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Propargyl 1,2-Orthoesters for a Catalytic and Stereoselective Synthesis of Pyrimidine Nucleosides

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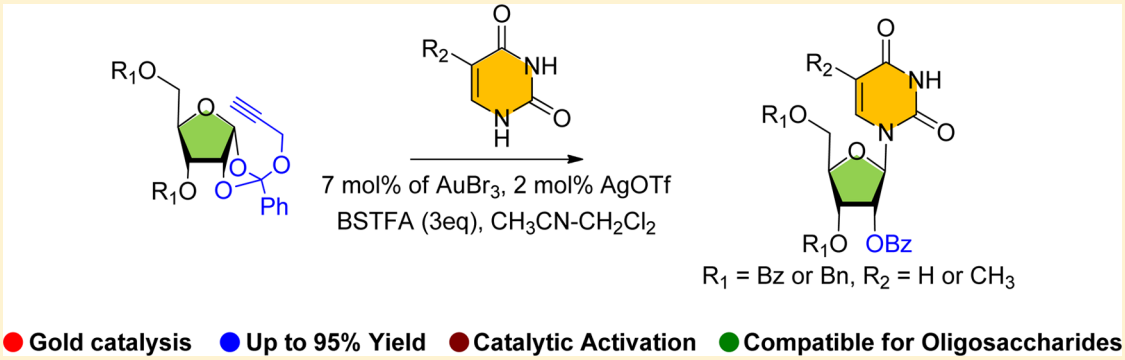
Supporting Information



ABSTRACT: Pyrimidine nucleosides are synthesized by using propargyl 1,2-orthoesters and Au(III) salt as a catalyst. Strategically positioned 1,2-orthoesters are found to yield only 1,2-*trans* nucleosides and enable preparation of 2′-OH containing pyrimidine nucleosides. The glycosyl donor employed in this study is stable and easily accessible. The identified high-yielding protocol is mild, diastereoselective, and catalytic.

INTRODUCTION

The Vorbrüggen-modified silyl version of the Hilbert−Johnson nucleoside reaction is the most widely used method for the synthesis of nucleosides in a stereoselective manner utilizing *C*-1-acyloxy glycosyl donors.[1] The procedure requires installation of 2′-*O*-acyl group for achieving the stereoselectivity that was rationalized based on the neighboring group participation in the form of a 1,2-dioxolenium ion.[2] The presence of a 2′-*O*-acyl moiety deactivated the oxocarbenium ion intermediate and hence required high temperature and strong Lewis acids for activation of the glycosyl donor.[3] However, these harsh reaction conditions have serious consequences on the choice of functional and protecting groups that can be employed in the nucleoside synthesis.[4] Efforts to replace the leaving group at the anomeric position for better nucleoside synthesis had limited success, which could be attributed partially to the poor nucleophilicity of pyrimidines and unfavorable competition for glycosidation between the pyrimidine and the side product from the leaving group. A significant improvement to the original Vorbrüggen glycosyl ester method wherein the *o*-alkynyl benzoate leaving group was activated using catalytic amount of [$Ph_3PAuNTf_2$] in the presence of silylating agent BSTFA in acetonitrile at room temperature was recently reported.[5] Subsequently, *n*-pentenyl 1,2-orthoesters were employed to glycosylate the silylated nucleobases in the presence of a stoichiometric quantity of *N*-iodosuccinimide.[3] Introduction of 1,2-orthoesters to the nucleoside synthesis is significant because it enables differentiation of the 2′-hydroxyl group from the rest of the hydroxyls. Incidentally, several 2′-*O*-modified oligonucleosides derivatives are currently under investigation for applications in antisense therapeutics.[6] Traditionally, 2′-hydroxyl-free nucleosides are synthesized after protecting group adjustments which increase the total number of steps for the monomer synthesis, and often, the reagents are costlier as well. In the era of green chemistry, processes that give higher yields by catalytic means are very important to increase the overall atom economy.[7] Our laboratory reported[8] that propargyl 1,2-orthoesters behave as glycosyl donors in the presence of gold(III) salts in a diastereoselective fashion and were subsequently shown to be suitable for the synthesis of glycomimetics,[8b,c] glycopolymers,[8d−f] glycoconjugates,[8g] and oligosaccharides.[8h] Herein, gold catalysis repertoire was investigated for the synthesis of pyrimidine nucleosides.

RESULTS AND DISCUSSION

We explored the utility of gold-catalyzed glycosidation conditions[8] for the synthesis of pyrimidine nucleosides such as uridine, thymidine, and cytosine with the propargyl 1,2-orthoester of ribofuranose. Accordingly, a CH_3CN solution of uracil (**2a**) and easily accessible propargyl 1,2-orthoester (**1a**)[8i] was treated with silylating agent *N*,*O*-bis(trimethylsily)-trifluoroacetamide (BSTFA) and $AuBr_3$ (7 mol %) but gave a poor yield (30%) of the nucleoside **3a**;[3] addition of AgOTf (2 mol %) improved the yield to 42%.[8j] Previous studies showed that the propargyl orthoesters are activated better in CH_2Cl_2,

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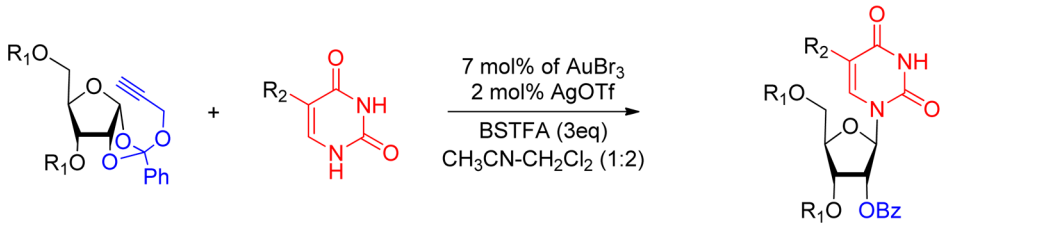
Scheme 1. Gold-Catalyzed Glycosidation for Pyrimidine Nucleosides



1a R_1 = -COPh
1b R_1 = -CH_2Ph

2a R_2 = -H
2b R_2 = -CH_3

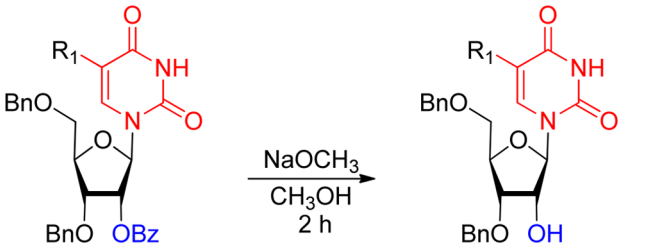
3a R_1 = -COPh, R_2 = -H (6 h, 85%)
4a R_1 = -COPh, R_2 = -CH_3 (6 h, 85%)
3b R_1 = -CH_2Ph, R_2 = -H (3 h, 93%)
4b R_1 = -CH_2Ph, R_2 = -CH_3 (3 h, 95%)

and hence, various combinations of CH_3CN and CH_2Cl_2 were used. We found that a 1:2 mixture of CH_3CN/CH_2Cl_2 is best suited (85% of **3a**) for the nucleosidation (Scheme 1).

Further, the coupling reaction between the orthoester **1a** and thymine **2b** was performed under the aforementioned conditions to afford the nucleoside **4a**[3] in 85% yield. Improved yield (93 and 95%) and faster completion of the reaction (3 h) were observed with nucleobases **2a** and **2b** when the protecting group was modified as a benzyl ether (**1b**) affording protected nucleosides **3b**[3] and **4b**, respectively (Scheme 1).[9] Orthoester **1a** was also subjected to nucleosidation reaction with cytosine **2c** to afford protected cytidine **3c** in 85% yield (Table 1).

The persence of 2′-benzoate in nucleosides **3b** and **4b** is beneficial as it can be easily saponified under Zemplén conditions to obtain nucleosides containing 2′-OH (**5**[10a] and **6**[10b]), which can be further extrapolated to various 2′-*O*-modified oligonucleoside for applications as antisense therapeutics (Scheme 2).

Scheme 2. Synthesis of 2′-OH Pyrimidine Nucleosides



3b R_1 = -H
4b R_1 = -CH_3

5 R_1 = -H (94%)
6 R_1 = -CH_3 (95%)

The scope of the reaction was further investigated with other xylo and arabinofuranosyl orthoester donors **7** and **8**. The nucleosidation reaction of donors **7**[8i] and **8**[8i] smoothly occurred under the aforementioned conditions to afford nucleosides **9**,[10c] **10a**,[10d] and **10b** in very high yields (81, 78, and 83%) and in a fully diastereoselective fashion (Table 1). The occurrence of the 1,2-*trans* relationship between C-1,2 was confirmed on the basis of the ^{13}C NMR spectral signatures where the anomeric carbon of the compound **9** was noticed at δ 88.3 ppm, whereas the anomeric carbon of the nucleoside **10a** was identified at δ 91.2 ppm.[9,10] Compounds **9** and **10a** showed unexpected 2D-NOESY correlations between H-1 and H-2,3, which may be due to the puckering of the sugar ring; however, $^1J_{C-H}$ values were noticed around 171.6, 171.1 Hz, respectively, in the HSQC spectra, confirming the 1,2-*trans* linkage unambiguously.[9] Furthermore, the utility of the gold(III)-catalyzed nucleosidation protocol was found to be highly useful for synthesizing pyranosyl nucleosides **12a,b** and **14** from the corresponding propargyl orthoesters **11**[8a] and **13**[8a] of galactopyranose and glucopyranose, respectively. The identified nucleosidation was found to be applicable for the synthesis of trisaccharide nucleoside **16** from the propargyl orthoester of maltotriose **15**[8k] in 70% yield. Purine nucleosides could not be synthesized by the above reaction conditions.

Next, we turned our attention to the synthesis of partial deprotection of the substitutions on the sugar ring for which orthogonally cleavable protecting groups were needed. Benzyl, benzoate, and silyl ethers were identified toward this objective as these protecting groups can be orthogonally installed and deprotected as well. Accordingly, compound **1a** was saponified under Zempén conditions[8i] to obtain an orthoester−diol **17** and treated with 1 equiv of TBDPSCl to afford 5-*O*-TBDPS ether **18** in 80% yield, which was further converted into the benzyl ether **19** by the use of NaH/BnBr/TBAI/DMF in excellent yield. Further, orthoester **19** smoothly underwent the nucleosidation reaction with nucleobase **2b** under gold(III) catalysis conditions to afford the required nucleoside **20**. Saponification of nucleoside **20** under Zemplén conditions afforded 2′-OH containing nucleoside **21** without affecting the other two protecting groups, whereas the hydrogenolysis resulted in the formation of 3′-OH containing nucleoside **22**, and finally, the fluoride ion mediated cleavage of the silyl ether moiety furnished the nucleoside with free 5′-OH **23** (Scheme 3).

CONCLUSIONS

In conclusion, easily accessible propargyl 1,2-orthoesters are shown to be good synthons for the synthesis of pyrimidine nucleosides under gold(III) catalysis conditions. The nucleosidation reaction is catalytic, mild, and high-yielding and enables facile preparation of pyrimidine nucleosides with an orthogonally protected 2′-hydroxyl group for further functional group interconversion. However, the procedure is not suitable for the synthesis of purine nucleosides. Thus, synthesized nucleosides were deprotected to obtain either 2′, 3′, or 5′ free hydroxyl groups in an orthogonal fashion. The gold(III)-catalyzed nucleosidation reaction was shown to be suitable for synthesizing the nucleoside of a model trisaccharide as well.

EXPERIMENTAL SECTION

General Methods. Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Unless otherwise reported, all reactions were performed

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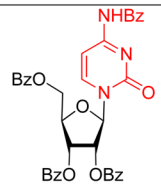
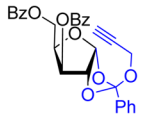
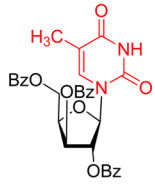
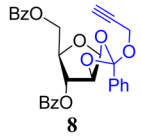
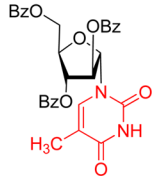
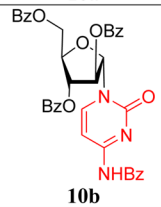
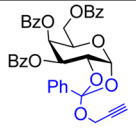
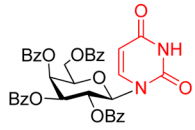
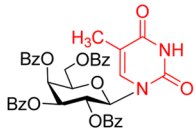
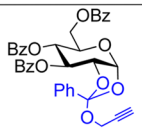
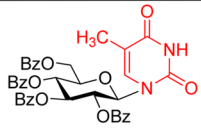
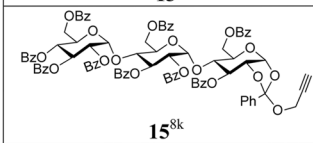
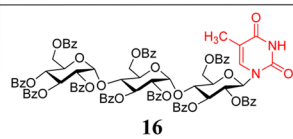
Table 1. Synthesis of Nucleosides

Orthoester	Nucleobase	Product	% Yield	Ref.
1a	**2c**	 **3c**	85	3
 **7**	**2b**	 **9**	81	10c
 **8**	**2b**	 **10a**	78	10d
8	**2c**	 **10b**	83	
 **11**	**2a**	 **12a**	80	
11	**2b**	 **12b**	83	
 **13**	**2b**	 **14**	78	10e
 **15**[8k]	**2b**	 **16**	70	

under argon atmosphere. Removal of solvent in vacuo refers to distillation using a rotary evaporator attached to an efficient vacuum pump. Products obtained as solids or syrups were dried under high vacuum. BSTFA, $AuBr_3$, and AgOTf were purchased from multinational commercial vendors. Analytical thin-layer chromatography was performed on precoated silica plates (F_{254}, 0.25 mm thickness); compounds were visualized by UV light or by staining with anisaldehyde spray. Optical rotations were measured on a digital polarimeter. IR spectra were recorded on an FT-IR spectrometer. NMR spectra were recorded either at 400 or 500 MHz with $CDCl_3$ or DMSO-d_6 as the solvent and TMS as the internal standard. High-resolution mass spectroscopy (HRMS) was performed using an ESI-TOF mass analyzer. Low-resolution mass spectroscopy (LRMS) was performed on UPLC−MS or TLC−MS.

General Procedure for the Synthesis of Pyrimidine Nucleosides. To a solution of nucleobase **2a** (100 mg, 0.89 mmol) was added BSTFA (689 mg, 709 μL, 2.68 mmol) and the solution stirred at 25 °C until it became a clear (~40 min) solution. A solution of orthoester **1a** (446 mg, 0.89 mmol) in CH_2Cl_2 was added dropwise at 25 °C and stirred for 5 min, and then $AuBr_3$ (27 mg, 0.06 mmol) and AgOTf (4.5

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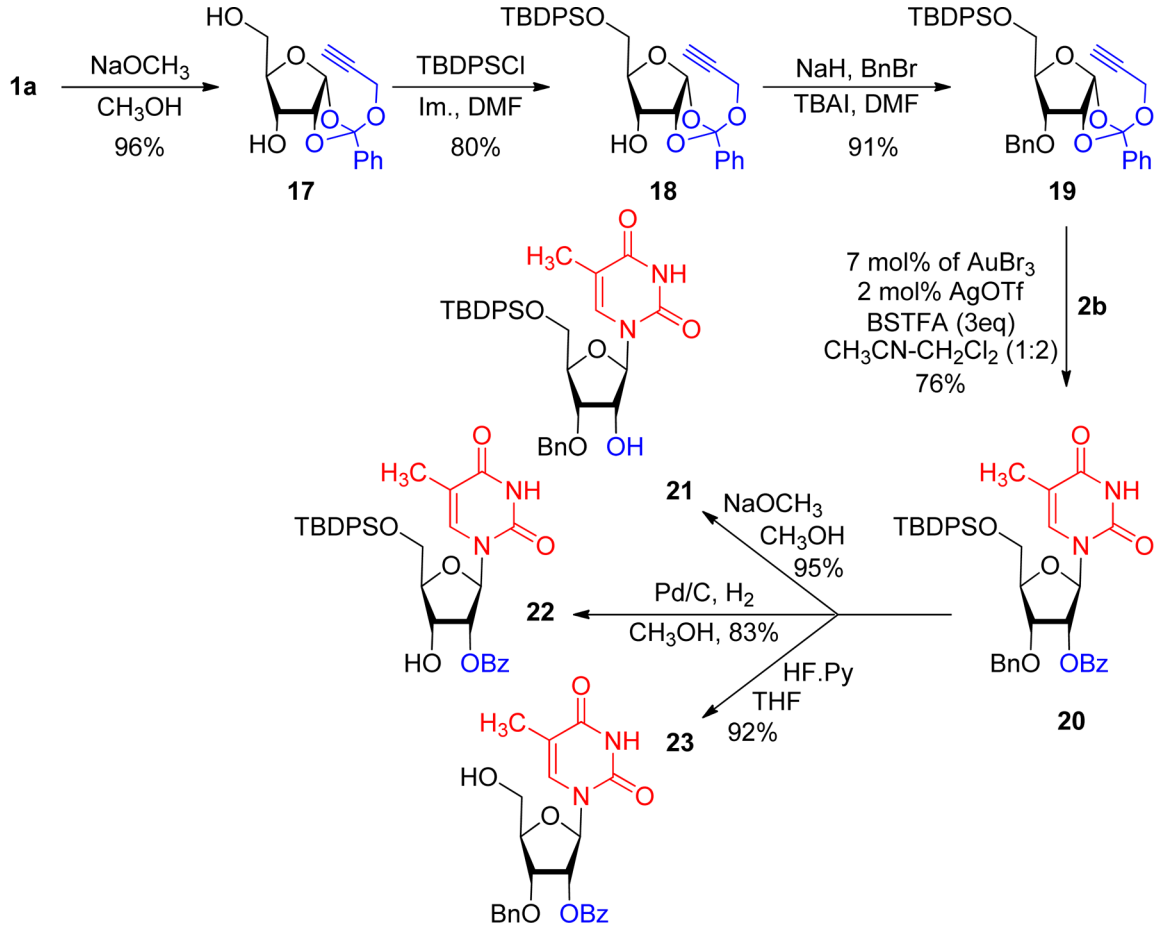
Scheme 3. Synthesis of Orthogonally Protected Thymine Nucleoside



mg, 0.02 mmol) were added and stirred at 25 °C. After the reaction was complete (as judged by TLC–MS analysis), the reaction mixture was concentrated in vacuo and the residue was purified by silica gel column chromatography using petroleum ether–ethyl acetate as the mobile phase to afford the nucleoside **3a** (422 mg, 85%) as a colorless gum.

*3,5-Di-O-benzoyl-α-D-ribofuranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**1a**).*[8h,i] This compound was prepared by employing the already reported procedure starting from D-ribose (5.0 g, 33.3 mmol): yield 9.3 g, 56% over four steps; $[\alpha]^{25}_{D}$ = +122.9 (*c* 2.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 2.42 (t, *J* = 2.4 Hz, 1H), 4.09 (dABq, *J* = 3.4, 2.6 Hz, 2H), 4.22–4.27 (m, 1H), 4.42 (dd, *J* = 12.3, 4.8 Hz, 1H), 4.64 (dd, *J* = 12.3, 3.3 Hz, 1H), 5.10 (dd, *J* = 9.3, 5.3 Hz, 1H), 5.35 (d, *J* = 4.8 Hz, 1H), 6.27 (d, *J* = 4.2 Hz, 1H), 7.34–7.48 (m, 7H), 7.49–7.55 (m, 1H), 7.57–7.63 (m, 1H), 7.67–7.72 (m, 2H), 8.00 (tt, *J* = 8.5, 1.2 Hz, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 51.5, 62.5, 72.9, 74.0, 76.3, 77.8, 79.2, 104.7, 123.6, 126.3, 126.3, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.8, 129.7, 129.7, 129.7, 129.7, 129.9, 129.9, 133.2, 133.6, 135.9, 165.5, 166.0; IR ($CHCl_3$) 710, 1099, 1271, 1451, 1602, 1725, 2930, 3066, 3291 cm^{-1}; HRMS (TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{24}O_8Na^+$ 523.1363, found 523.1369.

*3,5-Di-O-benzyl-α-D-ribofuranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**1b**).*[8h,i] This compound was prepared from compound **1a** (4.0 g, 8 mmol) as the starting material: yield 3.5 g, 93%; $[\alpha]^{25}_{D}$ = +21.1 (*c* 0.7, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.36–2.41 (m, 1H), 3.47–3.55 (m, 1H), 3.69 (d, *J* = 11.3 Hz, 1H), 3.88–3.95 (m, 2H), 4.01–4.06 (m, 2H), 4.42–4.57 (m, 3H), 4.72–4.78 (m, 1H), 4.86–4.93 (m, 1H), 6.09 (dd, *J* = 4.1, 1.4 Hz, 1H), 7.23–7.37 (m, 13H), 7.67–7.74 (m, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 51.8, 67.4, 72.2, 73.5, 73.7, 77.1, 77.6, 78.5, 79.7, 104.8, 123.4, 126.6, 126.6, 127.7, 127.8, 127.8, 128.1, 128.1, 128.1, 128.4, 128.4, 128.4, 128.4, 128.5, 128.5, 129.7, 135.5, 137.5, 137.9; IR ($CHCl_3$) 707, 1110, 1262, 1450, 1590, 1722, 2928, 3060, 3290 cm^{-1}; HRMS (TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{28}NaO_6^+$ 495.1778, found 495.1784.

*1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)uracil (**3a**).*[3,5] This compound was prepared following the above-mentioned general procedure using uracil **2a** (0.1 g, 0.89 mmol) as the starting material: yield 0.42 g, 85%; $[\alpha]^{25}_{D}$ = −35.3 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 4.63–4.72 (m, 2H), 4.82 (dd, *J* = 11.8, 2.5 Hz, 1H), 5.60 (dd, *J* = 8.1, 1.6 Hz, 1H), 5.75 (t, *J* = 5.7 Hz, 1H), 5.86–5.91 (m, 1H), 6.30 (d, *J* = 5.5 Hz, 1H), 7.31–7.60 (m, 10H), 7.89–7.98 (m, 4H), 8.05–8.11 (m, 2H), 9.50 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 63.9, 71.2, 73.9, 80.6, 88.3, 103.5, 128.4, 128.6, 128.6, 128.6, 128.7, 128.8, 128.8, 128.9, 129.3, 129.7, 129.7, 129.9, 129.9, 130.0, 130.0, 133.7, 133.8, 133.9, 139.8, 150.3, 163.2, 165.4, 165.4, 166.2; IR ($CHCl_3$) 2924, 1724, 1455, 1268, 1112, 765 cm^{-1}; HRMS (TOF) *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{25}N_2O_9^+$ 557.1555, found 557.1552.

*1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)thymine (**4a**).*[3,5] This compound was prepared following the above-mentioned general procedure using thymine **2b** (0.1 g, 0.79 mmol) as the starting material: yield 0.39 g, 85%; $[\alpha]^{25}_{D}$ = −76.2 (*c* 1.00,$CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.58 (s, 3H), 4.62–4.73 (m, 2H), 4.84–4.91 (m, 1H), 5.79 (t, *J* = 6.1 Hz, 1H), 5.94 (dd, *J* = 6.0, 3.8 Hz, 1H), 6.45 (d, *J* = 6.3 Hz, 1H), 7.30–7.62 (m, 10H), 7.96 (dd, *J* = 11.9, 7.4 Hz, 4H), 8.13 (d, *J* = 7.4 Hz, 2H), 9.82 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.1, 64.0, 71.5, 73.5, 80.6, 87.1, 112.2, 128.4, 128.5, 128.5, 128.6, 128.6, 128.7, 128.8, 128.9, 129.3, 129.7, 129.7, 129.8, 129.9, 129.9, 130.0, 133.7, 133.7, 133.8, 135.0, 150.6, 163.9, 165.4, 165.4, 166.0; IR ($CHCl_3$) 3025, 1725, 1267, 1109, 711 cm^{-1}; HRMS (TOF) *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{27}N_2O_9^+$ 571.1711, found 571.1723.

*1-(2-O-Benzoyl-3,5-di-O-benzyl-β-D-ribofuranosyl)uracil (**3b**).*[3] This compound was prepared following the above-mentioned general procedure using uracil **2a** (0.1 g, 0.89 mmol) as the starting material: yield 0.44 g, 93%; $[\alpha]^{25}_{D}$ = +63.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$,

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399.78 MHz) δ 3.59 (dd, J = 10.8, 2.1 Hz, 1H), 3.87 (dd, J = 10.7, 2.2 Hz, 1H), 4.22−4.50 (m, 5H), 4.65 (d, J = 11.8 Hz, 1H), 5.37 (d, J = 8.2 Hz, 1H), 5.50−5.59 (m, 1H), 6.30 (d, J = 4.0 Hz, 1H), 7.19−7.46 (m, 12H), 7.56 (dd, J = 7.2, 1.3 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 8.08 (dt, J = 8.3, 1.6 Hz, 2H), 9.82 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 68.7, 73.3, 73.8, 75.1, 75.8, 77.5, 82.3, 87.9, 102.5, 128.1, 128.1, 128.1, 128.2, 128.2, 128.4, 128.5, 128.5, 128.6, 128.6, 128.7, 128.8, 129.2, 130.1, 130.1, 133.6, 137.3, 140.3, 150.5, 163.8, 165.6; IR ($CHCl_3$) 3201, 3062, 2921, 2866, 1721, 1454, 1381, 1266, 1122, 700 cm^{-1}; HRMS (TOF) m/z [M + H]$^+$ calcd for $C_{30}H_{29}N_2O_7^+$ 529.1969, found 529.1974.

*1-(2-O-Benzoyl-3,5-di-O-benzyl-β-D-ribofuranosyl)thymine (**4b**).* This compound was prepared following the above-mentioned general procedure using thymine **2b** (0.1 g, 0.79 mmol) as the starting material: yield 0.41 g, 95%; $[\alpha]^{25}_D$ = +25.9 (c 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.51 (s, 3H), 3.54 (dd, J = 10.8, 2.1 Hz, 1H), 3.83 (dd, J = 10.8, 2.0 Hz, 1H), 4.24−4.29 (m, 1H), 4.37 (t, J = 5.1 Hz, 1H), 4.41−4.55 (m, 3H), 4.61 (d, J = 11.7 Hz, 1H), 5.51 (t, J = 4.8 Hz, 1H), 6.29 (d, J = 4.5 Hz, 1H), 7.15−7.34 (m, 10H), 7.40 (t, J = 7.7 Hz, 2H), 7.48−7.59 (m, 2H), 8.04 (d, J = 7.6 Hz, 2H), 9.04 (d, J = 25.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.1, 68.9, 73.2, 73.7, 75.0, 76.1, 82.3, 87.4, 111.3, 127.8, 127.8, 128.0, 128.0, 128.1, 128.2, 128.4, 128.5, 128.5, 128.6, 128.7, 128.7, 129.1, 130.0, 130.0, 133.6, 135.8, 137.3, 137.3, 150.4, 163.9, 165.6; HRMS (TOF) m/z [M + H]$^+$ calcd for $C_{31}H_{31}N_2O_7^+$ 543.2126, found 543.2131.

*1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-N-benzoylcytosine (**3c**).*[3] This compound was prepared following the above-mentioned general procedure using cytosine **2c** (0.1 g, 0.47 mmol) as the starting material: yield 0.25 g, 85%; $[\alpha]^{25}_D$ = −41.3 (c 1.00, $CHCl_3$); ^{1}H NMR (DMSO-d_6, 399.78 MHz) δ 4.63−4.87 (m, 3H), 5.96−6.10 (m, 2H), 6.24 (d, J = 2.7 Hz, 1H), 7.36−7.58 (m, 9H), 7.64 (q, J = 7.7, 4H), 7.91 (dd, J = 13.2, 7.4 Hz, 4H), 8.02 (d, J = 7.4 Hz, 4H), 8.33 (d, J = 7.3 Hz, 1H), 11.42 (s, 1H); ^{13}C NMR (DMSO-d_6, 100.53 MHz) δ 64.2, 71.1, 74.4, 79.6, 92.5, 97.3, 128.9, 129.0, 129.1, 129.1, 129.1, 129.2, 129.2, 129.2, 129.2, 129.3, 129.3, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 129.9, 133.3, 133.5, 134.1, 134.3, 134.5, 147.9, 154.8, 164.5, 165.1, 165.2, 166.0, 167.9; IR ($CHCl_3$) 3021, 1726, 1556, 1483, 1262, 750, 712 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$ calcd for $C_{37}H_{29}NaN_3O_9^+$ 682.1796, found 682.1801.

*1-(3,5-Di-O-benzyl-β-D-ribofuranosyl)uracil (**5**).*[10a] This compound was prepared following the above-mentioned general procedure using nucleoside **3b** (0.1 g, 0.20 mmol) as the starting material: yield 0.75 g, 94%; $[\alpha]^{25}_D$ = +14.8 (c 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 3.55 (dd, J = 10.7, 2.0 Hz, 1H), 3.81 (dd, J = 10.7, 2.4 Hz, 2H), 4.07 (t, J = 5.1 Hz, 1H), 4.22−4.29 (m, 2H), 4.46 (s, 2H), 4.53−4.72 (m, 2H), 5.33 (d, J = 8.1 Hz, 1H), 5.94 (d, J = 4.0 Hz, 1H), 7.11−7.42 (m, 10H), 7.75 (d, J = 8.1 Hz, 1H), 9.77 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 69.1, 72.7, 73.8, 74.1, 76.7, 81.5, 90.1, 102.3, 128.0, 128.0, 128.1, 128.1, 128.3, 128.3, 128.7, 128.7, 128.7, 128.7, 137.1, 137.3, 140.4, 151.0, 163.7; IR ($CHCl_3$) 3419, 3060, 2923, 2857, 1692, 1458, 1271, 1119, 699 cm^{-1}; HRMS (TOF) m/z [M + H]$^+$ calcd for $C_{23}H_{25}N_2O_6^+$ 425.1707, found 425.1712.

*1-(3,5-Di-O-benzyl-β-D-ribofuranosyl)thymine (**6**).*[10b] This compound was prepared following the above-mentioned general procedure using nucleoside **4b** (0.1 g, 0.19 mmol) as the starting material: yield 0.77 g, 95%; $[\alpha]^{25}_D$ = −10.3 (c 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.49 (s, 3H), 3.52 (dd, J = 10.7, 1.7 Hz, 1H), 3.79 (dd, J = 10.7, 2.1 Hz, 1H), 4.08 (t, J = 4.8 Hz, 1H), 4.21−4.25 (m, 1H), 4.27 (t, J = 4.9 Hz, 1H), 4.44−4.53 (m, 2H), 4.54−4.71 (m, 2H), 5.94 (d, J = 4.5 Hz, 1H), 7.18−7.34 (m, 11H), 7.49 (s, 1H), 9.60 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.1, 69.4, 72.7, 73.7, 74.1, 77.0, 77.4, 81.6, 89.7, 111.1, 127.7, 127.7, 128.1, 128.1, 128.2, 128.3, 128.7, 128.7, 128.7, 136.0, 137.2, 137.4, 151.0, 164.2; IR ($CHCl_3$) 3421, 3032, 2924, 1694, 1469, 1118 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$ calcd for $C_{24}H_{26}N_2NaO_6^+$ 461.1683, found461.1689.

*3,5-Di-O-benzoyl-α-D-xylofuranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**7**).*[8h] This compound was prepared by adopting the reported procedure from D-xylose (5.0 g, 33.3 mmol) as the starting material: yield 9.0 g, 53% over four steps; $[\alpha]^{25}_D$ = +0.6 (c 1.00, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.40 (t, J = 2.5 Hz, 1H), 4.04−4.07 (m, 2H), 4.44−4.49 (m, 1H), 4.53−4.59 (m, 2H), 5.04 (d, J = 4.1 Hz, 1H), 5.66 (d, J = 3.1 Hz, 1H), 6.37 (d, J = 4.1 Hz, 1H), 7.36−7.72 (m, 11H), 7.92−8.06 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 51.9, 61.7, 74.0, 76.2, 77.9, 79.3, 84.2, 105.4, 122.9, 126.3, 128.4, 128.4, 128.6, 128.6, 128.7, 128.7, 128.9, 129.5, 129.8, 129.8, 129.9, 129.9, 129.9, 130.0, 133.3, 133.9, 135.1, 165.2, 166.1; IR ($CHCl_3$) 706, 1105, 1268, 1447, 1591, 1725, 2930, 3068, 3290 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$ calcd for $C_{29}H_{24}O_8Na^+$ 523.1363, found 523.1368.

*3,5-Di-O-benzoyl-β-D-arabinofuranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**8**).*[8h,i] This compound was prepared by adopting the reported procedure from D-arabinose (5.0 g, 33.3 mmol) as the starting material: yield 9.6 g, 56% over four steps; $[\alpha]^{25}_D$ = −13.83 (c 1.00, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.39 (t, J = 2.6 Hz, 1H), 3.98 (dd, J = 2.3, 0.8 Hz, 2H), 4.29 (d, J = 7.3 Hz, 2H), 4.66 (t, J = 7.2 Hz, 1H), 5.19 (d, J = 4.2 Hz, 1H), 5.54 (s, 1H), 6.40 (d, J = 4.3 Hz, 1H), 7.38−7.47 (m, 7H), 7.49−7.55 (m, 1H), 7.56−7.61 (m, 1H), 7.66−7.71 (m, 2H), 8.00−8.06 (m, 4H); 13C NMR (100.53 MHz, $CDCl_3$) δ 52.2, 63.9, 74.0, 77.8, 79.4, 84.6, 85.0, 106.8, 122.9, 126.6, 126.6, 128.4, 128.5, 128.6, 128.6, 128.7, 128.7, 129.0, 129.7, 129.8, 129.9, 129.9, 129.9, 130.2, 133.2, 133.8, 134.3, 165.3, 165.9; IR ($CHCl_3$) 717, 1107, 1268, 1450, 1594, 1723, 2974, 3071, 3293 cm^{-1}; HRMS (TOF) m/z [M + Na]$^+$ calcd for $C_{29}H_{24}O_8Na^+$ 523.1363, found 523.1367.

*1-(2,3,5-Tri-O-benzoyl-β-D-xylofuranosyl)thymine (**9**).*[10c] This compound was prepared following the above-mentioned general procedure using nucleobase **2b** (0.1 g, 0.79 mmol) as the starting material: yield 0.37 g, 81%; $[\alpha]^{25}_D$ = 49.5 (c 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.76 (d, J = 0.9 Hz, 3H), 4.68−4.79 (m, 2H), 4.83 (dt, J = 6.1, 4.1 Hz, 1H), 5.64 (dd, J = 2.5, 1.8 Hz, 1H), 5.86 (dd, J = 3.9, 1.6 Hz, 1H), 6.33 (d, J = 2.6 Hz, 1H), 7.39 (dt, J = 19.9, 7.7 Hz, 6H), 7.47−7.61 (m, 4H), 7.97 (d, J = 7.6 Hz, 4H), 8.02−8.06 (m, 2H), 9.75 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.5, 61.7, 75.4, 79.0, 80.3, 88.3, 111.7, 128.5, 128.6, 128.6, 128.6, 128.7, 128.7, 128.7, 128.9, 129.3, 129.8, 129.8, 129.8, 129.9, 130.1, 130.2, 133.5, 134.0, 134.2, 135.1, 150.4, 164.0, 164.8, 164.9, 166.2; IR ($CHCl_3$) 3201, 3023, 1725, 1458, 1209, 1101, 760 cm^{-1}; HRMS (TOF) m/z [M + H]$^+$ calcd for $C_{31}H_{27}N_2O_9^+$ 571.1711, found 571.1720.

*1-(2,3,5-Tri-O-benzoyl-α-D-arabinofuranosyl)thymine (**10a**).*[10d] This compound was prepared following the above-mentioned general procedure using nucleobase **2b** (0.1 g, 0.79 mmol) as the starting material: yield 0.35 g, 78%; $[\alpha]^{25}_D$ = 0.8 (c 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.90 (d, J = 0.6 Hz, 3H), 4.63−4.78 (m, 2H), 4.99 (q, J = 5.1 Hz, 1H), 5.77 (t, J = 3.0 Hz, 1H), 5.96 (t, J = 2.9 Hz, 1H), 6.30 (d, J = 3.1 Hz, 1H), 7.29−7.32 (m, 1H), 7.41 (dt, J = 24.6, 7.5 Hz, 6H), 7.52−7.62 (m, 3H), 8.02 (td, J = 7.9, 1.4 Hz, 4H), 8.08 (dd, J = 8.7, 1.1 Hz, 2H), 9.76 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.7, 63.9, 77.4, 80.6, 83.6, 91.2, 111.4, 128.5, 128.6, 128.6, 128.6, 128.7, 128.7, 128.8, 128.8, 129.5, 129.9, 129.9, 129.9, 129.9, 130.1, 130.1, 133.4, 134.0, 134.0, 136.1, 150.5, 164.2, 165.3, 165.4, 166.2; IR ($CHCl_3$) 3198, 3023, 1723, 1266, 1103, 763, 711 cm^{-1}; HRMS (TOF) m/z [M + H]$^+$ calcd for $C_{31}H_{27}N_2O9^+$ 571.1711, found 571.1723.

*1-(2,3,5-Tri-O-benzoyl-α-D-arabinofuranosyl)-4-N-benzoylcytosine (**10b**).* This compound was prepared following the above-mentioned general procedure using cytosine **2c** (0.1 g, 0.47 mmol) as the starting material: yield 0.25 g, 83%; $[\alpha]^{25}_D$ = −14.7 (c 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 4.61−4.78 (m, 2H), 5.05−5.11 (m, 1H), 5.72 (t, J = 2.4 Hz, 1H), 6.04 (t, J = 1.6 Hz, 1H), 6.28 (d, J = 1.5 Hz, 1H), 7.32−7.62 (m, 13H), 7.88−7.95 (m, 5H), 8.01−8.10 (m, 4H), 9.36 (brs, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 63.9, 77.4, 80.7, 85.3, 93.7, 127.8, 128.5, 128.5, 128.5, 128.6, 128.7, 128.7, 128.7, 128.7, 129.1, 129.1, 129.5, 129.9, 129.9, 129.9, 130.0, 130.0, 130.1, 130.1, 133.0, 133.4, 133.4, 133.9, 133.9, 134.0, 134.0, 145.1, 154.8, 163.1, 165.1, 165.2, 166.2; IR ($CHCl_3$) 3126, 1723, 1485, 1258, 1104, 751, 711 cm^{-1}; HRMS (TOF) m/z [M + H]$^+$ calcd for $C_{37}H_{29}NaN_3O_9^+$ 682.1796, found 571.1798.

*3,4,6-Tri-O-benzoyl-α-D-galactopyranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**11**).*[8a] This compound was prepared from D-galactose (5.0 g, 27.7 mmol) as the starting material: yield 10.7 g,

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75% over three steps; $[\alpha]^{25}_{D}$ = +70.53 (*c* 1.00, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.41 (t, *J* = 2.3 Hz, 1H), 4.06 (d, *J* = 2.4 Hz, 2H), 4.41 (dd, *J* = 10.9, 5.1 Hz, 1H), 4.53−4.59 (m, 1H), 4.60−4.68 (m, 1H), 4.86 (t, *J* = 5.5 Hz, 1H), 5.62 (d, *J* = 5.9 Hz, 1H), 5.82−5.88 (m, 1H), 6.28 (d, *J* = 5.1 Hz, 1H), 7.31−7.43 (m, 11H), 7.47−7.53 (m, 3H), 7.70 (dd, *J* = 6.6, 2.9 Hz, 2H), 7.90−7.98 (m, 4H); ^{13}C NMR (100.53 MHz, $CDCl_3$) 52.1, 62.3, 66.4, 69.0, 70.0, 73.5, 74.0, 79.3, 98.4, 120.2, 126.1, 126.2, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.8, 129.0, 129.4, 129.7, 129.7, 129.7, 129.7, 129.8, 129.8, 130.0, 133.2, 133.4, 133.6, 135.2, 165.2, 165.2, 165.9; IR ($CHCl_3$) 709, 1097, 1269, 1727, 2400, 2950, 3300 cm^{-1}; HRMS (TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{37}H_{30}NaO_{10}^+$ 657.1731, found 657.1739.

1-(2,3,4,6-Tetra-O-benzoyl-β-D-galactopyranosyl)uracil (**12a**). This compound was prepared following the above-mentioned general procedure using nucleobase **2a** (0.1 g, 0.89 mmol) as the starting material: yield 0.50 g, 80%; $[\alpha]^{25}_{D}$ = 123.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 4.47 (dd, *J* = 11.3, 5.5 Hz, 1H), 4.58−4.74 (m, 2H), 5.87−5.97 (m, 3H), 6.15 (s, 1H), 6.37 (p, *J* = 6.4 Hz, 1H), 7.25 (dt, *J* = 21.5, 7.8 Hz, 4H), 7.34−7.44 (m, 4H), 7.47−7.67 (m, 5H), 7.75−7.80 (m, 2H), 7.84−7.88 (m, 2H), 7.93−8.02 (m, 2H), 8.06 (dd, *J* = 7.8, 1.3 Hz, 2H), 9.72 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 62.2, 68.2, 68.4, 71.8, 74.5, 80.9, 104.1, 128.1, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.7, 129.0, 129.0, 129.0, 129.2, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 133.5, 133.6, 133.9, 134.0, 139.3, 150.6, 163.0, 165.4, 165.5, 165.6, 166.1; IR ($CHCl_3$) 3436, 3067, 1728, 1455, 1270, 1102, 1025, 762 cm^{-1}; HRMS (TOF) *m*/*z* [M + H]$^+$ calcd for $C_{38}H_{31}N_2O_{11}^+$ 691.1922, found 691.1929.

1-(2,3,4,6-Tetra-O-benzoyl-β-D-galactopyranosyl)thymine (**12b**). This compound was prepared following the above-mentioned general procedure using nucleobase **2b** (0.1 g, 0.79 mmol) as the starting material: yield 0.47 g, 83%; $[\alpha]^{25}_{D}$ = 58.0 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.99−2.03 (m, 3H), 4.43−4.51 (m, 1H), 4.56−4.67 (m, 2H), 5.81−5.96 (m, 2H), 6.11 (d, *J* = 3.2 Hz, 1H), 6.31 (d, *J* = 9.1 Hz, 1H), 7.18−7.29 (m, 2H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.33−7.47 (m, 5H), 7.48−7.56 (m, 3H), 7.66 (tt, *J* = 7.0, 1.2 Hz, 1H), 7.76−7.81 (m, 2H), 7.84−7.88 (m, 2H), 7.95−8.01 (m, 2H), 8.03−8.09 (m, 2H), 9.29 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.9, 62.2, 68.2, 68.4, 71.9, 74.4, 77.4, 80.9, 112.4, 128.2, 128.4, 128.4, 128.5, 128.5, 128.6, 128.6, 128.9, 128.9, 129.1, 129.2, 129.8, 129.8, 129.9, 129.9, 129.9, 129.9, 130.0, 130.0, 133.4, 133.6, 133.8, 134.0, 134.7, 150.6, 163.5, 165.3, 165.4, 165.6, 166.1; IR ($CHCl_3$) 3262, 3066, 1726, 1457, 1268, 1103, 763, 711 cm^{-1}; HRMS (TOF) *m*/*z* [M + H]$^+$ calcd for $C_{39}H_{33}N_2O_{11}^+$ 705.2079, found 705.2083.

3,4,6-Tri-O-benzoyl-α-D-glucopyranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**13**).[8a] This compound was prepared from D-glucose (5.0 g, 27.7 mmol) as the starting material: yield 11.8 g, 83% over three steps; $[\alpha]^{25}_{D}$ = −5.94 (*c* 1.00, $CHCl_3$); ^{1}H NMR (399.78 MHz, $CDCl_3$) δ 2.39 (t, *J* = 2.5 Hz, 1H), 3.89−4.05 (m, 2H), 4.16 (ddd, *J* = 8.1, 4.6, 3.0 Hz, 1H), 4.40 (dd, *J* = 12.1, 4.8 Hz, 1H), 4.55 (dd, *J* = 12.1, 2.9 Hz, 1H), 4.88 (ddd, *J* = 5.4, 3.0, 1.1 Hz, 1H), 5.53 (dt, *J* = 8.8, 1.1 Hz, 1H), 5.78 (dd, *J* = 3.0, 1.3 Hz, 1H), 6.11 (d, *J* = 5.3 Hz, 1H), 7.21−7.28 (m, 2H), 7.39−7.50 (m, 8H), 7.54−7.64 (m, 2H), 7.77−7.82 (m, 2H), 7.95 (ddd, *J* = 9.2, 7.4, 1.3 Hz, 4H), 8.09 (dd, *J* = 8.5, 1.2 Hz, 2H); ^{13}C NMR (100.53 MHz, $CDCl_3$) δ 52.5, 64.0, 67.6, 68.5, 69.1, 72.1, 74.1, 79.3, 97.9, 121.3, 126.6, 126.6, 128.3, 128.4, 128.6, 128.6, 128.6, 128.6, 128.7, 128.7, 129.0, 129.1, 129.7, 129.7, 129.8, 130.0, 130.0, 130.1, 130.1, 130.2, 133.1, 133.7, 133.8, 134.1, 164.7, 165.3, 166.1; IR ($CHCl_3$) 3743, 2339, 1719, 1249, 1092, 1019, 703 cm^{-1}; HRMS (TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{37}H_{30}NaO_{10}^+$ 657.1731, found 657.1737.

1-(2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl)thymine (**14**).[5] This compound was prepared following the above-mentioned general procedure using nucleobase **2b** (0.1 g, 0.79 mmol) as the starting material: yield 0.44 g, 78%; $[\alpha]^{25}_{D}$ = +5.0 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$,399.78 MHz) δ 1.93 (d, *J* = 1.2 Hz, 3H), 4.39 (ddd, *J* = 10.0, 5.0, 2.7 Hz, 1H), 4.48 (dd, *J* = 12.4, 5.1 Hz, 1H), 4.67 (dd, *J* = 12.4, 2.7 Hz, 1H), 5.67 (t, *J* = 9.5 Hz, 1H), 5.78 (t, *J* = 9.8 Hz, 1H), 6.08 (t, *J* = 9.7 Hz, 1H), 6.26 (d, *J* = 9.5 Hz, 1H), 7.27−7.60 (m, 13H), 7.78−7.94 (m, 6H), 8.00−8.06 (m, 2H), 8.51 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.7, 62.7, 68.9, 70.2, 73.0, 75.4, 77.3, 80.6, 112.3, 128.0, 128.5, 128.5, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 129.4, 129.8, 129.8, 129.9, 129.9, 129.9, 130.0, 130.0, 130.1, 130.1, 133.4, 133.5, 133.8, 133.9, 134.6, 150.3, 163.1, 165.3, 165.3, 165.5, 166.1; IR ($CHCl_3$) 1727, 1456, 1267, 1088, 711 cm^{-1}; HRMS (TOF) *m*/*z* [M + H]$^+$ calcd for $C_{39}H_{33}N_2O_{11}^+$ 705.2079, found705.2091.

1-(2,3,6-Tri-O-benzoyl-4-O-[2,3,6-tri-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl α-D-Glucopyranosyl)-α-D-glucopyranosyl] β-D-glucopyranosyl)thymine (**16**). This compound was prepared following the above-mentioned general procedure using nucleobase **2b** (0.1 g, 0.79 mmol) as the starting material: yield 0.92 g, 70%; $[\alpha]^{25}_{D}$ = +59.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 399.78 MHz) δ 1.84 (d, *J* = 0.7 Hz, 3H), 4.21−4.29 (m, 2H), 4.35−4.51 (m, 5H), 4.62−4.72 (m, 2H), 4.82 (dd, *J* = 12.2, 1.4 Hz, 1H), 5.02 (dd, *J* = 12.2, 1.6 Hz, 1H), 5.12 (dd, *J* = 9.9, 3.9 Hz, 1H), 5.28 (dd, *J* = 10.5, 3.9 Hz, 1H), 5.39 (t, *J* = 9.5 Hz, 1H), 5.64 (d, *J* = 3.9 Hz, 1H), 5.69 (t, *J* = 9.7 Hz, 1H), 5.79 (d, *J* = 3.9 Hz, 1H), 5.82−5.95 (m, 2H), 6.12 (t, *J* = 9.9 Hz, 2H), 7.07−7.25 (m, 12H), 7.29−7.67 (m, 25H), 7.67−7.77 (m, 6H), 7.87 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.96 (dd, *J* = 8.3, 1.1 Hz, 2H), 8.03−8.08 (m, 2H), 8.14−8.20 (m, 2H), 8.55 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.6, 62.4, 62.8, 63.0, 69.1, 69.3, 70.0, 70.5, 70.6, 70.7, 71.0, 71.7, 73.3, 73.7, 75.1, 76.0, 77.4, 80.2, 96.8, 96.9, 112.1, 127.9, 128.1, 128.1, 128.2, 128.2, 128.2, 128.2, 128.3, 128.3, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5, 128.5, 128.5, 128.7, 128.7, 128.7, 128.8, 128.8, 128.9, 129.1, 129.4, 129.5, 129.6, 129.6, 129.7, 129.7, 129.7, 129.7, 129.8, 129.8, 129.8, 129.9, 129.9, 129.9, 130.0, 130.0, 130.0, 130.0, 130.0, 130.0, 130.1, 130.1, 130.1, 130.2, 133.1, 133.1, 133.2, 133.3, 133.4, 133.4, 133.5, 133.6, 133.7, 133.7, 134.6, 150.2, 163.2, 164.7, 164.8, 165.2, 165.4, 165.4, 165.7, 165.7, 165.9, 166.0, 166.1; IR ($CHCl_3$) 3598, 2925, 2853, 2361, 1732, 1415, 1315, 1269, 1095, 1028, 709 cm^{-1}; HRMS (TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{93}H_{76}N_2O_{27}Na^+$ 1675.4528, found 1675.4519.

β-D-Ribofuranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**17**). This compound was prepared from orthoester **1a** (5.0 g, 10.0 mmol) as the starting material: yield 2.8 g, 96%; $[\alpha]^{25}_{D}$ = +36.1 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$,399.78 MHz) δ 2.42 (t, *J* = 2.4 Hz, 1H), 3.25 (bs, 2H), 3.50−3.60 (m, 2H), 3.69−3.79 (m, 1H), 3.97 (dd, *J* = 8.3, 5.4 Hz, 1H), 4.01 (d, *J* = 2.4 Hz, 2H), 4.78 (t, *J* = 4.4, 3.9 Hz, 1H), 5.99 (d, *J* = 4.0 Hz, 1H), 7.32−7.40 (m, 3H), 7.64 (dd, *J* = 6.7, 2.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 51.6, 59.8, 70.3, 73.9, 79.2, 79.5, 80.5, 104.0, 122.9, 126.0, 126.1, 128.2, 128.3, 129.6, 135.0; IR ($CHCl_3$) 770, 960, 1039, 1291, 1451, 1537, 1641, 2352, 2928, 3285, 3397 cm^{-1}; HRMS (TOF) *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{16}NaO_6^+$ 315.0839, found 315.0839.

5-O-(tert-Butyldiphenylsilyl)-β-D-arabinofuranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**18**). This compound was prepared from compound **17** (2.8 g, 9.6 mmol) as the starting material: yield 4.1 g, 80%; $[\alpha]^{25}_{D}$ = +21.7 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$,399.78 MHz) δ 1.06 (d, *J* = 1.6 Hz, 9H), 2.18 (bs, 1H), 2.42 (td, *J* = 2.5, 1.0 Hz, 1H), 3.53−3.60 (m, 1H), 3.78 (ddd, *J* = 11.8, 3.8, 1.1 Hz, 1H), 3.88−3.94 (m, 1H), 4.12 (ddd, *J* = 5.9, 2.3, 0.8 Hz, 2H), 4.15−4.21 (m, 1H), 4.93 (t, *J* = 4.7 Hz, 1H), 6.15 (d, *J* = 4.1 Hz, 1H), 7.36−7.44 (m, 10H), 7.64−7.71 (m, 5H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.4, 26.9, 26.9, 26.9, 51.8, 62.0, 71.2, 73.9, 79.5, 79.7, 81.7, 104.6, 123.3, 126.3, 126.3, 127.8, 127.8, 127.8, 127.8, 128.6, 128.6, 129.8, 129.8, 129.9, 133.2, 133.3, 134.9, 135.6, 135.7, 135.7, 135.7; IR ($CHCl_3$) 700, 771, 1039, 1109, 1285, 1455, 1722, 2353, 2864, 2935, 3062, 3289, 3546 cm^{-1}; HRMS (TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{34}O_6NaSi^+$ 553.2017, found 553.2022.

2-O-Benzoyl-5-O-(tert-butyldiphenylsilyl)-β-D-arabinofuranoside (Prop-2-yn-1-yl)-1,2-orthobenzoate (**19**). This compound was prepared from compound **18** (4.1 g, 7.7 mmol) as the starting material: yield 4.4 g, 91%; $[\alpha]^{25}_{D}$ = +66.7 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$,399.78 MHz) δ 1.15 (s, 9H), 2.50 (t, *J* = 2.5 Hz, 1H), 3.89 (dd, *J* = 11.8, 3.0 Hz, 1H), 3.98 (dt, *J* = 8.9, 2.4 Hz, 1H), 4.05 (dd, *J* = 11.8, 1.4 Hz, 1H), 4.19−4.21 (m, 2H), 4.24 (dd, *J* = 8.9, 4.7 Hz, 1H), 4.71 (d, *J* = 11.7 Hz, 1H), 4.93 (d, *J* = 11.7 Hz, 1H), 5.07 (t, *J* = 4.4 Hz, 1H), 6.23 (d, *J* = 4.1 Hz, 1H), 7.41−7.52 (m, 13H), 7.74−7.80 (m, 5H), 7.83−7.89 (m, 2H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 19.4, 26.8, 26.8, 26.9, 51.6, 61.3, 72.2, 73.6, 76.6, 77.4, 77.9, 79.9, 104.8,

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123.4, 126.5, 126.5, 127.7, 127.7, 127.7, 127.7, 127.9, 127.9, 128.0, 128.3, 128.5, 128.5, 129.5, 129.7, 129.7, 133.1, 133.4, 134.9, 135.5, 135.5, 135.6, 135.6, 135.8, 137.6; IR ($CHCl_3$) 1046, 1108, 1290, 1455, 2334, 2359, 2856, 2927, 2959, 3036, 3067, 3291 cm^{-1}; HRMS (TOF) m/z $[M + Na]^+$ calcd for $C_{38}H_{40}NaO_6Si^+$ 643.2486, found 643.2491.

*1-(2-O-Benzoyl-3-O-benzyl-5-O-(tert-butyldiphenylsilyl)-β-D-ribofuranosyl)thymine (**20**).* This compound was prepared from compound **19** (1.0 g, 1.6 mmol) as the starting material: yield 0.9 g, 76%; $[\alpha]^{25}_D$ = +12.6 (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$, 399.78 MHz) δ 1.14 (s, 9H), 1.59 (d, *J* = 0.7 Hz, 3H), 3.73 (dd, *J* = 11.7, 2.1 Hz, 1H), 4.03 (dd, *J* = 11.7, 1.9 Hz, 1H), 4.19−4.23 (m, 1H), 4.40−4.55 (m, 2H), 4.64 (d, *J* = 11.6 Hz, 1H), 5.50 (t, *J* = 5.9 Hz, 1H), 6.47 (d, *J* = 6.2 Hz, 1H), 7.16−7.25 (m, 5H), 7.38−7.49 (m, 9H), 7.56−7.63 (m, 1H), 7.66−7.73 (m, 4H), 8.03−8.17 (m, 2H), 9.13 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.1, 19.5, 27.2, 27.2, 27.2, 63.6, 73.4, 75.0, 76.2, 77.4, 84.0, 86.2, 111.8, 128.0, 128.1, 128.1, 128.1, 128.1, 128.1, 128.2, 128.5, 128.5, 128.7, 128.7, 129.1, 130.2, 130.2, 130.3, 132.3, 132.9, 133.7, 135.2, 135.4, 135.4, 135.7, 135.7, 137.3, 150.6, 163.9, 165.8; IR ($CHCl_3$)3196, 3068, 2930, 2857, 1706, 1466, 1427, 1267, 1111, 704 cm^{-1}; HRMS (TOF) m/z $[M + H]^+$ calcd for $C_{40}H_{43}N_2O_7Si^+$ 691.2834, found 691.2844.

*1-(3-O-Benzyl-5-O-(tert-butyldiphenylsilyl)-β-D-ribofuranosyl)-thymine (**21**).* This compound was prepared from compound **20** (0.1 g, 0.14 mmol) as the starting material: yield 81 mg, 95%; $[\alpha]^{25}_D$ = +14.4 (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$, 399.78 MHz) δ 1.08 (s, 9H), 1.59 (d, *J* = 1.1 Hz, 3H), 3.34 (s, 1H), 3.65 (dd, *J* = 11.5, 2.0 Hz, 1H), 3.94 (dd, *J* = 11.6, 2.1 Hz, 1H), 4.10−4.16 (m, 2H), 4.25 (s, 1H), 4.62 (q, *J* = 11.7 Hz, 2H), 6.01 (d, *J* = 6.4 Hz, 1H), 7.28−7.49 (m, 12H), 7.57−7.67 (m, 4H), 8.86 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.1, 19.5, 27.1, 27.1, 27.2, 63.9, 73.0, 74.2, 77.4, 83.1, 88.5, 111.6, 128.1, 128.1, 128.2, 128.2, 128.3, 128.3, 128.5, 128.8, 128.8, 130.2, 130.3, 132.4, 132.9, 135.3, 135.4, 135.4, 135.6, 135.7, 136.9, 150.9, 163.7; IR ($CHCl_3$) 3187, 3068, 2928, 2856, 1696, 1468, 1427, 1267, 1112, 703 cm^{-1}; HRMS (TOF) m/z $[M + H]^+$ calcd for $C_{33}H_{39}N_2O_6Si^+$ 587.2572, found 587.2577.

*1-(2-O-Benzoyl-5-O-tert-butyldiphenylsilyl-β-D-ribofuranosyl)-thymine (**22**).* This compound was prepared from compound **20** (0.1 g, 0.14 mmol) as the starting material: yield 72 mg, 83%; $[\alpha]^{25}_D$ = −19.9 (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$, 399.78 MHz) δ 1.11 (s, 9H), 1.49 (d, *J* = 0.9 Hz, 3H), 4.02−4.12 (m, 2H), 4.32 (d, *J* = 2.3 Hz, 1H), 4.42 (d, *J* = 9.1 Hz, 1H), 4.46−4.58 (m, 1H), 5.54 (dd, *J* = 5.7, 2.5 Hz, 1H), 6.33 (d, *J* = 7.1 Hz, 1H), 7.33−7.48 (m, 8H), 7.49−7.61 (m, 2H), 7.62−7.75 (m, 4H), 8.16 (dd, *J* = 8.2, 1.2 Hz, 2H), 9.85 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.0, 19.5, 27.1, 27.1, 27.2, 63.9, 73.4, 74.5, 77.3, 83.8, 87.6, 112.1, 128.1, 128.1, 128.2, 128.2, 128.5, 129.3, 130.2, 130.2, 130.2, 130.3, 132.0, 133.0, 133.6, 135.1, 135.3, 135.3, 135.6, 135.6, 151.4, 164.2, 166.3; IR ($CHCl_3$) 3623, 2927, 2855, 2413, 2116, 1650, 1268, 1110, 772 cm^{-1}; HRMS (TOF) m/z $[M + H]^+$ calcd for $C_{33}H_{37}N_2O_7Si^+$ 601.2365, found 601.2370.

*1-(2-O-Benzoyl-3-O-benzyl-β-D-ribofuranosyl)thymine (**23**).* This compound was prepared from compound **20** (0.1 g, 0.14 mmol) as the starting material: yield 60 mg, 92%; $[\alpha]^{25}_D$ = −15.8 (*c* 1.00, $CHCl_3$); ^1H NMR ($CDCl_3$, 399.78 MHz) δ 1.91 (d, *J* = 1.0 Hz, 3H), 2.61 (s, 1H), 3.74 (dd, *J* = 12.7, 2.5 Hz, 1H), 3.97 (dd, *J* = 12.2, 2.2 Hz, 1H), 4.23 (dt, *J* = 5.2, 2.4 Hz, 1H), 4.48−4.59 (m, 2H), 4.65 (d, *J* = 11.4 Hz, 1H), 5.65 (dd, *J* = 5.5, 4.6 Hz, 1H), 5.96 (d, *J* = 4.5 Hz, 1H), 7.24 (s, 5H), 7.35 (d, *J* = 1.3 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.54−7.65 (m, 1H), 8.07 (dd, *J* = 8.2, 1.3 Hz, 2H), 8.83 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.53 MHz) δ 12.6, 61.7, 73.5, 74.6, 75.7, 83.7, 90.9, 111.5, 128.1, 128.1, 128.2, 128.5, 128.5, 128.6, 128.6, 129.1, 130.0, 130.1, 133.7, 137.3, 137.5, 150.3, 163.7, 165.9; IR ($CHCl_3$) 3649, 2924, 2853, 2101, 1660, 1455, 1266, 1115, 762 cm^{-1}; HRMS (TOF) m/z $[M + H]^+$ calcd for $C_{24}H_{25}N_2O_7^+$ 453.1656, found 453.1662.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H, ^{13}C, and DEPT NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

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