Analogues of the Antiviral Acyclonucleoside 9-(4-Hydroxy-3-hydroxymethylbutyl)guanine. Part 4.[1] Substitution on the 2-Amino Group

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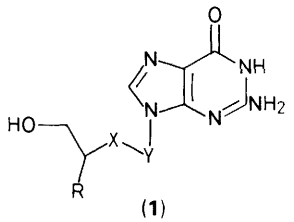
Syntheses of 2-*N*-substituted derivatives of antiviral acyclonucleosides are described. Analogues of 9-(4-hydroxy-3-hydroxymethylbutyl)guanine (**1b**) with alkyl (**6**), aryl (**7**) and (**8**), amino (**9**), methoxy (**10**), and hydroxy (**11**) substituents on the 2-amino group were prepared by reaction of the appropriate amine with the 2-chloropurine (**5**). The 2-*N*-hydroxy derivatives (**23a, b**) of the 9-alkoxyguanines (**1c, d**) were synthesized by cyclisation of imidazole intermediates (**20a, b**) to the 2-thiopurines (**21a, b**) followed by oxidation and hydroxylamine displacement at the 2-position. The 2-*N*-hydroxyguanines (**11**) and (**23a**) showed potent antiherpes virus activity in cell culture tests.

Since the discovery of the potent and selective antiherpes virus activity of acyclovir (**1a**)[2,3] several groups of workers have investigated the synthesis and properties of analogues of acyclovir in which the heterocyclic base has been modified. The guanine moiety has been replaced with other purines,[4] pyrimidines,[5–7] and imidazoles,[8] aza and deaza variants[9–11] have been prepared, and substituents at C-8 have been investigated.[12] All of these modifications to the structure of (**1a**) have resulted in substantial loss of antiviral potency, the most active analogues being at least 10-fold less active than the guanine derivative.



(**1**)

	X	Y	R
a;	O	CH_2	H
b;	CH_2	CH_2	CH_2OH
c;	CH_2	O	H
d;	CH_2	O	CH_2OH

As part of our studies on the related antiviral acyclonucleoside 9-(4-hydroxy-3-hydroxymethylbutyl)guanine (BRL 39123) (**1b**)[1, 13–17] we have already described its hypoxanthine and xanthine analogues (which lack the 2-amino group) as well as a series of compounds modified at the 6-position of the base.[14] None of these compounds had high antiviral activity in cell culture but some of them proved to be efficient pro-drugs of (**1b**) in animals.[18] Although it appeared that the 2-amino function of (**1b**) was necessary for antiviral activity, we considered that it might be possible to monosubstitute on this amino group with retention of activity. We reasoned that substitution on an exocyclic position should have minimal effect on the electronic parameters of the purine ring system and that replacing just one hydrogen of the amino group would still allow Watson–Crick hydrogen bonding to complementary cytosine residues. Support for this approach was provided by the observation that 2-*N*-aryl derivatives of guanine nucleosides and nucleotides, including the 2-*N*-(4-butylphenyl) derivative of acyclovir, inhibit DNA polymerase α,[19–21] although the latter compound does not inhibit herpesvirus replication.[21]

In this paper we describe the synthesis and antiviral activity of a structurally diverse series of 2-*N*-substituted derivatives of (**1b**) and the extension of the most interesting modification to analogues of the more recently reported antiviral 9-alkoxyguanines (**1c**) and (**1d**).[22,23]

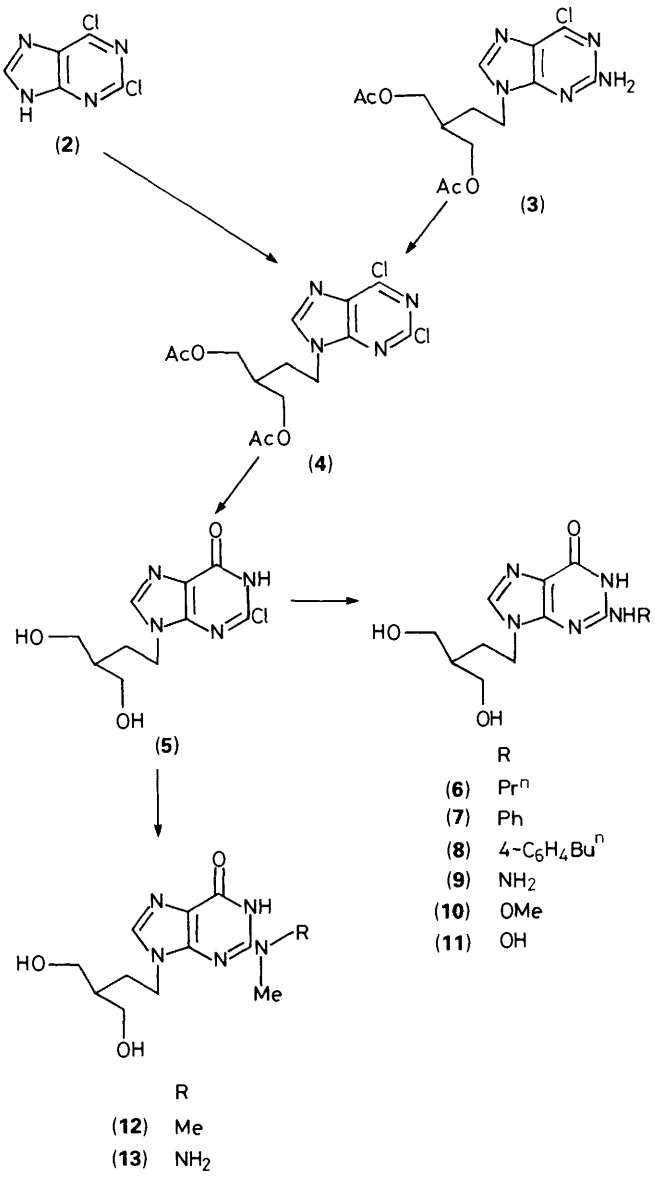
Results and Discussion

The 9-alkyl-2,6-dichloropurine (**4**) (Scheme 1) was prepared in two ways. Alkylation of 2,6-dichloropurine (**2**) with 2-acetoxymethyl-4-iodobutyl acetate afforded the 9-isomer (**4**) in 39% yield along with substantial quantities of the 7-isomer (13% yield). Alternatively, the 2-amino-6-chloropurine[24] (**3**) was chlorinated by the free-radical method using amyl nitrite† in carbon tetrachloride[25] which afforded compound (**4**) in 40% yield. Alkaline hydrolysis of (**4**) with refluxing aqueous sodium hydroxide resulted in removal of the acetate protecting groups and hydrolysis of the 6-chlorine to give compound (**5**) in 60% yield. Compound (**5**) was treated with a variety of amines in aqueous diglyme (1,2-dimethoxyethane) or in 2-methoxyethanol at 100—120 °C. Reaction with the arylamines, with propylamine, and with the hydroxylamines required 10—20 h, but reaction with hydrazine was complete in less than 2 h. The isolated yields of the 2-*N*-substituted guanines (**6**)—(**9**) were between 40 and 55% but the methoxyamine (**10**) and hydroxyamine (**11**) were obtained in lower yields (33 and 17% respectively). When compound (**5**) was treated with 1,1-dimethylhydrazine, none of the 2,2-dimethylhydrazine product was obtained. The major isolated products were the 2-dimethylamine compound (**12**) and the 2-(1-methylhydrazine) compound (**13**). It would appear that attack by the tertiary nitrogen of 1,1-dimethylhydrazine occurs, followed by *in situ* cleavage of either the N–N bond or an N–CH_3 bond of the quaternary species.

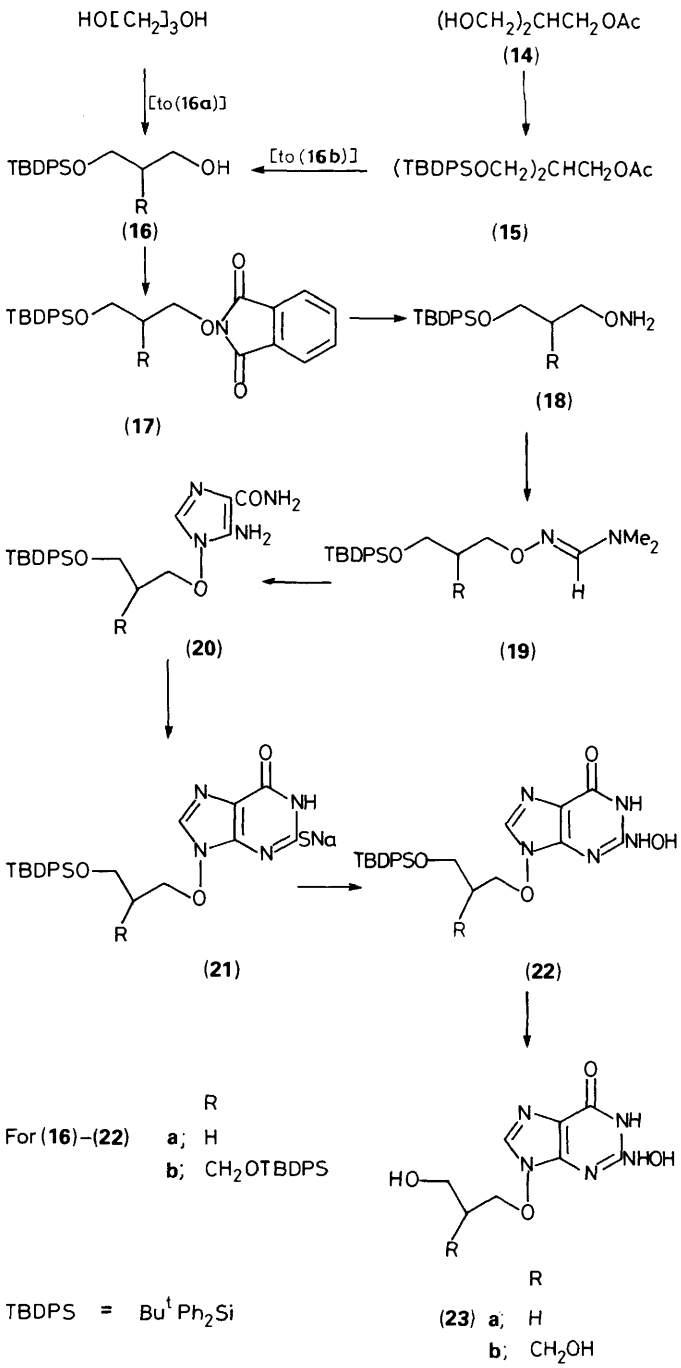
The synthesis of the 2-*N*-hydroxy-substituted derivatives of (**1c**) and (**1d**) required construction of the purine system with a potential leaving group at the 2-position. We elected for the method of Yamazaki *et al.*[26] in which an imidazole precursor is cyclised with sodium methylxanthate to give a 2-thiopurine which can be oxidised and displaced with amine nucleophiles.

Treatment of the acetate-protected triol (**14**)[27] (Scheme 2) with t-butylchlorodiphenylsilane and imidazole in *N*,*N*-dimethylformamide (DMF) followed by deacetylation with catalytic potassium carbonate in methanol afforded the alcohol (**16b**). The alcohol (**16a**) was obtained in 75% yield by reaction of the sodium salt of propane-1,3-diol with t-butylchloro-

† Commercial amyl nitrite is essentially pure 3-methylbutyl nitrite.



Scheme 1.



Scheme 2.

diphenylsilane using the method described for t-butyldimethylsilyl monoethers.[28] The alcohols (**16a** and **b**) were converted into the alkoxyphthalimides (**17a** and **b**) in 78% yield by diethyl azodicarboxylate(DEAD)–triphenylphosphine-mediated coupling with *N*-hydroxyphthalimide and cleavage with methylhydrazine in methylene dichloride afforded the alkoxyamines (**18a** and **b**) in 80% yield. Reaction of the alkoxyamines with DMF dimethyl acetal gave the formamidines (**19a** and **b**). Transamidination with α-amino-α-cyanoacetamide in methanolic hydrogen chloride followed by boron trifluoride-catalysed cyclisation[22] afforded the imidazoles (**20a** and **b**) in 28% and 8% yields, respectively. It seems likely that the much lower yield of compound (**20b**) is due to steric factors as the **b** series also gave significantly lower yields than the **a** series in all subsequent steps.

The imidazoles were cyclised to purines using sodium methyl xanthate in DMF[26] and the products were most conveniently isolated as their sodium salts (**21a**) in 57% yield and (**21b**) in 35% yield. The purine thiolates were oxidised with 3-chloroperbenzoic acid in DMF and the intermediate sulphonates were treated directly with hydroxylamine in 2-methoxyethanol to give the hydroxyamino compounds (**22a** and **b**) in 69 and 29% yield, respectively. Deprotection was achieved by treatment of the compounds with 67% trifluoroacetic acid (TFA) at room temperature for 30—45 min and this afforded the 2-*N*-hydroxyguanines (**23a** and **b**) in yields of 75 and 63%, respectively.

The 2-*N*-hydroxy substitution in products (**11**), (**23a**), and (**23b**) did not appear to have a large effect on the electronic parameters of the guanine ring. Thus the $\lambda_{max.}$ shifted by *ca.* 4 nm to longer wavelength in the ultraviolet spectrum. In the proton n.m.r. spectrum the 8-H resonance had a slight downfield shift (0.05—0.1 p.p.m.) and, as expected, there was a substantial downfield shift (*ca.* 3 p.p.m.) of the 2-NH resonance. These three compounds were noticeably more water soluble

than the corresponding guanines but under alkaline conditions compound (**23a**) was appreciably unstable.

Biological Data.—The acyclonucleosides prepared in this study were tested at concentrations up to 100 μg ml^{-1} in cell culture systems (MRC-5 cells or Vero cells) for activity against viruses of the herpes family and the 50% inhibitory concentrations (IC_{505}) were determined. Compounds (**6**), (**8**), and (**10**) had no significant antiviral activity against herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) in either cell line. Slight activity was seen for the 2-*N*-phenyl (**7**) and 2-*N*-amino (**9**) compounds against HSV-1 in MRC-5 cells (IC_{50} 50 μg ml^{-1} and 67 μg ml^{-1}, respectively). In contrast, the 2-*N*-hydroxy derivative (**11**) not only had moderate activity against HSV-1 and HSV-2 in MRC-5 cells ($IC_{50} \approx 20$ μg ml^{-1}) but showed activity similar to that of (**1b**) against both viruses in Vero cells ($IC_{50} \approx 1$ μg ml^{-1}).

The potent activity of compound (**11**) encouraged us to synthesize and evaluate the 2-*N*-hydroxy analogues of the more recently discovered 9-alkoxyguanine acyclonucleosides.[22,23] Compound (**23a**) was a potent antiviral, being active against HSV-1 and HSV-2 in both cell lines at 0.2—2 μg ml^{-1}. Compound (**23b**) was tested against both viruses in MRC-5 cells, but showed only weak activity (IC_{50} 30—40 μg ml^{-1}). The activity of the three 2-*N*-hydroxy compounds (**11**), (**23a**), and (**23b**) against varicella zoster virus broadly reflected their HSV activity (IC_{50} 5, 17, and 86 μg ml^{-1}, respectively), but neither (**11**) nor (**23a**) was active against cytomegalovirus. None of the compounds showed toxicity to the cell monolayers used in these tests.

The high degree of activity of compounds (**11**) and (**23a**) relative to the parent guanines is quite exceptional for base-modified guanine acyclonucleosides. Because of the markedly different effects on antiviral activity obtained by introducing the 2-*N*-hydroxy substituent into (**1b**), (**1c**), and (**1d**), we think it likely that the activity is attributable to the 2-*N*-hydroxy compound *per se*. However, it remains a possibility that the 2-*N*–OH bond is subject to reductive cleavage in the test systems, in which case the observed activities would be due to formation of the parent guanine acyclonucleosides.

Experimental

M.p.s were determined using a Reichert Kofler apparatus and are uncorrected. ^{1}H N.m.r. spectra were recorded with a Jeol GX-270 MHz spectrometer. I.r. spectra were recorded with a Perkin-Elmer 580 spectrometer and u.v. spectra with a Cary 219 or a Unikon 810 spectrometer. Mass spectra were recorded on a VG 70-70 instrument and accurate masses were measured on a VG ZAB spectrometer. Microanalyses were performed on a Carlo Erba model 1106 analyser. Column chromatography was carried out on Merck 7736 silica gel. All compounds were homogeneous by t.l.c. on silica gel $60F_{254}$-coated aluminium sheets.

9-(4-*Acetoxy*-3-*acetoxymethylbutyl*)-2,6-*dichloropurine* (**4**).—*Method A.* A mixture of the purine (**3**) (14.24 g, 40 mmol) and isopentyl nitrite (32.2 ml, 240 mmol) in carbon tetrachloride (1.4 l) was heated under reflux for 2 h. The solution was evaporated and the residue purified by column chromatography on silica gel with chloroform, followed by chloroform–methanol (50:1) as eluant. The product was crystallised from ether to afford the *dichloropurine* (**4**) (6.0 g, 40%), m.p. 92—94 °C; $\lambda_{max.}$(EtOH) 214 (ε 22 500) and 275 nm (9 300); $\nu_{max.}$(KBr) 1 740, 1 725, 1 590, and 1 555 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.95 (3 H, m, 2′-H_2 and 3′-H), 2.00 (6 H, s, 2 × Me), 3.97 (4 H, d, *J* 3.8 Hz, 2 × CH_2O), 4.35 (2 H, t, *J* 7.0 Hz, 1′-H_2), and 8.77 (1 H, s, 8-H) (Found: C, 44.5; H, 4.3; N, 14.8. $C_{14}H_{16}Cl_2N_4O_4$ requires C, 44.82; H, 4.30; N, 14.93%).

Method B. 2-Acetoxymethyl-4-iodobutyl acetate (4.71 g, 15 mmol) was added to a solution of 2,6-dichloropurine (2.83 g, 15 mmol) and potassium carbonate (2.07 g, 15 mmol) in DMF (45 ml) and the solution was stirred at room temperature for 20 h. The solution was evaporated, the residue was partitioned between chloroform (60 ml) and water (60 ml), and the organic layer was dried ($MgSO_4$) and evaporated. The residue was purified by column chromatography on silica gel with chloroform–methanol (100:1; 50:1) as eluant to afford the 9-substituted dichloropurine (**4**) (2.2 g, 39%). Further elution of the column yielded the 7-isomer (0.75 g, 13%).

2-*Chloro*-9-(4-*hydroxy*-3-*hydroxymethylbutyl*)*hypoxanthine* (**5**).—A suspension of the purine (**4**) (2.44 g, 6.5 mmol) in aqueous sodium hydroxide (2.5M; 11 ml) was heated under reflux for 40 min. The solution was allowed to cool, filtered, and neutralised with 5M-hydrochloric acid. The solution was evaporated and the residue was extracted with chloroform–methanol (1:1; 15 ml). Column chromatography on silica gel eluting with chloroform–methanol mixtures (1:1; 2:3) afforded the 2-*chloropurine* (**5**) which was recrystallised from ethanol (1.06 g, 60%); $\lambda_{max.}$(H_2O) 255 nm (11 400); $\nu_{max.}$(KBr) 3 400, 2 920, 1 720, 1 695, 1 595, and 1 570 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.43 (1 H, m, 3′-H), 1.73 (2 H, q, *J* 7.2 Hz, 2′-H_2), 3.38 (4 H, AB of ABX, $J_{AX} = J_{BX} = 5.6$ Hz, J_{AB} 10.7 Hz, 2 × CH_2O), 4.09 (2 H, t, *J* 7.3 Hz, 1′-H_2), 4.47 (2 H, br, D_2O-exchangeable, 2 × OH), and 7.89 (1 H, s, 8-H) (Found: C, 42.0; H, 4.7; N, 19.2%; M^+, 272.0675. $C_{10}H_{13}ClN_4O_3 \cdot 0.7H_2O$ requires C, 42.10; H, 5.09; N, 19.64%; *M*, 272.0677).

9-(4-*Hydroxy*-3-*hydroxymethylbutyl*)-2-N-*propylguanine* (**6**).—A solution of the purine (**5**) (0.14 g, 0.5 mmol) and propylamine (0.50 ml, 6.0 mmol) in 2-methoxyethanol (2 ml) was stirred at 110 °C for 16 h. The solution was evaporated and the residue was recrystallised from aqueous ethanol to afford the 2-N-*propylguanine* (**6**) (80 mg, 54%), m.p. 268—273 °C; $\lambda_{max.}$(H_2O) 253 (13 900) and 277sh nm (8 300); $\nu_{max.}$(KBr) 3 240, 2 960, 2 930, 2 870, 1 705, 1 680, 1 610, 1 575, 1 520, and 1 465 cm^{-1}; δ_H [$(CD_3)_2SO$] 0.91 (3 H, t, *J* 7.4 Hz, Me), 1.42 (1H, m, 3′-H), 1.58 (2 H, sextet, *J* 7.3 Hz, CH_2Me), 1.73 (2 H, q, *J* 7.0 Hz, 2′-H_2), 3.24 (2 H, q, *J* 6.5 Hz, NHCH_2), 3.40 (4 H, m, 2 × CH_2O), 4.02 (2 H, t, *J* 7.1 Hz, 1′-H_2), 4.36 (2 H, t, *J* 5.2 Hz, D_2O-exchangeable, 2 × OH), 6.32 (1 H, t, *J* 5.5 Hz, D_2O-exchangeable, 2-NH), 7.67 (1 H, s, 8-H), and 10.34 (1 H, s, D_2O-exchangeable, 1-H) (Found: C, 51.8; H, 7.1; N, 22.7%; M^+, 295.1652. $C_{13}H_{21}N_5O_3 \cdot 0.45H_2O$ requires C, 51.46; H, 7.27; N, 23.08%; *M*, 295.1644).

9-(4-*Hydroxy*-3-*hydroxymethylbutyl*)-2-N-*phenylguanine* (**7**).—A solution of the purine (**5**) (0.14 g, 0.5 mmol) and aniline (0.23 ml, 2.5 mmol) in diglyme (2 ml) and water (0.35 ml) was stirred at 120 °C for 18 h. The solution was allowed to cool and the solid was filtered off to afford the 2-N-*phenylguanine* (**7**) (83 mg, 50%), m.p. >300 °C (from ethanol–water); $\lambda_{max.}$(MeOH) 275 nm (21 300); $\nu_{max.}$(KBr) 3 300, 1 715, 1 690, 1 615, 1 590, and 1 570 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.49 (1 H, m, 3′-H), 1.80 (2 H, q, *J* 7.1 Hz, 2′-H_2), 3.42 (4 H, AB of ABX, $J_{AX} = J_{BX} = 5.7$ Hz, J_{AB} 10.3 Hz, 2 × CH_2O), 4.11 (2 H, t, *J* 7.3 Hz, 1′-H_2), 4.46 (2 H, br s, D_2O-exchangeable, 2 × OH), 7.0–7.7 (5-H, m, Ph), 7.84 (1 H, s, 8-H), 8.83 (1 H, s, D_2O-exchangeable, 2-NH), and 10.50 (1 H, s, D_2O-exchangeable, 1-H) (Found: C, 56.45; H, 5.8; N, 20.6%; M^+, 329.1493. $C_{16}H_{19}N_5O_3 \cdot 0.6H_2O$ requires C, 56.49; H, 5.99; N, 20.59%; *M*, 329.1488).

2-N-(4-*Butylphenyl*)-9-(4-*hydroxy*-3-*hydroxymethylbutyl*)-*guanine* (**8**).—A solution of the purine (**5**) (0.41 g, 1.5 mmol) and 4-butylaniline (0.95 ml, 6 mmol) in a mixture of diglyme (6 ml) and water (1 ml) was stirred at 120 °C for 16 h. The solution was

allowed to cool, filtered and the solid obtained was washed with ether to afford the 2-N-(*4-butylphenyl*)*guanine* (**8**) (230 mg, 40%), m.p. >260 °C (decomp.) (from methanol); $\lambda_{max.}$ 279 nm (23 000); $\nu_{max.}$(KBr) 3 400—3 100, 2 930, 1 690, 1 620, 1 595, 1 460, 1 430, and 1 415 cm^{-1}; δ_H [$(CD_3)_2SO$] 0.90 (3 H, t, *J* 7.3 Hz, Me), 1.31 (2 H, sextet, *J* 7.4 Hz, CH_2Me), 1.54 (3 H, m, 3′-H and CH_2CH_2Me), 1.82 (2 H, q, *J* 7.1 Hz, 2′-H_2), 2.55 (2 H, t, *J* 7.4 Hz, $CH_2CH_2CH_2$Me), 3.43 (4 H, AB of ABX, $J_{AX} = J_{BX}$ = 5.8 Hz, J_{AB} 10.6 Hz, 2 × CH_2O), 4.12 (2 H, t, *J* 7.2 Hz, 1′-H_2), 4.46 (2 H, br t, D_2O-exchangeable, 2 × OH), 7.16 (2 H, d, *J* 8.5 Hz, ArH), 7.58 (2 H, d, *J* 8.3 Hz, ArH), 7.81 (1 H, s, 8-H), 8.91 (1 H, s, D_2O-exchangeable, 2-NH), and 10.54 (1 H, s, D_2O-exchangeable, 1-H) (Found: C, 62.2; H, 7.2; N, 18.3. $C_{20}H_{27}N_5O_3$ requires C, 62.32; H, 7.06; N, 18.17%).

2-N-*Amino*-9-(*4-hydroxy*-3-*hydroxymethylbutyl*)*guanine Hydrochloride* (**9**).—A solution of the purine (**5**) (0.14 g, 0.5 mmol) and hydrazine hydrate (0.12 ml, 2.5 mmol) in 2-methoxyethanol (2 ml) was stirred at 110 °C for 110 min. The solution was evaporated and the residue was recrystallised from ethanol–water to afford the 2-N-*aminoguanine hydrochloride* (**9**) (78 mg, 51%), m.p. 234—237 °C; $\lambda_{max.}$ 253 (14 300) and 275sh nm (10 000); $\nu_{max.}$(KBr) 3 310, 3 110, 2 920, 1 685, 1 600, 1 570, 1 525, and 1 465 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.44 (1 H, m, 3′-H), 1.72 (2 H, q, *J* 7.1 Hz, 2′-H_2), 3.39 (4 H, AB of ABX, J_{AX} 5.5, J_{BX} 5.8, and J_{AB} 10.6 Hz, 2 × CH_2O), 4.01 (2 H, t, *J* 7.3 Hz, 1′-H_2), 4.41 (2 H, br, D_2O-exchangeable, 2 × OH), 5.0 (2 H, v br, D_2O-exchangeable, NH_2), 7.71 (1 H, s, 8-H), and 8.31 (1 H, br, D_2O-exchangeable, NH) (Found: C, 40.1; H, 5.6; N, 27.7%; M^+, 268.1276. $C_{10}H_{16}N_6O_3$·HCl requires C, 39.41; H, 5.62; N, 27.58%; *M*, 268.1284).

9-(*4-Hydroxy*-3-*hydroxymethylbutyl*)-2-N-*methoxyguanine* (**10**).—A solution of the purine (**5**) (0.14 g, 0.5 mmol), *O*-methylhydroxylamine hydrochloride (0.167 g, 2.0 mmol), and triethylamine (0.28 ml, 2.0 mmol) in 2-methoxyethanol (2 ml) was stirred at 110 °C for 11 h. The solution was evaporated and the residue was purified by preparative h.p.l.c. on a reverse-phase C_{18} μ-Bondapak column with 13% methanol in water as eluant to afford the 2-N-*methoxyguanine* (**10**) (47 mg, 33%), m.p. 169—173 °C (decomp.); $\lambda_{max.}$(H_2O) 256 nm (13 700); $\nu_{max.}$(KBr) 3 390, 3 160, 2 940, 1 735, 1 685, 1 600, and 1 570 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.44 (1 H, m, 3′-H), 1.73 (2 H, q, *J* 7.1 Hz, 2′-H_2), 3.38 (4 H, AB of ABX, J_{AX} 5.5, J_{BX} 5.8, and J_{AB} 10.7 Hz, 2 × CH_2O), 3.64 (3 H, s, Me), 4.04 (2 H, t, *J* 7.4 Hz, 1′-H_2), 4.30 (2 H, br, D_2O-exchangeable, 2 × OH), 7.86 (1 H, s, 8-H), 10.23 (1 H, s, D_2O-exchangeable, 1-H), and 11.16 (1 H, s, D_2O-exchangeable, 2-NH); *m/z* (f.a.b. +ve ion; thioglycerol) 284 (MH^+) (Found: C, 44.7; H, 5.9; N, 23.5. $C_{11}H_{17}N_5O_4$·0.7 H_2O requires C, 44.65; H, 6.27; N, 23.67%).

2-N-*Hydroxy*-9-(*4-hydroxy*-3-*hydroxymethylbutyl*)*guanine* (**11**).—A mixture of the purine (**5**) (0.14 g, 0.5 mmol), hydroxylamine hydrochloride (0.14 g, 2.0 mmol), and triethylamine (0.35 ml, 2.5 mmol) in 2-methoxyethanol (2 ml) was stirred at 100 °C for 16 h. The solution was evaporated and the residue was purified by preparative h.p.l.c. on a reverse-phase C_{18} μ-Bondapak column with 3% methanol in ammonium acetate buffer (50 mM; pH 4.5) as eluant to afford crude product, which was rechromatographed under similar conditions with 2% methanol in NH_4OAc buffer as eluant to afford the pure 2-N-*hydroxyguanine* (**11**) (23 mg, 17%), m.p. 187—189 °C (decomp.); $\lambda_{max.}$(H_2O) 257 nm (14 200); $\nu_{max.}$(KBr) 3 380, 3 200, 2 930, 2 890, 1 670, 1 585, and 1 470 cm^{-1}; δ_H [$(CD)_3SO$] 1.44 (1 H, m, 3′-H), 1.72 (2 H, q, *J* 7.1 Hz, 2′-H_2), 3.38 (4 H, m, 2 × CH_2O), 4.02 (2 H, t, *J* 7.4 Hz, 1′-H_2), 4.39 (2 H, t, *J* 5.2 Hz, D_2O-exchangeable, 2 × CH_2OH), 7.75 (1 H, s, 8-H), 9.16 (1 H, br, D_2O-exchangeable, NHOH), 9.66 (1 H, br, D_2O-exchangeable, NHOH), and 10.50 (1 H, br, D_2O-exchangeable, 1-H); *m/z* (f.a.b. +ve ion; thioglycerol) 270 (MH^+) (Found: C, 43.8; H, 5.8; N, 25.4. $C_{10}H_{15}N_5O_4$·0.3H_2O requires C, 43.73; H, 5.73; N, 25.50%).

Reaction of compound (**5**) *with* 1,1-*Dimethylhydrazine*.—A solution of the purine (**5**) (0.14 g, 0.5 mmol), 1,1-dimethylhydrazine (0.15 ml, 2.0 mmol), and triethylamine (0.14 ml, 1.0 mmol) in 2-methoxyethanol (2 ml) was stirred at 80—85 °C for 3 h. The solution was evaporated and the residue was purified by preparative h.p.l.c. on a reverse-phase C_{18} μ-Bondapak column with 4—25% methanol in ammonium acetate butter (50 mM; pH 4.5) as eluant. The first product to elute was 2-N-*amino*-9-(*4-hydroxy*-3-*hydroxymethylbutyl*)-2-N-*methylguanine* (**13**) (17 mg, 12%); $\lambda_{max.}$(H_2O) 256 (13 600) and 278sh nm (7 900); $\nu_{max.}$(KBr) 3 440, 3 300, 3 260, 1 690, 1 650, 1 580, and 1 540 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.42 (1 H, m, 3′-H), 1.73 (2 H, q, *J* 7.1 Hz, 2′-H_2), 3.23 (3 H, s, Me), 3.40 (4 H, AB of ABX, J_{AX} 5.4, J_{BX} 5.9, and J_{AB} 10.6 Hz, 2 × CH_2O), 4.03 (2 H, t, *J* 7.3 Hz, 1′-H_2), 5.5 (10 H, v br, D_2O-exchangeable, H_2O, 2 × OH, NH_2, and 1-H), and 7.71 (1 H, s, 8-H) (Found: M^+, 282.1441. $C_{11}H_{18}N_6O_3$ requires *M*, 282.1440).

The second product to elute was 9-(*4-hydroxy*-3-*hydroxymethylbutyl*)-2-N-2-N-*dimethylguanine* (**12**) (16 mg, 11%); $\lambda_{max.}$(H_2O) 256 (15 500) and 280sh nm (8 700); $\nu_{max.}$(KBr) 3 390, 3 180, 3 120, 2 930, 1 670, 1 600, and 1 575 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.41 (1 H, m, 3′-H), 1.74 (2 H, q, *J* 7.1 Hz, 2′-H_2), 3.06 (6 H, s, 2 × Me), 3.40 (4 H, m, 2 × CH_2O), 4.03 (2 H, t, *J* 7.1 Hz, 1′-H_2) 4.36 (2 H, br t, D_2O-exchangeable, 2 × OH), 7.69 (1 H, s, 8-H), and 10.58 (1 H, br, D_2O-exchangeable, 1-H) (Found: M^+, 281.1494. $C_{12}H_{19}N_5O_3$ requires *M*, 281.1488).

3-(*t-Butyldiphenylsiloxy*)-2-(*t-butyldiphenylsiloxymethyl*)-*propyl Acetate* (**15**).—Imidazole (8.85 g, 130 mmol) was added to a solution of the diol (**14**) (5.45 g, 40 mmol) and t-butylchlorodiphenylsilane (22.1 ml, 85 mmol) in DMF (50 ml) and the mixture was stirred at room temperature for 1 h. Water (50 ml) was added and the solution was extracted with hexane (80 ml). The organic layer was washed successively with 1M-hydrochloric acid (60 ml) and aqueous sodium hydrogen carbonate (60 ml), dried ($MgSO_4$), and the solution was evaporated. The residue was purified by column chromatography on silica gel with hexane–acetone (40:1) as eluant to afford *compound* (**15**) as a viscous liquid (18.16 g, 73%); $\nu_{max.}$(film) 2 960, 2 930, 2 860, 1 740, 1 470, and 1 425 cm^{-1}; δ_H ($CDCl_3$) 1.02 (18 H, s, 2 × CMe_3), 1.92 (3 H, s, COMe), 2.14 (1 H, m, CH), 3.75 (4 H, m, 2 × CH_2OSi), 4.18 (2 H, d, *J*, 6.3 Hz, CH_2OOC), and 7.3—7.65 (20 H, m, 4 × Ph) (Found: C, 73.4; H, 8.0. $C_{38}H_{48}O_4Si_2$ requires C, 73.03; H, 7.74%).

3-(*t-Butyldiphenylsiloxy*)*propan*-1-*ol* (**16a**).—Propane-1,3-diol (4.3 ml, 60 mmol) was added to a suspension of sodium hydride (60% dispersion in oil, hexane-washed; 2.4 g, 60 mmol) in tetrahydrofuran (THF) (120 ml) and the mixture was stirred at room temperature for 1 h. t-Butylchlorodiphenylsilane (15.6 ml, 60 mmol) was added and the mixture was stirred for a further 45 min. The mixture was partitioned between ether (400 ml) and aqueous potassium carbonate (10%; 250 ml). The organic layer was washed with brine (200 ml), dried ($MgSO_4$), and the solution was evaporated. The residue was purified by column chromatography on silica gel with ethyl acetate–hexane (1:4) as eluant to afford the alcohol (**16a**) as a white solid (45.15 g, 75%), m.p. 35—40 °C; $\nu_{max.}$(film) 3 270, 3 070, 2 960, 2 930, 2 880, 2 860, 1 470, and 1 425 cm^{-1}; δ_H [$(CD_3)_2SO$] 0.99 (9 H, s, CMe_3), 1.69 (2 H, quintet, *J* 6.3 Hz, CCH_2C), 3.52 (2 H, q, *J* 5.9 Hz, CH_2OH), 3.72 (2 H, t, *J* 6.5 Hz, CH_2OSi), 4.40 (1 H, t, *J* 5.1 Hz, D_2O-exchangeable, OH), and 7.40—7.65 (10 H, m, 2 × Ph); *m/z* (c.i., NH_3) 315 (100, MH^+).

3-(*t-Butyldiphenylsiloxy*)-2-(*t-butyldiphenylsiloxymethyl*)-*propan-1-ol* (**16b**).—Potassium carbonate (0.55 g, 4 mmol) was added to a solution of the acetate (**15**) (17.5 g, 28 mmol) in methanol (80 ml), and the solution was stirred at room temperature for 3 h. Acetic acid was added to neutralise the solution, which was then evaporated. The residue was partitioned between chloroform (80 ml) and aqueous sodium hydrogen carbonate (80 ml); the organic layer was dried ($MgSO_4$) and then evaporated. The residue was purified by column chromatography on silica gel with hexane–acetone (12:1) as eluant to afford the *alcohol* (**16b**) as an oil (10.94 g, 67%); $\nu_{max.}$(film) 3 450, 2 960, 2 930, 2 860, 1 470, and 1 425 cm^{-1}; δ_H ($CDCl_3$) 1.01 (18 H, s, 2 × CMe_3), 2.05 (1 H, m, CH), 2.59 (1 H, br, D_2O-exchangeable, OH), 3.69 (6 H, m, 3 × CH_2O), and 7.3—7.65 (20 H, m, 4 × Ph) (Found: C, 74.0; H, 8.1. $C_{36}H_{46}O_3Si_2$ requires C, 74.18; H, 7.95%).

N-(3-*t-Butyldiphenylsiloxypropoxy*)*phthalimide* (**17a**).—DEAD (10.4 ml, 66 mmol) was added to an ice-cooled solution of the alcohol (**16a**) (13.8 g, 44 mmol), triphenylphosphine (17.3 g, 66 mmol), and *N*-hydroxyphthalimide (10.8 g, 66 mmol) in THF (130 ml) and the solution was then stirred at room temperature for 3 h. The solution was evaporated, the residue was extracted twice with ether–hexane (1:1), and the combined solutions were evaporated. The residue was purified by column chromatography on silica gel with hexane–acetone (5:1) as eluant to afford the *alkoxyphthalimide* (**17a**) as a white solid (35.22 g, 78%), m.p. 74—76 °C; $\nu_{max.}$(KBr) 2 960, 2 930, 2 880, 2 860, 1 775, and 1 740 cm^{-1}; δ_H ($CDCl_3$) 1.05 (9 H, s, CMe_3), 2.03 (2 H, quintet, *J* 6.2 Hz, CCH_2C), 3.88 (2 H, t, *J* 6.1 Hz, CH_2OSi), 4.40 (2 H, t, *J* 6.6 Hz, CH_2ON), and 7.35—7.85 (14 H, m, ArH) (Found: C, 70.3; H, 6.3; N, 3.0. $C_{27}H_{29}NO_4Si$ requires C, 70.56; H, 6.36; N, 3.05%).

N-[3-(*t-Butyldiphenylsiloxy*)-2-(*t-butyldiphenylsiloxymethyl*)-*propoxy*]*phthalimide* (**17b**).—The *alkoxyphthalimide* (**17b**), prepared in a similar way to (**17a**) but from the alcohol (**16b**), was obtained as a gum (10.11 g, 77%); $\nu_{max.}$(KBr) 2 950, 2 930, 2 880, 2 850, 1 690, 1 635, 1 470, and 1 425 cm^{-1}; δ_H ($CDCl_3$) 1.01 (18 H, s, 2 × CMe_3), 2.30 (1 H, m, CH), 3.90 (4 H, m, 2 × CH_2OSi), 4.36 (2 H, d, *J* 6.3 Hz, CH_2ON), and 7.3—7.85 (24 H, m, ArH) (Found: C, 72.2; H, 6.9; N, 2.0. $C_{44}H_{49}NO_5Si_2$ requires C, 72.59; H, 6.78; N, 1.92%).

3-(*t-Butyldiphenylsiloxy*)*propoxyamine* (**18a**).—Methylhydrazine (2.39 ml, 45 mmol) was added to a solution of the alkoxyphthalimide (**17a**) (16.09 g, 35 mmol) in methylene dichloride (140 ml) and the mixture was stirred at room temperature for 45 min. The mixture was filtered and the filtrate was washed with aqueous sodium carbonate (3%; 100 ml). The organic layer was dried ($MgSO_4$) and the solution was evaporated. The residue was purified by column chromatography on silica gel with hexane–ethyl acetate (3:1) as eluant to afford the *alkoxyamine* (**18a**) as an oil (9.65 g, 81%); $\nu_{max.}$(film) 3 320, 2 960, 2 930, 2 860, 1 470, and 1 425 cm^{-1}; δ_H ($CDCl_3$) 1.05 (9 H, s, CMe_3), 1.83 (2 H, quintet, *J* 6.3 Hz, CCH_2C), 3.74 (2 H, t, *J* 6.3 Hz, CH_2O), 3.79 (2 H, t, *J* 6.3 Hz, CH_2O), 5.3 (2 H, br D_2O-exchangeable, NH_2), and 7.35—7.7 (10 H, m, 2 × Ph); *m/z* (c.i., isobutane) 330 (100, MH^+).

3-(*t-Butyldiphenylsiloxy*)-2-(*t-butyldiphenylsiloxymethyl*)-*propoxyamine* (**18b**).—The *alkoxyamine* (**18b**), prepared in a similar way to (**18a**) but from the alkoxyphthalimide (**17b**), was obtained as an oil (6.11 g, 79%); $\nu_{max.}$(KBr) 2 960, 2 930, 2 890, 2 860, 1 470, and 1 425 cm^{-1}; δ_H [$(CD_3)_2SO$] 0.95 (18 H, s, 2 × CMe_3), 2.14 (1 H, m, CH), 3.61 (2 H, d, *J* 6.3 Hz, CH_2ON), 3.75 (4 H, d, *J* 5.8 Hz, 2 × CH_2OSi), 5.87 (2 H, s, D_2O-exchangeable, NH_2), and 7.35—7.6 (20 H, m, 4 × Ph); *m/z* (c.i., NH_3) 598 (100, MH^+) (Found: C, 71.3; H, 8.3; N, 2.2. $C_{36}H_{47}NO_3Si_2 \cdot 0.5H_2O$ requires C, 71.24; H, 7.97; N, 2.31%).

N^2-[3-(*t-Butyldiphenylsiloxy*)*propoxy*]-N^1,N^1-*dimethylformamidine* (**19a**).—The alkoxyamine (**18a**) (9.39 g, 28.5 mmol) was dissolved in DMF dimethylacetal (40 ml) and the solution was stirred at room temperature for 30 min. The solution was evaporated, the residue was dissolved in methylene dichloride (80 ml), the solution was washed with water (2 × 80 ml), dried ($MgSO_4$), and evaporated to afford the *formamidine* (**19a**) as an oil (10.71 g, 98%); $\nu_{max.}$(film) 2 960, 2 930, 2 860, and 1 630 cm^{-1}; δ_H ($CDCl_3$) 1.04 (9 H, s, CMe_3), 1.89 (2 H, quintet, *J* 6.3 Hz, CCH_2C), 2.75 (6 H, s, NMe_2), 3.76 (2 H, t, *J* 6.3 Hz, CH_2OSi), 3.99 (2 H, t, *J* 6.3 Hz, CH_2ON), and 7.35—7.7 (11 H, m, 2 × Ph and HC=N) (Found: C, 68.9; H, 8.4; N, 7.4. $C_{22}H_{32}N_2O_2Si$ requires C, 68.71, H, 8.39; N, 7.28%).

N^2-[3-(*t-Butyldiphenylsiloxy*)-2-(*t-butyldiphenylsiloxymethyl*)-*propoxy*]-N^1,N^1-*dimethylformamidine* (**19b**).—The *formamidine* (**19b**), prepared in a similar way to (**19a**) but from the alkoxyamine (**18b**), was obtained as a viscous liquid (5.73 g, 88%); $\nu_{max.}$(KBr) 2 960, 2 930, 2 890, 2 850, 1 630, 1 470, and 1 425 cm^{-1}; δ_H ($CDCl_3$) 1.02 (18 H, s, 2 × CMe_3), 2.43 (1 H, m, CH), 2.72 (6 H, s, NMe_2), 3.84 (4 H, m, 2 × CH_2OSi), 3.96 (2 H, d, *J* 6.3 Hz, CH_2ON), and 7.3—7.7 (21 H, m, 4 × Ph and HC=N) (Found: C, 71.5; H, 8.2; N, 4.3. $C_{39}H_{52}N_2O_3Si_2$ requires C, 71.73; H, 8.03; N, 4.29%).

5-*Amino*-1-[3-(*t-butyldiphenylsiloxy*)*propoxy*-1H-*imidazole*-4-*carboxamide* (**20a**).—2-Amino-2-cyanoacetamide (2.5 g, 25 mmol) was dissolved in 2% methanolic hydrogen chloride (75 ml) and the solution was evaporated. The residue was taken up in methanol (20 ml) and to this solution was added the formamidine (**19a**) (9.62 g, 25 mmol). The solution was stirred for 20 h and the solution was evaporated. The residue was dissolved in ethyl acetate (125 ml), and the solution was washed with water (5 ml), dried ($MgSO_4$), and the solvent was removed. The residue was taken up in 1,2-dimethoxyethane (250 ml) and to this solution was added boron trifluoride–diethyl ether (3 ml, 25 mmol). The solution was stirred at 80 °C for 45 min and evaporated. The residue was taken up in chloroform (200 ml) and washed with aqueous sodium hydrogen carbonate (200 ml). The aqueous solution was diluted with water (100 ml) and extracted with chloroform. The combined organic layers were washed with brine (100 ml), dried ($MgSO_4$), and the solvent was removed. The residue was purified by column chromatography on silica gel with chloroform–methanol (60:1) as eluant to afford the *imidazole* (**20a**) as a white solid (3.1 g, 28%), m.p. 120—124 °C; $\lambda_{max.}$(EtOH) 264 nm (14 000); $\nu_{max.}$(KBr) 3 420, 3 340, 2 950, 2 930, 1 660, 1 620, 1 600, 1 550, 1 460, and 1 425 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.00 (9 H, s, CMe_3), 1.97 (2 H, quintet, *J* 6.5 Hz, CCH_2C), 3.81 (2 H, t, *J* 6.2 Hz, CH_2OSi), 4.28 (2 H, t, *J* 6.6 Hz, CH_2ON), 5.85 (2 H, s, D_2O-exchangeable, NH_2), 6.75 (2 H, br, D_2O-exchangeable, NH_2), 7.33 (1 H, s, 2-H), and 7.42—7.64 (10 H, m, 2 × Ph) (Found: C, 62.9; H, 7.0; N, 12.8. $C_{23}H_{30}N_4O_3Si$ requires C, 62.98; H, 6.89; N, 12.77%).

5-*Amino*-1-[3-(*t-butyldiphenylsiloxy*)-2-(*t-butyldiphenylsiloxymethyl*)*propoxy*]-1H-*imidazole*-4-*carboxamide* (**20b**).—2-Amino-2-cyanoacetamide (0.86 g, 8.6 mmol) was dissolved in 1.4% methanolic hydrogen chloride (20 ml) and the solution was evaporated. The residue was taken up in a mixture of methanol (6 ml) and DMF (6 ml) and to this solution was added the formamidine (**19b**) (5.62 g, 8.6 mmol). The solution was stirred for 64 h and was then evaporated. The residue was dissolved in ethyl acetate (45 ml), and the solution washed with water (4 ml), dried ($MgSO_4$), and evaporated. The residue was taken up in 1,2-dimethoxyethane and to this solution was added boron trifluoride–diethylether (1.05 ml, 8.6 mmol). The solu-

tion was stirred at 80 °C for 80 min and evaporated. The residue was taken up in chloroform (70 ml), and the solution was washed with aqueous sodium hydrogen carbonate (100 ml), dried ($MgSO_4$), and evaporated. The residue was purified by column chromatography on silica gel with chloroform–methanol (100:1) as eluant to afford the *imidazole* (**20b**) (0.50 g, 8%); δ_H [$(CD_3)_2SO$] 0.96 (18 H, s, 2 × CMe_3), 2.34 (1 H, m, CH), 3.86 (4 H, d, *J* 4.7 Hz, 2 × CH_2OSi), 4.26 (2 H, d, *J* 6.3 Hz, CH_2ON), 5.82 (2 H, s, D_2O-exchangeable, NH_2), 6.74 (2 H, br, D_2O-exchangeable, NH_2), 7.16 (1 H, s, 2-H) and 7.35—7.60 (20 H, m, 4 × Ph) (Found: M^+, 706.3386. $C_{40}H_{50}N_4O_4Si_2$ requires *M*, 706.3371).

9-[3-(*t-Butyldiphenylsiloxy*)*propoxy*]-2-*mercaptohypoxanthine Sodium Salt* (**21a**).—A solution of the imidazole (**20a**) (3.05 g, 7 mmol) in DMF (30 ml) was added to a solution of carbon disulphide (2.53 ml, 42 mmol) and sodium methoxide (2.27 g, 42 mmol) in DMF (40 ml). The mixture was heated under reflux for 75 min and the solution was evaporated. The residue was triturated with water, filtered off, and washed with aqueous methanol. The solid was suspended in warm methanol, the mixture was cooled, and the solid was filtered off to afford the 2-*mercaptopurine sodium salt* (**21a**) as a white solid (2.01 g, 57%), m.p. 200 °C (decomp.); $\lambda_{max.}$(MeOH) 293 nm (18 100); $\nu_{max.}$(KBr) 3 400, 2 960, 2 930, 2 860, 1 660, 1 560, 1 515, and 1 470 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.00 (9 H, s, CMe_3), 1.94 (2 H, quintet, *J* 6.5 Hz, CCH_2C), 3.82 (2 H, t, *J* 6.2 Hz, CH_2OSi), 4.39 (2 H, t, *J* 6.5 Hz, CH_2ON), 7.45—7.65 (10 H, m, 2 × Ph), 7.68 (1 H, s, 8-H), and 10.06 (1 H, s, D_2O-exchangeable, 1-H) (Found: C, 55.1; H, 5.5; N, 10.5. $C_{24}H_{27}N_4NaO_3SSi{\cdot}H_2O$ requires C, 55.37; H, 5.61; N, 10.76%).

9-[3-(*t-Butyldiphenylsiloxy*)-2-(*t-butyldiphenylsiloxymethyl*)*propoxy*]-2-*mercaptohypoxanthine Sodium Salt* (**21b**).—A solution of the imidazole (**20b**) (0.48 g, 0.68 mmol) in DMF (3 ml) was added to a solution of carbon disulphide (0.24 ml, 4 mmol) and sodium methoxide (0.22 g, 4 mmol) in DMF (4 ml). The mixture was heated under reflux for 105 min and the solution was evaporated. The residue was partitioned between chloroform (10 ml) and water (10 ml). The organic layer was applied to a silica gel plug and this was eluted with chloroform–methanol (15:1). The product was crystallised from aqueous methanol to afford the 2-*mercaptopurine sodium salt* (**21b**) (185 mg, 35%), m.p. 120—140 °C; $\lambda_{max.}$(MeOH) 295 nm (17 200); $\nu_{max.}$(KBr) 3 400, 2 960, 2 930, 2 860, 1 665, 1 565, 1 475, and 1 440 cm^{-1}; δ_H [$(CD_3)_2SO$] 0.95 (18 H, s, 2 × CMe_3), 2.30 (1 H, m, CH), 3.86 (4 H, m, 2 × CH_2OSi), 4.36 (2 H, d, *J* 6.1 Hz, CH_2ON), and 7.35—7.60 (21 H, m, 4 × Ph and 8-H) (Found: C, 63.8; H, 6.2; N, 7.25. $C_{41}H_{47}N_4NaO_4SSi_2$ requires C, 63.87; H 6.14; N, 7.27%).

9-[3-(*t-Butyldiphenylsiloxy*)*propoxy*]-2-N-*hydroxyguanine* (**22a**).—3-Chloroperbenzoic acid (85%; 2.42 g) was added to an ice-cooled solution of the 2-mercaptopurine sodium salt (**21a**) (1.66 g, 3.3 mmol) in DMF (8 ml), and the solution was stirred for 5 min at this temperature followed by 1 h at room temperature. The solution was cooled again and neutralised by addition of 2M-hydroxylamine in 2-methoxyethanol (7 ml). The solution was evaporated and the residue was taken up in 2M-hydroxylamine in 2-methoxyethanol (8 ml) and stirred at 100 °C for 30 min. The solution was allowed to cool, diluted with ethyl acetate (20 ml), washed with water (2 × 10 ml), and the organic layer was filtered to give the 2-N-*hydroxyguanine* (**22a**) as a white solid (1.09 g, 69%), m.p. 225—229 °C; $\lambda_{max.}$(MeOH) 260 nm (15 400) nm; $\nu_{max.}$(KBr) 3 120, 2 960, 2 930, 2 890, 2 860, 1 680, and 1 585 cm^{-1}; δ_H [$(CD_3)_2SO$] 0.98 (9 H, s, CMe_3), 1.93 (2 H, quintet, *J* 6.3 Hz, CCH_2C), 3.80 (2 H, t, *J* 6.0 Hz, CH_2OSi), 4.40 (2 H, t, *J* 6.5 Hz, CH_2ON), 7.40—7.62 (10 H, m, 2 × Ph), 7.92 (1 H, s, 8-H), and 10.00 (2 H, v br, NHOH) (Found: C, 59.9; H, 6.1; N, 14.4. $C_{24}H_{29}N_5O_4Si$ requires C, 60.10; H, 6.09; N, 14.60%).

9-[3-(*t-Butyldiphenylsiloxy*)-2-(*t-butyldiphenylsiloxymethyl*)*propoxy*]-2-N-*hydroxyguanine* (**22b**).—3-Chloroperbenzoic acid (85%; 0.15 g) was added to a solution of the 2-mercaptopurine sodium salt (**21b**) (0.16 g, 0.21 mmol) in DMF (0.6 ml) and the solution was stirred for 1 h. The solution was neutralised by addition of 2M-hydroxylamine in 2-methoxyethanol (0.45 ml) and the solution was evaporated. The residue was taken up in 2M-hydroxylamine in 2-methoxyethanol (0.5 ml) and was stirred at 100 °C for 40 min. The solution was partitioned between water (4 ml) and ethyl acetate (4 ml) and the organic layer was washed with aqueous sodium hydrogen carbonate (4 ml), dried ($MgSO_4$), and evaporated. The residue was purified by column chromatography on silica gel with chloroform–methanol (100:1; 30:1) as eluant to give the 2-N-*hydroxyguanine* (**22b**) (45 mg, 29%), m.p. 183—188 °C; $\lambda_{max.}$(MeOH) 260 nm (14 900); $\nu_{max.}$(KBr) 3 390, 3 080, 2 970, 2 940, 2 870, 1 690, 1 585, 1 475, and 1 430 cm^{-1}; δ_H [$(CD_3)_2SO$] 0.93 (18 H, s, 6 × Me), 2.24 (1 H, m, CH), 3.83 (4 H, AB of ABX, $J_{AX} = J_{BX}$ = 5.8, and J_{AB} 10.2 Hz, 2 × CH_2OSi), 4.38 (2 H, d, *J* 6.1 Hz, CH_2ON), 7.35—7.60 (20 H, m, 4 × Ph), 7.72 (1 H, s, 8-H), 9.28 (1 H, br, D_2O-exchangeable, NHOH), 9.84 (1 H, br, D_2O-exchangeable, NHOH), and 10.78 (1 H, br, D_2O-exchangeable, 1-H) (Found: C, 66.1; H, 6.7; N, 9.4. $C_{41}H_{49}N_5O_5Si_2$ requires C, 65.83; H, 6.60; N, 9.36%).

2-N-*Hydroxy*-9-(3-*hydroxypropoxy*)*guanine* (**23a**).—The protected 2-N-hydroxyguanine (**22a**) (1.05 g, 2.2 mmol) was dissolved in a mixture of water and TFA (1:2; 6 ml) and the solution was stirred for 30 min. The solution was diluted with water (2 ml), washed with hexane (2 × 4 ml), the aqueous layer was evaporated, and the residue was azeotroped with ethanol (2 × 5 ml). The residue was taken up in water and neutralised with aqueous sodium hydrogen carbonate. Recrystallisation afforded the 2-N-*hydroxyguanine* (**23a**) (270 mg), and passage of the mother liquors down a C_{18} reverse-phase silica gel column with 1% acetic acid in water as eluant gave further product (125 mg; total 75%), m.p. 235—238 °C; $\lambda_{max.}$(H_2O) 258 nm (13 600); $\nu_{max.}$(KBr) 3 400, 3 180, 3 120, 2 960, 1 690, 1 650, and 1 580 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.81 (2 H, quintet, *J* 6.5 Hz, CCH_2C), 3.56 (2 H, t, *J* 5.8 Hz, CH_2OH), 4.33 (2 H, t, *J* 6.6 Hz, CH_2ON), 4.60 (1 H, br D_2O-exchangeable, OH), 8.00 (1 H, s, 8-H), 9.35 (1 H, br, D_2O-exchangeable, NHOH), 9.90 (1 H, br, D_2O-exchangeable, NHOH), and 10.73 (1 H, br, D_2O-exchangeable, 1-H) (Found: C, 39.7; H, 4.6; N, 28.9. $C_8H_{11}N_5O_4$ requires C, 39.84; H, 4.60; N, 29.03%).

2-N-*Hydroxy*-9-(3-*hydroxy*-2-*hydroxymethylpropoxy*)*guanine* (**23b**).—The protected 2-N-hydroxyguanine (**22b**) (40 mg, 53 μmol) was dissolved in a mixture of water and TFA (1:2; 1 ml) and the solution was stirred for 45 min. The solution was diluted with water (1 ml), washed with hexane (2 × 2 ml), the aqueous layer was evaporated, and the residue was azeotroped with ethanol (2 × 3 ml). The residue was taken up in water and brought to pH 5 with aqueous sodium hydrogen carbonate. The solution was purified by reverse-phase h.p.l.c. on a C_{18} μ-Bondapak column with 2% methanol in ammonium acetate buffer (50 mM; pH 4.5) as eluant and the product was lyophilised to give the 2-N-*hydroxyguanine* (**23b**) (9 mg, 63%); $\lambda_{max.}$ (H_2O) 257 nm (13 000); $\nu_{max.}$(KBr) 3 180, 2 930, 1 690, 1 615, and 1 590 cm^{-1}; δ_H [$(CD_3)_2SO$] 1.92 (1 H, m, CH), 3.51 (4 H, m, 2 × CH_2OH), 4.26 (2 H, d, *J* 6.6 Hz, CH_2ON), 4.55 (2 H, br, D_2O-exchangeable, 2 × OH), 7.98 (1 H, s, 8-H), and 9.45 (3 H, v br, D_2O-exchangeable, NHOH and 1-H) (Found: C, 37.6; H, 4.6; N, 23.1. $C_9H_{13}N_5O_5{\cdot}0.5H_2CO_3$ requires C, 37.75; H, 4.67; N, 23.17%).

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