SYNTHESIS OF NOVEL RACEMIC CONFORMATIONALLY LOCKED CARBOCYCLIC NUCLEOSIDES DERIVED FROM 7-SUBSTITUTED BICYCLO[2.2.1]HEPT-5-ENE-2,2-DIMETHANOLS

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(1*R**,4*R**,7*S**)-7-Aminobicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**15**) was prepared in four easy steps from bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**10**). Reaction of amine **15** with ethyl *N*-((*E*)-3-ethoxymethacryloyl)carbamate afforded thymine derivatives **17a**. The amine **15** was used to construct 6-chloro-9*H*-purine derivative **19a**, 2-amino-6-chloro-9*H*-purine derivative **22a**. Ammonolysis of **19a** led to the adenine derivative **20a**. Treatment of **22a** with trifluoroacetic acid afforded guanine nucleoside **23a**. (1*R**,4*R**,7*S**)-7-[6-(Cyclopropylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**21a**) and (1*R**,4*R**,7*S**)-7-[2-amino-6-(cyclopropylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**24a**) were prepared by aminolysis of **19a** and **22a**. Saturated nucleosides **17b**, **20b**, **21b**, **23b**, **24b** were obtained by hydrogenation on palladium catalyst.

Keywords: Carbanucleosides; Carbocyclic nucleosides; Nucleosides; Norbornenes; Locked nucleosides; Conformation analysis; Wagner–Meerwein rearrangement; Purines; Thymine; Antiviral activity.

Carbocyclic nucleoside analogues, in which a methylene group replaces the hemiacetal oxygen atom of the furanose ring, are an important class of potentially active therapeutic agents. For example, carbocyclic 2,3-didehydro-2,3-dideoxyguanosine (carbovir) (**1**) and the structurally related abacavir (ZIAGEN™) (**2**) are potent and selective inhibitors of HIV-1 replication and have cytopathic effects in a variety of human *t*-lymphoblastoic cell lines[1,2]. U.S. Food and Drug Administration approved ZIAGEN for the treatment of HIV-1 infections. Also other synthetic carbocyclic nucleoside analogues such as BCA (**3**)[3], Lobucavir (**4**)[4], bicyclic compound **5** (ref.[5]), and cyclohexene nucleoside analogues **6** and **7** (ref.[6]) are potent inhibitors of virus replication (Chart 1).

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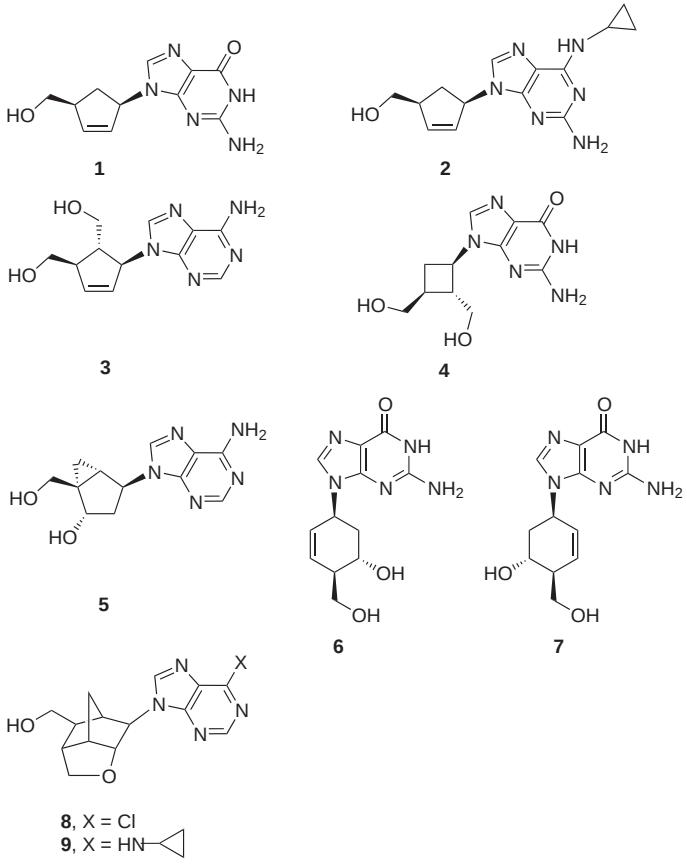


CHART 1

The carbocyclic nucleoside **1**–**3** and **5** are conformationally restricted analogues of natural nucleosides. Compound **4** (Lobucavir) is a conformationally locked analogue of the antiviral acyclic nucleoside ganciclovir[4]. Recently, novel conformationally locked carbocyclic nucleoside analogues containing the 2-oxabicyclo[2.2.1]heptane ring system were described[7]. Bisphosphate of the 2-iodo-(6-methylamino)purine analogue of this ring system displayed a potent binding affinity to the human $P2Y_1$ receptor[8]. We reported the synthesis of novel racemic conformationally locked carbocyclic purine nucleoside analogues derived from 5-oxatricyclo[4.2.1.$0^{3,7}$]-nonane-3-methanol[9]. Its 6-chloropurine (**8**) and 6-(cyclopropylamino)-purine (**9**) derivatives show a certain anti-HIV-1 and anti-HIV-2 activity in human T-lymphocyte (CEM) cells.

This study concerns a synthesis of novel racemic conformationally locked nucleoside analogues with bicyclo[2.2.1]hept-2-ene or -heptane ring substi-

tuted with nucleobase at position 7. These bicyclic compounds are conformationally locked carbapentofuranose nucleoside analogues. General formulae of target compounds are shown in Chart 2.

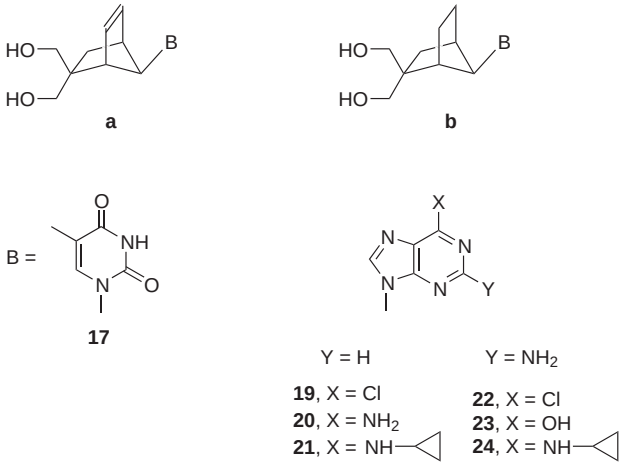
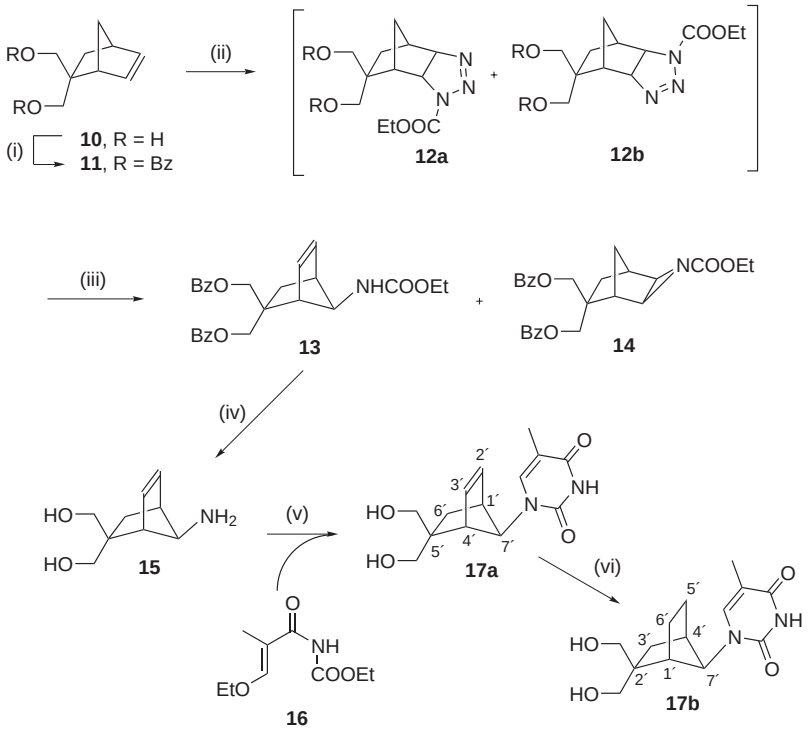


CHART 2

The synthetic strategy was based on construction of the nucleobases from appropriate aminobicycloalkene. Key intermediate *syn*-amine **7** was prepared in three simple steps from commercially available bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**10**) (Scheme 1). Diol **10** was benzoylated[10] with benzoyl chloride in pyridine and the dibenzoyl derivative **11** was treated with ethyl azidoformate[11]. Intermediate triazoline derivatives **12a** and **12b** were treated without isolation with silica gel (Wagner–Meerwein rearrangement[12]). This reaction afforded a mixture of carbamates **13** and **14**. The products were easily separated by chromatography on a silica gel column. The ratio of these products (2:3) was in agreement with literature data[13] for this reaction on similar bicyclic systems. Attempts[13] to increase yield of carbamate **13** by changing reaction conditions (different solvents and acids) or to convert aziridinecarboxylate **14** to carbamate **13** by treatment with various organic and inorganic acids or trimethylsilyl bromide were unsuccessful. Free amine **15** was obtained in good yield (83%) by deprotection with potassium hydroxide.

Thymine nucleoside **17a** was prepared in moderate yield (50%) by reaction of amine **15** with carbamate **16** in 1,4-dioxane at 100 °C and following pyrimidine ring closure catalyzed with Dowex 50 (ref.[10]). Saturated nucleoside **17b** was obtained by hydrogenation using palladium(II) hydroxide as a catalyst (71%).

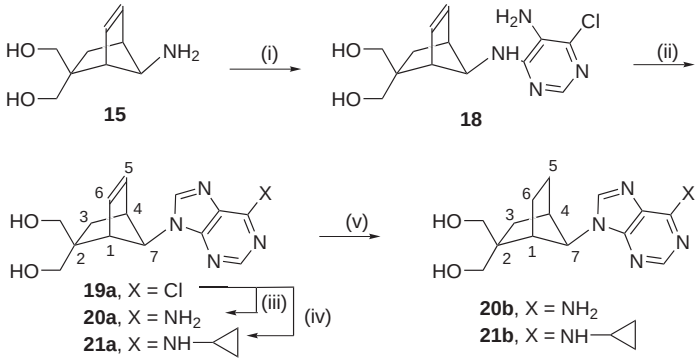


(i) BzCl, pyridine, 91%; (ii) ethyl azidoformate, toluene; (iii) silica gel, CH_2Cl_2, 33% of **13**, 47% of **14**; (iv) KOH, EtOH-H_2O, 83%; (v) 1. dioxane, 100 °C, 2. Dowex 50, dioxane, 100 °C, 50%; (vi) H_2, $Pd(OH)_2$/C, MeOH-H_2O, 71%

SCHEME 1

Amine **15** was treated[9,14] with 4,6-dichloropyrimidin-5-amine in ethanol in the presence of triethylamine to give the pyrimidylamino derivative **18** in excellent yield (97%) (Scheme 2). Ring closure of **18** with triethyl orthoformate in the presence of concentrated hydrochloric acid gave 6-chloropurine derivative **19a** (80%). Ammonolysis of **19a** with liquid ammonia at 75 °C led to adenine derivative **20a** (95%). The reaction of 6-chloropurine **19a** with cyclopropylamine gave cyclopropylamino nucleoside **21a** (92%). Both unsaturated nucleosides were hydrogenated to give saturated nucleosides in excellent yields – **20b** (87%) and **21b** (86%).

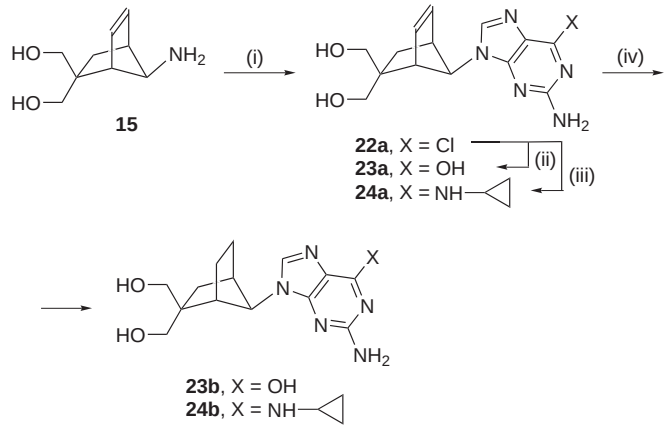
The commonly used procedure[14,15] for preparation of 2-amino-6-chloropurine analogues from amino derivatives is based on condensation of amine with 4,6-dichloropyrimidin-2-amine followed by treatment with 4-chlorobenzene-1-diazonium chloride, reduction of the resulting azo de-



(i) 4,6-dichloropyrimidin-5-amine, Et_3N, EtOH, 100 °C, 97%; (ii) 1. $CH(OEt)_3$, HCl, 2. HCl, THF-H_2O, 79%; (iii) NH_3 (l), 75 °C, 95%; (iv) cyclopropylamine, MeOH, 92%; (v) H_2, $Pd(OH)_2$/C, MeOH-H_2O, 87% of **20b**, 86% of **21b**

SCHEME 2

rivative, and cyclization with triethyl orthoformate. Guanine derivatives **22**–**24a** were synthesized by a simpler method described by Legrawerend and coworkers[16]. This procedure reduces the number of reaction steps and increases overall yield of the purine nucleoside (Scheme 3). Amine **15** was coupled with 4,6-dichloropyrimidine-2,5-diamine in the presence of triethylamine in ethanol, the obtained product was purified by chromatography and immediately was treated with triethyl orthoformate and concen-



(i) 1. 4,6-dichloropyrimidin-2,5-diamine, Et_3N, EtOH, 100 °C, 2. $CH(OEt)_3$, HCl, 3. HCl, THF-H_2O, 78%; (ii) CF_3COOH-H_2O, r.t., 94%; (iii) cyclopropylamine, MeOH, 94%; (iv) H_2, $Pd(OH)_2$/C,DMF, 87% of **23b** or MeOH-H_2O, 80% of **24b**

SCHEME 3

trated hydrochloric acid to give 2-amino-6-chloropurine nucleoside **22a** in good overall yield (78% based on amine **15**). The nucleoside analogue **22a** was converted to guanine compound **23a** (94%) by treatment with trifluoroacetic acid[17]. The reaction of **22a** with cyclopropylamine in methanol afforded compound **24a** (94%). Saturated derivatives **23b** and **24b** were prepared by hydrogenation (yields 87 and 80%, respectively) using the same method as described above for preparation of saturated adenine nucleosides. Compound **23a** was hydrogenated in a large volume of dimethylformamide because of its insolubility in various water–methanol mixtures.

The structure of the prepared compounds was determined by ^{1}H and ^{13}C NMR spectroscopy. Coupling constants *J*(H,H) were determined in decoupling experiments. Assignment signal to protons and carbon atoms in NMR spectra of **20b** was performed by HETCOR. All the unsaturated nucleoside analogues have long-range interaction between proton H-7 and hydrogens H-5, H-6 attached to the double bond (*J* = 0.7 to 1.0 Hz). The NOE experiment with the 6-chloropurine derivative **19a** showed correlation between the proton H-8′ (8.47 ppm) and protons H-5 (6.02 ppm) and H-6 (6.07 ppm) indicating *syn*-position of the nucleobase (Fig. 1). Correlation was also observed between H-8′ and H-1 (3.43 ppm), H-4 (3.56 ppm) and H-7 (4.80 ppm). No NOE correlation between H-8′ and H-3*exo* was observed.

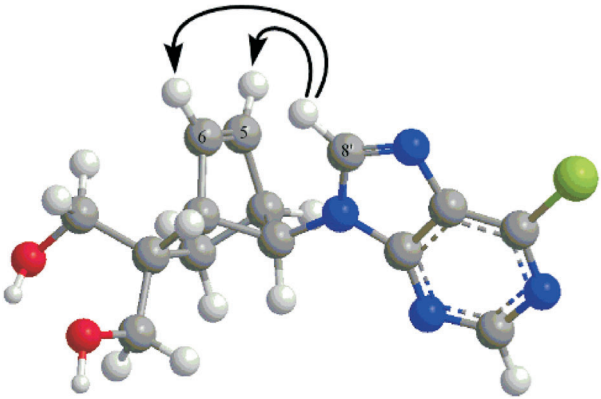


FIG. 1
NOE interaction between the proton H-8′ and protons H-5 and H-6 in chloropurine **19a**

We have synthesized a novel series of conformationally locked carbocyclic nucleosides based on the norbornene or norbornane skeleton. The target compounds were tested for inhibition of cell growth of the following cell cultures: mouse leukemia L1210 cells (ATCC CCL 240), human cervix carcinoma HeLaS3 cells (ATCC CCL 2.2), human promyelocytic leukemia HL60 cells (ATCC CCL 240), and human T lymphoblastoid CCRF-CEM cell line (ATCC CCL 119). None of the compounds exhibited a considerable activity[18]. The compounds were also tested for anti-HIV-1 and anti-HIV-2 activity in human T-lymphocyte (CEM) cells. Preliminary data showed that only compounds **19a** and **22a** exhibit a certain activity (**19a**, EC_{50} > 13 μM and CC_{50} = 30 ± 0.62 μM; **22a**, EC_{50} > 62 μM and CC_{50} was 139 ± 2.2 μM)[19].

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. NMR spectra (δ, ppm; *J*, Hz) were measured on a Varian Unity 500 instrument (500 MHz for ^{1}H and 125.7 MHz for ^{13}C) in hexadeuteriated dimethyl sulfoxide and referenced to the solvent signal (δ 2.50 and 39.70, respectively). Mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer using the FAB (ionization with Xe, accelerating voltage 8 kV, thioglycerol–glycerol 3:1 mixture or bis(2-hydroxyethyl) disulfide were used as a matrix). Column chromatography was performed on Silica gel 60 (Fluka) and thin-layer chromatography (TLC) on Silufol UV 254 foils (Kavalier, Votice). Solvents were evaporated at 2 kPa and bath temperature 30–60 °C; compounds were dried at 13 Pa and 50 °C.

(1*R**,4*R**)-(Bicyclo[2.2.1]hept-5-ene-2,2-diyl)dimethyl Dibenzoate (**11**)

Dibenzoate **11** (6.3 g, 87%) was prepared according to published procedure[10] from diol **10** (3.08 g, 20 mmol), m.p. 63–65 °C.

{(1*R**,4*R**,7*S**)-7-[(Ethoxycarbonyl)amino]bicyclo[2.2.1]hept-5-ene-2,2-diyl}dimethyl Dibenzoate (**13**) and [(1*R**,2*R**,4*S**,5*S**)-3-(Ethoxycarbonyl)-3-azatricyclo[3.2.1.0^{2,4}]-octane-6,6-diyl]dimethyl Dibenzoate (**14**)

A solution of dibenzoate **11** (3 g, 8.3 mmol) and ethyl azidoformate (3 ml, 29 mmol) in toluene (15 ml) was heated at 80 °C for 6 h and evaporated. Residue was dissolved in dichloromethane (15 ml) and silica gel (3 g) was added. After 2 h of stirring silica gel was filtered off and filtrate was evaporated. The products were separated by column chromatography on silica gel (400 g). Elution with toluene–ethyl acetate (15:1) afforded 1.76 g (47%) of **6** as an oil and following elution with toluene–ethyl acetate (10:1) gave 1.23 g (33%) of **5** as an oil.

{(1R,4R*,7RS*)-7-[(Ethoxycarbonyl)amino]bicyclo[2.2.1]hept-5-ene-2,2-diyl}dimethyl dibenzoate* (**13**). ^{1}H NMR: 0.98 d, 1 H, J_{gem} = 12.6 (H-3en); 1.12 t, 3 H, *J*(CH_3,CH_2) = 7.1 ($CH_2C\mathbf{H}_3$); 1.83 dd, 1 H, *J*(3ex,4) = 3.7 (H-3ex); 2.89 m, *J*(4,1) ~ *J*(4, 6) ~ *J*(4,7) ~ 1.0 (H-4); 2.97 brdq, 1 H, *J*(1,5) = 3.1, *J*(1,6) ~ *J*(1,7) ~ 1.0 (H-1); 3.91 brd, 1 H, *J*(7,NH) = 5.9 (H-7); 3.94 q, 2 H ($C\mathbf{H}_2CH_3$); 3.97 d, 1 H and 4.17 d, 1 H, J_{gem} = 11.4 (CH_2O); 4.56 d, 1 H and 4.60 d, 1 H, J_{gem} = 11.4 (CH_2O); 6.03 brdd, 1 H, *J*(6,5) = 5.7 (H-6); 6.16 brdd, 1 H, *J*(5,4) = 2.9 (H-5); 7.09 d, 1 H (NH); 7.48 t,

4 H, 7.64 t, 2 H, 7.94 d, 2 H and 7.96 d, 2 H (H-arom.). ^{13}C NMR: 14.84 ($CH_2\mathbf{C}H_3$); 31.27 (C-3); 44.82 (C-2); 45.90 (C-1); 49.85 (C-4); 59.61 ($\mathbf{C}H_2CH_3$); 67.13 (C-7); 67.21 (OCH_2); 68.10 (OCH_2); 128.90, 4 C, 129.34, 2 C, 129.36, 2 C, 129.71, 129.74 (C-arom); 131.28 (C-5); 133.53, 133.55 (C-arom); 134.43 (C-6); 156.29 (NH**C**OOEt); 165.59 (C=O); 165.75 (C=O). FAB MS, *m/z* (%): 450 (2) [M + H], 105 (100) [PhCO]. For $C_{26}H_{27}NO_6$ (449.5) calculated: 69.47% C, 6.05% H, 3.12% N; found: 69.71% C, 6.23% H, 2.87% N.

[(1R,2R*,4S*,5S*)-3-(Ethoxycarbonyl)-3-azatricyclo[3.2.1.0^{2,4}]octane-6,6-diyl]dimethyl dibenzoate* (**14**). ^{1}H NMR: 1.16 t, 3 H, *J*(CH_3,CH_2) = 7.1 ($CH_2C\mathbf{H}_3$); 1.22 dd, 1 H, *J*(7,8b) = 2.1, J_{gem} = 12.9 (H-7en); 1.31 dm, 1 H, J_{gem} = 10.7 (H-8b); 1.35 dm, 1 H (H-8a); 1.53 dd, 1 H, *J*(7ex,1) = 4.2 (H-7ex); 2.54 brdq, 1 H, *J*(1,2) ~ *J*(1,8a) ~ *J*(1,8b) ~ 1.3 (H-1); 2.68 brq, 1 H, *J*(5,4) = 1.2, *J*(5,8a) ~ *J*(5,8b) ~ 1.5 (H-5); 2.91 dd, 1 H, *J*(2,4) = 5.3 (H-2); 2.96 dd, 1 H (H-4); 4.02 m, 2 H ($C\mathbf{H}_2CH_3$); 4.28 d, 1 H and 4.34 d, 1 H, J_{gem} = 11.4 (CH_2O); 4.37 d, 1 H and 4.49 d, 1 H, J_{gem} = 11.5 (CH_2O); 7.46 t, 2 H, 7.49 t, 2 H, 7.63 t, 2 H, 7.65 t, 2 H, 7.94 d, 2 H, and 7.96 d, 2 H (H-arom.). ^{13}C NMR: 14.40 ($CH_2\mathbf{C}H_3$); 26.04 (C-8); 33.33 (C-7); 36.59 (C-1); 36.76 (C-4); 38.06 (C-6); 39.41 (C-5); 46.24 (C-6); 61.84 ($\mathbf{C}H_2CH_3$); 65.81 (OCH_2); 67.48 (OCH_2); 128.89, 2 C, 128.94, 2 C, 129.38, 2 C, 129.39, 2 C, 129.73, 129.69, 133.57, 133.54 (C-arom.); 161.68 (NH**C**OOEt); 165.63 (C=O); 165.79 (C=O). FAB MS, *m/z* (%): 450 (4) [M + H], 105 (100) [PhCO]. For $C_{26}H_{27}NO_6$ (449.5) calculated: 69.47% C, 6.05% H, 3.12% N; found: 69.78% C, 6.12% H, 2.89% N.

(1*R**,4*R**,7*S**)-7-Aminobicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**15**)

To a solution of carbamate **13** (3.48 g, 7.75 mmol) in ethanol–water (30 ml, 1:1) potassium hydroxide (3.1 g, 55 mmol) was added and the reaction mixture was refluxed for 10 h in argon atmosphere. Then second portion of potassium hydroxide (0.8 g, 14 mmol) was added and heating was continued for 4 h. The reaction mixture was neutralized with 6 M hydrochloric acid and solution was applied onto a Dowex 50 (H^+ form; 100 ml). The column was eluted with methanol–water (1:1, 300 ml), water (300 ml), methanol (300 ml) and then with 3.5 M methanolic ammonia. Fractions containing the product were evaporated to yield 1.08 g (82%) of the desired amine **15**. Crude amine was crystallized from ethanol–ether, m.p. 165–168 °C. ^{1}H NMR: 0.47 d, 1 H, J_{gem} = 12.2 (H-3*endo*); 1.30 brs, 2 H (NH_2); 1.41 dd, 1 H, *J*(3,4) = 3.7 (H-3*exo*); 2.37 m, 1 H (H-1); 2.47 m, 1 H (H-4); 3.20 m, 1 H (H-7); 3.01 d, 1 H and 3.12 d, 1 H, J_{gem} = 10.2 (CH_2O); 3.20 brs, 1 H (OH); 3.55 brs, 1 H (OH); 3.50 d, 1 H and 3.65 d, 1 H, J_{gem} = 10.4 (CH_2O); 6.01 m, 2 H (H-5, H-6). ^{13}C NMR: 31.55 (C-3); 48.54 (C-2); 49.02 (C-4); 52.49 (C-1); 64.26 (OCH_2); 65.38 (OCH_2); 68.58 (C-7); 132.52 (C-6); 132.80 (C-5). FAB MS, *m/z* (%): 170 (80) [M + H], 79 (100). For $C_9H_{15}NO_2$ (169.2) calculated: 63.88% C, 8.93% H, 8.28% N; found: 63.60% C, 9.07% H, 7.98% N.

1-[(1*R**,4*R**,7*S**)-5,5-Bis(hydroxymethyl)bicyclo[2.2.1]hept-2-en-7-yl]-5-methylpyrimidine-2,4(1*H*,3*H*)-dione (**17a**)

A solution of amine **15** (305 mg, 1.8 mmol) and acyl carbamate **16** (335 mg, 1.8 mmol) in 1,4-dioxane (15 ml) was heated at 100 °C for 3 h. Dowex 50 (H^+ form; 5 ml) was washed with 1,4-dioxane and then added to the mixture. The mixture was heated at 100 °C for 2.5 h, the resin was filtered off, washed with methanol and the collected filtrates were evaporated. The residue was crystallized from acetone to yield 250 mg (50%) of the thymine nucleoside **17a**, m.p. 198–199 °C. ^{1}H NMR: 0.63 d, 1 H, J_{gem} = 12.3 (H-6′*endo*); 1.66 dd, 1 H,

J(6′*exo*,1′) = 3.8 (H-6′*exo*); 1.72 d, 3 H, *J*(CH_3,6) = 1.0 (CH_3); 2.97 dm, 1 H, *J*(4′,1′) ~ *J*(4′,2′) ~ *J*(4′,7′) ~ 1.2, *J*(4′,3′) = 2.8 (H-4′); 3.16 m, 1 H, *J*(1′,3′) ~ *J*(1′,7′) ~ 1.2, *J*(1′,2′) = 2.7 (H-1′); 3.04 dd, 1 H, *J*(CH,OH) = 5.2 and 3.23 dd, 1 H, *J*(CH,OH) = 5.0, J_{gem} = 10.4 (CH_2O); 3.57 dd, 1 H, *J*(CH,OH) = 5.1 and 3.70 dd, 1 H, *J*(CH,OH) = 5.5, J_{gem} = 10.6 (CH_2O); 4.20 m, 1 H (H-7′); 4.40 t, 1 H (CH_2O**H**); 4.66 t, 1 H (CH_2O**H**); 6.01 ddt, 1 H, *J*(2′,7′) = 0.7, *J*(2′,3′) = 5.6 (H-2′); 6.06 ddt, 1 H, *J*(3′,7′) = 0.7 (H-3′); 7.18 brq, 1 H (H-6); 11.13 brs (NH). ^{13}C NMR: 12.19 (CH_3); 30.42 (C-6′); 44.75 (C-1′); 48.10 (C-4′); 48.14 (C-5′); 63.55 (CH_2O); 64.69 (CH_2O); 72.67 (C-7′); 106.84 (C-5); 132.17 (C-3′); 132.26 (C-2′); 141.45 (C-6); 151.51 (C-2); 164.30 (C-4). FAB MS, *m/z* (%): 279 (100) [M + H], 127 (98). For $C_{14}H_{18}N_2O_4 \cdot CH_3COCH_3$ (336.4) calculated: 60.70% C, 7.19% H, 8.33% N; found: 60.44% C, 7.14% H, 8.41% N.

(1*R**,4*R**,7*S**)-7-[(5-Amino-6-chloropyrimidin-4-yl)amino]bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**18**)

A mixture of amine **15** (510 mg, 3 mmol), 4,6-dichloropyrimidin-5-amine (984 mg, 6 mmol), and triethylamine (2.4 ml) in ethanol (18 ml) was heated in a pressure vessel at 105 °C for 6 days and, after cooling, it was evaporated. The residue was chromatographed on a column of silica gel (200 g) in ethyl acetate–acetone–ethanol–water (100:15:6:4) to afford 866 mg (97%) of **18** as a foam. Analytical sample was obtained by crystallization from ethyl acetate, m.p. 225–227 °C. ^{1}H NMR: 0.57 d, 1 H, J_{gem} = 12.2 (H-3*endo*); 1.60 dd, 1 H, *J*(3*exo*,4) = 3.8 (H-3*exo*); 2.68 brdq, 1 H, *J*(1,5) = 0.7, *J*(1,4) ~ *J*(1,7) ~ 1.5, *J*(1,6) = 2.9 (H-1); 2.90 m, 1 H, *J*(4,6) = 0.7, *J*(4,7) = 1.5, *J*(4,5) = 2.9 (H-4); 3.05 dd, 1 H, *J*(CH,OH) = 5.2 and 3.21 dd, 1 H, *J*(CH,OH) = 5.2, J_{gem} = 10.4 (CH_2O); 3.58 dd, 1 H, *J*(CH,OH) = 5.1 and 3.72 dd, 1 H, *J*(CH,OH) = 5.5, J_{gem} = 10.6 (CH_2O); 4.24 dm, 1 H, *J*(7,5) ~ *J*(7,6) ~ 0.7, *J*(7,NH) = 6.2 (H-7); 4.31 t, 1 H (CH_2O**H**); 4.62 t, 1 H (CH_2O**H**); 5.11 brs, 2 H (NH_2); 6.03 ddt, 1 H, *J*(5,6) = 5.7 (H-5); 6.09 ddt, 1 H (H-6); 6.57 d, 1 H (NH); 7.70 s, 1 H (H-2′). ^{13}C NMR: 30.85 (C-3); 45.82 (C-4); 48.24 (C-2); 49.23 (C-1); 63.07 (CH_2O); 65.07 (CH_2O); 67.81 (C-7); 123.63 (C-5′); 132.05 (C-6); 132.99 (C-6); 136.83 (C-4′); 145.76 (C-2′); 152.18 (C-6′). FAB MS, *m/z* (%): 299/297 (100/50) [M + H], 263 (73). For $C_{13}H_{17}ClN_4O_2$ (296.8) calculated: 52.62% C, 5.77% H, 11.95% Cl, 18.88% N; found: 52.56% C, 5.88% H, 11.77% Cl, 18.48% N.

(1*R**,4*R**,7*S**)-7-(6-Chloro-9*H*-purin-9-yl)bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**19a**)

To a suspension of pyrimidine **18** (800 mg, 2.7 mmol) in triethyl orthoformate (80 ml) concentrated hydrochloric acid (1.4 ml) was added and the reaction mixture was vigorously stirred for 3 days (suspension dissolved) at room temperature. The solution was evaporated and the residue was redissolved in a mixture of tetrahydrofuran (15 ml) and 0.5 M hydrochloric acid (15 ml) and stirred at room temperature for 4 h. After neutralization with solid sodium hydrogencarbonate, the mixture was evaporated to a fourth of the original volume and adsorbed on silica gel and this silica gel was placed on the top of a silica gel column (200 g). Elution with ethyl acetate–acetone–ethanol–water (100:15:6:4) gave 655 mg (79%) of the chloropurine nucleoside **19a**, m.p. 193.5–195 °C (H_2O). ^{1}H NMR: 0.77 d, 1 H, J_{gem} = 12.3 (H-3*endo*); 1.80 dd, 1 H, *J*(3*exo*,4) = 3.8 (H-3*exo*); 3.43 brdq, 1 H, *J*(1,4) ~ *J*(1,5) ~ *J*(1,7) ~ 1.2, *J*(1,6) = 2.8 (H-1); 3.12 dd, 1 H, *J*(CH,OH) = 5.2 and 3.28 dd, 1 H, *J*(CH,OH) = 4.9, J_{gem} = 10.4 (CH_2O); 3.56 brt, 1 H, *J*(4,1) ~ *J*(4,6) ~ *J*(4,7) ~ 0.7, *J*(4,5) = 2.8 (H-4); 3.70 dd, 1 H, *J*(CH,OH) = 5.0 and 3.79 dd, 1 H, *J*(CH,OH) = 5.4, J_{gem} = 10.6 (CH_2O); 4.49 t, 1 H (CH_2O**H**);

4.78 t, 1 H (CH_2O**H**); 4.80 m, 1 H (H-7); 6.02 brdd, 1 H, *J*(5,7) = 1.0, *J*(5,6) = 5.6 (H-5); 6.07 brdd, 1 H, *J*(6,7) = 1.0 (H-6); 8.47 s, 1 H and 8.70 s, 1 H (H-2′, H-8′). ^{13}C NMR: 30.13 (C-3); 45.55 (C-4); 48.28 (C-2); 49.19 (C-1); 63.81 (CH_2O); 64.82 (CH_2O); 70.03 (C-7); 131.01 (C-5′); 132.53 (C-6); 132.58 (C-5); 147.81 (C-8′); 149.03 (C-6′); 151.49 (C-2′); 152.93 (C-4′). FAB MS, *m/z* (%): 309/307 (40/100) [M + H]. For $C_{14}H_{15}ClN_4O_2 \cdot 1/4H_2O$ (311.2) calculated: 54.02% C, 5.02% H, 11.39% Cl, 18.00% N; found: 54.07% C, 4.95% H, 11.32% Cl, 18.05% N.

(1*R**,4*R**,7*S**)-7-(6-Amino-9*H*-purin-9-yl)bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**20a**)

Chloropurine **19a** (400 mg, 1.3 mmol) was heated with liquid ammonia (25 ml) and methanol (4 ml) in an autoclave at 75 °C for 48 h. Ammonia was then evaporated and residue was crystallized from water to give 387 mg (95%) adenine nucleoside (**20a**), m.p. 259–261 °C. ^{1}H NMR: 0.73 d, 1 H, J_{gem} = 12.3 (H-3*endo*); 1.75 dd, 1 H, *J*(3*exo*,4) = 3.7 (H-3*exo*); 3.12 dd, 1 H, *J*(CH,OH) = 5.3 and 3.27 dd, 1 H, *J*(CH,OH) = 5.1, J_{gem} = 10.4 (CH_2O); 3.33 dm, 1 H, *J*(1,4) ~ *J*(1,5) ~ *J*(1,7) ~ 1.2, *J*(1,6) = 2.8 (H-1); 3.47 brt, 1 H, *J*(4,6) ~ *J*(4,7) ~ 1.2, *J*(4,5) = 2.8 (H-4); 3.68 dd, 1 H, *J*(CH,OH) = 5.2 and 3.78 dd, 1 H, *J*(CH,OH) = 5.4, J_{gem} = 10.6 (CH_2O); 4.44 t, 1 H (CH_2O**H**); 4.62 m, 1 H (H-7); 4.75 t, 1 H (CH_2O**H**); 6.01 ddt H, *J*(5,7) = 0.7, *J*(5,6) = 5.6 (H-5); 6.07 ddt H, *J*(6,7) = 0.7 (H-6); 7.11 brs, 1 H (NH_2); 7.85 s, 1 H and 8.11 s, 1 H (H-2′, H-8′). ^{13}C NMR: 30.35 (C-3); 45.60 (C-4); 48.28 (C-2); 49.06 (C-1); 63.87 (CH_2O); 64.92 (CH_2O); 69.25 (C-7); 118.91 (C-5′); 132.42 (C-6), 132.43 (C-5); 140.98 (C-8′); 150.60 (C-4′); 152.38 (C-2′); 156.02 (C-6′). FAB MS, *m/z* (%): 288 (100) [M + H], 200 (15). For $C_{14}H_{17}N_5O_2 \cdot 1H_2O$ (305.3) calculated: 55.07% C, 6.27% H, 22.94% N; found: 55.44% C, 6.18% H, 23.05% N.

(1*R**,4*R**,7*S**)-7-[6-(Cyclopropylamino)-9*H*-purin-9-yl]bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**21a**)

A mixture of chlorpurine **19a** (390 mg, 1.27 mmol), cyclopropylamine (2 ml) and methanol (2 ml) was left standing overnight and evaporated. The product was purified by chromatography on silica gel (120 g) in ethyl acetate–acetone–ethanol–water (36:6:5:3). It was obtained 384 mg (92%) of the product, m.p. 208–210.5 °C (ethanol–water). ^{1}H NMR: 0.58 m, 2 H, 0.61 m, 2 H, and 3.02 m, 1 H (cyclopropyl); 0.73 d, 1 H, J_{gem} = 12.3 (H-3*endo*); 1.76 dd, 1 H, *J*(3*exo*,4) = 3.8 (H-3*exo*); 3.12 dd, 1 H, *J*(CH,OH) = 5.3 and 3.27 dd, 1 H, *J*(CH,OH) = 5.0, J_{gem} = 10.4 (CH_2O); 3.33 brdq, 1 H, *J*(1,5) = 0.7, *J*(1,4) ~ *J*(1,7) ~ 1.6, *J*(1,6) = 2.8 (H-1); 3.48 brt, 1 H, *J*(4,6) ~ *J*(4,7) ~ 1.2, *J*(4,5) = 2.8 (H-4); 3.68 dd, 1 H, *J*(CH,OH) = 5.0 and 3.78 dd, 1 H, *J*(CH,OH) = 5.5, J_{gem} = 10.6 (CH_2O); 4.63 m, 1 H (H-7); 4.44 t, 1 H (CH_2O**H**); 4.75 t, 1 H (CH_2O**H**); 6.00 brdd, 1 H, *J*(5,7) = 0.7, *J*(5,6) = 5.6 (H-5); 6.06 brdd, 1 H, *J*(6,7) = 0.7 (H-6); 7.76 brs, 1 H (NH); 7.85 s, 1 H and 8.20 s, 1 H (H-2′, H-8′). ^{13}C NMR: 6.61, 2 C (2 × CH_2); 24.40 (NCH); 30.33 (C-3); 45.58 (C-4); 48.28 (C-2); 49.08 (C-1); 63.87 (CH_2O); 64.92 (CH_2O); 69.26 (C-7); 119.01 (C-5′); 132.41, 2 C (C-5, C-6); 140.81 (C-8′); 149.84 (C-4′); 152.27 (C-2′); 155.60 (C-6′). FAB MS, *m/z* (%): 328 (100) [M + H], 201 (30), 176 (40), 110 (45). For $C_{17}H_{21}N_5O_2$ (327.4) calculated: 62.37% C, 6.47% H, 21.39% N; found: 62.32% C, 6.44% H, 21.09% N.

(1*R**,4*R**,7*S**)-7-(2-Amino-6-chloro-9*H*-purin-9-yl)bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**22a**)

A mixture of amine **15** (510 mg, 3 mmol), 2,5-diamino-4,6-dichloropyrimidine (600 mg, 3.35 mmol), and triethylamine (2.4 ml) in ethanol (18 ml) was heated in a pressure vessel at 105 °C for 6 days and, after cooling, was evaporated. The residue was chromatographed on a column of silica gel (200 g) in ethyl acetate–acetone–ethanol–water (100:15:6:4) to afford 919 mg (98%) of pyrimidine intermediate, which was immediately used in the next step. Concentrated hydrochloric acid (1.4 ml) was added to a suspension of pyrimidine intermediate in triethyl orthoformate (100 ml) and the reaction mixture was vigorously stirred for 4 days (suspension not dissolved) at room temperature. The solution was evaporated, the residue was dissolved in a mixture of tetrahydrofuran (15 ml) and 0.5 M hydrochloric acid (15 ml) and stirred at room temperature for 4 h. After neutralization with solid sodium hydrogencarbonate, the mixture was evaporated to one fourth of the original volume and adsorbed on silica gel. This silica gel was placed on the top of the silica gel column (200 g). Chromatography in ethyl acetate–acetone–ethanol–water (100:15:6:4) gave 748 mg (yield 78% based on amine **7**) of the 2-amino-6-chloropurine nucleoside **22a**. The solid was recrystallized from water–methanol (95:5), m.p. 237–239 °C (decomp.). ^{1}H NMR: 0.73 d, 1 H, J_{gem} = 12.3 (H-3*endo*); 1.72 dd, 1 H, *J*(3*exo*,4) = 3.8 (H-3*exo*); 3.10 dd, 1 H, *J*(CH,OH) = 5.1 and 3.26 dd, 1 H, *J*(CH,OH) = 5.1, J_{gem} = 10.4 (CH_2O); 3.45 brt, 1 H, *J*(4,6) = 0.7, *J*(4,1) ~ *J*(4,7) ~ 1.5, *J*(4,5) = 2.9 (H-4); 3.65 dd, 1 H, *J*(CH,OH) = 5.1 and 3.75 dd, 1 H, *J*(CH,OH) = 5.6, J_{gem} = 10.6 (CH_2O); 3.92 brdq, 1 H, *J*(1,5) = 0.7, *J*(1,7) = 1.6, *J*(1,6) = 2.9 (H-1); 4.47 t, 1 H (CH_2O**H**); 4.54 m, 1 H (H-7); 4.74 t, 1 H (CH_2O**H**); 5.98 ddt, 1 H, *J*(5,7) = 0.7, *J*(5,6) = 5.6 (H-5); 6.12 ddt, 1 H, *J*(6,7) = 0.7 (H-6); 6.86 brs, 2 H (NH_2); 7.86 s, 1 H (H-8′). ^{13}C NMR: 30.26 (C-3); 45.54 (C-4); 48.18 (C-2); 48.77 (C-1); 63.77 (CH_2O); 64.85 (CH_2O); 69.29 (C-7); 123.53 (C-5′); 132.33 (C-5); 132.67 (C-6); 143.45 (C-8′); 149.32 (C-6′); 155.11 (C-2′); 159.74 (C-4′). FAB MS, *m/z* (%): 322/324 (3/2) [M + H], 257 (8), 197 (8), 181 (30), 110 (62), 75 (80), 57 (100). For $C_{14}H_{16}ClN_5O_2 \cdot 1/4H_2O$ (317.3) calculated: 51.54% C, 5.10% H, 10.87% Cl, 21.47% N; found: 51.71% C, 5.02% H, 10.78% Cl, 21.15% N.

2-Amino-9-[(1*R**,4*R**,7*S**)-5,5-bis(hydroxymethyl)bicyclo[2.2.1]hept-2-en-7-yl]-9*H*-purin-6(1*H*)-one (**23a**)

A solution of **22a** (625 mg, 1.94 mol) in CF_3COOH–H_2O (3:1, 16 ml) was left standing at room temperature for 3 days. The solution was concentrated, the residue was coevaporated with water (2 × 5 ml), then treated with NH_4OH and evaporated. The residue was crystallized from water to give 555 mg (94%) of guanine nucleoside **23a**, m.p. 329–331 °C (decomp.). ^{1}H NMR: 0.70 d, 1 H, J_{gem} = 12.3 (H-6′*endo*); 1.68 dd, 1 H, *J*(6′*exo*,1′) = 3.8 (H-6′*exo*); 3.16 brdq, 1 H, *J*(4′,1′) ~ *J*(4′,2′) ~ *J*(4′,7′) ~ 1.2, *J*(4′,3′) = 2.8 (H-4′); 3.10 dd, 1 H, *J*(CH,OH) = 5.1 and 3.24 dd, 1 H, *J*(CH,OH) = 5.1, J_{gem} = 10.4 (CH_2O); 3.34 brt, 1 H, *J*(1′,3′) ~ *J*(1′,7′) ~ 1.0, *J*(1′,2′) = 2.8 (H-1′); 3.63 dd, 1 H, *J*(CH,OH) = 5.2 and 3.72 dd, 1 H, *J*(CH,OH) = 5.6, J_{gem} = 10.8 (CH_2O); 4.42 m, 1 H (H-7′); 4.44 t, 1 H (CH_2O**H**); 4.71 t, 1 H (CH_2O**H**); 5.96 brdd, 1 H, *J*(2′,7′) < 1.0, *J*(2′,3′) = 5.6 (H-2′); 6.12 brdd, 1 H, *J*(3′,7′) < 1.0 (H-3′); 6.38 brs, 2 H (NH_2); 7.39 s, 1 H (H-8′); 10.45 brs (NH). ^{13}C NMR: 30.44 (C-6′); 45.79 (C-1′); 48.20 (C-5′); 48.79 (C-4′); 63.70 (CH_2O); 64.89 (CH_2O); 68.98 (C-7′); 116.76 (C-5); 132.06 (C-3′); 132.64 (C-2′); 137.61 (C-8); 152.22 (C-4); 153.35 (C-4); 156.93 (C-6). FAB MS, *m/z* (%): 304 (2) [M + H], 215 (20), 86 (100), 57 (90). For $C_{14}H_{17}N_5O_3 \cdot 1/3H_2O$ (309.3) calculated: 54.36% C, 5.76% H, 22.64% N; found: 54.55% C, 5.67% H, 22.41% N.

(1*R**,4*R**,7*S**)-7-[2-Amino-6-(cyclopropylamino)-9*H*-purin-9-yl]-bicyclo[2.2.1]hept-5-ene-2,2-dimethanol (**24a**)

A mixture of chloropurine **22a** (350 mg, 1.09 mmol), cyclopropylamine (6 ml) and methanol (8 ml) was vigorously stirred overnight and evaporated. Crystallization of the residue from water–methanol (9:1) afforded 300 mg (81%) of the product. A second crop (50 mg, 13.4%) was obtained by chromatography of the mother liquor on silica gel (50 g) in ethyl acetate–acetone–ethanol–water (36:6:5:3), m.p. 261–264 °C. ^{1}H NMR: 0.55 m, 2 H, 0.63 m, 2 H, and 3.00 m, 1 H (cyclopropyl); 0.71 d, 1 H, J_{gem} = 12.3 (H-3*endo*); 1.70 dd, 1 H, *J*(3*exo*,4) = 3.8 (H-3*exo*); 3.11 dd, 1 H, *J*(CH,OH) = 5.2 and 3.25 dd, 1 H, *J*(CH,OH) = 5.0, J_{gem} = 10.4 (CH_2O); 3.20 brdq, 1 H, *J*(1,4) ~ *J*(1,5) ~ *J*(1,7) ~ 1.2, *J*(1,6) = 2.8 (H-1); 3.39 m, 1 H (H-4); 3.64 dd, 1 H, *J*(CH,OH) = 5.2 and 3.74 dd, 1 H, *J*(CH,OH) = 5.5, J_{gem} = 10.6 (CH_2O); 4.43 m, 1 H (H-7); 4.43 t, 1 H (CH_2O**H**); 4.72 t, 1 H (CH_2O**H**); 5.77 brs, 2 H (NH_2); 5.95 brdd, 1 H, *J*(5,7) = 0.7, *J*(5,4) = 2.8, *J*(5,6) = 5.6 (H-5); 6.12 brdd, 1 H, *J*(6,7) ~ *J*(6,7) ~ 1.0 (H-6); 7.18 brs, 1 H (NH); 7.40 s, 1 H (H-8′). ^{13}C NMR: 6.63, 2 C (2 × CH_2); 24.18 (NCH); 30.50 (C-3); 45.68 (C-4); 48.23 (C-2); 48.71 (C-1); 63.76 (CH_2O); 64.92 (CH_2O); 68.73 (C-7); 113.59 (C-5′); 132.13 (C-6); 132.61 (C-5); 137.30 (C-8′); 151.80 (C-4′); 155.93 (C-2′); 160.12 (C-6′). FAB MS, *m/z* (%): 343 (40) [M + H], 255 (12), 191 (35) [base + H], 93 (100). For $C_{17}H_{22}N_6O_2 \cdot 1/4H_2O$ (346.9) calculated: 58.86% C, 6.54% H, 24.23% N; found: 58.94% C, 6.58% H, 24.61% N.

Preparation of Saturated Nucleosides **17b**, **20b**, **21b**, **23b** and **24b**. General Method

A mixture of unsaturated nucleoside **a** (160 mg) and $Pd(OH)_2$ (20% on charcoal, 80 mg) in appropriate solvent was stirred in atmosphere of hydrogen for 3 days. The catalyst was filtered off and washed with methanol and filtrate was evaporated. Residue was crystallized or chromatographed on silica gel column and crystallized.

1-[(1R,4S*,7S*)-2,2-Bis(hydroxymethyl)bicyclo[2.2.1]heptan-7-yl]-5-methylpyrimidine-2,4(1H,3H)-dione* (**17b**). Solvent: methanol–water (11 ml, 10:1), residue was chromatographed on silica gel (10 g) in ethyl acetate–acetone–ethanol–water (100:15:6:4) to afford 130 mg (72%) of the oily product, which crystallized from acetone, m.p. 166–168.5 °C. ^{1}H NMR: 0.67 d, 1 H, J_{gem} = 12.7 (H-3′*endo*); 1.21 ddd, 1 H, *J*(5′*endo*,6′*exo*) = 6.4, *J*(5′*endo*,6′*endo*) = 8.9, J_{gem} = 12.6 (H-5′*endo*); 1.25 brtdd, 1 H, *J*(6′*exo*,1′) = 4.1, *J*(6′*exo*,5′*exo*) = 10.6, J_{gem} = 12.6 (H-6′*exo*); 1.51 ddd, 1 H, *J*(3′*exo*,5′*exo*) = 2.9, *J*(3′*exo*,4′) = 4.1 (H-3′*exo*); 1.60 brtdd, 1 H, *J*(5′*exo*,4′) = 4.5 (H-5′*exo*); 1.68 m, 1 H (H-6′*endo*); 1.76 d, 3 H, *J*(CH_3,6) = 1.0 (CH_3); 2.53 brdt, 1 H, *J*(1′,4′) = *J*(1′,7′) = 1.5 (H-1′); 2.69 brt, 1 H, *J*(4′,7′) = 1.5 (H-4′); 3.22 dd, 1 H, *J*(CH,OH) = 4.9 and 3.48 dd, 1 H, *J*(CH,OH) = 4.6, J_{gem} = 10.6 (CH_2O); 3.28 dd, 1 H, *J*(CH,OH) = 4.9 and 3.55 dd, 1 H, *J*(CH,OH) = 5.2, J_{gem} = 10.4 (CH_2O); 3.92 m, 1 H (H-7′); 4.43 t, 1 H (CH_2O**H**); 4.52 t, 1 H (CH_2O**H**); 7.37 q, 1 H (H-6); 11.12 s, 1 H (NH). ^{13}C NMR: 12.17 (CH_3); 20.96 (C-6′); 26.14 (C-5′); 34.79 (C-3′); 38.19 (C-4′); 42.69 (C-1′); 45.46 (C-2′); 62.77 (CH_2O); 64.28 (CH_2O); 65.71 (C-7′); 107.90 (C-5); 140.17 (C-6); 151.45 (C-2); 164.37 (C-4). FAB MS, *m/z* (%): 281 (100) [M + H], 127 (60) [thymine]. For $C_{14}H_{18}N_2O_4$ (280.3) calculated: 59.99% C, 7.19% H, 9.99% N; found: 59.67% C, 7.14% H, 9.75% N.

(1R,4S*,7S*)-7-(6-Amino-9H-purin-9-yl)bicyclo[2.2.1]heptane-2,2-dimethanol* (**20b**). Solvent: methanol–water (20 ml, 3:1), the residue was crystallized from water to afford 140 mg (87%) of the saturated nucleoside, m.p. 139–142 °C (hydrate), 231–233 °C. ^{1}H NMR: 0.77 d, 1 H, J_{gem} = 12.7 (H-3*endo*); 1.11 brtdd, 1 H, *J*(6*exo*,1) = 4.3, *J*(6*exo*,5*endo*) = 6.2, *J*(6*exo*,5*exo*) = 11.5, J_{gem} = 12.8 (H-6*exo*); 1.24 ddd, 1 H, *J*(5*endo*,6*endo*) = 9.0, J_{gem} = 12.6 (H-5*endo*); 1.55 brtq, 1 H,

J(5*exo*,6*endo*) = 2.2, *J*(5*exo*, 3*exo*) = 2.5, *J*(5*exo*,4) = 4.3 (H-5*exo*); 1.59 ddd, 1 H, *J*(3*exo*,4) = 4.5 (H-3*exo*); 1.68 brddd, 1 H, *J*(6*endo*,7) = 1.0 (H-6*endo*); 3.01 brdt, 1 H, *J*(1,4) = *J*(1,7) = 1.5 (H-1); 3.10 brt, 1 H, *J*(4,7) = 1.5 (H-4); 3.25 dd, 1 H, *J*(CH,OH) = 4.9 and 3.53 dd, 1 H, *J*(CH,OH) = 4.5, J_{gem} = 10.6 (CH_2O); 3.39 dd, 1 H, *J*(CH,OH) = 4.8 and 3.61 dd, 1 H, *J*(CH,OH) = 5.3, J_{gem} = 10.4 (CH_2O); 4.37 m, 1 H (H-7); 4.50 t, 1 H (CH_2O**H**); 4.62 t, 1 H (CH_2O**H**); 7.13 brs, 2 H (NH_2); 8.09 s, 1 H and 8.11 s, 1 H (H-2′, H-8′). ^{13}C NMR: 21.24 (C-6); 26.33 (C-5); 34.85 (C-3); 39.08 (C-4); 43.26 (C-1); 45.67 (C-2); 62.43 (C-7); 63.13 (CH_2O); 64.66 (CH_2O); 119.06 (C-5′); 140.92 (C-8′); 150.23 (C-4′); 152.41 (C-2′); 156.13 (C-6′). FAB MS, *m/z* (%): 290 (40) [M + H], 181 (25), 110 (55), 75 (80), 57 (100). For $C_{14}H_{19}N_5O_2 \cdot 1H_2O$ (307.3) calculated: 54.71% C, 6.89% H, 22.79% N; found: 54.49% C, 6.85% H, 22.56% N.

(1R,4S*,7S*)-7-[6-(Cyclopropylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptane-2,2-dimethanol* (**21b**). Solvent: methanol (10 ml), the residue was crystallized from acetone–ethanol (10:1) to afford 139 mg (86%) of the saturated nucleoside, m.p. 173–175 °C. ^{1}H NMR: 0.60 m, 2 H, 0.69 m, 2 H, and 3.05 m, 1 H (cyclopropyl); 0.77 d, 1 H, J_{gem} = 12.1 (H-3*endo*); 1.10 m, 1 H (H-6*exo*); 1.23 brddd, 1 H, *J*(5*endo*,6*exo*) = 6.0, *J*(5*endo*,6*endo*) = 8.8, J_{gem} = 12.2 (H-5*endo*); 1.56 m, 1 H (H-5*exo*); 1.59 ddd, 1 H, *J*(3*exo*,5*exo*) = 2.3, *J*(3*exo*,4) = 4.0 (H-3*exo*); 1.68 brddd, 1 H, *J*(6*endo*,5*exo*) = 3.2, J_{gem} = 12.6 (H-6*endo*); 3.01 brdt, 1 H, *J*(1,4) = *J*(1,7) = 1.5, *J*(1,6*exo*) = 3.8 (H-1); 3.10 brt, 1 H, *J*(4,7) = 1.5, *J*(4,6*exo*) = 4.0 (H-4); 3.29 d, 1 H, 3.39 d, 1 H and 3.53 dd, 1 H, 3.61 d, 1 H, J_{gem} = 10.6 (2 × CH_2O); 4.37 m, 1 H (H-7); 4.54 brs, 1 H and 4.66 brs, 1 H (2 × CH_2O**H**); 7.79 brs, 1 H (NH); 8.10 s, 1 H and 8.21 s, 1 H (H-2′, H-8′). ^{13}C NMR: 6.55, 2 C (2 × CH_2); 24.04 (NCH); 21.22 (C-6); 26.32 (C-5); 34.85 (C-3); 39.06 (C-4); 43.27 (C-1); 45.67 (C-2); 62.42 (C-7); 63.09 (CH_2O); 64.61 (CH_2O); 119.39 (C-5′); 140.71 (C-8′); 149.67 (C-4′); 152.30 (C-2′); 155.65 (C-6′). FAB MS, *m/z* (%): 330 (100) [M + H], 176 (55). For $C_{17}H_{23}N_5O_2 \cdot 1/3H_2O$ (335.4) calculated: 60.88% C, 7.11% H, 20.88% N; found: 60.83% C, 7.00% H, 20.65% N.

2-Amino-9-[(1R,4S*,7S*)-2,2-bis(hydroxymethyl)bicyclo[2.2.1]heptan-7-yl]-9H-purin-6(1H)-one* (**23b**). Solvent: dimethylformamide (50 ml), the residue was crystallized from water to afford 152 mg (87%) of the saturated nucleoside, m.p. 307–309 °C (decomp.). ^{1}H NMR: 0.71 d, 1 H, J_{gem} = 12.7 (H-3′*endo*); 1.20 m, 2 H (H-5′*endo*, H-6′*exo*); 1.55 m, 2 H (H-5′*exo*, H-3′*exo*); 1.68 m, 1 H (H-6′*endo*); 2.86 m, 1 H (H-1′); 3.01 brt, 1 H, *J*(4′,3′*exo*) ~ *J*(4′,3′*exo*) ~ 4.3 (H-4′); 3.22 dd, 1 H, *J*(CH,OH) = 4.9 and 3.51 dd, 1 H, *J*(CH,OH) = 4.5, J_{gem} = 10.6 (CH_2O); 3.34 dd, 1 H, *J*(CH,OH) = 4.8 and 3.59 dd, 1 H, *J*(CH,OH) = 5.2, J_{gem} = 10.5 (CH_2O); 4.18 m, 1 H (H-7); 4.50 t, 1 H (CH_2O**H**); 4.56 t, 1 H (CH_2O**H**); 6.32 brs, 2 H (NH_2); 7.64 s, 1 H (H-8); 10.53 brs, 1 H (NH). ^{13}C NMR: 21.20 (C-6′); 26.25 (C-5′); 34.73 (C-3′); 39.17 (C-4′); 43.10 (C-1′); 46.70 (C-2′); 62.21 (C-7′); 62.87 (CH_2O); 64.48 (CH_2O); 117.01 (C-5); 137.39 (C-8); 151.92 (C-4); 153.06 (C-2); 157.01 (C-6). FAB MS, *m/z* (%): 306 (100) [M + H], 137 (65), 73 (100). For $C_{14}H_{19}N_5O_3 \cdot 1H_2O$ (323.3) calculated: 52.00% C, 6.55% H, 21.66% N; found: 51.96% C, 6.42% H, 21.59% N.

(1R,4S*,7S*)-7-[2-Amino-6-(cyclopropylamino)-9H-purin-9-yl]bicyclo[2.2.1]heptane-2,2-dimethanol* (**24b**). Solvent: methanol–water (10:1, 11 ml), the residue was crystallized from acetone–ethanol (10:1) to afford 128 mg (80%) of the saturated nucleoside, m.p. 248–251 °C (decomp.). ^{1}H NMR: 0.57 m, 2 H, 0.65 m, 2 H, and 3.01 m, 1 H (cyclopropyl); 0.72 d, 1 H, J_{gem} = 12.4 (H-3*endo*); 1.18 ddd, 1 H, *J*(5*endo*,6*exo*) = 6.7, *J*(5*endo*,6*endo*) = 9.0, J_{gem} = 12.6 (H-5*endo*); 1.22 m, 1 H (H-6*exo*); 1.51 brtdd, 1 H, *J*(5*exo*,3*exo*) = 2.7, *J*(5*exo*,4) = 4.0, *J*(5*exo*,6) = 10.5 (H-5*exo*); 1.56 ddd, 1 H, *J*(3*exo*,4) = 4.0 (H-3*exo*); 1.68 m, 1 H, J_{gem} = 12.8 (H-6*endo*); 2.91 brdt, 1 H, *J*(1,4) = *J*(1,7) = 1.5, *J*(1,6*exo*) = 3.8 (H-1); 3.07 brt, 1 H, *J*(4,7) = 1.5 (H-4);

3.27 dd, 1 H, *J*(CH,OH) = 4.8 and 3.53 dd, 1 H, *J*(CH,OH) = 4.3, J_{gem} = 10.6 (CH_2O); 3.35 dd, 1 H, *J*(CH,OH) = 4.3 and 3.60 dd, 1 H, *J*(CH,OH) = 4.9, J_{gem} = 10.6 (CH_2O); 4.17 m, 1 H (H-7); 4.51 t, 1 H (CH_2O**H**); 4.58 t, 1 H (CH_2O**H**); 5.72 brs, 2 H (NH_2); 7.19 brs, 1 H (NH); 7.65 s, 1 H (H-8′). ^{13}C NMR: 6.61, 2 C (2 × CH_2); 24.00 (NCH); 21.28 (C-6); 26.34 (C-5); 34.79 (C-3); 39.04 (C-4); 42.96 (C-1); 45.69 (C-2); 61.93 (C-7); 62.97 (CH_2O); 64.57 (CH_2O); 113.77 (C-5′); 137.14 (C-8′); 152.02 (C-4′); 155.96 (C-6′); 160.01 (C-2′). FAB MS, *m/z* (%): 345 (100) [M + H], 191 (45). For $C_{17}H_{24}N_6O_2 \cdot 1/3H_2O$ (347.4) calculated: 58.27% C, 7.10% H, 23.98% N; found: 58.32% C, 7.29% H, 23.55% N.

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