Asymmetric Synthesis and Antiviral Activities of L-Carbocyclic 2′,3′-Didehydro-2′,3′-dideoxy and 2′,3′-Dideoxy Nucleosides

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Asymmetric syntheses of L-carbocyclic 2′,3′-didehydro-2′,3′-dideoxy- and 2′,3′-dideoxypyrimidine and purine nucleoside analogues were accomplished, and their anti-HIV and anti-HBV activities were evaluated. The key intermediate, (1*S*,4*R*)-1-benzoyloxy-4-(*tert*-butoxymethyl)cyclopent-2-ene (**7**), was prepared by benzoylation of the alcohol **2**, selective deprotection of the isopropylidene group of **3**, followed by thermal elimination via cyclic ortho ester or deoxygenation via cyclic thionocarbonate. The target compounds were also synthesized by thermal elimination via cyclic ortho esters from protected nucleosides. It was found that L-carbocyclic 2′,3′-didehydro-2′,3′-dideoxyadenosine (**34**) exhibited potent anti-HBV activity (EC_{50} = 0.9 μM) and moderate anti-HIV activity (EC_{50} = 2.4 μM) in vitro without cytotoxicity up to 100 μM.

Introduction

Since the discovery of the natural products (−)-aristeromycin and neplanocin A as biologically interesting carbocyclic nucleosides, a number of carbocyclic nucleosides have been synthesized and have shown interesting antitumor[1] and antiviral activity against herpes virus,[2] cytomegalovirus,[3] hepatitis B virus,[4] and human immunodeficiency virus (HIV).[5] These compounds possess greater metabolic stability to nucleoside phosphorylases, which cleave the glycosidic bond of normal nucleosides.[6] Among them, carbovir[7] and its 6-cyclopropylamino analogue 1592U89 (abacavir)[8] are the most interesting compounds as they both exhibit potent anti-HIV activity. Abacavir has been reported to reduce the viral load of greater than 99% with significant improvement in CD4 counts, and it has recently been approved by the FDA. More recently, a novel carbocyclic nucleoside, BMS-200475, has been reported to have potent anti-hepatitis B virus activity and is currently undergoing phase II clinical trials.[9]

Recently, a number of nucleosides with the unnatural L-configuration have emerged as potent antiviral agents against HIV and HBV, which include (−)-(2′*R*,5′*S*)-1-(2-hydroxymethyloxathiolan-5-yl)cytosine (3TC),[10,11] (−)-β-L-2′,3′-dideoxy-5-fluoro-3′-thiacytidine (FTC),[12] β-L-2′,3′-dideoxy-5-fluorocytidine (L-FddC),[13] and β-L-2′-fluoro-5-methylarabinofuranosyl uracil (L-FMAU).[14] Both 3TC and FTC were found to have more potent antiviral activity against HIV and HBV than their D-counterparts with reduced toxicity.[15,16] Two other L-nucleosides, β-L-d4C and β-L-Fd4C, were reported to exhibit potent anti-HIV and anti-HBV activities.[17] The synthesis of the enantiomers of abacavir was reported[18] and the D-enantiomer of abacavir also exhibited anti-HBV activity.[19] In connection with L-nucleosides, we have reported the synthesis and antiviral activity of β-L-2′,3′-didehydro-2′,3′-dideoxy purine nucleoside analogues, among which the adenosine derivative (β-L-d4A) exhibited significant anti-HIV and anti-HBV activities.[20] The racemic mixtures of some carbocyclic 2′,3′-didehydro-2′,3′-dideoxy purine derivatives were reported to exhibit anti-HIV activity.[21] Carbovir was the first carbocyclic nucleoside analogue which exhibits potent anti-HIV activity in vitro. The first preparation of the D- and L-isomers of carbovir was reported by Vince et al.[22] The L-carbovir was prepared either by chemoenzymatic syntheses,[22−24] or by a stereoselective method via [2+3] asymmetric cycloaddition.[25] The anti-HIV and anti-HBV activities of carbovir reside in its natural β-D-enantiomer.[26] It was reported that the triphosphates of β-D- and β-L-carbovir are approximately equipotent as HIV reverse transcriptase inhibitors[24] and the β-L-carbovir triphosphate exhibited more potent anti-HBV activity.[27]

These findings prompted us to synthesize L-carbocyclic nucleosides in the search for new antiviral agents. Recently, we have reported a preliminary result of carbocyclic β-L-2′,3′-didehydro-2′,3′-dideoxy adenine as an anti-HIV agent.[28] As part of our ongoing drug discovery efforts, herein we report the full account of the asymmetric syntheses of carbocyclic β-L-2′,3′-didehydro-2′,3′-dideoxy and β-L-2′,3′-dideoxy pyrimidine and purine nucleoside analogues together with their anti-HIV and anti-HBV activities.

For the synthesis of L-carbocyclic nucleosides, we utilized the reported (+)-cyclopentenone **1** as a chiral starting material, which was prepared in three steps from D-ribose.[29] The alcohol **2** was previously reported by our group from the regioselective addition of *tert*-butoxymethyl group to the enone **1**, followed by DIBAL-H

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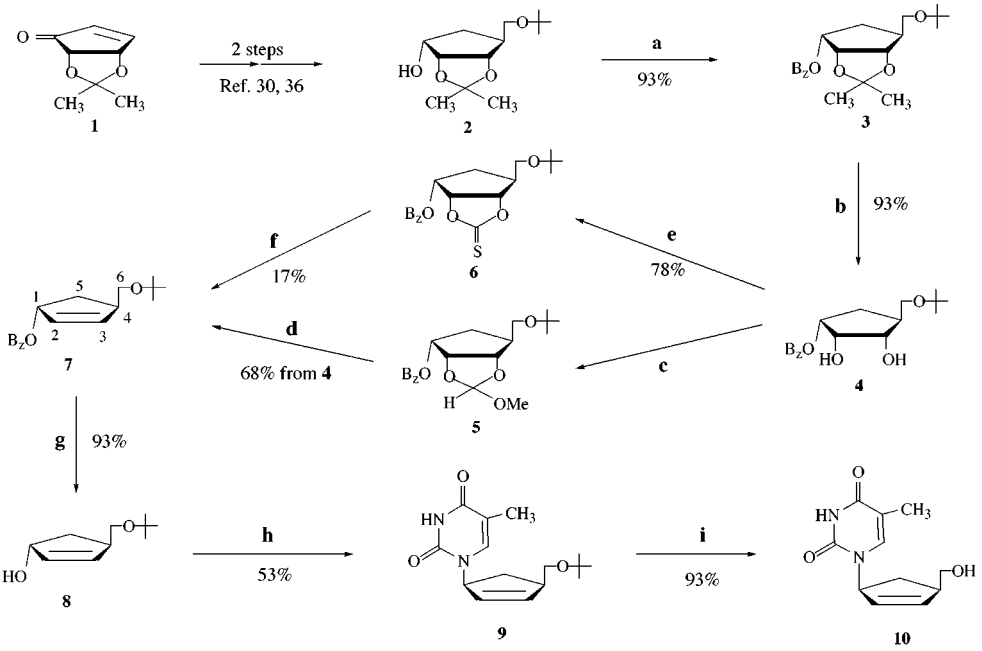
Scheme 1[a]



[a] Reagents and conditions: (a) BzCl, Pyr, rt, 12 h; (b) concentrated HCl:MeOH (1:70, v/v), rt, 2.5 h; (c) $CH(OMe)_3$, pyridinium *p*-toluene-sulfonate, rt, 2 h; (d) Ac_2O, 120−130 °C, 6 h; (e) 1,1′-thiocarbonyldiimidazole, MeCN, rt, 24 h; (f) 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine, THF, rt, 20 h; (g) 2 N NaOH/MeOH, rt, 1.5 h; (h) (1) N^3-benzoylthymine, Ph_3P, diethyl azodicarboxylate, dioxane, rt, 6 h; (2) NH_3/MeOH, rt; (i) CF_3CO_2H/H_2O (2:1), 50 °C, 3 h.

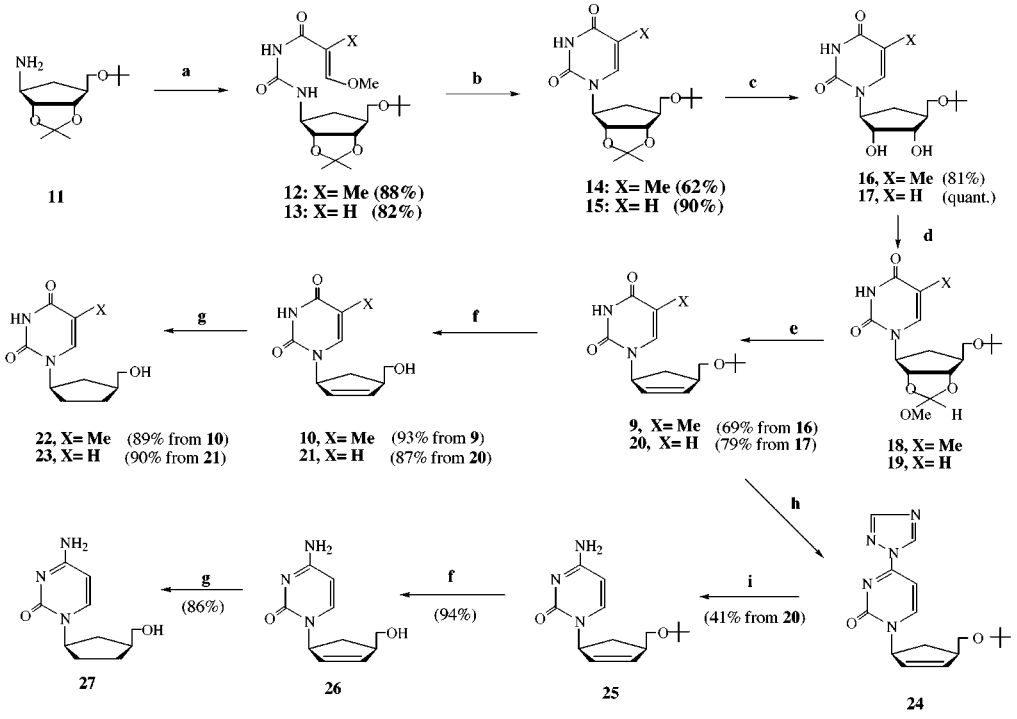
reduction (Scheme 1).[30] Treatment of compound **2** with benzoyl chloride in pyridine gave the benzoate **3** in 93% yield. Selective deprotection of the isopropylidene protection group of compound **3** with a mixture of concentrated HCl and methanol (1: 70, v/v) at room temperature for 2.5 h gave the diol **4** in 93% yield. The diol **4** was treated with trimethyl orthoformate at room temperature for 2 h in the presence of catalytic amounts of pyridinium *p*-toluene-sulfonate to afford the cyclic ortho ester **5**, which was subjected to a thermal elimination reaction[31] with acetic anhydride at 120−130 °C for 6 h to give the required cyclopentene **7**. Another method of deoxygenation of the diol **4** to **7** via cyclic thionocarbonates was also explored. The yield was, however, lower than that of the above method as briefly described below: Compound **4** was treated with 1,1′-(thiocarbonyl)-diimidazole at room temperature to give cyclic thionocarbonate **6**, which was deoxygenated to **7** under mild conditions using 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine.[32]

For structural identification, NOESY experiments were performed, which indicated that there is a correlation between H-1 and H-6 of compound **7**, suggesting that H-1 and H-6 are on the same side. The benzoyl group of compound **7** was removed with 2 N NaOH in methanol to give the alcohol **8**, which was then reacted with a heterocyclic base under Mitsunobu conditions.[33,34] Thymidine analogue was prepared by the reaction of **8** with N^3-benzoylthymine[35] in the presence of triphenylphosphine and DEAD at room temperature to give **9** in 53% yield. Deblocking of compounds **9** with trifluoroacetic acid/H_2O (2:1) at 50 °C for 3 h provided thymine analogue **10** in 93% yield.

Other carbocyclic L-2′,3′-didehydro-2′,3′-dideoxy and 2′,3′-dideoxy pyrimidine and purine nucleosides were also prepared by thermal elimination reactions via cyclic ortho esters from protected nucleosides (Scheme 2 and Scheme 3). Treatment of **11**[30,36] with β-methoxy-α-methacryloyl isocyanate and β-methoxy acryloyl isocyanate using the methodology reported by Shealy et al.[37,38] gave acrylurea **12** (X = Me) and **13** (X = H), respectively. Reaction of **12** and **13** with 30% NH_4OH and ethanol at 80−100 °C in a steel bomb gave the corresponding thymine **14** and uracil **15** derivatives, respectively. Treatment of compound **14** and **15** with a mixture of concentrated HCl and methanol (1: 65, v/v) at room temperature for 2.5 h gave the diol **16** and **17** in 81% and quantitative yields, respectively. Ortho esterification of compound **16** and **17** with trimethyl orthoformate in the presence of pyridinium *p*-toluene-sulfonate gave the cyclic ortho esters **18** and **19**, which were then heated with acetic anhydride at 120−130 °C to afford **9** and **20**, respectively. Deprotection of compounds **9** and **20** employing the conditions described above provided **10** (93% yield) and **21** (87% yield), respectively. Preparation of the cytosine derivative **26** was accomplished by the reported method.[39] The treatment of **20** with 4-chlorophenyl dichlorophosphate and 1,2,4-triazole in pyridine gave the triazole derivative **24**. Subsequent hydrolysis of **24** with concentrated NH_4OH gave **25** (41% yield), which was deblocked with trifluoroacetic acid/H_2O to afford the cytosine nucleoside **26** in 94% yield.

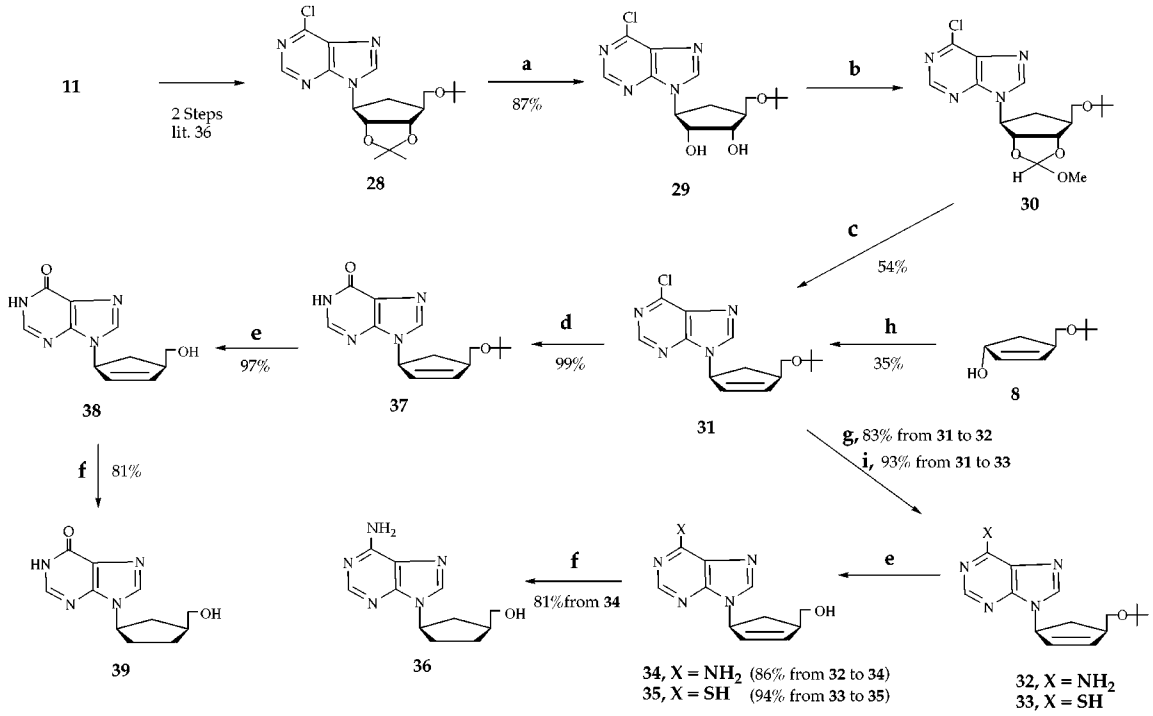
The 6-chloropurine derivative **28** was prepared in two steps from **11** (Scheme 3).[36] The isopropylidene protection group of compound **28** was removed using a mixture of HCl and methanol (1: 70, v/v) to give compound **29** in 87% yield. Treatment of the diol **29** with trimethyl orthoformate in the presence of pyridinium *p*-toluene-sulfonate gave **30**, which was then subjected to a thermal elimination reaction with acetic anhydride to give compound **31**. The 6-chloropurine nucleoside analogue **31** was also obtained in 35% yield by the reaction of alcohol **8** with 6-chloropurine in the presence of

Scheme 2[a]



[a] Reagents and conditions: (a) β-methoxy-α-methacryloyl isocyanate, DMF, −20 to 20 °C, 10 h (for **12**) or β-methoxyacryloyl isocyanate, DMF, −20 to 20 °C, 10 h (for **13**); (b) 30% NH_4OH, EtOH or/and dioxane, 80−100 °C, 10−24 h; (c) concentrated HCl:MeOH (1:65 to 70, v/v), rt, 2.5−3 h; (d) $CH(OMe)_3$, pyridinium *p*-toluene-sulfonate; rt, 30 min; (e) Ac_2O, 120−130 °C, 8 h; (f) CF_3CO_2H/H_2O (2:1), 50 °C, 3 h; (g) 10% Pd/C, MeOH, 15 psi; (h) *p*-chlorophenylphosphorodichloridate, 1,2,4-triazole, Py, rt, 24 h; (i) 30% NH_4OH, dioxane, rt, 24 h.

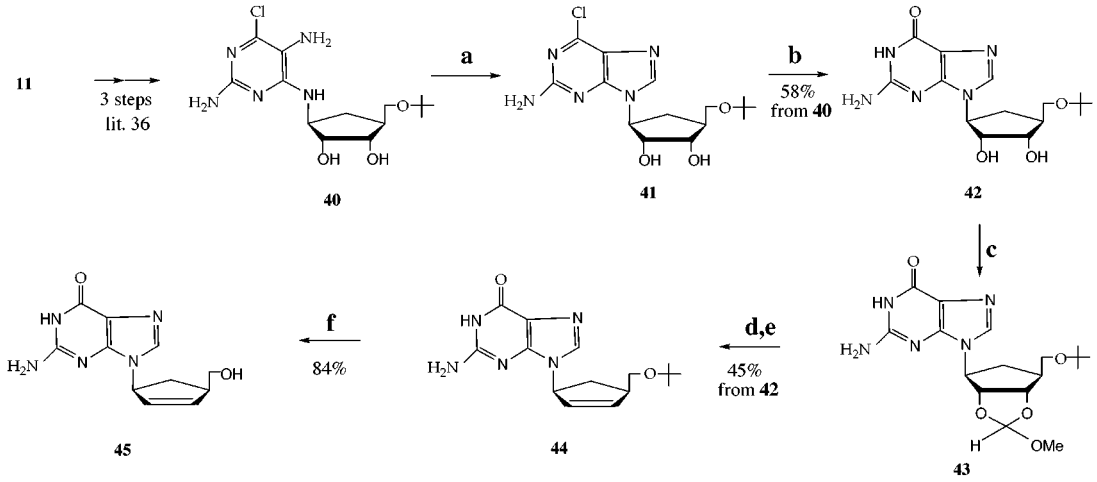
Scheme 3[a]



[a] Reagents and conditions: (a) concentrated HCl:MeOH (1:70, v/v), rt, 3 h; (b) $CH(OMe)_3$, pyridinium *p*-toluene-sulfonate, rt, 2 h; (c) Ac_2O, 120−130 °C, 12 h; (d) $HSCH_2CH_2OH$, MeOH, reflux, 24 h; (e) CF_3CO_2H/H_2O (2:1), 50 °C, 3 h; (f) 10% Pd/C, MeOH, rt, 15 psi, 3 h; (g) NH_3/MeOH, 80−90 °C, 20 h; (h) 6-chloropurine, Ph_3P, diethyl azodicarboxylate, dioxane, rt, 10 h; (i) thiourea, EtOH, reflux, 1 h.

triphenylphosphine and diethyl azodicarboxylate (DEAD) at room temperature (Scheme 3). Treatment of the compound **31** with saturated ammonia in methanol in a steel bomb at 80 to 90 °C provided the adenine derivative **32** in 83%. The *tert*-butyl group of **32** was removed by CF_3CO_2H/H_2O (2:1, v/v) at 50 °C to afford β-L-2′,3′-didehydro-2′,3′-dideoxyadenosine **34** in 86% yield. The 6-mercaptopurine analogue **35** was obtained by the reaction of **31** with thiourea in refluxing ethanol followed by deprotection with a mixture of CF_3CO_2H and

Scheme 4[a]



[a] Reagents and conditions: (a) $CH(OMe)_3$, HCl, DMF, 0−5 °C, 8 h then rt 18 h; (b) $HSCH_2CH_2OH$, MeOH, reflux, 18 h; (c) $CH(OMe)_3$, pyridinium *p*-toluene-sulfonate, rt, 1 h; (d) Ac_2O, 120−130 °C, , 12 h; (e) 30% NH_4OH, MeOH, H_2O, 65 °C, 1.25 h; (e) CF_3CO_2H/H_2O (2:1), 50 °C, 3 h.

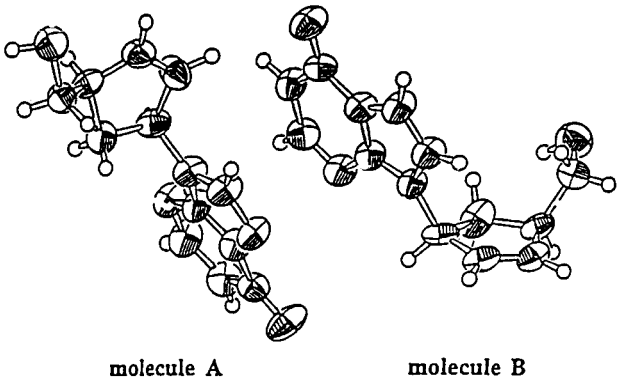


Figure 1. ORTEP drawing of compound **38** (C-L-d4I).

H_2O. Treatment of compound **31** with mercaptoethanol and sodium methoxide in refluxing methanol followed by deblocking with CF_3CO_2H/H_2O gave carbocyclic β-L-2′,3′-didehydro-2′,3′-dideoxyinosine (**38**). 2′,3′-Saturated carbocyclic pyrimidine (**22, 23,** and **27**) and purine (**36, 39**) nucleosides were prepared by the catalytic hydrogenation of the corresponding 2′,3′-unsaturated nucleosides with palladium on activated carbon (Schemes 2 and 3).

For the synthesis of L-carbovir **45**, we utilized 6-chloro-2,5-diaminopyrimidine analogue **40** as an intermediate, which was synthesized from cyclopentylamine **11** in three steps (Scheme 4).[30,36] Treatment of **40** with triethyl orthoformate in the presence of concentrated HCl gave the 2-amino-6-chloropurine analogue **41**, which was treated with a mixture of mercaptoethanol and sodium methoxide in methanol to give the guanine derivative **42**. Conversion of **42** to L-carbovir **45** was accomplished via a thermal elimination reaction with acetic anhydride described as above (Scheme 4).

The X-ray structure of the inosine derivative **38**[40] contains two molecules (**A** and **B**) with different conformational features (Figure 1). One molecule (molecule **A**) adopts a sugar puckering with the pseudorotation phase angle $P = 264.4°$ and $\nu_{max} = 23.60°$, the 5′-OH orientation $\gamma = 68.1°$ ($C_{3'}$-$C_{4'}$-$C_{6'}$-$O_{6'}$), and the base orientation, $\chi = 98.9°$ ($C_{5'}$-$C_{1'}$-N_9-C_4). The other (molecule **B**) has the C5′-exo conformation with $P = 80.8°$ and $\nu_{max} = 9.97°$, the 5′-OH orientation $\gamma = -171.6°$ ($C_{3'}$-$C_{4'}$-$C_{6'}$-$O_{6'}$), and the base orientation, $\chi = 68.5°$ ($C_{5'}$-$C_{1'}$-N_9-C_4) (Table 1).

The anti-HIV and anti-hepatitis B virus (HBV) activities of synthesized L-carbocyclic nucleosides were evaluated in peripheral blood mononuclear (PBM) and 2.2.15 cells, respectively (Table 2). It was found that β-L-carbocyclic 2′,3′-didehydro-2′,3′-dideoxyadenosine (**34**) exhibited potent anti-HBV activity ($EC_{50} = 0.9$ μM in 2.2.15 cells) and moderately potent anti-HIV activity ($EC_{50} = 2.4$ μM, $EC_{90} = 11.7$ μM in PBM cells) without cytotoxicity up to 100 μM in PBM, CEM, and Vero cells. The cytosine analogue **26** displayed some anti-HBV activity ($EC_{50} = 10.0$ μM in 2.2.15 cells) and anti-HIV activity ($EC_{50} = 35.8$ μM, $EC_{90} = 65.9$ μM in PBM cells). In the carbocyclic L-d2N series, only adenine analogue **36** exhibited weak anti-HIV activity with an EC_{50} value of 27 μM. The thymine derivative **10** did not display any antiviral activity, but showed weak cytotoxicity.

Experimental Section

Melting points were determined on a Mel-temp II apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on a Bruker 400 AMX spectrometer at 400 MHz for ^{1}H NMR and 100 MHz for ^{13}C NMR with tetramethylsilane as the internal standard. Chemical shifts (δ) are reported in parts per million (ppm), and signals are reported as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), or br s (broad singlet). UV spectra were recorded on a Beckman DU-650 spectrophotometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. Mass spectra were recorded on a Micromass Autospec high-resolution mass spectrometer. TLC was performed on Uniplates (silica gel) purchased from Analtech Co. Column chromatography was performed using silica gel G (TLC grade, >440 mesh) for vacuum flash column chromatography. Elemental analyses were performed by Atlantic Microlab Inc., Norcross, GA.

(1*R*,2*R*,3*S*,4*S*)-1-Benzoyloxy-4-(*tert*-butoxymethyl)-2,3-(isopropylidenedioxy)cyclopentane (3). Benzoyl chloride (0.28 mL, 2.4 mmol) was added dropwise to a solution of alcohol **2** (0.2 g, 0.81 mmol) in pyridine (2 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h at room temperature for 12 h. After the reaction mixture was quenched by adding ice, it was stirred for 15 min and then the solvent was removed in vacuo. The residue was treated with ethyl acetate (15 mL) and water (5 mL). The organic layer was washed with saturated $NaHCO_3$ (5 mL) and brine (5 mL) and dried

Table 1. Conformational Parameters for Compound **38**

compd **38**	pseudorotation angle, *P* (deg)	torsion angles (deg) $C_{3'}-C_{4'}-C_{6'}-O_{6'}$ (γ)	torsion angles (deg) $C_{5'}-C_{1'}-N_{9'}-C_4$ (χ)	conformation
A	264.4	68.1	98.9	C5′-endo
B	80.8	−171.6	68.5	C5′-exo

Table 2. Anti-HIV and Anti-HBV Activity and Cytotoxicities of L-Carbocyclic d4- and d2-Nucleosides[a]

	anti-HIV (μM) in PBM cells		anti-HBV (μM) in 2.2.15 cells	cytotoxicities (IC_{50}, μM)		
no.	EC_{50}	EC_{90}	EC_{50}	PBM	CEM	Vero
10 (C-L-d4T)	>100	-	>10	66.6	>100	49.4
21 (C-L-d4U)	>100	-	>10	>100	>100	>100
22 (C-L-d2T)	>100	-	>10	>100	>100	171
23 (C-L-d2U)	>100	-	>10	>100	>100	>100
26 (C-L-d4C)	35.8	65.9	10.0	>100	>100	>100
30 (C-L-d2C)	>100	-	>10	>100	>100	>100
34 (C-L-d4A)	2.4	11.7	0.9	>100	>100	>100
35 (C-L-d4MP)	>100	-	>10	>100	>100	>100
36 (C-L-d2A)	27.0	-	>50	>100	>100	>100
38 (C-L-d4I)	>100	-	>10	>100	>100	>100
39 (C-L-d2I)	>100	-	>10	>100	>100	>100
45 L-carbovir	>200[22]	-	>200[26]	-	-	-

[a] -: not determined.

($MgSO_4$). After filtration and evaporation, the residue was purified by silica gel column chromatography with 1−3% EtOAc in hexanes to give **3** (265 mg, 93.4%) as a syrup: $[\alpha]^{25}_D$ 55.61° (*c* 0.82, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.41−8.10 (m, 5H, Ar−H), 5.28 (m, 1H, 1-H), 4.77 (t, J = 5.6 Hz, 1H, 2-H), 4.50 (d, J = 5.5 Hz, 1H, 3-H), 3.38 (dd, J = 4.3, 8.7 Hz, 1H, 6-Ha), 3.31 (dd, J = 4.3, 8.7 Hz, 1H, 6-Hb), 2.26−2.37 (m, 2H, 5-H), 1.98 (m, 1H, 4-H), 1.41 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.19 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 349.1998; Calcd for $C_{20}H_{28}O_5$, *m*/*z* 349.2015 $(M + H)^+$. Anal. ($C_{20}H_{28}O_5$) C, H.

(1*R*,2*R*,3*S*,4*S*)-1-Benzoyloxy-2,3-dihydroxy-4-(*tert*-butoxymethyl)cyclopentane (4). A solution of compound **3** (3.15 g, 9.04 mmol) in a mixture of concentrated HCl and MeOH (324 mL, concentrated. HCl: MeOH = 1:70, v/v) was stirred at room temperature for 2.5 h. The reaction mixture was cooled in an ice bath, neutralized with $NaHCO_3$ solid, and filtered. The filtrate was concentrated to dryness, and the residue was purified by silica gel column chromatography with 10−25% EtOAc in hexanes to give **4** (2.60 g, 93.3%) as a syrup: $[\alpha]^{25}_D$ −28.61° (*c* 0.87, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 7.49−8.04 (m, 5H, Ar−H), 5.04 (m, 1H, 1-H), 4.74 (d, J = 5.1 Hz, 1H, OH, D_2O exchangeable), 4.52 (d, J = 6.5 Hz, 1H, OH, D_2O exchangeable), 3.97 (dd, J = 4.6, 9.2 Hz, 1H, 2-H), 3.70 (dd, J = 6.7, 11.3 Hz, 1H, 3-H), 3.14−3.37 (m, 2H, 6-H), 2.17 (m, 1H, 5-Ha), 1.77−1.95 (m, 2H, 4-H and 5-Hb), 1.13 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 309.1711; Calcd for $C_{17}H_{25}O_5$, *m*/*z* 309.1702 $(M + H)^+$. Anal. ($C_{17}H_{24}O_5$) C, N.

(1a*S*,3a*S*,4*R*,6*S*)-4-Benzoyloxy-6-(*tert*-butoxymethyl)-3a,4,5,6,6a-tetrahydrocyclopenta-1,3-dioxole-2-thione (6). 1,1′-Thiocarbonyldiimidazole (295 mg, 1.61 mmol) was added to a solution of compound **4** (0.2 g, 0.649 mmol) in dry MeCN (15 mL). The mixture was stirred under nitrogen at room temperature for 24 h. The solvent was removed in a vacuum, and the residue was purified by silica gel column chromatography with 1−3% EtOAc in hexanes to give **6** (177 mg, 78%) as a solid: mp 68−70 °C; $[\alpha]^{28}_D$ 122.35° (*c* 0.27, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.43−8.08 (m, 5H, Ar−H), 5.61 (m, 1H, 1-H), 5.39 (t, J = 6.1 Hz, 1H, 2-H), 5.17 (d, J = 6.5 Hz, 1H, 3-H), 3.55 (dd, J = 3.4, 8.9 Hz, 1H, 6-Ha), 3.37 (dd, J = 3.1, 8.9 Hz, 1H, 6-Hb), 2.73 (m, 1H, 5-Ha), 2.16−2.29 (m, 2H, 4-H and 5-Hb), 1.19 (s, 9H, *tert*-butyl); ^{13}C NMR ($CDCl_3$) δ 191.51, 165.88, 133.41, 129.94, 128.46, 89.40, 84.25, 74.05, 73.55, 62.65, 42.56, 32.11, 27.35; HR-FAB MS Obsd, *m*/*z* 351.1251; Calcd for $C_{18}H_{23}O_5S$, *m*/*z* 351.1266 $(M + H)^+$. Anal. ($C_{18}H_{22}O_5S$) C, H, S.

(1*S*,4*R*)-1-Benzoyloxy-4-(*tert*-butoxymethyl)cyclopent-2-ene (7). Method a. A suspension of compound **4** (1.69 g, 5.48 mmol) and pyridinium *p*-toluene-sulfonate (1.54 g, 6.0 mmol) in trimethyl orthoformate (12 mL) was stirred at room temperature for 2 h. The reaction mixture was diluted with ether (160 mL) and washed with aqueous $NaHCO_3$ (2 × 40 mL) and brine (40 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to dryness. The residue, after being coevaporated with benzene (2 × 10 mL), was treated with acetic anhydride (17 mL). The reaction mixture was heated at 120−130 °C for 6 h, and the mixture was concentrated to dryness. The residue was purified by silica gel column chromatography with 1−2% EtOAc in pentane to **7** (1.023 g, 68% from **4**).

Method b. A solution of compound **6** (148 mg, 0.42 mmol) in dry THF was treated with 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine (120 mg, 0.6 mmol) and then stirred at room temperature for 20 h. The reaction mixture was concentrated to dryness, and the residue was purified by silica gel column chromatography with 1% Et_2O in hexanes to give **7** (19.4 mg, 17%): $[\alpha]^{27}_D$ 259.89° (*c* 1.45, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.40−8.03 (m, 5H, Ar−H), 6.15 (m, 1H, 2-H), 5.98 (m, 1H, 3-H), 5.95 (m, 1H, 1-H), 3.28 (d, J = 6.9 Hz, 1H, 6-H), 3.13 (m, 1H, 4-H), 2.10 (m, 1H, 5-Hab), 1.19 (s, 9H, *tert*-butyl); ^{13}C NMR ($CDCl_3$) δ 166.59, 140.05, 132.76, 130.65, 130.07, 129.60, 128.27, 80.66, 72.69, 65.50, 45.68, 34.35, 27.52; HR-FAB MS Obsd, *m*/*z* 275.1645; Calcd for $C_{17}H_{23}O_3$, *m*/*z* 275.1647 $(M + H)^+$. Anal. ($C_{17}H_{22}O_3$) C, H.

(1*S*,4*R*)-4-(*tert*-Butoxymethyl)-1-hydroxycyclopent-2-ene (8). Compound **7** (578 mg, 2.1 mmol) was treated with a mixture of MeOH (35 mL) and 2 N NaOH (4.5 mL). The

reaction mixture was stirred at room temperature for 1.5 h and then neutralized with dry ice. The mixture was concentrated in a vacuum to dryness, and the residue was treated with EtOAc (75 mL) and washed with aqueous $NaHCO_3$ (2 × 10 mL) and brine (15 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to give crude **8** (335 mg, 93.4%) as a syrup, which was used for the next step without further purification.

(1′*S*,4′*R*)-1-[4-(*tert*-Butoxymethyl)cyclopent-2-enyl]-thymine (9). Method a. A solution of diethyl azodicarboxylate (DEAD) (160 mg, 0.92 mmol) in dioxane (3 mL) was slowly added to a suspension of compound **8** (78 mg, 0.46 mmol), triphenylphosphine (240 mg, 0.92 mmol), and N^3-benzoylthymine (211 mg, 0.92 mmol) in dry dioxane (4.5 mL). The mixture was stirred at room temperature for 6 h. The solvent was removed under reduced pressure, and the residue was treated with saturated ammonia in MeOH (5 mL). The mixture was stirred at room temperature for 10 h and then concentrated to dryness under reduced pressure. The residue was purified by preparative TLC with 1% MeOH in $CHCl_3$ to give **9** (68 mg, 53.4%) as a white solid.

Method b. A suspension of compound **16** (119 mg, 0.38 mmol) and pyridinium *p*-toluene-sulfonate (105 mg, 0.42 mmol) in trimethyl orthoformate (3 mL) was stirred at room temperature for 30 min. The reaction mixture was diluted with EtOAc (20 mL) and washed with saturated $NaHCO_3$ (2 × 5 mL) and brine (10 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The residue was coevaporated with benzene (2 × 5 mL) and treated with Ac_2O (2 mL). The mixture was heated at 120−130 °C for 8 h and concentrated to dryness. The residue was treated with saturated ammonia in MeOH (8 mL), and the mixture was stirred at room temperature for 8 h. The residue was purified by silica gel column chromatography with 2−5% EtOAc in $CHCl_3$ to give **9** (73 mg, 68.8%) as a solid: mp 122−124 °C; UV (MeOH) λ_{max} 272 nm; $[\alpha]^{24}_D$ 59.38° (*c* 0.33, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.32 (br s, 1H, NH, D_2O exchangeable, 2-H), 7.22 (s, 1H, 6-H), 6.08 (m, 1H, 2′-H), 5.72 (m, 1H, 1′-H), 5.59 (m, 1H, 3′-H), 3.50 (dd, J = 8.9, 4.1 Hz, 1H, 6′-Ha), 3.34 (dd, J = 8.9, 4.6 Hz, 1H, 6′-Hb), 2.95 (m, 1H, 4′-H), 2.66 (dt, J = 14.0, 9.1, 9.1 Hz, 1H, 5′-Ha), 1.90 (s, 3H, 5-CH_3), 1.49 (m, 1H, 5′-Hb), 1.18 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 279.1699; Calcd for $C_{15}H_{23}N_2O_3$, *m*/*z* 279.1709 (M + H)$^+$. Anal. ($C_{15}H_{22}N_2O_3$) C, H, N.

(1′*S*,4′*R*)-1-[4-(Hydroxymethyl)cyclopent-2-enyl]thymine (10). A mixture of compound **9** (50 mg, 0.18 mmol), CF_3CO_2H (8 mL), and H_2O (4 mL) was heated at 50 °C for 3 h. The solution was then concentrated to dryness and coevaporated with EtOH (2 × 5 mL). The residue was purified by silica gel column chromatography with 3% MeOH in $CHCl_3$ to give **10** (37 mg, 93%) as a white solid: mp 162−164 °C; $[\alpha]^{24}_D$ 71.66° (*c* 0.30, MeOH); UV (H_2O) λ_{max} 273.5 (ϵ 12757) (pH 2), 273.5 (ϵ 12893) (pH 7), 272.0 nm (ϵ 9453) (pH 11); ^{1}H NMR (DMSO-d_6) δ 7.34 (s, 1H, 6-H), 6.08 (m, 1H, 2′-H), 5.68 (m, 1H, 3′-H), 5.49 (m, 1H, 1′-H), 4.74 (t, J = 5.2 Hz, 1H, OH, D_2O exchangeable), 3.45 (m, 2H, 6′-Ha,b), 2.78 (m, 1H, 4′-H), 2.46 (m, 1H, 5′-Ha), 1.74 (s, 3H, CH_3), 1.33 (m, 1H, 5′-Hb); ^{13}C NMR (DMSO-d_6) δ 163.05, 150.00, 138.31, 136.63, 128.96, 108.10, 62.55, 59.36, 46.32, 32.06, 11.31; HR-FAB MS Obsd, *m*/*z* 223.1082; Calcd for $C_{11}H_{15}N_2O_3$, *m*/*z* 223.1083 (M + H)$^+$. Anal. ($C_{11}H_{14}N_2O_3$) C, H, N.

***N*-[[(1*S*,2*R*,3*S*,4*S*)-4-(*tert*-Butoxymethyl)-2,3-(isopropylidenedioxy)cyclopentyl]aminocarbonyl]-3-methoxy-2-methyl-2-propenamide (12).** To a solution of β-methoxy-α-methacryloyl chloride (1.274 g, 9.46 mmol) in anhydrous benzene (13.2 mL) was added silver cyanate (3.04 g). The mixture was refluxed for 30 min and allowed to cool to room temperature. After the solid phase had settled, 6.33 mL of the supernatant solution which contained β-methoxy-α-methacryloyl isocyanate was added to a solution of amine **11** (820 mg) in dried DMF (16 mL) at −15 to −20 °C during 15 min. The reaction mixture was stirred at −15 °C for 2 h and then at room temperature for 8 h under nitrogen. The mixture was evaporated under reduced pressure, and the residue was purified by flash silica gel column chromatography with 5% MeOH in $CHCl_3$ to afford **12** (1.12 g, 88%) as a solid: mp 129−130 °C; $[\alpha]^{27}_D$ 22.52° (*c* 0.54, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.30 (s, 1H, 6-H), 4.45 (m, 2H, 1′-H and 2′-H), 4.20 (m, 1H, 3′-H), 3.86 (s, 3H, OCH_3), 3.38 (m, 2H, 6′-H), 2.37 (m, 1H, 5′-H), 2.27 (m, 1H, 4′-H), 1.76 (s, 3H, 5-CH_3), 1.59 (s, 1H, NH), 1.57 (m, 1H, 5′-H), 1.49 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.17 (s, 9H, *tert*-butyl). Anal. ($C_{19}H_{32}N_2O_6$) C, H, N.

(1′*S*,2′*R*,3′*S*,4′*S*)-1-[4-(*tert*-Butoxymethyl)-2,3-(isopropylidenedioxy)cyclopentan-1-yl]thymine (14). Compound **12** (550 mg, 1.43 mmol) was dissolved in dioxane (4 mL), ethanol (4 mL), and aqueous ammonia (30%, 3 mL). The reaction mixture was heated at 80−100 °C in a sealed bomb for 10 h. The solution was evaporated to dryness. The residue was purified by flash silica gel column chromatography with 0.3% MeOH in $CHCl_3$ to give **14** (314 mg, 62%) as a solid: mp 154−156 °C; $[\alpha]^{25}_D$ 35.53° (*c* 0.53, $CHCl_3$); UV (MeOH) λ_{max} 272.5 nm; ^{1}H NMR ($CDCl_3$) δ 7.08 (s, 1H, 6-H), 4.68 (m, 2H, 1′-H and 2′-H), 4.46 (m, J = 4.2, 6.0 Hz, 1H, 3′-H), 3.46 (m, 2H, 6′-H), 2.33 (m, 2H, 4′-H and 5′-H), 1.97 (m, 1H, 5′-H), 1.93 (s, 3H, 5-CH_3), 1.54 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.20 (s, 9H, *tert*-butyl). Anal. ($C_{18}H_{28}N_2O_5$) C, H, N.

***N*-[[(1*S*,2*R*,3*S*,4*S*)-4-(*tert*-Butoxymethyl)-2,3-(isopropylidenedioxy)cyclopentyl]aminocarbonyl]-3-methoxy-2-propenamide (13).** Conversion of **11** (1.6 g, 6.6 mmol) to **13** was accomplished using a procedure similar to that described for **12**. The residue obtained was purified by silica gel column chromatography with 15% EtOAc in hexanes to give **13** (2.0 g, 82.1%) as a solid: mp 121−122 °C; $[\alpha]^{27}_D$ 26.63° (*c* 0.57, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.76 (br s, 1H, NH), 7.67 (d, J = 12.2 Hz, 1H, 6-H), 5.41 (d, J = 12.2 Hz, 1H, 5-H), 4.45 (m, 2H, 1′-H and 2′-H), 4.20 (m, 1H, 3′-H), 3.73 (s, 3H, OCH_3), 3.33−3.42 (m, 2H, 6′-H), 2.36−2.43 (m, 1H, 5′-H), 2.28 (m, 1H, 4′-H), 1.57 (m, 1H, 5′-H), 1.46 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.17 (s, 9H, *tert*-butyl); ^{13}C NMR ($CDCl_3$) δ 167.98, 163.06, 155.09, 111.47, 97.64, 86.46, 82.45, 72.80, 62.51, 57.48, 56.54, 45.08, 33.91, 27.38, 27.21, 24.85. Anal. ($C_{18}H_{30}N_2O_6$) C, H, N.

(1′*S*,2′*R*,3′*S*,4′*S*)-1-[4-(*tert*-Butoxymethyl)-2,3-(isopropylidenedioxy)cyclopentan-1-yl]uracil (15). A mixture of compound **13** (600 mg, 1.62 mmol), ethanol (10 mL), and aqueous ammonia (30%, 2.5 mL) was heated at 80−90 °C in a steel bomb for 24 h. After cooling, the solution was evaporated to dryness. The residue was purified by preparative TLC (3% MeOH in $CHCl_3$) to give **15** (493 mg, 90%) as an oil: $[\alpha]^{25}_D$ 43.16° (*c* 0.67, $CHCl_3$); UV (MeOH) λ_{max} 266.5 nm; ^{1}H NMR ($CDCl_3$) δ 7.35 (d, J = 8.0 Hz, 1H, 6-H), 5.73 (d, J = 8.0 Hz, 1H, 6-H), 4.72 (m, 2H, 1′-H and 2′-H), 4.48 (m, 1H, 3′-H), 3.46 (m, 2H, 6′-H), 2.37 (m, 2H, 4′-H and 5′-H), 1.97 (m, 1H, 5′-H), 1.55 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 1.19 (s, 9H, *tert*-butyl); ^{13}C NMR ($CDCl_3$) δ 167.98, 163.05, 155.09, 111.47, 97.64, 86.46, 82.45, 72.80, 62.51, 57.48, 56.54, 45.08, 33.91, 27.38, 27.21, 24.85. Anal. ($C_{17}H_{26}N_2O_5 \cdot 0.5H_2O$) C, H, N.

(1′*S*,2′*R*,3′*S*,4′*S*)-1-[4-(*tert*-Butoxymethyl)-2,3-dihydroxycyclopentan-1-yl]thymine (16). A solution of compound **14** (362 mg, 1.03 mmol) in a mixture of concentrated HCl and MeOH (35.5 mL, concentrated HCl:MeOH = 1:70, v/v) was stirred at room temperature for 2.5 h. The reaction mixture was cooled in an ice bath and neutralized with $NaHCO_3$ solid. The mixture was concentrated to dryness. The residue was purified by silica gel column chromatography with 2−4% MeOH in CH_2Cl_2 to give **16** (258.5 mg, 80.6%) as a syrup: UV (MeOH) λ_{max} 273.5 nm; $[\alpha]^{24}_D$ 38.57° (*c* 0.12, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 11.20 (s, 1H, NH, D_2O exchangeable), 7.51 (s, 1H, 6-H), 4.82 (d, J = 6.5 Hz, 1H, OH, D_2O exchangeable), 4.63 (dd, 1H, J = 9.3, 18.5 Hz, 1′-H), 4.57 (d, J = 3.9 Hz, 1H, OH, D_2O exchangeable), 4.01 (m, 1H, 3′-H), 3.29 (m, 2H, 6′-Ha,b), 2.03−1.94 (m, 2H, 5′-Ha and 4′-H), 1.78 (s, 3H, CH_3), 1.24 (m, 1H, 5′-Hb), 1.14 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 313.1766; Calcd for $C_{15}H_{25}N_2O_5$, *m*/*z* 313.1763 (M + H)$^+$. Anal. ($C_{15}H_{24}N_2O_5 \cdot 0.2H_2O$) C, H, N.

(1′*S*,2′*R*,3′*S*,4′*S*)-1-[4-(*tert*-Butoxymethyl)-2,3-dihydroxycyclopentan-1-yl]uracil (17). A solution of compound **15** (3.2 g, 9.45 mmol) in a mixture of concentrated HCl and MeOH (341.2 mL, concentrated HCl:MeOH = 1:65, v/v) was stirred at room temperature for 3 h. The reaction mixture was cooled

in an ice bath and neutralized with solid $NaHCO_3$. The mixture was concentrated to dryness. The residue was purified by silica gel column chromatography with 5−8% MeOH in $CHCl_3$ to give **17** (2.82 g, 100%) as a syrup: $[\alpha]^{25}_D$ 36.73° (*c* 0.65, $CHCl_3$); UV (MeOH) λ_{max} 267.5 nm; ^{1}H NMR (DMSO-d_6) δ 7.68 (d, J = 8.0 Hz, 1H, 6-H), 5.60 (d, J = 8.0 Hz, 1H, 5-H), 4.88 (d, J = 6.4 Hz, 1H, OH, D_2O exchangeable), 4.65 (m, 1H, 1′-H), 4.61 (d, J = 6.0 Hz, 1H, OH, D_2O exchangeable), 3.65 (m, 1H, 3′-H), 3.27 (m, 2H, 6′-Ha,b), 2.07−1.95 (m, 2H, 5′-Ha and 4′-H), 1.23 (m, 1H, 5′-Hb), 1.13 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m/z* 299.1605; Calcd for $C_{14}H_{23}N_2O_5$, *m/z* 299.1607 $(M + H)^+$.

(1′*S*,4′*R*)-1-[4-(*tert*-Butoxymethyl)cyclopent-2-enyl]-uracil (20). Conversion of **17** (952 mg, 3.2 mmol) to **20** was accomplished using a procedure similar to that described for **9** (method b). The obtained residue was purified by silica gel column chromatography with 1% MeOH in $CHCl_3$ to give **20** (665 mg, 78.8%) as a solid: mp 107−110 °C; $[\alpha]^{26}_D$ 77.58° (*c* 0.99, $CHCl_3$); UV (MeOH) λ_{max} 267.5 nm; ^{1}H NMR ($CDCl_3$) δ 8.76 (br s, 1H, NH, D_2O exchangeable), 7.69 (d, J = 8.0 Hz, 1H, 5-H), 6.06 (m, 1H, 2′-H), 5.75 (m, 1H, 1′-H), 5.65 (d, J = 8.0 Hz, 1H, 6-H), 5.58 (m, 1H, 3′-H), 3.52 (dd, J = 9.0, 3.6 Hz, 1H, 6′-Ha), 3.34 (dd, J = 8.9, 4.1 Hz, 1H, 6′-Hb), 2.96 (m, 1H, 4′-H), 2.69 (dt, J = 14.4, 9.5, 9.5 Hz, 1H, 5′-Ha), 1.52 (m, 1H, 5′-Hb), 1.16 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m/z* 265.1562; Calcd for $C_{14}H_{21}N_2O_3$, *m/z* 265.1552 $(M + H)^+$. Anal. ($C_{14}H_{20}N_2O_3$) C, H, N.

(1′*S*,4′*R*)-1-[4-(Hydroxymethyl)cyclopent-2-enyl]uracil (21). Conversion of **20** (165 mg, 0.65 mmol) to **21** was accomplished using a procedure similar to that described for **10**. The residue obtained was purified by silica gel column chromatography with 1−3% MeOH in $CHCl_3$ to give **21** (117 mg, 87%) as a white solid: mp 196−198 °C; $[\alpha]^{25}_D$ 104.68° (*c* 0.81, MeOH); UV (H_2O) λ_{max} 268.5 (ϵ 10540) (pH 2), 268.0 (ϵ 11562) (pH 7), 265.5 nm (ϵ 10019) (pH 11); ^{1}H NMR (DMSO-d_6) δ 11.25 (br s, 1H, NH, D_2O exchangeable), 7.46 (d, J = 8.0 Hz, 1H, 5-H), 6.09 (m, 1H, 2′-H), 5.69 (m, 1H, 3′-H), 5.58 (d, J = 8.0 Hz, 1H, 6-H), 5.49 (m, 1H, 1′-H), 4.73 (t, J = 5.2 Hz, 1H, OH, D_2O exchangeable), 3.45 (m, 2H, 6′-Ha,b), 2.79 (m, 1H, 4′-H), 2.47 (m, 1H, 5′-Ha), 1.34 (m, 1H, 5′-Hb); HR-FAB MS Obsd, *m/z* 209.0926; Calcd for $C_{10}H_{13}N_2O_3$, *m/z* 209.0926 $(M + H)^+$. Anal. ($C_{10}H_{12}N_2O_3$) C, H, N.

(1′*S*,4′*R*)-1-[4-(Hydroxymethyl)cyclopentan-1-yl]thymine (22). Compound **10** (40 mg, 0.45 mmol) in MeOH (10 mL) was hydrogenated at 15 psi in the presence of 10% Pd/C (30 mg) for 3 h at room temperature. The reaction mixture was filtered, and the filtrate was evaporated. The residue was purified by silica gel column chromatography with 2−3% MeOH in $CHCl_3$ to give **22** (36 mg, 89.2%) as a white solid: mp 172−174 °C; $[\alpha]^{28}_D$ 11.30° (*c* 0.18, MeOH); UV (H_2O) λ_{max} 274.0 (ϵ 10601) (pH 2), 273.5 (ϵ 10764) (pH 7), 273.0 nm (ϵ 6055) (pH 11); ^{1}H NMR (DMSO-d_6) δ 11.19 (br s, 1H, NH, D_2O exchangeable), 7.57 (s, 1H, 6-H), 4.72 (m, 1H, 1′H), 4.57 (t, 1H, OH, D_2O exchangeable), 3.36 (d, 2H, J = 6.3 Hz, 6′-Ha,b), 2.06−1.33 (m, 7H, 2′-Ha,b, 3′-Ha,b, 4′-H, and 5′-Ha,b), 1.77 (s, 3H, CH_3); HR-FAB MS Obsd, *m/z* 225.1245; Calcd for $C_{11}H_{17}N_2O_3$, *m/z* 225.1239 $(M + H)^+$. Anal. ($C_{11}H_{16}N_2O_3$) C, H, N.

(1′*S*,4′*R*)-1-[4-(Hydroxymethyl)cyclopentan-1-yl]uracil (23). Conversion of **21** (72 mg, 0.45 mmol) to **23** was accomplished using a procedure similar to that described for **22**. The residue obtained was purified by silica gel column chromatography with 1−3% MeOH in $CHCl_3$ to give **23** (65 mg, 90%) as a syrup: $[\alpha]^{28}_D$ 21.28° (*c* 0.42, MeOH); UV (H_2O) λ_{max} 269.0 (ϵ 9949) (pH 2), 268.5 (ϵ 10085) (pH 7), 266.0 nm (ϵ 7646) (pH 11); ^{1}H NMR (DMSO-d_6) δ 11.22 (br s, 1H, NH, D_2O exchangeable), 7.70 (d, J = 8.0 Hz, 1H, 5-H), 5.57 (d, J = 8.0 Hz, 1H, 6-H), 4.73 (m, 1H, 1′H), 4.57 (t, 1H, OH, D_2O exchangeable), 3.38 (m, 2H, 6′-Ha,b), 2.08−1.31 (m, 7H, 2′-Ha,b, 3′-Ha,b, 4′-H, and 5′-Ha,b); HR-FAB MS Obsd, *m/z* 211.1081; Calcd for $C_{10}H_{15}N_2O_3$, *m/z* 211.1083 $(M + H)^+$. Anal. ($C_{10}H_{14}N_2O_3 \cdot 0.85H_2O$) C, H, N.

(1′*S*,4′*R*)-1-[4-(*tert*-Butoxymethyl)cyclopent-2-enyl]cytosine (25). To a solution of compound **20** (400 mg, 1.51 mmol) in pyridine (23 mL) while stirring in a cold water bath was added dropwise 4-chlorophenyl dichlorophosphate (0.74 mL, 6.05 mmol), followed by the addition of 1,2,4-triazole (418 mg, 6 mmol). The mixture was stirred at room temperature for 24 h, and then the reaction mixture was evaporated in vacuo to dryness under 40 °C. The residue was dissolved in CH_2Cl_2 (25 mL), and the solution was washed with water (2 × 50 mL), and saturated $NaHCO_3$ (50 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to dryness to give crude **24** which was used for the next step without further purification. The crude **24** was stirred in a mixture of 30% aqueous ammonia (30 mL) and 1,4-dioxane (30 mL) at room temperature for 24 h. The solution was removed to dryness, and the residue was purified by silica gel column chromatography with 1−3% MeOH in $CHCl_3$ to give **25** (163 mg, 41%) as a white solid: mp >220 °C (dec); $[\alpha]^{28}_D$ 102.31° (*c* 0.50, $CHCl_3$); UV (MeOH) λ_{max} 276 nm; ^{1}H NMR ($CDCl_3$) δ 7.71 (d, J = 7.0 Hz, 1H, 5-H), 6.04 (m, 1H, 2′-H), 5.90 (m, 1H, 1′-H), 5.63 (d, J = 7.0 Hz, 1H, 6-H), 5.59 (m, 1H, 3′-H), 3.49 (dd, J = 3.9, 8.9 Hz, 1H, 6′-Ha), 3.31 (dd, J = 4.4, 8.8, Hz, 1H, 6′-Hb), 2.94 (m, 1H, 4′-H), 2.74 (dt, J = 14.4, 9.5, 9.4 Hz, 1H, 5′-Ha), 1.45 (dt, J = 14.3, 5.5, 5.1 Hz, 1H, 5′-Hb), 1.16 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m/z* 264.1714; Calcd for $C_{14}H_{22}N_3O_2$, *m/z* 264.1712 $(M + H)^+$. Anal. ($C_{14}H_{21}N_3O_2$) C, H, N.

(1′*S*,4′*R*)-1-[4-(Hydroxymethyl)cyclopent-2-enyl]cytosine (26). Conversion of **25** (136 mg, 0.52 mmol) to **26** was accomplished using a procedure similar to that described for **10**. The obtained residue was purified by silica gel column chromatography with 10% MeOH in $CHCl_3$ to give **26** (101 mg, 94%) as a white solid:. mp 150−153 °C; $[\alpha]^{28}_D$ 133.89° (*c* 0.44, MeOH); UV (H_2O) λ_{max} 284.5 (ϵ 10022) (pH 2), 274.5 (ϵ 7419) (pH 7), 274.5 nm (ϵ 7141) (pH 11); ^{1}H NMR (DMSO-d_6) δ 7.46 (d, J = 7.3 Hz, 1H, 5-H), 6.08 (m, 1H, 2′-H), 5.73 (d, J = 7.3 Hz, 1H, 6-H), 5.66 (m, 1H, 3′-H), 5.54 (m, 1H, 1′H), 4.70 (t, J = 5.0 Hz, 1H, OH, D_2O exchangeable), 4.12 (br s, 2H, NH_2, D_2O exchangeable), 3.38 (m, 2H, 6′-Ha,b), 2.77 (m, 1H, 4′-H), 2.47 (m, 1H, 5′-Ha), 1.25 (m, 1H, 5′-Hb); HR-FAB MS Obsd, *m/z* 208.1078; Calcd for $C_{10}H_{13}N_3O_2$, *m/z* 208.1086 $(M + H)^+$. Anal. ($C_{10}H_{15}N_3O_2 \cdot 0.2H_2O$) C, H, N.

(1′*S*,4′*R*)-1-[4-(Hydroxymethyl)cyclopentan-1-yl]cytosine (27). Compound **26** (52 mg, 0.25 mmol) in MeOH (15 mL) was hydrogenated at 15 psi in the presence of 10% Pd/C (40 mg) for 1 h at room temperature. The reaction mixture was filtered, and the filtrate was evaporated. The residue was purified by silica gel column chromatography with 8−10% MeOH in $CHCl_3$ to give **27** (45 mg, 85.6%) as a solid: mp 103−105 °C; $[\alpha]^{28}_D$ 41.29° (*c* 0.22, MeOH); UV (H_2O) λ_{max} 285 (ϵ 12707) (pH 2), 275 (ϵ 8529) (pH 7), 275.5 nm (ϵ 9402) (pH 11); ^{1}H NMR (DMSO-d_6) δ 7.63 (d, J = 7.3 Hz, 1H, 6-H), 7.00 (br s, 2H, NH_2, D_2O exchangeable), 5.68 (d, J = 7.1 Hz, 1H, 5-H), 4.77 (m, 1H, 1′-H), 4.55 (t, J = 5.3 Hz, 1H, OH, D_2O exchangeable), 3.35 (m, 2H, 6′-Ha,b), 2.07−1.23 (m, 7H, 2′-Ha,b, 3′-Ha,b, 4′-H, and 5′-Ha,b); HR-FAB MS Obsd, *m/z* 210.1243; Calcd for $C_{10}H_{16}N_3O_2$, *m/z* 210.1243 $(M + H)^+$. Anal. ($C_{10}H_{15}N_3O_2 \cdot 0.1CHCl_3$) C, H, N.

(1′*S*,2′*R*,3′*S*,4′*S*)-9-[4-(*tert*-Butoxymethyl)-2,3-dihydroxycyclopentan-1-yl]-6-chloropurine (29). A solution of compound **28** (1.53 g, 4.01 mmol) in a mixture of concentrated HCl (2.62 mL) and MeOH (170 mL) was stirred at room temperature for 3 h. The reaction mixture was cooled in an ice−water bath and then neutralized with $NaHCO_3$ solid. The mixture was concentrated to dryness, and the residue was purified by silica gel column chromatography with 1−3% MeOH in $CHCl_3$ to give **29** (1.19 g, 86.8%) as a foam: $[\alpha]^{25}_D$ 19.92° (*c* 0.67, $CHCl_3$); UV (MeOH) λ_{max} 263.5 nm; ^{1}H NMR (DMSO-d_6 + D_2O) δ 8.79 and 8.77 (two s, 2H, 2-H and 8-H), 4.85 (dd, J = 9.5, 18.7 Hz, 1H, 1′-H), 3.88 (dd, J = 5.0, 9.2 Hz, 1H, 2′-H), 3.80 (dd, J = 2.4, 4.9 Hz, 1H, 3′-H), 3.36 (m, 2H, 6′-Hab), 2.35 (dt, J = 8.9, 8.9, 13.0 Hz, 1H, 5-Ha), 2.08 (m, 1H, 4′-H), 1.78 (m, 1H, 5-Hb), 1.15 (s, 9H, *tert*-butyl); FAB MS *m/z* 341 $(M + H)^+$.

(1′*S*,4′*R*)-9-[4-(*tert*-Butoxymethyl)cyclopent-2-enyl]-6-chloropurine (31). Method a. A solution of diethyl azodicarboxylate (DEAD) (512 mg, 2.94 mmol) in dioxane (4.5 mL) was slowly added to a suspension of compound **8** (250 mg, 1.47 mmol), triphenylphosphine (770 mg, 2.94 mmol), and 6-chlo-

ropurine (454 mg, 2.94 mmol) in dry dioxane (15 mL). The mixture was stirred at room temperature for 10 h. The solvent was removed under reduced pressure, and the residue was purified by preparative TLC with 30% EtOAc in hexanes to give **31** (156 mg, 34.6%) as white solid.

Method b. A suspension of compound **29** (880 mg, 2.58 mmol) and pyridinium *p*-toluene-sulfonate (710 mg, 2.83 mmol) in trimethyl orthoformate (3 mL) was stirred at room temperature for 2 h. The reaction mixture was diluted with EtOAc (100 mL) and washed with saturated $NaHCO_3$ solution (2 × 15 mL) and brine (15 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to dryness. The residue was coevaporated with benzene (2 × 15 mL) and then treated with Ac_2O (14 mL). The mixture was heated at 120−130 °C for 12 h and then concentrated to dryness. The residue was purified by silica gel column chromatography with 15% EtOAc in hexanes to give **31** (429 mg, 54.2%) as a white solid: mp 111−114 °C; $[\alpha]^{22}_D$ 17.69° (*c* 1.21, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.75 (s, 1H, 2-H), 8.45 (s, 1H, 8-H), 6.02 (m, 1H, 2′-H), 5.84 (m, 2H, 1′-H and 3′-H), 3.53 (dd, J = 4.2, 8.9 Hz, 1H, 6′-Ha), 3.39 (dd, J = 4.6, 8.9 Hz, 1H, 6′-Hb), 3.10 (m, 1H, 4′-H), 2.87 (dt, J = 14.3, 9.2, 9.2 Hz, 1H, 5′-Ha), 1.78 (m, 1H, 5′-Hb), 1.18 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 307.1326; Calcd for $C_{15}H_{20}N_4ClO$, *m*/*z* 307.1326 $(M + H)^+$. Anal. ($C_{15}H_{19}N_4ClO$) C, H, N.

(1′*S*,4′*R*)-9-[4-(*tert*-Butoxymethyl)cyclopent-2-enyl]-adenine (32). A solution of compound **31** (145 mg, 0.47 mmol) and saturated NH_3 in methanol (20 mL) was heated at 80−90 °C in a steel bomb for 20 h. After cooling, the solvent was removed under vacuum and the residue was purified by silica gel column chromatography with 0−1% MeOH in $CHCl_3$ to give compound **32** (112 mg, 82.5%) as a white solid: mp 182 °C; UV (MeOH) λ_{max} 261 nm; $[\alpha]^{24}_D$ 19.86° (*c* 0.70, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.36 (s, 1H, 2-H), 8.04 (s, 1H, 8-H), 6.16 (m, 1H, 2′-H), 5.82 (m, 1H, 3′-H), 5.74 (m, 1H, 1′-H), 5.61 (br s, 2H, NH_2, D_2O exchangeable), 3.46 (dd, J = 4.8, 8.8 Hz, 1H, 6′-Ha), 3.35 (dd, J = 5.1, 8.8 Hz, 1H, 6′-Hb), 3.04 (m, 1H, 4′-H), 2.82 (dt, J = 14.1, 9.1, 9.1 Hz, 1H, 5′-Ha), 1.69 (m, 1H, 5′-Hb), 1.16 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 288.1818; Calcd for $C_{15}H_{22}N_5O$, *m*/*z* 288.1824 $(M + H)^+$. Anal. ($C_{15}H_{21}N_5O$) C, H, N.

(1′*S*,4′*R*)-9-[4-(*tert*-Butoxymethyl)cyclopent-2-enyl]-9*H*-purine-6-thiol (33). A solution of compound **31** (165 mg, 0.54 mmol) and thiourea (52 mg, 0.67 mmol) in EtOH (17 mL) was refluxed for 1 h and cooled in an ice−water bath. The white precipitate formed was filtered and washed with EtOH (2 mL) to give a white solid of **33** (152 mg, 93%): mp 220 °C (dec); UV (MeOH) λ_{max} 325.0 nm; $[\alpha]^{28}_D$ −89.08° (*c* 0.21, $CHCl_3$); ^{1}H NMR (DMSO-d_6) δ 8.23 (s, 1H, 2-H), 8.05 (s, 1H, 8-H), 6.19 (m, 1H, 2′-H), 5.80 (m, 1H, 3′-H), 5.68 (m, 1H, 1′-H), 4.48 (dd, J = 8.7, 4.8 Hz, 1H, 6′-Ha), 3.38 (dd, J = 8.9, 5.0 Hz, 1H, 6′-Hb), 3.05 (m, 1H, 4′-H), 2.82 (dt, J = 14.1, 9.3, 9.2 Hz, 1H, 5′-Ha), 1.73 (m, 1H, 5′-Hb), 1.18 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 305.1410; Calcd for $C_{15}H_{21}N_4OS$, *m*/*z* 305.1436 $(M + H)^+$.

(1′*S*,4′*R*)-9-[4-(Hydroxymethyl)cyclopent-2-enyl]adenine (34). Conversion of **32** (50 mg, 0.18 mmol) to **34** was accomplished using a procedure similar to that described for **10**. The residue obtained was purified by silica gel column chromatography with 3−5% MeOH in $CHCl_3$ to give **34** (34.5 mg, 86%) as a white solid: mp 189−192 °C; $[\alpha]^{24}_D$ 4.81° (*c* 0.52, MeOH); UV (H_2O) λ_{max} 260.5 (ϵ 14944) (pH 2), 261.5 (ϵ 16043) (pH 7), 261.5 nm (ϵ 15151) (pH 11); ^{1}H NMR (DMSO-d_6) δ 8.13 (s, 1H, 2-H), 8.04 (s, 1H, 8-H), 7.21 (br s, 2H, NH_2, D_2O exchangeable), 6.14 (m, 1H, 2′-H), 5.92 (m, 1H, 3′-H), 5.58 (m, 1H, 1′-H), 4.75 (t, J = 5.4 Hz, 1H, OH, D_2O exchangeable), 3.46 (m, 2H, 6′-Ha,b), 2.90 (m, 1H, 4′-H), 2.67 (dt, J = 13.7, 8.8, 8.6 Hz, 1H, 5′-Ha), 1.63 (m, 1H, 5′-Hb); ^{13}C NMR (DMSO-d_6) δ 154.80, 151.34, 151.31, 137.96, 137.44, 128.63, 117.80, 62.84, 58.12, 46.69, 33.29; HR-FAB MS Obsd, *m*/*z* 232.1181; Calcd for $C_{11}H_{14}N_5O$, *m*/*z* 232.1198 $(M + H)^+$. Anal. ($C_{11}H_{13}N_5O$) C, H, N.

(1′*S*,4′*R*)-9-[4-(Hydroxymethyl)cyclopentan-1-yl]-9*H*-purine-6-thiol (35). Conversion of **33** (143 mg, 0.47 mmol) to **35** was accomplished using a procedure similar to that described for **10**. The residue obtained was purified by silica gel column chromatography with 3% MeOH in $CHCl_3$ to give **35** (110 mg, 94%) as a solid: mp 235−238 °C; $[\alpha]^{28}_D$ −41.61° (*c* 0.22, Pyr); UV (H_2O) λ_{max} 322.5 (ϵ 12953) (pH 2), 320.0 (ϵ 19421) (pH 7), 310.5 nm (ϵ 20659) (pH 11); ^{1}H NMR (DMSO-d_6) δ 13.72 (br s, 1H, NH, D_2O exchangeable), 8.20 (s, 1H, 2-H), 8.19 (s, 1H, 8-H), 6.17 (m, 1H, 2′-H), 5.92 (m, 1H, 3′-H), 5.58 (m, 1H, 1′-H), 4.74 (t, J = 5.3 Hz, 1H, OH, D_2O exchangeable), 3.45 (t, J = 5.6 Hz, 2H, 6′-Ha,b), 2.90 (m, 1H, 4′-H), 2.67 (dt, J = 13.8, 8.8, 8.7 Hz, 1H, 5′-Ha), 1.63 (dt, J = 13.8, 5.6, 5.6 Hz, 1H, 5′-Hb); HR-FAB MS Obsd, *m*/*z* 249.0821; Calcd for $C_{11}H_{13}N_4O_2$, *m*/*z* 249.0810 $(M + H)^+$. Anal. ($C_{11}H_{12}N_4OS$) C, H, N.

(1′*S*,4′*R*)-9-[4-(Hydroxymethyl)cyclopentan-1-yl]adenine (36). Conversion of **34** (55 mg, 0.24 mmol) to **36** was accomplished using a procedure similar to that described for **22**. The residue obtained was purified by silica gel column chromatography with 3−5% MeOH in $CHCl_3$ to give **36** (54 mg, 81%) as a white solid: mp 124−126 °C; $[\alpha]^{28}_D$ −1.56° (*c* 0.29, MeOH); UV (H_2O) λ_{max} 260 (ϵ 15415) (pH 2), 261 (ϵ 16055) (pH 7), 261 nm (ϵ 16360) (pH 11); ^{1}H NMR (DMSO-d_6) δ 8.23 (s, 1H, 2-H), 8.12 (s, 1H, 8-H), 7.21 (br s, 2H, NH_2, D_2O exchangeable), 4.79 (m, 1H, 1′-H), 4.63 (br s, 1H, OH, D_2O exchangeable), 3.44 (m, 2H, 6′-Ha,b), 1.61−2.33 (m, 7H, 2′-Ha,b, 3′-Ha,b, 4′-H, and 5′-Ha,b); HR-FAB MS Obsd, *m*/*z* 234.1351; Calcd for $C_{11}H_{16}N_5O$, *m*/*z* 234.1355 $(M + H)^+$. Anal. ($C_{11}H_{15}N_5O$·0.3MeOH) C, H, N.

(1′*S*,4′*R*)-9-[4-(Hydroxymethyl)cyclopent-2-enyl]hypoxanthine (38). A mixture of chloropurine analogue **31** (150 mg, 0.49 mmol), 2-mercaptoethanol (140 mg, 1.9 mmol), and NaOMe (105 mg, 1.95 mmol) in methanol (25 mL) was refluxed for 24 h. The mixture was cooled, neutralized with glacial AcOH, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography with 3% MeOH in $CHCl_3$ to give **37** (140 mg, 99.3%) as a white solid which was used for the next step without further purification. Conversion of **37** (135 mg, 0.47 mmol) to **38** was accomplished using a procedure similar to that described for **10**. The obtained residue was purified by silica gel column chromatography with 10% MeOH in $CHCl_3$ to give **38** (105 mg, 96.6%) as a white solid: mp 270−272 °C; $[\alpha]^{28}_D$ −3.83° (*c* 0.38, MeOH); UV (H_2O) λ_{max} 250.5 (ϵ 12128) (pH 2), 250.0 (ϵ 12873) (pH 7), 255.0 nm (ϵ 12095) (pH 11); ^{1}H NMR (DMSO-d_6) δ 12.29 (br s, 1H, NH, D_2O exchangeable), 8.04 (s, 1H, 2-H), 7.99 (s, 1H, 8-H), 6.15 (m, 1H, 2′-H), 5.91 (m, 1H, 3′-H), 5.56 (m, 1H, 1′-H), 4.73 (t, J = 5.2 Hz, 1H, OH, D_2O exchangeable), 3.45 (t, J = 5.7 Hz, 2H, 6′-Ha,b), 2.87 (m, 1H, 4′-H), 2.67 (dt, J = 13.7, 8.7, 8.7 Hz, 1H, 5′-Ha), 1.63 (dt, J = 13.7, 5.8, 5.8 Hz, 1H, 5′-Hb); HR-FAB MS Obsd, *m*/*z* 233.1047; Calcd for $C_{11}H_{13}N_4O_2$, *m*/*z* 233.1039 $(M + H)^+$. Anal. ($C_{11}H_{12}N_4O_2$) C, H, N.

(1′*S*,4′*R*)-9-[4-(Hydroxymethyl)cyclopentan-1-yl]hypoxanthine (39). Conversion of **38** (66 mg, 0.28 mmol) to **39** was accomplished using a procedure similar to that described for **22**. The obtained residue was purified by silica gel column chromatography with 10% MeOH in $CHCl_3$ to give **39** (54 mg, 81%) as a white solid: mp 246−248 °C; $[\alpha]^{28}_D$ −1.04° (*c* 0.20, MeOH); UV (H_2O) λ_{max} 249.5 (ϵ 11108) (pH 2), 249.5 (ϵ 11999) (pH 7), 254.5 nm (ϵ 15312) (pH 11); ^{1}H NMR (DMSO-d_6) δ 12.26 (br s, 1H, NH, D_2O exchangeable), 8.18 (s, 1H, 2-H), 8.02 (s, 1H, 8-H), 4.78 (m, 1H, 1′-H), 4.63 (t, 1H, OH, D_2O exchangeable), 3.41 (m, 2H, 6′-Ha,b), 2.28−1.62 (m, 7H, 2′-Ha,b, 3′-Ha,b, 4′-H, and 5′-Ha,b); HR-FAB MS Obsd, *m*/*z* 235.1196; Calcd for $C_{11}H_{15}N_4O_2$, *m*/*z* 235.1195 $(M + H)^+$. Anal. ($C_{11}H_{14}N_4O_2$·0.1H_2O) C, H, N.

(1′*S*,2′*R*,3′*S*,4′*S*)-9-[4-(*tert*-Butoxymethyl)-2,3-dihydroxycyclopentan-1-yl]guanine (42). A solution of compound **40** (880 g, 2.54 mmol), dimethyl formamide (10.3 mL), triethyl orthoformate (20.5 mL), and concentrated HCl (0.82 mL) was stirred at 0−5 °C for 8 h and then at room temperature for 12 h. The solvent was removed, and the residue was stirred with 50% HAc (47 mL) for 16 h. The mixture was concentrated to dryness, and the residue was purified by silica gel column chromatography with 1−2% MeOH in $CHCl_3$ to give

(1′*S*,2′*R*,3′*S*,4′*S*)-9-[4-(*tert*-butoxymethyl)-2,3-dihydroxycyclopentan-1-yl]-2-amino-6-chloropurine (**41**) (638 g, 70.5%) as a foam: UV (MeOH) λ_{max} 306.5 nm. A solution of the above 2-amino-6-chloropurine analogue **41** (275 mg, 0.77 mmol), 2-mercaptoethanol (300 mg, 3.84 mmol), NaOMe (325 mg, 6.0 mmol), and MeOH (40 mL) was refluxed for 18 h. The mixture was cooled and neutralized with glacial acetic acid, and the solvent was removed. The residue was purified by silica gel column chromatography with 8−10% MeOH in $CHCl_3$ to give **42** (150 mg, 58%) as a white solid: mp 237−240 °C; $[\alpha]^{25}_D$ 16.13° (*c* 0.48, MeOH); UV (MeOH) λ_{max} 254 nm; ^{1}H NMR (DMSO-d_6) δ 7.79 (s, 1H, 8-H), 6.42 (br s, 2H, NH_2), 4.93 (d, J = 5.9 Hz, 1H, OH, D_2O exchangeable), 4.60 (d, J = 3.3 Hz, 1H, OH, D_2O exchangeable), 4.53 (dd, J = 9.6, 18.4 Hz, 1H, 1′-H), 4.20 (m, 1H, 2′-H), 3.75 (m, 1H, 3′-H), 3.47 (m, 2H, 6′-Hab), 2.24 (m, 1H, 5-Ha), 2.00 (m, 1H, 4′-H), 1.37 (m, 1H, 5-Hb), 1.15 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 338.1843; Calcd for $C_{15}H_{24}N_5O_4$, *m*/*z* 338.1828 $(M + H)^+$.

(1′*S*,4′*R*)-9-[4-(*tert*-Butoxymethyl)cyclopent-2-enyl]guanine (44). Conversion of **42** (140 mg, 0.41 mmol) to **44** was accomplished using a procedure similar to that described for **20**. The residue obtained was heated with a mixture of aqueous ammonia (1 mL), methanol (6 mL), and H_2O (1 mL) at 65 °C for 1.25 h. The solvent was removed, and the residue was purified by silica gel column chromatography with 5% MeOH in $CHCl_3$ to give **44** (56 mg, 45%): UV (MeOH) λ_{max} 254 nm; ^{1}H NMR ($CDCl_3$) δ 12.08 (br s, 1H, NH), 7.68 (s, 1H, 8-H), 6.38 (br s, 2H, NH_2), 6.12 (m, 1H, 2′-H), 5.82 (m, 1H, 1′-H), 5.48 (m, 1H, 3′-H), 3.30−3.50 (m, 2H, 6′-H), 2.98 (m, 1H, 4′-H), 2.75 (dt, J = 8.8, 9.0, 14.0 Hz, 1H, 5′-Ha), 1.64 (m, 1H, 5′-Hb), 1.16 (s, 9H, *tert*-butyl); HR-FAB MS Obsd, *m*/*z* 304.1780; Calcd for $C_{15}H_{22}N_5O_2$, *m*/*z* 304.1774 $(M + H)^+$.

(1′*S*,4′*R*)-9-[4-(Hydroxymethyl)cyclopent-2-enyl]guanine, L-Carbovir (45). Conversion of **44** (40 mg, 0.13 mmol) to **45** was accomplished using a procedure similar to that described for **10**. The residue obtained was purified by silica gel column chromatography with 10% MeOH in $CHCl_3$ to give **45** (27 mg, 84%) as a solid: mp 223−224 °C (decomp.) [lit[23] for D-(−) form, 210−220 °C (decomp.); lit[7] for (±) form, 254−256 °C; lit[22] for l-form, 265−270 °C]; $[\alpha]^{28}_D$ 59.03° (*c* 0.51, MeOH) [lit[25] for L-carbovir, $[\alpha]^{20}_D$ 60° (*c* 0.25, MeOH); lit[22] for L-carbovir, $[\alpha]^{23}_D$ 61.1° (*c* 0.3, MeOH)]; UV (MeOH) λ_{max} 253.5 nm; ^{1}H NMR (DMSO-d_6) δ 10.35 (br s, 1H, NH, D_2O exchangeable), 7.58 (s, 1H, 8-H), 6.43 (br s, 2H, NH_2), 6.10 (m, 1H, 2′-H), 5.86 (m, 1H, 3′-H), 5.34 (m, 1H, 1′-H), 4.71 (t, J = 5.4 Hz, 1H, OH, D_2O exchangeable), 3.43 (t, J = 5.8 Hz, 2H, 6′-Ha,b), 2.85 (m, 1H, 4′-H), 2.58 (m, 1H, 5′-Ha), 1.56 (dt, J = 13.7, 5.8, 5.7 Hz, 1H, 5′-Hb); HR-FAB MS Obsd, *m*/*z* 248.1148; Calcd for $C_{11}H_{14}N_5O_2$, *m*/*z* 248.1147 $(M + H)^+$.

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