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Note

Synthesis of *N*-homobicyclic dideoxynucleoside analogues

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ABSTRACT

Syntheses of six *N*-homobicyclic dideoxynucleoside analogues are described. The reaction of mannose diacetonide with trimethylsulfoxonium iodide gave a mixture of diastereomeric hydroxymethyl mannose diacetonides in a ratio of 2:5, which was separated by fractional crystallization. The two stereoisomers were converted to bicyclic furanolactols each of which was coupled with three nucleoside bases. Further debenzylations gave the six target *N*-homobicyclic dideoxynucleosides.

1. Introduction

The synthesis of modified nucleosides has been of interest for over four decades. The finding that 3′-azido-3′-deoxy thymidine (AZT) is a therapeutic agent for the treatment of AIDS[1] triggered explosive new development in this area. Nucleoside modification has been reviewed extensively[2–10] and specialized reviews published on the synthesis of sugar-modified nucleosides such as ketonucleosides,[11] 3-branched nucleoside analogues,[12] AIDS-driven nucleosides chemistry,[13] bicyclic heterocyclic nucleosides,[14] *C*-nucleosides[10,15–19] *C*-branched nucleoside analogues,[20] carbocyclic nuleosides,[21–24] nucleosides with six-membered carbohydrate moieties,[25–27] nucleoside antibiotics,[28,29] azanucleosides,[30] L-nucleosides,[31,32] 2′,3′-dideoxynucleosides,[33,34] 4′,5′-unsaturated nucleosides,[35] *C*-alkenylated pyrimidine nucleosides,[36] anomeric spironucleosides,[37] and isonucleosides.[38] Most of the nucleosides are reverse transcriptase inhibitors like Zidovudine, Zalcitabine, and Stavudine; a few non-nucleosides such as Nevirapine, Delavirdine, and Efavirenzes also inhibit HIV reverse transcriptase. Many 2,3-dideoxyribonucleosides possess significant antiviral activity against HIV and other viruses. It has been suggested that proper puckering of the five-membered monocyclic carbohydrate moiety is required for antiviral activity.[39] However, bicyclic nucleosides from a conformationally different class, such as fused ring cytidine analogues[40–42] and oxytanylthymidine,[43] were recently found to have moderate to significant activity against HIV through the inhibition of HIV reverse transcriptase. These findings led to an investigation of the conformational requirements for dideoxynucleosides as inhibitors of HIV-RT[44] and further studies on bicyclic nucleosides.[45–49] Certain members of the class possess interesting cellular activities, for example, naturally occurring bicyclic nucleosides called griseolic acids, isolated from the cultured broth of *Streptomyces griseoaurantiacus*, show significant inhibitory activity against 3′,5′-cyclic nucleotide phosphodiesterases.[50,51]

Synthetic guanosine analogues of griseolic acids are even more potent against these enzymes[51]; other derivatives are potent antihypertensive agents.[52] Recently, bicyclic nucleosides have also received attention in studies of the stabilities of antisense oligonucleotides.[53–57] Bicyclic nucleosides exhibit increased affinity for complementary RNA or DNA and are also important in the preparation of triple-helix-forming oligonucleotides.[53,56]

Several authors have used similar nucleosides to prepare oligonucleotides.[58–60] As a continuation of our efforts in the discovery of antiviral agents, we chose the synthesis of the bicyclic nucleosides **1**–**6** (Fig. 1).

2. Results and discussion

The synthesis started from mannose diacetonide **7**,[61] readily obtainable from D-mannose in 85% yield (Scheme 1). The reaction of mannose diacetonide **7** with trimethylsulfoxonium iodide and potassium *tert*-butoxide at room temperature for 3 h[62] gave the diastereomeric mixture of key intermediates **8** and **9** in the ratio of 2:5 (by NMR), as a viscous oil in 79% yield.[63] Among the bases (NaH, *n*-BuLi, LiHMDS, NaHMDS, LDA, *t*-BuOK) tried, *t*-BuOK gave the best result for **8**, **9** in terms of yield and separation of the diastereomeric mixture. Here, the lactol moiety reacted with the in situ generated dimethyloxosulfonium methylide to form an epoxide to give hydroxymethyl mannose diacetonide. Fractional crystallization of this mixture (CH_2Cl_2–hexane 1:4) gave **8**, as a

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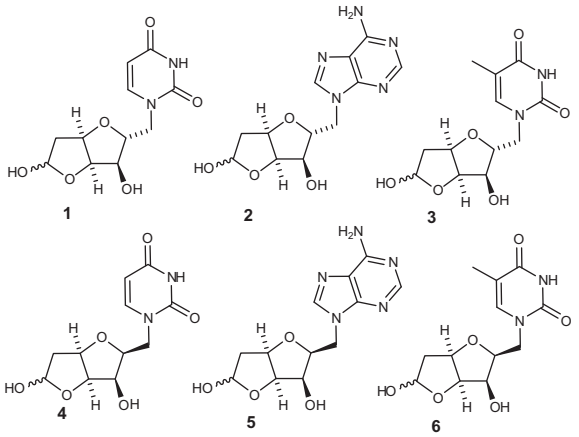
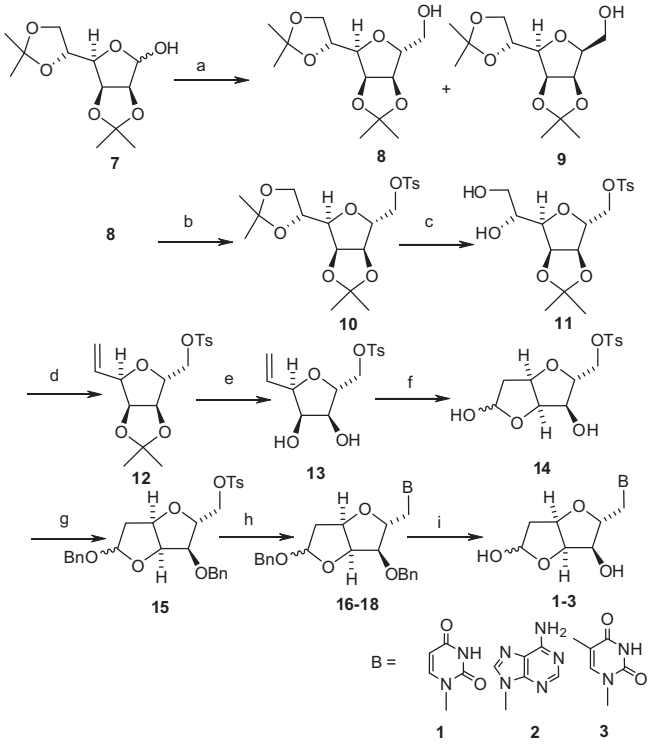
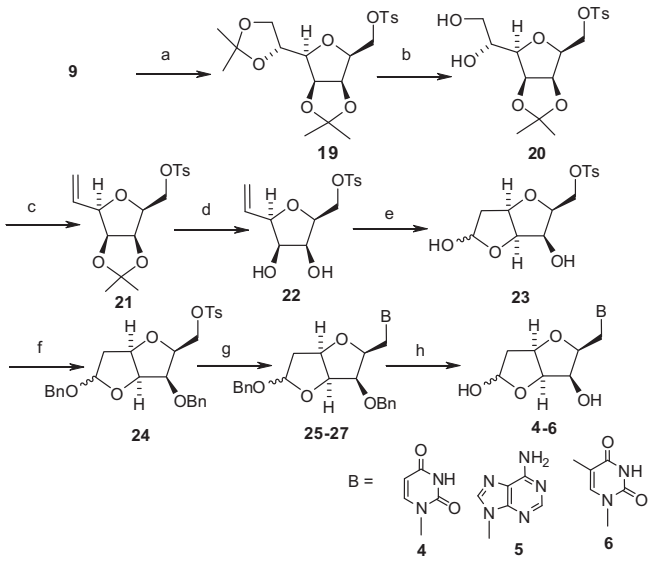


Figure 1. *N*-Homobicyclic dideoxynucleoside analogues.

crystalline compound (30%), mp 83–85 °C and **9** as viscous oil (70%). Tosylation of **8** with *p*-toluenesulfonyl chloride in pyridine to give tosylate **10** in 92% yield. Regioselective hydrolysis of isopropylidene of **10** with $BiCl_3$[64,65] in DCM gave diol **11** in 85% yield. Treatment of diol **11** with triphenylphosphine imidazole and iodine in toluene at 80 °C by reductive elimination gave vinyl furan **12** in 87% yield as viscous oil. Removal of isopropylidene group of vinyl furan **12** with 5% aq H_2SO_4 in 1,4-dioxane gave the desired hydroxy vinyl furan **13**. The crucial step of converting **13** to lactol **14** was achieved in 90% yield using $PdCl_2$, CuCl, DMF, H_2O, and O_2 at room temperature for 4 h.[66,67] Treatment of **14** with NaH, BnBr in DMF gave benzyl derivative **15** in 95% yield. Intermediate **15** was used for the synthesis of bicyclic dideoxynucleosides.



Scheme 1. Synthesis of *N*-homobicyclic-dideoxy nucleosides **1**–**3**. Reagents and conditions: (a) TMSOI, $KOBu^t$, DMSO (b) TsCl, pyridine, DMAP, (c) $BiCl_3$, DCM, (d) TPP, imidazole, I_2, toluene, 80 °C; (e) 5% aq H_2SO_4, 1,4-dioxane; (f) $PdCl_2$, CuCl, O_2, DMF, H_2O, rt; (g) NaH, BnBr, DMF, rt; (h) NaH, DMF, nucleoside base, 90 °C; (i) $Pd(OH)_2$–H_2.



Scheme 2. Synthesis of *N*-homobicyclic-dideoxy nucleosides **4**–**6**. Reagents and conditions: (a) TsCl, pyridine, DMAP, (b) $BiCl_3$, DCM; (c) TPP, imidazole, I_2, toluene, 80 °C; (d) 5% aq H_2SO_4, 1,4-dioxane; (e) $PdCl_2$, CuCl, O_2, DMF, H_2O; (f) NaH, BnBr, DMF; (g) NaH, DMF, nucleoside base, 90 °C; (h) $Pd(OH)_2$–H_2.

Thus uracil on treatment with NaH in DMF at 90 °C for 15 min followed by addition of tosylate **15** gave *N*-homobicyclic dideoxyuridine nucleoside **16**. Further deprotection of benzyl groups with 20% $Pd(OH)_2$ in methanol under hydrogen atmosphere gave the corresponding *N*-homobicyclic dideoxyuridine nucleoside **1**. Using similar reactions of dibenzyl homobicyclic tosylate **15** with adenine and thymine gave the *N*-homobicyclic dideoxy nucleosides **2** and **3**, respectively. As described in Scheme 2 compound **9** was subjected to similar reactions to obtain *N*-homobicyclo dideoxy nucleosides **4**–**6**.

3. Experimental section

3.1. General methods

Melting points were measured on a Buchi-510 instrument and are uncorrected. Spectra were recorded with the following instruments: IR, Perkin Elmer spectrophotometer; NMR, 200 MHz (Varian) and Unity 300 MHz (Bruker) and mass spectra LC–MS and Micro mass VG 7070H (70 eV). Column chromatography was performed with silica gel (Achme 60–120 mesh or >300 mesh flash chromatography) and TLC with silica gel MERCK GF_{254} (precoated). Visualization of the spots on TLC plates was carried out either in UV light (short wave 250 nm) or by exposing the plates to iodine vapors or spraying with 10% sulfuric acid in CH_3OH and subsequently heating on a hot plate.

3.2. Experimental procedures and spectral data

3.2.1. 2,3;5,6-Di-*O*-isopropylidene–D-mannofuranose (7)

Anhydrous $CuSO_4$ (30 g, 188.6 mmol) was added in one portion to a suspension of D-mannose (20 g, 111.1 mmol) in dry acetone (200 mL); then sulfuric acid (6 drops) was added. The suspension was stirred for 8 h. The solution was filtered under vacuum and then stirred with potassium carbonate (3.4 g) at room temperature until (pH 8). The mixture was filtered through Celite and evaporation of solvent in vacuum gave a white solid, which was dissolved in CH_2Cl_2, and filtered through a bed of silica gel topped with Celite. Evaporation of solvent under reduced pressure gave a white solid. Recrystallisation from diethyl ether–hexane gave **7** as colorless

crystals in (24.6 g 94.4 mmol) 85% yield. Mp 119–121 °C; $[\alpha]_D$ +12.1 (*c* 1.1, $CHCl_3$); IR: ν_{max} (KBr) 3441 cm^{-1} (OH); ^1H NMR (200 MHz, $CDCl_3$): δ 1.3 (s, 3H), 1.32 (s, 3H), 1.35 (s, 3H), 1.4 (s, 3H), 3.0 (br s, 1H, OH), 4.0 (dd, 1H, *J* = 5.1, 8.6 Hz, H-6), 4.1 (dd, 1H, *J* = 6.0, 8.6 Hz, H-6^1), 4.15 (dd, 1H, *J* = 3.7, 7.2 Hz, H-4), 4.3–4.4 (m, 1H, H-5), 4.6 (d, 1H, *J* = 5.9 Hz, H-2), 4.8 (dd, 1H, *J* = 3.7, 5.9 Hz, H-3), 5.31 (br s, 1H, H-1); FABMS: 261 $(M+1)^+$; Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.37; H, 7.74. Found: C, 55.33; H, 7.71.

3.2.2. 3,6-Anhydro-1,2,4,5-di-*O*-isopropylidene-D-*glycero*-D-*manno*-heptitol (8), and 3,6-anhydro-1,2;4,5-di-*O*-isopropylidene-D-*glycero*-D-*galacto*-heptitol (9)[63]

A mixture of trimethylsulfoxonium iodide (25.2 g, 114.5 mmol) and potassium-*tert*-butoxide (11.2 g, 100 mmol) in dry dimethylsulfoxide (100 mL) was stirred for 30 min at 10 °C. A solution of 2,3;5,6-di-*O*-isopropylidene-α-D-mannofuranose **7** (20 g, 76.92 mmol) in dimethylsulfoxide (50 mL) was added to the above reaction mixture and brought to room temperature and stirred for 1 h. When the reaction was complete, it was quenched by the addition of saturated aqueous ammonium chloride solution (100 mL) and was extracted into diethyl ether (3 × 75 mL). The combined organic phase was washed with water (2 × 50 mL), dried over Na_2SO_4, and concentrated under reduced pressure to obtain a residue that was filtered on a bed of Silica Gel 60–120 mesh eluted with hexane–EtOAc (1:1). This gave a diastereomeric mixture of **8** and **9** (16.65 g, 79%) from which the title compound **8** (4.75 g, 17.3 mmol) was separated as white needles by fractional crystallization using dichloromethane–hexane (1:4) **8** and **9** (2:5 ratio). This mixture was passed through silica gel column chromatography using 30% ethylacetate and hexane to give the pure diastereomers **8** and **9**. Data for **8**: mp 83–85 °C; $[\alpha]_D$ −12.6 (*c* 1.0, $CHCl_3$); IR: ν_{max} (KBr) 3600 cm^{-1} (OH); ^1H NMR (300 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.32 (s, 3H), 1.42 (s, 3H), 1.51 (s, 3H), 3.6 (m, 2H, H-6,7), 4.0 (m, 1H, H-1), 4.15 (m, 2H, H-1^1, 6), 4.41 (m, 1H, H-2), 4.62 (m, 1H, H-3), 4.81 (m, 1H, H-4); ^{13}C NMR (50 MHz, $CDCl_3$): δ 112.7, 108.9, 84.7, 82.4, 81.3, 80.9, 73.6, 66.4, 62.0, 26.5, 25.8, 24.8, 24.3; FABMS: 276 $(M+1)^+$; Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 56.84; H, 7.95. Data for **9**: Obtained **9** (11.9 g, 43 mmol) as viscus liquid. $[\alpha]_D$ −9.0 (*c* 2.6, $CHCl_3$); IR: ν_{max} (KBr) 3600 cm^{-1} (OH); ^1H NMR (200 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.35 (s, 3H), 1.45 (s, 3H), 1.49 (s, 3H), 2.21 (br s, 1H, OH), 3.49 (d, 1H, *J* = 3.0 Hz), 3.6–4.10 (m, 5H, 1^1, 3, 6, 7, 7^1), 4.35 (m, 1H, H-2), 4.6–4.7 (m, 2H, H-4, H-5); ^{13}C NMR (50 MHz, $CDCl_3$): δ 112.7, 108.9, 84.8, 82.4, 81.3, 80.9, 73.6, 66.4, 62.0, 26.5, 25.8, 24.8, 24.3; FABMS: 275 $(M+1)^+$; Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.84; H, 7.95. Found: C, 56.77, H, 7.89.

3.2.3. 6-(2,2-Dimethyl-1,3-dioxolan-4yl)-2,2-dimethyl-4(4-methylphenylsulfonyloxymethyl)-(3a*R*,4*S*,6a*S*)-perhydrofuro[3,4-*d*][1,3]dioxole (10)

To a stirred solution of the alcohol **8** (15 g, 54.7 mmol) in pyridine (100 mL) at 0 °C were added *p*-toluenesulfonyl chloride (12.48 g, 65.7 mmol) and catalytic amount of DMAP (100 mg) and the mixture stirred for 30 min and brought to room temperature and stirred for 3 h. The reaction mixture was diluted with chilled water (200 mL) and ether was added and the organic layer was separated. The aqueous phase was extracted with diethyl ether (2 × 75 mL) and the combined organic layer was dried over Na_2SO_4, filtered, and concentrated to obtain **10** in 92% yield (21.50 g, 50.36 mmol); mp 105–107 °C; $[\alpha]_D$ +2.0 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.35 (s, 3H), 1.40 (s, 3H), 1.45 (s, 3H), 2.42 (s, 3H), 3.80–3.85 (m, 2H, H-7, H-7^1), 3.92–4.15 (m, 4H, H-3, H-1. H-1^1, H-6), 4.21 (m, 1H, H-2), 4.85 (m, 2H, H-4, H-5), 7.39 (d, 2H, *J* = 8.0 Hz, Ar), 7.81 (d, 2H, *J* = 8.0 Hz, Ar); ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.5, 132.7, 130.0, 128.0, 113.2, 109.2, 83.0, 81.0, 80.0, 73.5, 69.8, 66.8, 27.0, 26.0, 25.0, 24.5, 21.8; FABMS: 429 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{20}H_{29}O_8S$ 429.2267, observed 429.2260 $(M+H)^+$.

3.2.4. 6-(2,2-Dimethyl-1,3-dioxolan-4yl)-2,2-dimethyl-4(4-ethylphenylsulfonyloxymethyl)-(3a*R*,4*R*,6a*S*)-perhydrofuro[3,4-*d*][1,3]-dioxole (19)

Same procedure as above. Obtained **19** from **9** in 93% yield (8.71 g, 20.36 mmol) as viscous oil. $[\alpha]_D$ +2.5 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.35 (s, 6H), 1.45 (s, 3H), 2.41 (s, 3H), 3.50 (dd, 1H, $J_{7,7^1}$ = 10.4 Hz, $J_{6,7}$ = 5.5 Hz, H-7), 3.8–4.40 (m, 5H, H-1, H-1^1, H-2), 4.61–4.72 (m, 2H, H-4, H-5), 7.30 (d, 2H, *J* = 8.0 Hz), 7.81 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.5, 132.7, 130.0, 128.0, 113.2, 109.2, 83.0, 81.0, 80.0, 73.5, 69.8, 66.8, 27.0, 26.0, 25.0, 24.5, 21.8; FABMS: 429 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{20}H_{29}O_8S$ 429.2267, observed 429.2262 $(M+H)^+$.

3.2.5. 6-(1,2-Dihydroxyethyl)-2,2-dimethyl-4-(4-methylphenylsulfonyloxymethyl)-(3a*R*,4*S*,6a*S*)-perhydrofuro[3,4-*d*][1,3]-dioxole (11)

To a solution of compound **10** (10 g, 23.41 mmol) in CH_2Cl_2 (35 mL) was added bismuth trichloride (150 mg) and stirred at room temperature for 2 h. Reaction was monitored by TLC and on completion of the reaction, $NaHCO_3$ (3 g) and water (50 mL) were added and extracted into CH_2Cl_2 (3 × 25 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to give a residue, which was chromatographed SiO_2, 60–120 mesh; hexane–EtOAc (2:1) to yield **11** in 85% (7.70 g, 19.90 mmol) yield. $[\alpha]_D$ +2.7 (*c* 1.0, CH_3OH); IR: ν_{max} (KBr) 3481.5, 3569 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1. 51 (s, 3H), 2.0 (br s, 1H, OH), 2.52 (s, 3H), 2.61 (br s, 1H, OH), 3.51–3.71 (m, 2H, H-7, H-7^1), 3.72–3.91 (m, 2H, H-1, H-1^1), 3.95 (d, 1H, *J* = 5.0 Hz, H-3), 4.05 (d, 1H, *J* = 5.5 Hz, H-6), 4.25 (d, 1H *J* = 5.5 Hz, H-6), 4.81 (d, 1H, *J* = 7.0 Hz), 7.41 (d, 2H, *J* = 8.0 Hz), 7.82 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.2, 132.5, 129.9, 127.8, 113.09, 82.2, 81.4, 70.5, 69.5, 64.2, 28.8, 26.1, 24.6, 21.5; FABMS: 389 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{17}H_{25}O_8S$ 389.4407, observed 389.4406 $(M+H)^+$.

3.2.6. 6-(1,2-Dihydroxyethyl)-2,2-dimethyl-4-(4-methylphenylsulfonyloxymethyl)-(3a*R*,4*R*,6a*S*)-perhydrofuro[3,4-*d*][1,3]-dioxole (20)

Same procedure as above. Obtained **20** from **19** (5.39 g, 13.90 mmol) in 85% as syrup. $[\alpha]_D$ +6.5 (*c* 1.0, MeOH); ^1H NMR (300 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.42 (s, 3H), 2.5 (s, 3H) 3.5 (dd, 1H, *J* = 5.0, 8.0 Hz), 3.61–3.71 (m, 1H), 3.72–3.8 (m, 1H), 3.81–3.92 (m, 1H), 4.11–4.21 (m, 2H), 4.22–4.31 (m, 1H), 4.61–4.71 (m, 1H), 4.75–4.81 (m, 1H), 7.31 (d, 2H, *J* = 8.0 Hz, Ar), 7.81 (d, 2H, *J* = 8.0 Hz, Ar); ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.2, 132.5, 129.9, 127.8, 113.1, 82.2, 81.4, 70.5, 69.5, 64.2, 28.8, 26.1, 24.7, 21.5; FABMS: 389 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{17}H_{25}O_8S$ 389.4407, observed 389.4404 $(M+H)^+$.

3.2.7. 2,2-Dimethyl-4-(4-methylphenylsulfonyloxymethyl)-6-vinyl-(3a*R*,4*R*,6a*S*)-perhydrofuro[3,4-*d*][1,3]-dioxole (12)

A mixture of compound **11** (7 g, 22.29 mmol), triphenylphosphine (18.95 g, 72.35 mmol) and imidazole (4.91 g, 72.2 mmol) was heated to 78 °C in toluene (150 mL) with stirring, while adding iodine (18.37 g, 144.70 mmol) in small portions. The white, finely dispersed complex that initially formed was transformed into clear yellow solution that darkened as an iodine tarry complex was formed from which the product was gradually dissolved. After 15 min, the reaction mixture was cooled and iodine (18.37 g, 144.70 mmol) was added, followed by aqueous 10% sodium hydroxide (100 mL). The mixture was stirred until virtually all of the tarry red deposits were dissolved and extracted into EtOAc

(3 × 50 mL) the combined organic layer was washed successively with water, saturated aqueous sodium thiosulphate, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuum. The residue was purified by column chromatography 60–120 mesh; 2–5% EtOAc in hexane as the eluant to gave **12** in 87% yield (5.57 g, 15.74 mmol); mp 109–111 °C; $[\alpha]_D$ −19.3 (*c* 1.0, $CHCl_3$); IR: ν_{max} (KBr) 1598.9 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.42 (s, 3H), 2.51 (s, 3H), 4.0–4.11 (m, 1H), 4.12 (m, 1H), 4.29 (d, 1H, *J* = 4.0 Hz), 4.33 (d, 1H, *J* = 4.0 Hz), 4.62 (d, 1H, *J* = 4.0 Hz), 4.71 (d, 1H, *J* = 4.0 Hz), 5.32 (d, 1H, *J* = 5.0 Hz), 5.33 (d, 1H, *J* = 8.0 Hz), 5.81–5.92 (m, 1H), 7.4 (d, 2H, *J* = 7.0 Hz, Ar), 7.8 (d, 2H, *J* = 7.0 Hz, Ar); ^{13}C NMR (50 MHz, $CDCl_3$): δ 133.9, 131.3, 129.3, 120.1, 114.1, 84.9, 83.9, 82.7, 71.5, 27.5, 26.1, 22.9; FABMS: 355 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{17}H_{23}O_6S$ 355.4260, observed 355.4262 $(M+H)^+$.

3.2.8. 2,2-Dimethyl-4-(4-methylphenylsulfonyloxymethyl)-6-vinyl-(3a*R*,4*S*,6a*S*)-perhydrofuro[3,4-*d*][1,3]-dioxole (21)

Same procedure as above. Obtained **21** from **20** (3.93 g, 11.1 mmol) in 86% as viscous oil. $[\alpha]_D$ +12.6 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.42 (s, 3H), 2.51 (s, 3H), 3.72 (dd, 1H, *J* = 5.0, 8.0 Hz), 3.92 (dd, 1H, *J* = 5.0, 8.0 Hz), 4.0–4.21 (m, 1H), 4.31–4.36 (m, 1H), 4.6–4.7 (m, 1H), 4.75 (m, 1H), 5.32 (d, 1H, *J* = 9.0 Hz), 5.36 (d, 1H, *J* = 9.0 Hz), 5.82–5.92 (m, 1H), 7.31 (d, 2H, *J* = 8.0 Hz, Ar), 7.92 (d, 1H, *J* = 8.0 Hz, Ar); FABMS: 355 $(M^+ + 1)$; HRMS (ESI^+): calcd for $C_{17}H_{23}O_6S$ 355.4260, observed 355.4266 $(M+H)^+$.

3.2.9. 3,4-Dihydroxy-2-(4-methylphenylsulfonyloxymethyl)-5-vinyl-(2*R*,3*S*,4*S*)-tetrahydrofuran (13)

To a solution of **12** (4.5 g, 14.33 mmol) in 1,4-dioxane (20 mL) was added 5% aq sulfuric acid (5 mL), stirred at 80 °C temperature for 2 h. After completion of the reaction, solvent was removed in vacuum to obtain a residue, which was extracted in to EtOAc (3 × 50 mL). The combined organic layer was washed with saturated $NaHCO_3$ solution, water, dried anhydrous Na_2SO_4 (5 g), filtered, and concentrated to obtain the corresponding diol as viscous oil, which was purified by column chromatography 60–120 mesh; hexane–EtOAc (1:3) to yield **13** in 85% yield (3.39 g, 10.80 mmol) as a syrup. $[\alpha]_D$ +32.5 (*c* 1.0, $CHCl_3$); IR: ν_{max} (KBr): 3414, 1716, 1682, 1599 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 2.5 (s, 3H), 4.0 (m, 1H), 4.12 (m, 1H), 4.2–4.3 (m, 3H), 4.35–4.4 (m, 1H), 5.31 (d, 1H, *J* = 6.0 Hz), 5.35 (d, 1H, *J* = 8.0 Hz), 5.8–6.0 (m, 1H), 7.4 (d, 2H, *J* = 8.0 Hz, Ar), 7.81 (d, 2H, *J* = 8.0 Hz, Ar); ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.1, 133.2, 132.8, 130.0, 128.01, 118.9, 82.1, 79.7, 73.2, 73.0, 70.0, 21.7; FABMS: 315 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{14}H_{19}O_6S$ 315.3621, observed 315.3622 $(M+H)^+$.

3.2.10. 3,4-Dihydroxy-2-(4-methylphenylsulfonyloxymethyl)-5-vinyl-(2*S*,3*S*,4*S*)-tetrahydro furan (22)

Same procedure as above. Obtained **22** from **21** (2.6 g, 8.3 mmol) in 84% yield as syrup. $[\alpha]_D$ −27.6 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 2.41 (s, 3H), 3.22 (br s, 2H, OH), 3.9–4.0 (m, 1H), 4.11 (m, 1H), 4.22 (m, 1H), 4.31 (m, 1H), 4.31–4.41 (m, 2H), 5.22–5.31 (m, 2H), 5.81–5.91 (m, 1H), 7.31 (d, 2H, *J* = 8.0 Hz), 7.81 (d, 2H, *J* = 8.0 Hz); FABMS: 315 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{14}H_{19}O_6S$ 315.3621, observed 315.3620 $(M+H)^+$.

3.2.11. ((2R,3R,3aR,6aR)-3,5-Dihydroxyhexahydrofuro[3,2-*b*]-furan-2-yl)methyl 4-methylbenzenesulfonate (14)

To a solution of **13** (3 g, 9.55 mmol) in DMF–H_2O (4:1, 20 mL) was added palladium(II) chloride (0.169 g, 0.955 mmol), copper(I) chloride (1.04 g, 10.50 mmol), and oxygen was bubbled in for 4 h at room temperature. After completion of the reaction 2% HCl was added and the mixture was extracted with diethyl ether (3 × 50 mL). The combined ethereal solution was washed with water, dried over Na_2SO_4, filtered, and concentrated to obtain **14** in 90% yield (2.83 g, 8.57 mmol) as an oil. $[\alpha]_D$ +50.7 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.91 (br s, 1H, OH), 2.11–2.21 (m, 2H), 2.52 (s, 3H), 3.41 (br s, 1H, OH), 4.0–4.11 (m, 2H), 4.21–4.52 (m, 2H), 4.61 (m, 1H), 4.82 (m, 1H), 5.71 (m, 1H), 7.41 (d, 2H, *J* = 8.0 Hz, Ar), 7.81 (d, 2H, *J* = 8.0 Hz, Ar); ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.4, 133.1, 130.3, 128.3, 100.7, 100.2, 84.0, 82.6, 81.7, 81.1, 80.8, 79.3, 73.1, 73.0, 70.1, 69.7, 42.8, 42.1, 22.0; FABMS: 330 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{14}H_{19}O_7S$ 331.3841, observed 330.3844 $(M+H)^+$.

3.2.12. ((2*S*,3*R*,3a*R*,6a*R*)-3,5-Dihydroxyhexahydrofuro[3,2-*b*]-furan-2-yl)methyl 4-methylbenzenesulfonate (23)

Same procedure as above. Obtained **23** from **22** (2.33 g, 7.08 mmol) in 89% yield as semisolid. $[\alpha]_D$ −44.5 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 0.91 (br s, 1H, OH), 2.21 (m, 2H), 2.51 (m, 3H), 3.41 (br s, 1H, OH), 4.11 (m, 2H), 4.31 (m, 2H), 4.61 (m, 1H), 4.81 (m, 1H), 5.61 (m, 1H), 7.32 (d, 2H, *J* = 8.0 Hz, Ar), 7.82 (d, 2H, *J* = 8.0 Hz, Ar). FABMS: 331 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{14}H_{19}O_7S$ 331.3841, observed 331.3842 $(M+H)^+$.

3.2.13. 3,5-Di(benzyloxy)-2-(4-methylphenylsulfonyloxymethyl)-(2*R*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]furan (15)

To a cool stirred suspension of NaH (60% 0.545 g, 22.72 mmol) in dry DMF (15 mL), was added a solution of compound **14** (2.5 g, 7.57 mmol) in dry DMF (10 mL). After 15 min, benzyl bromide (1 mL 9.09 mmol) was added to the reaction mixture, stirring was continued for 1 h at 0 °C temperature, the reaction was quenched by the addition of crushed ice, and diluted with water (25 mL). The reaction mixture was extracted into ether (3 × 100 mL). The combined organic layer was washed with brine solution, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude product, which was purified on a silica gel column, eluting with 3–5% EtOAc in hexane to give **15** as a pale yellow gum (3.67 g, 7.19 mmol) in 95% yield as syrup. $[\alpha]_D$ +89.2 (*c* 1.0, MeOH); ^1H NMR (200 MHz, $CDCl_3$): δ 2.11 (dd, 1H, *J* = 7.5, 11.5 Hz), 2.31 (dd, 1H, *J* = 7.5, 11.5 Hz), 2.41 (s, 3H), 3.81 (m, 1H), 3.91 (m, 1H), 4.11 (m, 1H, *J* = 7.5, 11.5 Hz), 4.32 (dd, 1H, *J* = 7.5, 11.5 Hz), 4.41 (m, 1H), 4.51 (d, 2H), 4.61 (d, 2H), 4.71–4.81 (m, 1H), 5.41 (d, 1H, *J* = 7.5 Hz), 7.21–7.42 (m, 12H, Ar), 7.81 (d, 2H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$): δ 144.8, 138.0, 137.4, 129.8, 128.5, 128.4, 128.1, 127.9, 127.8, 127.7, 105.2, 81.8, 78.5, 76.5, 72.5, 69.6, 68.6, 41.8, 21.6; FABMS: 512 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{28}H_{31}O_7S$ 512.6066, observed 512.6060 $(M+H)^+$.

3.2.14. 3,5-Di(benzyloxy)-2-(4-methylphenylsulfonyloxymethyl)-(2*S*,3*R*,3a*R*,6a*S*)-perhydro furo[3,2-*b*]furan (24)

Same procedure as above. Obtained **24** from **23** (2.93 g, 5.75 mmol) in 95% yield as semisolid. $[\alpha]_D$ +19.5 (*c* 1.0, MeOH); ^1H NMR (200 MHz, $CDCl_3$): δ 2.0–2.21 (m, 2H), 2.51 (s, 3H), 3.81–3.91 (m, 1H), 4.11–4.21 (m, 2H), 4.25 (d, 1H, *J* = 7.0 Hz), 4.41 (d, 1H, *J* = 7.5 Hz), 4.51 (d, 1H, *J* = 7.5 Hz), 4.61 (m, 1H), 4.70 (m, 1H), 4.81 (m, 2H); FABMS: 512 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{28}H_{31}O_7S$ 512.6066, observed 512.6062 $(M+H)^+$.

3.2.15. 1-[3,5-Di(benzyloxy)-(2*R*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]furan-2-yl-methyl]-1,2,3,4-tetrahydro-2,4-pyrimidinedione (16)

A mixture of uracil (0.043 g, 0.39 mmol) and NaH (60% 0.028 g, 1.16 mmol) in DMF (5 mL) was stirred at 90 °C for 15 min. Then, compound **15** (0.1 g, 0.19 mmol) in DMF (5 mL) was added to the reaction mixture and heated at 90 °C for 3 h. The reaction mixture was cooled to room temperature and the solvent was removed in vacuo to give the crude product which was filtered on a bed of Silica Gel 60–120 mesh, eluting with hexane–EtOAc (1:10) to obtain

16 in 60% yield (0.052 g, 0.11 mmol) as semisolid. $[\alpha]_D$ +3.0 (*c* 0.5, MeOH); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.0–2.11 (m, 1H), 2.61 (m, 1H), 3.51 (m, 1H), 3.91–4.0 (m, 3H), 4.41 (m, 1H), 4.45–4.6 (m, 4H), 4.71 (d, 1H, *J* = 6.0 Hz), 4.75–4.82 (m, 1H), 5.42 (d, 1H, *J* = 7.5 Hz), 5.51 (d, 1H, *J* = 8.0 Hz) 7.21–7.41 (m, 10H, Ar), 8.51 (br s, 1H, NH); ^{13}C NMR (50 MHz, $CDCl_3$): δ 145.4, 137.8, 137.3, 128.4, 128.3, 128.9, 127.8, 127.6, 104.9, 101.6, 81.6, 80.1, 78.3, 76.3, 72.6, 69.4, 47.9, 41.8; FABMS: 451 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{25}H_{27}N_2O_6$ 451.4917, observed 451.4916 $(M+H)^+$.

3.2.16. 1-[3,5-Di(benzyloxy)-(2*S*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]furan-2-ylmethyl]-1,2,3,4-tetrahydro-2,4-pyrimidinedione (25)

Same procedure as above. Obtained **25** from **24** in 59% yield (0.052 g, 0.11 mmol) as a semisolid. $[\alpha]_D$ +37.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11–2.21 (m, 2H), 3.62 (m, 1H), 3.81 (m, 2H), 4.11–4.21 (m, 1H), 4.31–4.41 (m, 1H), 4.45 (d, 1H, *J* = 8.0 Hz), 4.61 (d, 1H, *J* = 8.0 Hz), 4.72 (d, 1H, *J* = 7.0 Hz), 4.72–4.82 (m, 3H), 5.31 (d, 1H, *J* = 6.0 Hz) 5.51 (d, 1H, *J* = 7.0 Hz); FABMS: 451 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{25}H_{27}N_2O_6$ 451.4917, observed 451.4912 $(M+H)^+$.

3.2.17. 9-[3,5-Di(benzyloxy)-(2*R*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]furan-2-yl-methyl]-9*H*-pyrinamine (17)

A mixture of adenine, (0.10 g, 0.39 mmol) and NaH (60% 0.028 g, 1.17 mmol) in dry DMF (5 mL) was stirred at 90 °C for 15 min. Then, compound **15** (0.1 g, 0.19 mmol) in DMF (5 mL) was added and the reaction mixture was kept at 90 °C for 3 h. The reaction mixture was cooled to room temperature and the solvent was removed in vacuo to give the crude product, which was filtered on a bed of silica gel (SiO_2, 60–120 mesh; hexane–EtOAc (1:10) to obtain **17** in 58% yield (0.053 g, 0.11 mmol) as semisolid. $[\alpha]_D$ +60.7 (*c* 1.0, MeOH); ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.11–2.21 (m, 1H), 2.31–2.35 (m, 1H), 3.30 (m, 1H), 4.11 (m, 1H), 4.31 (m, 1H), 4.41 (dd, 1H, *J* = 6.0, 11.0 Hz), 4.51 (dd, 3H, *J* = 6.0, 11.0 Hz), 4.61 (d, 2H, *J* = 9.0 Hz), 4.71 (m, 1H), 5.41 (d, 1H, *J* = 8.0 Hz), 5.91 (br s, 2H, NH_2), 7.21–7.41 (m, 10H, Ar), 7.81 (s, 1H), 8.41 (s, 1H); FABMS: 474 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{26}H_{28}N_5O_4$ 474.5317, observed 474.5322 $(M+H)^+$.

3.2.18. 9-[3,5-Di(benzyloxy)-(2*S*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]furan-2-yl-methyl]-9*H*-6-pyrinamine (26)

Same procedure as above. Obtained **26** from **24** in 57% yield (0.052 g, 0.11 mmol) as semisolid. $[\alpha]_D$ +4.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.41–2.51 (m, 2H), 3.52 (m, 1H), 4.31–4.41 (m, 1H), 4.51 (d, 1H, *J* = 7.5 Hz), 4.51 (d, 1H, *J* = 7.5 Hz), 4.61–4.71 (m, 1H), 4.77–4.81 (m, 3H), 4.86 (d, 2H, *J* = 9.0 Hz), 5.31 (d, 1H, *J* = 7.0 Hz), 6.11 (br s, 2H), 7.21–7.41 (m, 10H, Ar), 7.71 (s, 1H, base), 8.31 (s, 1H); FABMS: 474 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{26}H_{28}N_5O_4$ 474.5317, observed 474.5320 $(M+H)^+$.

3.2.19. 1-[3,5-Di(benzyloxy)-(2*R*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]furan-2-yl-methyl]-5-methyl-1,2,3,4-tetrahydro-2,4-pyrimidinedione (18)

To a mixture of thymine, (0.049 g, 0.096 mmol) and NaH (60%, 0.028 g, 1.17 mmol) in DMF (5 mL) was stirred at 90 °C for 15 min. Then compound **15** (0.1 g, 0.19 mmol) in DMF (5 mL) was added and the reaction mixture was kept at 90 °C for 3 h. The reaction mixture was cooled to room temperature and the solvent was removed in vacuo to give the crude product, which was filtered on a bed of Silica Gel 60–120 mesh; hexane–EtOAc (1:10) to obtain **18** in 57% yield (0.051 g, 0.11 mmol), as semisolid. $[\alpha]_D$ −31.6 (*c* 1.0, MeOH); ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.91 (s, 3H), 2.1 (m, 1H), 2.31–2.41 (m, 1H), 3.51–3.61 (m, 1H), 3.91–4.0 (m, 2H), 4.31–4.41 (m, 1H), 4.51–4.71 (m, 4H), 4.61–4.81 (m, 1H), 5.41 (d, 1H, *J* = 6.0 Hz), 7.0 (s, 1H), 7.22–7.42 (m, 10H, Ar), 8.41 (br s, 1H, NH); FABMS: 465 $(M+1)^{+\cdot}$; HRMS (ESI^+): calcd for $C_{26}H_{29}N_2O_6$ 465.5183, observed 465.5184 $(M+H)^+$.

3.2.20. 1-[3,5-Di(benzyloxy)-(2*S*,3*R*,3a*R*,6a*S*)-perhydrofuro-[3,2-*b*]-furan-2-yl-methyl]-5-methyl,1,2,3,4-tetrahydro-2,4-pyrimidinedione (27)

Same procedure as above. Obtained **27** from **24** in 56% yield (0.050 g, 0.10 mmol) as a semisolid. $[\alpha]_D$ +49.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.81 (s, 3H), 2.12–2.21 (m, 2H), 3.61–3.71 (m, 1H), 3.81–3.92 (m, 2H), 4.31–4.41 (m, 1H), 4.45 (d, 1H, *J* = 9.0 Hz), 4.67 (d, 1H, *J* = 9.0 Hz), 4.69 (m, 1H), 4.75 (m, 2H), 4.81 (d, 1H, *J* = 7.0 Hz), 5.31 (d, 1H, *J* = 6.0 Hz), 6.91 (br s, 1H), 7.21–7.31 (m, 8H, Ar), 7.41 (d, 2H, *J* = 8.0 Hz), 9.71 (br s, 1H, NH); FABMS: 465 $(M+1)^{+\cdot}$; HRMS (ESI^+): calcd for $C_{26}H_{29}N_2O_6$ 465.5183, observed 465.5182 $(M+H)^+$.

3.2.21. 1-[3,5-Dihydroxy-(2*R*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]-furan-2-yl-methyl]-1,2,3,4-tetrahydro-2,4-pyrimidinedione (1)

A solution of **16** (0.04 g, 0.08 mmol) in MeOH (5 mL), palladium hydroxide (5 mg) was stirred under hydrogen atmosphere (1 atm) at room temperature. After 3 h, catalyst was filtered washed with MeOH (2 × 10 mL). The filtrate was concentrated under reduced pressure, which was purified on a small bed of silica gel (5–95% $CHCl_3$–CH_3OH) to afford the title compound **1** (0.022 g, 0.084 mmol) in 95% yield, as a semisolid. $[\alpha]_D$ +68.0 (*c* 2.0, CH_3OH); ^{1}H NMR (300 MHz, CD_3OD): δ 2.0–2.11 (m, 2H), 2.6 (br s, 1H, OH), 3.41–3.62 (m, 1H), 3.71–3.92 (m, 2H), 4.11–4.21 (m, 1H), 4.51 (m, 1H), 4.71 (m, 1H), 5.11 (m, 1H), 5.61 (d, 1H, *J* = 5.0 Hz), 7.52 (d, 1H, *J* = 5.0 Hz); ^{13}C NMR (50 MHz, CDCl3): δ 148.1, 107.9, 101.8, 85.5, 82.3,82.1, 79.5, 78.8, 75.8, 75.6, 50.6, 50.4, 44.6, 42.5, 42.2, 31.9; FABMS: 271 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{11}H_{15}N_2O_6$ 271.2467, observed 271.2464 $(M+H)^+$.

3.2.22. 1-[3,5-Dihydroxy-(2*R*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]-furan-2-ylmethyl]-1,2,3,4-tetrahydro-2,4-pyrimidinedione (4)

Same procedure as above. Obtained **4** from **25** yield (0.022 g, 0.084 mmol) in 94% yield as semisolid. $[\alpha]_D$ +73.0 (*c* 2.0, CH_3OH); ^{1}H NMR (300 MHz, CD_3OD): δ 2.0–2.21 (m, 2H), 2.62 (br s, 1H, OH), 3.41–3.61 (m, 1H), 3.71–3.91 (m, 2H), 4.11–4.21 (m, 1H), 4.51 (m, 1H), 4.81 (m, 1H), 5.21 (m, 1H), 5.61 (d, 1H, *J* = 5.0 Hz), 7.51 (d, 1H, *J* = 5.0 Hz); FABMS: 271 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{11}H_{15}N_2O_6$ 271.2467, observed 271.2468 $(M+H)^+$.

3.2.23. 5-(6-Amino-9*H*-9-purinylmethyl)-(3a*S*,5*R*,6*R*,6a*R*)-perhydrofuro[3,2-*b*]-furan 2,6-diol (2)

A solution of **17** (0.045 g, 0.095 mmol) in CH_3OH (5 mL), palladium hydroxide (5 mg) was stirred under hydrogen atmosphere (1 atm) at room temperature. After 3.5 h catalyst was filtered washed with CH_3OH (2 × 10 mL). The filtrate was concentrated under reduced pressure, which was purified on a small bed of silica gel (20–30% EtOAc hexane) to afford the title compound **2** (0.027 g, 0.095 mmol) in 94% yield as a semisolid. $[\alpha]_D$ +60.7 (*c* 1.0, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.11–2.21 (m, 1H), 2.81–2.31 (m, 1H), 3.31–3.41 (m, 1H), 4.1–4.15 (m, 1H), 4.21–4.31 (m, 1H), 4.41 (m, 1H), 4.51 (m, 3H), 4.61 (d, 2H, *J* = 9.0 Hz), 4.71–4.81 (m, 1H), 5.41 (d, 1H, *J* = 8.0 Hz), 5.91 (br s, 2H, NH_2), 7.21–7.31 (m, 10H, Ar), 7.81 (s, 1H), 8.42 (s, 1H); FABMS: 294 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{12}H_{16}N_5O_4$ 294.2866, observed 294.2864 $(M+H)^+$.

3.2.24. 5-(6-Amino-9*H*-9-purinylmethyl)-(3a*S*,5*S*,6*R*,6a*R*)-perhydrofuro[3,2-*b*]-furan-2,6-diol (5)

Same procedure as above. Obtained **5** from **26** yield (0.027 g, 0.095 mmol) in 94% yield as a semisolid. $[\alpha]_D$ +4.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (200 MHz, CD_3OD): δ 2.12–2.21 (m, 2H), 3.81 (m, 2H), 4.0–4.11 (m, 2H), 4.12 (m, 2H), 4.41–4.51 (m, 1H), 4.61–4.71 (m,

1H), 5.41 (d, 2H), 8.21 (d, 1H), 7.91 (d, 1H); FABMS: 294 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{12}H_{16}N_5O_4$ 294.2866, observed 294.2865 $(M+H)^+$.

3.2.25. 1-[3,5-Dihydroxy-(2*R*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]-furan-2-yl-methyl]-5-methyl-1,2,3,4-tetrahydro-2,4-pyrimidinedione (3)

To a solution of **18** (0.04 g, 0.086 mmol) in CH_3OH (5 mL), palladium hydroxide (5 mg) was stirred under hydrogen atmosphere (1 atm) at room temperature. After 3 h catalyst was filtered and washed with CH_3OH (2 × 10 mL). The filtrate was concentrated under reduced pressure, which was purified on a small bed of silica gel (5–95% $CHCl_3$–CH_3OH) to afford the title compound **3** (0.024 g, 0.086 mmol) in 93% yield as a semisolid. $[\alpha]_D$ +32.2 (*c* 2.0, CH_3OH); ^1H NMR (300 MHz, CD_3OD): δ 1.81 (s, 3H), 2.11–2.22 (m, 2H), 3.71–3.81 (m, 2H), 4.01–4.21 (m, 1H), 4.41–4.05 (m, 1H), 4.51–4.81 (m, 2H, OH), 5.11 (br d, 1H, *J* = 5.0 Hz), 7.42 (s, 1H); FABMS: 285 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{12}H_{17}N_2O_6$ 285.2732, observed 285.2734 $(M+H)^+$.

3.2.26. 1-[3,5-Dihydroxy-(2*S*,3*R*,3a*R*,6a*S*)-perhydrofuro[3,2-*b*]-furan-2-ylmethyl]-5-methyl-1,2,3,4-tetrahydro-2,4-pyrimidinedione (6)

Same procedure as above. Obtained **6** from **27** yield (0.024 g, 0.086 mmol) in 93% yield as a semisolid. $[\alpha]_D$ +2.0 (*c* 2, CH_3OH); ^1H NMR (300 MHz, CD_3OD), δ 1.81 (s, 3H), 2.11–2.22 (m, 2H), 3.71–3.81 (m, 2H), 4.11–4.22 (m, 1H), 4.31–4.41 (m, 1H), 4.45–4.85 (m, 2H, OH), 5.61 (m, 1H), 7.32 (s, 1H); FABMS: 285 $(M+1)^+$; HRMS (ESI^+): calcd for $C_{12}H_{17}N_2O_6$ 285.2732, observed 285.2736 $(M+H)^+$.

4. Conclusions

The syntheses of six *N*-homobicyclic-dideoxy nucleosides have been achieved. These bicyclic nucleosides containing [3.3.0] fused bicyclic carbohydrate moieties may be of biological importance, as other members of this class are known to possess interesting cellular activities.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2012.01.018.

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