Carbohydrate Research, 35 (1974) 87–96

A NEW METHOD OF ACETONATION. SYNTHESIS OF 4,6-*O*-ISOPROPYLIDENE-D-GLUCOPYRANOSE*†

MELVILLE L. WOLFROM, ATMANAND B. DIWADKAR, JACQUES GELAS‡, AND DEREK HORTON**
Department of Chemistry, The Ohio State University, Columbus, Ohio 43210 (U.S.A.)
(Received December 11th, 1973; accepted for publication, January 2nd, 1974)

ABSTRACT

Ethyl isopropenyl ether reacts with D-glucose in *N*,*N*-dimethylformamide containing a trace of *p*-toluenesulfonic acid to give crystalline 4,6-*O*-isopropylidene-α,β-D-glucopyranose (**2**) in near-quantitative yield. The structure of **2** was established by n.m.r. spectroscopy of it and of its β-triacetate **3**, and by conversion of **3** through deacetonation and subsequent acetylation into β-D-glucopyranose pentaacetate (**5**). The acetonation reagent operates under kinetic control, with favored attack at primary hydroxyl groups, instead of by the thermodynamic control associated with conventional acetonation methods. The reagents converts methyl α-D-glucopyranoside (**7**) into the 4,6-isopropylidene acetal **8**, and D-mannitol (**9**) into a 2:1 mixture of the 1,2:5,6-di-isopropylidene acetal **10** and the 1,2:3,4:5,6-tri-isopropylidene acetal **11**.

INTRODUCTION

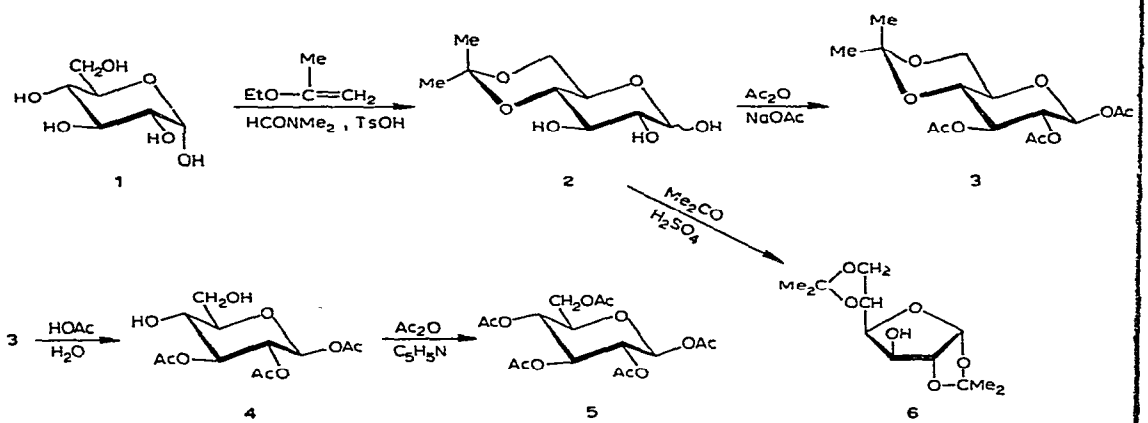
In a program evaluating the reaction of vinyl ethers with carbohydrates, the late Professor M. L. Wolfrom and his associates described[2] various 1-alkoxyethyl ethers and ethylidene acetals formed from sugars by reaction with alkyl vinyl ethers in the presence of a trace of acid. As a route to analogs that would not introduce additional asymmetry at the acetal carbon atom, the use of ethyl isopropenyl ether[3] was initiated, and it was shown[4] that this ether reacts with D-glucose to form a new monoisopropylidene acetal of then unknown structure.

This paper is concerned with the application of ethyl isopropenyl ether as an acetonation reagent for sugars, and with the characterization of the new monoisopropylidene acetal as 4,6-*O*-isopropylidene-α,β-D-glucopyranose (**2**).

*Dedicated to Dr. Horace S. Isbell, in honor of his 75th birthday.
† For a preliminary report, see ref. 1.
‡ Permanent address: Groupe de chimie organique 1, Université de Clermont-Ferrand, Ensemble scientifique des Cézeaux, BP 45, 63170 Aubière (France).
**To whom inquiries should be addressed.

DISCUSSION

D-Glucose (**1**) was brought into reaction with a twofold excess of ethyl isopropenyl ether[3] and a catalytic amount of *p*-toluenesulfonic acid in a solvent (*N*,*N*-dimethylformamide) that did not decompose the ether and permitted a homogeneous reaction-medium. Scrupulously anhydrous conditions were required, otherwise reaction of **1** was incomplete. After ~5 h at 0–5°, all of the starting material had reacted, and the water-soluble product was isolated crystalline in practically quantitative yield. The structure 4,6-*O*-isopropylidene-α,β-D-glucopyranose (**2**) was assigned to this product on the basis of chemical and physical evidence.



The product had the empirical formula $C_9H_{16}O_6$, corresponding to a product of condensation between one molecule of D-glucose and one molecule of acetone, but it was clearly different from the well-known 1,2-*O*-isopropylidene-α-D-glucofuranose. A molecular formula of $C_9H_{16}O_6$ (mol. wt. 220) was indicated by the mass spectrum, which showed at highest mass a peak having *m/e* 205 ($M^+ - \cdot CH_3$). The product reduced Fehling solution but gave a negative Schiff test, and it showed mutarotation (downward) but no carbonyl-group absorption in the infrared; these data indicate that a hemiacetal structure is present. The compound was thus formulated as a mono-*O*-isopropylidene-D-glucose having the anomeric position in the hemiacetal form. The compound consumed two moles of periodate per mole and gave a triacetate having no remaining hydroxyl-group absorption in the infrared, demonstrating that three contiguous hydroxyl groups are present, one of them being the anomeric hydroxyl group. All of these data accord equally well with the structures 4,6-*O*-isopropylidene-D-glucopyranose and 5,6-*O*-isopropylidene-D-glucofuranose, and the 4,5-acetal of the septanose form could not be excluded. Deacetonation of the triacetate with aqueous acetic acid, followed by acetylation of the product, gave a high yield of β-D-glucopyranose pentaacetate (**5**). This conversion establishes the structure of the triacetate as 1,2,3-tri-*O*-acetyl-4,6-*O*-isopropylidene-β-D-glucopyranose (**3**);

tautomeric change during the deacetonation–acetylation sequence can be ruled out because O-1 remains substituted in the intermediate 1,2,3-tri-*O*-acetyl-β-D-glucopyranose (4).

The structure 3 is confirmed by n.m.r. spectroscopy (Table I). The H-1 signal appears as a wide doublet at lowest field, and H-2 and H-3 resonate substantially downfield of the remaining protons, as anticipated for ring protons at positions substituted by acetoxyl groups; the chemical shifts and spin-couplings observed for H-1, 2, and 3 correspond closely with those found for β-D-glucopyranose pentaacetate (5), and confirm the triaxial disposition of these three protons. The H-4 signal of 3 resonates at much higher field than it does in 5, as expected for a structure having O-4 engaged in an acetal bridge, whereas the H-5 resonances of the two compounds have approximately the same chemical shifts.

TABLE I

P.M.R.-SPECTRAL DATA FOR 1,2,3-TRI-*O*-ACETYL-4,6-*O*-ISOPROPYLIDENE-β-D-GLUCOPYRANOSE (3) AND β-D-GLUCOPYRANOSE PENTAACETATE (5)

Solvent	*Compd.*	*Chemical shifts (δ)*								*CMe₂*
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6′*	*Ac*	
$(CD_3)_2CO$	3	5.79	4.97	5.21	←———	3.95 —	3.50 ——→		2.05, 2.00, 1.93	1.47, 1.28
	5	5.37	4.63	4.93	4.67 ←	—4.10 —	3.65 —→			
C_6D_6	3	5.83	5.40	5.32	3.64	3.10	3.50	3.71	1.71, 1.69, 1.60	1.31, 1.14
$CDCl_3$	3	5.75	5.10	5.25	←———	4.10 —	3.40 ——→		2.15, 2.12, 2.10	1.55, 1.48
		First-order couplings (Hz)								
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$		
$(CD_3)_2CO$	3	8	9	9	9.5	9.5	6	10.5		
$(CD_3)_2CO$	5	7.2	8.3	8.2	8.1					

In a recent report[5], Hasegawa and Fletcher described the treatment of D-glucose with 2,2-dimethoxypropane–*N*,*N*-dimethylformamide–*p*-toluenesulfonic acid to give an amorphous mixture which, after acetylation and chromatography, gave 42% of a crystalline product. It was concluded that the latter was, most probably, 1,2,3-tri-*O*-acetyl-4,6-*O*-isopropylidene-β-D-glucopyranose, as it could be converted into the pentaacetate 5. Their product had m.p. and specific rotation in good agreement with values reported here for 3.

The firm structural evidence obtained for the triacetate 3 allows the non-acetylated precursor to be identified as 4,6-*O*-isopropylidene-D-glucopyranose (2), but does not permit assignment of anomeric configuration to 2 because anomerization is possible under the acetylation conditions used. The observed downward mutarotation of 2 suggests the α-D configuration but does not exclude the possibility of an

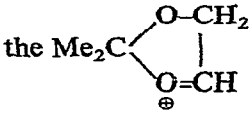
anomeric mixture richer in the α anomer than is the equilibrium mixture of anomers in water.

Direct evidence that the crystalline **2** obtained is an anomeric mixture was afforded by g.l.c. and n.m.r. data. G.l.c. of the per-*O*-(trimethylsilyl) derivative of **2**, in comparison with per(trimethylsilylated) D-glucose, 1,2-*O*-isopropylidene-α-D-glucofuranose, and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6**, reference standard, T_R 1.0), showed two peaks, in approximately equal proportion, migrating respectively faster (T_R 2.4) and slower (T_R 3.4) than the single peak from the derivative of 1,2-*O*-isopropylidene-α-D-glucofuranose (T_R 2.8); by comparison, the derivative of mutarotated D-glucose showed peaks for the two anomers (T_R 5.0 for α, 8.7 for β) at much longer retention-times.

The n.m.r. spectrum of **2** (m.p. 169.5–170.5°) in dry methyl sulfoxide-d_6 showed low-field resonances for the 1-OH protons of the two anomeric forms, and hydroxyl-proton exchange by deuterium oxide left at low field only two signals, that for H-1α (as a narrow doublet) downfield of that for H-1β (a wide doublet). The ratios of intensities of these two signals, and those of the 1-OH protons, indicated that the initial, crystalline product **2** was an 11:9 mixture of the α and β anomers. Such anomeric mixtures have been encountered in previous examples in this laboratory[6] and characterized[7] by n.m.r. spectroscopy in methyl sulfoxide-d_6.

A sample of **2** that had been recrystallized three times from acetone had a higher m.p. (174–175°), and g.l.c. of the pertrimethylsilylated derivative indicated that it contained ~75% of the α form and 25% of the β form. In dry methyl sulfoxide-d_6, the HO-1α and HO-1β signals for this sample showed intensities in a similar ratio, also observed, after deuteration, in the initial, relative intensities of the H-1α and H-1β signals. At mutarotational equilibrium, this ratio changed to α:β = 1:1, and in deuterium oxide alone the α:β ratio was 2:3. This higher-melting preparation of **2** mutarotated from about +36° (initial) to −6.7° (equilibrium) in water. Assuming a Hudson 2A value[8] (M_α—M_β, the rotatory contribution of the anomeric center) of ~37,500 (as observed for a range of anomeric pairs of D-glucopyranose derivatives), the specific rotations of the pure α and β anomers may be estimated at about +100° and −70°, respectively.

For D-glucose at mutarotational equilibrium in water, Isbell and Pigman[9] found the α:β ratio to be 36.2:63.8, as determined accurately from polarimetric data on the pure anomers. For compound **2**, the α:β ratio of ~40:60, as estimated by n.m.r. spectroscopy, is in close accord, indicating that the 4,6-substituent does not greatly affect the relative free-energies of the anomers in aqueous solution.

The mass spectra of the acetal **2** and its triacetate **3** were useful for assigning molecular weight from the M−15 peaks, but the observed fragment-ions should be interpreted with caution. Thus, the weak peak at *m/e* 101 in the spectrum of **2** might be considered[10] as indicative of the  ion arising from a 5,6-*O*-isopro-

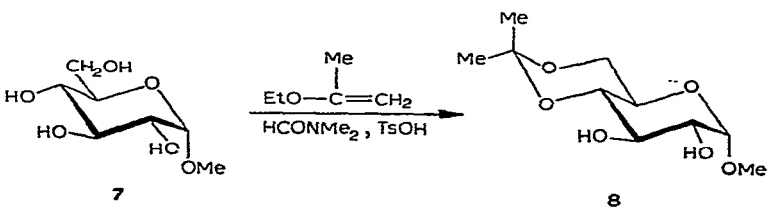
pylidenehexofuranose structure by C-4–C-5 cleavage. However, other pathways to a fragment of *m/e* 101 are available, as evident from the fact that 4,6-*O*-ethylidene-D-glucopyranose also displays a weak peak at this mass number. Only when the *m/e* 101 peak is of high intensity should it be considered strongly indicative of the 5,6-acetal structure.

The acetonation reagent evidently operates under kinetic conditions, presumably by initial attack at the most accessible (primary) hydroxyl group in **1**, with subsequent ring-closure at O-4 to give **2** while the intermediate retains the original pyranoid ring-form. When **2** is conventionally acetonated (acetone–sulfuric acid), it gives, in high yield, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, the thermodynamic product of acetonation with excess reagent.

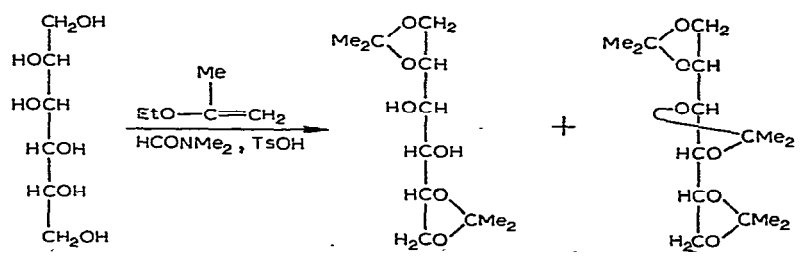
The furanoid analog of **2**, 5,6-*O*-isopropylidene-D-glucofuranose, has evidently not yet been prepared; a claim[11] that it is produced by partial hydrolysis of 1,2:5,6-di-*O*-isopropylidene-3-*O*-vinyl-α-D-glucofuranose with acid is not supported by structural evidence, and the preparative route, together with the m.p. (161–162.5°) cited, suggest that the product was 1,2-*O*-isopropylidene-α-D-glucofuranose.

Acetonation of methyl α-D-glucopyranoside (**7**) with ethyl isopropenyl ether gave a high yield of methyl 4,6-*O*-isopropylidene-α-D-glucopyranoside (**8**); in this instance, the tautomeric form of the initial sugar is fixed, and the product is the same as that obtained[12,13] by use of 2,2-dimethoxypropane or acetone as the acetonation reagent.

D-Mannitol (**9**), when allowed to react with excess ethyl isopropenyl ether until all of the starting material had disappeared, gave a mixture from which 1,2:5,6-di-*O*-isopropylidene-D-mannitol[14] (**10**) and 1,2:3,4:5,6-di-*O*-isopropylidene-D-mannitol[14] (**11**) could be obtained, in ~60 and ~30% yields, respectively.



7 8



9 10 11

EXPERIMENTAL

General methods. — Evaporations were effected *in vacuo* below 40°. Melting points were determined with a Thomas–Hoover "Unimelt" apparatus and are uncorrected. T.l.c. was performed on 0.25-mm plates of Silica Gel G (Merck) activated at 110°, and 10% aqueous sulfuric acid was employed for detection. Column chromatography was conducted with Silica Gel No. 7734 (70–325 mesh, Merck). Chromatographic solvents were either ethyl acetate or 4:1 ethyl acetate–methanol. I.r. spectra were recorded with a Perkin–Elmer Model 237 spectrophotometer. Optical rotations were determined with a Perkin–Elmer Model 141 polarimeter with use of 1-dm tubes. N.m.r. spectra were recorded at 100 MHz with a Varian HA-100 spectrometer with Me_4Si as the internal standard and the source of a lock signal. Chemical shifts are given in p.p.m. and the couplings given are first-order spacings. Mass spectra were recorded with an AEI-MS-9 spectrometer at an ionizing potential of 70 eV and an accelerating potential of 8 kV; a direct-insertion probe was employed. Analyses were performed by W. N. Rond. X-Ray powder diffraction data give interplanar spacings in Å for CuKα radiation (camera diameter = 114.59 mm). Relative intensities are estimated visually: m, medium; s, strong; v, very; w, weak.

4,6-O-Isopropylidene-α,β-D-glucopyranose (**2**). — (*a*) *Synthesis.* To a solution of D-glucose (**1**, 5.4 g, 30 mmoles) in *N,N*-dimethylformamide (100 ml, dried over Drierite) kept below 5° in an ice bath was added ethyl isopropenyl ether[3] (5.2 g, 60 mmoles) and *p*-toluenesulfonic acid (~10 mg). The mixture was stirred magnetically at 0–5° until t.l.c. monitoring indicated that all of the starting material had disappeared (about 5–6 h), whereupon anhydrous sodium carbonate (~5 g) was added, with energetic stirring of the cold mixture for 1 h. The mixture was refrigerated overnight and then filtered, and the filtrate was poured into ice–water (50 ml). The resultant solution was extracted with dichloromethane (3 × 50 ml), and the combined organic extracts were washed with water (4 × 20 ml). The aqueous phase and combined aqueous extracts were freeze-dried (48 h) to yield **2** as a white solid (6.25 g, 95%) that was homogeneous by t.l.c. and after trimethylsilylation showed no appreciable peaks for components other than the α and β anomers of **2**. It reduced Fehling solution, gave a negative Schiff test, and consumed 2 moles per mole of periodate[15].

Recrystallization could be effected from ethanol–hexane to give small white granules, m.p. 169.5–170.5°, $[\alpha]_D^{27}$ +24 ±2 (initial, extrapolated) → +8.5 ($t_{0.5}$ 9 min) → −7.3° (final, 48 h; *c* 2.1, water); R_F (t.l.c.) 0.2 (ethyl acetate), 0.6 (4:1 ethyl acetate–methanol); λ_{max}^{KBr} 2.98 (OH), 7.29 (CMe_2), 11.72 μm (α anomer[16]); mass spectrum* *m/e* 205 (8, $M^+ - \cdot CH_3$), 187 (1, 205 − H_2O), 145 (3, 205 − AcOH), 131 (5), 127 (4, 205 − H_2O − AcOH), 101 (3), 73 (23), 59 (100, Me_2COH^+), 43 (97, $MeCO^+$); X-ray powder diffraction data: 11.87 m, 6.66 m, 5.84 m, 5.37 m, 5.31 vw, 4.92 vs (1), 4.65 vw, 4.46 m, 3.94 s (2), 3.67 w.

*A sample of 4,6-*O*-ethylidene-D-glucopyranose[17] showed the following mass-spectral data: *m/e* 205 (1), 191 (1, $M^+ - \cdot CH_3$), 144 (11), 117 (24), 116 (10), 103 (12), 101 (11), 87 (18), 73 (100), 60 (50), 57 (39), 45 (65), 43 (49).

Anal. Calc. for $C_9H_{16}O_6$: C, 49.09; H, 7.27. Found: C, 49.33; H, 7.55.

Recrystallization of the product 3 times from acetone gave material having m.p. 174–175°, $[\alpha]_D^{23}$ +36 ±2 (initial, extrapolated) → +13 ($t_{0.5}$, 12 min) → −6.7° (final, 48 h; *c* 2, water); this product appeared to be richer in α anomer than the product obtained from ethanol–hexane.

Evaporation of the dried (magnesium sulfate) dichloromethane extract gave a residue that by t.l.c. showed two components migrating faster than **2**; the latter was absent from this fraction. The faster-moving components are under investigation. These components were usually very minor, but on certain occasions the procedure gave a somewhat lower yield of **2** and a greater proportion of these side-products.

If the reaction was not conducted under scrupulously anhydrous conditions, some D-glucose accompanied **2** in the initial freeze-dried product. Pure **2** could readily be isolated by chromatography of the product (3 g) from a column (45 × 3 cm) of silica gel (90 g) with 4:1 ethyl acetate–methanol.

(*b*) *Anomeric composition of* **2**. The 100-MHz n.m.r. spectrum of a sample of **2** (crystallized from ethanol–hexane) dissolved in methyl sulfoxide-d_6 showed, at lowest field, two doublets at δ 6.45 ($J_{1\beta,OH}$ 6 Hz, HO-1β) and 6.15 ($J_{1\alpha,OH}$ 4.5 Hz, HO-1α); their intensity ratio indicated an α:β anomeric ratio of ~11:9. These peaks disappeared when a drop of deuterium oxide was added to the solution, and the only signals remaining below δ 3.9 were a narrow doublet at δ 4.84 ($J_{1\alpha,2}$ 3.5 Hz, H-1α) and a wide one at δ 4.26 ($J_{1\beta,2}$ 7.5 Hz, H-1β) in the intensity ratio ~5:4. Before deuteration, the H-1α and H-1β signals appeared as narrow and wide apparent triplets, respectively, and the additional splitting of each signal permitted differentiation of the HO-1α and HO-1β signals. Also observed in the spectrum before deuteration were doublets at δ 4.65 ($J_{H,OH}$ 4.5 Hz) and 4.45 ($J_{H,OH}$ 6.5 Hz), assigned to HO-2 and HO-3 but not individually differentiated. The spectrum showed a poorly resolved multiplet, δ 2.52–3.52 for the remaining ring-proton resonances, together with 3-proton singlets at δ 1.43 and 1.32 for the CMe_2 group. At equilibrium in deuterium oxide, **2** showed (at 40°) the H-1α and H-1β signals in the relative-intensity ratio of ~40:60.

The product **2** (10 mg) was per(trimethylsilylated) by heating it with shaking in a closed vial for a few min at 60–70° with *N*-trimethylsilylimidazole in pyridine (Tri-Sil Z, Pierce Chemicals, 1 ml). After 15 min, it was analyzed by g.l.c. on a Beckman GC-5 dual-column instrument with flame-ionization detectors, and helium as the carrier gas. A column (3.18 mm × 1.83 m) of 3% SE-30 on 80–100 mesh Chromosorb P was used, with a helium flow-rate of 75 ml.min^{-1}, an injection temperature of 210–220°, and a column temperature of 145°. Both the initial freeze-dried product, and **2** that had been crystallized from ethanol–hexane, gave only two peaks, T_R 2.4 and 3.4, corresponding to the α and β anomeric forms of trimethylsilylated **2**; no components corresponding to per(trimethylsilylated) D-glucose [T_R 5.0 (α) and 8.7 (β)], 1,2-*O*-isopropylidene-α-D-glucofuranose (T_R 2.8), or 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6**, T_R 1.0) were detected.

The sample of **2** (m.p. 174–175°) that had been thrice recrystallized from

acetone gave two peaks having the same T_R values as before, with an α:β ratio of ~3:1. In dry methyl sulfoxide-d_6, this sample showed n.m.r. resonances for HO-1α and HO-1β in 3:1 ratio, and this same ratio was observed, after addition of one drop of deuterium oxide, in the intensities of the H-1α and H-1β signals, changing to 1:1 after 48 h.

Equilibrium acetonation of **2** *to give* **6**. — To a solution of **2** (60 mg) in dry acetone (25 ml) was added one drop of conc. sulfuric acid, and the mixture was stirred for 15 h at ~25°. Sodium carbonate (0.3 g) was added and, after 2 h, the mixture was filtered and the filtrate evaporated. Crystallization of the residue from chloroform–hexane gave 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**6**; 45 mg, 63%), m.p. 110°, indistinguishable from authentic[18] material by mixture m.p.

*1,2,3-Tri-*O*-acetyl-4,6-*O*-isopropylidene-β-*D*-glucopyranose* (**3**). — A mixture of compound **2** (2.2 g, 10 mmoles), acetic anhydride (6.1 g, 60 mmoles), and sodium acetate (9.8 g, 120 mmoles) was stirred thoroughly and heated for 1 h at 100°. The cooled mixture was poured onto ice and the product was extracted with dichloromethane. The dried (magnesium sulfate) extract was evaporated and the crystalline residue was recrystallized from ethanol to give **3** as microscopic needles (2.9 g, 81%), m.p. 171–172°, $[\alpha]_D^{27}$ −30° (*c* 1, chloroform) (Hasegawa and Fletcher[5] gave m.p. 169°, $[\alpha]_D^{20}$ −34° in chloroform); R_F 0.9 (ethyl acetate); λ_{max}^{KBr} 5.80 (C=O), 7.23 μm (CMe_2); for n.m.r. data, see Table I; mass spectrum: *m/e* 331 (26, $M^+ - \cdot CH_3$), 245 (24, $M^+ - Me_2COH^+ - CH_2CO$), 226 (26, $M^+ - 2AcOH$), 203 (16), 169 (46), 157 (38, $AcOCH{=}\overset{+}{C}HCHOAc$), 143 (69), 127 (44), 115 (200, $157 - CH_2CO$), 109 (58), 103 (26, Ac_2OH^+), 101 (44), 97 (26), 73 (52), 59 (100, Me_2COH^+), 43 (1160, CH_3CO^+); X-ray powder diffraction 11.75 m, 11.18 m, 8.93 vs (1), 6.92 w, 6.19 m, 5.59 m, 5.22 s (2), 4.81 m, 4.43 s (3), 4.21 w, 4.03 m.

Anal. Calc. for $C_{15}H_{22}O_9$: C, 52.02; H, 6.36. Found: C, 52.01; H, 6.64.

The n.m.r. spectrum in acetone-d_6 showed first-order behavior for H-1, H-2, and H-3. The spectrum in benzene-d_6 showed second-order character in the H-1 signal because of the close proximity of the H-2 and H-3 signals, but the H-5,6,6′ signals were essentially first-order (see Table I). A comparison of data for **3** and β-D-glucopyranose penta-acetate[19] (**5**) is given in Table I.

Deacetonation of **3** *and acetylation to give β-D-glucopyranose pentaacetate* (**5**). — A solution of **3** (200 mg) in 1:3 acetic acid–water (10 ml) was heated for 1 h at 70°. T.l.c. then indicated disappearance of the starting material and formation of a single component having a lower R_F value. The solution was freeze-dried to give amorphous 1,2,3-tri-*O*-acetyl-β-D-glucopyranose. To this product was added a solution of acetic anhydride (177 mg) in pyridine (137 mg) at ~0°. After 15 h at ~0°, the mixture was poured onto ice and the product was extracted with dichloromethane. The dried (magnesium sulfate) extract was evaporated to give **5** (248 mg, 97%), m.p. 127–128°, which was recrystallized from ethanol to give pure **5** (220 mg, 86%), m.p. 131–132°, undepressed on admixture with authentic **5** and indistinguishable from it by n.m.r. (Table I) and mass spectra.

Methyl 4,6-O-isopropylidene-α-D-glucopyranoside (**8**). — Methyl α-D-glucopyranoside (**7**, 5.0 g, 25 mmoles) was dispersed in dry *N,N*-dimethylformamide (10 ml, dried over Linde molecular sieves), and Drierite (0.7 g) was added. To the stirred mixture at ~25° was added ethyl isopropenyl ether (2.22 g, 25 mmoles) followed by *p*-toluenesulfonic acid (27 mg). The mixture was stirred for 3 h at ~25°, and filtered to remove Drierite and unreacted **7**, and the filtrate was treated with sodium carbonate (0.5 g) and water (0.1 ml). After 2 h at ~25°, the mixture was filtered and the filtrate evaporated at 15 torr. The resulting syrup (5.6 g) was dissolved in 1:1 chloroform–acetone and transferred to a column (24×4 cm) of silica gel (Davison, grade 950, 60–200 mesh, W. R. Grace Co.), which was eluted with the same solvent to give fractions containing only the product **8**. Crystallization from benzene gave **8** as clusters of needles (4.25 g, 82% on the basis of unrecovered **7**), m.p. 84–86°, $[\alpha]_D^{25}$ +105° (*c* 5.0, water); lit.[12] m.p. 84–86°, $[\alpha]_D^{20}$ +94° (*c* 5.0 water), and[13] m.p. 82–83.5°, $[\alpha]_D^{25}$ +105° (*c* 4.7, water). The product was indistinguishable from an authentic sample by mixed m.p., i.r. spectrum, and X-ray powder diffraction data.

Conversion of D-*mannitol* (**9**) *into 1,2:5,6-di-*O*-isopropylidene-*D*-mannitol* (**10**) *and 1,2:3,4:5,6-tri-*O*-isopropylidene-*D*-mannitol* (**11**). — To a solution of D-mannitol (**9**, 1 g, 5.5 mmoles) in anhydrous *N,N*-dimethylformamide (2 ml) was added Drierite (0.14 g) followed by ethyl isopropenyl ether (2.4 g, 27 mmoles) and *p*-toluenesulfonic acid (5.4 mg). The mixture was stirred for 75 min at ~25° (conditions for maximal conversion as judged by t.l.c.) and then filtered. The filtrate was stirred with sodium carbonate (0.1 g) and water (0.1 ml) for 30 min at ~25°, the mixture filtered, and the filtrate evaporated at 40° (bath)/15 torr. T.l.c. of the solid residue (1.8 g) showed two components, R_F 0.3 and 0.7 (1:9 methanol–benzene), and it was resolved on a column of silica gel G (150 g) by elution with the t.l.c. solvent. The component having R_F 0.3 was obtained crystalline (0.87 g, 60%), and was indistinguishable from the authentic[14] diacetal **10** by mixture m.p. and i.r. spectrum. The pure component having R_F 0.7 was likewise obtained crystalline (0.48 g, 29%), and was indistinguishable by mixture m.p. and i.r. spectrum from the authentic[14] triacetal **11**.

ACKNOWLEDGMENTS

The authors thank Dr. J. D. Wander for recording the 100-MHz spectra, and R. Weisenberger for the mass spectra. The initial phase of this study was supported by Grant No. 12-14-100-7652(71) (O.S.U. Research Foundation Project 1856) from the Agricultural Research Service, U. S. Department of Agriculture, administered by the Northern Regional Research Laboratory, Peoria, Illinois. One of us (J.G.) thanks the NATO organization in Paris for a grant.

REFERENCES

1 Preliminary report: J. GELAS AND D. HORTON, *Abstr. Papers Amer. Chem. Soc. Meeting*, 167 (1974) CARB 26.

2 M. L. WOLFROM AND G. G. PAREKH, *Carbohyd. Res.*, 11 (1969) 547; M. L. WOLFROM, S. S. BHATTACHARJEE, AND R. M. DE LEDERKREMER, *ibid.*, 11 (1969) 148; and earlier papers in this series.

3 L. A. YANOVSKAYA, S. S. YUFIT, AND V. F. KUCHEROV, *Izv. Akad. Nauk SSSR, Ser. Khim.*, (1960) 1246, S. CHLÁDEK AND J. SMRT, *Coll. Czech. Chem. Commun.* 28 (1963) 1301.
4 M. L. WOLFROM AND A. B. DIWADKAR, *Abstr. Papers Amer. Chem. Soc. Meeting*, 158 (1969) CARB-3.
5 A. HASEGAWA AND H. G. FLETCHER, JR., *Carbohyd. Res.*, 29 (1973) 209.
6 D. HORTON, J. S. JEWELL, AND K. D. PHILIPS, *J. Org. Chem.*, 31 (1966) 3843.
7 B. CASU, M. REGGIANI, G. G. GALLO, AND A. VIGEVANI, *Tetrahedron Lett.*, (1964) 2839; (1965) 2253; A. S. PERLIN, *Can. J. Chem.*, 44 (1966) 539.
8 C. S. HUDSON, *J. Amer. Chem. Soc.*, 31 (1909) 66; F. J. BATES AND ASSOCIATES, *Nat. Bur. Stand. Circ.* C440 (1942) 411.
9 H. S. ISBELL AND W. PIGMAN, *J. Res. Nat. Bur. Stand.*, 18 (1937) 142; compare R. U. LEMIEUX AND J. D. STEVENS, *Can. J. Chem.*, 44 (1966) 249; D. HORTON, J. S. JEWELL, AND K. D. PHILIPS, *J. Org. Chem.*, 31 (1966) 4022.
10 D. C. DEJONGH AND K. BIEMANN, *J. Amer. Chem. Soc.*, 86 (1964) 67; N. K. KOCHETKOV AND O. S. CHIZHOV, *Advan. Carbohyd. Chem.*, 21 (1966) 39.
11 B. I. MIKHANTEV AND V. L. LAPENKO, *Zh. Obshch. Khim.*, 27 (1957) 2840.
12 J. K. N. JONES, *Can. J. Chem.*, 34 (1956) 840.
13 M. E. EVANS, F. PARRISH, AND L. LONG, JR., *Carbohyd. Res.*, 3 (1967) 453.
14 E. BAER AND H. O. L. FISCHER, *J. Amer. Chem. Soc.*, 61 (1939) 761.
15 R. D. GUTHRIE, *Methods Carbohyd. Chem.*, 1 (1962) 435.
16 S. A. BARKER, E. J. BOURNE, AND D. H. WHIFFEN, *Methods Biochem. Anal.*, 3 (1956) 213; J. J. CAEL, J. L. KOENIG, AND J. BLACKWELL, *Carbohyd. Res.*, 32 (1974) 79.
17 R. C. HOCKETT, D. V. COLLINS, AND A. SCATTERGOOD, *J. Amer. Chem. Soc.*, 73 (1951) 599.
18 O. T. SCHMIDT, *Methods Carbohyd. Chem.*, 2 (1963) 318.
19 Compare R. U. LEMIEUX AND J. D. STEVENS, *Can. J. Chem.*, 43 (1965) 2059.