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A stereospecific synthesis of L-deoxyribose, L-ribose and L-ribosides

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Abstract—Using an inexpensive D-galactose from the chiral pool, L-deoxyribose, L-ribose and their derivatives were synthesized via mild reaction conditions. During the synthesis of L-deoxyribose, the key deoxygenation of the 2-hydroxy group of 3,5-*O*-dibenzyl-methyl-L-arabinofuranoside was performed by reduction of the corresponding triflate with tetrabutylammonium borohydride in high yield. During the synthesis of L-ribose, the key step of inversion of the 2-hydroxy group in the same substrate was carried out by intramolecular S_N2 tandem reaction. Then the L-ribosyl donors were submitted to glycosidations according to Vorbrüggen's conditions to give L-ribosides (L-uridine, L-5-fluorouridine, L-iodouridine, L-thymidine, L-puridine, L-adenosine and L-guanosine) in excellent yields.

1. Introduction

Since the discovery of the acquired immunodeficiency syndrome (AIDS) infected by human immunodeficiency virus (HIV), intensive efforts in the search for effective antiviral agents which inhibit the replication of HIV have been made. Nucleoside analogues with modified sugar moieties have become active antiviral drugs, such as 3′-azido-3′-deoxythymidine (AZT),[1] 2′,3′-dideoxycytidine (ddC),[2] and 2′,3′-didehydro-3′-deoxythymidine (d_4T).[3] All these nucleoside analogues act by their conversion into the corresponding 5′-triphosphates as competitive inhibitors or as DNA chain terminators. However, owing to inherent drug resistance[4] and toxicity of the used anti-HIV drugs,[5] recently several modified L-nucleosides, such as (−)-(2′*R*, 5′*S*)-1-(2-hydroxymethyl oxathiolan-5-yl)-cytosine (3TC),[6] L-thymidine (L-T),[7] L-3′-thiacytidine (L-3-TC),[8] L-5-fluoro-3′-thia-cytidine (L-FTC),[9] L-2′,3′-dideoxycytidine (L-ddC),[10] L-5-fluoro-2′,3′-dideoxy-cytidine (L-5-FddC),[11] and L-2′-fluoro-5-methylarabinofuranosyl uracil (L-FMAU)[12] have been developed as more actively antiviral and less toxic agents. Their antiviral mechanism shows that L-nucleosides are phosphorylated by cellular kinases which interact selectively with viral polymerases but seldomly with cellular polymerases.

For these reasons, studies on L-carbohydrates, modified L-nucleosides, especially L-deoxyribosides, L-ribosides and their derivatives are being considered. It is also of interest to synthesize L-deoxyribose, L-ribose, L-ribosides and their derivatives. Up to now, there have been several reports of syntheses of L-deoxyribose and L-ribose from L-arabinose,[13–15] D-glucose,[16] D-ribose[17] and L-xylose.[18] Herein we reported a stereospecific synthesis of L-deoxyribose **2**, L-ribose **3** and L-ribosides from D-galactose **1**.

2. Results and discussion

2.1. Proposed synthesis of L-deoxyribose and L-ribose

Comparing their structures (Fig. 1), some useful information on D-galactose **1** in relation to L-deoxyribose **2** and L-ribose **3** was acquired. D-Galactose is a hexose while L-deoxyribose and L-ribose are pentoses without C-6; they have the same configurations at C-3 and C-4 but different at C-2. Therefore, in our synthetic approach, the strategy employed for the conversion of D-galactose into L-deoxyribose **2** and L-ribose **3**, respectively, included two key steps to effect their structurally different points. One step was chemoselective oxidative cleavage of the 5,6-diol of D-galactose and the other was the deoxygenation of the

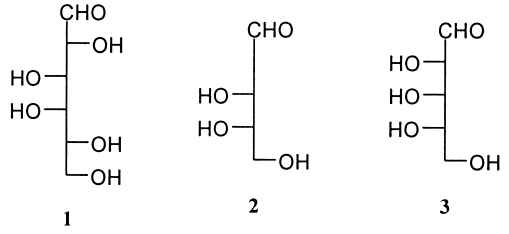

Figure 1. Structures of D-galactose **1**, L-deoxyribose **2** and L-ribose **3**.

Keywords: synthesis; L-deoxyribose; L-ribose; L-ribosides.

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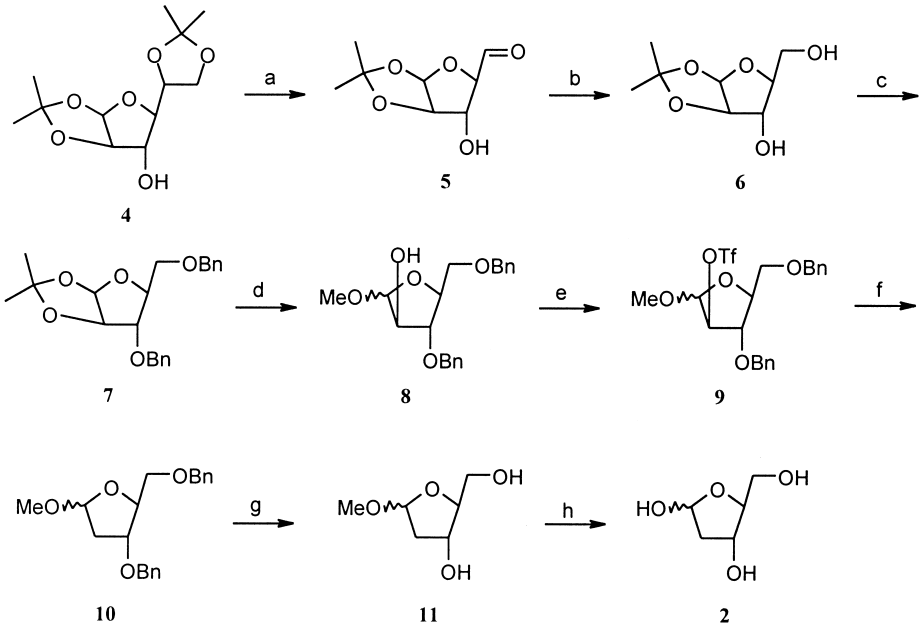
2-hydroxy group or the configurational inversion of the 2-hydroxy group.

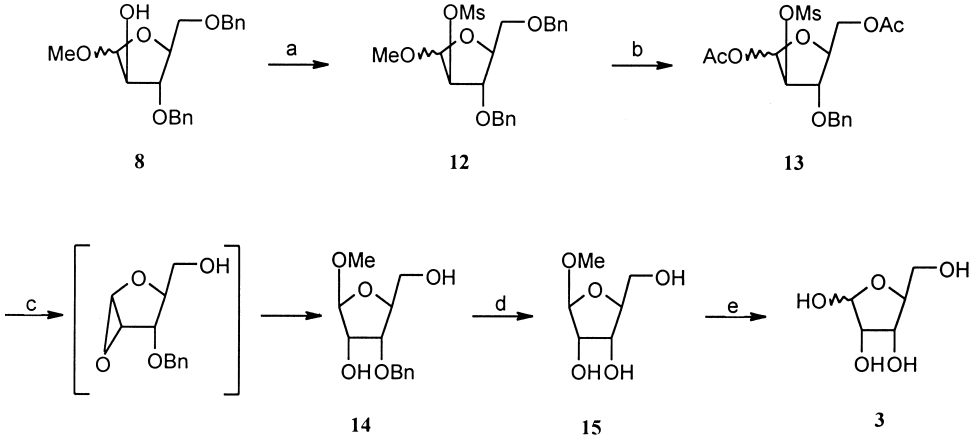
2.2. Synthesis of L-deoxyribose

According to literature,[19] 1,2,5,6-di-*O*-isopropylidene-D-galactofuranose **4** obtained from D-galactose was employed as the starting material. Then, there were two pathway chosen for the conversion of compound **4** into compound **6** (Scheme 1). For the first one, chemoselective hydrolysis and cleavage of the 5,6-*O*-isopropylidene acetal of **4** with $NaIO_4/H_5IO_6$ (1.0 equiv./0.5 equiv.) in one operation[20] and reduction of the corresponding aldehyde **5** with sodium borohydride furnished L-arabinose derivative **6** in 91% yield. For the second route, the 5,6-*O*-isopropylidene acetal of **4** was selectively hydrolyzed with 10% AcOH follwed by $NaIO_4$ cleavage of the resulting glycol and reduction. After protection of the 3,5-dihydroxyl groups of compound **6** with benzyl chloride and methanolysis of the resulting compound **7** with 10% HCl–MeOH, a substrate **8** for deoxygenation of the 2-hydroxy group was obtained.

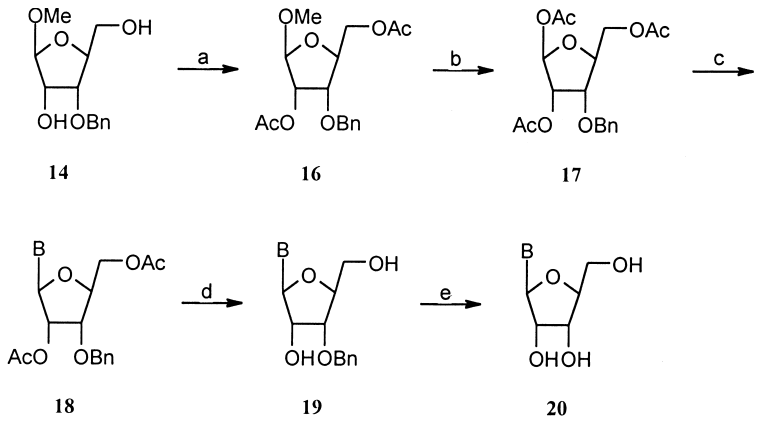
To realize the deoxygenation, several sulfonates (–OTs, –OMs, –OTf) prepared from compound **8** were tried as substrates for the reduction using several reductive agents ($NaBH_4$, $LiAlH_4$, n-Bu_4NBH_4) in different solvents (tetrahydrofuran, benzene, toluene). The other factors of reaction temperature and reaction time were also considered. One of the sulfonates, triflate **9**, was previously prepared almost quantitatively by reaction of **8** with triflic anhydride and pyridine in CH_2Cl_2. After a series of attempts at the deoxygenation, compound **10** was acquired by reduction of triflate **9** with tetrabutylammonium borohydride in benzene under reflux for 4 h in 95% yield. Subsequently, L-deoxyribose **2**



Scheme 1. *Reagents and conditions*: (a) $NaIO_4/H_5IO_6$ (1.0 equiv./0.5 equiv.), EtOAc, rt, 5 h, 94; or 10% AcOH–H_2O, rt, 24 h; $NaIO_4$, MeOH, H_2O, 3 h, two steps 92%; (b) $NaBH_4$, MeOH, rt, 2 h, 97%; (c) KOH, BnCl, 1,4-dioxane, reflux, 2 h, 96%; (d) 10% HCl–MeOH, rt, 3 h, 98%; (e) Tf_2O, py, CH_2Cl_2, −15–−10°C, 4 h, 99%; (f) n-Bu_4NBH_4, benzene, reflux, 4 h, 95%; (g) 10% Pd–C, H_2, rt, 3 h, 97%; (h) Dowex [H^+], H_2O, 60°C, 24 h, 98%.



Scheme 2. *Reagents and conditions*: (a) MsCl, Et_3N, rt, overnight, 98%; (b) Ac_2O, AcOH, H_2SO_4, 4°C, overnight, 89%; (c) NaOMe, MeOH, rt, 6 h, 86%; (d) 10% Pd–C, MeOH, H_2, 2 h, 97%; (e) Dowex [H^+], H_2O, 50°C, 24 h, 95% yield.



Scheme 3. *Reagents and conditions*: (a) Ac_2O, py, overnight, rt, 92%; (b) AcOH, Ac_2O, H_2SO_4, 4°C, overnight, 76%; (c) for **18a**: uracil, TMSOTf, BSA, CH_3CN, 60–65°C, overnight, 92%; for **18b**: thymine, TMSOTf, BSA, CH_3CN, 60–65°C, overnight, 88%; for **18c**: 5-fluorouracil, TMSOTf, BSA, CH_3CN, 60–65°C, overnight, 89%; (d) NH_3–H_2O, MeOH, 60°C, overnight; (e) 10% Pd–C, H_2, rt, 3 h, **20a**: L-uridine: 92%, two steps; **20b**: L-thymidine: 91%, two steps. **20c**: L-5-Fluorouridine: 87%, two steps.

was prepared by hydrogenation of **11** with 10% palladium–carbon in methanol, followed by hydrolysis of methyl glycoside with ion-exchange resin (H^+ form) in 98% yield.

2.3. Synthesis of L-ribose

L-Ribose was synthesized starting from the key intermediate compound **8** (Scheme 2). The most important task was to realize the configuration inversion of the 2-hydroxyl group in compound **8**. Inversion of the 2-hydroxyl group was attempted by several methods including oxidation/reduction procedures and methods of Mitsunobu and intermolecular S_N1 reaction, but unfortunately all of these were unsuccessful. An idea of inversion of the 2-hydroxyl group by using the chirality of C-1 occurred, which would be effected by a tandem reaction.

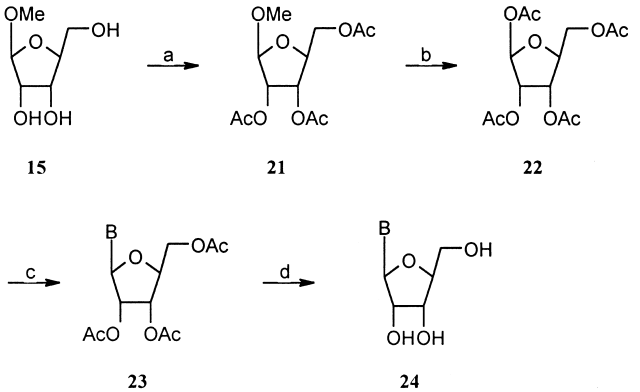
Preparation of compound **12** by methanesulfonylation of compound **8** and then acetylation of compound **12** with Ac_2O, AcOH and H_2SO_4 gave only the 1,5-diacetate **13**, with no monoacetate, in 89% yield. Hydrolysis of diacetate **13** followed by inversion of configuration of the 2-hydroxyl group using NaOMe/MeOH solution gave compound **14** in 86% yield. This reaction experienced mechanism of the intramolecular S_N2 tandem reaction. Two kinds of C-1 alkoxide and C-5 alkoxide were formed by removing 1,5-diacetate of compound **13** under the basic solution, but only structural advantage of C-1 alkoxide attacked methanesulfonyloxy group of C-2 from its back position, with producing the 1,2-epoxide intermediate. This intermediate was unstable under the reaction system and easily reacted regioselectively at the C-1 position with surrounding methoxyl alkoxide, then produced compound **14**.

After the same procedures of debenzylation and hydrolysis of methyl glycoside, L-ribose **3** was synthesized. The resulting structure was confirmed by comparison with a commercial sample from Aldrich.

2.4. Synthesis of L-ribosides

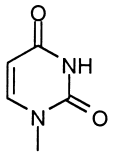
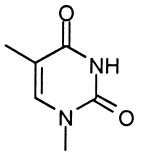
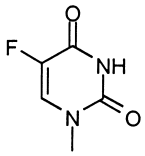
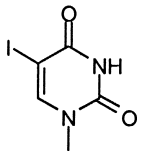
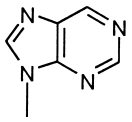
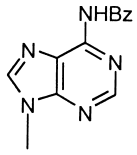
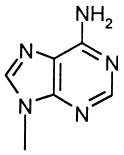
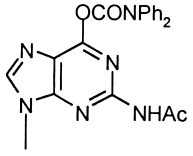
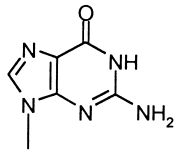
Diacetate **16** was prepared by diacetylation of the two hydroxyl groups of compound **14** and treated with Ac_2O/$AcOH/H_2SO_4$ to afford 1,2,5-tri-*O*-acetyl-3-*O*-benzyl-L-ribofuranose **17** as the β anomer of a separabale mixture (α/β=1:7), which was used for glycosidation (Scheme 3). According to the Vorbrüggen method,[21] the β-*N*-glycosidic bound linkage were formed by the L-ribosyl donor **17** and the protected bases. We therefore obtained **18a–c** by the treatment of **17** with the bases of uracil, thymine and 5-fluorouracil, respectively, in the presence of TMSOTf and BSA (*N*,*O*-bis-thrimethylsilylacetamide) in good yields (92, 88, 89% for **18a–c**, respectively). Then L-uridine **20a**, L-thymidine **20b** and L-5-fluorouridine **20c** were obtained by deacetylation of **18a–c** with NH_3–H_2O/MeOH and debenzylation with 10% palladium–carbon in methanol in high yield (92, 91, 87%, for **20a–c** respectively.

For some bases sensitive to debenzylation, like 5-iodouracil and purines, another synthetic route was applied (Scheme 4). Protection of the triol **15** with acetic anhydride and pyridine and treatment of the resulting triacetate **21** with $Ac_2O/AcOH/H_2SO_4$ afforded a separable mixture (α/β= 1:4) of tetra-*O*-acetyl-L-ribose, with the β anomer **22** as a



Scheme 4. *Reagents and conditions*: (a) Ac_2O, py, overnight, rt, 90%; (b) Ac_2O, AcOH, H_2SO_4, 4°C, overnight, 74%; (c) for **23a**: 5-iodouracil, TMSOTf, BSA, CH_3CN, 60–65°C, overnight, 94%; for **23b**: purine, TMSOTf, BSA, CH_3CN, 60–65°C, overnight, 83%; for **23c**: 6-*N*-benzoyl-adenine, TMSOTf, MFSTA, CH_3CN, 60–65°C, overnight, 81%; for **23d**: 2-*N*-6-*O*-diphenylcarbamoylguanine,[22] TMSOTf, BSA, toluene, 3 h, 80°C, 86%; (d) NH_3/H_2O, MeOH, 60°C, overnight, **24a**: L-iodouridine: 93%; **24b**: L-puridine: 91%; **24c**: L-adenosine: 94%; **24d**: L-guanosine: 91%.

Table 1. Bases structures of the synthesized ribosides and their derivatives

Base					
Compound no.	**18a** **19a** **20a**	**18b** **19b** **20b**	**18c** **19c** **20c**	**23a** **24a**	**23b** **24b**
Base					
Compound no.	**23c**	**24c**	**23d**	**24d**	

suitable L-ribosyl donor. Using the same procedures for glycosidation, we acquired the derivatives of L-ribosides (**23a**–**d**) in good yield (94, 83, 81, 86% for **23a**–**d**, respectively) on different bases (5-iodouracil, purine, N^6-benzoyladenine and N^2-O^6-diphenylcarbamoylguanine), selecting the reagents of BSA and MFSTA (*N*-methyl-*N*-trimethylsilyltrifluoroacetamide) and different solvents. After deprotection of **23a**–**d**, L-iodouridine **24a**, L-puridine **24b**, L-adenosine **24c** and L-guanosine **24d** were afforded in high yield (93, 91, 94, 91% for **24a**–**d**, respectively).

In order to be read more easily, structures of bases of the above synthesized L-ribosides and their derivatives were shown in Table 1.

3. Conclusion

From the easily available 1,2,5,6-di-*O*-isopropylidene-D-galactofuranose **4** we synthesized L-deoxyribose via eight steps in 75% overall yield and L-ribose via nine steps in 57% overall yield. We also successfully carried out the key steps of chemoselective hydrolysis and cleavage of the terminal isopropylidene acetal of compound **4** and the key steps of the inversion and deoxygenation of the 2-hydroxy group of compound **8**. Owing to these mild reaction conditions, cheap reagents and good yields, these procedures provide a practical synthesis of L-deoxyribose, L-ribose and L-ribosides. The biological activity of the L-ribosides and their derivatives are being assessed.

4. Experimental

4.1. General

IR spectra were recorded on a Digilab FT-IR instrument. ^{1}H NMR spectra were recorded on a Bruker AM-300 (300 MHz) and assigned in ppm (δ) downfield relative to TMS as internal standard. Optical rotations were measured at room temperature. MS spectra were conducted on a HP-5989A and VG QUATTRO mass spectrometers. Microanalyses were performed in the Microanalytical Laboratory at the Shanghai Institute of Organic Chemistry. Flash column chromatography was performed on silica gel (10–40 μm) using a mixture of petroleum ether and ethyl acetate or dichloromethane and methanol as the eluent. Solvents and reagents were purified and dried by standard methods prior to use.

4.1.1. 1,2-Isopropylidene-5-oxo-β-L-arabinofuranose (5). A solution of D-galactofuranose **4** (5.20 g, 20.0 mmol) in ethyl acetate (50 mL) was added to a well-stirred suspension of $NaIO_4$ (4.2 g, 20.0 mmol) and H_5IO_6 (2.28 g, 10.0 mmol) in ethyl acetate (50 mL). After 5 h at room temperature, the mixture was worked up by filtering and evaporating the solution. The residue was chromatographed (ethyl acetate/petroleum ether=1:1) to give aldehyde **5** (3.538 g, 94%) as a colorless oil. $[\alpha]_D^{20}=-22.8$ (*c* 1.2, MeOH); MS (EI) *m/z* 188 (M^+), 173 (M^+-CH_3); IR (film, cm^{-1}): 3402 (brs), 2990, 1733; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71 (s, 1H, HC(5)), 6.05 (d, $J_{1,2}$=3.5 Hz, 1H, HC(1)), 4.56 (d, $J_{1,2}$=3.5 Hz, 1H, HC(2)), 4.45 (s, 1H, HC(4)), 4.38 (s, 1H, HC(3)), 1.37 (s, 3H, CH_3), 1.27 (s, 3H, CH_3); HRMS (EI): (M^+-CH_3), found 173.0431. $C_7H_9O_5$ requires 173.0412.

4.1.2. 1,2-Isopropylidene-β-L-arabinofuranose (6). To a solution of aldehyde **5** (10.23 g, 54.41 mmol) in methanol (200 mL) was added $NaBH_4$ (6.59 g, 173 mmol). After the mixture was stirred at room temperature for 2 h, 10% AcOH was added to neutralize the mixture. Then the mixture was concentrated in vacuo and the residue was purified by flash chromatography (CH_2Cl_2/MeOH=15:1) to give alcohol **6** (10.03 g, 97%) as a colorless oil. $[\alpha]_D^{20}=-28.9$ (*c* 1.2, MeOH) [lit.[19] $[\alpha]_D^{20}=-28.9$ (H_2O)]; IR (film, cm^{-1}): 3397 (brs), 2940; MS (EI) *m/z* 175 (M^+-CH_3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 (d, $J_{1,2}$=4.1 Hz, 1H, HC(1)), 4.59 (d, $J_{1,2}$=4.1 Hz, 1H, HC(2)), 4.27 (d, $J_{3,4}$=2.5 Hz, 1H, HC(3)), 4.11 (m, 1H, HC(4)), 3.82 (dd, $J_{4,5a}$=6.9 Hz, $J_{5a,5b}$=11.8 Hz, 1H, HC(5a)), 3.75 (dd, $J_{4,5b}$=5.2 Hz, $J_{5a,5b}$=11.8 Hz, 1H, HC(5b)), 1.54 (s, 3H, CH_3), 1.34 (s, 3H, CH_3).

4.1.3. 1,2-Isopropylidene-3,5-*O*-dibenzyl-β-L-arabinofuranose (7). To a solution of alcohol **6** (12.454 g, 65.54 mmol) in anhydrous 1,4-dioxane (75 mL) was

added benzyl chloride (75 mL) and powdered potassium hydroxide (45 g). The mixture was refluxed under argon for 2 h. The dioxane was distilled and the residue was cooled and ice-water (150 mL) was added, then extracted with ether (4×100 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography (ethyl acetate/petroleum ether=1:20) to give **7** (23.30 g, 96%) as a yellow oil. $[\alpha]_D^{20}=-17.8$ (*c* 0.90, MeOH) [lit.[23] $[\alpha]_D^{20}=-10.4$ (*c* 0.8, $CHCl_3$)]; IR (film, cm^{-1}): 3032, 2939, 1497; MS (EI) *m/z* 371 (M^++1), 370 (M^+); ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.27 (m, 10H, Ph), 5.91 (d, $J_{1,2}$=4.1 Hz, 1H, HC(1)), 4.66 (d, $J_{1,2}$=4.1 Hz, 1H, HC(2)), 4.62–4.53 (m, 4H, CH_2OPh), 4.28 (td, $J_{3,4}$=3.0 Hz, $J_{4,5}$=6.3 Hz, 1H, HC(4)), 4.04 (d, $J_{3,4}$=3.0 Hz, 1H, HC(3)), 3.64 (d, $J_{4,5}$=6.3 Hz, 2H, HC(5)), 1.45 (s, 3H, CH_3), 1.33 (s, 3H, CH_3); Anal. calcd for $C_{22}H_{26}O_5$: C, 71.35; H, 7.03. Found: C, 71.92; H, 6.95.

4.1.4. 3,5-*O*-Dibenzyl-methyl-L-arabinofuranoside (8). A solution of **7** (7.84 g, 21.19 mmol) in 10% (w/w) hydrogen chloride in methanol (200 mL) was stirred at room temperature for 3 h. After the addition of $NaHCO_3$ (20 g), the mixture was concentrated to dryness. Ice-water was added to the residue, then extracted with ethyl acetate (4×100 mL) and the combined organic layers were washed with brine, dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography (ethyl acetate/petroleum ether=1:3) to give **8** (7.158 g, 98%) as a colorless oil. $[\alpha]_D^{20}=-72.1$ (*c* 1.5, MeOH); IR (film, cm^{-1}): 3443 (brs), 3032, 2915; MS (EI) *m/z* 344 (M^+); ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.25 (m, 10H, Ph), 4.92 (s, 0.57H, HC(1), α-anomer), 4.87 (d, $J_{1,2}$=4.7 Hz, 0.43H, HC(1), β-anomer), 4.78–4.46 (m, 4H, OCH_2Ph), 4.28 (dd, $J_{2,3}$=2.5 Hz, $J_{3,4}$=5.2 Hz, 1H, HC(3)), 4.14 (m, 1H, HC(3)), 3.86 (m, 1H, HC(4)), 3.67 (dd, $J_{4,5a}$=2.2 Hz, $J_{5a,5b}$=10.4 Hz, 1H, HC(5a)), 3.44 (dd, $J_{4,5b}$=2.5 Hz, $J_{5a,5b}$=10.4 Hz, 1H, HC(5b)), 3.42 (s, 3H, OMe); Anal. calcd for $C_{20}H_{24}O_5$: C, 69.77; H, 6.98. Found: C, 69.77; H, 7.08.

4.1.5. 3,5-*O*-Dibenzyl-2-*O*-triflate-methyl-L-arabinofuranoside (9). A 250 mL three-neck round bottom flask equipped with two addition funnels was charged with pyridine (0.80 mL, 10.23 mmol) and anhydrous CH_2Cl_2 (50 mL) under argon. A solution of triflic anhydride (1.0 mL, 6.5 mmol) in CH_2Cl_2 (40 mL) was placed in one addition funnel. The sugar **8** (2.037 g, 5.92 mmol) dissolved in CH_2Cl_2 (40 mL) was placed in the other addition funnel. The flask was cooled to −10 to −15°C in an ice/salt bath and the triflic anhydride solution was added dropwise for 30 min. The mixture was stirred for another 15 min. Then sugar solution was added dropwise for 30 min and stirring continued for additional 4 h. The reaction mixture was poured into ice-water (300 mL). The aqueous layer was extracted with CH_2Cl_2 (2×400 mL). The combined extract was dried over Na_2SO_4 and the residue purified by flash chromatography (ethyl acetate/petroleum ether=1:15) gave **9** (2.790 g, 99%) as a yellow oil. $[\alpha]_D^{20}=-124$ (*c* 1.9, MeOH); IR (film, cm^{-1}): 3034, 2935, 1498, 1419; MS (EI) *m/z* 476 (M^+); ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.22 (m, 10H, Ph), 5.20 (s, 0.73H, HC(1), α-anomer), 5.09 (m, 1H, HC(2)), 5.00 (d, $J_{1,2}$=4.4 Hz, 0.23H, HC(1), β-anomer), 4.73–4.48 (m, 4H, OCH_2Ph), 4.21–4.11 (m, 2H, HC(3), HC(4)), 3.64–3.48 (m, 2H, HC(5)), 3.42 (s, 2.19H, OCH_3, α-anomer), 3.38 (s, 0.81H, β-anomer); Anal. calcd for $C_{21}H_{23}O_7SF_3$: C, 52.94; H, 4.83. Found: C, 53.05; H, 4.83.

4.1.6. Methyl 3,5-*O*-dibenzyl-2-deoxy-L-ribofuranoside (10). To a solution of **9** (857 mg, 1.80 mmol) in anhydrous benzene (15 mL) was added *n*-Bu_4NBH_4 (1.38 g, 54 mmol). The mixture was refluxed for 4 h under argon. The reaction mixture was poured into ice-water (50 mL). The aqueous water was extracted with CH_2Cl_2 (3×100 mL). The combined organic layers were washed with water, brine, and dried over Na_2SO_4. The solvent was removed in vacuo. The residue was purified by flash chromatography (ethyl acetate/petroleum ether=1:12) to give β-anomer (212 mg, 36%), α-anomer (281 mg, 48%) and recovered starting material (72 mg, 11%). The yield was 95%. β-anomer: $[\alpha]_D^{20}=-14.3$ (*c* 0.8, MeOH) [D-enantiomer: lit.[24] $[\alpha]_D^{20}=-52$ (*c* 0.5, $CHCl_3$)]; IR (film, cm^{-1}): 3032, 2908, 1497; MS (EI) *m/z* 328 (M^+); ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.26 (m, 10H, Ph), 5.10 (dd, $J_{1,2a}$=5.1 Hz, $J_{1,2b}$=2.1 Hz, 1H, HC(1)), 4.60–4.56 (m, 4H, OCH_2Ph), 4.26 (m, 1H, HC(3)), 4.14 (m, 1H, HC(4)), 3.58–3.47 (m, 2H, HC(5)), 3.30 (s, 3H, OCH_3), 2.25–2.09 (m, 2H, HC(2a), HC(2b)); Anal. calcd for $C_{20}H_{24}O_4$: C, 73.17; H, 7.32. Found: C, 73.01, H, 7.14. α-anomer: $[\alpha]_D^{20}=-58.0$ (*c* 0.8, MeOH) [D-enantiomer: lit.[24] $[\alpha]_D^{20}=+106$ (*c* 0.5, $CHCl_3$)]; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.26 (m, 10H, Ph), 5.07 (d, $J_{1,2a}$=5.4 Hz, 1H, HC(1)), 4.58–4.46 (m, 4H, OCH_2Ph), 4.25 (dd, $J_{2a,3}$=8.7 Hz, $J_{3,4}$=4.3 Hz, 1H, HC(3)), 3.97 (m, 1H, HC(4)), 3.57–3.47 (m, 2H, HC(5)), 3.41 (s, 3H, OCH_3), 2.27–2.17 (m, 2H, HC(2a), HC(2b)).

4.1.7. Methyl 2-deoxy-L-ribofuranoside (11). To a solution of **10** (383 mg, 1.167 mmol) in MeOH (16 mL) was added 10% Pd–C (100 mg). The mixture was stirred under H_2 for 3 h at room temperature. The reaction was worked up by filtering and concentrating in vacuo. The residue was purified by flash chromatography (CH_2Cl_2/MeOH=10:1) to give **11** (168 mg, 97%) as a white solid. $[\alpha]_D^{20}=-48$ (*c* 0.8, MeOH); IR (KBr) ν_{max} 3393 (brs), 2935; MS (EI) *m/z* 148 (M^+), 117 (M^+-OMe); ^1H NMR (300 MHz, D_2O) δ 5.22 (m, 1H, HC(1)), 4.29 (m, 1H, H(3)), 4.07 (m, 1H, HC(4)), 3.64–3.56 (m, 2H, HC(5)), 3.37 (s, 3H, OMe), 2.38–1.87 (m, 2H, HC(2)) [lit.[25]]; HRMS (EI): (M^+-OMe), found 117.0552. $C_5H_9O_3$ requires 117.0559.

4.1.8. L-2-Deoxyribose (2). To a solution of **11** (140 mg, 0.95 mmol) in 10 mL water was added Dowex resin [H^+ form] (200 mg). The mixture was stirred at 60°C for 24 h. The reaction was worked up by filtering and concentrating in vacuo. The residue was purified by flash chromatography (CH_2Cl_2/MeOH=5:1) to give **2** (124 mg, 98%) as a white solid. $[\alpha]_D^{20}=+64.5$ (*c* 1.9, MeOH) [D-enantiomer: lit.[26] $[\alpha]_D^{20}=-59$ (*c* 1, H_2O)]; ^1H NMR (300 MHz, CD_3OD) δ 5.36 (dd, $J_{1,2a}$=3.2 Hz, $J_{1,2b}$=4.3 Hz, 0.4H, HC(1)), 4.91 (dd, $J_{1,2a}$=3.2 Hz, $J_{1,2b}$=7.2 Hz, 0.6H, HC(1)), 4.24–3.93 (m, 2H, HC(3), HC(4)), 3.90–3.51 (m, 2H, HC(5)), 2.35–1.83 (m, 2H, HC(2a), HC(2b)).

4.1.9. Methyl 3,5-*O*-dibenzyl-2-*O*-methanesulfonyl-L-arabinofuranoside (12). To a solution of **8** (5.00 g,

14.53 mmol) in anhydrous CH_2Cl_2 (125 mL) was added triethylamine (5.6 mL, 40 mmol) and methanesulfonyl chloride (1.66 mL, 21.8 mmol). The solution was stirred at room temperature overnight. Then the solution was diluted with CH_2Cl_2 (200 mL), washed with water, brine, dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography (ethyl acetate/petroleum ether=1:4) to give **12** (6.01 g, 98%) as a yellow oil. $[\alpha]_D^{20}=-72.7$ (*c* 1.5, MeOH); IR (film, cm^{-1}): 3032, 2937, 1497, 1364; MS (EI) *m/z* 423 ($M^+ +1$), 421 ($M^+ -1$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.28 (m, 10H, Ph), 5.09 (s, 0.67H, HC(1), α-anomer), 5.01 (m, 1H, HC(2)), 4.96 (d, $J_{1,2}$=4.4 Hz, 0.33H, β-anomer), 4.76–4.49 (m, 4H, OCH_2Ph), 4.22 (m, 1H, HC(3)), 4.13 (m, 1H, HC(4)), 3.67–3.53 (m, 2H, HC(5)), 3.43 (s, 2H, OCH_3, α-anomer), 3.40 (s, 1H, OCH_3, β-anomer), 3.04 (s, 1H, CH_3, β-anomer), 2.94 (s, 2H, CH_3, α-anomer); Anal. calcd for $C_{21}H_{26}O_7S$: C, 59.72; H, 6.16. Found: C, 59.79; H, 6.19.

4.1.10. 1,5-*O*-Diacetyl-3-*O*-benzyl-2-*O*-methanesulfonyl-L-arabinofuranose (13). Glacial acetic acid (30 mL) and Ac_2O (7.6 mL) were added to **12** (6.01 g, 14.24 mmol). The mixture was stirred for 5 min at 0°C, then H_2SO_4 (1.2 mL) was added dropwise during 30 min. The mixture was stirred until the precipitation occurred, then kept overnight at 4°C. Ice-water (200 mL) was added and stirred for 30 min, then the mixture was extracted with CH_2Cl_2 (3×200 mL). The combined organic layers were washed with a cold sat. $NaHCO_3$ solution (3×200 mL), brine, dried over Na_2SO_4. The solvent was removed in vacuo and the residue purified by flash chromatography (ethyl acetate/petroleum ether=1:3) gave **13** (5.10 g, 89%) as a colorless oil. $[\alpha]_D^{20}=+52.5$ (*c* 1.5, MeOH); IR (film, cm^{-1}): 3030, 2939, 1740, 1355; MS (EI) *m/z* 343 ($M^+ -OAc$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.35 (m, 5H, Ph), 6.24 (s, 1H, HC(1)), 5.14 (d, $J_{2,3}$=1.6 Hz, 1H, H(2)), 4.78 (d, *J*=11.9 Hz, 1H, OCH_2Ph), 4.62 (d, *J*=11.9 Hz, 1H, OCH_2Ph), 4.40 (m, 1H, HC (4)), 4.27 (dd, $J_{4,5a}$=3.8 Hz, $J_{5a,5b}$=12.3 Hz, 1H, HC(5a)), 4.18 (m, 1H, HC(3)), 4.15 (dd, $J_{4,5b}$=5.3 Hz, $J_{5a,5b}$=12.3 Hz, 1H, HC(5b)), 3.14 (s, 3H), 2.14 (s, 3H, OAc), 2.05 (s, 3H, OAc); HRMS (EI): ($M^+ -OAc-Ac$), found 300.0668. $C_{13}H_{16}SO_6$ requires 300.0631.

4.1.11. Methyl 3-*O*-Benzyl-β-L-ribofuranoside (14). To a solution of **13** (2.50 g, 6.22 mmol) in methanol (50 mL) was added NaOMe/MeOH solution (100 mL, 18.7 mmol). The mixture was stirred at room temperature for 6 h. HCl (1 mol/L) solution was added to neutralize the mixture. The mixture was concentrated in vacuo and the residue was purified by flash chromatography (CH_2Cl_2/MeOH=30:1) to give **14** (1.378 g, 87%) as a yellow residue. $[\alpha]_D^{20}=+9.1$ (*c* 0.5, MeOH); IR (film, cm^{-1}): 3415 (brs), 3032, 2931. MS (EI) *m/z* 254 (M^+); ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.31 (m, 5H, Ph), 4.87 (s, 1H, HC(1)), 4.56 (s, 2H, OCH_2Ph), 4.23–4.11 (m, 2H, HC(3), HC(4)), 4.04 (d, $J_{2,3}$=4.2 Hz, 1H, HC(2)), 3.77 (dd, $J_{4,5a}$=2.2 Hz, $J_{5a,5b}$=12.0 Hz, 1H, HC(5a)), 3.55 (dd, $J_{4,5b}$=3.3 Hz, $J_{5a,5b}$=12.0 Hz, 1H, HC(5b)), 3.40 (s, 3H, OMe); HRMS (EI): (M^+), found 254.1154. $C_{13}H_{18}O_5$ requires 254.1178.

4.1.12. Methyl β-L-ribofuranoside (15). To a solution of **14** (1.305 g, 5.14 mmol) in methanol (60 mL) was added 10% Pd–C (150 mg). The mixture was stirred under H_2 for 2 h at room temperature. The reaction was worked up by filtering and concentrating in vacuo. The residue was purified by flash chromatography (CH_2Cl_2/MeOH=8:1) to give **15** (818 mg, 97%) as a white solid. $[\alpha]_D^{20}=+64.8$ (*c* 2.0, H_2O) [lit.[27] $[\alpha]_D^{20}=+46$ (*c* 1.9, H_2O)]; IR (KBr): ν_{max} 3392 (brs), 2936. MS (EI) *m/z* 164 (M^+), 133 ($M^+ -OMe$); ^1H NMR (300 MHz, DMSO-d_6) δ 4.61 (d, $J_{1,2}$=2.9 Hz, 1H, HC(1)), 3.75–3.70 (m, 3H, HC(2), HC(3), HC(4)), 3.63 (dd, $J_{4,5a}$=3.6 Hz, $J_{5a,5b}$=11.8 Hz, HC(5a)), 3.56 (m, 1H, HC(5b)), 3.33 (s, 3H, OMe); HRMS (EI): ($M^+ -OMe$), found 133.0501. $C_5H_9O_6$ requires 133.0508.

4.1.13. L-Ribose (3). To a solution of **15** (750 mg, 4.57 mmol) in H_2O (40 mL) was added Dowex resin [H^+ form] (1.20 g). The mixture was stirred at 50°C for 24 h. The reaction was worked up by filtering and concentrating in vacuo. The residue was purified by flash chromatography (CH_2Cl_2/MeOH=4:1) to give **3** (653 mg, 95%) as a white solid. $[\alpha]_D^{20}=+19.2$ (*c* 2.0, H_2O) [lit.[26] $[\alpha]_D^{20}=+19$ (*c* 2.0, H_2O)]; IR (KBr) ν_{max} 3510 (brs), 2939; MS (EI) *m/z* 151 ($M^+ +1$), 133 ($M^+ -OH$); ^1H NMR (300 MHz, CD_3OD) δ 4.93 (d, $J_{1,2}$=5.0 Hz, 0.57H, HC(1), β-anomer), 4.78 (d, $J_{1,2}$=1.5 Hz, 0.43H, HC(1), α-anomer), 3.94–3.82 (m, 2H, HC(2), HC(3)), 3.77–3.61 (m, 2H, HC(4), HC(5a)), 3.48 (m, 1H, HC(5b)); Anal. calcd for $C_5H_{10}O_5 \cdot 0.1H_2O$: C, 39.53; H, 6.72. Found: C, 39.51; H, 6.79.

4.1.14. Methyl 2,5-*O*-diacetyl-3-*O*-benzyl-β-L-ribofuranoside (16). To a solution of **14** (4.46 g, 19.12 mmol) in pyridine (60 mL) was added Ac_2O (16 mL). The mixture was stirred at room temperature overnight. The mixture was evaporated in vacuo. Then a cold sat. $NaHCO_3$ solution (100 mL) was added to the residue. The mixture was extracted with CH_2Cl_2 (3×100 mL), washed with $CuSO_4$ solution, brine, dried over Na_2SO_4. The solvent was removed in vacuo. The residue was purified by flash chromatography (ethyl acetate/petroleum ether=1:10) to give **16** (5.571 g, 86%) as a colorless oil. $[\alpha]_D^{20}=-13.1$ (*c* 1.0, MeOH); IR (film, cm^{-1}): 3034, 2938, 1751, 1744, 1498; MS (EI) *m/z* 338 (M^+), 307 ($M^+ -OMe$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.29 (m, 5H, Ph), 5.21 (d, $J_{2,3}$=4.3 Hz, 1H, HC(2)), 4.86 (s, 1H, HC(1)), 4.61 (d, *J*=11.4 Hz, 1H, OCH_2Ph), 4.43 (d, *J*=11.4 Hz, 1H, OCH_2Ph), 4.29 (d, $J_{4,5a}$=3.1 Hz, $J_{5a,5b}$=11.5 Hz, 1H, HC(5a)), 4.21 (ddd, $J_{3,4}$=7.8 Hz, $J_{4,5a}$=3.1 Hz, $J_{4,5b}$=6.1 Hz, 1H, HC(4)), 4.12 (dd, $J_{2,3}$=4.3 Hz, $J_{3,4}$=7.8 Hz, 1H, HC(3)), 4.06 (dd, $J_{4,5b}$=6.1 Hz, $J_{5a,5b}$=11.6 Hz, 1H, HC(5b)), 3.34 (s, 3H, OMe), 2.13 (s, 3H, OAc), 2.05 (s, 3H, OAc); Anal. calcd for $C_{17}H_{22}O_7$: C, 60.36; H, 6.51. Found: C, 60.39; H, 6.62.

4.1.15. 1,2,5-*O*-Triacetyl-3-*O*-benzyl-β-L-ribofuranose (17). Compound **16** (2.814 g, 8.31 mmol) was treated as the preparation of compound **13**. Purification by flash chromatography (ethyl acetate/petroleum ether=1:4) gave **17** (β-anomer, 2.318 g, 76%) and its α-anomer (584 mg, 17%) as a colorless oil. β-anomer: $[\alpha]_D^{20}=-22.3$ (*c* 0.8, MeOH); IR (film, cm^{-1}): 3030, 2939, 1747, 1455; MS (EI) *m/z* 307 ($M^+ -OAc$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H, Ph), 6.15 (s, 1H, HC(1)), 5.32 (d, $J_{2,3}$=4.4 Hz, 1H, HC(2)), 4.65 (d, *J*=11.3 Hz, 1H, OCH_2Ph), 4.46 (d, *J*=11.3 Hz, 1H, OCH_2Ph), 4.29 (dd, $J_{4,5a}$=3.4 Hz, $J_{5a,5b}$=10.0 Hz, 1H, HC(5a)), 4.27 (dd, $J_{4,5b}$=3.0 Hz, $J_{5a,5b}$=

11.0 Hz, 1H, HC(5b)), 4.14–4.09 (m, 2H, HC(3), HC(4)), 2.15 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.03 (s, 3H, OAc); Anal. calcd for $C_{18}H_{22}O_8$ C, 59.02; H, 6.01. Found: C, 58.96; H, 6.11. α-anomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.33 (m, 5H, Ph), 7.06 (d, $J_{1,2}$=4.9 Hz, 1H, HC(1)), 5.43 (t, $J_{1,2}$=$J_{2,3}$=5.0 Hz, 1H, HC(2)), 5.28 (m, 1H, HC(4)), 4.68 (d, 1H, J=11.4 Hz, 1H, OCH_2Ph), 4.61 (d, J=11.4 Hz, 1H, OCH_2Ph), 4.44 (dd, $J_{4,5a}$=3.3 Hz, $J_{5a,5b}$=12.1 Hz, HC(5a)), 4.13 (dd, $J_{4,5b}$=6.2 Hz, $J_{5a,5b}$=12.1 Hz, 1H, HC(5b)), 3.84 (t, $J_{2,3}$=$J_{3,4}$=5.2 Hz, 1H, HC(3)), 2.13 (s, 3H, OAc), 2.06 (s, 3H, OAc), 2.02 (s, 3H, OAc).

4.1.16. 2′,5′-*O*-Diacetyl-3′-*O*-benzyl-β-L-uridine (18a). Compound **17** (364 mg, 1.0 mmol) and uracil (334 mg, 3.0 mmol) were co-evaporated three times with anhydrous CH_3CN under argon. Anhydrous CH_3CN (16 mL) and BSA (0.74 mL, 3.0 mmol) were added at room temperature. The mixture was stirred at 60–65°C until the base dissolved. TMSOTf (174 μL, 1.48 mmol) was added, the mixture stirred overnight at 65°C. CH_2Cl_2 (150 mL) was added and the mixture was washed with sat. $NaHCO_3$ solution and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography (ethyl acetate/petroleum ether=2:1) to afford **18a** (383 mg, 92%) as a white foam. $[\alpha]_D^{20}$=−190.5 (*c* 2.4, MeOH); IR (KBr) ν_{max} 3034, 2828, 1680, 1466, 1380; MS (EI) *m/z* 419 (M^++1), 359 (M^+−OAc), 307 (M^+−base); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.07 (s, 1H, NH), 7.40 (d, $J_{5,6}$= 8.1 Hz, 1H, HC(6)), 7.37–7.29 (m, 5H, Ph), 5.84 (d, $J_{1',2'}$=3.0 Hz, 1H, HC(1′)), 5.74 (dd, $J_{3,5}$=2.0 Hz, $J_{5,6}$= 8.0 Hz, 1H, HC(5)), 5.41 (dd, 1H, $J_{1',2'}$=3.0 Hz, $J_{2',3'}$= 5.4 Hz, 1H, HC(2′)), 4.63 (d, J=11.6 Hz, 1H, OCH_2Ph), 4.46 (d, J=11.6, 1H, OCH_2Ph), 4.30 (d, $J_{4',5a'}$=4.1 Hz, $J_{5a',5b'}$=13.1 Hz, 1H, HC(5a′)), 4.26–4.20 (m, 2H, HC(4′), HC(5b′)), 4.13 (m, 1H, HC(3′)), 2.16 (s, 3H, OAc), 2.03 (s, 3H, OAc); HRMS (EI): (M^+−base), found 307.1182. $C_{14}H_{17}O_5$ requires 307.1172.

4.1.17. 2′,5′-*O*-Diacetyl-3′-*O*-benzyl-β-L-thymidine (18b). Compound **17** (334 mg, 0.913 mmol) and thymine (345 mg, 2.74 mmol) were treated as described above. Purification by flash chromatography (ethyl acetate/petroleum ether=3:2) afforded **18b** (346 mg, 88%) as a white foam. $[\alpha]_D^{20}$= −23.4 (*c* 0.6, MeOH); IR (KBr) ν_{max} 3197 (brs), 2903, 1748, 1649, 1465, 1373; MS (EI) *m/z* 372 (M^+−AcOH), 307 (M^+−base); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (s, 1H, NH), 7.38–7.30 (m, 5H, Ph), 7.14 (s, 1H, HC(6)), 5.85 (d, $J_{1',2'}$=3.3 Hz, 1H, HC(1′)), 5.37 (dd, $J_{1',2'}$=3.3 Hz, $J_{2',3'}$= 5.2 Hz, 1H, HC(2′)), 4.62 (d, J=11.3 Hz, 1H, OCH_2Ph), 4.46 (d, J=11.3 Hz, 1H, OCH_2Ph), 4.31 (dd, $J_{4',5a'}$= 4.1 Hz, $J_{5a',5b'}$=13.1 Hz, 1H, HC(5a′)), 4.25–4.19 (m, 2H, HC(3′), HC(4′)), 4.15 (dd, $J_{4',5b'}$=6.3 Hz, $J_{5a',5b'}$=12.8 Hz, 1H, HC(5b′)), 2.14 (s, 3H, OAc), 2.04 (s, 3H, OAc), 1.91 (s, 3H, CH_3); Anal. calcd for $C_{21}H_{24}O_8N_2$: C, 58.33; H,5.56; N, 6.48. Found: C, 58.22; H, 5.56; N, 6.32.

4.1.18. 2′,5′-*O*-Diacetyl-3′-*O*-benzyl-β-L-5-flurouridine (18c). Compound **17** (350 mg, 0.96 mmol) and 5-flurouracil (373 mg, 2.87 mmol) were treated as described above. Purification by flash chromatography (ethyl acetate/petroleum ether=2:1) gave **18c** (371 mg, 89%) as a white foam. $[\alpha]_D^{20}$=−44.2 (*c* 1.0, MeOH); IR (KBr) ν_{max} 3013, 2919, 1739,1716, 1463, 1376; MS (EI) *m/z* 437 (M^++1), 307 (M^+−base); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (s, 1H, NH), 7.69 (d, J=6.3 Hz, 1H, HC(6)), 7.38–7.29 (m, 5H, Ph), 5.93 (dd, $J_{1',2'}$=2.6 Hz, $J_{1',4'}$=1.2 Hz, 1H, HC(1′)), 5.38 (dd, $J_{1',2'}$=2.6 Hz, $J_{2',3'}$=5.1 Hz, 1H, HC(2′)), 4.65 (d, J=11.5 Hz, 1H, OCH_2Ph), 4.44 (d, J=11.5 Hz, 1H, OCH_2Ph), 4.31–4.25 (m, 3H, HC(4′), HC(5a′), HC(5b′)), 4.04 (dd, $J_{2',3'}$=5.2 Hz, $J_{3',4'}$=7.2 Hz, 1H, HC (3′)), 2.18 (s, 3H, OAc), 2.03 (s, 3H, OAc); HRMS (EI): (M^+−base−Ac), found 264.0998. $C_{14}H_{16}O_5$ required 264.0991.

4.1.19. 3′-*O*-Benzyl-β-L-thymidine (19b). Compound **18b** (382 mg, 0.884 mmol) was dissolved in MeOH/THF (v/v=2:1, 6 mL), then NH_3 (35% in water, 11 mL) was added. The mixture was stirred overnight at 60°C in a sealed tube. After evaporation to dryness, the residue was purified by flash chromatography (CH_2Cl_2/MeOH=10:1) to afford **19b** (286 mg, 93%) as a white foam. $[\alpha]_D^{20}$=−27.5 (*c* 1.6, MeOH); IR (KBr) ν_{max} 3419 (brs), 3030, 2929, 1472; MS (EI) *m/z* 349 (M^++H); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.63 (s, 1H, NH), 7.35–7.32 (m, 6H, Ph, HC(6)), 5.63 (d, $J_{1',2'}$=5.2 Hz, 1H, HC(1′)), 5.29 (m, 1H, HC(4′)), 4.68 (d, J=11.7 Hz, 1H, OCH_2Ph), 4.63 (d, J=11.7 Hz, 1H, OCH_2Ph), 4.48 (dd, $J_{2',3'}$=5.4 Hz, $J_{3',4'}$=5.8 Hz, 1H, HC(3′)), 4.20 (dd, $J_{1',2'}$=4.3 Hz, $J_{2',3'}$=5.4 Hz, 1H, HC(2′)), 3.87 (m, 1H, HC(5a′)), 3.64 (m, 1H, HC(5b′)); Anal. calcd for $C_{17}H_{20}O_6N_2$: C, 58.62; H, 5.75; N, 8.05. Found: C, 58.18; H, 5.75; N, 7.73.

4.1.20. 3′-*O*-Benzyl-β-L-uridine (19a). Compound **18a** (235 mg, 0.562 mmol) and NH_3 (35% in water, 7 mL) were treated as described above. Purification by flash chromatography (CH_2Cl_2/MeOH=8:1) gave **19a** (179 mg, 95%) as a white foam. $[\alpha]_D^{20}$=−10.6 (*c* 0.6, MeOH); IR (KBr) ν_{max} 3389 (brs), 3037, 2819, 1464; MS (EI) *m/z* 335 (M^++1), 223 (M^+−base); ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.15 (s, 0.16H, NH), 7.89 (d, $J_{5,6}$=8.1 Hz, 1H, HC(6)), 7.40–7.28 (m, 5H, Ph), 5.83 (d, $J_{1',2'}$=5.8 Hz, 1H, HC(1′)), 5.66 (d, $J_{5,6}$=8.1 Hz, 1H, HC(5)), 4.71 (d, J=12.1 Hz, 1H, OCH_2Ph), 4.58 (d, J=12.1 Hz, 1H, OCH_2Ph), 4.23 (t, $J_{1',2'}$=5.6 Hz, $J_{2',3'}$=5.4 Hz, 1H, HC(2′)), 4.03 (m, 1H, HC(4′)), 3.92 (dd, $J_{2',3'}$=4.6 Hz, $J_{3',4'}$=4.1 Hz, 1H, HC(3′)), 3.62 (dd, $J_{4',5a'}$=3.3 Hz, $J_{5a',5b'}$=12.1 Hz, 1H, HC(5a′)), 3.53 (dd, $J_{4',5b'}$=3.0 Hz, $J_{5a',5b'}$=12.1 Hz, 1H, HC(5′)); HRMS (EI): (M^+−OBn), found 227.0668. $C_9H_{11}O_5N_2$ requires 227.0670.

4.1.21. 3′-*O*-Benzyl-β-L-5-fluorouridine (19c). Compound **18c** (207 mg, 0.475 mmol) and NH_3 (35% in water, 6 mL) were treated as described above. Purification by flash chromatography (CH_2Cl_2/MeOH=13:1) gave **19c** (152 mg, 91%) as a white foam. $[\alpha]_D^{20}$=−78.8 (*c* 1.8, MeOH); IR (KBr) ν_{max} 3449 (brs), 3066, 1474; MS (EI) *m/z* 353 (M^++1), 223 (M^+−base); ^{1}H NMR (300 MHz, CD_3OD) δ 8.30 (d, $J_{5,6}$=6.9 Hz, 1H, HC(6)), 7.43–7.29 (m, 5H, Ph), 5.93 (dd, $J_{1',2'}$=5.8 Hz, $J_{1',4'}$=1.5 Hz, 1H, HC(1′)), 4.76 (d, J=11.8 Hz, 1H, OCH_2Ph), 4.64 (d, J=11.8 Hz, 1H, OCH_2Ph), 4.31 (t, $J_{1',2'}$=4.9 Hz, $J_{2',3'}$=5.0 Hz, 1H, HC(2′)), 4.15 (ddd, $J_{3',4'}$=4.9 Hz, $J_{4',5a'}$=2.8 Hz, $J_{4',5b'}$= 1.5 Hz, 1H, HC(4′)), 4.06 (t, $J_{2',3'}$=5.0 Hz, $J_{3',4'}$=4.9 Hz, 1H, HC(3′)), 3.85 (dd, $J_{4',5a'}$=2.8 Hz, $J_{5a',5b'}$=12.3 Hz, 1H, HC(5a′)), 3.68 (dd, $J_{4',5b'}$=1.5 Hz, $J_{5a',5b'}$=12.1 Hz, 1H, HC(5b′)); HRMS (EI): (M^+−base), found 223.0970. $C_{12}H_{15}O_4$ requires 223.0969.

4.1.22. β-L-Thymidine (20b). To a solution of **19b** (200 mg, 0.575 mmol) in MeOH (10 mL) was added 10% Pd–C (50 mg). The mixture was stirred under H_2 for 1 h at room temperature. The reaction was worked up by filtering and concentrating in vacuo. The residue was purified by flash chromatography (CH_2Cl_2/MeOH=4:1) to give **20b** (147 mg, 98%) as a white solid. $[\alpha]_D^{20}$=+15.6 (*c* 1.1, MeOH) [D-enantiomer: lit.[28] $[\alpha]_D^{20}$=−9.7 (*c* 1.66, H_2O)]; MS (EI) *m/z* 258 (M^+); ^{1}H NMR (300 MHz, DMSO-d_6) δ 11.31 (s, 0.25H, NH), 7.74 (s, 1H, HC(6)), 5.78 (d, $J_{1',2'}$= 5.6 Hz, 1H, HC(1′)), 4.03 (t, $J_{1',2'}$=5.5 Hz, $J_{2',3'}$=5.3 Hz, 1H, HC(2′)), 3.96 (dd, $J_{2',3'}$=4.9 Hz, $J_{3',4'}$=3.9 Hz, 1H, HC(3′)), 3.80 (q, $J_{3',4'}$=3.9 Hz, $J_{4',5a'}$=3.4 Hz, $J_{4',5b'}$= 3.4 Hz, 1H, HC(4′)), 3.63 (dd, $J_{4',5a'}$=3.4, $J_{5a',5b'}$=12.1 Hz, 1H, HC(5a′)), 3.53 (dd, $J_{4',5b'}$=3.4 Hz, $J_{5a',5b'}$=12.2 Hz, 1H, HC(5b′)); Anal. calcd for $C_{10}H_{14}O_6N_2{\cdot}0.25H_2O$: C, 45.71; H, 5.52; N, 10.67. Found: C, 45.89; H, 5.44; N, 10.33.

4.1.23. β-L-Uridine (20a). Compound **19a** (157 mg, 0.470 mmol) was treated as described above. Purification by flash chromatography (CH_2Cl_2/MeOH=4:1) gave **20a** (111 mg, 97%) as a white foam. $[\alpha]_D^{20}$=−14.3 (*c* 0.4, H_2O) [lit.[18] $[\alpha]_{546}^{25}$=−16 (*c* 0.55, H_2O)]; MS (EI) *m/z* 244 (M^+), 227 (M^+−OH), 133 (M^+−base); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.87 (d, $J_{5,6}$=8.2 Hz, 1H, HC(6)), 5.78 (d, $J_{1',2'}$=5.2 Hz, 1H, HC(1′)), 5.64 (d, $J_{5,6}$=8.2 Hz, 1H, HC(5)), 4.02 (t, $J_{1',2'}$=5.2 Hz, $J_{2',3'}$=5.2 Hz, 1H, HC(2′)), 3.96 (dd, $J_{2',3'}$=4.9 Hz, $J_{3',4'}$=4.2 Hz, 1H, HC(3′)), 3.80 (q, $J_{3',4'}$=3.6 Hz, $J_{4',5a'}$=3.3 Hz, $J_{4',5b'}$= 3.3 Hz, 1H, HC(4′)), 3.62 (dd, $J_{4',5a'}$=3.3 Hz, $J_{5a',5b'}$= 12.1 Hz, 1H, HC(5a′)), 3.54 (dd, $J_{4',5b'}$=3.3 Hz, $J_{5a',5b'}$= 12.2 Hz, 1H, HC(5b′)); HRMS (EI): (M^+−H_2O), found 226.0590. $C_9H_{10}O_5N_2$ requires 226.0595.

4.1.24. β-L-5-Fluorouridine (20c). Compound **19c** (126 mg, 0.361 mmol) was treated as described above. Purification by flash chromatography (CH_2Cl_2/MeOH=4:1) gave **20c** (91 mg, 95%) as a white foam. $[\alpha]_D^{20}$=−8.2 (*c* 0.7, H_2O) [D-enantiomer: lit.[29] $[\alpha]_D^{20}$=+17 (*c* 2.0, H_2O)]; MS (EI) *m/z* 263 (M^++1); ^{1}H NMR (300 MHz, CD_3OD) δ 8.32 (d, $J_{5,6}$=7.0 Hz, 1H, HC(6)), 5.90 (dd, $J_{1',2'}$=3.8 Hz, $J_{1',4'}$=1.6 Hz, 1H, HC(1′)), 4.20–4.15 (m, 2H, HC(2′), HC(3)), 4.02 (m, 1H, HC(4′)), 3.88 (dd, $J_{4',5a'}$=2.6 Hz, $J_{5a',5b'}$=12.2 Hz, 1H, HC(5a′)), 3.76 (dd, $J_{4',5b'}$=2.6 Hz, $J_{5a',5b'}$=12.2 Hz, 1H, HC(5b′)); HRMS (EI): (M^+−base), found 133.0501. $C_5H_9O_4$ requires 133.0513.

4.1.25. Methyl 2,3,5-*O*-triacetyl-β-L-ribofuranoside (21). Compound **15** (717 mg, 4.37 mmol) was treated as the preparation of compound **16**. Purification by flash chromatography (ethyl acetate/petroleum ether=1:5) gave **21** (1.321 g, 98%) as a colorless oil. $[\alpha]_D^{20}$=+23.8 (*c* 0.8, MeOH) [lit.[30] $[\alpha]_D^{22}$=+14.6 (*c* 2.3, MeOH)]; IR (film, cm^{-1}): 2943, 1749, 1442; MS (EI) *m/z* 290 (M^+), 259 (M^+−OMe); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.34 (dd, $J_{2,3}$=4.8 Hz, $J_{3,4}$=6.6 Hz, 1H, HC(3)), 5.23 (d, $J_{2,3}$= 4.8 Hz, 1H, HC(2)), 4.91 (s, 1H, HC(1)), 4.37 (dd, $J_{4,5a}$= 3.8 Hz, $J_{5a,5b}$=11.5 Hz, 1H, HC(5a)), 4.30 (m 1H, HC(4)), 4.11 (dd, $J_{4,5b}$=5.3 Hz, $J_{5a,5b}$=11.5 Hz, 1H, HC(5b)), 3.39 (s, 3H, OMe), 2.12 (s, 3H, OAc), 2.10 (s, 3H, OAc), 2.06 (s, 3H, OAc).

4.1.26. 1,2,3,5-*O*-Tetracetyl-β-L-ribofuranose (22). Compound **21** (1.045 g, 3.60 mmol) was treated as the preparation of compound **13**. Purification by flash chromatography (ethyl acetate/petroleum ether=1:3) gave **22** (910 mg, 77%) as a colorless oil. $[\alpha]_D^{20}$=+40.8 (*c* 1.7, MeOH) [lit.[31] $[\alpha]_D^{20}$=+12.1 (*c* 2.47, $CHCl_3$)]; IR (film, cm^{-1}): 2931, 1748; MS (EI) *m/z* 259 (M^+−OAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.17 (s, 1H, HC(1)), 5.40–5.33 (m, 2H, HC(2), HC(3)), 4.39 (m, 1H, HC(4)), 4.34 (dd, $J_{4,5a}$=3.3 Hz, $J_{5a,5b}$=12.0 Hz, 1H, HC(5a)), 4.15 (dd, $J_{4,5b}$=5.1 Hz, $J_{5a,5b}$=12.0 Hz, 1H, HC(5b)), 2.15 (s, 3H, OAc), 2.08 (s, 3H, OAc), 2.03 (s, 3H, OAc); Anal. calcd for $C_{13}H_{18}O_9$: C, 49.06; H, 5.66. Found: C, 48.98; H, 5.69.

4.1.27. 2′,3′,5′-*O*-Triacetyl-β-L-5-iodouridine (23a). Compound **22** (112 mg, 0.352 mmol) and 5-iodouracil (251 mg, 1.06 mmol) were treated as the preparation of compound **18a**. Purification by flash chromatography (ethyl acetate/petroleum ether=1:1) afforded **23a** (164 mg, 94%) as a white foam. $[\alpha]_D^{20}$=+144.1 (*c* 3.2, MeOH); IR (KBr) ν_{max} 2906, 1750, 1720, 1693; MS (EI) *m/z* 497 (M^++1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (s, 1H, HC(6)), 6.08 (d, $J_{1',2'}$=4.7 Hz, 1H, HC(1′)), 5.37–5.29 (m, 2H, HC(2′), HC(3′)), 4.48–4.28 (m, 3H, HC(4′), HC(5a′), HC(5b′)), 2.26 (s, 3H, OAc), 2.14 (s, 3H, OAc), 2.12 (s, 3H, OAc); HRMS (EI): (M^+−AcOH), found 436.9846. $C_{15}H_{17}O_9N_2I$ requires 436.9877.

4.1.28. 2′,3′,5′-*O*-Triacetyl-β-L-puridine (23b). Compound **22** (171 mg, 0.538 mmol) and purine (195 mg, 1.62 mmol) were treated as described above. Purification by flash chromatography (CH_2Cl_2/MeOH=12:1) gave **23b** (169 mg, 83%) as a white foam. $[\alpha]_D^{20}$=+20.3 (*c* 3.0, MeOH) [D-enantiomer: lit.[32] $[\alpha]_D^{20}$=−10.8 (*c* 1.5, MeOH)]; IR (KBr) ν_{max} 3105, 1750,1641; MS (EI) *m/z* 378 (M^+), ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.17 (s, 1H, HC(6)), 9.00 (s, 1H, HC(2)), 8.25 (s, 1H, HC(8)), 6.25 (d, $J_{1',2'}$=5.2 Hz, 1H, HC(1′)), 5.98 (t, $J_{1',2'}$=5.2 Hz, $J_{2',3'}$= 5.5 Hz, 1H, HC(2′)), 5.68 (t, $J_{2',3'}$=5.5 Hz, $J_{3',4'}$=4.7 Hz, 1H, HC(3′)), 4.48–4.43 (m, 2H, HC(4′), HC(5a′)), 4.37 (dd, $J_{4',5b'}$=5.2 Hz, $J_{5a',5b'}$=12.9 Hz, 1H, HC (5b′)), 2.15 (s, 3H, OAc), 2.11 (s, 3H, OAc), 2.07 (s, 3H, OAc); HRMS (EI): (M^+−base), found 259.0818. $C_{11}H_{15}O_7$ requires 259.0777.

4.1.29. 2′,3′,5′-*O*-Triacetyl-N^6-benzoyl-β-L-adenosine (23c). Compound **22** (172 mg, 0.541 mmol) and 6-*N*-benzoyladenine (384 mg, 1.62 mmol) were co-evaporated three times with anhydrous CH_3CN under argon. Anhydrous CH_3CN (5 mL) and MFTSA (0.60 mL, 3.14 mmol) were added at room temperature. The mixture was stirred at 60–65°C until the base dissolved. TMSOTf (0.15 mL, 0.80 mmol) was added, the mixture stirred overnight at 65°C. CH_2Cl_2 (100 mL) was added and the mixture was washed with sat. $NaHCO_3$ solution, dried over Na_2SO_4. The solvent was removed in vacuo. The residue was purified by flash chromatography (CH_2Cl_2/MeOH=15:1) to afford **23c** (218 mg, 81%) as a white foam. $[\alpha]_D^{20}$=+16.8 (*c*, MeOH); IR (KBr) ν_{max} 3005, 1749, 1612, 1583; MS (EI) *m/z* 497 (M^+), 438 (M^+−OAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.20 (brs, 1H, NH), 8.81 (s, 1H, HC(8)), 8.20 (s, 1H, HC(2)), 8.05–7.51 (m, 5H, Ph), 6.27 (d, $J_{1',2'}$= 5.5 Hz, 1H, HC(1′)), 5.97 (t, $J_{1',2'}$=5.5 Hz, $J_{2',3'}$=5.2 Hz, 1H, HC(2′)), 5.68 (dd, $J_{2',3'}$=5.2 Hz, $J_{3',4'}$=4.4 Hz, 1H,

HC(3′)), 4.48–4.37 (m, 3H, HC(4′), HC (5a′), HC(5b′)), 2.16 (s, 3H, OAc), 2.14 (s, 3H, OAc), 2.09 (s, 3H, OAc); HRMS (EI): (M^+−base), found 259.0818. $C_{11}H_{15}O_7$ requires 259.0830.

4.1.30. N^2-Acetyl-6-*O*-diphenylcarbamoyl-2′,3′,5′-*O*-triacetyl-β-L-guanosine (23d). Compound **22** (107 mg, 0.336 mmol) and N^2-acetyl-O^6-diphenylcarbamoylguanine (190 mg, 0.51 mmol) were treated as described above. Purification by flash chromatography (ethyl acetate/petroleum ether=2:1) gave **23d** (187 mg, 86%) as a white foam. $[\alpha]_D^{20}$=+6.2 (*c* 0.4, MeOH); IR (KBr) ν_{max} 3107, 1744, 1622; MS (EI) *m/z* 259 (M^+−base); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (brs, 1H, NH), 8.06 (s, 1H, HC(8)), 7.45–7.20 (m, 10H, NPh_2), 6.11 (d, $J_{1',2'}$=4.7 Hz, 1H, HC(1′)), 5.90 (t, $J_{1',2'}$=5.2 Hz, $J_{2',3'}$=5.2 Hz, 1H, HC(2′)), 5.73 (t, $J_{2',3'}$=5.0 Hz, $J_{3',4'}$=5.0 Hz, 1H, HC(3′)), 4.49–4.43 (m, 2H, HC(4′), HC(5a′)), 4.41 (dd, $J_{4',5b'}$=6.3 Hz, $J_{5a',5b'}$=11.7 Hz, 1H, HC(5b′)), 2.47 (s, 3H, NHAc) 2.15 (s, 3H, OAc), 2.09 (s, 3H, OAc), 2.05 (s,3H, OAc).

Compound **23a–d** was treated as the preparation of compound **19a**. Purification by flash chromatography (CH_2Cl_2/MeOH=4:1) afforded **24a–d** as white foams.

4.1.31. β-L-5-Iodouridine (24a). Yield: 93%. $[\alpha]_D^{20}$=+67.6 (*c* 2.2, MeOH) [D-enantiomer: lit.[33] $[\alpha]_D^{25}$=−27.5 (*c* 0.13, H_2O)]; MS (EI) *m/z* 370 (M^+); MS (ESI) *m/z* 393.0 (M^++Na); ^{1}H NMR (300 MHz, CD_3OD) δ 8.71 (s, 1H, HC(6)), 6.07 (d, $J_{1',2'}$=3.5 Hz, 1H, HC(1′)), 4.39–4.34 (m, 2H, HC(2′), HC(3′)), 4.24 (m, 1H, HC(4′)), 4.07 (dd, $J_{4',5a'}$=2.6 Hz, $J_{5a',5b'}$=12.2 Hz, 1H, HC(5a′)), 3.94 (dd, $J_{4',5b'}$=2.5 Hz, $J_{5a',5b'}$=12.2 Hz, 1H, HC(5b′)).

4.1.32. β-L-Puridine (24b). Yield: 91%. $[\alpha]_D^{20}$=+36.0 (*c* 1.2, MeOH) [D-enantiomer: lit.[34] $[\alpha]_D^{35}$=−46.8 (*c* 2.0, H_2O)]; MS (EI) *m/z* 235 (M^+−OH); MS (ESI) *m/z* 252.1 (M^+); ^{1}H NMR (300 MHz, CD_3OD) δ 9.31 (s, 1H, HC(6)), 9.13 (s, 1H, HC(2)), 8.99 (s, 1H, HC(8)), 6.37 (d, $J_{1',2'}$=5.5 Hz, 1H, HC(1′)), 4.95 (t, $J_{1',2'}$=5.3 Hz, $J_{2',3'}$=5.3 Hz, 1H, HC(2′)), 4.58 (dd, $J_{2',3'}$=5.1 Hz, $J_{3',4'}$=3.7 Hz, 1H, HC(3′)), 4.37 (m, 1H, HC(4′)), 4.10 (dd, $J_{4',5a'}$=3.0 Hz, $J_{5a',5b'}$=12.3 Hz, 1H, HC (5a′)), 3.98 (dd, $J_{4',5b'}$=3.3 Hz, $J_{5a',5b'}$=12.3 Hz, 1H, HC(5b′)).

4.1.33. β-L-Adenosine (24c). Yield: 94%. $[\alpha]_D^{20}$=+30.7 (*c* 0.65, MeOH) [lit.[18] $[\alpha]_{546}^{25}$=+87 (*c* 0.45, 1.25 M NaOH)]; MS (EI) *m/z* 250 (M^+−OH); MS (ESI) *m/z* 290.1 (M^++Na); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.57 (s, 1H, HC(8)), 8.42 (s, 1H, HC(2)), 6.20 (d, $J_{1',2'}$=6.5 Hz, 1H, HC(1′)), 4.95 (dd, $J_{1',2'}$=6.2 Hz, $J_{2',3'}$=5.2 Hz, 1H, HC(2′)), 4.52 (dd, $J_{2',3'}$=5.0 Hz, $J_{3',4'}$=2.7 Hz, 1H, HC(3′)), 4.36 (m, 1H, HC(4′)), 4.06 (dd, $J_{4',5a'}$=2.7 Hz, $J_{5a',5b'}$=12.4 Hz, 1H, HC(5a′)), 3.94 (dd, $J_{4',5b'}$=2.9 Hz, $J_{5a',5b'}$=12.4 Hz, 1H, HC(5b′)).

4.1.34. β-L-Guanosine (24d). Yield: 91%. $[\alpha]_D^{20}$=+8.3 (*c* 0.5, MeOH) [lit.[18] $[\alpha]_{546}^{25}$=+80 (*c* 0.85, 1.25 M NaOH)]; MS (EI) *m/z* 283 (M^+); MS (ESI) *m/z* 306.1 (M^++Na); ^{1}H NMR (300 MHz, CD_3OD) δ 8.71 (s, 1H, HC(8)), 6.04 (d, $J_{1',2'}$=5.9 Hz, 1H, HC(1′)), 4.79 (t, $J_{1',2'}$=5.1 Hz, $J_{2',3'}$=5.4 Hz, 1H, HC(2′)), 4.48 (dd, $J_{2',3'}$=5.1 Hz, $J_{3',4'}$=3.4 Hz, 1H, HC(3′)), 4.28 (q, *J*=3.1 Hz, 1H, HC (4′)), 4.04 (dd, $J_{4',5a'}$=3.0 Hz, $J_{5a',5b'}$=12.2 Hz, 1H, HC(5a′)), 3.93 (dd, $J_{4',5b'}$=3.3 Hz, $J_{5a',5b'}$=12.3 Hz, 1H, HC(5b′)).

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