INTRAMOLECULAR CYCLIZATION OF SOME ACYCLIC NUCLEOSIDE ANALOGS*

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Reaction of stereoisomeric 8-bromo-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenines (**8**) with concentrated aqueous ammonia, sodium hydride, potassium *tert*-butoxide, or 1,8-diazabicyclo-[5,4,0]undec-7-ene afforded 4′-*O*,8-anhydro-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenines **9** (derivatives of 1,3-oxazepino[2,3-*e*]adenine). The CD spectra of optically active stereoisomers of **9** have been studied and it was found that for *threo* isomers **9a** and **9b** their character corresponds to 5′-*O*,8-cycloadenosine. The compounds **9** were also prepared by oxidative cyclization of 9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenines (**7**) with lead(IV) acetate in benzene. Reaction of 9-(4-hydroxybutyl)adenine (**14**) with lead(IV) acetate smoothly afforded the seven-membered ring derivative, 4′-*O*,8-anhydro-9-(4-hydroxybutyl)adenine (**15**); no anhydro products with five-, six-, and eight-membered ring were found. 2′,3′-*O*-Isopropylideneinosine (**16**) reacted with lead(IV) acetate to give 5′-*O*,8-cyclo-2′,3′-*O*-isopropylideneinosine (**17**) whereas 9-(4-hydroxybutyl)hypoxanthine (**18**) afforded no cyclic products.

Key words: Nucleosides; Acyclic analogs; Purine derivatives.

In the nucleoside chemistry, purine derivatives modified in the position 8 are of particular importance. Some of them (e.g. compounds derived from 8-amino- or 8-hydroxyguanine) exhibit significant biological (e.g. immunomodulatory) effects[1,2]. These derivatives are usually prepared by reaction of 8-halogenopurines with the corresponding nucleophile such as ammonia, amines, hydrazine, azides, alkoxides, etc. When the sugar moiety participates in such reactions, we can postulate (or even directly prove) a participation of the so-called cyclonucleosides[3].

Some time ago we investigated such reactions with acyclic nucleoside analogs in which the sugar (aldopentofuranose) residue is replaced by a chain bearing hydroxyl functionalities. We focused on adenine derivatives, particularly SAH hydrolase inhibitors such as 9-(*S*)-(2,3-dihydroxypropyl)adenine (DHPA)[4], which exhibit antiviral ac-

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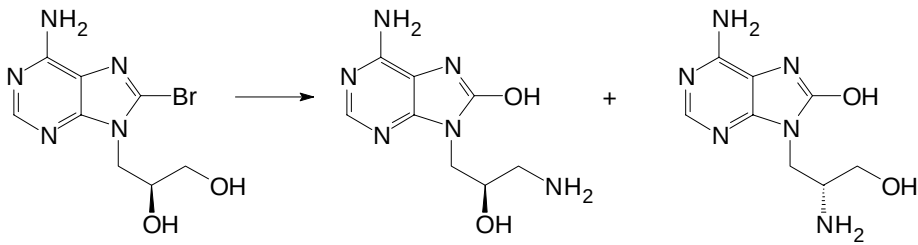
tivity and show further effects on proliferating systems. Most nucleophilic reactions of adenine bases, containing a bromine atom at C-8 and protected hydroxy groups, proceed analogously as those of nucleosides, i.e. under formation of products substituted in position 8 with the corresponding nucleophile[5].

However, compounds containing free hydroxy groups in the side chain react anomalously[6,7]: their reaction with ammonia or primary amines affords 8-hydroxyadenine derivatives with amino group in the side chain. In the reaction of 2,3-dihydroxypropyl derivative **1** two isomeric amino derivatives **2** and **3** were isolated (Scheme 1). One can assume that the reaction involves a cyclonucleoside analog which is opened by nucleophilic attack under formation of 8-hydroxyadenine derivative containing the nucleophilic group in the side chain. The existence of such cyclic form has been proven[7].

The original study on this subject has shown[7] that also 8-bromo-9-(2,3,4-trihydroxybutyl)adenine (**4**) on reaction with aqueous ammonia afforded the 3-amino-2,4-dihydroxybutyl derivative **5** whose formation requires a cyclic intermediate **6** (Scheme 2).

We set out to investigate the mentioned reaction under conditions allowing formation of a seven-membered ring derivative as the only possible intermediate, to prepare such cyclic structures independently and to assess their reactivity with nucleophiles. As a model we have chosen the mentioned group of 8-bromo-9-(2,3,4-trihydroxybutyl)adenines, protected in positions 2 and 3 of the side chain by a 1,3-dioxolane ring ("isopropylidene derivatives").

For the starting adenine derivatives of *threo* configuration both enantiomeric forms 2*S*,3*S* and 2*R*,3*R* have already been described (compounds **7a** and **7b**, respectively), whereas the *erythro* isomer **7c** is hitherto known only in the racemic form[6]. In this study we prepared the (2*S*,3*R*)-*erythro* isomer **7e** from 2′,3′-*O*-isopropylideneadenosine by reductive cleavage with excess of diisobutylaluminium hydride in dry tetrahydrofuran[8] and subsequent shortening of the aliphatic chain in the obtained 1-(adenin-9-yl)-1-deoxy-2,3-*O*-isopropylidene-D-ribitol.

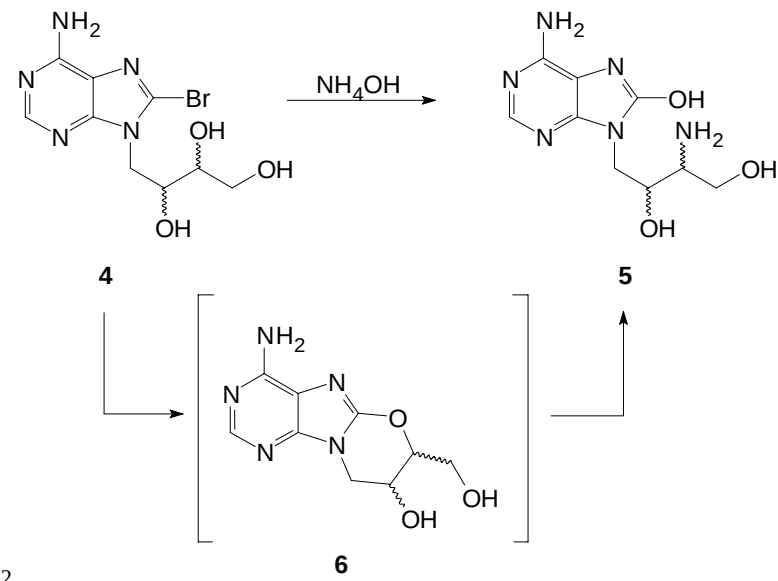


SCHEME 1

The (2*R*,3*S*)-*erythro* isomer **7d** was obtained by reduction of methyl ester of 2′,3′-*O*-isopropylidene-D-eritadenine[9] with Dowex 1 X 2 (BH_4^- form) in aqueous methanol[10].

The compounds **7** were converted into the bromo derivatives **8** by bromination with 2.5 equivalents of bromine in a mixture of dioxane and 10% aqueous solution of sodium dihydrogen phosphate. Intramolecular cyclization of the bromo compounds **8** was performed by treatment with 2 equivalents of sodium hydride in dioxane and gave 4′-*O*,8-anhydro-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenines **9** (1,3-oxazepino[2,3-*e*]adenine derivatives* (Scheme 3). The reaction with both the *threo* (**8a**, **8b**) and *erythro* (**8c**) isomers was complete on standing for 2–3 days at room temperature. After neutralization of the reaction mixture, the cyclic products **9** were obtained by crystallization from ethanol. The *erythro* derivative **9c** was only sparingly soluble in common organic solvents as well as in water and crystallized directly from the reaction mixture.

Compound **8b** was also cyclized by action of 2 equivalents of potassium *tert*-butoxide. Reaction of the *threo* derivatives **8a** and **8b** with DBU in acetonitrile, dimethylformamide or diethylene glycol dimethyl ether proceeded slowly and gave low yields



SCHEME 2

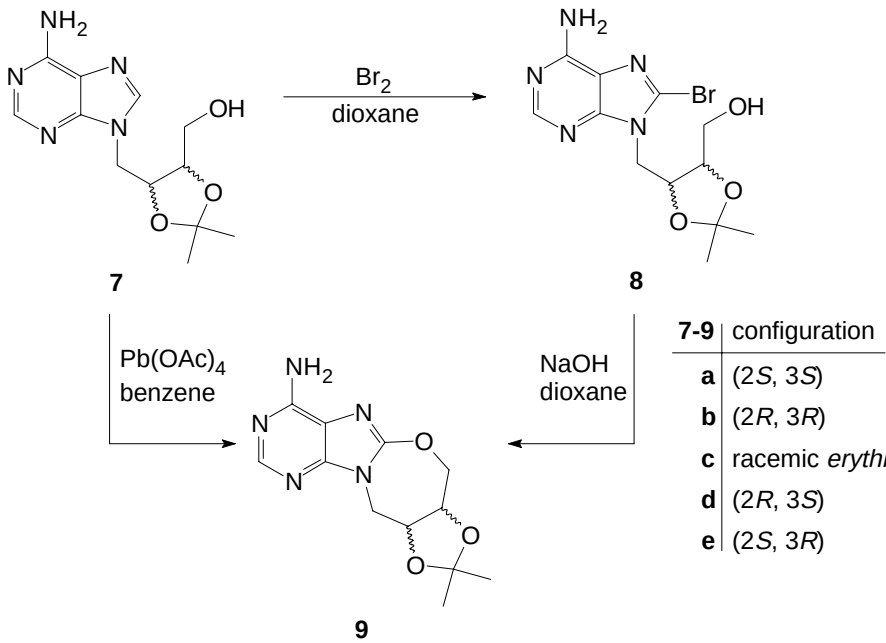
* Instead of the IUPAC-compatible name 1,3-oxazepino[2, 3-*e*]adenines we commonly use the name anhydro derivatives.

whereas the racemic *erythro* derivative **8c** on treatment with DBU in dimethylformamide gave the cyclic product **9c** in high yield.

When treated with aqueous ammonia[7] at 100 °C in an autoclave, bromo derivatives **8** afforded the cyclic anhydro compounds **9** (**9a**: 14%, **9b**: 10%, and **9c**: 79%). In addition, we observed the formation of the corresponding 8-hydroxy and 8-amino derivatives as products of nucleophilic substitution in the position 8. In the reaction of derivative **8b**, small amounts of hydroxy derivative **10** and 8-amino derivative **11** were isolated and characterized (Scheme 4). In no case, however, "anomalous" products with amino group in the side chain have been detected. As shown by direct experiments, the anhydro derivatives **9** did not react with ammonia under the given conditions.

The acyclic analogs of cyclonucleosides are also stable toward alkaline hydrolysis. Neither 4′-*O*,8-anhydro-9-(2*S*,3*S*)-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine (**9a**) nor 4′-*O*,8-anhydro-9-(4-hydroxybutyl)adenine (**15**) reacted with 1 M sodium hydroxide even at 50 °C.

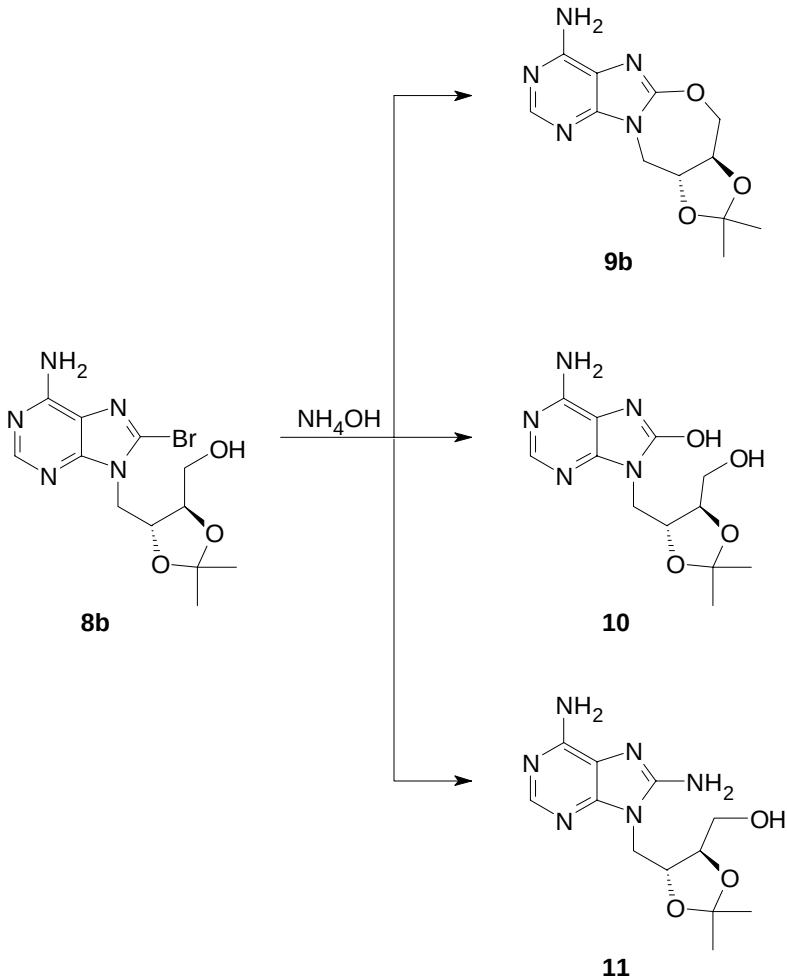
According to a recent paper of Japanese authors[11], a 5′-*O*,8-cycloadenosine derivative was prepared by oxidative cyclization of 2′,3′-*O*-isopropylideneadenosine with lead(IV) acetate. In our case, an analogous reaction of 9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenines **7** with lead(IV) acetate also afforded cyclic anhydro derivatives **9**, identical with those prepared from the 8-bromo derivatives **8**.



SCHEME 3

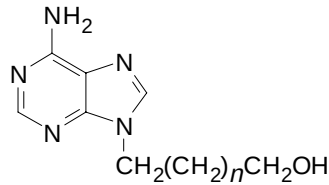
Compared with 2′,3′-*O*-isopropylideneadenosine, the reaction of the acyclic nucleoside analogs required a larger excess of lead(IV) acetate (1.7–1.8 equivalents) and a longer reaction time (in some cases longer than 20 h). Even then the yields of the products **9** were much lower (17–46%). As side products in the cyclization of compound **7b** and **7d** we isolated 9-(2*R*,3*R*)-(4-*O*-acetyl-2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine and 9-(2*R*,3*S*)-(4-*O*-acetyl-2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine, respectively.

In order to find out whether this reaction with lead(IV) acetate could afford anhydro derivatives with rings other than seven-membered, we selected monohydroxyalkyladenines as simple models. The six-membered ring structures, mentioned in the lite-



SCHEME 4

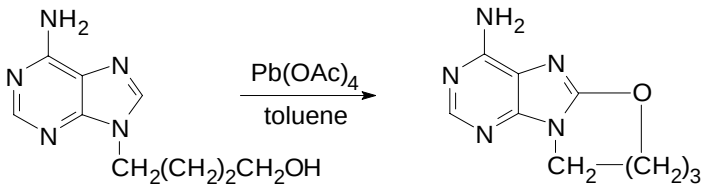
rature[7], could not be prepared by this method: even upon reflux for 24 h, 9-(3-hydroxypropyl)adenine (**12a**) did not react in the desired way and the reaction mixture contained only the *O*-acetyl derivative of the starting compound. On the other hand, reaction of 9-(4-hydroxybutyl)adenine (**14**) with 2 equivalents of lead(IV) acetate in refluxing toluene after 9 h gave 4′-*O*,8-anhydro-9-(4-hydroxybutyl)adenine (**15**) in a good yield (Scheme 5); this confirms that this oxidative cyclization easily affords anhydro derivatives with seven-membered ring. Treatment of 9-(5-hydroxypentyl)adenine (**12b**) with 2 equivalents of lead(IV) acetate in benzene, however, did not afford any eight-membered ring derivative.



12	*n*
a	1
b	3

When working with dioxane, *tert*-butyl alcohol or acetic acid instead of benzene or toluene, the reaction with lead(IV) acetate did not take place at all, even with racemic *erythro*-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine (**7c**) which otherwise is a good substrate.

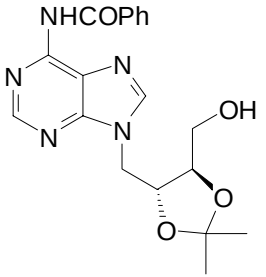
Since the original paper[11] mentioned a positive effect of N^6-benzoylation on the course of this reaction in the adenosine series, we prepared N^6-benzoyl-9-(2-hydroxyethyl)adenine, N^6-benzoyl-9-(2-hydroxybutyl)adenine and N^6-benzoyl-9-(3-hydroxybutyl)adenine by benzoylation with benzoyl chloride and chlorotrimethylsilane in



14 **15**

SCHEME 5

pyridine[12]. None of these compounds reacted with lead(IV) acetate in benzene or toluene. On prolonged treatment under otherwise the same conditions, (2*R*,3*R*)-N^6-benzoyl-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine (**13**) underwent complete debenzoylation to give (2*R*,3*R*)-4′-*O*,8-anhydro-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine (**9b**).



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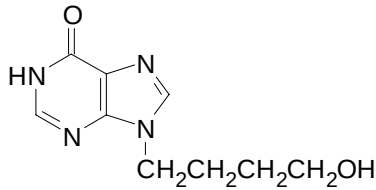

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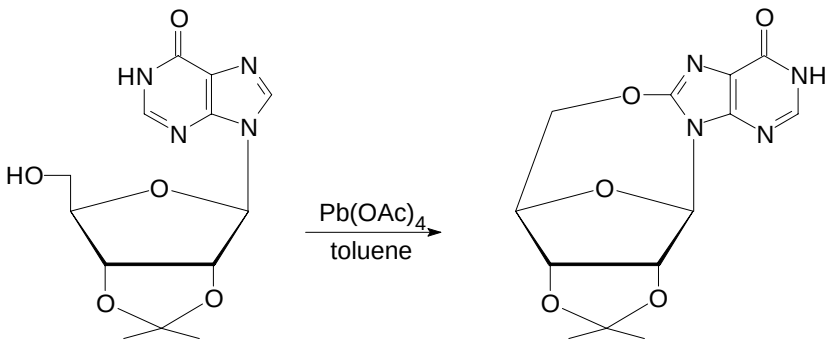
In this context, we also investigated the behaviour of guanine and hypoxanthine derivatives toward lead(IV) acetate. Whereas 2′,3′-*O*-isopropylideneinosine (**16**) on treatment with 2.5 equivalents of lead(IV) acetate in refluxing toluene for 7 h afforded the cyclic product **17** in 40% yield (Scheme 6), attempted cyclization of the analogous inosine derivative failed. The corresponding hypoxanthine derivative **18**, prepared by deamination of 9-(4-hydroxybutyl)adenine (**14**) with isoamyl nitrite in 80% acetic acid, did not react in benzene. No reaction was also observed with 2′,3′-*O*-isopropylideneguanosine[13] in refluxing benzene (6 h).

Detailed study of CD spectra of adenine cyclonucleosides[14] shows a considerable dependence on the conformation of the molecule, particularly on the angle between the



16 **17**

SCHEME 6

plane of the heterocyclic chromophore and the chiral part of the molecule (sugar). Therefore the CD spectra of 5′-*O*,8-cyclonucleosides differ markedly from those of 2′-*O*,8-cyclonucleosides and their 3′-*O*,8-isomers. The character of CD spectra of compounds **9a** and **9b** agrees qualitatively with that of adenine 5′-*O*,8-cyclonucleoside[14], the absolute molar elipticity value of the maximum being even by 30% higher than for 5′-*O*,8-cycloadenosine. The CD spectra of all the cyclic anhydro derivatives **9** consist of two bands of opposite sign (Fig. 1). One of them has a maximum at 260 nm, the other at about 206 nm for the *threo* and 212 nm for the *erythro* derivatives. The spectra of enantiomeric compounds **9a** and **9b** are mirror images of each other, confirming thus their optical purity. The same is true for the CD spectra of enantiomers **9d** and **9e**. Spectra of the *erythro* and *threo* compounds differ mainly in intensity of both bands.

EXPERIMENTAL

The compounds were dried over phosphorus pentoxide at 13 Pa. Melting points were determined on a Kofler block and are uncorrected. Thin-layer chromatography was performed on Silufol UV 254 foils (Kavalier, Votice, Czech Republic) in the systems chloroform–methanol (9 : 1) (S1), chloroform–methanol (85 : 15) (S2) and chloroform–methanol (4 : 1) (S3). Preparative thin-layer chromatography on silica gel was carried out on 40 × 17 × 0.4 cm plates (UV indicator, Kavalier, Votice, Czech Republic). Column chromatography was done on silica gel (30 μm) of the same provenience. Spots were detected by UV light at 254 nm.

CD spectra were measured in water on a Jobin Yvon Mark V instrument. The concentration of the measured solutions was determined from the absorbancies at the absorption maxima; the ε_{max} values for *threo* enantiomers **11a** and **11b** (ε_{260} = 15 800) and *erythro* enantiomers **11d** and **11e** (ε_{263} = 14 100) were determined experimentally.

UV spectra (λ_{max}, ε) were taken in aqueous solutions on a Beckmann DU-65 instrument. Mass spectra (*m/z*, rel.%) were measured on a ZAB-EQ (VG Analytical, Manchester, U.K.) mass spectrometer using FAB technique (Xe, accelerating voltage 8 kV). The samples were dissolved in methanol and a mixture of thioglycerol and glycerol (3 : 1) was used as a matrix.

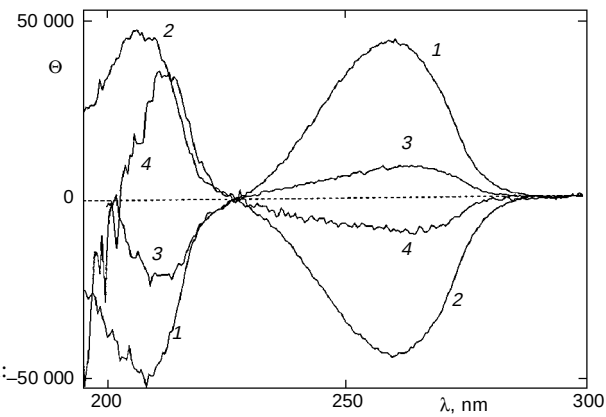


FIG. 1
CD spectra in aqueous solution: *1* **9b**, *2* **9a**, *3* **9e**, *4* **9d**

Proton NMR spectra (δ, ppm; *J*, Hz) were measured on Varian UNITY 200 (200 MHz) or Varian UNITY 500 (500 MHz) spectrometers in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard. ^{13}C NMR spectra were taken on a Varian UNITY-500 instrument (125.7 MHz) and the chemical shifts were referenced to the solvent signal ($\delta(CD_3SOCD_3)$ = 39.7 ppm) or, for solutions in D_2O, to dioxane as external standard (δ(dioxane) = 66.86 ppm). The carbon signals of the types C, CH, CH_2 and CH_3 were distinguished on the basis of J-modulated spectra ("Attached Proton Test Pulse Sequence")[15].

9-(4-Hydroxybutyl)adenine (**14**)

A mixture of adenine (18 g, 0.13 mol) and potassium carbonate (38.6 g, 0.28 mol) in dimethylformamide (230 ml) was stirred at 140 °C. After stirring for 0.5 h, 4-bromobutyl acetate (45 g, 0.23 mol) was added dropwise during 50 min and the reaction mixture was heated at 140 °C for 9 h. The insoluble portion was removed by filtration of the hot mixture and the filtrate was evaporated. The residue was codistilled with toluene and then chromatographed on a column. Crystallization from ethanol afforded 17.4 g (52%) of crystalline 9-(4-acetoxybutyl)adenine[16].

The obtained N^9-isomer (15 g, 60 mmol) was deacetylated by treatment with 0.1 M methanolic sodium methoxide (400 ml) for 0.5 h. The mixture deposited crystals which were collected, washed with ethanol and ether and dried in vacuo. The filtrate was neutralized with Dowex 50 (H^+ form), made slightly alkaline with triethylamine, and filtered. The solvent was evaporated and the residue was crystallized from ethanol. Total yield of 9-(4-hydroxybutyl)adenine (**14**) was 13.4 g (95%), m.p. 198–200 °C, R_F 0.37 (S4). For $C_9H_{13}N_5O$ (207.2) calculated: 52.12% C, 6.27% H, 33.78% N; found: 51.94% C, 6.29% H, 33.63% N. ^1H NMR spectrum: 8.145 s, 1 H and 8.14 s, 1 H (H-2 and H-8); 7.23 brs, 2 H (NH_2); 4.46 t, 1 H, *J*(OH,4′) = 4.9 (OH); 4.14 t, 2 H, *J*(1′,2′) = 7.1 (H-1′); 3.39 dt, 2 H, *J*(4′,3′) = 6.6 (H-4′); 1.82 m, 2 H (H-2′); 1.37 m, 2 H (H-3′). ^{13}C NMR spectrum: 156.16 (C-6); 152.56 (C-2); 149.76 (C-4); 141.06 (C-8); 118.96 (C-5); 60.34 (C-4′); 43.06 (C-1′); 29.69 (C-3′); 25.50 (C-2′). Mass spectrum: 208 (100, M + H).

The above chromatography also afforded 1.25 g (4%) of 3-(4-acetoxybutyl)adenine, m.p. 178–180 °C. For $C_{11}H_{15}N_5O_2$ (249.2) calculated: 52.97% C, 6.02% H, 28.09% N; found: 53.11% C, 6.14% H, 27.62% N. ^1H NMR spectrum: 8.36 s, 1 H and 7.78 s, 1 H (H-2 and H-8); 8.15 brs, 1 H and 7.90 brs, 1 H (NH_2); 4.33 t, 2 H, *J*(1′,2′) = 7.1 (H-1′); 4.00 t, 2 H, *J*(4′,3′) = 6.6 (H-4′); 1.97 s, 3 H (OAc); 1.94 m, 2 H (H-2′); 1.56 m, 2 H (H-3′). ^{13}C NMR spectrum: 170.58 (CO); 155.19 (C-6); 152.68 (C-8); 149.89 (C-4); 143.56 (C-2); 120.66 (C-5); 63.45 (C-4′); 49.11 (C-1′); 25.57 and 25.36 (C-2′ and C-3′); 20.87 (CH_3). Mass spectrum: 250 (100, M + H).

9-(4-Hydroxybutyl)hypoxanthine (**18**)

Isoamyl nitrite (5 ml) was added to a solution of 9-(4-hydroxybutyl)adenine (**14**; 1.0 g, 4.8 mmol) in 80% acetic acid (50 ml) and the reaction mixture was set aside for 2 days at room temperature. The solvent was evaporated, the residue was codistilled with water, deionized on Dowex 50 X 8 (H^+ form) and purified by column chromatography on silica gel. Crystallization from methanol afforded compound **18** (0.3 g, 30%), m.p. 165–168 °C, R_F 0.29 (S3). ^1H NMR spectrum: 12.27 brs, 1 H (NH); 8.09 s, 1 H and 8.03 s, 1 H (H-2 and H-8); 4.46 t, 1 H, *J*(OH,4′) = 5.1 (OH); 4.14 t, 2 H, *J*(1′,2′) = 7.3 (H-1′); 3.38 m, 2 H (H-4′); 1.81 m, 2 H and 1.36 m, 2 H (H-2′ and H-3′). ^{13}C NMR spectrum: 156.92 (C-6); 148.63 (C-4); 145.64 (C-2); 140.58 (C-8); 124.13 (C-5); 60.29 (C-4′); 43.47 (C-1′); 29.60 (C-3′); 26.66 (C-2′). Mass spectrum: 209 (100, M + H).

9-(2*S*,3*R*)-(2,3-*O*-Isopropylidene-2,3,4-trihydroxybutyl)adenine (**7e**)

Compound **7e** was prepared by a described procedure[8]. M.p. >250 °C, R_F 0.46 (S3). ^{1}H NMR spectrum: 8.13 s, 1 H and 8.08 s, 1 H (H-2 and H-8); 7.20 brs, 2 H (NH_2); 5.05 brs, 1 H (OH); 4.57 ddd, 1 H, *J*(2′,3′) = 6.4 (H-2′); 4.37 dd, 1 H, *J*(1a′,2′) = 2.9, *J*(gem) = 14.2 (Ha-1′); 4.26 q, 1 H, *J* = 6.2 (H-3′); 4.21 dd, 1 H, *J*(1b′,2′) = 10.3, *J*(gem) = 14.2 (Hb-1′); 3.63 d, 2 H, *J*(4′,3′) = 6.1 (H-4′); 1.43 s, 3 H and 1.21 s, 3 H (2 × CH_3). Mass spectrum: 280 (100, M + H).

9-(2*R*,3*S*)-(2,3-*O*-Isopropylidene-2,3,4-trihydroxybutyl)adenine (**7d**)

Compound **7d** was prepared by a described procedure[10]. Its m.p., R_F, and ^{1}H NMR and mass spectra were identical with those of compound **7e**.

N^6-Benzoyl-9-(2*R*,3*R*)-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine (**13**)

A solution of 9-(2*R*,3*R*)-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine (**7b**; 1.7 g, 6 mmol) and benzoyl chloride (3.6 ml) in pyridine (30 ml) was stirred in a stoppered flask for 1 h in the dark[17]. The reaction mixture was poured on ice, and the precipitate was taken up in chloroform. The chloroform phase was washed successively with water, a solution of sodium hydrogen carbonate and water, and dried over magnesium sulfate. The chloroform was evaporated, the residue was dissolved in pyridine (80 ml) and cooled with ice. Sodium hydroxide (1 M solution, 80 ml) was added and the reaction mixture was stirred for 10 min with cooling. After neutralization with acetic acid, the solvent was evaporated and the residue was partitioned between water and chloroform. The chloroform layer was washed with a solution of sodium hydrogen carbonate and with water, and dried. The solvent was evaporated and the crude residue was column chromatographed (chloroform–methanol (99 : 1)). Crystallization from ethanol afforded 0.75 g (32%) of compound **13**, m.p. 138–140 °C, R_F 0.43 (S2). For $C_{19}H_{21}N_5O_4$ (383.4) calculated: 59.52% C, 5.52% H, 18.27% N; found: 59.52% C, 5.45% H, 18.04% N. ^{1}H NMR spectrum: 11.17 s, 1 H (NH); 8.76 s, 1 H and 8.43 s, 1 H (H-2 and H-8); 8.06 d, 2 H and 7.64 t, 1 H and 7.55 t, 2 H (arom); 4.97 t, 1 H, *J*(OH,4′) = 5.5 (OH); 4.56 dd, 1 H, *J*(1a′,2′) = 3.9, *J*(gem) = 14.4 (Ha-1′); 4.47 dd, 1 H, *J*(1b′,2′) = 6.8, *J*(gem) = 14.4 (Hb-1′); 4.27 td, 1 H, *J*(2′,1a′) = 3.9, *J*(2′,1b′) = 6.8, *J*(2′,3′) = 7.8 (H-2′); 3.82 dt, 1 H, *J*(3′,4a′) = *J*(3′,4b′) = 4.9, *J*(3′,2′) = 7.8 (H-3′); 3.55 dt, 1 H, *J*(4a′,3′) = *J*(4a′,OH) = 5.2, *J*(gem) = 11.5 (Ha-4′); 3.52 dt, 1 H, *J*(4b′,3′) = *J*(4b′,OH) = 5.4, *J*(gem) = 11.5 (Hb-4′); 1.29 s, 3 H and 1.26 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 165.53 (C=O); 152.82 (C-6); 151.80 (C-2); 150.34 (C-4); 145.38 (C-8); 133.64, 132.62, 128.68 4C (C-arom), 125.30 (C-5); 109.16 (O–C–O); 79.11 (C-3′); 76.19 (C-2′); 61.40 (C-4′); 45.32 (C-1′); 27.22 and 27.11 (2 × CH_3). Mass spectrum: 384 (53%, M + H).

Benzoylation of Acyclic Adenine Nucleosides (Ref.[12])

A mixture of the corresponding adenine derivative (15 mmol), pyridine (80 ml) and chlorotrimethylsilane (13 ml) was stirred at room temperature (calcium chloride protecting tube) for 1 h. Benzoyl chloride (10 ml) was added and stirring was continued for further 2 h. The reaction mixture was cooled to 0 °C, water (15 ml) and concentrated ammonia (35 ml) were added dropwise during 5 min and the mixture was stirred at 0 °C for 30 min. The solvent was evaporated and the residue was codistilled with water and extracted with acetone. The product was crystallized from water and then from ethanol or ethyl acetate with ether added to turbidity, or purified by chromatography on a column of silica gel.

N^6-Benzoyl-9-(2-hydroxyethyl)adenine: yield 2.3 g (54%), m.p. 185–188 °C, R_F 0.58 (S2). For $C_{14}H_{13}N_5O_2$ (283.3) calculated: 59.36% C, 4.63% H, 24.72% N; found: 59.17% C, 4.56% H, 24.32% N. ^{1}H NMR spectrum: 11.15 brs, 1 H (NH); 8.74 s, 1 H and 8.43 s, 1 H (H-2 and H-8); 8.10–8.02 m,

2 H and 7.70–7.50 m, 3 H (arom); 5.08 t, 1 H, *J*(OH,2′) = 5.2 (OH); 4.34 t, 2 H, *J*(1′,2′) = 5.2 (H-1′); 3.82 q, 2 H, *J*(2′,1′) = *J*(2′,OH) = 5.2 (H-2′). ^{13}C NMR spectrum: 165.91 (CO); 152.86 (C-6); 151.56 (C-2); 150.23 (C-4); 145.48 (C-8); 133.77, 132.61, 128.69 4C (C arom); 125.70 (C-5); 59.36 (C-2′); 46.30 (C-1′). Mass spectrum: 284 (100, M + H).

N^6*-Benzoyl-9-(3-hydroxybutyl)adenine:* yield 1.54 g (50%), m.p. 155–157 °C, R_F 0.31 (S2). For $C_{16}H_{17}N_5O_2$ (311.3) calculated: 61.72% C, 5.46% H, 22.50% N; found: 61.65% C, 5.49% H, 22.33% N. ^{1}H NMR spectrum: 11.14 s, 1 H (NH); 8.74 s, 1 H and 8.49 s, 1 H (H-2 and H-8); 8.06 d, 2 H and 7.60 t, 1 H and 7.53 t, 2 H (arom); 4.75 d, 1 H, *J*(OH,3′) = 4.6 (OH); 4.38 ddd, 1 H, *J*(1′a,2′) = 5.9 and 7.8, *J*(gem) = 13.7 (Ha-1′); 4.32 brpent, 1 H, *J*(1′b,2′) = 7.3 and 7.3, *J*(gem) = 13.7 (Hb-1′); 3.61 m, 1 H (H-3′); 1.97 m, 1 H and 1.86 m, 1 H (H-2′); 1.10 d, 3 H, *J*(4′,3′) = 6.3 (H-4′). Mass spectrum: 312 (100, M + H).

Bromination of 9-(2,3-*O*-Isopropylidene-2,3,4-trihydroxybutyl)adenines (**7**)

Bromine (0.5 ml, 19.4 mmol) was added to a suspension of compound **7a**, **7b** or **7c** (2.0 g, 7 mmol) in a mixture of dioxane (90 ml) and 10% aqueous solution of sodium hydrogen phosphate (90 ml) and the mixture was stirred at room temperature for 24 h. Concentrated solution of sodium hydrogen sulfite was added until the mixture became colourless and the product was taken up in chloroform (6 × 30 ml). The chloroform extract was dried over magnesium sulfate, filtered, the solvent was evaporated and the product was crystallized from ethyl acetate.

A. Compound **8a**: yield 1.6 g (65%), m.p. 166–168 °C (ethyl acetate), R_F 0.74 (S3). For $C_{12}H_{16}BrN_5O_3$ (358.2) calculated: 40.24% C, 4.50% H, 19.55% N, 22.31% Br; found: 40.15% C, 4.53% H, 20.03% N, 22.21% Br. ^{1}H NMR spectrum: identical with that of **13b** (see *B*). UV (pH 7): 267.0 (14 700). Mass spectrum: 358 (100, M + H).

B. Compound **8b**: yield 1.8 g (71%), m.p. 166–168 °C (ethyl acetate), R_F 0.75 (S3). For $C_{12}H_{16}BrN_5O_3$ (358.2) calculated: 40.24% C, 4.50% H, 19.55% N, 22.31% Br; found: 40.17% C, 4.48% H, 19.87% N, 22.35% Br. ^{1}H NMR spectrum: 8.14 s, 1 H (H-2); 7.42 brs, 2 H (NH_2); 4.92 t, 1 H, *J*(OH,4′) = 5.4 (OH); 4.35 dd, 1 H, *J*(1a′,2′) = 5.4, *J*(gem) = 14.4 (Ha-1′); 4.31 dd, 1 H, *J*(1b′,2′) = 6.1, *J*(gem) = 14.4 (Hb-1′); 4.25 brdt, 1 H, *J*(2′,1a′) = *J*(2′,1b′) = 5.6, *J*(2′,3′) = 7.6 (H-2′); 3.95 dt, 1 H, *J*(3′,4a′) = *J*(3′,4b′) = 4.9, *J*(3′,2′) = 7.6 (H-3′); 3.47 t, 2 H, Σ*J* = 10.5 (H-4′); 1.27 s, 3 H and 1.26 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 154.95 (C-6); 153.08 (C-2); 151.02 (C-4); 127.25 (C-8); 119.05 (C-5); 109.18 (O–C–O); 79.48 (C-3′); 75.78 (C-2′); 61.31 (C-4′); 46.42 (C-1′); 27.25 and 27.01 (2 × CH_3). UV spectrum (pH 7): 267.0 (14 000). Mass spectrum: 358 (29, M + H).

C. Compound **8c**: yield 1.0 g (41%), m.p. 208–210 °C (ethanol), R_F 0.71 (S3). For $C_{12}H_{16}BrN_5O_3$ (358.2) calculated: 40.24% C, 4.50% H, 19.55% N, 22.31% Br; found: 39.88% C, 4.57% H, 19.80% N, 22.26% Br. ^{1}H NMR spectrum: 8.13 s, 1 H (H-2); 7.40 brs, 2 H (NH_2); 5.09 t, 1 H, *J*(OH,4′) = 5.4 (OH); 4.69 ddd, 1 H, *J* = 4.9, 6.3 and 8.6 (H-2′); 4.33–4.27 m, 3 H (H-1′and H-3′); 3.70 dt, 1 H, *J*(4a′,3′) = 5.1, *J*(4a′,OH) = 5.4, *J*(gem) = 11.2 (Ha-4′); 3.67 brdt, 1 H, *J*(4b′,3′) = 6.3, *J*(4b′,OH) = 5.4, *J*(gem) = 11.2 (Hb-4′); 1.42 s, 3 H and 1.18 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 154.97 (C-6); 152.87 (C-2); 151.08 (C-4); 127.14 (C-8); 119.19 (C-5); 108.56 (O–C–O); 76.74 (C-3′); 73.96 (C-2′); 59.10 (C-4′); 45.13 (C-1′); 27.79 and 25.34 (2 × CH_3). UV spectrum (pH 7): 267.0 (10 900). Mass spectrum: 358 (57, M + H).

4′-*O*,8-Anhydro-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenines (**9a–9d**)

A. By reaction of compound **8a** with NaH. To a solution of compound **8a** (0.5 g, 1.4 mmol) in dioxane (25 ml) was added 60% dispersion of sodium hydride in mineral oil (110 mg, 2.8 mmol). The mixture was stirred at room temperature for 2 days and then neutralized with acetic acid. After evaporation, the residue was crystallized from ethanol to give 0.24 g (61%) of compound **9a**, m.p.

274–276 °C, R_F 0.65 (S3). For $C_{12}H_{15}N_5O_3$ (277.3) calculated: 51.98% C, 5.45% H, 25.26% N; found: 51.51% C, 5.28% H, 24.78% N. ^{1}H NMR and ^{13}C NMR spectra were identical with those of compound **9b** (see procedure *B*). UV (pH 7): 260.0 (13 400). Mass spectrum: 278 (100, M + H).

B. By reaction of compound **8b** with potassium *tert*-butoxide. To a solution of compound **8b** (0.1 g, 0.3 mmol) in dioxane (5 ml) was added potassium *tert*-butoxide (68 mg, 0.6 mmol) and the mixture was stirred at room temperature under exclusion of moisture. After neutralization with acetic acid and filtration, the filtrate was evaporated and the residue crystallized from ethanol to give 85 mg (51%) of compound **9b**, m.p. 278–280 °C, R_F 0.61 (S3). For $C_{12}H_{15}N_5O_3$ (277.3) calculated: 51.98% C, 5.45% H, 25.26% N; found: 51.42% C, 5.38% H, 24.81% N. ^{1}H NMR spectrum: 8.13 s, 1 H (H-2); 7.07 s, 2 H (NH_2); 4.77–4.66 m, 2 H, 4.08 m, 2 H, 3.87–3.83 m, 2 H (NCH_2, OCH_2, H-2′ and H-3′); 1.45 s, 3 H and 1.37 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 154.96 (C-6); 153.86 (C-8); 152.10 (C-2); 148.82 (C-4); 114.22 (C-5); 110.67 (O–C–O); 79.24 (C-3′); 76.75 (C-2′); 70.93 (C-4′); 40.88 (C-1′); 26.68 and 26.62 (2 × CH_3). UV spectrum (pH 7): 260.0 (15 800). Mass spectrum: 278 (100, M + H).

C. By reaction of compound **8c** with NaH. To a solution of compound **8c** (0.5 g, 1.4 mmol) in dioxane (25 ml) was added 60% disperion of sodium hydride in mineral oil (110 mg, 2.8 mmol). After stirring at room temperature for 3 days, the mixture was neutralized with acetic acid, the crystals were collected and washed with water and acetone. Yield 0.31 g (66%) of compound **9c**, m.p. >250 °C, R_F 0.33 (S2). For $C_{12}H_{15}N_5O_3$ (277.3) calculated: 51.98% C, 5.45% H, 25.26% N; found: 51.50% C, 5.58% H, 25.63% N. For the ^{1}H NMR and ^{13}C NMR spectra see method *D*. MS: 278 (100, M + H).

D. By reaction of compound **8c** with DBU. A mixture of compound **8c** (0.7 g, 2 mmol), DBU (0.7 ml) and dimethylformamide (21 ml) was heated at 110 °C for 6 h. The deposited crystals were collected, washed with water and acetone, and dried. Yield 0.48 g (88%) of compound **9c**, m.p. >250 °C, R_F 0.35 (S2). For $C_{12}H_{15}N_5O_3$ (277.3) calculated: 51.98% C, 5.45% H, 25.26% N; found: 51.82% C, 5.32% H, 25.41% N. ^{1}H NMR spectrum: 8.06 s, 1 H (H-2); 6.49 brs, 2 H (NH_2); 4.75 dd, 1 H, J(1a′,2′) = 1.5, J(gem) = 13.7 (Ha-1′); 4.72 ddd, 1 H, J(3′,2′) = 7.3, J(3′,4a′) = 5.4, J(3′,4b′) = 1.7 (H-3′); 4.59 dd, 1 H, J(4a′,3′) = 5.4, J(gem) = 14.9 (Ha-4′); 4.58 ddd, 1 H, J(2′,1a′) = 1.5, J(2′,1b′) = 3.9, J(2′,3′) = 7.3 (H-2′); 4.43 dd, 1 H, J(1b′,2′) = 3.9, J(gem) = 13.7 (Hb-1′); 4.37 dd, 1 H, J(4b′,3′) = 1.7, J(gem) = 14.9; 1.32 s, 3 H and 1.23 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 153.65 and 153.59 (C-8 and C-6); 150.39 (C-2); 149.45 (C-4); 115.06 (C-5); 108.30 (O–C–O); 75.18 (C-3′); 73.04 (C-2′); 68.79 (C-4′); 41.41 (C-1′); 26.10 and 24.74 (2 × CH_3). Mass spectrum: 278 (52, M + H).

E. By reaction of compound **7c** with lead(IV) acetate. Compound **7c** (0.6 g, 2.1 mmol) was added to a solution of lead(IV) acetate (1.15 g, 2.6 mmol) in benzene (300 ml). After reflux for 11 h, another portion (0.5 g, 1.1 mmol) of lead(IV) acetate was added and the mixture was stirred and refluxed for another 12 h. The hot mixture was filtered and the filtrate was concentrated. Crystallization from methanol afforded 0.27 g (46%) of compound **9c**. For the ^{1}H NMR, ^{13}C NMR and mass spectra and m.p. see method *D*. UV spectrum (pH 7): 263.0 (11 573).

F. By reaction of compound **7b** with lead(IV) acetate. Compound **7b** (2 g, 7 mmol) was added to a solution of lead(IV) acetate (3.7 g, 8.4 mmol) in benzene (1 l) and the mixture was refluxed for 11 h. Another portion (1.9 g, 4.2 mmol) of lead(IV) acetate was then added and the refluxing was continued for another 11 h. The hot mixture was filtered and the filtrate was taken down. Column chromatography and crystallization from methanol gave 0.72 g (37%) of compound **9b**. For $C_{12}H_{15}N_5O_3$ (277.3) calculated: 51.98% C, 5.45% H, 25.26% N; found: 51.65% C, 5.34% H, 25.37% N. For ^{1}H NMR, ^{13}C NMR and mass spectra and m.p. see procedure *D*.

The procedure also gave 0.4 g (17%) of 9-(2*R*,3*R*)-(4-*O*-acetyl-2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine; ^{1}H NMR spectrum: 8.14 s, 1 H and 8.09 s, 1 H (H-2 and H-8); 7.30 brs, 2 H (NH_2); 4.43 dd, 1 H, J(1a′,2′) = 4.2, J(gem) = 14.6 (Ha-1′); 4.38 dd, 1 H, J(1b′,2′) = 5.6, J(gem) = 14.6 (Hb-1′); 4.27 dt, 1 H, J(2′,3′) = 7.8 (H-2′); 4.12 dd, 2 H, J(4a′,3′) = 3.9, J(gem) = 11.7 (Ha-4′); 4.06 dd, J(4b′,3′) = 5.8, J(gem) = 11.7 (Hb-4′); 3.94 ddd, 1 H, J(3′,2′) = 7.8 (H-3′); 2.01 s, 3 H (OAc); 1.30 s,

3 H and 1.22 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 170.23 (CO); 156.16 (C-6); 152.76 (C-2); 149.86 (C-4); 141.50 (C-8); 118.53 (C-5); 109.55 (O–C–O); 75.89 and 75.87 (C-3′ and C-2′); 63.50 (C-4′); 44.20 (C-1′); 26.99 and 26.96 (2 × CH_3). Mass spectrum: 322 (100, M + H).

G. By reaction of compound **7e** with lead(IV) acetate. Lead(IV) acetate (1.58 g, 3.6 mmol) was added to a solution of compound **7e** (0.5 g, 1.8 mmol) in dry benzene (400 ml). After reflux for 10 h, the hot mixture was filtered, the filtrate was evaporated and the crude product was crystallized from methanol to give 0.15 g (30%) of compound **9e**, m.p. >250 °C. Its ^1H NMR and ^{13}C NMR spectra were identical with those of compound **9d** (see procedure *H*). UV spectrum (pH 7): 263.0 (14 100). Mass spectrum: 278 (100, M + H).

H. By reaction of compound **7d** with lead(IV) acetate. Compound **7d** (0.43 g, 1.5 mmol) was added to lead(IV) acetate (1.43 g, 3.2 mmol) in dry toluene (300 ml). After reflux for 15 h, the hot mixture was filtered and the filtrate was evaporated. Crystallization from methanol afforded 0.1 g (23%) of compound **9d**, m.p. >250 °C. ^1H NMR spectrum: 8.05 s, 1 H (H-2); 6.59 brs, 2 H (NH_2); 4.76 dd, 1 H, *J*(1a′,2′) = 1.3, *J*(gem) = 13.4 (Ha-1′); 4.73 ddd, 1 H, *J*(3′,4a′) = 5.1, *J*(3′,4b′) = 1.6, *J*(3′,2′) = 7.5 (H-3′); 4.59 dd, 1 H, *J*(4a′,3′) = 5.1, *J*(gem) = 14.9 (Ha-4′); 4.57 ddd, 1 H, *J*(2′,1a′) = 1.3, *J*(2′,1b′) = 3.8, *J*(2′,3′) = 7.5 (H-2′); 4.42 dd, 1 H, *J*(1b′,2′) = 3.8, *J*(gem) = 13.4 (Hb-1′); 4.37 dd, 1 H, *J*(4b′,3′) = 1.6, *J*(gem) = 14.9 (Hb-4′); 1.32 s, 3 H and 1.22 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 153.79 and 153.77 (C-8 and C-6); 150.63 (C-2); 149.50 (C-4); 115.00 (C-5); 108.44 (O–C–O); 75.37 (C-3′); 73.14 (C-2′); 69.18 (C-4′); 41.53 (C-1′); 26.27 and 24.93 (2 × CH_3). UV spectrum (pH 7): 263.0 (13 900). Mass spectrum: 278 (100, M + H).

The reaction mixture also contained 9-(2*R*,3*S*)-(4-*O*-acetyl-2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine. ^1H NMR spectrum: 8.14 s, 1 H and 8.02 s, 1 H (H-2 and H-8); 7.24 brs, 2 H (NH_2); 4.67 ddd, 1 H, *J*(2′,1a′) = 3.4, *J*(2′,1b′) = 9.7, *J*(2′,3′) = 6.2 (H-2′); 4.45 td, 1 H, *J*(3′,4a′) = 4.6, *J*(3′,2′) = *J*(3′,4b′) = 6.6 (H-3′); 4.35 dd, 1 H, *J*(1a′,2′) = 3.4, *J*(gem) = 13.9 (Ha-1′); 4.27 dd, 1 H, *J*(4a′,3′) = 4.6, *J*(gem) = 11.7 (Ha-4′); 4.24 dd, 1 H, *J*(1b′,2′) = 9.7, *J*(gem) = 13.9 (Hb-1′); 4.16 dd, 1 H, *J*(4b′,3′) = 6.6, *J*(gem) = 11.7 (Hb-4′); 2.05 s, 3 H (OAc); 1.43 s, 3 H and 1.22 s, 3 H (2 × CH_3). Mass spectrum: 322 (100, M + H).

Reaction of 8-Bromo-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenines **8a–8c** with Ammonia

A. Compound **8a** (0.36 g, 1 mmol) in concentrated aqueous ammonia (45 ml) was heated at 100 °C in an autoclave for 16 h. After evaporation, the residue was subjected to preparative thin-layer chromatography (silica gel, S3). Yield 40 mg (14%) of compound **9a** and 80 mg (22%) of the starting **8a**.

B. Compound **8b** (1 g, 3 mmol) in concentrated aqueous ammonia (40 ml) was heated for 8 h at 100 °C in an autoclave. The solvent was evaporated and the residue was separated by preparative thin-layer chromatography on silica gel (S2). Yield 80 mg (10%) of compound **9b** (R_F 0.58 (S3)), 20 mg (2%) of the 8-hydroxy derivative **10** (R_F 0.39 (S3)) and 15 mg (2%) of the 8-amino derivative **11** (R_F 0.30 (S3)). A part of the starting compound **8b** (0.6 g, 60%) was recovered.

Compound **10**: ^1H NMR spectrum: 10.22 brs, 1 H (OH); 8.02 s, 1 H (H-2); 6.45 brs, 2 H (NH_2); 4.84 t, *J*(OH,4′) = 5.3 (OH); 4.21 brq, 1 H (H-2′); 3.97 dd, 1 H, *J*(1a′,2′) = 6.3, *J*(gem) = 13.9 (Ha-1′); 3.92 m, 1 H (H-3′); 3.86 dd, 1 H, *J*(1b′,2′) = 6.1, *J*(gem) = 13.9 (Hb-1′); 3.38 brt, 2 H, *J* = 5.1 (H-4′); 1.28 s, 3 H and 1.26 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 152.76 (C-6); 151.56 (C-2); 148.29 (C-8); 147.11 (C-4); 109.35 (O–C–O); 103.77 (C-5); 80.60 (C-3′); 75.53 (C-2′); 62.02 (C-4′); 42.67 (C-1′); 27.58 and 27.57 (2 × CH_3).

Compound **11**: ^1H NMR spectrum: 7.93 s, 1 H (H-2); 6.52 br, 2 H and 6.39 br, 2 H (2 × NH_2); 4.18 m, 3 H (NCH_2 and OCH); 3.90 m, 1 H (OCH); 3.42 m, 2 H (OCH_2); 1.28 s, 6 H (2 × CH_3). ^{13}C NMR spectrum: 152.43 (C-4); 152.18 (C-6); 150.11 (C-8); 148.97 (C-2); 116.80 (C-5); 108.89 (O–C–O); 79.45 (C-3′); 75.78 (C-2′); 61.22 (C-4′); 42.88 (C-1′); 27.23 and 26.98 (2 × CH_3).

C. Reaction of compound **8c**: A solution of compound **8c** (0.35 g, 1 mmol) in concentrated aqueous ammonia (46 ml) was heated at 100 °C for 20 h in an autoclave. The reaction mixture deposited crystals of compound **9c** which were collected, washed with methanol and ether, and dried. Yield 0.2 g (79%) of compound **9c**. The filtrate was subjected to preparative thin-layer chromatography on silica gel (S3). ^{1}H NMR spectrum identified 8-amino-9-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine as a side product: ^{1}H NMR spectrum: 7.89 s, 1 H (H-2); 6.32 s, 2 H and 6.30 s, 2 H (2 × NH_2); 4.90 br, 1 H (OH); 4.58 ddd, 1 H, *J*(2′,3′) = 6.6 (H-2′); 4.23 brq, 1 H, *J* = 6.1 (H-3′); 4.15 dd, 1 H, *J*(1a′,2′) = 9.8, *J*(gem) = 14.7 (Ha-1′); 4.08 dd, 1 H, *J*(1b′,2′) = 3.2, *J*(gem) = 14.7 (Hb-1′); 3.74 dd, 1 H, *J*(4a′,3′) = 5.8, *J*(gem) = 11.5 (Ha-4′); 3.59 dd, 1 H, *J*(4b′,3′) = 5.8, *J*(gem) = 11.5 (Hb-4′); 1.39 s, 3 H and 1.18 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 152.25 (C-4); 151.51 (C-6); 149.92 (C-8); 148.64 (C-2); 115.84 (C-5); 108.22 (O–C–O); 77.15 (C-3′); 73.99 (C-2′); 62.80 (C-4′); 41.67 (C-1′); 27.65 and 25.30 (2 × CH_3).

Reaction of N^6-Benzoyl-9-(2*R*,3*R*)-(2,3-*O*-isopropylidene-2,3,4-trihydroxybutyl)adenine (**13**) with Lead(IV) Acetate

Compound **13** (0.4 g, 1.04 mmol) was dried by codistillation with toluene (3 × 25 ml), then dissolved in toluene (300 ml) and lead(IV) acetate (0.7 g, 1.57 mmol) was added. After reflux for 8.5 h, the hot mixture was filtered and the filtrate was evaporated. The residue was separated by preparative thin-layer chromatography on silica gel (S3). Crystallization of the crude product from ethanol afforded 0.06 g (20%) of compound **9b**.

Reaction of 9-(3-Hydroxypropyl)adenine (**12a**) with Lead(IV) Acetate

A mixture of 9-(3-hydroxypropyl)adenine (**12a**; 0.35 g, 1.8 mmol), lead(IV) acetate (1.6 g, 3.6 mmol) and benzene (200 ml) was refluxed for 15 h. The usual workup afforded 0.12 g (34%) of the starting compound **12a** and 9-(3-acetoxypropyl)adenine (0.05 g, 11%) as the only product. ^{1}H NMR spectrum: 8.14 s, 1 H and 8.135 s, 1 H (H-2 and H-8); 7.23 brs, 2 H (NH_2); 4.22 t, 2 H, *J*(1′,2′) = 7.1 (H-1′); 3.97 t, 2 H, *J*(3′,2′) = 6.3 (H-3′); 2.13 pent, 2 H, Σ*J* = 26.5 (H-2′); 1.93 s, 3 H (OAc). Mass spectrum: 236 (100, M + H).

Reaction of 9-(4-Hydroxybutyl)adenine (**14**) with Lead(IV) Acetate in Acetic Acid

A suspension of 9-(4-hydroxybutyl)adenine (**14**; 0.1 g, 0.48 mmol) and lead(IV) acetate (0.33 g, 0.75 mmol) in acetic acid (25 ml) was stirred at room temperature overnight and then was heated at 100 °C for 5 h. Another portion of lead(IV) acetate (0.22 g, 0.50 mmol) was added and the heating at 100 °C was continued for another 3.5 h. The hot reaction mixture was filtered, the residue was codistilled with dioxane and extracted with chloroform. After evaporation of the solvent, the residue was separated by preparative thin-layer chromatography on silica gel (S1). ^{1}H NMR spectrum detected the *O*-acetyl derivative and the N^6,*O*-diacetyl derivative of the starting compound **14** as the only products.

N^6-Acetyl-9-(4-acetoxybutyl)adenine. ^{1}H NMR spectrum: 10.40 br, 1 H (NH); 8.61 s, 1 H and 8.47 s, 1 H (H-2 and H-8); 4.27 t, 2 H, *J*(1′,2′) = 7.1 (H-1′); 4.00 t, 2 H, *J*(4′,3′) = 6.4 (H-4′); 1.99 s, 3 H and 1.97 s, 3 H (NAc, OAc); 1.92–1.86 m, 2 H and 1.63–1.52 m, 2 H (H-2′ and H-3′).

9-(4-Acetoxybutyl)adenine. ^{1}H NMR spectrum: 8.15 s, 1 H and 8.14 s, 1 H (H-2 and H-8); 7.21 brs, 2 H (NH_2); 4.16 t, 2 H, *J*(1′,2′) = 7.0 (H-1′); 4.00 t, 2 H, *J*(4′,3′) = 6.6 (H-4′); 1.97 s, 3 H (OAc); 1.85 m, 2 H and 1.52 m, 2 H (H-2′ and H-3′).

4′,8-Anhydro-9-(4-hydroxybutyl)adenine (**15**)

A suspension of 9-(4-hydroxybutyl)adenine (**14**; 0.5 g, 2.4 mmol, pre-dried by codistillation with toluene (3 × 25 ml)) in dry toluene (300 ml) was stirred and refluxed. Lead(IV) acetate (2.15 g, 4.8 mmol) was added and the mixture was refluxed for 9 h. The mixture was filtered while hot and the filtrate was taken down. Crystallization from ethanol–ethyl acetate afforded compound **15** (0.1 g, 20%). Thin-layer chromatography (silica gel, S2) of the mother liquors afforded further 0.15 g of compound **15** and 0.1 g (20%) of the starting compound **14**. Total yield of the compound **15** was 0.25 g (51%). M.p. 245–247 °C, R_F 0.71 (S2). For $C_9H_{11}N_5O$ (205.2) calculated: 52.67% C, 5.40% H, 34.13% N; found: 52.80% C, 5.22% H, 33.90% N. ^{1}H NMR spectrum: 8.08 s, 1 H (H-2); 6.93 brs, 2 H (NH_2); 4.21 m, 2 H (H-1′); 4.08 m, 2 H (H-4′); 2.03 m, 2 H and 1.86 m, 2 H (H-2′ and H-3′). ^{13}C NMR spectrum: 156.43 (C-8); 154.73 (C-6); 151.56 (C-2); 148.89 (C-4); 114.83 (C-5); 73.70 (C-4′); 42.15 (C-1′); 30.68 (C-3′); 26.09 (C-2′). Mass spectrum: 206 (100, M + H).

5′-*O*,8-Cyclo-2′,3′-*O*-isopropylideneinosine (**17**)

Lead(IV) acetate (1.80 g, 4 mmol) was added to a solution of 2′,3′-*O*-isopropylideneinosine (**16**; 0.5 g, 1.62 mmol) in dry benzene (500 ml). After reflux for 7 h, the hot mixture was filtered and the filtrate was evaporated. Crystallization from ethanol afforded 0.2 g (40%) of compound **17**, m.p. >250 °C, R_F 0.63 (S3). For $C_{13}H_{14}N_4O_5$ (306.3) calculated: 50.98% C, 4.61% H, 18.29% N, found: 51.43% C, 5.10% H, 17.86% N. ^{1}H NMR spectrum: 12.40 brs, 1 H (NH); 8.06 s, 1 H (H-2); 6.00 brs, 1 H, J(1′,2′) = 0.5 (H-1′); 5.09 brd, 1 H, J(2′,1′) = 0.5, J(2′,3′) = 5.6 (H-2′); 4.93 brd, 1 H, J(3′,4′) = 0.5, J(3′,2′) = 5.6 (H-3′); 4.76 brs, 1 H (H-4′); 4.62 dd, 1 H, J(5a′,4′) = 2.2, J(gem) = 12.9 (Ha-5′); 4.11 brd, 1 H, J(5b′,4′) = 1.0, J(gem) = 12.9 (Hb-5′); 1.45 s, 3 H and 1.30 s, 3 H (2 × CH_3). ^{13}C NMR spectrum: 156.03 (C-6); 152.61 (C-8); 146.15 (C-2); 146.02 (C-4); 119.72 (C-5); 112.13 (O–C–O); 86.44 (C-1′); 85.62 (C-4′); 84.94 (C-2′); 81.07 (C-3′); 74.40 (C-5′); 26.04 and 24.43 (2 × CH_3). Mass spectrum: 307 (100, M + H).

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