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Synthetic Approaches To Novel Cis and Trans Dideoxynucleosides of the Apiose Family

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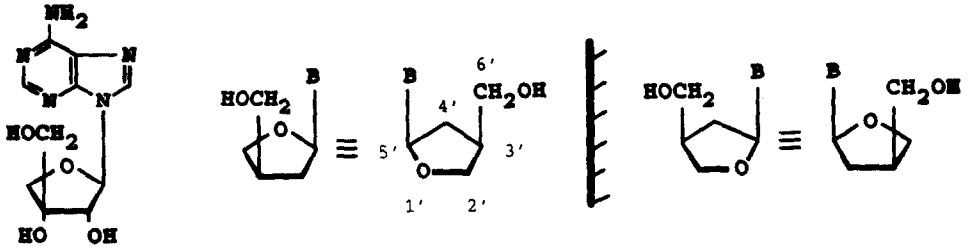
Abstract: Stereoselective synthesis of the complete family of optically active dideoxygenated nucleosides of the apiose family have been developed. The chiral aldodiol system **7**, a key intermediate in this synthesis, was prepared from the prochiral molecule **6**, through the action of the lipase from *Candida cylindracia*. Approaches to novel enantiomeric and diastereoisomeric dideoxynucleosides containing the tetrahydrofuranethanol moiety have also been discovered. A key intermediate in this approach was the optically active trans-allyllactone **61**, prepared from L-glutamic acid, and its isomerization product, the corresponding cis-allylbutyrolactone **62**. The methodologies developed have generality and allow synthetic access to a wide variety of new nucleosides.

INTRODUCTION

9-(β-D-Apio-D-furanosyl)adenine (**1**), a biologically-active, relatively non-cytotoxic nucleoside related to natural D-apiose,[1-3] is a regioisomer of adenosine through transposition of the C-4' hydroxymethyl to C-3'. Compounds belonging to the enantiomeric series represented by **2** (3'*S*,5'*R*) and **3** (3'*R*,5'*S*) are dideoxygenated analogs of D-apio-D-adenosine **1**. They may also be conceptualized as dideoxynucleosides with transposed hydroxymethyl groups or transposed oxygen atoms. A few dideoxynucleosides derived from the natural nucleosides have been found to be potently active against HIV through inhibition of HIV-encoded reverse transcriptase (RT).[4] The design and evaluation of additional novel nucleoside-based RT inhibitors are needed in order to develop analogs that exhibit increasingly more favorable toxicity profiles and are less susceptible to the development of resistant strains of HIV.[5] One essential feature in the design of these inhibitors is retention of the 2',3'-dideoxygenation which is necessary for termination of the viral DNA chain elongation.[6] Other modifications have included strategic substitution on the carbohydrate moiety, removal of the endocyclic heteroatom or introduction of an additional heteroatom.[7-12] An interesting new family of dideoxynucleosides involves transposition of the 5'-CH_2OH or transposition of the endocyclic oxygen.[13-17] These compounds are regioisomeric with respect to dideoxy analogs of the natural nucleosides and two representative classes are depicted by structures **2** and **3**. We wish to report on approaches to the stereoselective synthesis of the complete family of optically active 2',3'-dideoxygenated nucleosides

represented by 2 and 3. This study is supported by the observation[16] that one member of Class 3 has been reported to have anti-HIV activity in MT-4 cells with no apparent toxicity. Development of additional methodologies in this area has also allowed access to novel chiral isomeric dideoxynucleosides containing a furanethanol moiety and this is described.

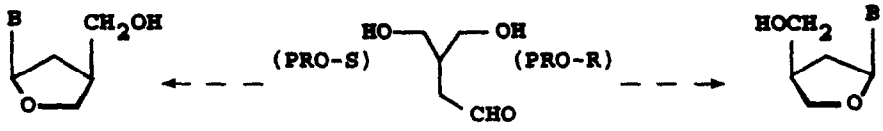


1 2 3

Figure 1

RESULTS AND DISCUSSION

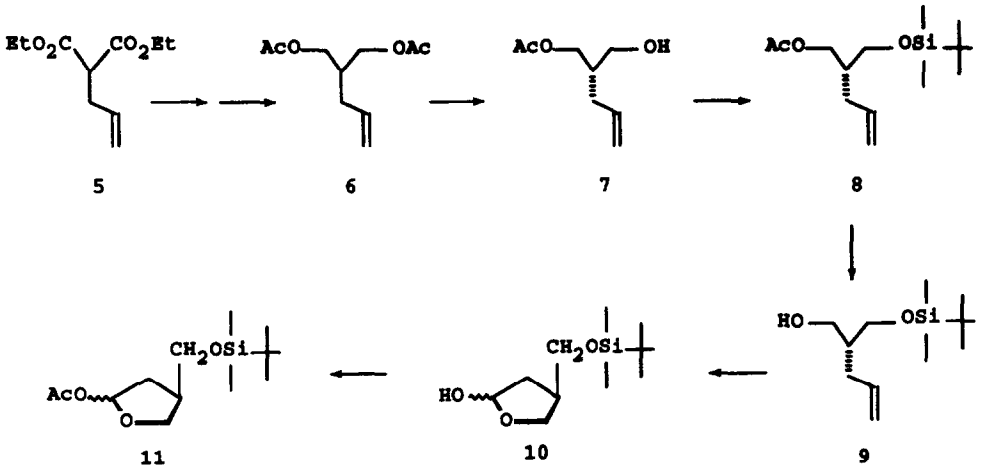
Potential strategies for the synthesis of the carbohydrate moiety of this family of optically active regioisomeric dideoxynucleosides could utilize apiose or its deoxygenated derivatives as precursors. However, due to the multistep syntheses required to obtain these chiral precursors,[18,19] alternative approaches were examined. Syntheses utilizing enzyme catalyzed reactions represent alternative approaches that have proven effective for the stereoselective synthesis of biologically active nucleosides.[20] Additionally, a divergent synthesis from a key chiral precursor would allow for an efficient approach to each enantiomeric series of these dideoxynucleosides. Such a divergent point would arise from the cyclization of a chiral derivative of the prochiral aldodiol 4 (Figure 2). Lactol formation with the *pro-S* hydroxymethyl group would allow for the formation of the dideoxygenated D-apiose [tetrahydro-3(S)-furanmethanol] nucleoside of class 2, while cyclization involving the *pro-R* hydroxymethyl allows entry into the L-apiose [tetrahydro-3(R)-furanmethanol] nucleoside of class 3.



2 4 3

Figure 2

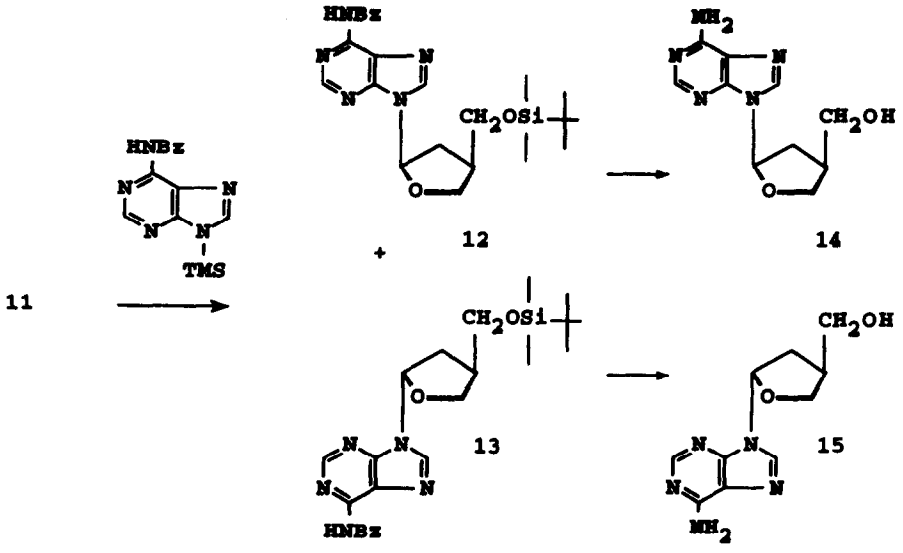
2-Allyl-1,3-propanediol was chosen as the starting material due to its potential ease of conversion into **4**. Chiral derivatives of the aldodiol system **4** are accessible through the resolution of diastereomeric urethanes,[21] or through stereoselective enzymatic hydrolysis of a suitable derivative.[22,23] The high stereoselectivity and relatively low cost of the latter method warranted its application in this synthetic work. 2-Allyl-1,3-propanediol was readily prepared by the reduction of diethyl allylmalonate **5**. Acetylation afforded 2-(2-propenyl)-1,3-propanediol diacetate (**6**) in an 80% overall yield (Scheme 1). Stereoselective ester hydrolysis with the lipase from *candida cylindracea* (Sigma, Type VII) in 30% aqueous acetone afforded the S-(-)-monoacetate **7** ($[\alpha]_D$ = -7.95°, $CHCl_3$) in a 50% yield and in high optical purity (98.7% ee). Consistently high optical purity was observed with reaction times of 7 - 10 hours at carefully maintained pH values between 6.95 - 7.00. More extended reaction times (>12 hrs) or higher pH resulted in a decrease in optical purity. Silylation of the S-(-)-monoacetate **7** produced the R-(+)-**8** which was chemically hydrolyzed to give, in near quantitative yields for two steps, the R-(+)-monosilyl ether **9**. For a key transformation, the attempted oxidative cleavage of the olefin **9** to form the tetrahydro-3(R)-furanmethanol **10**, the use of ruthenium dioxide (Aldrich) with sodium periodate[24] resulted in low and non-reproducible yields of the desired product. Contrary to previous reports,[23] no evidence for the formation of the corresponding lactone was observed. Ozonolysis (-78°C, dimethyl sulfide) of **9** and attempted acetylation did however produce the corresponding lactone of **10**, presumably *via* an *in situ* dimethyl sulfoxide - acetic anhydride oxidation[25] of



Scheme 1

the ozonolysis product. DIBAL reduction of the lactone afforded **10** in 54% overall yield from **9**. However, the most successful method employed for the conversion of **9** to **10** was the use of sodium periodate and catalytic osmium tetroxide (2.5 - 5.0 mole %),[26] which consistently afforded near quantitative yields of the desired **10**. Acetylation gave the diastereomeric mixture of protected tetrahydro-5(R,S)-acetyloxy-3(R)-furanmethanol **11** (5*R*:*S* = 2:1) in a combined yield of 78%.

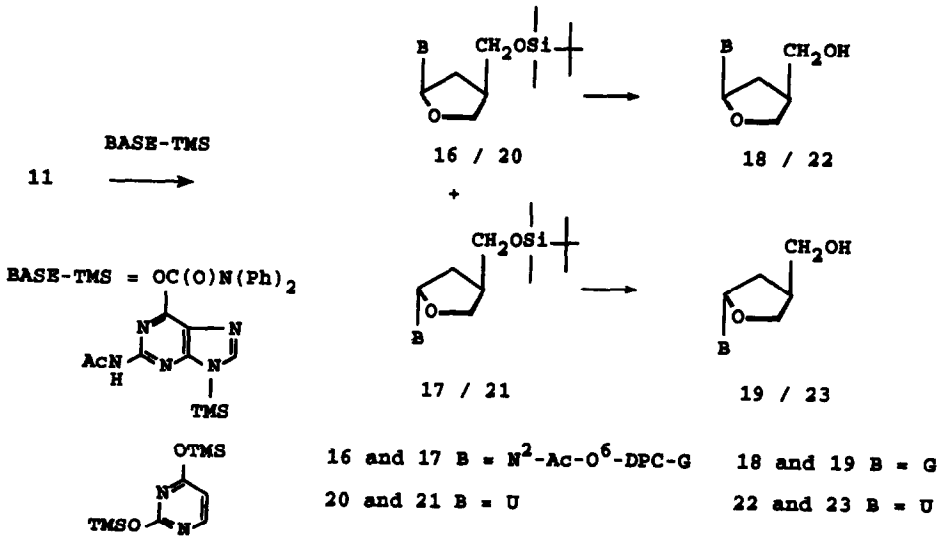
Glycosylation of **11** using stochiometric amounts of trimethylsilyl triflate (TMSOTf) [27] with silylated N^6-benzoyladenine [generated in situ with *bis*(trimethylsilyl)acetamide (BSA) in refluxing acetonitrile], afforded a 1:2 diastereomeric mixture of the adenine dideoxynucleosides **12** and **13** (Scheme 2). The use of Lewis acids such as stannic chloride were precluded, due to the reported low diastereomeric ratio of the desired cis isomer (cis:trans ratio = 1:4) in those glycosylations.[16] Differentiation between the cis and trans isomers was readily discerned from the different ^{1}H NMR chemical shifts of their tetrahydrofuran H-2' protons: δ 4.20 and 3.83 for the major isomer, **13**, and 4.08 and 3.98 for the minor isomer, **12**. These assignments were confirmed by extensive NOE experiments. Separation of the diastereomers by preparative layer chromatography with multiple immersions afforded pure 5'(R)-3'(R)-**12** (15%) and 5'(S)-3'(R)-**13** (27%). Deprotection [(i) NH_3, (ii) Et_4NF] of each isomer afforded 5(R)-(6-amino-9H-purin-9-yl)tetrahydro-3(S)-furanmethanol (**14**) ($[\alpha]_D$ = -22.6°, MeOH) and the trans compound [5'(S)-3'(S)], **15** ($[\alpha]_D$ = +39.8°, MeOH).



Scheme 2

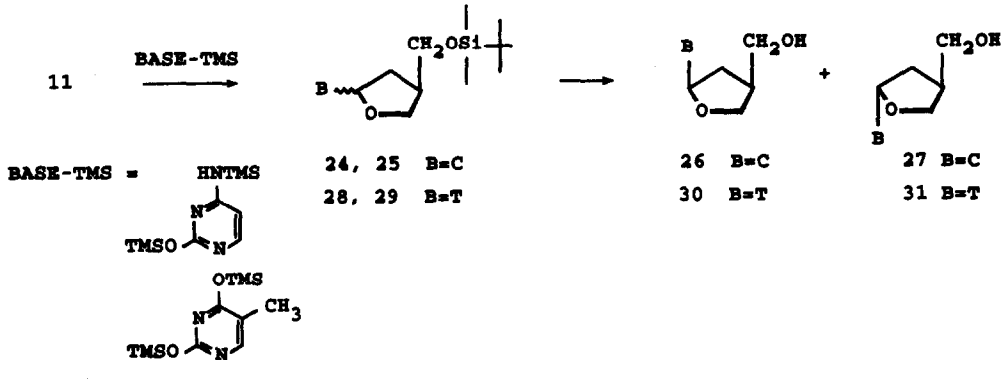
The anomeric stereochemical assignments for **14** and **15** were determined, in part, by ^{1}H NMR difference NOE data. Upon irradiation of the C-6' methylene protons a NOE of 3% was observed for both of the cis H-2' and H-4' protons of **14**. Irradiation of these protons resulted in NOEs of 2% and 8%, respectively, on the adenine base H-8. Similar results with **15** show, that upon irradiation of the C-6' methylene protons, NOEs of 2% and 3% on the cis H-2' and H-4' protons were observed. Irradiation of this H-4' proton resulted in a NOE of 6% on the anomeric H-5' proton. Additional support for the anomeric assignments is the levorotatory nature of **14**, which is consistent with that observed for 9-(D-apio-D-furanosyl)adenine,[1] and also for adenosine, and 2',3'-dideoxyadenosine.

Glycosylation of **11** with silylated N^2-acetyl-O^6-diphenylcarbamoylguanine[28] (Scheme 3) afforded a mixture of the cis-5'(R)-3'(R)-**16** and trans-5'(S)-3'(R)-**17** (1:2) in 21% yield. Separation of the diastereomers by preparative layer chromatography and deprotection of the individual anomers afforded 5(R)-(2-amino-1,9-dihydro-6H-purin-6-one)tetrahydro-3(S)-furanmethanol (**18**) and the trans-5'(S)-3'(S)-**19** in 76% and 86% yields, respectively. Similarly, under the standard glycosylation conditions (TMSOTf, 0°C - 25°C, CH_3CN), silylated uracil and **11** were coupled to form the separable compounds, **20** and **21**. Desilylation of the individual anomers afforded the regioisomeric dideoxyuridine nucleosides **22** and **23** in respective yields of 23% and 52%.



Scheme 3

Additionally, **11** was coupled with silylated cytosine and thymine (Scheme 4) to form the diastereoisomers **24, 25** and **28, 29**, respectively. In each case, the lack of significant difference in R_f values between the diastereomers prevented an efficient separation. Desilylation of the diastereoisomeric pairs also resulted in an inefficiently separable mixture of **26, 27** and **30, 31**. This problem could not be surmounted through the formation of chiral esters (e.g. camphanyl or N-benzoyl-L-phenylalaninyl) as these failed to significantly enhance separation of the diastereoisomers. Separation of **26, 27, 30,** and **31** could be achieved, albeit tediously, utilizing preparative layer chromatography (multiple immersion technique) and careful dissection of the diffused bands. The resulting fractions were analyzed (^{1}H NMR), appropriately combined, and re-chromatographed. Repeating this process provided pure products.

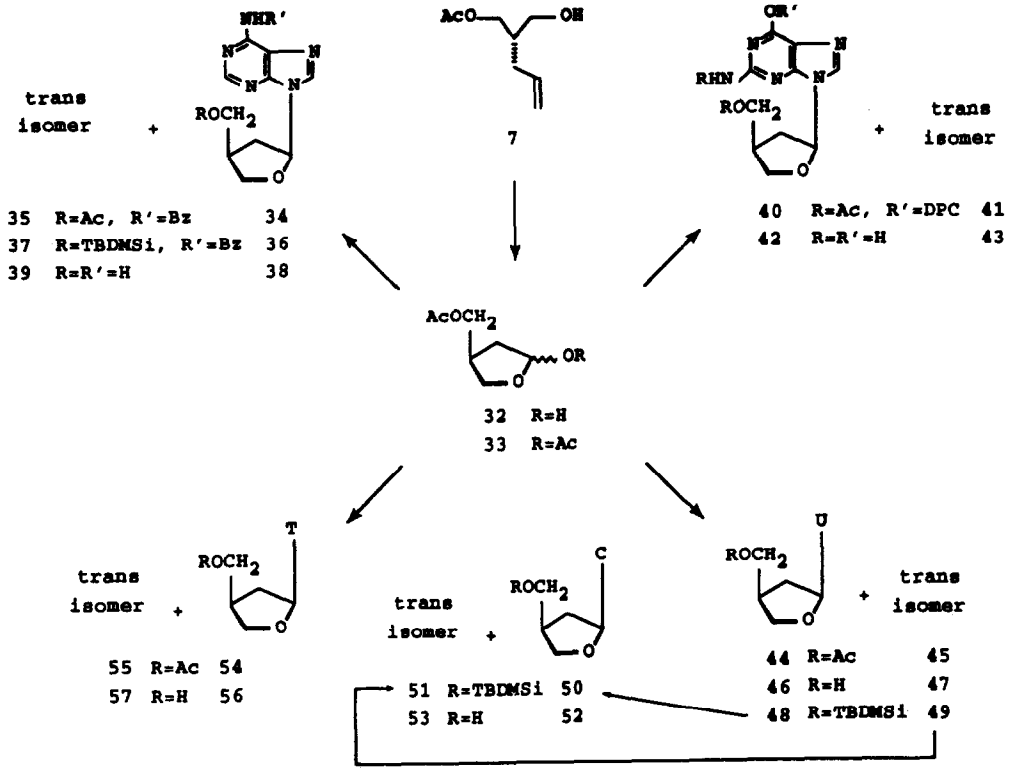


Scheme 4

In the case of the isodideoxycytidines **26** and **27**, the intricate chromatographic process was avoided through preparation of these compounds from the corresponding uridine analogs **20** and **21** in 61% and 65% yields utilizing the well established sequential phosphorous oxychloride ($POCl_3$)/1,2,4-triazole/ammonia methodology.[29] However, attempts to prepare the thymidine nucleosides **30** and **31** from the uridine nucleosides **22** and **23** using known chemical methodologies[30] were unsuccessful.

Entry into the enantiomeric tetrahydro-3(R)-furanmethanol class of regioisomeric dideoxynucleosides (i.e. of Class 3) was achieved through the key chiral intermediate **7** (Scheme 5). Treatment of **7** with OsO_4 and $NaIO_4$ readily afforded the lactol **32** (82%). Acetylation produced **33** in a 78% yield. Glycosylation, deprotection, separation and identification were carried out in a related manner to those of the enantiomeric

S-series to give the isomeric dideoxynucleosides **34-57**.



Scheme 5

These studies were extended to the novel homologous series represented by **58** and **59** (Fig. 3).

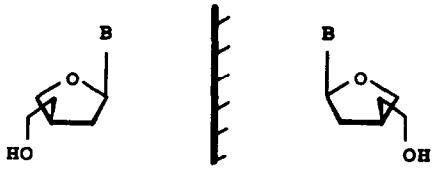
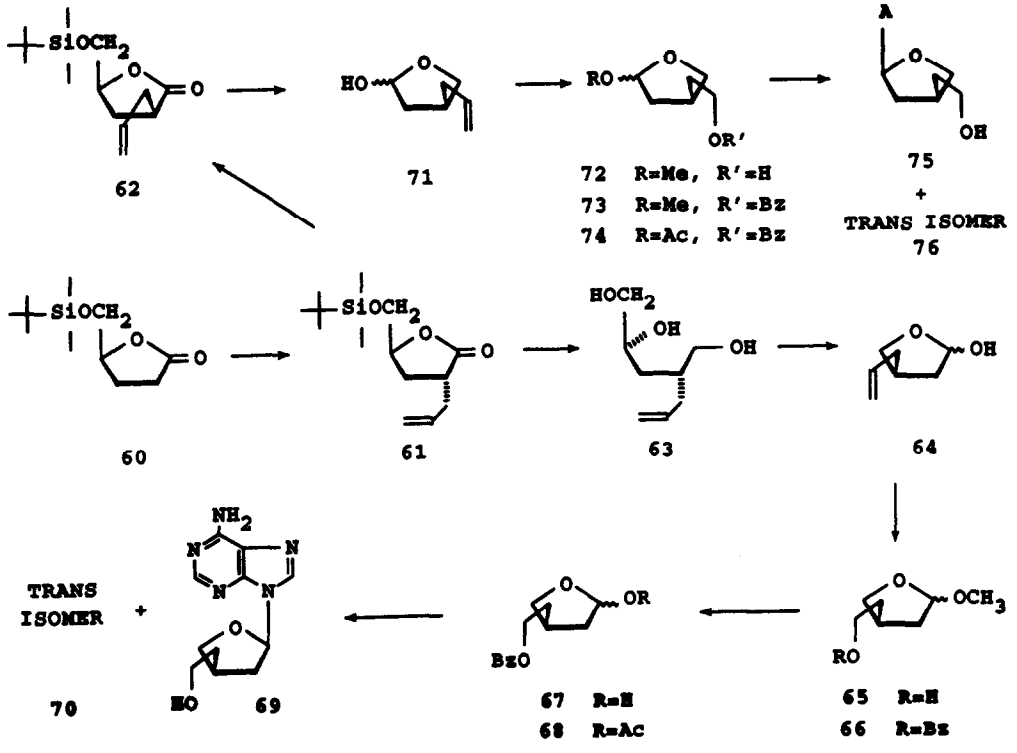


Figure 3

Approaches to the synthesis of these adenine tetrahydro-3-furanethanol nucleosides utilized the known enantiospecific formation of γ-butyrolactones from L-glutamic acid[31,32] and the potentially high stereoselectivity of alkylations of these compounds.[33-35] Thus, the silylated hydroxymethyl-γ-butyrolactone **60** served as the starting material for the synthesis. Treatment of **60** with LDA (1 equiv.) at -98 °C and subsequent reaction with allyl iodide afforded the separable diastereomeric allylbutyrolactones **61** and its cis-

isomer **62** (95:5) in a total yield of 95% (**Scheme 6**). The diastereoisomeric lactones **61** and **62** could be identified and differentiated by high-field ^{1}H NMR chemical shift data and extensive differential NOE experiments. Reduction of **61** followed by desilylation afforded the 4(R)-hydroxymethyl-6-hepten-1,2(S)-diol (**63**) in 90% yield ($[\alpha]_D$ = -19°, MeOH). The order of the reactions in this conversion of **61** to **63** is critical in order to prevent epimerization of the allyl group. Oxidative cleavage of the glycol in **63** ($NaIO_4$) was followed by spontaneous intramolecular hemiacetal formation of the resulting aldehyde to produce the tetrahydro-5-hydroxy-3(R)-allylfuran **64** (88%, $[\alpha]_D$ = +46°, MeOH). Protection of the anomeric hydroxyl group was then required for the successful conversion to the furanethanol system and to exclude the potential formation of the corresponding 4-hydroxymethylpyranoside. Thus, ozonolysis of the methyl furanoside followed by reduction of the resulting aldehyde gave the tetrahydro-3(R)-furanethanol **65** (75%, $[\alpha]_D$ = +29°, MeOH). Benzoylation, demethylation, and acetylation provided the glycosylation precursor **68** (56%, $[\alpha]_D$ = +10°, MeOH). Condensation of **68** in the presence of TMS triflate with silylated N^6-benzoyladenine (35 % yield), followed by debenzoylation and separation of the anomers by fractional crystallization and by



Scheme 6

preparative layer chromatography, produced the pure *cis*-compound, 5(R)-(6-amino-9H-purin-9-yl)-3(R)-furanethanol (**69**, 32%), and its *trans*-isomer [5'(S)-3'(R), **70**, 56%].

The enantiomeric 3(S)-furanethanol adenine dideoxynucleosides were obtained from the β-allylbutyrolactone **62** (**Scheme 6**). Treatment of the 95:5 mixture of allylbutyrolactones **61** (α) and **62** (β) with LDA, followed by quenching of the resulting enolate with water, resulted in isomerization to produce predominantly the β-allyl compound **62** (81%, **62:61** ratio = 84:16). Separation of the desired diastereoisomer **62** and subjecting it to the sequence of reactions previously described, converted **62** through the tetrahydro-3(S)-allylfuranoside **71** (71%, $[\alpha]_D$ = -44°, MeOH), to the 5-α,β mixture of acetylated tetrahydro-3(S)-furanethanols **74** ($[\alpha]_D$ = -10°, MeOH) in 31% yield. Glycosylation of the latter with N^6-benzoyladenine, deprotection and separation of the resulting diastereoisomers produced the *cis*-5(S)-(6-amino-9H-purin-9-yl)tetrahydro-3(S)-furanethanol, **75** (9%, $[\alpha]_D$ = +54.3°, MeOH) and its diastereoisomeric *trans*-5'(R),3'(S)-isomer, **76** (23%, $[\alpha]_D$ = -22.3°, MeOH). Finally, it should be mentioned that these approaches can be used to gain entry into the entire series of enantiomeric dideoxynucleosides of the tetrahydrofuranethanol family involving both purine and pyrimidine bases.

As hydrolysis (chemical and enzymatic) plays a major role in the catabolism of some potential anti-HIV nucleosides, the resistance toward enzymatic deamination and acid catalyzed glycosidic bond hydrolysis was studied. Marked resistance toward deamination by mammalian adenosine deaminase was seen for the cis-compound, **14**, and its enantiomer **38** (0.12% and 0.10%, respectively, of the rate of adenosine). Their trans-isomers, **15** and **39**, were even more resistant to deamination (0.015 % and 0.013 %, respectively, of adenosine). The corresponding tetrahydrofuranethanol compounds **69** and **75** were almost totally resistant to deamination by adenosine deaminase (< 0.005 % of the rate of adenosine). Studies of the relative rates of glycosidic bond hydrolysis [36] show that the cis-enantiomers **14** and **38** were slightly more stable (84%) than 2',3'-dideoxyadenosine (100%), while the trans-enantiomers **15** and **39** were significantly more stable (50%) at pH 3. Compounds **69** and **75** exhibited similar behavior.

In summary, approaches to enantiomeric pairs of isomeric dideoxynucleosides related to D- and L-apiose have also been developed. The key precursor for the construction of the dideoxyapiose ring was a chiral aldodiol system synthesized from a pro-chiral molecule through the action of the lipase from *Candida cylindracia*. Routes to novel enantiomeric dideoxynucleosides containing the tetrahydrofuranethanol moiety have also been discovered. Key steps in this approach, among others, were the preparation of two important intermediates, a trans-allylbutyrolactone and its cis-isomer which was accessible from the ready

isomerization of the trans-compound. The methodologies developed have generality and allow access to a wide variety of new nucleosides.

Experimental Section

Melting points reported are uncorrected and were determined on a Thomas-Hoover melting point apparatus fitted with a microscope. Nuclear magnetic resonance spectra were recorded on Bruker Models AMX-600, MSL-300, and AC-300 pulse Fourier transform spectrometers. Mass spectra were determined on a VG ZAB-HF high resolution mass spectrometer with FAB capability or a VG TRIO single quadrupole GC/MS system. Ultraviolet spectra were recorded on a Varian Cary Model 3 or a Gilford Response spectrophotometer. Infrared spectra were recorded on a Mattson Cygnus 25 Fourier transform instrument. Lyophilizations were performed with a Virtis freezemobile 3 unit. Preparative layer chromatography was carried out on plates prepared with E. Merck PF_{254} silica gel. Flash chromatography was carried out using glass columns packed with 230-400 mesh silica gel. High performance liquid chromatography was done at 80 psi using Altex columns packed with 40-60 m Amberlite XAD-4 resin (Rohm and Haas). Fractions were monitored by a Pharmacia UV-2 ultraviolet monitor and products were collected on a Gilson FC-100 fraction collector. Analytical and Preparative HPLC separations were also carried out with a Waters automated 600E system with photodiode array detector and FOXY fraction collector using Delta-Pak C_{18} and Hamilton PRP-1 columns. Elemental analyses were performed at Galbraith Laboratories, Inc., Knoxville, TN., and at the University of Iowa.

Diacetyl 2-allyl-1,3-propanediol (6). Diethyl allylmalonate (20 mL, 101.4 mmol) in anhydrous Et_2O (100 mL) was added dropwise to a stirred solution of $LiAlH_4$ (9.62 g, 253.5 mmol) in Et_2O (400 mL) at 0 °C over 1 hr. The reaction was then allowed to warm to room temperature and was stirred an additional 4 h. Wet Et_2O was then slowly added, followed by water, and the mixture was filtered through Celite, dried (Na_2SO_4), concentrated, and purified by flash chromatography (hexanes to 50% EtOAc/hexanes) to afford 10.13 g (87.20 mmol, 86%) of 2-allyl-1,3-propanediol[21]: ^1H NMR ($CDCl_3$) δ 1.9 (m, 3H), 3.4 (m, 4H), 4.0 (br s, 2H), 4.90 (m, 2H), 5.60 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 32.1, 41.7, 64.0, 116.0, 135.9. To a solution of the diol (3.50 g, 30.15 mmol) in CH_3CN (150 mL) were added DMAP (0.29 g, 2.41 mmol), Et_3N (12.6 mL, 90.40 mmol), and Ac_2O (8.53 mL, 90.41 mmol) at 0 °C. The reaction was allowed to stir at room temperature for 4 h then MeOH (10 mL) was added. The mixture was then concentrated under reduced pressure, dissolved in EtOAc, and washed with water (3 x 30 mL). The organics were then dried (Na_2SO_4) and purified by flash chromatography (hexanes to 25% EtOAc/hexanes) to afford 5.49 g (27.44 mmol, 91%) of **6**[23]: ^1H NMR ($CDCl_3$) δ 1.81 (s, 6H), 1.90 (m, 3H), 3.83 (m, 4H), 4.84 (m, 2H), 5.53 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.1, 32.2, 36.5, 63.2, 116.7, 134.6, 170.1.

S-(-)-1-O-Acetyl-2-allyl-1,3-propanediol (7). Lipase (sigma, Type VII, from *Candida cylindracea*, 4 g) was added to a rapidly stirred solution of the diacetate **6** (2.0 g, 10 mmol) and Triton X-100 (0.48 g) in a 30% aqueous acetone solution (290 mL). NaOH (1 N) was added dropwise to maintain a pH of 7. The reaction was allowed to proceed for 7.5 h and was then diluted with EtOAc (200 mL) and filtered through Celite. The filtrate was then washed with water, dried (Na_2SO_4), concentrated and purified by flash chromatography (hexanes to 50% EtOAc/hexanes) to afford 0.98 g (4.90 mmol, 49%) of the unreacted diacetate **6** and 0.79 g (5.00 mmol, 50%) [98% conversion] of the S-(-)-monoacetate isomer **7**: $[\alpha]_D$ = -7.95° (c = 1.21, $CHCl_3$), Lit.[23] $[\alpha]_D$ = -7.98° (c = 1.21, $CHCl_3$), Lit.[22] $[\alpha]_D$ = -7.65°; ^1H NMR ($CDCl_3$) δ 1.66 (m, 1H), 1.80 (s, 3H), 1.86 (m, 2H), 3.30 (m, 2H), 3.48 (br s, 1H), 3.85 (m, 2H), 4.80 (m, 2H), 5.52 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 20.2, 31.9, 39.5, 61.3, 63.7, 116.7, 135.3, 170.9.

Tetrahydro-5(R and S)-acetyloxy-3(R)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan (11). To a solution of **7** (1.10 g, 6.92 mmol) in CH_2Cl_2 (50 mL) was added *tert*-butyldimethylsilyl chloride (1.25 g, 8.31 mmol) and imidazole (0.57 g, 8.31 mmol) under nitrogen. The resulting heterogeneous mixture was stirred at room temperature for 24 h and then diluted with CH_2Cl_2, washed with water, dried (Na_2SO_4), concentrated, and was then flash chromatographed (hexanes) to afford 1.87 g (6.85 mmol, 99%) of R-(-)-3-O-acetyl-2-allyl-1-O-[(1,1-dimethylethyl)dimethylsilyl]-1,3-propanediol (**8**): $[\alpha]_D$ = -0.10° (c = 2.08, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.08 (s, 6H), 0.78 (s, 9H), 1.77 (m, 1H), 1.91 (s, 3H), 2.01 (m, 2H), 3.47 (m, 2H), 3.94 (m, 2H),

4.92 (m, 2H), 5.64 (m, 1H); ^{13}C NMR ($CDCl_3$) δ -5.8, 18.0, 20.6, 25.6, 32.3, 39.9, 61.9, 64.0, 116.4, 135.8, 170.5.

To a solution of **8** (0.28 g, 1.04 mmol) in MeOH (10 mL) was added sodium methoxide (0.07 g, 1.24 mmol) and the solution was stirred for 45 min. The reaction was then neutralized with 1 N HCl. The volatiles were then removed under reduced pressure and the product was purified by flash chromatography (hexanes to 25% EtOAc/hexanes) to afford 0.23 g (1.00 mmol, 97%) of R-(+)-2-allyl-1-O-[(1,1-dimethylethyl)dimethylsilyl]-1,3-propanediol (**9**): $[\alpha]_D$ = +3.73° (c = 1.76, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ -0.02 (s, 6H), 0.81 (s, 9H), 1.70 (m, 1H), 1.97 (m, 2H), 3.0 (br s, 1H), 3.55 (m, 4H), 4.93 (m, 2H), 5.68 (m, 1H); ^{13}C NMR ($CDCl_3$) δ -5.7, 18, 25.7, 32.2, 41.9, 64.9, 65.5, 116.1, 136.3.

Sodium metaperiodate (3.91 g, 18.3 mmol) in water (10.5 mL) was added to an etheral solution (10.5 mL) of **9** (1.41 g, 6.10 mmol) and OsO_4 (0.08 g, 0.30 mmol). The solution was vigorously stirred for 12 h then cooled to 0°C and $NaHSO_3$ (1 g) was slowly added. The mixture was allowed to stir for an additional 10 min, diluted with EtOAc, then transferred to a separatory funnel and washed with saturated $NaHSO_3$ and water. The organics were then dried (Na_2SO_4) and purified by flash chromatography (hexanes to 50% EtOAc/hexanes) to afford 1.39 g (5.98 mmol, 98%) of tetrahydro-5(R and S)-hydroxy-3(R)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan (**10**): $[\alpha]_D$ = +24.0° (c = 1.78, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ -0.15 (s, 6H), -0.10 (s, 6H), 0.70 (s, 9H), 0.72 (s, 9H), 1.49 (m, 2H, H-4α/β), 1.73 (ddd, 1H, J = 1.2, 7.9 and 13.1 Hz, H-4α), 1.97 (ddd, 1H, J = 5.3, 10.1 and 13.3 Hz, H-4β), 2.34 (m, 1H, H-3β), 2.44 (m, 1H, H-3α), 3.29 (dd, 1H, J = 7.5 and 9.8 Hz, H-6α), 3.37 (dd, 1H, J = 6.0 and 9.9 Hz, H-6α), 3.48 (m, 3H, H-6β and H-2β), 3.60 (dd, 1H, J = 6.5 and 8.6 Hz, H-2β), 3.80 (t, 1H, J = 8.3, H-2α), 3.88 (t, 1H, J = 7.9 Hz, H-2α), 4.74 (d, 1H, J = 3 Hz, C(5)-OHα), 4.86 (d, 1H, J = 6.3 Hz, C(5)-OHβ), 5.25 (t, 1H, J = 5.1 Hz, H-5β), 5.31 (s, 1H, H-5α): ^{13}C NMR ($CDCl_3$) δ -5.8, 17.8, 17.9, 25.5, 35.7, 36.3, 39.4, 64.3, 64.6, 68.7, 97.8, 97.9: Mass Spectrum (70 eV) *m/z* (rel. Intensity) 215 (.37), 201 (1.39), 173 (6.25), 157 (20.27), 83 (100).

To a solution of **10** (1.11 g, 4.78 mmol) in CH_3CN (10 mL) containing 0.5 g of molecular sieves were added Et_3N (0.93 mL, 6.67 mmol), DMAP (0.06 g, 0.48 mmol), and Ac_2O (0.54 mL, 5.72 mmol). The solution was stirred for 1 h then diluted with Et_2O and washed with water, dried (Na_2SO_4), concentrated, and flash chromatographed (hexanes to 20% EtOAc/hexanes) to afford 1.02 g (3.73 mmol, 78%) of predominantly the 5(R)-anomeric acetate of **11**: ^{1}H NMR ($CDCl_3$) δ -0.06 (s, 6H), -0.05 (s, 6H), 0.78 (s, 9H), 0.79 (s, 9H), 1.76 (m, 2H, H-4α/β), 1.95 (s and m, 7H, CH_3α/β and H-4β), 2.14 (m, 1H, H-4α), 2.41 (m, 1H, H-3β), 2.53 (m, 1H, H-3α), 3.46 (m, 2H, H-6α), 3.55 (m, 2H, H-6β), 3.67 (m, 2H, H-2α/β), 3.97 (m, 2H, H-2α/β), 6.16 (d, 2H, J = 4.7 Hz, H-5α/β); ^{13}C NMR ($CDCl_3$) δ -5.7, 18, 21, 25.6, 34.3, 34.7, 39.1, 39.8, 63.9, 64.2, 70.7, 71.1, 99, 169.9, 170. Anal. Calcd. for $C_{13}H_{26}O_4Si$: C, 56.90; H, 9.96. Found: C, 56.80; H, 9.99.

5(R)-(6-Amino-9H-purin-9-yl)tetrahydro-3(S)-furanmethanol (14). A solution of N^6-benzoyladenine (0.68 g, 2.82 mmol) and BSA (0.91 mL, 3.67 mmol) in CH_3CN (5 mL) was refluxed for 1 hr then cooled to 0 °C. The acetylated sugar **11** (0.77 g, 2.82 mmol) in CH_3CN (6 mL) was then added, followed by TMSOTf (0.60 mL, 3.10 mmol), and the reaction mixture was stirred for 2 h at 0°C and then at room temperature for an additional 2 h. A saturated solution of $NaHCO_3$ (20 mL) was then added, followed by EtOAc (100 mL), and the organics were washed with water, dried (Na_2SO_4), and purified by flash chromatography ($CHCl_3$ to 5% MeOH/$CHCl_3$) and by preparative layer chromatography with multiple elutions (20% hexanes/Et_2O to Et_2O) to afford 0.19 g (0.42 mmol, 15%) of 5(R)-[(6-benzoylamino)-9H-purin-9-yl]tetrahydro-3(R)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan **12**: U.V. (MeOH) λ_{max} = 279 nm; $[\alpha]_D$ = -10.5° (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ -0.03 (s, 6H), 0.81 (s, 9H), 2.36 (m, 1H), 2.62 (m, 2H), 3.65 (d, 2H, J = 5.1 Hz), 3.98 (t, 1H, J = 8.1 Hz), 4.08 (t, 1H, J = 7.9 Hz), 6.27 (t, 1H, J = 6.2 Hz), 7.40 (t, 2H, J = 7.4 Hz), 7.47 (t, 1H, J = 7.3 Hz), 7.95 (d, 2H, J = 7.3 Hz), 8.16 (s, 1H), 8.67 (s, 1H), 9.52 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.1, 25.7, 34.4, 41.5, 62.7, 71.2, 85.7, 123.6, 127.8, 128.6, 132.5, 133.6, 140.9, 149.5, 151.5, 152.3, 164.9; Mass Spectrum (70 eV) *m/z* (rel. intensity) 453 (M^+, 0.2), 424 (M^+-30, 0.3), 396 (M^+-57, 2.7); and 0.35 g (0.76 mmol, 27%) of 5(S)-[(6-benzoylamino)-9H-purin-9-yl]tetrahydro-3(R)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan **13**: U.V. (MeOH) λ_{max} = 279 nm; $[\alpha]_D$ = +20.5° (c = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ -0.03 (s, 6H), 0.81 (s, 9H), 2.27 (m, 1H), 2.54 (m, 1H), 2.67 (m, 1H), 3.57 (m, 2H), 3.83 (t, 1H, J = 7.4 Hz), 4.20 (t, 1H, J = 7.9 Hz), 6.24 (dd, 1H, J = 2.6 and 6.7 Hz), 7.33 (t, 2H, J = 7.4 Hz), 7.43 (t, 1H, J = 7.2 Hz), 7.91 (d, 2H, J = 7.5 Hz), 7.99 (s, 1H), 8.60 (s, 1H), 9.74 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.0, 25.6, 34.7, 40.1, 63.2, 71.7, 86.3, 123.7, 127.8, 128.4, 132.3, 133.5, 141, 149.5, 151.1, 152.1, 165.

A solution of **12** (0.19 g, 0.42 mmol) in MeOH (100 mL) was cooled to 0 °C and saturated with NH_3. The reaction was then warmed to room temperature and allowed to proceed for 24 h. The volatiles were then

removed under reduced pressure and the resulting oil was purified by preparative TLC (5% MeOH/$CHCl_3$) to give 0.15 g (0.42 mmol, 99%) of the debenzoylated product: U.V. (MeOH) λ_{max} = 259 nm; ^{1}H NMR ($CDCl_3$) δ -0.03 (s, 6H), 0.80 (s, 9H), 2.31 (m, 1H), 2.61 (m, 2H), 3.63 (d, 2H, J = 5.2 Hz), 3.95 (t, 1H, J = 8.0 Hz), 4.05 (t, 1H, J = 7.8 Hz), 6.22 (t, 1H, J = 6.0 Hz), 6.62 (br s, 2H), 7.98 (s, 1H), 8.25 (s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.1, 25.7, 34.3, 41.4, 62.8, 70.9, 85.3, 119.9, 138.1, 149.4, 152.7, 155.8. To a solution of this product (0.15 g, 0.42 mmol) in CH_3CN (10 mL) was added Et_4NF (0.09 g, 0.63 mmol) and the solution was stirred for 1 hr. The volatiles were then removed and the tan oil was purified by preparative TLC (10% MeOH/$CHCl_3$) followed by reverse-phase HPLC (20% EtOH/H_2O) to afford 0.07 g (0.31 mmol, 73%) of **14**: M.P. (lyophilized powder) 182-184 °C; U.V. (H_2O) λ_{max} = 259 nm (ε = 14,580); $[\alpha]_D$ = -22.6° (c = 0.25, MeOH); ^{1}H NMR (DMSO-d_6) δ 2.31 (m, 1H), 2.55 (m, 2H), 3.56 (m, 2H), 3.88 (t, 1H, J = 8.1 Hz), 3.99 (t, 1H, J = 7.7 Hz), 4.83 (t, 1H, J = 5.1 Hz), 6.23 (t, 1H, J = 6.5 Hz), 7.26 (br s, 2H), 8.14 (s, 1H), 8.32 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 33.7, 41.7, 61.7, 70.8, 84.3, 119.2, 139.1, 149.2, 152.5, 156. Anal. Calcd. for $C_{10}H_{13}N_5O_2$: C, 51.06; H, 5.57; N, 29.77. Found C, 50.91; H, 5.59; N, 29.68.

5(S)-(6-Amino-9H-purin-9-yl)tetrahydro-3(S)-furanmethanol (15). In a manner identical to that described for **14**, 0.35 g (0.77 mmol) of **13** was converted to 0.27 g (0.76 mmol, 99%) of the debenzoylated product: U.V. (MeOH) λ_{max} = 259 nm; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 6H), 0.82 (s, 9H), 2.25 (m, 1H), 2.52 (m, 1H), 2.66 (m, 1H), 3.58 (m, 2H), 3.83 (t, 1H, J = 7.4 Hz), 4.22 (t, 1H, J = 7.9 Hz), 6.26 (dd, 1H, J = 2.8 and 6.3 Hz), 6.69 (br s, 2H), 7.87 (s, 1H), 8.25 (s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.1, 25.7, 34.7, 40.2, 63.4, 71.6, 85.8, 120.0, 138.2, 149.0, 152.7, 155.8. To a solution of the debenzoylated product (0.27 g, 0.76 mmol) in CH_3CN (10 mL) was added Et_4NF (0.17 g, 1.15 mmol) and the solution was stirred for 1 hr. The volatiles were then removed under reduced pressure and the oil obtained was purified by preparative TLC and by reverse-phase HPLC to afford 0.16 g (0.67 mmol, 88%) of the 5'(S)-isomer **15**: M.P. (lyophilized powder) 138-140 °C; U.V. (H_2O) λ_{max} = 259 nm (ε = 14,180); $[\alpha]_D$ = +39.8° (c = 0.25, MeOH); ^{1}H NMR (DMSO-d_6) δ 2.22 (m, 1H), 2.56 (m, 1H), 2.76 (m, 1H), 3.43 (m, 2H), 3.75 (dd, 1H, J= 5.4 and 8.1 Hz), 4.17 (t, 1H, J = 7.6 Hz), 4.81 (t, 1H, J = 4.7 Hz), 6.27 (dd, 1H, J = 3.0 and 6.6 Hz), 7.24 (br s, 2H), 8.14 (s, 1H), 8.26 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.0, 40.5, 62.2, 70.9, 84.4, 119.2, 139.2, 149.0, 152.6, 156.0. Anal. Calcd. for $C_{10}H_{13}N_5O_2 \cdot 1/4\ H_2O$: C, 50.1; H, 5.68; N, 29.21. Found C, 50.19; H, 5.66; N, 29.14.

5(R)-(2-Amino-1,9-dihydro-6H-purin-6-one)tetrahydro-3(S)-furanmethanol (18). Under the standard glycosylation conditions, **11** (1.05 g, 3.82 mmol) in CH_3CN (6 mL) followed by TMSOTf (0.81 mL, 4.21 mmol) were added at 0 °C to a solution of silylated N^2-acetyl-O^6-diphenylcarbamoylguanine (1.78 g, 4.59 mmol), prepared with BSA (1.32 mL, 5.35 mmol) in CH_3CN (15 mL). The resulting solution was allowed to warm to room temperature and was stirred for 4 h. Workup, as previously described, followed by purification utilizing flash chromatography (5% MeOH/$CHCl_3$) and then preparative layer chromatography (25% hexanes/Et_2O) gave 0.16 g (0.27 mmol, 7.1%) of the slower migrating 5(R)-[2-(acetylamino)-6-(diphenylcarbamoyloxy)-9H-purin-6-yl]tetrahydro-3(R)-[((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan (**16**): U.V. (MeOH) λ_{max} = 276 nm; ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 6H), 0.84 (s, 9H), 2.30 (m, 1H), 2.46 (s, 3H), 2.55 (m, 1H), 2.61 (m, 1H), 3.66 (m, 2H), 3.96 (t, 1H, J = 8.2 Hz), 4.08 (t, 1H, J = 7.8 Hz), 6.18 (t, 1H, J = 6.2 Hz), 7.19 (t, 2H, J = 6.6 Hz), 7.30 (t, 4H, J = 7.7 Hz), 7.38 (d, 4H, J = 7.5 Hz), 8.14 (s, 1H), 8.42 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.1, 25.0, 25.7, 34.3, 41.5, 62.7, 71.0, 85.6, 121.1, 126.4, 126.8, 127.3, 127.5, 129.0, 141.6, 141.8, 150.2, 151.9, 154.4, 155.9, 170.7; and 0.30 g (0.50 mmol, 13%) of the faster migrating 5(S)-[2-(acetylamino)-6-(diphenylcarbamoyloxy)-9H-purin-6-yl]tetrahydro-3(R)-[((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan (**17**): U.V. (MeOH) λ_{max} = 276 nm; ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 6H), 0.87 (s, 9H), 2.30 (m, 1H), 2.44 (s, 3H), 2.56 (m, 1H), 2.72 (m, 1H), 3.61 (m, 2H), 3.87 (dd, 1H, J = 6.1 and 8.5 Hz), 4.25 (t, 1H, J = 7.9 Hz), 6.19 (dd, 1H, J = 2.7 and 6.6 Hz), 7.18 (t, 2H, J = 7.0 Hz), 7.29 (t, 4H, J = 7.6 Hz), 7.38 (d, 4H, J = 7.4 Hz), 8.02 (s, 1H), 8.49 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.1, 24.9, 25.7, 34.4, 40.2, 63.4, 71.7, 86.3, 121.3, 126.1, 126.8, 127.4, 127.7, 129.0, 141.6, 142.2, 150.3, 151.9, 154.1, 155.9, 170.6.

A solution of **16** (0.16 g, 0.27 mmol) in 95% ethanol (150 mL) at 0 °C was saturated with NH_3. The solution was then allowed to warm to room temperature and proceed for 48 h. The volatiles were then removed and the remaining white powder was purified by preparative TLC (10% MeOH/$CHCl_3$) to afford 0.08 g (0.22 mmol, 83%) of the silylated guanine dideoxynucleoside: U.V. (MeOH) λ_{max} = 252 nm (sh 274); ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 6H), 0.86 (s, 9H), 2.16 (m, 1H), 2.56 (m, 2H), 3.70 (m, 2H), 3.81 (t, 1H, J = 7.7 Hz), 3.95 (t, 1H, J = 7.4 Hz), 5.99 (t, 1H, J = 6.2 Hz), 6.49 (br s, 2H), 7.85 (s, 1H), 10.7 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.4, 17.9, 25.8, 33.6, 41.3, 63.3, 70.2, 83.6, 116.9, 134.8, 150.9, 153.6, 156.8. Et_4NF (0.06 g, 0.40 mmol) was added to a solution of the above product (0.08 g, 0.22 mmol) in CH_3CN (10 mL) and the mixture was stirred for 1 hr. The volatiles were then removed under reduced pressure and the resulting oil was purified by preparative TLC (15% MeOH/$CHCl_3$) and then with reverse-phase HPLC (10% EtOH/H_2O) to afford 0.05 g (0.19 mmol, 86%) of **18**: M.P. (lyophilized powder) >250 °C (decomp.); U.V. (H_2O) λ_{max} =

252 nm (ε = 13,138) 274 sh (ε = 8778); $[\alpha]_D$ = -22.3° (c = 0.25, 10% H_2O/MeOH); ^1H NMR (DMSO-d_6) δ 2.15 (m, 1H), 2.47 (m, 2H), 3.52 (m, 2H), 3.82 (t, 1H, J = 8.0 Hz), 3.93 (t, 1H, J = 7.7 Hz), 4.80 (br s, 1H), 5.98 (t, 1H, J = 6.5 Hz), 6.51 (br s, 2H), 7.87 (s, 1H), 10.68 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 33.7, 41.5, 61.6, 70.4, 83.5, 116.8, 135.1, 150.9, 153.9, 157.2. Anal. Calcd. for $C_{10}H_{13}N_5O_3 \cdot 1/4\ H_2O$: C, 46.96; H, 5.32; N, 27.38. Found C, 46.94, H, 5.34; N, 27.29.

5(S)-(2-Amino-1,9-dihydro-6H-purin-6-one)tetrahydro-3(S)-furanmethanol (19). In a similar fashion as described for the lactam deblocking of **16**, 0.32 g (0.54 mmol) of **17** was deblocked to give 0.18 g (0.49 mmol, 92%) of the silylated analog: U.V. (MeOH) λ_{max} = 252 nm (sh 274); ^1H NMR ($CDCl_3$) δ 0.05 (s, 6H), 0.87 (s, 9H), 2.16 (m, 1H), 2.40 (m, 1H), 2.74 (m, 1H), 3.59 (m, 2H), 3.69 (dd, 1H, J = 5.4 and 7.9 Hz), 4.13 (t, 1H, J = 7.6 Hz), 6.04 (dd, 1H, J = 2.9 and 6.6 Hz), 6.47 (br s, 2H), 7.82 (s, 1H), 10.68 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ -5.4, 17.9, 25.8, 33.7, 39, 63.6, 70.3, 83.6, 116.9, 135.2, 150.6, 153.6, 156.8. This product 0.17 g (0.45 mmol) was then similarly desilylated with Et_4NF (0.14 g, 0.91 mmol) to afford 0.11 g (0.42 mmol, 93%) of **19**; M.P. (lyophilized powder) >250 °C (decomp.); U.V. (H_2O) λ_{max} = 252 nm (ε = 12,600) 274 sh (ε = 8435); $[\alpha]_D$ = +18.7° (c = 0.27, 10% H_2O/MeOH); ^1H NMR (DMSO-d_6) δ 2.16 (m, 1H), 2.37 (m, 1H), 2.67 (m, 1H), 3.42 (m, 2H), 3.70 (dd, 1H, J = 5.4 and 8.4 Hz), 4.12 (dd, 1H, J = 7.4 and 8.1 Hz), 4.80 (br s, 1H), 6.03 (dd, 1H, J= 3.7 and 7.0 Hz), 6.48 (br s, 2H), 7.81 (s, 1H), 10.68 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.1, 40.2, 62.1, 70.6, 83.6, 116.8, 135.1, 150.7, 153.6, 156.9. Anal. Calcd. for $C_{10}H_{13}N_5O_3$: C, 47.81; H, 5.22; N, 27.87. Found C, 47.73; H, 5.23; N, 27.79.

5(R)-[2,4(1H,3H)-Pyrimidinedione]tetrahydro-3(S)-furanmethanol (22). Under the standard glycosylation conditions, **11** (1.0 g, 3.65 mmol) in CH_3CN (6 mL) followed by TMSOTf (0.78 mL, 4.02 mmol) were added at 0 °C to a solution of silylated uracil (0.49 g, 4.38 mmol), prepared with BSA (2.38 mL, 9.64 mmol) in CH_3CN (3 mL). The resulting solution was allowed to warm to room temperature and was stirred for 4 h. After workup and purification using flash chromatography ($CHCl_3$ to 5% MeOH/$CHCl_3$), separation of the anomers by preparative TLC (25% hexanes/Et_2O) yielded 0.30 g (0.91 mmol, 25%) of the faster migrating 5(R)-[2,4(1H,3H)-pyrimidinedione]tetrahydro-3(R)-[(((1,1-dimethylethyl)dimethylsilyl)oxy) methyl]furan (**20**): U.V. (MeOH) λ_{max} = 261 nm; ^1H NMR ($CDCl_3$) δ 0.01 (s, 6H), 0.82 (s, 9H), 1.70 (m, 1H), 2.54 (m, 2H), 3.52 (dd, 1H, J = 5.6 and 10.1 Hz), 3.60 (dd, 1H, J = 4.4 and 10.2 Hz), 3.86 (t, 1H, J = 7.8 Hz), 4.01 (t, 1H, J = 7.9 Hz), 5.70 (d, 1H, J = 8.1 Hz), 6.0 (t, 1H, J = 6.2 Hz), 7.42 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ -5.7, 18.0, 25.6, 34.6, 40.6, 62.6, 70.9, 86.7, 102.0, 139.2, 150.5, 163.8; and 0.68 g (2.08 mmol, 57%) of the slower migrating 5(S)-[2,4(1H,3H)-pyrimidinedione]tetrahydro-3(R)-[(((1,1-dimethylethyl)-dimethylsilyl)oxy)methyl]furan (**21**): U.V. (MeOH) λ_{max} = 261.5 nm; ^1H NMR ($CDCl_3$) δ -0.11 (s, 6H), 0.72 (s, 9H), 1.93 (m, 1H), 2.09 (m, 1H), 2.37 (m, 1H), 3.42 (m, 1H), 3.48 (m, 1H), 3.67 (t, 1H, J = 7.7 Hz), 4.09 (t, 1H, J = 7.7 Hz), 5.58 (d, 1H, J = 8.0 Hz), 5.85 (m, 1H), 7.26 (d, 1H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$) δ -5.7, 18.0, 25.6, 35.2, 39.7, 63.0, 72.1, 87.3, 101.6, 139.2, 150.2, 163.9.

Treatment of **20** (0.17 g, 0.53 mmol) with Et_4NF (0.16 g, 1.06 mmol) in CH_3CN (50 mL) afforded, after purification by preparative TLC (7% MeOH/$CHCl_3$) and by reverse-phase HPLC (20% EtOH/H_2O), 0.10 g (0.49 mmol, 92%) of **22**: M.P. (MeOH) 88-89 °C; U.V. (H_2O) λ_{max} = 262 nm (ε = 10,370); $[\alpha]_D$ = +30.9° (c = 0.33, MeOH); ^1H NMR (DMSO-d_6) δ 1.72 (m, 1H), 2.34 (m, 1H), 2.51 (m, 1H), 3.44 (m, 2H), 3.82 (t, 1H, J = 8.0 Hz), 3.94 (t, 1H, J = 7.9 Hz), 4.76 (br s, 1H), 5.62 (d, 1H, J = 8.2 Hz), 5.96 (t, 1H, J = 6.7 Hz), 7.66 (d, 1H, J = 8.2 Hz) 11.28 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ34.0, 40.9, 61.7, 71.0, 85.9, 101.6, 140.5, 150.4, 163.2. Anal. Calcd. for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.20. Found C, 50.79; H, 5.69; N, 13.16.

5(S)-[2,4(1H,3H)-Pyrimidinedione]tetrahydro-3(S)-furanmethanol (23). In an identical manner 0.45 g (1.37 mmol) of **21** was treated with Et_4NF (0.41 g, 2.74 mmol) to give 0.28 g (1.32 mmol, 96%) of **23**: M.P. (lyophilized powder) 93-95 °C; U.V. (H_2O) λ_{max} = 262 nm (ε = 10,100); $[\alpha]_D$ = -17.7° (c = 0.48, MeOH); ^1H NMR (DMSO-d_6) δ 2.04 (m, 2H), 2.46 (m, 1H), 3.38 (m, 2H), 3.64 (dd, 1H, J = 6.5 and 8.3 Hz), 4.18 (dd, 1H, J = 7.3 and 8.2 Hz), 4.78 (br s, 1H), 5.56 (d, 1H, J = 8.1 Hz), 5.93 (dd, 1H, J = 4.4 and 6.3 Hz); 7.58 (d, 1H, J = 7.9 Hz), 11.2 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.4, 39.9, 61.8, 71.6, 86.2, 101.3, 140.6, 150.4, 163.3. Anal. Calcd. for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.20. Found C, 50.87; H, 5.69; N, 13.15.

5(R)-[4-Amino-2(1H)-pyrimidinone]tetrahydro-3(S)-furanmethanol (26) and 5(S)-[4-Amino-2(1H)-pyrimidinone]tetrahydro-3(S)-furanmethanol (27). Under the standard glycosylation conditions, **11** (1.03 g, 3.76 mmol) in CH_3CN (6 mL) followed by TMSOTf (0.80 mL, 4.13 mmol) were added at 0 °C to a solution of silylated cytosine (0.50 g, 4.51 mmol), prepared with BSA (2.23 mL, 9.02 mmol) in CH_3CN (3 mL). The resulting solution was allowed to warm to room temperature and was stirred for 3 h. The reaction was then worked up under standard conditions to give, after purification by flash chromatography (10% MeOH/$CHCl_3$) 1.03 g (3.16 mmol, 84%) of a 1/1 anomeric mixture of the nucleosides **24**: U.V. (MeOH) λ_{max} = 272 nm; ^1H

NMR ($CDCl_3$) δ -0.04 (s, 6H), 0.80 (s, 9H), 1.57 (m, 1H), 2.56 (m, 2H), 3.46 (m, 1H), 3.54 (dd, 1H, J = 5.0 and 10.1 Hz), 3.82 (t, 1H, J = 7.5 Hz), 4.0 (t, 1H, J = 7.4 Hz), 5.72 (d, 1H, J = 7.4 Hz), 5.96 (t, 1H, J = 5.9 Hz), 7.52 (d, 1H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.1, 25.7, 35.5, 41.0, 63.4, 71.3, 88.0, 94.8, 140.5, 156.2, 166.1; and **25**: U.V. (MeOH) λ_{max} = 272 nm; ^1H NMR ($CDCl_3$) δ -0.01 (s, 6H), 0.83 (s, 9H), 2.05 (m, 1H), 2.17 (m, 1H), 2.40 (m, 1H), 3.50 (t, 1H, J = 7.5Hz), 3.61 (dd, 1H, J = 5.1 and 9.8 Hz), 3.78 (t, 1H, J = 8.0 Hz), 4.17 (t, 1H, J = 7.8 Hz), 5.82 (d, 1H, J = 7.3 Hz), 5.98 (m, 1H), 7.35 (d, 1H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ -5.5, 18.2, 25.8, 35.8, 39.7, 63.4, 72.3, 88.1, 94.3, 139.8, 156.1, 166.1. To a solution of **24** and **25** (0.96 g, 2.96 mmol) in CH_3CN (50 mL) was added Et_4NF (0.88 g, 5.91 mmol). Purification utilizing flash chromatography (15% MeOH/$CHCl_3$) afforded 0.56 g (2.63 mmol, 89%) of the 1/1 anomeric mixture of **26** and **27**. Pure anomers were isolated through multiple developments by preparative TLC (Et_2O 78%, $CHCl_3$ 18%, MeOH 2%, EtOH 2%) and further purified by reverse-phase HPLC (10% EtOH/H_2O) to give pure **26** and **27**. Data for **26**: low melting point solid; U.V. (H_2O) λ_{max} = 272 nm (ε = 8890); $[\alpha]_D$ = +56.5° (c = 0.23, MeOH); ^1H NMR (DMSO-d_6) δ 1.58 (m, 1H), 2.36 (m, 1H), 2.47 (m, 1H), 3.40 (m, 2H), 3.82 (t, 1H, J = 7.8 Hz), 3.93 (t, 1H, J = 7.8 Hz), 4.73 (br s, 1H), 5.73 (d, 1H, J = 7.4 Hz), 5.92 (t, 1H, J = 6.5 Hz), 7.10 (d, 2H, J = 12.4 Hz), 7.58 (d, 1H, J = 7.4 Hz); ^{13}C NMR (DMSO-d_6) δ 34.9, 41.0, 62.0, 70.9, 86.5, 93.9, 140.6, 155.2, 165.7. Anal. Calcd. for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89. Found C, 51.11; H, 6.20; N, 19.85.
Data for **27**: M.P. (lyophilized powder) 192-195 °C; U.V. (H_2O) λ_{max} = 272 nm (ε = 9900); $[\alpha]_D$ = -39.5° (c = 0.47, MeOH); ^1H NMR (DMSO-d_6) δ 1.91 (m, 1H), 2.04 (m, 1H), 2.39 (m, 1H), 3.42 (m, 2H), 3.64 (t, 1H, J = 7.4 Hz), 4.19 (t, 1H, J = 7.6 Hz), 4.77 (t, 1H, J = 4.4 Hz), 5.71 (d, 1H, J = 7.3 Hz), 5.90 (dd, 1H, J = 3.6 and 6.3 Hz), 7.11 (d, 2H, J = 11.2 Hz), 7.54 (d, 1H, J = 7.3 Hz); ^{13}C NMR (DMSO-d_6) δ 35.2, 40.7, 61.8, 71.5, 86.6, 93.5, 140.7, 155.1, 165.7. Anal. Calcd. for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89. Found C, 51.0; H, 6.18; N, 19.87.

From **20**: To a solution of **20** (0.12 g, 0.36 mmol) in pyridine (5 mL) was added a heterogeneous solution of $POCl_3$ (0.07 mL, 0.71 mmol) and 1,2,4-triazole (0.20 g, 2.85 mmol) in pyridine (5 mL). The resulting solution was stirred for 1 hr and then cooled to 0 °C. NH_4OH (conc., 1.5 mL) was then added and the reaction was allowed to warm to room temperature and was stirred for 12 h. The volatiles were then removed and the brown residue was purified by flash and preparative layer chromatography (10% MeOH/$CHCl_3$) to afford 0.09 g (0.27 mmol, 75%) of **24**. A solution of **24** (0.09 g, 0.27 mmol) in CH_3CN was treated with Et_4NF (0.12 g, 0.81 mmol) to afford, after purification by preparative layer chromatography (15% MeOH/$CHCl_3$) and with reverse-phase HPLC (10% EtOH/H_2O), 0.05 g (0.22 mmol, 81%) of **26**.

From **21**: In an identical manner, **21** (0.21 g, 0.65 mmol) was treated with $POCl_3$ (0.12 mL, 1.30 mmol), triazole (0.36 g, 5.22 mmol), and NH_4OH (conc., 5 mL) to afford 0.17 g (0.51 mmol, 79%) of **25**. Desilylation with Et_4NF (0.15 g, 1.03 mmol) afforded, after final purification by reverse-phase HPLC, 0.09 g (0.42 mmol, 83%) of **27**.

5(R)-[5-Methyl-2,4(1H,3H)-pyrimidinedione]tetrahydro-3(S)-furanmethanol (30) and 5(S)-[5-Methyl-2,4(1H,3H)-pyrimidinedione]tetrahydro-3(S)-furanmethanol (31). Under the standard glycosylation conditions, **11** (0.51 g, 1.84 mmol) in CH_3CN (6 mL) followed by TMSOTf (0.39 mL, 2.03 mmol) were added at 0 °C to a solution of silylated thymine (0.23 g, 1.84 mmol), prepared with BSA (1.18 mL, 4.79 mmol) in CH_3CN (3 mL). The resulting solution was allowed to warm to room temperature and stir for 4 h. Workup and purification by flash chromatography (5% MeOH/$CHCl_3$) yielded 0.49 g (1.45 mmol, 79%) of an anomeric mixture (1/2) of the 5'(R)-anomer **28**: U.V. (MeOH) λ_{max} = 267 nm; ^1H NMR ($CDCl_3$) δ -0.08 (s, 6H), 0.76 (s, 9H), 1.65 (m, 1H), 1.79 (s, 3H), 2.43 (m, 2H), 3.53 (m, 2H), 3.81 (t, 1H, J = 8.0 Hz), 3.92 (t, 1H, J = 8.1 Hz), 5.97 (t, 1H, J = 6.4 Hz), 7.10 (s, 1H), 10.25 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.8, 12.2, 17.8, 25.5, 34.2, 40.5, 62.4, 70.6, 86.3, 110.4, 134.6, 150.3, 164.1; and the 5'(S)-anomer **29**: U.V. (MeOH) λ_{max} = 267 nm; ^1H NMR ($CDCl_3$) δ -0.08 (s, 6H), 0.76 (s, 9H), 1.79 (s, 3H), 1.95 (m, 1H), 2.10 (m, 1H), 2.43 (m, 1H), 3.47 (m, 2H), 3.69 (t, 1H, J = 7.7 Hz), 4.13 (t, 1H, J = 7.9 Hz), 5.92 (dd, 1H, J = 4.3 and 6.2 Hz), 7.06 (s, 1H), 10.25 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.8, 12.2, 17.8, 25.5, 34.9, 39.8, 63.1, 71.8, 86.7, 110.0, 134.9, 150.5, 164.2. Et_4NF (0.50 g, 3.38 mmol) was added to a solution of **28** and **29** (0.58 g, 1.69 mmol) in CH_3CN (50 mL). The solution was allowed to stir for 1 h, concentrated, and purified by flash chromatography (10% MeOH/$CHCl_3$) to afford 0.34 g (1.50 mmol, 89%) of the anomeric mixture. Preparative TLC utilizing multiple elutions (ether 78%, chloroform 18%, MeOH 2%, ethanol 2%), dissection of the resulting band, and reelution of appropriately combined fractions provided, after final purification by reverse phase HPLC (20% EtOH/H_2O), pure 5'(R)-anomer (faster migrating component on normal phase silica) **30**: M.P. (lyophilized powder) 134-135 °C; U.V. (MeOH) λ_{max} = 267 nm (ε = 9400); $[\alpha]_D$ = +17.2° (c = 0.52, MeOH); ^1H NMR ($CDCl_3$) δ 1.90 (m, 1H), 2.0 (s, 3H), 2.68 (m, 2H), 3.78 (m, 2H), 4.04 (t, 1H, J = 7.6 Hz), 4.18 (t, 1H, J = 7.7 Hz), 6.08 (t, 1H, J = 6.3 Hz), 7.35 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 34.7, 40.7, 63.1, 71.2, 87.1, 110.7, 135.4, 150.5, 164.0. Anal. Calcd. for $C_{10}H_{14}N_2O_4$: C, 53.09; H, 6.24; N, 12.38.

Found C, 52.94; H, 6.27; N, 12.34.

Data for the 5'(S)-anomer **31**: M.P. (lyophilized powder) 131-133 °C; U.V. (MeOH) λ_{max} = 267 nm (ε = 9100); $[\alpha]_D$ = +2.84° (c = 0.56, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.98 (s, 3H), 2.19 (m, 1H), 2.35 (m, 1H), 2.68 (m, 1H), 3.73 (m, 2H), 3.91 (t, 1H, J = 7.3 Hz), 4.35 (t, 1H, J = 7.6 Hz), 6.10 (dd, J =4.3, 6.5 Hz, 1H), 7.33 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.6, 35.5, 40.1, 63.3, 72.2, 87.1, 110.6, 135.3, 150.6, 164.3.
Anal. Calcd. for $C_{10}H_{14}N_2O_4$: C, 53.09; H, 6.24; N, 12.38. Found C, 52.88; H, 6.26; N, 12.35.

Tetrahydro-5(R and S)-acetyloxy-3(S)-[(acetyloxy)methyl]furan (33). To a solution of the S-(-)-monoacetate of 2-ally-1,3-propanediol (**7**, 2.49 g, 15.74 mmol) in Et_2O (100 mL) and water (30 mL) was added $NaIO_4$ (10.10 g, 47.21 mmol). The mixture was cooled to 0 °C and OsO_4 (0.10 g, 0.39 mmol) in THF (4 mL) was then added dropwise. The reaction was warmed to room temperature and then allowed to stir for 12 h. The reaction mixture was filtered and saturated $NaHSO_3$ was then slowly added. The resulting solution was stirred for 10 min and Na_2SO_4 was then added and the dried organics were filtered. The remaining solids were washed with EtOAc and the combined organics were concentrated and purified by flash chromatography (hexanes to 50% EtOAc/hexanes) to give 2.07 g (12.9 mmol, 82%) of tetrahydro-5(R and S)-hydroxy-3(S)-[(acetyloxy)methyl]furan (**32**): $[\alpha]_D$ = -31.1° (c = 0.39, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.63 (m, 1H), 1.94 (s, 3H), 2.07 (m, 1H), 2.67 (m, 1H), 3.52 - 4.10 (m, 4H), 4.32 (t, 1H, J = 8.2 Hz), 5.43 (d, 1H, J = 2.2 Hz); ^{13}C NMR ($CDCl_3$) δ 20.6, 36.2, 36.9, 65.6, 66.1, 68.9, 69.3, 98.0, 98.2, 170.9.

Molecular sieves (0.30 g) were added to a solution of tetrahydro-5(R and S)-hydroxy-3(S)-[(acetyloxy)methyl]furan (**32**) (2.07 g, 12.97 mmol) in CH_3CN (20 mL). DMAP (0.16 g, 1.30 mmol), Et_3N (2.71 mL, 19.45 mmol), and Ac_2O (1.47 mL, 15.56 mmol) were then added and the reaction mixture was stirred under nitrogen with exclusion of moisture for 1.5 h. The solution was cooled to 0 °C and quenched with MeOH (10 mL). The volatiles were then removed under reduced pressure (bath temperature <40 °C) and the remaining oil was purified by flash chromatography (hexanes to 30% EtOAc/hexanes) to afford 2.03 g (10.1 mmol, 78%) of the product as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.80 (m, 1H), 1.91 (s, 3H), 1.92 (s, 3H), 2.20 (m, 1H), 2.60 (m, 1H), 3.50 - 4.04 (m, 4H), 6.15 (d, 1H, J = 4.6 Hz); ^{13}C NMR ($CDCl_3$) δ 20.3, 20.7, 34.5, 34.9, 35.6, 36.0, 64.8, 65.3, 70.3, 70.8, 98.1, 169.7, 170.2. Anal. Calcd. for $C_9H_{14}O_5$: C, 53.46; H, 6.98. Found: C, 53.31; H, 6.99.

5(S)-(6-Amino-9H-purin-9-yl)tetrahydro-3(R)-furanmethanol (38). Under the standard glycosylation conditions, N^6-benzoyladenine (0.68 g, 2.83 mmol) was treated with BSA (0.82 mL, 3.33 mmol), **33** (0.52 g, 2.57 mmol), and TMSOTf (0.55 mL, 2.82 mmol). After workup and purification by flash chromatography (5% MeOH/$CHCl_3$) an anomeric mixture [5(S):5(R) = 2:3] of the acetylated products (0.54 g, 1.41 mmol, 55%) were isolated. The mixture (0.46 g, 1.20 mmol) was dissolved in DMF (3 mL) and sodium amide (0.07 g, 1.79 mmol) was added. The resulting solution was allowed to stir for 8 h and additional sodium amide (0.04 g, 1.02 mmol) was added. After stirring 6 h the solution was neutralized with 0.1 N HCl, concentrated to dryness under reduced pressure, and purified by flash chromatography ($CHCl_3$ to 8% MeOH/$CHCl_3$) to afford 0.39 g (1.14 mmol, 95%) of the de-acetylated anomers. Silylation of the anomeric mixture with imidazole (0.15 g, 2.15 mmol) and *tert*-butyldimethylsilyl chloride (0.23 g, 1.53 mmol) in CH_2Cl_2 (5 mL) gave the separable anomers, 5(S)-[(6-benzoylamino)-9H-purin-9-yl]tetrahydro-3(S)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan (**36**) (0.18 g, 0.39 mmol, 34%): U.V. (MeOH) λ_{max} = 279 nm; $[\alpha]_D$ = +14.5° (c = 1.0, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 6H), 0.85 (s, 9H), 2.40 (m, 1H), 2.66 (m, 2H), 3.68 (m, 2H), 4.03 (t, 1H, J = 8.1 Hz), 4.13 (t, 1H, 7.9 Hz), 6.32 (t, 1H, J = 6.2 Hz), 7.46 (t, 2H, J = 7.4 Hz), 7.54 (t, 1H, J = 7.3 Hz), 8.00 (d, 2H, J = 7.2 Hz), 8.20 (s, 1H), 8.75 (s, 1H), 9.29 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.5, 18.3, 25.8, 34.6, 41.6, 62.8, 71.3, 85.9, 123.7, 127.9, 128.8, 132.7, 133.7, 141.0, 149.5, 151.5, 152.5, 164.7; and 5(R)-[(6-benzoylamino)-9H-purin-9-yl]tetrahydro-3(S)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl] furan (**37**) (0.30 g, 0.66 mmol, 58%): U.V. (MeOH) λ_{max} = 279 nm; $[\alpha]_D$ = -19.7° (c = 1.0, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.02 (s, 6H), 0.86 (s, 9H), 2.34 (m, 1H), 2.58 (m, 1H), 2.72 (m, 1H), 3.62 (m, 2H), 3.88 (dd, 1H, J = 6.4 and 8.4 Hz), 4.26 (t, 1H, J = 7.9 Hz), 6.29 (dd, 1H, J = 2.6 and 6.7 Hz), 7.40 (t, 1H, J = 7.5 Hz), 7.50 (t, 1H, J = 7.3 Hz), 7.96 (d, 2H, J = 7.5 Hz), 8.05 (s, 1H), 8.69 (s, 1H), 9.79 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.5, 18.2, 25.8, 34.8, 40.3, 63.4, 71.8, 86.3, 123.7, 127.9, 128.6, 132.5, 133.7, 141.1, 149.5, 151.3, 152.1, 164.9.

Under identical conditions as previously described, **36** (0.12 g, 0.26 mmol) was debenzoylated (NH_3/MeOH) and then treated with Et_4NF (0.08 g, 0.52 mmol) to afford, after purification by preparative TLC and reverse-phase HPLC 0.06 g (0.24 mmol, 91%) of the desired **38**: M.P. (lyophilized powder) 180-183 °C; U.V. (H_2O) λ_{max} = 259 nm (ε = 14,250); $[\alpha]_D$ = +22.3° (c = 0.18, MeOH); ^{1}H NMR (DMSO-d_6) δ 2.27 (m, 1H), 2.54 (m, 2H), 3.52 (m, 2H), 3.84 (t, 1H, J = 8.0 Hz), 3.95 (t, 1H, J = 7.6 Hz), 4.78 (br s, 1H), 6.18 (t, 1H

J = 6.4 Hz), 7.21 (br s, 2H), 8.10 (s, 1H), 8.28 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 33.7, 41.6, 61.6, 70.7, 84.2, 119.1, 139.0, 149.1, 152.5, 156. Anal. Calcd. for $C_{10}H_{13}N_5O_2$: C, 51.06; H, 5.57; N, 29.77. Found C, 50.94; H, 5.54; N, 29.70.

5(R)-(6-Amino-9H-purin-9-yl)tetrahydro-3(R)-furanmethanol (39). Under identical conditions previously described, 0.20 g (0.45 mmol) of **37** was converted to 0.10 g (0.43 mmol, 96%) of **39**: M.P. (lyophilized powder) 139-140 °C; U.V. (H_2O) λ_{max} = 259 nm (ε = 13,800); $[\alpha]_D$ = -38.6° (c = 0.35, MeOH); ^{1}H NMR (DMSO-d_6) δ 2.21 (m, 1H), 2.54 (m, 1H), 2.76 (m, 1H), 3.44 (m, 2H), 3.75 (dd, 1H, J = 5.4 and 8.2 Hz), 4.17 (t, 1H, J = 7.7 Hz), 4.81 (br s, 1H), 6.26 (dd, 1H, J = 3.4 and 7.0 Hz), 7.24 (br s, 2H), 8.14 (s, 1H), 8.25 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 33.9, 40.4, 62.2, 70.8, 84.3, 119.2, 139.2, 148.9, 152.5, 156. Anal. Calcd. for $C_{10}H_{13}N_5O_2$: C, 51.06; H, 5.57; N, 29.77. Found C, 50.98; H, 5.59; N, 29.73.

5(S)-(2-Amino-1,9-dihydro-6H-purin-6-one)tetrahydro-3(R)-furanmethanol (42). Under the standard glycosylation conditions, N^2-acetyl-O^6-diphenylcarbamoylguanine (0.79 g, 2.04 mmol) was treated with BSA (0.92 mL, 3.73 mmol), **33** (0.34 g, 1.87 mmol), and TMSOTf (0.36 mL, 1.87 mmol) to afford, after workup and purification by preparative TLC (Et_2O 78%, $CHCl_3$ 19%, MeOH 1%, EtOH 2%) 0.08 g (0.15 mmol, 9%) of 5(S)-[2-(acetylamino)-6-(diphenylcarbamoyloxy)-9H-purin-6-yl]tetrahydro-3(S)-[(acetyloxy) methyl]furan (**40**): U.V. (MeOH) λ_{max} = 276 nm; ^{1}H NMR ($CDCl_3$) δ 2.00 (s, 3H), 2.35 (m, 1H), 2.43 (s, 3H), 2.61 (m, 1H), 2.74 (m, 1H), 4.11 (m, 4H), 6.11 (t, 1H, J = 6.4 Hz), 7.25 (m, 10H), 8.05 (s, 1H), 8.64 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.7, 24.9, 34.4, 38.5, 64.3, 71.3, 85.9, 121.4, 125.9, 126.9, 127.6, 127.8, 129.0, 141.6, 142.4, 150.3, 151.8, 154.2, 155.9, 170.1, 170.7; and 0.11 g (0.21 mmol, 13%) of the faster migrating 5(R)-[2-(acetylamino)-6-(diphenylcarbamoyloxy)-9H-purin-6-yl]tetrahydro-3(S)-[(acetyloxy)methyl]furan (**41**): U.V. (MeOH) λ_{max} = 276 nm; ^{1}H NMR ($CDCl_3$) δ 2.07 (s, 3H), 2.30 (m, 1H), 2.46 (s, 3H), 2.77 (m, 1H), 2.98 (m, 1H), 3.86 (dd, 1H, J = 5.8 and 8.8 Hz), 4.07 (dd, 1H, 7.2 and 11.0 Hz), 4.15 (dd, 1H, J = 6.3 and 11.0 Hz), 4.34 (dd, 1H, J = 7.5 and 8.5 Hz), 6.21 (dd, 1H, J = 2.8 and 6.9 Hz), 7.25 (m, 10H), 8.00 (s, 1H), 8.66 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 20.6, 24.8, 34.5, 37.2, 64.6, 71.7, 86.0, 121.3, 126.2, 126.7, 127.2, 127.4, 129.0, 141.5, 142.4, 150.2, 151.8, 154.0, 155.9, 170.1, 170.7.

In a manner identical to that previously described, **40** (0.10 g, 0.19 mmol) was deblocked with ethanolic ammonia to afford, after purification, 0.04 g (0.16 mmol, 86%) of **42**: M.P. (lyophilized powder) >250 °C (decomp); U.V. (H_2O) λ_{max} = 252 nm (ε = 13,160) 274 sh (ε = 8990); $[\alpha]_D$ = +23.7° (c = 0.25, 10% H_2O/MeOH); ^{1}H NMR (DMSO-d_6) δ 2.15 (m, 2H), 2.47 (m, 2H), 3.53 (m, 2H), 3.81 (t , 1H, J = 8.0 Hz), 3.93 (t, 1H, J = 7.7 Hz), 4.81 (br s, 1H), 5.98 (t, 1H, J = 6.5 Hz), 6.46 (br s, 2H), 7.89 (s, 1H), 10.64 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 33.7, 41.5, 61.6, 70.4, 83.5, 116.8, 135.1, 150.9, 153.5, 156.8. Anal. Calcd. for $C_{10}H_{13}N_5O_3.H_2O$: C, 44.61; H, 5.61; N, 26.01. Found C, 44.44; H, 5.63; N, 25.99.

5(R)-(2-Amino-1,9-dihydro-6H-purin-6-one)tetrahydro-3(R)-furanmethanol (43). In an identical manner, **41** (0.11 g, 0.21 mmol) was converted to 0.05 g (0.19 mmol, 94%) of **43**: M.P. (lyophilized powder) >250 °C (decomp.); U.V. (H_2O) λ_{max} = 252 nm (ε = 13,060) 274 sh (ε = 8880); $[\alpha]_D$ = -18.3° (c = 0.41, 10% H_2O/MeOH); ^{1}H NMR (DMSO-d_6) δ 2.14 (m, 1H), 2.38 (ddd, 1H, J = 3.7, 8.0, and 13.4 Hz), 2.67 (m, 1H), 3.41 (m, 2H), 3.70 (dd, 1H, J = 5.4 and 8.4 Hz), 4.12 (dd, 1H, J = 7.4 and 8.1 Hz), 4.82 (br s, 1H), 6.03 (dd, 1H, J = 3.8 and 7.0 Hz), 6.55 (br s, 2H), 7.80 (s, 1H), 10.67 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.1, 40.2, 62.1, 70.5, 83.6, 116.8, 135.0, 150.7, 153.9, 157.3. Anal. Calcd. for $C_{10}H_{13}N_5O_3.H_2O$: C, 44.61; H, 5.61; N, 26.01. Found C, 44.56; H, 5.59; N, 25.93.

5(S)-[2,4(1H,3H)-Pyrimidinedione]tetrahydro-3(R)-furanmethanol (46). Under the standard glycosylation conditions, uracil (0.58 g, 5.18 mmol) was reacted with BSA (2.77 mL, 11.22 mmol), **33** (0.87 g, 4.31 mmol), and TMSOTf (0.92 mL, 4.75 mmol) to afford, after flash chromatography (5% MeOH/$CHCl_3$), 0.80 g (3.15 mmol, 73%) of the inefficiently separable anomeric mixture [5'(S):5'(R) = 1:2] of the acetylated **44** and **45**. Treatment with sodium methoxide (0.26 g, 4.75 mmol) in MeOH (50 mL) afforded 0.66 g (3.08 mmol, 98%) of the anomeric **46** and **47** which were silylated with *tert*-butyldimethylsilyl chloride (0.56 g, 3.73 mmol) and imidazole (0.32 g, 4.66 mmol) in DMF (10 mL) to afford the separable 5(S)-[2,4(1H,3H)-pyrimidinedione] tetrahydro-3(S)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan (**48**) (0.26 g, 0.80 mmol, 26%): U.V. (MeOH) λ_{max} = 262 nm; ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 6H), 0.80 (s, 9H), 1.65 (m, 1H), 2.50 (m, 2H), 3.59 (m, 2H), 3.80 (t, 1H, J = 7.9 Hz), 3.95 (t, 1H, J = 7.9 Hz), 5.70 (d, 1H, J = 8.1 Hz), 5.98 (t, 1H, J = 6.2 Hz), 7.38 (d, 1H, J = 8.1 Hz), 9.10 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.0, 25.7, 34.7, 40.7, 62.7, 71.0, 86.8, 102.1, 139.1, 150.7, 163.9; and 5(R)-[2,4(1H,3H)-pyrimidinedione]tetrahydro-3(S)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]furan (**49**) (0.53 g, 1.63 mmol, 53%): U.V. (MeOH) λ_{max} = 262 nm; ^{1}H NMR ($CDCl_3$) δ -0.01 (s, 6H), 0.83 (s, 9H), 2.05 (m, 1H), 2.18 (m, 1H), 2.46 (m, 1H), 3.57 (m, 2H), 3.78 (t, 1H, J = 7.8 Hz), 4.18 (t, 1H J = 7.8 Hz), 5.68 (d, 1 H, J = 7.9 Hz), 5.96 (m, 1H), 7.37 (d, 1H, J = 8.0 Hz), 9.09 (br s, 1H); ^{13}C

NMR ($CDCl_3$) δ -5.6, 18.1, 25.7, 35.4, 39.8, 63.1, 72.2, 87.5, 101.7, 139.2, 150.5, 163.9.

Compound **48** (0.06 g, 0.19 mmol) was treated with Et_4NF (0.06 g, 0.38 mmol) in CH_3CN (10 mL) and upon purification yielded 0.03 g (0.16 mmol, 83%) of **46** as a low melting lyophilized solid: U.V. (H_2O) λ_{max} = 262 nm (ε = 9400); $[\alpha]_D$ = -32.9° (c = 0.30, MeOH); ^1H NMR (DMSO-d_6) δ 1.72 (m, 1H), 2.36 (m, 1H), 2.48 (m, 1H), 3.44 (m, 2H), 3.82 (t, 1H, J = 8.0 Hz), 3.94 (t, 1H, J = 7.9 Hz), 4.77 (br s, 1H), 5.62 (d, 1H, J = 8.0 Hz), 5.94 (t, 1H, J = 6.5 Hz), 7.66 (d, 1H, J = 8.0 Hz), 11.20 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.0, 40.9, 61.7, 71.0, 85.9, 101.6, 140.5, 150.5, 163.3. Anal. Calcd. for $C_9H_{12}N_2O_4 \cdot 1/2\ H_2O$: C, 48.87; H, 5.92; N, 12.66. Found C, 48.72; H, 5.94; N, 12.64.

5(R)-[2,4(1H,3H)-Pyrimidinedione]tetrahydro-3(R)-furanmethanol (47). Under identical conditions, **49** (0.13 g, 0.41 mmol) was treated with Et_4NF (0.12 g, 0.82 mmol) to afford, after purification, 0.08 g (0.39 mmol, 95%) of **47**: M.P. (lyophilized powder) 97-99 °C: U.V. (H_2O) λ_{max} = 262 nm (ε = 10,190); $[\alpha]_D$ = +20.2° (c = 0.30, MeOH); ^1H NMR (DMSO-d_6) δ 2.06 (m, 2H), 2.48 (m, 1H), 3.39 (m, 2H), 3.65 (t, 1H, J = 7.3 Hz), 4.20 (t, 1H, J = 7.8 Hz), 4.80 (br s, 1H), 5.58 (d, 1H, J = 8.0 Hz), 5.94 (t, 1H, J = 4.9 Hz), 7.60 (d, 1H, J = 8.2 Hz), 11.2 (br s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.4, 39.9, 61.8, 71.6, 86.2, 101.7, 140.6, 150.4, 163.4. Anal. Calcd. for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.20. Found C, 50.84; H, 5.72; N, 13.15.

5(S)-[4-Amino-2(1H)-pyrimidinone]tetrahydro-3(R)-furanmethanol (52). Under similar conditions as described for **26**, 0.21 g (0.65 mmol) of the protected uridine **48** was treated with a solution of triazole (0.36 g, 5.16 mmol) and $POCl_3$ (0.12 mL, 1.29 mmol) in pyridine (15 mL). After treatment with NH_4OH (conc., 3 mL) and purification utilizing flash and preparative layer chromatography 0.14 g (0.44 mmol, 69%) of the protected cytidine analog **50** was isolated: U.V. (MeOH) λ_{max} = 272 nm; ^1H NMR ($CDCl_3$) δ 0.0 (s, 6H), 0.83 (s, 9H), 1.63 (m, 1H), 2.61 (m, 1H), 3.48 (dd, 1H, J = 6.0 and 9.8 Hz), 3.57 (dd, 1H, J = 4.5 and 10.2 Hz), 3.90 (t, 1H, J = 7.8 Hz), 4.08 (t, 1H, J = 7.9 Hz), 5.76 (d, 1H, J = 7.4 Hz), 6.02 (t, 1H, J = 6.0 Hz), 7.58 (d, 1H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ -5.5, 18.2, 25.8, 35.7, 41.0, 63.2, 71.5, 88.1, 94.4, 140.5, 156.4, 166.0. Treatment with Et_4NF (0.19 g, 1.26 mmol) followed by purification afforded 0.09 g (0.42 mmol, 94%) of the desired **52** as a low melting lyophilized solid: U.V. (H_2O) λ_{max} = 272 nm (ε = 9290); $[\alpha]_D$ = -59.9° (c = 0.40, MeOH); ^1H NMR (DMSO-d_6) δ 1.58 (m, 1H), 2.36 (m, 1H), 2.47 (m, 1H), 3.40 (m, 2H), 3.82 (t, 1H, J = 7.8 Hz), 3.94 (t, 1H, J = 7.8 Hz), 4.73 (br s, 1H), 5.73 (d, 1H, J = 7.4 Hz), 5.92 (t, 1H, J = 6.4 Hz), 7.12 (br s, 2H), 7.58 (d, 1H, J = 7.4 Hz); ^{13}C NMR (DMSO-d_6) δ 34.9, 40.9, 61.9, 70.8, 86.4, 93.8, 140.6, 155.1, 165.6. Anal Calcd. for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89. Found C, 51.16; H, 6.23; N, 19.85.

5(R)-[4-Amino-2(1H)-pyrimidinone]tetrahydro-3(R)-furanmethanol (53). Identically, **49** (0.23 g, 0.70 mmol) in pyridine (5 mL) was treated with $POCl_3$ (0.13 mL, 1.4 mmol) and triazole (0.39 g, 5.59 mmol) in pyridine (15 mL) followed by NH_4OH (conc. 5 mL) to yield, after purification, 0.19 g (0.57 mmol, 81%) of **51**: U.V. (MeOH) λ_{max} = 272 nm; ^1H NMR ($CDCl_3$) δ -0.01 (s, 6H), 0.83 (s, 9H), 2.05 (ddd, 1H, J = 2.4, 7.8, and 13.7 Hz), 2.19 (m, 1H), 2.40 (m, 1H), 3.50 (dd, 1H, J = 7.1 and 10.0 Hz), 3.61 (dd, 1H, J = 5.2 and 10.0 Hz), 3.79 (t, 1H, J = 8.0 Hz), 4.18 (t, 1H, J = 7.9 Hz), 5.78 (d, 1H, J = 7.4 Hz), 5.98 (dd, 1H, J = 2.6 and 6.0 Hz), 7.38 (d, 1H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ -5.5, 18.2, 25.8, 35.8, 39.7, 63.3, 72.4, 88.2, 94.3, 140.0, 156.3, 166.0. Desilylation with Et_4NF (0.17 g, 1.14 mmol) in CH_3CN (10 mL) gave after purification 0.11 g (0.54 mmol, 95%) of **53**: M.P. (lyophilized powder) 194-196 °C; U.V. (H_2O) λ_{max} = 272 nm (ε = 9980); $[\alpha]_D$ = +39.64° (c = 0.47, MeOH); ^1H NMR (DMSO-d_6) δ 1.91 (m, 1H), 2.04 (m, 1H), 2.39 (m, 1H), 3.40 (m, 2H), 3.64 (t, 1H, J = 7.6 Hz), 4.19 (t, 1H, J = 7.7 Hz), 4.75 (t, 1H, J = 4.4 Hz), 5.70 (d, 1H, J = 7.4 Hz), 5.91 (dd, 1H, J = 3.6 and 6.3 Hz), 7.08 (d, 2H, J = 11.2 Hz), 7.54 (d, 1H, J = 7.4 Hz); ^{13}C NMR (DMSO-d_6) δ 35.2, 40.7, 61.8, 71.5, 86.6, 93.5, 140.7, 155.1, 165.7. Anal Calcd. for $C_9H_{13}N_3O_3$: C, 51.18; H, 6.20; N, 19.89. Found C, 51.15; H, 6.22; N, 19.83.

5(S)-[5-Methyl-2,4(1H,3H)-pyrimidinedione]tetrahydro-3(R)-furanmethanol (56) and 5(R)-[5-Methyl-2,4(1H,3H)-pyrimidinedione]tetrahydro-3(R)-furanmethanol (57). Under the standard glycosylation conditions, thymine (0.49 g, 3.87 mmol) was treated with BSA (2.10 mL, 8.51 mmol), **33** (0.78 g, 3.87 mmol), and TMSOTf (0.82 mL, 4.25 mmol) to afford after purification by flash chromatography 0.88 g (3.29 mmol, 85%) of an inefficiently separable mixture of the anomeric [5'(S):5'(R) = 1:2] nucleosides **54** and **55**. Deprotection with methanolic sodium methoxide (0.29 g, 5.31 mmol) afforded 0.68 g (2.99 mmol, 91%) of the anomeric mixture. Preparative TLC (Et_2O 78%, $CHCl_3$ 18%, MeOH 2%, and EtOH 2%) utilizing multiple elutions, dissection of the resulting band, and re-elution of the appropriately combined fractions provided pure 5'(S)-anomer **56**: M.P. (lyophilized powder) 135-136 °C; U.V. (H_2O) λ_{max} = 266 nm (ε = 8940); $[\alpha]_D$ = -17.5° (c = 0.56, MeOH); ^1H NMR ($CDCl_3$) δ 1.81 (m, 1H), 1.92 (s, 3H), 2.60 (m, 2H), 3.67 (dd, 1H, J = 6.2 and 10.4 Hz), 3.74 (dd, 1H, J = 5.0 and 10.4 Hz), 3.96 (t, 1H, J = 7.9 Hz), 4.10 (t, 1H, J = 8.1 Hz), 6.00 (t, 1H, J = 6.5 Hz), 7.26 (s, 1H), 8.20 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.5, 34.7, 40.7, 63.0, 71.2,

86.9, 110.7, 135.4, 150.5, 164.1. Anal. Calcd. for $C_{10}H_{14}N_2O_4$: C, 53.09; H, 6.24; N, 12.38. Found C, 52.99; H, 6.26; N, 12.33. And pure 5'(R)-anomer **57**: M.P. (lyophilized powder) 132-134 °C; U.V. (H_2O) λ_{max} = 267 nm (ε = 9470); $[\alpha]_D$ = -2.24° (c = 0.45, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.90 (s, 3H), 2.09 (ddd, 1H, J = 4.2, 7.9, and 13.8 Hz), 2.27 (m, 1H), 2.59 (m, 1H), 3.63 (dd, 1H, J = 6.8 and 10.6 Hz), 3.68 (dd, 1H, J = 6.5 and 10.6 Hz), 3.83 (dd, 1H, J = 6.5 and 8.8 Hz), 4.27 (dd, 1H, J = 7.1 and 8.8 Hz), 6.01 (dd, 1H, J = 4.2 and 6.4 Hz), 7.29 (s, 1H), 8.20 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 12.5, 35.4, 40.0, 63.0, 72.1, 87.0, 110.7, 135.2, 150.6, 164.4. Anal. Calcd. for $C_{10}H_{14}N_2O_4$: C, 53.09; H, 6.24; N, 12.38. Found C, 52.99; H, 6.23; N, 12.34.

(+)-α(R)-allyl-γ(S)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]-γ-butyrolactone (61). LDA (1.59 mL, 2.39 mmol) was added dropwise to a solution of the lactone **60**[32] (0.5 g, 2.17 mmol) in THF (2 mL) at -98 °C. The solution was allowed to stir for 40 min and then allyl iodide (0.3 mL, 3.26 mmol) was rapidly added. After stirring for an additional 30 min the reaction was quenched with a saturated ammonium chloride and then diluted with EtOAc. The organics were then washed until neutral, dried (Na_2SO_4), concentrated and purified by flash chromatography (hexanes to 3% EtOAc/hexanes) to afford 0.52 g (1.93 mmol, 89%) of **61**: $[\alpha]_D$ = +18.6° (c = 0.84, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 6H), 0.86 (s, 9H), 2.00 (dt, 1H, J = 8.8, 8.9 and 12.9 Hz), 2.24 (m, 2H), 2.55 (ddd, 1H, 4.5, 6.4 and 14.4 Hz), 2.80 (ddd, 1H, J = 4.4, 9.3 and 18.4 Hz), 3.63 (dd, 1H, J = 2.8 and 11.2 Hz), 3.80 (dd, 1H, J = 3.3 and 11.2 Hz), 4.49 (m, 1H), 5.09 (m. 2H), 5.73 (m, 1H); ^{13}C NMR ($CDCl_3$) δ -5.6, 18.2, 25.8, 29.3, 35.3, 39.1, 65.1, 77.2, 117.6, 134.6, 179.1. Anal. Calcd. for $C_{14}H_{26}O_3S$: C, 62.18; H, 9.69. Found: 62.04; H, 9.72.

Compound **62** [S,S (+) isomer] was the minor product [0.03 g, 0.11 mmol, 5%]: $[\alpha]_D$ = +53.5° (c = 0.99, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.05 (s, 6H), 0.86 (s, 9H), 1.88 (m, 1H), 2.25 (m, 2H), 2.66 (m, 2H), 3.67 (dd, 1H, J = 3.9 and 11.4 Hz), 3.83 (dd, 1H, J = 3.5 and 11.4 Hz), 4.42 (m, 1H), 5.08 (m, 2H), 5.74 (m, 1H); ^{13}C NMR ($CDCl_3$) δ -5.5, 18.1, 25.7, 28.8, 34.4, 39.9, 63.8, 78.4, 117.2, 134.5, 177.9. Anal. Calcd. for $C_{14}H_{26}O_3S$: C, 62.18; H, 9.69. Found: 62.07; H, 9.70.

Tetrahydro-5(R and S)-hydroxy-3(R)-allylfuran (64). A solution of **61** (0.21 g, 0.77 mmol) in Et_2O (5 mL) was added dropwise to $LiAlH_4$ (0.04 g, 1.16 mmol) in Et_2O (5 mL). The resulting mixture was stirred for 1 h and then wet ether, followed by water, was added. The mixture was then filtered through Celite, dried (Na_2SO_4) and concentrated. Desilylation with Et_4NF (0.16 g, 1.04 mmol) provided, after purification by flash chromatography ($CHCl_3$ to 10% MeOH/$CHCl_3$), 0.12 g (0.75 mmol, 98%) of 4(R)-hydroxymethyl-6-hepten-1,2(S)-diol (**63**): $[\alpha]_D$ = -18.9° (c = 0.82, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.43 (m, 2H), 1.79 (m, 1H), 2.04 (m, 2H), 3.50 (m, 4H), 3.79 (m, 1H), 4.43 (br s, 3H), 5.00 (m, 2H), 5.73 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 35.0, 36.1, 36.5, 65.1, 66.7, 69.5, 116.6, 136.5.

Sodium periodate (0.52 g, 2.43 mmol) was added to a solution of **63** (0.26 g, 1.62 mmol) in Et_2O (10 mL) and water (4 mL). The resulting heterogeneous solution was stirred for 1 h and then filtered through Celite, dried (Na_2SO_4), concentrated and purified by flash chromatography ($CHCl_3$ to 5% MeOH/$CHCl_3$) to afford 0.18 g (1.41 mmol, 87%) of **64**; $[\alpha]_D$ = +45.5° (c = 0.91, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.42 (m, 1H), 2.10 (m, 3H), 2.43 (m, 1H), 3.37 (t, H-2α, J = 7.5 Hz), 3.52 (t, H-2β, J = 7.9 Hz), 3.83 (t, H-2β, J = 8.0), 4.01 (t, H-2α, J = 7.8 Hz), 4.66 (br s, 1H), 5.00 (m, 2H), 5.40 (d, 1H, J = 4.9 Hz), 5.75 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 36.1, 36.4, 37.4, 37.8, 39.2, 71.4, 71.7, 98.3, 98.7, 115.6, 115.8, 136.3, 136.5. Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.66; H, 9.47.

Tetrahydro-5(R and S)-acetyloxy-3(R)-(2-benzoyloxyethyl)furan (68). Anhydrous methanolic HCl (0.47 mL, 0.47 mmol) was added to a solution of **64** (1.20 g, 9.39 mmol) in MeOH (5 mL). The mixture was stirred for 20 min and then neutralized with Dowex-OH^-. The mixture was filtered, concentrated and then briefly dried under vacuum to yield 1.09 g (7.7 mmol, 82%) of the volatile methyl furanoside: $[\alpha]_D$ = +17.4° (c = 0.38, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.5 - 2.43 (m, 5H), 3.26 (s, 3H), 3.45 (m, 1H), 3.91 (m, 1H), 4.93 (m, 3H), 5.67 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 36.2, 36.3, 37.5, 38.0, 38.4, 38.5, 54.4, 54.7, 71.4, 71.6, 105.1, 105.5, 115.6, 115.9, 136.4, 136.7. A freshly prepared solution of the methyl allylfuranoside (0.32 g, 2.25 mmol) in MeOH (20 mL) was cooled to -78 °C and ozonized (3 min), treated with dimethyl sulfide (3 mL) and allowed to stir for 3 h. The solution was then concentrated, redissolved in ethanol (10 mL) and treated with $NaBH_4$ (0.13 g, 3.37 mmol). The resulting solution was stirred for 1 h and then neutralized with 1 N HCl. The solution was evaporated to dryness, dissolved in $CHCl_3$ and filtered. The organics were concentrated and purified by flash chromatography ($CHCl_3$ to 5% MeOH/$CHCl_3$) to afford 0.30 g (2.07 mmol, 92%) of tetrahydro-5(R and S)-methoxy-3(R)-(2-hydroxyethyl)furan (**65**): $[\alpha]_D$ = +28° (c = 1.39, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.59 (m, 2H), 1.65 (m, 1H), 2.01 (m, 1H), 2.26 (m, 1H), 3.27 (s, $OCH_3\beta$), 3.29 (s, $OCH_3\alpha$), 3.48 (m, 1H), 3.59 (m, 2H), 4.02 (m, 1H), 4.96 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 33.9, 35.1, 35.9, 36.5, 38.7, 39.0, 54.5, 54.8, 61.5, 71.7, 72.4, 105.0, 105.5.

Benzoyl chloride (0.16 mL, 1.35 mmol) was added dropwise, at 0 °C, to a solution of **65** (0.16 g, 1.12 mmol) and Et_3N (0.31 mL, 2.24 mmol) in CH_2Cl_2 (3 mL). The resulting solution was stirred for 1 h at room temperature and then diluted with EtOAc and the organics were washed until neutral. Purification by flash chromatography afforded 0.24 g (0.96 mmol, 86%) of tetrahydro-5(R and S)-methoxy-3(R)-(2-benzoyloxyethyl)furan (**66**): $[\alpha]_D$ = +24.4° (c = 0.98, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.64 (m, 1H), 1.85 (m, 2H), 2.10 (m, 1H), 2.45 (m, 1H), 3.30 (s, $OCH_3\alpha$), 3.32 (s, $OCH_3\beta$), 3.56 (m, 1H), 4.10 (t, 1H, J = 8.0 Hz), 4.30 (m, 2H), 4.99 (m, 1H), 7.4 (t, 2H, J = 7.5 Hz), 7.52 (t, 1H, J = 7.9 Hz), 8.0 (d, 2H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 32.0, 32.6, 34.2, 35.6, 38.7, 39.0, 54.3, 54.7, 63.9, 71.4, 72.2, 104.9, 105.3, 128.2, 129.4, 130.0, 132.8, 166.3. A solution of **66** (0.24 g, 0.96 mmol) in dioxane (10 mL) and aqueous HCl (2.4 mL, 0.24 mmol) was stirred at room temperature for 16 h. The solution was then neutralized, concentrated, extracted with EtOAc, and purified by flash chromatography (hexanes to 30 % EtOAc/hexanes) to afford 0.19 g (0.80 mmol, 83%) of tetrahydro-5(R and S)-hydroxy-3(R)-(2-benzoyloxyethyl)furan (**67**): $[\alpha]_D$ = +8.4° (c = 1.66, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.63 (m, 1H), 1.95 (m, 2H), 2.34 (m, 1H), 2.63 (m, 1H), 3.53 (t, 1H, J = 7.9 Hz), 4.22 (t, 1H, J = 7.9 Hz), 4.33 (m, 2H), 5.54 (m, 1H), 7.41 (t, 2H, J = 7.5 Hz), 7.53 (t, 1H, J = 7.3 Hz), 8.0 (d, 2H, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ 32.0, 32.3, 34.2, 36.1, 39.7, 39.9, 63.9, 64.0, 71.9, 72.7, 98.5, 98.9, 128.4, 129.5, 130.1, 133, 166.5.

Acetic anhydride (0.16 mL, 1.64 mmol) was added to a solution of **67** (0.32 g, 1.37 mmol), DMAP (0.04 g, 0.34 mmol) and Et_3N (0.29 mL, 2.0 mmol) in acetonitrile (2 mL). After stirring for 1 h MeOH (3 mL) was added and the solution was concentrated, extracted (EtOAc / H_2O) and purified by flash chromatography (hexanes to 20% EtOAc/hexanes) to afford 0.30 g (1.08 mmol, 79%) of **68**: $[\alpha]_D$ = +10.1° (c = 1.40, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.85 (m, 2H), 1.98 (s, $C(O)CH_3\alpha$), 2.0 (s, $C(O)CH_3\beta$), 2.19 (dd, 1H, J = 7.1 and 13.2 Hz), 2.42 (m, 1H), 2.61 (m, 1H), 3.59 (t, 1H, J = 8.1 Hz), 4.21 (t, 1H, J = 8.1 Hz), 4.32 (m, 2H), 6.25 (d, 1H, J = 4.7 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.53 (t, 1H, J = 7.4 Hz), 7.98 (d, 2H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 21.2, 32.0, 32.1, 34.1, 38.2, 38.7, 63.8, 73.5, 73.9, 98.8, 99.0, 128.4, 129.5, 130.0, 133.0, 166.4, 170.3. Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.98; H, 6.54.

5(R)-(6-Amino-9H-purin-9-yl)tetrahydro-3(R)-furanethanol (69) and 5(S)-(6-Amino-9H-purin-9-yl)tetrahydro-3(R)-furanethanol (70). Under the standard glycosylation conditions N^6-benzoyladenine (0.36 g, 1.50 mmol), persilylated with BSA (0.62 mL, 2.51 mmol) in CH_3CN (3 mL), was treated with the lactol **68** (0.35 g, 1.25 mmol), in CH_3CN (6 mL), and TMSOTf (0.27 mL, 1.38 mmol) to afford 0.20 g (0.44 mmol, 35%) of the inseparable mixture of the dibenzoylated products. A mixture of the anomers (0.06 g, 0.14 mmol) in MeOH (2 mL) and sodium methoxide (0.2 g, 0.35 mmol) was stirred for 12 h and then neutralized with 0.1 N HCl. The solution was evaporated to dryness and the trans-5'(S)-3'(R) **70** was isolated by fractional crystalization from MeOH (0.02 g, 0.08 mmol, 56%). The filtrate was purified by preparative layer chromatography (10% MeOH/$CHCl_3$) to afford 0.01 g (0.04 mmol, 32%) of the cis-5'(R)-3'(R) **69**: M.P. (lyophilized powder) 118-120 °C; U.V. (H_2O) λ_{max} = 259 nm (ε = 13,420); $[\alpha]_D$ = -55.6° (c = 0.45, MeOH); ^{1}H NMR (DMSO-d_6) δ 1.68 (m, 2H), 2.30 (m, 1H), 2.47 (m, 1H), 2.58 (m, 1H), 3.45 (m, 2H), 3.78 (t, 1H, J = 8.5 Hz), 4.03 (t, 1H, J = 6.9 Hz), 4.53 (br s, 1H), 6.20 (t, 1H, J = 6.3 Hz), 7.24 (br s, 2H), 8.15 (s, 1H), 8.32 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.2, 36.9, 37.0, 59.8, 73.1, 84.2, 119.3, 139.4, 149.1, 152.4, 156.0: Anal. Calcd. for $C_{11}H_{15}N_5O_2$: C, 53.00; H, 6.07; N, 28.1. Found C, 52.87; H, 6.09; N, 27.96.

Data for **70**: M.P. (H_2O) 248-249 °C; U.V. (H_2O) λ_{max} = 259 (ε = 13,700); $[\alpha]_D$ = +23° (C = 0.2, H_2O); ^{1}H NMR (DMSO-d_6) δ 1.59 (m, 2H), 2.11 (m, 1H), 2.55 (m, 1H), 2.65 (m, 1H), 3.44 (m, 2H), 3.56 (t, 1H, J = 7.7 Hz), 4.28 (t, 1H, J = 7.8 Hz), 4.52 (br s, 1H), 6.25 (dd, 1H, J = 2.4 and 7.1 Hz), 7.23 (br s, 2H), 8.13 (s, 1H), 8.20 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.6, 35.5, 37.7, 59.6, 73.8, 84.2, 119.1, 138.9, 148.9, 152.4, 155.8. Anal. Calcd. for $C_{11}H_{15}N_5O_2 \cdot 1/2H_2O$: C, 51.15; H, 6.24; N, 27.12. Found C, 51.28; H, 6.26; N, 27.01.

(+)-α(S)-allyl-γ(S)-[(((1,1-dimethylethyl)dimethylsilyl)oxy)methyl]-γ-butyrolactone (62). LDA (3.54 mL, 5.31 mmol) was added to a solution of predominantly the lactone **61** (1.43 g, 5.30 mmol) in THF (3.5 mL) at -78 °C. After stirring for 1 h the solution was quenched with a saturated ammonium chloride solution, extracted with EtOAc, and purified by column chromatography (hexanes to 3% EtOAc/hexanes) to afford 0.19 g (0.69 mmol, 13%) of the α(R)-allyl-**61** and 0.97 g (3.60 mmol, 68%) of the α(S)-allyl-**62**: for physical data see experimental for **61**.

Tetrahydro-5(R and S)-hydroxy-3(S)-allylfuran (71). Identical to the method described for the conversion of **61** to **64**, 1.39 g (5.06 mmol) of **62** was treated with $LiAlH_4$ (0.29 g, 7.59 mmol) in Et_2O (20 mL) followed by Et_4NF (1.51 g, 10.12 mmol) in CH_3CN (20 mL) to afford after purification 0.73 g (4.54 mmol, 90%) of the 4(S)-hydroxymethyl-6-heptene-1,2(S)-diol: $[\alpha]_D$ = -17.5° (c = 1.58, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.29 (m,

2H), 1.72 (m, 1H), 2.0 (m, 2H), 3.29 (dd, 1H, J = 7.5 and 14.6 Hz), 3.27 (dd, 1H, J = 7.8 and 12.1 Hz), 3.52 (dd, 1H, J = 3.2 and 11.2 Hz), 3.61 (dd, 1H, J = 3.9 and 11.0 Hz), 3.69 (m, 1H), 4.45 (br s, 3H), 4.98 (m, 2H), 5.72 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 36.3, 37.1, 39.1, 66.2, 67.3, 71.6, 116.4, 136.6. The above product (0.81 g, 5.05 mmol) in Et_2O (40 mL) and water (5 mL) was then treated with sodium periodate (1.62 g, 7.57 mmol) to afford after purification 0.54 g (4.19 mmol, 83%) of **71**: $[\alpha]_D$ = -43.7° (c = 1.01, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.57 (m, 1H), 2.14 (m, 3H), 2.42 (m, 1H), 3.46 (m, 1H), 3.95 (m, 1H), 4.99 (m, 2H), 5.35 (m, 1H), 5.72 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 36.3, 36.4, 37.4, 37.9, 38.7, 71.7, 71.9, 98.5, 98.8, 115.7, 116.0, 136.5, 136.6. Anal. Calcd. for $C_7H_{12}O_2$: C, 65.59; H, 9.44. Found: C, 65.85; H, 9.48.

Tetrahydro-5(R and S)-acetyloxy-3(S)-(2-benzoyloxyethyl)furan (74). Using the method described for **65**, compound **71** (0.72 g, 5.58 mmol) in MeOH (3 mL) was treated with anhydrous methanolic HCl (0.28 mL, 0.28 mmol). After neutralization with Dowex-OH$^-$ the filtrate was ozonized (-78 °C), treated with DMS (3 mL) and allowed to stir for 3 h. The volatiles were then removed under reduced pressure and the remaining oil was redissolved in EtOH (5 mL) cooled to 0 °C and treated with $NaBH_4$ (0.32 g, 8.37 mmol) to afford after purification 0.43 g (2.96 mmol, 53%) of tetrahydro-5(R and S)-methoxy-3(S)-(2-hydroxyethyl)furan (**72**): $[\alpha]_D$ = -27.8° (c = 1.50, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.57 (m, 2H), 1.64 (m, 1H), 2.00 (dd, 1H, J = 7.5 and 12.8 Hz), 2.25 (m, 1H), 3.26 (s, $OCH_3\beta$), 3.28 (s, $OCH_3\alpha$), 3.46 (m, 1H), 3.56 (m, 2H), 4.00 (m, 1H), 4.95 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 33.8, 35.2, 35.9, 36.5, 38.7, 39.0, 54.5, 54.8, 61.5, 71.7, 72.4, 105.0, 105.5.

Using the method described for the preparation of **66**, 0.43 g (2.96 mmol) of **72** was treated with Et_3N (0.83 mL, 5.92 mmol) and benzoyl chloride (0.52 mL, 4.44 mmol) in CH_2Cl_2 (3 mL) to afford after purification 0.56 g (2.25 mmol, 76%) of tetrahydro-5(R and S)-methoxy-3(S)-(2-benzoyloxyethyl)furan (**73**): $[\alpha]_D$ = -23.8° (c = 1.14, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.60 (m, 1H), 1.82 (m, 2H), 2.05 (m, 1H), 2.40 (m, 1H), 3.26 (s, $OCH_3\beta$), 3.29 (s, $OCH_3\alpha$), 3.52 (m, 1H), 4.08 (t, 1H, J = 8.0 Hz), 4.26 (m, 1H), 4.96 (m, 1H), 7.37 (t, 2H, J = 7.5 Hz), 7.49 (t, 1H, J = 7.4 Hz), 7.96 (d, 2H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 32.1, 32.7, 34.4, 35.7, 38.9, 39.2, 54.5, 54.9, 63.9, 64.0, 71.6, 72.3, 105.1, 105.5, 128.3, 129.5, 130.5, 132.9, 166.5.

As described for **68**, 0.39 g (1.57 mmol) of **73** was treated with 3.92 mL of 0.1 N HCL in dioxane (14 mL) to afford, after purification, 0.37 g (1.57 mmol) of the demethylated lactol: $[\alpha]_D$ = -8.0° (c = 1.41, MeOH), ^{1}H NMR ($CDCl_3$) δ 1.58 (m, 1H), 1.89 (m, 2H), 2.28 (m, 1H), 2.58 (m, 1H), 3.46 (m, 1H), 4.16 (m, 1H), 4.26 (m, 2H), 5.47 (m, 1H), 7.36 (t, 1H, J = 7.4 Hz), 7.48 (t, 1H, J = 7.3 Hz), 7.94 (d, 2H, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 31.7, 32.1, 34.1, 35.9, 39.5, 39.7, 63.5, 63.8, 71.5, 72.3, 98.2, 98.6, 128.2, 129.3, 129.9, 132.8, 166.3 Treatment with DMAP (0.05 g, 0.39 mmol), Et_3N (0.33 mL, 2.35 mmol), and Ac_2O (0.18 mL, 1.88 mmol) in CH_3CN (2 mL) afforded after purification 0.34 g (1.22 mmol, 78%) of **74**: $[\alpha]_D$ = -10.4° (c = 2.26, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.86 (m, 2H), 1.99 (s, 3H), 2.17 (m, 1H), 2.40 (m, 1H), 2.61 (m, 1H), 3.58 (m, 1H), 4.21 (m, 1H), 4.31 (m, 2H), 6.24 (d, 1H, J = 4.3 Hz), 7.40 (t, 2H, J = 7.5 Hz), 7.52 (t, 1H, J = 7.2 Hz), 7.99 (d, 2H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 21.2, 31.9, 32.0, 34.1, 38.1, 38.6, 63.7, 73.4, 73.9, 98.7, 98.9, 128.3, 129.4, 129.9, 132.9, 166.3, 170.3. Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.94; H, 6.53.

5(S)-(6-Amino-9H-purin-9-yl)tetrahydro-3(S)-furanethanol (75) and 5(R)-(6-Amino-9H-purin-9-yl)tetrahydro-3(S)-furanethanol (76). Identical to the method described for **69** and **70**, **74** (0.34 g, 1.22 mmol) followed by TMSOTf (0.26 mL, 1.34 mmol) were added to a solution of N^6-benzoyladenine (0.35 g, 1.46 mmol), persilylated with BSA (0.6 mL, 2.43 mmol) in CH_3CN (3 mL). After work-up and purification 0.20 g (0.43 mmol, 35%) of the dibenzoylated anomeric mixture was isolated. Sodium methoxide (0.07 g, 1.29 mmol) deprotection in MeOH (5 mL) afforded after purification 0.027 g (0.11 mmol, 25 %) of the cis-5'(R)-3'(R)-isomer, **75**: M.P. (lyophilized powder) 119-121 °C; U.V. (H_2O) λ_{max} = 260 nm (ε = 13,100); $[\alpha]_D$ = +54.3° (c = 0.56, MeOH); ^{1}H NMR (DMSO-d_6) δ 1.68 (m, 2H), 2.32 (m, 1H), 2.46 (m, 1H), 2.59 (m, 1H), 3.46 (m, 2H), 3.79 (t, 1H, J = 8.7 Hz), 4.03 (t, 1H, 7.14 Hz), 4.52 (br s, 1H), 6.20 (t, 1H, J = 6.54 Hz), 7.24 (br s, 2H), 8.14 (s, 1H), 8.32 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.2, 36.9, 37.0, 59.8, 73.1, 84.2, 119.3, 139.4, 149.1, 152.4, 156.0; Anal. Calcd. for $C_{11}H_{15}N_5O_2$: C, 53.00; H, 6.07; N, 28.1: Found : C, 52.90; H, 6.09; N, 27.99: and 0.07 g (0.28 mmol, 65%) of **76**: M.P. (H_2O) 247-249 °C; U.V. (H_2O) λ_{max} = 260 nm (ε = 13,500); $[\alpha]_D$ = -22.3° (c = 0.28, H_2O); ^{1}H NMR (DMSO-d_6) δ 1.59 (m, 2H), 2.11 (dt, 1H, J = 7.4, 8.2 and 13.2 Hz), 2.55 (m, 1H), 2.64 (m, 1H), 3.43 (m, 2H), 3.55 (t, 1H, J = 7.8 Hz), 4.28 (t, 1H, J = 7.6 Hz), 4.51 (br s, 1H), 6.25 (dd, 1H, J = 2.5 and 7.0 Hz), 7.22 (br s, 2H), 8.13 (s, 1H), 8.21 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 34.6, 35.4, 37.7, 59.6, 73.8, 84.2, 119.1, 138.8, 148.8, 152.4, 155.9. Anal. Calcd. for $C_{11}H_{15}N_5O_2 \cdot 1/2H_2O$: C, 51.15; H, 6.24; N, 27.12. Found C, 51.23; H, 6.26; N, 27.05.

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