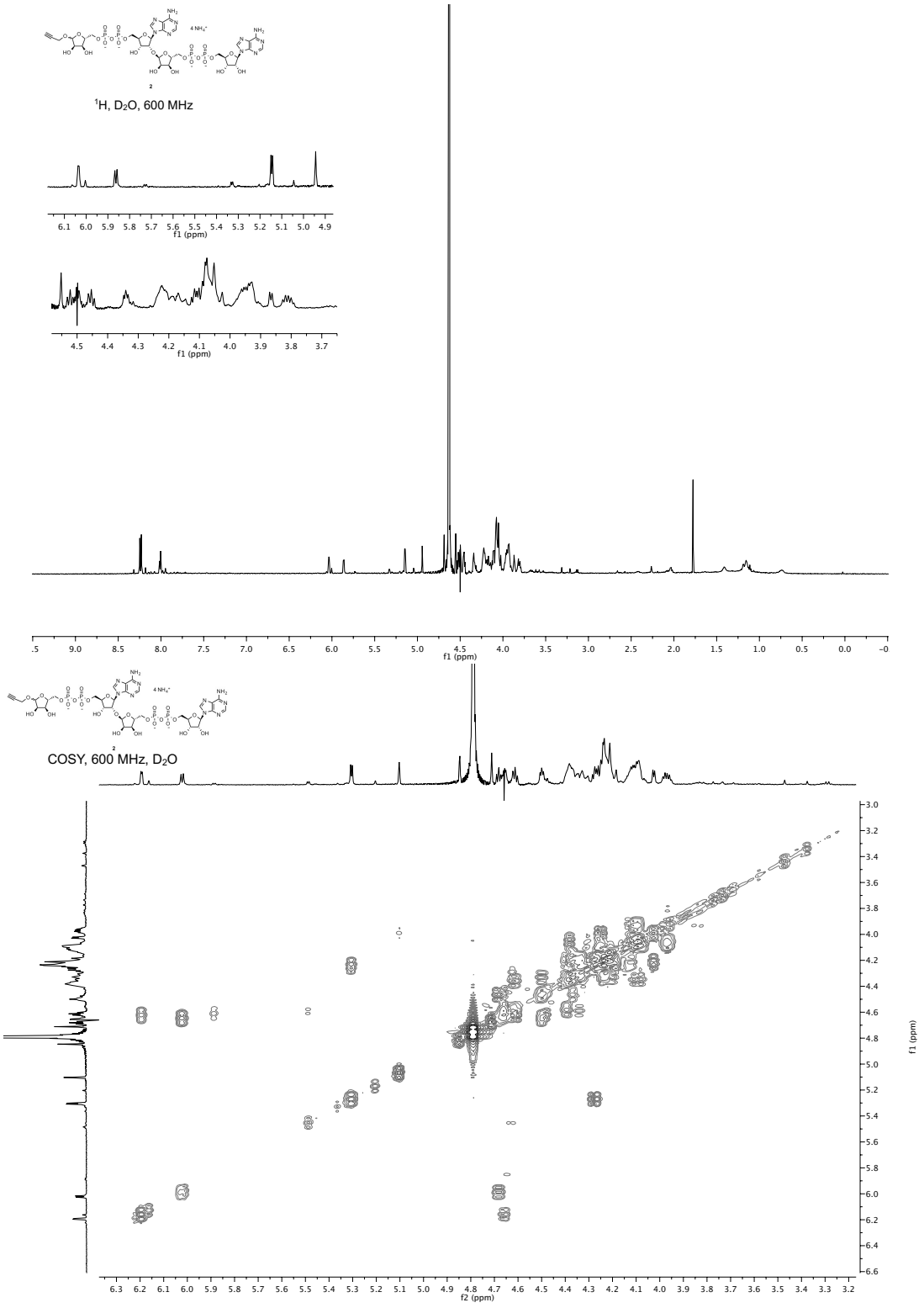
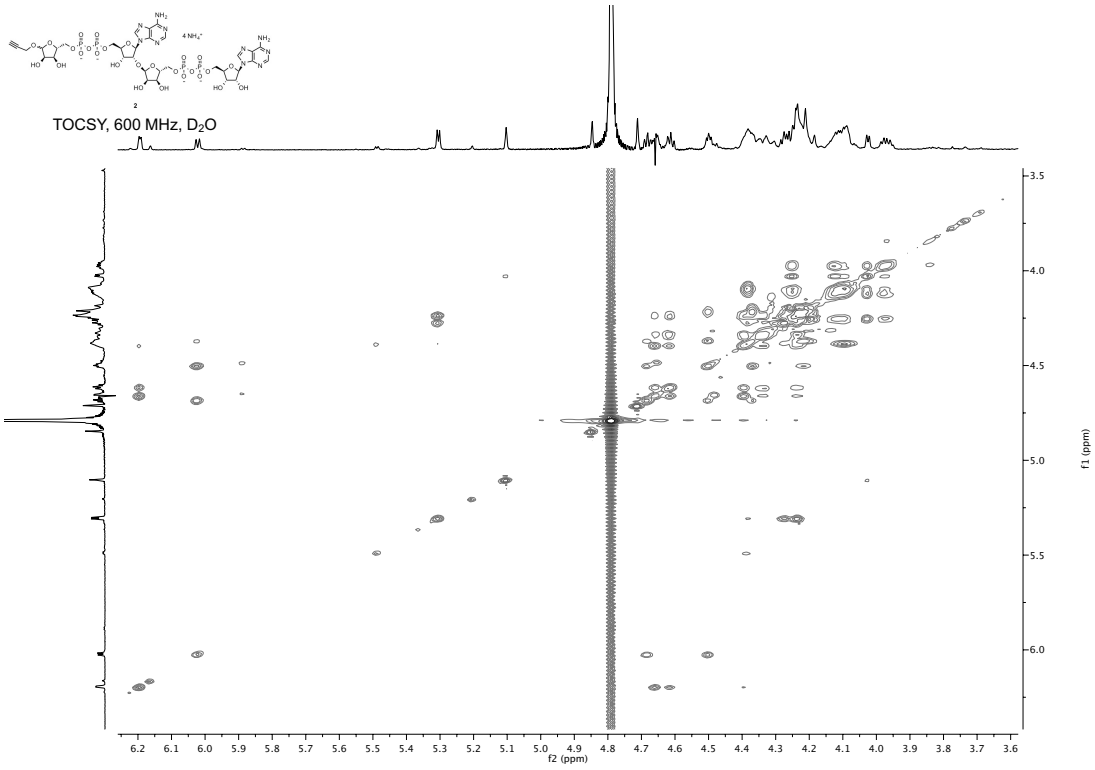
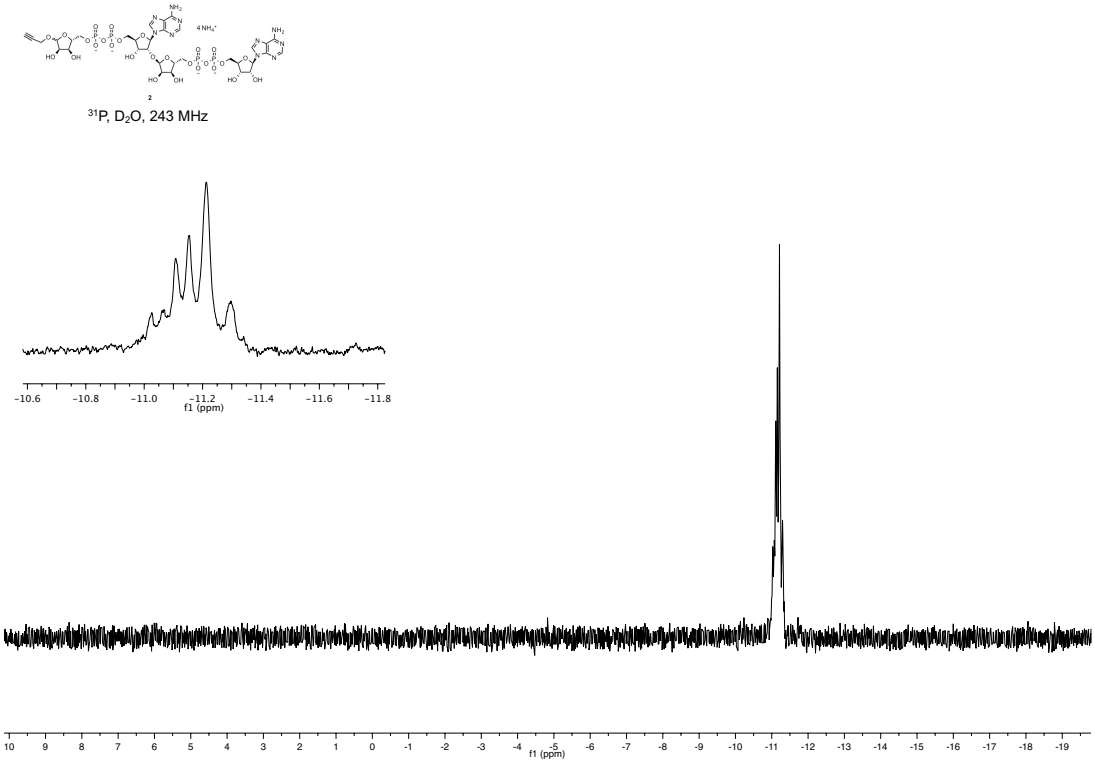
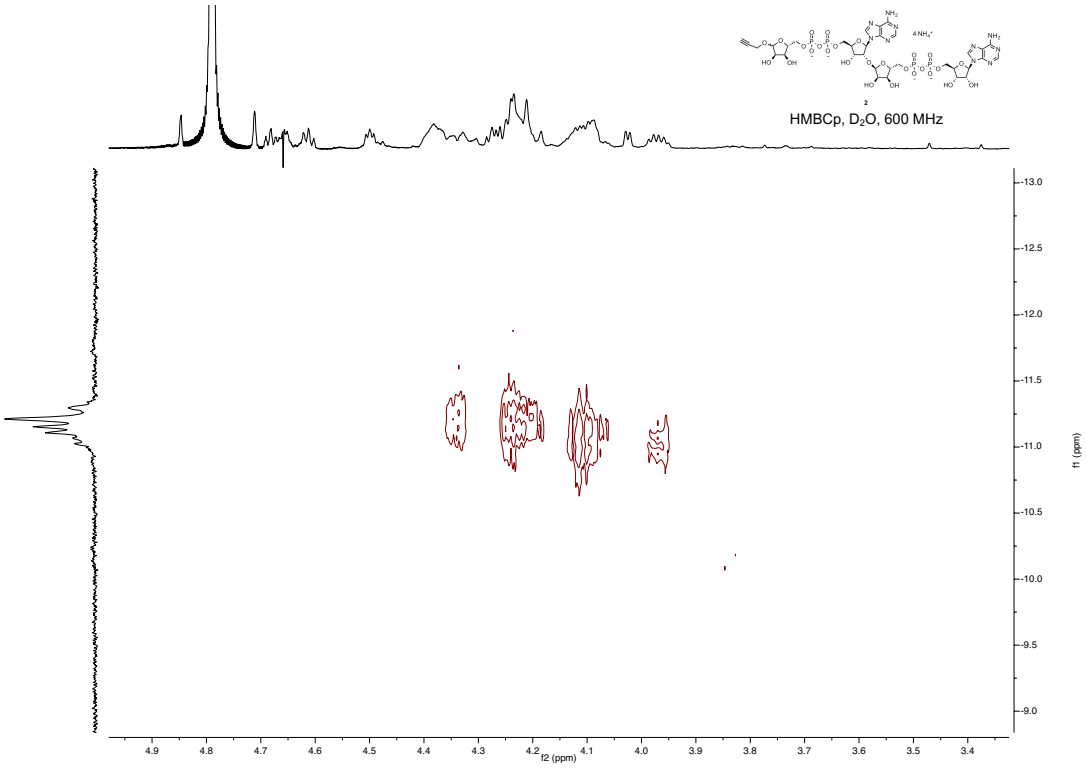
HSQC, 750 MHz, D2O
f2 (ppm)
f1 (ppm)

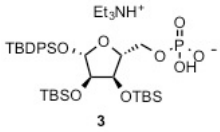

4 Et3NH+
1 (ADP-Ribose Dimer)
HMBC, 750 MHz, D2O
f2 (ppm)
f1 (ppm)


2
^{1}H, D$_2$O, 600 MHz
f1 (ppm)
2
COSY, 600 MHz, D$_2$O
f2 (ppm)
f1 (ppm)


TOCSY, 600 MHz, D_2O
f2 (ppm)
f1 (ppm)

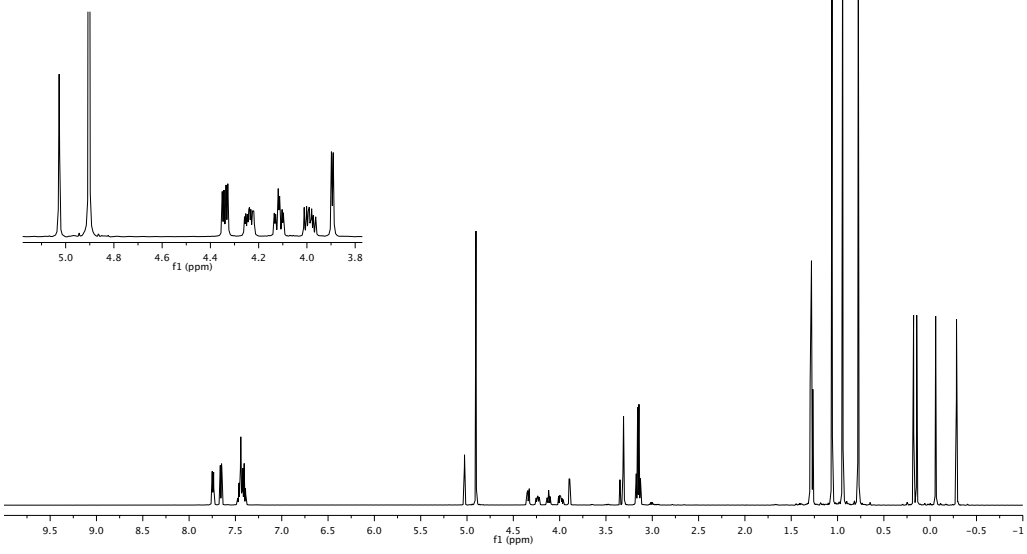

^{31}P, D_2O, 243 MHz
f1 (ppm)

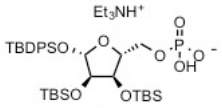




3

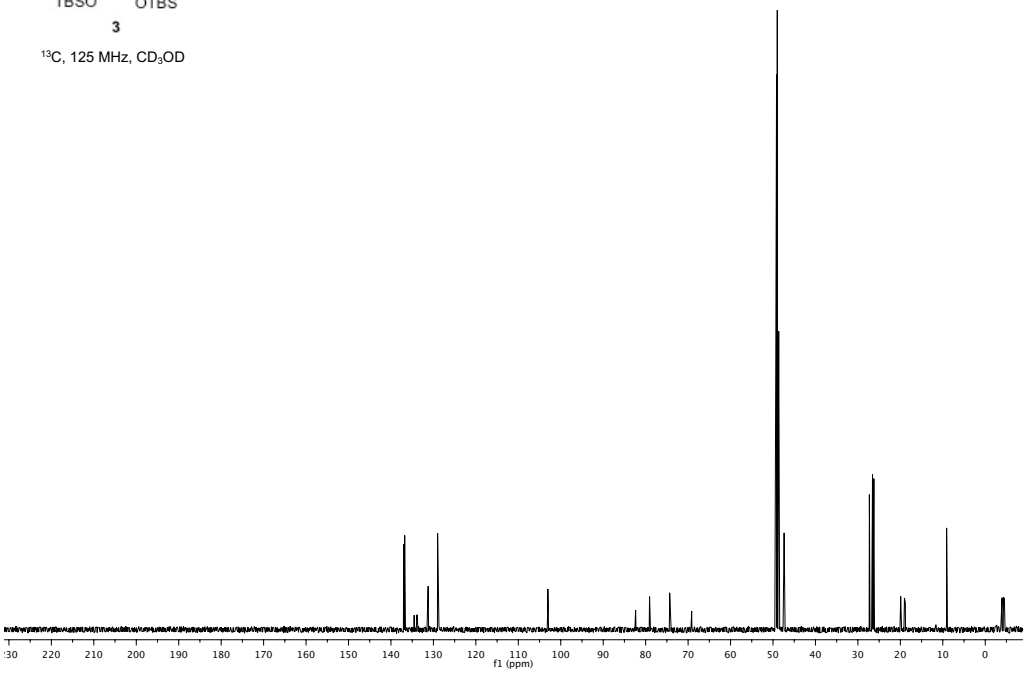
^{1}H, 500 MHz, CD_3OD

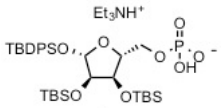




3

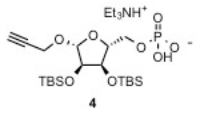
^{13}C, 125 MHz, CD_3OD





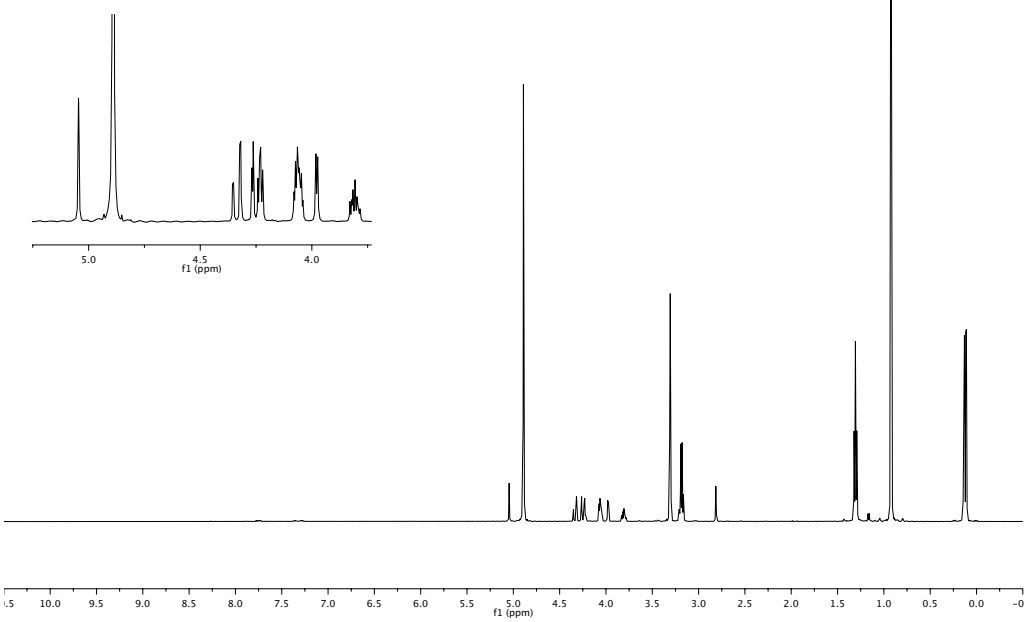
3

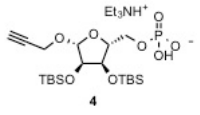
^{31}P, 202 MHz, CD_3OD



4

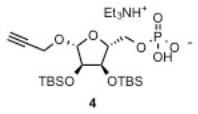
^{1}H, 500 MHz, CD_3OD





4

^{13}C, 125 MHz, CD_3OD



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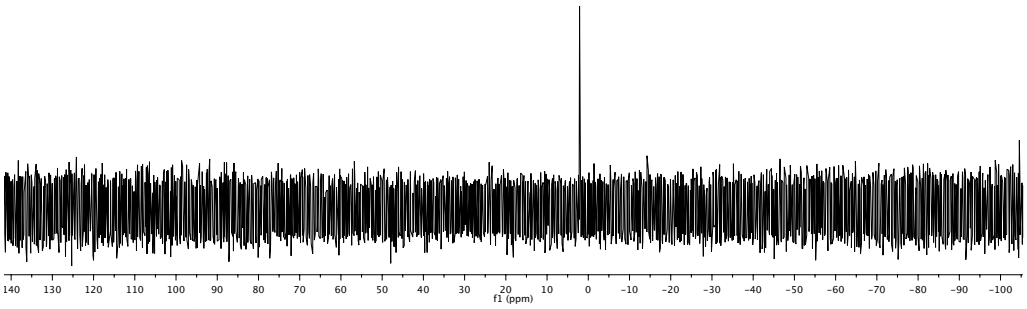
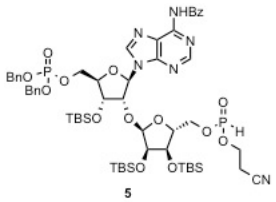
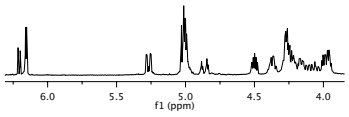
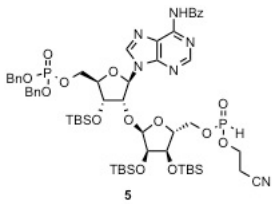




5

^{1}H, 500 MHz, $CDCl_3$





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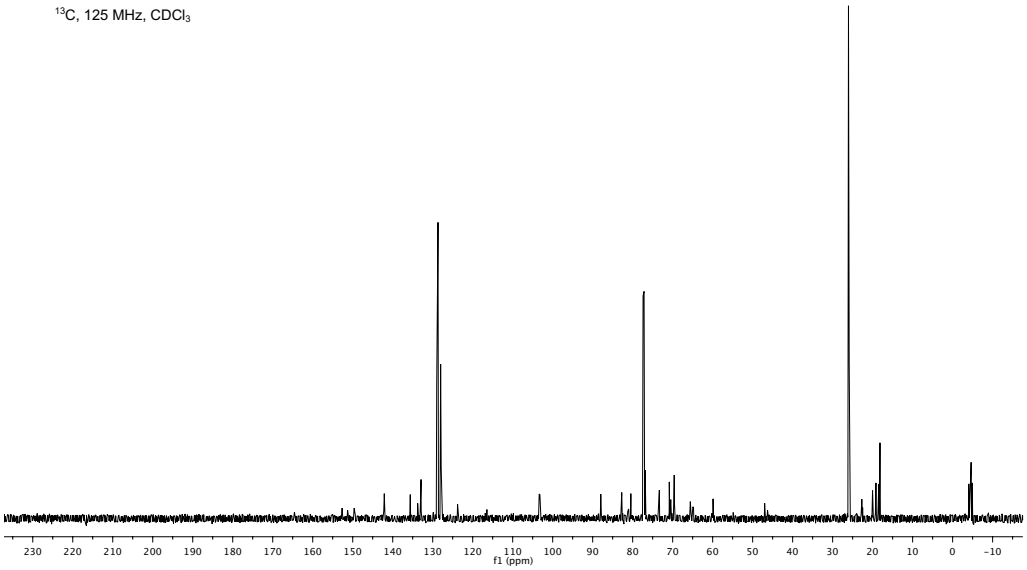
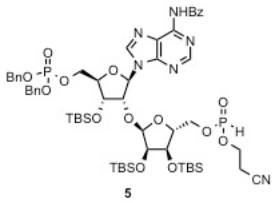
^{13}C, 125 MHz, $CDCl_3$





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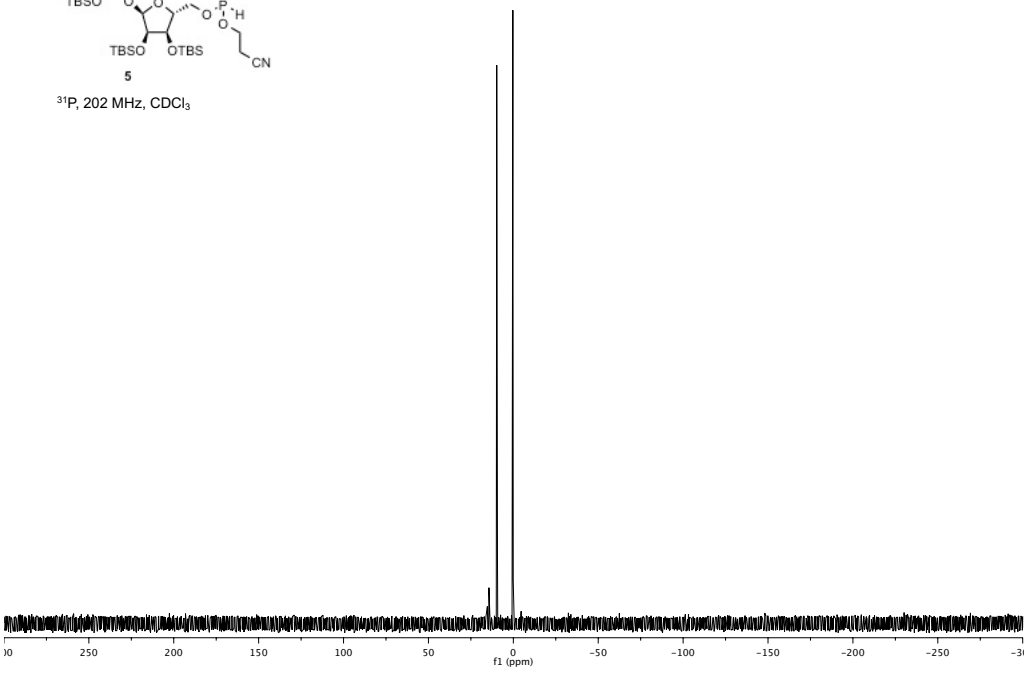
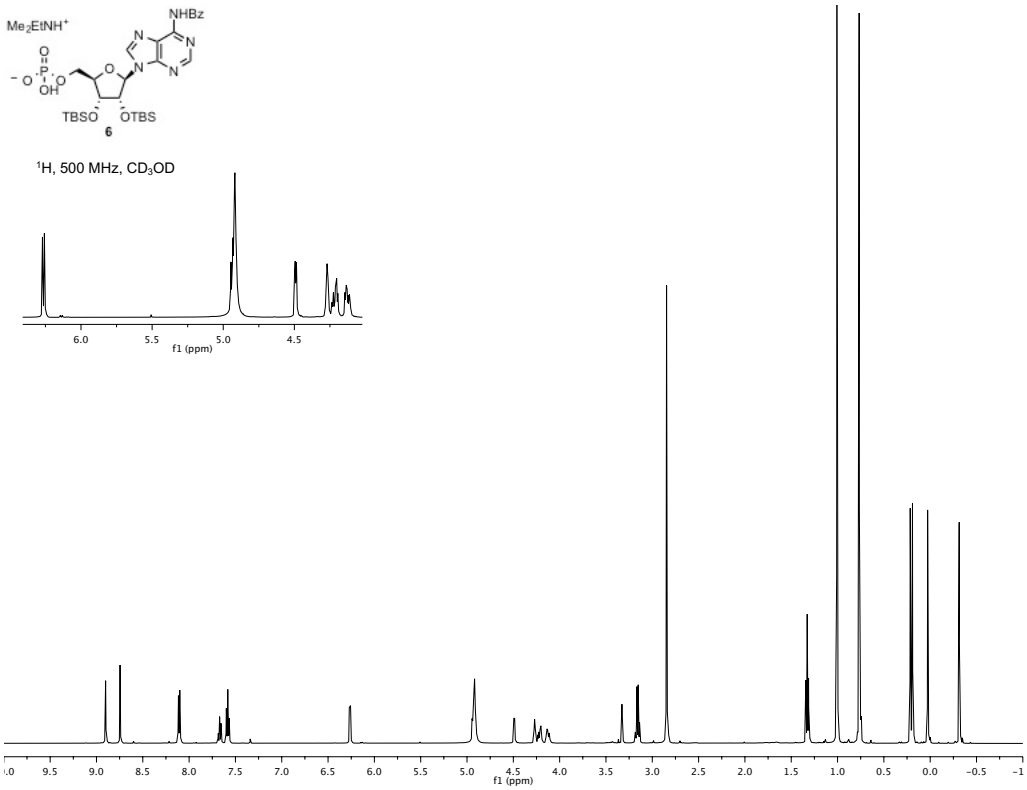
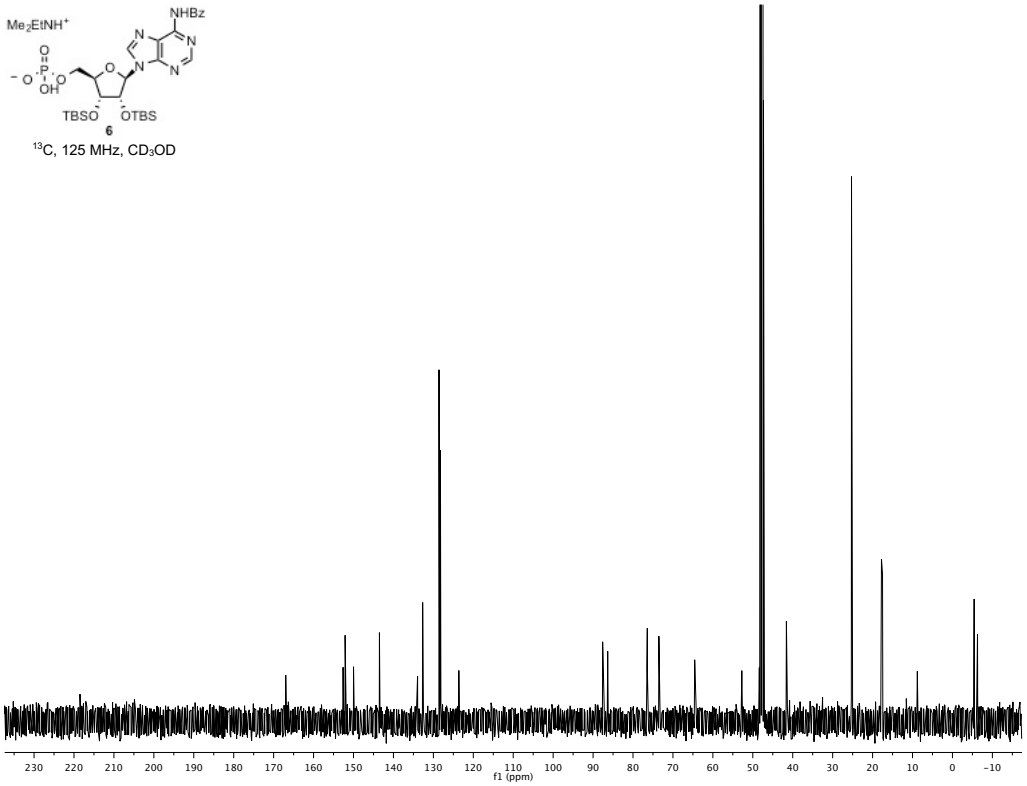
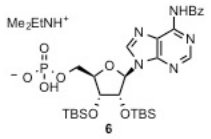
^{31}P, 202 MHz, $CDCl_3$

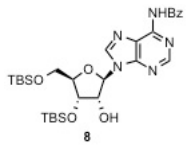



Me2EtNH+
NHBz
TBSO
OTBS
6
1H, 500 MHz, CD3OD
f1 (ppm)

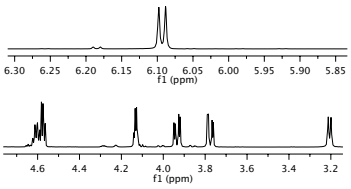

Me2EtNH+
NHBz
TBSO
OTBS
6
13C, 125 MHz, CD3OD
f1 (ppm)

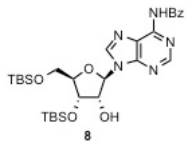


^{31}P, 202 MHz, CD_3OD



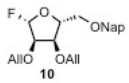
^{1}H, 500 MHz, $CDCl_3$





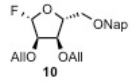
8

^{13}C, 125 MHz, $CDCl_3$



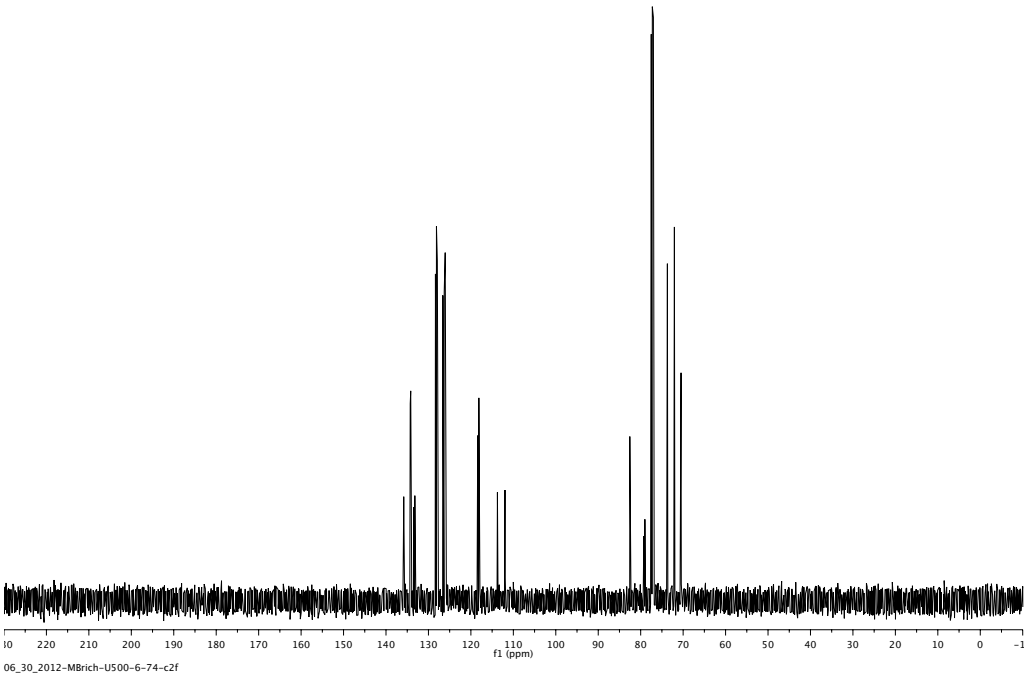
10

^{1}H, 500 MHz, $CDCl_3$



10

^{13}C, 125 MHz, $CDCl_3$



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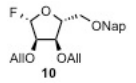
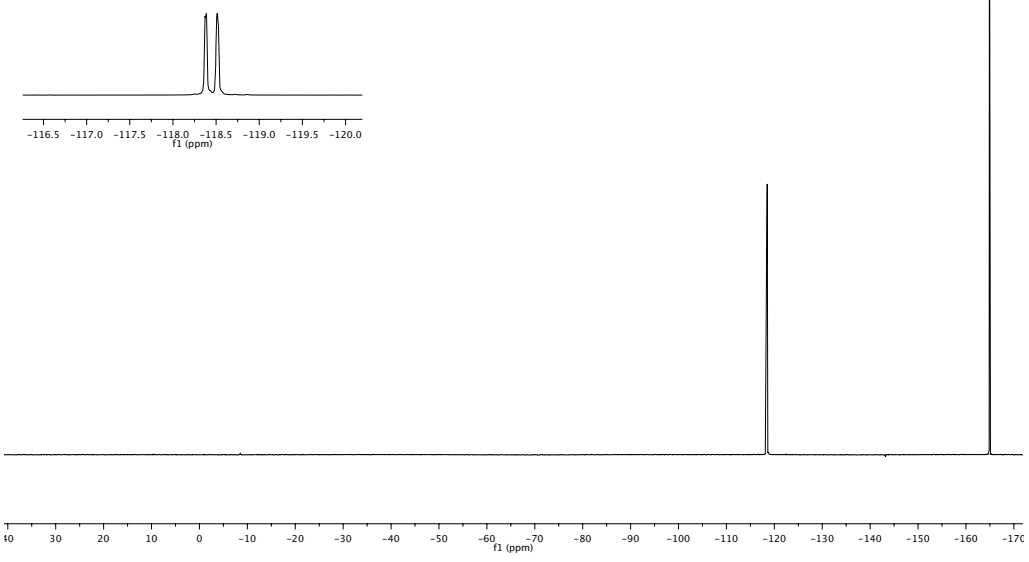
06_30_2012-MBrich-U500-6-74-c2f

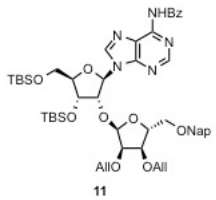


10

^{19}F (^{1}H coupled), 470 MHz, $CDCl_3$

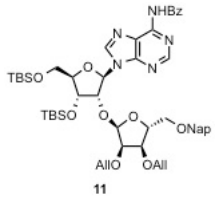
C_6F_6 (Reference Std.)





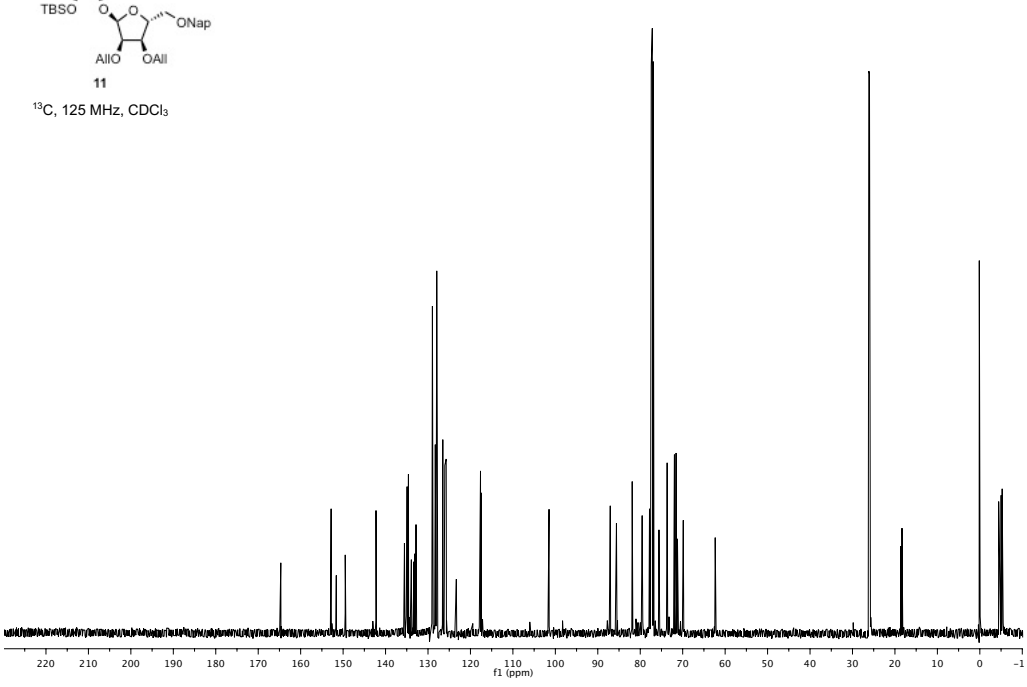
11

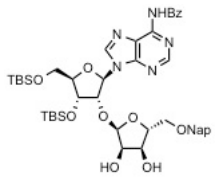
^{1}H, 500 MHz, $CDCl_3$



11

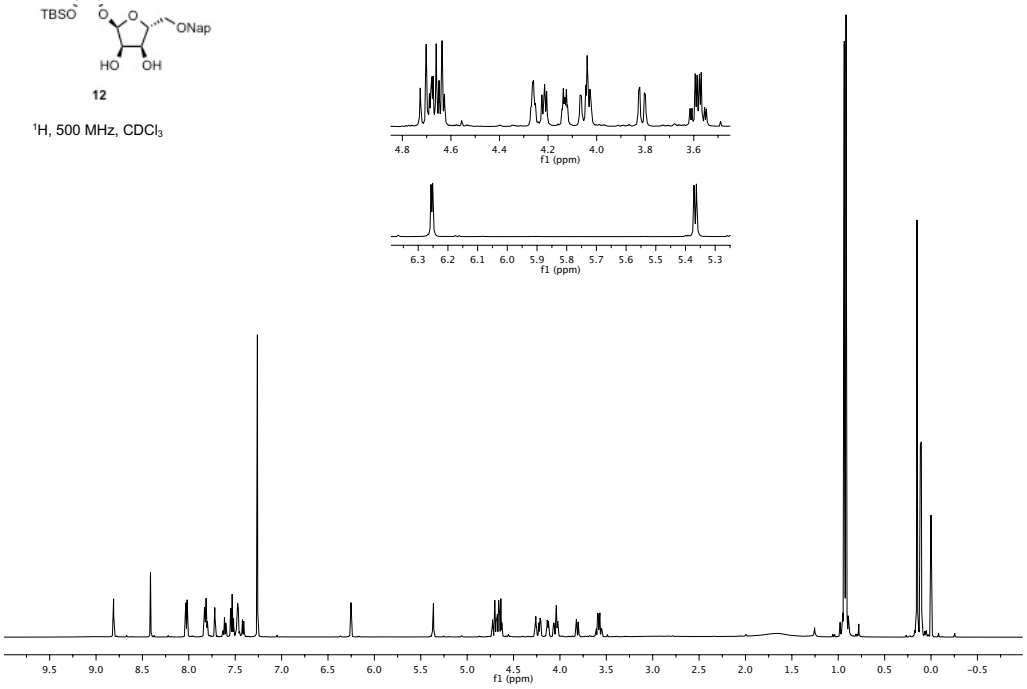
^{13}C, 125 MHz, $CDCl_3$

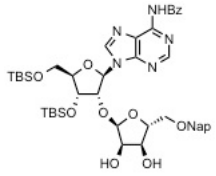




12

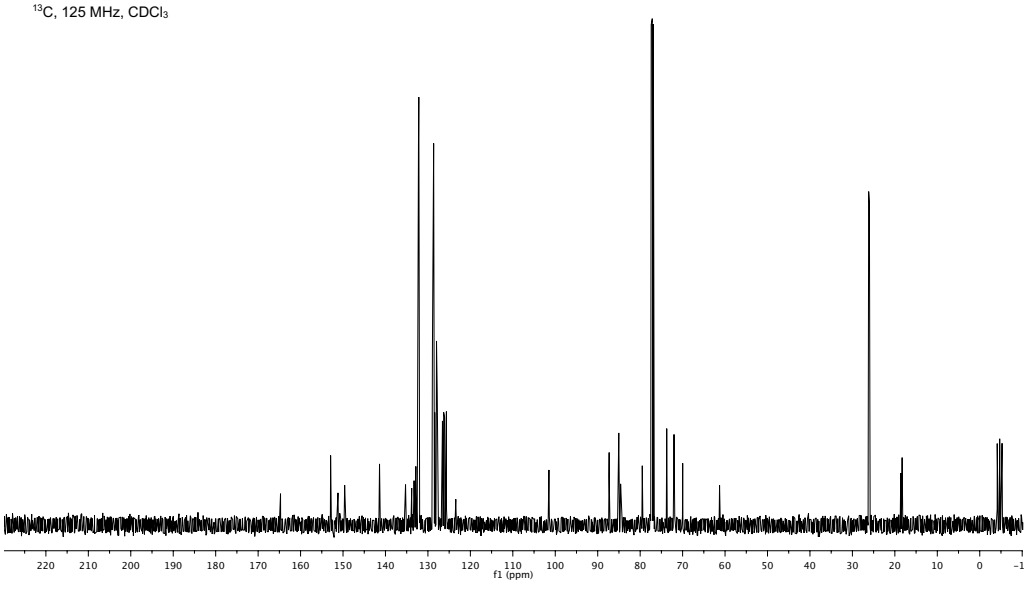
^{1}H, 500 MHz, $CDCl_3$

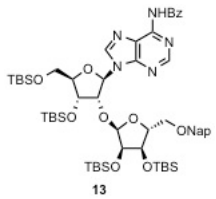




12

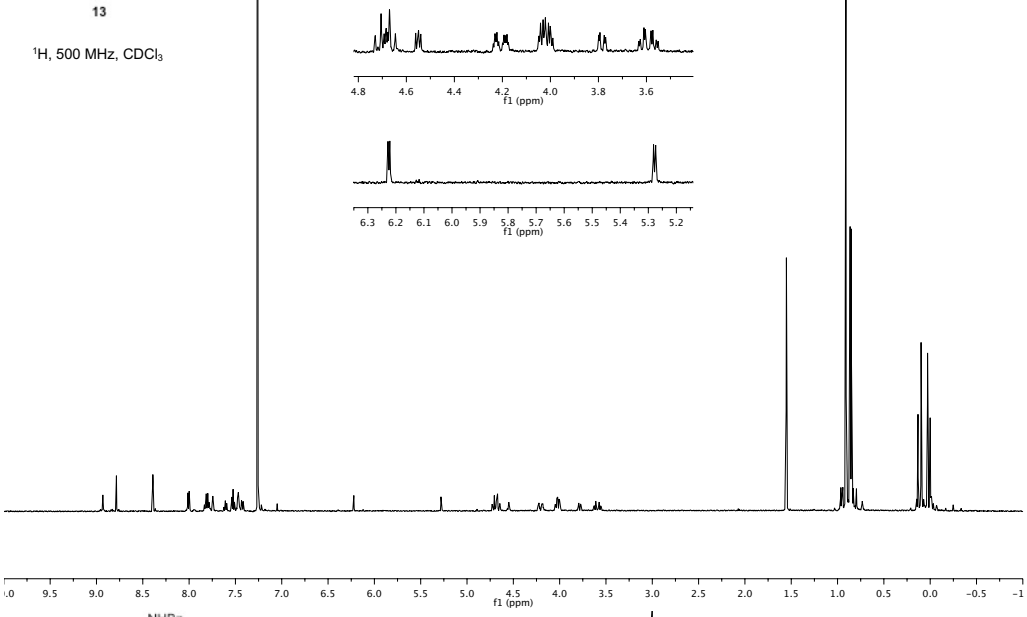
^{13}C, 125 MHz, $CDCl_3$

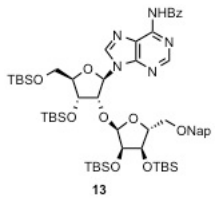




13

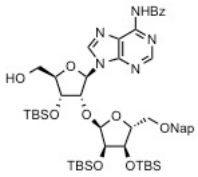
^{1}H, 500 MHz, $CDCl_3$





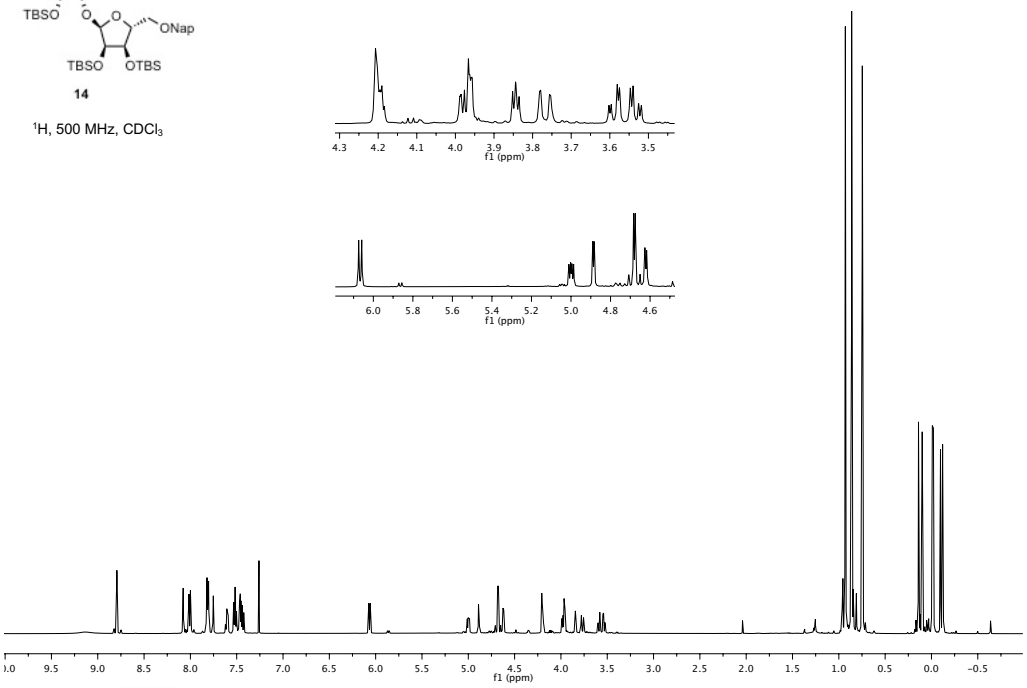
13

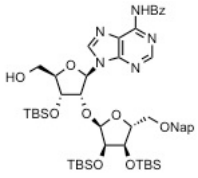
^{13}C, 125 MHz, $CDCl_3$



14

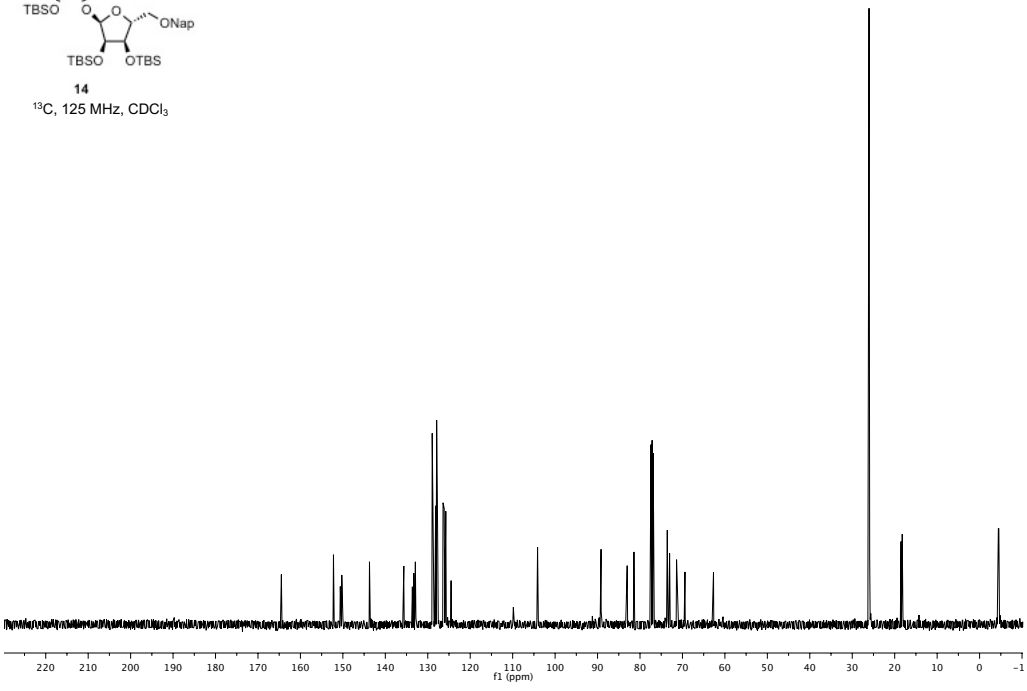
^{1}H, 500 MHz, $CDCl_3$

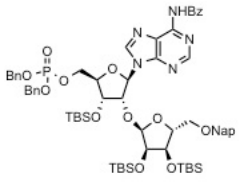




14

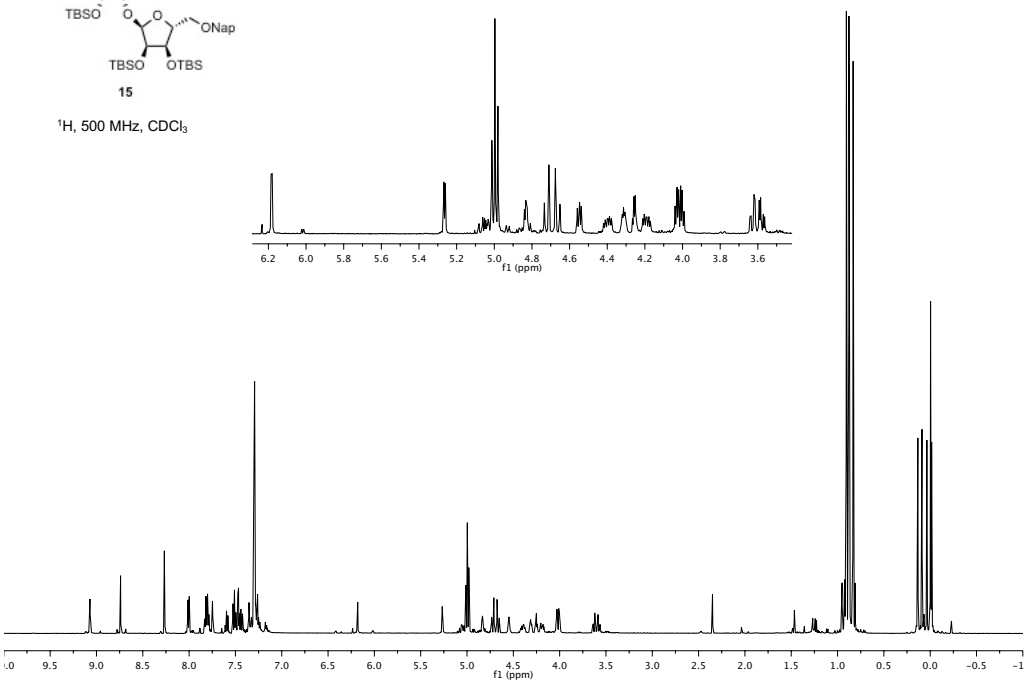
^{13}C, 125 MHz, $CDCl_3$

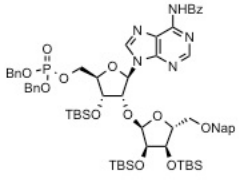




15

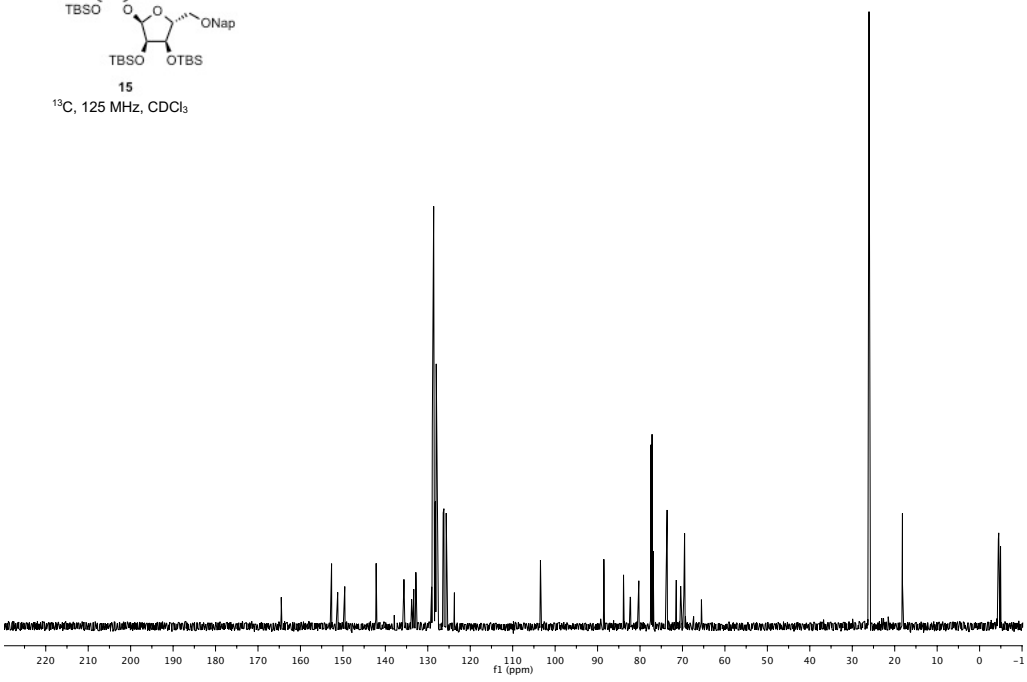
^{1}H, 500 MHz, $CDCl_3$

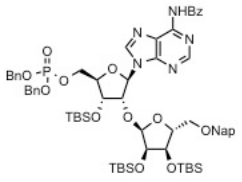




15

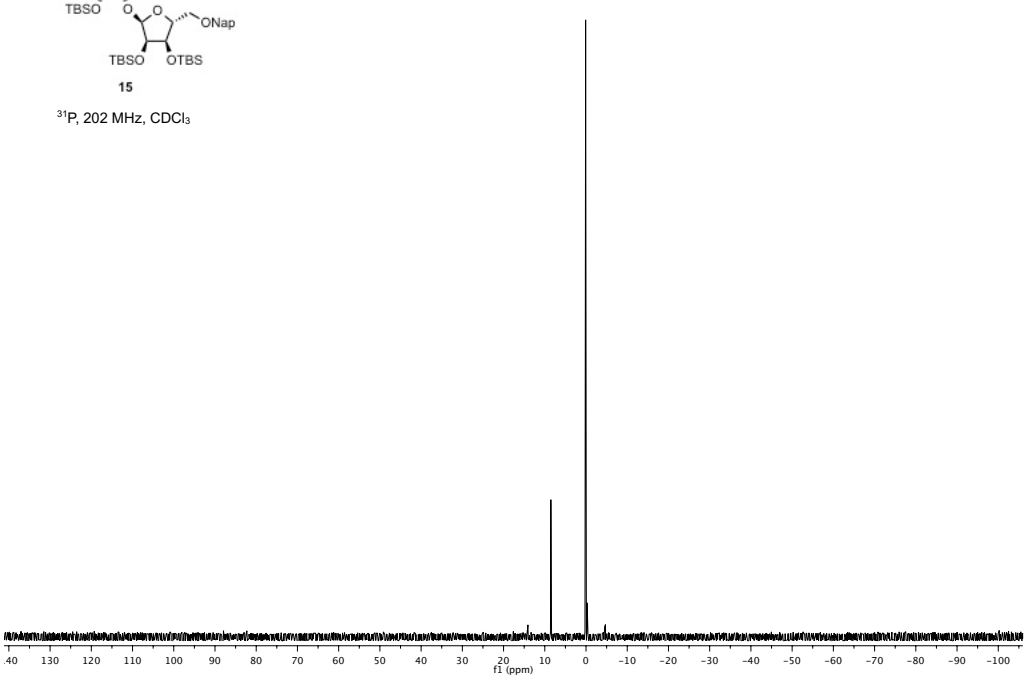
^{13}C, 125 MHz, $CDCl_3$

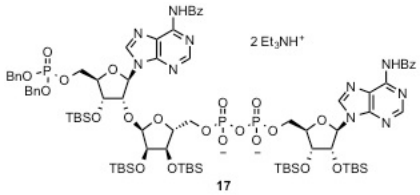




15

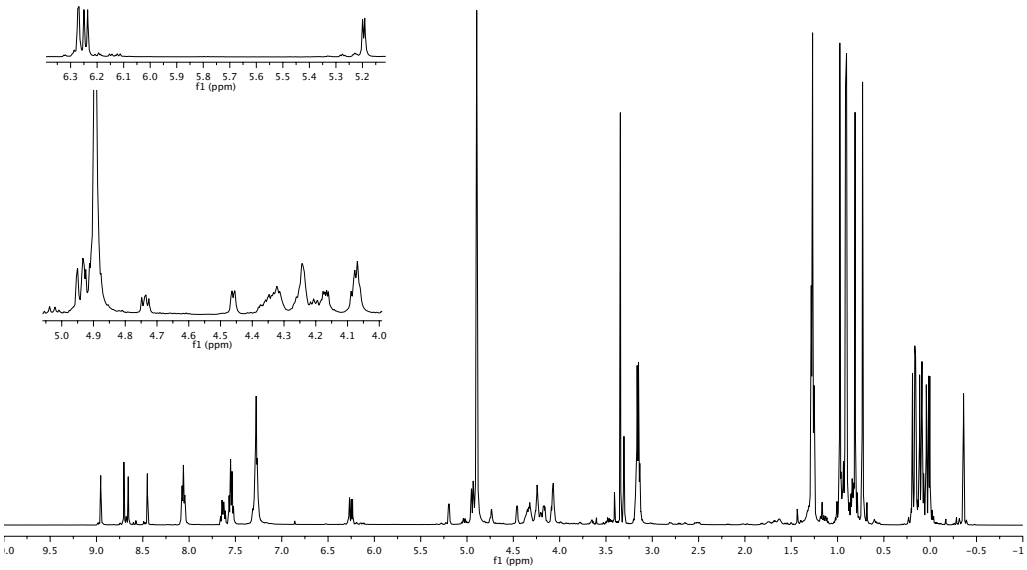
^{31}P, 202 MHz, $CDCl_3$

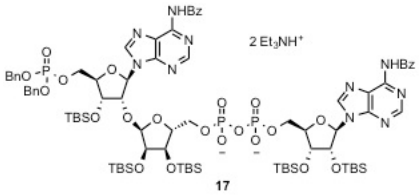




17

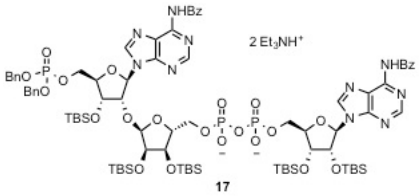
^{1}H, 500 MHz, CD_3OD





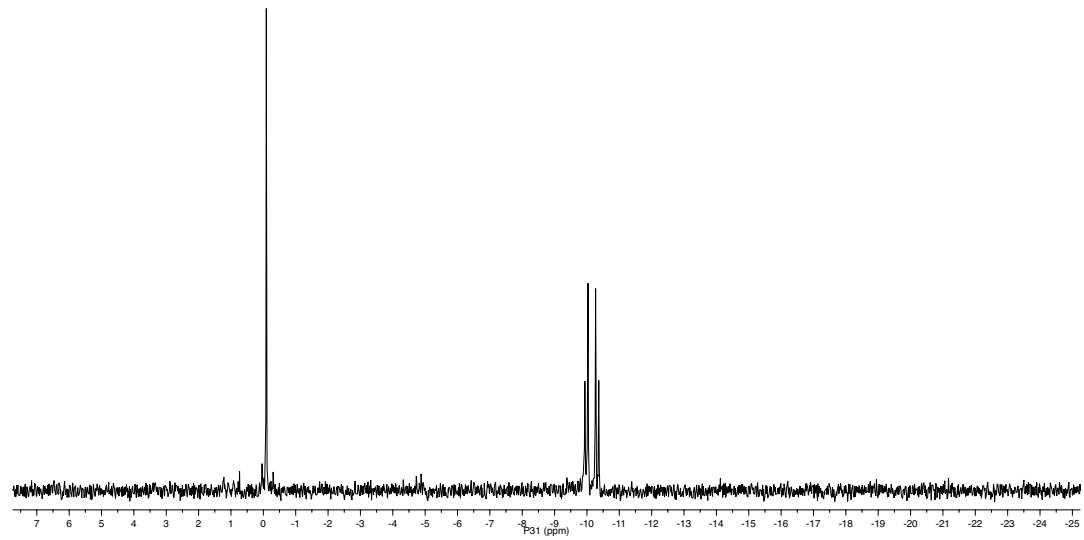
17

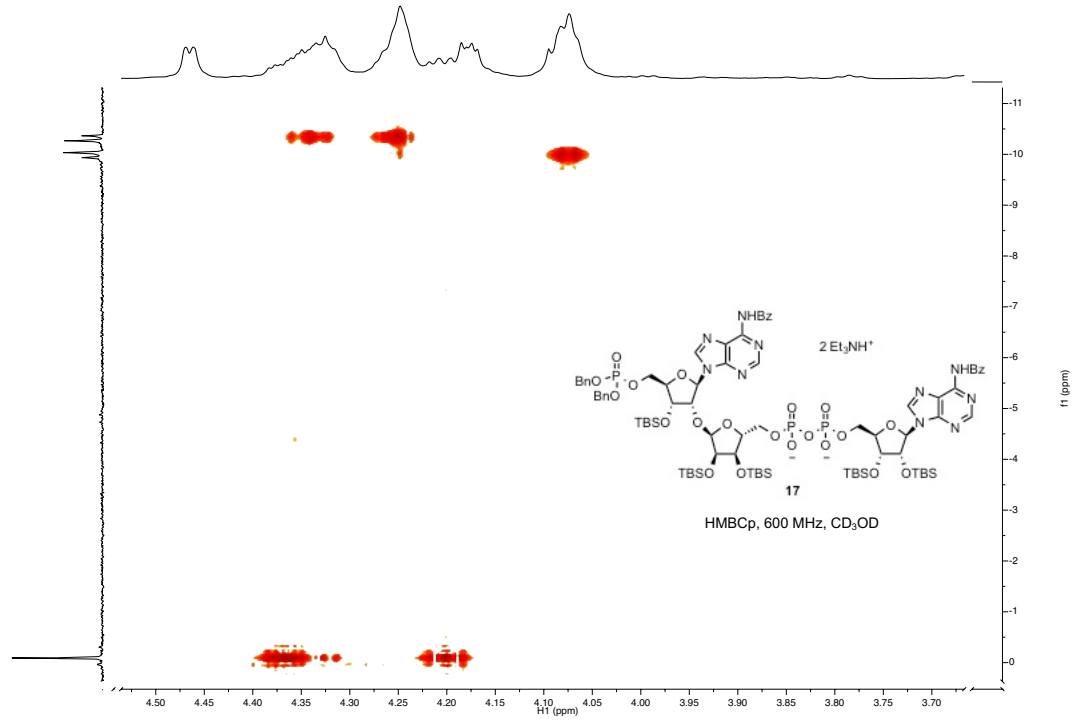
^{13}C, 125 MHz, CD_3OD

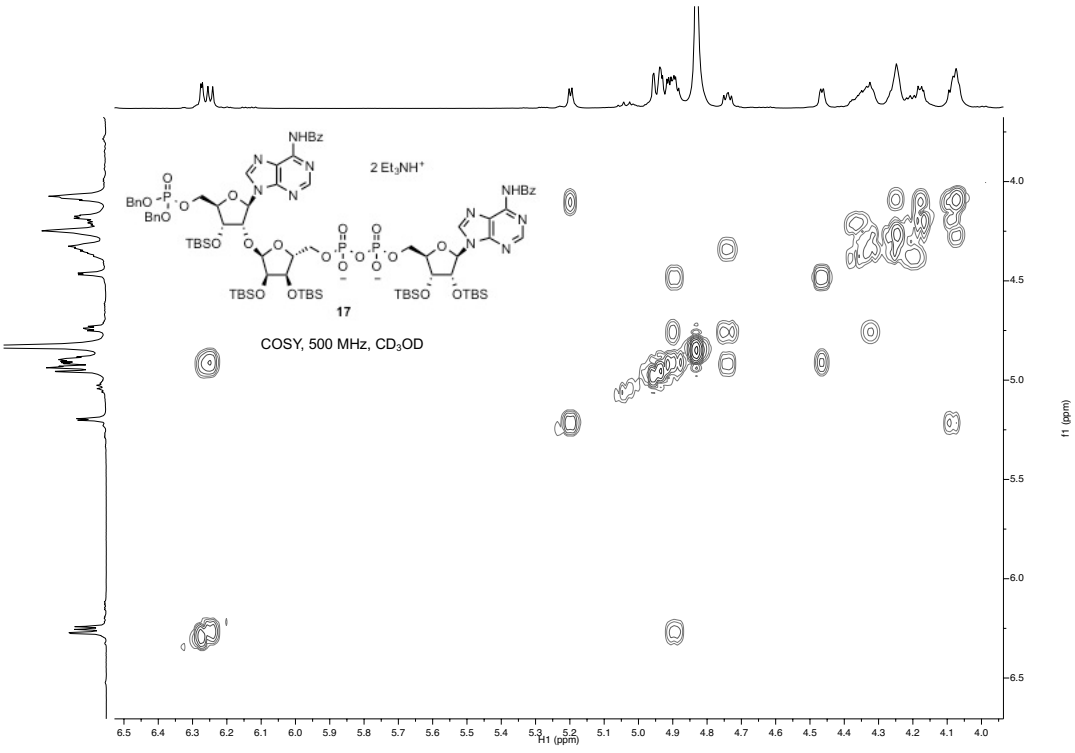


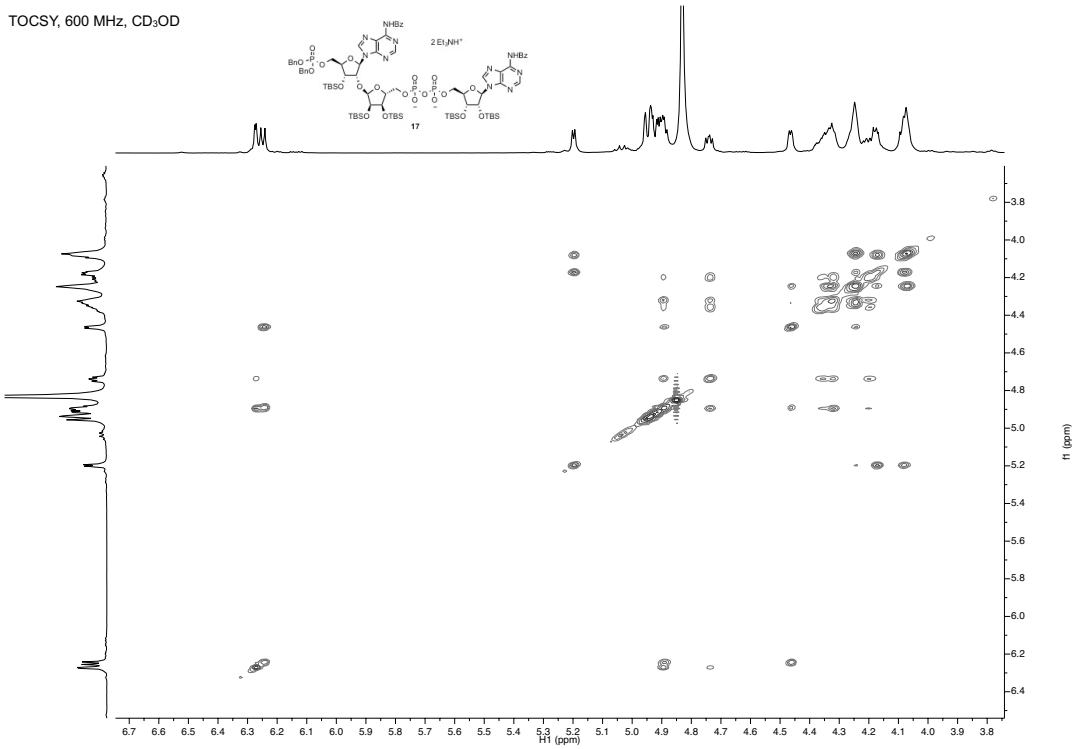
17

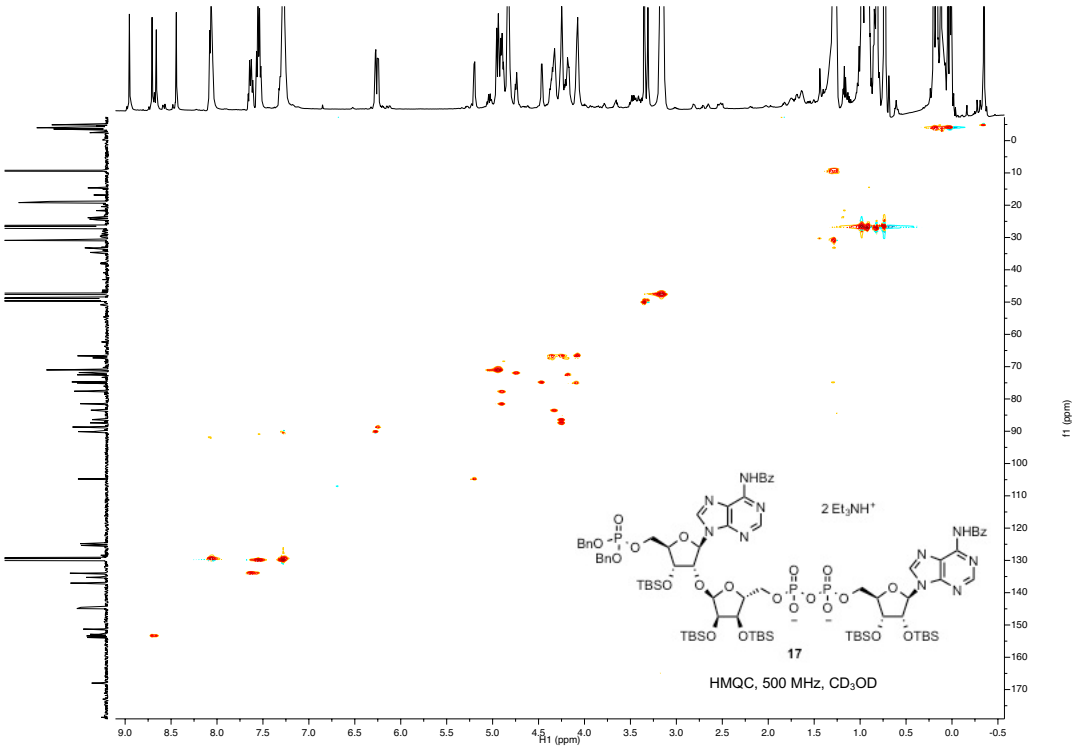
^{31}P, 202 MHz, CD_3OD

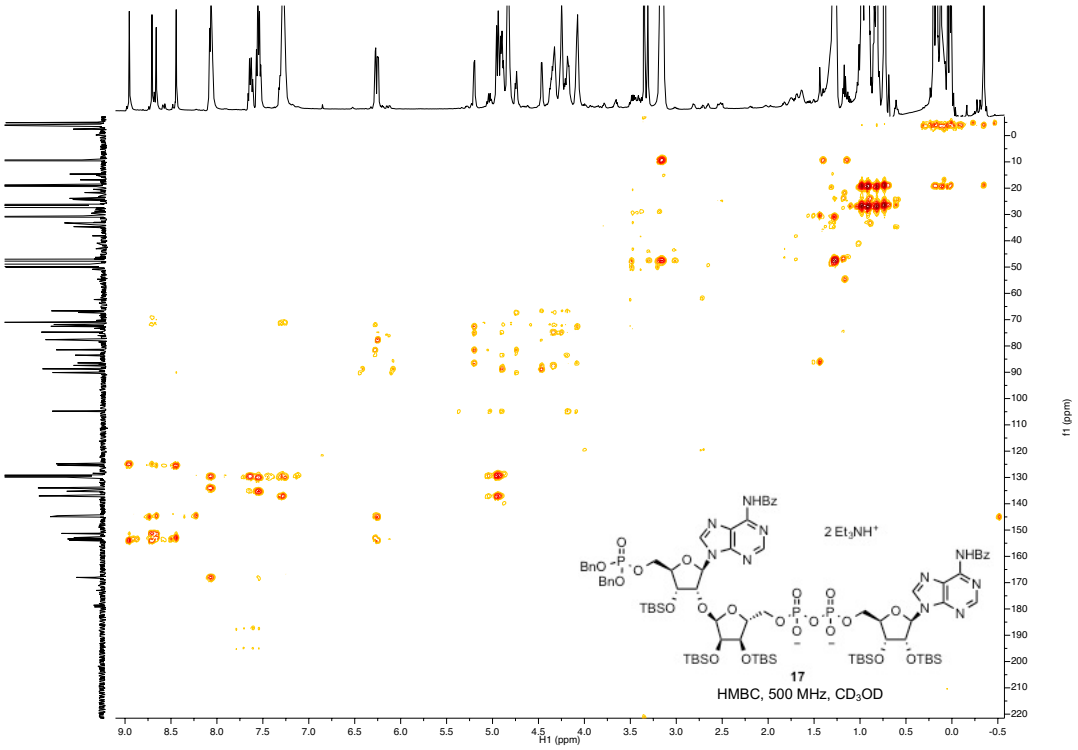



NHBz
2 Et3NH+
BnO
BnO
TBSO
TBSO
OTBS
TBSO
OTBS
17
HMBCp, 600 MHz, CD3OD
H1 (ppm)
f1 (ppm)


NHBz
2 Et3NH+
BnO
BnO
TBSO
TBSO
OTBS
TBSO
OTBS
17
COSY, 500 MHz, CD3OD
H1 (ppm)
f1 (ppm)

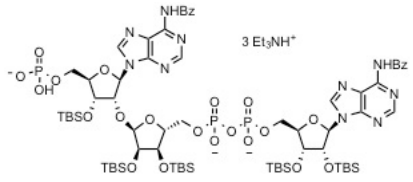

TOCSY, 600 MHz, CD3OD
NHBz
2 Et3NH+
BnO
BnO
TBSO
TBSO
OTBS
TBSO
OTBS
17
f1 (ppm)
H1 (ppm)


NHBz
2 Et3NH+
BnO
BnO
TBSO
TBSO
OTBS
TBSO
OTBS
17
HMQC, 500 MHz, CD3OD
f1 (ppm)
H1 (ppm)



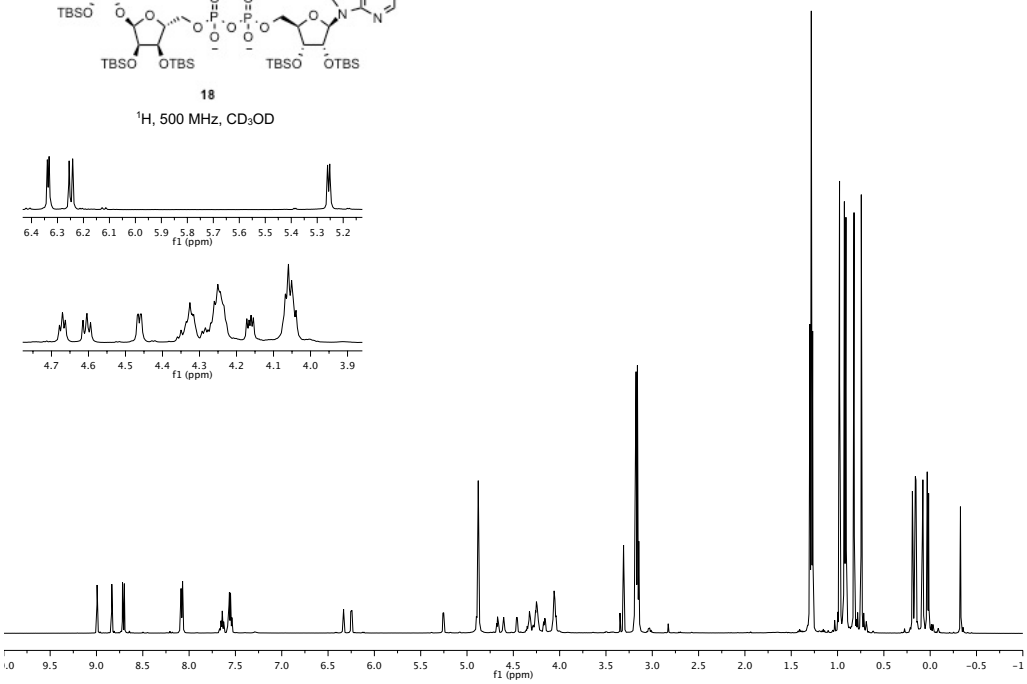
17

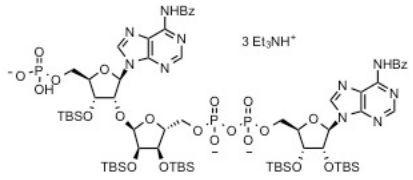
HMBC, 500 MHz, CD_3OD



18

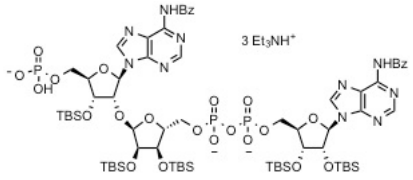
^1H, 500 MHz, CD_3OD





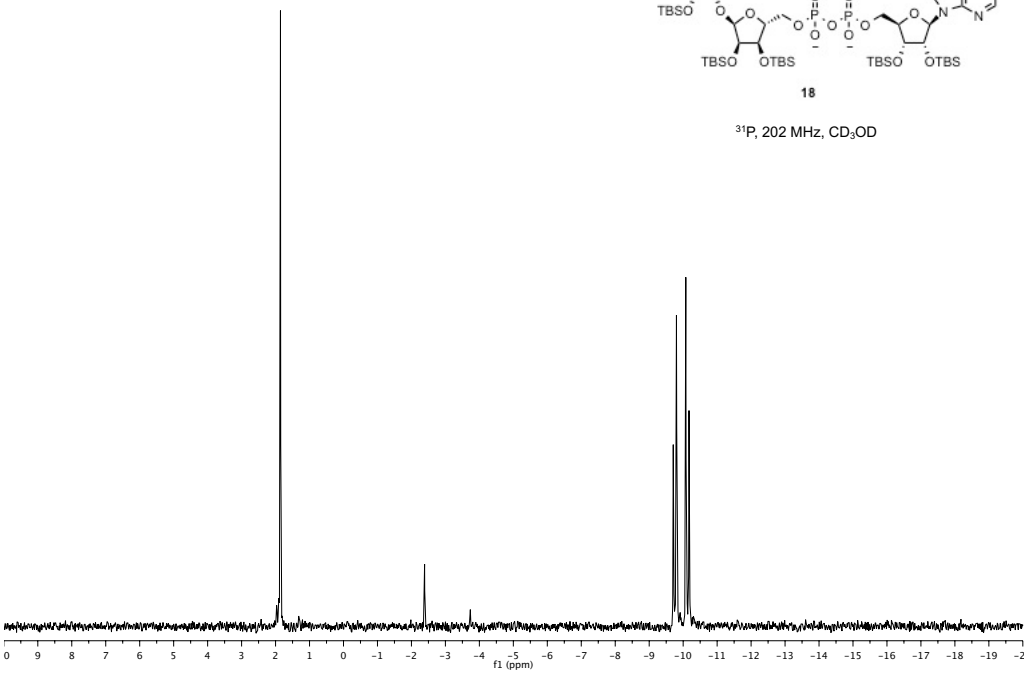
18

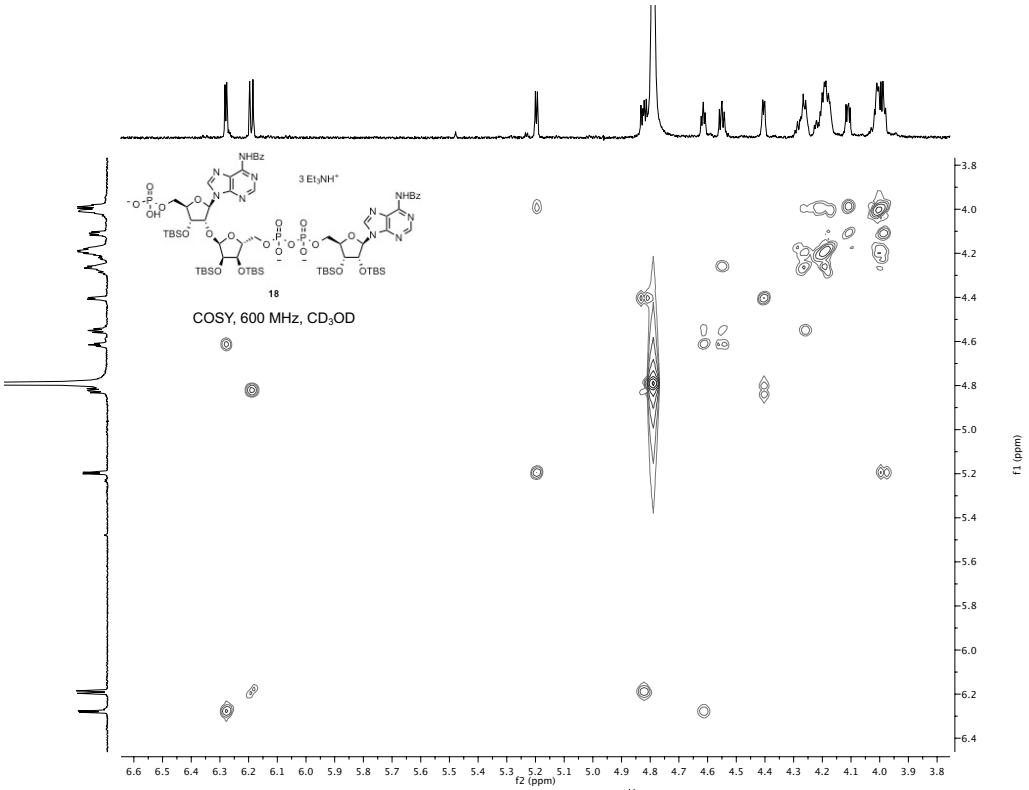
^{13}C, 125 MHz, CD_3OD

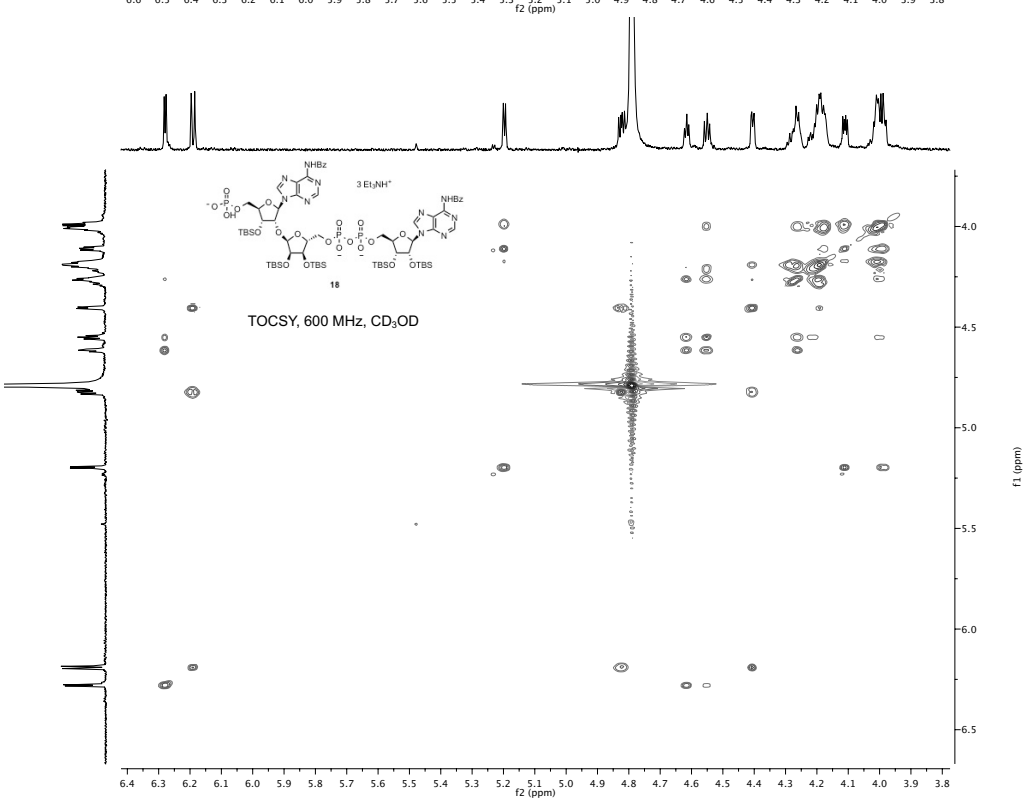


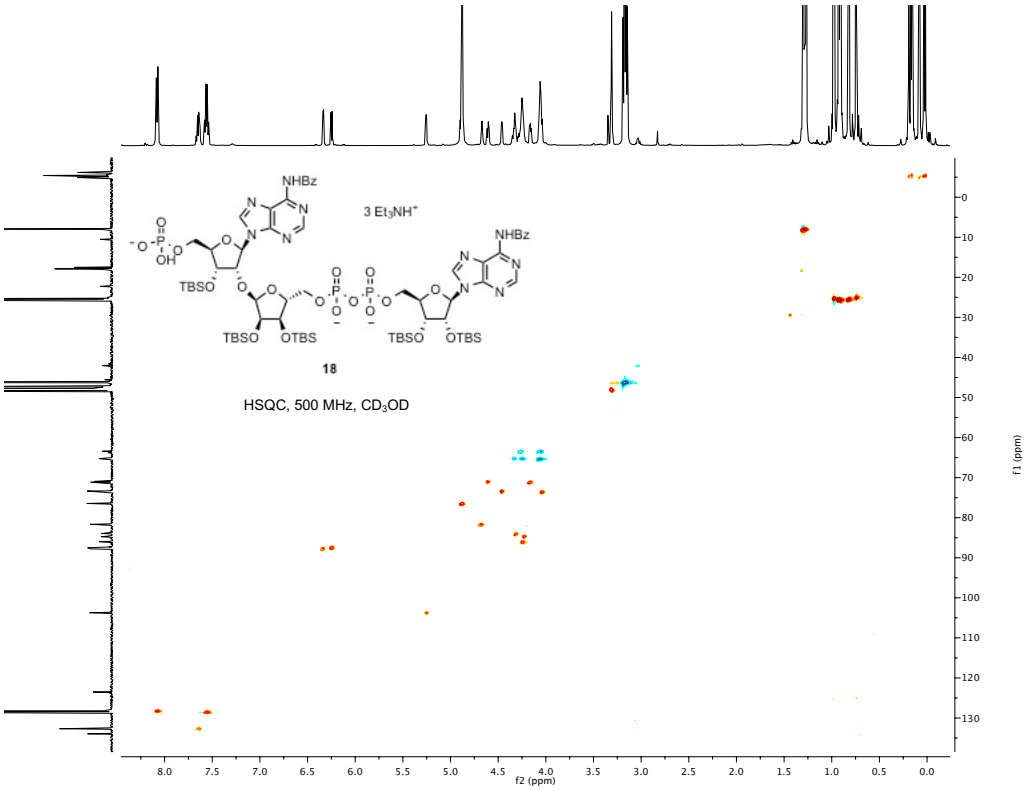
18

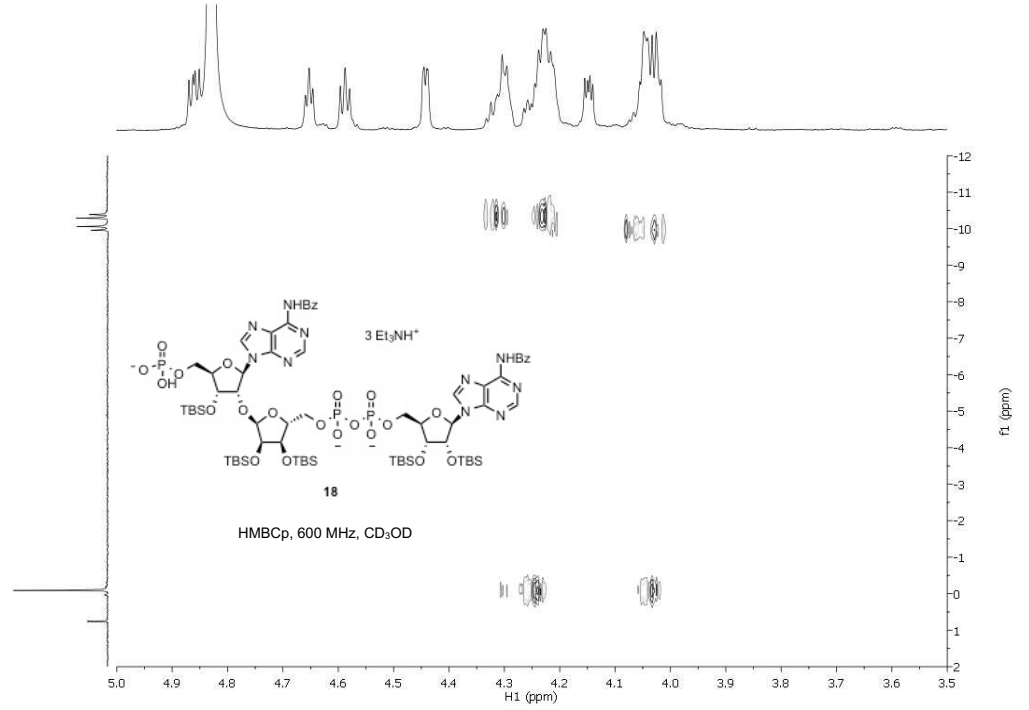
^{31}P, 202 MHz, CD_3OD

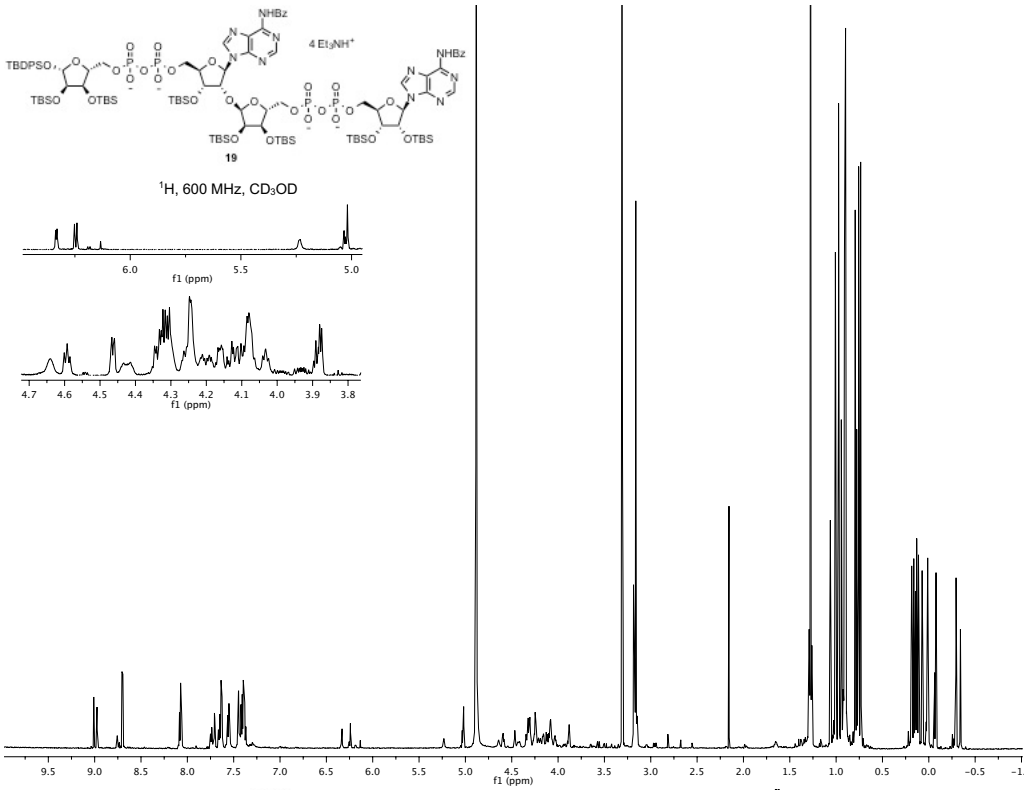


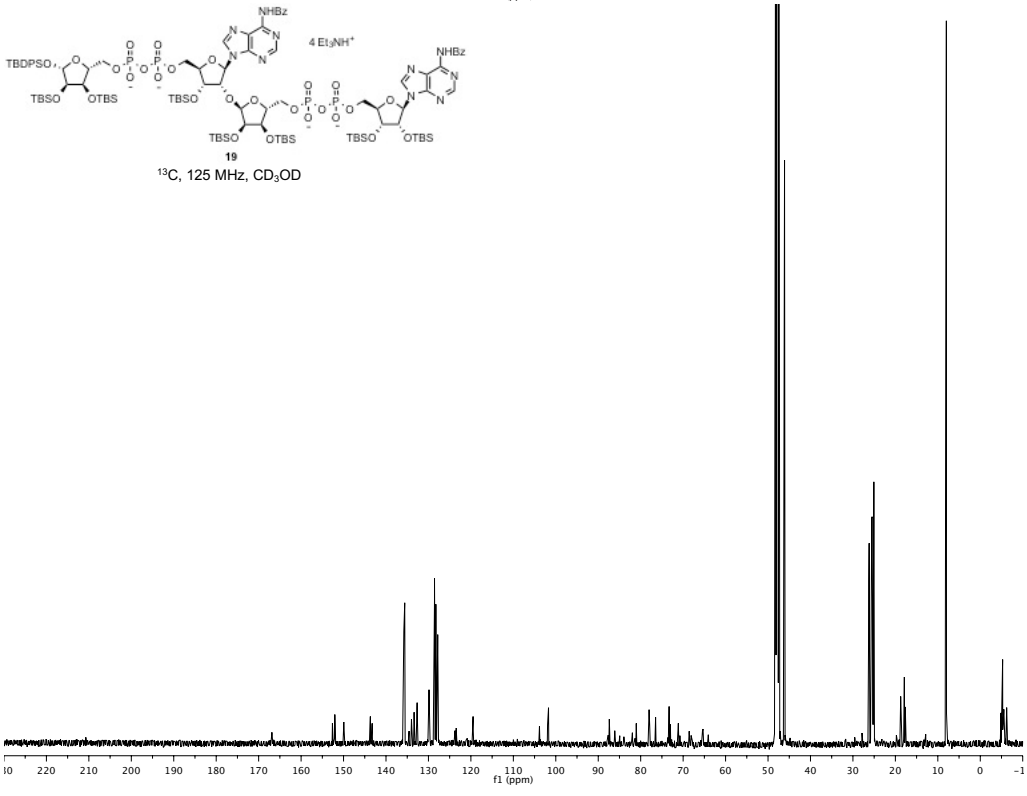

NHBz
3 Et3NH+
TBSO
OTBS
18
COSY, 600 MHz, CD3OD
f2 (ppm)
f1 (ppm)

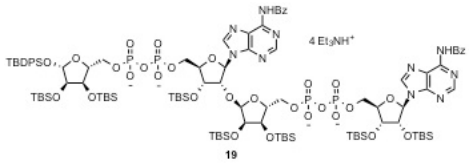

NHBz
3 Et3NH+
TBSO
OTBS
18
TOCSY, 600 MHz, CD3OD
f2 (ppm)
f1 (ppm)


NHBz
3 Et3NH+
TBSO
OTBS
18
HSQC, 500 MHz, CD3OD
f2 (ppm)
f1 (ppm)


NHBz
3 Et3NH+
TBSO
OTBS
18
HMBCp, 600 MHz, CD3OD
H1 (ppm)
f1 (ppm)

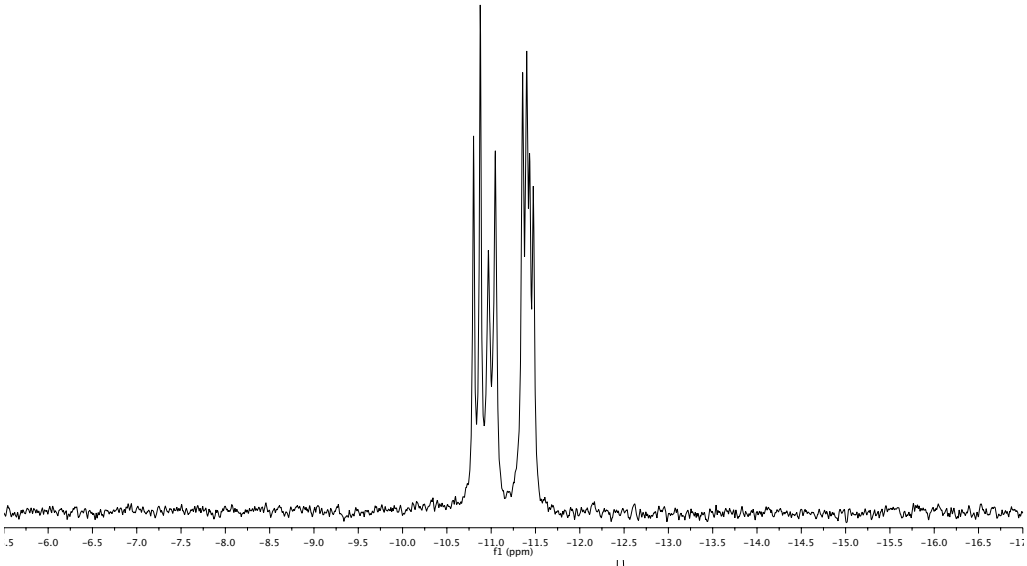

NHBz
4 Et3NH+
TBDPSO
TBSO
OTBS
19
1H, 600 MHz, CD3OD
f1 (ppm)


NHBz
4 Et3NH+
TBDPSO
TBSO
OTBS
19
13C, 125 MHz, CD3OD
f1 (ppm)

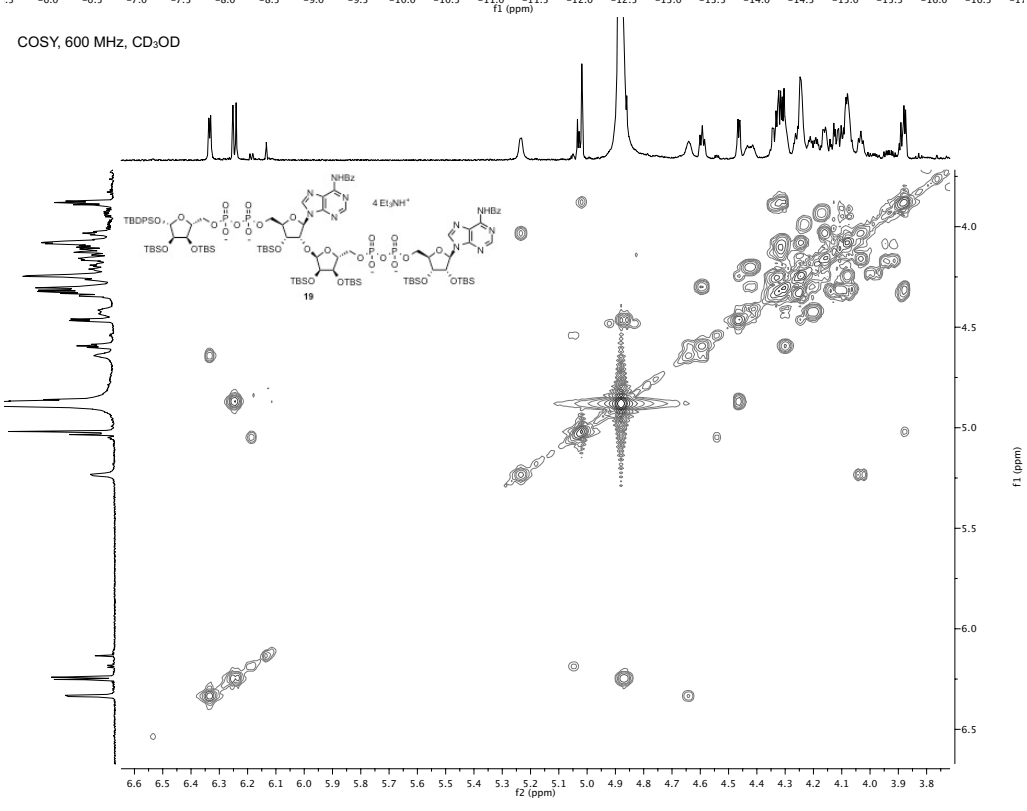


19

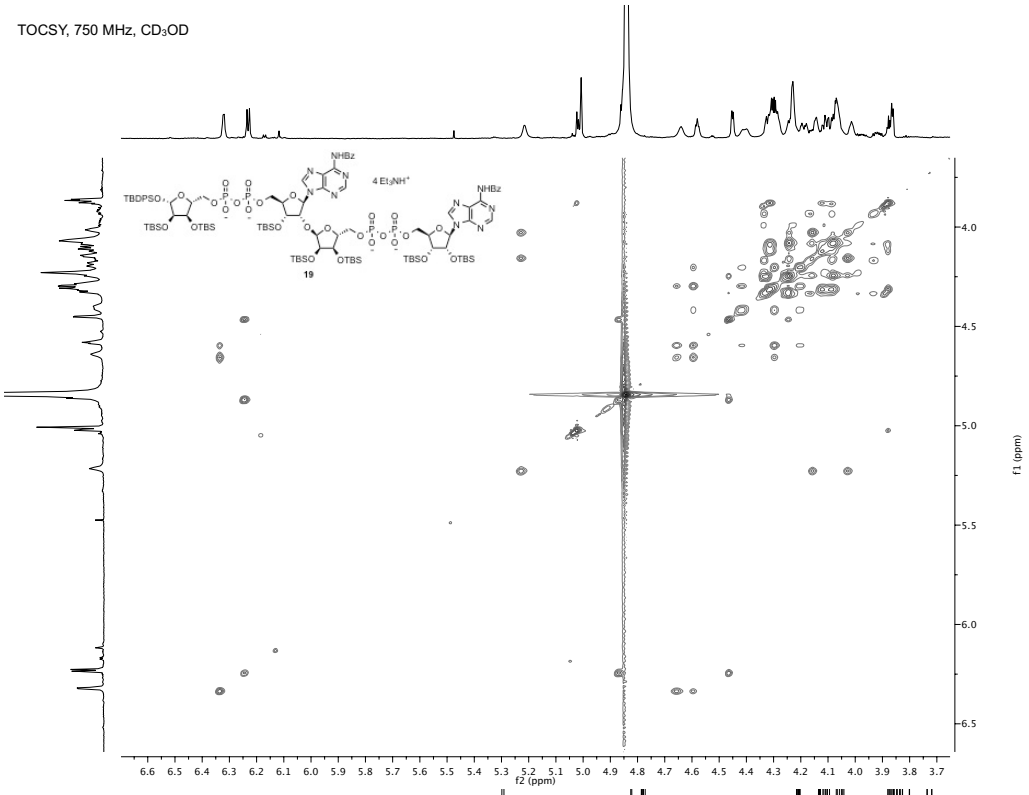
^{31}P, 243 MHz, CD_3OD



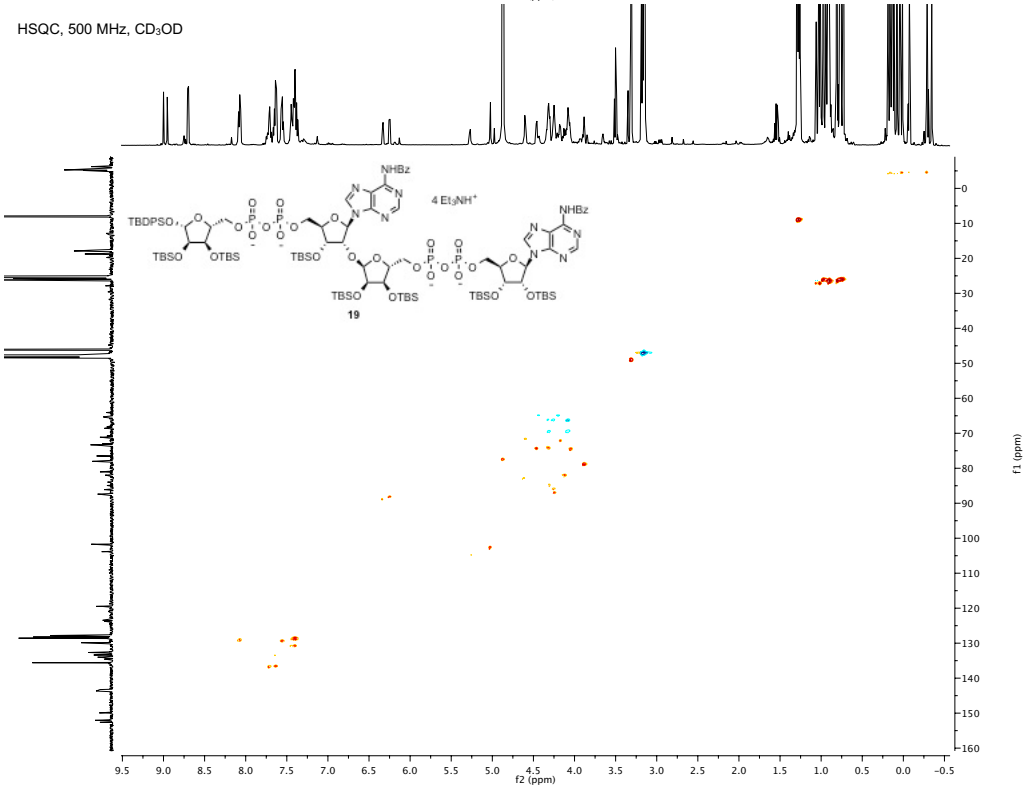
COSY, 600 MHz, CD_3OD



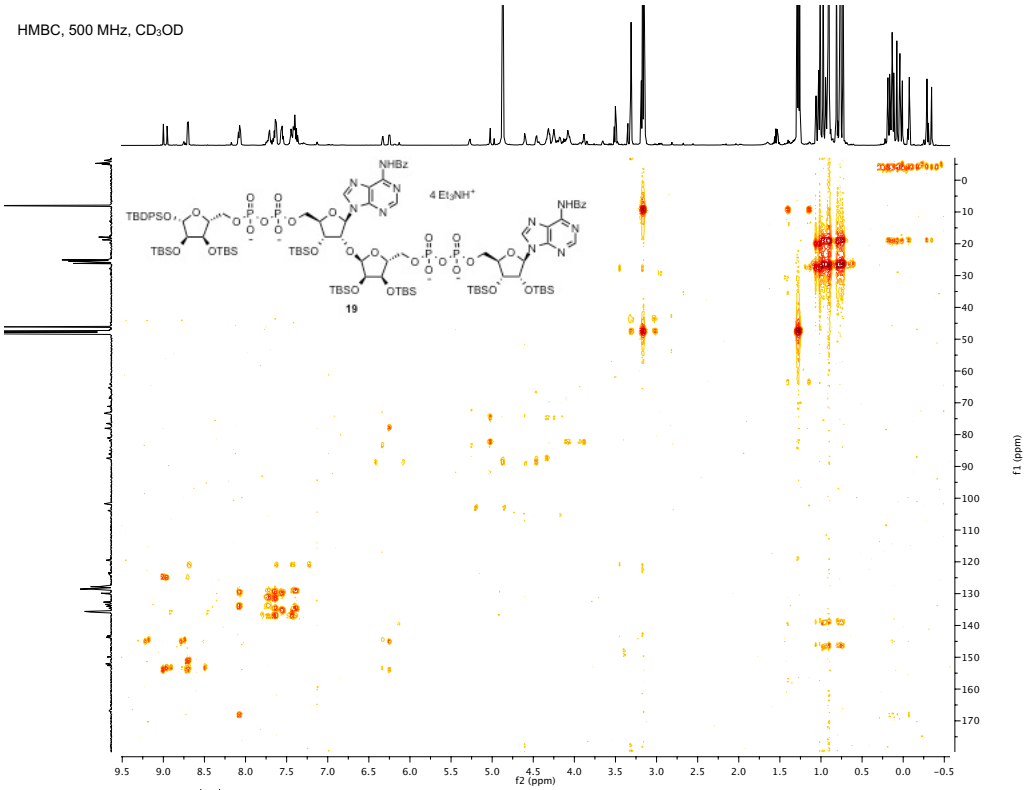
TOCSY, 750 MHz, CD_3OD



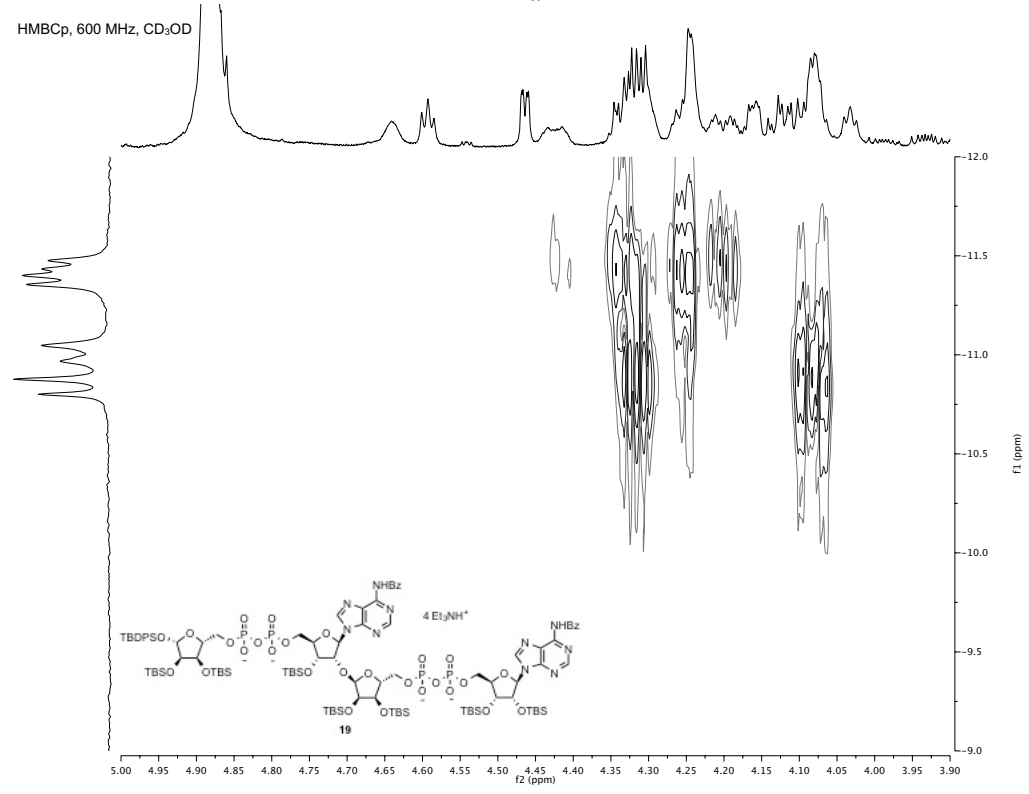
HSQC, 500 MHz, CD_3OD

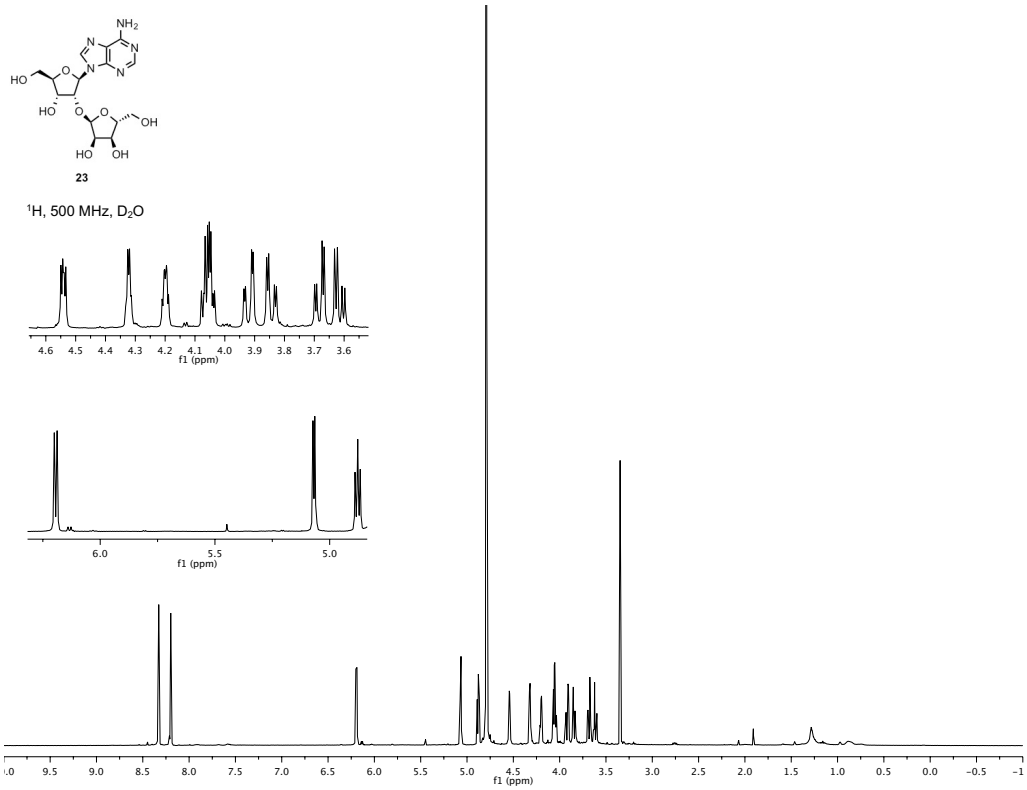


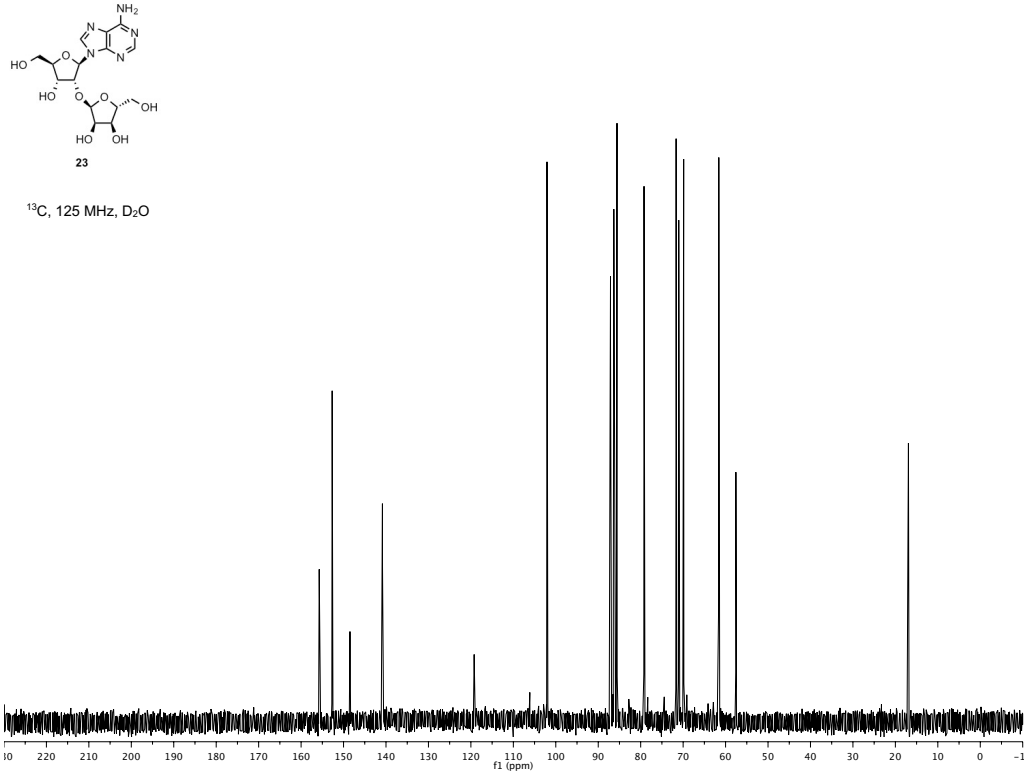
HMBC, 500 MHz, CD_3OD

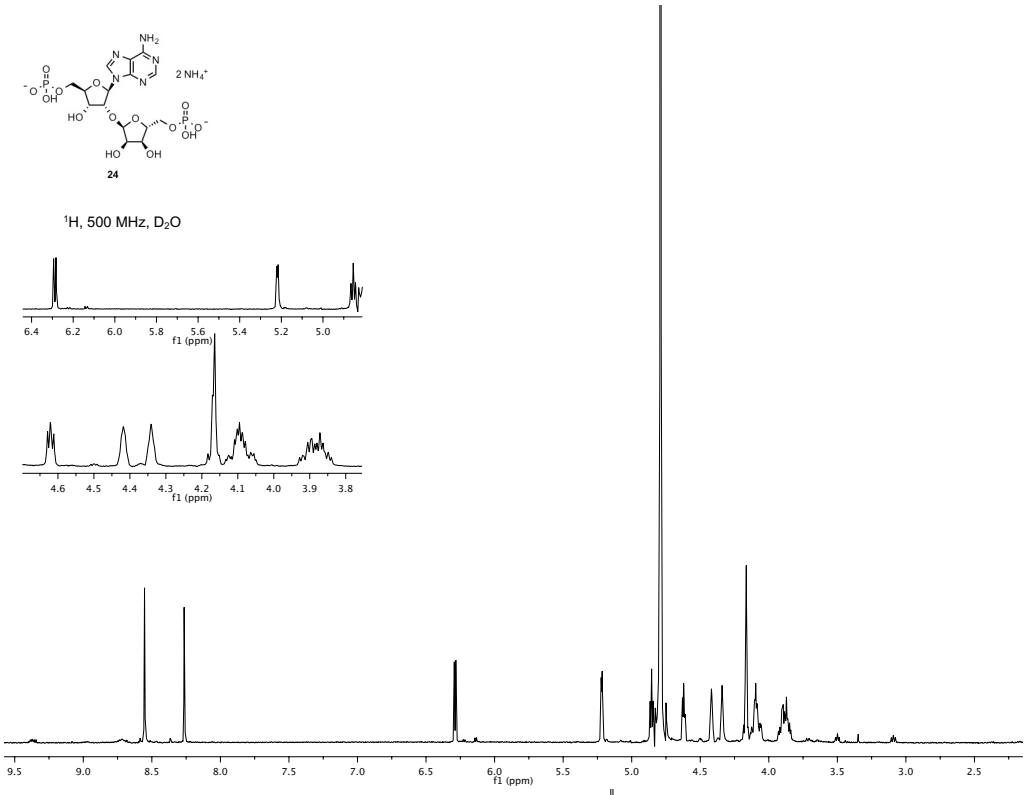


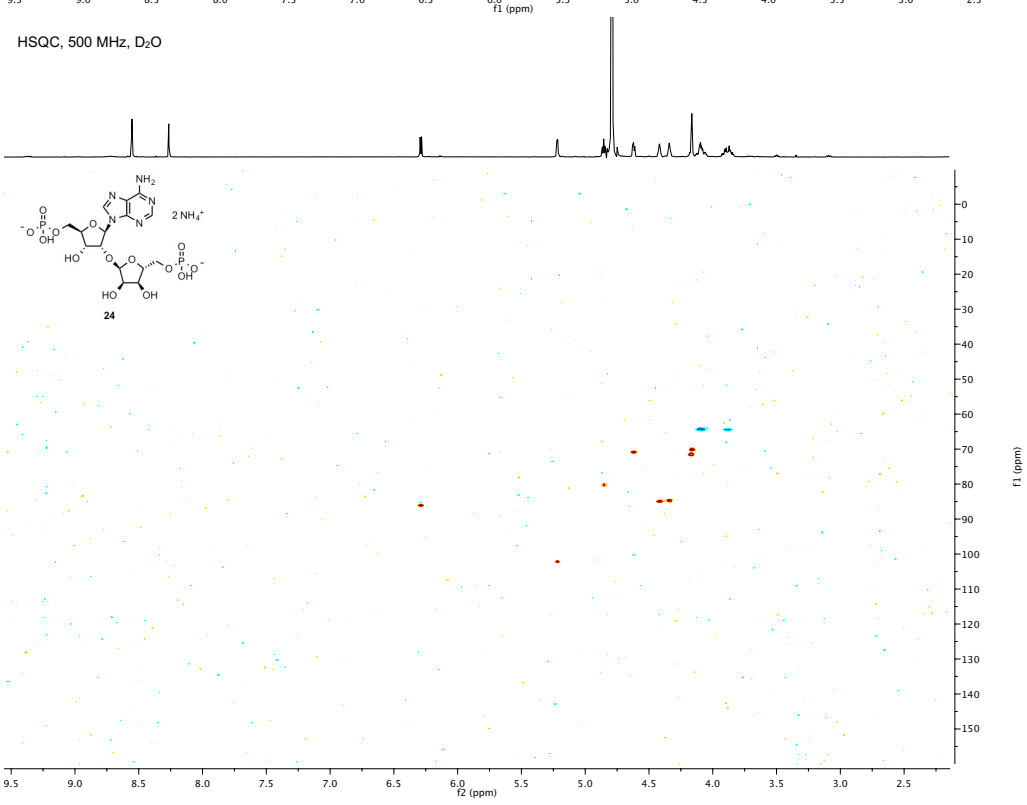
HMBCp, 600 MHz, CD_3OD



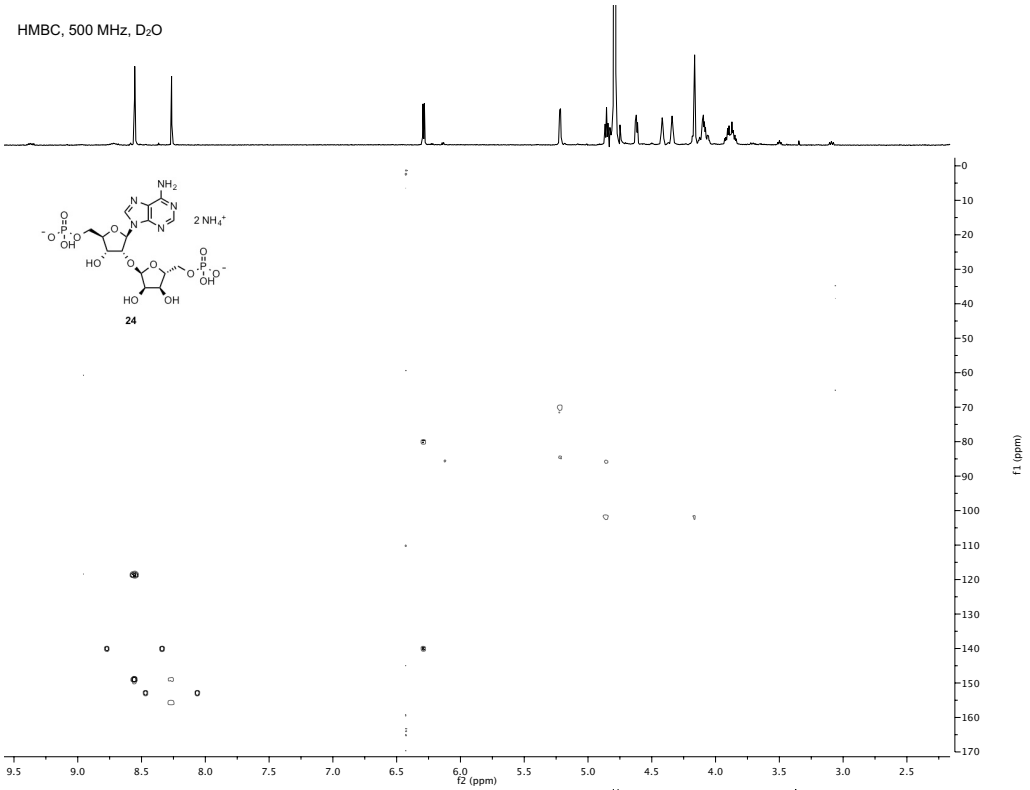

NH2
HO
HO
OH
HO
OH
23
1H, 500 MHz, D2O
4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6
f1 (ppm)
6.0 5.5 5.0
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
f1 (ppm)


NH2
HO
HO
OH
HO
OH
23
13C, 125 MHz, D2O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

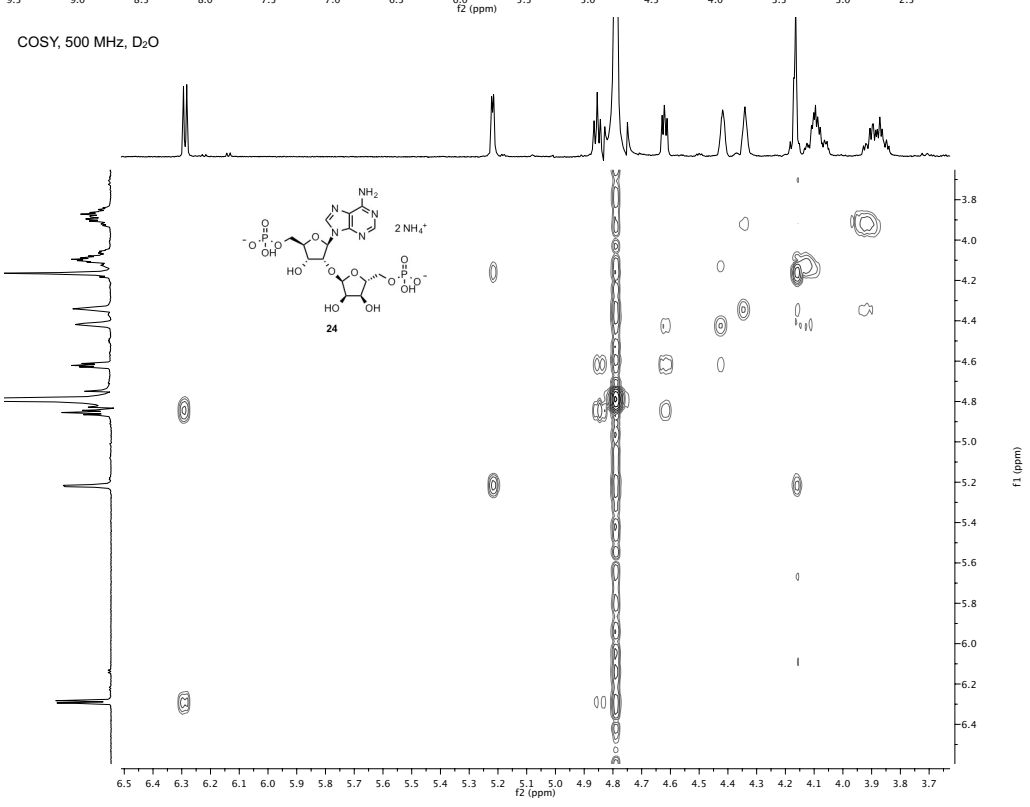

2 NH4+
24
1H, 500 MHz, D2O
f1 (ppm)


HSQC, 500 MHz, D2O
2 NH4+
24
f2 (ppm)
f1 (ppm)

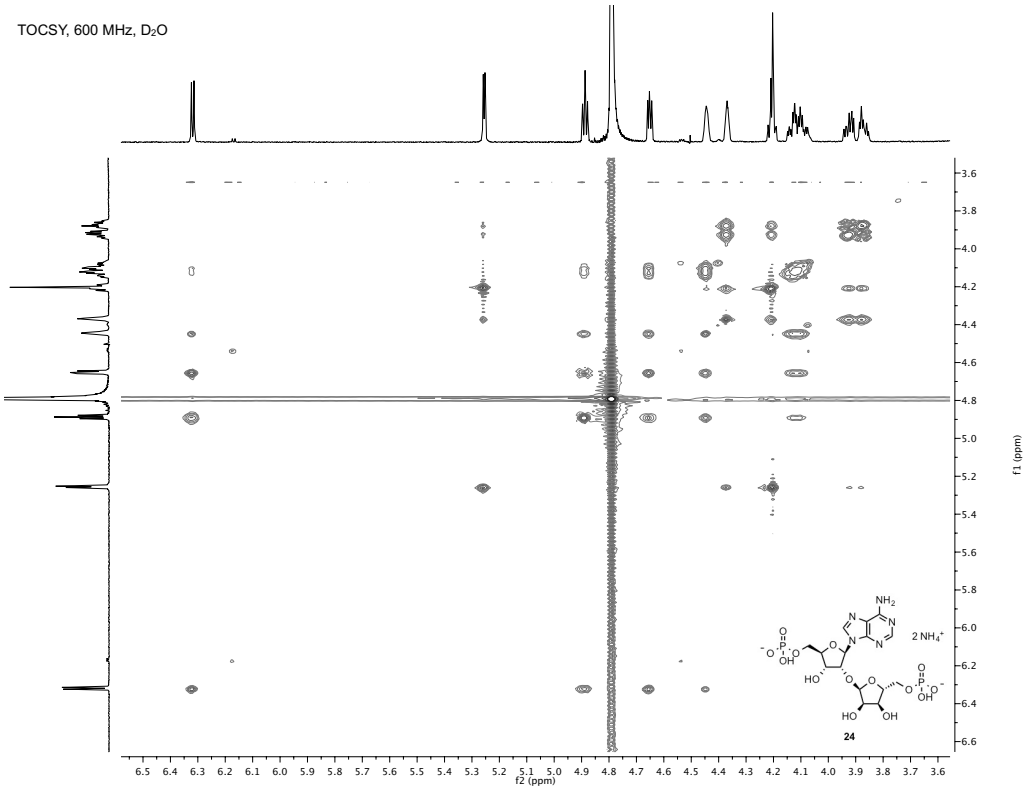
HMBC, 500 MHz, D_2O



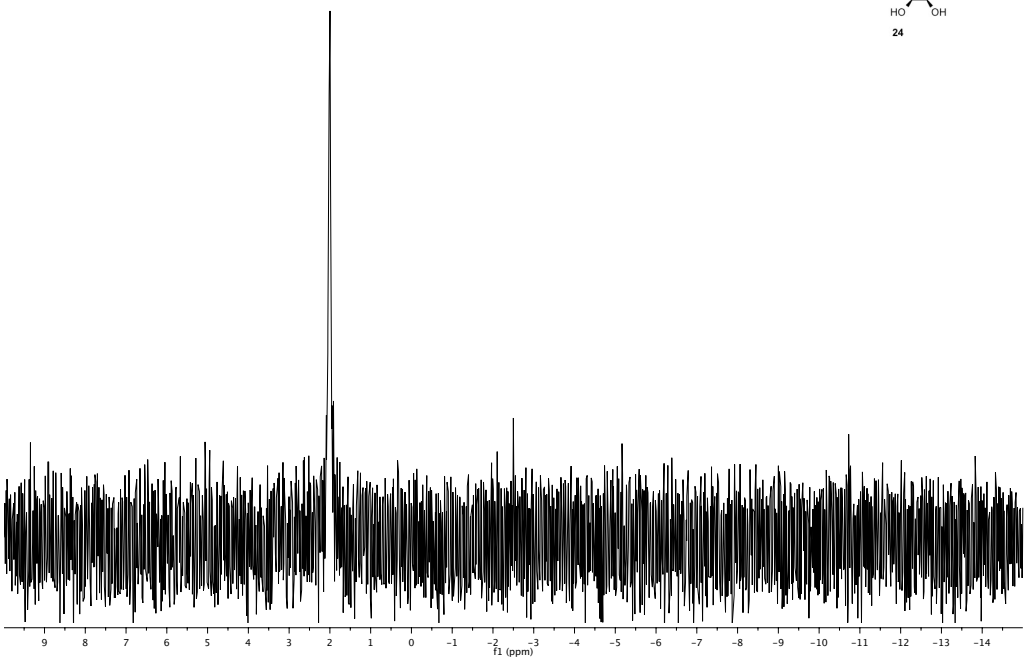
COSY, 500 MHz, D_2O

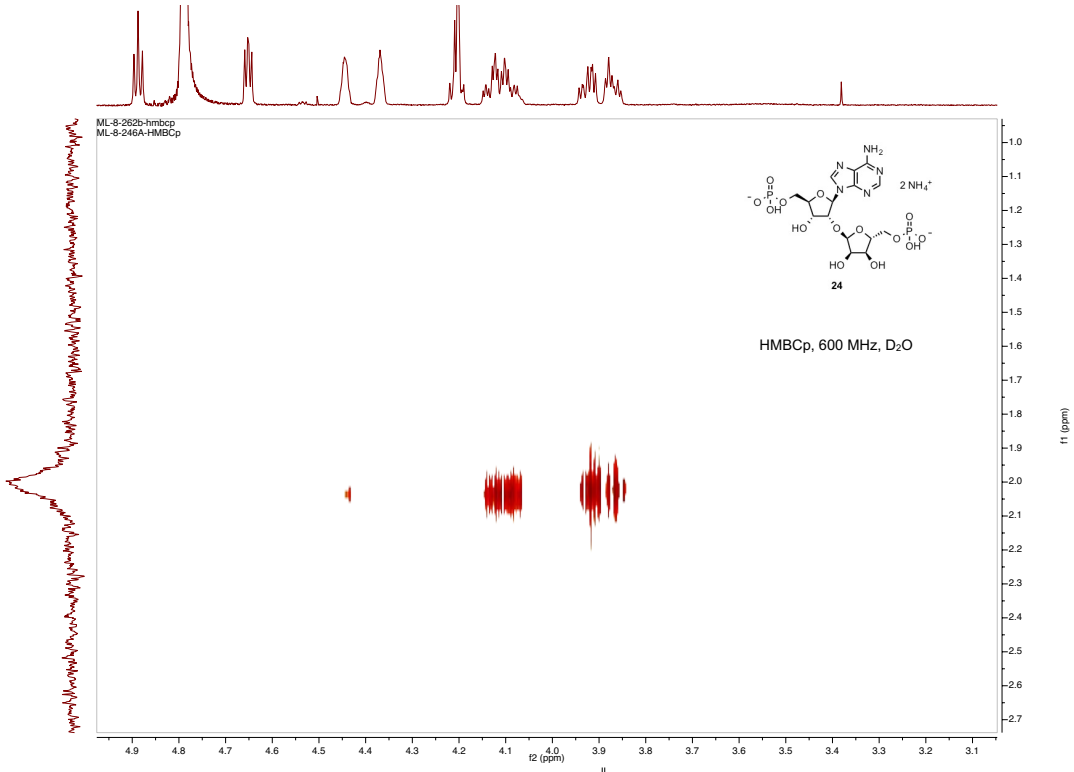


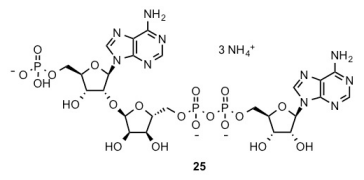
TOCSY, 600 MHz, D_2O



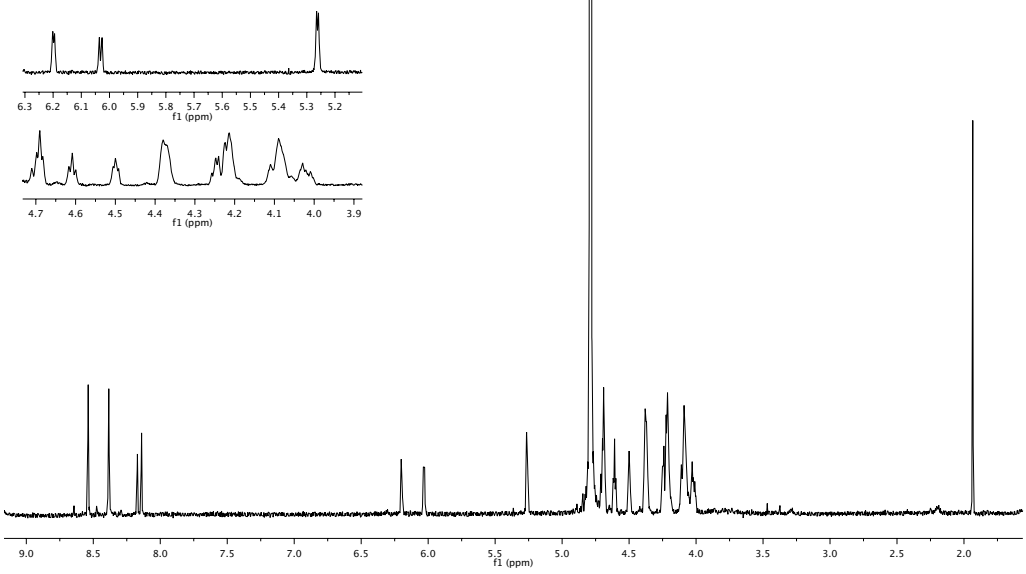
^{31}P, 243 MHz, D_2O

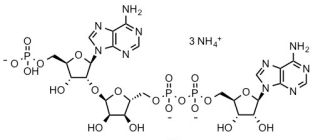




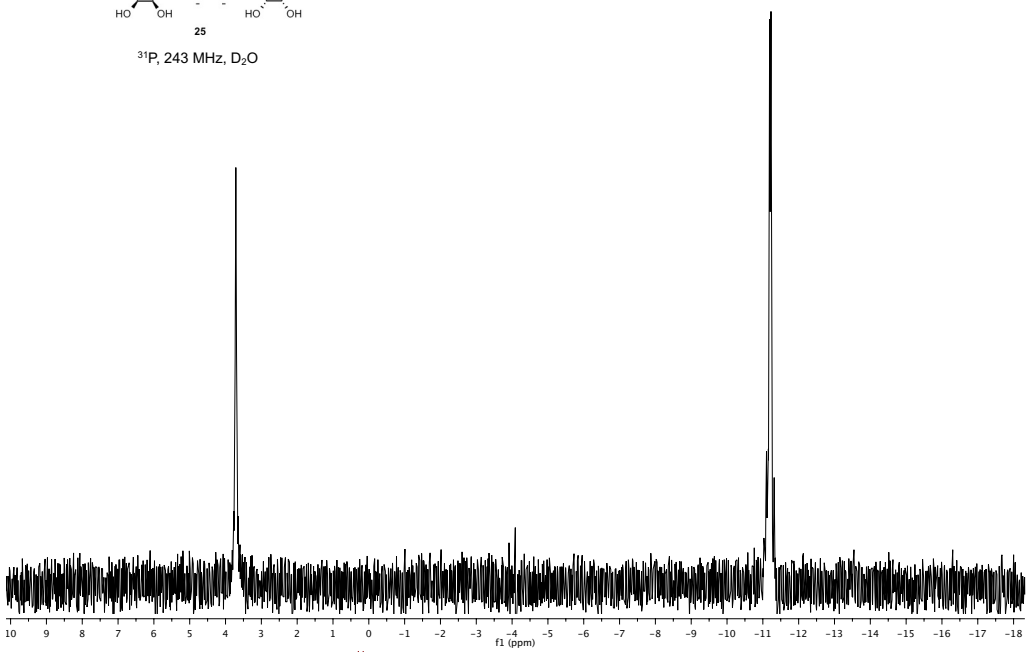


^{1}H, 500 MHz, D_2O

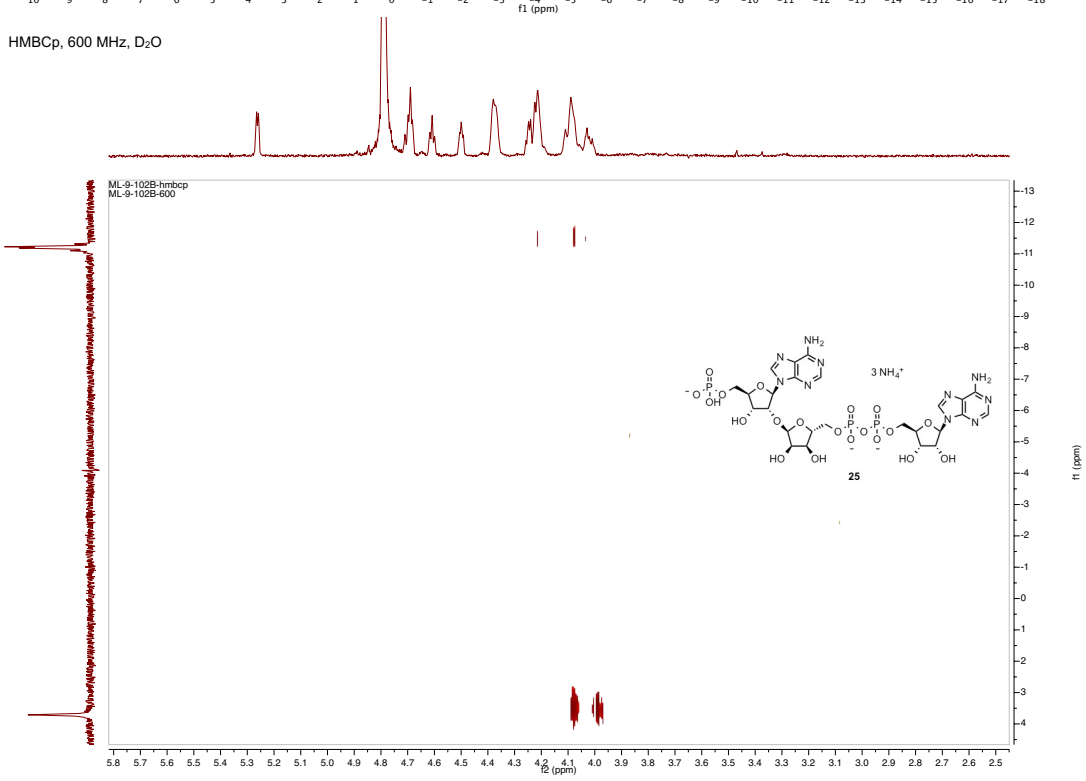




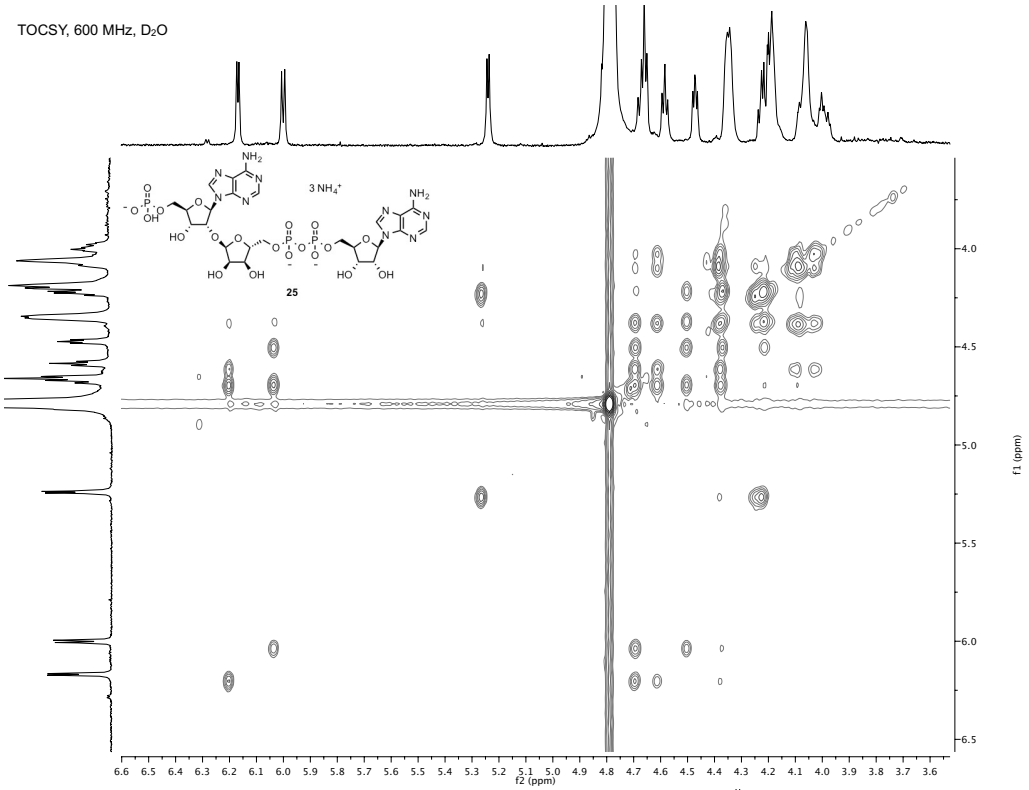
^{31}P, 243 MHz, D_2O



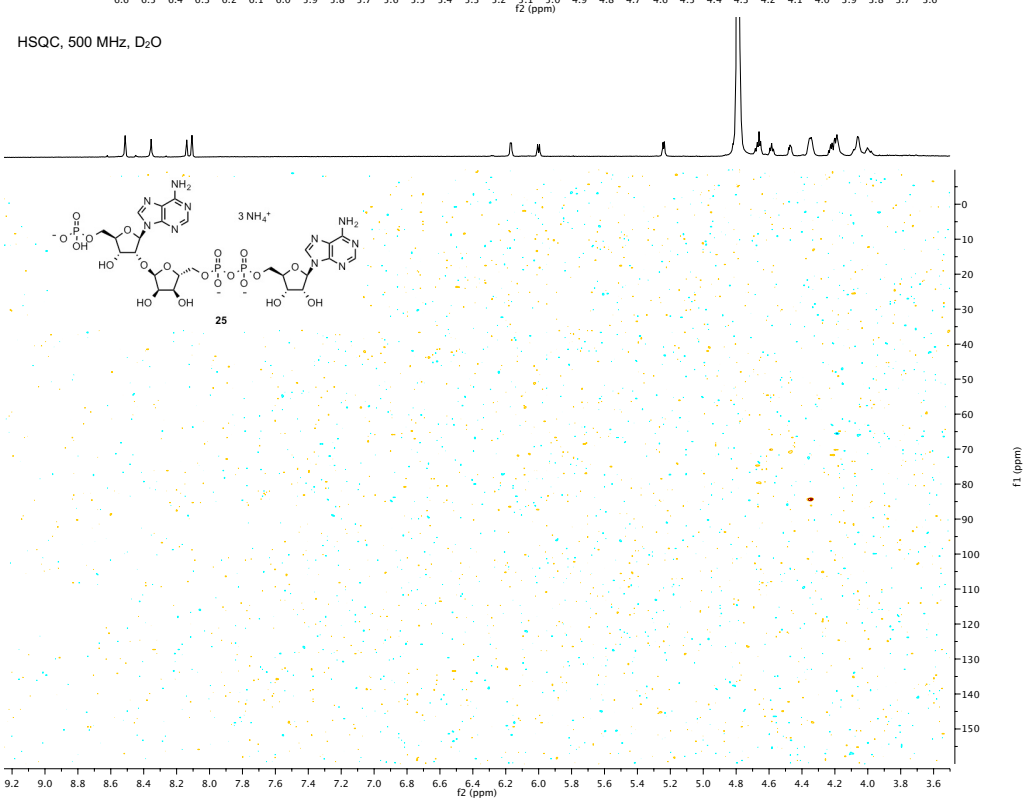
HMBCp, 600 MHz, D_2O



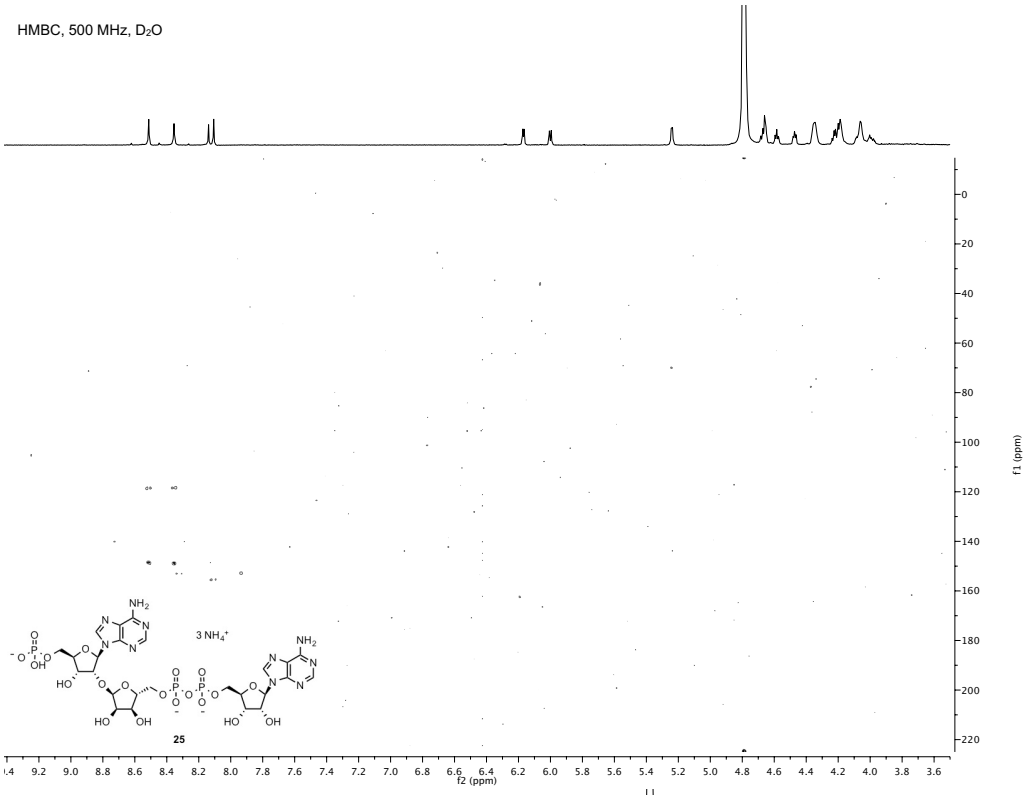
TOCSY, 600 MHz, D_2O



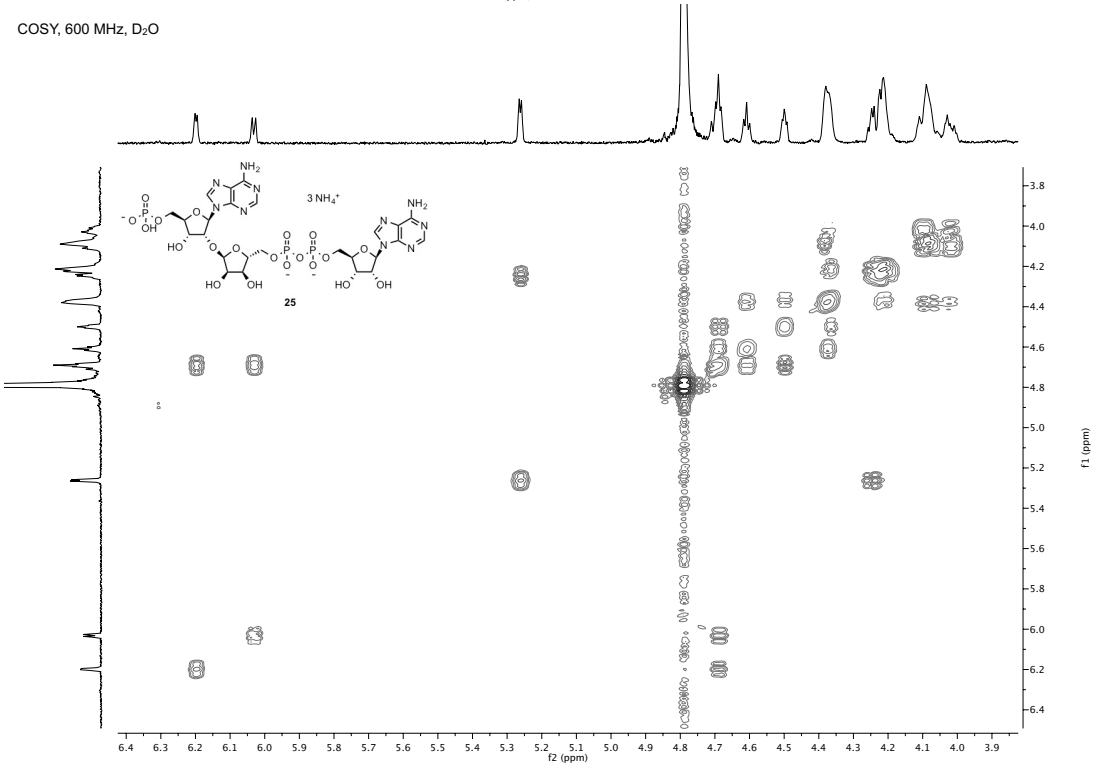
HSQC, 500 MHz, D_2O

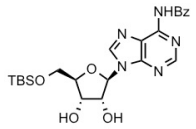


HMBC, 500 MHz, D_2O



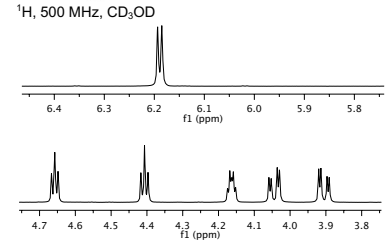
COSY, 600 MHz, D_2O

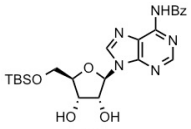




26

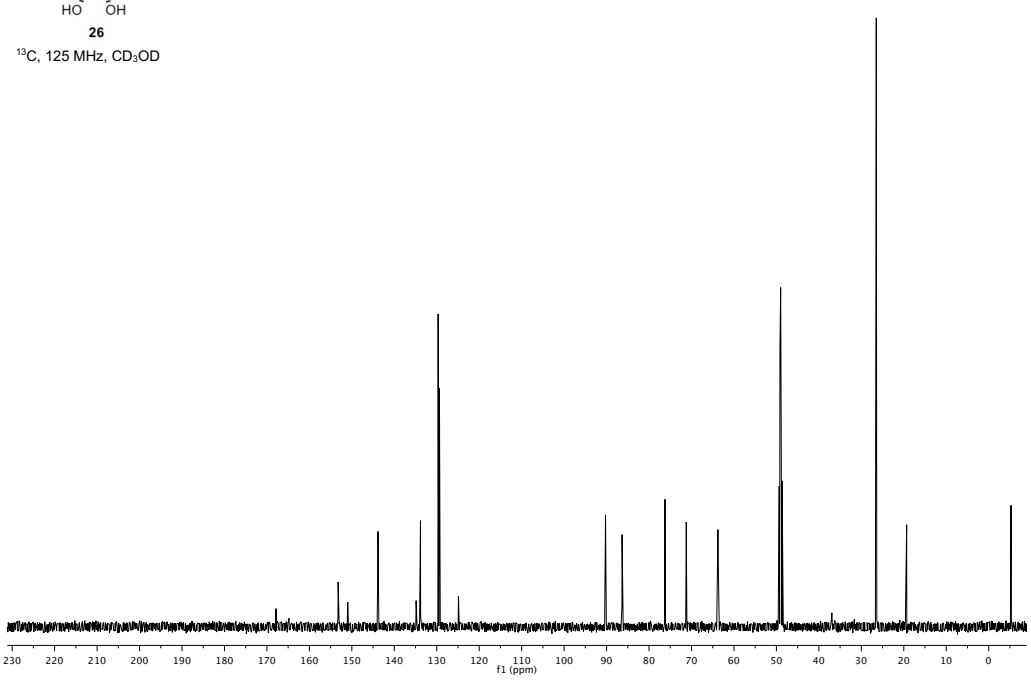
^{1}H, 500 MHz, CD_3OD

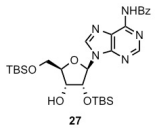




26

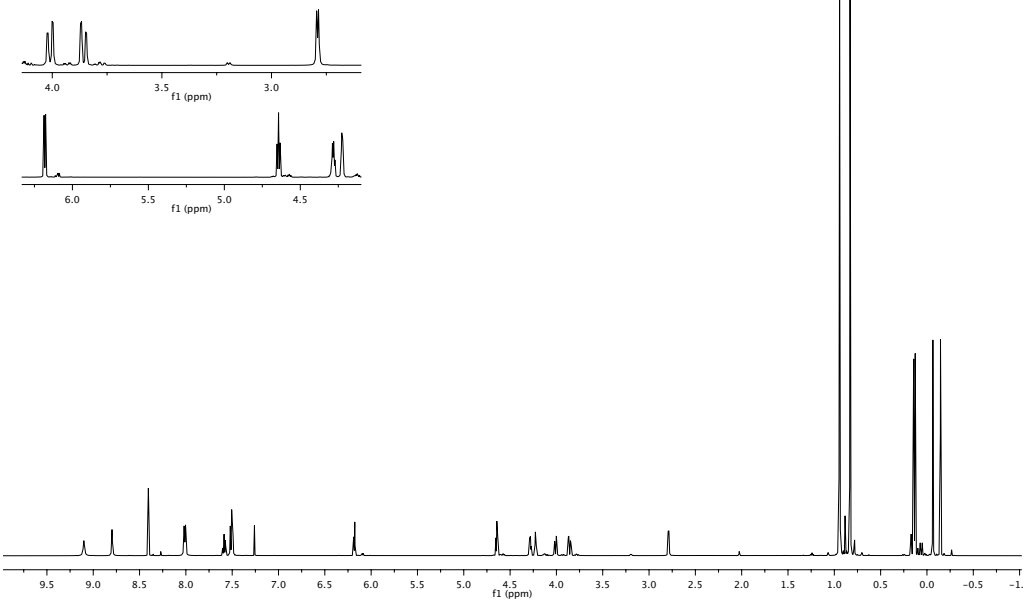
^{13}C, 125 MHz, CD_3OD

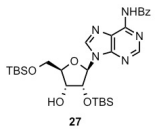




27

^{1}H, 500 MHz, $CDCl_3$

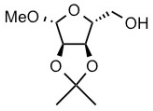




27

^{13}C, 125 MHz, $CDCl_3$

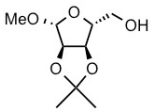
ml-5-220a
ml-5-220a



28

^{1}H, 500 MHz, $CDCl_3$

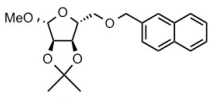
ml-5-220a-13c
ml-5-220a-13c



28

^{13}C, 125 MHz, $CDCl_3$

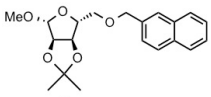
05_12_2012-MBrich-U500-5-274-a1
05_12_2012-MBrich-U500-5-274-a1



29

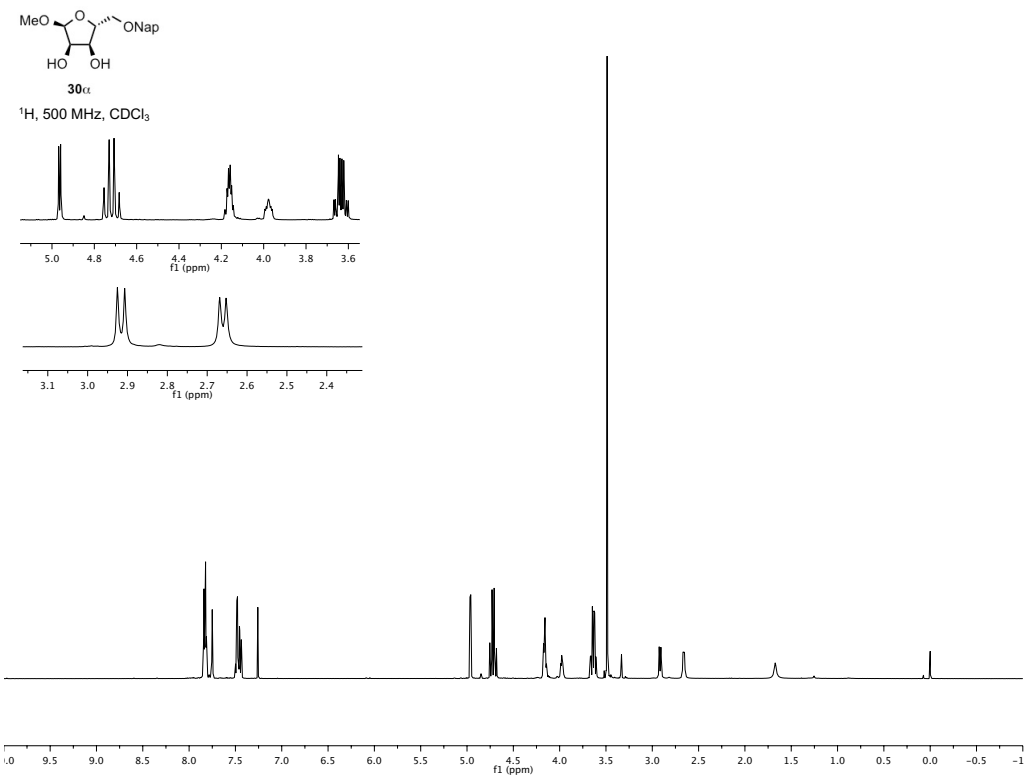
^{1}H, 500 MHz, $CDCl_3$

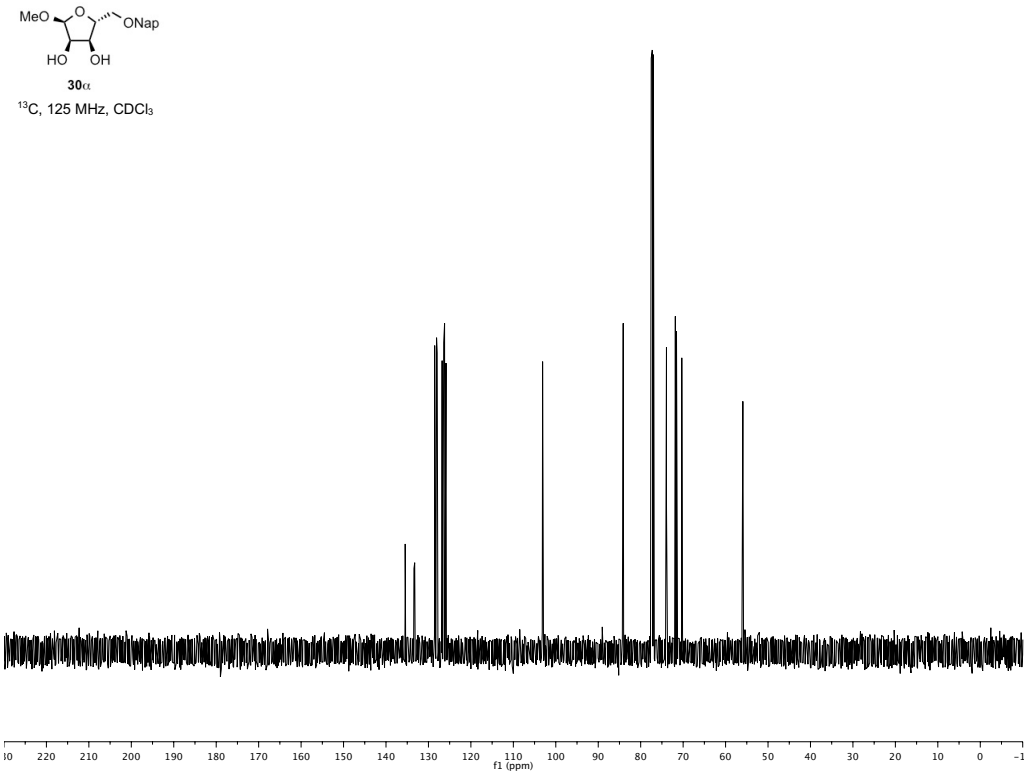
05_12_2012-MBrich-U500-5-278-b2c
05_12_2012-MBrich-U500-5-278-b2c

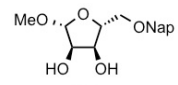


29

^{13}C, 125 MHz, $CDCl_3$

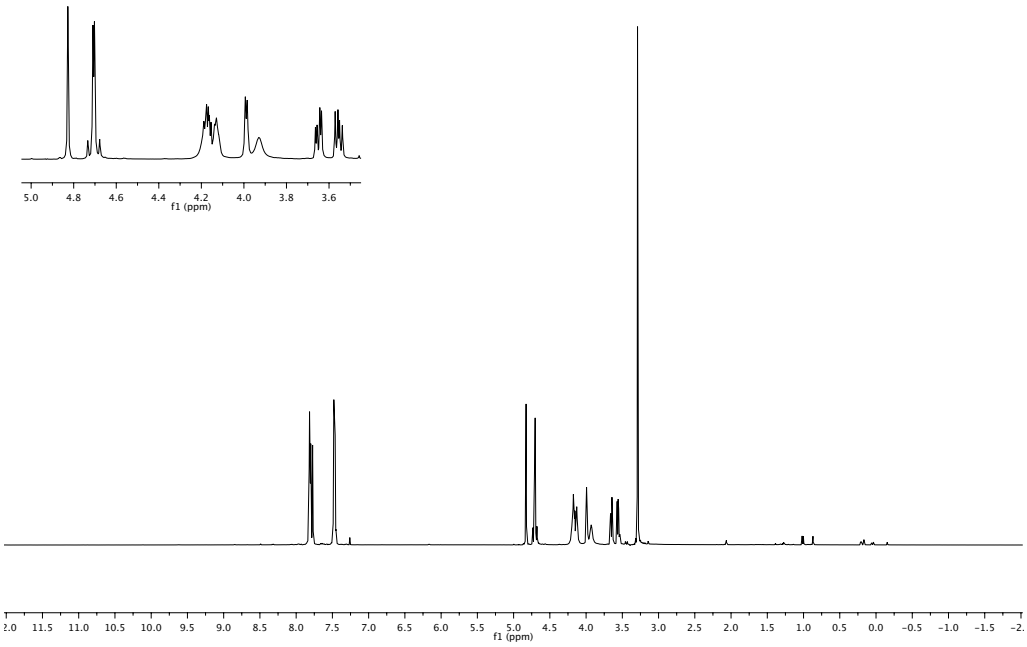

MeO
O
ONap
HO
OH
30α
1H, 500 MHz, CDCl3
f1 (ppm)
f1 (ppm)

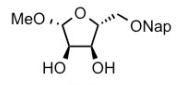

MeO
O
ONap
HO
OH
30α
13C, 125 MHz, CDCl3
f1 (ppm)



30β

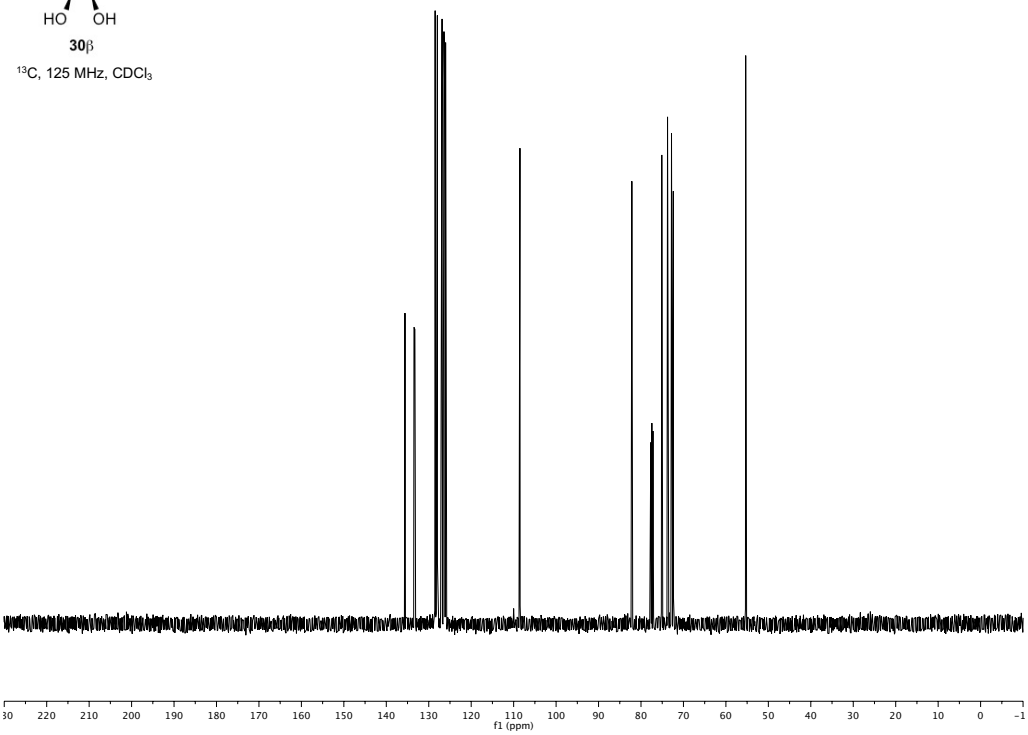
^{1}H, 500 MHz, $CDCl_3$

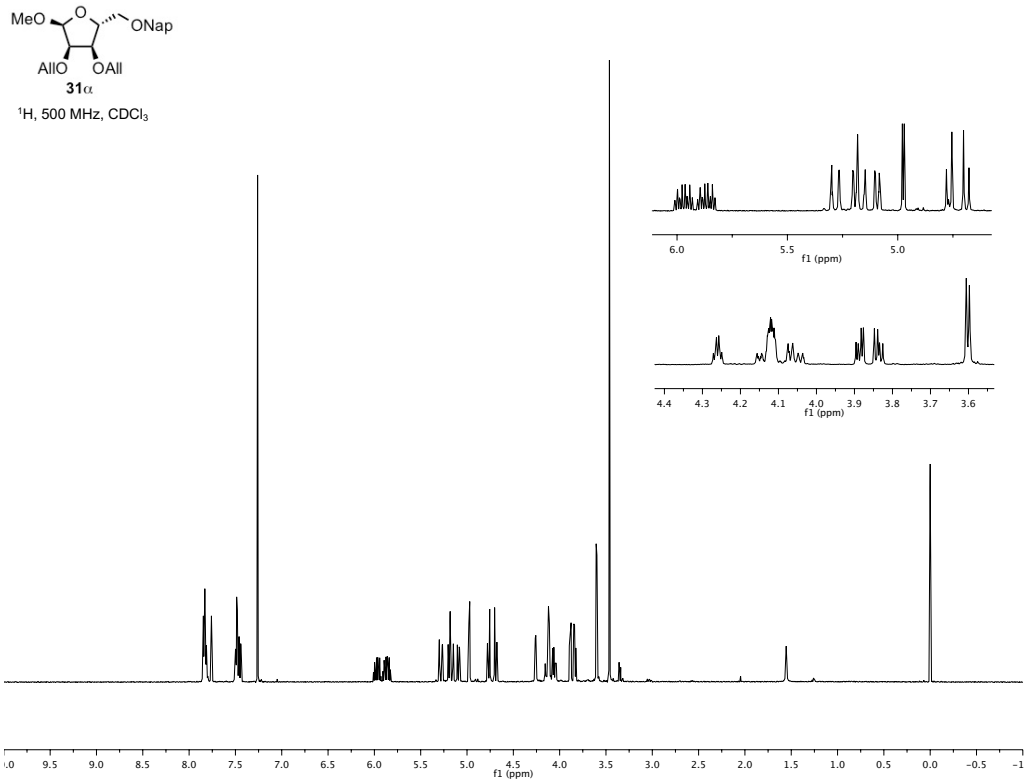


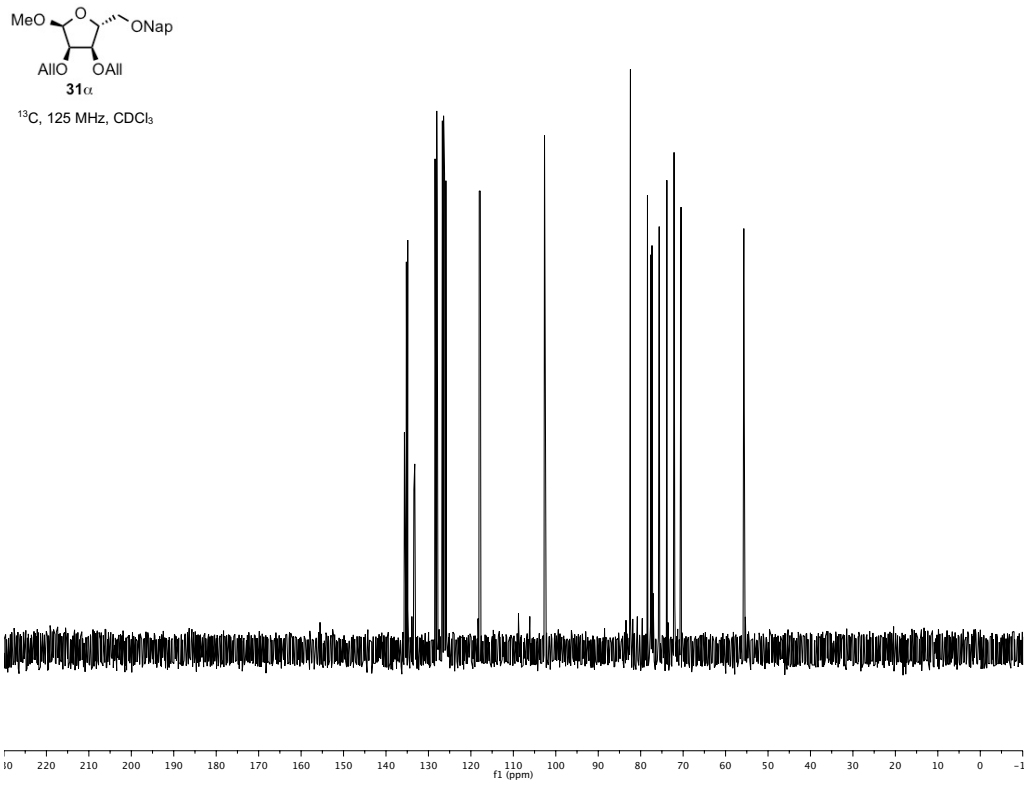


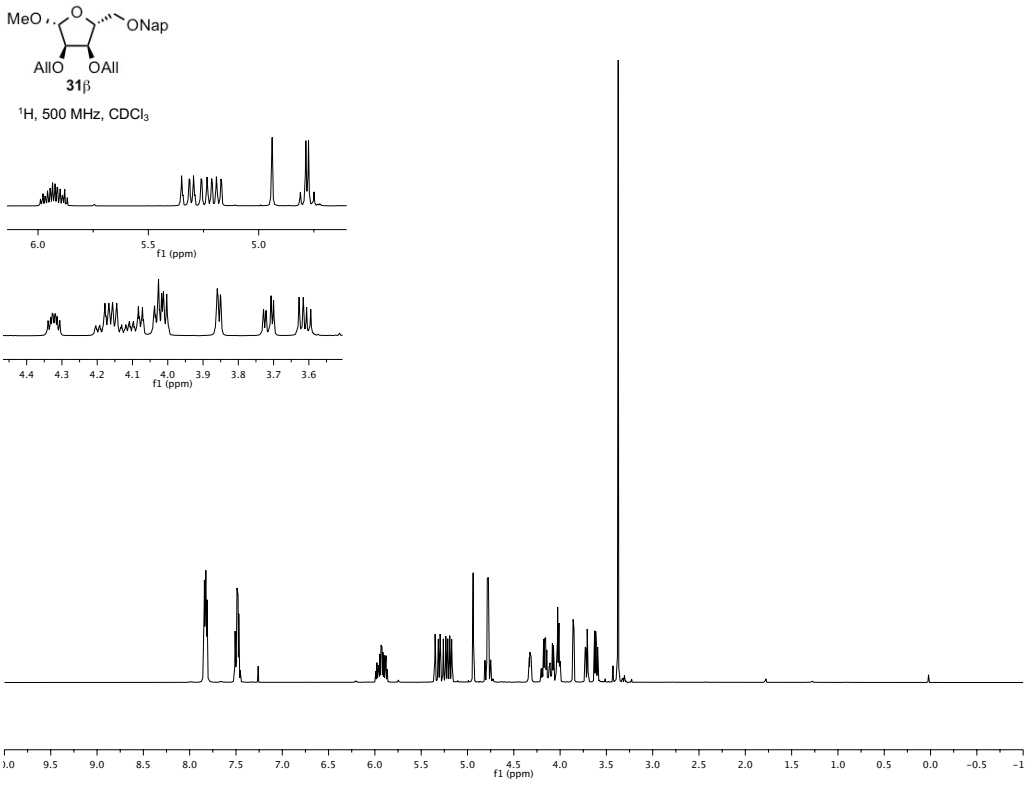
30β

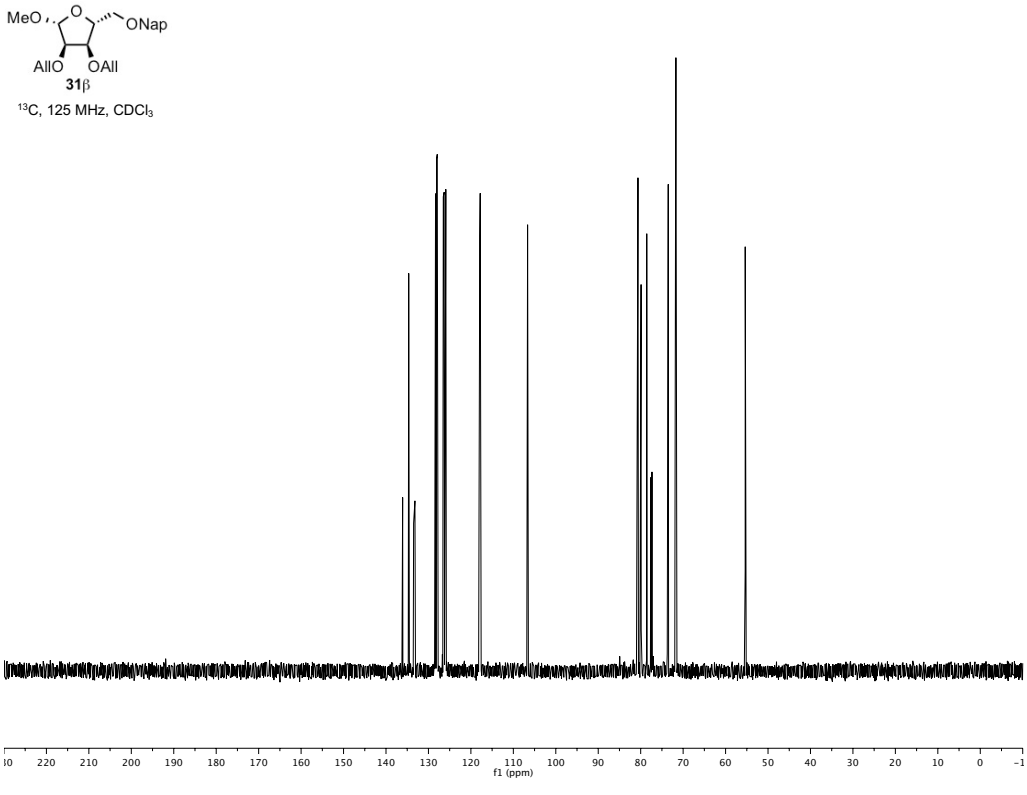
^{13}C, 125 MHz, $CDCl_3$

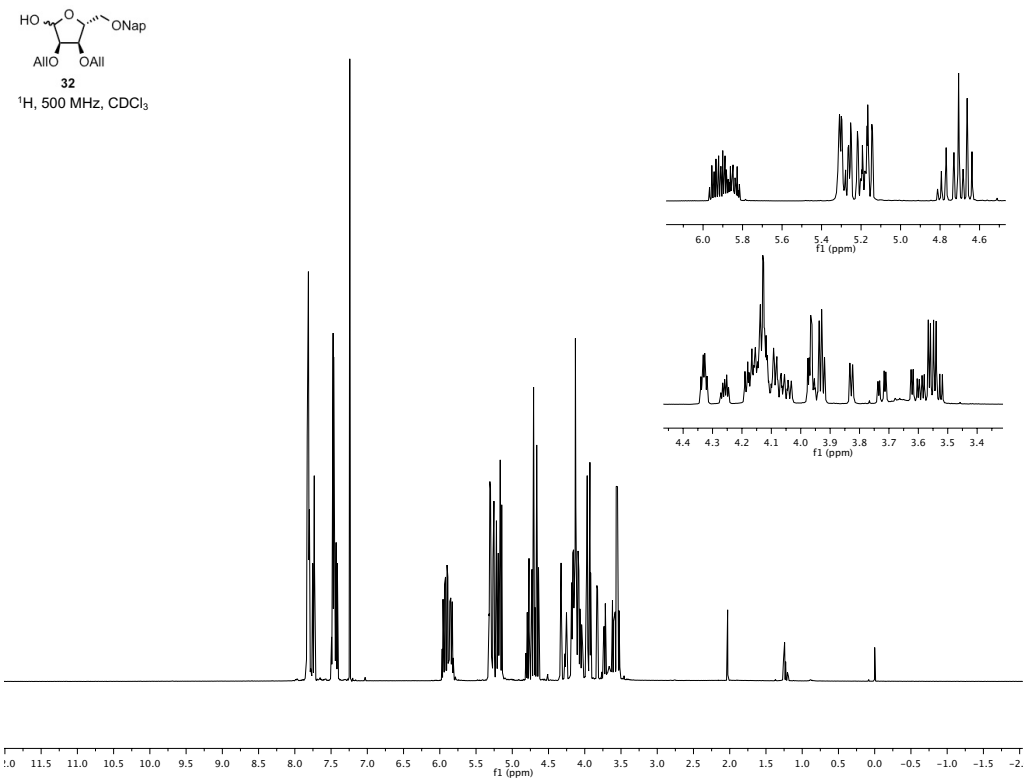


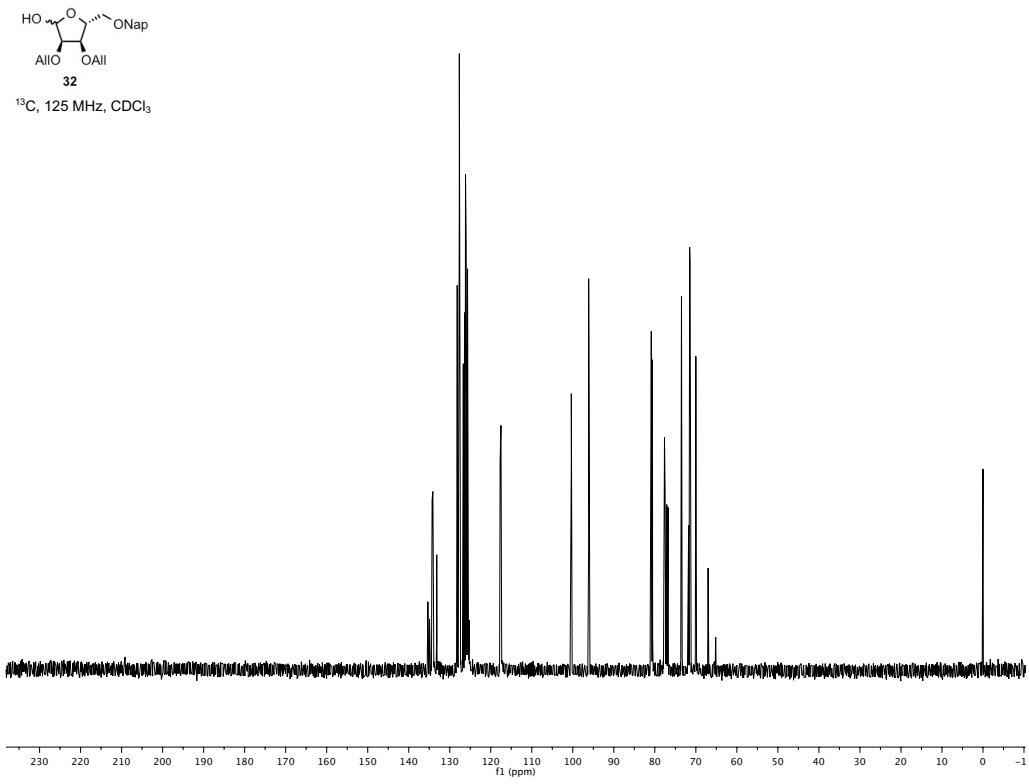

MeO
ONap
AllO
OAll
31α
1H, 500 MHz, CDCl3
6.0
5.5
5.0
f1 (ppm)
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
f1 (ppm)
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

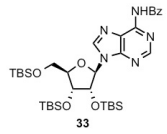

MeO
ONap
AllO
OAll
31α
13C, 125 MHz, CDCl3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


MeO
ONap
AllO
OAll
31β
¹H, 500 MHz, CDCl₃
f1 (ppm)


MeO
ONap
AllO
OAll
31β
¹³C, 125 MHz, CDCl₃
f1 (ppm)

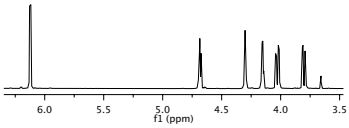

HO
O
ONap
AllO
OAll
32
^{1}H, 500 MHz, $CDCl_3$
f1 (ppm)

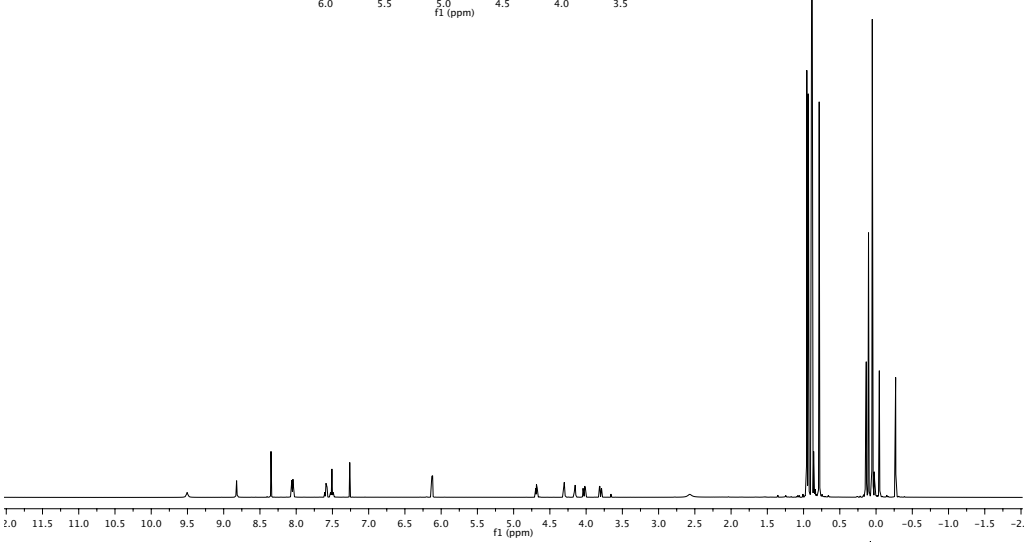

HO
O
ONap
AllO
OAll
32
^{13}C, 125 MHz, $CDCl_3$
f1 (ppm)

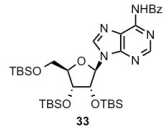


33

^{1}H, 500 MHz, $CDCl_3$

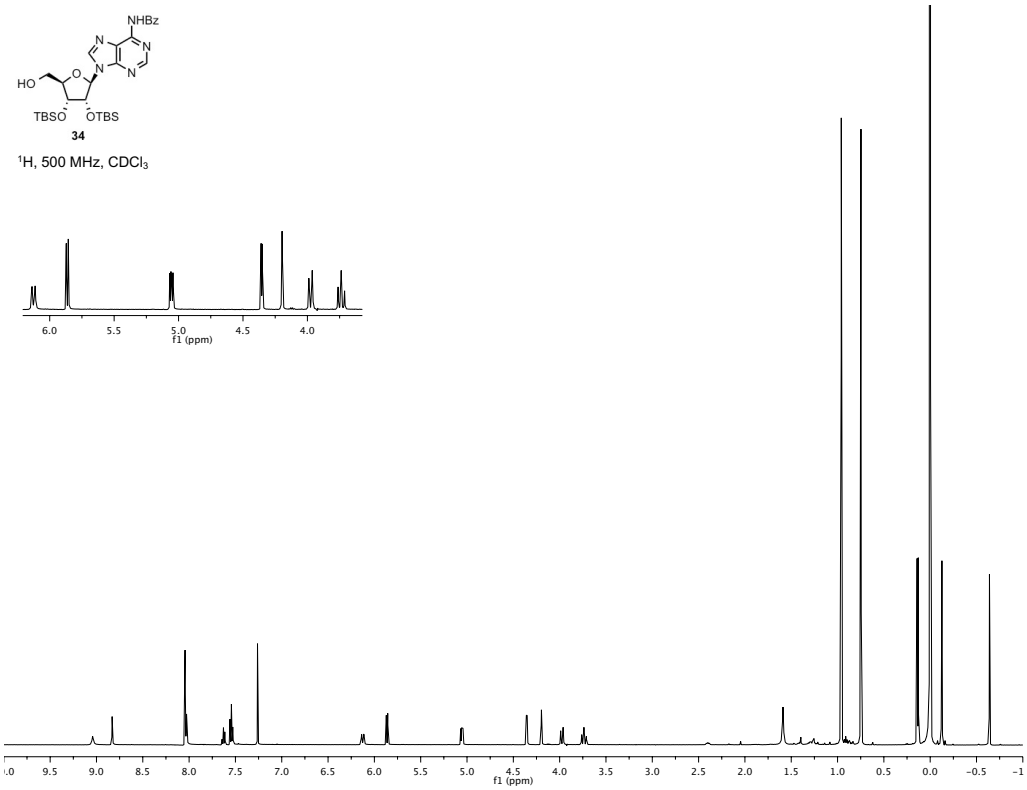


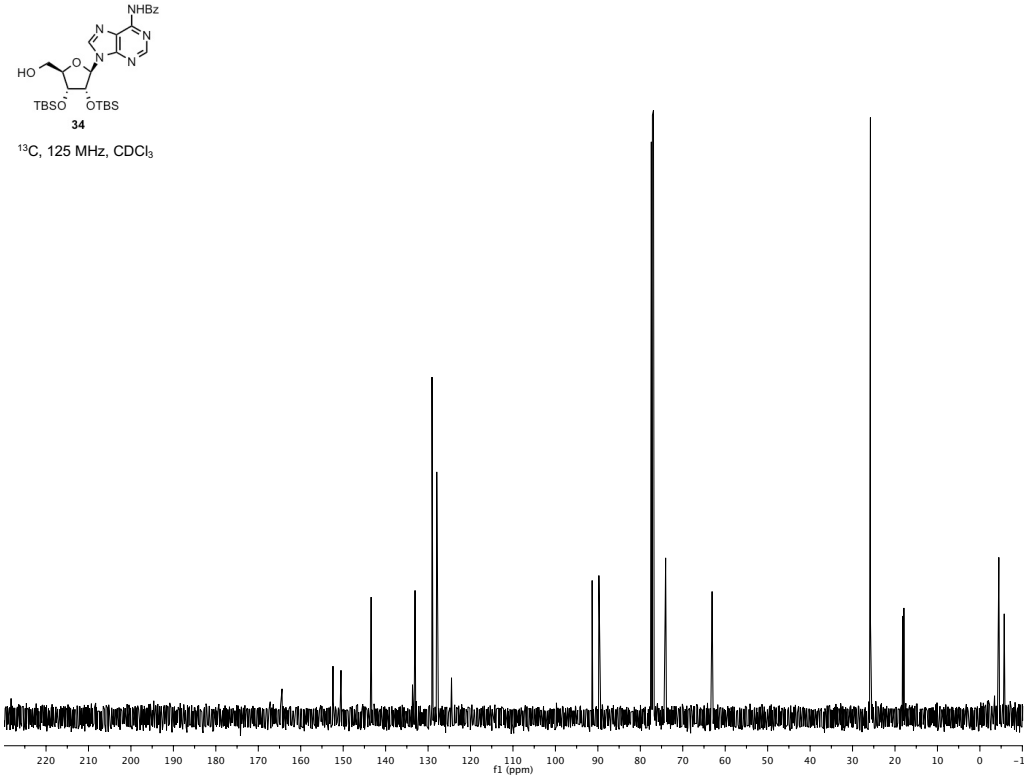




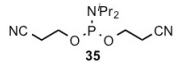
33

^{13}C, 125 MHz, $CDCl_3$


NHBz
HO
TBSO
OTBS
34
1H, 500 MHz, CDCl3
f1 (ppm)


NHBz
HO
TBSO
OTBS
34
13C, 125 MHz, CDCl3
f1 (ppm)

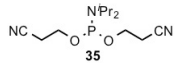
ml-5-020a
ml-5-020a



35

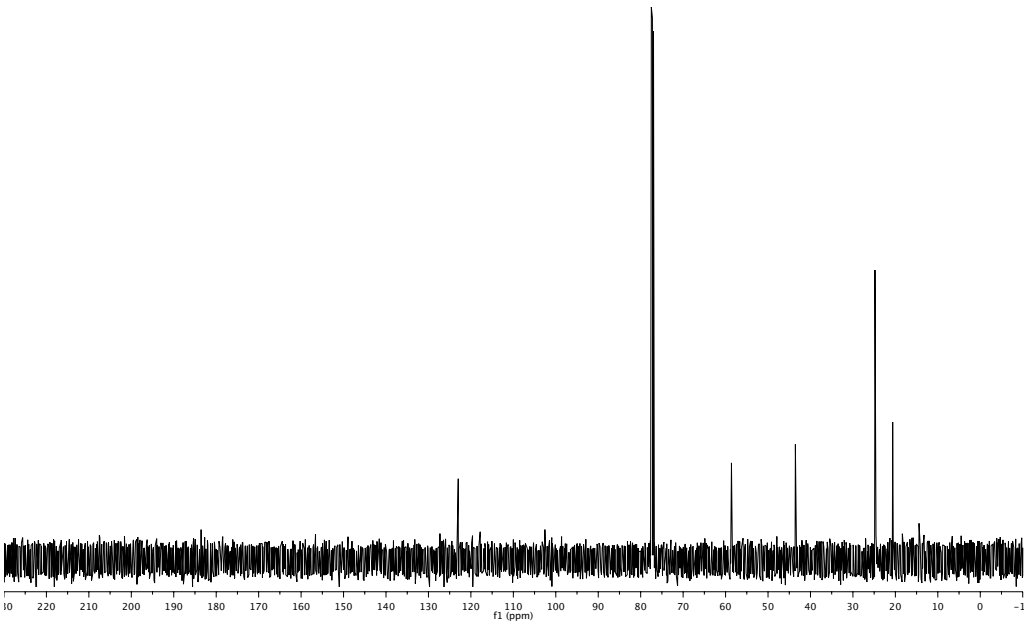
^{1}H, 500 MHz, $CDCl_3$

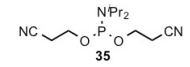
03_21_2012-MBrich-U500-5-176-a3c
03_21_2012-MBrich-U500-5-176-a3c



35

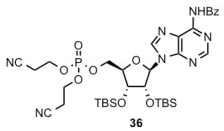
^{13}C, 125 MHz, $CDCl_3$





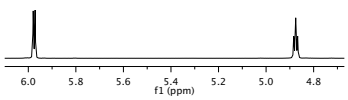
35

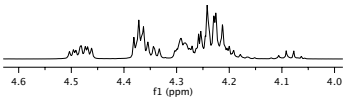
^{31}P, 202 MHz, $CDCl_3$

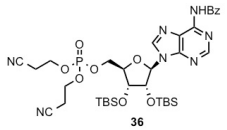


36

^{1}H, 500 MHz, $CDCl_3$

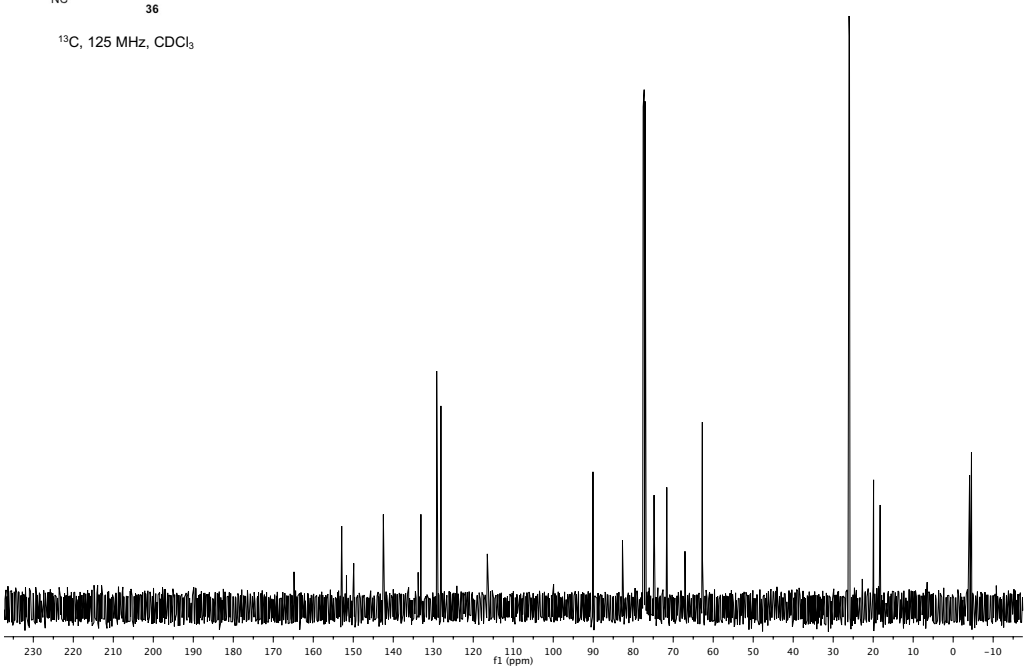


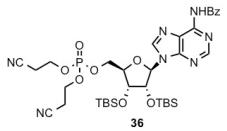




36

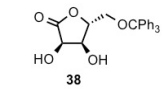
^{13}C, 125 MHz, $CDCl_3$





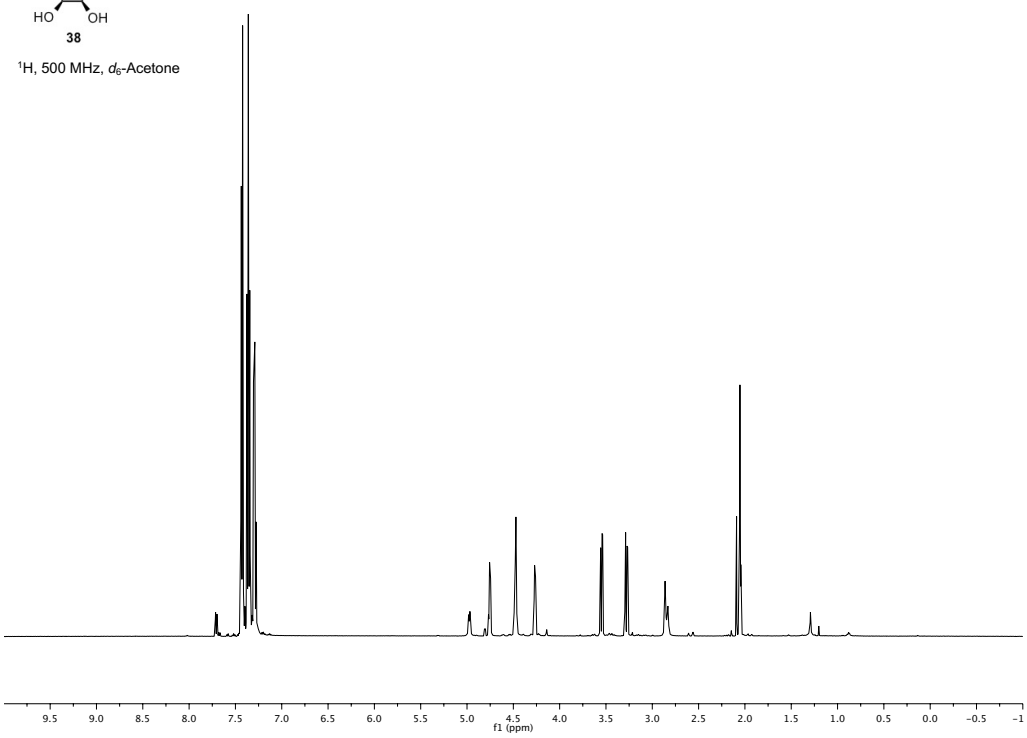
36

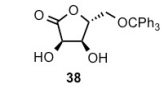
^{31}P, 202 MHz, $CDCl_3$



38

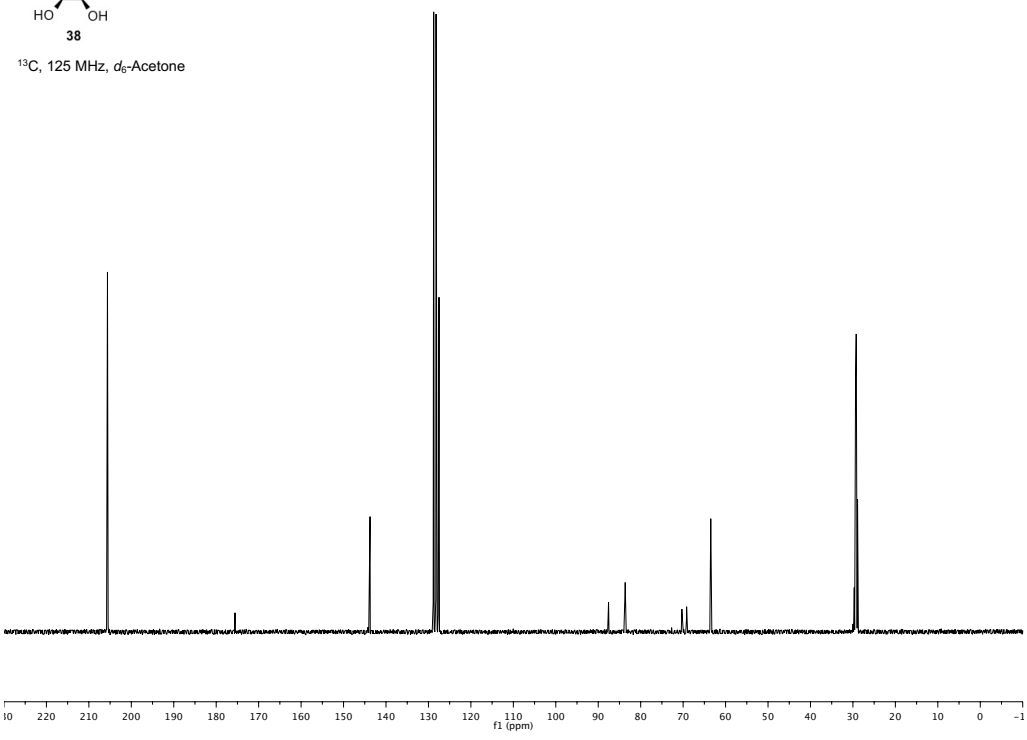
^{1}H, 500 MHz, d_6-Acetone

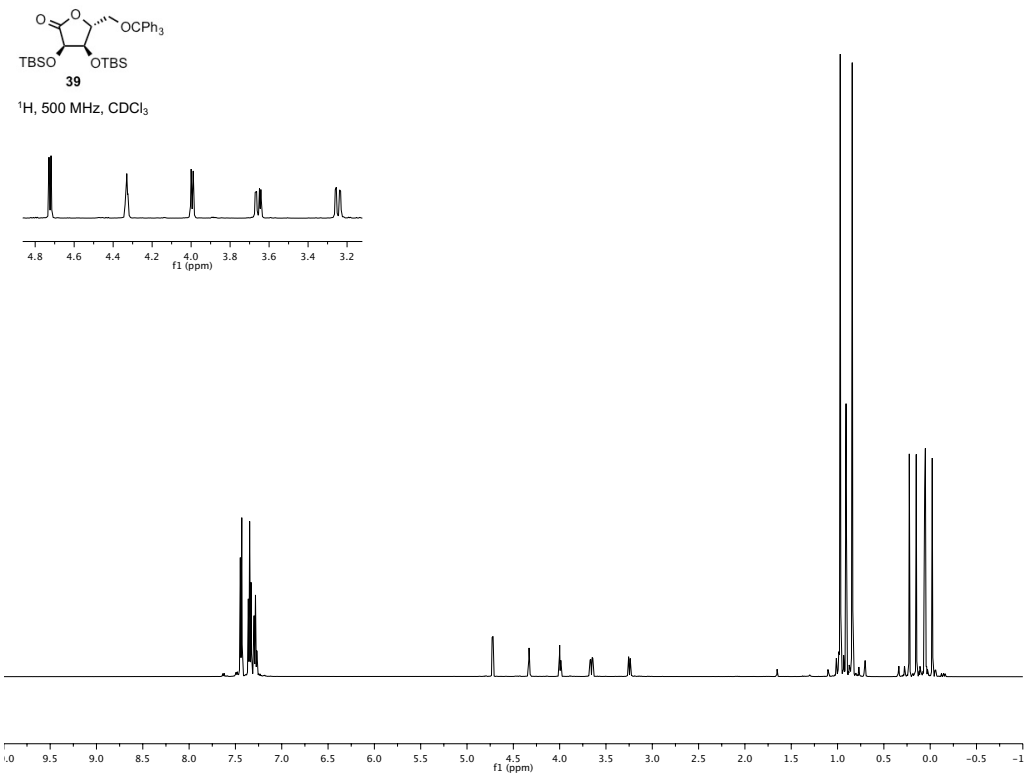


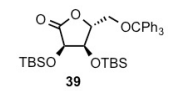


38

^{13}C, 125 MHz, d_6-Acetone

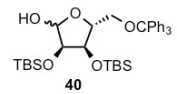



O
O
OCPh3
TBSO
OTBS
39
1H, 500 MHz, CDCl3
4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2
f1 (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1
f1 (ppm)



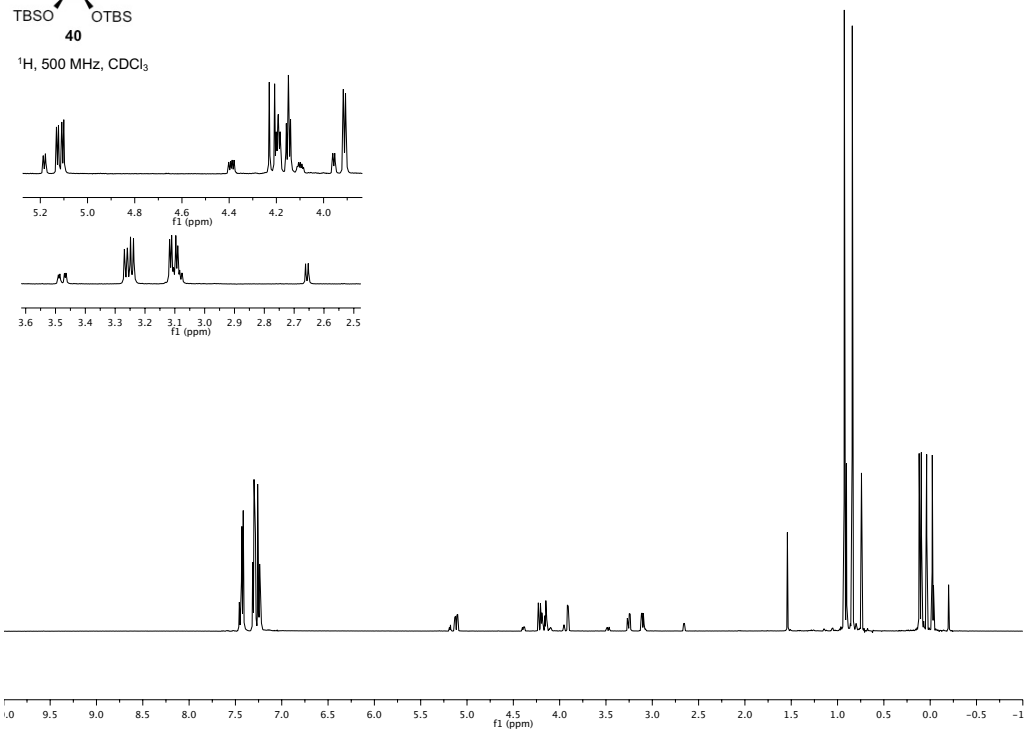
39

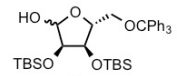
^{13}C, 125 MHz, $CDCl_3$



40

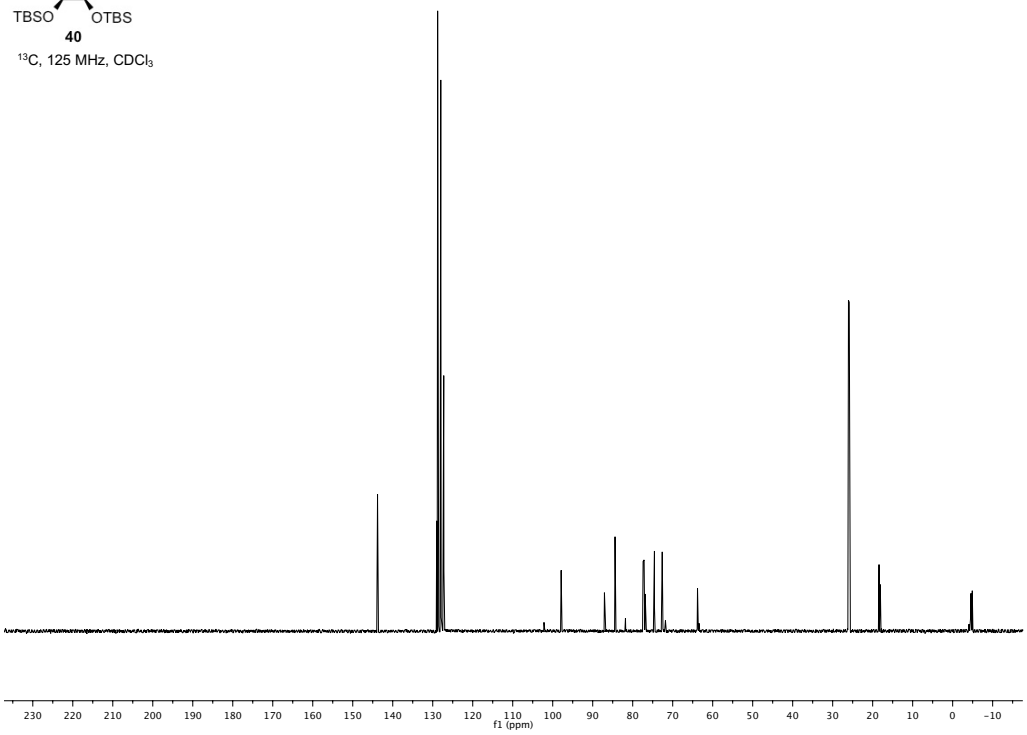
^{1}H, 500 MHz, $CDCl_3$

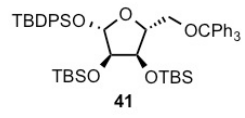




40

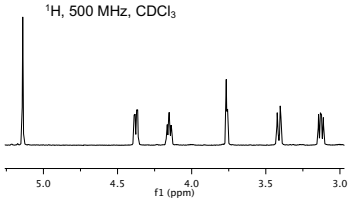
^{13}C, 125 MHz, $CDCl_3$

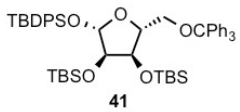




41

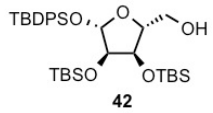
^{1}H, 500 MHz, $CDCl_3$





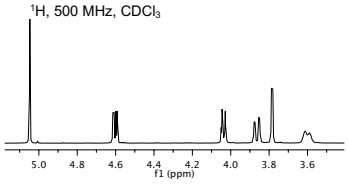
41

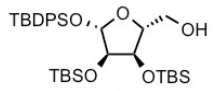
^{13}C, 125 MHz, $CDCl_3$



42

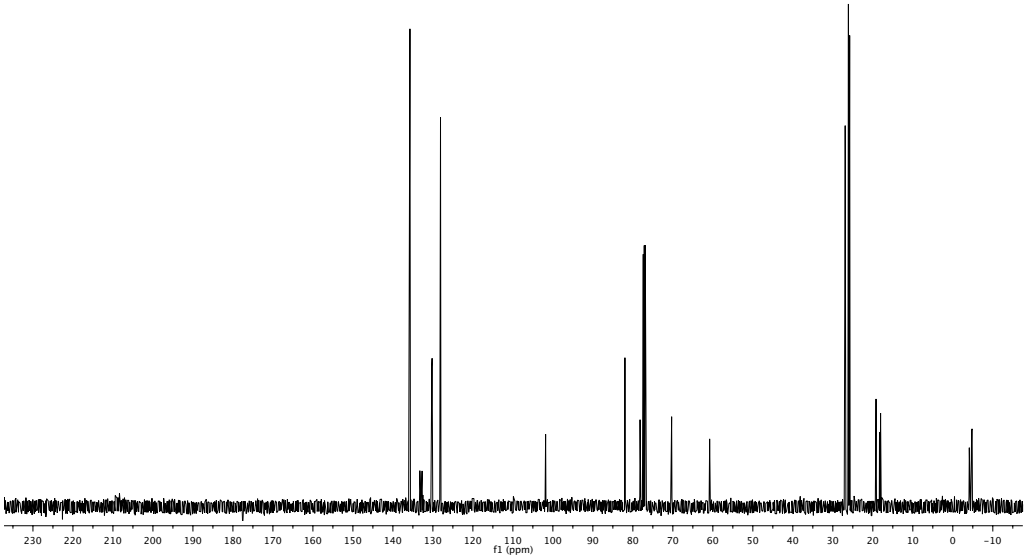
^{1}H, 500 MHz, $CDCl_3$

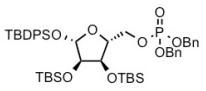




42

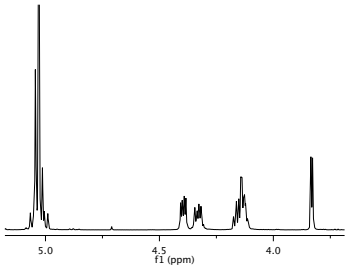
^{13}C, 125 MHz, $CDCl_3$

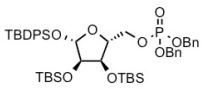




43

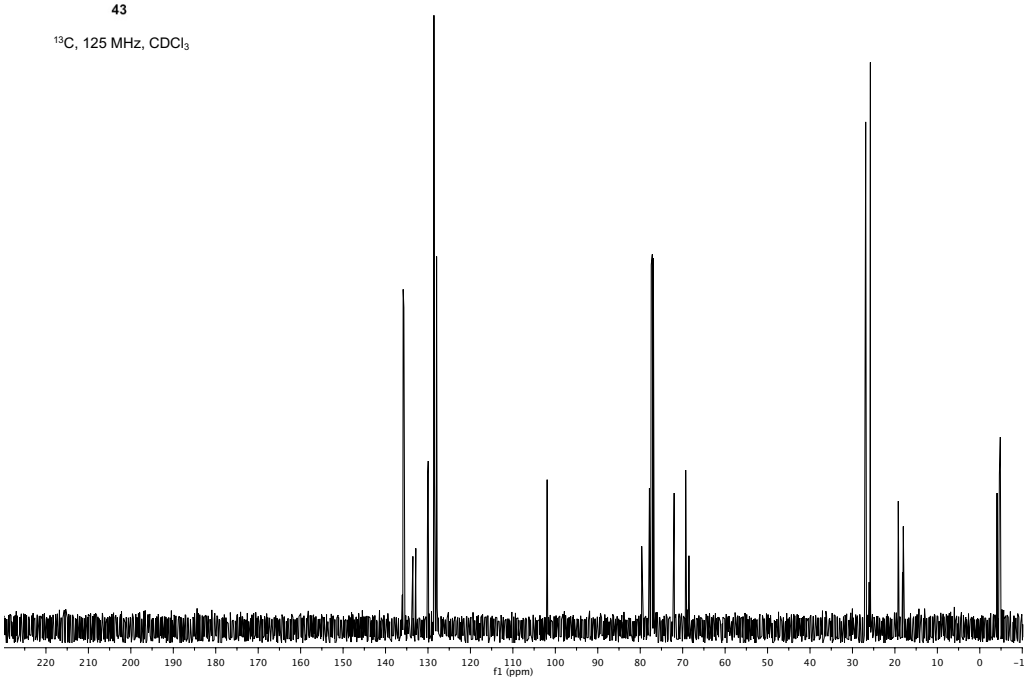
^{1}H, 500 MHz, $CDCl_3$

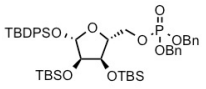




43

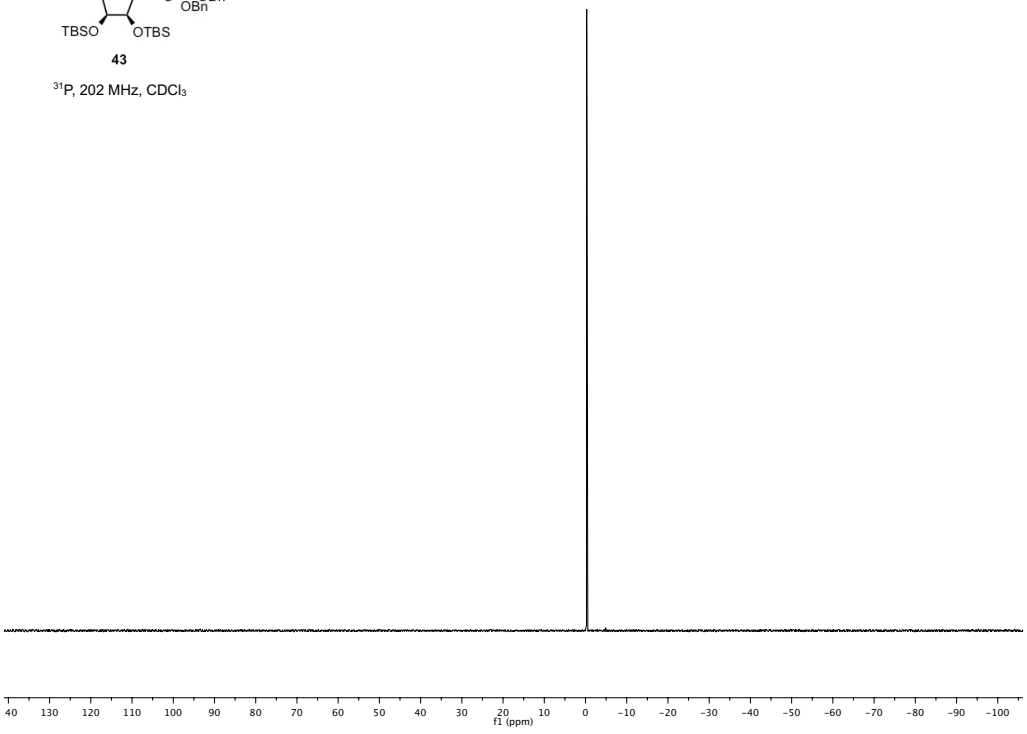
^{13}C, 125 MHz, $CDCl_3$

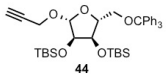




43

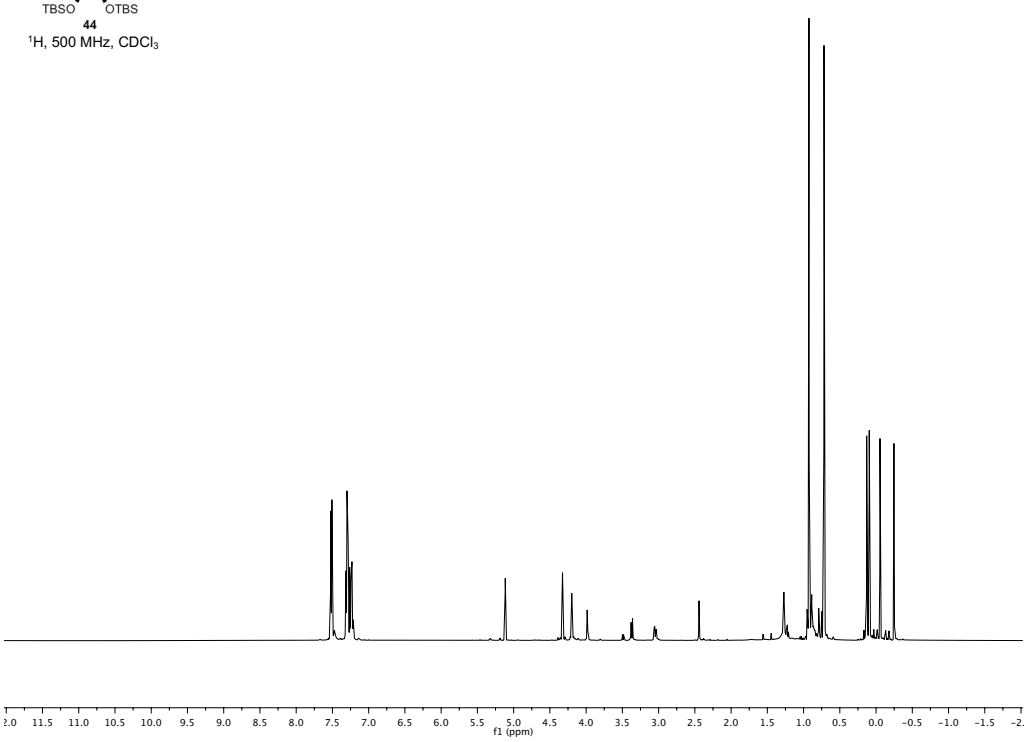
^{31}P, 202 MHz, $CDCl_3$

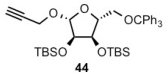




44

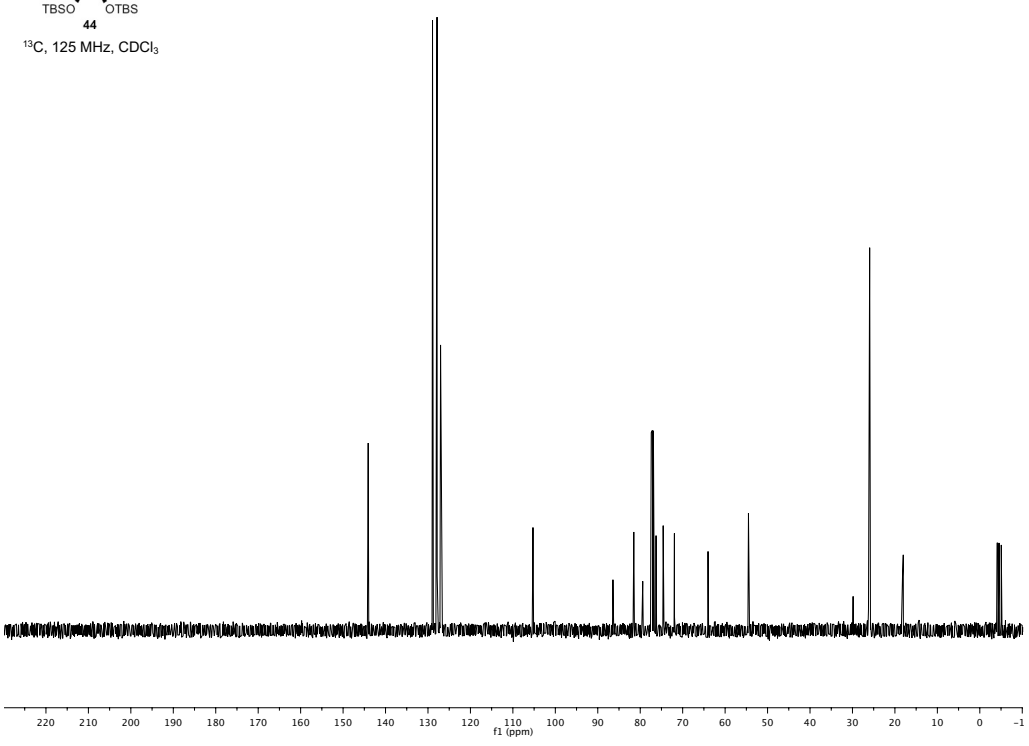
^{1}H, 500 MHz, $CDCl_3$

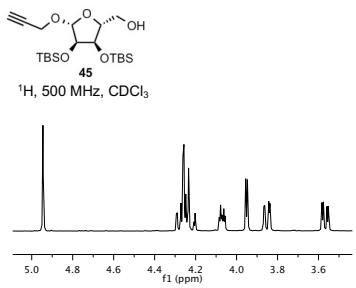




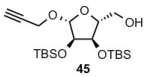
44

^{13}C, 125 MHz, $CDCl_3$

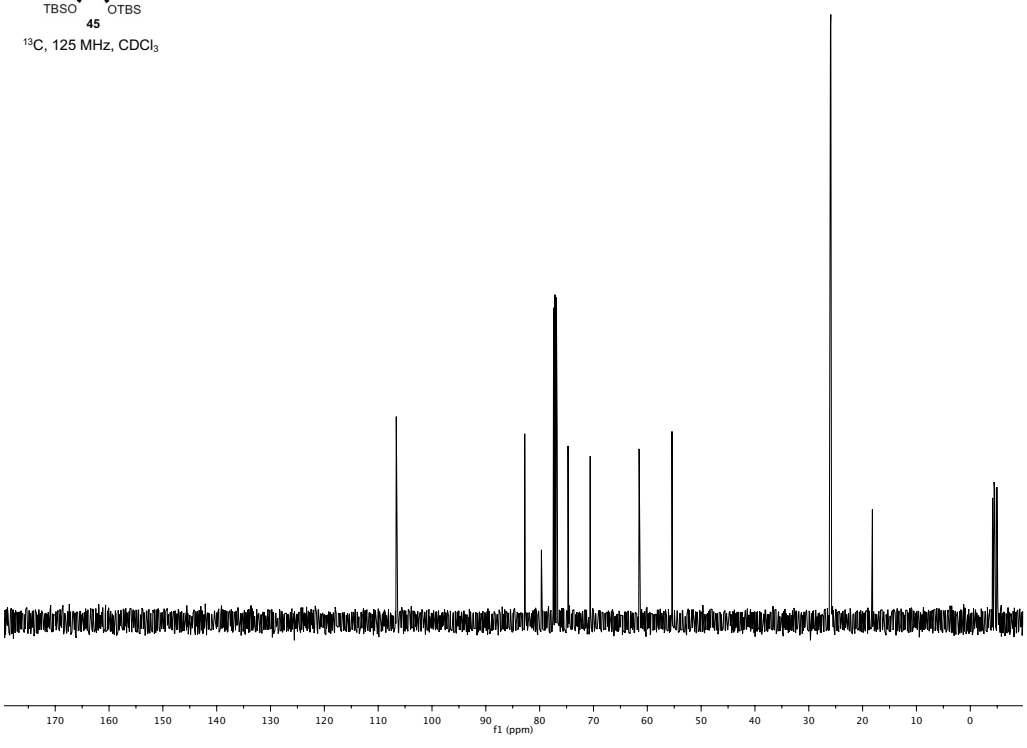




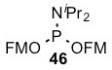
^{1}H, 500 MHz, $CDCl_3$



^{13}C, 125 MHz, $CDCl_3$



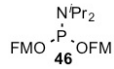
ml-5-198a
ml-5-198a



46

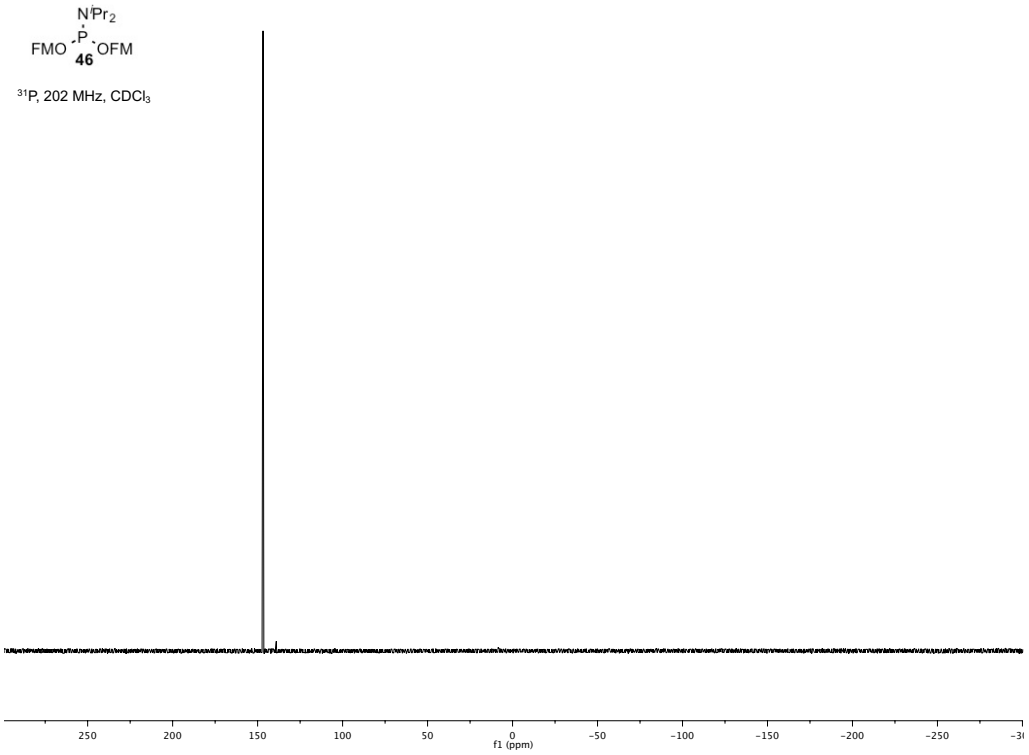
^{1}H, 500 MHz, $CDCl_3$

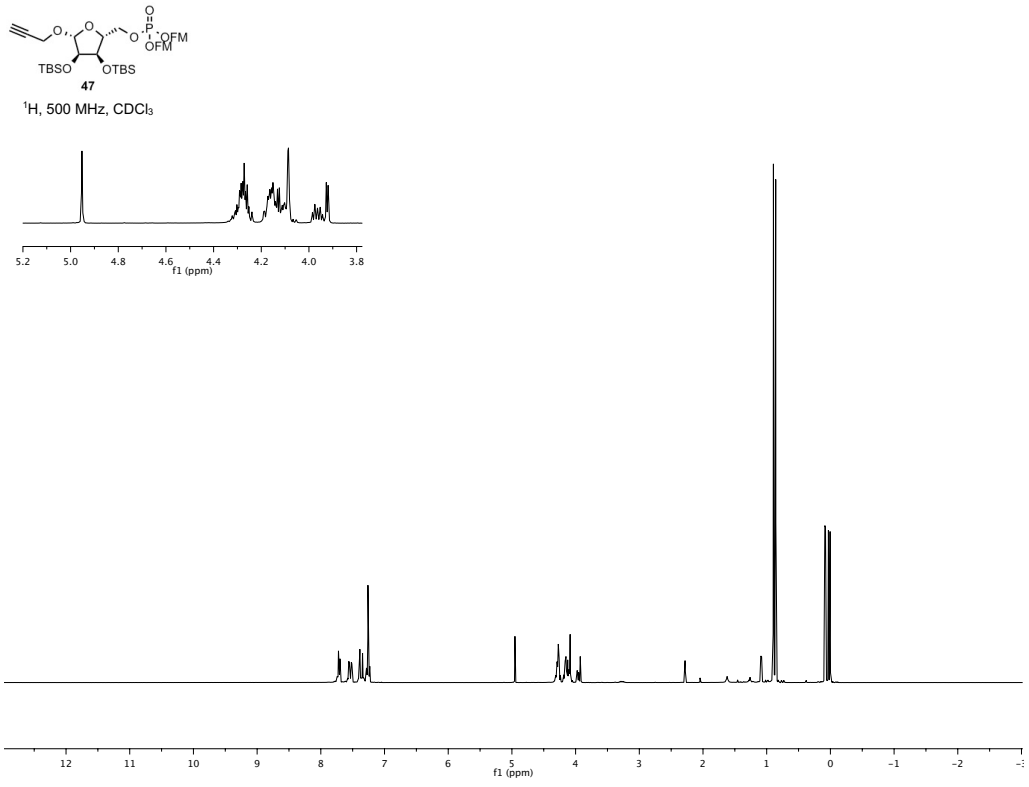
ml-5-198a-13c
STANDARD CARBON PARAMETERS

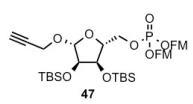


46

^{13}C, 125 MHz, $CDCl_3$

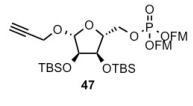

N/Pr2
FMO
P
OFM
46
31P, 202 MHz, CDCl3
250
200
150
100
50
0
−50
−100
−150
−200
−250
f1 (ppm)


O
O
O
O
P
OFM
OFM
TBSO
OTBS
47
1H, 500 MHz, CDCl3
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
f1 (ppm)
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)



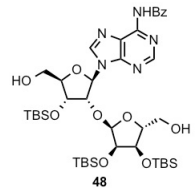
47

^{13}C, 125 MHz, $CDCl_3$



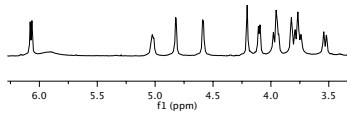
47

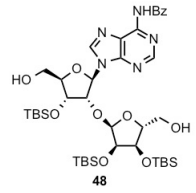
^{31}P, 202 MHz, $CDCl_3$



48

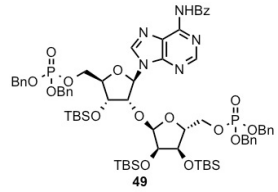
^{1}H, 500 MHz, $CDCl_3$





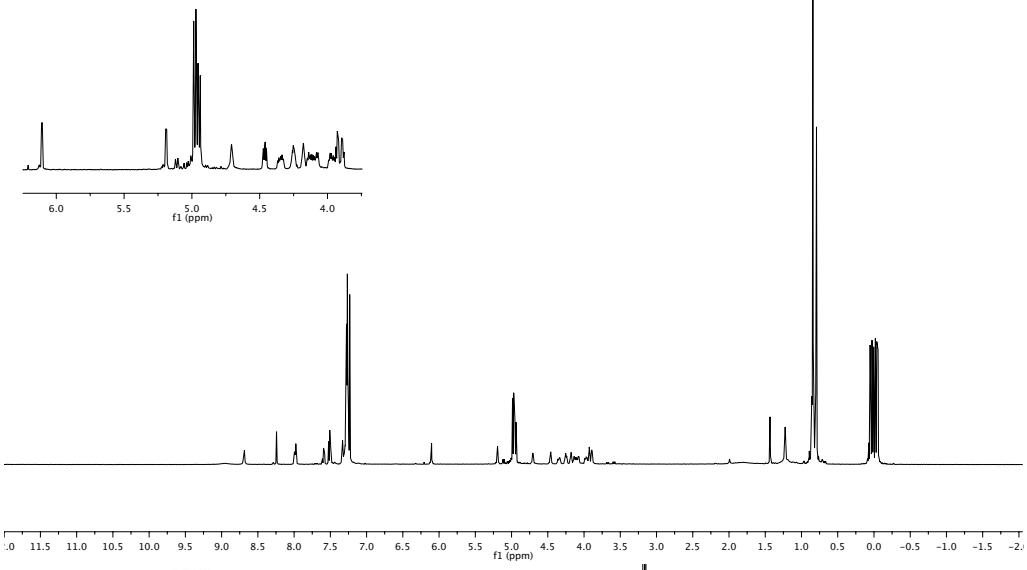
48

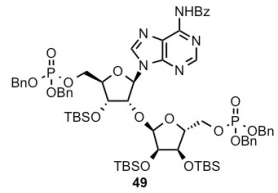
^{13}C, 125 MHz, $CDCl_3$



49

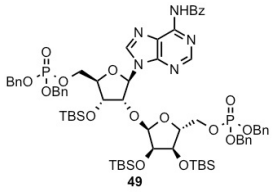
^{1}H, 500 MHz, $CDCl_3$





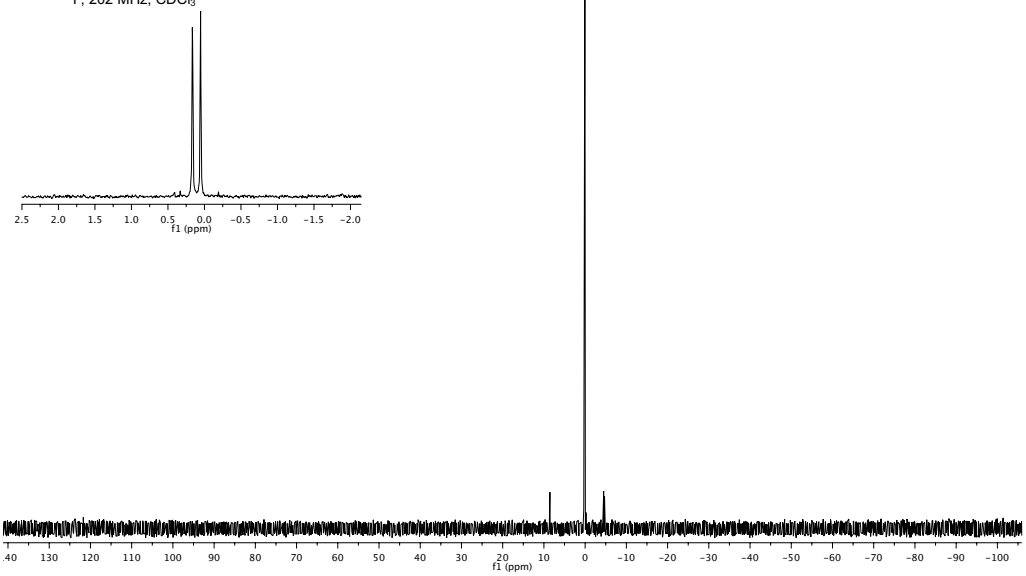
49

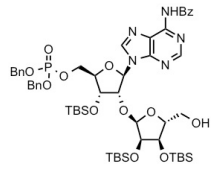
^{13}C, 125 MHz, $CDCl_3$



49

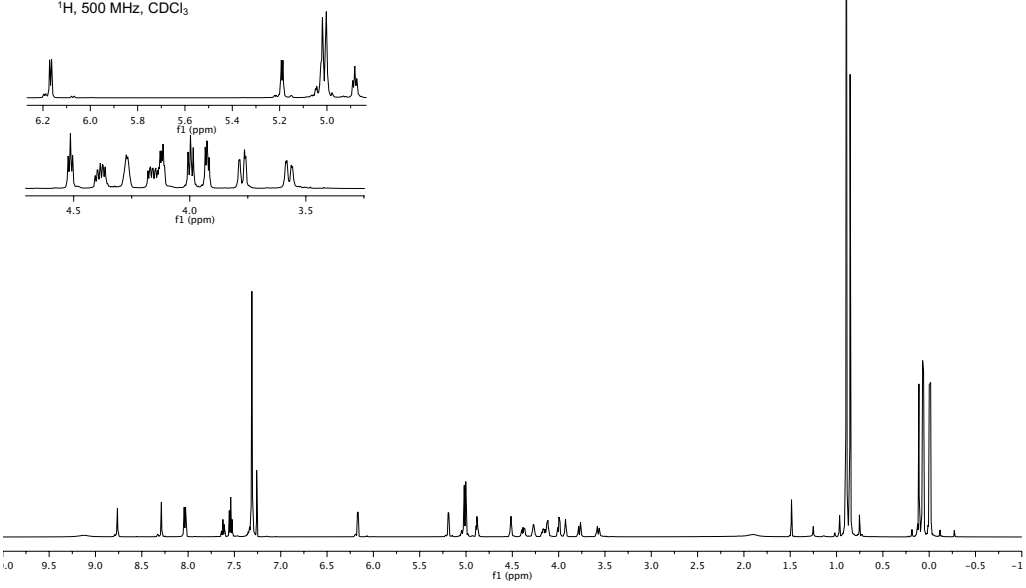
^{31}P, 202 MHz, $CDCl_3$

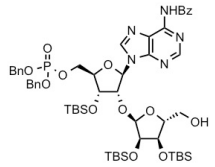




50

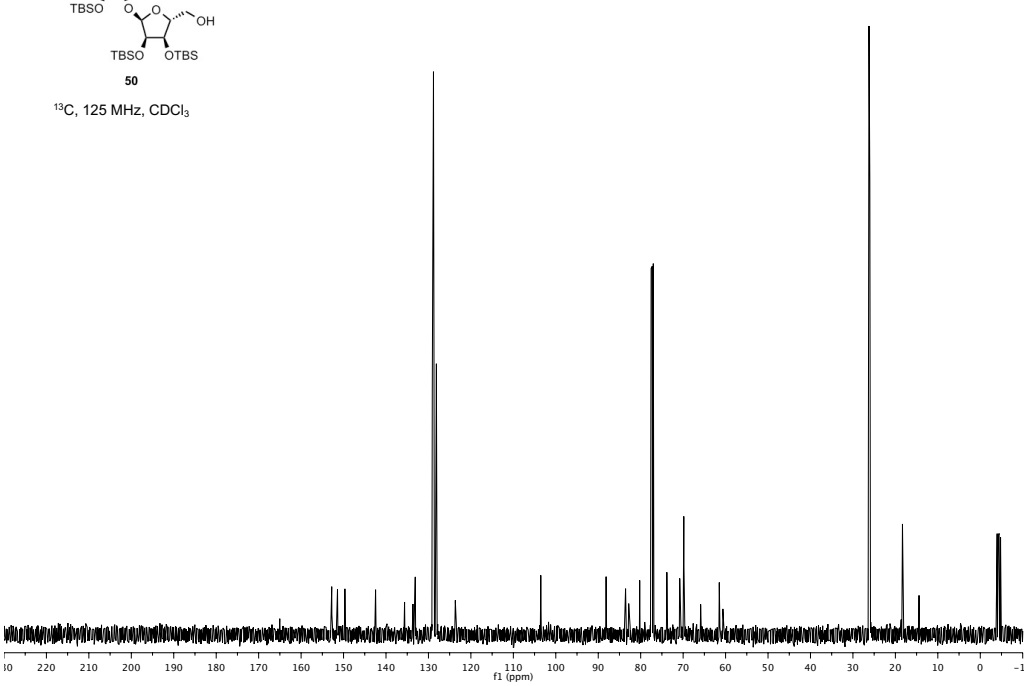
^{1}H, 500 MHz, $CDCl_3$

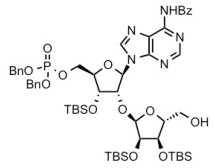




50

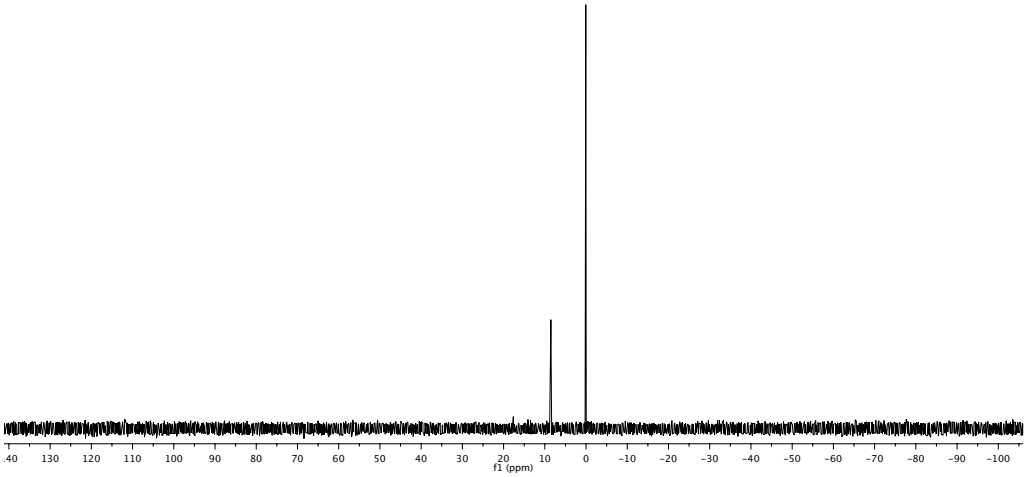
^{13}C, 125 MHz, $CDCl_3$

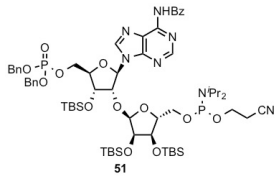




50

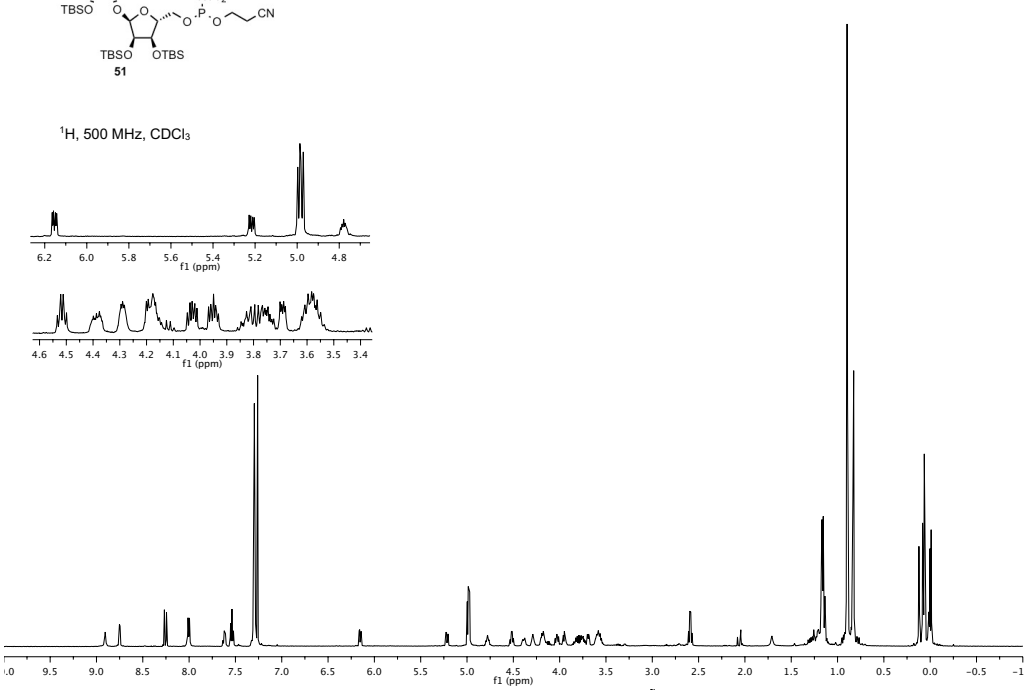
^{31}P, 202 MHz, $CDCl_3$

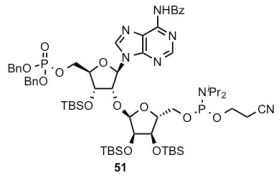




51

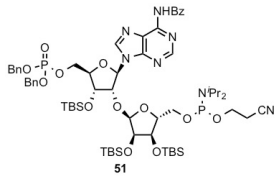
^{1}H, 500 MHz, $CDCl_3$





51

^{13}C, 125 MHz, $CDCl_3$



51

^{31}P, 202 MHz, $CDCl_3$