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NEW SYNTHESES OF 2′-*C*-METHYLNUCLEOSIDES STARTING FROM D-GLUCOSE AND D-RIBOSE*

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ABSTRACT

Effective general methods have been developed for the synthesis of 2′-*C*-methylnucleosides starting from D-glucose and D-ribose. 3-*O*-Benzyl-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose was prepared in 5 steps from D-glucose and converted into 1,2,3-tri-*O*-acetyl-2-*C*-methyl-5-*O*-*p*-methylbenzoyl-D-ribofuranose (**5**), the starting compound for nucleoside synthesis. Compound **5** was also synthesised from 2-*C*-hydroxymethyl-2,3-*O*-isopropylidene-5-*O*-trityl-D-ribofuranose, prepared in 3 steps from D-ribose. Condensation of **5** with the bis-trimethylsilyl derivatives of uracil, N^4-benzoylcytosine, and N^6-benzoyladenine in the presence of $F_3CSO_2OSiMe_3$ followed by removal of the protecting acyl groups yielded the corresponding 2′-*C*-methylnucleosides.

INTRODUCTION

We have described synthesis of 5′- and 3′-*C*-methylnucleosides and nucleotides and oligonucleotides derived therefrom[1–5] and used them in studies of enzyme-catalysed hydrolysis of internucleotide bonds[5–7] in relation to the mechanism of enzyme action in nucleic acid transformations. We now report on the synthesis of 2′-*C*-methylnucleosides.

Walton *et al.* prepared 2′-*C*-methyladenosine[8] and 2′-*C*-methylcytidine[9] starting from 2-*C*-methyl-D-ribonolactone obtained in a yield of 11% by treatment[10] of D-fructose with alkali. Later, Novak and Šorm[11] used the same starting compound to synthesise derivatives of 2-*C*-methyl-D-ribose. However, the overall yields of the compounds prepared by these methods were low.

RESULTS AND DISCUSSION

The development of stereospecific methods for the synthesis of *C*-branched

*Dedicated to Professor W. Pfleiderer on the occasion of his 60th birthday.
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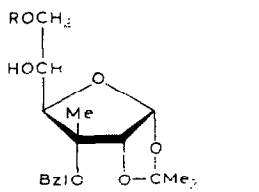
monosaccharides has made it possible to prepare derivatives of 2-*C*-alkyl-D-ribose by routes in which the incorporation of an alkyl substituent is the key step. The stereospecificity of nucleophilic attack on derivatives of pentopyranosid-2-uloses and the development of methods for the synthesis of 2-*C*-methyl-D-ribose, 2-*C*-methyl-D-arabinose, and hamamelose derivatives have been studied[12-14]. The synthesis of 2′-*C*-methylnucleosides requires furanose derivatives; the reactions of derivatives of pentofuranosid-2-uloses with organometallic compounds have been reported[15,16], but the starting ketones were difficult to prepare and unstable.

Aldol condensation of 2,3-*O*-isopropylidene-D-ribose with formaldehyde to produce 2-*C*-hydroxymethyl-2,3-*O*-isopropylidene-D-ribose in a high yield[17] is another route to 2-*C*-branched derivatives of D-ribose. Moffatt and Cook[18] failed to react derivatives of 2′-ketonucleosides with MeMgI and MeLi, but derivatives of 2′-deoxy-2′-methyleneuridine and the uridine nucleoside of D-hamamelose have been prepared[19] using the Wittig reaction.

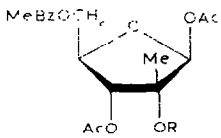
We now report on two procedures for the synthesis of 2-*C*-methyl-ribofuranoses and related nucleosides. The first procedure involved 1,2:5,6-di-*O*-isopropylidene-3-*C*-methyl-D-allofuranose[1,20], hydrolysis of which yields 3-*C*-methyl-D-allose, which can be used for the synthesis of both 3′- and 2′-*C*-methyl-nucleosides by removal of C-6 and C-1, respectively. Since the conventional degradations of ketoses to pentoses usually give low yields of products, periodate oxidation was used by Fox *et al.*[21] who synthesised 2-deoxy-2-fluoro-D-arabino-furanose derivatives from 3-deoxy-3-fluoro-1,2:5,6-di-*O*-isopropylidene-α-D-gluco-furanose. The tertiary hydroxyl group must be blocked in the periodate oxidation of 3-*C*-methyl-D-ribose derivatives[22] and benzylation was preferred to acylation since tertiary acyl groups can migrate[23] to secondary positions in acid-catalysed hydrolysis of the 1,2-*O*-isopropylidene group.

1,2:5,6-Di-*O*-isopropylidene-3-*C*-methyl-α-D-allofuranose was converted *via* two steps into **1** in a high yield using conventional techniques[24]. Selective incorporation of the *p*-methylbenzoyl group into **1**(→**2**) was accomplished *via* the 5,6-*O*-dibutylstannylidene derivative[25]. Treatment of **2** with aqueous 90% trifluoroacetic acid for 15 min at 20° followed by periodate oxidation, elimination of the formyl group, and acetylation gave 77% of **3**.



1 R = H

2 R = *p*-methylbenzoyl



3 R = Bzl

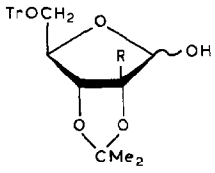
4 R = H

5 R = Ac

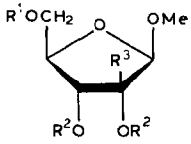
Homogeneous hydrogenolysis[26] of **3** over $Pd(OH)_2/C$ in ethanol–cyclohexene yielded 82% of **4**. Acetylation in the presence of 4-dimethylaminopyridine then gave the crystalline 2-*C*-methyl-D-ribofuranose derivative **5**, which was used for the synthesis of the nucleosides.

The structures of **2–5** were confirmed by the ^{1}H-n.m.r. data. It was difficult to prove the anomeric configuration of **3–5** because of the absence of $J_{1,2}$ values. However, since $J_{1,2} + J_{3,4}$ is constant for related compounds[27], $J_{3,4}$ may be used to determine the anomeric configuration, values of >5 and <3 Hz being typical of β- and α-D-ribofuranose derivatives, respectively[28,29]. The ^{1}H-n.m.r. spectra of acylated 2-*C*-methyl-β-D-ribofuranose contained a 3-proton doublet ($J_{3,4}$ 7.3–7.5 Hz), whereas the corresponding signal in the α anomers appeared as a broad singlet[8]. Since the $J_{3,4}$ values for **3–5** are 7.2–7.8 Hz, they are β anomers.

The second procedure involved aldol condensation of formaldehyde with the furanose derivative **6** obtained in a high yield in two steps from D-ribose[30,31], and which could be protected variously at position 5. Aldol condensation was conducted using methanol–K_2CO_3 under nitrogen for 20–24 h to give **7**. Treatment of **7** with a small excess of toluene-*p*-sulfonyl chloride in pyridine at 0° yielded 70% of the tosylate **8**. The ^{1}H-n.m.r. data indicated **7** and **8** to be 1:1 α,β-mixtures. Kuhn methylation[32] of **8** was stereoselective and gave 90% of **9**. Reduction of **9** with $LiAlH_4$ in boiling tetrahydrofuran for 15 h yielded **10** (77%) and **11** (6%).



6 R = H
7 R = CH_2OH
8 R = CH_2OTs



9 R^1 = Tr, R^2 = >CMe_2, R^3 = CH_2OTs
10 R^1 = Tr, R^2 = >CMe_2, R^3 = Me
11 R^1 = Tr, R^2 = >CMe_2, R^3 = CH_2OH
12 R^1 = H, R^2 = >CMe_2, R^3 = Me
13 R^1 = R^2 = H, R^3 = Me
14 R^1 = *p*-methylbenzoyl, R^2 = >CMe_2, R^3 = Me
15 R^1 = *p*-methylbenzoyl, R^2 = H, R^3 = Me
16 R^1 = *p*-methylbenzoyl, R^2 = Ac, R^3 = Me

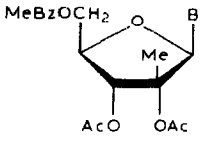
Detritylation of **10** was effected with $SnCl_4$ in 1,2-dichloroethane, which gave 90% of known[11] **12**. Acid-catalysed hydrolysis of the isopropylidene group from **12** gave known[11] **13**. Treatment of **12** with *p*-methylbenzoyl chloride in pyridine yielded **14**, acid hydrolysis of which afforded the furanoside **15** in high yield. Acetylation of **15** required harsh conditions[11], namely, boiling with an excess of Ac_2O in pyridine for 2 h, which gave 83% of **16**.

The methyl furanosides **9–16** must be β because their negative $[\alpha]_D$ values are typical of methyl β-D-ribofuranosides[33] and the ^{1}H-n.m.r. spectra of **15** and **16** each

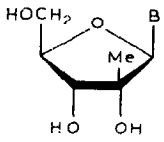
contained a 3-proton doublet with $J_{3,4}$ 7.0–7.3 Hz. The conversion **9**→**16** involved a high yield at each step and only one anomer was isolated. The ^{13}C resonances of C-1 for **12** and **13** were in the range characteristic of β anomers[34].

Acetolysis of **16** yielded a complex mixture of compounds which was partially fractionated by chromatography on silica gel and characterised by ^1H-n.m.r. spectroscopy; 60% of α,β-**5** was obtained and α,β-**4** was identified amongst the products of acetolysis. In their spectral and chromatographic behaviour, the β anomers of **4** and **5** were identical with the compounds prepared from D-glucose by the first procedure. The yield of the α,β-**5** was increased to 90% by acetylation of the products of acetolysis of **16**. Novak and Šorm[11] obtained 1,2,3,5-tetra-*O*-acetyl-2-*C*-methyl-β-D-ribofuranose in yields of 19% and 24% by acetolysis of **13** and its triacetate, respectively.

On attempted glycosylation of **5** or α,β-**5** by the method of Vorbrüggen *et al.*[35], the reaction was roughly ten times slower than with D-ribofuranose derivatives, and several carbohydrate and nucleoside derivatives were obtained the structures of which were not established unambiguously. Apparently, the slow reaction and the formation of by-products were due to steric hindrance by the *C*-methyl group and the rapid formation of carbocations from the tertiary alcohols. The yields of nucleosides **17**–**19** were highest when the reaction was performed at 20° with a 1.5-fold excess of bis-trimethylsilyl derivatives of uracil, N^4-benzoylcytosine, and N^6-benzoyladenine and a 2-fold excess of trimethylsilyl trifluoromethane sulfonate in 1,2-dichloroethane for 7 days. The 2′-*C*-methylnucleosides **20**–**22** were obtained in high yields after deacylation of **17**–**19** with methanolic ammonia.



17 B = Ura
18 B = Cyt^{Bz}
19 B = Ade^{Bz}



20 B = Ura
21 B = Cyt
22 B = Ade

The structures of **20**–**22** were confirmed by the u.v., c.d., and ^1H-n.m.r. data. The u.v. spectra of the 2′-*C*-methylnucleosides **20**–**22** were identical to those of natural nucleosides. In the c.d. spectra, the positive Cotton effect at 260–280 nm is typical of β-pyrimidine nucleosides[36], and the negative Cotton effect is characteristic of β-purine nucleosides[37] (Fig. 1). The amplitude of the long-wavelength Cotton effect was much greater for **20**–**22** than for natural nucleosides and comparable with that for β-D-arabinofuranosyl nucleosides[36,37].

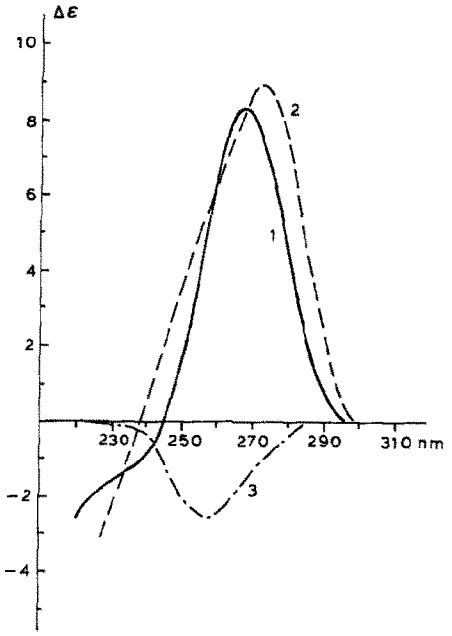


Fig. 1. C.d. spectra in water at 20°: 1, 2′-*C*-methyluridine (**20**); 2, 2′-*C*-methylcytidine (**21**); 3, 2′-*C*-methyladenosine (**22**).

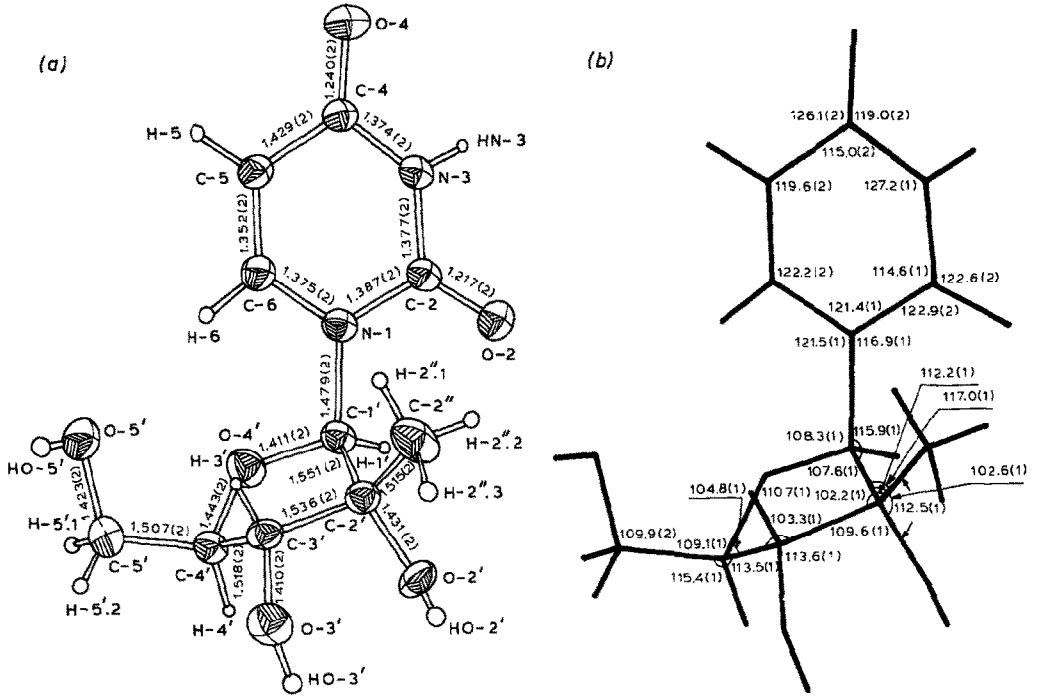


Fig. 2. (*a*) Numbering of atoms, and interatomic distances (in Å), and (*b*) bond angles in the structure of 2′-*C*-methyluridine (**20**).

These data and the ^{1}H-n.m.r. data indicate that the conformation of 2′-*C*-methylnucleosides in solution is mainly *anti*. The ^{1}H-n.m.r. spectra of solutions of **20–22** in D_2O each contained singlets for the methyl group and H-1′, the latter being in the region typical of nucleosides that are mainly in the *anti* conformation[27]. The other signals of ribofuranose residue could not be resolved at 400 MHz.

The structure of **20** was proved by X-ray diffraction analysis of crystals obtained from aqueous solution. The furanose ring was shown to have a C-3′-*endo*–C-4′-*exo* ($^3T_4$) conformation. The phase angle of pseudo-rotation P was 24.8° and the maximal amplitude of pseudo-rotation Φ_{max} was 33.4°. The conformation was *anti* to the glycoside bond, and the torsion angle O-4′–C-1′–N-1–C-2 was −145.5°. The conformation of the exocyclic $HOCH_2$-5′ group was *gauche–gauche*, and the torsion angle C-3′–C-4′–C-5′–O-5′ was 60.8° (Fig. 2).

The syntheses of 2′-*C*-methyl-D-ribose described above should be applicable to other 2-*C*-branched derivatives of D-ribose.

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} plates with *A*, $CHCl_3$; *B*, 97.5:2.5 $CHCl_3$–EtOH; *C*, 95:5 $CHCl_3$–EtOH; *D*, 9:1 $CHCl_3$–EtOH; *E*, 3:2 PhMe–EtOAc; *F*, 7:1:2 ^{i}PrOH–conc. NH_4OH–H_2O; with detection by heating at 150–200° or with u.v. light. ^{1}H-N.m.r. spectra were recorded with a Varian XL-100, Varian XL-200, or Bruker WP-400 spectrometer, using solutions in $CDCl_3$, pyridine-d_5, $(CD_3)_2SO$ (internal Me_4Si), and D_2O (internal *tert*-butyl alcohol, δ 1.27). The signals were assigned by using double resonance. ^{13}C-N.m.r. spectra (15.08 MHz) were recorded with a Bruker–Physik WP-60 spectrometer with proton decoupling on solutions in $CDCl_3$ (internal Me_4Si).

Crystals for X-ray analysis were obtained from a saturated aqueous solution of 2′-*C*-methyluridine (**20**) by slowly evaporating the solvent at 20°. The space group of the crystals is $P2_12_12_1$, with a = 7.288(1), b = 10.298(1), c = 17.303(2) Å, V = 1298.6(2) Å^3, and Z = 4. The intensities of 2104 independent reflections were used with $I > 3\sigma(I)$, and measured with a CAD-4 Hilger–Watts diffractometer ($\theta/2\theta$-scanning, Mo$K\alpha$ radiation, graphite monochromator). The data were corrected for the Lorentz and polarisation factors. The structure was determined by a direct method using the MULTAN program and refined by the full-matrix, least-squares method in an anisotropic approximation for pseudo hydrogen atoms. The co-ordinates of hydrogen atoms were found from the Fourier series of difference syntheses and refined by the least-squares method in an isotropic approximation.

3-O-Benzyl-1,2-O-isopropylidene-3-C-methyl-6-O-methylbenzoyl-α-D-allofuranose (**2**). — A solution of **1** (ref. 24) (2.7 g, 8.33 mmol) in dry methanol (100 mL) was boiled with dibutylstannoxane (2.11 g, 8.44 mmol) until dissolution was complete (1 h) and then cooled to 20°, and triethylamine (3.55 mL, 25.32 mmol) and *p*-methylbenzoyl chloride (3.91 g, 25.32 mmol) were added with stirring. The suspension was stored for 2 h at 20° and filtered, the precipitate was washed with chloroform (2 × 30 mL), and the combined filtrate and washings were concentrated *in vacuo* to dryness. A solution of the residue in chloroform (70 mL) was washed successively with water (10 mL), aqueous 10% $NaHCO_3$ (10 mL), and water (10 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo* to dryness. Elution of the residue (5.0 g) from a column of silica gel (200 g) with solvent *A* gave, in the appropriate fractions, **2**, isolated as a thick syrup (3.0 g, 81%), R_F 0.5 (solvent *A*), $[\alpha]_D^{20}$ +34° (*c* 1, chloroform). ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 7.86 (d, 2 H, *J* 7.0 Hz, Me*Bz*), 7.44–7.04 (m, 7 H, Me*Bz*, CH_2*Ph*), 5.71 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.98 (d, 1 H, $J_{OH,5}$ 5.5 Hz, HO-5, exchangeable with D_2O), 4.64 (d, 1 H, *J* −11.5 Hz, C*H*HPh), 4.54 (d, 1 H, *J* −11.5 Hz, CH*H*Ph), 4.48 (d, 1 H, $J_{2,1}$ 3.7 Hz, H-2), 4.50–3.82 (m, 4 H, H-4,5,6,6′), 2.38 (s, 3 H, *Me*Bz), 1.48 (s, 3 H, Me), 1.32 (s, 6 H, Me, C–Me-3).

Anal. Calc. for $C_{25}H_{30}O_7$: C, 67.86; H, 6.83. Found: C, 67.54; H, 6.79.

1,3-Di-O-acetyl-2-O-benzyl-2-C-methyl-5-O-p-methylbenzoyl-β-D-ribofuranose (**3**). — A solution of **2** (4.1 g, 9.26 mmol) in aqueous 90% CF_3COOH (40 mL) was kept for 15 min at 20°. T.l.c. (solvent *C*) then showed the reaction to be complete. Toluene (20 mL) was added to the solution, the mixture was concentrated *in vacuo* to dryness, and toluene (3 × 10 mL) was evaporated from the residue, a solution of which in chloroform (70 mL) was then washed successively with cold water (10 mL), cold aqueous 10% $NaHCO_3$ (10 mL), and cold water (10 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. To a solution of the residue (3.2 g) in 1,4-dioxane (60 mL) and water (20 mL) was added M $NaIO_4$ (10 mL), and the mixture was stirred for 16 h at 20°. T.l.c. (solvent *E*) then showed the reaction to be complete. The mixture was diluted with ethanol (80 mL), and filtered, the precipitate was washed with ethanol (2 × 20 mL), and the combined filtrate and washings were concentrated *in vacuo* to dryness. A solution of the residue in chloroform (70 mL) was washed with water (2 × 10 mL), dried (Na_2SO_4), and concentrated *in vacuo* to dryness. To a solution of the residue in dry methanol (50 mL) was added methanolic M MeONa (0.3 mL), and the solution was stored for 25 min at 20°. T.l.c. (solvent *E*) then showed that deformylation was complete. The mixture was neutralised with Dowex 50 (H^+) resin and filtered, the resin was washed with methanol (2 × 5 mL), the combined filtrates and washings were concentrated to dryness, and pyridine (2 × 30 mL) was evaporated from the residue which was then treated with acetic anhydride (10 mL) in dry pyridine (50 mL). Conventional work-up and elution of the product from a column of silica gel (100 g) with solvent *A* gave **3**, isolated as a thick syrup (3.2 g, 77%), R_F 0.51 (solvent *B*), $[\alpha]_D^{20}$ +12° (*c* 0.9, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.82 (d, 2 H, *J* 7.0

Hz, Me*Bz*), 7.22–7.02 (m, 7 H, Me*Bz*, CH_2*Ph*), 6.14 (s, 1 H, H-1), 5.29 (d, 1 H, $J_{3,4}$ 7.8 Hz, H-3), 4.54 (bs, 2 H, CH_2Ph), 4.58–4.20 (m, 3 H, H-4,5,5'), 2.30 (s, 3 H, *Me*Bz), 2.02 (s, 3 H, Ac), 1.90 (s, 3 H, Ac), 1.34 (s, 3 H, C-Me-2).

Anal. Calc. for $C_{25}H_{28}O_8$: C, 65.78; H, 6.18. Found: C, 65.42; H, 6.14.

*1,3-Di-*O*-acetyl-2-*C*-methyl-5-*O*-*p*-methylbenzoyl-β-*D*-ribofuranose* (**4**). — 20% $Pd(OH)_2$/C (400 mg) and cyclohexene (50 mL) were added to a solution of **3** (910 mg, 2.0 mmol) in dry EtOH (70 mL). The mixture was boiled under reflux for 2.5 h, then cooled, and filtered, the insoluble material was washed with ethanol (2 × 30 mL), and the combined filtrate and washings were concentrated *in vacuo* to dryness. Elution of the residue from a column of silica gel (50 g) with solvent *A* gave **4**, isolated as a thick syrup (0.6 g, 82%), R_F 0.35 (solvent *B*), $[\alpha]_D^{20}$ −26° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.88 (d, 2 H, *J* 7.0 Hz, Me*Bz*), 7.15 (d, 2 H, *J* 7.0 Hz, Me*Bz*), 5.98 (s, 1 H, H-1), 5.28 (d, 1 H, $J_{3,4}$ 7.2 Hz, H-3), 4.64–4.24 (m, 3 H, H-4,5,5'), 2.40 (s, 3 H, *Me*Bz), 2.14 (s, 3 H, Ac), 2.00 (s, 3 H, Ac), 1.32 (s, 3 H, C-Me-2).

Anal. Calc. for $C_{18}H_{24}O_9$: C, 58.82; H, 6.05. Found: C, 58.45; H, 6.01.

*1,2,3-Tri-*O*-acetyl-2-*C*-methyl-5-*O*-*p*-methylbenzoyl-β-*D*-ribofuranose* (**5**). — A solution of **4** (800 mg, 2.2 mmol) in dry pyridine (10 mL) was concentrated *in vacuo* to dryness and to a solution of the residue in dry pyridine (30 mL) were added acetic anhydride (5 mL) and 4-dimethylaminopyridine (50 mg). The mixture was stored for 16 h at 20°. Conventional work-up and elution of the product from a column of silica gel (50 g) with solvent *A* yielded **5** (800 mg, 90%), R_F 0.96 (solvent *B*), m.p. 88° (from EtOH), $[\alpha]_D^{20}$ −1.25° (*c* 1.2, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.87 (d, 2 H, *J* 7.0 Hz, Me*Bz*), 7.17 (d, 2 H, *J* 7.0 Hz, MeBz), 6.45 (s, 1 H, H-1), 5.40 (d, 1 H, $J_{3,4}$ 7.3 Hz, H-3), 4.60–4.20 (m, 3 H, H-4,5,5'), 2.38 (s, 3 H, *Me*Bz), 2.10 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 1.98 (s, 3 H, Ac), 1.60 (s, 3 H, C-Me-2).

Anal. Calc. for $C_{20}H_{24}O_9$: C, 58.82; H, 5.92. Found: C, 58.70; H, 5.90.

*2-*C*-Hydroxymethyl-2,3-*O*-isopropylidene-5-*O*-trityl-α,β-*D*-ribofuranose* (**7**). — K_2CO_3 (10.45 g, 75.7 mmol) and aqueous 37% HCHO (145 mL) were added to a solution of **6** (ref. 30) (30.3 g, 70.1 mmol) in methanol (300 mL). The solution was boiled under reflux under nitrogen for 20 h, then cooled to 20°, and diluted with chloroform (300 mL). The organic layer was separated and concentrated to dryness, and a solution of the residue in chloroform (100 mL) was dried (Na_2SO_4), filtered, and concentrated to dryness. Elution of the residue from a column of silica gel (500 g) with solvent *B* yielded **7** (23.3 g, 72%), R_F 0.23 (solvent *B*), $[\alpha]_D^{20}$ −6° (*c* 1.1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.51–7.21 (m, 15 H, Tr), 5.34 (d, 0.5 H, $J_{1,OH}$ 5.5 Hz, transformed into a singlet on addition of D_2O, H-1), 5.27 (d, 0.5 H, $J_{1,OH}$ 10.0 Hz, transformed into a singlet on addition of D_2O, H-1), 4.58 (d, 0.5 H, $J_{3,4}$ 1.0 Hz, H-3), 4.52 (d, 0.5 H, $J_{3,4}$ 2.0 Hz, H-3), 4.43–4.23 (m, 1 H, H-4), 3.77 (bs, 3 H, OH, CH_2OH), 3.47–3.10 (m, 2 H, H-5,5'), 2.37 (bs, 0.5 H, OH, exchangeable with D_2O), 1.96 (bs, 0.5 H, OH, exchangeable with D_2O), 1.63 (s, 1.5 H, Me), 1.53 (s, 1.5 H, Me), 1.51 (s, 1.5 H, Me), 1.47 (s, 1.5 H, Me); α,β-ratio 1:1.

Anal. Calc. for $C_{18}H_{30}O_6$: C, 63.13; H, 8.83. Found: C, 62.90; H, 8.78.

2,3-O-Isopropylidene-2-C-tosyloxymethyl-5-O-trityl-α,β-D-ribofuranose (**8**). — A solution of **7** (16.0 g, 34.6 mmol) in dry pyridine (70 mL) was concentrated to dryness. To a solution of the residue in dry pyridine (100 mL) at 0° was added a solution of tosyl chloride (7.25 g, 38.06 mmol) in dry 1,2-dichloroethane (20 mL) during 1 h at 0°, and the mixture was stored for 16 h at 20°. Conventional work-up and elution of the product from a column of silica gel (500 g) with solvent *A* gave **8** (15.5 g, 72%), R_F 0.27 (solvent *A*), m.p. 121–122° (from chloroform–hexane), $[\alpha]_D^{20}$ +20° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.78–7.02 (m, 19 H, Tr, Ts), 5.20 (s, 0.5 H, $J_{1,OH}$ 10.5 Hz, converted into a singlet on addition of D_2O, H-1), 5.15 (d, 0.5 H, $J_{1,OH}$ 7.5 Hz, converted into a singlet on addition of D_2O, H-1), 4.57 (bs, 0.5 H, H-3), 4.44 (d, 0.5 H, $J_{3,4}$ 2.0 Hz, H-3), 4.30–4.06 (m, 3 H, CH_2OTs, H-4), 3.70 (d, 0.5 H, $J_{OH,1}$ 10.5 Hz, exchangeable with D_2O, OH), 3.68 (d, 0.5 H, $J_{OH,1}$ 7.5 Hz, exchangeable with D_2O, OH), 3.47–3.07 (m, 2 H, H-5,5′), 2.42 (s, 3 H, Ts Me), 1.50 (s, 1.5 H, Me), 1.40 (s, 1.5 H, Me), 1.37 (s, 1.5 H, Me), 1.34 (s, 1.5 H, Me); α,β-ratio 1:1.

Anal. Calc. for $C_{35}H_{36}O_8$: C, 68.17; H, 5.88. Found: C, 68.30; H, 5.82.

Methyl 2,3-O-isopropylidene-2-C-tosyloxymethyl-5-O-trityl-β-D-ribofuranose (**9**). — A solution of **8** (13.4 g, 21.64 mmol) in dry *N,N*-dimethylformamide (40 mL) was concentrated to dryness and to a solution of the residue in dry *N,N*-dimethylformamide (100 mL) were added freshly precipitated silver oxide (25.0 g, 107.9 mmol) and methyl iodide (50 mL, 0.8 mol). The mixture was stirred in the dark for 16 h at 20° and then filtered, the precipitate was washed with *N,N*-dimethylformamide (2 × 30 mL), and the combined filtrate and washings were concentrated to dryness. A solution of the residue in chloroform (100 mL) was filtered, washed with aqueous 10% sodium thiosulfate (30 mL) and water (50 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. Elution of the residue (13.0 g) from a column of silica gel (300 g) with solvent *A* yielded **9** (2.6 g, 92%), R_F 0.70 (solvent *A*), m.p. 92–93.5° (from dichloromethane–hexane), $[\alpha]_D^{20}$ −18° (*c* 0.6, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.78 (d, 2 H, *J* 8.4 Hz, Ts), 7.54–7.22 (m, 17 H, Tr, Ts), 4.79 (s, 1 H, H-1), 4.36 (bs, 1 H, H-3), 4.28 (t, 1 H, $J_{4,5} = J_{4,5'} = 6.8$ Hz, H-4), 4.01 (d, 1 H, *J* −11.5 Hz, C*H*HOTs), 3.96 (d, 1 H, *J* −11.5, CH*H*OTs), 3.38–3.00 (m, 2 H, H-5,5′), 3.05 (s, 3 H, OMe), 2.41 (s, 3 H, Ts Me), 1.44 (s, 3 H, Me), 1.33 (s, 3 H, Me).

Anal. Calc. for $C_{36}H_{38}O_8$: C, 68.56; H, 6.07. Found: C, 68.56; H, 6.09.

Methyl 2,3-O-isopropylidene-2-C-methyl-5-O-trityl-β-D-ribofuranoside (**10**) *and methyl 2-C-hydroxymethyl-2,3-O-isopropylidene-5-O-trityl-β-D-ribofuranoside* (**11**). — $LiAlH_4$ (1.14 g, 30.0 mmol) was added to a solution of **9** (6.6 g, 10.5 mmol) in dry tetrahydrofuran (150 mL). The mixture was boiled under reflux and protected from moisture for 15 h and then cooled to 0°. Ethyl acetate (5 mL), water (1 mL), aqueous 15% NaOH (1 mL), and water (3 mL) were added consecutively to the stirred mixture and stirring was continued for 20 min at 20°. The precipitate was collected and washed with tetrahydrofuran (2 × 30 mL), and the combined

filtrate and washings were concentrated to dryness *in vacuo*. A solution of the residue in chloroform (100 mL) was washed with water (20 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was recrystallised from ethanol to give **10** (3.7 g, 77%), R_F 0.70 (solvent *A*), m.p. 134–134.5°, $[\alpha]_D^{20}$ −45° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.47–7.13 (m, 15 H, Tr), 4.67 (s, 1 H, H-1), 4.23 (t, 1 H, $J_{4,5} = J_{4,5'}$ = 6.8 Hz, H-4), 4.15 (s, 1 H, H-3), 3.25–3.00 (m, 2 H, H-5,5'), 3.06 (s, 3 H, OMe), 1.40 (s, 3 H, Me), 1.32 (s, 3 H, Me), 1.14 (s, 3 H, Me-2).

Anal. Calc. for $C_{29}H_{32}O_5$: C, 75.62; H, 7.01; Found: C, 75.80; H, 7.03.

Column chromatography on silica gel (100 g; solvent *B*) of the material in the mother liquors and crystallisation from dichloromethane–hexane gave **11** (0.3 g, 6%), R_F 0.30 (solvent *A*), m.p. 132–133°, $[\alpha]_D^{20}$ −34° (*c* 0.9, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.48–7.23 (m, 15 H, Tr), 4.90 (s, 1 H, H-1), 4.48 (d, $J_{3,4}$ 0.9 Hz, H-3), 4.37 (ddd, 1 H, $J_{4,3}$ 0.9, $J_{4,5}$ 6.5, $J_{4,5'}$ 8.1 Hz, H-4), 3.63 (dd, 1 H, $J_{2'a,OH}$ 7.1, $J_{2'a,2'b}$ −12.6 Hz, C*H*HOH), 3.52 (dd, 1 H, $J_{2'b,OH}$ 7.5, $J_{2'b,2'a}$ −12.6 Hz, CH*H*OH), 3.21 (dd, 1 H, $J_{5,4}$ 6.5, $J_{5,5'}$ −9.5 Hz, H-5), 3.18 (s, 3 H, OMe), 3.09 (dd, 1 H, $J_{5',4}$ 8.1, $J_{5',5}$ −9.5 Hz, H-5'), 2.18 (dd, 1 H, $J_{OH,2'a}$ 7.1, $J_{OH,2'b}$ 7.5 Hz, CH_2OH, exchangeable with D_2O), 1.50 (s, 3 H, Me), 1.41 (s, 3 H, Me).

Anal. Calc. for $C_{29}H_{32}O_6$: C, 73.09; H, 6.77. Found: C, 73.09; H, 6.98.

*Methyl 2,3-O-isopropylidene-2-C-methyl-β-*D*-ribofuranoside* (**12**). — A M solution of $SnCl_4$ in 1,2-dichloroethane (4 mL) was added to a solution of **10** (3.7 g, 8.04 mmol) in dry 1,2-dichloroethane (75 mL). After 5 min, chloroform (30 mL) and aqueous 10% $NaHCO_3$ (20 mL) were added, and the organic layer was separated, washed with water (10 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. Elution of the residue from a column of silica gel (100 g), using solvent *A*, gave **12**, isolated as an oil (1.6 g, 90%), R_f 0.45 (solvent *A*), $[\alpha]_D^{20}$ −86° (*c* 0.9, ethanol); lit.[11] $[\alpha]_D^{20}$ −84° (ethanol). N.m.r. data ($CDCl_3$): ^{1}H, δ 4.81 (s, 1 H, H-1), 4.43 (d, 1 H, $J_{3,4}$ 1.0 Hz, H-3), 4.28 (dt, 1 H, $J_{4,3}$ 1.0, $J_{4,5} = J_{4,5'}$ = 3.2 Hz, H-4), 3.67 (dd, 1 H, $J_{5,4}$ 3.2, $J_{5,5'}$ −12.0 Hz, H-5), 3.60 (dd, 1 H, $J_{5',4}$ 3.2, $J_{5',5}$ −12.0 Hz, H-5'), 3.44 (s, 3 H, OMe), 2.77 (bs, 1 H, OH, exchangeble with D_2O), 1.48 (s, 3 H, Me), 1.44 (s, 3 H, Me-2), 1.41 (s, 3 H, Me); ^{13}C, δ 112.6 (CMe_2), 111.2 (1-C), 92.1 (2-C), 88.1 (4-C), 87.6 (3-C), 64.0 (5-C), 55.9 (OMe), 28.2 (Me), 27.7 (Me), 19.8 (C–Me-2).

*Methyl 2-C-methyl-β-*D*-ribofuranoside* (**13**). — A solution of **12** (330 mg, 1.54 mmol) in aqueous 90% CF_3COOH (15 mL) was stored for 5 min, then toluene (15 mL) was added, and the mixture was concentrated to dryness. The residue was recrystallised from ethanol to yield **13** (220 mg, 82%), R_F 0.20 (solvent *D*), m.p. 111–111.5°, $[\alpha]_D^{20}$ −91° (*c* 0.2, ethanol); lit.[11] m.p. 109°, $[\alpha]_D^{20}$ −82.1° (ethanol). n.m.r. data [$(CD_3)_2SO$]: ^{1}H, δ 4.75 (d, 1 H, $J_{OH,3}$ 7.0 Hz, exchangeable with D_2O, HO-3), 4.50 (s, 1 H, exchangeable with D_2O, HO-2), 4.48 (t, 1 H, $J_{OH,5} = J_{OH,5'}$ = 5.5 Hz, exchangeable with D_2O, HO-5), 4.42 (s, 1 H, H-1), 3.80–3.30 (m, 4 H, H-3,4,5,5'), 3.25 (s, 3 H, OMe), 1.11 (s, 3 H, Me-2); ^{13}C (D_2O–CD_3OD), δ 109.8 (1-C), 82.9 (4-C), 79.0 (2-C), 75.3 (3-C), 63.6 (5-C), 55.8 (OMe), 18.6 (Me-2).

Methyl 2,3-O-isopropylidene-2-C-methyl-5-O-p-methylbenzoyl-β-D-ribofuranoside (**14**). — A solution of **12** (800 mg, 3.67 mmol) in dry pyridine (20 mL) was concentrated to dryness. To a solution of the residue in dry pyridine (50 mL) was added *p*-methylbenzoyl chloride (0.53 mL, 4.04 mmol), and the mixture was stored for 2 h at 20°. The usual work-up and elution of the product from a column of silica gel (100 g) with solvent *A* gave **14** (1.1 g, 89%), R_F 0.70 (solvent *A*), m.p. 55–56.5° (from CH_2Cl_2–hexane), $[\alpha]_D^{20}$ −47° (*c* 1.1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.97 (d, 2 H, *J* 8.3 Hz, *Bz*Me), 7.25 (d, 2 H, *J* 8.3 Hz, *Bz*Me), 4.86 (s, 1 H, H-1), 4.43–4.31 (m, 4 H, H-3,4,5,5′), 3.37 (s, 3 H, OMe), 2.42 (s, 3 H, Bz*Me*), 1.49 (s, 3 H, Me), 1.47 (s, 3 H, Me-2), 1.44 (s, 3 H, Me).

Anal. Calc. for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found: C, 64.03; H, 7.16.

Methyl 2-C-methyl-5-O-p-methylbenzoyl-β-D-ribofuranoside (**15**). — A solution of **14** (900 mg, 2.68 mmol) in aqueous 90% CF_3COOH (50 mL) was kept for 5 min at 20° and then concentrated to dryness, and toluene (2 × 30 mL) was evaporated from the residue. Elution of the residue from a column of silica gel (50 g) with solvent *B*, after washing with solvent *A*, gave **15** (750 mg, 95%), R_F 0.27 (solvent *B*), m.p. 92.5–93.5° (from CH_2Cl_2–hexane), $[\alpha]_D^{20}$ −57° (*c* 0.9, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.96 (d, 2 H, *J* 8.2 Hz, *Bz*Me), 7.23 (d, 2 H, *J* 8.2 Hz, *Bz*Me), 4.66 (s, 1 H, H-1), 4.53 (dd, 1 H, $J_{5,4}$ 3.6, $J_{5,5'}$ −11.8 Hz, H-5), 4.37 (dd, 1 H, $J_{5',4}$ 5.2, $J_{5,5'}$ −11.8 Hz, H-5′), 4.19 (ddd, 1 H, $J_{4,3}$ 7.3, $J_{4,5}$ 3.6, $J_{4,5'}$ 5.2 Hz, H-4), 4.02 (d, 1 H, $J_{3,4}$ 7.3 Hz, H-3), 3.33 (s, 3 H, OMe), 2.41 (s, 3 H, Bz*Me*), 1.32 (s, 3 H, Me-2).

Anal. Calc. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.91; H, 6.83.

Methyl 2,3-di-O-acetyl-2-C-methyl-5-O-p-methylbenzoyl-β-D-ribofuranoside (**16**). — A solution of **15** (750 mg, 2.5 mmol) in dry pyridine (20 mL) was concentrated to dryness and to a solution of the residue in dry pyridine (50 mL) was added Ac_2O (5 mL). The mixture was boiled under reflux in the absence of moisture for 2 h. Conventional work-up and elution of the product from a column of silica gel (100 g), using solvent *A*, gave **16** (800 mg, 83%), R_F 0.90 (solvent *B*), $[\alpha]_D^{20}$ +4° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.89 (d, 2 H, *J* 7.5 Hz, *Bz*Me), 7.18 (d, 2 H, *J* 7.5 Hz, *Bz*Me), 5.38 (d, 1 H, $J_{3,4}$ 7.0 Hz, H-3), 5.20 (s, 1 H, H-1), 4.63–4.03 (m, 3 H, H-4,5,5′), 3.38 (s, 3 H, OMe), 2.42 (s, 3 H, Bz*Me*), 2.07 (s, 6 H, 2 Ac), 1.61 (s, 3 H, Me-2).

Anal. Calc. for $C_{19}H_{24}O_8$: C, 59.99; H, 6.36. Found: C, 60.14; H, 6.51.

1,2,3-Tri-O-acetyl-2-C-methyl-5-O-p-methylbenzoyl-α,β-D-ribofuranose (*α,β*-**5**) *and 1,3-di-O-acetyl-2-C-methyl-5-O-p-methylbenzoyl-β-D-ribofuranose* (*β*-**4**). — Aqueous 96% H_2SO_4 (2.5 mL) was added, with cooling to +5°, to a solution of **16** (4.6 g, 12.1 mmol) in HOAc (40 mL) and Ac_2O (5 mL). The mixture was stored for 16 h at 20°, then diluted with chloroform (100 mL), washed successively with water (10 mL), aqueous 10% $NaHCO_3$ (2 × 30 mL) and water (2 × 10 mL), dried (Na_2SO_4), filtered, and concentrated to dryness. The residue was treated by either of two procedures.

(*a*) The residue was eluted from a column of silica gel with solvent *A* to afford, first, **α,β-5**, isolated as an oil (3.0 g, 61%). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.87 (d, 2 H, *J* 7.0 Hz, *Bz*Me), 7.17 (d, 2 H, *J* 7.0 Hz, *Bz*Me), 6.45 (s, 0.4 H, H-1β), 6.28 (s, 0.6 H, H-1α), 5.40 (d, 0.4 H, $J_{3,4}$ 7.3 Hz, H-3β), 5.04 (d, 0.6 H, $J_{3,4}$ 4.0 Hz, H-3α), 4.64–4.10 (m, 3 H, H-4,5,5′), 2.38 (s, 3 H, Bz*Me*), 2.10 (s, 1.2 H, Acβ), 2.08 (s, 1.2 H, Acβ), 2.06 (s, 3.6 H, 2 Acα), 2.04 (s, 1.8 H, Acα), 1.98 (s, 1.2 H, Acβ), 1.65 (s, 1.8 H, Me-2α), 1.60 (s, 1.2 H, Me-2β); α,β-ratio 3:2.

Anal. Calc. for $C_{20}H_{24}O_9$: C, 58.82; H, 5.92. Found: C, 59.03; H, 6.05.

Eluted second was an oily mixture (0.7 g, 14%) of triacetate **α-5** and diacetate **α-4**. ^{1}H-N.m.r. data ($CDCl_3$): δ 7.87 (d, 2 H, *J* 7.0 Hz, *Bz*Me), 7.17 (d, 2 H, *J* 7.0 Hz, *Bz*Me), 6.28 (s, 0.5 H, H-1 of **5**α), 5.92 (s, 0.5 H, H-1 of **4**α), 5.04 (d, 0.5 H, $J_{3,4}$ 4.0 Hz, H-3 of **5**α), 4.82 (d, 0.5 H, $J_{3,4}$ 4.0 Hz, H-3 of **4**α), 4.64–4.12 (m, 3 H, H-4,5,5′), 2.38 (s, 3 H, Bz*Me*), 2.18 (s, 3 H, 2 Ac of **4**α), 2.08 (s, 3 H, 2 Ac of **5**α), 2.04 (s, 1.5 H, Ac of **5**α), 1.65 (s, 1.5 H, Me-2 of **5**α), 1.50 (s, 1.5 H, Me-2 of **4**α); the ratio of **4**α:**5**α was 1:1.

Eluted third was **β-4** (0.4 g, 7%), identical with that prepared from **3**.

(*b*) A solution of the residue in dry pyridine (30 mL) was concentrated to dryness and then dissolved in dry pyridine (50 mL), Ac_2O (5 mL) was added, and the mixture was boiled under reflux for 2 h in the absence of moisture and then cooled. Conventional work-up and elution of the product from a column of silica gel, using solvent *A*, gave **5** (4.3 g, 90%) with an α,β-ratio of 1:1.

*1-(2,3-Di-*O*-acetyl-2-*C*-methyl-5-*O*-*p*-methylbenzoyl-β-*D*-ribofuranosyl)uracil* (**17**). — A suspension of dry uracil (400 mg, 3.55 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 × 30 mL) was evaporated from the residue. A solution of **5** (900 mg, 2.2 mmol) in dry 1,2-dichloroethane (40 mL) and M $CF_3SO_2SiMe_3$ in 1,2-dichloroethane (4 mL) were added to the residue, and the mixture was stored for 16 h at 20°. T.l.c. (solvent *B*) then revealed that reaction was incomplete. More M $CF_3SO_2OSiMe_3$ solution (1.5 mL) was added and the mixture was stored for ~6 days at 20° until **5** had disappeared completely. The mixture was then diluted with chloroform (30 mL), aqueous 10% $NaHCO_3$ (10 mL) was added, the mixture was stirred for 20 min at 20°, and the organic layer was separated, washed with 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), which had been washed with solvent *A* to afford **17**, isolated as a foam (750 mg, 74%), R_F 0.48 (solvent *B*), $[\alpha]_D^{20}$ +23° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 8.14 (bs, 1 H, NH), 7.84 (d, 2 H, *J* 7.0 Hz, *Bz*Me), 7.34 (d, 1 H, $J_{6,5}$ 8.0 Hz, H-6), 7.20 (d, 2 H, *J* 7.0 Hz, *Bz*Me), 6.21 (s, 1 H, H-1′), 5.54 (dd, 1 H, $J_{NH,5}$ 2.0, $J_{5,6}$ 8.0 Hz, H-5), 5.29 (d, 1 H, $J_{3',4'}$ 6.5 Hz, H-3′), 4.70–4.30 (m, 3 H, H-4′,5′,5″), 2.40 (s, 3 H, Bz*Me*), 2.09 (s, 6 H, 2 Ac), 1.53 (s, 3 H, Me-2′).

Anal. Calc. for $C_{22}H_{24}N_2O_9$: C, 57.39; H, 5.25; N, 6.08. Found: C, 57.54; H, 5.34; N, 6.19.

*1-(2,3-Di-*O*-acetyl-2-C-methyl-5-*O*-p-methylbenzoyl-β-*D*-ribofuranosyl)-*N*⁴-benzoylcytosine* (**18**). — The nucleoside **18** (55%), prepared in the same way as **17** starting from N^4-benzoylcytosine and **5**, had R_F 0.55 (solvent *B*), m.p. 213–214° (from ethanol), $[\alpha]_D^{20}$ +56° (*c* 1, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 9.02 (bs, 1 H, NH), 7.92–7.12 (m, 11 H, *Bz*Me, Bz, H-5,6), 6.46 (s, 1 H, H-1′), 5.32 (d, 1 H, $J_{3',4'}$ 6.2 Hz, H-3′), 4.72–4.40 (m, 3 H, H-4′,5′,5″), 2.42 (s, 3 H, Bz*Me*), 2.12 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 1.50 (s, 3 H, Me-2′).

Anal. Calc. for $C_{29}H_{29}N_3O_9$: C, 61.80; H, 5.19; N, 7.46. Found: C, 61.92; H, 5.28; N, 7.53.

*9-(2,3-Di-*O*-acetyl-2-C-methyl-5-*O*-p-methylbenzoyl-β-*D*-ribofuranosyl)-*N*⁶-benzoyladenine* (**19**). — The nucleoside **19** (72%), prepared in the same way as **17** starting from N^6-benzoyladenine and **5** at room temperature for 7 days, and isolated as a foam, had R_F 0.65 (solvent *B*), $[\alpha]_D^{20}$ −11° (*c* 0.7, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 9.08 (bs, 1 H, NH), 8.70 (s, 1 H, H-8), 8.08 (s, 1 H, H-2), 8.02–7.40 (m, 7 H, Bz, *Bz*Me), 7.18 (d, 2 H, *J* 7.5 Hz, *Bz*Me), 6.50 (s, 1 H, H-1′), 5.84 (d, 1 H, $J_{3',4'}$ 6.5 Hz, H-3′), 4.73 (m, 2 H, H-5′,5″), 4.45 (m, 1 H, H-4′), 2.38 (s, 3 H, Bz*Me*), 2.15 (s, 6 H, 2 Ac), 1.42 (s, 3 H, Me-2).

Anal. Calc. for $C_{30}H_{29}N_5O_8$: C, 66.04; H, 5.36; N, 5.14. Found: C, 66.34; H, 5.47; N, 5.32.

1-(2-C-Methyl-β-D-ribofuranosyl)uracil (**20**). — A solution of **17** (200 mg, 0.43 mmol) in methanol (12 mL) semi-saturated with ammonia at 0° was kept for 48 h at 20° and then concentrated *in vacuo* to dryness. The residue was partitioned between chloroform (10 mL) and water (20 mL), and the organic layer was washed with water (2 × 10 mL). The combined aqueous extracts were washed with chloroform (10 mL) and concentrated *in vacuo* to dryness, and the residue was recrystallised from water to yield **20** (80 mg, 72%), R_F 0.68 (solvent *F*), m.p. 118–119° (softening at 101°), $[\alpha]_D^{20}$ +82° (*c* 0.7, water); $\lambda_{max}^{pH\ 1-7}$ 262 nm (ε 10000), $\lambda_{max}^{pH\ 13}$ 262 nm (ε 7660). ^{1}H-N.m.r. data (D_2O): δ 7.60 (d, 1 H, $J_{6,5}$ 7.8 Hz, H-6), 5.80 (s, 1 H, H-1′), 5.76 (d, 1 H, $J_{5,6}$ 7.8 Hz, H-5), 3.76 (m, 2 H, H-3′,4′), 3.59 (m, 2 H, H-5′,5″), 1.14 (s, 3 H, Me-2′).

Anal. Calc. for $C_{10}H_{14}N_2O_6 \cdot 2\ H_2O$: C, 40.81; H, 6.17; N, 9.52. Found: C, 40.63; H, 6.14; N, 9.23.

1-(2-C-Methyl-β-D-ribofuranosyl)cytosine (**21**). — Prepared from **18** as described above, **21** (75%) had R_F 0.58 (solvent *F*), m.p. 235–238°, $[\alpha]_D^{20}$ +128° (*c* 1, water); lit.[9] m.p. 243–245°, $[\alpha]_D^{20}$ +132° (water); $\lambda_{max}^{pH\ 1}$ 281 nm (ε 12500), $\lambda_{max}^{pH\ 7-13}$ 273 nm (ε 8800). ^{1}H-N.m.r. data (D_2O): δ 7.60 (d, 1 H, $J_{6,5}$ 7.6 Hz, H-6), 5.80 (s, 1 H, H-1′), 5.78 (d, 1 H, $J_{5,6}$ 7.6 Hz, H-5), 3.77 (m, 2 H, H-3′,4′), 3.60 (m, 2 H, H-5′,5″), 1.14 (s, 3 H, Me-2′).

Anal. Calc. for $C_{10}H_{15}N_3O_5$: C, 46.69; H, 5.88; N, 16.33. Found: C, 46.64; H, 5.81; N, 16.29.

9-(2-C-Methyl-β-D-ribofuranosyl)adenine (**22**). — Prepared from **19** as described above, **22** (76%) had R_F 0.71 (solvent *F*), m.p. 248–250°, $[\alpha]_D^{20}$ −18° (*c* 0.8, water); lit.[8] m.p. 256–258°, $[\alpha]_D^{20}$ −21° (water); $\lambda_{max}^{pH\ 1}$ 258 nm (ε 14800), $\lambda_{max}^{pH\ 7-13}$ 260

nm (ε 15000). ^{1}H-N.m.r. data (C_5D_5N): δ 9.06 (s, 1 H, H-8), 8.57 (s, 1 H, H-2), 8.00 (bs, 2 H, NH_2), 6.75 (s, 1 H, H-1'), 4.93 (d, 1 H, $J_{3',4'}$ 8.5 Hz. H-3'), 4.62 (ddd, 1 H, $J_{4',3'}$ 8.5, $J_{4',5'}$ 2.2, $J_{4',5''}$ 2.4 Hz, H-4'), 4.34 (dd, 1 H, $J_{5',4'}$ 2.2, $J_{5',5''}$ −12.2 Hz, H-5'), 4.29 (dd, 1 H, $J_{5'',4'}$ 2.4, $J_{5'',5'}$ −12.2 Hz, H-5''), 1.22 (s, 3 H, Me-2').

Anal. Calc. for $C_{11}H_{15}N_5O_4$: C, 46.97; H, 5.38; N, 24.90. Found: C, 46.83; H, 5.27; N, 24.73.

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