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SYNTHESIS OF AN ANALOGUE OF THE POLYOXINS

X-RAY STRUCTURE OF STARTING CARBOHYDRATE AND ACETAL MIGRATION ACCOMPANYING ACETOLYSIS

A. J. BRINK†, J. COETZER‡, O. G. DE VILLIERS†, R. H. HALL†, A. JORDAAN*† and G. J. KRUGER‡

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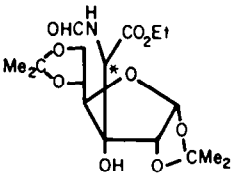
Abstract—An analogue of the polyoxins has been prepared from 1,5 - di - O - acetyl - 3 - C - (*R*) - ethoxycarbonylmethyl - 5(*R*),1′(*R*) - N - formylepimino - 2,3 - O - isopropylidene - β - D - ribofuranose (**13**). The structure of **13** was determined by X-ray analysis. Intramolecular acetal migrations were observed during acetolysis under acid conditions.

Interest in the polyoxins[1] has led to the preparation of several carbon–carbon linked sugar α-amino-acids[2] as well as the nucleoside amino-acid, 1-(5-amino-5-deoxy-β-D-allofuranosyluronic acid) uracil[3] which is the basic skeleton of the polyoxins. We report the preparation of a novel nucleoside amino-acid derivative, 1 - (5 - O - acetyl - 3 - *C* - (*R*) - ethoxycarbonylmethyl - 5(*R*),1′(*R*) - *N* - formylepimino - 2,3 - O - isopropylidene - β - D - ribofuranosyl)uracil (**6**) where the amino-acid moiety is linked to C-3′ of the nucleoside. During the preparation an acetal migration, which occurred during the acetolysis of a 1,2-O-isopropylidene compound, was observed. This migration during acetolysis was investigated using other compounds with similar configurational properties.

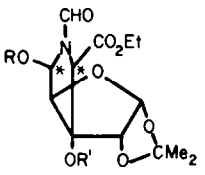
Removal, by mild acid hydrolysis, of the 5,6 - O - isopropylidene group of 3 - C - (*R*) - ethoxycarbonyl-(formylamino)methyl - 1,2:5,6 - di - O - isopropylidene - α

†National Chemical Research Laboratory, Council for Scientific and Industrial Research, P.O. Box 395, Pretoria 0001, Republic of South Africa.

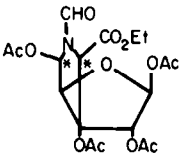
‡National Physical Research Laboratory, Council for Scientific and Industrial Research, P.O. Box 395, Pretoria 0001, Republic of South Africa.



1



2 R = R′ = H
3 R = Ac, R′ = H
4 R = R′ = Ac



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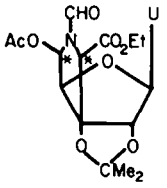
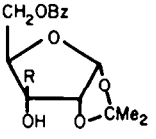
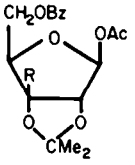


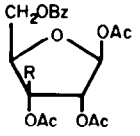
U = uracil
6



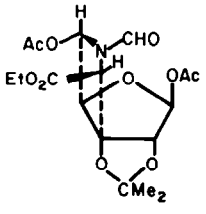
7 R = CH_2NO_2
8 R = CH_3



9 R = CH_2NO_2
10 R = CH_3



11 R = CH_2NO_2
12 R = CH_3



13

* Denotes *R* stereochemistry

- D - allofuranose (**1**)[4] gave the 5,6-glycol which with sodium metaperiodate gave an epimeric mixture of the carbinolamides (**2**). During column chromatography this mixture was converted into a single epimer which, after recrystallization, was obtained in 74% yield. The NMR spectrum of the epimer with a singlet at τ 4·60 (H-5) indicated that it was the 5 - *R* - epimer,3 - C - (*R*) - ethoxycarbonylmethyl - 5 - (*R*),1'(*R*) - N - formylepimino - 1,2 - O - isopropylidene - α - D - ribofuranose (**2**): a Dreiding model of this compound showed that the H(4)-C(4)-C(5)-H(5) dihedral angle is approximately 120°, whereas the 5 - *S* - isomer would have a dihedral angle of approximately 0°. Attempts to open the epimino-ring with sodium borohydride were unsuccessful.

Acetolysis of **2** gave a crystalline product. The NMR spectrum of this product showed that the H-5 signal remained a singlet whereas the H-1 signal had moved downfield and had changed from a doublet to a singlet. The presence of one isopropylidene and two acetyl groups was also indicated. These data[5] and the microanalytical figures indicated that the product was a 2,3 - O - isopropylidene - β - D - ribofuranose and not the tetra acetate (**5**). X-ray analysis (see later) confirmed that an acetal migration had taken place and that the product was 1,5 - di - O - acetyl - 3 - C - (*R*) - ethoxycarbonylmethyl - 5(*R*),1'(*R*) - N - formylepimino - 2,3 - O - isopropylidene - β - D - ribofuranose (**13**).

Reaction of **13** with bis(trimethylsilyl)uracil gave a protected nucleoside in high yield which, because of the $J_{1',2'}$ coupling of 2 Hz, was assumed[6] to be the β-nucleoside (**6**). Unfortunately it has not proved possible to remove the protecting groups from **6** without also hydrolysing the N-glycosyl linkage. To circumvent these difficulties it was decided to prepare the tetraacetate (**5**) by another route, and to use it for the preparation of an uracil nucleoside derivative with readily removable blocking groups.

Acetylation of **2** with acetic anhydride-pyridine gave the 5-O-acetyl compound (**3**), whereas with acid catalysis, the 3,5-di-O-acetyl compound (**4**) was obtained. Acetolysis of **4**, gave the tetra acetate (**5**). With compounds **3**–**5** the 5-(*R*)-stereochemistry is assumed from the H-5 singlets in their NMR spectra whereas the H-1 singlet of compound **5** shows[5,6] that it is the β-anomer.

Attempts to react **5** with bis(trimethylsilyl)uracil under the same conditions employed for the preparation of **6** gave unchanged starting material, while with other bases, using a variety of reaction conditions, intractable mixtures of products were obtained. These difficulties probably arise from the presence of two "anomeric" sites in **5** as C-5 can be regarded as the anomeric position of an amino-sugar having a nitrogen atom in its 5-membered ring.

Acetal migration accompanying acetolysis. The acid catalysed migration of the 1,2 - O - isopropylidene group of sugar derivatives with the 3-OH group unprotected and orientated *cis* to the 1,2 - O - isopropylidene group, to give a 2,3 - O - isopropylidene compound, is well known in acetone[7] and methanol[8,9] solutions. A 2,3-O - isopropylidene derivative is also formed[10] as an intermediate during the hydrolysis of 1,6 - anhydro - 3,4 - O - isopropylidene - β - D - talopyranose in 80% aqueous acetic acid. However such migrations under acetolysis conditions have not been reported, and the formation of compound **13** from **2** was unexpected. Consequently the acetolysis of two branched-chain compounds with similar geometry to that of **2** was studied.

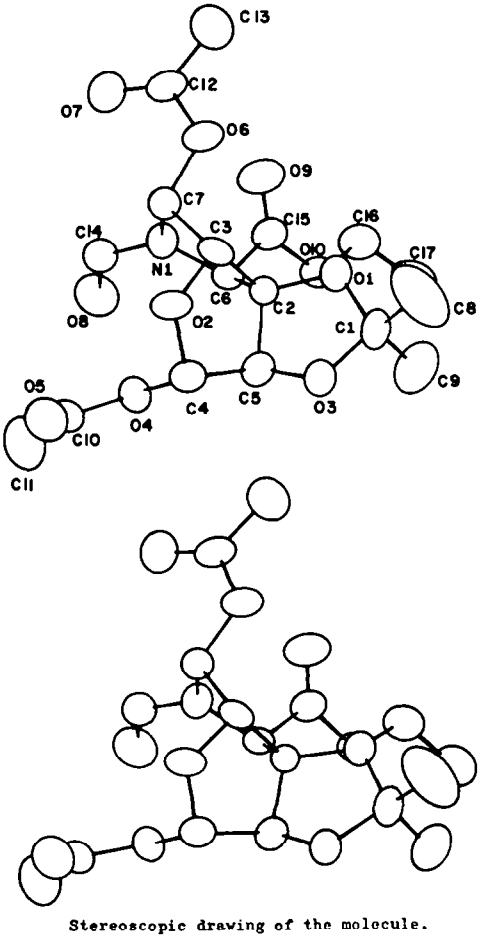
Although the workup of the product mixture after the acetolysis of the nitro-sugar (**7**) was complicated by the decomposition[11] of the tri-O-acetate (**11**) during chromatography, the crystalline 2,3 - O - isopropylidene derivative (**9**) was obtained in 36% yield. The NMR spectrum of the mixture before attempts at separation clearly indicated the presence of the tri-O-acetate (**11**) (Experimental).

Acetolysis of the branched-chain compound (**8**)[9] similarly gave a mixture of the tri-O-acetate (**12**) (74%) (mainly β-anomer) and the 2,3 - O - isopropylidene derivative (**10**) (8%). These results indicate that such migrations occur readily under acetolysis conditions but that the yields vary over a wide range.

X-ray analysis of compound (**13**)†. A complete single

Molecular Formula	$C_{17}H_{23}O_{10}N$.
Orthorhombic	$P2_12_12_1$
a	19·36 ± 0·02 Å
b	10·14 ± 0·01
c	10·05 ± 0·01
D_m	1·36 g cm^{-3}
D_c	1·35 g cm^{-3}
M	401·4
Z	4

Crystal data



Stereoscopic drawing of the molecule.

†The final atomic parameters are available on request from Dr. J. Coetzer or Dr. G. J. Kruger.

crystal X-ray analysis of **13** was carried out on material obtained from a methanol solution. The crystals were found to be orthorhombic with space group $P2_12_12_1$.

The structure was solved by direct methods.[12] All the atoms, including the hydrogens, were located on a series of Fourier and difference Fourier maps. Refinement of the trial structure was done by full-matrix least-squares methods. The Figure shows a stereoscopic drawing[13] of the molecule and the atomic numbering used in the X-ray analysis.

All the bond lengths are normal, the mean sp^3C–sp^3C, sp^3C–sp^3O and C=O bond lengths being 1·53, 1·44 and 1·18 Å, respectively.

EXPERIMENTAL

TLC and column chromatography were performed with silica gel (Merck GF_{254}). M.ps were determined with a hot-stage apparatus. IR spectra were recorded with a Perkin–Elmer 257 spectrophotometer and optical rotations were measured for solns in chloroform with a Bendix-NPL Automic Polarimeter type 143 (*c* 1·0 ± 0·3). NMR spectra were recorded with a Varian HA-100 instrument with tetramethylsilane as internal standard for $CDCl_3$ solns and mass spectra with an A.E.I. MS9 spectrometer by direct insertion.

3 - C - (*R*) - *Ethoxycarbonylmethyl* - 5 - (*R*),1′(*R*) - N - *formylepimino* - 1,2 - O - *isopropylidene* - α - D - *ribofuranose* (**2**). Compound **1** (10 g, 25·7 mmole in aqueous AcOH (75%, 250 ml) was kept at 75° until all the starting material had reacted (TLC). The solvent was removed *in vacuo* to give an oil (*ca.* 10 g) which was dissolved in aqueous EtOH (96%, 200 ml). An aqueous soln of $NaIO_4$ (6·42 g, 30 mmole, 100 ml) was added dropwise with stirring and the mixture was kept at 25° for 18 hr. Ethylene glycol (1 ml) was then added and the solvents removed *in vacuo*. The residue was stirred with chloroform (300 ml), the mixture was filtered, and the filtrate was dried ($MgSO_4$). Filtration and evaporation gave an oil (*ca.* 8 g) which contained two main components (TLC). Chromatography with EtOAc as eluant gave a solid mixture of two compounds (TLC). It was clear that the compound with lower R_f was isomerising on the column to the other compound. Rechromatography of the mixture gave a solid which crystallized from acetone-hexane as pure compound **2** (5·99 g, 73·5%), m.p. 159–161°. $[\alpha]_D^{22}$ + 40°; ν_{max}($CHCl_3$) 3540 (OH), 1745 (ester), and 1680 cm^{-1} (amide); *m/e* 302 (M^+–CH_3); NMR: τ 1·61 (1 H, s, CHO), 4·14 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 4·60 (1 H, s, H-5), 5·34 (1 H, d, $J_{2,1}$ 4 Hz, H-2), 5·53 and 5·69 (2 H, 2 s, H-4,1′), 5·74 (2 H, q, J 7 Hz, OCH_2CH_3), 8·41 (3 H, s, Me), 8·60 (3 H, s, Me) and 8·70 (3 H, t, J 7 Hz, OCH_2CH_3). (Found: C, 48·9; H, 6·0; N, 4·4. $C_{13}H_{19}NO_8$ requires: C, 49·2; H, 6·0; N, 4·4%).

1,5 - O - *Acetyl* - 3 - C - (*R*) - *ethoxycarbonylmethyl* - 5(*R*),1′(*R*) - N - *formylepimino* - 2,3 - O - *isopropylidene* - β - D - *ribofuranose* (**13**). Compound **2** (2 g, 6·3 mmole) was reacted over 3 days at 0° with a mixture of AcOH (40 ml), Ac_2O (4 ml), and conc. H_2SO_4 (1·2 ml) and then added to ice-water (250 ml). The aqueous mixture was extracted with chloroform and the combined extracts washed with water, sat. $NaHCO_3$ aq until free from acid, and finally water. The organic soln was dried ($MgSO_4$) and the solvent removed *in vacuo* to give an oil (*ca.* 2 g) which was chromatographed with chloroform-ethanol (99 : 1) as eluant to give **13** as a syrup which crystallized from acetone-hexane as needles, (1·78, 70%), m.p. 89–91°. $[\alpha]_D^{22}$ *ca.* 0°; ν_{max} ($CHCl_3$) 1745 (ester) and 1685 cm^{-1} (amide); *m/e* 385 (M^+–CH_3); NMR: τ 1·44 (1 H, s, CHO), 3·70 and 3·89 (2 H, 2 s, H-1,5), 4·88 (1 H, S, H-2), 5·37 and 5·46 (2 H, 2 s, H-4,1′), 5·78 (2 H, q, J 7 Hz, OCH_2CH_3), 7·86 (3 H, s, OAc), 8·00 (3 H, s, OAc), 8·48 (3 H, s, Me), 8·58 (3 H, s, Me), 8·72 (3 H, t, J 7 Hz, OCH_2CH_3). (Found: C, 50·8; H, 5·7; N, 3·3. $C_{17}H_{23}NO_{10}$ requires: C, 50·9; H, 5·8; N, 3·5%).

1(5 - O - *Acetyl* - 3 - C - (*R*) - *ethoxycarbonylmethyl* - 5(*R*),1′(*R*) - N - *formylepimino* - 2,3 - O - *isopropylidene* - β - D - *ribofuranosyl*)*uracil* (**6**). Bis(trimethylsilyl)uracil (550 mg, 2·15 mmole) and $SnCl_4$ (0·3 ml) were added to a soln of **3** (445 mg, 1·1 mmole) in 1,2 - dichloroethane (50 ml). The mixture was stirred under N_2 at 25° for 24 hr, and poured into sat, $NaHCO_3$aq (100 ml). The mixture was extracted with EtOAc (4 × 30 ml), the combined extracts dried ($MgSO_4$), filtered and removed *in vacuo* to give a yellow oil (492 mg) which was purified by chromatography with chloroform–ethanol 9 : 1 as eluant to give **6** as an oil (360 mg, 72%). $[\alpha]_D^{23}$ + 67°; ν_{max} ($CHCl_3$) 1725 (ester) and 1660 cm^{-1} (amide); NMR: τ 1·56 (1 H, s, CHO), 2·71 (1 H, d, $J_{5,6}$ 8 Hz, H-6), 3·49 (1 H, d, $J_{1',2'}$ 2 Hz, H-1′), 3·62 (1 H, s, H-5′), 4·26 (1 H, d, $J_{5,6}$ 8 Hz, H-5), 4·78 (1 H, d, $J_{2',1'}$ 2 Hz, H-2′), 4·97 and 5·40 (2 H, 2 s, H-4′,1″), 5·80 (2 H, m, OCH_2CH_3), 7·94 (3 H, s, OAc), 8·48 (3 H, s, Me), 8·51 (3 H, s, Me), 8·72 (3 H, t, J 7 Hz, OCH_2CH_3). (Found: *m/e* 438·114. $C_{18}H_{20}N_4O_{11}$ requires: M^+–CH_3, 438·115).

5 - O - *Acetyl* - 3 - C - (*R*) - *ethoxycarbonylmethyl* - 5(*R*),1′(*R*) - N - *formylepimino* - 1,2 - O - *isopropylidene* - α - D - *ribofuranose* (**3**). Compound **2** (317 mg, 1 mmole) was dissolved in a mixture of Ac_2O (0·5 ml) and pyridine (2 ml) and the solution left at 25° for 20 hr before it was poured into ice-water (20 ml) and extracted with chloroform (3 × 10 ml). The combined extracts were washed with cold IN HCl (20 ml), water (50 ml), and sat $NaHCO_3$aq until the soln was acid-free. The soln was then dried ($MgSO_4$) and the solvent removed *in vacuo* to give **3** as an oil which crystallised from acetone-hexane as needles (291 mg, 81%) m.p. 178–180°. $[\alpha]_D^{22}$ + 106°; ν_{max} ($CHCl_3$) 3550 (OH), 1745 (acetate), and 1690 cm^{-1} (amide), *m/e* 344 (M^+–CH_3); NMR: τ 1·42 (1 H, s, CHO), 3·76 (1 H, s, H-5), 4·09 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 5·28 (1 H, d, $J_{2,1}$ 4 Hz, H-2), 5·53 and 5·64 (2 H, 2 s, H-4,1′), 5·72 (2 H, q, J 7 Hz, OCH_2CH_3), 6·72 (1 H, s, disappears on addition of D_2O, OH), 7·74 (3 H, s, OAc), 8·41 (3 H, s, Me), 8·59 (3 H, s, Me), 8·69 (3 H, t, J 7 Hz, OCH_2CH_3). (Found: C, 50·4; H, 6·0; N, 4·0. $C_{15}H_{21}NO_9$ requires: C, 50·1; H, 5·9; N, 3·9%).

3,5 - *Di* - O - *acetyl* - 3 - C - (*R*) - *ethoxycarbonylmethyl* - 5(*R*),1′(*R*) - N - *formylepimino* - 1,2 - O - *isopropylidene* - α - D - *ribofuranose* (**4**). Compound **2**, (3·17 g, 10 mmole) was dissolved in Ac_2O (60 ml) containing *p*-toluenesulphonic acid (600 mg) and the mixture kept at 25° for 18 hr and poured into cold, sat., $NaHCO_3$aq (1·5 l). The mixture was stirred for 30 min and extracted with chloroform (3 × 150 ml). The combined extracts were dried ($MgSO_4$), filtered, and the solvent removed *in vacuo* to give **4** as an oil (3·62 g) which crystallized from acetone-hexane as needles (3·11 g, 82%), m.p. 148–150°. $[\alpha]_D^{22}$ + 122°; ν_{max}($CHCl_3$) 1745 (acetate) and 1690 cm^{-1} (amide); *m/e* 386 (M^+–CH_3); NMR: τ 1·42 (1 H, s, CHO), 3·76 (1 H, s, H-5), 4·11 (1 H, d, $J_{1,2}$ 4 Hz, H-1), 4·72 (1 H, d, $J_{2,1}$ 4 Hz, H-2), 5·28 and 5·62 (2 H, 2 s, H-4, 1′), 5·86 (2 H, m, OCH_2CH_3), 7·83 (3 H, s, OAc), 7·90 (3 H, s, OAc), 8·42 (3 H, s, Me), 8·63 (3 H, s, Me) and 8·70 (3 H, t, J 7 Hz, OCH_2CH_3). (Found: C, 50·7; H, 5·9; N, 3·6. $C_{17}H_{23}NO_{10}$ requires: C, 50·9; H, 5·8; N, 3·5%).

1,2,3,5 - *Tetra* - O - *acetyl* - 3 - C - (*R*) - *ethoxycarbonylmethyl* - 5(*R*),1′(*R*) - N - *formylepimino* - β - D - *ribofuranose* (**5**). Compound (**4**) (2·80 g, 7 mmole) was acetolysed as described for compound (**2**). Similar work up gave an oil which was chromatographed with chloroform-ethanol (95 : 5) as eluant to give **5** as a homogeneous oil (2·65 g, 85%). $[\alpha]_D^{23}$ + 20°; ν_{max}($CHCl_3$) 1745 (acetate) and 1690 cm^{-1} (amide), *m/e* 386 (M^+–CH_3CO_2); NMR: τ 1·44 (1 H, s, CHO), 3·78 and 3·85 (2 H, 2s, H-1,5), 4·18 (1 H, s, H-2), 4·76 and 5·11 (2 H, 2s, H-4,1′), 5·86 (2 H, m, OCH_2CH_3), 7·79 (3 H, s, OAc), 7·83 (3 H, s, OAc), 7·91 (3 H, s, OAc), 7·95 (3 H, s, OAc), and 8·71 (3 H, t, OCH_2CH_3) (Found: *m/e* 386·109. $C_{16}H_{20}NO_{10}$ requires M^+–CH_3CO_2, 386·108).

5 - O - *Benzoyl* - 1,2 - O - *isopropylidene* - 3 - C - *nitromethyl* - α - D - *ribofuranose* (**7**). NaH (50% dispersion in oil, 0·6 g, 12·5 mmole) was added in portions to dry nitromethane (30 ml) at − 25° with stirring. The temp. of the mixture was allowed to rise slowly to 25° by which time all the hydride had reacted and the mixture was again cooled to − 25°. A soln of 5 - O - benzoyl - 1,2 - O - isopropylidene - α - D - *erythro* - pentos - 3 - ulose[9] (2·92 g, 10 mmole) in dry nitromethane (10 ml) at − 25° was added to the suspension and the mixture was stirred at 25° for 1 hr, neutralized with AcOH and the solvent removed *in vacuo*. Water (100 ml) was added to the residue, and the mixture extracted with chloroform (2 × 50 ml). The combined extracts were washed (sat. $NaHCO_3$aq, water), dried ($MgSO_4$), and the solvent removed *in vacuo* to give **7** which crystallized from EtOAc–hexane, as needles (2·86 g, 81%), m.p. 166–167°. $[\alpha]_D^{22}$ + 27°; ν_{max} ($CHCl_3$) 3530 (OH), 1720(CO), 1560 cm^{-1}(NO_2); *m/e* 338 (M^+–CH_3); NMR: τ 1·92–2·68 (5 H, m,

Ph), 4·06 (1 H, d, $J_{1,2}$ 3·5 Hz, H-1), 5·18–5·80 (6 H, m, H-2, 4,5, 5', CH_2), 6·68 (1 H, s, lost on addition of D_2O, OH), 8·38 (3 H, s, Me), and 8·58 (3 H, s, Me). (Found: C, 54·4; H, 5·2; N, 3·9. $C_{16}H_{19}NO_8$ requires: C, 54·4; H, 5·4; N, 4·0%).

1 - O - *Acetyl* - 5 - O - *benzoyl* - 2,3 - O - *isopropylidene* - 3 - C - *nitromethyl* - β - D - *ribofuranose* (**9**). Compound **7** (1 g, 2·83 mmole) was acetolysed as described for **2**. Similar work up gave an oil which slowly crystallized but consisted of two major components (TLC). Fractional crystallization from ethyl acetate-hexane gave **9** as needles (89 mg, 7%), m.p. 129–130°. $[\alpha]_D^{22} - 64°$; ν_{max} ($CHCl_3$) 1740 and 1720 (CO), 1560 cm^{-1} (NO_2); *m/e* 380 (M^+–CH_3); NMR: τ 1·90–2·61 (5 H, m, Ph), 3·74 (1 H, s, H-1), 4·89–5·61 (6 H, m, H-2,4,5,5', CH_2), 8.08 (3 H, s, OAc), 8.43 (3 H, s, CH_3) and 8·56 (3 H, s, CH_3). (Found: C, 54·7; H, 5·1; N, 3·5. $C_{18}H_{21}NO_9$ requires: C, 54·7; H, 5·4; N; 3·5%).

Chromatography, with ethyl acetate-hexane (1 : 1) as eluant, of the residue obtained on evaporation of the mother liquors from the fractional crystallization gave more **9** (286 mg, 23%), as well as a mixture from which a further crop of **9** was obtained by fractional crystallization (75 mg, 6%) (total yield of **9**: 36%). The other major compound decomposed during chromatography, but the NMR spectrum of the mixture obtained on acetolysis of **7** showed that it was **11**. NMR: (Signals additional to those of **9**) τ 3·77 (s, H-1), 7·84 (s, OAc), and 7·88 (s, 2 x OAc).

1,2,3 - *Tri* - O - *acetyl* - 5 - O - *benzoyl* - 3 - C - *methyl* - α,β - D - *ribofuranose* (**12**) *and* 1 - O - *acetyl* - 5 - O - *benzoyl* - 2,3 - O - *isopropylidene* - 3 - C - *methyl* - β - D - *ribofuranose* (**10**). 5 - O - Benzoyl - 1,2 - O - isopropylidene - 3 - C - methyl - α - D - ribofuranose[9] (1 g, 3·24 mmole) was acetolysed as described for **2**. Similar work up gave an oil containing two main components (TLC). Chromatography with ethyl acetate-hexane (1 : 2) as eluant gave **10** as a syrup (95 mg, 8%). $[\alpha]_D^{22} - 22°$; ν_{max} ($CHCl_3$) 1720 and 1740 cm^{-1} (CO); *m/e* 335 (M^+–CH_3); NMR: τ 1·90–2·62 (5 H, m, Ph), 3·81 (1 H, s. H-1), 5·36–5·77 (4 H, m, H-2, 4, 5, 5'), 7·99 (3 H, s, OAc), 8·42 (3 H, s, CH_3), 8·50 (3 H, s, CH_3), and 8·57 (3 H, s, CH_3). (Found: *m/e* 335·112. $C_{17}H_{19}O_7$ requires: M^+–CH_3, 335·113).

Further elution gave **12** as a syrup (936 mg, 73%); ν_{max} ($CHCl_3$) 1710 and 1740 cm^{-1} (CO); *m/e* 351 (M^+–CH_3CO) NMR: τ 1·90–2·61 (5 H, m, Ph), 3·62 (1 H, d, $J_{1,2}$ 4 Hz, α H-1), 3·89 (1 H, d, $J_{1,2}$ 1 Hz, β H-1), 4·41 (1 H, d, $J_{2,1}$ 1 Hz, β H-2), 4·50 (1 H, d, $J_{2,1}$ 4 Hz, α H_2), 5·14–5·62 (3 H, m, H-4, 5, 5'), 7·87 (3 H, s, OAc), 7·90 (3 H, s, OAc), 7·96 (3 H, s, OAc), 8·34 (3 H, s, α Me), 8·43 (3 H, s, β Me) (In mixture α : β = *ca.* 1:4). (Found: *m/e* 355·112. $C_{17}H_{19}O_7$ requires: M^+–CH_3CO_2, 335·113).

X-ray data and structure determination of compound (**13**). A small roughly cubical crystal of dimensions 0·15 × 0·15 × 0·14 mm was used for the accurate measurement of the cell constants and 1425 independent reflections on a Philips PW 1100 four-circle automatic diffractometer [MoK_α radiation (λ = 0·7107 Å), ω–2θ scan mode and θ_{max} = 22°]. A summary of the crystal data is given in the Table. Background intensity was measured for half the total scan time on each side of the reflection. A total of 219 reflections was considered to be unobserved with intensity, $I < 2\sigma(I)$. Lorentz and polarization corrections were applied but no absorption corrections were made.

The structure was solved by the multisolution approach as used in the program Multan 74.[12] In the refinement of the atomic parameters, using a full-matrix least-squares procedure, the thermal factors of the H atoms were kept constant at the value of the overall temperature factor estimated during structure factor normalization. All the other atoms were refined anisotropically. The function minimized was $\Sigma\omega(|F_o| - |F_c|)^2$ with $1/\sigma_F^2$ weights. The final R index is 0·048 (R_w = 0·045). The scattering factors of Stewart, Davidson and Simpson[14] were used for the hydrogen atoms and those for all other atoms were generated from the analytical expressions of Cromer and Mann.[15] All the Fourier and refinement calculations were done with the X-ray system of crystallographic programs (1972).[16]

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