

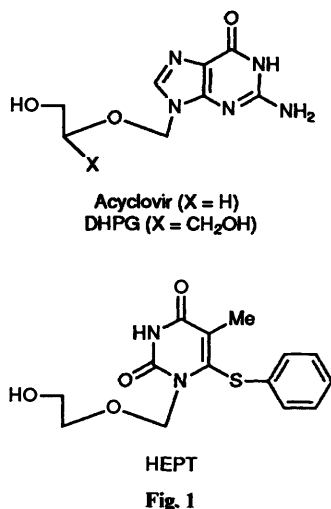
Potential Antiviral Agents. Stereospecific Synthesis of Purines and Pyrimidines Substituted with Chiral Acyclic Chains by Sugar-Ring Opening of α -L-Arabinopyranosyl Nucleosides

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3',4'-Seco-nucleosides as well as their derivatives lacking C-3', all retain the carbon framework and chirality of the β -D-ribofuranosyl moiety of the nucleosides occurring in nucleic acids, have been synthesized and their antiviral properties examined. Most of these chiral acyclic nucleosides were hitherto unknown and they were stereospecifically prepared by ring opening of α -L-arabinopyranosyl nucleosides by means of periodate oxidation followed by borohydride reduction. All the prepared compounds were tested for their activity against a variety of RNA and DNA viruses, but they did not show significant antiviral activity.

Today, several acyclic nucleoside analogues¹ are known potent antiviral agents. Among them, 9-[2-(hydroxyethoxy)methyl]guanine (Acyclovir)² and 9-[(1,3-dihydroxypropan-2-yloxy)methyl]guanine (DHPG)³ (Fig. 1) have been approved for clinical use against herpes simplex virus type 1 and human cytomegalovirus infections, respectively. More recently, it was also reported that various 6-substituted acyclic pyrimidine nucleosides related to acyclovir, such as 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine (HEPT) (Fig. 1), are selective inhibitors of human immunodeficiency virus in various human lymphocytes.⁴



Since the acyclic nucleosides have the potential for chemotherapeutic activity a large number of compounds of this class have been synthesized. Among them are the 1',2'-⁵ and 2',3'-seco-nucleosides⁶ which retain the carbon framework and chirality of the β -D-ribofuranosyl moiety of the natural nucleosides at their two asymmetrical carbon atoms (Fig. 2). On the other hand, little attention has been given to either 3',4'-seco-nucleosides or to β -D-ribofuranosyl nucleosides lacking C-3' (Fig. 2). Russian authors envisaged the possibility of preparing 1-[(1*R*,2*R*)-2,3-dihydroxy-1-(2-hydroxyethoxy)propyl]uracil (3',4'-seco-uridine) by periodate oxidation of 1-(α -L-arabinopyranosyl)uracil, followed by reduction with sodium borohydride.⁷ However, no full paper concerning this possibility has been published and only the preparation of achiral 3',4'-seco-

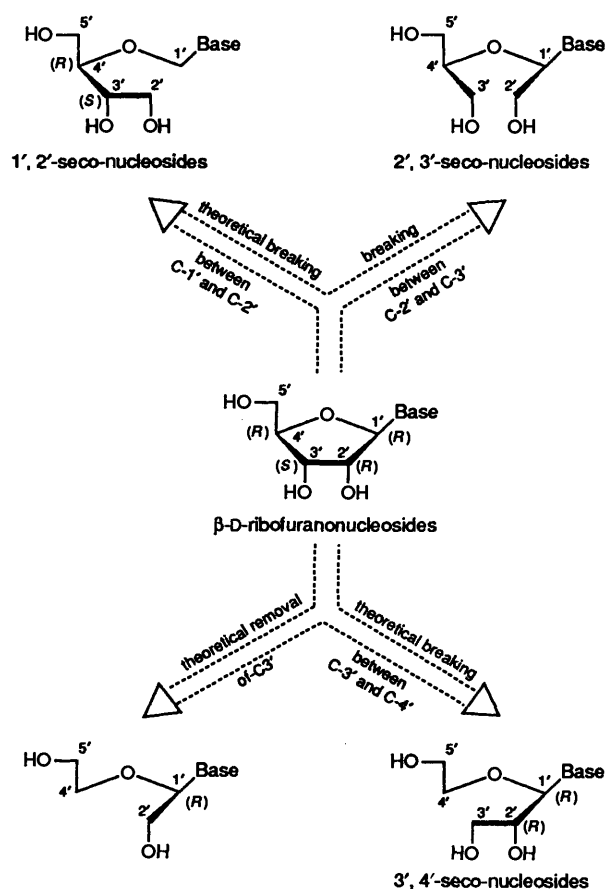


Fig. 2 For convenience, we adopted a 'ribose-like' numbering of the acyclic nucleosides

nucleosides by condensation of silylated bases with 1,4,5,6-tetraacetoxy-3-oxahexane in the presence of Lewis acids, followed by deacylation, has been reported.⁸ Regarding nucleosides lacking C-3', racemic acyclic compounds of the five bases occurring in nucleic acids have been prepared previously following different procedures,⁹⁻¹² but only the pure enantiomers having adenine¹⁴ or uracil¹² as aglycone have been reported, and were prepared by ring opening of appropriate pentopyranonucleosides.

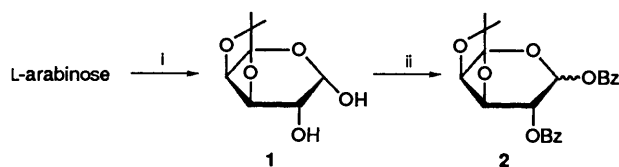
In continuation of our research programme on sugar-

modified nucleoside analogues as potential antiviral agents,¹⁵⁻²³ we now describe the stereospecific synthesis and biological evaluation of open-ring β -D-ribofuranonucleoside derivatives lacking the C-3'-C-4' bond or the C-3' atom.

Results and Discussion

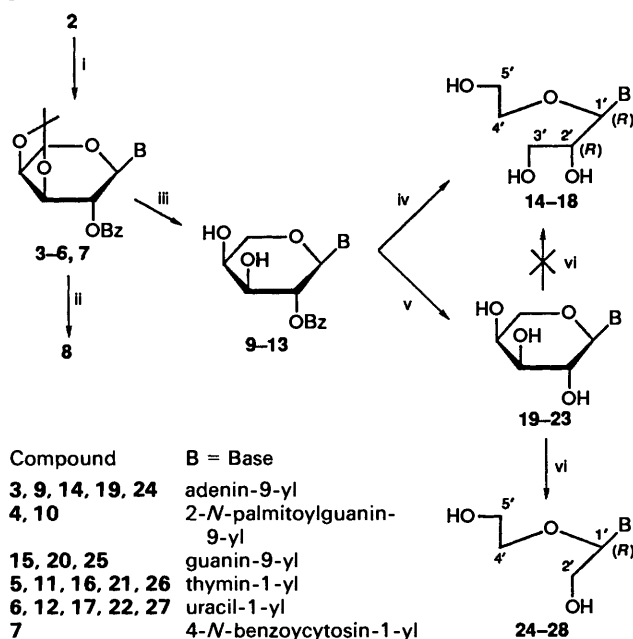
The synthetic route chosen to the chiral acyclic nucleosides consisted of periodate oxidation of a preformed pyranonucleoside and reduction of the resulting dialdehyde with sodium borohydride. Among the various starting materials which could be used, we opted for the α -L-arabinopyranosyl nucleosides, as these compounds: (i) possess the requisite *R* configuration at the 1'- and 2'-carbon, (ii) are not well documented, and (iii) the evaluation of their biological properties seemed to us to be of interest.

Condensation of a suitably protected L-arabinopyranose and the purine or pyrimidine bases was employed to prepare the α -L-arabinopyranosyl nucleosides. In accord with Baker's rule²⁴ and owing to 2-*O*-acyl participation during the condensation, a 2-*O*-benzoyl-L-arabinopyranose was used for exclusive formation of the α (*trans*-1',2') anomers in the arabinose series. As starting sugar we selected the syrupy 1,2-di-*O*-benzoyl-3,4-*O*-isopropylidene-L-arabinopyranose **2**, hitherto unknown and readily prepared from inexpensive, commercial L-arabinose in two steps (Scheme 1).



Scheme 1 Reagents: i, (MeO)₂CMe₂, PTSA, DMF; ii, BzCl, pyridine

Glycosylations were effected by various procedures which, except for the guanine and cytosine series, did not require prior protection of the heterocyclic bases (Scheme 2). Hence, the



Scheme 2 Reagents and conditions: i, Adenine, SnCl₄, MeCN for **3**; 2-*N*-palmitoylguanine, BSA, TMSTf, MeCN for **4**; thymine or uracil, HMDS, TMSCl, SnCl₄, MeCN for **5** or **6**; silylated 4-*N*-benzoylcytosine, TMSTf, ClCH₂CH₂Cl for **7**; ii, NH₂NH₂·H₂O, AcOH, C₃H₅N; iii, aq. AcOH; iv, NaIO₄; then NaBH₄, aq. 1,4-dioxane; then NH₃, MeOH; v, NH₃, MeOH; vi, NaIO₄; then NaBH₄, aq. 1,4-dioxane

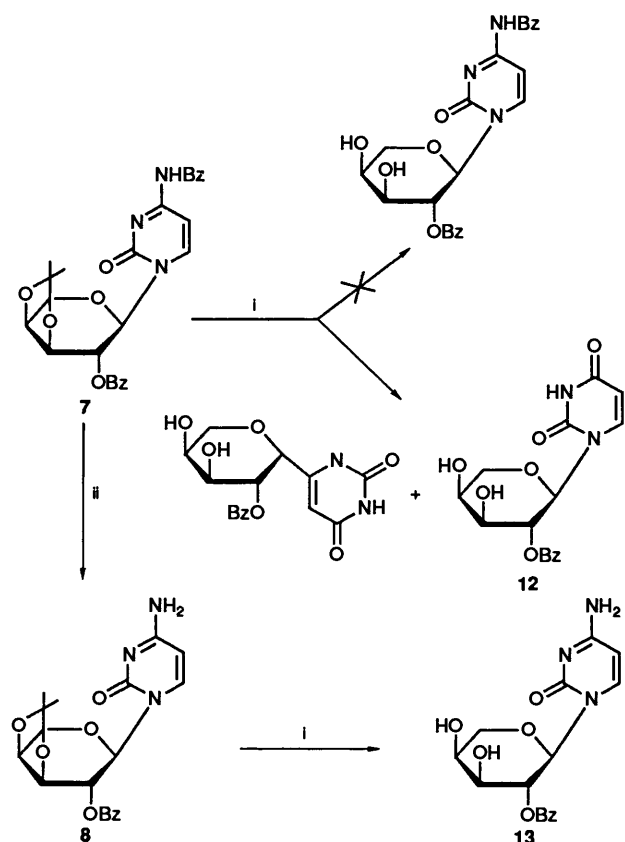
method of Saneyoshi *et al.*²⁵ was successful with adenine, while the nucleosides of thymine and uracil were obtained by Vorbruggen procedures.²⁶ Only the expected α -L-9-N **3** isomer (in the case of adenine) and α -L-1-N **5,6** isomers (in the case of thymine and uracil, respectively) were obtained after purification by silica gel column chromatography or direct crystallization. In the guanine series, application of the procedure of Wright and Dudycz²⁷ to 2-*N*-palmitoylguanin²⁸ afforded a separable mixture of the expected α -L-9-N **4** and undesirable α -L-7-N isomers. Contrary to all expectations, attempts to prepare 1-(2-*O*-benzoyl-3,4-*O*-isopropylidene- α -L-arabinopyranosyl)cytosine **8** by condensation of the sugar **2** with cytosine following the procedures usually implemented in the pentofuranosyl series^{15,16,23,26} were unsuccessful. That is why we first protected the exocyclic amine function of cytosine with a benzoyl group. After silylation, 4-*N*-benzoylcytosine²⁹ was treated with compound **2** in 1,2-dichloroethane in the presence of trimethylsilyl triflate (TMSTf) to afford the fully protected nucleoside **7** in 67% yield.

Removal of the *O*-isopropylidene protecting group from compounds **3-6** with aqueous acetic acid afforded the desired 2'-*O*-benzoyl- α -L-arabinopyranosyl nucleosides **9-12**. On the other hand, when 4-*N*-benzoyl-1-(2-*O*-benzoyl-3,4-*O*-isopropylidene- α -L-arabinopyranosyl)cytosine **7** was treated with aqueous acetic acid the expected product, 4-*N*-benzoyl-1-(2-*O*-benzoyl- α -L-arabinopyranosyl)cytosine, could not be obtained. Two new compounds were observed on TLC and were isolated by silica gel column chromatography. From their physical properties (data not shown) they were characterized as being the α and β anomers of 1-(2-*O*-benzoyl-L-arabinopyranosyl)uracil (Scheme 3). These reactions of deamination³⁰ and partial anomerization are peculiar to the 4-*N*-benzoylcytosine derivative **7** since under the same acidic conditions the cytosine derivatives **8** and **13** were not deaminated and uracils **6** and **12** did not anomerize.

Selective 4-*N*-deacylation of nucleoside **7** could be effected by the procedure of Letsinger *et al.*³¹ with hydrazine hydrate in a buffered acetic acid-pyridine mixture to give compound **8**, which was subsequently de-*O*-isopropylidened to afford compound **13** (Scheme 3).

The 2'-*O*-benzoyl- α -L-arabinopyranosyl nucleosides **9-13** are the key intermediates in our synthetic approach (Scheme 2). On the one hand scission of their 3',4'-bond by periodate oxidation,^{32,33} followed first by sodium borohydride reduction of the formed dialdehydes and then by deacylation with ammonia in methanol, resulted in the formation of the hitherto unknown chiral (1'*R*,2'*R*) 3',4'-seco analogues **14-18** of the natural β -D-ribofuranosyl nucleosides. On the other hand, deacylation of compounds **9-13** in methanolic ammonia yielded the unprotected α -L-arabinopyranosyl nucleosides **19-32** in good yield. When these nucleosides **19-23** were treated with two mole equivalents of sodium metaperiodate and then with sodium borohydride, successive scissions of the 3',4' and 2',3' bonds followed by reduction of the intermediary dialdehydes resulted in the formation of the expected chiral β -D-ribofuranosyl nucleoside derivatives lacking C-3', diols **24-28**. Among them, only those bearing adenine, **24**,¹⁴ or uracil, **27**,¹² have been reported previously but in the latter case no physical properties were described.

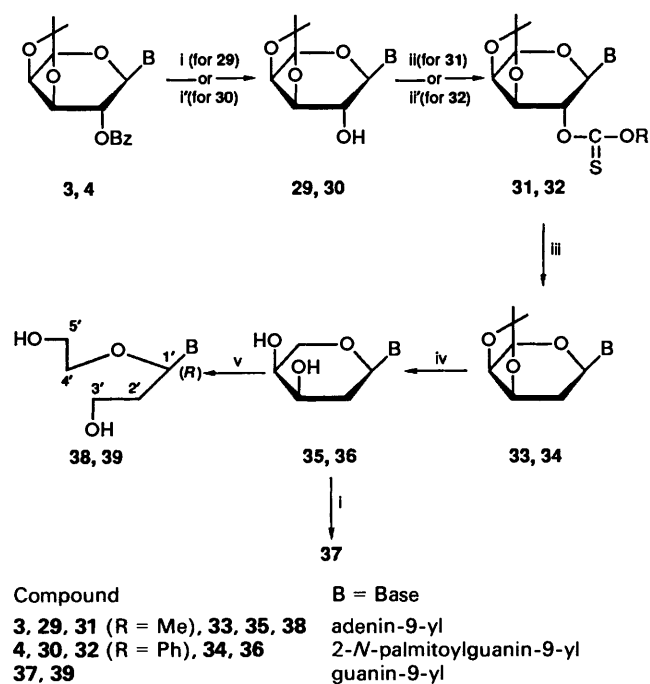
It is noteworthy that we also studied the possibility of preparing the 3',4'-seco nucleosides **14-18** directly from the unprotected compounds **19-23** by using only one mole equivalent of sodium metaperiodate. This possibility, which has been expressed in the literature,⁷ implies that the periodate cleavage of the 2',3' α -hydroxy carbonyl function generated by scission of the 3',4'-bond occurs more slowly than does the 3',4'-bond scission. However, all attempts were unsuccessful and we could detect by TLC only the acyclic nucleosides **24-28** lacking C-3' and the remaining starting compounds **19-23**.



Scheme 3 Reagents and conditions: i, aq. AcOH; ii, $\text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O}$, AcOH, $\text{C}_5\text{H}_5\text{N}$

Finally, it seemed worthwhile to synthesize the chiral 9-[(1*R*)-3-hydroxy-1-(2-hydroxyethoxy)propyl]-adenine **38** and -guanine **39** for which only racemic mixtures had been described previous to our starting this work,^{9,34,35} and for which the synthesis has been mentioned very recently.^{36,37} Therefore (Scheme 4), selective 2'-*O*-debenzoylation of protected nucleosides **3,4** by methanolic ammonia or aqueous sodium hydroxide in a pyridine-ethanol mixture, respectively, gave the 3',4'-*O*-isopropylidene derivatives **29** and **30**. Barton-type deoxygenative hydrogenolysis of thionocarbonate esters³⁸ was chosen for the preparation of the 2'-deoxy- α -L-arabinopyranosyl nucleosides. In the guanine series, reaction of compound **30** with *O*-phenyl chlorothiocarbonate and 4-(dimethylamino)pyridine (DMAP) in acetonitrile^{17,39} gave the corresponding 2'-*O*-[phenoxy(thiocarbonyl)] derivative **32**, which was treated with tributyltin hydride and the free-radical initiator α,α' -azoisobutyronitrile (AIBN) in toluene to afford, after purification by column chromatography, the protected 2'-deoxygenated product **34**. In the adenine series, treatment of compound **29** with excess of *N,N'*-thiocarbonyldiimidazole in dimethylformamide (DMF) gave an intermediate imidazolide which, upon reaction with anhydrous methanol at 60 °C for 2 h,⁴⁰ yielded the crystalline methyl thiocarbonate **31** in 58% yield. Reduction of thioester **31** with tributyltin hydride in toluene containing AIBN afforded crystalline compound **33** after column chromatography. The hitherto unknown 9-(2-deoxy- α -L-erythro-pentopyranosyl)-adenine **35** and -guanine **37** were obtained by deisopropylideneation of compounds **33** and **34** under acidic conditions, followed in the latter case by *N*-deacylation of the intermediate **36** with methanolic ammonia. Scission of the 3',4'-bond of intermediates **35** and **36** by periodate oxidation, followed by sodium borohydride reduction, resulted in the formation of the chiral (1'*R*)-3',4'-*seco* derivatives **38,39** of the

natural β -D-2'-deoxyribofuranosyl nucleosides, which were obtained pure after silanized silica gel column chromatography. The physical data for these acyclic nucleosides **38,39** were more or less in accord with literature data for their racemates^{9,34,35} and for the *R* enantiomers reported during the course of this work.^{36,37}



Scheme 4 Reagents and conditions: i, NH_3 , MeOH; i', NaOH, $\text{C}_5\text{H}_5\text{N}$ -EtOH; ii, $(\text{Im})_2\text{CS}$, DMF; then MeOH; ii', DMAP, PhOCSCl, MeCN; iii, Bu_3ShH , AIBN, toluene; iv, aq. AcOH; v, NaIO_4 ; then NaBH_4 , aq. 1,4-dioxane (followed by NH_3 , MeOH in the case of compound **36**)

Biological Evaluation

All the prepared α -L-pentopyranosyl nucleosides **19–23**, **35**, **36** and chiral acyclic nucleosides **14–18**, **24–28**, **38**, **39** were tested for their *in vitro* inhibitory effects on the replication of a number of DNA viruses (*i.e.*, human cytomegalovirus, herpes simplex virus type 1 and type 2, vaccinia virus) and RNA viruses (parainfluenza virus type III, respiratory syncytial virus, Sindbis virus, Coxsackie virus B3 and polio virus-1) in three cell systems (MRC-5, Vero and KB cells). None of these compounds showed marked antiviral effects or detectable alteration of host cell morphology at the highest concentration tested (generally 1 mmol dm^{-3}). When evaluated in two anti-human immunodeficiency virus (anti-HIV) assays, none of the tested compounds showed marked antiviral effect at a concentration less than 10-fold lower than the minimal concentration causing a detectable alteration of MT-4 and CEM host cell viability ($\approx 1 \text{ mmol dm}^{-3}$). Furthermore, two compounds, namely 9-(2-deoxy- α -L-erythro-pentopyranosyl)guanine **37** and 9-[(1*R*)-3-hydroxy-1-(2-hydroxyethoxy)propyl]guanine **39**, were significantly cytotoxic against MT-4 cells ($100 > \text{CD}_{50} > 10 \text{ } \mu\text{mol dm}^{-3}$ and $10 > \text{CD}_{50} > 1 \text{ } \mu\text{mol dm}^{-3}$, respectively).

Conclusions.—From the present work, it is obvious that an α -L-pentopyranose structure or the lack of the 3',4'-bond or C-3' atom in nucleosides does not induce inhibition of virus multiplication. Among the several hypotheses that can explain this lack of activity, the inability of these compounds to enter cells, to serve as substrate for the intracellular enzymes catalysing triphosphorylation or to inhibit enzymes involved in the metabolism of nucleic acids can be proposed. Further research

is needed to test these hypotheses, but the present data obtained with substrates **15**, **25** and **39** show that introduction of an additional chain on the C-1' atom of acyclovir leads to loss of antiviral activity.

Experimental

Evaporation of solvents was done with rotary evaporator under reduced pressure. M.p.s were determined in open capillary tubes on a Gallenkamp MFB-595-010 M apparatus and are uncorrected. UV spectra were recorded on an Uvikon 810 (KONTRON) spectrophotometer. ¹H NMR spectra were run at ambient temperature in (CD₃)₂SO with a Bruker WM 360 WB spectrometer. Chemical shifts are given in δ-values (CD₃)-(CD₂H)SO being set at δ_H 2.49 as a reference. Deuterium exchange and decoupling experiments were performed in order to confirm proton assignments. All *J*-values are in Hz. FAB mass spectra were recorded in the positive-ion or negative-ion mode on a JEOL DX 300 mass spectrometer operating with a JMA-DA 5000 mass data system. Xe atoms were used for the gun at 3 kV with a total discharge current of 20 mA. The matrix was glycerol (G), a mixture (50:50, v/v) of glycerol and thioglycerol (G-T) or 3-nitrobenzyl alcohol (NBA). Specific rotations were measured on a Perkin-Elmer Model 241 spectropolarimeter (path length 1 cm), and are given in units of 10⁻¹ deg cm² g⁻¹. Elemental analyses were carried out by the Service de Microanalyses du CNRS, Division de Vernaison (France). TLC was performed on precoated aluminium sheets of Silica Gel 60 F₂₅₄ (Merck, Art. 5554), visualization of products being accomplished by UV absorbance followed by charring with 10% ethanolic sulfuric acid and heating. Column chromatography was carried out on Silica Gel 60 (Merck, Art. 9385) or on Silanized Silica Gel RP2 (Merck, Art. 7719) at atmospheric pressure. High-performance liquid chromatographic (HPLC) purifications were carried out on a Waters Associates Unit equipped with two Model 6000 A solvent delivery systems, a Model 680 solvent programmer, a Model U6K sample injector, a Waters 990 photodiode array detector, and a NEC-APC IV microprocessor-controlled data system. The column was a Waters C₁₈ 'Radial Pak' (100 × 8 mm id, 10 μm particle size), inserted into a Waters Associates Radial Compression module RCM 100 and protected by a prefilter and a precolumn C₁₈ 'Guard Pak'. Light petroleum refers to the fraction boiling in the range 40–60 °C.

3,4-O-Isopropylidene-β-L-arabinopyranose 1.—This compound was prepared as described⁴¹ for the D-enantiomer by treatment of L-arabinose (8.00 g, 53.3 mmol) with 2,2-dimethoxypropane (20 cm³, 163 mmol) in dry DMF (100 cm³) in the presence of toluene-4-sulfonic acid (PTSA) (0.12 g, 0.63 mmol). Column chromatography of the product on silica gel using a stepwise gradient of methanol (0–10%) in dichloromethane afforded the title compound **1** (8.4 g, 83%), which was crystallized from light petroleum, m.p. 84–85 °C (lit.,⁴² 80 °C; lit.,⁴³ 78–80 °C and 80–81 °C) (for the D-enantiomer: lit.,⁴¹ 84–85 °C; lit.,⁴⁴ 78 °C; lit.⁴⁵ 82–85 °C; lit.,⁴⁶ 82–84 °C); [α]_D²⁰ + 111.0 (c 1.0, water) {lit.,⁴² [α]_D²⁰ + 128.8 (c 0.93, water)} {for the D-enantiomer: lit.,⁴¹ [α]_D²⁰ – 111.1 (c 0.5, water); lit.,⁴⁴ – 111 (c 1.1, water); lit.,⁴⁶ [α]_D²⁰ from –156 to –111 (c 1.1, water)}; ¹H NMR data (CD₃)₂SO were in accord with literature data.^{43,46}

1,2-Di-O-benzoyl-3,4-O-isopropylidene-L-arabinopyranose 2.—A solution of 3,4-O-isopropylidene-β-L-arabinopyranose **1** (1.90 g, 10 mmol) in anhydrous pyridine (10 cm³) was cooled in an ice-bath, and benzoyl chloride (3.49 cm³, 30 mmol) was added dropwise to the stirred mixture. The reaction mixture was stirred at room temperature overnight with exclusion of moisture. A mixture of water and ice (~30 cm³) was added, and

the mixture was stirred for 1 h. The products were extracted into dichloromethane (3 × 10 cm³). The combined organic layers were washed successively with ice-cold 3 mol dm⁻³ aq. sulfuric acid (3 × 50 cm³), water (3 × 50 cm³), saturated aq. sodium hydrogen carbonate, and water, then dried over sodium sulfate, filtered, and evaporated to dryness under reduced pressure. The resulting syrup consisted of an anomeric mixture of the *title compound 2* (3.39 g, 85%; ratio β/α ~ 2:1 as determined from its ¹H NMR spectrum) and was sufficiently pure to be directly used in the condensation steps; δ_H 8.0–7.5 (10 H total sum, 3 m, 2 × Ph for α- and β-anomer), 6.41 and 5.99 [1 H total sum, 2 d, *J*_{1,2} 3.4, 1-H β-anomer and *J*_{1,2} 7.6, 1-H α-anomer, respectively], 5.37 and 5.27 [1 H total sum, t and dd, *J* 7.5, 2-H α-anomer and *J*_{1,2} 3.4, *J*_{2,3} 7.6, 2-H β-anomer, respectively], 4.71 (dd, *J*_{2,3} 7.5, *J*_{3,4} 5.7, 3-H β-anomer), 4.56 (1 H, total sum, m, 3-H α-anomer and 4-H β-anomer), 4.41 (m, 5-H β-anomer), 4.2–4.1 (m, 4-H, 5-H, 5'-H α-anomer and 5'-H β-anomer), 1.52 and 1.32 (2 s, CMe₂ α-anomer), 1.50 and 1.34 (2 s, CMe₂ β-anomer). Crystallization from methanol afforded the pure β-anomer **2** (1.83 g, 46%), m.p. 156–157 °C (Found: C, 66.5; H, 5.3. C₂₂H₂₂O₇ requires C, 66.3; H, 5.6%); [α]_D²⁰ + 191 (c 1.0, Me₂SO); λ_{max}(95% EtOH)/nm 280sh (ε 3600 dm³ mol⁻¹ cm⁻¹), 273 (4100) and 229 (24 800); λ_{min}/nm 255 (ε 3200).

9-(2-O-Benzoyl-3,4-O-isopropylidene-α-L-arabinopyranosyl)-adenine 3.—This compound was prepared by treatment of adenine (1.32 g, 9.77 mol) with the sugar **2** (3.99 g, 10.0 mmol) and tin(IV) chloride (2.35 cm³, 20.0 mmol) in anhydrous acetonitrile (200 cm³) as described for other adenine nucleoside analogue series.^{15,23} After the usual work-up, the residue was subjected to silica gel column chromatography, with a stepwise gradient of methanol (0–7%) in dichloromethane. Crystallization of the product in the appropriate fractions from dichloromethane afforded the *title compound 3* (2.97 g, 74%), m.p. 226–227 °C (Found: C, 56.95; H, 5.1; N, 16.8. C₂₀H₂₁N₅O₅·1/5CH₂Cl₂ requires C, 56.6; H, 5.0; N, 16.35%); [α]_D²⁰ + 13.0 (c 1.0, Me₂SO); λ_{max}(95% EtOH)/nm 258 (ε 16 200) and 233 (16 900); λ_{min}/nm 245 (ε 13 100) and 221 (12 600); δ_H 8.27 and 8.09 (1 H each, 2 s, 2- and 8-H), 7.7–7.4 (5 H, m, Ph), 7.13 (2 H, s, NH₂), 5.90 (1 H, d, *J*_{1,2} 9.6, 1'-H), 5.73 (1 H, dd, *J*_{2,3} 7.4, 2'-H), 4.63 (1 H, t, 3'-H), 4.5–4.3 (2 H, m, 4'- and 5'-H), 4.21 (1 H, dd, *J*_{5,5'} 13.6, 5'-H) and 1.59 and 1.33 (3 H each, 2 s, CMe₂); *m/z* (FAB > 0, NBA) 412 (M + H)⁺, 277 (s)⁺, 136 (BH₂)⁺ and 105 (C₆H₅CO)⁺.

9-(2-O-Benzoyl-3,4-O-isopropylidene-α-L-arabinopyranosyl)-2-N-palmitoylguanine 4.—This compound was prepared by treatment of silylated 2-N-palmitoylguanine [obtained by reflux of 2-N-palmitoylguanine²⁸ (4.68 g, 12.0 mmol) with bis(trimethylsilyl)acetamide (BSA) (11.8 cm³, 48.3 mmol) in anhydrous acetonitrile (50 cm³) for 30 min] with the sugar **2** [3.99 g, 10.0 mmol; added in solution in acetonitrile (50 cm³)] and TMSTf (2.73 cm³, 15.1 mmol) as described for other guanine nucleoside analogue series.²³ After the usual work-up, the residue was subjected to silica gel column chromatography, with a stepwise gradient of methanol (0–3%) in dichloromethane. Crystallization of the product in the appropriate fractions from methanol afforded the *title compound 4* (3.2 g, 48%), m.p. 199–200 °C (Found: C, 63.2; H, 7.3; N, 10.35. C₃₆H₅₁N₅O₇·H₂O requires C, 63.2; H, 7.8; N, 10.2%); [α]_D²⁰ + 57.0 (c 1.0, in Me₂SO); λ_{max}(95% EtOH)/nm 281 (ε 13 000), 276 (13 000), 259 (16 100), 254 (16 200) and 234 (18 100); λ_{min}/nm 278 (ε 12 900), 270 (12 600), 256 (16 100) and 246 (14 600); δ_H 11.9 and 11.7 (1 H each 2 br s, 1-H and 2-NH), 8.12 (1 H, s, 8-H), 7.8–7.4 (5 H, m, Ph), 5.6 (2 H, m, 1'- and 2'-H), 4.59 (1 H, t, *J* 5.9, 3'-H), 4.4 (2 H, m, 4'- and 5'-H), 4.14 (1 H, dd, *J*_{4,5} 2.1, *J*_{5,5'} 13.7, 5'-H), 2.45 (2 H, t, COCH₂), 1.6–1.5 [5 H, m, CMeMe and COCH₂CH₂ (δ 1.58, s, CMeMe)], 1.34 (3 H, s, CMeMe), 1.21

(24 H, m, $[\text{CH}_2]_{12}$) and 0.83 (3 H, t, J 6.8, CH_2Me); m/z (FAB > 0, NBA) 666 ($\text{M} + \text{H}$)⁺, 390 (BH_2)⁺, 277 (s)⁺, 152 ($\text{BH}_2 - \text{CH}_3[\text{CH}_2]_{14}\text{CO} + \text{H}$)⁺ and 105 ($\text{C}_6\text{H}_5\text{CO}$)⁺.

1-(2-O-Benzoyl-3,4-O-isopropylidene- α -L-arabinopyranosyl)-thymine 5 and -uracil 6.—These compounds were prepared by treatment of thymine (1.26 g, 10.0 mmol) or uracil (1.12 g, 10.0 mmol) with the sugar **2** (3.99 g, 10.0 mmol), hexamethyl-disilazane (HMDS) (1.67 cm³, 8.0 mmol), chlorotrimethylsilane (TMSCl) (1.01 cm³, 8.0 mmol) and tin(IV) chloride (1.41 cm³, 12.0 mmol) as described for other thymine and uracil nucleoside analogue series.^{15,16,23} After the usual work-up, the residues were directly crystallized to afford the *title compounds* **5** and **6**.

Compound 5 (2.82 g, 70%), m.p. 168–169 °C (from dichloromethane) (Found: C, 55.2; H, 5.2; N, 6.2. $\text{C}_{20}\text{H}_{22}\text{N}_2\text{O}_7 \cdot \frac{1}{2}\text{CH}_2\text{Cl}_2$ requires C, 55.3; H, 5.2; N, 6.3%); $[\alpha]_{\text{D}}^{20} + 53.0$ (c 1.0 in Me_2SO); λ_{max} (95% EtOH)/nm 262 (ϵ 9600) and 230 (14 800); λ_{min} /nm 248 (ϵ 8100); δ_{H} 11.3 (1 H, br s, 3-H), 7.9–7.5 (6 H, m, Ph and 6-H), 5.77 (1 H, d, $J_{1,2}$ 9.6, 1'-H), 5.26 (1 H, dd, $J_{2,3}$ 7.3, 2'-H), 4.60 (1 H, dd, $J_{3,4}$ 5.7, 3'-H), 4.4–4.3 (2 H, m, 4'- and 5'-H), 4.13 (1 H, dd, $J_{4,5}$ 2.3, $J_{5,5'}$ 13.7, 5'-H'), 1.77 (3 H, d, J 1.0, Me) and 1.55 and 1.31 (3 H each, 2 s, CMe_2); m/z (FAB > 0, NBA) 403 ($\text{M} + \text{H}$)⁺.

Compound 6 (2.64 g, 68%), m.p. 176–177 °C (from diisopropyl ether) (Found: C, 58.4; H, 5.1; N, 6.3. $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_7$ requires C, 58.8; H, 5.2; N, 7.2%); $[\alpha]_{\text{D}}^{20} + 80.0$ (c 1.0 in Me_2SO); λ_{max} (95% EtOH)/nm 260 (ϵ 10 100) and 232 (16 200); λ_{min} /nm 252 (ϵ 9700); δ_{H} 11.3 (1 H, br s, 3-H), 7.9–7.5 [6 H, m, Ph and 6-H (δ 7.63, d, $J_{5,6}$ 8.2, 6-H)], 5.78 (1 H, d, $J_{1,2}$ 9.6, 1'-H), 5.64 (1 H, d, 5-H), 5.25 (1 H, dd, $J_{2,3}$ 7.4, 2'-H), 4.60 (1 H, dd, $J_{3,4}$ 5.6, 3'-H), 4.3 (2 H, m, 4'- and 5'-H), 4.14 (1 H, dd, $J_{4,5}$ 2.1, $J_{5,5'}$ 13.7, 5'-H') and 1.53 and 1.31 (3 H each, 2 s, CMe_2); m/z (FAB > 0, G–T) 389 ($\text{M} + \text{H}$)⁺, 277 (s)⁺, 113 (BH_2)⁺ and 105 ($\text{C}_6\text{H}_5\text{CO}$)⁺; m/z (FAB < 0, G–T) 479 ($\text{M} + \text{G} - \text{H}$)⁻, 387 ($\text{M} - \text{H}$)⁻ and 111 (B)⁻.

4-N-Benzoyl-1-(2-O-benzoyl-3,4-O-isopropylidene- α -L-arabinopyranosyl)cytosine 7.—A suspension of 4-*N*-benzoylcytosine²⁹ (2.48 g, 11.5 mmol) and ammonium sulfate (0.12 g, 0.9 mmol) in HMDS (62 cm³, 297 mmol) was heated under reflux overnight. After cooling, the excess of HMDS was removed under reduced pressure and by co-distillation with anhydrous xylene.

The resulting silylated 4-*N*-benzoylcytosine was dissolved in anhydrous 1,2-dichloroethane (37 cm³), then a solution of the sugar **2** (3.99 g, 10.0 mmol) in 1,2-dichloroethane (108 cm³) and a solution of TMSTf (2.18 cm³, 12.6 mmol) in the same solvent (15 cm³) were added successively. The reaction mixture was heated under reflux for 1 h, cooled to room temperature, and then poured into ice-cold, saturated, aq. sodium hydrogen carbonate (160 cm³). The organic layer was separated, washed with water (2 \times 150 cm³), dried over sodium sulfate, filtered, and evaporated to dryness under reduced pressure. Column chromatography of the residue on silica gel with stepwise gradient of methanol (0–2%) in dichloromethane afforded the *title compound* **7** (3.3 g, 67%), which was crystallized from methanol, m.p. 202–203 °C (Found: C, 63.5; H, 5.2; N, 8.7. $\text{C}_{26}\text{H}_{25}\text{N}_3\text{O}_7$ requires C, 63.5; H, 5.1; N, 8.55%); $[\alpha]_{\text{D}}^{20} + 60.0$ (c 1.0 in Me_2SO); λ_{max} (95% EtOH)/nm 302 (ϵ 9500), 260 (27 300) and 232 (22 400); λ_{min} /nm (ϵ 9000) and 244 (19 500); δ_{H} 11.1 (1 H, br s, 4-NH), 8.15 (1 H, d, $J_{5,6}$ 7.5, 6-H), 8.0–7.5 (10 H, m, 2 \times Ph), 7.31 (1 H, d, 5-H), 5.99 (1 H, d, $J_{1,2}$ 9.4, 1'-H), 5.30 (1 H, t, 2'-H), 4.63 (1 H, t, 3'-H), 4.3 (2 H, m, 4'- and 5'-H), 4.19 (1 H, d, $J_{5,5'}$ 13.5, 5'-H') and 1.56 and 1.32 (3 H each, 2 s, CMe_2); m/z (FAB > 0, G–T) 492 ($\text{M} + \text{H}$)⁺, 277 (s)⁺, 216 (BH_2)⁺ and 105 ($\text{C}_6\text{H}_5\text{CO}$)⁺.

1-(2-O-Benzoyl-3,4-O-isopropylidene- α -L-arabinopyranosyl)-

cytosine 8.—To a solution of the nucleoside **7** (1.0 g, 2.04 mmol) in an acetic acid–pyridine mixture (1:4; 16 cm³) was added hydrazine hydrate (0.49 cm³, 10.08 mmol). The solution was stirred for 24 h at room temperature, and then evaporated to dryness under reduced pressure. Column chromatography of the residue on silica gel with stepwise gradient of methanol (0–5%) in dichloromethane afforded the *title compound* **8** (0.36 g, 46%), which was crystallized from ethyl acetate, m.p. 252–253 °C (Found: C, 58.9; H, 5.4; N, 10.9. $\text{C}_{19}\text{H}_{21}\text{N}_3\text{O}_6$ requires C, 58.9; H, 5.5; N, 10.9%); $[\alpha]_{\text{D}}^{20} + 97.0$ (c 1.0, Me_2SO); λ_{max} (95% EtOH)/nm 270 (ϵ 8900) and 231 (20 600); λ_{min} /nm 258 (ϵ 8700); δ_{H} 7.9–7.5 (6 H, m, Ph and 5-H), 7.2 and 7.1 (1 H each, 2 \times br s, 4-NH₂), 5.87 (1 H, d, $J_{1,2}$ 9.7, 1'-H), 5.72 (1 H, d, $J_{5,6}$ 7.6, 6-H), 5.23 (1 H, dd, $J_{2,3}$ 7.5, 2'-H), 4.57 (1 H, dd, $J_{3,4}$ 5.5, 3'-H), 4.3 (2 H, m, 4'- and 5'-H), 4.08 (1 H, dd, $J_{4,5}$ 2.0, $J_{5,5'}$ 13.6, 5'-H') and 1.53 and 1.30 (3 H each, 2 \times s, CMe_2); m/z (FAB > 0, G–T) 775 [$\text{M} + \text{H}$]⁺, 388 ($\text{M} + \text{H}$)⁺, 112 (BH_2)⁺ and 105 ($\text{C}_6\text{H}_5\text{CO}$)⁺; m/z (FAB < 0, G–T) 386 ($\text{M} - \text{H}$)⁻ and 110 (B)⁻.

General Procedure for the Preparation of 2'-O-Benzoyl- α -L-arabinopyranosyl Nucleosides 9–13.—A suspension of the foregoing appropriate isopropylidene derivative (1.0 mmol) in an acetic acid–water mixture (7:3; 10 cm³) was stirred and heated at 60 °C for 3 h. After cooling, the reaction mixture was evaporated to dryness under reduced pressure and the residue was co-evaporated under reduced pressure several times with ethanol to give a solid residue. The deisopropylidened nucleosides **9–13** were purified by either silica gel column chromatography or direct crystallization.

9-(2-O-Benzoyl- α -L-arabinopyranosyl)adenine 9 (0.32 g, 86%, after direct crystallization from methanol), m.p. 237–238 °C (Found: C, 54.7; H, 4.7; N, 18.7. $\text{C}_{17}\text{H}_{17}\text{N}_5\text{O}_5$ requires C, 55.0; H, 4.6; N, 18.9%); $[\alpha]_{\text{D}}^{20} - 39.2$ (c 1.0, Me_2SO); λ_{max} (95% EtOH)/nm 258 (ϵ 15 600) and 232 (16 000); λ_{min} /nm 246 (ϵ 12 300) and 222 (12 300); δ_{H} 8.25 and 8.05 (1 H each, 2 s, 2- and 8-H), 7.7–7.4 (5 H, m, Ph), 7.16 (2 H, s, NH₂), 5.8–5.7 (2 H, m, 1'- and 2'-H), 5.29 (1 H, d, J 5.9, 3'-OH), 5.11 (1 H, d, J 5.5, 4'-OH), 4.0 (1 H, m, 3'-H) and 4.1–3.9 (3 H, m, 4'-H and 5'-H₂); m/z (FAB > 0, NBA) 372 ($\text{M} + \text{H}$)⁺ and 136 (BH_2)⁺.

9-(2-O-Benzoyl- α -L-arabinopyranosyl)-2-N-palmitoylguanine 10 (0.57 g, 91%, after direct crystallization from methanol), m.p. 204 °C (start of decomposition) (Found: C, 59.9; H, 7.4; N, 11.0. $\text{C}_{33}\text{H}_{47}\text{N}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$ requires C, 59.9; H, 7.8; N, 10.6%); $[\alpha]_{\text{D}}^{20} + 55.6$ (c 1.0, Me_2SO); λ_{max} (95% EtOH)/nm 274 (ϵ 13 500), 256 (17 100), 254 (17 000) and 233 (15 600); λ_{min} /nm 270 (ϵ 13 400) and 243 (14 100); δ_{H} 12.1–11.5 (2 H, br s, 1-H and 2-NH), 8.09 (1 H, s, 8-H), 7.8–7.3 (5 H, m, Ph), 5.65 (1 H, t, J 9.3, 2'-H), 5.51 (1 H, d, 1'-H), 5.4 and 5.2 (1 H each, 2 br s, 3'- and 4'-OH), 4.0–3.8 (4 H, m, 3'- and 4'-H, and 5'-H₂), 2.42 (2 H, t, J 7.3, COCH_2), 1.6 (2 H, m, COCH_2CH_2), 1.3–1.2 (24 H, m, $[\text{CH}_2]_{12}$) and 0.83 (3 H, t, J 6.6, CH_2Me); m/z (FAB > 0, G) 626 ($\text{M} + \text{H}$)⁺.

1-(2-O-Benzoyl- α -L-arabinopyranosyl)thymine 11 (0.33 g, 91%, after direct crystallization from a methanol–dichloromethane mixture), m.p. 223–224 °C (Found: C, 56.2; H, 5.1; N, 7.6. $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_7$ requires C, 56.35; H, 5.0; N, 7.7%); $[\alpha]_{\text{D}}^{20} - 13.0$ (c 1.0 in Me_2SO); λ_{max} (95% EtOH)/nm 262 (ϵ 9900) and 229 (14 800); λ_{min} /nm 248 (ϵ 8100); δ_{H} 11.2 (1 H, br s, 3-H), 7.9–7.5 (6 H, m, Ph and 6-H), 5.68 (1 H, d, $J_{1,2}$ 8.9, 1'-H), 5.35 (1 H, t, 2'-H), 5.3 and 5.1 (1 H each, 2 br s, 3'- and 4'-OH), 4.0 (1 H, m, 3'-H), 3.9–3.8 (3 H, m, 4'-H and 5'-H₂) and 1.78 (3 H, s, Me); m/z (FAB > 0, NBA) 363 ($\text{M} + \text{H}$)⁺.

1-(2-O-Benzoyl- α -L-arabinopyranosyl)uracil 12 {0.30 g, 86%, after chromatography [eluent: stepwise gradient of methanol (0–10%) in dichloromethane], and then crystallization from diisopropyl ether}, m.p. 157–159 °C (Found: C, 52.2; H, 4.9; N, 7.35. $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_7 \cdot \text{H}_2\text{O}$ requires C, 52.5; H, 4.95; N, 7.65%); $[\alpha]_{\text{D}}^{20} + 28.4$ (c 1.0 in Me_2SO); λ_{max} (95% EtOH)/nm 260 (ϵ 10 100) and 231 (14 900); λ_{min} /nm 247 (ϵ 8500); δ_{H} 11.2 (1 H, br s,

3-H), 7.9–7.5 [6 H, m, Ph and 6-H (δ 7.71, d, $J_{5,6}$ 8.2, 6-H)], 5.70 (2 H, m, 1'- and 5-H), 5.35 (1 H, t, $J_{9,4}$, 2'-H), 5.27 (1 H, d, J 6.0, 3'-OH), 5.08 (1 H, d, J 5.9, 4'-OH), 4.0 (1 H, m, 3'-H) and 3.9–3.8 (3 H, m, 4'-H and 5'-H₂); m/z (FAB > 0, G-T) 349 (M + H)⁺, 237 (s)⁺, 113 (BH₂)⁺ and 105 (C₆H₅CO)⁺; m/z (FAB < 0, G-T) 347 (M - H)⁻ and 111 (B)⁻.

1-(2-O-Benzoyl- α -L-arabinopyranosyl)cytosine **13** {0.29 g, 84%, after chromatography [eluent: stepwise gradient of methanol (0–15%) in dichloromethane], and then crystallization from methanol}, m.p. 179 °C (decomposition) (Found: C, 53.45; H, 5.1; N, 10.8. C₁₆H₁₇N₃O₆·CH₃OH requires C, 53.8; H, 5.6; N, 11.1%). $[\alpha]_D^{20} + 23.8$ (c 0.8 in Me₂SO); λ_{\max} (95% EtOH)/nm 270 (ϵ 8600) and 232 (18 500); λ_{\min} /nm 258 (ϵ 8100); δ_H 7.9–7.5 (6 H, m, Ph and 6-H), 7.2 and 7.0 (1 H each, 2 br s, NH₂), 5.79 (1 H, d, $J_{1,2}$ 9.4, 1'-H), 5.72 (1 H, d, $J_{5,6}$ 7.5, 5-H), 5.33 (1 H, t, 2'-H), 5.22 (1 H, d, $J_{5,6}$, 3'-OH), 5.05 (1 H, d, J 5.6, 4'-OH), 3.9 (1 H, m, 3'-H) and 3.9–3.7 (3 H, m, 4'-H and 5'-H₂); m/z (FAB > 0, G-T) 348 (M + H)⁺, 237 (s)⁺ and 112 (BH₂)⁺; m/z (FAB < 0, G-T) 454 (M + T - H)⁻, 346 (M - H)⁻ and 110 (B)⁻.

General Procedure for the Preparation of 9- and 1-[(1R,2R)-2,3-Dihydroxy-1-(2-hydroxyethoxy)propyl]-purines and -pyrimidines 14–18.—A solution of sodium metaperiodate (1.12 g, 5.24 mmol) in water (12.5 cm³) was added to a solution of the foregoing appropriate deisopropylidened derivative (3.5 mmol) in a 1,4-dioxane–water mixture (9:1, 35 cm³). The reaction mixture was stirred overnight at room temperature, filtered, and the insoluble sodium iodate was washed with 1,4-dioxane. The combined filtrate and washings were concentrated to ~50 cm³, and sodium borohydride (0.2 g, 5.29 mmol) was added in portions. The solution was stirred for 1 h at room temperature after the addition was complete, then was neutralized by careful addition of acetic acid, and evaporated to dryness under reduced pressure. The residue was dissolved in stirred methanolic ammonia (previously saturated at -10 °C and tightly stoppered; 90 cm³) and stirred overnight at room temperature. The solution was then evaporated to dryness under reduced pressure and the residue was co-evaporated under reduced pressure with ethanol to give a crude compound. The title compounds were purified by chromatography, and then crystallized or lyophilized.

9-[(1R,2R)-2,3-Dihydroxy-1-(2-hydroxyethoxy)propyl]adenine **14** [0.25 g, 27%, after purification by HPLC (eluent: 3% acetonitrile in water; flow rate 6.75 cm³/min), and then crystallization from water], m.p. > 260 °C (Found: C, 41.6; H, 5.6; N, 24.25. C₁₀H₁₃N₅O₄·H₂O requires C, 41.8; H, 6.0; N, 24.4%). $[\alpha]_D^{20} + 9.6$ (c 0.5, Me₂SO); λ_{\max} (95% EtOH)/nm 258 (ϵ 14 500); λ_{\min} /nm 226 (ϵ 1900); δ_H 8.23 and 8.13 (1 H each, 2 s, 2- and 8-H), 7.20 (2 H, s, NH₂), 5.63 (1 H, d, $J_{1,2}$ 6.9, 1'-H), 5.2, 4.7 and 4.6 (1 H each, 3 br s, 2', 3'- and 5'-OH), 4.1 (1 H, m, 2'-H) and 3.5–3.2 (6 H, m, 3 × CH₂); m/z (FAB > 0, G-T) 270 (M + H)⁺ and 136 (BH₂)⁺.

9-[(1R,2R)-2,3-Dihydroxy-1-(2-hydroxyethoxy)propyl]guanine **15** [0.38 g, 38%, after purification by HPLC (eluent: 0.5% acetonitrile in water; flow rate 6.75 cm³/min), and then repetitive crystallization from water], m.p. > 260 °C (Found: C, 37.5; H, 5.4; N, 21.4. C₁₀H₁₃N₅O₅·2H₂O requires C, 37.4; H, 5.95; N, 21.8%). $[\alpha]_D^{20} + 10.0$ (c 0.5, Me₂SO); λ_{\max} (95% EtOH)/nm 270sh (ϵ 9400) and 253 (13 200); λ_{\min} /nm 221 (ϵ 2800); δ_H 10.5 (1 H, br s, 1-H), 7.76 (1 H, s, 8-H), 6.43 (2 H, s, NH₂), 5.39 (1 H, d, $J_{1,2}$ 7.0, 1'-H), 5.08 (1 H, d, J 5.5, 2'-OH), 4.6 (2 H, m, 3'- and 5'-OH), 4.0 (1 H, m, 2'-H) and 3.5–3.2 (6 H, m, 3 × CH₂ partially obscured by water).

1-[(1R,2R)-2,3-Dihydroxy-1-(2-hydroxyethoxy)propyl]thymine **16** {0.55 g, 60%, after purification by silica gel column chromatography [eluent: stepwise gradient of methanol (0–17%) in dichloromethane], and then lyophilization from water}, m.p. 148 °C (decomp.); $[\alpha]_D^{20} + 57.0$ (c 0.9, Me₂SO); λ_{\max} (95%

EtOH)/nm 266 (ϵ 9700); λ_{\min} /nm 239 (ϵ 4000); δ_H 11.1 (1 H, br s, 3-H), 7.45 (1 H, s, 6-H), 5.54 (1 H, d, $J_{1,2}$ 7.6, 1'-H), 4.99 (1 H, d, J 5.2, 2'-OH), 4.6 (2 H, m, 3'- and 5'-OH), 3.7 (1 H, m, 2'-H), 3.6–3.4 (6 H, m, 3 × CH₂) and 1.77 (3 H, s, Me); m/z (FAB > 0, G-T) 261 (M + H)⁺ and 127 (BH₂)⁺.

1-[(1R,2R)-2,3-Dihydroxy-1-(2-hydroxyethoxy)propyl]uracil **17** {0.55 g, 64%, after purification first by silica gel column chromatography [eluent: stepwise gradient of methanol (0–20%) in dichloromethane], then by silanized silica gel column chromatography [eluent: linear gradient of methanol (0–100%) in water], and finally lyophilization from water} (Found: C, 42.4; H, 6.0; N, 10.4. C₉H₁₄N₂O₆·½H₂O requires C, 42.35; H, 5.9; N, 11.0%). $[\alpha]_D^{20} + 21.0$ (c 1.6, Me₂SO); λ_{\max} (95% EtOH)/nm 262 (ϵ 9100); λ_{\min} /nm 230 (ϵ 1800); δ_H 11.2 (1 H, br s, 3-H), 7.58 (1 H, d, $J_{5,6}$ 8.0, 6-H), 5.59 (1 H, d, 5-H), 5.55 (1 H, d, $J_{1,2}$ 7.2, 1'-H), 5.4–4.2 (3 H, br s, 2', 3'- and 5'-OH), 3.6 (1 H, m, 2'-H) and 3.6–3.3 (6 H, m, 3 × CH₂ partially obscured by water); m/z (FAB > 0, G-T) 339 (M + G + H)⁺, 247 (M + H)⁺ and 113 (BH₂)⁺; m/z (FAB < 0, G-T) 337 (M + G - H)⁻, 245 (M - H)⁻ and 111 (B)⁻.

1-[(1R,2R)-2,3-Dihydroxy-1-(2-hydroxyethoxy)propyl]cytosine **18** {0.38 g, 44%, after purification by silanized silica gel column chromatography [eluent: linear gradient of methanol (0–100%) in water], and then crystallization from water}, m.p. 198 °C (start of decomposition); $[\alpha]_D^{20} + 13.3$ (c 0.5, Me₂SO); λ_{\max} (95% EtOH)/nm 271 (ϵ 9000) and 238 (8600); λ_{\min} /nm 255 (ϵ 7500); δ_H 7.52 (1 H, d, $J_{5,6}$ 7.4, 6-H), 7.2–6.9 (2 H, br s, NH₂), 5.71 (1 H, d, 5-H), 5.67 (1 H, d, $J_{1,2}$ 5.9, 1'-H), 5.1–4.5 (3 H, br s, 2', 3'- and 5'-OH), 3.7 (1 H, m, 2'-H) and 3.5–3.2 (6 H, m, 3 × CH₂ partially obscured by water); m/z (FAB > 0, G-T) 246 (M + H)⁺, 133 (s)⁺ and 112 (BH₂)⁺.

General Procedure for the Preparation of α -L-Arabinopyranosyl Nucleosides 19–23.—A solution of the foregoing appropriate 2'-O-benzoyl- α -L-arabinopyranosyl nucleoside (2.0 mmol) in methanolic ammonia (previously saturated at -10 °C and tightly stoppered; 50 cm³) was stirred overnight at room temperature. The solution was evaporated to dryness under reduced pressure and the residue was co-evaporated under reduced pressure several times with methanol. The α -L-arabinopyranosylguanine **20** and the other title compounds were purified by either silanized silica gel column chromatography or by direct crystallization.

9- α -L-Arabinopyranosyladenine **19** (0.44 g, 82%, after direct crystallization from water) (Found: C, 42.7; H, 5.3; N, 23.6. Calc. for C₁₀H₁₃N₅O₄·H₂O: C, 42.1; H, 5.3; N, 24.55%), m.p. 165–166 °C (lit.⁴⁷ 269–270 °C and 235–236 °C; lit.⁴⁸ 164–166 °C); $[\alpha]_D^{20} + 35.5$ (c 1.0, water) {lit.⁴⁷ $[\alpha]_D^{25} + 35.3$ (c 1, water); lit.⁴⁸ + 35.9 (c 1.02, water)}; λ_{\max} (95% EtOH)/nm 258 (ϵ 13 800); λ_{\min} /nm 226 (ϵ 2400); δ_H 8.31 and 8.14 (1 each, 2 s, 2- and 8-H), 7.23 (2 H, s, NH₂), 5.30 (1 H, d, $J_{1,2}$ 9.2, 1'-H), 5.19 (1 H, d, J 5.8, 2'-OH), 4.95 (1 H, d, J 5.6, 3'-OH), 4.71 (1 H, d, J 4.7, 4'-OH), 4.2 (1 H, m, 2'-H), 3.8–3.7 (3 H, m, 4'-H and 5'-H₂) and 3.6 (1 H, m, 3'-H); m/z (FAB > 0, G) 268 (M + H)⁺ and 136 (BH₂)⁺.

9- α -L-Arabinopyranosylguanine **20** {0.42 g, 74%, after chromatography [eluent: linear gradient of methanol (0–100%) in water], and then crystallization from water}, m.p. > 260 °C; $[\alpha]_D^{20} + 36.7$ (c 1.0, Me₂SO); λ_{\max} (95% EtOH)/nm 270sh (ϵ 9200) and 253 (ϵ 13 100); λ_{\min} /nm 225 (ϵ 5400); δ_H 10.6 (1 H, br s, 1-H), 7.75 (1 H, s, 8-H), 6.47 (2 H, s, NH₂), 5.2 (1 H, br s, OH), 5.03 (1 H, d, $J_{1,2}$ 9.2, 1'-H), 5.0–4.8 (1 H, br s, OH), 4.7 (1 H, br s, OH), 4.02 (1 H, t well resolved after D₂O exchange, 2'-H), 3.8–3.7 (2 H, m, 4'- and 5'-H), 3.61 (1 H, d, $J_{5,5'}$ 12.2, 5'-H') and 3.49 (1 H, dd well resolved after D₂O exchange, $J_{2,3}$ 9.2, $J_{3,4}$ 3.1, 3'-H); m/z (FAB > 0, NBA) 284 (M + H)⁺.

1- α -L-Arabinopyranosylthymine **21** (0.46 g, 89%, after direct crystallization from ethanol) (Found: C, 46.3; H, 5.4; N, 10.7. Calc. for C₁₀H₁₄N₂O₆: C, 46.5; H, 5.5; N, 10.9%), m.p. 248–

249 °C (lit.,⁴⁹ 250–251 °C; lit.,⁵⁰ 248–250 °C; lit.,⁵¹ 246–248 °C); $[\alpha]_D^{20} + 89.0$ (c 1.0, Me₂SO) and +66.0 (c 1.0, water) {lit.,⁴⁹ $[\alpha]_D^{25} + 69$ (c 3, water); lit.,⁵¹ $[\alpha]_D^{20} + 66.1$ (c 1.34, water)}; $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 262 (ϵ 9700); λ_{\min}/nm 232 (ϵ 2400); δ_{H} 11.2 (1 H, br s, 3-H), 7.46 (1 H, d, *J* 0.8, 6-H), 5.22 (1 H, d, *J* 9.1, 1'-H), 5.17 (1 H, d, *J* 4.8, 2'-OH), 4.9 (1 H, br s, 3'-OH), 4.63 (1 H, d, *J* 5.0, 4'-OH), 3.8–3.7 (3 H, m, 2', 4'- and 5'-H), 3.61 (1 H, d, *J*_{5,5'} 12.3, 5'-H'), 3.5 (1 H, dd well resolved after D₂O exchange, *J* 3.2, 9.2, 3'-H) and 1.79 (3 H, d, *J* 0.8, Me); *m/z* (FAB > 0, NBA) 259 (M + H)⁺.

1- α -L-Arabinopyranosyluracil **22** (0.39 g, 80%, after direct crystallization from aq. ethanol) (Found: C, 43.4; H, 4.85; N, 11.05. Calc. for C₉H₁₂N₂O₆· $\frac{1}{2}$ H₂O: C, 43.5; H, 5.1; N, 11.3%), m.p. 254–255 °C (lit.,⁴⁷ 254–255 °C; lit.,⁵² 253–254 °C; lit.,¹³ 251–253 °C); $[\alpha]_D^{20} + 102.9$ (c 1.0, Me₂SO) and +84.1 (c 1.1, water) {lit.,⁴⁷ $[\alpha]_D^{25} + 86.4$ (c 1.0, water); lit.,¹³ +88 (c 0.5, water)}; $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 259 (ϵ 10 100); λ_{\min}/nm 226 (ϵ 1300); δ_{H} 11.2 (1 H, br s, 3-H), 7.58 (1 H, d, *J*_{5,6} 8.1, 6-H), 5.65 (1 H, d, 5-H), 5.2 [2 H, m, 1'-H and 2'-OH; δ 5.20 (1 H, d, *J*_{1,2} 9.3, 1'-H) after D₂O exchange], 4.9 (1 H, br s, 4'-OH), 4.66 (1 H, d, *J* 5.0, 3'-OH), 3.8–3.6 (4 H, m, 2', 4'- and 5'-H) and 3.5 [1 H, m (dd well resolved after D₂O exchange, *J* 2.8, 9.1), 3'-H]; *m/z* (FAB > 0, G–T) 337 (M + G + H)⁺, 245 (M + H)⁺ and 113 (BH₂)⁺; *m/z* (FAB < 0, G–T) 335 (M + G – H)⁻, 243 (M – H)⁻ and 111 (B)⁻.

1- α -L-Arabinopyranosylcytosine **23** (0.43 g, 88%, after direct crystallization from ethanol) (Found: C, 44.2; H, 5.4; N, 17.0. Calc. for C₉H₁₃N₃O₅: C, 44.4; H, 5.4; N, 17.3%), m.p. >260 °C (lit.,⁴⁷ 266–267 °C); $[\alpha]_D^{20} + 90.0$ (c 1.0, Me₂SO) {lit.,⁴⁷ $[\alpha]_D^{25} + 99.9$ (c 1, water)}; $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 270 (ϵ 9200) and 239 (7900); λ_{\min}/nm 255 (ϵ 7500) and 225 (7700); δ_{H} 7.50 (1 H, d, *J*_{5,6} 7.5, 6-H), 7.2–7.0 (2 H, br s, NH₂), 5.72 (1 H, d, 5-H), 5.35 (1 H, d, *J*_{1,2} 9.3, 1'-H), 4.99 (1 H, d, *J* 5.6, 2'- or 4'-OH), 4.83 (1 H, d, *J* 5.4, 3'-OH), 4.62 (1 H, d, *J* 4.9, 4'- or 2'-OH), 3.8–3.6 (3 H, m, 2', 4'- and 5'-H), 3.55 (1 H, d, *J*_{5,5'} 12.1, 5'-H') and 3.34 [1 H, m (dd well resolved after D₂O exchange, *J* 3.0, 9.2), 3'-H]; *m/z* (FAB > 0, G–T) 336 (M + G + H)⁺, 244 (M + H)⁺ and 112 (BH₂)⁺; *m/z* (FAB < 0, G–T) 426 (M + 2G – H)⁻, 334 (M + G – H)⁻, 242 (M – H)⁻ and 110 (B)⁻.

General Procedure for the Preparation of 9- and 1-[(1R)-2-Hydroxy-1-(2-hydroxyethoxy)ethyl]-purines and -pyrimidines 24–28.—A solution of sodium metaperiodate (0.45 g, 2.10 mmol) in water (5 cm³) was added to a solution of the foregoing appropriate α -L-arabinopyranosyl nucleoside (1.0 mmol) in a 1,4-dioxane–water mixture (9:1; 10 cm³). The reaction mixture was stirred for 1 h at room temperature. Work-up, and reduction with sodium borohydride (0.08 g, 2.1 mmol), were performed as described previously for the synthesis of compounds **14–18**. The known adenine **24** and uracil **27** derivatives as well as the three other title compounds (new) were purified by chromatography.

9-[(1R)-2-Hydroxy-1-(2-hydroxyethoxy)ethyl]adenine **24** {0.16 g, 68%, after purification by silanized silica gel column chromatography [eluent: linear gradient of methanol (0–100%) in water], and then lyophilization from water} was obtained as very hygroscopic material in accord with previously reported data¹⁴ (for racemic **24**: m.p. lit.,¹¹ 188–190 °C; lit.,¹² 150–151 °C); $[\alpha]_D^{20} + 35.7$ (c 1.0, water) {lit.,¹⁴ $[\alpha]_D^{25} + 34.5$ (c 3.05, water)}; $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 259 (ϵ 15 000); λ_{\min}/nm 225 (ϵ 3800); δ_{H} 8.25 and 8.15 (1 H each, 2 s, 2- and 8-H), 7.21 (2 H, s, NH₂), 5.69 (1 H, t, *J* 5.8, 1'-H), 5.15 and 4.59 (1 H each, 2 t, *J* 5.9, 5.8, 2'- and 5'-OH), 3.9 (2 H, m, 2'-H₂) and 3.5–3.2 (4 H, m, 4'- and 5'-H₂), in accord with literature data for racemic **24**;^{9,12} *m/z* (FAB > 0, G) 332 (M + G + H)⁺, 240 (M + H)⁺ and 136 (BH₂)⁺.

9-[(1R)-2-Hydroxy-1-(2-hydroxyethoxy)ethyl]guanine **25** {0.13 g, 58%, after purification by silanized silica gel column

chromatography [eluent: linear gradient of methanol (0–100%) in water], and then crystallization from water}, m.p. >260 °C (lit.,¹⁰ >300 °C for racemic **25**); $[\alpha]_D^{20} + 1.7$ (c 1.2, Me₂SO); $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 270sh (ϵ 9200) and 253 (13 200); λ_{\min}/nm 223 (ϵ 4200); δ_{H} 11.0 (1 H, br s, 1-H), 7.75 (1 H, s, 8-H), 6.60 (2 H, s, NH₂), 5.43 (1 H, t, *J* 5.8, 1'-H), 5.1 and 4.6 (1 H, each, 2 br s, 2'- and 5'-OH), 3.79 (2 H, d, 2'-H₂) and 3.5–3.2 (4 H, m, 4'- and 5'-H₂), in accord with literature data for racemic **25**;¹⁰ *m/z* (FAB > 0, G–T) 256 (M + H)⁺ and 152 (BH₂)⁺.

1-[(1R)-2-Hydroxy-1-(2-hydroxyethoxy)ethyl]thymine **26** {0.15 g, 67%, after purification by silica gel column chromatography [eluent: stepwise gradient of methanol (0–12%) in dichloromethane], and then lyophilization from water}, m.p. 171 °C (decomp.); $[\alpha]_D^{20} + 57.3$ (c 1.0, Me₂SO); $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 266 (ϵ 9700); λ_{\min}/nm 234 (ϵ 2800); δ_{H} 11.2 (1 H, br s, 3-H), 7.49 (1 H, d, *J* 1.0, 6-H), 5.58 (1 H, t, *J* 5.7, 1'-H), 5.0 and 4.6 (1 H each, 2 br s, 2'- and 5'-OH), 3.6–3.4 (6 H, m, 2', 4'- and 5'-H₂) and 1.77 (3 H, d, *J* 1.0, Me), in accord with literature data for racemic **26**;¹² *m/z* (FAB > 0, G–T) 323 (M + G + H)⁺, 231 (M + H)⁺ and 127 (BH₂)⁺.

1-[(1R)-2-Hydroxy-1-(2-hydroxyethoxy)ethyl]uracil **27**¹² {0.13 g, 61%, after purification by silanized silica gel column chromatography [eluent: linear gradient of methanol (0–100%) in water], and then lyophilization from water} (Found: C, 42.9; H, 5.45; N, 12.2. Calc. for C₈H₁₂N₂O₅· $\frac{1}{2}$ H₂O: C, 42.7; H, 5.8; N, 12.4%); m.p. 133–134 °C; $[\alpha]_D^{20} + 58.3$ (c 1.0, Me₂SO); $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 262 (ϵ 10 100); λ_{\min}/nm 230 (ϵ 1300); δ_{H} 11.2 (1 H, br s, 3-H), 7.56 (1 H, d, *J*_{5,6} 7.9, 6-H), 5.60 (1 H, d, 5-H), 5.58 (1 H, t, *J* 5.4, 1'-H), 5.1 and 4.7 (1 H each, 2 br s, 2'- and 5'-OH) and 3.6–3.4 (6 H, m, 2', 4'- and 5'-H₂), in accord with literature data for racemic **27**;¹² *m/z* (FAB > 0, G–T) 433 (2 M + H)⁺, 309 (M + G + H)⁺, 217 (M + H)⁺ and 113 (BH₂)⁺; *m/z* (FAB < 0, G–T) 431 (2 M – H)⁻, 307 (M + G – H)⁻, 215 (M – H)⁻ and 111 (B)⁻.

1-[(1R)-2-Hydroxy-1-(2-hydroxyethoxy)ethyl]cytosine **28** {0.14, 67%, after purification by silica gel column chromatography [eluent: stepwise gradient of methanol (0–25%) in dichloromethane], and then lyophilization from water} was obtained as hygroscopic material; $[\alpha]_D^{20} + 50.7$ (c 1.5, Me₂SO); $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 272 (ϵ 9100) and 238 (7800); λ_{\min}/nm 252 (ϵ 7300) and 230 (7700); δ_{H} 7.49 (1 H, d, *J*_{5,6} 7.4, 6-H), 7.2–7.0 (2 H, br s, NH₂), 5.71 (1 H, d, 5-H), 5.64 (1 H, t, *J* 5.1, 1'-H), 5.0–4.0 (2 H, br s, 2'- and 5'-OH) and 3.6–3.3 (6 H, m, 2', 4'- and 5'-H₂), in accord with literature data for racemic **28**;¹² *m/z* (FAB > 0, G–T) 216 (M + H)⁺ and 112 (BH₂)⁺; *m/z* (FAB < 0, G–T) 214 (M – H)⁻ and 110 (B)⁻.

9-(3,4-O-Isopropylidene- α -L-arabinopyranosyl)adenine **29**.—A solution of 9-(2-O-benzoyl-3,4-O-isopropylidene- α -L-arabinopyranosyl)adenine **3** (0.41 g, 1.0 mmol) in methanolic ammonia (previously saturated at –10 °C and tightly stoppered; 25 cm³) was stirred overnight at room temperature. The solution was evaporated to dryness under reduced pressure and the residue was co-evaporated under reduced pressure several times with methanol. Crystallization of the product from methanol afforded the *title compound* **29** (0.29 g, 95%), m.p. >260 °C (Found: C, 50.7; H, 5.7; N, 22.7. C₁₃H₁₇N₅O₄ requires C, 50.8; H, 5.6; N, 22.8%); $[\alpha]_D^{20} + 86.3$ (c 1.0, Me₂SO); $\lambda_{\max}(95\% \text{ EtOH})/\text{nm}$ 258 (ϵ 14 500); λ_{\min}/nm 226 (ϵ 2800); δ_{H} 8.32 and 8.14 (1 H each, 2 s, 2- and 8-H), 7.21 (2 H, s, NH₂), 5.6 (1 H, br s, 2'-OH), 5.35 (1 H, d, *J*_{1,2} 9.5, 1'-H), 4.3–4.1 (4 H, m, 2', 3', 4'- and 5'-H), 4.01 (1 H, dd, *J*_{4,5'} 2.6, *J*_{5,5'} 13.5, 5'-H') and 1.54 and 1.33 (3 H, each, 2 s, CMe₂); *m/z* (FAB > 0, G) 400 (M + G + H)⁺, 308 (M + H)⁺ and 136 (BH₂)⁺.

9-(3,4-O-Isopropylidene- α -L-arabinopyranosyl)-2-N-palmitoylguanine **30**.—To a stirred, ice-cooled solution of 9-(2-O-benzoyl-3,4-O-isopropylidene- α -L-arabinopyranosyl)-2-N-

palmitoylguanine **4** (0.67 g, 1.0 mmol) in a pyridine-ethanol mixture (7:3; 17 cm³) was added aq. 2 mol dm⁻³ sodium hydroxide (5 cm³). The reaction mixture was stirred at 0 °C for 2 h, neutralized with acetic acid (*d* 1.05; 0.57 cm³), and then diluted with dichloromethane (50 cm³). The organic layer was washed with water (3 × 20 cm³), dried over sodium sulfate, filtered, and evaporated to dryness. Crystallization of the product from methanol afforded the *title compound 30* (0.46 g, 81%), m.p. 186 °C (Found: C, 59.9; H, 8.4; N, 11.9. C₂₉H₄₇N₅O₆·H₂O requires C, 60.1; H, 8.5; N, 12.1%); [α]_D²⁰ +44.1 (*c* 0.9, Me₂SO); λ_{max}(95% EtOH)/nm 280 (ε 12 700), 259 (16 700) and 254 (16 800); λ_{min}/nm 271 (ε 12 000), 257 (16 600) and 229 (5700); δ_H 12.1 and 11.6 (1 H each, 2 br s, 1-H and 2-NH), 8.17 (1 H, s, 8-H), 5.65 (1 H, d, *J* 5.7, 2'-OH), 5.15 (1 H, d, *J*_{1',2'} 9.5, 1'-H), 4.29 (1 H, m, 4'-H), 4.22 (1 H, d, *J*_{5',5''} 13.6, 5'-H), 4.13 (1 H, m, 3'-H), 4.06 (1 H, m, 2'-H), 3.91 (1 H, dd, *J*_{4',5'} 2.5, 5'-H'), 2.44 (2 H, t, *J* 7.4, COCH₂), 1.6–1.5 [5 H, m, CMeMe and COCH₂CH₂ (δ 1.53, s, CMeMe)], 1.32 (3 H, s, CMeMe), 1.2 (24 H, m, [CH₂]₁₂) and 0.83 (3 H, t, *J* 6.6, CH₂Me); *m/z* (FAB > 0, NBA) 562 (M + H)⁺, 390 (BH₂)⁺ and 152 (BH₂ - CH₃[CH₂]₁₄CO + H)⁺.

9-[3,4-O-Isopropylidene-2-O-methoxy(thiocarbonyl)-α-L-arabinopyranosyl]adenine **31**.—To a solution of 9-(3,4-O-isopropylidene-α-L-arabinopyranosyl)adenine **29** (3.1 g, 10.1 mmol) in DMF (80 cm³) was added *N,N'*-thiocarbonyldiimidazole (2.67 g, 15.0 mmol), and the reaction mixture was heated and stirred at 80 °C for 3 h under argon. The solvent was removed under reduced pressure and the residue was dissolved in anhydrous methanol (80 cm³); the solution was heated and stirred at 60 °C for 2 h, then evaporated to dryness. Crystallization of the product from methanol afforded the *title compound 31* (2.2 g, 58%), m.p. 166–167 °C (Found: C, 47.2; H, 5.0; N, 18.2; S, 8.2. C₁₅H₁₉N₅O₅S requires C, 47.2; H, 5.0; N, 18.4; S, 8.4%); [α]_D²⁰ +84.6 (*c* 0.5, Me₂SO); λ_{max}(95% EtOH)/nm 259 (ε 15 500) and 238sh (9900); λ_{min}/nm 224 (ε 7300); δ_H 8.23 and 8.15 (1 H, each, 2 s, 2- and 8-H), 7.27 (2 H, s, NH₂), 6.00 (1 H, dd, *J* 7.3, 9.4, 2'-H), 5.85 (1 H, d, *J*_{1',2'} 9.4, 1'-H), 4.6 (1 H, m, 3'-H), 4.4–4.3 (2 H, m, 4'- and 5'-H), 4.18 (1 H, dd, *J*_{4',5'} 2.5, *J*_{5',5''} 13.7, 5'-H'), 3.78 (3 H, s, OMe) and 1.58 and 1.34 (3 H each, 2 s, CMe₂); *m/z* (FAB > 0, G) 474 (M + G + H)⁺, 382 (M + H)⁺, 247 (s)⁺ and 136 (BH₂)⁺.

9-(2-Deoxy-3,4-O-isopropylidene-α-L-erythro-pentopyranosyl)adenine **33**.—A solution of 9-[3,4-O-isopropylidene-2-O-methoxy(thiocarbonyl)-α-L-arabinopyranosyl]adenine **31** (2.0 g, 5.2 mmol), tributyltin hydride (15.2 cm³, 57.3 mmol) and AIBN (136 mg, 0.83 mmol) in toluene (270 cm³) was stirred at 80 °C for 2 h under argon. The solvent was evaporated off under reduced pressure and the residue was subjected to silica gel column chromatography, with a stepwise gradient of methanol (0–7%) in dichloromethane. Crystallization of the product in the appropriate fractions from methanol afforded the *title compound 33* (1.41 g, 92%), m.p. 200–201 °C (Found: C, 51.6; H, 6.15; N, 22.8. C₁₃H₁₇N₅O₃· $\frac{2}{3}$ H₂O requires C, 51.5; H, 6.1; N, 23.1%); [α]_D²⁰ +46.0 (*c* 1.0, Me₂SO); λ_{max}(95% EtOH)/nm 259 (ε 14 300); λ_{min}/nm 226 (ε 2100); δ_H 8.40 and 8.15 (1 H, each, 2 s, 2- and 8-H), 7.24 (2 H, s, NH₂), 5.71 (1 H, dd, *J* 2.9, 10.3, 1'-H), 4.5 (1 H, m, 3'-H), 4.1 (2 H, m, 4'- and 5'-H), 3.97 (1 H, dd, *J*_{4',5'} 3.2, *J*_{5',5''} 13.7, 5'-H'), 2.45 (1 H, m, 2'-H partially obscured by Me₂SO), 2.3 (1 H, m, 2'-H') and 1.52 and 1.31 (3 H each, 2 s, CMe₂); *m/z* (FAB > 0, G) 384 (M + G + H)⁺, 292 (M + H)⁺ and 136 (BH₂)⁺.

9-(2-Deoxy-3,4-O-isopropylidene-α-L-erythro-pentopyranosyl)-2-N-palmitoylguanine **34**.—To a solution of 9-(3,4-O-isopropylidene-α-L-arabinopyranosyl)-2-N-palmitoylguanine **30** (0.42 g, 0.75 mmol) in anhydrous acetonitrile (75 cm³) were

added *O*-phenyl chlorothiocarbonate (0.15 cm³, 1.08 mmol) and DMAP (0.28 g, 2.29 mmol). The solution was stirred overnight at room temperature, and then the solvent was removed under reduced pressure. Ethyl acetate (50 cm³) and water (50 cm³) were added. The organic phase was separated and washed successively with ice-cold 10% aq. acetic acid saturated with sodium chloride, water, saturated aq. sodium hydrogen carbonate, and water (50 cm³ each) before being dried over sodium sulfate, filtered and evaporated to dryness. The residue was dissolved in dry toluene, the solution was evaporated under reduced pressure, and this process was repeated three times to give crude thiocarbonate **32** which was directly dissolved in dry toluene (7.5 cm³) and treated with tributyltin hydride (0.5 cm³, 1.89 mmol) and AIBN (37 mg, 0.23 mmol) at 80 °C for 2 h under argon. The solvent was evaporated off under reduced pressure and the residue was subjected to silica gel column chromatography, with a stepwise gradient of methanol (0–2%) in dichloromethane. Crystallization of the product in the appropriate fractions from methanol afforded the *title compound 34* (0.25 g, 61%), m.p. 149–150 °C (Found: C, 63.8; H, 8.4; N, 12.8. C₂₉H₄₇N₅O₅ requires C, 63.8; H, 8.7; N, 12.8%); [α]_D²⁰ +22.7 (*c* 1.0 in Me₂SO); λ_{max}(95% EtOH)/nm 278 (ε 12 900), 259 (16 300) and 254sh (16 100); λ_{min}/nm 270 (ε 12 600) and 225 (3000); δ_H 12.0 and 11.7 (1 H each, 2 br s, 1-H and 2-NH), 8.26 (1 H, s, 8-H), 5.54 (1 H, dd, *J* 5.2, 7.7, 1'-H), 4.49 (1 H, m, 3'-H), 4.1 (2 H, m, 4'- and 5'-H), 3.86 (1 H, dd, *J*_{4',5'} 2.9, *J*_{5',5''} 13.3, 5'-H'), 2.44 (2 H, t, *J* 7.4, COCH₂), 2.3 (2 H, m, 2'-H₂), 1.6 (2 H, m, COCH₂CH₂), 1.50 and 1.31 (3 H each, 2 s, CMe₂), 1.2 (24 H, m, [CH₂]₁₂) and 0.84 (3 H, t, *J* 6.7, CH₂Me); *m/z* (FAB > 0, NBA) 568 (M + Na)⁺, 546 (M + H)⁺ and 390 (BH₂)⁺.

9-(2-Deoxy-α-L-erythro-pentopyranosyl)adenine **35** and 9-(2-(Deoxy-α-L-erythro-pentopyranosyl)-2-N-palmitoylguanine **36**.—The foregoing appropriate isopropylidene derivatives **33** (0.29 g, 1.0 mmol) and **34** (0.54 g, 1.0 mmol) were de-isopropylidened following the general procedure used for the preparation of compounds **9**–**13**. Direct crystallization afforded the *title compounds 35* and **36**.

Compound 35 (0.23 g, 92% after crystallization from aq. ethanol (Found: C, 45.4; H, 5.3; N, 26.1. C₁₀H₁₃N₅O₃· $\frac{2}{3}$ H₂O requires C, 45.6; H, 5.5; N, 26.6%), m.p. 248 °C (for the *D*-enantiomer: lit.,⁵³ 232–235 °C; lit.,⁵⁴ 231–232 °C; lit.,⁵⁵ 266 °C; lit.,³⁷ 235 °C); [α]_D²⁰ +13.6 (*c* 1.0, water) {for the *D*-enantiomer: lit.⁵³ [α]_D²⁵ +6.0 (*c* 1.0, water); lit.,⁵⁴ -11.4 (*c* 0.7, water); lit.,⁵⁵ [α]_D²⁵ -17; lit.,³⁷ [α]_D²¹ +5.66 (*c* 1.1, water)}; λ_{max}(95% EtOH)/nm 259 (ε 14 800); λ_{min}/nm 226 (ε 2500); δ_H 8.30 and 8.14 (1 H each, 2 s, 2- and 8-H), 7.22 (2 H, s, NH₂), 5.64 (1 H, dd, *J* 2.0, 11.1, 1'-H), 4.88 (1 H, d, *J* 5.1, OH), 4.62 (1 H, d, *J* 4.3, OH), 3.8 (2 H, m, 3'- and 4'-H), 3.7 (2 H, m, 5'-H₂), 2.5 (1 H, m, 2'-H partially obscured by Me₂SO) and 1.9 (1 H, m, 2'-H'), in close agreement with literature data for the *D*-enantiomer;³⁷ *m/z* (FAB > 0, G) 252 (M + H)⁺ and 136 (BH₂)⁺.

Compound 36 (0.44 g, 87% after crystallization from methanol) (Found: C, 60.7; H, 8.9; N, 13.7. C₂₆H₄₃N₅O₅· $\frac{1}{2}$ H₂O requires C, 60.7; H, 8.6; N, 13.6%), m.p. >250 °C; [α]_D²⁰ +43.6 (*c* 1.0, Me₂SO); λ_{max}(95% EtOH)/nm 277sh (ε 12 700), 259 (16 100) and 254sh (16 000); λ_{min}/nm 228 (ε 3700); δ_H 12.0 (2 H, br s, 1-H and 2-NH), 8.15 (1 H, s, 8-H), 5.45 (1 H, m, 1'-H), 4.9 (1 H, br s, OH), 4.7 (1 H, br s, OH), 3.8 (2 H, m, 3'- and 4'-H), 3.6 (2 H, m, 5'-H₂), 2.4 (3 H, m, 2'-H and COCH₂ partially obscured by Me₂SO), 1.9 (1 H, m, 2'-H'), 1.6 (2 H, m, COCH₂CH₂), 1.2 (24 H, m, [CH₂]₁₂) and 0.84 (3 H, t, *J* 6.5, CH₂Me); *m/z* (FAB > 0, G–T) 506 (M + H)⁺, 390 (BH₂)⁺ and 152 (BH₂ - CH₃[CH₂]₁₄CO + H)⁺.

9-(2-Deoxy-α-L-erythro-pentopyranosyl)guanine **37**.—A suspension of 9-(2-deoxy-α-L-erythro-pentopyranosyl)-2-N-palmi-

toylguanine **36** (0.10 g, 0.20 mmol) in methanolic ammonia (previously saturated at -10°C and tightly stoppered; 5 cm^3) was stirred overnight at room temperature, and then evaporated to dryness. The residue was purified by HPLC (eluent: 0.5% acetonitrile in water; flow rate $6.75\text{ cm}^3/\text{min}$) to afford the title compound **37** (0.036 g, 67%), which was first lyophilized and then crystallized from water; m.p. 186°C (decomp.); $[\alpha]_{\text{D}}^{20} + 25.4$ (c 0.6, Me_2SO); $\lambda_{\text{max}}(95\% \text{ EtOH})/\text{nm}$ 267sh (ϵ 11 000) and 254 (13 100); δ_{H} 10.6 (1 H, br s, 1-H), 7.83 (1 H, s, 8-H), 6.47 (2 H, s, NH_2), 5.35 (1 H, dd, J 2.0, 11.1, 1'-H), 4.9 (1 H, br s, OH), 4.6 (1 H, br s, OH), 3.8 (2 H, m, 3'- and 4'-H), 3.6 (2 H, m, 5'- H_2), 2.3 (1 H, m, 2'-H) and 1.9 (1 H, m, 2'-H'); m/z (FAB > 0 , NBA) 268 ($\text{M} + \text{H}$)⁺.

9-[(1R)-3-Hydroxy-1-(2-hydroxyethoxy)propyl]adenine **38**.—This compound was synthesized from 9-(2-deoxy- α -L-erythro-pentopyranosyl)adenine **35** (0.25 g, 1.0 mmol) following the general procedure used for the preparation of compounds **24–28**. After the usual work-up, the residue was subjected to silanized silica gel column chromatography, with a linear gradient of methanol (0–100%) in water. Lyophilization of the product in the appropriate fractions from water afforded the title compound **38** (0.12 g, 47%) (Found: C, 45.8; H, 5.9; N, 27.3. Calc. for $\text{C}_{10}\text{H}_{15}\text{N}_5\text{O}_3 \cdot \frac{1}{2}\text{H}_2\text{O}$: C, 45.8; H, 6.15; N, 26.7%) as a hygroscopic compound [lit.,³⁷ m.p. 138°C (from water)]; $[\alpha]_{\text{D}}^{20} + 17.0$ (c 1.0, Me_2SO) {lit.,⁵³ $[\alpha]_{\text{D}}^{26} + 10.2$; lit.,³⁷ $[\alpha]_{\text{D}}^{20} + 10.14$ (c 0.7, water)}; $\lambda_{\text{max}}(95\% \text{ EtOH})/\text{nm}$ 259 (ϵ 14 200); $\lambda_{\text{min}}/\text{nm}$ 226 (ϵ 5200); δ_{H} 8.29 and 8.14 (1 H each, 2 s, 2- and 8-H), 7.21 (2 H, s, NH_2), 5.86 (1 H, dd, J 6.2, 7.1, 1'-H), 4.6 (2 H, m, 2 \times OH), 3.6–3.2 (6 H, m, 3 \times CH_2 partially obscured by water), 2.4 (1 H, m, 2'-H), 2.2 (1 H, m, 2'-H'), more or less in accord with literature data for the (*R*) enantiomer^{36,37} and for racemic **38**,^{9,34} m/z (FAB > 0 , G) 346 ($\text{M} + \text{G} + \text{H}$)⁺, 254 ($\text{M} + \text{H}$)⁺ and 136 (BH_2)⁺.

9-[(1R)-3-Hydroxy-1-(2-hydroxyethoxy)propyl]guanine **39**.—This compound was synthesized from 9-(2-deoxy- α -L-erythro-pentopyranosyl)-2-*N*-palmitoylguanine **36** (0.51 g, 1.0 mmol) following the general procedure used for the preparation of compounds **14–18**. After the usual work-up, the residue was subjected to silanized silica gel column chromatography, with a linear gradient of methanol (0–100%) in water. Crystallization of the product in the appropriate fractions from water afforded the title compound **39** (0.11 g, 41%), m.p. $> 260^{\circ}\text{C}$ (for racemic **39**: lit.,³⁴ 305°C ; lit.,³⁵ $> 300^{\circ}\text{C}$); $[\alpha]_{\text{D}}^{20} + 8.3$ (c 0.5, Me_2SO); $\lambda_{\text{max}}(95\% \text{ EtOH})/\text{nm}$ 268sh (ϵ 11 100) and 253 (13 200); δ_{H} 10.6 (1 H, br s, 1-H), 7.80 (1 H, s, 8-H), 6.45 (2 H, s, NH_2), 5.62 (1 H, t, J 6.7, 1'-H), 4.5 (2 H, br s, 2 \times OH), 3.5–3.2 (6 H, m, 3 \times CH_2 partially obscured by water), 2.3 (1 H, m, 2'-H), 2.0 (1 H, m, 2'-H'), in accord with literature data for the (*R*) enantiomer³⁶ and for racemic **39**,³⁴ m/z (FAB > 0 , G–T) 270 ($\text{M} + \text{H}$)⁺ and 152 (BH_2)⁺; m/z (FAB < 0 , G–T) 268 ($\text{M} - \text{H}$)⁻ and 150 (B)⁻.

Biological Methods.—The broad antiviral assays on cell culture and the anti-HIV assays were performed by following previously established procedures as described in refs. 22 and 23.

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