Carbohydrate Research, 181 (1988) 77–88
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

EPIMERIZATION DURING THE ACETOLYSIS OF 3-*O*-ACETYL-5-*O*-BENZOYL-1,2-*O*-ISOPROPYLIDENE-3-*C*-METHYL-α-D-RIBOFURANOSE. SYNTHESIS OF 3′-*C*-METHYLNUCLEOSIDES WITH THE β-D-*ribo*- AND α-D-*arabino* CONFIGURATIONS

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(Received October 9th, 1987; accepted for publication, January 26th, 1988)

ABSTRACT

Acetolysis of 3-*O*-acetyl-5-*O*-benzoyl-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-ribofuranose with a high concentration of acetic acid yielded 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-D-arabinofuranose, which was used for the preparation of 3-*C*-methyl-α-D-arabinofuranosyl nucleosides. 3′-*C*-Methylribonucleosides were also synthesized starting from 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-D-ribofuranose.

INTRODUCTION

Pyrimidine 3′-*C*-alkylnucleosides and their phosphoric esters have been prepared[1–3] and their physicochemical and biological properties studied. 3′-*C*-Methyluridine 5′-triphosphate inhibits RNA synthesis[4] catalysed by *E. coli* RNA polymerase and can be used for nucleic acid sequencing. We now report on the synthesis of purine 3′-*C*-methylnucleosides in continuation of studies of the synthesis of functionally competent analogs of nucleosides, nucleotides, and oligonucleotides.

RESULTS AND DISCUSSION

Two methods have been developed for converting 5-*O*-benzoyl-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-ribofuranose[2,3,5] (**1a**) into the acylated derivatives[2,3] **3a** and **4a** of 3-*C*-methyl-D-ribofuranose: (*a*) acid hydrolysis of the 1,2-*O*-isopropylidene group followed by acetylation, and (*b*) acetylation of the tertiary alcohol group (→**2a**) followed by acetolysis. A mixture of the anomers **3a** and **4a** synthesized by method (*a*) was then converted in high yield into pyrimidine 3′-*C*-methylribo-

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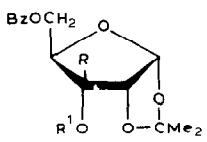
0008-6215/88/$ 03.50

TABLE I

ACETOLYSIS OF 3-*O*-ACETYL-5-*O*-BENZOYL-3-*C*-METHYL-1,2-*O*-ISOPROPYLIDENE-α-D-RIBOFURANOSE (**2a**): ^{1}H-N.M.R. DATA OF ACETOLYSIS PRODUCTS **3a–6a** ($CDCl_3$, 37°)[a]

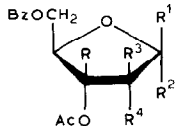
Product	*Relative proportions of the products Conditions*			*Chemical shifts (δ) and J values (Hz)*						
	A	B	C	*H-1* ($J_{1,2}$)	*H-2*	*H-4* ($J_{4,5}$; $J_{4,5'}$)	*H-5* ($J_{5,5'}$)	*H-5'*	*Me-3*	*Ac*
3a (*β-ribo*)	20	20	50	6.03d (1.5)	5.43d	4.62dd (4.0; 7.5)	4.56dd (−12.0)	4.40dd	1.72s	2.10s, 2.04s, 2.03s
4a (*α-ribo*)	10	10	20	6.36d (4.5)	5.37d	4.76–4.32m			1.64s	2.12s, 2.08s, 2.05s
5a (*α-arabino*)	50	50	20	6.05d (1.3)	5.56d	4.79dd (4.3; 6.8)	4.62dd (−11.9)	4.47dd	1.58s	2.15s, 2.12s, 2.05s
6a (*β-arabino*)	20	20	10	6.34d (5.0)	5.48d	4.80–4.30m			1.68s	2.14s, 2.07s, 2.06s

[a]Signals for Bz at δ 8.15–7.30. The parameters were determined from the spectra of **3a** and **5a**, and for **4a** and **6a**, by analysing the spectra of the mixtures **3a,4a, 5a,6a,** and **3a–6a**.



1 R^1 = H
2 R^1 = Ac

a R = Me
b R = H



3 $R^1 = R^4$ = OAc, $R^2 = R^3$ = H
4 $R^1 = R^3$ = H, $R^2 = R^4$ = OAc
5 $R^1 = R^4$ = H, $R^2 = R^3$ = OAc
6 $R^1 = R^3$ = OAc, $R^2 = R^4$ = H

nucleosides[2,3]. Method (*b*) gave a low yield of the products and isomers were formed. Method (*b*) has now been studied in detail.

Epimerization at C-2 in acetolysis was discovered in 1963 by Jerkeman[6], studied further by others[7–10], and used by Lerner[11–15] to prepare rare monosaccharides and nucleosides. Epimerization occurs during the acetolysis of 1,2(and 2,3)-*O*-isopropylidene-furanose derivatives with HO-2,3 *cis* and is favoured at high concentrations of acetic acid. Acetolysis of D-ribofuranose derivatives[9] yielded, after deacetylation, D-ribose and D-arabinose, in the ratio 3–6:1, and Sowa[8] proposed a mechanism involving a 2,3-acetoxonium ion.

The acetolysis of 3-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-1,2-*O*-isopropylidene-α-D-ribofuranose (**2a**) was studied using AcOH–Ac_2O–H_2SO_4 mixtures 10:1:0.5 (*A*), 7:1:0.5 (*B*), and 17:17:1 v/v (*C*). The products, isolated (80–85% yield) by chromatography on silica gel and analysed by ^{1}H-n.m.r. spectroscopy (see Table I), were a mixture of the four acetates **3a–6a** which could not be completely separated by chromatography on silica gel.

Acid hydrolysis of **1a** followed by acetylation[2,3] yielded a mixture of the anomers **3a** and **4a**, from which the crystalline β anomer **3a** was isolated after chromatography on silica gel. The α anomer **5a** was isolated by crystallization of the mixture **3a–6a** from dichloromethane–hexane.

The chemical shifts of signals for the anomeric protons of **3a–6a** are similar (see Table I) and do not allow the configuration of the anomeric center to be determined if only a single isomer is available. However, for each pair of anomers, the chemical shifts of the H-1 signals where H-1,2 are *cis* are more downfield than where H-1,2 are *trans* ($J_{1,2}$ 1.3–1.5 Hz). These data are consistent with the empirical rules formulated earlier[16]. The proposed assignment is confirmed by the X-ray data for the α anomer **5a** (see Fig. 1). In the crystal, the furanose ring of **5a** has C-1*exo*,C-2*endo* ($_1T^2$ conformation). The phase pseudorotation angles P was 136.4° and the maximal amplitude of pseudorotation Φ_{max} was 35.9°.

The ratios of the products of acetolysis are also shown in Table I. At a high concentration of acetic acid, 70% epimerization occurred and the α anomer **5a** was the main product. When the AcOH–Ac_2O ratio was 1:1, 30% of the 3-*C*-methyl-D-arabinose derivatives **5a** and **6a** were produced with a *trans*/*cis* ratio of H-1,2 of 7:3.

Acetolysis of the D-ribofuranose derivative **2b** under conditions *A* and *B* (Table I) gave the four isomers **3b–6b**, for which the ^{1}H-n.m.r. data indicated the

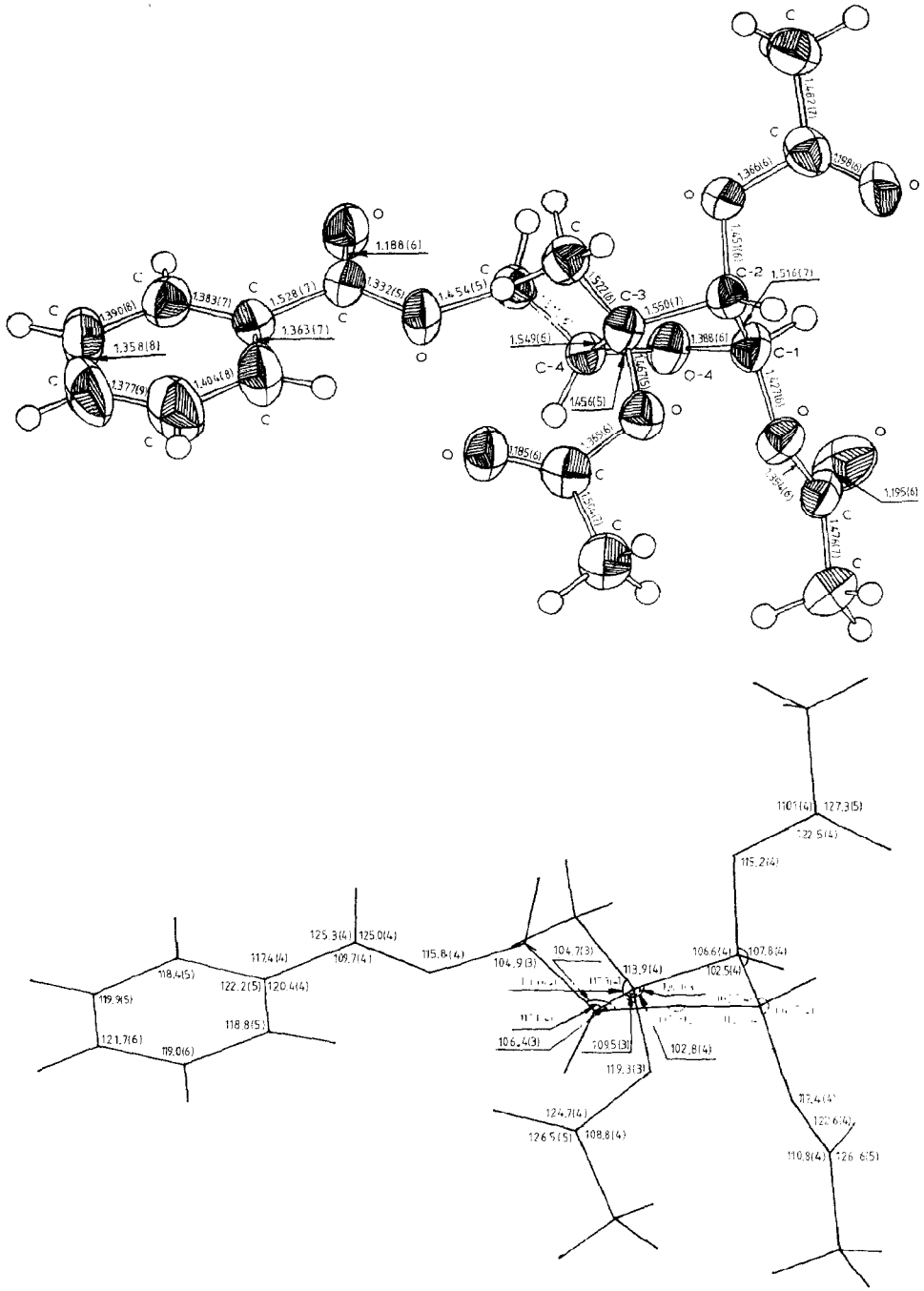


Fig. 1. Numbering of atoms, interatomic distances (in Å), and bond angles for 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-α-D-arabinofuranose (**5a**).

ratio of D-*ribo* and D-*arabino* compounds to be 2.3:1. No *arabino* derivatives were produced under conditions *C*.

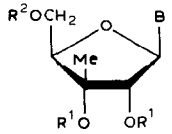
In order to determine whether or not epimerization occurred during or after removal of the isopropylidene group, the acetolysis of **3a, 3b,** and **5a** was studied under conditions *A*. The ^{1}H-n.m.r. data indicated that an α,β-mixture of products was formed, but no epimerization was detected. As in the acetolysis of **2a**, the ratio between isomers where H-1,2 were *trans* and *cis* was 7:3.

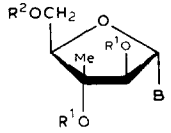
Thus, acetolysis of 1,2-*O*-isopropylidene derivatives in the presence of a high concentration of acetic anhydride (conditions *C*) makes it possible to obtain only completely acylated D-ribofuranose derivatives. This approach cannot be used for *C*-branched derivatives, but acid hydrolysis of the isopropylidene group followed by acetylation is an alternative strategy. Acetolysis under conditions *A* or *B* provides a new method for the synthesis of 3-*C*-methyl-D-arabinofuranose derivatives.

Glycosylation of bis-trimethylsilyluracil with a mixture of isomers **3a–6a**, prepared under conditions *A* or *B*, in the presence of trimethylsilyl trifluoromethanesulfonate by the method of Vorbrüggen[17] yielded a mixture of the acylated uridine derivatives **7** and **10** which were separated by chromatography on silica gel; the derivative **7** is known[2,3]. Likewise, glycosylation of the trimethylsilyl derivatives of N^6-benzoyladenine and N^2-palmitoylguanine with a mixture of **3a–6a** gave the nucleoside derivatives **8** and **11**, and **9** and **12**, respectively, as well as other *N*-isomers. The main products **11** and **12** were isolated by chromatography on silica gel.

The purine ribonucleoside derivatives **8** and **9** were prepared from a mixture of **3a** and **4a**. The structure of these compounds was corroborated by the ^{1}H-n.m.r. data (see Table II): a $J_{1,2}$ value of 7.5–8.0 Hz is typical for 3′-*C*-methylribonucleosides[1–3,5,18]. The signal of H-4′ of the α-nucleosides **10–12** is shifted downfield as compared to the corresponding signal in the β-nucleosides **7–9**, apparently due to the anisotropic effect of the heterocyclic base.

Deacylation of **7–12** with ammonia in methanol gave nucleosides **13–18** in high yield, and their u.v. spectra were identical with those of corresponding natural nucleosides. Fig. 2 contains the c.d. spectra of these compounds (for the guanine nucleoside **15**, the amplitude of the Cotton effect at 240–280 nm was close to zero).





7	B = Ura, R^1 = Ac, R^2 = Bz	**10**
8	B = Ade^{Bz}, R^1 = Ac, R^2 = Bz	**11**
9	B = Gua^{Pal}, R^1 = Ac, R^2 = Bz	**12**
13	B = Ura, R^1 = R^2 = H	**16**
14	B = Ade, R^1 = R^2 = H	**17**
15	B = Gua, R^1 = R^2 = H	**18**

TABLE II

^{1}H-N.M.R. DATA FOR **7**–**18** AT 37°

Compound (solvent)	*Chemical shifts (δ) and J values (Hz)*									
	Carbohydrate residue						*Heterocycle*			*Other protons*[a]
	H-1 ($J_{1,2}$)	*H-2* ($J_{2,OH}$)	*H-4* ($J_{4,5}$; $J_{4,5'}$)	*H-5* ($J_{5,5'}$)	*H-5'*	*Me-3*	*H-8* *H-6* ($J_{5,6}$)	*H-2* *H-5* ($J_{NH\text{-}5}$)	*NH* NH_2	
7 ($CDCl_3$)	6.16d (7.5)	5.36d	4.88dd (3.3; 3.6)	4.70dd (−12.8)	4.50dd	1.73s	7.36d (8.0)	5.43dd (2.0)	8.55bs	2.16s (2 Ac)
8 ($CDCl_3$)	6.29d (7.5)	6.07d	4.97dd (3.5; 4.5)	4.80dd (−12.5)	4.56dd	1.83s	8.63s	8.07s	8.95bs	2.17s; 2.09s (Ac)
9 ($CDCl_3$)	6.03d (7.5)	5.88d	5.13t (3.5; 3.5)	4.72–4.56m		1.27s	7.58s		8.96bs 8.25bs	2.18s; 2.08s (Ac)
10 ($CDCl_3$)	5.98d (3.8)	5.68d	5.11t (5.5; 5.5)	4.50d		1.60s	7.34d (8.0)	5.70dd (2.0)	8.56bs	2.13s; 2.03s (Ac)
11 ($CDCl_3$)	6.20d (4.0)	6.16d	5.25t (5.5; 5.5)	4.58d		1.68s	8.70s	8.14s	9.00bs	2.14s; 2.02s (Ac)
12 ($CDCl_3$)	6.04d (3.2)	5.88d	5.18t (3.2; 3.2)	4.51m		1.21s	7.80s		9.94bs 9.46bs	2.02s; 1.90s (Ac)
13 (D_2O)	5.96d (7.8)	4.18d	4.09dd (3.8; 4.9)	3.90–3.70m		1.40s	7.90d (8.0)	5.90d		
14 (D_2O)	5.96d (8.0)	4.62d	4.20t (3.0; 3.0)	4.00–3.70m		1.49s	8.25s	8.12s		
15 [$(CD_3)_2SO$]	5.66d (8.0)	4.28dd (6.0)	3.90–3.50m			1.30s	7.87s		10.65bs 6.38bs	5.32d (HO-2) 5.10t (HO-5) 4.66s (HO-3)
16 (D_2O)	5.79d (3.3)	4.18d	4.38dd (4.5; 6.5)	3.97m		1.33s	7.86d (8.0)	5.83d		
17 (D_2O)	5.98d (4.0)	4.45d	4.52dd (4.5; 6.5)	3.78m		1.32s	8.22s	8.12s		
18 [$(CD_3)_2SO$]	5.55d (5.0)	4.28dd (6.0)	4.12dd (6.0; 6.5)	3.63m		1.10s	7.84s		10.30bs 6.28bs	5.65d (HO-2) 5.12s (HO-3) 4.80t (HO-5)

[a]Signals for Bz of **7**–**12** at δ 8.06–7.32 and for the Pal group protons for **9** and **12** at δ 2.66–0.76.

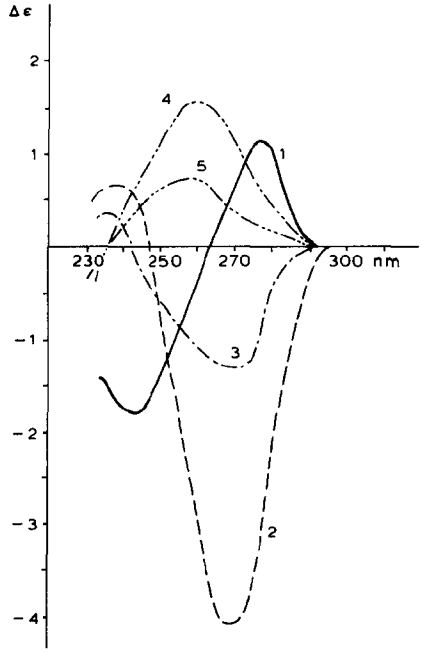


Fig. 2. C.d. spectra (H_2O, 20°): 1, 3′-*C*-methyluridine (**13**); 2, **16**; 3, 3′-*C*-methyladenosine (**14**); 4, **17**; 5, **18**.

The positive Cotton effect is typical of β-pyrimidine nucleosides[19] and the negative one for β-purine nucleosides[20]. The opposite correlations was found for α-nucleosides.

The structure of the compounds synthesized was corroborated further by the results of periodate oxidation. The oxidations were monitored by t.l.c., and at 20°, the reactions of uridine and 3′-*C*-methyluridine **13** were complete in 20 min, reflecting the presence of a *cis*-2,3-diol group[21]. Under similar conditions, 1-(α-D-arabinofuranosyl)uracil and its 3′-*C*-methyl derivative **16** required 2.5 and 72 h, respectively, reflecting the presence of a *trans*-2,3-diol group[21].

EXPERIMENTAL

General methods. — All melting points (uncorrected) were determined with a TP (U.S.S.R.) instrument. Optical rotations were measured with a Perkin–Elmer Model 141 automatic polarimeter, u.v. spectra with a Specord UV-VIS instrument, and c.d. spectra with a Jobin–Yvon Dichrograph III. Silica gel L (40–100 μm) (Czechoslovakia) was used for column chromatography. T.l.c. was conducted on Silufol UV_{254}, using *A*, $CHCl_3$; *B*, 98:2 $CHCl_3$–EtOH; *C*, 8:2 $CHCl_3$–EtOH; with detection by heating to 150–200° or with u.v. light. ^{1}H-N.m.r. spectra were recorded with a Varian XL-100 or Varian XL-200 spectrometer, using solutions in

$CDCl_3$, $(CD_3)_2SO$ (internal Me_4Si), and D_2O (internal *tert*-butyl alcohol, δ 1.27). The signals were assigned by using double resonance.

Crystals of **5a** are rhombic; a = 8.678(1), b = 11.354(1), c = 20.000(3) Å, V = 1970.5 Å^3; the space group is $P2_12_12_1$, and Z = 4 ($C_{19}H_{22}O_9$). The intensities of 1732 independent reflections were measured with a CAD-4 automatic Hilger–Watts diffractometer (Mo$K\alpha$, a graphite monochromator, $\theta/2\theta$ scanning). The data were corrected for the Lorentz and polarization factors. The structure was determined by direct method (MULTAN) programme and refined by the least-squares method in an anisotropic approximation for carbon and oxygen atoms. Hydrogen atom positions were calculated geometrically after each refinement cycle by the least-squares method and refined at fixed values of the thermal parameter B_{iso} = 5 Å^2. The final value of the factor R was 4.2% for 1507 reflections with $I \geq 4\sigma(I)$.

1,2,3-Tri-O-acetyl-5-O-benzoyl-3-C-methyl-β-D-ribofuranose (**3a**). — A solution of **1a**[3,5] (3.1 g, 10 mmol) in aqueous 90% CF_3COOH (50 mL) was kept for 20 min at 20°. Toluene (30 mL) was added, the mixture was concentrated *in vacuo* to dryness, and toluene (2 × 30 mL) and pyridine (2 × 20 mL) were evaporated from the residue, which was treated with dry pyridine (50 mL) and Ac_2O (10 mL) in the presence of 4-dimethylaminopyridine (50 mg) for 3 days at 20°. Conventional work-up and elution of the product from a column of silica gel (100 g) with solvent *A* gave, first, **3a** as a syrup which slowly crystallized on storage to give material (1 g, 25%) having R_F 0.49 (solvent *A*), m.p. 55°, $[\alpha]_D^{20}$ +16° (*c* 1.1, chloroform).

Anal. Calc. for $C_{19}H_{22}O_9$: C, 57.87; H, 5.62. Found: C, 57.77; H, 5.53.

Further elution afforded a mixture of **3a** and **4a** as a thick syrup (2.5 g, 63.5%).

Acetolysis of 3-O-acetyl-5-O-benzoyl-1,2-O-isopropylidene-3-C-methyl-α-D-ribofuranose (**2a**). — *Conditions* A. Aqueous 96% H_2SO_4 (1.2 mL) was added to a solution of **2a**[2,3] (2.1 g, 6 mmol) in AcOH (24.0 mL) and Ac_2O (2.4 mL). The mixture was stored for 16 h at 20°, then diluted with chloroform (50 mL), washed successively with ice-cold water (10 mL), cold aqueous 10% $NaHCO_3$ (3 × 10 mL), and water (10 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was purified by chromatography on silica gel (50 g) with solvent *A* to give a partially crystalline mixture (2.0 g, 85%) of triacetates **3a–6a**. The ^{1}H-n.m.r. data are given in Table I. Crystallization of the mixture from CH_2Cl_2–hexane gave 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-α-D-arabinofuranose (**5a**; 620 mg, 27%), m.p. 99–100°, $[\alpha]_D^{20}$ +68° (*c* 1.0, chloroform).

Anal. Calc. for $C_{19}H_{22}O_9$: C, 57.87; H, 5.62. Found: C, 57.71; H, 5.59.

Conditions B. Aqueous 96% H_2SO_4 (0.4 mL) was added to a solution of **2a** (700 mg, 2 mmol) in AcOH (5.6 mL) and Ac_2O (0.8 mL). The mixture was stored for 16 h at 20°, then worked-up as described above to give the mixture **3a–6a** (630 mg, 80%).

Conditions C. Aqueous 96% H_2SO_4 (0.42 mL) was added to a solution of **2a** (700 mg, 2 mmol) in AcOH (7.1 mL) and Ac_2O (7.1 mL). The reaction was stored for 16 h at 20° and then worked-up as described above to give **3a–6a** (630 mg, 80%).

Acetolysis of 3-O-acetyl-5-O-benzoyl-1,2-O-isopropylidene-α-D-ribofuranose (**2b**). — Compound **1b**[22] (2.1 g, 7.14 mmol) was acetylated with Ac_2O in dry pyridine (20 mL) for 16 h at 20°. Conventional work-up and elution of the product from a column of silica gel (50 g) with solvent *A* gave **2b**, isolated as a thick syrup (2.1 g, 87.5%), R_F 0.68 (solvent *A*). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.02–7.92 (m, 2 H, Bz), 7.54–7.32 (m, 3 H, Bz), 5.81 (d, 1 H, $J_{1,2}$ 3.7, H-1), 4.88–4.28 (m, 5 H, H-2,3,4,5,5′), 2.10 (s, 3 H, Ac), 1.56 (s, 3 H, Me), 1.34 (s, 3 H, Me).

Aqueous 96% H_2SO_4 (0.4 mL) (conditions *A*) was added to a solution of **2b** (2 mmol) in AcOH (8 mL) and Ac_2O (0.8 mL). The mixture was stored for 16 h at 20°, then treated as in the acetolysis of **2a**. A mixture (600 mg, 80%) of triacetates **3b–6b** was obtained as an oil which crystallized upon storage, R_F 0.39 (solvent *A*). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.10–7.28 (m, 5 H, Bz), 6.40 (d, $J_{1,2}$ 4.8 Hz, *α-ribo*-H-1), 6.35 (d, $J_{1,2}$ 5.0 Hz, *β-arabino*-H-1), 6.18 (d, $J_{1,2}$ 0.5 Hz, *α-arabino*-H-1), 6.13 (d, $J_{1,2}$ 0.8 Hz, *β-ribo*-H-1), 5.58–5.02 (m, 2 H, H-2,3), 4.74–4.20 (m, 3 H, H-4,5,5′), 2.14 (s, Ac), 2.12 (s, Ac), 2.10 (s, Ac), 2.04 (s, Ac), 1.94 (s, Ac). The ratios of isomers **3b, 4b, 5b,** and **6b** were 5:2:2:1. Crystallization of this mixture from ethanol gave 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-β-D-ribofuranose (**3b**; 150 mg, 20%), R_F 0.38 (solvent *A*), m.p. 114–115°, $[\alpha]_D^{20}$ −9.2° (*c* 0.6, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.04–7.92 (m, 2 H, Bz), 7.50–7.32 (m, 3 H, Bz), 6.13 (d, 1 H, $J_{1,2}$ 0.8 Hz, H-1), 5.44 (dd, 1 H, $J_{3,2}$ 4.9, $J_{3,4}$ 5.2 Hz, H-3), 5.34 (dd, H-2), 4.68–4.30 (m, 3 H, H-4,5,5′), 2.12 (s, 3 H, Ac), 2.04 (s, 3 H, Ac), 1.94 (s, 3 H, Ac).

Anal. Calc. for $C_{18}H_{20}O_9$: C, 56.84; H, 5.30. Found: C, 57.03; H, 5.63.

Acetolysis of **2b** (2 mmol), using conditions *B*, gave a mixture (82%) of **3b–6b** in the ratios 11:3:4:2.

Acetolysis of **2b**, using conditions *C*, gave a mixture (83%) of **3b** and **4b** in the ratio 7:3.

Acetolysis of 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-β-D-ribofuranose (**3a**) under conditions *A* afforded a mixture (80%) of **3a** and **4a** in the ratio 7:3.

Acetolysis of 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-α-D-arabinofuranose (**5a**) under conditions *A* gave a mixture of **5a** and **6a** in the ratio 7:3.

Acetolysis of 1,2,3-tri-*O*-acetyl-5-*O*-benzoyl-β-D-ribofuranose (**3b**) under conditions *A* afforded a mixture (84%) of **3b** and **4b** in the ratio 7:3.

1-(2,3-Di-O-acetyl-5-O-benzoyl-3-C-methyl-β-D-ribofuranosyl)uracil (**7**) *and 1-(2,3-di-O-acetyl-5-O-benzoyl-3-C-methyl-α-D-arabinofuranosyl)uracil* (**10**). — A mixture of dry uracil (500 mg, 4.44 mmol) in hexamethyldisilazane (10 mL) and dry pyridine (5 mL) was boiled under reflux in the absence of moisture until dissolution was complete (4 h). The mixture was concentrated *in vacuo* to dryness and dry toluene (2 × 20 mL) was evaporated from the residue. A solution of **3a–6a** (1.6 g, 4.06 mmol), prepared by acetolysis of **2a** under conditions *B*, in dry 1,2-dichloroethane (40 mL) and M $CF_3SO_2SiMe_3$ in 1,2-dichloroethane (5 mL) were added to the residue, and the mixture was stored for 16 h at 20°. Chloroform (50 mL) was added to the mixture, which was washed successively with aqueous 10% $NaHCO_3$ (10 mL) and water (10 mL), dried (Na_2SO_4), filtered, and concentrated

to dryness. The residue was eluted with solvent *B* from a column of silica gel (100 g) to afford, first, **7**[3], isolated as a foam (450 mg, 25%), R_F 0.49 (solvent *B*), $[\alpha]_D^{20}$ −41° (*c* 1, chloroform). Further elution afforded **10** (1.3 g, 63.5%), m.p. 212–213° (from ethanol), R_F 0.47 (solvent *B*), $[\alpha]_D^{20}$ −1.6° (*c* 1, chloroform).

Anal. Calc. for $C_{21}H_{22}N_2O_9$: C, 56.50; H, 4.97; N, 6.28. Found: C, 56.28; H, 4.68; N, 6.13.

Trimethylsilyl derivatives of N^6-benzoyladenine and N^2-palmitoylguanine were glycosylated in a similar manner with a mixture of acetates **3a–6a** in the presence of $CF_3SO_2OSiMe_3$ (1.2–1.25 equiv.) by boiling for 1.5–2 h in 1,2-dichloroethane, to afford the following main products.

9-(2,3-Di-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-α-D-arabinofuranosyl)-N^6-benzoyladenine (**11**, 52%), isolated as a foam, R_F 0.55 (solvent *B*), $[\alpha]_D^{20}$ +34° (*c* 1, chloroform).

9-(2,3-Di-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-α-D-arabinofuranosyl)-N^2-palmitoylguanine (**12**, 46%), isolated as a foam, R_F 0.35 (solvent *B*), $[\alpha]_D^{20}$ +11° (*c* 1, chloroform).

*9-(2,3-Di-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-β-D-ribofuranosyl)-*N^6*-benzoyladenine* (**8**). — A mixture of dry N^6-benzoyladenine (741 mg, 3.1 mmol) in hexamethyldisilazane (10 mL) and dry pyridine (5 mL) was boiled under reflux in the absence of moisture until dissolution was complete (3 h) and then concentrated *in vacuo* to dryness, and dry toluene (2 × 10 mL) was evaporated from the residue. A solution of **3a** and **4a** (1.2 g, 3 mmol) in dry 1,2-dichloroethane (40 mL) and M $CF_3SO_2OSiMe_3$ in 1,2-dichloroethane (3.5 mL) were added to the residue. The mixture was boiled under reflux in the absence of moisture for 1.5 h and then allowed to cool to 20°. Chloroform (50 mL) was added and the organic layer was washed consecutively with aqueous 10% $NaHCO_3$ (10 mL) and water (10 mL), dried (Na_2SO_4), and concentrated to dryness. The residue was eluted with solvent *B* from a column of silica gel (100 g), which had been washed with solvent *A*, to afford **8**, isolated as a foam (1.35 g, 78%), R_F 0.45 (solvent *B*), $[\alpha]_D^{20}$ −61° (*c* 1, chloroform).

*9-(2,3-Di-*O*-acetyl-5-*O*-benzoyl-3-*C*-methyl-β-D-ribofuranosyl)-*N^2*-palmitoylguanine* (**9**). — Glycosylation of the trimethylsilyl derivative of N^2-palmitoylguanine, as described for **8**, with a mixture of **3a** and **4a** in the presence of $CF_3SO_2OSiMe_3$ (1.2 equiv.) and boiling for 2 h in 1,2-dichloroethane, gave **9** (46%), isolated as a foam, R_F 0.30 (solvent *B*), $[\alpha]_D^{20}$ −46° (*c* 1, chloroform).

Deacylation of nucleosides **7–12**. — A solution of the protected nucleoside (2 mmol) in methanolic 5M ammonia (30 mL) was kept for 2 days at 20° and then concentrated to dryness. The residue was partitioned between chloroform (20 mL) and water (30 mL), the organic layer was washed with water (2 × 10 mL), the combined aqueous extracts were washed with chloroform (2 × 5 mL) and concentrated *in vacuo* to dryness, and the residue was recrystallized from water. This procedure was used to prepare the following nucleosides.

1-(3-*C*-Methyl-β-D-ribofuranosyl)uracil (**13**, 75%), m.p. 213–214°, R_F 0.45 (solvent *C*); lit.[3] m.p. 213–214°.

9-(3-*C*-methyl-β-D-ribofuranosyl)adenine (**14**, 72%), R_F 0.3 (solvent *C*), m.p. 207–208° (softening at 172°), $[\alpha]_D^{20}$ −53° (*c* 1, water) {lit.[18] m.p. 213–215° (softening at 165°), $[\alpha]_D^{20}$ −58° (water)}; $\lambda_{max}^{pH\ 1}$ 258 nm (ε 14700), $\lambda_{max}^{pH\ 7-13}$ 260 nm (ε 15000).

9-(3-*C*-Methyl-β-D-ribofuranosyl)guanine (**15**, 70%), R_F 0.17 (solvent *C*), m.p. 250° (dec.), $[\alpha]_D^{20}$ −16° (*c* 1, methyl sulfoxide); $\lambda_{max}^{pH\ 1}$ 255 nm (ε 12000), $\lambda_{max}^{pH\ 13}$ 263 nm (ε 11000).

Anal. Calc. for $C_{11}H_{15}N_5O_5$: C, 44.44; H, 5.09; N, 23.56. Found: C, 44.57; H, 5.21; N, 23.52.

1-(3-*C*-Methyl-α-D-arabinofuranosyl)uracil (**16**, 72%), R_F 0.40 (solvent *C*), m.p. 120–122°, $[\alpha]_D^{20}$ +30° (*c* 1, methyl sulfoxide); $\lambda_{max}^{pH\ 1-7}$ 262 nm (ε 10600), $\lambda_{max}^{pH\ 7-13}$ 262 nm (ε 7800).

Anal. Calc. for $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.46; N, 10.85. Found: C, 46.61; H, 5.39; N, 10.70.

9-(3-*C*-Methyl-α-D-arabinofuranosyl)adenine (**17**, 75%), R_F 0.25 (solvent *C*), m.p. 217–218°, $[\alpha]_D^{20}$ +34° (*c* 1, methyl sulfoxide); $\lambda_{max}^{pH\ 1}$ 258 nm (ε 14700), $\lambda_{max}^{pH\ 7-13}$ 260 nm (ε 15000).

Anal. Calc. for $C_{11}H_{15}N_5O_4$: C, 46.97; H, 5.38; N, 24.90. Found: C, 46.83; H, 5.29; N, 24.78.

9-(3-*C*-Methyl-α-D-arabinofuranosyl)guanine (**18**, 75%), R_F 0.13 (solvent *C*), m.p. 240° (dec.), $[\alpha]_D^{20}$ +69° (*c* 1, methyl sulfoxide); $\lambda_{max}^{pH\ 1}$ 254 nm (ε 12100), $\lambda_{max}^{pH\ 13}$ 263 nm (ε 11100).

Anal. Calc. for $C_{11}H_{15}N_5O_5$: C, 44.44; H, 5.09; N, 23.56. Found: C, 44.53; H, 5.18; N, 23.53.

Periodate oxidation. — 0.1M $NaIO_4$ (0.25 mL) was added to the solution of the nucleoside (0.02 mmol) in water (0.5 mL). The reaction was monitored by t.l.c. (solvent *C*). The starting compounds had R_F 0.35–0.45, and the products had R_F 0.55–0.60.

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