SYNTHESIS OF PURINE NUCLEOSIDE ANALOGUES DERIVED FROM CARBOCYCLIC 5-*C*-(HYDROXYMETHYL)HEXOPYRANOSES

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(1*R*,2*R*,3*R*,4*S*)-3-(Benzyloxy)-5,5-bis(hydroxymethyl)cyclohexane-1,2,4-triol (**1**) was converted to (3a*S*,4*R*,5*S*,7a*R*)-4-(benzyloxy)-2-oxo-6,6-bis[(trityloxy)methyl]hexahydro-2λ^4-1,3,2-benzodioxathiol-5-ol (**3**) and subsequently to (3a*S*,4*R*,5*S*,7a*R*)-4-(benzyloxy)-2,2-dioxo-6,6-bis[(trityloxy)methyl]hexahydro-2λ^4-1,3,2-benzodioxathiol-5-yl benzoate (**4**). Treatment of sulfate **4** with adenine and DBU afforded, after deprotection, **7** and **22** in low yields. Reaction of sulfite **3** with lithium azide gave (1*R*,2*R*,3*S*,6*S*)-6-azido-2-(benzyloxy)-4,4-bis[(trityloxy)methyl]-cyclohexane-1,3-diol (**10**) and (1*S*,4*R*,5*S*,6*S*)-5-azido-6-(benzyloxy)-2,2-bis[(trityloxy)methyl]-cyclohexane-1,4-diol (**11**) which were, after separation, reduced with LAH to (1*R*,2*R*,3*S*,6*S*)-6-amino-2-(benzyloxy)-4,4-bis[(trityloxy)methyl]cyclohexane-1,3-diol (**9**) and (1*S*,4*R*,5*S*,6*S*)-5-amino-6-(benzyloxy)-2,2-bis[(trityloxy)methyl]cyclohexane-1,4-diol (**12**). Amino derivatives **9** and **12** were transformed to (1*R*,2*R*,3*S*,6*S*)-6-(6-amino-9*H*-purin-9-yl)-4,4-bis(hydroxymethyl)cyclohexane-1,2,3-triol (**7**), (1*R*,2*R*,3*S*,6*S*)-6-[6-(cyclopropylamino)-9*H*-purin-9-yl]-4,4-bis(hydroxymethyl)cyclohexane-1,2,3-triol (**16**), (1*S*,2*S*,3*S*,4*R*)-3-[6-(cyclopropylamino)-9*H*-purin-9-yl]-6,6-bis(hydroxymethyl)cyclohexane-1,2,4-triol (**20**), (1*S*,2*S*,3*S*,4*R*)-3-(6-amino-9*H*-purin-9-yl)-6,6-bis(hydroxymethyl)cyclohexane-1,2,4-triol (**22**), and 2-amino-9-[(1*S*,2*R*,3*R*,4*S*)-2,3,4-trihydroxy-5,5-bis(hydroxymethyl)cyclohexyl]-9*H*-purin-6(1*H*)-one (**27**).

Keywords: Carbasugars; Carbocyclic hexopyranoses; Cyclohexanes; Azides; Nucleosides; Carbocyclic nucleosides; Purines; 6-(Cyclopropylamino)purine; Adenine; Guanine.

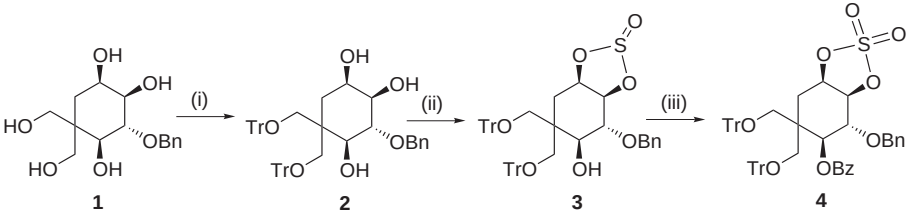
The development of new modified nucleosides as antiviral agents has remained a very active field of research. As the hexitol nucleosides exhibit antiviral activity[1], a variety of their carbocyclic congeners and cyclohexene analogues were prepared[2]. Recently, a potent antiviral activity of such compounds was found[2l,2m]. Cyclohexenyl nucleosides were also incorporated in DNA chains[3].

This communication is a continuation of our program[4,2s] aimed at the syntheses and structure-antiviral activity study of carbocyclic nucleosides, dealing with the synthesis of purine nucleoside analogues derived from

5a-carba-5-*C*-(hydroxymethyl)-α-D-idopyranose and 5a-carba-5-*C*-(hydroxymethyl)-β-D-gulopyranose.

Some time ago[4d], we reported preparation of (1*R*,2*R*,3*R*,4*S*)-3-(benzyloxy)-5,5-bis(hydroxymethyl)cyclohexane-1,2,4-triol (5a-carba-5-*C*-(hydroxymethyl)-β-D-idopyranose) which was used as a starting compound for preparation of the target nucleoside analogues.

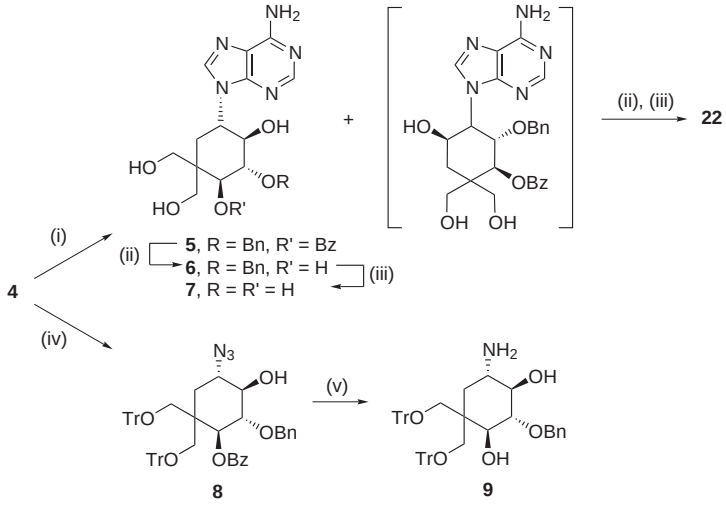
Tritylation of the carbocyclic sugar **1** afforded dityrityl derivative **2**, which was treated with thionyl chloride and triethylamine in ether at –75 °C to give a mixture of sulfites **3** (90%). The mixture of stereoisomers, which differ in orientation of the S=O bond, was not separated. The ratio of isomers (3:10) was determined by ^{1}H NMR spectroscopy. The mixture of sulfites **3** was benzoylated with benzoyl chloride in pyridine and the obtained crude benzoates were converted to sulfate **4** following the procedure by Gao and Sharpless[5] (Scheme 1).



(i) TrCl/pyridine, 77%; (ii) $SOCl_2$/TEA/ether, -75 °C, 90%;
(iii) 1. BzCl/pyridine, 2. $KIO_4/RuCl_3/CH_3CN/CCl_4/H_2O$, 65%

SCHEME 1

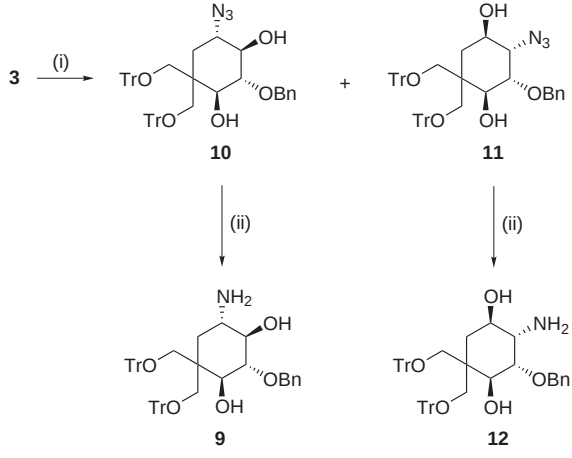
Treatment of adenine with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) followed by sulfate **4** in dimethylformamide at 125 °C afforded, after hydrolysis with a mixture of tetrahydrofuran, sulfuric acid, and water, adenine derivative **5** (16.6% based on sulfate **4**; Scheme 2). Methanolysis of the benzoate **5** with methanolic ammonia gave **6** (89%) and subsequent transfer hydrogenation[6], performed with 20% palladium hydroxide on carbon in a refluxing mixture of ethanol and cyclohexene, afforded free nucleoside analog **7** (83%). The mother liquor from crystallization of compound **5** contained a mixture of **5** and another compound which could not be chromatographically separated. The mixture was methanolyzed, subsequently hydrogenolyzed and purified by chromatography to give **7** (1.2%) and **22** (1% both based on sulfate **4**). As the yield of compound **5** was low, an alternative approach was used. Sulfate **4** was treated with lithium azide in dimethylformamide at 60 °C to give, after hydrolysis, the azido derivative **8** (68%). The other isomer was not found in the reaction mixture. Reduction



(i) 1. adenine/DBU/DMF, 125 °C, 1. 80% aq. TFA, 16.6%; (ii) NH_3/MeOH, 89% of **6**; (iii) EtOH/cyclohexane/20% Pd/C, 83%; (iv) LiN_3/DMF, 60 °C, 68%; (v) LAH/THF, reflux, 76%

SCHEME 2

of azide **8** with $LiAlH_4$ yielded the amino derivative **9** (61%). Reaction of sulfites **3** with lithium azide in dimethylformamide at 130 °C led to a mixture of azides **10** (42%) and **11** (19%) which were separated by chromatography on a silica gel column. Reduction of azides **10** and **11** with $LiAlH_4$ gave amino derivatives **9** (76%) and **12** (71%), respectively (Scheme 3).

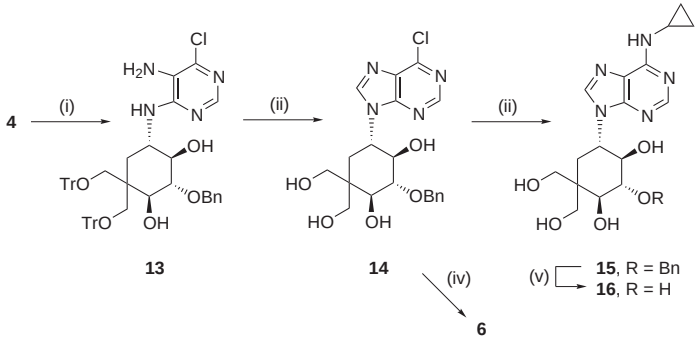


(i) LiN_3/DMF, 130 °C, 42% of **10**, 19% of **11**; (ii) $LiAlH_4$/THF, 76% of **9**, 71% of **12**

SCHEME 3

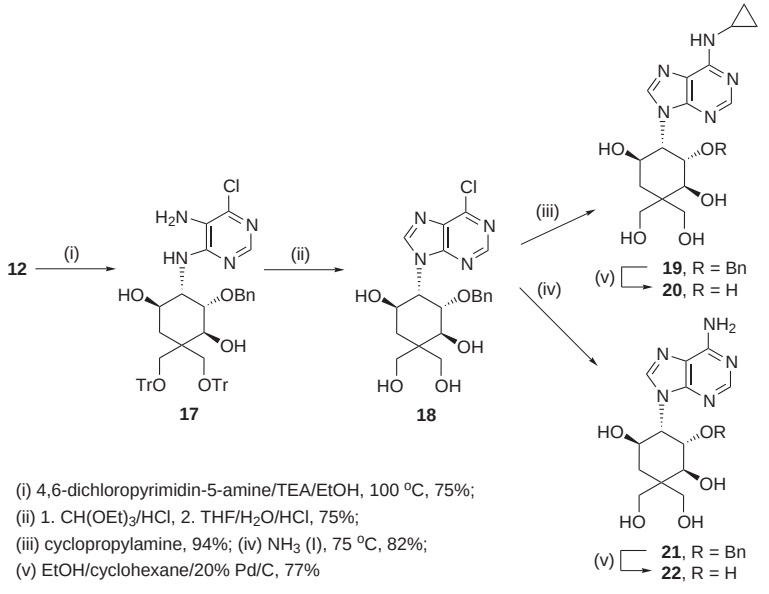
Treatment of sulfites **3** with adenine and DBU in dimethylformamide at 130 °C led to a reaction mixture which contained neither starting sulfites nor substituted adenine.

The amino derivatives **9** and **12** were converted to the 6-chloropurine derivatives by described procedures[7]. Coupling **9** or **12** with 4,6-dichloropyrimidin-5-amine in ethanol in the presence of triethylamine gave pyrimidinylamino derivative **13** (61%) or **17** (75%) (Schemes 4 and 5). Ring



(i) 4,6-dichloropyrimidin-5-amine/TEA/EtOH, 100 °C, 61%; (ii) 1. $CH(OEt)_3$/HCl, 2. THF/H_2O/HCl, 77%; (iii) cyclopropylamine, 93%; (iv) NH_3 (l), 75 °C, 80%; (v) EtOH/cyclohexane/20% Pd/C, 83%

SCHEME 4

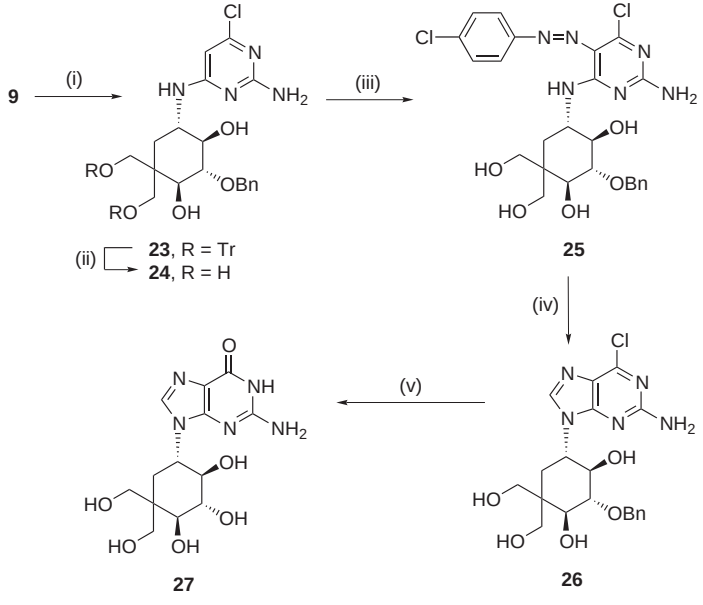


(i) 4,6-dichloropyrimidin-5-amine/TEA/EtOH, 100 °C, 75%;
(ii) 1. $CH(OEt)_3$/HCl, 2. THF/H_2O/HCl, 75%;
(iii) cyclopropylamine, 94%; (iv) NH_3 (l), 75 °C, 82%;
(v) EtOH/cyclohexane/20% Pd/C, 77%

SCHEME 5

closure and detritylation of **13** or **17** with triethyl orthoformate in the presence of concentrated hydrochloric acid gave 6-chloropurine derivative **14** (77%) or **18** (75%). As the reaction of **17** with orthoformate proceeded more slowly, a higher concentration of hydrochloric acid was used. Aminolysis of **14** and **18** with cyclopropylamine afforded substituted (cyclopropylamino)purine **15** (93%) and **19** (94%), respectively. Treatment of **14** or**18** with liquid ammonia at 75 °C gave adenine derivative **6** (80%) or **21** (82%), respectively. Free nucleoside analogues **7**, **16**, **20**, and **22** were obtained by transfer hydrogenation.

The synthesis of guanine analog **28** is shown in Scheme 6. Amine **9** was condensed with 4,6-dichloropyrimidin-2-amine to afford pyrimidinylamino derivative **23** (68%). Detritylation of compound **23** with trifluoroacetic acid gave **24** (85%). It was then treated with 4-chlorobenzenediazonium chloride to give azopyrimidine **25** (67%). Reduction of **25** with zinc in the presence of acetic acid, followed by cyclization with triethyl orthoformate and concentrated hydrochloric acid, yielded chloropurine derivative **26** (50%). Hydrolysis of **26** with 1 M HCl under reflux afforded guanine derivative **27** (50%).



(i) 4,6-dichloropyrimidin-2-amine/TEA/EtOH, 100 °C, 68%; (ii) 80% aq. TFA, 85%; (iii) 4-chloroaniline/HCl/$NaNO_2$/AcOH/NaOAc, 67%; (iv) 1. Zn/EtOH/H_2O/AcOH, 2. $CH(OEt)_3$/HCl, 3. THF/H_2O/HCl, 50%; (v) 1M HCl, reflux, 50%

SCHEME 6

The structure of prepared compounds was determined by ^{1}H NMR spectra. Compounds **5**–**10**, **13**–**16**, and **23**–**27** have all cyclohexane substituents, except one hydroxymethyl group, in equatorial positions; thus, only one proton of the endocyclic methylene group is equatorial with corresponding values of vicinal coupling constants *J*(eq,ax) 3.7–4.6. Trans axial orientation of the other cyclohexane ring protons is in accord with values of vicinal coupling constants *J*(ax,ax) 8.8–13.3 (*cf.* Fig. 1, structure A). In compounds **11**, **12**, and **17**–**22** (structure B), substituents in positions 1 and 2 of the cyclohexane ring are in equatorial positions and substituents 3 and 4 have axial orientation, which corresponds with the values of the following coupling constants: *J*(1ax,6ax) 11.6–12.8, *J*(1ax,6eq) 3.4–4.4, *J*(1ax,2ax) 8.2–11.1, *J*(2ax,3eq) 2.1–3.4, and *J*(3eq,4eq) 3.3–3.6. Assignment of the signals to protons and carbon atoms in NMR spectra of compounds **7** and **22** was also confirmed by gs HSQC.

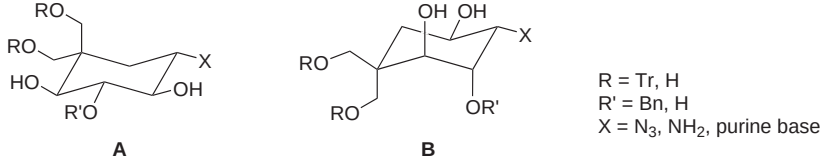


FIG. 1

In conclusion, new nucleoside analogues of adenine, 6-(cyclopropylamino)purine, and guanine derived from 5a-carba-5-*C*-(hydroxymethyl)-α-D-idopyranose and 5a-carba-5-*C*-(hydroxymethyl)-β-D-gulopyranose were prepared.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were obtained at 20 °C with a Autopol IV polarimetr (Rudolph Research Analytical, U.S.A.) and are given in 10^{-1} deg cm^2 g^{-1}. Mass spectra were recorded on a ZAB-EQ (VG Analytical) spectrometer using FAB (ionization by Xe, accelerating voltage 8 kV, glycerol matrix). 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 hexadeuteriodimethyl sulfoxide (referenced to the solvent signal) and deuteriochloroform (referenced to the signal of tetramethylsilane as internal standard). 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 36–60 °C; the compounds were dried at 13 Pa and 50 °C.

(1*R*,2*R*,3*R*,4*S*)-3-(Benzyloxy)-5,5-bis[(trityloxy)methyl]cyclohexane-1,2,4-triol (**2**)

A solution of alcohol **1** (2.98 g, 10 mmol; dried by codistillation with pyridine) and trityl chloride (7.92 g, 28 mmol) in pyridine (80 ml) was heated at 100 °C for 1 h. The mixture

was taken down and the residue was partitioned between ethyl acetate (250 ml) and water (60 ml).The organic layer was separated and washed with water (2 × 50 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. Column chromatography of the residue on silica gel (400 g) in toluene–ethyl acetate (2:1) afforded 6.05 g (77%) of trityl derivative **2**. For $C_{53}H_{50}O_6$ (783.0) calculated: 81.30% C, 6.44% H; found: 81.46% C, 6.52% H. $[\alpha]_D$ +8.2 (*c* 0.720, chloroform). ^{1}H NMR (DMSO-d_6): 1.54 dd, 1 H, *J*(6a,1) = 2.9, J_{gem} = 14.0 (H-6a); 1.67 dd, 1 H, *J*(6b,1) = 5.3 (H-6b); 3.03 d, 1 H and 3.51 d, 1 H, J_{gem} = 8.6 (CH_2O); 3.24 t, 2 H and 3.35–3.42 m, 2 H (CH_2O, H-2, H-3); 3.60 t, 1 H, *J*(4,3) = 6.8 (H-4); 3.65 m, 1 H (H-1); 4.36 d, 1 H, *J* = 4.0 (OH); 4.41 d, 1 H, *J* = 6.6 (OH); 4.56 d, 1 H and 4.60 d, 1 H, J_{gem} = 11.5 (CH_2Ph); 4.79 d, 1 H, *J* = 5.3 (OH); 7.18–7.31 m, 35 H (arom.). ^{1}H NMR ($CDCl_3$): 1.56 dd, 1 H, *J*(6a,1) = 2.8, J_{gem} = 15.2 (H-6a); 1.96 dd, 1 H, *J*(6b-1) = 4.5 (H-6b); 3.37 dd, 1 H, *J*(2,1) = 3.5 (H-2); 3.39 d, 1 H and 3.61 d, 1 H, J_{gem} = 8.8 (CH_2O); 3.53 dd, 1 H, *J*(3,2) = 8.3, *J*(3,4) = 6.6 (H-3); 3.66 brd, 1 H (H-4); 3.75 s, 2 H (CH_2O); 3.82 m, 1 H (H-1); 4.34 d, 1 H and 4.78 d, 1 H, J_{gem} = 11.4 (CH_2Ph); 7.20–7.34 m, 30 H and 7.43–7.46 m, 5 H (arom.).

(3a*S*,4*R*,5*S*,7a*R*)-4-(Benzyloxy)-2-oxo-6,6-bis[(trityloxy)methyl]hexahydro-2λ^4-1,3,2-benzodioxathiol-5-ol (**3**)

Thionyl chloride (7.4 ml) was added to a stirred solution of *cis*-diol **2** (7.83 g, 10 mmol) and triethylamine (38 ml) in ether (300 ml), and cooled to –75 °C. In the course of 4 h, the mixture was warmed up to –20 °C and poured on crushed ice (0.5 kg). The organic phase was separated, washed with water (3 × 100 ml), and dried over anhydrous sodium sulfate. The solvent was evaporated and the residue was codistilled with toluene (2 × 100 ml). The obtained product **3** (7.47 g; 90%) was used in the next reaction step. A sample of the compound for spectral measurement and analysis was purified by chromatography on a silica gel column with toluene–ethyl acetate (93:7). For $C_{53}H_{48}O_7S$ (829.0) calculated: 76.79% C, 5.84% H, 3.87% S; found: 76.50% C, 5.91% H, 3.61% S. ^{1}H NMR (DMSO-d_6): 2.04 dd, 0.3 H, *J*(7,7a) = 2.5, J_{gem} =14.9 (H-7 of isomer B); 2.15 m, 2 H (2 × H-7 of isomer A); 2.28 dd, 0.3 H, *J*(7′,7a) = 2.3 (H-7′ of isomer B); 2.87 d, 0.3 H, J_{gem} = 9.1 (CH**H**-O of isomer B); 2.96–3.01 m, 1.6 H (C**H**H-O of isomer B, H-4 of both isomers); 3.06 s, 2 H (CH_2O of isomer A); 3.30 d, 1 H and 3.31 d, 1 H, J_{gem} = 9.1 (CH_2O of isomer A); 3.82 dd, 1.3 H, *J*(5,4) = 10.1 (H-5 of both isomers); 4.59 d, 1 H and 4.66 d, 1 H, J_{gem} = 11.6 (CH_2Ph of isomer A); 4.66 d, 0.3 H and 4.71 d, 0.3 H, J_{gem} = 11.4 (CH_2Ph of isomer B); 4.77–4.80 m, 0.6 H (H-3a, H-7a of isomer B); 4.88–4.93 m, 2 H (H-3a, H-7a of isomer A); 5.12 d, 0.3 H, *J*(OH,5) = 5.6 (5-OH of isomer B); 5.17 d, 1 H, *J*(OH,5) = 5.8 (5-OH of isomer A); 7.13–7.46 m, 45.5 H (arom. of both isomers).

(3a*S*,4*R*,5*S*,7a*R*)-4-(Benzyloxy)-2,2-dioxo-6,6-bis[(trityloxy)methyl]hexahydro-2λ^4-1,3,2-benzodioxathiol-5-yl Benzoate (**4**)

Benzoyl chloride (2 ml, 17 mmol) was added under stirring to a solution of sulfite **3** (6.63 g, 8 mmol) in pyridine (35 ml) and the mixture was set aside at room temperature overnight. Water (1 ml) was then added and, after 10 min, the mixture was concentrated, and the residue was partitioned between ethyl acetate (50 ml) and water (25 ml). The organic phase was washed with water (2 × 50 ml) and 10% aqueous sodium hydrogencarbonate (2 × 50 ml), then dried over anhydrous sodium sulfate, and the solvent was evaporated. To a stirred and ice-cooled mixture of the residue, acetonitrile (20 ml), tetrachloromethane (10.5 ml), and water (38 ml), potassium periodate (3.63 g) and ruthenium(III) chloride hydrate (25 mg)

were added. The mixture was stirred at 0 °C for 20 min and, at room temperature, for 10 min. Additional amount of potassium periodate (1.81 g) was then added, the mixture was stirred at room temperature for 30 min, and then diluted with ethyl acetate (230 ml). The organic layer was separated, washed with water (3 × 100 ml), dried over anhydrous sodium sulfate, and filtered through a silica gel pad (90 g). Silica gel was washed with ethyl acetate and the collected filtrates were evaporated. Crystallization of the residue from methanol afforded 4.95 g (65%) of sulfate **4**, m.p. 147.5–150 °C. For $C_{60}H_{52}O_9S$ (949.1) calculated: 75.93% C, 5.52% H, 3.38% S; found: 76.16% C, 5.38% H, 3.21% S. $[\alpha]_D$ –21.7 (*c* 0.475, chloroform). ^{1}H NMR (DMSO-d_6): 2.37 d, 1 H and 3.13 d, 1 H, J_{gem} = 10.0 (CH_2O); 2.43 dd, 1 H, *J*(7,7a) = 3.5, J_{gem} = 16.2 (H-7); 2.55 dd, 1 H, *J*(7′,7a) = 2.0 (H-7′); 3.04 d, 1 H and 3.75 d, 1 H, J_{gem} = 9.8 (CH_2O); 4.04 dd, 1 H, *J*(4,3a) = 7.8, *J*(4,5) = 10.6 (H-4); 4.32 d, 1 H and 4.57 d, 1 H, J_{gem} = 11.6 (CH_2Ph); 5.56 d, 1 H (H-5); 5.59 m, 1 H (H-7a); 5.63 dd, 1 H, *J*(3a,4) = 7.8, *J*(3a,7a) = 5.1 (H-3a); 6.90–7.60 m, 46 H (arom.). ^{13}C NMR (DMSO-d_6): 26.87 (C-7); 43.19 (C-6); 70.44 (C-5); 74.05 (OCH_2Ph); 76.49 (C-4); 83.80 (C-7a); 87.88 (C-3a); 86.39, 86.48, 126.80, 2 C, 126.97, 2 C, 127.18, 2 C, 127.56, 3 C, 127.69, 4 C, 127.79, 4 C, 127.92, 3 C, 127.94, 4 C, 128.11, 3 C, 128.34, 4 C, 128.40, 4 C, 128.47, 128.67, 129.21, 129.42, 133.53, 137.35, 143.19, 3 C, 143.32, 3 C, 147.94 (arom.).

(1*S*,4*S*,5*R*,6*S*)-4-(6-Amino-9*H*-purin-9-yl)-5-hydroxy-2,2-bis(hydroxymethyl)-6-(benzyloxy)cyclohexyl Benzoate (**5**)

A solution of adenine (1.08 g, 8 mmol) and DBU (1.2 ml, 8 mmol) in dimethylformamide (20 ml) was stirred under argon at 125 °C (bath). To the mixture, a solution of sulfate **4** (3.80 g, 4 mmol) in dimethylformamide (12 ml) was added and the mixture was heated to 125 °C for 1 h. After cooling, the mixture was neutralized with dilute sulfuric acid and evaporated. A mixture of the residue, tetrahydrofuran (36 ml), concentrated sulfuric acid (1.8 ml) and water (1.8 ml) was stirred at room temperature overnight and then neutralized with solid sodium hydrogencarbonate. The insoluble material was filtered off and washed with methanol. The collected filtrates were evaporated and the residue was stirred with 80% aqueous trifluoroacetic acid (60 ml) at room temperature for 30 min. The mixture was taken down and the residue was stirred with 50% aqueous methanol (40 ml). The deposited triphenylmethanol was filtered off, washed with 50% aqueous methanol and the combined filtrates were neutralized with Dowex 1 (HCO_3^-). The resin was filtered off, washed with aqueous methanol, and the collected filtrates were evaporated. Chromatography of the residue on a silica gel column (160 g) in ethyl acetate–acetone–ethanol–water (95:15:9:6) afforded, after crystallization from aqueous propan-2-ol, 346 mg (16.6% based on sulfate **4**) of **5**, m.p. 268–270 °C. For $C_{27}H_{29}N_5O_6$ (519.6) calculated: 62.42% C, 5.63% H, 13.48% N; found: 62.28% C, 5.71% H, 13.36% N. $[\alpha]_D$ +57.5 (*c* 0.532, 2-methoxyethanol). ^{1}H NMR (DMSO-d_6): 1.97 dd, 1 H, *J*(3a,4) = 4.4, J_{gem} = 13.4 (H-3a); 2.40 t, 1 H, *J*(3b,4) = 13.4 (H-3b); 3.17 dd, 1 H and 3.27 dd, 1 H, J_{gem} = 10.6 (CH_2O); 3.63 dd, 1 H and 3.93 dd, 1 H, J_{gem} = 11.3 (CH_2O); 4.04 t, 1 H (H-6); 4.29 ddd, 1 H, *J*(5,6) = 10.1 (H-5); 4.48 d, 1 H and 4.78 d, 1 H, J_{gem} = 11.4 (CH_2Ph); 4.59 t, 1 H, *J*(OH,CH_2) = 5.0 (CH_2O**H**); 4.85 ddd, 1 H, *J*(4,5) = 10.3 (H-4); 4.92 t, 1 H, *J*(OH,CH_2) = 5.0 (CH_2O**H**); 5.42 d, 1 H, *J*(OH,5) = 6.6 (5-OH); 5.47 d, 1 H, *J*(1,6) = 10.1 (H-1); 7.03–7.11 m, 5 H (arom., benzyl); 7.14 brs, 2 H (NH_2); 7.54 t, 2 H, 7.66 t, 1 H and 8.00 d, 2 H (arom., benzoyl); 8.15 s, 1 H and 8.22 s, 1 H (H-2′, H-8′).

The mother liquors from crystallization of **5** were evaporated and a solution of the residue (72 mg) in methanolic ammonia (saturated at 0 °C, 1.5 ml) was set aside in a pressure

vessel at room temperature for 48 h. Then, the reaction mixture was evaporated, palladium hydroxide (20% Pd/C, 120 mg) was added to a solution of the residue in ethanol (3 ml) and cyclohexene (3 ml), and the mixture was refluxed under argon for 9 h. The catalyst was then filtered off, washed with ethanol, and the combined filtrates were evaporated. Chromatography of the residue on a silica gel column (10 g) in ethyl acetate–acetone–ethanol–water (90:15:11:9) afforded 25 mg (1.2%) of **7** and 20 mg (1%, both based on sulfate **4**) of **22**. (For spectra and characteristics see synthesis of **7** and **22**.)

(1*R*,2*R*,3*S*,6*S*)-6-(6-Amino-9*H*-purin-9-yl)-2-(benzyloxy)-4,4-bis(hydroxymethyl)-cyclohexane-1,3-diol (**6**)

A) A solution of benzoate **5** (260 mg, 0.5 mmol) in methanolic ammonia (saturated at 0 °C, 5 ml) was set aside in a pressure vessel at room temperature for 48 h and then the reaction mixture was evaporated. Chromatography of the residue on a silica gel column (10 g) in ethyl acetate–acetone–ethanol–water (90:15:11:9) afforded 185 mg (89%) of **6**. For $C_{20}H_{25}N_5O_5$ (415.5) calculated: 57.82% C, 6.07% H, 16.86% N; found: 57.59% C, 5.96% H, 16.60% N. $[\alpha]_D$ +15.1 (*c* 0.543, methanol). ^{1}H NMR (DMSO-d_6): 1.80 dd, 1 H, *J*(5a,6) = 4.3, J_{gem} = 13.2 (H-5a); 2.21 t, 1 H, *J*(5b,6) = 13.2 (H-5b); 3.34 dd, 1 H and 3.46 dd, 1 H, *J*(CH_2,OH) = 5.3, J_{gem} = 10.4 (CH_2O); 3.55 dd, 1 H and 3.69 dd, 1 H, *J*(CH_2,OH) = 5.0, J_{gem} = 11.1 (CH_2O); 3.57 t, 1 H, *J*(2,1) = *J*(2,3) = 9.6 (H-2); 3.71 dd, 1 H, *J*(3,OH) = 5.5 (H-3); 4.06 ddd, 1 H (H-1); 4.52 t, 1 H (CH_2O**H**); 4.57 t, 1 H (CH_2O**H**); 4.62 ddd, 1 H, *J*(6,1) = 10.6 (H-6); 4.80 d, 1 H (OH); 4.81 s, 2 H (CH_2Ph); 5.06 d, 1 H, *J*(OH,1) = 6.6 (1-OH); 7.07 s, 2 H (NH_2); 7.21–731 m, 3 H and 4.72 d, 2 H (arom.); 8.11 s, 2 H (H-2′, H-8′).

B) Liquid ammonia (10 ml) was added to a solution of **14** (217 mg, 0.5 mmol) in methanol (2.5 ml) at –70 °C and the mixture was heated in an autoclave at 75 °C for 48 h. Ammonia and methanol were evaporated and the residue was chromatographed on a silica gel column (25 g) in ethyl acetate–acetone–ethanol–water (90:15:11:9) to give 166 mg (80%) of **6**.

(1*R*,2*R*,3*S*,6*S*)-6-(6-Amino-9*H*-purin-9-yl)-4,4-bis(hydroxymethyl)-cyclohexane-1,2,3-triol (**7**)

Palladium hydroxide on carbon (20% Pd, 230 mg) was added to a solution of benzyl derivative **6** (208 mg, 0.5 mmol) in ethanol (10 ml) and cyclohexene (10 ml), and the mixture was refluxed under argon for 3 h. Then, more catalyst (200 mg) was added and the heating was continued for the following 6 h. The catalyst was then filtered off, washed with water, and the combined filtrates were evaporated. Crystallization of the residue from aqueous ethanol gave 135 mg (83%) of **7**, m.p. 245–248 °C. For $C_{13}H_{19}N_5O_5 \cdot H_2O$ (343.4) calculated: 45.48% C, 6.07% H, 20.40% N; found: 45.34% C, 5.96% H, 20.26% N. FAB MS, *m/z*: 326 [M + H]. $[\alpha]_D$ +26.9 (*c* 0.565, water). ^{1}H NMR (DMSO-d_6): 1.82 dd, 1 H, *J*(5eq,6) = 4.4, J_{gem} = 13.4 (H-5eq); 2.19 brt, 1 H, *J*(5ax,6) = 13.2 (H-5ax); 3.32 d, 1 H and 3.44 d, 1 H, J_{gem} = 10.5 (CH_2O); 3.49 dd, 1 H, *J*(2,1) = 8.3, *J*(2,3) = 9.4 (H-2); 3.51 d, 1 H and 3.62 d, 1 H, J_{gem} = 11.2 (CH_2O); 3.83 dd, 1 H, *J*(1,6) = 10.4 (H-1); 4.52 d, 1 H (H-3); 4.58 ddd, 1 H (H-6); 4.60 brs, 3 H and 4.95 brs, 2 H (5 × OH); 7.90 brs, 2 H (NH_2); 8.24 s, 1 H (H-2′); 8.28 s, 1 H (H-8′). ^{13}C NMR (DMSO-d_6): 31.29 (C-5); 44.36 (C-4); 56.21 (C-6); 60.65 and 64.69 (2 × CH_2O); 73.51 (C-1); 74.09 (C-3); 75.14 (C-2); 119.20 (C-5′); 142.26 (C-8′); 149.38 (C-2′); 149.70 (C-4′); 153.94 (C-6′).

(1*S*,4*S*,5*R*,6*S*)-4-Azido-5-hydroxy-6-(benzyloxy)-2,2-bis[(trityloxy)methyl]-cyclohexyl Benzoate (**8**)

A solution of sulfate **4** (1.90 g, 2 mmol) and lithium azide (392 mg, 8 mmol) in dimethylformamide (20 ml) was heated at 60 °C for 1.5 h and evaporated to dryness. A mixture of the residue, tetrahydrofuran (19 ml), sulfuric acid (0.9 ml) and water (0.9 ml) was stirred at room temperature overnight and then neutralized with sodium hydrogencarbonate. The mixture was partitioned between ethyl acetate (80 ml) and water (40 ml), the organic layer was separated, washed with water (2 × 40 ml), dried over anhydrous sodium sulfate, and evaporated. Chromatography of the residue on a silica gel column (200 g, pretreated with triethylamine) in toluene–ethyl acetate (93:7) gave 1.24 g (68%) of azide **8**. For $C_{60}H_{53}N_3O_6$ (912.1) calculated: 79.01% C, 5.86% H, 4.61% N; found: 79.17% C, 5.92% H, 4.47% N. $[\alpha]_D$ +4.7 (*c* 0.676, chloroform). ^{1}H NMR ($CDCl_3$): 1.66 t, 1 H, *J*(3a,4) = J_{gem} = 13.2 (H-3a); 2.04 dd, 1 H, *J*(3b,4) = 4.6 (H-3b); 2.97 d, 1 H and 3.17 d, 1 H, J_{gem} = 9.4 (CH_2O); 3.30 d, 1 H and 3.33 d, 1 H, J_{gem} = 9.6 (CH_2); 3.38 ddd, 1 H, *J*(4.5) = 9.1 (H-4); 3.57 brt, 1 H (H-5); 3.62 t, *J*(6,5) = 9.9 (H-6); 4.45 d, 1 H and 4.51 d, 1 H, J_{gem} = 11.1 (CH_2Ph); 5.55 d, 1 H, *J*(1,6) = 9.9 (H-1); 7.07–7.36 m, 37 H, 7.55 t, 1 H and 7.66 d, 2 H (arom.).

(1*R*,2*R*,3*S*,6*S*)-6-Amino-2-(benzyloxy)-4,4-bis[(trityloxy)methyl]-cyclohexane-1,3-diol (**9**)

A) A solution of azide **8** (1.82 g, 2 mmol) in tetrahydrofuran (8 ml) was added dropwise under stirring to a boiling 1 M solution of lithium aluminium hydride (8 ml) in argon atmosphere. The mixture was refluxed for 2.5 h, cooled, and ethyl acetate (4 ml) was added, followed after 15 min by water. The mixture was taken down, the residue was extracted with warm toluene (3 × 15 ml), and the combined extracts were evaporated. Crystallization from ether afforded 1.05 g (61%) of compound **9**, m.p. 115–118 °C. For $C_{53}H_{51}NO_5 \cdot (C_2H_5)_2O$ (856.1) calculated: 79.97% C, 7.18% H, 1.64% N; found: 79.77% C, 7.15% H, 1.52% N. $[\alpha]_D$ +2.7 (*c* 0.686, chloroform). ^{1}H NMR (DMSO-d_6): 0.59 t, 6 H, *J*(CH_3,CH_2) = 7.0 (2 × CH_3); 1.28 t, 1 H, *J*(5a,6) = J_{gem} = 13.5 (H-5a); 1.40 brs, 2 H (NH_2); 1.76 dd, 1 H, *J*(5b,6) = 3.9 (H-5b); 2.13–2.19 m, 1 H (H-6); 2.83–2.90 m, 2 H (H-1, H-2); 2.88 q, 4 H (2 × $MeCH_2$); 2.98 d, 1 H and 3.10 d, 1 H, J_{gem} = 9.3 (CH_2O); 3.20 s, 2 H (CH_2O); 3.68 dd, 1 H, *J*(3,OH) = 5.3, *J*(3,2) = 9.2 (H-3); 4.61 d, 1 H (3-OH); 4.62 d, 1 H and 4.70 d, H, J_{gem} = 11.4 CH_2Ph); 4.81 d, 1 H, *J*(OH,1) = 3.5 (1-OH); 7.18–7.42 m, 35 H (arom.).

B) Using the same procedure as described above, the azido derivative **10** (1.62 g, 2 mmol) produced 1.30 g (76%) of compound **9**.

(1*R*,2*R*,3*S*,6*S*)-6-Azido-2-(benzyloxy)-4,4-bis[(trityloxy)methyl]cyclohexane-1,3-diol (**10**) and (1*S*,4*R*,5*S*,6*S*)-5-Azido-6-(benzyloxy)-2,2-bis[(trityloxy)methyl]cyclohexane-1,4-diol (**11**)

A solution of sulfite **3** (4.15 g, 5 mmol) and lithium azide (1.22 g, 25 mmol) in dimethylformamide (45 ml) was heated under argon at 130 °C for 2.5 h. The mixture was evaporated and the residue residue was partitioned between ethyl acetate (200 ml) and water (50 ml). The organic layer was separated and washed with water (2 × 50 ml), dried over anhydrous sodium sulfate, and the solvent was evaporated. Chromatography of the residue on a silica gel column (400 g, pretreated with triethylamine) in toluene–ethyl acetate (93:7) gave 1.70 g (42%) of **10** and 0.78 g (19%) of **11** (both after crystallization from ethanol).

Compound **10**: M.p. 216–218 °C. For $C_{53}H_{49}N_3O_5$ (808.0) calculated: 78.79% C, 6.11% H, 5.20% N; found: 78.52% C, 6.20% H, 5.02% N. $[\alpha]_D$ –19.0 (*c* 0.538, chloroform). ^{1}H NMR ($CDCl_3$): 0.94 t, 1 H, *J*(5a,6) = J_{gem} = 13.2 (H-5a); 1.92 dd, 1 H, *J*(5b,6) = 4.8 (H-5b); 2.59 ddd, 1 H, *J*(6,1) = 9.6 (H-6); 2.98 dd, 1 H, *J*(2,1) = 9.2, *J*(2,3) = 9.6 (H-2); 3.20 td, 1 H, *J* = 1.8 (H-1); 3.23 d, 1 H and 3.67 d, 1 H, J_{gem} = 8.8 (CH_2O); 3.25 d, 1 H and 3.80 d, 1 H, J_{gem} = 9.7 (CH_2O); 3.59 dd, 1 H, *J* = 2.4 (H-3); 4.54 d, 1 H and 4.86 d, 1 H, J_{gem} = 11.2 (CH_2Ph); 7.24–7.46 m, 35 H (arom.). ^{1}H NMR (DMSO-d_6): 1.27 t, 1 H, *J*(5a,6) = J_{gem} = 12.8 (H-5a); 1.64 dd, 1 H, *J*(5b,6) = 3.7 (H-5b); 2.62 ddd, 1 H (H-6); 2.94 d, 1 H, J_{gem} = 8.5 (CH^aH-O); 2.95 t, 1 H, *J* = 9.1 (H-2); 3.13–3.33 m, 4 H (CH_2O, CH^aH-O, H-1); 3.71 dd, 1 H, *J*(3,OH) = 5.5, *J*(3,2) = 9.1 (H-3); 4.67 d, 1 H and 4.71 d, 1 H, J_{gem} = 11.6 (CH_2Ph); 5.04 d, 1 H, *J* = 5.5 (OH); 5.61 d, 1 H, *J* = 5.5 (OH); 7.15–7.42 m, 35 H (arom.).

Compound **11**: M.p. 193–195 °C. For $C_{53}H_{49}N_3O_5$ (808.0) calculated: 78.79% C, 6.11% H, 5.20% N; found: 78.92% C, 6.36% H, 4.92% N. $[\alpha]_D$ +7.9 (*c* 0.629, chloroform). ^{1}H NMR (DMSO-d_6): 0.98 brt, 1 H (H-3a); 1.78 dd, 1 H, *J*(3b,4) = 4.0, J_{gem} = 12.6 (H-3b); 3.14 d, 1 H, J_{gem} = 7.8 (C**H**H-O); 3.18 m, 1 H (H-5); 3.25–3.33 m, 3 H (2 × CH**H**O, H-4); 3.50 d, 1 H, J_{gem} = 9.1 (C**H**H-O); 3.60 t, 1 H, *J*(6,5) = *J*(6,1) = 3.3 (H-6); 3.77 dd, 1 H, *J*(OH,1) = 4.0 (H-1); 4.35 d, 1 H and 4.45 d, 1 H, J_{gem} = 11.6 (CH_2Ph); 4.65 d, 1 H, *J* = 4.0 (OH); 4.69 d, 1 H, *J* = 5.3 (OH); 7.11–7.34 m, 35 H (arom.).

(1*S*,4*R*,5*S*,6*S*)-5-Amino-6-(benzyloxy)-2,2-bis[(trityloxy)methyl]cyclohexane-1,4-diol (**12**)

Using the same procedure as described in the preparation of compound **9**, azide **11** (1.62 g, 2 mmol) was converted to amino derivative **12** (1.11 g; 71%, crystallized from ethanol), m.p. 118–120 °C. For $C_{53}H_{51}NO_5$ (782.0) calculated: 81.40% C, 6.57% H, 1.79% N; found: 81.21% C, 6.63% H, 1.82% N. $[\alpha]_D$ +7.5 (*c* 0.516, chloroform). ^{1}H NMR (DMSO-d_6): 0.89 t, 1 H, *J*(3a,4) = J_{gem} = 11.6 (H-3a); 1.19 brs, 2 H (NH_2); 1.69 dd, 1 H, *J*(3b,4) = 3.8 (H-3b); 2.73 m, 1 H (H-5); 3.17 d, 1 H, J_{gem} = 7.6 (CH**H**-O); 3.29–3.34 m, 3 H (2 × C**H**H-O, H-4); 3.44 dd, 1 H, *J*(6,1) = 3.6, *J*(6,5) = 3.3 (H-6); 3.51 d, 1 H, J_{gem} = 9.1 (CH**H**-O); 3.79 dd, 1 H, *J*(1,OH) = 4.1 (H-1); 4.12 d, 1 H (1-OH); 4.32 d, 1 H, *J*(4,OH) = 4.5 (4-OH); 4.34 s, 2 H (CH_2Ph); 7.11–7.26 m, 30 H and 7.33–7.36 m, 5 H (arom.).

(1*R*,2*R*,3*S*,6*S*)-6-[(5-Amino-6-chloropyrimidin-4-yl)amino]-2-(benzyloxy)-4,4-bis[(trityloxy)methyl]cyclohexane-1,3-diol (**13**)

A solution of amine **9** (1.28 g, 1.5 mmol), 4,6-dichloropyrimidin-5-amine (492 mg, 3 mmol), and triethylamine (0.7 ml) in ethanol (12 ml) was heated in a pressure vessel at 100 °C for 4 days and, after cooling, was taken down. Chromatography of the residue on a silica gel column (100 g) in toluene–ethyl acetate (2:1) afforded 835 mg (61%) of compound **13** as a solid foam. For $C_{57}H_{53}ClN_4O_5$ (909.5) calculated: 75.27% C, 5.87% H, 3.90% Cl, 6.16% N; found: 74.99% C, 5.97% H, 3.81% Cl, 6.01% N. $[\alpha]_D$ –14.4 (*c* 0.667, chloroform). ^{1}H NMR (DMSO-d_6): 1.57 dd, 1 H, *J*(5a,6) = 12.8, J_{gem} = 13.2 (H-5a); 2.08 dd, 1 H, *J*(5b,6) = 3.9 (H-5b); 2.98 d, 1 H and 3.21 d, 1 H, J_{gem} = 9.6 (CH_2O); 3.01 d, 1 H and 3.09 d, 1 H, J_{gem} = 8.7 (CH_2O); 3.15 t, 1 H, *J*(2,1) = *J*(2,3) = 9.3 (H-2); 3.44 dt, 1 H, *J*(1,6) = 9.1, *J*(1,OH) = 5.5 (H-1); 3.77 dd, 1 H, *J*(3,OH) = 5.2 (H-3); 4.22–4.31 m, 1 H (H-6); 4.67 d, 1 H and 4.78 d, 1 H, J_{gem} = 11.2 (CH_2Ph); 4.70 d, 1 H (3-OH); 4.96 d, 1 H (1-OH); 5.01 brs, 2 H (NH_2); 6.57 d, 1 H, *J* = 7.6 (NH); 7.20–7.42 m, 35 H (arom.); 7.46 s, 1 H (H-2′).

(1*R*,2*R*,3*S*,6*S*)-2-(Benzyloxy)-6-(6-chloro-9*H*-purin-9-yl)-4,4-bis(hydroxymethyl)-cyclohexane-1,3-diol (**14**)

Concentrated hydrochloric acid (0.12 ml) was added to a solution of compound **13** (910 mg, 1 mmol) in triethyl orthoformate (9 ml), the solution was set aside at room temperature for 16 h and then evaporated. The residue was dissolved in tetrahydrofuran (12 ml). To the stirred solution, 0.5 M hydrochloric acid (12 ml) was added, the mixture was stirred at room temperature for 2.5 h and then neutralized with solid sodium hydrogencarbonate. The organic layer was separated and evaporated. The residue was dissolved in methanol (5 ml), the crystalline triphenylmethanol was filtered off and washed with methanol. The aqueous layer was taken down and the residue was extracted with methanol (3 × 5 ml). The combined methanolic extracts and filtrates were evaporated. Column chromatography of the residue on silica gel (50 g) in ethyl acetate–acetone–ethanol–water (95:15:9:6) afforded 337 mg (77%) of chloropurine **14**. For $C_{20}H_{23}ClN_4O_5$ (434.9) calculated: 55.24% C, 5.33% H, 8.15% Cl, 12.88% N; found: 55.02% C, 5.52% H, 7.95% Cl, 12.62% N. FAB MS, *m/z* (rel.%): 437/435 (25/68) [M + H], 91 (100). $[\alpha]_D$ +10.9 (*c* 0.730, methanol). ^{1}H NMR (DMSO-d_6): 1.88 dd, 1 H, *J*(5eq,6) = 4.3, J_{gem} = 13.3 (H-5eq); 2.30 t, 1 H, *J*(5ax,6) = 13.3 (H-5ax); 3.31 d, 1 H and 3.46 d, 1 H, J_{gem} = 10.5 (CH_2O); 3.51 d, 1 H and 3.71 d, 1 H, J_{gem} = 11.2 (CH_2O); 3.62 dd, 1 H, *J*(2,1) = 8.9, *J*(2,3) = 9.6 (H-2); 3.73 dd, 1 H, *J*(3,OH) = 4.0 (H-3); 4.04 ddd, 1 H, *J*(1,6) = 10.5, *J*(1,OH) = 5.2 (H-1); 4.60 brs, 1 H and 4.65 brs, 1 H (2 × CH_2O**H**); 4.80 s, 2 H (CH_2Ph); 4.83 ddd, 1 H (H-6); 4.90 d, 1 H (3-OH); 5.21 d, 1 H (1-OH); 7.22 t, 1 H, 7.28 t, 2 H and 7.40 d, 2 H (arom.); 8.74 s, 1 H and 8.75 s, 1 H (H-2′, H-8′). ^{13}C NMR (DMSO-d_6): 30.90 (C-5); 44.70 (C-4); 57.20 (C-6); 60.78 and 64.34 (2 × OCH_2); 73.01 (C-1); 73.94 (C-3); 74.43 (OCH_2Ph); 84.30 (C-2); 127.29, 127.85, 2 C, 128.17, 2 C, 140.07 (arom.); 131.67 (C-5′); 147.50 (C-8′); 149.22 (C-6′); 151.34 (C-2′); 152.50 (C-4′).

(1*R*,2*R*,3*S*,6*S*)-2-(Benzyloxy)-6-[6-(cyclopropylamino)-9*H*-purin-9-yl]-4,4-bis(hydroxymethyl)cyclohexane-1,3-diol (**15**)

A solution of chloropurine **14** (326 mg, 0.75 mmol) in cyclopropylamine (1.7 ml) was set aside at room temperature overnight and then evaporated. Chromatography of the residue on a silica gel column (50 g) in ethyl acetate–acetone–ethanol–water (90:15:11:9) afforded 318 mg (93%) of compound **15** as a solid foam. For $C_{23}H_{29}N_5O_5$ (455.5) calculated: 60.65% C, 6.42% H, 15.37% N; found: 60.37% C, 6.56% H, 15.10% N. $[\alpha]_D$ +11.7 (*c* 0.541, methanol). ^{1}H NMR (DMSO-d_6): 0.60 m, 2 H, 0.72 m, 2 H and 3.05 brs, 1 H (cyclopropyl); 1.80 dd, 1 H, *J*(5a,6) = 4.3, J_{gem} = 13.3 (H-5a); 2.22 t, 1 H, *J*(5b,6) = 13.3 (H-5b); 3.34 dd, 1 H and 3.47 dd, 1 H, *J*(CH_2,OH) = 5.4, J_{gem} =10.5 (CH_2O); 3.53–3.57 m, 1 H and 3.67–3.73 m, 2 H (CH_2O, H-3); 3.57 t, 1 H, *J*(2,1) = *J*(2,3) = 9.1 (H-2); 4.07 ddd, 1 H, *J*(1,OH) = 6.7, *J*(1,6) = 10.4 (H-1); 4.54 t, 1 H, *J*(CH_2,OH) = 5.4 (CH_2O**H**); 4.59 t, 1 H, *J*(CH_2,OH) = 5.0 (CH_2O**H**); 4.63 ddd, 1 H (H-6); 4.81 brs, 2 H (CH_2Ph); 4.83 d, 1 H, *J*(OH,3) = 5.3 (3-OH); 5.08 d, 1 H (1-OH); 7.21–7.32 m, 3 H and 7.41–7.43 m, 2 H (arom.); 7.75 brd, 1 H, *J* = 3.4 (NH); 8.13 s, 1 H and 8.21 s, 1 H (H-2′, H-8′).

(1*R*,2*R*,3*S*,6*S*)-6-[6-(Cyclopropylamino)-9*H*-purin-9-yl]-4,4-bis(hydroxymethyl)-cyclohexane-1,2,3-triol (**16**)

Palladium hydroxide on carbon (20% Pd, 230 mg) was added to a solution of benzyl derivative **15** (228 mg, 0.5 mmol) in ethanol (10 ml) and cyclohexene (10 ml), and the mixture

was refluxed under argon for 3 h. The catalyst was then filtered off, washed with ethanol, and the combined filtrates were evaporated. Chromatography of the residue on a silica gel (20 g) column in ethyl acetate–acetone–ethanol–water (90:15:11:9) afforded 130 mg (71%) of **16** as an amorphous solid. For $C_{16}H_{23}N_5O_5$ (365.4) calculated: 52.59% C, 6.34% H, 19.17% N; found: 52.19% C, 6.60% H, 18.82% N. FAB MS, *m/z* (rel.%): 366 (100) [M + H], 176 (54), 102 (14). $[\alpha]_D$ +29.7 (*c* 0.708, water). ^{1}H NMR (DMSO-d_6): 0.59 m, 2 H, 0.71 m, 2 H and 3.02 brs, 1 H (cyclopropyl); 1.79 dd, 1 H, *J*(5eq,6) = 4.3, J_{gem} = 13.4 (H-5eq); 2.21 brt, 1 H, *J*(5ax,6) = 13.2 (H-5ax); 3.33 dd, 1 H and 3.44 dd, 1 H, *J*(CH_2,OH) = 5.1, J_{gem} = 10.6 (CH_2O); 3.47 ddd, 1 H, *J*(2,1) = 8.5, *J*(2,3) = 9.8, *J*(2,OH) = 4.4 (H-2); 3.51 dd, 1 H, *J*(3,OH) = 4.1 (H-3); 3.52 dd, 1 H and 3.62 dd, 1 H, *J*(CH_2,OH) = 5.3, J_{gem} = 11.2 (CH_2O); 3.86 ddd, 1 H, *J*(1,6) = 10.6, *J*(1,OH) = 5.5 (H-1); 4.51 brt, 2 H (2 × CH_2O**H**); 4.53 ddd, 1 H (H-6); 4.64 d, 1 H (3-OH); 4.88 d, 1 H (1-OH); 4.89 d, 1 H (2-OH); 7.78 brs, 1 H (NH); 8.10 s, 1 H and 8.20 s, 1 H (H-2′, H-8′). ^{13}C NMR (DMSO-d_6): 6.76, 2 C (2 × CH_2); 24.10 (NCH); 31.21 (C-5); 44.22 (C-4); 55.86 (C-6); 60.60 and 64.68 (2 × OCH_2); 73.55 (C-1); 73.88 (C-3); 75.19 (C-2); 119.88 (C-5′); 140.91 (C-8′); 149.60 (C-4′); 152.04 (C-2′); 155.71 (C-6′).

(1*S*,4*R*,5*S*,6*S*)-5-[(5-Amino-6-chloropyrimidin-4-yl)amino]-6-(benzyloxy)-2,2-bis[(trityloxy)methyl]cyclohexane-1,4-diol (**17**)

Amine **12** (1.17 g, 1.5 mmol) was reacted with 4,6-dichloropyrimidin-5-amine (492 mg, 3 mmol) as described for **13**. Chromatography of the product on a silica gel column in ethyl acetate–toluene (4:3) afforded 1.02 g (75%) of compound **17** as a solid foam. For $C_{57}H_{53}ClN_4O_5$ (909.5) calculated: 75.27% C, 5.87% H, 3.90% Cl, 6.16% N; found: 74.98% C, 6.01% H, 3.96% Cl, 6.01% N. $[\alpha]_D$ +15.9 (*c* 0.564, chloroform). ^{1}H NMR (DMSO-d_6): 1.16 brt, 1 H, *J*(3a,4) ≈ J_{gem} ≈ 12.0 (H-3a); 2.10 dd, 1 H, *J*(3b,4) = 3.4 (H-3b); 3.09 d, 1 H and 3.47 d, 1 H, J_{gem} = 7.5 (CH_2O); 3.14 d, 1 H, J_{gem} = 8.7 (CH^aH-O); 3.57–3.64 m, 2 H and 3.75–3.83 m, 2 H (CH^bH-O, H-1, H-4, H-6); 4.15 d, 1 H, *J* = 4.1 (OH); 4.17 d, 1 H and 4.25 d, 1 H, J_{gem} = 12.4 (CH_2Ph); 4.34 ddd, 1 H, *J*(5,4) = 9.5, *J*(5,NH) = 7.9, *J*(5,6) = 2.1 (H-5); 4.41 d, 1 H, *J* = 5.4 (OH); 5.18 s, 2 H (NH_2); 6.16 d, 1 H (NH); 7.02–7.42 m, 35 H (arom.); 7.62 s, 1 H (H-2′).

(1*S*,4*R*,5*S*,6*S*)-6-(Benzyloxy)-5-(6-chloro-9*H*-purin-9-yl)-2,2-bis(hydroxymethyl)-cyclohexane-1,4-diol (**18**)

Concentrated hydrochloric acid (1 ml) was added to a solution of compound **17** (910 mg, 1 mmol) in triethyl orthoformate (18 ml), the solution was set aside at room temperature for 3 days and then evaporated. The residue was worked up using the same procedure as in preparation of **14**. Column chromatography of the residue on silica gel (50 g) in ethyl acetate–acetone–ethanol–water (90:15:11:9) afforded, after crystallization from ethanol, 326 mg (75%) of chloropurine **18**, m.p. 203.5–205.5 °C. For $C_{20}H_{23}ClN_4O_5 \cdot H_2O$ (452.9) calculated: 53.04% C, 5.56% H, 7.83% Cl, 12.37% N; found: 52.91% C, 5.66% H, 7.80% Cl, 12.21% N. $[\alpha]_D$ –128.8 (*c* 0.845, methanol). ^{1}H NMR (DMSO-d_6): 1.40 t, 1 H, *J*(3a,4) = J_{gem} = 12.8 (H-3a); 1.83dd, 1 H, *J*(3b,4) = 4.3 (H-3b); 3.49 m, 2 H (CH_2O); 3.67 dd, 1 H, *J*(OH,CH_2) = 5.2 and 3.83 dd, 1 H, *J*(OH,CH_2) = 5.1, J_{gem} = 10.6 (CH_2O); 3.73 t, 1 H, *J*(6,1) = *J*(6,5) = 3.4 (H-6); 4.00 brt, 1 H (H-1); 4.06 d, 1 H and 4.50 d, 1 H, J_{gem} = 11.9 (CH_2Ph); 4.30 m, 2 H (2 × OH); 4.44 m, 1 H (H-4); 4.84 dd, 1 H, *J*(5,4) = 11.1 (H-5); 4.89 d, 1 H, *J* = 6.1 (OH); 5.23 d, 1 H, *J* = 4.8 (OH); 6.92 dd, 2 H and 7.06–7.11 m, 3 H (arom.); 8.57 s, 1 H and 8.66 s, 1 H (H-2′, H-8′).

(1*S*,4*R*,5*S*,6*S*)-6-(Benzyloxy)-5-[6-(cyclopropylamino)-9*H*-purin-9-yl]-2,2-bis(hydroxymethyl)cyclohexane-1,4-diol (**19**)

Using the same procedure as in preparation of **15**, chloropurine **18** (340 mg, 0.75 mmol) was treated with cyclopropylamine to give 321 mg (94%) of compound **19** as a solid foam. For $C_{23}H_{29}N_5O_5$ (455.5) calculated: 60.65% C, 6.42% H, 15.37% N; found: 60.31% C, 6.61% H, 15.08% N. FAB MS, *m/z* (rel.%): 366 (100) [M + H], 176 (69), 102 (14). $[\alpha]_D$ –98.5 (*c* 0.443, methanol). ^{1}H NMR (DMSO-d_6): 0.62 m, 2 H, 0.73 m, 2 H and 3.08 brs, 1 H (cyclopropyl); 1.40 dd, 1 H, *J*(3a,4) = 11.6, J_{gem} = 12.8 (H-3a); 1.80 dd, 1 H, *J*(3b,4) = 4.6 (H-3b); 3.45 dd, 1 H and 3.51 dd, 1 H, *J*(CH_2,OH) = 5.5, J_{gem} = 10.4 (CH_2O); 3.64 dd, 1 H and 3.80 dd, 1 H, *J*(CH_2,OH) = 5.2, J_{gem} = 10.6 (CH_2O); 3.71 t, 1 H, *J*(6,1) = 3.3 (H-6); 3.98 dd, 1 H (H-1); 4.00 d, 1 H and 4.47 d, 1 H, J_{gem} = 11.7 (CH_2Ph); 4.31 m, 1 H (H-4); 4.35 t, 1 H, *J*(OH,CH_2) = 5.5 (CH_2O**H**); 4.36 t, 1 H, *J*(OH,CH_2) = 5.2 (CH_2O**H**); 4.78 dd, 1 H, *J*(5,6) = 3.4, *J*(5,4) = 11.0 (H-5); 4.79 d, 1 H, *J* = 6.6 (4-OH); 5.16 d, 1 H, *J*(OH,1) = 4.8 (1-OH); 6.97–6.99 m, 2 H and 7.15–7.19 m, 3 H (arom.); 7.80 brs, 1 H (NH); 8.01 s, 1 H and 8.17 s, 1 H (H-2′, H-8′).

(1*S*,2*S*,3*S*,4*R*)-3-[6-(Cyclopropylamino)-9*H*-purin-9-yl]-6,6-bis(hydroxymethyl)-cyclohexane-1,2,4-triol (**20**)

Using the same procedure as in preparation of **16**, benzyl derivative **19** (228 mg, 0.5 mmol) was deprotected to give 128 mg (70%) of **20**. For $C_{16}H_{23}N_5O_5$ (365.4) calculated: 52.59% C, 6.34% H, 19.17% N; found: 52.28% C, 6.54% H, 18.90% N. $[\alpha]_D$ –76.3 (*c* 0.711, water). ^{1}H NMR (DMSO-d_6): 0.60 m, 2 H, 0.71 m, 2 H and 3.08 m, 1 H (cyclopropyl); 1.37 dd, 1 H, *J*(5ax,4) = 11.5, J_{gem} = 12.8 (H-5ax); 1.80 ddd, 1 H, *J*(5eq,1) = 1.0, *J*(5eq,4) = 4.5 (H-5eq); 3.41 dd, 1 H, *J*(CH,OH) = 5.5 and 3.46 dd, 1 H, *J*(CH,OH) = 5.5, J_{gem} = 10.4 (CH_2O); 3.56 dd, 1 H, *J*(CH,OH) = 5.0 and 3.86 dd, 1 H, *J*(CH,OH) = 5.6, J_{gem} = 11.0 (CH_2O); 3.61 ddd, *J*(1,2) = 3.3, *J*(1,OH) = 4.5 (H-1); 3.82 dt, 1 H, *J*(2,3) = 3.3, *J*(2,OH) = 5.0 (H-2); 4.30 t, 1 H, *J*(OH,CH_2) = 5.6 (CH_2O**H**); 4.32 tdd, 1 H, *J*(4,OH) = 6.5 (H-4); 4.36 t, 1 H, *J*(OH,CH_2) = 5.3 (CH_2O**H**); 4.69 d, 1 H (4-OH); 4.70 dd, 1 H, *J*(3,4) = 11.0 (H-3); 5.07 d, 1 H (1-OH); 5.46 d, 1 H (2-OH); 7.78 brs, 1 H (NH); 8.05 s, 1 H and 8.21 s, 1 H (H-2′, H-8′). ^{13}C NMR (DMSO-d_6): 6.89, 2 C (2 × CH_2); 24.10 (NCH); 34.25 (C-5); 45.08 (C-6); 59.36 (C-3); 63.21 (C-4); 70.67 (C-1); 73.52 (C-2); 118.92 (C-5′); 141.10 (C-8′); 150.10 (C-4′); 152.19 (C-2′); 155.65 (C-6′).

(1*S*,4*R*,5*S*,6*S*)-5-(6-Amino-9*H*-purin-9-yl)-6-(benzyloxy)-2,2-bis(hydroxymethyl)-cyclohexane-1,4-diol (**21**)

Using the same procedure as in preparation of **6** (method *B*), chloro derivative **18** (monohydrate, 226 mg, 0.5 mmol) was ammonolyzed to give 170 mg (82%) of **21**. For $C_{20}H_{25}N_5O_5$ (415.5) calculated: 57.82% C, 6.07% H, 16.86% N; found: 57.53% C, 6.18% H, 16.57% N. $[\alpha]_D$ –107.7 (*c* 0.562, methanol). ^{1}H NMR (DMSO-d_6): 1.41 t, 1 H, *J*(3a,4) = J_{gem} = 12.8 (H-3a); 1.80 dd, 1 H, *J*(3b,4) = 4.3 (H-3b); 3.44–3.53 m, 2 H (CH_2O); 3.64 d, 1 H and 3.81 d, 1 H, *J*(CH_2,OH) = 4.8, J_{gem} = 10.6 (CH_2O); 3.72 t, 1 H, *J*(6,1) = *J*(6,5) = 3.4 (H-6); 3.98 brdd, 1 H (H-1); 4.01 d, 1 H and 4.47 d, 1 H, J_{gem} 11.7 (CH_2Ph); 4.29–4.37 m, 3 H (2 × CH_2O**H**, H-1); 4.77 dd, 1 H, *J*(5,4) = 11.0 (H-5); 4.77 d, 1 H, *J* = 6.3 (OH); 5.14 d, 1 H, *J* = 4.8 (OH); 6.97–7.00 m, 2 H and 7.18 t, 3 H (arom.); 7.10 s, 2 H (NH_2); 8.01 s, 1 H and 8.08 s, 1 H (H-2′, H-8′).

(1*S*,2*S*,3*S*,4*R*)-3-(6-Amino-9*H*-purin-9-yl)-6,6-bis(hydroxymethyl)-cyclohexane-1,2,4-triol (**22**)

Using the same procedure as in preparation of **16**, benzyl derivative **21** (208 mg, 0.5 mmol) was deprotected to give, after crystallization from water, 126 mg (77%) of **22**, m.p. 317–319 °C. For $C_{13}H_{19}N_5O_5$ (325.3) calculated: 48.00% C, 5.89% H, 21.53% N; found: 47.81% C, 5.83% H, 21.37% N. FAB MS, *m/z*: 326 [M + H]. $[\alpha]_D$ –85.1 (*c* 0.536, water). ^{1}H NMR (DMSO-d_6): 1.38 dd, 1 H, *J*(5ax,4) = 11.5, J_{gem} = 12.8 (H-5ax); 1.79 ddd, 1 H, *J*(5eq,1) = 1.0, *J*(5eq,4) = 4.6 (H-5eq); 3.41 dd, 1 H and 3.45 dd, 1 H, *J*(CH_2,OH) = 5.6, J_{gem} = 10.3 (CH_2O); 3.55 dd, 1 H and 3.86 dd, 1 H, *J*(CH_2,OH) = 5.6, J_{gem} = 11.0 (CH_2O); 3.60 ddd, 1 H, *J*(1,2) = 3.5, *J*(1,OH) = 4.4 (H-1); 3.81 dt, *J*(2,3) = 3.2, *J*(2,OH) = 5.0 (H-2); 4.28 t, 1 H (CH_2O**H**); 4.31 tdd, 1 H, *J*(4,OH) = 6.5 (H-4); 4.35 t, 1 H (CH_2O**H**); 4.67 dd, 1 H, *J*(3,4) = 11.1 (H-3); 4.68 d, 1 H (4-OH); 5.05 d, 1 H (1-OH); 5.46 d, 1 H (2-OH); 7.11 brs, 2 H (NH_2); 8.04 s, 1 H (H-8′); 8.10 s, 1 H (H-2′). ^{13}C NMR (DMSO-d_6): 34.25 (C-5); 45.07 (C-6); 59.40 (C-3); 61.37 (OCH_2); 63.18 (C-4); 64.74 (OCH_2); 70.66 (C-1); 73.50 (C-2); 118.51 (C-5′); 141.34 (C-8′); 150.43 (C-4′); 152.19 (C-2′); 155.91 (C-6′).

(1*R*,2*R*,3*S*,6*S*)-6-[(2-Amino-6-chloropyrimidin-4-yl)amino]-4,4-bis[(trityloxy)methyl]-2-(benzyloxy)cyclohexane-1,3-diol (**23**)

Following the procedure used for preparation of compound **13**, reaction of amine **9** (1.28 g, 1.5 mmol) and 4,6-dichloropyrimidin-2-amine (492 mg, 3 mmol) gave 931 mg (68%) of **23** as a solid foam. For $C_{57}H_{53}ClN_4O_5$ (909.5) calculated: 75.27% C, 5.87% H, 3.90% Cl, 6.16% N; found: 75.03% C, 5.69% H, 3.76% Cl, 5.99% N. $[\alpha]_D$ +6.5 (*c* 0.572, chloroform). ^{1}H NMR (DMSO-d_6): 1.65 brs, 1 H (H-5a); 1.88 brd, 1 H, $J_{gem} \approx 12$ (H-5b); 3.03–3.19 m, 5 H (2 × CH_2, H-2); 3.29 ddd, 1 H, *J*(1,2) = *J*(1,6) = 9.3, *J*(1,OH) = 5.5 (H-1); 3.70 dd, 1 H, *J*(3,2) = 9.6, *J*(3,OH) = 5.5 (H-3); 4.68 d, 1 H and 4.76 d, 1 H, J_{gem} = 11.1 (CH_2Ph); 4.82 brs, 1 H (OH); 5.08 d, 1 H, *J* = 5.5 (OH); 5.54 brs, 1 H (H-5′); 6.19 brs, 2 H (NH_2); 6.90 brs, 1 H (NH); 7.13–7.41 m, 35 H (arom.).

(1*R*,2*R*,3*S*,6*S*)-6-[(2-Amino-6-chloropyrimidin-4-yl)amino]-4,4-bis(hydroxymethyl)-2-(benzyloxy)cyclohexane-1,3-diol (**24**)

A solution of trityl derivative **23** (1.36 g, 1.5 mmol) in 80% aqueous trifluoroacetic acid (20 ml) was set aside at room temperature for 15 min and then evaporated. The residue was stirred with 30% aqueous methanol (20 ml) for 10 min, the mixture was filtered, and the filtrate was neutralized with Dowex 1 (HCO_3^-). The resin was filtered off and washed with methanol. The combined filtrates were evaporated. Chromatography of the residue on a silica gel column (45 g) in ethyl acetate–acetone–ethanol–water (90:15:11:9) gave 543 mg (85%) of **24**, m.p. 144–146 °C (aqueous ethanol). For $C_{19}H_{25}ClN_4O_5 \cdot H_2O$ (442.9) calculated: 51.53% C, 6.14% H, 8.00% Cl, 12.65% N; found: 51.46% C, 6.17% H, 8.02% Cl, 12.58% N. $[\alpha]_D$ –16.1 (*c* 0.520, methanol). ^{1}H NMR (DMSO-d_6): 1.21 t, 1 H, *J*(5a,6) = J_{gem} = 13.1 (H-5a); 3.22–3.56 m, 7 H (2 × CH_2O, H-1, H-2, H-3); 4.70 brt, 2 H (2 × OH); 4.70 brs, 1 H (OH); 4.77 d, 1 H and 4.81 d, 1 H, J_{gem} = 11.6 (CH_2Ph); 4.88 brs, 1 H (OH); 5.75 brs, 1 H (H-5′); 6.31 brs, 2 H (NH_2); 6.98 brs, 1 H (NH); 7.23 t, 1 H, 7.30 t, 2 H and 7.42 d, 2 H (arom.).

(1*R*,2*R*,3*S*,6*S*)-6-({2-Amino-6-chloro-5-[(4-chlorophenyl)azo]pyrimidin-4-yl}amino)-2-(benzyloxy)-4,4-bis(hydroxymethyl)cyclohexane-1,3-diol (**25**)

A cold diazonium salt solution was prepared from 4-chloroaniline (166 mg, 1.3 mmol) in 3 M HCl (2.8 ml) and sodium nitrite (103 mg, 1.5 mmol) in water (0.8 ml). This solution was added to a mixture of **24** (443 mg, 1 mmol), acetic acid (5.6 ml), water (5.6 ml), and anhydrous sodium acetate (1.4 g). The mixture was set aside overnight. The precipitate was filtered, washed with cold water until neutral, and then air-dried. Yield 391 mg (67%) of azo compound **25**, m.p. 174.5–176 °C. For $C_{25}H_{28}Cl_2N_6O_5 \cdot H_2O$ (581.5) calculated: 51.64% C, 5.20% H, 12.19% Cl, 14.45% N; found: 51.74% C, 5.14% H, 12.06% Cl, 14.31% N. $[\alpha]_D$ +122 (*c* 0.573, methanol). ^{1}H NMR (DMSO-d_6): 1.30 t, 1 H, J(5a,6) = J_{gem} = 12.9 (H-5a); 1.92 dd, 1 H, J(5b,6) = 4.3 (H-5b); 3.35–3.46 m, 3 H and 3.59–3.67 m, 3 H (2 × CH_2O, H-1, H-3); 3.46 t, 1 H, J(2,1) = J(2,3) = 8.8 (H-2); 4.40 m, 1 H (H-6); 4.45 t, 1 H, J(OH,CH_2) = 5.0 (CH_2O**H**); 4.49 t, 1 H, J(OH,CH_2) = 5.6 (CH_2O**H**); 4.81 s, 2 H (CH_2Ph); 4.85 d, 1 H, J = 5.3 (OH); 5.12 d, 1 H, J = 5.8 (OH); 7.24 t, 1 H, 7.31 t, 2 H and 7.43 d, 2 H (arom., benzyl); 7.39 brs, 2 H (NH_2); 7.57 d, 2 H, J = 8.8 and 7.79 d, 2 H, J = 8.8 (4-chlorophenyl); 10.29 d, 1 H, J = 7.8 (NH).

(1*R*,2*R*,3*S*,6*S*)-6-(2-Amino-6-chloro-9*H*-purin-9-yl)-2-(benzyloxy)-4,4-bis(hydroxymethyl)cyclohexane-1,3-diol (**26**)

A mixture of azo compound **25** (581 mg, 1 mmol), ethanol (13 ml), water (7 ml), acetic acid (0.3 ml), and zinc dust (0.6 g) was refluxed under argon for 3 h. Zinc was filtered off, washed with ethanol, and combined filtrates and washings were evaporated. The residue was chromatographed on a silica gel column (80 g) in ethyl acetate–acetone–ethanol–water (90:15:11:9). The main UV absorbing fraction was concentrated, the residue was dissolved in triethyl orthoformate (18 ml), concentrated hydrochloric acid (1 ml) was added, and the mixture was set aside at room temperature for 48 h. The solvent was evaporated and a solution of the residue in a mixture of tetrahydrofuran (12 ml) and 0.5 M HCl (12 ml) was set aside at room temperature for 2.5 h. The mixture was neutralized with sodium hydrogencarbonate and evaporated. The residue was extracted with methanol (3 × 5 ml). Combined methanolic extracts and filtrates were taken down. Chromatography of the residue on a silicagel column (60 g) in ethyl acetate–acetone–ethanol–water (90:15:11:9) afforded 225 mg (50%) aminochloropurine **26** as a solid foam. For $C_{20}H_{24}ClN_5O_5$ (449.9) calculated: 53.39% C, 5.38% H, 7.88% Cl, 15.57% N; found: 53.08% C, 5.51% H, 7.69% Cl, 15.29% N. $[\alpha]_D$ +25.4 (*c* 0.574, methanol). ^{1}H NMR (DMSO-d_6): 1.79 dd, 1 H, J(5a,6) = 4.2, J_{gem} = 13.3 (H-5a); 2.12 t, 1 H, J(5b,6) = 13.3 (H-5b); 3.37 dd, 1 H and 3.45 dd, 1 H, J(OH,CH_2) = 5.1, J_{gem} = 10.4 (CH_2O); 3.54 dd, 1 H and 3.69 dd, 1 H, J(OH,CH_2) = 5.3, J_{gem} = 9.6 (CH_2O); 3.54 t, 1 H, J(2,1) = J(2,3) = 9.1 (H-2); 3.66 dd, 1 H (H-3); 3.99 ddd, 1 H, J(OH,1) = 6.1, J(1,6) = 10.4 (H-1); 4.52–4.59 m, 3 H (2 × CH_2O**H**, H-6); 4.80 s, 2 H (CH_2Ph); 4.85 d, 1 H, J(OH,3) = 5.0 (3-OH); 5.15 d, 1 H, J(OH,1) = 6.1 (1-OH); 6.82 s, 2 H (NH_2); 7.21–7.31 m, 3 H and 7.41 d, 2 H (arom.); 8.19 s, 1 H (H-8′).

2-Amino-9-[(1*S*,2*R*,3*R*,4*S*)-2,3,4-trihydroxy-5,5-bis(hydroxymethyl)-cyclohexyl]-9*H*-purin-6(1*H*)-one (**27**)

A solution of chloropurine **26** (135 mg, 0.3 mmol) in 1 M HCl (8 ml) was refluxed for 7 h and then evaporated. A solution of the residue in water (10 ml) was neutralized with

Dowex 1 (HCO_3^-), the resin was filtered off, washed with water, and the filtrates and washings were taken down. Crystallization of the residue from dimethylformamide afforded 51 mg (50%) of **27**, m.p. 221–226 °C. For $C_{13}H_{19}N_5O_6$ (341.3) calculated: 45.75% C, 5.61% H, 20.52% N; found: 45.49% C, 5.50% H, 20.31% N. FAB MS, *m/z*: 342 [M + H]. $[\alpha]_D$ +11.7 (*c* 0.214, DMF). ^{1}H NMR (DMSO-d_6): 1.74 dd, 1 H, *J*(5a,6) = 4.3, J_{gem} = 13.2 (H-5a); 1.96 t, 1 H, *J*(5b,6) = 13.2 (H-5b); 3.34–3.59 m, 6 H (2 × CH_2O, H-2, H-3); 3.70 ddd, 1 H, *J*(1,OH) = 5.1, *J*(1,2) = 8.6, *J*(1,6) = 10.6 (H-1); 4.32 ddd, 1 H (H-6); 4.45 t, 1 H, *J*(CH_2,OH) = 4.8 (CH_2O**H**); 4.51 t, 1 H, *J*(CH_2,OH) = 5.3 (CH_2O**H**); 4.64 brd, 1 H (OH); 4.87 d, 2 H, *J* = 5.1 (2 × OH); 6.35 s, 2 H (NH_2); 7.68 s, 1 H (H-8′); 10.48 brs, 1 H (NH).

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