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First example of 5/6-O-linked pseudosaccharides: synthesis of bicyclic nucleosides containing azido or extended carbohydrate moiety

Joy Krishna Maity,[a] Subhranshu Mukherjee,[a] Michael G. B. Drew,[b] Basudeb Achari[a] and Sukhendu B. Mandal[a,*]

[a]*Division of Chemistry, Indian Institute of Chemical Biology, 4, Raja S. C. Mullick Road, Jadavpur, Kolkata 700 032, India*
[b]*Department of Chemistry, University of Reading, Whiteknights, Reading RG6 6AD, UK*

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Abstract—Treatment of the D-glucose-derived substrate **1** with sodium hydride in tetrahydrofuran provided 3,6-anhydro monosaccharide **2**, along with the 5,6-ether linked pseudodisaccharide **3**, and pseudotrisaccharide **4**. However, reaction of **1** with sodium ethoxide in ethanol afforded **2** as the sole product, elaborated to the bicyclic azidonucleosides **9** and **16**. Acetylated bicyclic nucleosides **17**–**19** with extended carbohydrate residues have been synthesized from **3**.

Keywords: Pseudosaccharides; Synthesis; Azido bicyclic nucleosides; Carbohydrate; D-Glucose

1. Introduction

Bicyclic nucleosides[1] are derived by the replacement of the natural furanose sugar moiety with a bicyclic ring structure. Such replacement results in the diminution of the conformational freedom of the nucleosides.[2] A plethora of conformationally restricted bicyclic nucleosides have been synthesized for potential antiviral, antitumor, and other biological activities. Bicyclic nucleosides have been encountered in natural sources too. Among them, the most notable are the griseolic acids[3] (having furano-furan skeleton), which are known to inhibit the 3′,5′-cyclic nucleotide phosphodiesterase. Other bicyclic nucleosides such as ezomycins, quantamycin, and malayamycins (all with furanopyran skeleton) are antibiotics having interesting properties.[4] The common structural motif present in some of these products is an extended carbohydrate moiety. The fact that the location of such structural features in the nucleosides imparts various antibiotic properties encouraged researchers to take up programs on the synthesis of conformationally restricted glycotriazole-tethered nucleoside/nucleotide analogues,[5] which have not been adequately explored so far. Keeping this in mind, we took up the synthesis of glucose-derived bicyclic nucleosides with azido functionality at C-2′ and C-5′. In the process, we could also synthesize the hitherto unknown 5,6-ether linked pseudosaccharides and characterize a representative member unequivocally through X-ray crystallographic structure determination. It is pertinent to mention here that a 5,4-ether linked disaccharide has been identified as a structural element of the exotoxin of *Bacillus thuringiensis* and synthesized by Prystaš and Šorm,[6] while 6,6′-ether linked disaccharides have been synthesized by Ikegami's group[7] and by Haines[8] to establish the structure of a natural product[9] having antidiabetic activity.

2. Results and discussion

2.1. Synthesis of pseudosaccharides 2–4 from 1

We initially treated the glucose-derived precursor **1**[10] with sodium hydride in tetrahydrofuran, hoping to

* Corresponding author. Tel.: +91 33 2473 3491; fax: +91 33 24735197; e-mail: sbmandal@iicb.res.in

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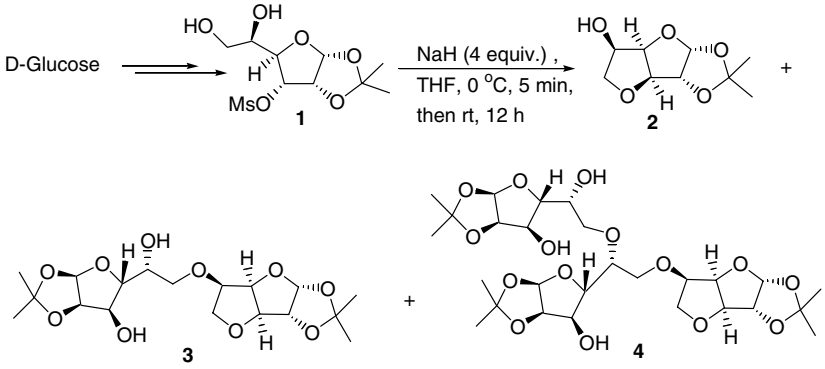
produce the fused bis-tetrahydrofuran (the skeleton present in furanodictines[11]) analogue **2**.[12] Interestingly, the reaction mixture yielded (Scheme 1), in addition to **2**, the hitherto unknown pseudodisaccharide **3** and pseudotrisaccharide **4** (both 5,6-ether linked). On the other hand, treatment of **1** with sodium ethoxide in ethanol furnished **2** as the sole product (in 76% yield). Previous workers[6–8] used the reaction of an appropriate sugar alkoxide with a suitable sugar–iodide/–tosylate/–triflate to obtain 5,4- and 6,6′-ether linked disaccharides. The present transformation, however, differs in having an internal functional group migration, which precedes the coupling step.

Formation of products **2**–**4** was found to depend on the concentration of the starting material **1** (Table 1). As the concentration of **1** increases, the yields of **2** and **3** decrease with simultaneous increase in the yield of **4**.

The occurrence of these products suggested that the nucleophilic attack of the C-6 hydroxyl group in **1** occurred in two different ways. Intramolecular attack on C-3 (bearing mesyl group) resulted in the formation of the cyclic product **2**. On the other hand, an intramolecular transfer of the mesyl functionality from C-3 to C-6 through the nucleophilic attack of the C-6 hydroxyl group (or stepwise migration of the mesyl group via C-5) produced the non-isolable intermediate **5a**, which could also lead to epoxide **5b** (Fig. 1). Either of these intermediates upon reaction with the hydroxyl group of **2** could have generated **3**, which subsequently yielded **4** after reaction with another molecule of **5a** or **5b**. The possible formation of the C-5 epimer of **5b** through the attack of C-6 OH on the C-5 mesylate could be ruled out from the structure of product **3**.

The presence of signals for four methyl groups and two anomeric centers together with other expected signals in the ^{1}H and ^{13}C NMR, and the location of a peak at m/z 427 $(MNa)^{+}$ in the mass spectrum of **3** proved helpful for deducing the gross structure. Finally, the structure and relative stereochemistry were established from an X-ray analysis (Fig. 2), which showed that there are two molecules in the asymmetric unit with equivalent geometries. With **4**, the location of the molecular ion peak m/z: 629 $(M+Na)^{+}$ in the mass spectrum coupled with the preliminary analysis of the NMR spectra suggested the coupling of another molecule of monoacetonide glucose. Almost all the NMR signals of **3** were repeated, pointing to the presence of this moiety in **4**. Due to the close chemical shifts of virtually all proton and carbon signals assigned to the two monocyclic units, an unambiguous structure assignment was difficult. However, starting from the anomeric proton signals of the two furanoside units, analysis of the ^{1}H–^{1}H COSY spectrum revealed that the two H-3 signals resonated at 4.14 ppm. These were coupled to the two OH doublet signals located at δ 3.15 and δ 3.27, ruling out an ether linkage involving either of the hydroxyl groups. This



Scheme 1. One-pot generation of pseudosaccharides **2**, **3**, and **4** from **1**.

Table 1. Concentration dependent formation of **2**, **3**, and **4** from **1**

1 $\xrightarrow[\text{THF, 0 °C, 5 min, then rt,12 h}]{\text{4 molar equiv. NaH,}}$ **2** + **3** + **4**

1 g[a] (mmol)	THF (mL)	Concn (mM)	**2** g[a] (%)[b]	**3** g[a] (%)[b]	**4** g[a] (%)[b]
0.25 (0.84)	250	3.36	0.068 (40)	0.108 (32)	—
2.0 (6.71)	75	89.5	0.474 (35)	0.758 (28)	0.122 (3)
5.0 (16.8)	50	336.0	1.080 (32)	1.550 (23)	0.506 (5)

[a] Amount taken/isolated.
[b] Isolated yield.

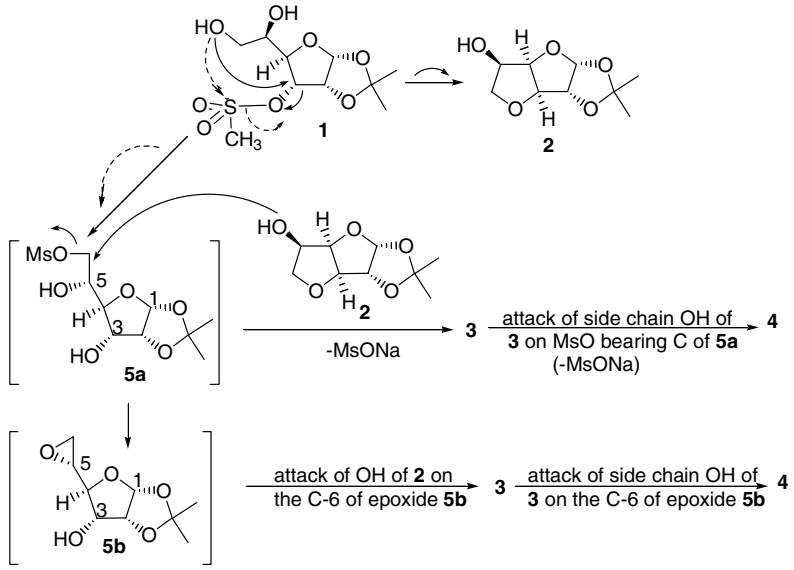


Figure 1. Proposed mechanism for the formation of **2**, **3**, and **4**.

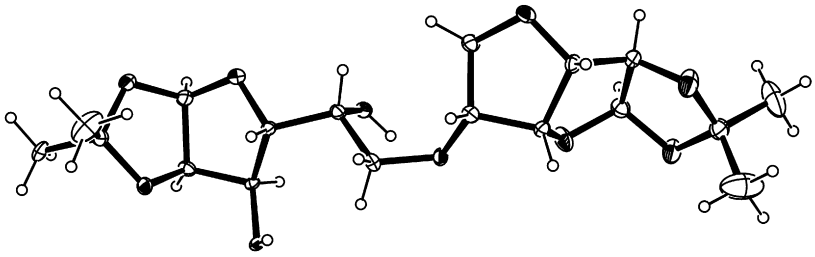


Figure 2. ORTEP diagram of **3**, with ellipsoids at 25% probability.

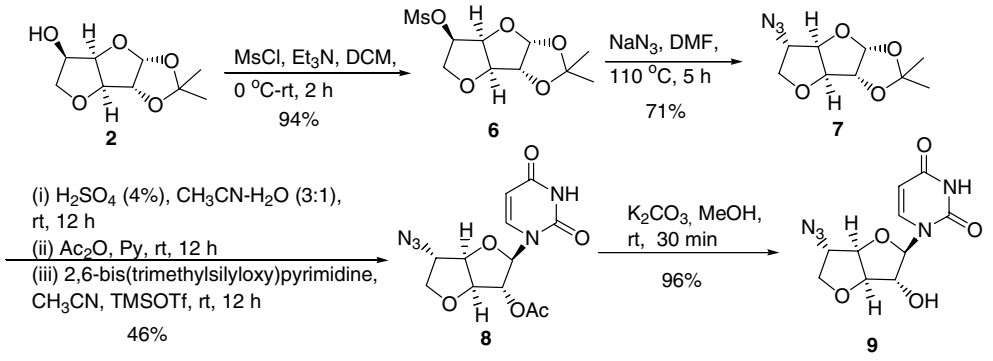
pointed to a 5,6-ether linkage, taking into account the preference for such bonding in the co-occurring product **3**.

We then focused our attention on the synthesis of azido nucleosides. For this, **2** was treated with methane sulfonylchloride to produce **6**. An azido group was then introduced by heating with sodium azide in dimethyl formamide to furnish **7** (inversion of stereochemistry expected through S_N2 displacement of the mesyloxy substituent[13]). Removal of the 1,2-*O*-isopropylidene group of **7** (Scheme 2) and peracetylation thereafter yielded a mixture of anomeric acetates. Installation of a uracil moiety at C-1 of the acetates under Vorbrüggen glycosidation condition[14] (to afford **8**) followed by deacetylation smoothly furnished the targeted nucleoside derivative **9**.

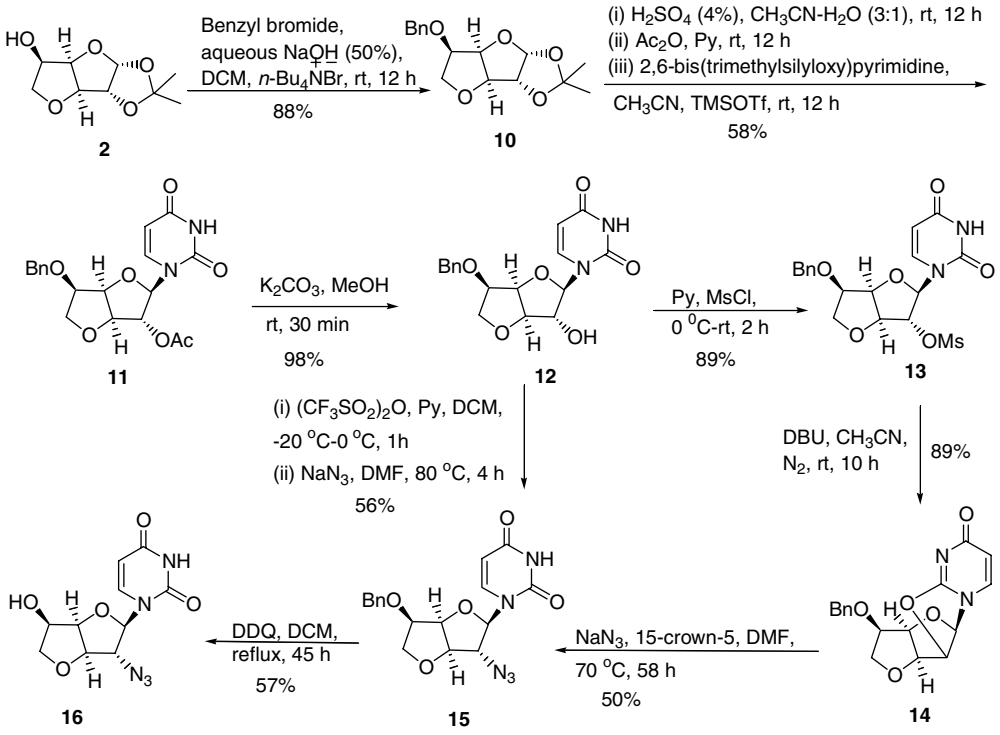
For the synthesis of the 2′-azido analogues, we next chose to protect the free hydroxyl group of **2** by benzylation, since benzyl ether is stable in the basic conditions that are required for subsequent functional group manipulations. Thus, **2** was initially treated with benzyl bromide to yield **10**[15] (Scheme 3). This after acetonide cleavage followed by peracetylation and reaction with uracil using Vorbrüggen procedure yielded **11**, which was deacetylated to **12**. Mesylation of the hydroxyl group of **12** furnished **13**. Exposure of this product to DBU triggered an intramolecular S_N2 attack producing the 2,2′-anhydro derivative **14**. Finally, introduction of azido group at 2′-C was successfully accomplished by heating **14** with sodium azide in DMF to furnish azidonucleoside **15**, which after debenzylation[16] afforded the fully deprotected bicyclic azidonucleoside **16** in good yield.

2.2. Synthesis of azido bicyclic nucleosides

In an attempt to obtain the azido epimer of **15**, we next subjected **12** to treatment with triflic anhydride and pyridine at low temperature. The product was then directly heated with NaN_3 to isolate the azido nucleoside, which, however, proved to be identical with **15** by spectroscopic analysis. Evidently, the reaction with triflic anhydride was also accomplished by an initial intramolecular S_N2 displacement to produce the cyclic ether **14** prior to substitution by azide during heating of the reaction mixture in DMF.



Scheme 2. Synthesis of 5′-azido bicyclic nucleoside **9**.



Scheme 3. Synthesis of 2′-α-azido bicyclic nucleoside **16**.

Regarding the structures of the azidonucleosides, the presence of the azido functionality was confirmed by the appearance of a peak at $\nu_{max} \sim 2100\ cm^{-1}$ in their IR spectra. Presence of the uracil unit could be deduced from the usual NMR spectral evidences. In the ^1H NMR spectrum of **8**, for example, signals for H-5 and H-6 were observed at δ 5.82 (d) and 7.34 (d), while the ^{13}C NMR spectrum contained signals for two olefinic methine carbons (δ 103.9 and 139.8) and two carbonyl carbons (δ 150.3 and 163.1). The incoming heterocyclic ring must be trans to the 2′-OAc group, as a dioxolonium intermediate with cis-geometry is known to be formed in such cases owing to the participation of the C-2′–OAc group.

In support, the ^1H NMR spectrum of **8** displayed two doublets at δ 6.11 and 5.20 ($J_{1',2'} = 3.0$ Hz, $J_{2',3'} = 0$ Hz) for the protons H-1′ and H-2′ (glucose numbering), respectively, the $J_{2',3'}$ value suggesting a trans relationship between H-2′ and H-3′. The relative disposition of H-4′ and H-5′ was also established from the appearance of a doublet at δ 4.59, ascribed to H-4′ with $J_{4',5'} = 0$ Hz. The peak observed at m/z 324 $(M+H)^+$ in the ESIMS of **8** was in agreement with the structure. Similar spectral data (^1H and ^{13}C NMR) were also obtained for the bicyclic nucleosides **9**, **11**–**13**, **15**, and **16**. Cis-disposition of H-4′ and H-5′ in **11**–**13**, **15**, and **16** was ascertained by the presence of a triplet ($J = 4.5$ Hz) around δ 4.8–5.0 assigned to H-4′. Mass

spectra and IR spectra of these nucleosides were also in conformity with their assigned structures.

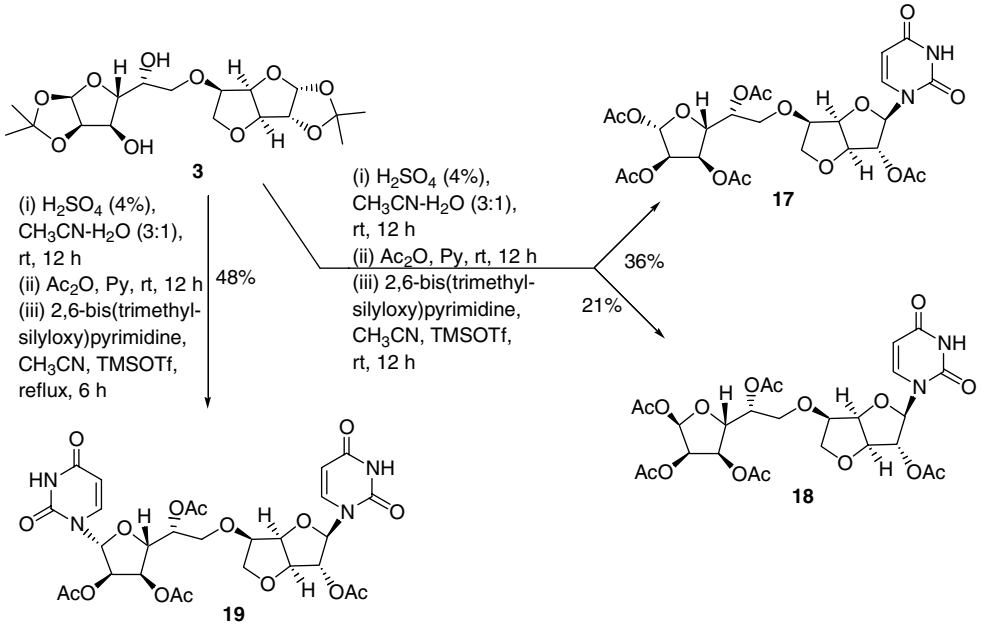
2.3. Conversion of 3 to the bicyclic nucleosides

The serendipitous formation of pseudosaccharide **3** by treating **1** with sodium hydride prompted us to attempt the synthesis of bicyclic nucleosides with a 5,6-ether linked carbohydrate residue and of a bisnucleoside. To this end, removal of the two acetonide protections of **3** by acid treatment (Scheme 4) was followed by peracetylation. Finally, partial introduction of one uracil moiety could be smoothly effected at room temperature under Vorbrüggen glycosidation condition. This afforded the C-1 isomeric nucleosides **17** (36%) and **18** (21%). However, the same reaction when carried out at refluxing temperature afforded bisnucleoside **19** (48%).

The FABMS of the pseudodisaccharide nucleosides **17** and **18** showed protonated molecular ion peaks at *m/z* 629 indicating their isomeric nature (with one uracil moiety). On the other hand, ESIMS of **19** displayed a peak at *m/z* 703 $(M+Na)^+$ agreeable with the presence of two uracil moieties. The ^1H–^1H COSY, ^1H–^{13}C HSQC, and ^1H–^{13}C HMBC spectra of **18** clearly identified all the signals establishing the disposition of the uracil heterocycle in the bicyclic framework. The anomeric proton (and carbon) resonances of the two halves of **18** were quite close (δ 6.13 and 5.97), but the δ 6.13 signal showed distinct HMBC correlation with the uracil C-2 and C-6 resonances, while the δ 5.97 signal was correlated with one of the acetate carbonyl resonances (δ 169.4). The *J* value for the proton signal (δ 6.13) carrying the base was lower (~3.0 Hz) compared to the other proton (δ 5.97, $J = 8.5$ Hz), which bears cis relationship with the neighboring proton. The other signals could be assigned easily based mainly on ^1H–^1H COSY spectrum. Of particular importance was the fact that the H-3 resonance assigned to the bicyclic unit was observed as a doublet (though showing a weak cross peak with the H-2 resonance) while the corresponding proton of the monocyclic unit forms a triplet. This is expected due to the inversion at C-3 during the formation of the second furan ring. The formation of the two products **17** and **18** at room temperature, while that of **19** requiring heating condition, suggests the greater reactivity of the bicyclic system under the reaction condition. However, the exact cause of the difference in reactivity of the two units is not apparent at the moment. Similar spectra (^1H and ^{13}C NMR) were obtained for **17** also. The $J_{1,2}$ values for the furanoside units in **17** and **18** (3.8 Hz and 8.4 Hz, respectively) are indicative of the 1,2-trans and -cis relationships (in the non-nucleosidic part).

3. Conclusion

In conclusion, a simple one-pot reaction has generated 5,6-ether linked pseudosaccharides from a D-glucose-derived substrate. A change in the reaction condition afforded the cyclic 3,6-anhydro pseudomonosaccharide exclusively. X-ray crystal structure determination (Supplementary data) of **3** has conclusively established the structure. Some of these products were elaborated to bicyclic azidonucleosides and related bicyclic nucleosides, which could be potential antiviral agents. Investigation on the scope of the strategy to synthesize other



Scheme 4. Conversion of **3** to the bicyclic nucleosides **17**–**19**.

complex bicyclic nucleoside ring systems utilizing click chemistry is under study.

4. Experimental

4.1. General experimental

Melting points were taken in open capillaries and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$, C_5D_5N, or D_2O as solvent using TMS as internal standard. Mass spectra were recorded using EI or FAB or ESI mode. Specific rotations were measured at 589 nm. Pre-coated plates (0.25 mm, Silica Gel 60 F_{254}) were used for TLC.

4.1.1. 3,6-Anhydro-1,2-*O*-isopropylidene-α-D-glucofuranose (2), 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-(1,2-*O*-isopropylidene-α-D-allofuranos-6-yl)-α-D-glucofuranose (3), 3,6-anhydro-1,2-*O*-isopropylidene-5-*O*-(1,2-*O*-isopropylidene-5-*O*-[1,2-*O*-isopropylidene-α-D-allofuranos-6-yl]-α-D-allofuranos-6-yl)-α-D-glucofuranose (4). (i) Using NaH: Oil-free NaH (4.0 equiv) was added portionwise to a solution of **1** (1 equiv) in dry THF (specified volumes in Table 1) at 0 °C under N_2 and the mixture was stirred for 30 min at room temperature for 12 h, when TLC showed complete disappearance of **1**. Excess NaH was destroyed by adding aqueous NH_4Cl solution. The solvent was evaporated in vacuo and the residue was extracted with $CHCl_3$ (3 × 40 mL). The $CHCl_3$ solution was washed with brine, dried (Na_2SO_4), and concentrated to afford a solid mass, which was then purified by column chromatography on silica gel (60–120 mesh). Elution with $CHCl_3$–petroleum ether (80:20) furnished **2**[15] and elution with $CHCl_3$–MeOH in 99:1 and 98:2 ratios afforded **3** and **4**, respectively, as white solids.

(ii) Using NaOEt: To a solution of sodium ethoxide [NaOEt was prepared by the addition of Na (350 mg) to dry EtOH (20 mL) at 0 °C and stirring for 1 h] was added a solution of **1** (503 mg, 1.69 mmol) in dry EtOH (20 mL) and the reaction mixture was stirred at 0 °C for 2 h. The reaction was quenched by the addition of satd aq NH_4Cl solution. The solvent was evaporated in vacuo and the residue was extracted with $CHCl_3$ (3 × 25 mL). The $CHCl_3$ solution was washed with H_2O (2 × 20 mL), dried (Na_2SO_4) and concentrated. The crude product was chromatographed using $CHCl_3$–petroleum ether (80:20) as eluent to give **2** (260 mg, 76%).

Compound **2**: Syrup; $[\alpha]_D^{25}$ +32.0 (*c* 0.50, $CHCl_3$) [lit.[15] $[\alpha]_D^{20}$ +15.0 (*c* 1, $CHCl_3$) and $[\alpha]_D^{20}$ +30.0 (*c* 1, H_2O)].

Compound **3**: Crystalline solid; mp 124 °C; $[\alpha]_D^{25}$ +61.5 (*c* 0.13, $CHCl_3$); IR (KBr): ν_{max} 3384, 1646, 1453, 1375, 1225, 1164, 1124, 1089, 1060, 1018, 886 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 3H), 1.37 (s, 3H), 1.49 (s, 3H), 1.59 (s, 3H), 3.67 (t, 1H, J = 8.0 Hz), 3.75 (dd, 1H, J = 6.0, 10.0 Hz), 3.81 (dd, 1H, J = 3.4, 10.0 Hz), 3.87 (dd, 1H, J = 4.0, 8.5 Hz, overlapping a multiplet, 1H), 4.00 (t, 1H, J = 7.0 Hz), 4.05–4.19 (m, 4H), 4.51 (d, 1H, J = 3.5 Hz), 4.59 (d, 1H, J = 3.4 Hz), 4.63 (d, 1H, J = 4.3 Hz), 4.86 (t, 1H, J = 3.6 Hz), 5.79 (d, 1H, J = 3.6 Hz), 5.98 (d, 1H, J = 3.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 26.3 (CH_3), 26.5 (CH_3), 26.6 (CH_3), 27.2 (CH_3), 69.5 (CH_2), 69.9 (CH), 71.0 (CH), 71.5 (CH_2), 79.5 (CH), 80.2 (2 × CH), 80.4 (CH), 84.9 (CH), 85.6 (CH), 103.7 (CH), 106.9 (CH), 112.4 (C), 112.8 (C); ESIMS, *m*/*z*: 427 (M+Na)$^+$. Anal. Calcd for $C_{18}H_{28}O_{10}$: C, 53.46; H, 6.98. Found: C, 53.18; H, 6.70.

Compound **4**: White solid; $[\alpha]_D^{25}$ +42.4 (*c* 0.22, $CHCl_3$); IR (KBr): ν_{max} 3400, 1452, 1373, 1215, 1166, 1130, 1106, 1060, 1025, 880 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz): δ 1.32 (s, 3H), 1.36 (s, 3H), 1.37 (s, 3H), 1.49 (s 3H), 1.56 (s, 3H), 1.59 (s, 3H), 3.15 (d, 1H, J = 9.6 Hz), 3.27 (d, 1H, J = 6.0 Hz), 3.66 (t-like, 1H, J = 7.8, 9.0 Hz, overlapping a broad signal, 1H), 3.71 (dd, 1H, J = 2.4, 8.4 Hz), 3.79 (m, 1H), 3.85 (m, 4H), 3.90 (dd, 1H, J = 9.6, 11.4 Hz), 3.96 (d, 1H, J = 7.2 Hz), 3.97 (d, 1H, J = 7.2 Hz), 4.06 (m, 1H), 4.14 (m, 2H), 4.51 (d, 1H, J = 3.6 Hz), 4.59 (d, 1H, J = 4.2 Hz), 4.60 (partially merged t, 1H, J = 4.5 Hz), 4.62 (t, 1H, J = 4.2 Hz), 4.87 (t, 1H, J = 4.2 Hz), 5.78 (d, 1H, J = 3.6 Hz), 5.79 (d, 1H, J = 3.6 Hz), 6.00 (d, 1H, J = 3.6 Hz); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 26.4 (CH_3), 26.5 (CH_3), 26.6 (CH_3), 26.7 (CH_3), 26.7 (CH_3), 27.3 (CH_3), 69.4 (CH_2), 70.5 (CH), 70.6 (CH_2), 71.5 (CH), 71.6 (CH), 73.5 (CH), 79.2 (CH), 79.5 (CH), 79.7 (CH), 80.1 (CH), 80.2 (2 × CH), 80.3 (CH), 85.0 (CH), 85.8 (CH), 103.77 (CH), 103.83 (CH), 107.1 (CH), 112.5 (C), 112.8 (C), 112.9 (C); ESIMS, *m*/*z*: 629 (M+Na)$^+$. Anal. Calcd for $C_{27}H_{42}O_{15}$: C, 53.46; H, 6.98. Found: C, 53.22; H, 6.73.

4.1.2. 3,6-Anhydro-1,2-*O*-isopropylidene-5-*O*-mesyl-α-D-glucofuranose (6). Methane sulfonyl chloride (0.46 mL, 5.90 mmol) was added to an ice-cold solution of **2** (496 mg, 2.46 mmol) in dry CH_2Cl_2 (20 mL) and the mixture was stirred for 5 min. Et_3N (1.16 mL, 8.36 mmol) was added dropwise to the mixture and the stirring was continued for 2 h. The organic solvent was washed repeatedly with satd aq $NaHCO_3$ (3 × 30 mL) and water (3 × 30 mL), dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography on silica gel using CH_3CO_2Et–petroleum ether (15:85) as eluent to furnish **6** (650 g, 94%) as a whitish yellow solid: $[\alpha]_D^{25}$ +49.7 (*c* 0.55, $CHCl_3$); IR (KBr): ν_{max} 1376, 1318, 1267, 1210, 1177, 1163, 1070, 1037, 850 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.34 (s, 3H), 1.49 (s, 3H), 3.14 (s, 3H), 3.81 (t-like, 1H, J = 8.0, 8.7 Hz), 4.09 (dd, 1H, J = 6.9, 8.8 Hz), 4.55 (d, 1H, J = 3.4 Hz), 4.62 (d, 1H, J = 3.5 Hz), 4.97 (t, 1H, J = 3.6 Hz), 5.02–5.08 (m, 1H), 5.98 (d, 1H,

$J = 3.4$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 27.1 (CH_3), 27.8 (CH_3), 39.6 (CH_3), 69.2 (CH_2), 77.5 (CH), 81.0 (CH), 85.2 (CH), 85.6 (CH), 107.7 (CH), 113.4 (C); ESIMS, *m/z*: 303 $(M+Na)^+$. Anal. Calcd for $C_{10}H_{16}O_7S$: C, 42.85; H, 5.75. Found: C, 42.68; H, 5.67.

4.1.3. 3,6-Anhydro-5-azido-5-deoxy-1,2-*O*-isopropylidene-β-L-ido-furanose (7). A mixture of **6** (600 mg, 2.14 mmol) and NaN_3 (1.39 g, 21.4 mmol) in anhydrous DMF (15 mL) was heated at 110 °C for 6 h. The reaction mixture was cooled to room temperature and the solvent was evaporated under reduced pressure. The residue was extracted with $CHCl_3$ (3×30 mL); the combined extract was washed with water, dried (Na_2SO_4), and evaporated in vacuo. The crude product was chromatographed using CH_3CO_2Et–petroleum ether (10:90) as eluent to give **7** (346 mg, 71%) as a colorless liquid: mp 45–47 °C; $[\alpha]_D^{25}$ +30.3 (*c* 0.75, $CHCl_3$) [lit.[15] mp 48–49 °C, $[\alpha]_D^{20}$ +42.0 (*c* 0.5, $CHCl_3$)]; IR (KBr): ν_{max} 3345, 2095, 1459, 1384, 1374, 1342, 1283, 1242, 1082, 1028, 927, 895 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.33 (s, 3H), 1.50 (s, 3H), 3.29 (br d, 1H, 9.5 Hz), 4.00 (dd, 1H, $J = 3.9$, 9.9 Hz), 4.09 (br d, 1H, $J = 3.4$ Hz), 4.61 (t-like, 2H, $J = 3.8$, 4.5 Hz), 4.76 (d, 1H, $J = 3.0$ Hz), 5.85 (d, 1H, $J = 3.5$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 27.0 (CH_3), 27.7 (CH_3), 65.4 (CH), 72.1 (CH_2), 84.5 (CH), 85.9 (CH), 86.5 (CH), 106.9 (CH), 112.9 (C); FABMS, *m/z*: 228 $(M+H)^+$. Anal. Calcd for $C_9H_{13}N_3O_4$: C, 47.57; H, 5.77; N, 18.49. Found: C, 47.50; H, 5.69; N,18.25.

4.1.4. 1-(2-*O*-Acetyl-3,6-anhydro-5-azido-5-deoxy-α-L-ido-furanosyl)uracil (8). Compound **7** (245 mg, 1.08 mmol) was dissolved in 10 mL of H_2SO_4–CH_3CN–H_2O (1:18:6) and stirred at room temperature for 12 h. The solution was neutralized by portionwise addition of solid $CaCO_3$. The precipitate was filtered off and the filtrate was evaporated in vacuo to a gummy mass, which was dried (P_2O_5) under vacuum. It was then treated with pyridine (3 mL) and Ac_2O (1 mL), and the mixture was stirred at room temperature for 12 h. The solvent was evaporated, and the sticky material was dried in vacuo to furnish a diacetate mixture (220 mg), which was subsequently used without purification. A solution of uracil (256 mg, 2.28 mmol) in hexamethyldisilazane (10 mL) and chlorotrimethylsilane (two drops) was heated at 135–140 °C under N_2 for 12 h. The solvent was distilled off under vacuum, and a solution of the residue in CH_3CN (7 mL) was added to a stirred solution of the above diacetate mixture in CH_3CN (5 mL) containing TMSOTf (0.21 mL, 1.17 mmol). The solution was stirred at room temperature for 12 h under N_2, when TLC showed complete disappearance of the starting material. The reaction mixture was neutralized with solid $NaHCO_3$, water (2–3 drops) was added to it, and the solvent was evaporated to a residue, which was extracted with $CHCl_3$–MeOH (98:2; 3×30 mL). The combined extract was washed with brine (2×20 mL), dried (Na_2SO_4) and concentrated to a gummy residue. The crude product was purified by column chromatography on silica gel (60–120 mesh) using CH_3CO_2Et as eluent to afford **8** (160 mg, 46%) as a white solid: $[\alpha]_D^{25}$ +62.2 (*c* 0.38, CH_3OH); IR (KBr): ν_{max} 3195, 2107, 1751, 1702, 1665, 1457, 1376, 1339, 1294, 1236, 1061, 902, 814 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.14 (s, 3H), 3.97 (d, 1H, $J = 9.0$ Hz), 4.00–4.29 (m, 2H), 4.59 (d, 1H, $J = 2.8$ Hz), 4.64 (d, 1H, $J = 2.8$ Hz), 5.20 (d, 1H, $J = 2.8$ Hz), 5.82 (d, 1H, $J = 8.0$ Hz), 6.11 (d, 1H, $J = 3.0$ Hz), 7.34 (d, 1H, $J = 8.1$ Hz), 9.45 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.4 (CH_3), 64.3 (CH), 72.2 (CH_2), 78.9 (CH), 85.2 (CH), 86.1 (CH), 90.1 (CH), 103.9 (CH), 139.8 (CH), 150.3 (C), 163.1 (C), 169.5 (C). ESIMS, *m/z*: 324 $(M+H)^+$; Anal. Calcd for $C_{12}H_{13}N_5O_6$: C, 44.59; H, 4.05; N, 21.66. Found: C, 44.40; H, 4.10; N, 21.38.

4.1.5. 1-(3,6-Anhydro-5-azido-5-deoxy-α-L-idofuranosyl)-uracil (9). To a solution of **8** (88 mg, 0.27 mmol) in dry MeOH (10 mL) was added K_2CO_3 (47 mg, 0.34 mmol), and the mixture was stirred at room temperature for 30 min. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography on silica gel. Elution with CH_3CO_2Et–MeOH (97:3) furnished **9** (73 mg, 96%) as a foamy solid: $[\alpha]_D^{25}$ +30.9 (*c* 0.29, CH_3OH); IR (KBr): ν_{max} 3300, 2111, 1726, 1476, 1395, 1260, 1061, 829 cm^{-1}; ^{1}H NMR (C_5D_5N, 300 MHz): δ 4.01 (dd, 1H, $J = 1.3$, 10.0 Hz), 4.35 (dd, 1H, $J = 4.8$, 10.0 Hz), 4.47 (d, 1H, $J = 3.3$ Hz), 4.91 (s, 3H), 5.85 (d, 1H, $J = 8.1$ Hz), 6.59 (d, 1H, $J = 3.6$ Hz), 7.37 (d, 1H, $J = 8.1$ Hz), 8.21 (br s, 1H), 13.38 (br s, 1H); ^{13}C NMR (C_5D_5N, 75 MHz): δ 65.5 (CH), 72.3 (CH_2), 78.8 (CH), 86.6 (CH), 89.1 (CH), 93.2 (CH), 103.6 (CH), 140.8 (CH), 152.0 (C), 164.2 (C); ESIMS, *m/z*: 304 $(M+Na)^+$. Anal. Calcd for $C_{10}H_{11}N_5O_5$: C, 42.71; H, 3.94; N, 24.90. Found: C, 42.45; H, 3.90; N, 24.65.

4.1.6. 3,6-Anhydro-5-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (10). Benzyl bromide (1.8 mL, 14.85 mmol) was added to a stirred heterogeneous mixture of **2** (2.00 g, 9.90 mmol), CH_2Cl_2 (50 mL), 50% aqueous NaOH solution (40 mL), and *n*-tetrabutylammonium bromide (319 mg, 0.99 mmol), and the mixture was stirred at room temperature for 12 h. The organic layer was taken out, washed with water until neutral and dried (Na_2SO_4). The solvent was evaporated and the resulting crude product was purified by column chromatography on silica gel using $CHCl_3$–petroleum ether (30:70) as eluent to furnish **10** (2.54 g, 88%) as a white solid: mp 90–91 °C; $[\alpha]_D^{25}$ +85.5 (*c* 0.93, $CHCl_3$) [lit.[15] mp 86.6–90.8 °C, $[\alpha]_D^{20}$ +84.0 (*c* 5, $CHCl_3$)].

4.1.7. 1-(2-*O*-Acetyl-3,6-anhydro-5-*O*-benzyl-β-D-glucofuranosyl)uracil (11). Compound **10** (2.5 g, 8.56 mmol) was treated with 30 mL of 4% H_2SO_4 in aqueous CH_3CN (75%). The residue obtained after solvent removal was acetylated with pyridine (20 mL) and Ac_2O (2.5 mL) mixture to give a diacetate mixture (2.25 g), which was subjected to the protocol described for preparation of **8** utilizing uracil (2.11 g, 18.83 mmol), hexamethyldisilazane (20 mL), TMSCl (two drops), TMSOTf (1.46 mL, 8.04 mmol), and CH_3CN (25 mL) to get **11** (1.5 g, 58%) as a foamy solid: $[\alpha]_D^{25}$ +102.6 (*c* 0.81, CH_3OH); IR (KBr): ν_{max} 3198, 1749, 1693, 1456, 1379, 1274, 1229, 1114, 1053, 816, 751, 700, 649, 606, 565 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 2.11 (s, 3H), 3.91–4.02 (m, 2H), 4.26 (dd, 1H, $J = 5.8$, 10.8 Hz), 4.48 (d, 1H, $J = 3.0$ Hz), 4.56 (d, 1H, $J = 11.5$ Hz), 4.70 (d, 1H, $J = 11.5$ Hz), 4.79 (t, 1H, $J = 4.5$ Hz), 5.23 (d, 1H, $J = 1.5$ Hz), 5.63 (d, 1H, $J = 7.8$ Hz), 6.18 (d, 1H, $J = 3.3$ Hz), 7.35 (br s, 5H), 7.71 (d, 1H, $J = 8.1$ Hz), 8.99 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.9 (CH_3), 69.6 (CH_2), 72.1 (CH_2), 78.9 (CH), 80.3 (CH), 82.2 (CH), 85.8 (CH), 91.2 (CH), 103.4 (CH), 128.5 (2 × CH), 128.7 (CH), 129.1 (2 × CH), 137.3 (C), 140.5 (CH), 150.6 (C), 163.3 (C), 169.9 (C); ESIMS, *m/z*: 411 $(M+Na)^+$. Anal. Calcd for $C_{19}H_{20}N_2O_7$: C, 58.76; H, 5.19; N, 7.21. Found: C, 58.48; H, 5.14; N, 6.95.

4.1.8. 1-(3,6-Anhydro-5-*O*-benzyl-β-D-glucofuranosyl) uracil (12). To a solution of **11** (1.40 g, 3.60 mmol) in dry MeOH (20 mL) was added K_2CO_3 (622 mg, 4.50 mmol), and the mixture was stirred at room temperature for 30 min. Usual workup and purification by column chromatography on silica gel using with CH_3CO_2Et–MeOH (95:5) as eluent furnished **12** (1.22 g, 98%) as a foamy solid: $[\alpha]_D^{25}$ +107.5 (*c* 0.81, CH_3OH); IR (KBr): ν_{max} 3383, 1688, 1463, 1391, 1274, 1211, 1111, 1063, 1024, 814 cm^{-1}; ^1H NMR (C_5D_5N, 300 MHz): δ 4.03 (dd, 1H, $J = 6.7$, 9.4 Hz), 4.09 (dd, 1H, $J = 5.4$, 9.4 Hz), 4.33 (dd, 1H, $J = 5.2$, 11.4 Hz), 4.56 (d, 1H, $J = 11.4$ Hz), 4.74 (1H, unresolved), 4.79 (d, 1H, $J = 11.4$ Hz), 4.95 (br s, 1H), 5.09 (t, 1H, $J = 4.3$ Hz), 5.71 (d, 1H, $J = 8.1$ Hz), 6.64 (d, 1H, $J = 2.7$ Hz), 7.25–7.37 (m, 3H), 7.46 (d, 2H, $J = 7.2$ Hz), 8.18 (d, 1H, $J = 8.1$ Hz), 8.27 (br s, 1H), 13.27 (br s, 1H); ^{13}C NMR (C_5D_5N, 75 MHz): δ 73.9 (CH_2), 74.1 (CH_2), 81.2 (CH), 81.6 (CH), 84.4 (CH), 90.9 (CH), 96.3 (CH), 103.9 (CH), 129.8 (CH), 130.0 (2 × CH), 130.5 (2 × CH) 140.1 (C), 142.5 (CH), 153.7 (C), 166.0 (C); ESIMS, *m/z*: 369 $(M+Na)^+$. Anal. Calcd for $C_{17}H_{18}N_2O_6$: C, 58.96; H, 5.24; N, 8.09. Found: C, 58.90; H, 5.21; N, 7.94.

4.1.9. 1-(3,6-Anhydro-5-*O*-benzyl-2-*O*-mesyl-β-D-glucofuranosyl)uracil (13). To a solution of **12** (825 mg, 2.38 mmol) in pyridine (20 mL) at 0 °C was added mesyl chloride (0.79 mL, 10.25 mmol) and the mixture was stirred for 30 min. The temperature was raised to 25 °C and the solution was stirred for 1.5 h. The solvent was evaporated in vacuo and the crude residue was extracted CH_3CO_2Et (3 × 30 mL). The combined extract was washed with water (2 × 30 mL), dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by silica gel column chromatography using CH_3CO_2Et–petroleum ether (80:20) as eluent to afford **13** (895 mg, 89%) as a yellow foamy solid: $[\alpha]_D^{25}$ +111.3 (*c* 0.22, MeOH); IR (KBr): ν_{max} 3235, 1699, 1678, 1630, 1447, 1406, 1387 1358, 1280, 1176, 1128, 1034, 974, 877 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 3.27 (s, 3H), 3.89 (dd, 1H, $J = 4.5$, 10.0 Hz), 3.99 (dd, 1H, $J = 6.8$, 10.0 Hz), 4.35–4.41 (m, 1H), 4.56 (d, 1H, $J = 11.0$ Hz), 4.59 (d, 1H, $J = 3.6$ Hz), 4.74 (d, 1H, $J = 11.0$ Hz), 4.99 (t, 1H, $J = 4.2$ Hz), 5.19 (s, 1H), 5.62 (d, 1H, $J = 8.1$ Hz), 6.01 (d, 1H, $J = 3.6$ Hz), 7.36–7.41 (m, 5H), 7.98 (d, 1H, $J = 8.1$ Hz), 9.73 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 38.6 (CH_3), 72.8 (CH_2), 73.0 (CH_2), 79.1 (CH), 84.0 (CH), 84.8 (CH), 85.8 (CH), 92.0 (CH), 102.2 (CH), 128.1 (2 × CH), 128.4 (CH), 128.7 (2 × CH), 136.7 (C), 139.6 (CH), 150.9 (C), 163.5 (C); ESIMS, *m/z*: 447 $(M+Na)^+$. Anal. Calcd for $C_{18}H_{20}N_2O_8S$: C, 50.94, H, 4.75; N, 6.60. Found C, 50.66; H, 4.58; N, 6.38.

4.1.10. 2,2′-Anhydro-1-(3,6-anhydro-5-*O*-benzyl-β-D-mannofuranosyl)-2-hydroxy-(1*H*)-pyrimidin-4-one (14). To a solution of **13** (600 mg, 1.42 mmol) in CH_3CN (15 mL) was added DBU (0.32 mL, 2.12 mmol), and the mixture was stirred at room temperature for 10 h under N_2. The solvent was evaporated under reduced pressure and the crude product was chromatographed on silica gel using CH_3CO_2Et–MeOH (92:8) as eluent to furnish **14** (415 mg, 89%) as a white solid: $[\alpha]_D^{25}$ +99.8 (*c* 0.21, MeOH); IR (KBr): ν_{max} 1655, 1620, 1530, 1478, 1347, 1261, 1236, 1139, 938, 831 cm^{-1}; ^1H NMR (C_5D_5N, 300 MHz): δ 3.69 (t-like, 1H, $J = 7.0$, 8.5 Hz), 3.95 (t-like, 1H, $J = 6.4$, 8.8 Hz), 4.09 (apparent dd, 1H, $J = 5.6$, 13.3 Hz), 4.49 (d, 1H, $J = 12.0$ Hz), 4.62 (d, 1H, $J = 12.0$ Hz), 4.99–5.04 (2H, merged with solvent), 5.65 (t, 1H, $J = 5.8$ Hz), 6.10 (d, 1H, $J = 7.4$ Hz), 6.50 (d, 1H, $J = 5.8$ Hz), 7.30–7.35 (m, 5H), 7.75 (d, 1H, $J = 7.4$ Hz); ^{13}C NMR (C_5D_5N, 75 MHz): δ 72.2 (CH_2), 72.7 (CH_2), 78.3 (CH), 81.4 (CH), 82.4 (CH), 84.8 (CH), 92.8 (CH), 109.6 (CH), 128.0 (CH), 128.1 (2 × CH), 128.7 (2 × CH), 136.1 (CH), 138.4 (C), 161.3 (C), 172.1 (C); ESIMS, *m/z*: 351 $(M+Na)^+$. Anal. Calcd for $C_{17}H_{16}N_2O_5$: C, 62.19; H, 4.91; N, 8.53. Found C, 62.02; H, 4.81; N, 8.38.

4.1.11. 1-(3,6-Anhydro-2-azido-5-*O*-benzyl-2-deoxy-β-D-glucofuranosyl)uracil (15). *Preparation of* **15** *from* **14**: A mixture of **14** (306 mg, 0.93 mmol), NaN_3 (182 mg, 2.79 mmol), 15-crown-5 (0.56 mL, 2.79 mmol), and

DMF (8 mL) was heated at 70 °C for 58 h under N_2. The solvent was evaporated in vacuo. The crude product was extracted with CH_3CO_2Et–MeOH (99:1) mixture (3 × 20 mL). The extract was washed with brine (2 × 20 mL), dried (Na_2SO_4), and concentrated in vacuo to a crude product, which was purified by preparative TLC on silica gel plates using $CHCl_3$–MeOH (96:4) mixture as the developing solvent to give **15** (82 mg, 22%) as a foamy solid: $[\alpha]_D^{25}$ +82.6 (*c* 0.26, CH_3OH); IR (KBr): ν_{max} 3259 (broad), 2114, 1692, 1455, 1383, 1271, 1114 cm^{-1}; ^1H NMR (C_5D_5N, 300 MHz): δ 4.00 (dd, 1H, $J = 6.9$, 9.6 Hz), 4.07 (dd, 1H, $J = 5.0$, 9.6 Hz), 4.33 (dd, 1H, $J = 4.8$, 11.2 Hz), 4.55–4.59 (m, 2H), 4.76 (d, 1H, $J = 11.2$ Hz), 4.86 (br s, 1H), 4.94 (t, 1H, $J = 4.4$ Hz), 5.69 (d, 1H, $J = 8.1$ Hz), 6.42 (d, 1H, $J = 3.3$ Hz), 7.28–7.39 (m, 3H), 7.47 (d, 2H, $J =$ 7.2 Hz), 8.13 (d, 1H, $J = 8.1$ Hz), 13.44 (br s, 1H); ^{13}C NMR (C_5D_5N, 75 MHz): δ 71.4 (CH), 72.2 (CH_2), 74.2 (CH_2), 81.3 (CH), 84.9 (CH), 88.2 (CH), 93.8 (CH), 104.1 (CH), 129.9 (CH), 130.1 (2 × CH), 130.5 (2 × CH), 139.9 (C), 141.5 (CH), 153.4 (C), 165.9 (C); ESIMS, *m*/*z*: 394 $(M+Na)^+$. Anal. Calcd for $C_{17}H_{17}N_5O_5$: C, 54.98; H, 4.61; N, 18.86. Found: C, 54.70; H, 4.73; N, 18.68.

Preparation of **15** *from* **12**: To a solution of **12** (180 mg, 0.52 mmol) in CH_2Cl_2 (10 mL) at −20 °C under N_2 were added pyridine (0.05 mL, 0.57 mmol) and trifluromethanesulfonic anhydride (0.10 mL, 0.62 mmol), and the mixture was stirred for 30 min. The temperature of the reaction was raised to 0 °C and the stirring was continued for 30 min when TLC showed complete disappearance of the starting material. The reaction mixture was cooled, neutralized with aqueous $NaHCO_3$ solution, and extracted quickly with CH_2Cl_2 (3 × 20 mL). The combined extract was dried (Na_2SO_4) and evaporated to a crude residue, which was dried under vacuum to give the corresponding triflic acid ester as a gummy mass (230 mg). To a solution of the above material in dry DMF (8 mL) was added NaN_3 (75 mg, 1.15 mmol), and the mixture was heated at 80 °C for 5 h under N_2. The solvent was evaporated in vacuo and the residual mass was extracted with $CHCl_3$–MeOH (99:1) mixture (20 mL). The solution was dried (Na_2SO_4), and the solvent was evaporated. The crude product was purified by preparative TLC on silica gel plates using $CHCl_3$–MeOH (98:2) as the developing solvent to afford **15** (48 mg, 27%) as a foamy solid.

4.1.12. 1-(3,6-Anhydro-2-azido-2-deoxy-β-D-glucofuranosyl) uracil (16). DDQ (9 mg, 0.038 mmol) was added to a solution of **15** (12 mg, 0.032 mmol) in dry CH_2Cl_2 (10 mL), and the mixture was heated at reflux for 45 h under N_2. The solvent was evaporated in vacuo and the crude product obtained was purified by preparative TLC on silica gel coated plates using $CHCl_3$–MeOH (90:10) mixture as the developing solvent to yield **16** (5 mg, 57%) as a foamy solid: $[\alpha]_D^{25}$ +65.3 (*c* 0.45, CH_3OH); IR (KBr): ν_{max} 3413, 2115, 1697, 1463, 1386, 1270, 1114, 1072, 819 cm^{-1}; ^1H NMR (C_5D_5N, 300 MHz): δ 4.13 (d, 2H, $J = 6.0$ Hz), 4.68 (m, 2H), 4.84 (t, 1H,$J = 4.5$ Hz), 4.91 (dd-like, 1H, $J = 2.2$, 3.7 Hz), 5.80 (d, 1H, $J = 8.1$ Hz), 6.49 (d, 1H, $J = 4.2$ Hz), 8.34 (d, 1H, $J = 8.1$ Hz), 13.45 (br s, 1H), signal for 1H not discernible; ^{13}C NMR (C_5D_5N, 75 MHz): δ 71.6 (CH), 73.9 (CH), 76.0 (CH_2), 86.0 (CH), 87.7 (CH), 93.1 (CH), 104.4 (CH), 142.0 (CH), 153.5 (C), 165.9 (C); ESIMS, *m*/*z*: 304 $(M+Na)^+$. Anal. Calcd for $C_{10}H_{11}N_5O_5$: C, 42.71; H, 3.94; N, 24.90. Found: C, 42.46; H, 3.80; N, 24.63.

4.1.13. 1-(2-*O*-Acetyl-3,6-anhydro-5-*O*-[1,2,3,5-tetra-*O*-acetyl-β-D-allofuranos-6-yl]-β-D-glucofuranosyl)uracil (17), 1-(2-*O*-acetyl-3,6-anhydro-5-*O*-[1,2,3,5-tetra-*O*-acetyl-α-D-allofuranos-6-yl]-β-D-glucofuranosyl)uracil (18). Compound **3** (285 mg, 0.705 mmol) was subjected to a procedure similar to that described for the conversion of **7** to **8** and using the protocol: (i) 7 mL of H_2SO_4–CH_3CN–H_2O (1:18:6) for acetonide deprotection; (ii) pyridine (10 mL), Ac_2O (0.6 mL) for acetylation; (iii) uracil (273 mg, 2.44 mmol), hexamethyldisilazane (10 mL), TMSCl (2 drops), TMSOTf (0.33 mL. 1.82 mmol), and CH_3CN (15 mL) for nucleosidation. The reaction yielded **17** (155 mg, 36% overall) and **18** (88 mg, 21% overall) as white foamy solids after purification by preparative TLC on silica gel plate using $CHCl_3$–petroleum ether (98:2) as the developing solvent.

Compound **17**: $[\alpha]_D^{25}$ +47.7 (*c* 0.34, $CHCl_3$); IR (KBr): ν_{max} 3215 (broad), 1752, 1695, 1458, 1373, 1222, 1067 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.95 (s, 3H), 2.08 (s, 3H), 2.13 (s, 3H), 2.15 (s, 3H), 2.17 (s, 3H), 3.72 (br s, 2H), 3.83 (t, 1H $J = 9.0$ Hz), 4.09 (t, 1H, $J = 7.4$ Hz), 4.29 (m, 2H), 4.46 (d, 1H, $J = 2.5$ Hz), 4.73 (apparent t, 1H), 5.00 (dd, 1H, $J = 2.5$, 10.5 Hz), 5.09 (apparent t, 1H), 5.17 (d, 1H, $J = 2.5$ Hz), 5.65 (br s, 1H), 5.82 (d, 1H, $J = 7.2$ Hz, with finer splitting), 6.13 (d, 1H, $J = 2.8$ Hz), 6.23 (d, 1H, $J = 3.8$ Hz), 7.57 (d, 1H, $J = 8.1$ Hz), 8.12 (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.8, 20.9, 21.1, 21.3 (5 × CH_3), 65.8 (CH), 66.3 (CH), 67.3 (CH), 68.1 (CH), 69.2 (CH_2), 71.5 (CH_2), 80.6 (CH), 81.3 (CH), 81.8 (CH), 86.2 (CH), 88.8 (CH), 91.3 (CH), 103.8 (CH), 140.4 (CH), 150.4 (C), 162.7 (C), 169.2 (C), 169.6 (2 × C), 169.8 (C), 170.4 (C); FABMS, *m*/*z*: 629 $(M+H)^+$. Anal. Calcd for $C_{26}H_{32}N_2O_{16}$: C, 49.68; H, 5.13; N, 4.46. Found: C, 49.40; H, 5.01; N, 4.18.

Compound **18**: $[\alpha]_D^{25}$ +68.2 (*c* 0.26, $CHCl_3$); IR (KBr): ν_{max} 1750, 1695, 1376, 1226, 1049 cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz): δ 1.95 (s, 3H), 2.02 (s, 3H), 2.11 (s, 3H), 2.12 (s, 3H), 2.16 (s, 3H), 3.69 (dd, 1H, $J = 1.2$, 11.0 Hz), 3.72 (dd, 1H, $J = 4.2$, 11.0 Hz), 3.84 (dd, 1H, $J = 6.6$, 9.0 Hz), 4.07 (dd, 1H, $J = 7.2$,

9.0 Hz), 4.15 (br d, 1H, $J = 9.6$ Hz), 4.28 (dd, 1H, $J = 6.6$, 11.0 Hz), 4.45 (d, 1H, $J = 3.6$ Hz), 4.74 (t, 1H, $J = 3.6$ Hz), 4.97 (dd, 1H, $J = 3.0$, 9.0 Hz), 4.99 (dd, 1H, $J = 2.4$, 10.0 Hz), 5.18 (d, 1H, $J = 2.4$ Hz), 5.68 (t, 1H, $J = 3.0$ Hz), 5.82 (d, 1H, $J = 7.8$ Hz), 5.97 (d, 1H, $J = 8.4$ Hz), 6.13 (d, 1H, $J = 3.0$ Hz), 7.59 (d, 1H, $J = 8.4$ Hz), 8.40 (br s, 1H); ^{13}C NMR ($CDCl_3$, 150 MHz): δ 20.46, 20.52, 20.6, 20.7, 20.9 ($5 \times CH_3$), 65.7 (CH), 67.9 (CH), 68.2 (CH), 68.5 (CH_2), 71.2 (CH_2), 72.5 (CH), 80.2 (CH), 80.4 (CH), 81.4 (CH), 85.7 (CH), 90.2 (CH), 90.8 (CH), 103.3 (CH), 139.9 (CH), 150.1 (C), 162.5 (C), 168.8 (C), 169.0 (C), 169.4 ($2 \times C$), 169.8 (C); FABMS, *m/z*: 629 $(M+H)^+$. Anal. Calcd for $C_{26}H_{32}N_2O_{16}$: C, 49.68; H, 5.13; N, 4.46. Found: C, 49.47; H, 4.98; N, 4.18.

4.1.14. 1-(2-*O*-Acetyl-3,6-anhydro-5-*O*-[2,3,5-tri-*O*-acetyl-1-deoxy-1β-{uracil-1-yl}-D-allofuranos-6-yl]-β-D-glucofuranosyl)uracil (19). Compound **3** (668 mg, 1.65 mmol) was subjected to the same procedure as described for the conversion of **2** to **8** [except for nucleosidation when the reaction mixture was heated at reflux for 6 h] using the protocol: (i) 10 mL of H_2SO_4–CH_3CN–H_2O (1:18:6) for acetonide deprotection; (ii) pyridine (15 mL), Ac_2O (1.2 mL) for acetylation; (iii) uracil (656 g, 5.85 mmol), hexamethyldisilazane (15 mL), TMSCl (two drops), TMSOTf (0.45 mL. 2.50 mmol), and CH_3CN (20 mL) for nucleosidation. The crude product was purified by preparative TLC on silica gel plates using $CHCl_3$–MeOH (19:1) as solvent system. Compound **19** (540 mg, 48%, overall) was obtained as a white foamy solid: $[\alpha]_D^{25}$ +47.9 (*c* 0.38, CH_3OH); IR (KBr): ν_{max} 3448, 1749, 1696, 1462, 1379, 1239, 1052, 818 cm^{-1}; ^{1}H NMR ($C_5D_5N+D_2O$, 300 MHz): δ 1.90 (s, 3H), 2.06 (s, 3H), 2.08 (s, 3H), 2.21 (s, 3H), 4.09–4.23 (m, 4H), 4.59 (m, 2H), 4.73 (d, 1H, $J = 2.6$ Hz), 5.02 (br s, 1H), 5.55–5.62 (2H, merged with HOD), 5.87–6.00 (m, 3H), 6.31 (br s, 1H), 6.55 (d, 1H, $J = 2.7$ Hz), 6.70 (d, 1H, $J = 9.0$ Hz), 7.96 (d, 1H, $J = 8.0$ Hz), 8.06 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.8, 20.9, 21.0, 21.1 ($4 \times CH_3$), 66.4 (CH), 67.2 (CH), 68.5 (CH_2), 72.3 (CH_2), 74.2 (CH), 80.3 (CH), 80.5 (CH), 80.7 (CH), 81.9 (CH), 86.4 (CH), 91.3 (CH), 91.5 (CH), 103.2 (CH), 103.5 (CH), 139.7 (CH), 140.7 (CH), 150.7 (C), 150.9 (C), 163.6 (C), 163.8 (C), 169.6 (C), 169.7 (C), 169.9 (C), 170.2 (C); ESIMS, *m/z*: 703 $(M+Na)^+$. Anal. Calcd for $C_{28}H_{32}N_4O_{16}$: C, 49.41; H, 4.74; N, 8.23. Found C, 49.13; H, 4.62; N, 8.97.

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Supplementary data

Supplementary data (X-ray crystallographic data for **3**, and ^{1}H and ^{13}C NMR spectra of **3**, **4**, **17**, and **18**) associated with this article can be found, in the online version, at doi:10.1016/j.carres.2007.08.013.

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12. The synthesis of **2** (in low to good yields) was previously carried out through (i) base induced ring opening of 5,6-cyclic sulfate or sulfite of 3-*O*-acetyl-1,2-*O*-isopropylidene-α-D-glucofuranose followed by cyclization;[15] (ii) thiourea mediated selective opening of 5,6-*O*-isopropylidene group of 1,2:5,6-di-*O*-isopropylidene-3-mesyloxy-α-D-allofuranaose and then etherification by alkali treatment;[17] (iii) phosphonium ion induced iodination on 1,2-*O*-isopropylidene-α-D-glucofuranose and subsequent base catalyzed Williamson etherification.[18]
13. This compound has been earlier prepared by Horton and co-workers (Wolfrom, M. L.; Bernsmann, J.; Horton, D. *J. Org. Chem.* **1962**, *27*, 4505–4509) through the displacement of 5-tosyloxy group using NaN_3, but the spectral data, particularly the NMR data, were not reported.
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