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Synthesis of (*E*)-3′-Phosphonoalkenyl Modified Nucleoside Phosphonates via a Highly Stereoselective Olefin Cross-Metathesis Reaction

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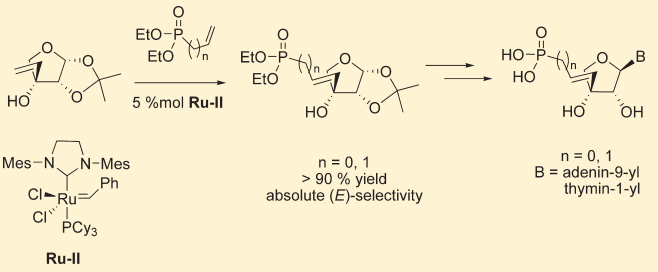
Supporting Information

ABSTRACT: The synthesis of (*E*)-3′-phosphonoalkenyl and 3′-phosphonoalkyl modified nucleoside analogues with a β-D-erythrofuranose moiety is reported. The highly stereoselective olefin cross-metathesis reaction was applied to introduce the phosphonoalkenyl group at the 3′-position of the sugar moiety with absolute (*E*)-selectivity. The 3′,6′-cyclomonophosphonic acids of 3′-phosphonoethyl-β-D-erythrofuranosyl nucleosides were synthesized via a dehydrative intramolecular cyclization reaction. None of the synthesized compounds shows significant in vitro activity against HIV, HCV, and RSV.



INTRODUCTION

Unsaturated phosphonates are primarily formed under Michaelis−Arbuzov[1] or Hornor−Wadsworth−Emmons[2] reaction conditions or by a transition-metal-catalyzed cross-coupling reaction[3] (e.g., Suzuki,[4] Stille,[5] and Heck[6] reaction). However, these methods often suffer from low *E*/*Z*-selectivity for the olefination reaction. In addition, activation of functional groups is generally necessary for both coupling partners. In recent years, olefin cross-metathesis (CM) has emerged as a powerful and convenient synthetic pathway to functionalized olefins from simple alkene precursors.[7] However, the major drawback of olefin CM is the lack of predictability in product selectivity and stereoselectivity despite the existence of a general model for product selectivity.[8] Only few examples were reported for the synthesis of unsaturated phosphonate nucleosides using olefin CM.[9] A mixture of *E*/*Z* isomers is often obtained with low to moderate yield for these olefin CM protocols.

Phosphorus-modified nucleoside analogues, bearing a phosphonate group in the sugar moiety, have shown potent antiviral activity.[10] Since the antiviral activity is often associated with the nucleoside analogues bearing a phosphonomethoxy group in the sugar moiety,[11] little attention has been paid to exploring the properties and scope of other phosphonate functions in relationship to biological activity. As part of our ongoing program to search for nucleoside phosphonate analogues as potential antivirals, we synthesized the 3′-phosphonoalkenyl modified β-D-erythrosyl nucleoside phosphonate analogues (**1a**, **1b**, and **1e**, Figure 1). The 3′-phosphonoalkyl analogues (**1c**, **1d**, **1f**, and **1g**, Figure 1) were prepared by reduction of the related unsaturated alkenyl derivatives. The key step in the synthesis is the introduction of the phosphonoalkenyl group to the 3′- position of the sugar moiety in the (*E*)-form. This transformation could be successfully achieved by reaction of dialkylphosphonoalkene with 3′-vinyl-α-D-erythrosyl derivatives via a highly stereoselective olefin cross-metathesis reaction. In addition, the saturated 3′,6′-cyclomonophosphonic acids (**1c** and **1d**) were prepared via a dehydrative intramolecular cyclization reaction. All of these synthesized compounds (**1a**−**1g**) were evaluated for their *in vitro* activity against HIV, HCV, and RSV in cell assays.

RESULTS AND DISCUSSION

Compound **1a**, bearing a 3′-phosphonovinyl group at the sugar moiety, was selected as the model compound for retrosynthetic analysis. Compound **1a** was proposed to be synthesized via two synthetic routes (Scheme 1). In the proposed synthetic route A (Scheme 1), compound **1a** could be prepared by coupling of compound **7** or **8** with vinyl dialkylphosphonate via a stereoselective olefin cross-metathesis reaction. Compound **7** or **8** could be obtained by glycosylation of compound **6** with silylated adenine under Vorbrüggen conditions.[12] Compound **6** is derived from compound **4**. Addition of a vinyl group in the 3-keto group of compound **3** in the β-configuration may give rise to compound **4**. Compound **3** can be prepared by oxidation of the 3-hydroxyl group of compound **2**. In the proposed synthetic route B, compound **1a** is synthesized by glycosylation of compound **11** with silylated adenine under Vorbrüggen conditions.[12] Compound **11** could be derived from compound **9** or **10**. Introduction of the phosphonovinyl group at the 3-position of **4** or **5** in (*E*)-form could lead to the formation of compound **9** or **10** via a stereoselective olefin cross-metathesis reaction.

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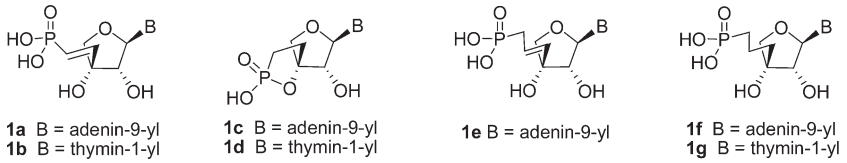
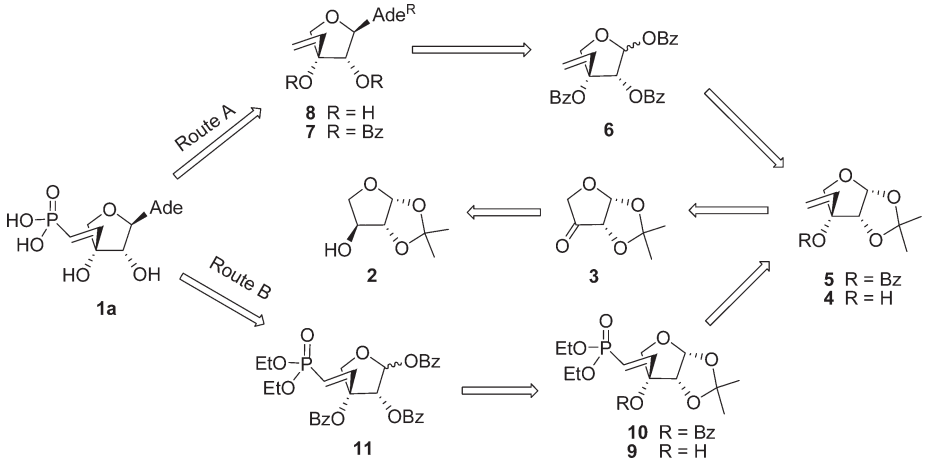


Figure 1. Structure of synthesized nucleoside phosphonate analogues.

Scheme 1. Retrosynthetic Analysis of Compound 1a



Compound **4** and **5** can be derived from protected L-threose (**2**) as described in route A.

As shown in Scheme 2, 1,2-*O*-isopropylidene-β-L-threose (**2**) was prepared starting from D-xylose according to reported procedures.[13] Oxidation of the 3-hydroxyl group of **2** in the presence of PCC provided ketone **3**.[14] The presence of a bulky 1,2-*O*-isopropylidene group at the α-position of **3** allows stereoselective introduction of the vinyl group at the 3-position in the β-configuration. Compound **4** was obtained as a single isomer by reaction of **3** with vinylmagnesium bromide using anhydrous $CeCl_3$ as additive at −78 °C.[15] Protection of the free hydroxyl group of **4** with a benzoyl group afforded compound **5**. Removal of the isopropylidene group of **5** and replacement with two benzoyl groups gave **6**. The presence of the 2-*O*-benzoyl group in **6** allows introduction of the base moiety in the β-configuration. Glycosylation of **6** with silylated N^6-benzoyladenine using $SnCl_4$ as Lewis catalyst under Vorbrüggen conditions provided the desired nucleoside **7** with a β-configured nucleobase. It should be mentioned that the glycosylation was not successful when using TMSOTf as Lewis catalyst. The benzoyl protecting groups of **7** were cleaved by treatment with ammonia saturated in methanol to give **8**. Unfortunately, all attempts to react **7** and **8** with vinyl diethylphosphonate via an olefin cross-metathesis reaction in the presence of Grubbs catalyst (**Ru-II**)[16] were not successful. The formation of the expected product **12** and **14** could not be observed. Therefore, we changed our reaction scheme.

As shown in Scheme 3, an alternative strategy was applied by first introducing the diethyl vinylphosphonate linker in the sugar moiety, followed by introducing the base moiety. However, both compound **5** and **6**, bearing a 3-*O*-benzoyl protecting group in the sugar moiety, are unable to couple with diethyl vinylphosphonate under cross-metathesis conditions. In contrast, coupling of the diethyl vinylphosphonate with the 3-vinyl group of **4** under cross-metathesis conditions in the presence of Grubbs catalyst (**Ru-II**)[16] provided the expected phosphonate **9** as a single isomer. ^{1}H NMR data indicates that the coupling constant between the two vinyl protons is 17.1 Hz, suggesting the vinyl group of **9** is in (*E*)-form. Protection of the free hydroxyl group of **9** with a benzoyl group gave compound **10**. Removal of the isopropylidene protecting group of **10** and replacement with two benzoyl protecting groups provided compound **11**, which is ready for glycosylation. The presence of a 2-*O*-benzoyl group allows selective introduction of the base moiety in the β-configuration. The nucleobase N^6-benzoyladenine and thymine were introduced after silylation and using $SnCl_4$ as Lewis catalyst, giving **12** and **13**. Deprotection of **12** and **13** was done in two steps. First, removal of the benzoyl protecting groups by treatment with ammonia in methanol (yielding **14** and **15**), and second, hydrolysis of the two ethyl protecting groups with TMSBr at room temperature. After purification by reverse phase C_{18} HPLC and Dowex (Na^+ form) ion-exchange resin, the nucleoside phosphonates **1a** and **1b** were obtained as a sodium salt.

gHMBC of 2D NMR was used to illustrate the correct connection of the nucleobase to the sugar moiety. For compound **1a**, the gHMBC spectrum shows the proton of C-1′ of the sugar moiety is coupled with the C-4 and C-8 of the adenine moiety, proving the C-1′ of the sugar moiety is linked to the N-9 of the adenine moiety via a C−N bond. Likewise, for the compound **1b**, the gHMBC spectrum indicates the proton of C-1′ of the sugar moiety is coupled with the C-6 of the thymine moiety, suggesting the desired connection between C-1′ of the sugar moiety and N-1 of the thymine moiety.

Reduction of the vinyl group of **14** and **15** by transfer hydrogenation in the presence of Pd/C catalyst provided **16** and **17**. However, to our surprise, deprotection of the phosphonate ester groups of **16** and **17** with TMSBr in the presence of 2,6-lutidine underwent a dehydrative intramolecular cyclization

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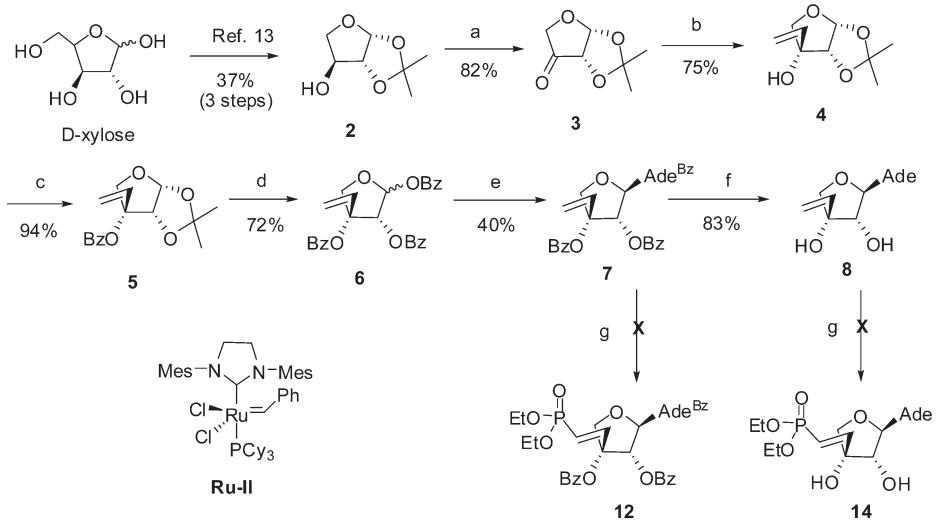
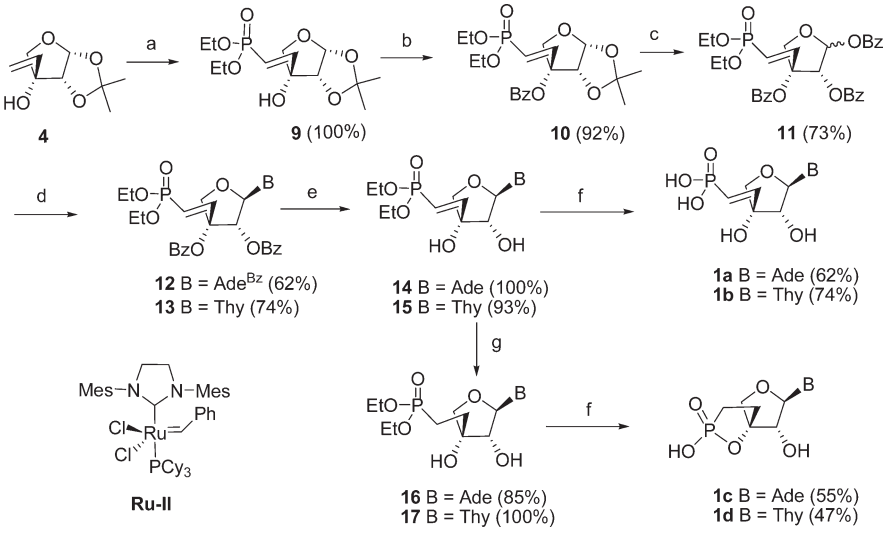
Scheme 2[a]



[a] Reagents and conditions: (a) PCC, molecule sieves (powder), CH_2Cl_2; (b) vinylmagnesium bromide, $CeCl_3$, THF, −78°C; (c) BzCl, DMAP, CH_2Cl_2, 0°C; (d) (1) CF_3CO_2H/H_2O (3:1); (2) BzCl, DMAP, CH_2Cl_2, 0°C; (e) $SnCl_4$, silylated N^6-benzoyladenine, CH_3CN; (f) ammonia saturated in methanol; (g) Grubbs catalyst **Ru-II** (5% mol), diethylvinylphosphonate, CH_2Cl_2, refluxed.

Scheme 3[a]



[a] Reagents and conditions: (a) Grubbs catalyst **Ru-II** (5% mol), diethylvinylphosphonate, CH_2Cl_2, refluxed; (b) BzCl, DMAP, CH_2Cl_2, 0°C; (c) (1) CF_3CO_2H/H_2O (3:1); (2) BzCl, DMAP, CH_2Cl_2, 0 °C; (d) $SnCl_4$, silylated N^6-benzoyladenine or silylated thymine, CH_3CN; (e) ammonia saturated in methanol; (f) (1) bromotrimethylsilane, 2,6-lutidine,CH_2Cl_2; (2): C_{18} HPLC, Dowex-Na^+; (g) Pd/C, cyclohexene, MeOH, refluxed.

to give rise to 3′,6′-cyclo-monophosphonic acid **1c** and **1d**, which were confirmed by NMR spectroscopy data and HRMS data. After purification by reverse phase C_{18} HPLC and Dowex (Na^+ form) ion-exchange resin, nucleoside phosphonates **1c** and **1d** were obtained as a sodium salt.

The synthesis of 3′-phosphonoallyl nucleoside analogue **1e** followed the same strategy as that of **1a** and **1b**. As shown in Scheme 4, coupling of allyl diethylphosphonate with the 3-vinyl group of **4** under cross-metathesis conditions in the presence of Grubbs catalyst (**Ru-II**)[16] provided **18** as a single isomer. ^1H NMR data indicates that the coupling constant between the two vinyl protons is 15.7 Hz, suggesting the vinyl group is in (*E*)-form. Protection of the free hydroxyl group of **18** with a benzoyl group gave compound **19**. Removal of the isopropylidene protecting group of **19** and replacement with two benzoyl groups provided compound **20**, which is ready for glycosylation. The presence of a 2-*O*-benzoyl group in **20** allows selective introduction of the base moiety in the β-configuration. The nucleobase N^6-benzoyladenine and thymine were introduced after silylation and using $SnCl_4$ as Lewis catalyst, giving **21** and **22**. However, attempts to remove the benzoyl protecting groups of compound **21** under different conditions, such as methanolic ammonia, catalytic MeONa in MeOH, 1% NaOH, Et_3N in MeOH and K_2CO_3 in MeOH, predominantly gave rise to the formation of side products, identified as **23b** and **23c**, as the geometric isomers, which are difficult to separate on reverse phase C_{18}

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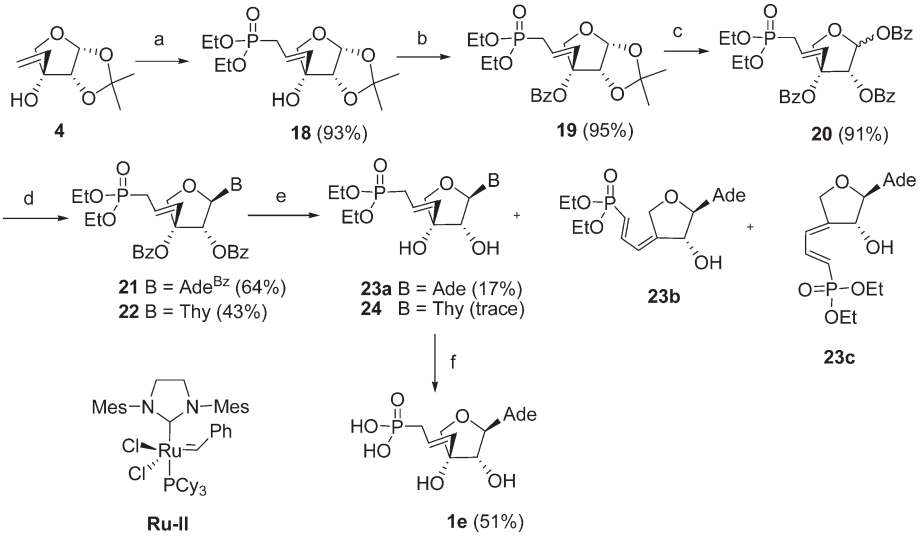
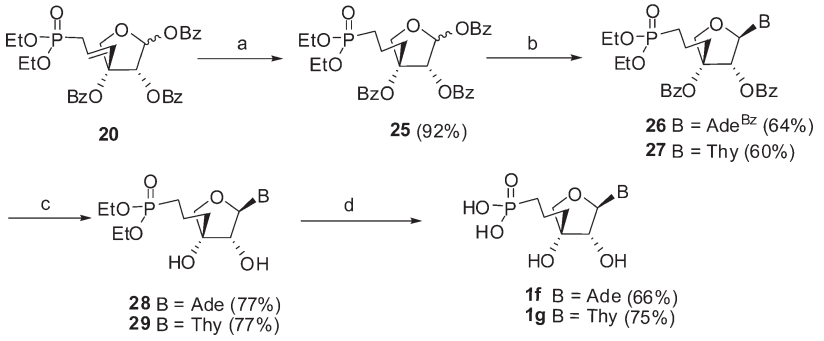
Scheme 4[a]



[a] Reagents and conditions: (a) Grubbs catalyst **Ru-II** (5% mol), diethylallylphosphonate, CH_2Cl_2, refluxed; (b) BzCl, DMAP, CH_2Cl_2, 0 °C; (c) (1) CF_3CO_2H/H_2O (3:1); (2) BzCl, DMAP, CH_2Cl_2, 0 °C; (d) $SnCl_4$, silylated N^6-benzoyladenine or silylated thymine, CH_3CN; (e) ammonia saturated in methanol; (f) (1) bromotrimethylsilane, 2,6-lutidine, CH_2Cl_2; (2): C_{18} RP column (HPLC), Dowex-Na^+.

Scheme 5[a]



[a] Reagents and conditions: (a) Pd/C, H_2, MeOH; (b) $SnCl_4$, silylated N^6-benzoyladenine or silylated thymine, CH_3CN; (c) ammonia saturated in methanol; (d) (1) Bromotrimethylsilane, 2,6-lutidine, CH_2Cl_2; (2) C_{18} RP column (HPLC), Dowex-Na^+.

HPLC. The best result was obtained by treatment of **21** with methanolic ammonia to give **23a** in 17% yield. However, only a trace amount of **24** was obtained by treatment of **22** with methanolic ammonia. Hydrolysis of the diethyl protecting groups of **23a** was achieved with TMSBr in the presence of 2,6-lutidine at room temperature. After purification by reverse phase C_{18} HPLC and Dowex (Na^+ form) ion-exchange resin, nucleoside phosphonic diacids **1e** was obtained as a sodium salt.

As shown in Scheme 5, reduction of the allyl group of **20** was achieved by catalytic hydrogenation in the presence of Pd/C to give **25**. The presence of 2-*O*-benzoyl group in **25** allows selective introduction of the base moiety in β-configuration. The nucleobase N^6-benzoyladenine and thymine were introduced after silylation and using $SnCl_4$ as Lewis catalyst, giving **26** and **27**. Deprotection of **26** and **27** was done in two steps. First, removal of the benzoyl groups by treatment with methanolic ammonia (yielding **28** and **29**) and, second, hydrolysis of the diethyl ester groups with TMSBr at room temperature. After purification by reverse phase C_{18} HPLC and Dowex (Na^+ form) ion-exchange resin, nucleoside phosphonate **1f** and **1g** were obtained as a sodium salt.

CONCLUSION

In conclusion, starting from the D-xylose, we have developed synthetic schemes for the synthesis of nucleoside phosphonates (**1a**, **1b**, and **1e**), characterized by bearing a *trans* phosphonovinyl or phosphonoallyl group at the 3′-position of D-erythrosyl sugar moiety. The phosphonovinyl and phosphonoallyl group was introduced in the 3′-position of the sugar moiety via a highly stereoselective olefin cross-metathesis reaction, and the (*E*)-isomer was exclusively obtained. Reduction of the related unsaturated alkenyl derivatives, followed by hydrolysis of the phosphonate ester groups, gave rise to the 3′-phosphonopropyl modified analogues (**1f** and **1g**) as well as 3′-phosphonoethyl modified 3′,6′-cyclomonophosphonic acids (**1c** and **1d**) via a dehydrative intramolecular cyclization. Unfortunately, none of these synthesized compounds (**1a**−**1g**) shows any significant *in vitro* activity against HIV, HCV, and RSV, as well as cytotoxicity at the concentration up to 50 μM. The lack of antiviral activity for these compounds could result from the poor metabolic activation to their diphosphates and/or the lack of affinity of their diphosphates toward viral polymerases (in this case, HIV RT, HCV NS5B RdRp, and RSV RNA polymerase).

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EXPERIMENTAL SECTION

For all reactions, analytical grade solvents were used. All moisture-sensitive reactions were carried out in oven-dried glassware (135 °C) under a nitrogen or argon atmosphere. Anhydrous THF was refluxed over sodium/benzophenone and distilled. ^{1}H, ^{31}P, and ^{13}C NMR spectra were recorded on 300 and 500 MHz spectrometer. 2D NMR (H, H−COSY, gHSQC and gHMBC) were used for the assignment of the final compounds. Exact mass measurements were performed on a time-of-flight mass spectrometer utilizing electrospray ionization (ESI); samples were infused in *i*-PrOH/H_2O (1:1) at 3 μL/min. Precoated aluminum sheets (254 nm) were used for TLC; the spots were examined with UV light and visualized with ceric ammonium molybdate (CAM) stains. Column chromatography was performed on silica gel 63−200, 60 Å. For sake of clarity, NMR signals of sugar protons and carbons are indicated with a prime, and signals of base protons and carbons are given without a prime.

1,2-*O*-Isopropylidene-α-D-xylofuranose (2a)[13a]**.** Finely powdered D-xylose (10.0 g, 67 mmol) was dissolved in acetone (260 mL) containing 10 mL of 96% H_2SO_4. After 30 min of stirring, a solution of sodium bicarbonate (13.0 g, 120 mmol) in H_2O (112 mL) was slowly added under external cooling so as to keep the temperature of the reaction mixture at 20 °C, and the mixture was stirred for a further 2.5 h. Then, solid Na_2CO_3 (27.0 g, 250 mmol) was added. The inorganic salt was filtered off and washed with acetone, and the combined filtrate was evaporated below 40 °C. The crude product was purified by silica gel column chromatography ($CHCl_3$/CH_3OH = 30:1) to give **2a** (11.1 g, 58 mmol) in 86% yield as white crystal after standing at −20 °C. Data for **2a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 3.28 (br, 1H, OH), 3.96−4.15 (m, 3H, OH, (H_5, 2H)), 4.23−4.29 (m, 2H, H_3, H_4), 4.49 (d, J = 3.6 Hz, 1H, H_2), 5.94 (d, J = 3.6 Hz, 1H, H_1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.1 (CH_3), 26.7 (CH_3), 60.9 (C-5), 76.6 (C-4), 78.8 (C-3), 85.6 (C-2), 104.8 (C-1), 111.8 (OCO); HRMS calcd for $C_8H_{14}O_5Na$ $[M + Na]^+$ 213.0739, found 213.0742.

1,2-*O*-Isopropylidene-5-*O*-(*N*-phthalimido)-α-D-xylofuranose (2b)[13b]**.** To a solution of 1,2-*O*-isopropylidene-α-D-xylofuranose **2a** (5.72 g, 0.03 mol), *N*-hydroxyphthalimide (6.85 g, 0.042 mol), and triphenyl phosphine (7.86 g, 0.03 mol) in dry THF (150 mL) at 0 °C was added DIAD (8.49 g, 0.042 mol) dropwise. The reaction mixture was stirred for 6 h at room temperature before adding 100 mL of water. Extraction with ethyl acetate (100 mL × 3), drying over Na_2SO_4, and concentrating *in vacuo* gave a yellow oil, and further purification on a silica gel column (EtOAc/hexane = 1:2 and 1:1) gave **2b** (9.0 g, 0.027 mol, 90% yield) as white solid. Data for **2b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 3.88 (br, 1H, OH), 4.29 (m, 1H, H_{5a}), 4.48−4.52 (m, 2H, H_{5b}, H_4), 4.61−4.68 (m, 2H, H_3, H_2), 5.92 (d, J = 3.6 Hz, 1H, H_1), 7.76−7.87 (m, 4H, Ar H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.3 (CH_3), 26.9 (CH_3), 74.8 (C-5), 75.1 (C-4), 77.4 (C-3), 85.1 (C-2), 105.1 (C-1), 112.0 (OCO), 123.9, 128.6, 134.8, 163.7 (C=O); HRMS calcd for $C_{16}H_{18}NO_7$ $[M + H]^+$ 336.1083, found 336.1086.

1,2-*O*-Isopropylidene-β-L-threofuranose (2)[13c]**.** To a solution of 1,2-isopropylidene-5-*O*-(*N*-phthalimidoxy)-α-D-xylofuranose **2b** (8.62 g, 25.68 mmol) and AIBN (2.11 g, 12.84 mmol) in 400 mL of anhydrous and degassed toluene was added *n*-Bu_3SnH (10.4 mL, 38.52 mmol). This solution was degassed three times under argon. The reaction mixture was heated at 80 °C for 3 h until the starting material was completed consumed. The volatile was evaporated under reduced pressure, and the residue was purified by column chromatography with EtOAc/hexane (1:2) to give a crude product, which was precipitated in a mixture of EtOAc and hexane (1:2) to remove the impurity as crystals. The resulted solution was concentrated and dried *in vacuo* to give **2** as a pale yellow solid (1.97 g, 12.32 mmol) in 48% yield. Data for **2**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 3.85 (dd, J_1 = 10.1 Hz, J_2 = 1.0 Hz, 1H, H_{4a}), 4.07 (dd, J_1 = 10.1 Hz, J_2 = 2.7 Hz, 1H, H_{4b}), 4.26 (d, J = 2.6 Hz, 1H, H_3), 4.49 (d, J = 3.6 Hz, 1H, H_2), 5.94 (d, J = 3.6 Hz, 1H, H_1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.2 (CH_3), 26.7 (CH_3), 72.9 (C-4), 75.3 (C-3), 84.9 (C-2), 105.2 (C-1), 111.8 ($OC(CH_3)_2$); HRMS calcd for $C_7H_{12}O_4Na$ $[M + Na]^+$ 183.0634, found 183.0640.

1,2-*O*-Isopropylidene-3-deoxy-3-keto-β-L-threofuranose (3). To a suspension of PCC (16.16 g, 74.96 mmol) and 4 Å molecular sieves (powder, 12.49 g) in dry DCM (140 mL) at 0 °C under Ar (caution: addition of PCC to DCM is exothermic) was added dropwise a solution of compound **2** (4.0 g, 24.98 mmol) in DCM (20 mL). The reaction mixture was stirred at room temperature overnight. Diethyl ether and Celite were added to the mixture and stirred for 1 h. The whole mixture was filtered through a short pad of a Celite. After evaporation, the residue was purified by column chromatography on a silica gel column (EtOAc/*n*-hexane = 1:2) to give **3** (3.24 g, 20.48 mmol) as white solid in 82% yield. Data for **3**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 4.07−4.13 (m, 1H, H_{4a}), 4.34−4.41 (m, 2H, H_{4b}, H_2), 6.08 (d, J = 4.4 Hz, 1H, H_1); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.1 (CH_3), 27.4 (CH_3), 68.9 (C-4), 75.7 (C-2), 104.1 (C-1), 114.2 ($OC(CH_3)_2$), 208.9 (C=O); HRMS calcd for $C_7H_{11}O_4$ $[M + H]^+$ 159.0657, found 159.0665.

1,2-*O*-Isopropylidene-3-vinyl-α-D-erythrofuranose (4). Preparation of anhydrous Cerium(III) chloride: Commercial available anhydrous $CeCl_3$ was transferred to a 2-necked flask and heated with an oil bath to 140−150 °C with slow stirring under vacuum (0.1 mmHg) for at least 2 h. The vessel was purged with Ar, and the oil bath was replaced with an ice bath. After the $CeCl_3$ had cooled (*J. Am. Chem. Soc.* **1989**, *111*, 4392), the appropriate volume of dried THF (freshly distilled from sodium/benzophenone) was added in one portion with vigorous stirring and the resultant slurry was stirred overnight.

Preparation of Compound 4. To a suspension of anhydrous $CeCl_3$ (10.0 g, 40.55 mmol) in dry THF (200 mL) at −78 °C was added 1.0 M vinyl magnesium bromide (38 mL, 38.34 mmol) over 20 min. The mixture was stirred for 1.5 h at the same temperature, whereupon a solution of dried compound **3** (3.03 g, 19.17 mmol) in dry THF (20 mL) was transferred in via cannula over 15−20 min. After the reaction mixture was stirred at the same temperature for 1 h, TLC showed no detectable starting material **3**, whereupon the dry ice/acetone bath was removed and 50 mL of satd NH_4Cl was poured into the reaction mixture. After being allowed to warm to room temperature, the mixture was extracted with ether (×2). The combined organic phases were then dried over Na_2SO_4 and concentrated. The resulting residue was purified by silica gel column chromatography (EtOAc/*n*-hexane = 1:9 and 1:1) to give **4** (2.7 g, 14.51 mmol) as white solid in 75% yield. Data for **4**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 3H, CH_3), 1.60 (s, 3H, CH_3), 2.83 (d, J = 0.7 Hz, 1H, OH), 3.77 (d, J = 8.8 Hz, 1H, H_{4a}), 3.81 (d, J = 8.8 Hz, 1H, H_{4b}), 4.21 (d, J = 3.8 Hz, 1H, H_2), 5.25 (dd, J_1 = 10.9 Hz, J_2 = 1.2 Hz, 1H, CH_2=C), 5.45 (dd, J_1 = 17.4 Hz, J_2 = 1.2 Hz, 1H, CH_2=C), 5.83 (d, J = 3.8 Hz, 1H, H_1), 5.91 (dd, J_1 = 17.4 Hz, J_2 = 10.9 Hz, 1H, CH_2=CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.6 (CH_3), 26.7 (CH_3), 73.5 (C-4), 78.5 (C-3), 82.6 (C-2), 105.4 (C-1), 112.9 ($OC(CH_3)_2$), 115.4 (CH=CH_2), 137.4 (CH=CH_2); HRMS calcd for $C_9H_{14}O_4Na$ $[M + Na]^+$ 209.0790, found 209.0793.

1,2-*O*-Isopropylidene-3-*O*-benzoyl-3-vinyl-α-D-erythrofuranose (5). To a solution of **4** (2.7 g, 14.51 mmol), Et_3N (6.0 mL, 43.53 mmol), and DMAP (3.55 g, 29.02 mmol) in dry CH_2Cl_2 (70 mL) was added dropwise BzCl (3.4 mL, 29.02 mmol) at 0 °C under Ar. The reaction mixture was warmed to room temperature and stirred for 2 h. The reaction mixture was partitioned between DCM and water, the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*, and the residue was purified by chromatography on a silica gel column (*n*-hexane/EtOAc = 24:1) to give compound **5** (3.97 g, 13.64 mmol) as white solid in 94%

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yield. Data for **5**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 4.18 (d, J = 8.5 Hz, 1H, H_{4a}), 4.31 (d, J = 8.5 Hz, 1H, H_{4b}), 4.87 (d, J = 3.6 Hz, 1H, H_2), 5.33 (d, J = 11.1 Hz, 1H, CH_2=C), 5.38 (d, J = 17.6 Hz, 1H, CH_2=CH), 5.84 (d, J = 3.6 Hz, 1H, H_1), 6.12 (dd, J_1 = 17.6 Hz, J_2 = 11.1 Hz, 1H, CH_2=CH), 7.42−7.60 (m, 3H, Ar-H), 8.04−8.07 (m, 2H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.5 (CH_3), 71.5 (C-4), 82.0 (C-2), 83.4 (C-3), 104.6 (C-1), 112.8 ($OC(CH_3)_2$), 116.7 (CH=CH_2), 128.1 (Bz, C), 129.5 (Bz, C), 129.6 (Bz, C), 132.9 (Bz, C), 135.6 (CH=CH_2), 164.6 (Bz, C=O); HRMS calcd for $C_{16}H_{18}O_5Na$ $[M + Na]^+$ 313.1052, found 313.1048.

1,2,3-*O*-Tribenzoyl-3-vinyl-D-erythrofuranose (6). Compound **5** (1.43 g, 4.92 mmol) was dissolved in 4 mL of a solution of CF_3CO_2H and H_2O (3:1) at 0 °C. The reaction mixture was stirred at room temperature for 1.5 h. Saturated $NaHCO_3$ solution and solid $NaHCO_3$ were added to neutralize the excess acid at 0 °C. The reaction mixture was extracted with DCM (×2), the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by chromatography on a silica gel column (EtOAc/*n*-hexane = 1:3) to give 3-*O*-benzoyl-3-vinyl-D-erythrose (1.16 g, 4.64 mmol) in 94% yield as an anomeric mixture (3.2:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.88−3.92 (m, 2H, H_4, $\alpha + \beta$ anomer), 4.12−4.15 (m, 2H, H_4, $\alpha + \beta$ anomer), 5.07 (d, J = 4.6 Hz, 1H, H_2), 5.21−5.31 (m, 3H, (CH_2=C, 2H, $\alpha + \beta$ anomer), (H_2, 1H)), 5.44−5.62 (m, 4H, (CH_2=C, 2H, $\alpha + \beta$ anomer), (H_1, 2H, $\alpha + \beta$ anomer)), 5.83 (dd, J_1 = 17.2 Hz, J_2 = 10.7 Hz, 1H, CH=CH_2), 5.98 (dd, J_1 = 17.2 Hz, J_2 = 10.7 Hz, 1H, CH_2=CH), 7.38−7.58 (m, 6H, Ar-H, $\alpha + \beta$ anomer), 8.01−8.07 (m, 4H, Ar-H, $\alpha + \beta$ anomer); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.7 (C-4), 75.8 (C-4), 76.1 (C-2), 79.1 (C-3), 80.1 (C-3), 83.0 (C-2), 95.7 (C-1), 101.1 (C-1), 116.2 (CH=CH_2), 117.1 (CH=CH_2), 128.5 (Bz, C), 129.1 (Bz, C), 129.9 (Bz, C), 133.5 (Bz, C), 133.6 (Bz, C), 133.7 (Bz, C), 136.2 (CH=CH_2), 137.2 (CH=CH_2), 165.7 (Bz, C=O), 165.8 (Bz, C=O).

To a solution of 3-*O*-benzoyl-3-vinyl-D-erythrose (1.16 g, 4.64 mmol), Et_3N (3.2 mL, 23.18 mmol) and DMAP (1.69 g, 13.91 mmol) in dry CH_2Cl_2 (50 mL) was added dropwise BzCl (2.15 mL, 18.55 mmol) at 0 °C under Ar. The reaction mixture was warmed to room temperature and stirred for 7 h. The reaction mixture was partitioned between DCM and water, the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*, and the residue was purified by chromatography on a silica gel column (*n*-hexane/EtOAc = 14:1 and 6:1) to give compound **6a** (0.536 g, 1.17 mmol) in 25% yield and **6b** (1.1 g, 2.41 mmol) in 52% yield. It was not identified at this stage which compound represents which isomer (α or β), but the anomeric mixture of **6a** and **6b** was used in the glycosylation reaction with the protected nucleobase. Data for **6a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.58 (d, J = 10.2 Hz, 1H, H_{4a}), 4.84 (d, J = 10.2 Hz, 1H, H_{4b}), 5.50 (d, J = 10.9 Hz, 1H, (CH_2=CH, terminal)), 5.59 (d, J = 17.5 Hz, 1H, (CH_2=CH, terminal)), 5.91 (d, J = 0.9 Hz, 1H, H_2), 6.39 (dd, J_1 = 17.5 Hz, J_2 = 10.9 Hz, 1H, CH_2=CH), 6.62 (d, J = 0.9 Hz, 1H, H_1), 7.25−7.60 (m, 9H, Ar-H), 7.87−8.12 (m, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.7 (C-4), 80.6 (C-2), 83.7 (C-3), 99.6 (C-1), 118.1 (CH=CH_2), 128.4 (Bz, C), 128.6 (Bz, C), 129.1 (Bz, C), 129.3 (Bz, C), 129.5 (Bz, C), 129.8 (Bz, C), 129.9 (Bz, C), 133.4 (Bz, C), 133.6 (Bz, C), 133.7 (Bz, C), 135.6 (CH=CH_2), 164.8 (Bz, C=O), 164.9 (Bz, C=O), 165.2 (Bz, C=O); HRMS calcd for $C_{27}H_{22}O_7Na$ $[M + Na]^+$ 481.1264, found 481.1259. Data for **6b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.65 (d, J = 10.6 Hz, 1H, H_{4a}), 4.75 (d, J = 10.6 Hz, 1H, H_{4b}), 5.39 (d, J = 10.9 Hz, 1H, (CH_2=CH, terminal)), 5.47 (d, J = 17.5 Hz, 1H, (CH_2=CH, terminal)), 5.69 (d, J = 4.5 Hz, 1H, H_2), 6.27 (dd, J_1 = 17.5 Hz, J_2 = 10.9 Hz, 1H, CH_2=CH), 6.81 (d, J = 4.5 Hz, 1H, H_1), 7.21−7.56 (m, 9H, Ar-H), 7.91−8.07 (m, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 74.8 (C-4), 76.2 (C-2), 82.2 C-3), 94.5 (C-1), 116.78 (CH=CH_2), 127.9 (Bz, C), 128.1 (Bz, C), 128.2 (Bz, C), 128.3 (Bz, C), 128.7 (Bz, C), 129.0 (Bz, C), 129.1 (Bz, C), 129.5 (Bz, C), 129.9 (Bz, C), 133.0 (Bz, C), 133.1 (Bz, C), 133.3 (Bz, C), 133.5 (Bz, C), 135.4 (CH=CH_2), 164.8 (Bz, C=O), 164.9 (Bz, C=O), 171.8 (Bz, C=O); HRMS calcd for $C_{27}H_{22}O_7Na$ $[M + Na]^+$ 481.1264, found 481.1266.

1-(N^6-Benzoyladenin-9-yl)-2,3-*O*-dibenzoyl-3-vinyl-β-D-erythrofuranose (7). N^6-Benzoyladenine (68 mg, 0.282 mmol), ammonium sulfate (2.4 mg, 0.018 mmol), and 3 mL of HMDS were added to a dried flask. The mixture was refluxed overnight under N_2. HMDS was removed *in vacuo*. To the flask with the residue was added a solution of compound **6** (81 mg, 0.177 mmol) in 3 mL of dried CH_3CN, followed by dropwise addition of $SnCl_4$ (84 μL, 0.712 mmol) at room temperature under N_2. The reaction mixture was allowed to stir for 1.5 h. The reaction was quenched with cold saturated $NaHCO_3$ and partitioned between H_2O (10 mL) and EtOAc (80 mL). The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 99:1) to afford **7** (40 mg, 0.069 mmol) as a colorless amorphous solid in 40% yield. Data for **7**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.82 (d, J = 10.6 Hz, 1H, $H_{4'a}$), 5.04 (d, J = 10.6 Hz, 1H, $H_{4'b}$), 5.44 (d, J = 11.0 Hz, 1H, (CH_2=CH, terminal)), 5.57 (d, J = 17.5 Hz, 1H, (CH_2=CH, terminal)), 6.30 (dd, J_1 = 17.5 Hz, J_2 = 11.0 Hz, 1H, CH_2=CH), 6.39 (d, J = 5.4 Hz, 1H, $H_{2'}$), 6.54 (d, J = 5.4 Hz, 1H, $H_{1'}$), 7.40−7.60 (m, 10H, Ar-H), 8.02−8.08 (m, 5H, Ar-H), 8.18 (s, 1H, H_2), 8.82 (s, 1H, H_8), 9.18 (br, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 74.7 (C-4′), 78.9 (C-2′), 84.7 C-3′), 87.8 (C-1′), 118.8 (CH=CH_2), 123.7 (C-5), 127.9 (Bz, C), 128.3 (Bz, C), 128.6 (Bz, C), 128.7 (Bz, C), 128.8 (Bz, C), 129.7 (Bz, C), 129.9 (Bz, C), 132.7 (Bz, C), 133.4 (Bz, C), 133.6 (Bz, C), 133.9 (CH=CH_2), 149.8 (C-4), 151.8 (C-6), 152.9 (C-2), 164.5 (Bz, C=O), 164.6 (Bz, C=O), 165.1 (Bz, C=O), the signal of C-8 of the adenine moiety was obscure in the noise; HRMS calcd for $C_{32}H_{26}N_5O_6$ $[M + H]^+$ 576.1883, found 576.1866.

1-(Adenin-9-yl)-3-vinyl-β-D-erythrofuranose (8). A solution of **7** (100 mg, 0.173 mmol) in methanol saturated with ammonia (8 mL) was stirred at room temperature overnight. The mixture was concentrated, and the residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 19:1) to afford **8** (38 mg, 0.143 mmol) as a white powder in 83% yield. Data for **8**: ^{1}H NMR (300 MHz, $CDCl_3$ + MeOD) δ 4.02 (d, J = 9.8 Hz, 1H, $H_{4'a}$), 4.44 (d, J = 9.8 Hz, 1H, $H_{4'b}$), 4.86 (d, J = 6.8 Hz, 1H, $H_{2'}$), 5.34 (d, J = 10.4 Hz, 1H, (CH_2=CH, terminal)), 5.57 (d, J = 17.1 Hz, 1H, (CH_2=CH, terminal)), 5.96 (d, J = 6.8 Hz, 1H, $H_{1'}$), 5.97 (dd, J_1 = 17.1 Hz, J_2 = 10.4 Hz, 1H, CH_2=CH), 8.06 (s, 1H, H_2), 8.25 (s, 1H, H_8); ^{13}C NMR (75 MHz, $CDCl_3$ + MeOD) δ 77.0 (C-4′), 78.3 (C-2′), 79.3 (C-3′), 89.9 (C-1′), 116.6 (CH=CH_2), 136.2 (CH=CH_2), 139.9 (C-8), 152.5 (C-2), the signals of (C-5), (C-4) and (C-6) of the adenine moiety were obscure in the noise; HRMS calcd for $C_{11}H_{14}N_5O_3$ $[M + H]^+$ 264.1096, found 264.1094.

1,2-*O*-Isopropylidene-(*E*)-3-(diethylphosphono)vinyl-α-D-erythrofuranose (9). To a solution of **4** (94 mg, 0.5 mmol) and vinyl diethylphosphonate (492 mg, 3 mmol) in 10 mL of dried DCM was added Grubbs II generation catalyst (**Ru-II**) (22 mg, 0.025 mmol) under Ar. The reaction mixture was refluxed overnight under Ar. Evaporation of the solvent and purification of the residue by silica gel column chromatography (EtOAc/hexane = 1:2 and EtOAc) gave **9** (173 mg, 0.53 mmol), which was contaminated with a small amount of vinyl diethylphosphonate derivatives. Data for **9**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.31−1.37 (m, 9H, CH_3), 1.60 (s, 3H, CH_3), 3.20 (s, 1H, OH), 3.80 (s, 2H, H_4), 4.07−4.14 (m, 4H, OCH_2), 4.21 (d, J = 3.8 Hz, 1H, H_2), 5.89 (d, J = 3.8 Hz, 1H, H_1), 6.13 (dd, J_1 = 19.9 Hz, J_2 = 17.1 Hz, 1H, CH=CH), 6.70 (dd, J_1 = 22.6 Hz, J_2 = 17.1 Hz, 1H, CH=CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3 (CH_3), 16.4 (CH_3), 26.4 (CH_3), 26.7 (CH_3), 61.8 (OCH_2), 61.9 (OCH_2), 73.1 (C-4), 78.7 (d, $J_{P,C}$ = 19.9 Hz, C-3), 81.9 (d, $J_{P,C}$ = 2.0 Hz, C-2), 105.3 (C-1), 113.2 ($OC(CH_3)_2$), 115.9 (d, $J_{P,C}$ = 186.9 Hz, CH=CH), 149.8 (d, $J_{P,C}$ = 6.0 Hz, CH=CH);

^{31}P NMR (121.5 MHz, $CDCl_3$) δ 17.9; HRMS calcd for $C_{13}H_{24}O_7P$ $[M + H]^+$ 323.1259, found 323.1260.

1,2-*O*-Isopropylidene-3-*O*-benzoyl-(*E*)-3-(diethylphosphono)vinyl-α-D-erythrofuranose (10). To a solution of **9** (550 mg, 1.707 mmol), Et_3N (0.467 mL, 3.414 mmol), and DMAP (417 mg, 3.414 mmol) in dry CH_2Cl_2 (8 mL) was added dropwise BzCl (0.397 mL, 3.414 mmol) at 0 °C under Ar. The reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was partitioned between DCM and water, the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*, and the residue was purified by chromatography on a silica gel column (*n*-hexane/EtOAc = 1:1 and 1:2) to give compound **10** (671 mg, 1.57 mmol) as a colorless oil in 92% yield. Data for **10**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29−1.35 (m, 9H, CH_3), 1.51 (s, 3H, CH_3), 4.03−4.13 (m, 4H, OCH_2), 4.20 (d, J = 8.8 Hz, 1H, H_{4a}), 4.28 (d, J = 8.8 Hz, 1H, H_{4b}), 4.86 (d, J = 3.7 Hz, 1H, H_2), 5.83 (t, J = 17.2 Hz, 1H, CH═CH), 5.90 (d, J = 3.7 Hz, 1H, H_1), 6.88 (dd, J_1 = 23.0 Hz, J_2 = 17.5 Hz, 1H, CH═CH), 7.44−7.63 (m, 3H, Ar-H), 8.03−8.06 (m, 2H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.4 (CH_3), 16.5 (CH_3), 26.7 (CH_3), 26.9 (CH_3), 62.2 (OCH_2), 62.3 (OCH_2), 71.9 (C-4), 82.1 (C-2), 83.6 (d, $J_{P,C}$ = 21.5 Hz, C-3), 105.1 (C-1), 113.5 ($OC(CH_3)_2$), 117.3 (d, $J_{P,C}$ = 186.3 Hz, CH═CH), 128.6 (Bz, C), 129.5 (Bz, C), 130.0 (Bz, C), 133.6 (Bz, C), 148.8 (d, $J_{P,C}$ = 5.9 Hz, CH═CH), 164.8 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 16.6; HRMS calcd for $C_{20}H_{28}O_8P$ $[M + H]^+$ 427.1522, found 427.1510.

1,2,3-*O*-Tribenzoyl-(*E*)-3-(diethylphosphono)vinyl-D-erythrofuranose (11). Compound **10** (0.671 g, 1.57 mmol) was dissolved in a solution (2.8 mL) of CF_3CO_2H and H_2O (3:1) at 0 °C. The reaction mixture was stirred at room temperature for 2 h. Saturated $NaHCO_3$ solution and solid $NaHCO_3$ was added to neutralize the excess acid at 0 °C. The reaction mixture was extracted with DCM (×2), the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by chromatography on a silica gel column (DCM/MeOH = 29:1) to give 3-*O*-benzoyl-(*E*)-3-(diethylphosphono)vinyl-D-erythrose (0.522 g, 1.35 mmol) in 86% yield as an anomeric mixture.

To a solution of 3-*O*-benzoyl-(*E*)-3-(diethylphosphono)vinyl-D-erythrose (0.522 g, 1.35 mmol), Et_3N (0.739 mL, 5.405 mmol) and DMAP (0.495 g, 4.054 mmol) in dry CH_2Cl_2 (15 mL) were added dropwise BzCl (0.628 mL, 5.405 mmol) at 0 °C under Ar. The reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was partitioned between DCM and water, the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*, and the residue was purified by chromatography on a silica gel column (*n*-hexane/EtOAc = 2:1 and 1:1) to give compound **11a** (0.285 g, 0.473 mmol) in 35% yield and **11b** (0.394 g, 0.675 mmol) in 50% yield. It was not identified at this stage which compound represents which isomer (α or β), but the anomeric mixture of **11a** and **11b** was used in the glycosylation reaction with the protected nucleobase. Data for **11a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22−1.30 (m, 6H, CH_3), 4.03−4.13 (m, 4H, OCH_2), 4.56 (d, J = 10.3 Hz, 1H, H_{4a}), 4.83 (d, J = 10.3 Hz, 1H, H_{4b}), 5.89 (d, J = 0.6 Hz, 1H, H_2), 6.08 (dd, J_1 = 17.3 Hz, J_2 = 16.6 Hz, 1H, CH═CH), 6.66 (d, J = 0.6 Hz, 1H, H_1), 7.26−7.60 (m, 10H, (CH═CH, 1H), (Ar-H, 9H)), 7.84−8.13 (m, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.2 (CH_3), 16.3 (CH_3), 16.4 (CH_3), 62.2 (OCH_2), 62.3 (OCH_2), 75.9 (C-4), 80.4 (C-2), 83.3 (d, $J_{P,C}$ = 21.7 Hz, C-3), 99.2 (C-1), 118.5 (d, $J_{P,C}$ = 185.7 Hz, CH═CH), 128.5 (Bz, C), 128.6 (Bz, C), 128.7 (Bz, C), 128.8 (Bz, C), 128.9 (Bz, C), 129.8 (Bz, C), 129.9 (Bz, C), 130.2 (Bz, C), 133.7 (Bz, C), 133.8 (Bz, C), 133.9 (Bz, C), 148.5 (d, $J_{P,C}$ = 6.4 Hz, CH═CH), 164.5 (Bz, C═O), 164.9 (Bz, C═O), 165.1 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 16.4; HRMS calcd for $C_{31}H_{31}O_{10}PNa$ $[M + Na]^+$ 617.1553, found 617.1556. Data for **11b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25−1.34 (m, 6H, CH_3), 4.05−4.15 (m, 4H, OCH_2), 4.68 (d, J = 11.0 Hz, 1H, H_{4a}), 4.74 (d, J = 11.0 Hz, 1H, H_{4b}), 5.66 (d, J = 4.6 Hz, 1H, H_2), 5.92 (dd, J_1 = 17.3 Hz, J_2 = 16.1 Hz, 1H, CH═CH), 6.86 (d, J = 4.6 Hz, 1H, H_1), 7.08 (dd, J_1 = 22.4 Hz, J_2 = 17.3 Hz, 1H, CH═CH), 7.22−7.58 (m, 9H, Ar-H), 7.93−8.02 (m, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3 (CH_3), 16.4 (CH_3), 62.3 (OCH_2), 62.4 (OCH_2), 75.8 (C-4), 76.4 (C-2), 81.9 (d, $J_{P,C}$ = 22.7 Hz, C-3), 94.8 (C-1), 117.2 (d, $J_{P,C}$ = 186.1 Hz, CH═CH), 128.4 (Bz, C), 128.6 (Bz, C), 128.7 (Bz, C), 128.8 (Bz, C), 129.3 (Bz, C), 129.4 (Bz, C), 129.9 (Bz, C), 130.0 (Bz, C), 133.5 (Bz, C), 133.8 (Bz, C), 149.2 (d, $J_{P,C}$ = 6.4 Hz, CH═CH), 164.5 (Bz, C═O), 164.9 (Bz, C═O), 165.1 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 16.5; HRMS calcd for $C_{31}H_{32}O_{10}P$ $[M + H]^+$ 595.1733, found 595.1749.

1-(N^6-Benzoyladenin-9-yl)-2,3-*O*-dibenzoyl-(*E*)-3-(diethylphosphono)vinyl-β-D-erythrofuranose (12). N^6-benzoyladenine (159 mg, 0.663 mmol), ammonium sulfate (2.6 mg, 0.02 mmol) and 8 mL of HMDS were added to a dried flask. The mixture was refluxed overnight under N_2. HMDS was removed *in vacuo*. To the flask with the residue was added a solution of compound **11** (197 mg, 0.331 mmol) in 10 mL of dried CH_3CN, followed by dropwise addition of $SnCl_4$ (117 μL, 0.994 mmol) at room temperature under N_2. The reaction mixture was allowed to stir for 50 min. The reaction was quenched with cold saturated $NaHCO_3$ and partitioned between H_2O (10 mL) and EtOAc (80 mL). The organic layer was washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH=49:1) to afford **12** (146 mg, 0.205 mmol) as a colorless amorphous solid in 62% yield. Data for **12**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22−1.30 (m, 6H, CH_3), 4.01−4.10 (m, 4H, OCH_2), 4.84 (d, J = 10.8 Hz, 1H, $H_{4'a}$), 5.05 (d, J = 10.8 Hz, 1H, $H_{4'b}$), 6.08 (dd, J_1 = 17.4 Hz, J_2 = 16.4 Hz, 1H, CH═CH), 6.38 (d, J = 6.1 Hz, 1H, $H_{2'}$), 6.86 (d, J = 6.1 Hz, 1H, $H_{1'}$), 7.16 (dd, J_1 = 22.5 Hz, J_2 = 17.4 Hz, 1H, CH═CH), 7.41−7.62 (m, 9H, Ar-H), 8.00−8.07 (m, 6H, Ar-H), 8.17 (s, 1H, H_2), 8.84 (s, 1H, H_8), 9.23 (br, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3 (CH_3), 16.4 (CH_3), 62.2 (d, $J_{P,C}$ = 2.1 Hz, OCH_2), 62.3 (d, $J_{P,C}$ = 2.1 Hz, OCH_2), 75.3 (C-4′), 78.4 (C-2′), 84.7 (d, $J_{P,C}$ = 22.4 Hz, C-3′), 88.1 (C-1′), 118.8 (d, $J_{P,C}$ = 185.1 Hz, CH═CH), 124.0 (C-5), 128.0 (Bz, C), 128.3 (Bz, C), 128.8 (Bz, C), 128.9 (Bz, C), 129.4 (Bz, C), 129.9 (Bz, C), 130.0 (Bz, C), 132.8 (Bz, C), 133.6 (Bz, C), 133.9 (Bz, C), 134.1 (Bz, C), 142.1 (C-8), 146.1 (d, $J_{P,C}$ = 6.6 Hz, CH═CH), 150.0 (C-4), 151.8 (C-6), 153.0 (C-2), 164.4 (Bz, C═O), 164.7 (Bz, C═O), 164.9 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ_P 16.0; HRMS calcd for $C_{36}H_{35}N_5O_9P$ $[M + H]^+$ 712.2172, found 712.2170.

1-(Thymin-1-yl)-2,3-*O*-dibenzoyl-(*E*)-3-(diethylphosphono)-vinyl-β-D-erythrofuranose (13). Thymine (60 mg, 0.479 mmol), ammonium sulfate (1.9 mg, 0.014 mmol) and 4 mL of HMDS were added to a dried flask. The mixture was refluxed overnight under N_2. HMDS was removed *in vacuo*. To the flask with the residue was added a solution of compound **11** (142 mg, 0.239 mmol) in 10 mL of dried CH_3CN, followed by dropwise addition of $SnCl_4$ (84 μL, 0.717 mmol) at room temperature under N_2. The reaction mixture was allowed to stir for 1 h. The reaction was quenched with cold saturated $NaHCO_3$ and partitioned between H_2O (10 mL) and EtOAc (80 mL). The organic layer was washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH=49:1) to afford **13** (107 mg, 0.178 mmol) as a colorless amorphous solid in 74% yield. Data for **13**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22−1.29 (m, 6H, CH_3), 1.95 (s, 3H, CH_3), 3.99−4.09 (m, 4H, OCH_2), 4.56 (d, J = 10.8 Hz, 1H, $H_{4'a}$), 4.85 (d, J = 10.8 Hz, 1H, $H_{4'b}$), 5.81 (d, J = 6.1 Hz, 1H, $H_{2'}$), 5.99 (dd, J_1 = 17.4 Hz, J_2 = 16.4 Hz, 1H, CH═CH), 6.22 (d, J = 6.1 Hz, 1H, $H_{1'}$), 7.05 (dd, J_1 = 22.4 Hz, J_2 = 17.4 Hz, 1H, CH═CH), 7.16 (d, J = 0.9 Hz, 1H, H_6), 7.34−7.63 (m, 6H, Ar-H), 7.93−8.08 (m, 4H, Ar-H), 9.40 (br, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6 (CH_3), 16.3 (CH_3), 16.4 (CH_3), 62.3 (OCH_2), 62.4 (OCH_2), 74.6 (C-4′), 78.2 (C-2′), 83.1 (d, $J_{P,C}$ = 22.3 Hz, C-3′), 88.6 (C-1′), 112.2 (C-5), 118.8 (d, $J_{P,C}$ = 185.3 Hz,

CH=CH), 128.5 (Bz, C), 128.7 (Bz, C), 128.8 (Bz, C), 129.1 (Bz, C), 129.9 (Bz, C), 130.1 (Bz, C), 133.9 (Bz, C), 134.1 (Bz, C), 135.6 (C-6), 147.1 (d, $J_{P,C}$ = 6.6 Hz, CH=CH), 150.5 (C-2), 163.7 (C-4), 164.4 (Bz, C=O), 165.3 (Bz, C=O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 16.1; HRMS calcd for $C_{29}H_{32}N_2O_{10}P$ $[M + H]^+$ 599.1794, found 599.1799.

1-(Adenin-9-yl)-(*E*)-3-(diethylphosphono)vinyl-β-D-erythrofuranose (14). A solution of **12** (144 mg, 0.202 mmol) in methanol saturated with ammonia (5 mL) was stirred at room temperature overnight. The mixture was concentrated, and the residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH= 19:1 and 9:1) to afford **14** (82 mg, 0.202 mmol) as a white powder in 100% yield. Data for **14**: ^{1}H NMR (300 MHz, MeOD) δ 1.30−1.36 (m, 6H, CH_3), 3.93 (d, J = 9.7 Hz, 1H, $H_{4'a}$), 4.05−4.15 (m, 4H, OCH_2), 4.54 (d, J = 9.7 Hz, 1H, $H_{4'b}$), 5.09 (d, J = 7.1 Hz, 1H, $H_{2'}$), 6.01 (d, J = 7.1 Hz, 1H, $H_{1'}$), 6.21 (dd, J_1 = 20.8 Hz, J_2 = 17.0 Hz, 1H, CH=CH), 6.89 (dd, J_1 = 22.2 Hz, J_2 = 17.0 Hz, 1H, CH=CH), 8.22 (s, 1H, H_2), 8.84 (s, 1H, H_8); ^{13}C NMR (75 MHz, MeOD) δ 16.6 (CH_3), 16.7 (CH_3), 63.5 (OCH_2), 63.6 (OCH_2), 77.7 (C-4′), 79.0 (C-2′), 81.1 (d, $J_{P,C}$ = 20.5 Hz, C-3′), 90.7 (C-1′), 118.2 (d, $J_{P,C}$ = 187.5 Hz, CH=CH), 120.9 (C-5), 142.1 (C-8), 150.9 (C-4), 153.0 (d, $J_{P,C}$ = 6.2 Hz, CH=CH), 153.9 (C-2), 157.4 (C-6); ^{31}P NMR (121.5 MHz, MeOD) δ 17.3; HRMS calcd for $C_{15}H_{23}N_5O_6P$ $[M + H]^+$ 400.1386, found 400.1374.

1-(Thymin-1-yl)-(*E*)-3-(diethylphosphono)vinyl-β-D-erythrofuranose (15). A solution of **13** (160 mg, 0.267 mmol) in methanol saturated with ammonia (5 mL) was stirred at room temperature overnight. The mixture was concentrated, and the residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH= 19:1) to afford **15** (97 mg, 0.248 mmol) as a white powder in 93% yield. Data for **15**: ^{1}H NMR (300 MHz, MeOD) δ 1.30−1.34 (m, 6H, CH_3), 1.90 (d, J = 0.9 Hz, 3H, CH_3), 3.84 (d, J = 9.7 Hz, 1H, $H_{4'a}$), 4.03−4.13 (m, 4H, OCH_2), 4.34 (d, J = 9.7 Hz, 1H, $H_{4'b}$), 4.49 (d, J = 7.3 Hz, 1H, $H_{2'}$), 5.90 (d, J = 7.3 Hz, 1H, $H_{1'}$), 6.16 (dd, J_1 = 20.9 Hz, J_2 = 17.0 Hz, 1H, CH=CH), 6.79 (dd, J_1 = 22.2 Hz, J_2 = 17.0 Hz, 1H, CH=CH), 7.57 (d, J = 1.1 Hz, 1H, H_6); ^{13}C NMR (75 MHz, MeOD) δ 12.2 (CH_3), 16.6 (CH_3), 16.7 (CH_3), 63.5 (OCH_2), 63.6 (OCH_2), 77.4 (C-4′), 78.5 (C-2′), 80.8 (d, $J_{P,C}$ = 20.5 Hz, C-3′), 91.9 (C-1′), 112.0 (C-5), 118.0 (d, $J_{P,C}$ = 187.5 Hz, CH=CH), 139.2 (C-6), 152.8 (C-2), 153.2 (d, $J_{P,C}$ = 6.3 Hz, CH=CH), 166.3 (C-4); ^{31}P NMR (121.5 MHz, MeOD) δ 17.3; HRMS calcd for $C_{15}H_{24}N_2O_8P$ $[M + H]^+$ 391.1270, found 391.1272.

1-(Adenin-9-yl)-(*E*)-3-phosphonovinyl-β-D-erythrofuranose (1a). To a solution of compound **14** (113 mg, 0.282 mmol) and 2,6-lutidine (2 mL, 17.23 mmol) in 20 mL of dry CH_2Cl_2 was added bromotrimethylsilane (744 μL, 5.64 mmol) at room temperature under nitrogen. The reaction mixture was continuously stirred for 2 day in the darkness. The reaction mixture was concentrated under high vacuum at room temperature, and the residue was coevaporated with MeOH and 0.5 M TEAB solution. Purification by HPLC using reverse phase C_{18} column (mobile phase A: MeCN + 50 mM TEAB; mobile phase B: H_2O + 50 mM TEAB) and ion exchange with Dowex-Na^+ resin offered **1a** (69 mg, 0.178 mmol) as a colorless solid after lyophilization in 62% yield. Data for **1a**: ^{1}H NMR (500 MHz, D_2O) δ 4.08 (d, J = 10.3 Hz, 1H, $H_{4'a}$), 4.55 (d, J = 10.3 Hz, 1H, $H_{4'b}$), 5.00 (d, J = 7.6 Hz, 1H, $H_{2'}$), 6.11 (d, J = 7.6 Hz, 1H, $H_{1'}$), 6.28 (dd, $J_{H,H}$ = 17.2 Hz, $J_{P,H}$ = 15.7 Hz, 1H, PCH=C), 6.45 (dd, $J_{H,P}$ = 19.7 Hz, $J_{H,H}$ = 17.2 Hz, 1H, PC=CH), 8.23 (s, 1H, H_2), 8.38 (s, 1H, H_8); ^{13}C NMR (125 MHz, D_2O) δ 76.0 (C-4′), 77.2 (C-2′), 79.2 (d, $J_{P,C}$ = 18.8 Hz, C-3′), 87.1 (C-1′), 118.7 (C-5), 127.8 (d, $J_{P,C}$ = 170.5 Hz, PCH=CH), 139.1 (d, $J_{P,C}$ = 5.4 Hz, PCH=CH), 140.3 (C-8), 148.7 (C-4), 152.5 (C-2), 155.2 (C-6); ^{31}P NMR (121.5 MHz, D_2O) δ 10.6; HRMS calcd for $C_{11}H_{13}N_5O_6P$ $[M-H]^-$ 342.0604, found 342.0602.

1-(Thymin-1-yl)-(*E*)-3-phosphonovinyl-β-D-erythrofuranose (1b). Compound **1b** was prepared as described for **1a**, using **15** (114 mg, 0.292 mmol) as starting material, 2,6-lutidine (2 mL, 17.23 mmol) and bromotrimethylsilane (771 μL, 5.86 mmol). **1b** (82 mg, 0.217 mmol) was obtained as a colorless solid after lyophilization in 74% yield. Data for **Ib**: ^{1}H NMR (500 MHz, D_2O) δ 1.92 (d, J = 1.0 Hz, 3H, CH_3), 4.00 (d, J = 10.3 Hz, 1H, $H_{4'a}$), 4.41 (d, J = 10.3 Hz, 1H, $H_{4'b}$), 4.58 (d, J = 7.5 Hz, 1H, $H_{2'}$), 5.98 (d, J = 7.5 Hz, 1H, $H_{1'}$), 6.21 (dd, $J_{H,H}$ = 17.3 Hz, $J_{H,P}$ = 15.4, 1H, PCH=C), 6.31 (dd, $J_{H,H}$ = 17.2 Hz, $J_{H,P}$ = 19.4 Hz, 1H, PC=CH), 7.59 (d, J = 1.2 Hz, 1H, H_6); ^{13}C NMR (125 MHz, D_2O) δ 11.1 (CH_3), 76.3 (C-4′), 77.1 (C-2′), 79.3 (d, $J_{P,C}$ = 18.5 Hz, C-3′), 89.0 (C-1′), 111.6 (C-5), 128.3 (d, $J_{P,C}$ = 169.0 Hz, PCH=CH), 137.6 (C-6), 138.3 (d, $J_{P,C}$ = 5.2 Hz, PCH=CH), 151.7 (C-2), 166.2 (C-4); ^{31}P NMR (121.5 MHz, D_2O) δ_P 10.2; HRMS calcd for $C_{11}H_{14}N_2O_8P$ $[M-H]^-$ 333.0488, found 333.0478.

1-(Adenin-9-yl)-3-(diethylphosphono)ethyl-β-D-erythrofuranose (16). A solution of **14** (58 mg, 0.145 mmol) in methanol (12 mL) was added Pd/C (32 mg, 0.029 mmol) and cyclohexene (0.588 mL, 5.8 mmol) under Ar. The reaction mixture was refluxed for 30 h. The mixture was filtered through a Celite pad to remove the catalyst and purified on a silica gel column (CH_2Cl_2/MeOH= 9:1) to afford **16** (50 mg, 0.124 mmol) as a white powder in 85% yield. Data for **16**: ^{1}H NMR (300 MHz, MeOD + $CDCl_3$) δ 1.31−1.36 (m, 6H, CH_3), 1.76−2.18 (m, 4H, ($H_{5'}$, 2H), ($H_{6'}$, 2H)), 4.07−4.12 (m, 5H, ($H_{4'a}$, 1H), ((OCH_2)$_2$, 4H)), 4.31 (d, J = 9.6 Hz, 1H, $H_{4'b}$), 4.71 (d, J = 6.6 Hz, 1H, $H_{2'}$), 5.91 (d, J = 6.6 Hz, 1H, $H_{1'}$), 8.02 (s, 1H, H_2), 8.22 (s, 1H, H_8); ^{13}C NMR (75 MHz, MeOD + $CDCl_3$) δ 16.2 (CH_3), 16.3 (CH_3), 18.8 (d, $J_{P,C}$ = 142.8 Hz, C-6′), 28.6 (d, $J_{P,C}$ = 4.2 Hz, C-5′), 62.1 (d, $J_{P,C}$ = 3.5 Hz, OCH_2), 62.2 (d, $J_{P,C}$ = 3.5 Hz, OCH_2), 77.5 (C-4′), 77.7 (C-3′), 78.2 (C-2′), 90.4 (C-1′), 119.7 (C-5), 139.9 (C-8), 149.2 (C-4), 152.4 (C-2), 155.4 (C-6); ^{31}P NMR (121.5 MHz, MeOD + $CDCl_3$) δ 33.1; HRMS calcd for $C_{15}H_{25}N_5O_6P$ $[M + H]^+$ 402.1542, found 402.1536.

1-(Thymin-1-yl)-3-(diethylphosphono)ethyl-β-D-erythrofuranose (17). A solution of **15** (50 mg, 0.126 mmol) in methanol (10 mL) was added Pd/C (14 mg, 0.012 mmol) and cyclohexene (0.5 mL, 5.0 mmol) under Ar. The reaction mixture was refluxed for 3.5 h. The mixture was filtered through a Celite pad to remove the catalyst and purified on a silica gel column (CH_2Cl_2/MeOH= 19:1) to afford **17** (52 mg, 0.126 mmol) as a white powder in 100% yield. Data for **17**: ^{1}H NMR (300 MHz, MeOD) δ 1.31−1.36 (m, 6H, CH_3), 1.77−2.16 (m, 7H, ($H_{5'}$, 2H), ($H_{6'}$, 2H), (CH_3, 3H)), 3.87 (d, J = 9.5 Hz, 1H, $H_{4'a}$), 4.05−4.14 (m, 4H, (OCH_2)$_2$), 4.15 (d, J = 9.5 Hz, 1H, $H_{4'b}$), 4.23 (d, J = 7.2 Hz, 1H, $H_{2'}$), 5.83 (d, J = 7.2 Hz, 1H, $H_{1'}$), 7.52 (d, J = 1.1 Hz, 1H, H_6); ^{13}C NMR (75 MHz, MeOD) δ 12.2 (CH_3), 16.6 (CH_3), 16.7 (CH_3), 19.6 (d, $J_{P,C}$ = 142.1 Hz, C-6′), 29.8 (d, $J_{P,C}$ = 4.4 Hz, C-5′), 63.3 (OCH_2), 63.4 (OCH_2), 78.2 (C-4′), 78.4 (C-3′), 78.6 (C-2′), 92.3 (C-1′), 111.9 (C-5), 139.2 (C-6), 152.8 (C-2), 166.4 (C-4); ^{31}P NMR (121.5 MHz, MeOD) δ 33.5; HRMS calcd for $C_{15}H_{26}N_2O_8P$ $[M + H]^+$ 393.1427, found 393.1427.

{[1-(Adenin-9-yl)-5-deoxy-5-methyl]-β-D-apiofuranosyl}-3,6-cyclomonophosphonic Acid Sodium Salt (1c). Compound **1c** was prepared as described for **1a**, using **16** (98 mg, 0.244 mmol) as starting material, 2,6-lutidine (2 mL, 17.23 mmol) and bromotrimethylsilane (646 μL, 4.88 mmol). **1c** (50 mg, 0.134 mmol) was obtained as a colorless solid after lyophilization in 55% yield. Data for **1c**: ^{1}H NMR (600 MHz, D_2O) δ 1.72−1.89 (m, 2H, $H_{6'}$), 2.26−2.45 (m, 2H, $H_{5'}$), 4.23 (d, J = 10.4 Hz, 1H, $H_{4'a}$), 4.39 (d, J = 10.4 Hz, 1H, $H_{4'b}$), 4.81 (d, J = 7.9 Hz, 1H, $H_{2'}$), 5.99 (d, J = 7.8 Hz, 1H, $H_{1'}$), 8.15 (s, 1H, H_2), 8.27 (s, 1H, H_8); ^{13}C NMR (150 MHz, D_2O) δ 19.7 (d, $J_{P,C}$ = 117.1 Hz, C-6′), 27.1 (C-5′), 76.3 (C-4′), 77.4 (d, $J_{P,C}$ = 1.5 Hz, C-2′), 85.3 (d, $J_{P,C}$ = 9.7 Hz, C-3′), 87.6 (C-1′), 119.1 (C-5), 140.8 (C-8), 148.8 (C-4), 152.7 (C-2), 155.5 (C-6); ^{31}P NMR (121.5 MHz, D_2O) δ 44.2; HRMS calcd for $C_{11}H_{13}N_5O_5P$ $[M-H]^-$ 326.0655, found 326.0613.

{[1-(Thymin-1-yl)-5-deoxy-5-methyl]-β-D-apiofuranosyl}-3,6-cyclomonophosphonic Acid Sodium Salt (1d). Compound **1d** was prepared as described for **1a**, using **17** (58 mg, 0.147 mmol) as starting material, 2,6-lutidine (1 mL, 8.61 mmol) and bromotrimethylsilane (388 μL, 2.94 mmol). **1d** (25 mg, 0.069 mmol) was obtained as a

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colorless solid after lyophilization in 47% yield. Data for **1d**: ^{1}H NMR (500 MHz, D_2O) δ 1.70−1.87 (m, 2H, $H_{6'}$), 1.90 (d, J = 1.2 Hz, 3H, CH_3), 2.20−2.41 (m, 2H, $H_{5'}$), 4.19 (d, J = 10.3 Hz, 1H, $H_{4'a}$), 4.26 (d, J = 10.4 Hz, 1H, $H_{4'b}$), 4.40 (d, J = 7.6 Hz, 1H, $H_{2'}$), 5.87 (d, J = 7.6 Hz, 1H, $H_{1'}$), 7.52 (d, J = 1.2 Hz, 1H, H_6); ^{13}C NMR (125 MHz, D_2O) δ 11.1 (CH_3), 19.3 (d, $J_{P,C}$ = 117.1 Hz, C-6′), 26.8 (C-5′), 76.1 (C-4′), 77.0 (d, $J_{P,C}$ = 3.7 Hz, C-2′), 84.9 (d, $J_{P,C}$ = 9.6 Hz, C-3′), 89.4 (C-1′), 111.4 (C-5), 137.7 (C-6), 151.6 (C-2), 166.2 (C-4); ^{31}P NMR (121.5 MHz, D_2O) δ 44.1; HRMS calcd for $C_{11}H_{14}N_2O_7P$ $[M\text{-}H]^-$ 317.0540, found 317.0535.

1,2-*O*-Isopropylidene-(*E*)-3-(diethylphosphono)allyl-α-D-erythrofuranose (18). To a solution of **4** (279 mg, 1.5 mmol) and allyl diethylphosphonate (802 mg, 4.5 mmol) in 24 mL of dried DCM was added Grubbs II generation catalyst **Ru-II** (64 mg, 0.075 mmol) under Ar. The reaction mixture was stirred under reflux overnight under Ar. Evaporation of the solvent and purification of the residue by silica gel column chromatography (EtOAc) gave **18** (468 mg, 1.39 mmol) in 93% yield. Data for **18**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30−1.36 (m, 9H, CH_3), 1.58 (s, 3H, CH_3), 2.57 (d_{AB}, J_{AB} = 7.1 Hz, $J_{P,H}$ = 21.9 Hz, 2H, PCH_2), 2.82 (s, 1H, OH), 3.77 (s, 2H, H_4), 4.05−4.15 (m, 4H, OCH_2), 4.20 (d, J = 3.8 Hz, 1H, H_2), 5.71 (dd, J_1 = 15.7 Hz, J_2 = 4.6 Hz, 1H, CH═CH), 5.81 (d, J = 3.8 Hz, 1H, H_1), 5.84−5.96 (ddt, J_1 = 14.0 Hz, J_2 = 14.0 Hz, J_3 = 7.2 Hz, 1H, CH═CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5 (CH_3), 16.6 (CH_3), 26.7 (CH_3), 26.8 (CH_3), 29.7 (d, $J_{P,C}$ = 139.1 Hz, PCH_2), 62.1 (OCH_2), 62.2 (OCH_2), 73.7 (d, $J_{P,C}$ = 2.0 Hz, C-4), 78.3 (d, $J_{P,C}$ = 2.0 Hz, C-3), 82.8 (d, $J_{P,C}$ = 4.1 Hz, C-2), 105.5 (C-1), 113.1 ($OC(CH_3)_2$), 120.7 (d, $J_{P,C}$ = 10.8 Hz, CH═CH), 134.5 (d, $J_{P,C}$ = 14.3 Hz, CH═CH); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 26.6; HRMS calcd for $C_{14}H_{26}O_7P$ $[M + H]^+$ 337.1416, found 337.1412.

1,2-*O*-Isopropylidene-3-*O*-benzoyl-(*E*)-3-(diethylphosphono)allyl-α-D-erythrofuranose (19). To a solution of **18** (572 mg, 1.701 mmol), Et_3N (0.466 mL, 3.402 mmol) and DMAP (416 mg, 3.402 mmol) in dry CH_2Cl_2 (12 mL) were added dropwise BzCl (0.395 mL, 3.402 mmol) at 0 °C under Ar. The reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was partitioned between DCM and water, the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*, and the residue was purified by chromatography on a silica gel column (*n*-hexane/EtOAc = 1:1 and EtOAc) to give compound **19** (714 mg, 1.616 mmol) as a colorless oil in 95% yield. Data for **19**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24−1.29 (m, 6H, CH_3), 1.35 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 2.58 (d_{AB}, J_{AB} = 7.1 Hz, $J_{P,H}$ = 21.9 Hz, 2H, PCH_2), 4.01−4.11 (m, 4H, OCH_2), 4.17 (d, J = 8.6 Hz, 1H, H_{4a}), 4.31 (d, J = 8.6 Hz, 1H, H_{4b}), 4.87 (d, J = 3.5 Hz, 1H, H_2), 5.82 (d, J = 3.5 Hz, 1H, H_1), 5.85−5.93 (m, 1H, CH═CH), 5.98 (dd, J_1 = 16.0 Hz, J_2 = 4.6 Hz, 1H, CH═CH), 7.32−7.60 (m, 3H, Ar-H), 8.02−8.05 (m, 2H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3 (CH_3), 16.4 (CH_3), 26.7 (CH_3), one signal of CH_3 was overlapped, 29.7 (d, $J_{P,C}$ = 138.7 Hz, PCH_2), 62.0 (OCH_2), 62.1 (OCH_2), 71.8 (C-4), 82.3 (C-2), 83.1 (d, $J_{P,C}$ = 1.8 Hz, C-3), 104.8 (C-1), 113.1 ($OC(CH_3)_2$), 122.9 (d, $J_{P,C}$ = 10.8 Hz, CH═CH), 128.4 (Bz, C), 129.7 (Bz, C), 129.8 (Bz, C), 132.7 (d, $J_{P,C}$ = 14.6 Hz, CH═CH), 133.2 (Bz, C), 164.8 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 25.8; HRMS calcd for $C_{21}H_{30}O_8P$ $[M + H]^+$ 441.1679, found 441.1680.

1,2,3-*O*-Tribenzoyl-(*E*)-3-(diethylphosphono)allyl-D-erythrofuranose (20). Compound **19** (714 mg, 1.616 mmol) was dissolved in a solution (2.8 mL) of CF_3CO_2H and H_2O (3:1) at 0 °C. The reaction mixture was stirred at room temperature for 2 h. Saturated $NaHCO_3$ solution and solid $NaHCO_3$ was added to neutralize the excess acid at 0 °C. The reaction mixture was extracted with DCM (×2), the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by chromatography on a silica gel column (DCM/MeOH = 49:1) to give 3-*O*-benzoyl-(*E*)-3-(diethylphosphono)allyl-D-erythrose (608 mg, 1.519 mmol) in 94% yield as an anomeric mixture.

To a solution of 3-*O*-benzoyl-(*E*)-3-(diethylphosphono)allyl-D-erythrose (608 mg, 1.519 mmol), Et_3N (0.829 mL, 6.065 mmol) and DMAP (0.556 g, 4.548 mmol) in dry CH_2Cl_2 (18 mL) was added dropwise BzCl (0.705 mL, 6.065 mmol) at 0 °C under Ar. The reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was partitioned between DCM and water, the organic layer was washed with water and brine, dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*, and the residue was purified by chromatography on a silica gel column (*n*-hexane/EtOAc = 1:1 and 1:2) to give compound **20a** (0.414 g, 0.682 mmol) in 45% yield and **20b** (0.482 g, 0.788 mmol) in 52% yield. It was not identified at this stage which compound represents which isomer (α or β), but the anomeric mixture of **20a** and **20b** was used in the glycosylation reaction with the protected nucleobase. Data for **20a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17−1.26 (m, 6H, CH_3), 2.67 (d_{AB}, J_{AB} = 7.1 Hz, $J_{P,H}$ = 21.9 Hz, 2H, PCH_2), 3.99−4.06 (m, 4H, OCH_2), 4.59 (d, J = 10.2 Hz, 1H, H_{4a}), 4.78 (d, J = 10.2 Hz, 1H, H_{4b}), 5.90 (s, 1H, H_2), 5.98 (ddt, J_1 = 14.6 Hz, J_2 = 14.6 Hz, J_3 = 7.3 Hz, 1H, CH═CH), 6.26 (dd, J_1 = 15.8 Hz, J_2 = 4.7 Hz, 1H, CH═CH), 6.60 (s, 1H, H_1), 7.28−7.63 (m, 9H, Ar-H), 7.86−8.10 (m, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.7 (CH_3), 16.8 (CH_3), 30.2 (d, $J_{P,C}$ = 139.1 Hz, PCH_2), 62.6 (d, $J_{P,C}$ = 12.1 Hz, OCH_2), 62.7 (OCH_2), 76.4 (C-4), 81.2 (C-2), 83.8 (C-3), 100.1 (C-1), 124.3 (d, $J_{P,C}$ = 10.8 Hz, CH═CH), 128.9 (Bz, C), 129.0 (Bz, C), 129.1 (Bz, C), 129.5 (Bz, C), 129.7 (Bz, C), 129.9 (Bz, C), 130.2 (Bz, C), 130.3 (Bz, C), 130.4 (Bz, C), 133.1 (d, $J_{P,C}$ = 14.8 Hz, CH═CH), 133.9 (Bz, C), 134.2 (Bz, C), 165.1 (Bz, C═O), 165.4 (Bz, C═O), 165.6 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 25.6; HRMS calcd for $C_{32}H_{34}O_{10}P$ $[M + H]^+$ 609.1890, found 609.1887. Data for **20b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21−1.28 (m, 6H, CH_3), 2.64 (d_{AB}, J_{AB} = 7.1 Hz, $J_{P,H}$ = 21.9 Hz, 2H, PCH_2), 4.03−4.09 (m, 4H, OCH_2), 4.63 (d, J = 10.6 Hz, 1H, H_{4a}), 4.74 (d, J = 10.6 Hz, 1H, H_{4b}), 5.69 (d, J = 4.5 Hz, 1H, H_2), 5.91 (ddt, J_1 = 15.2 Hz, J_2 = 15.2 Hz, J_3 = 7.3 Hz, 1H, CH═CH), 6.13 (dd, J_1 = 15.8 Hz, J_2 = 4.5 Hz, 1H, CH═CH), 6.80 (d, J = 4.5 Hz, 1H, H_1), 7.20−7.56 (m, 9H, Ar-H), 7.89−8.06 (m, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.4 (CH_3), 16.5 (CH_3), 29.7 (d, $J_{P,C}$ = 138.8 Hz, PCH_2), 62.3 (OCH_2), 62.4 (OCH_2), 75.1 (C-4), 76.6 (C-2), 82.1 (d, $J_{P,C}$ = 1.9 Hz, C-3), 94.8 (C-1), 123.2 (d, $J_{P,C}$ = 11.1 Hz, CH═CH), 128.4 (Bz, C), 128.5 (Bz, C), 128.6 (Bz, C), 129.1 (Bz, C), 129.5 (Bz, C), 129.9 (Bz, C), 130.0 (Bz, C), 132.5 (d, $J_{P,C}$ = 14.7 Hz, CH═CH), 133.4 (Bz, C), 133.5 (Bz, C), 133.7 (Bz, C), 164.7 (Bz, C═O), 165.2 (Bz, C═O), one signal of (Bz, C═O) was overlapped; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 25.8; HRMS calcd for $C_{32}H_{34}O_{10}P$ $[M + H]^+$ 609.1890, found 609.1891.

1-(N^6-Benzoyladenin-9-yl)-2,3-*O*-dibenzoyl-(*E*)-3-(diethylphosphono)allyl-β-D-erythrofuranose (21). N^6-Benzoyladenine (144 mg, 0.6 mmol), ammonium sulfate (2.4 mg, 0.018 mmol), and 8 mL of HMDS were added to a dried flask. The mixture was refluxed overnight under N_2. HMDS was removed *in vacuo*. To the flask with the residue was added a solution of compound **20** (183 mg, 0.3 mmol) in 15 mL of dried CH_3CN, followed by dropwise addition of $SnCl_4$ (106 μL, 0.9 mmol) at room temperature under N_2. The reaction mixture was allowed to stir for 50 min. The reaction was quenched with cold saturated $NaHCO_3$ and partitioned between H_2O (10 mL) and EtOAc (80 mL). The organic layer was washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 49:1) to afford **21** (140 mg, 0.193 mmol) as a colorless amorphous solid in 64% yield. Data for **21**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16−1.25 (m, 6H, CH_3), 2.61 (d_{AB}, J_{AB} = 7.1 Hz, $J_{P,H}$ = 21.9 Hz, 2H, PCH_2), 3.98−4.07 (m, 4H, OCH_2), 4.78 (d, J = 10.5 Hz, 1H, $H_{4'a}$), 5.02 (d, J = 10.5 Hz, 1H, $H_{4'b}$), 6.03−6.13 (m, 1H, CH═CH), 6.18 (dd, J_1 = 15.8 Hz, J_2 = 4.5 Hz, 1H, CH═CH), 6.39 (d, J = 5.4 Hz, 1H, $H_{2'}$), 6.47 (d, J = 5.4 Hz, 1H, $H_{1'}$), 7.38−7.60 (m, 9H, Ar-H), 8.01−8.07 (m, 6H, Ar-H), 8.24 (s, 1H, H_2), 8.82 (s, 1H, H_8), 9.10 (br, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.4 (d, $J_{P,C}$ = 2.6 Hz, CH_3), 16.5 (d, $J_{P,C}$ = 2.6 Hz, CH_3), 29.8

(d, $J_{P,C}$ = 142.6 Hz, PCH_2), 62.2 (d, $J_{P,C}$ = 1.9 Hz, OCH_2), 62.3 (d, $J_{P,C}$ = 1.9 Hz, OCH_2), 74.7 (C-4′), 79.2 (d, $J_{P,C}$ = 3.1 Hz, C-2′), 84.2 (d, $J_{P,C}$ = 2.1 Hz, C-3′), 87.7 (C-1′), 123.7 (C-5), 125.0 (d, $J_{P,C}$ = 10.9 Hz, CH═CH), 127.9 (Bz, C), 128.7 (Bz, C), 128.8 (Bz, C), 128.9 (Bz, C), 129.8 (Bz, C), 129.9 (Bz, C), 130.1 (Bz, C), 130.4 (d, $J_{P,C}$ = 14.6 Hz, CH═CH), 132.9 (Bz, C), 133.7 (Bz, C), 133.8 (Bz, C), 134.0 (Bz, C), 141.9 (C-8), 149.9 (C-4), 151.9 (C-6), 153.1 (C-2), 164.6 (Bz, C═O), 164.7 (Bz, C═O), 165.2 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 25.4; HRMS calcd for $C_{37}H_{37}N_5O_9P$ $[M + H]^+$ 726.2329, found 726.2319.

1-(Thymin-1-yl)-2,3-*O*-dibenzoyl-(*E*)-3-(diethylphosphono)allyl-β-D-erythrofuranose (22). Thymine (46 mg, 0.36 mmol), ammonium sulfate (1.4 mg, 0.011 mmol), and 6 mL of HMDS were added to a dried flask. The mixture was refluxed overnight under N_2. HMDS was removed *in vacuo*. To the flask with the residue was added a solution of compound **20** (109 mg, 0.18 mmol) in 9 mL of dried CH_3CN, followed by dropwise addition of $SnCl_4$ (64 μL, 0.54 mmol) at room temperature under N_2. The reaction mixture was allowed to stir for 1 h. The reaction was quenched with cold saturated $NaHCO_3$ and partitioned between H_2O (10 mL) and EtOAc (80 mL). The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 49:1) to afford **22** (48 mg, 0.078 mmol) as a colorless amorphous solid in 43% yield. Data for **22**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18−1.24 (m, 6H, CH_3), 1.97 (s, 3H, CH_3), 2.61 (d_{AB}, J_{AB} = 7.1 Hz, $J_{P,H}$ = 22.0 Hz, 2H, PCH_2), 4.00−4.04 (m, 4H, OCH_2), 4.53 (d, J = 10.7 Hz, 1H, $H_{4'a}$), 4.83 (d, J = 10.7 Hz, 1H, $H_{4'b}$), 5.73 (d, J = 5.8 Hz, 1H, $H_{2'}$), 5.98−6.08 (m, 1H, CH═CH), 6.12 (dd, J_1 = 15.9 Hz, J_2 = 4.5 Hz, 1H, CH═CH), 6.21 (d, J = 5.8 Hz, 1H, $H_{1'}$), 7.19 (s, 1H, H_6), 7.31−7.62 (m, 6H, Ar-H), 7.90−8.10 (m, 4H, Ar-H), 9.28 (br, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.6 (CH_3), 16.4 (CH_3), 16.5 (CH_3), 29.6 (d, $J_{P,C}$ = 138.5 Hz, PCH_2), 62.2 (OCH_2), 62.3 (OCH_2), 74.3 (C-4′), 78.9 (d, $J_{P,C}$ = 3.0 Hz, C-2′), 82.9 (d, $J_{P,C}$ = 2.0 Hz, C-3′), 88.5 (C-1′), 112.1 (C-5), 124.5 (d, $J_{P,C}$ = 11.0 Hz, CH═CH), 128.6 (Bz, C), 128.7 (Bz, C), 128.8 (Bz, C), 128.9 (Bz, C), 129.7 (Bz, C), 129.8 (Bz, C), 130.0 (Bz, C), 130.1 (Bz, C), 131.5 (d, $J_{P,C}$ = 14.6 Hz, CH═CH), 133.6 (Bz, C), 133.9 (Bz, C), 135.7 (C-6), 150.6 (C-2), 163.7 (C-4), 164.6 (Bz, C═O), 165.5 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 25.5; HRMS calcd for $C_{30}H_{34}N_2O_{10}P$ $[M + H]^+$ 613.1951, found 613.1957.

1-(Adenin-9-yl)-(*E*)-3-(diethylphosphono)allyl-β-D-erythrofuranose (23a). A solution of **21** (180 mg, 0.248 mmol) in methanol saturated with ammonia (4 mL) was stirred at room temperature overnight. The mixture was concentrated, and the residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH= 19:1 and 9:1) to afford a crude product, which was further purified by HPLC on a C_{18} column to give **23a** (18 mg, 0.043 mmol) as colorless oil in 17% yield. Data for **23a**: ^{1}H NMR (300 MHz, MeOD) δ 1.29−1.34 (m, 6H, CH_3), 2.70 (d_{AB}, J_{AB} = 7.0 Hz, $J_{P,H}$ = 22.1 Hz, 2H, PCH_2), 3.91 (d, J = 9.5 Hz, 1H, $H_{4'a}$), 4.06−4.16 (m, 4H, OCH_2), 4.44 (d, J = 9.5 Hz, 1H, $H_{4'b}$), 4.98 (d, J = 7.1 Hz, 1H, $H_{2'}$), 5.87−5.97 (m, 2H, CH═CH), 6.00 (d, J = 7.1 Hz, 1H, $H_{1'}$), 8.20 (s, 1H, H_2), 8.30 (s, 1H, H_8); ^{13}C NMR (75 MHz, MeOD) δ 16.7 (CH_3), 16.8 (CH_3), 29.5 (d, $J_{P,C}$ = 138.4 Hz, PCH_2), 63.7 (OCH_2), 63.8 (OCH_2), 78.2 (d, $J_{P,C}$ = 3.6 Hz, C-4′), 79.3 (C-2′), 80.3 (d, $J_{P,C}$ = 2.3 Hz, C-3′), 90.7 (C-1′), 120.8 (C-5), 122.2 (d, $J_{P,C}$ = 10.9 Hz, CH═CH), 135.9 (d, $J_{P,C}$ = 14.2 Hz, CH═CH), 142.1 (C-8), 150.8 (C-4), 153.8 (C-2), 157.3 (C-6); ^{31}P NMR (121.5 MHz, MeOD) δ 28.2; HRMS calcd for $C_{16}H_{25}N_5O_6P$ $[M + H]^+$ 414.1543, found 414.1542.

Data for **23b**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.29−1.31 (m, 6H, CH_3), 4.03−4.06 (m, 4H, OCH_2), 4.79 (d, J = 14.9 Hz, 1H, $H_{4'a}$), 4.87 (d, J = 14.9 Hz, 1H, $H_{4'b}$), 5.45 (s, 1H, $H_{2'}$), 5.69 (dd, J_1 = 18.3 Hz, J_2 = 17.6 Hz, 1H, $H_{7'}$), 6.03 (s, 1H, $H_{1'}$), 6.21 (br, 2H, NH_2), 6.25 (d, J = 9.1 Hz, 1H, $H_{5'}$), 7.63 (ddd, J_1 = 20.8 Hz, J_2 = 16.9 Hz, J_3 = 11.2 Hz, 1H, $H_{6'}$), 7.88 (s, 1H, H_8), 8.18 (s, 1H, H_2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.3 (CH_3), 16.4 (CH_3), 61.9 (OCH_2), 62.0 (OCH_2), 71.6 (C-4′), 74.3 (C-2′), 92.2 (C-1′), 118.3 (d, $J_{P,C}$ = 190.3 Hz, C-7′), 119.7 (C-5), 123.6 (d, $J_{P,C}$ = 28 Hz, C-5′), 138.3 (C-8), 143.8 (d, $J_{P,C}$ = 6.8 Hz, C-6′), 145.8 (C-3′), 149.2 (C-4), 152.8 (C-2), 155.5 (C-6); ^{31}P NMR (121.5 MHz, MeOD) δ 18.6; HRMS calcd for $C_{16}H_{23}N_5O_5P$ $[M + H]^+$ 396.1437, found 396.1427. Data for **23c**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.32−1.35 (m, 6H, CH_3), 4.07−4.12 (m, 4H, OCH_2), 4.97 (s, 2H, H_4), 5.20 (s, 1H, $H_{2'}$), 5.77 (d, J = 6.2 Hz, 1H, $H_{1'}$), 5.79 (d, J = 17.8 Hz, 1H, $H_{7'}$), 6.27 (br, 2H, NH_2), 6.41 (d, J = 11.5 Hz, 1H, $H_{5'}$), 6.99 (ddd, J_1 = 20.5 Hz, J_2 = 16.7 Hz, J_3 = 11.5 Hz, 1H, $H_{6'}$), 7.94 (s, 1H, H_8), 8.22 (s, 1H, H_2); ^{13}C NMR (150 MHz, $CDCl_3$) δ 16.3 (CH_3), 16.4 (CH_3), 61.9 (d, $J_{P,C}$ = 9.8 Hz, OCH_2), 62.0 (OCH_2), 69.0 (C-4′), 76.0 (C-2′), 90.5 (C-1′), 119.0 (d, $J_{P,C}$ = 189.9 Hz, C-7′), 119.6 (C-5), 122.0 (d, $J_{P,C}$ = 27.5 Hz, C-5′), 138.6 (C-8), 142.7 (d, $J_{P,C}$ = 5.8 Hz, C-6′), 145.7 (C-3′), 149.1 (C-4), 152.6 (C-2), 155.6 (C-6); ^{31}P NMR (121.5 MHz, MeOD) δ 18.1; HRMS calcd for $C_{16}H_{23}N_5O_5P$ $[M + H]^+$ 396.1437, found 396.1434.

1-(Thymin-1-yl)-3-(diethylphosphono)allyl-β-D-erythrofuranose (24). A solution of **22** (48 mg, 0.078 mmol) in methanol saturated with ammonia (3 mL) was stirred at room temperature overnight. The mixture was concentrated, and the residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 19:1) to afford a crude product, which was further purified by HPLC on a C_{18} column to provide **24** in trace amount. HRMS calcd for $C_{16}H_{26}N_2O_8P$ $[M + H]^+$ 405.1427, found 405.1421.

1-(Adenin-9-yl)-(*E*)-3-phosphonoallyl-β-D-erythrofuranose (1e). To a solution of compound **23a** (52 mg, 0.125 mmol) and 2,6-lutidine (1 mL, 8.61 mmol) in 8 mL of dry CH_2Cl_2 was added bromotrimethylsilane (293 μL, 2.52 mmol) at room temperature under nitrogen. The reaction mixture was continuously stirred for 2 days in the darkness. The reaction mixture was concentrated under high vacuum at room temperature, and the residue was coevaporated with MeOH and 0.5 M TEAB solution. Purification by HPLC using reverse phase C_{18} column (mobile phase A: MeCN + 50 mM TEAB; mobile phase B: H_2O + 50 mM TEAB) and ion exchange with Dowex-Na^+ resin offered **1e** (26 mg, 0.064 mmol) as a colorless solid after lyophilization in 51% yield. Data for **1e**: ^{1}H NMR (600 MHz, D_2O) δ 2.46 (d_{AB}, J_{AB} = 7.7 Hz, $J_{P,H}$ = 20.8 Hz, 2H, PCH_2), 4.01 (d, J = 10.2 Hz, 1H, $H_{4'a}$), 4.43 (d, J = 10.2 Hz, 1H, $H_{4'b}$), 4.89 (d, J = 7.6 Hz, 1H, $H_{2'}$), 5.72 (dd, J_1 = 15.6 Hz, J_2 = 4.7 Hz, 1H, $H_{5'}$), 5.93 (ddt, J_1 = 13.9 Hz, J_2 = 13.9 Hz, J_3 = 7.5 Hz, 1H, $H_{6'}$), 6.03 (d, J = 7.6 Hz, 1H, $H_{1'}$), 8.16 (s, 1H, H_2), 8.30 (s, 1H, H_8); ^{13}C NMR (150 MHz, D_2O) δ 32.3 (d, $J_{P,C}$ = 129 Hz, PCH_2), 76.6 (C-2′), 77.5 (C-4′), 79.0 (C-3′), 87.4 (C-1′), 118.9 (C-5), 126.2 (d, $J_{P,C}$ = 10.5 Hz, $H_{6'}$), 129.7 (d, $J_{P,C}$ = 12 Hz, $H_{5'}$), 140.6 (C-8), 148.9 (C-4), 152.7 (C-2), 155.5 (C-6); ^{31}P NMR (121.5 MHz, D_2O) δ 19.7; HRMS calcd for $C_{12}H_{15}N_5O_6P$ $[M - H]^-$ 356.0761, found 356.0758.

1,2,3-*O*-Tribenzoyl-3-(diethylphosphono)propyl-D-erythrofuranose (25). To a solution of **20** (613 mg, 1.01 mmol) in methanol (20 mL) was added Pd/C (106 mg, 0.1 mmol) under Ar. The reaction mixture was stirred under hydrogen atmosphere for 21 h. The mixture was filtered through a Celite pad to remove the catalyst and purified on a silica gel column (EtOAc/*n*-hexane = 1:1 and 2:1) to afford **25** (571 mg, 0.935 mmol) as an anomeric mixture (**25a** and **25b**) in 92% yield. Data for **25a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19−1.25 (m, 6H, CH_3), 1.71−2.05 (m, 4H, (H_5, 2H), (H_6, 2H)), 2.51−2.67 (m, 2H, PCH_2), 3.96−4.09 (m, 4H, OCH_2), 4.59 (s, 2H, H_4), 5.89 (d, J = 0.6 Hz, 1H, H_2), 6.60 (d, J = 0.6 Hz, 1H, H_1), 7.30−7.62 (m, 9H, Ar-H), 7.86−8.10 (m, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3 (CH_3), 16.4 (CH_3), 17.2 (d, $J_{P,C}$ = 4.7 Hz, C-6), 24.7 (d, $J_{P,C}$ = 140.7 Hz, PCH_2), 34.8 (d, $J_{P,C}$ = 15.3 Hz, C-5), 61.5 (OCH_2), 61.6 (OCH_2), 76.6 (C-4), 78.8 (C-2), 85.2 (d, $J_{P,C}$ = 1.6 Hz, C-3), 100.1 (C-1), 128.4 (Bz, C), 128.5 (Bz, C), 128.6 (Bz, C), 128.9 (Bz, C), 129.2 (Bz, C), 129.3 (Bz, C), 129.6 (Bz, C), 129.8 (Bz, C), 129.9 (Bz, C), 133.4 (Bz, C), 133.6 (Bz, C), 133.7 (Bz, C), 164.9 (Bz, C═O), 165.0 (Bz, C═O), 165.1 (Bz, C═O),

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^{31}P NMR (121.5 MHz, $CDCl_3$) δ 30.8; HRMS calcd for $C_{32}H_{35}O_{10}PNa$ $[M + Na]^+$ 633.1866, found 633.1871. Data for **25b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17−1.25 (m, 6H, CH_3), 1.73−1.84 (m, 4H, (H_5, 2H), (H_6, 2H)), 2.27−2.37 (m, 1H, PCH_a), 2.55−2.66 (m, 1H, PCH_b), 3.95−4.08 (m, 4H, OCH_2), 4.42 (d, J = 10.6 Hz, 1H, H_{4a}), 4.70 (d, J = 10.6 Hz, 1H, H_{4b}), 5.64 (d, J = 4.6 Hz, 1H, H_2), 6.81 (d, J = 4.6 Hz, 1H, H_1), 7.16−7.57 (m, 9H, Ar-H), 7.85−8.06 (m, 6H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.3 (d, $J_{P,C}$ = 2.7 Hz, CH_3), 16.4 (d, $J_{P,C}$ = 2.7 Hz, CH_3), 17.1 (d, $J_{P,C}$ = 4.7 Hz, C-6), 24.7 (d, $J_{P,C}$ = 141.0 Hz, PCH_2), 35.7 (d, $J_{P,C}$ = 15.7 Hz, C-5), 61.6 (OCH_2), 61.7 (OCH_2), 75.4 (C-4 overlapped with C-2), 83.6 (d, $J_{P,C}$ = 2.0 Hz, C-3), 95.0 (C-1), 128.3 (Bz, C), 128.5 (Bz, C), 128.6 (Bz, C), 129.1 (Bz, C), 129.4 (Bz, C), 129.9 (Bz, C), 130.0 (Bz, C), 133.3 (Bz, C), 133.5 (Bz, C), 133.6 (Bz, C), 165.0 (Bz, C═O), 165.1 (Bz, C═O), one signal of (Bz, C═O) was overlapped; ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 30.7; HRMS calcd for $C_{32}H_{35}O_{10}PNa$ $[M + Na]^+$ 633.1866, found 633.1857.

1-(N^6-Benzoyladenin-9-yl)-2,3-*O*-dibenzoyl-3-(diethylphosphono)propyl-β-D-erythrofuranose (26). N^6-Benzoyladenine (124 mg, 0.52 mmol), ammonium sulfate (2 mg, 0.016 mmol), and 4 mL of HMDS were added to a dried flask. The mixture was refluxed overnight under N_2. HMDS was removed *in vacuo*. To the flask with the residue was added a solution of compound **25** (159 mg, 0.26 mmol) in 13 mL of dried CH_3CN, followed by dropwise addition of $SnCl_4$ (92 μL, 0.78 mmol) at room temperature under N_2. The reaction mixture was allowed to stir for 1 h. The reaction was quenched with cold saturated $NaHCO_3$ and partitioned between brine (10 mL) and EtOAc (80 mL). The organic layer was washed with water and brine, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 49:1) to afford **26** (122 mg, 0.168 mmol) as a colorless amorphous solid in 64% yield. Data for **26**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14−1.24 (m, 6H, CH_3), 1.76−1.90 (m, 4H, ($H_{5'}$, 2H), ($H_{6'}$, 2H)), 2.51−2.67 (m, 2H, PCH_2), 3.93−4.07 (m, 4H, OCH_2), 4.80 (s, 2H, $H_{4'}$), 6.36 (d, J = 5.7 Hz, 1H, $H_{2'}$), 6.57 (d, J = 5.7 Hz, 1H, $H_{1'}$), 7.31−7.61 (m, 9H, Ar-H), 7.96−8.06 (m, 6H, Ar-H), 8.22 (s, 1H, H_2), 8.79 (s, 1H, H_8), 9.51 (br, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.2 (d, $J_{P,C}$ = 3.9 Hz, CH_3), 16.3 (d, $J_{P,C}$ = 3.9 Hz, CH_3), 17.1 (d, $J_{P,C}$ = 4.7 Hz, C-6′), 24.6 (d, $J_{P,C}$ = 140.7 Hz, PCH_2), 34.4 (d, $J_{P,C}$ = 15.7 Hz, C-5′), 61.5 (OCH_2), 61.6 (OCH_2), 75.5 (C-4′), 77.9 (C-2′), 86.4 (d, $J_{P,C}$ = 1.8 Hz, C-3′), 88.9 (C-1′), 123.9 (C-5), 127.9 (Bz, C), 128.4 (Bz, C), 128.5 (Bz, C), 128.7 (Bz, C), 129.7 (Bz, C), 129.8 (Bz, C), 132.6 (Bz, C), 133.5 (Bz, C), 133.6 (Bz, C), 133.8 (Bz, C), 142.4 (C-8), 149.9 (C-4), 151.7 (C-6), 152.7 (C-2), 164.8 (Bz, C═O), 165.0 (Bz, C═O), 165.1 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 30.7; HRMS calcd for $C_{37}H_{39}N_5O_9P$ $[M + H]^+$ 728.2485, found 728.2481.

1-(Thymin-1-yl)-2,3-*O*-dibenzoyl-3-(diethylphosphono)-propyl-β-D-erythrofuranose (27). Thymine (66 mg, 0.52 mmol), ammonium sulfate (2 mg, 0.015 mmol), and 4 mL of HMDS were added to a dried flask. The mixture was refluxed overnight under N_2. HMDS was removed *in vacuo*. To the flask with the residue was added a solution of compound **25** (159 mg, 0.26 mmol) in 13 mL of dried CH_3CN, followed by dropwise addition of $SnCl_4$ (92 μL, 0.78 mmol) at room temperature under N_2. The reaction mixture was allowed to stir for 1 h. The reaction was quenched with cold saturated $NaHCO_3$ and partitioned between brine (10 mL) and EtOAc (80 mL). The organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 49:1) to afford **27** (96 mg, 0.156 mmol) as a colorless amorphous solid in 60% yield. Data for **27**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15−1.24 (m, 6H, CH_3), 1.73−1.88 (m, 4H, ($H_{5'}$, 2H), ($H_{6'}$, 2H)), 1.95 (s, 3H, CH_3), 2.34−2.58 (m, 2H, PCH_2), 3.93−4.05 (m, 4H, OCH_2), 4.56 (d, J = 10.6 Hz, 1H, $H_{4a'}$), 4.62 (d, J = 10.6 Hz, 1H, $H_{4b'}$), 5.87 (d, J = 5.9 Hz, 1H, $H_{2'}$), 6.06 (d, J = 5.9 Hz, 1H, $H_{1'}$), 7.21 (d, J = 0.8 Hz, 1H, H_6), 7.35−7.59 (m, 6H, Ar-H), 7.98−8.01 (m, 4H, Ar-H), 9.85 (br, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.5 (CH_3), 16.3 (CH_3), 16.4 (CH_3), 17.1 (d, $J_{P,C}$ = 4.4 Hz, C-6′), 24.4 (d, $J_{P,C}$ = 140.8 Hz, PCH_2), 34.9 (d, $J_{P,C}$ = 14.5 Hz, C-5′), 61.5 (d, $J_{P,C}$ = 1.5 Hz, OCH_2), 61.6 (d, $J_{P,C}$ = 1.7 Hz, OCH_2), 75.7 (C-4′), 77.7 (C-2′), 85.8 (d, $J_{P,C}$ = 1.4 Hz, C-3′), 91.0 (C-1′), 111.5 (C-5), 128.5 (Bz, C), 128.7 (Bz, C), 129.7 (Bz, C), 129.8 (Bz, C), 129.9 (Bz, C), 133.5 (Bz, C), 133.7 (Bz, C), 136.7 (C-6), 150.7 (C-2), 164.1 (C-4), 165.1 (Bz, C═O), 165.4 (Bz, C═O); ^{31}P NMR (121.5 MHz, $CDCl_3$) δ 30.9; HRMS calcd for $C_{30}H_{36}N_2O_{10}P$ $[M + H]^+$ 615.2107, found 615.2112.

1-(Adenin-9-yl)-3-(diethylphosphono)propyl-β-D-erythrofuranose (28). A solution of **26** (217 mg, 0.298 mmol) in methanol saturated with ammonia (5 mL) was stirred at room temperature overnight. The mixture was concentrated, and the residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 19:1 and 9:1) to afford **28** (96 mg, 0.231 mmol) as a white powder in 77% yield. Data for **28**: ^{1}H NMR (300 MHz, MeOD) δ 1.29−1.34 (m, 6H, CH_3), 1.66−1.94 (m, 6H, ($H_{5'}$, 2H), ($H_{6'}$, 2H), (PCH_2, 2H)), 3.99 (d, J = 9.4 Hz, 1H, $H_{4'a}$), 4.04−4.17 (m, 4H, OCH_2), 4.36 (d, J = 9.4 Hz, 1H, $H_{4'b}$), 4.81 (d, J = 7.1 Hz, 1H, $H_{2'}$), 5.97 (d, J = 7.1 Hz, 1H, $H_{1'}$), 8.20 (s, 1H, H_2), 8.29 (s, 1H, H_8); ^{13}C NMR (75 MHz, MeOD) δ 16.7 (CH_3), 16.8 (CH_3), 18.2 (d, $J_{P,C}$ = 4.7 Hz, C-6′), 25.3 (d, $J_{P,C}$ = 139.4 Hz, PCH_2), 37.4 (d, $J_{P,C}$ = 16.1 Hz, C-5′), 63.1 (OCH_2), 63.2 (OCH_2), 78.3 (C-4′), 79.2 (C-2′), 79.4 (d, $J_{P,C}$ = 1.6 Hz, C-3′), 90.8 (C-1′), 120.8 (C-5), 142.0 (C-8), 150.8 (C-4), 153.8 (C-2), 157.3 (C-6); ^{31}P NMR (121.5 MHz, MeOD) δ 33.0; HRMS calcd for $C_{16}H_{27}N_5O_6P$ $[M + H]^+$ 416.1699, found 416.1696.

1-(Thymin-1-yl)-3-(diethylphosphono)propyl-β-D-erythrofuranose (29). A solution of **27** (171 mg, 0.278 mmol) in methanol saturated with ammonia (5 mL) was stirred at room temperature overnight. The mixture was concentrated, and the residue was purified by chromatography on a silica gel column (CH_2Cl_2/MeOH = 19:1) to give **29** (87 mg, 0.214 mmol) as a white powder in 77% yield. Data for **29**: ^{1}H NMR (300 MHz, MeOD) δ 1.30−1.35 (m, 6H, CH_3), 1.53−1.82 (m, 6H, ($H_{5'}$, 2H), ($H_{6'}$, 2H), (PCH_2, 2H)), 1.89 (d, J = 1.1 Hz, 3H, CH_3), 3.89 (d, J = 9.5 Hz, 1H, $H_{4'a}$), 4.05−4.15 (m, 4H, OCH_2), 4.16 (d, J = 9.5 Hz, 1H, $H_{4'b}$), 4.19 (d, J = 7.2 Hz, 1H, $H_{2'}$), 5.81 (d, J = 7.2 Hz, 1H, $H_{1'}$), 7.49 (d, J = 1.1 Hz, 1H, H_6); ^{13}C NMR (75 MHz, MeOD) δ 12.3 (CH_3), 16.7 (CH_3), 16.8 (CH_3), 18.1 (d, $J_{P,C}$ = 4.8 Hz, C-6′), 25.3 (d, $J_{P,C}$ = 139.4 Hz, PCH_2), 37.6 (d, $J_{P,C}$ = 16.0 Hz, C-5′), 63.1 (OCH_2), 63.2 (OCH_2), 78.2 (C-4′), 78.8 (C-2′), 79.1 (d, $J_{P,C}$ = 2.8 Hz, C-3′), 92.2 (C-1′), 111.8 (C-5), 139.2 (C-6), 152.7 (C-2), 166.3 (C-4); ^{31}P NMR (121.5 MHz, MeOD) δ 33.1; HRMS calcd for $C_{16}H_{28}N_2O_8P$ $[M + H]^+$ 407.1583, found 407.1587.

1-(Adenin-9-yl)-3-phosphonopropyl-β-D-erythrofuranose (1f). Compound **1f** was prepared as described for **1e**, using **28** (68 mg, 0.164 mmol) as starting material, 2,6-lutidine (2 mL, 17.23 mmol) ,and bromotrimethylsilane (436 μL, 3.28 mmol). **1f** (44 mg, 0.108 mmol) was obtained as a colorless solid after lyophilization in 66% yield. Data for **1f**: ^{1}H NMR (500 MHz, D_2O) δ 1.61−1.67 (m, 3H, ($H_{7'}$, 2H), ($H_{6'a}$, 1H)), 1.76−1.83 (m, 2H, ($H_{6'b}$, 1H), ($H_{5'a}$, 1H)), 1.90−1.95 (m, 1H, $H_{5'b}$), 4.11 (d, J = 10.1 Hz, 1H, $H_{4'a}$), 4.40 (d, J = 10.1 Hz, 1H, $H_{4'b}$), 4.73 (d, J = 7.3 Hz, 1H, $H_{2'}$), 6.00 (d, J = 7.5 Hz, 1H, $H_{1'}$), 8.18 (s, 1H, H_2), 8.31 (s, 1H, H_8); ^{13}C NMR (125 MHz, D_2O) δ 17.6 (d, $J_{P,C}$ = 3.9 Hz, C-6′), 27.4 (d, $J_{P,C}$ = 133.4 Hz, C-7′), 35.5 (d, $J_{P,C}$ = 16.4 Hz, C-5′), 76.4 (C-4′), 77.4 (C-2′), 78.3 (C-3′), 87.3 (C-1′), 118.6 (C-5), 140.3 (C-8), 148.6 (C-4), 152.4 (C-2), 155.1 (C-6); ^{31}P NMR (121.5 MHz, D_2O) δ 24.2; HRMS calcd for $C_{12}H_{17}N_5O_6P$ $[M - H]^-$ 358.0917, found 358.0894.

1-(Thymin-1-yl)-3-phosphonopropyl-β-D-erythrofuranose (1g). Compound **1g** was prepared as described for **1e**, using **29** (75 mg, 0.184 mmol) as starting material, 2,6-lutidine (2 mL, 17.23 mmol), and bromotrimethylsilane (428 μL, 3.689 mmol). **1g** (55 mg, 0.139 mmol) was obtained as a colorless solid after lyophilization in 75% yield. Data for **1g**: ^{1}H NMR (500 MHz, D_2O) δ 1.58−1.65 (m, 3H, ($H_{7'}$, 2H), ($H_{6'a}$, 1H)), 1.72−1.74 (m, 2H, ($H_{6'b}$, 1H), ($H_{5'a}$, 1H)), 1.84−1.88 (m, 1H,

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$H_{5'b}$), 1.91 (d, J = 0.5 Hz, 3H, CH_3), 4.05 (d, J = 10.1 Hz, 1H, $H_{4'a}$), 4.29 (d, J = 10.1 Hz, 1H, $H_{4'b}$), 4.34 (d, J = 7.3 Hz, 1H, $H_{2'}$), 5.88 (d, J = 7.3 Hz, 1H, $H_{1'}$), 7.53 (d, J = 0.8 Hz, 1H, H_6); ^{13}C NMR (125 MHz, D_2O) δ 11.1 (CH_3), 17.6 (d, $J_{P,C}$ = 4.8 Hz, C-6′), 27.3 (d, $J_{P,C}$ = 133.1 Hz, C-7′), 35.4 (d, $J_{P,C}$ = 16.3 Hz, C-5′), 76.6 (C-4′), 77.2 (C-2′), 78.3 (C-3′), 89.6 (C-1′), 111.4 (C-5), 137.8 (C-6), 151.7 (C-2), 166.2 (C-4); ^{31}P NMR (121.5 MHz, D_2O) δ 21.9; HRMS calcd for $C_{12}H_{18}N_2O_8P$ $[M - H]^-$ 349.0801, found 349.0807.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H NMR and ^{13}C NMR spectra of compounds **1**−**29** and HPLC spectra of compounds **1a**−**1g**. This material is available free of charge via the Internet at http://pubs.acs.org.

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