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Synthesis and Biological Evaluation of 4′-*C*,3′-*O*-Propylene-Linked Bicyclic Nucleosides

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A set of pyrimidine nucleosides fused with a 4′-*C*,3′-*O*-propylene bridge was successfully synthesised in 12 steps from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, an inexpensive starting material, based on a ring-closing metathesis (RCM) reaction followed by Vorbrüggen-type nucleobase coupling. Antiviral and cytotoxicity activities of the targeted modified nucleosides, as well as their phosphoramidate prodrugs, are described.

Introduction

There has been a continuing interest in the synthesis of modified nucleosides as potent antiviral and antitumor agents, and a plethora of compounds has been evaluated over the years.[1] In this context, various bridged nucleosides, in which the carbohydrate conformation is restricted or locked by the introduction of an additional link on the carbohydrate moiety, have been reported.[2] Some of these carbohydrate-modified nucleosides have also been incorporated into oligonucleotides to increase resistance toward enzymatic degradation and to form stable duplexes with complementary DNA and RNA strands.[3] All these modified nucleosides have been designed to optimise their recognition by their target enzymes or oligonucleotide strands based on a preorganisation of the sugar moiety to an appropriate conformation. Among the large number of modified nucleosides, various restricted analogues on the sugar ring, with a bridge of different sizes containing one oxygen atom, have been evaluated for their biological activities.

In the antisense field, the most intriguing examples are the 2′-*O*,4′-*C*-methylene-bridged nucleic acids (named locked nucleic acids, or LNA,[4] now commercially available) and ENA[5] (2′-*O*,4′-*C*-ethylene-bridged nucleic acids) as outlined in Figure 1. It is worth pointing out that LNA are conformationally restricted RNA mimics, with an *N*-type sugar pucker that is present exclusively in A-form duplexes. LNA display a markedly increased duplex stability with complementary RNA and a greater nuclease resistance compared to native DNA. In addition, some bicyclic nucleoside analogues containing a fused oxirane (**1**),[6] oxetane (**2**)[7] and tetrahydrofuran (**3**–**4**[8] and **5**)[9] rings (Figure 1) have been reported to exhibit anti-HIV activity.

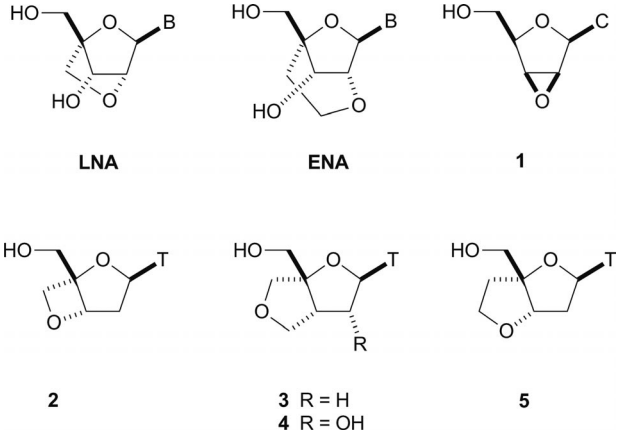

Figure 1. Structures of **LNA**, **ENA** and nucleoside derivatives **1**–**5** (T = thymin-1-yl, C = cytosin-1-yl, B = pyrimidin-1-yl and purin-9-yl).

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Besides LNA and ENA, some oxygenated bicyclic nucleosides, such as **6**,[10] **7**,[11] **8**,[12] **9**[13] and **10**[14] (Figure 2), have been incorporated into oligonucleotides and evaluated for antisense application. To the best of our knowledge, since our previous work[15] on the synthesis of the 4′-*C*,3′-*O*-propylene-bridged nucleosides **11** and **12** starting from thymidine (Scheme 1), no effort to prepare such bicyclic nucleosides has been described in the literature, with the exception of a publication by Morita et al.[14]

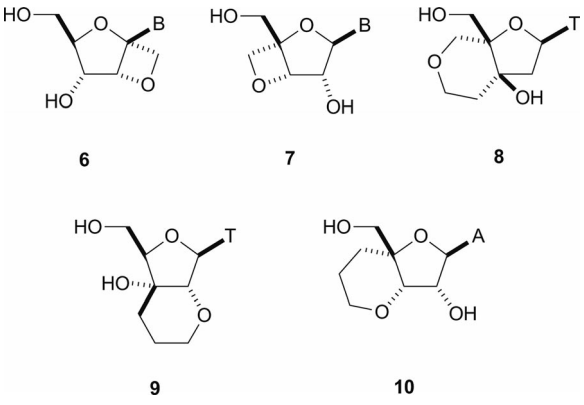
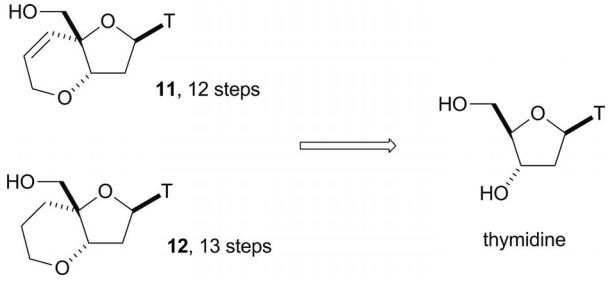


Figure 2. Selected oxygenated bicyclic nucleoside derivatives **6**–**10** incorporated into oligonucleosides (T = thymin-1-yl, B = pyrimidin-1-yl and purin-9-yl and A = adenin-9-yl).



Scheme 1. Structure of 3′-*O*,4′-*C*-propylene-bridged nucleosides **11** and **12** in the 2′-deoxyribose series.

These authors reported the biological evaluation of 2′,5′-oligoadenylate-5′-triphosphate analogues containing 4′-*C*,3′-*O*-bridged adenosine as potent RNase L agonists, but without any information about the preparation of the bicyclic nucleoside derivative **10**.

As a continuation of our interest in the preparation of new nucleoside analogues, we herein report full details related to the synthesis of bicyclic nucleosides **13**–**18** (Figure 3) in the D-ribose series containing natural pyrimidine nucleobases (thymine, uracil and cytosine) and present their biological evaluation.

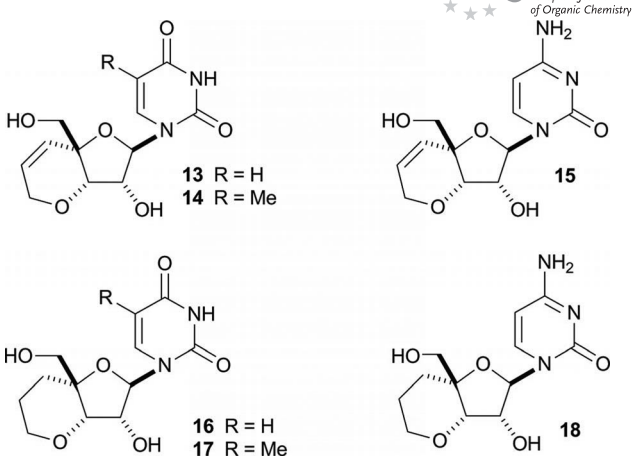
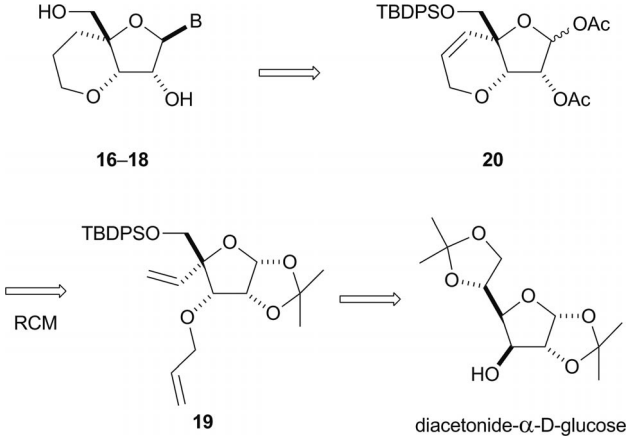


Figure 3. Targeted bicyclic nucleosides **13**–**18**.

Results and Discussion

Chemical Synthesis

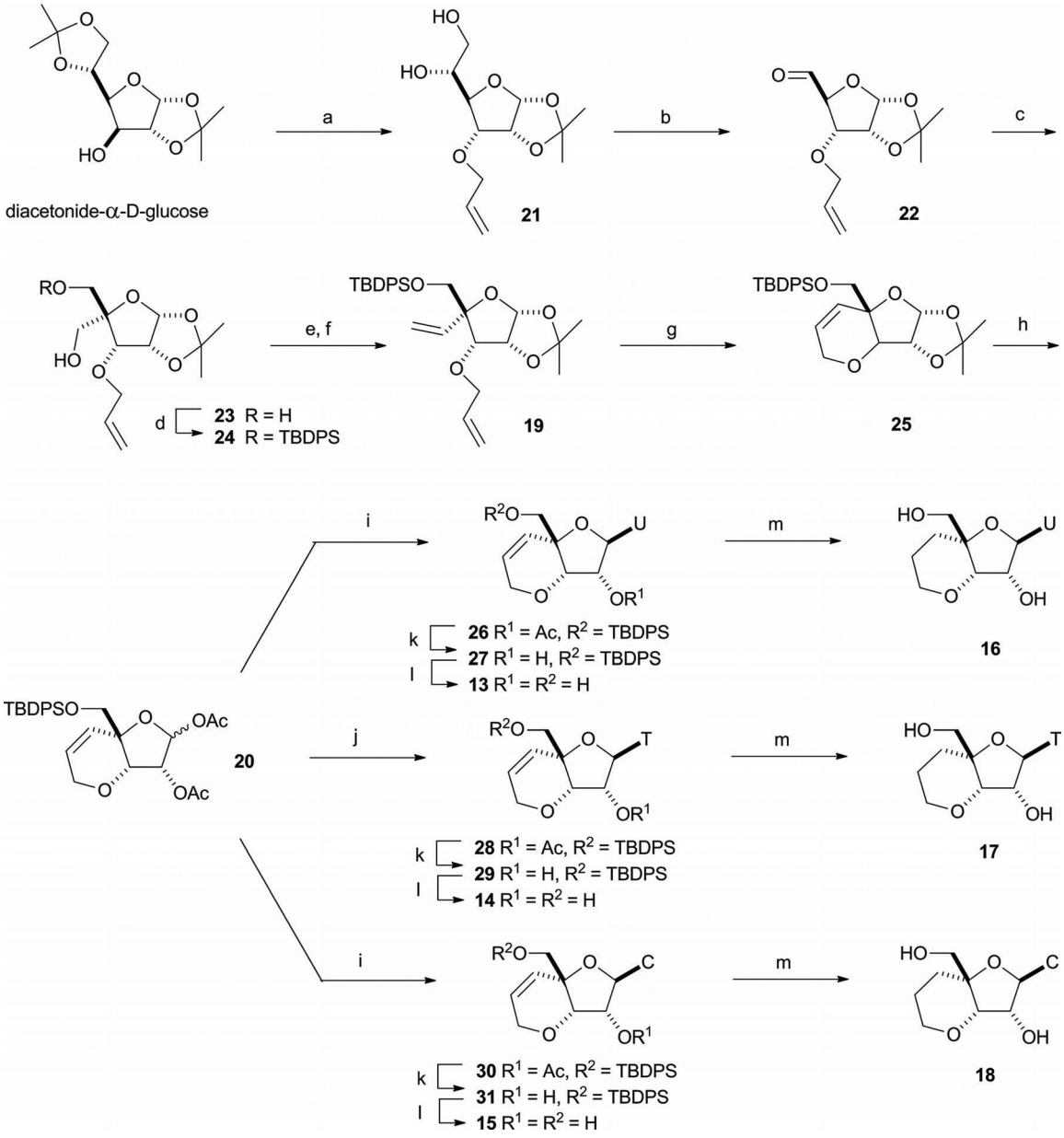
For the synthesis of the 4′-*C*-,3′-*O*-bridged nucleosides **13**–**18**, a convergent strategy was used in which the modified glycosyl donor **20** was synthesised from the inexpensive 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and then coupled to the nucleobase, leading to the targeted D-*ribo* analogues. This strategy was designed based on the retrosynthetic analysis involving a ring-closing metathesis (RCM)[16] reaction as the key step (Scheme 2). RCM is a useful method in organic chemistry for the synthesis of different nucleoside analogues that have restricted conformations, such as bicyclonucleosides[2f] and cyclonucleosides.[2g]



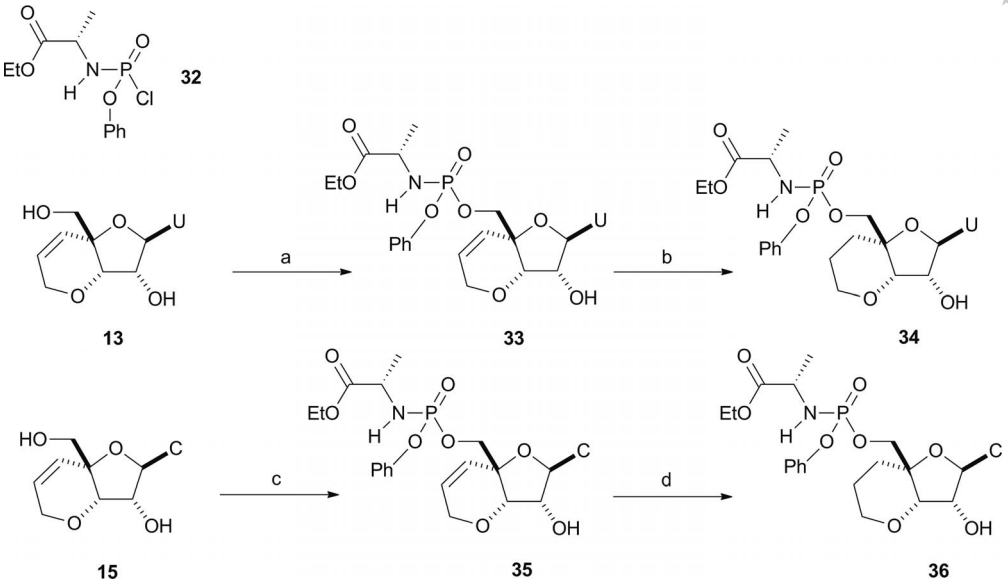
Scheme 2. Retrosynthetic scheme.

As the entry on the D-*ribo* derivatives, we envisaged that the chiral compound **20** could serve as the common glycosyl donor to reach our target nucleosides, as outlined in Scheme 3. The precursor of our key glycosyl donor **20** was synthesised via the diene **19** according to a known sequence described for the 3-*O*-benzyl derivative.[17] In our case, the choice to use diacetoneglucose as the starting material led

us to invert the absolute configuration of the carbon atom in position 3 [(*S*) to (*R*)] to have the D-allose configuration. Then the oxidative cleavage of the diol in position 5,6 would furnish the pentose analogue in similar configuration with that of the natural nucleoside. The chiral starting material **21** was prepared on a large scale in 4 steps from a glucose derivative following known procedures.[18] Oxidative cleavage of the diol **21** by treatment with $NaIO_4$ in a mixture of dioxane and water furnished the aldehyde **22**. Without isolation, treatment of the aldehyde **22** with excess formaldehyde and sodium hydroxide afforded the corresponding aldol, which was then trapped by reduction with sodium borohydride to yield the desired diol **23**.[19] According to previously reported examples, the less hindered 5′β-hydroxy group of diol **23** was stereoselectively protected as a silyl ether in 64% yield.[11b,17] The structure of **24** was confirmed by NOE correlation between the methylene bearing the free hydroxy function and the methyl of the isopropylidene group oriented toward the *endo* face of the bicyclic system (see Supporting Information).[17a] Next, Swern oxidation of



Scheme 3. Reagents and conditions: (a) see ref.[18], 4 steps, 50% overall yield. (b) $NaIO_4$, H_2O/dioxane (1:1), 0 °C, 30 min. (c) HCHO aq., NaOH aq., room temp., dioxane, 6 h, then $NaBH_4$, room temp., 30 min., 51% yield for the three steps. (d) TBDPSCl, Et_3N, CH_2Cl_2, 0 °C then r.t., overnight, 64%. (e) ClCOCOCl, DMSO, DIPEA, CH_2Cl_2, –78 °C. (f) $Ph_3P{=}CH_2$, THF, –78 °C, room temp., 3 h, 45% for the two steps. (g) Grubbs' catalyst second generation, CH_2Cl_2, room temp., 16 h, 97%. (h) AcOH, Ac_2O, cat. H_2SO_4, room temp., 3 h, 77%. (i) Uracil, BSA, TMSOTf, CH_3CN, 0 °C then r.t., 12 h, for **26** 73%, for **30** same conditions with cytosine, 77%. (j) Thymine, HMDS, TMSCl, TMSOTf, DCE, –35 °C, then r.t., 24 h, 76%. (k) K_2CO_3, MeOH, room temp., for **27**, 3 h, 88%; for **29**, 3 h, 79%; for **31**, 2 h, 85%. (l) TBAF, THF, room temp., for **13**, 4 h, 95%; for **14**, 4 h, 95%; for **15**, 4 h, 76%. (m) 1 atm. H_2, 10% Pd/C, EtOH, r.t. for **16**, 24 h, 93%; for **17**, 24 h, 87%; for **18**, 24 h, 79%.



Scheme 4. Reagents and conditions: (a) compound **32**, *N*-methylimidazole, THF, –78 °C, 2 h, then r.t., 12 h, 65%. (b) 1,4-cyclohexadiene, Pd/C, EtOH, room temp., 3 h, 98%. (c) *tert*-BuMgCl, THF, 30 min, –78 °C, then compound **32**, –78 °C, 2 h, then r.t., 12 h, 48%. (d) 1 atm. H_2, Pd/C, EtOH, room temp., 3 h, 94%.

the remaining primary alcohol of **24** gave the corresponding aldehyde, which was treated with methylenetriphenylphosphorane to afford the diene **19** in 45% overall yield for the two-step sequence. The subsequent RCM reaction performed with the second generation Grubbs' catalyst at room temperature in dichloromethane on compound **19** led to the desired cyclised intermediate **25** in high yield.

Successive hydrolysis of the acetonide group of compound **25** and acetylation of the resulting diol with acidic treatment in a one-pot reaction delivered the diacetate **20** as an anomeric mixture. It should be noted that the two anomers have been separated on silica gel chromatography for NMR analysis. At this point, from this key intermediate **20** as an α,β-anomeric mixture, the desired β-nucleoside analogues could be efficiently obtained in around 75% yield after purification by stereoselective coupling in the presence of TMSOTf with the silylated pyrimidines formed in situ following the method of Vorbrüggen.[20] The attack of the nucleobase from the favourable β-face is due to anchimeric assistance by neighbouring group participation of the 2′-*O*-Ac to give only the β-anomer. From **26**, **28** and **30**, subsequent methanolysis and cleavage of the TBDPS group with TBAF afforded the first bicyclic nucleosides **13**, **14** and **15**, respectively, and the hydrogenation of the double bond of the compounds so obtained gave the saturated analogues **16**–**18** in around 60% yield for the three steps. In our hands, standard hydrogenation of **13** [1 atm. H_2 (balloon) 10% Pd/C, EtOH, room temp., 24 h] furnished the target uridine analogue **16** without the unwanted reduction of the C5–C6 uracil double bond.[17b,21b–21d] Nevertheless, some reports in the literature[21a] mention the hydrogenation of the uracil nucleobase under these later conditions, which could depend on the quality of Pd/C. Also, the use of transfer hydrogenation conditions prevents this potential side reaction (vide infra).

In addition to this work, the aryl phosphoramidate derivatives of **13**, **15**, **16** and **18** were prepared according to reported methodology[22] to evaluate the importance of the rate-limiting monophosphorylation step on the antiviral activity (Scheme 4). It should be also pointed out that the resulting less polar aryl phosphoramidites prodrugs **33**–**36** may more efficiently cross the plasma membrane. The masking groups are then cleaved by chemical or enzymatic hydrolysis to liberate the charged phosphates inside the cell. Starting from nucleoside analogue **13**, the phosphoramidate **33** was prepared by addition of compound **32** in the presence of *N*-methylimidazole. The later compound **33** was then subjected to hydrogenation by catalytic hydrogen transfer to minimize reduction of the double bound of the uracil base,[23] affording the pronucleotide **34** in 65% yield for the two steps. Starting from nucleoside analogue **15**, the phosphoramidate **35** was obtained following the Uchigawa procedure[24] in the presence of *tert*-butylmagnesium chloride in 48% yield. Then, classical hydrogenation of nucleotide analogue **35** furnished the target pronucleotide **36** in 94% yield. All of the phosphoramidate derivatives **33**–**36** were obtained as diastereomeric mixtures (R_P:S_P = 1:1), as measured by ^{1}H and ^{31}P NMR spectra.

Conformational Analysis of Nucleosides 13 and 16

We performed the conformational analysis of both dihydro- and tetrahydro-2*H*-pyrano-fused uridines **13** and **16** to study their ribofuranose sugar conformations. In both cases, our proton NMR studies (Bruker 500 MHz Avance III spectrometer) in D_2O from 283 to 323 K showed no variation of the $J_{1',2'}$ values: 8.45 ± 0.15 Hz and 8.25 ± 0.15 Hz for **13** and **16**, respectively. These results indicated unambiguously that their ribofuranose ring puck-

ering was restricted in the *S*-type conformation by the 3′-*O*,4′-*C*-bridge, which is the appropriate conformation for phosphorylation.[9,25]

Biological Evaluation

All final nucleoside analogs and phosphoramidates were tested against HIV-1 (strain LAI) in an assay using human peripheral blood mononuclear (PBM) cells and demonstrated no significant activity (median effective concentration, $EC_{50} > 100$ μM) when compared with 3′-azido-3′-deoxythymidine (AZT, zidovudine) which had an EC_{50} value of 0.004 μM.[26] These compounds were also evaluated for their potential toxic effects on uninfected phytohaemagglutinin-stimulated human PBM cells, and also in lymphoblastoid CEM cells as well as anchored Vero (African green monkey kidney) cells: no cytotoxicity up to 100 μM was detected for any of the compounds.[27] Although none of these 3′-*O*,4′-*C*-propylene-bridged nucleosides presented any cytotoxicity, they had no anti-HIV activity when tested up to 100 μM. Therefore, we also evaluated the compounds for activity against HCV, an RNA virus, using a well defined Huh-7 replicon assay system.[28] Unfortunately, none of the compounds were effective, but they were also not cytotoxic toward Huh-7 cells, whereas the positive control 2′-*C*-methylcytidine had significant antiviral activity (EC_{50} = 3 μM). Concerning the aryl phosphoramidate derivatives of **13**, **15**, **16** and **18**, the biological data showed no appreciable differences in antiviral potency compared to their parent structures against HIV-1 or HCV. All final nucleoside analogues and phosphoramidates were tested against *Herpes simplex* virus type 1 (HSV-1) by cell viability.[29,30] After 3 days of treatment, microscopically visible alteration of normal Vero cell morphology was observed and viability assay showed destruction of cell layer. For those compounds, the 50% cytotoxic concentration (CC_{50}) fell within the range of 0.49 to 3.0 μM. The cytosine analogues **15** and **18** showed the lowest toxicity (3.0 and 2.2 μM respectively), compared with Acyclovir [Zovirax®, 2-amino-9-(propoxymethyl)-1*H*-purin-6(9*H*)-one], which has a CC_{50} above 4.4 μM. No *anti*-HSV activity was observed for any of the final nucleoside analogues **13**–**18** nor phosphoramidates **33**–**36**. The lack of recognition of the corresponding 5′-triphosphate of these bicyclic nucleosides by viral polymerases or lack of conversion to the triphophates by cellular kinases are the most likely explanations for the lack of antiviral activity.

Conclusions

In summary, we have prepared a set of novel pyrimidine ribonucleosides fused with a 4′-*C*,3′-*O*-propylene bridge in 12 steps from diacetonide-α-D-glucose using a simple and flexible synthetic route. None of the synthesised nucleoside analogues were cytotoxic, but they exhibited no significant anti-HIV or *anti*-HCV activities, suggesting that these compounds are probably not substrates for the various cellular kinases, or alternatively, their corresponding 5′-triphosphates (if they are formed) are not recognized by the viral DNA or RNA polymerases.

Experimental Section

All reactions were performed using anhydrous solvents and monitored by TLC (Kieselgel $60F_{254}$ MERCK aluminium sheet) with detection by UV light and/or with ethanolic phosphomolybdic acid solution. Flash column chromatography was performed on silica gel 60 ACC 40–63 μM (SDS). ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz, respectively, with a Bruker Avance 300 MHz spectrometer. Chemical shifts (δ) are quoted in ppm, and are referenced to TMS as an internal standard. Coupling constants (J) are quoted in Hz. Mass spectra and HRMS spectra were recorded at the Centre Commun de Spectrométrie de Masse-Claude Bernard, University of Lyon, with a Thermo-Finnigan MAT 95 XL apparatus. Melting points (m.p.) were measured on a Stuart Scientific apparatus 7SMP3 or Kofler Heating Plate (type WME). Optical rotations were measured with a Perkin–Elmer 241 MC polarimeter.

3-*O*-Allyl-4-*C*-hydroxymethyl-1,2-*O*-isopropylidene-α-D-erythrofuranose (23): To a stirred solution of diol **21** (14.2 g, 54.6 mmol) in water and dioxane (1:1, 38 mL), $NaIO_4$ (14.0 g, 65.5 mmol, 1.2 equiv.) was added at 0 °C. After stirring for 30 min, 1.5 mL of ethylene glycol was added, and the resulting mixture was extracted with AcOEt (3 × 50 mL) and then with CH_2Cl_2. The organic layer was then dried with $MgSO_4$, filtered and concentrated under reduced pressure to obtain the aldehyde **22**. To the crude aldehyde dissolved in dioxane (185 mL) was added an aqueous formaldehyde solution (37%, 6.0 mL) and an aqueous solution of NaOH (2 M, 27.3 mL). After stirring for 6 h at room temp., the mixture was cooled to 0 °C, and $NaBH_4$ (3.8 g, 99.1 mmol, 2.0 equiv.) was slowly added. The solution was stirred for 30 min at room temp., and a pyridine/acetic acid mixture (4:1, 200 mL) was added. After stirring for an additional 30 min at 0 °C, the crude mixture was concentrated under reduced pressure. Purification by chromatography on silica gel (petroleum ether/AcOEt, 30:70) afforded the diol **23** as a colourless syrup (6.6 g, 51% over two steps). Spectroscopic data of this compound were consistent with those reported by Kierzek et al., see ref.[19]. $[\alpha]_D^{25}$ = +78.3 (c = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3429, 2975, 2930, 2880, 1644, 1456, 1386, 1377, 1106, 1055, 876 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.94–5.84 (m, 1 H, H_2C=C*H*-CH_2), 5.73 (d, J = 3.6 Hz, 1 H, H$^{1'}$), 5.28 [syst. ABM*X*Y, J = 17.1, 1.2 Hz, 1 H, H-(*H*)C=CH-CH_2], 5.20 [syst. ABM*X*Y, J = 10.5, 1.2 Hz, 1 H, *H*-(H)C=CH-CH_2], 4.63 (dd, J = 5.1, 3.6 Hz, 1 H, H$^{2'}$), 4.22 (d, J = 5.1 Hz, 1 H, H$^{3'}$), 4.21 and 4.06 (syst. *AB*MXY, J = 12.7, 5.8 Hz, 2 H, H_2C=CH-CH_2), 3.92 and 3.60 (syst. AB, J = 12.0 Hz, 2 H, H$^{5'\alpha}$), 3.83 and 3.78 (syst. AB, J = 5.8 Hz, 2 H, H$^{5'\beta}$), 1.57 {s, 3 H, [C(CH_3)-CH_3(*endo*)]}, 1.29 {s, 3 H, [C(CH_3)-CH_3(*exo*)]} ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 134.0 (H_2C=*C*H-), 118.3 (H_2*C*=CH-), 113.5 [2 × O-*C*(O)CH_3], 104.3 (C$^{1'}$), 86.2 (C$^{4'}$), 78.5 (C$^{2'}$), 78.2 (C$^{3'}$), 71.9 (O-*C*H_2-CH=CH_2), 64.0, 63.1 (2 × *C*H_2-OH), 26.5 [C(CH_3)-*C*H_3(*endo*)], 25.8 [C(CH_3)-*C*H_3(*exo*)] ppm.

3-*O*-Allyl-5-*tert*-butyldiphenylsilyl-4-*C*-hydroxymethyl-1,2-*O*-isopropylidene-α-D-erythrofuranose (24): Diol **23** (6.6 g, 25.4 mmol) was dissolved in dry CH_2Cl_2 (150 mL), and then Et_3N (11.3 mL, 93.9 mmol, 3.7 equiv.) and *tert*-butyldiphenylsilylchloride (19.7 mL, 76.2 mmol, 3.0 equiv.) were added at 0 °C. After stirring overnight at room temp., a saturated aqueous solution of $NaHCO_3$ was added, and the aqueous layer was extracted three times with CH_2Cl_2. The organic layers were combined, dried with $MgSO_4$,

filtered and concentrated under reduced pressure. After purification by chromatography on silica gel (petroleum ether/AcOEt, 90:10), the monoprotected alcohol **24** was obtained as white crystals (8.3 g, 64%); m.p. 67–69 °C. IR (KBr): $\tilde{\nu}$ = 3500, 3133, 2987, 2952, 2857, 1471, 1429, 1385, 1136, 1007 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.68–7.65 (m, 4 H, H^{Ar}), 7.43–7.38 (m, 6 H, H^{Ar}), 5.99–5.86 (syst. AB*M*XY, 1 H, H_2C=C*H*-CH_2), 5.83 (d, *J* = 3.3 Hz, 1 H, $H^{1'}$), 5.30 [syst. ABMX*Y*, *J* = 17.1, 1.5 Hz, 1 H, H-(*H*)C=CH-CH_2], 5.24 [syst. ABM*X*Y, *J* = 10.3, 1.5 Hz, 1 H, *H*-(H)C=CH-CH_2], 4.70 (dd, *J* = 5.1, 3.8 Hz, 1 H, $H^{2'}$), 4.43 (d, *J* = 5.1 Hz, 1 H, $H^{3'}$), 4.22 and 4.02 (syst. *AB*MXY, *J* = 12.6, 5.4, 1.5 Hz, 2 H, H_2C=CH-CH_2), 3.84 and 3.78 (syst. AB, *J* = 11.9 Hz, 2 H, -C*H*$_2$OH), 3.82 and 3.75 (syst. AB, *J* = 9.0 Hz, 2 H, $H^{5'}$), 1.64 {s, 3 H, [C(CH_3)-C*H*$_3$(*endo*)]}, 1.37 {s, 3 H, [C(CH_3)-C*H*$_3$(*exo*)]}, 1.06 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.6 (*C*H^{Ar}), 134.1 (H_2C=*C*H-), 133.3, 133.0 (*C*^{Ar}-Si), 129.8, 127.7 (*C*H^{Ar}), 118.2 (H_2C=CH-), 113.7 [2 × O-*C*(O)CH_3], 104.4 ($C^{1'}$), 87.3 ($C^{4'}$), 79.2 ($C^{2'}$), 78.1 ($C^{3'}$), 71.9 (O-*C*H_2-CH=CH_2), 65.5 (*C*H_2-O-Si), 63.2 (*C*H_2-OH), 26.8 [(*C*H_3)$_3$C-Si], 26.7 [C(CH_3)-*C*H_3(*endo*)], 26.3 [C(CH_3)-*C*H_3(*exo*)], 19.3 [(CH_3)$_3$*C*-Si] ppm.

3-*O*-Allyl-5-(*tert*-butyldiphenylsilyl)-1,2-*O*-isopropylidene-4-*C*-vinyl-α-D-erythrofuranose (19): To a solution of oxalyl chloride (2.9 mL, 33.1 mmol, 2.0 equiv.) in anhydrous CH_2Cl_2 (70 mL) at –78 °C was added a solution of dry DMSO (3.9 mL, 10.3 mmol, 3.3 equiv.) in anhydrous CH_2Cl_2 (35 mL). After stirring for 20 min at –78 °C, alcohol **24** (8.3 g, 16.5 mmol) in anhydrous CH_2Cl_2 (35 mL) was added dropwise. The reaction mixture was stirred for 30 min at –78 °C, Et_3N (12.4 mL, 102.5 mmol, 6.2 equiv.) was added, and the reaction was warmed to room temp. before being cooled to 0 °C for addition of H_2O. After extraction with CH_2Cl_2, the organic layer was washed with H_2O and brine, dried with $MgSO_4$, filtered and concentrated under reduced pressure. The aldehyde (8.2 g) was then used crude for the next reaction. To a suspension of triphenylphosphonium bromide (23.6 g, 66.1 mmol, 4.0 equiv.) in dry THF (300 mL) at 0 °C was added *n*BuLi (1.6 M in hexanes, 23.8 mL, 59.5 mmol, 3.6 equiv.). After stirring for 5 min at 0 °C and 1 h at room temp., the reaction mixture was cooled to –78 °C. A solution of the previous crude aldehyde (8.2 g, 16.5 mmol) in dry THF (200 mL) was added dropwise. The reaction was stirred for 30 min at –78 °C then for 2 h at 0 °C and finally for 1 h at room temperature before being cooled to 0 °C for the addition of a saturated aqueous solution of NH_4Cl. After extraction with CH_2Cl_2, the combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (petroleum ether/AcOEt, 95:5), and the unsaturated compound **19** was obtained as a colourless oil (3.7 g, 45% over two steps). $[\alpha]_D^{25}$ = –1.0 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2980, 2858, 1472, 1428, 1265, 1250, 1113, 1028 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.66 (m, 4 H, H^{Ar}), 7.45–7.35 (m, 6 H, H^{Ar}), 6.14 (syst. AB*X*, *J* = 17.3, 11.0 Hz, 1 H, *H*C=CH_2 vinyl), 6.08–5.94 (m, 1 H, H_2C=C*H*-CH_2 allyl), 5.85 (d, *J* = 3.8 Hz, 1 H, $H^{1'}$), 5.45 [syst. A*B*X, *J* = 17.3, 1.8 Hz, 1 H, HC=C(H)-*H* vinyl], 5.35 [syst. ABMX*Y*, *J* = 17.3, 1.4, 1.1 Hz, 1 H, *H*-(H)C=CH-CH_2 allyl], 5.25–5.22 [m, 1 H, *H*-(H)-C=CH-CH_2 allyl], 5.18 [syst. *A*BX, *J* = 11.0, 1.8 Hz, 1 H, H-C=C(H)-*H* vinyl], 4.72 (dd, *J* = 4.9, 3.8 Hz, 1 H, $H^{2'}$), 4.48 (d, *J* = 4.9 Hz, 1 H, $H^{3'}$), 4.30–4.12 (m, 2 H, H_2C=CH-C*H*$_2$ allyl), 3.57 (s, 2 H, $H^{5'}$), 1.54 {s, 3 H, [C(CH_3)-C*H*$_3$(*endo*)]}, 1.38 {s, 3 H, [C(CH_3)-C*H*$_3$(*exo*)]}, 1.05 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.7, 135.5 (*C*H^{Ar}), 134.8 (H_2C=*C*H- vinyl), 133.9 (H_2C=*C*H- allyl), 133.5, 133.0 (*C*^{Ar}-Si), 129.7, 127.7 (*C*H^{Ar}), 117.9 (H_2C=CH- allyl), 116.2 (H_2C=CH- vinyl), 113.5 [2 × O-*C*(O)CH_3], 103.9 ($C^{1'}$), 87.1 ($C^{4'}$), 79.5 ($C^{2'}$), 77.0 ($C^{3'}$), 72.0 (O-*C*H_2-CH=CH_2), 66.3 (*C*H_2-O-Si), 26.8 [(*C*H_3)$_3$C-Si], 26.2 [C(CH_3)-*C*H_3(*endo*)], 25.8 [C(CH_3)-*C*H_3(*exo*)], 19.3 [(CH_3)$_3$*C*-Si] ppm.

(3ξ)-3,7-Anhydro-5,6-dideoxy-1,2-*O*-(1-methylethylidene)-4-{[(*tert*-butyldiphenylsilyl)oxy]methyl}-β-L-*threo*-hept-5-enofuranose (25): To a solution of compound **19** (3.7 g, 7.5 mmol) in dry CH_2Cl_2 (850 mL) was added Grubbs' type-II catalyst (670 mg, 0.75 mmol, 0.1 equiv.). The reaction mixture was stirred for 16 h at room temp., and then the solvent was evaporated. The crude residue was purified by chromatography on silica gel (petroleum ether/AcOEt, 95:5) to give the bicyclic compound **25** as a brown oil (3.4 g, 97%). $[\alpha]_D^{25}$ = –3.1 (*c* = 1.0, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2931, 2857, 1428, 1381, 1372, 1113, 1018 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.63–7.72 (m, 4 H, H^{Ar}), 7.35–7.45 (m, 6 H, H^{Ar}), 5.97 (d, *J* = 4.3 Hz, 1 H, $H^{1'}$), 6.00–5.93 (m, 1 H, H_2C=C*H*-CH_2), 5.73 [syst. ABM*X*, *J* = 10.6, 2.2 Hz, 1 H, H-(*H*)C=CH-CH_2], 4.94 (dd, *J* = 5.9, 4.3 Hz, 1 H, $H^{2'}$), 4.50 and 4.04 (syst. *AB*MX, *J* = 16.4, 3.0, 2.2 Hz, 2 H, HC=CH-C*H*$_2$), 4.39 (d, *J* = 5.9 Hz, 1 H, $H^{3'}$), 3.65 and 3.43 (syst. AB, *J* = 10.8 Hz, 2 H, $H^{5'}$), 1.54 {s, 3 H, [C(CH_3)-C*H*$_3$(*endo*)]}, 1.38 {s, 3 H, [C(CH_3)-C*H*$_3$(*exo*)]}, 1.05 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.7 (*C*H^{Ar}), 133.0, 132.8 (*C*^{Ar}-Si), 129.8 (*C*H^{Ar}, HC=*C*H-CH_2), 127.8 (*C*H^{Ar}), 124.3 (H*C*=CH-CH_2), 114.1 [O-*C*(O)$(CH_3)_2$], 105.4 ($C^{1'}$), 82.2 ($C^{2'}$), 80.2 ($C^{4'}$), 74.4 ($C^{3'}$), 68.1 ($C^{5'}$), 63.8 (HC=CH-*C*H_2-O), 27.2 [C(CH_3)-*C*H_3], 26.8 [(*C*H_3)$_3$-C-Si], 26.4 [C(CH_3)-*C*H_3], 19.2 [(CH_3)$_3$*C*-Si] ppm.

1,2-Di-*O*-acetyl-3,7-anhydro-5,6-dideoxy-4-{[(*tert*-butyldiphenylsilyl)oxy]methyl}-α/β-L-*lyxo*-hept-5-enofuranose (20): To a solution of the bicyclic compound **25** (3.4 g, 7.3 mmol) in acetic acid (95 mL) was added acetic anhydride (10.2 mL, 87.5 mmol, 12.0 equiv.) and a concentrated solution of H_2SO_4 (95 µL, 14 µmol, 0.002 equiv.). After stirring for 3 h at room temp., an aqueous saturated solution of $NaHCO_3$ was added, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (petroleum ether/AcOEt, 80:20) to give anomer β-**20** as a colourless oil (1.7 g, 46%) and anomer α-**20** as a colourless oil (1.2 g, 31%). **β-Anomer:** $[\alpha]_D^{25}$ = +67.0 (*c* = 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.74–7.66 (m, 4 H, H^{Ar}), 7.46–7.36 (m, 6 H, H^{Ar}), 6.51 (d, *J* = 5.1 Hz, 1 H, $H^{1'}$), 6.15–6.08 (syst. AB*M*X, *J* = 10.4, 4.3, 1.6 Hz, 1 H, HC=C*H*-CH_2), 5.70–5.66 (m, 2 H, *H*C=CH-CH_2, $H^{2'}$), 4.38 (d, *J* = 5.0 Hz, 1 H, $H^{3'}$), 4.28 and 3.90 (syst. *AB*MX, *J* = 16.4, 4.3, 2.0 Hz, 2 H, HC=CH-C*H*$_2$), 3.59 and 3.38 (syst. AB, *J* = 11.0 Hz, 2 H, $H^{5'}$), 2.19, 2.11 [s, 3 H, O-C(=O)-C*H*$_3$], 1.10 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6, 170.0 [2 × O-*C*(=O)-CH_3], 135.6, 132.7 (*C*H^{Ar}), 132.3 (*C*^{Ar}), 130.8 (HC=*C*H-CH_2), 129.9, 127.8 (*C*H^{Ar}), 124.7 (H*C*=CH-CH_2), 94.5 ($C^{1'}$), 81.5 ($C^{4'}$), 74.3 ($C^{3'}$), 72.6 ($C^{2'}$), 68.0 ($C^{5'}$), 62.8 (HC=CH-*C*H_2), 26.8 [(*C*H_3)$_3$C-Si], 21.4, 20.7 [2 × O-C(=O)-*C*H_3], 19.1 [(CH_3)$_3$*C*-Si] ppm. **α-Anomer:** $[\alpha]_D^{25}$ = –59.0 (*c* = 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.74–7.66 (m, 4 H, H^{Ar}), 7.46–7.36 (m, 6 H, H^{Ar}), 6.38 (d, *J* = 5.4 Hz, 1 H, $H^{1'}$), 6.08 (syst. AB*M*X, *J* = 10.4, 4.3, 1.5 Hz, 1 H, HC=C*H*-CH_2), 5.64 (syst. ABM*X*, *J* = 10.4, 2.0 Hz, 1 H, *H*C=CH-CH_2), 5.60 (dd, *J* = 5.3, 5.0 Hz, 1 H, $H^{2'}$), 4.50 and 4.04 (syst. *AB*MX, *J* = 16.4, 4.3, 2.0 Hz, 2 H, HC=CH-CH_2), 4.40 (d, *J* = 5.0 Hz, 1 H, $H^{3'}$), 3.66 and 3.43 (syst. AB, *J* = 11.0 Hz, 2 H, $H^{5'}$), 2.18, 2.00 [s, 3 H, O-C(=O)-C*H*$_3$], 1.10 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7, 170.1 [2 × O-*C*(=O)-CH_3], 135.6 (*C*H^{Ar}), 132.6 (*C*^{Ar}), 130.0 (HC=*C*H-CH_2) 129.9, 127.8 (*C*H^{Ar}), 124.1 (H*C*=CH-CH_2), 99.2 ($C^{1'}$), 82.0 ($C^{4'}$), 80.2 ($C^{3'}$), 75.2 ($C^{2'}$), 67.6 ($C^{5'}$), 63.0 (HC=CH-*C*H_2), 26.7 [(*C*H_3)$_3$C-Si], 21.0 [2 × O-C(=O)-*C*H_3], 19.2 [(CH_3)$_3$*C*-Si] ppm.

Uridine Derivative 26: To a suspension of uracil (203 mg, 0.37 mmol, 1.5 equiv.) in freshly distilled CH_3CN (3 mL) was

added BSA [*N*,*O*-bis(trimethylsilyl)acetamide] (185 μL, 0.75 mmol, 3.0 equiv.). The mixture was stirred for 20 min at room temp., and a solution of glycoside **20** (116 mg, 0.25 mmol, 1 equiv.) in freshly distilled CH_3CN (2 mL) was added. After cooling to 0 °C, TMSOTf (46 μL, 0.25 mmol) was added, and the reaction was stirred at room temp. overnight. After dilution with CH_2Cl_2, an aqueous saturated solution of $NaHCO_3$ was added. The aqueous layer was extracted three times with CH_2Cl_2, and then the organic layers were recombined, dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by chromatography on silica gel (petroleum ether/AcOEt, 60:40) to afford compound **26** (181 mg, 73%) as a white solid; m.p. 61–62 °C. $[\alpha]_D^{25}$ = +46.5 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.20 (s, 1 H, NH), 7.79 [d, *J* = 8.1 Hz, 1 H, N-(*H*)C=CH], 7.70–7.63 (m, 4 H, H^{Ar}), 7.47–7.38 (m, 6 H, H^{Ar}), 6.46 (d, *J* = 8.4 Hz 1 H, H$^{1'}$), 6.13 (syst AB*M*X, *J* = 10.3, 4.7, 1.6 Hz, 1 H, HC=C*H*-CH_2), 5.58–5.49 (m, 2 H, *H*C=CH-CH_2, H$^{2'}$), 5.37 [d, *J* = 8.1 Hz, 1 H, N-(H)C=C*H*], 4.35 (d, *J* = 4.8 Hz, 1 H, H$^{3'}$), 4.23 [syst. A*B*MX, *J* = 16.4, 4.7, 1.2 Hz, 1 H, HC=CH-C(*H*)-H], 3.88–3.81 [m, 1 H, HC=CH-C(H)-*H*], 3.83 and 3.50 (syst. AB, *J* = 11.3 Hz, 2 H, H$^{5'}$), 2.16 [s, 3 H, H_3C-C(=O)], 1.13 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 163.0, 150.6 (C=O), 140.0 [N-(H)*C*=CH], 135.7, 135.3 (CH^{Ar}), 131.6 (HC=*C*H-CH_2), 130.3, 130.2 (C^{Ar}-Si), 128.1, 127.8 (CH^{Ar}), 123.2 (H*C*=CH-CH_2), 102.9 [N-(H)C=*C*H], 84.1 (C$^{1'}$), 79.6 (C$^{4'}$), 75.2 (C$^{3'}$), 74.6 (C$^{2'}$), 68.5 (C$^{5'}$), 62.6 (HC=CH-*C*H_2), 27.0 [(*C*H_3)$_3$C-Si], 20.6 [O-C(=O)-*C*H_3], 19.3 [(CH$_3$)$_3$*C*-Si] ppm. HRMS (CI): calcd. for $C_{30}H_{35}N_2O_7Si$ [M + H]$^+$ 563.2214; found 563.2214.

Uridine Derivative 27: Compound **26** (181 mg, 0.32 mmol) was dissolved in MeOH (14 mL), and K_2CO_3 (126 mg, 0.96 mmol, 3 equiv.) was added. After stirring for 3 h at room temp., an aqueous solution of HCl (1 N) was added until neutral pH, and then the solvent was evaporated under reduced pressure. The crude mixture was purified by chromatography on silica gel (petroleum ether/AcOEt, 50:50) to obtain alcohol **27** (147 mg, 88%) as a white solid; m.p. 90–91 °C. $[\alpha]_D^{25}$ = +51.4 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.58 (br. s, 1 H, NH), 7.73 [d, *J* = 8.1 Hz, 1 H, N-(*H*)-C=CH], 7.65–7.59 (m, 4 H, H^{Ar}), 7.47–7.38 (m, 6 H, H^{Ar}), 6.17 (d, *J* = 8.4 Hz, 1 H, H$^{1'}$), 6.12 (syst AB*M*X, *J* = 10.5, 3.9 Hz, 1 H, HC=C*H*-CH_2), 5.57 (d, *J* = 10.5 Hz, 1 H, *H*C=CH-CH_2), 5.42 [dd, *J* = 8.1, 1.5 Hz, 1 H, N-(H)C=C*H*], 4.54 (dd, *J* = 8.4, 4.8 Hz, 1 H, H$^{2'}$), 4.28 and 3.94 (syst. *AB*MX, *J* = 16.5, 3.9 Hz, 2 H, HC=CH-CH_2), 4.07 (d, *J* = 4.8 Hz, 1 H, H$^{3'}$), 3.79 and 3.47 (syst. AB, *J* = 11.1 Hz, 2 H, H$^{5'}$), 1.10 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.2, 151.1 (C=O), 140.0 [N-(H)*C*=CH], 135.6, 135.2, 130.2, 128.0 (CH^{Ar}), 135.3, 131.6 (C^{Ar}-Si), 123.7 (H*C*=CH-CH_2), 102.8 [N-(H)C=*C*H], 86.9 (C$^{1'}$), 79.0 (C$^{4'}$), 76.1 (C$^{3'}$), 75.3 (C$^{2'}$), 68.3 (C$^{5'}$), 62.7 (HC=CH-*C*H_2), 27.0 [(*C*H_3)$_3$C-Si], 19.2 [(CH$_3$)$_3$*C*-Si] ppm. HRMS (CI): calcd. for $C_{28}H_{33}N_2O_6Si$ [M + H]$^+$ 521.2108; found 521.2109.

Uridine Derivative 13: Alcohol **27** (147 mg, 0.28 mmol) was dissolved in THF (4 mL), and a solution of TBAF (1 M in THF, 565 μL, 0.56 mmol, 2 equiv.) was added. The mixture was stirred for 4 h at room temp. and then concentrated under reduced pressure. Purification of the crude mixture by chromatography on silica gel (AcOEt/MeOH, 70:30) afforded nucleoside analogue **13** contaminated with a small amount of TBAF-derived materials (83 mg, 95%) as a white powder; m.p. 197–198 °C. $[\alpha]_D^{25}$ = +70.8 (*c* = 1.0, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 8.10 [d, *J* = 8.1 Hz, 1 H, N-(*H*)C=CH], 6.23 (syst. AB*M*X, *J* = 10.5, 4.8, 1.8 Hz, 1 H, HC=C*H*-CH_2), 6.11 (d, *J* = 8.1 Hz, 1 H, H$^{1'}$), 5.75 [d, *J* = 8.1 Hz, 1 H, N-(H)C=C*H*], 5.67 (syst. ABM*X*, *J* = 10.5, 2.4, 1.8 Hz, 1 H, *H*C=CH-CH_2), 4.62 (dd, *J* = 8.1, 4.8 Hz, 1 H, H$^{2'}$), 4.27 and 3.99 (syst. *AB*MX, *J* = 16.2, 4.8, 1.8 Hz, 2 H, HC=CH-CH_2), 4.01 (d, *J* = 4.8 Hz, 1 H, H$^{3'}$), 3.60 and 3.49 (syst AB, *J* = 11.7 Hz, 2 H, H$^{5'}$) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 168.1, 152.8 (C=O), 142.9 [N-(H)*C*=CH], 132.5 (HC=*C*H-CH_2), 125.2 (H*C*=CH-CH_2), 103.4 [N-(H)C=*C*H], 88.4 (C$^{1'}$), 80.9 (C$^{4'}$), 78.5 (C$^{3'}$), 75.3 (C$^{2'}$), 67.4 (C$^{5'}$), 63.8 (HC=CH-*C*H_2) ppm. HRMS (CI): calcd. for $C_{12}H_{15}N_2O_6$ [M + H]$^+$ 283.0930; found 283.0931.

Uridine Derivative 16: To a solution of nucleoside analogue **14** (83 mg, 0.38 mmol) in EtOH (17 mL) was added Pd/C 10% (17 mg). After 24 h of stirring at room temp. under H_2 atmosphere (balloon), the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (AcOEt and AcOEt/MeOH, 70:30) to give the diol **16** as a white powder (75 mg, 93%); m.p. 224–225 °C. $[\alpha]_D^{25}$ = –39.8 (*c* = 1.0, MeOH). ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 11.27 (s, 1 H, NH), 8.02 [d, *J* = 8.1 Hz, 1 H, N-(*H*)-C=CH], 6.02 (d, *J* = 8.4 Hz, 1 H, H$^{1'}$), 5.67 [d, *J* = 8.1 Hz, 1 H, N-(H)C=C*H*], 5.35 (t, *J* = 1.2 Hz, 1 H, CH_2-O*H*), 5.15 (d, *J* = 7.5 Hz, 1 H, CH-O*H*), 4.57–4.50 (m, 1 H, H$^{2'}$), 3.90–3.86 (m, 1 H, CH_2-CH_2-O), 3.83 (d, *J* = 3.9 Hz, 1 H, H$^{3'}$), 3.39–3.37 (m, 2 H, H$^{5'}$), 3.30–3.27 (m, 1 H, CH_2-CH_2-O), 1.59–1.51 [m, 4 H, H_2C-CH_2-O, H_2C-(CH$_2$)$_2$-O] ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 162.9, 151.1 (C=O), 141.0 [N-(H)*C*=CH], 102.0 [N-(H)C=*C*H], 86.8 (C$^{1'}$), 81.6 (C$^{4'}$), 76.4 (C$^{3'}$), 73.2 (C$^{2'}$), 66.4 (C$^{5'}$), 63.7 (CH_2-*C*H_2-O), 28.1 (*C*H_2-CH_2-O), 20.5 [*C*H_2-(CH$_2$)$_2$-O] ppm. HRMS (CI): calcd. for $C_{12}H_{17}N_2O_6$ [M + H]$^+$ 285.1087; found 285.1088.

Thymidine Derivative 28: To a suspension of thymine (475 mg, 3.8 mmol, 2.1 equiv.) in dry HMDS (50 mL) was added trimethylsilyl chloride (7.5 mL, 59.0 mmol, 33.0 equiv.). The reaction mixture was heated under reflux overnight and then concentrated under reduced pressure. The crude mixture was diluted with dry 1,2-dichloroethane (5 mL) and a solution of compound **20** (935 mg, 1.8 mmol) in dry 1,2-dichloroethane (10 mL) was added. The reaction mixture was cooled to –35 °C and TMSOTf (720 μL, 4.0 mmol, 2.0 equiv.) was added dropwise. After 24 h of stirring at room temp., an aqueous saturated solution of $NaHCO_3$ was added, and the resulting mixture was stirred for 40 min at room temp. After extraction with CH_2Cl_2, the organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (petroleum ether/AcOEt, 40:60) to give the thymidine derivative **28** as a white solid (790 mg, 76%); m.p. 82–83 °C. $[\alpha]_D^{25}$ = +103.3 (*c* = 1.0, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3360, 2874, 1700, 1458, 1129, 1060 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.90 (br. s, 1 H, NH), 7.72–7.66 (m, 4 H, H^{Ar}), 7.53 (s, 1 H, HC=C^{thy}), 7.47–7.37 (m, 6 H, H^{Ar}), 6.40 (d, *J* = 8.6 Hz, 1 H, H$^{1'}$), 6.18–6.10 (syst. AB*M*X, *J* = 10.3, 3.8 Hz, 1 H, HC=C*H*-CH_2), 5.61–5.51 (m, 2 H, H$^{2'}$, *H*C=CH-CH_2), 4.40 (d, *J* = 4.9 Hz, 1 H, H$^{3'}$), 4.23 [syst. A*B*MX, *J* = 16.3, 4.7 Hz, 1 H, HC=CH-C(*H*)-H], 3.91–3.82 [m, 1 H, HC=CH-C(*H*)-H], 3.86 and 3.50 (syst. A*B*, *J* = 11.2 Hz, 2 H, H$^{5'}$), 2.16 [s, 3 H, O-C(=O)-CH_3], 1.68 (s, 3 H, CH_3^{thy}), 1.11 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6 [O-*C*(=O)-CH_3], 163.6, 150.7 (C=O), 135.6 (CH^{Ar}), 135.3 (*C*H^{thy}), 131.8, 132.6 (C^{Ar}), 131.5 (H*C*=CH-CH_2), 128.1, 130.2, 130.3 (CH^{Ar}), 123.4 (HC=*C*H-CH_2), 111.8 (C^{thy}), 83.7 (C$^{1'}$), 79.3 (C$^{4'}$), 75.0 (C$^{3'}$), 74.3 (C$^{2'}$), 62.6 (C$^{5'}$), 60.4 (HC=CH-*C*H_2), 27.1 [(*C*H_3)$_3$C-Si], 20.7 [O-C(=O)-*C*H_3], 19.4 [(CH$_3$)$_3$*C*-Si], 11.7 (CH_3^{thy}) ppm. HRMS (CI): calcd. for $C_{31}H_{37}N_2O_7Si$ [M + H]$^+$ 577.2371; found 577.2370.

Thymidine Derivative 29: To a solution of thymidine derivative **28** (380 mg, 0.7 mmol) in MeOH (30 mL) was added K_2CO_3 (288 mg, 2.1 mmol, 3.2 equiv.). After stirring for 3 h at room temp., the reaction mixture was neutralised with an aqueous solution of HCl (1 M)

until neutral pH, and then concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (petroleum ether/AcOEt, 60:40) to give the alcohol **29** as a white solid (278 mg, 79%); m.p. 89–90 °C. $[\alpha]_D^{25}$ = +106.4 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.21 (br. s, 1 H, NH), 7.66–7.63 (m, 4 H, H^{Ar}), 7.49–7.39 (m, 7 H, HC=C^{thy}, H^{Ar}), 6.17–6.10 (m, 2 H, $H^{1'}$, HC=C*H*-CH_2), 5.58 (syst. ABM*X*, *J* = 10.2 Hz, 1 H, *H*C=CH-CH_2), 4.58 (m, 1 H, $H^{2'}$), 4.25 and 3.95 (syst. *AB*MX, *J* = 16.4, 4.5 Hz, 1 H, HC=CH-C*H*$_2$), 4.11 (d, *J* = 5.0 Hz, 1 H, $H^{3'}$), 3.83 and 3.50 (syst. AB, *J* = 11.0 Hz, 2 H, $H^{5'}$), 3.02 (d, *J* = 11.0 Hz, 1 H, OH), 1.52 (s, 3 H, CH_3^{thy}), 1.11 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.2, 150.8 (C=O), 135.6 (CH^{Ar}), 135.4 (HC=C^{thy}), 135.3, 132.6, 131.9 (C^{Ar}), 131.1 (HC=*C*H-CH_2), 130.4, 130.3, 128.1 (CH^{Ar}), 124.0 (H*C*=CH-CH_2), 111.6 (C^{thy}), 86.7 ($C^{1'}$), 78.8 ($C^{4'}$), 75.9 ($C^{3'}$), 74.8 ($C^{2'}$), 68.4 (*C*H$_2$-O-Si), 62.7 (H-C=CH-*C*H$_2$), 27.1 [(*C*H$_3$)$_3$C-Si], 19.4 [(CH$_3$)$_3$*C*-Si], 11.8 (CH_3^{thy}) ppm. HRMS (CI): calcd. for $C_{29}H_{35}N_2O_6Si$ [M + H]$^+$ 534.2264; found 535.2263.

Thymidine Derivative 14: To a solution of alcohol **29** (200 mg, 0.37 mmol) in dry THF (5 mL) was added TBAF (1 M in THF, 750 µL, 0.75 mmol, 2 equiv.). After 4 h of stirring at room temp., the reaction mixture was concentrated under reduced pressure. The crude mixture was purified by chromatography on silica gel (AcOEt/MeOH, 85:15) to give the diol **14** as a white solid contaminated with a small amount of TBAF-derived materials (110 mg, 95%); m.p. 210–211 °C. $[\alpha]_D^{25}$ = +69.5 (*c* = 1.0, MeOH). IR (KBr): $\tilde{\nu}$ = 3465, 3257, 2925, 1724, 1658, 1477, 1368, 1259, 1129, 1060, 1040 cm^{-1}. ^{1}H NMR (300 MHz, CD_3OD): δ = 7.82 (s, 1 H, C*H*^{thy}), 6.12 (syst. AB*M*X, *J* = 10.0, 5.0, 1.0 Hz, 1 H, HC=C*H*-CH_2), 6.00 (d, *J* = 8.4 Hz, 1 H, $H^{1'}$), 5.57 (syst. ABM*X*, *J* = 10.0 Hz, 1 H, *H*C=CH-CH_2), 4.54 (dd, *J* = 5.8 Hz, 1 H, $H^{2'}$), 4.16 and 3.87 (syst. *AB*MX, *J* = 16.3, 4.6 Hz, 1 H, C=CH-C*H*$_2$-H), 3.95 (d, *J* = 5.0 Hz, 1 H, $H^{3'}$), 3.52 and 3.37 (syst. AB, *J* = 11.0, 7.0 Hz, 2 H, $H^{5'}$) 1.8 (s, 3 H, CH_3^{thy}) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 166.3, 153.1 (C=O), 138.5 (CH^{thy}), 132.4 (HC=*C*H-CH_2), 125.3 (*H*C=CH-CH_2), 112.1 (C^{thy}), 88.3 ($C^{1'}$), 80.7 ($C^{4'}$), 78.4 ($C^{3'}$), 75.0 ($C^{2'}$), 67.5 (H-C=CH-*C*H$_2$), 63.9 ($C^{5'}$), 12.5 (CH_3^{thy}) ppm. HRMS (CI): calcd. for $C_{13}H_{17}N_2O_6$ [M + H]$^+$ 297.1087; found 297.1087.

Thymidine Derivative 17: To a solution of diol **14** (110 mg, 0.37 mmol) in MeOH (20 mL) was added Pd/C 10% (26 mg). After 24 h of stirring at room temp. under H_2 atmosphere (balloon), the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (AcOEt and AcOEt/MeOH, 95:5) to give the diol **17** as a white powder (95 mg, 87%); m.p. 123–124 °C. $[\alpha]_D^{25}$ = –40.7 (*c* = 1.0, CD_3OD). IR (KBr): $\tilde{\nu}$ = 3429, 3064, 2928, 1696, 1473, 1283, 1074 cm^{-1}. ^{1}H NMR (300 MHz, CD_3OD): δ = 8.00 (s, 1 H, C*H*^{thy}), 6.13 (d, *J* = 8.0 Hz, 1 H, $H^{1'}$), 4.73–4.69 (m, 1 H, $H^{2'}$), 3.95–3.92 (m, 1 H, CH_2-C*H*$_2$-O), 3.91 (d, *J* = 4.2 Hz, 1 H, $H^{3'}$), 3.52 (syst. *AB*, *J* = 11.7 Hz, 2 H, $H^{5'}$), 3.38–3.27 (m, 1 H, CH_2-C*H*$_2$-O), 1.90 (s, 3 H, CH_3^{thy}), 1.80–1.75 {m, 2 H, [HC(*H*)-CH_2-O, HC(*H*)-$(CH_2)_2$-O]}, 1.64–1.54 {m, 2 H, [HC(*H*)-CH_2-O, HC(*H*)-$(CH_2)_2$-O]} ppm. ^{13}C NMR (75 MHz, MeOD): δ = 166.3, 153.2 (C=O), 138.8 (CH^{thy}), 111.8 (C^{thy}), 89.5 ($C^{1'}$), 83.6 ($C^{4'}$), 78.3 ($C^{3'}$), 75.6 ($C^{2'}$), 68.5 ($C^{5'}$), 65.7 (CH_2-*C*H$_2$-O), 29.6, 22.0 [*C*H$_2$-$(CH_2)_2$-O, *C*H$_2$-CH_2-O], 12.5 (CH_3^{thy}) ppm. HRMS (CI): calcd. for $C_{13}H_{19}N_2O_6$ [M + H]$^+$ 299.1243; found 299.1241.

Cytidine Derivative 30: To a suspension of cytosine (36 mg, 0.33 mmol, 1.5 equiv.) in freshly distilled CH_3CN (2.5 mL) was added BSA (163 µL, 0.67 mmol, 3 equiv.). The mixture was stirred for 30 min at room temp., and a solution of glycoside **20** (102 mg, 0.22 mmol) in freshly distilled CH_3CN (1.5 mL) was added. After cooling to 0 °C, TMSOTf (40 µL, 0.22 mmol) was added, and the reaction mixture was stirred at room temp. overnight. After dilution with CH_2Cl_2, an aqueous saturated solution of $NaHCO_3$ was added. The aqueous layer was extracted three times with CH_2Cl_2, and then the organic layers were recombined, dried with Na_2SO_4, filtered and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel ($CHCl_3$/MeOH, 97:3) to afford compound **30** as a white solid (95 mg, 77%); m.p. 69–70 °C. $[\alpha]_D^{25}$ = +70.7 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 [d, *J* = 7.5 Hz, 1 H, N-(*H*)C=CH], 7.66–7.60 (m, 4 H, H^{Ar}), 7.42–7.34 (m, 6 H, H^{Ar}), 6.49 (d, *J* = 8.4 Hz, 1 H, $H^{1'}$), 6.34, 6.24 (br. s, 2 H, NH_2), 6.10 (syst AB*M*X, *J* = 10.5, 4.5 Hz, 1 H, HC=C*H*-CH_2), 5.56–5.43 [m, 3 H, N-(H)C=C*H*, $H^{2'}$, *H*C=CH-CH_2], 4.30 (d, *J* = 5.1 Hz, 1 H, $H^{3'}$), 4.16 [syst. A*B*MX, *J* = 16.8, 4.5 Hz, 1 H, HC=CH-C(*H*)-H], 3.82–3.76 [m, 1 H, HC=CH-C(H)-*H*], 3.75 and 3.43 (syst. AB, *J* = 11.1 Hz, 2 H, $H^{5'}$), 2.07 [s, 3 H, O-C(=O)-C*H*$_3$], 1.07 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2 (CH_3*C*=O), 165.6, 156.0 (C=N and C=O), 140.9 [N-(H)*C*=CH], 135.6, 135.3 (CH^{Ar}), 132.3, 131.6 (C^{Ar}), 131.3 (HC=*C*H-CH_2), 130.1–129.8, 123.5 (CH^{Ar}), 113.9 (*H*C=CH-CH_2), 95.6 [N-(H)C=*C*H], 84.2 ($C^{1'}$), 78.9 ($C^{4'}$), 75.1 ($C^{3'}$), 75.0 ($C^{2'}$), 68.2 ($C^{5'}$), 62.5 (HC=CH-*C*H$_2$), 26.9 [(*C*H$_3$)$_3$C-Si], 20.6 [O-C(=O)-*C*H$_3$], 19.1 [(CH$_3$)$_3$*C*-Si] ppm. HRMS (CI): calcd. for $C_{30}H_{36}N_3O_6Si$ [M + H]$^+$ 562.2373; found 562.2374.

Cytidine Derivative 31: Compound **30** (135 mg, 0.24 mmol) was dissolved in MeOH (10 mL), and K_2CO_3 (100 mg, 0.72 mmol, 3 equiv.) was added. After stirring for 2 h at room temp., an aqueous solution of HCl (1 N) was added until neutral pH, and then the solvent was evaporated under reduced pressure. The crude mixture was purified by chromatography on silica gel ($CHCl_3$/MeOH, 95:5) to obtain alcohol **31** as a white solid (107 mg, 85%); m.p. 82–83 °C. $[\alpha]_D^{25}$ = +53.9 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 [d, *J* = 7.2 Hz, 1 H, N-(*H*)C=CH], 7.60–7.57 (m, 4 H, H^{Ar}), 7.45–7.34 (m, 6 H, H^{Ar}), 6.21 (m, 4 H, $H^{1'}$, HC=C*H*-CH_2, NH_2), 5.62–5.57 [m, 2 H, N-(H)C=C*H*, *H*C=CH-CH_2], 4.46 (dd, *J* = 7.5, 5.1 Hz, 1 H, $H^{2'}$), 4.25 and 3.90 (syst. *AB*MX, *J* = 16.5, 4.5 Hz, 2 H, HC=CH-C*H*$_2$), 4.07 (d, *J* = 5.1 Hz, 1 H, $H^{3'}$), 3.68 and 3.46 (syst. AB, *J* = 11.1 Hz, 2 H, $H^{5'}$), 1.03 (s, 9 H, *t*Bu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7, 157.0 (C=N and C=O), 140.8 [N-(H)*C*=CH], 135.5, 135.4 (CH^{Ar}), 132.3, 132.0 (C^{Ar}), 131.4 (HC=*C*H-CH_2), 130.1, 127.9 (CH^{Ar}), 123.9 (H*C*=CH-CH_2), 95.0 [N-(H)C=C*H*], 89.1 ($C^{1'}$), 79.8 ($C^{4'}$), 76.8 ($C^{3'}$), 76.5 ($C^{2'}$), 67.9 ($C^{5'}$), 62.9 (HC=C-*C*H$_2$), 26.9 [(*C*H$_3$)$_3$C-Si], 19.1 [(CH$_3$)$_3$-*C*-Si] ppm. HRMS (CI): calcd. for $C_{28}H_{33}N_3O_5Si$ [M + H]$^+$ 520.2268; found 520.2266.

Cytidine Derivative 15: Alcohol **31** (107 mg, 0.33 mmol) was dissolved in THF (4 mL), and a solution of TBAF 1 M in THF (654 µL, 0.66 mmol, 2 equiv.) was added. The mixture was stirred for 4 h at room temp., and then concentrated under reduced pressure. Purification of the crude mixture by chromatography on silica gel (AcOEt/MeOH, 80:20) afforded nucleoside analogue **15** as a white powder (70 mg, 76%); m.p. 159–160 °C. $[\alpha]_D^{25}$ = +89.1 (*c* = 1.0, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.99 [d, *J* = 7.5 Hz, 1 H, N-(*H*)C=CH], 6.23 (syst. AB*M*X, *J* = 10.2, 4.5, 1.5 Hz, 1 H, HC=C*H*-CH_2), 6.10 (d, *J* = 8.4 Hz, 1 H, $H^{1'}$), 5.94 [d, *J* = 7.5 Hz, 1 H, N-(H)C=C*H*], 5.69 (syst. ABM*X*, *J* = 10.2, 2.4, 1.5 Hz, *H*C=CH-CH_2), 5.68 (dd, *J* = 8.4, 4.8 Hz, 1 H, $H^{2'}$), 4.27 and 4.00 (syst. *AB*MX, *J* = 16.2, 4.5, 1.5 Hz, 2 H, HC=CH-C*H*$_2$), 4.06 (d, *J* = 4.8 Hz, 1 H, $H^{3'}$), 3.61 and 3.47 (syst. AB, *J* = 11.7 Hz, 2 H, $H^{5'}$) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 167.5, 158.9 (C=N and C=O), 143.9 [N-(H)*C*=CH], 132.4 (HC=*C*H-CH_2), 125.3 (H*C*=CH-CH_2), 96.8 [N-(H)C=*C*H], 90.2 ($C^{1'}$), 80.8 ($C^{4'}$), 78.5 ($C^{3'}$), 75.5 ($C^{2'}$), 67.5 ($C^{5'}$), 61.6 (HC=C-*C*H$_2$) ppm.

HRMS (CI): calcd. for $C_{12}H_{16}N_3O_5$ [M + H]$^+$ 282.1090; found 282.1090.

Cytidine Derivative 18: To a solution of nucleoside analogue **15** (70 mg, 0.25 mmol) in EtOH (14 mL) was added Pd/C 10% (14 mg). After stirring for 24 h at room temp. under H_2 atmosphere (balloon), the reaction mixture was filtered through Celite and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (AcOEt/MeOH, 80:20) to give the diol **18** as a white powder (56 mg, 79%); m.p. 190–191 °C. $[\alpha]_D^{25}$ = –31.4 (c = 1.0, MeOH). ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 7.87 [d, J = 7.5 Hz, 1 H, N-(*H*)C=CH], 7.19, 7.11 (br. s, 2 H, NH_2), 6.04 (d, J = 8.4 Hz, 1 H, H$^{1'}$), 5.74 [d, J = 7.5 Hz, 1 H, N-(H)-C=C*H*], 5.26 (t, J = 5.4 Hz, 1 H, *H*O-CH$^{5'}$), 4.99 (d, J = 7.8 Hz, 1 H, *H*O-CH$^{2'}$), 4.50 (m, 1 H, H$^{2'}$), 3.89–3.87 (m, 1 H, CH$_2$-C*H*$_2$-O), 3.82 (d, J = 4.2 Hz, 1 H, H$^{3'}$), 3.41–3.23 (m, 3 H, H$^{5'}$, CH$_2$-C*H*$_2$-O), 1.64–1.57 [m, 3 H, *H*$_2$C-(CH$_2$)$_2$-O, C*H*$_2$-CH$_2$-O], 1.48–1.42 (m, 1 H, C*H*$_2$-CH$_2$-O) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 165.3, 155.8 (C=N and C=O), 141.9 [N-(H)*C*=CH], 94.3 [N-(H)C=*C*H], 88.2 (C$^{1'}$), 81.2 (C$^{4'}$), 76.3 (C$^{3'}$), 73.6 (C$^{2'}$), 68.4 (C$^{5'}$), 63.7 (CH$_2$-*C*H$_2$-O), 28.1, 20.6 [*C*H$_2$-CH$_2$-O, *C*H$_2$-(CH$_2$)$_2$-O] ppm. HRMS (CI): calcd. for $C_{12}H_{18}N_3O_5$ [M + H]$^+$ 284.1246; found 284.1245.

Uridine Derivative 33: To a solution of **13** (100 mg, 0.35 mmol) and **32** (130 mg, 0.44 mmol, 1.3 equiv.) in anhydrous THF (10 mL) at –78 °C was added *N*-methylimidazole (0.14 mL, 1.75 mmol, 5 equiv.) over 5 min under argon. After stirring for 2 h at –78 °C, the reaction was maintained for 12 h at room temp. The solvent was removed under reduced pressure and the residue was dissolved in CH_2Cl_2 (20 mL), washed with cold 0.5 M HCl (5 mL × 2), cold water (10 mL), and brine (5 mL). The organic layer was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography (CH_2Cl_2/MeOH, 20:1) to give **33** (120 mg, 65%) as a diastereomeric mixture (R_P/S_P = 1:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.14–7.98 (m, 1 H), 7.33–7.24 (m, 2 H), 7.21–7.07 (m, 3 H), 6.30–6.17 (m, 2 H), 5.71–5.60 (m, 2 H), 5.39–5.23 (m, 1 H), 4.21–3.84 (m, 7 H), 3.60–3.56 (m, 1 H), 3.45–3.42 (m, 1 H), 1.36–1.34–1.15 (m, 6 H) ppm. ^{31}P NMR (162 MHz, CD_3OD): δ = 4.30, 4.17 ppm. MS-ESI$^+$: m/z = 538 [M + H$^+$]. HRMS-ESI$^+$: m/z calcd. for $C_{23}H_{29}N_3O_{10}P$ [M + H$^+$] 538.1582; found 538.1585.

Uridine Derivative 34: To a solution of **33** (50 mg, 0.09 mmol) in EtOH (5 mL) was added 1,4-cyclohexadiene (0.50 mL) and 10% Pd/C (5 mg) at room temp. After stirring for 3 h at room temp., the reaction mixture was treated with Celite (1.0 g) and stirred for 30 min with the septa removed. The suspension was filtered, and the resulting solid was washed with MeOH (3 × 15 mL). The collected solution was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 20:1) to give **34** (490 mg, 98%) as a diastereomeric mixture (R_P/S_P = 1:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.26–8.14 (m, 1 H), 7.32–7.24 (m, 2 H), 7.20–7.07 (m, 3 H), 6.39–6.31 (m, 1 H), 5.69–5.58 (m, 1 H), 5.53–5.39 (m, 1 H), 4.18–3.83 (m, 6 H), 3.57–3.54 (m, 1 H), 3.49–3.45 (m, 1 H), 3.34–3.31 (m, 1 H), 1.80–1.70 (m, 2 H), 1.58–1.49 (m, 2 H), 1.34–1.17 (m, 6 H) ppm. ^{31}P NMR (162 MHz, CD_3OD): δ = 4.31, 4.15 ppm. MS-ESI$^+$: m/z = 540 [M + H$^+$]. HRMS-ESI$^+$: m/z calcd. for $C_{23}H_{31}N_3O_{10}P$ [M + H$^+$] 540.1738; found 540.1742.

Cytidine Derivative 35: To a solution of **15** (80 mg, 0.285 mmol) in anhydrous THF (5 mL) at –78 °C was added *t*BuMgCl (1.0 M in THF, 0.65 mL, 0.650 mmol, 2.3 equiv.) under argon. After stirring for 30 min at –78 °C followed by 30 min at 0 °C, the solution was cooled to –78 °C, and **32** (110 mg, 0.377 mmol, 1.3 equiv.) was added in anhydrous THF (5 mL) under argon. After stirring for 2 h at –78 °C, the reaction mixture was maintained for 12 h at room temp. The solution was treated with saturated NH_4Cl (0.2 mL) at 0 °C and then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (20 mL), washed with cold water (10 mL) and brine (5 mL). The organic layer was dried with Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography (CH_2Cl_2/MeOH, 20:1 to 10:1) to give **35** (74 mg, 0.138 mmol) in 48% yield as a diastereomeric mixture (R_P/S_P = 1:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 7.83–7.69 (br. s, 1 H), 7.68–7.64 (m, 1 H), 7.35–7.30 (m, 2 H), 7.22–7.12 (m, 3 H), 6.34–6.31 (m, 1 H), 6.27–6.24 (m, 1 H), 5.96–5.90 (m, 1 H), 5.85–5.65 (m, 1 H), 4.37–3.84 (m, 8 H), 3.43 (s, 1 H), 3.18 (m, 1 H), 3.10 (m, 1 H), 1.29–1.15 (m, 6 H) ppm. ^{31}P NMR (162 MHz, CD_3OD): δ = 4.53, 4.37 ppm. MS-ESI$^+$: m/z = 537 [M + H$^+$]. HRMS-ESI$^+$: m/z calcd. for $C_{23}H_{30}N_4O_9P$ [M + H$^+$] 537.1741; found 537.1745.

Cytidine Derivative 36: To a solution of **35** (30 mg, 0.056 mmol) in EtOH (5 mL) was added 10% Pd/C (5 mg) at room temp. The mixture was stirred for 3 h under an H_2 atmosphere (1 atm), and then treated with Celite (1.0 g) and stirred for 30 min with the septa removed. The suspension was filtered, and the resulting solid was washed with MeOH (5 × 5 mL). The collected solution was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 10:1) to give **36** (28 mg, 94%) as a diastereomeric mixture (R_P/S_P = 1:1). ^{1}H NMR (400 MHz, CD_3OD): δ = 8.02–7.99 (m, 1 H), 7.37–7.33 (m, 2 H), 7.24–7.13 (m, 3 H), 6.42–6.38 (m, 1 H), 5.93–5.90 (m, 1 H), 4.14–3.83 (m, 8 H), 3.64 (m, 1 H), 3.58 (br. s, 1 H), 3.30 (m, 1 H), 1.95–1.88 (m, 1 H), 1.84–1.79 (m, 2 H), 1.59–1.50 (m, 1 H), 1.33–1.14 (m, 6 H) ppm. ^{31}P NMR (162 MHz, CD_3OD): δ = 4.36, 4.31 ppm. MS-ESI$^+$: m/z = 539 [M + H$^+$]. HRMS-ESI$^+$: m/z calcd. for $C_{23}H_{32}N_4O_9P$ [M + H$^+$] 539.1897; found 539.1901.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H- and ^{13}C-NMR spectra for compounds **13**–**18**, NOESY data for compound **24** and copies of ^{1}H-, ^{31}P-NMR and mass spectra for compounds **33**–**36**.

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