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KINETIC ACETONATION OF D-MANNOSE: PREPARATION OF 4,6-MONO- AND 2,3:4,6-DI-*O*-ISOPROPYLIDENE-D-MANNOPYRANOSE*

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ABSTRACT

The major product obtained on acetonation of D-mannose with a 2-molar excess of isopropenyl methyl (or ethyl) ether is 4,6-*O*-isopropylidene-α-D-mannopyranose (**3a**), the product of kinetic acetonation; a larger excess of the reagent leads to the 2,3:4,6-diisopropylidene acetal (**6**). The course of the reaction and side-products formed were examined in detail. The 1,2,3-triacetate of **3a** was deacetonated to give α-D-mannopyranose 1,2,3-triacetate; similar reactions were performed on the β anomers. The 1-acetate of the diacetal **6** could be selectively deacetonated to give 1-*O*-acetyl-2,3-*O*-isopropylidene-α-D-mannopyranose. The reactions provide access to protected derivatives of D-mannose, and partially acylated derivatives, having modes of substitution different from those obtainable by classical acetonation procedures conducted under conditions of thermodynamic control.

INTRODUCTION

Earlier reports[2,3] in this series have shown that alkyl isopropenyl ethers can be used to effect acetonation of sugars under kinetic control, to give products having a mode of substitution different from that in the products of classical, thermodynamically controlled acetonation; the kinetic procedure favors attack at primary hydroxyl groups, and subsequent ring-closure to give isopropylidene acetals of the 1,3-dioxane type when groups are sterically available. D-Glucose thus gives[2] the pyranoid 4,6-isopropylidene acetal; D-ribose and D-arabinose, which do not have the primary hydroxyl group free in the preponderant tautomers, give mainly the pyranoid 3,4-isopropylidene acetals[3].

It is now shown that methyl (or ethyl) isopropenyl ether, used in suitable proportion, can be used to convert D-mannose in high yield into either its pyranoid 4,6-monoisopropylidene acetal or its pyranoid 2,3:4,6-diisopropylidene acetal.

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DISCUSSION

Treatment of D-mannose (**1**) in *N*,*N*-dimethylformamide with a 2-molar excess of isopropenyl methyl ether (**2**) (or ethyl isopropenyl ether) in the cold, under strictly anhydrous conditions and in the presence of a trace of *p*-toluenesulfonic acid, gave a major, water-soluble, solid product identified as 4,6-*O*-isopropylidene-D-mannopyranose (**3**); recrystallization from ethyl acetate afforded in 82% yield the pure, crystalline α anomer (**3a**), which showed downward mutarotation and gave a crystalline triacetate (**7a**). Acetylation of the crude monoacetal **3** (in which the β anomer **3b** was present in much lower proportion than the α anomer **3a**), followed by chromatographic resolution of the product-mixture, permitted isolation of crystalline 1,2,3-tri-*O*-acetyl-4,6-*O*-isopropylidene-β-D-mannopyranose (**7b**).

The gross structures attributed to **3a**, **7a**, and **7b** were evident from their microanalytical data and mass spectra (see Experimental section); the latter further gave evidence for the structural formulations assigned, and the corresponding ^{1}H-n.m.r. spectra (see Tables I and II) furnished decisive confirmation of the structures. The ^{1}H-n.m.r. spectrum of **3a** in dimethyl sulfoxide-d_6 showed signals for the two *C*-methyl groups of the isopropylidene group, and exchangeable doublets for each of the hydroxyl groups; the lack of a triplet signal for one of the hydroxyl groups established that the primary hydroxyl group was engaged in the acetal substitution. The triacetate **7a** showed the H-1 signal at lowest field, and the H-2 and H-3 signals also at low field (and only slightly separated), as expected for the 1,2,3-tri-*O*-acyl mode of substitution. The anomeric triacetate **7b** showed a similar pattern, but with larger separation of the H-2 and H-3 signals, permitting attribution by spin-decoupling, and assignment of $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ in clear accord with the β-D-mannopyranoid formulation, and thus with the 4,6-monoisopropylidene acetal structures for **3a** and **3b**, and, consequently, for **7a** and **7b**.

Additional, chemical evidence for the structures was provided by acid-catalyzed deacetonation of **7a** and **7b** to the corresponding 1,2,3-tri-*O*-acetyl-α- and -β-D-mannopyranoses (**9a** and **9b**), whose n.m.r. spectra showed the low-field signals anticipated for H-1, H-2, and H-3. Acetylation of **9a** and **9b** with an excess of acetic anhydride in pyridine gave the known α- and β-D-mannopyranose pentaacetates (**10a** and **10b**, respectively), thus proving that the precursors **7a**, **7b** (and **3a**, **3b**) all had the pyranoid ring-form. Repetition of the acetylation of **9a** and **9b**, but with use of acetic anhydride-d_6, afforded the corresponding pentaacetates (**11a** and **11b**) in which the 4- and 6-substituents were trideuterated in the methyl groups; two of the acetyl-group signals in the spectra of **10a** and **10b** were absent from the spectra of the 4,6-di-*O*-(trideuterioacetyl) derivatives **11a** and **11b**.

The product of acetonation of **1** by 2 mol of **2** was mainly a water-soluble fraction (Fraction A), from which **3a** was readily isolated in high yield; a minor, dichloromethane-soluble fraction (B) was also isolated. Both of these fractions were analyzed in detail by t.l.c., by g.l.c. of the per(trimethylsilyl)ated products, and, after acetylation of the two fractions, by column-chromatographic resolution. In the

TABLE I

PROTON CHEMICAL-SHIFT DATA FOR ISOPROPYLIDENE ACETALS OF D-MANNOSE AND ACETYLATED DERIVATIVES

Compd.	*Solvent*	*Chemical shifts*[a] (δ)									
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	CMe_2	*OAc*	*OH*
3a	Me_2SO-d_6	5.00d[b]			3.4–4.0m				1.42, 1.33		6.47d, 4.83d, 4.68d
5	Me_2SO-d_6	5.27d[c]	4.54d	4.83dd	3.7–4.4m				1.38(6), 1.26, 1.23		6.50d[d]
6	Me_2SO-d_6	5.33d[e]			3.60–4.35m				1.33, 1.50[f]		6.84d
7a	$CDCl_3$	6.12d	5.40m		4.27dd	~4.0m		~3.9m	1.56, 1.43	2.20(6), 2.07(3)	—
7a	$(CD_3)_2CO$	6.07d	5.33dd	5.27dd	4.27m	~4.0m		~3.9m	1.53, 1.36	2.20, 2.15, 1.99	—
7a	C_6D_6	6.41d	5.77m		4.47dd	4.13m		~3.9m	1.44, 1.32	1.75(6), 1.50(3)	—
7a	C_6D_6[g]	6.28	5.64m		4.36dd	4.02sx	3.84dd	3.76dd	1.45, 1.36	1.84, 1.80, 1.64	—
7b	$CDCl_3$	6.00d	5.63dd	5.17dd	4.12dd	3.50m		3.93m	1.56, 1.44	2.25, 2.12, 2.07	—
7b	$(CD_3)_2CO$	6.12d	5.60dd	5.25dd	4.16dd	3.57m		3.89m	1.55, 1.37	2.19, 2.09, 2.02	—
7b	C_6D_6	5.87m		5.34m	4.30dd	3.27m		3.83m	1.40, 1.28	1.90, 1.76, 1.48	—
8	$CDCl_3$	6.27s	4.75d	4.87dd	4.33dd	5.40o	4.69dd	4.23dd	1.50, 1.36	2.13(9)	—
8	$(CD_3)_2CO$	6.16s	4.82d	5.00dd	4.33dd	5.34o	4.65dd	4.12dd	1.44, 1.33	2.07, 2.03, 2.02	—
8	C_6D_6	6.49s	4.53d	4.67dd	4.36dd	5.70o	4.96dd	4.33dd	1.43, 1.17	1.84, 1.80, 1.75	—
9a	$CDCl_3$	6.16d	5.34m		3.6–4.4m				—	2.21, 2.19, 2.13	5.78(2)[d]
9a	Me_2SO-d_6	6.03d	5.10m		3.6–4.4m				—	2.15, 2.12, 2.02	~5(2)[d]
9b	$CDCl_3$	6.02d	4.48dd	5.13dd	3.4–4.2m				—	2.21(3), 2.12(6)	~4(2)[d]
9b	Me_2SO-d_6	6.04d	5.41dd	5.05dd	3.4–4.0m				-	2.13, 2.07, 2.02	~5.3(2)[d]
10a	$CDCl_3$[h]	6.21d	5.23–5.53m		4.10m		4.17–4.55m		—	2.20(6), 2.12, 2.09, 2.04	—
10a	$(CD_3)_2CO$[i]	6.18d	5.27–5.60m		4.07m		4.13–4.57m			2.22, 2.20, 2.08, 2.07, 2.01	—
10a	C_6D_6[j]	6.43d	5.60–5.90m		4.13m		4.20–4.70m			1.77(6), 1.74, 1.62, 1.53	—

(Table continued on p. 374)

TABLE I (*continued*)

Compd.	*Solvent*	*Chemical shifts*[a] (δ)									
		H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	CMe_2	*OAc*	*OH*
10b	$CDCl_3$[k]	6.02d	5.58m	5.27m	5.42m	3.93m	4.44m	4.17m	—	2.24, 2.13(6), 2.10, 2.03	—
10b	$(CD_3)_2CO$[l]	6.12d	5.57m	5.28m	5.40m	4.02m	4.40m	4.15m	—	2.18, 2.08(9), 1.98	—
11b	C_6D_6[m]	5.98d	5.82dd	5.40dd	5.73dd	3.67o	4.49dd	4.22dd	—	1.84(6), 1.70	—
12	$CDCl_3$	6.22s	4.75d	4.93dd	~4.2m	4.46m ← 4.25–4.0m →			1.51(6), 1.41, 1.38	2.11	—
12	$(CD_3)_2CO$	6.11s	4.77d	4.96dd	3.98m	4.42dd	4.13m	3.93m	1.45, 1.38 1.34(6)	2.07	—
12	C_6D_6	6.53s	← 4.0–4.8m →						1.45, 1.38, 1.33, 1.13	1.62	—
13	$CDCl_3$	6.40s	← 3.6–4.4m →						1.59, 1.55, 1.47, 1.40	2.32	—
13	$(CD_3)_2CO$	6.28s	← 3.6–4.4m →						1.52(6), 1.37(6)	2.13	—
13	C_6C_6	6.68s	← 3.6–4.4m →						1.53, 1.47, 1.31, 1.25	1.67	—
15	Me_2SO-d_6	6.22s	← 3.80–4.16m →						1.45, 1.30	2.10	5.33d 4.60[n]
16	$CDCl_3$[o]	6.51s	← 5.25dd–3.80–4.50m →						1.62, 1.40	2.18, 2.15, 2.13	—
16	$(CD_3)_2CO$[o]	6.33s	← 5.17dd–3.80–4.50m →						1.53, 1.37	2.15, 2.10, 2.03	—
16	C_6D_6[o]	6.67s	← 5.52dd–3.70–4.70m →						1.61, 1.23	1.80, 1.75, 1.70	—

[a]From spectra recorded at 60 MHz. Signal multiplities: d, doublet; m, multiplet; o, octet; s, singlet; and sx, sextet. Spectral integrals were sufficiently accurate for assignment of each signal. Numbers in parentheses indicate number of protons. [b]$^3J_{OH,H-1}$ 4.5 Hz; became a singlet at δ 5.07, after addition of D_2O to the solution, wich concurrent disappearance of the corresponding OH signals. [c]$^3J_{OH,H-1}$ 4.2 Hz; became a singlet after addition of D_2O. [d]Protons exchangeable by addition of D_2O. [e]$^3J_{HOCH-1}$ 4.5 Hz; became a singlet after addition of D_2O to the solution, with concurrent disappearance of the corresponding OH signal. [f]The integration of these signals corresponds to four methyl groups, which is consistent with the formula of a diisopropylidene derivative. [g]Spectra recorded at 250 MHz with a Cameca apparatus. [h]Spectrum of the deuterio derivative **11a** gave similar chemical shifts, but showed OAc signals only at 2.20(6) and 2.04. [i]As for *h*, with OAc signals at δ 2.21, 2.19, and 2.00. [j]As for *h*,with OAc signals at δ 1.75, 1.67, and 1.59. [k]Spectrum of the deuterio derivative **11b** gave similar chemical shifts, but showed OAc signals only at δ 2.24, 2.14, and 2.04. [l]Same as for *k*, with OAc signals at δ 2.20, 2.10, and 2.00. [m]The spectrum reported here was that of the deuterio derivative; the non-deuterated compound **10b** showed OAc signals at δ 1.76(9) 1.68, and 1.58. [n]The triplet ($^3J_{HOCH_2-5}$ ~5 Hz) and the doublet ($^3J_{HOCH-4}$ ~3 Hz) disappeared after addition of D_2O to the solution. [o]Spectra of the deuterio derivative **17** gave similar chemical shifts, and showed an OAc signal only at 2.17 ($CDCl_3$), 2.16 [$(CD_3)_2CO$], and 1.67 (C_6D_6).

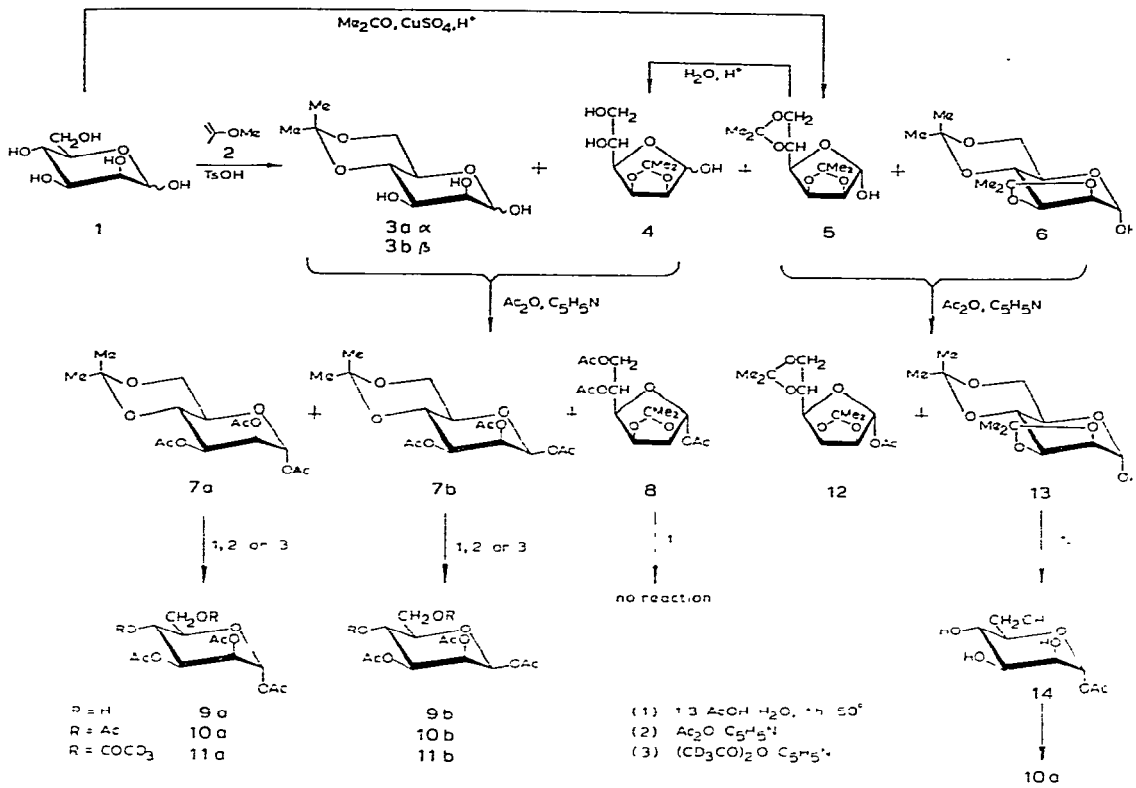


TABLE II

PROTON–PROTON SPIN-COUPLING DATA FOR ISOPROPYLIDENE ACETALS OF D-MANNOSE AND ACETYLATED DERIVATIVES

Compd.	*Solvent*	*First-order couplings*[a] *(Hz)*						
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$
5	Me_2SO-d_6	~0.5	6.0	3.2				
7a	C_6D_6	1.4	3.4[b]	9.8[b]	9.5[b]	5.2[b]	9.5[b]	10.5[b]
7b	$(CD_3)_2CO$	1.4	3.4	9.6	~9.5			
8	$(CD_3)_2CO$	~0.5	5.4	3.2	7.5	2.6	5.6	11.8
9a	$CDCl_3$	1.4						
9b	$CDCl_3$	~1	3.4	9.5				
10a	C_6D_6	1.5				5.0		12.2
11b	C_6D_6	1.0	3.0	10.0	9.0	4.6	2.5	12.3
12	$(CD_3)_2CO$	~0.5	6.0	2.8	5.5	6.2	4.8	~12
16	C_6D_6	<0.5		7.5	9.8			

[a]Spacings were measured on an expanded 60-MHz spectrum (sweep-width, 100 Hz) in the solvent that allowed the best first-order spectrum. Even when a multiplet was analyzable, the spacing is not given if second-order effects were evident. [b]Couplings measured from spectra recorded with a 250-MHz Cameca spectrometer.

water-soluble fraction (A) there was detected, in addition to the preponderant acetal **3a** and the β anomer **3b**, a small proportion of 2,3-*O*-isopropylidene-D-mannofuranose (**4**), which was extremely difficult to resolve from **3b** by t.l.c., or by g.l.c. of the per(trimethylsilyl) ethers; acetylation of the mixture, followed by column-chromatographic resolution of the acetates, permitted separation of all three compounds present, namely, the major product (**7a**) and its anomer (**7b**), together with a small proportion of the α-1,5,6-triacetate (**8**) of **4**. The latter was identified by direct comparison with a known[4,5] sample of **8** obtained by acetylation of **4** prepared by the general literature procedure of partial deacetonation of the classic acetonation-product of D-mannose, namely, 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose[5] (**5**). Compound **4** probably arises through concurrent, kinetic[2,3] acetonation of **1** by a route less favored than the major pathway (to **3**), and subsequent tautomerization to the furanose form; the possibility that it arises by thermodynamic control is considered unlikely, as no 5,6-acetal was found in the products.

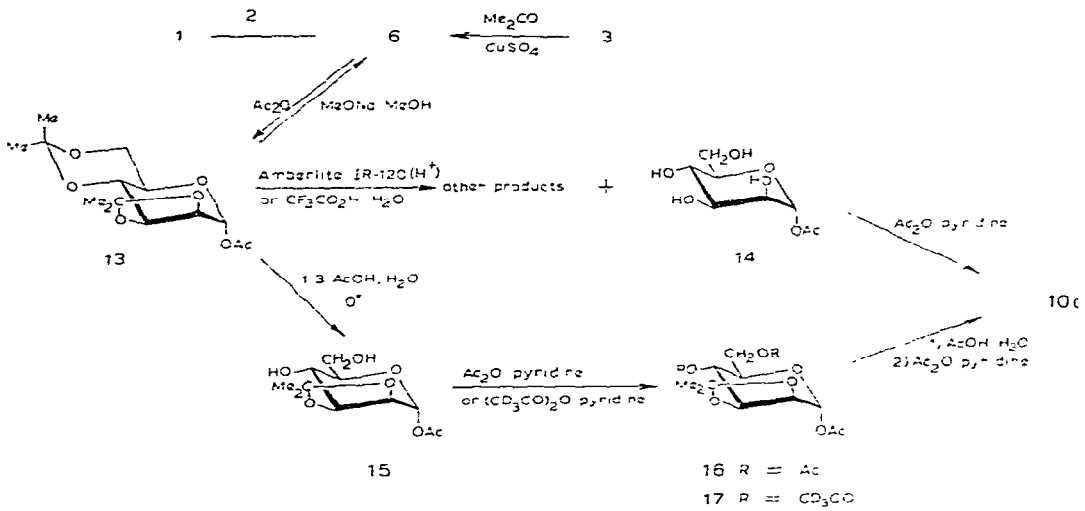
The minor, organic-soluble fraction (B) obtained from the monoacetonation of **1** with **2** showed essentially a single component in t.l.c., but the material was a mixture of two compounds, as was evident from g.l.c. analysis of the per(trimethylsilyl)ated product. One of these products, that in lesser proportion, behaved as the known diacetal **5**; the other, present in greater proportion, appeared to be a different diacetal, and was shown by subsequent experiments to be the pyranoid 2,3:4,6-diacetal **6**. The two products were resolved by acetylation followed by column chromatography on silica gel; the slower-migrating product, obtained in low yield, was the 1-acetate[6] (**12**) of **5**, and the faster-migrating, preponderant product was shown to be 1-*O*-acetyl-2,3:4,6-di-*O*-isopropylidene-α-D-mannopyranose (**13**).

Conditions favorable for kinetic diacetonation of D-mannose (**1**) were established by treating **1** with a 2-molar excess of **2**, as in the monoacetonation procedure for the preparation of **3**, with subsequent treatment of the mixture with an additional, 2-molar equivalent of **2**. The product of diacetonation, the pyranoid 2,3:4,6-diacetal (**6**), was isolated most readily by acetylation; this afforded the crystalline α-1-acetate (**13**) of **6** in 65% net yield from **1**. *O*-Deacetylation of **13** by catalytic transesterification then afforded the crystalline diacetal **6** in essentially quantitative yield. The crude diacetonation product from **1** contained very little monoacetonated material; the diacetal **6** that constituted the principal product was accompanied by a very small proportion of the classic diacetal **5**, as shown by g.l.c. (after trimethylsilylation) and by t.l.c. of the acetylated product, where traces of **12** were detected in the mother liquors from crystallization of **13**.

Evidence for the structure **6** accorded the new diacetal was provided from spectral data (see Tables I and II, and the Experimental section) and from chemical transformations. The ^{1}H-n.m.r. spectrum of **6** in dimethyl sulfoxide-d_6 showed the presence of two isopropylidene groups, and a single hydroxyl group that showed OH–H-1 coupling. Furthermore, treatment of the monoacetal **3** with acetone–copper(II) sulfate under strictly nonacidic conditions gave 89% of the diacetal **6** and a negligible proportion of the furanoid isomer **5**; this reaction was, however, subject

to profound change of course according to the precise procedural conditions, and, on certain occasions, extensive conversion into the isomer **5** took place. It is evident that copper(II) sulfate–acetone cannot be considered to be a strictly neutral reagent, a conclusion previously suggested by Maeda *et al.*[7].

Additional, structural evidence for **6** was provided by selective deacetonation studies on its 1-acetate **13**. Various procedures were examined for effecting partial or complete deacetonation of **13**. The action of Amberlite IR-120 (H^+) resin in methanol for 18 h at ~20° caused complete deacetonation, and formation of syrupy 1-*O*-acetyl-α-D-mannopyranose (**14**), acetylation of which gave α-D-mannopyranose pentaacetate (**10a**). This sequence of conversions provided firm evidence for the pyranoid ring in the acetal **6** and its acetate **13**. Trifluoroacetic acid–water[8] converted **13** into **14**, but gave a complex mixture of accompanying side-products. Selective deacetonation of **13** was satisfactorily accomplished by use of 1:3 acetic acid–water for 1 h at ~20°: the



4,6-*O*-isopropylidene group was removed, and crystalline 1-*O*-acetyl-2,3-*O*-isopropylidene-α-D-mannopyranose (**15**) was obtained in 74% yield. The n.m.r. spectrum of **15** in dimethyl sulfoxide-d_6 showed that one *O*-isopropylidene group remained, and two signals for OH protons were observed (one a doublet and one a triplet), thus establishing that the acetal group removed was that involving O-6.

Acetylation of **15** gave the crystalline triacetate **16**, which showed the anticipated three acetyl-group and two *C*-methyl-group signals in its n.m.r. spectrum; acetylation of **15** with acetic anhydride-d_6 gave the 4,6-bis(deuterioacetyl) analog **17**, which showed only one acetyl-group signal in its n.m.r. spectrum. Complete deacetonation of **16** with acetic acid–water gave amorphous 1,4,6-tri-*O*-acetyl-α-D-mannopyranose, acetylation of which afforded α-D-mannopyranose pentaacetate (**10a**).

The foregoing reactions demonstrate the considerable synthetic utility of the

acetonation procedure with alkyl isopropenyl ethers for the preparation, in high yield, of novel, partially substituted derivatives of D-mannopyranose linked through each of the ring-positions. The reactions proceed almost exclusively under kinetic control, with attack at the primary hydroxyl group followed by cyclization to the 1,3-dioxane ring-system the most-favored mode, and further attack to bridge a *cis*-vicinal diol grouping being the next-favored reaction. In contrast, the classic acetonation procedure with copper(II) sulfate–acetone, which requires a small proportion of a mineral acid for the reaction to proceed at an effective rate (see Experimental section), leads exclusively to the thermodynamic product, the diacetal **5**, partial deacetonation of which causes removal of the 5,6-*O*-isopropylidene group, to give **4**.

There have been several recent reports[9,10] on acetonation of sugars and their derivatives with 2,2-dimethoxypropane–*p*-toluenesulfonic acid; this reagent evidently affords mixtures containing both kinetic and thermodynamic products, from which the kinetic products may be isolated. For example, acetonation of D-mannose (**1**) with this reagent gives[9] the thermodynamic acetal **5** and not the kinetic product (**3** or **6**). Comparative studies in our hands have indicated that the method employing alkyl isopropenyl ether provides a superior, preparative route for the kinetic products, which are formed almost exclusively. The preparative procedure is simple, and affords the acetals in higher yields than by other methods.

EXPERIMENTAL

General methods. — The procedures used were as described in a previous report[3]. The g.l.c. injector was maintained at 250°, and two different column-packings (OV-1, 2% and 5%) were used. N.m.r. chemical-shifts are given in Table I, and Table II records spin-coupling data. The intensities of mass-spectral fragments are expressed as percentages of the base peak, and *m/e* values are recorded for major fragments only. Assignments are in general accord with interpretations reported in the literature for other *O*-isopropylidenehexoses and their acetates, but the possibility of alternative formulations is not excluded.

Acetonation of D-*mannose* (**1**) *with isopropenyl methyl ether* (**2**)*; preparation of 4,6-*O*-isopropylidene-*D*-mannopyranose* (**3**). — A solution of D-mannose (**1**; 5.4 g, 30 mmol) in dry *N*,*N*-dimethylformamide (20 ml) containing Drierite (1 g) was maintained below 5° (ice-bath), and isopropenyl methyl ether (4.3 g, 60 mmol) and *p*-toluenesulfonic acid (~20 mg) were added. The mixture was stirred magnetically at 0–5° until monitoring by t.l.c. indicated that all of the starting-material had disappeared (~5 h), whereupon anhydrous sodium carbonate (~5 g) was added, and the cold mixture was stirred vigorously for one h more. The mixture was filtered, and the filtrate poured into ice–water (50 ml). The product was extracted with dichloromethane (4×20 ml), and the extracts were combined, and washed with water (4×20 ml). The aqueous phase and the combined, aqueous extracts were freeze-dried, to yield an amorphous solid (mono-*O*-isopropylidene derivatives, Fraction A; 6.0 g). Evaporation of the dried (sodium sulfate) dichloromethane extract gave a syrup

(di-*O*-isopropylidene derivatives, Fraction B; 0.7 g). Detailed analytical characterization of Fractions A and B is given later; Fraction A was essentially a mixture of the anomers of **3**, with the α anomer (**3a**) strongly preponderant.

4,6-O-Isopropylidene-α-D-mannopyranose (**3a**). — The amorphous solid (Fraction A, yield 91% of crude monoisopropylidene acetals) was recrystallized twice from ethyl acetate to give **3a** as a microcrystalline, white powder, yield 5.4 g (82%), m.p. 156–157°, $[\alpha]_D^{20}$ −1 (3 min) → −16 (5 min) → −24° (final, 48 h; *c* 1.2, water); λ_{max}^{KBr} 2.90 broad (OH), 7.28 (CMe_2), and 9–10 μm (COCOC); *m/e* 205 (4.5, $M^+ - Me$), 187 (1.2, $205 - H_2O$, m* 170.6), 161 (0.7, $M^+ - Me_2C\overset{+}{O}H$), 145 (1.2, 205 − AcOH), 131 (3.3), 115 (1.5), 103 (1.2), 102 (1), 101 (6.5), 85 (2.4), 73 (7), 59 (30), 58 (26), and 43 (100); X-ray powder diffraction data: 6.88 s (3), 6.00 s (2), 5.37 vw, 4.75 vs (1), 4.39 m, 4.08 s, 3.90 w, 3.58 m, 3.20 m, 3.08 w, 2.91 w, and 2.75 m.

Anal. Calc. for $C_9H_{16}O_6$: C, 49.09; H, 7.27; O, 43.65. Found: C, 49.53; H, 7.12; O, 43.67.

Compound **3a** thus obtained was essentially the pure α anomer, as shown by g.l.c. of a per(trimethylsilyl)ated sample; the major peak for the derivative of **3a** was contaminated by less than 1–3% of that of **3b** (see later, for g.l.c. data).

1,2,3-Tri-O-acetyl-4,6-O-isopropylidene-α-D-mannopyranose (**7a**). — A solution of acetic anhydride (5.1 g, 30 mmol) in anhydrous pyridine (5 ml) was added at 0° to a stirred solution of pure compound **3a** (1.1 g, 5 mmol) in pyridine (5 ml) that was prepared and utilized as rapidly as possible, in order to prevent possible anomerization. The mixture was stirred for 24 h at ~20° and then poured onto ice. The product was extracted with dichloromethane, and the extract was washed with saturated, aqueous sodium hydrogencarbonate (3 × 10 ml), dried (sodium sulfate), and evaporated, to give **7a** as a syrup that crystallized on slow evaporation of a solution in ethyl acetate that had been passed through a small pad of Celite; yield 1.5 g (87%); m.p. 49° (modification of form; remelting at 55°), $[\alpha]_D^{20}$ +48° (*c* 1.0, chloroform); R_F 0.75 (1:1 ethyl acetate–petroleum ether); $\lambda_{max}^{CCl_4}$ 5.70 (C=O), 7.50 (CMe_2), and 8.5–10 μm (COCOC), no OH absorption; *m/e* 331 (8, $M^+ - Me\cdot$), 287 (0.6, $M^+ - AcO\cdot$), 245 (6.5, $287 - CH_2CO$), 227 (0.9, 287 − AcOH, m* 179.5), 226 (1.3, $M^+ - 2$ AcOH), 203 (1.4, $245 - CH_2CO$, m* 168.2), 169 (8, $227 - Me_2CO$), 157 (2, $AcO\overset{+}{C}H{=}CH{-}CHOAc$), 143 (6.5, 203 − AcOH, m* 100.7), 127 (3.5, $169 - CH_2CO$, m* 85.4), 115 (10, $157 - CH_2CO$), 109 (8, 169 − AcOH, m* 70.3), 103 (1.3), 101 (5), 97 (1.9), 73 (3.5), 59 (6), and 43 (100).

Anal. Calc. for $C_{15}H_{22}O_9$: C, 52.02; H, 6.36; O, 41.62. Found: C, 52.06; H, 6.40; O, 41.55.

Analytical characterization of products of acetonation of **1**. — *Chromatographic analyses.* The amorphous solid (Fraction A) and the syrup (Fraction B) from the first experiment were analyzed by t.l.c. and g.l.c. The solid (A) showed only a single, slow-migrating spot (R_F 0.27, ethyl acetate); with 4:1 ethyl acetate–methanol, it also showed a single spot (R_F 0.55), but with a tail. These R_F values are very similar to those of 2,3-*O*-isopropylidene-D-mannofuranose (**4**), so that differentiation of **3** and **4**

by t.l.c. is difficult. Analysis of a per(trimethylsilyl)ated sample of Fraction A by g.l.c. revealed two peaks, in the ratio of ~4:1, whose retention times (T_R) are given (*a*) relative to that of per(trimethylsilyl)ated 2,3:5,6-di-*O*-isopropylidene-D-mannose (Me_3Si-**5**), and also (*b*) (in parentheses) as absolute retention-times in sec (column OV-1, 2%, 150°): T_R (Me_3Si-**5**) 1.00 (558), T_R (major peak, Me_3Si-**3a**) 1.49 (830), T_R (minor peak, Me_3Si-**3b** + Me_3Si-**4**) 1.86 (1039). Within the limits of experimental error, the T_R value for a reference sample of 2,3-*O*-isopropylidene-1,5,6-tri-*O*-(trimethylsilyl)-D-mannofuranose (Me_3Si-**4**) was identical to that of the minor peak.

After the following experiment on the acetylated products had shown that the minor peak was probably a mixture of two compounds [per(trimethylsilyl)ated **3b** and **4**], further g.l.c. analysis was performed with a column packed with 5% of OV-1. The major peak remained a single component [T_R (Me_3Si-**5**) 1.00 (1340), T_R (major peak, Me_3Si-**3a**) 1.49 (2000) at 150°], but the minor peak was separated into two extremely closely spaced components [T_R 1.90 (2540)] that were better resolved at 170°.

The syrupy fraction (B) showed one major, fast-migrating spot (R_F 0.73, ethyl acetate) followed by two very minor components (R_F 0.56 and 0.47). It was purified by column chromatography on silica gel (eluant 1:1 ethyl acetate–petroleum ether), in order to remove the minor, slow-migrating contaminants (not isolated). A white, crystalline solid was obtained whose m.p. [118° (modification) to 132° (total fusion)] indicated that it was a mixture: $[\alpha]_D^{20}$ − 20° (*c* 1.2, chloroform); R_F 0.73 (ethyl acetate), 0.53 (1:2 ethyl acetate–petroleum ether) identical to those of an authentic sample of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**5**) [lit.[11] for **5**: m.p. 122–123°; $[\alpha]_D$ + 16° (ethanol)]. A per(trimethylsilyl)ated aliquot was analyzed by g.l.c. (column OV-1, 5%, 150°). It revealed two major peaks [T_R 1.00 (1340) and T_R 1.24 (1660) in the ratio of ~3:7], the first peak having a retention time identical to that of authentic per(trimethylsilyl)ated **5**; the second one corresponded to per(trimethylsilyl)ated **6** (see later data for **6**). A very minor component [T_R 1.13 (1520)] was also detected.

*Acetylation of the crude monoisopropylidene acetals (Fraction A), and isolation of 1,2,3-tri-*O*-acetyl-4,6-*O*-isopropylidene-β-D-mannopyranose* (**7b**). — For isolative characterization of the minor components of Fraction A, a sample (6.6 g, 30 mmol) in pyridine (20 ml) was acetylated with acetic anhydride (18.4 g, 180 mmol in pyridine (20 ml) according to the procedure described for preparation of **7a**. The syrup thus obtained (9.1 g, crude yield 88%) showed three spots (*a*, *b*, and *c*) in t.l.c. (R_F 0.75, 0.70, and 0.66, with 1:1 ethyl acetate–petroleum ether; R_F 0.45, 0.38, and 0.33 with 1:2 ethyl acetate–petroleum ether). The mixture was resolved on a column (4 × 100 cm) of silica gel (500 g) with 1:2 ethyl acetate–petroleum ether as the eluant, and collection of 10-ml fractions. Fractions 130–185 (spot *a*) contained the pure α-triacetate **7a** (4.5 g, 43%). Fractions 186–191 were a mixture (0.2 g) of spot *a* and spot *b*. Fractions 192–210 were exclusively spot *b*, isolated as a pure, crystalline compound (1.4 g, 13%) that was identified as *1,2,3-tri-*O*-acetyl-4,6-*O*-isopropylidene-β-D-mannopyranose* (**7b**): m.p. 53–62°, $[\alpha]_D^{20}$ −39° (*c* 1.0, chloroform); $\lambda_{max}^{CHCl_3}$ 5.75 strong (C=O), 7.30 (CMe_2), and 8.5–10 μm (COCOC), no OH absorption; *m/e* 331 (13, $M^+ - Me\cdot$), 287 (0.5, $M^+ - AcO\cdot$), 245 (11, $287 - CH_2CO$), 227 (0.5, 287–

AcOH), 226 (0.5, $M^{+}-2$ AcOH), 203 (2.5, $245-CH_2CO$, m* 168.2), 169 (4.5, $227-Me_2CO$), 157 (4.5, AcOCH=CH–$\overset{+}{C}$HOAc), 143 (10, 203–AcOH, m* 100.7), 127 (3, $169-CH_2CO$, m* 95.4), 115 (18, $157-CH_2CO$, m* 84.2), 109 (5.5, 169–AcOH, m* 70.3), 103 (2.2), 101 (7), 97 (2.5), 73 (4.5), 59 (9), and 43 (100).

Anal. Calc. for $C_{15}H_{22}O_9$: C, 52.02; H, 6.36; O, 41.62. Found: C, 52.00; H, 6.38; O, 41.64.

Fractions 211–216 contained a mixture (0.4 g) of spots *b* and *c*. Finally, fractions 217–250 contained spot *c* alone, isolated as a pure syrup (0.8 g, 8%) and identified as *1,5,6-tri-O-acetyl-2,3-O-isopropylidene-α-D-mannofuranose* (**8**), slightly contaminated (n.m.r.) by the *β* anomer; $[\alpha]_D^{20}$ +40° (*c* 1.4, chloroform) {lit.[4] m.p. 58.5–59°, $[\alpha]_D^{20}$ +49.9° (tetrachloroethane)}; *m/e* 331 (32, $M^{+}-Me.$), 287 (8, $M^{+}-AcO\cdot$), 245 (4, $287-\cdot CH_2CO$), 226 (2.5, $M^{+}-2$ AcOH), 203 (1.5, $245-CH_2CO$), 169 (15, $227-Me_2CO$), 157 (2.7, AcOCH=CH–$\overset{-}{C}$HOAc), 143 (3.5, 203–AcOH), 127 (8, $169-Me_2CO$, m* 95.4), 115 (11, $157-CH_2CO$), 109 (9, 169–AcOH), 103 (3), 101 (7), 98 (10.5), 97 (5), 85 (7.5), 73 (2.5), 71 (7), 59 (7), and 43 (100).

The ratio of pyranose to furanose forms isolated in this experiment was ~9:1, and the ratio of the α to *β* pyranose anomers was ~4:1. The n.m.r. spectrum of the crude mixture of the three acetates showed the presence of α and *β* anomers in the ratio of ~3:1.

Acetylation of crude diisopropylidene acetals (Fraction B), and isolation of 1-O-acetyl-2,3:4,6-di-O-isopropylidene-α-D-mannopyranose (**13**) *and its isomer* **12**. — As direct separation of the two major derivatives in Fraction B appeared to be practically impossible, acetylation was performed on a further 2.0 g of the mixture, following the procedure already described for Fraction A, but with twice the stoichiometric amount of acetic anhydride. Analysis of the resulting syrup (2.1 g, 91%) by t.l.c. showed two components (R_F 0.64 and 0.55; 1:2 ethyl acetate–petroleum ether), which were separated by column chromatography on silica gel (same eluant). First eluted was compound **13**; yield 1.15 g (50%), m.p. 145–147° (after recrystallization from methanol–water), $[\alpha]_D^{20}$ +3° (*c* 1.0, chloroform); $\lambda_{max}^{CHCl_3}$ 5.75 (C=O), 7.25 and 7.30 (CMe_2), and 8.5–10 μm (COCOC), no OH absorption; *m/e* 287 (20, $M^{+}-Me\cdot$), 259 (0.9, $M^{+}-MeCO\cdot$), 244 (12, $287-MeCO\cdot$), 243 (5.5, $287-AcO\cdot$), 229 (1.5, $287-Me_2CO$, m* 182.7), 227 (1.5, 287–AcOH, m* 179.5), 202 (1.6, $244-CH_2CO$), 201 (10, $287-2\ MeCO\cdot$, m* 140.8), 187 (1), 186 (1), 185 (3.5, $227-AcO\cdot$, m* 150.7), 173 (1.6), 169 (5, 229–AcOH), 143 (11, $201-Me_2CO$, m* 101.7), 141 (3), 129 (2), 127 (8), 115 (12), 101 (23), 100 (3), 97 (9), 85 (13), 73 (2.5), 71 (3.5), 59 (21), 57 (4), and 43 (100); X-ray powder diffraction data: 9.84 s (2), 8.22 m, 7.43 m, 5.95 vw, 5.07 vs (1), 4.68 m, 4.45 s (3), 4.29 w, 4.11 m, 3.83 w, 3.73 vw, and 3.43 w.

Anal. Calc. for $C_{14}H_{22}O_7$: C, 55.63; H, 7.28; O, 37.09. Found: C, 55.44; H, 7.19; O, 36.95.

Eluted after **13** was *1-O-acetyl-2,3:5,6-di-O-isopropylidene-α-D-mannofuranose*

(**12**; 0.45 g, 19%), isolated as a syrup; $[\alpha]_D^{20}$ +45° (*c* 1.6, chloroform) (lit.[6] $[\alpha]_D^{20}$ +45° in chloroform); λ_{max}^{film} 5.75 strong (C=O), 7.30 strong (CMe_2), and 8.5–10 μm (COCOC) no OH absorption; *m/e* 287 (43, $M^+ - Me\cdot$), 259 (0.4, $M^+ - MeCO\cdot$), 243 (1.6, 287 – AcO·), 229 (12, 287 – Me_2CO), 201 (1.5, 287 – 2 MeCO·, m* 140.8), 195 (16), 194 (2.5), 169 (1.5, 229 – AcOH, m* 124.7), 143 (3, 201 – Me_2CO), 141 (2.5), 128 (2.5), 127 (38), 115 (2.5), 109 (4), 102 (2.8), 101 (63), 99 (4.5), 98 (3.5), 97 (2.5), 85 (9.5), 72 (9), 59 (15), and 43 (100).

Deacetonation of **7a** *to* **9a**, *and subsequent acetylation to give* α-D-*mannopyranose pentaacetate* (**10a**) *and its 4,6-bis(trideuterioacetyl) analog* (**11a**). — A solution of **7a** (1.7 g, 5 mmol) in 1:3 acetic acid–water (50 ml) was heated for 1 h at 50°, whereupon t.l.c. (ethyl acetate) indicated disappearance of **7a** and formation of a single component having R_F 0.46. The solution was freeze-dried, to afford amorphous *1,2,3-tri-O-acetyl-*α-D-*mannopyranose* (**9a**; 1.4 g, 93%); m.p. 62–64°, $[\alpha]_D^{20}$ +45° (*c* 0.9, chloroform); λ_{max}^{KBr} ~3 (very broad, OH), 5.80 (C=O), and 8.5–10 μm (COCOC); *m/e* 247 (2.5, $M^+ - AcO\cdot$), 246 (0.3, $M^+ - AcOH$), 245 (2.2, $M^+ - H_2O - MeCO\cdot$), 217 (2), 215 (1.6, 246 – $\cdot CH_2OH$), 203 (0.6, 245 – CH_2CO), 173 (0.7), 158 (3, 246 – AcOCH=O), 157 (10, $AcOCH{=}CH{-}\overset{+}{C}HOAc$, m* 100.6 from *m/e* 245), 145 (1.8), 144 (1.5), 143 (2.5, 203 – AcOH, m* 100.7), 127 (1.8), 126 (0.9), 116 (3.3, 158 – CH_2CO, m* 85.2), 115 (32, 157 – CH_2CO, m* 84.2), 103 (3.5), 102 (2), 101 (0.7), 98 (6), 97 (2.5), 85 (4), 73 (20, 115 – CH_2CO, m* 46.3), 60 (7), and 43 (100).

A solution of acetic anhydride (5 ml) in pyridine (5 ml) was slowly added at 0° to a stirred solution of **9a** (0.5 g) in pyridine (5 ml). After 12 h at ~25°, the solution was processed as already described for the isolation of **7a**, to give **10a** as a syrup (0.55 g, 85%) that crystallized after a few days. Recrystallization from methanol plus a few drops of water gave pure **10a**, m.p. 75–76°, $[\alpha]_D^{20}$ +53° (*c* 1.0, chloroform) {lit.[12] m.p. 74°, $[\alpha]_D^{22}$ +56.6° (chloroform)}: R_F 0.27, ethyl acetate; λ_{max}^{KBr} 5.8 μm very strong (C=O), no OH absorption.

The foregoing procedure was repeated with 0.5 g of **9a**, but with use of acetic anhydride-d_6. All data recorded for the product **11a** thus obtained were closely comparable to those given for **10a**, except for the n.m.r. spectrum (see Table I), which showed signals for only three of the five acetyl groups.

Deacetonation of **7b** *to* **9b**, *and subsequent acetylation to give* β-D-*mannopyranose pentaacetate* (**10b**) *and its 4,6-bis(trideuterioacetyl) analog* (**11b**). — The deacetonation procedure used in the foregoing experiment was repeated with 1.0 g of **7b**, to give *1,2,3-tri-O-acetyl-*β-D-*mannopyranose* (**9b**; 0.8 g, 91%); m.p. 147–149°, $[\alpha]_D^{20}$ −32° (*c* 1.5, chloroform); R_F 0.43 (ethyl acetate); λ_{max}^{KBr} ~3 very broad (OH), 5.75 (C=O), and 8.5–10 μm (COCOC); *m/e* 288 (0.5, $M^+ - H_2O$), 247 (0.7, $M^+ - AcO\cdot$), 246 (0.5, $M^+ - AcOH$), 245 (4, 288 – MeCO·), 217 (2.5), 215 (3.5, 246 – $\cdot CH_2OH$), 203 (1.2, 245 – CH_2CO), 173 (1.3), 158 (3.5, 246 – AcOCH=O), 157 (17, $AcO{-}CH{=}CH{-}\overset{+}{C}HOAc$), 145 (3.5), 144 (3), 143 (5.5, 203 – AcOH), 127 (6), 126 (5.5), 116 (6, 158 – CH_2CO), 115 (55, 157 – CH_2CO), 103 (9.5), 102 (4), 101 (7), 98 (13), 97 (7), 85 (11), 73 (30), 60 (9.5), and 43 (100); X-ray powder diffraction data:

9.13 s (3), 8.78 m, 7.67 vw, 6.94 vs (1), 5.89 m, 5.42 m, 5.42 m, 5.11 m, 4.45 s (2), 4.33 m, 4.20 w, 3.96 w, and 3.81 m.

Compound **9b** (0.3 g) was treated with acetic anhydride, and an additional 0.3 g was treated with acetic anhydride-d_6, by the procedure described for the α anomer. The former experiment gave 0.30 g (80%) of crystalline **10b**, m.p. 116–117° (from methanol–water), $[\alpha]_D^{20}$ −24° (*c* 1.2, chloroform) (lit.[13] m.p. 117–118°, $[\alpha]_D^{20}$ −25.3° in chloroform); λ_{max}^{KBr} 5.8 μm (very strong C=O), no OH absorption. For the 4,6-bis(trideuterioacetyl) analog **11b**, all of the data were essentially identical to those recorded for **10b**, but the n.m.r. spectrum (see Table I) showed signals for only three of the five acetyl groups.

Preparative diacetonation of D-*mannose* (**1**) *with isopropenyl methyl ether* (**2**) *to give 2,3:4,6-di-*O*-isopropylidene-α-*D*-mannopyranose* (**6**), *isolated via its 1-acetate* **13**. — A solution of D-mannose (**1**; 5.4 g, 30 mmol) in dry *N*,*N*-dimethylformamide (20 ml) containing Drierite (1 g) was maintained at ~ −10°, and isopropenyl methyl ether (**2**; 4.3 g, 60 mmol) and *p*-toluenesulfonic acid (~20 mg) were added. The mixture was stirred magnetically for ~3 h, and then a further amount of the ether **2** (4.3 g, 60 mmol) was added dropwise during ~2 h, the temperature being kept at ~ −10°. T.l.c. (ethyl acetate) indicated that slow-migrating components (R_F <0.5) were absent. The mixture was then treated exactly as described for the preparation of the monoacetal **3**. In the present experiment, the aqueous phase contained only traces of monoacetals. Evaporation of the dichloromethane extract gave an amorphous solid whose properties in t.l.c. (1:2 ethyl acetate–petroleum ether) were very similar to those of the syrup (B) described in the first experiment, except for the presence of very minor, fast-migrating contaminants. G.l.c. of a per(trimethylsilyl)ated sample showed the same two major peaks, in 3:17 ratio (in order of elution). The mixture was acetylated conventionally with acetic anhydride and pyridine. Evaporation of the solvents, and nucleation with crystalline **13** (nucleation was not needed in subsequent preparations) gave solid **13**. One recrystallization from methanol–water gave reasonably pure **13**; a second recrystallization afforded analytically pure *1-*O*-acetyl-2,3:4,6-di-*O*-isopropylidene-α-*D*-mannopyranose* (**13**), yield 5.9 g (65% from D-mannose), having physical and spectral data identical to those already described.

The mother liquors contained additional **13** (0.2 g was recovered crystalline after long keeping), together with 1-*O*-acetyl-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose; the latter was not isolated.

The acetate **13** was deacetylated conventionally: a solution prepared from sodium (0.05 g) in anhydrous methanol (10 ml) was added to a solution of **13** (1 g) in methanol (10 ml). After 2 h at ~20°, all of the starting material had disappeared. Sodium ions were removed by shaking the solution with Amberlite IR-120 (H^+) resin, to bring it to neutrality (it was necessary to check the pH carefully during addition of the resin, because of the acid-sensitivity of the isopropylidene groups; see later). The resin was filtered off, and the filtrate was evaporated, to give the crystalline diacetal **6**; yield 0.85 g (93%). The product could be recrystallized from hexane, or ethyl acetate; it had m.p. 139–141°, $[\alpha]_D^{20}$ −39 (initial) → −50° (final, 48 h; *c* 1.0,

chloroform); the R_F and T_R values were identical to those already given; λ_{max}^{KBr} 2.9 broad (OH), 7.30 (CMe_2), and 8.5–10 μm (COCOC); *m/e* 260 (0.5, M^+), 245 (50, $M^+ - Me\cdot$), 217 (2.5, $M^+ - MeCO\cdot$), 202 (0.8, $M^+ - Me_2CO$), 187 (6.5, 245 – Me_2CO, m* 142.7). 185 (0.5, 245 – AcOH), 169 (1.8, 187 – H_2O), 159 (17), 145 (2.5), 141 (2.5), 131 (25), 130 (2.5), 129 (13), 127 (9), 115 (4.2), 113 (3), 102 (2), 101 (16), 100 (22), 99 (4.5), 98 (5), 97 (3.2), 85 (13), 81 (8), 73 (11), 71 (6), 69 (19), 59 (95), and 43 (100): X-ray powder diffraction data: 9.82 s (2), 5.54 vs (1), 4.24 m (3), and 3.87 vw.

Anal. Calc. for $C_{12}H_{20}O_6$: C, 55.38; H, 7.69; O, 36.92. Found: C, 55.21; H, 7.65; O, 37.20.

Conversion of 4,6-O-isopropylidene-D-mannopyranose (**3**) *into the 2,4:4,6-diacetal* **6**. — A suspension of the monoacetal **3** (1 g) and anhydrous copper(II) sulfate (5 g) in pure acetone (20 ml) was shaken vigorously for 48 h and then filtered. Evaporation of the filtrate gave 1.05 g (89%) of the diacetal **6**. G.l.c. of a per(trimethylsilyl)ated aliquot showed a principal peak corresponding to the (trimethylsilyl)ated diacetal **6** contaminated by <5% of the derivative of the furanoid isomer **5**.

It should be noted that, in one experiment performed with a different sample of copper(II) sulfate, complete isomerization of **6** to the thermodynamically favored, furanose form **5** occurred.

Selective deacetonation of the diacetal **13**: *preparation of 1-O-acetyl-2,3-O-isopropylidene-α-D-mannopyranose* (**15**). — *Deacetonation with acetic acid–water*. A suspension of **13** (0.5 g) in 1:3 acetic acid–water (20 ml) was stirred at room temperature until dissolution was complete (~1 h). The solution was then refrigerated (~0°) overnight. T.l.c. then indicated the presence of **15** as the major component (R_F 0.43, ethyl acetate) and a slow-migrating, minor component (R_f 0.05). The solution was freeze-dried, to give crude **15** as a microcrystalline powder that could be effectively purified by recrystallization from ethyl acetate: yield 0.32 g (74%). In a similar experiment performed with 1 g of **13**, the mixture was chromatographed (silica gel, 30 g: ethyl acetate) to give pure **15**; yield 0.62 g (70%) as a microcrystalline powder, m.p. 130–131°, $[\alpha]_D^{20}$ +24.5° (*c* 0.9, chloroform); R_f 0.43 (ethyl acetate); λ_{max}^{KBr} 2.95 and 3.03 (OH), 7.30 (CMe_2), 5.67 (C=O), and 8.35–10 μm (COCOC): *m/e* 247 (10, $M^+ - Me\cdot$), 229 (0.2, 247 – H_2O, m* 212.3), 219 (0.8, $M^+ - MeCO\cdot$), 204 (0.7, $M^+ - Me_2CO$), 203 (6.5, $M^+ - AcO\cdot$), 202 (6.5, $M^+ - AcOH$), 188 (0.7, 219 – $\cdot CH_2OH$, or 247 – $AcO\cdot$), 187 (8, 247 – AcOH, m* 141.6), 169 (0.5, 187 – H_2O, m* 152.7), 161 (2), 145 (9), 144 (3), 143 (1.5), 131 (2.5), 129 (9), 127 (10, 187 – AcOH, m* 86.2), 116 (2), 115 (6), 109 (3.5), 101 (4), 100 (5), 99 (6), 98 (9), 97 (7), 85 (20), 73 (22), 71 (9), 59 (40), and 43 (100); X-ray powder diffraction data: 8.38 vs (1), 746 m (3), 4.74 vs (2), 4.47 m, 4.12 m, and 3.83 m.

Anal. Calc. for $C_{11}H_{18}O_7$: C, 50.38; H, 6.87; O, 42.75. Found: C, 50.32; H, 6.69; O, 42.51.

G.l.c. analysis (OV-1, 5%, 170°, with Me_3Si-**5** as reference; T_R 1.00) of a per(trimethylsilyl)ated aliquot of the freeze-dried, crude product revealed the presence of a major component having T_R 1.74 (1020) (~80%, Me_3Si-**15**), a minor

one having T_R 2.52 (1475) (~15%, Me_3Si-**14**), plus four trace-products having T_R 1.88 (1100), 2.15 (1260), 3.60 (2105), and 3.85 (2255), these last amounting altogether to ~5% of the total mixture. (All of these components were detected in the mixtures obtained during deacetonation with trifluoroacetic acid or Amberlite IR-120; see following paragraphs.) A preliminary experiment conducted at room temperature resulted in an increase of these by-products. None of them corresponded to a per(trimethylsilyl)ated sample of D-mannose which, under the same conditions, gave a peak having T_R 2.35.

Deacetonation with trifluoroacetic acid–water. A suspension of **13** (0.5 g) in 1:9 trifluoroacetic acid–water (20 ml) was stirred at room temperature until a homogeneous solution was formed (~1 h), and the solution was kept overnight at ~0°. T.l.c. then indicated complete disappearance of starting material, and the presence of a major, slow-migrating spot (R_F 0.05, ethyl acetate), presumably the monoacetate **14**. The solution was freeze-dried to a glass. A per(trimethylsilyl)ated aliquot thereof showed, in g.l.c. (OV-1 5%, 170°; reference Me_3Si-**5**), a peak [T_R 2.52 (1475)] that amounted to ~40% of a mixture of about ten peaks. The mixture was acetylated conventionally, and column chromatography (30 g of silica gel; eluant 1:2 ethyl acetate–petroleum ether) of the resulting syrup allowed isolation of a crystalline compound identified, by mixed m.p. and n.m.r. spectrum, as α-D-mannopyranose pentaacetate (**10a**; 0.2 g, 30%).

Deacetonation with Amberlite IR-120 (H^+) resin. A solution of **13** (0.5 g) in methanol (20 ml) was stirred overnight at ~20° with Amberlite IR-120 (H^+) resin (3 ml). T.l.c. then indicated complete disappearance of starting material, and the presence of one major spot (**14**; R_F 0.05 in ethyl acetate). The resin was filtered off, and the filtrate evaporated. G.l.c. of a per(trimethylsilyl)ated aliquot thereof showed the same major peak (T_R 2.50, same conditions and reference as the preceding) as was detected in the foregoing experiment, but, in this instance, it comprised ~85% of the mixture (the other 15% arose from no more than four peaks). The mixture was acetylated, and the resulting solid was recrystallized from methanol–water, to give α-D-mannopyranose pentaacetate (**10a**): yield 0.33 g (51%), identified by mixed m.p. and n.m.r. spectrum.

1,4,6-Tri-O-acetyl-2,3-O-isopropylidene-α-D-mannopyranose (**16**) *and its 4,6-bis(trideuterioacetyl) analog* (**17**). — Selective deacetonation of **13** (1 g) was conducted with acetic acid–water as already described. The microcrystalline, freeze-dried compound (0.76 g) was divided into two equal parts. The first was acetylated with acetic anhydride–pyridine, to give an amorphous solid (one major spot in t.l.c.); it was twice crystallized (methanol–water), to give pure **16**; yield 0.76 g (66%), m.p. 126–127°, $[\alpha]_D^{20}$ −2° (*c* 1.0, chloroform); R_F 0.40 (1:2 ethyl acetate–petroleum ether); $\lambda_{max}^{CHCl_3}$ 5.7 strong (C=O), 7.30 (CMe_2), and 9–10 μm (COCOC), no OH absorption; *m/e* 331 (4.2, $M^+ - Me\cdot$), 303 (0.6, $M^+ - MeCO\cdot$), 288 (0.5, $M^+ - Me_2CO$), 287 (3.5, $M^+ - AcO\cdot$), 286 (0.6, $M^+ - AcOH$), 271 (0.2, 331 − AcOH, m* 221.9), 245 (0.5, 287 − CH_2CO), 229 (1.1, 288 − $AcO\cdot$, m* 182.1), 169 (18, 229 − AcOH), 157 (2), 145 (1.8), 139 (3.5), 127 (6), 115 (5), 109 (15, 169 − AcOH, m* 70.3), 103 (2), 101 (1.5),

100 (2), 99 (1.5), 98 (7), 97 (6), 85 (7), 81 (3.8), 73 (2), 69 (2), 59 (4), and 43 (100); X-ray powder diffraction data: 11.25 m, 9.68 vw, 7.11 2, 6.65 m (3), 6.25 m, 5.55 w, 4.68 w, 4.26 s (2), 4.12 s (1), 4.83 vw, and 3.58 vw.

Anal. Calc. for $C_{15}H_{22}O_9$: C, 52.02; H, 6.36; O, 41.62. Found: C, 52.75; H, 6.44; O, 41.71.

The other half was acetylated with acetic anhydride-d_6. All data recorded for compound **17** thus obtained were closely comparable to those given for **16**, except for the n.m.r. spectrum (see Table I), which showed a signal for only one of the three acetyl groups.

Deacetonation of **16**, *and acetylation to give* α-D-*mannopyranose pentaacetate* (**10a**). — A suspension of **16** (0.2 g) in 1:3 acetic acid–water (20 ml) was stirred for 1 h at ~50°. The resulting solution was freeze-dried, and the amorphous solid acetylated (acetic anhydride–pyridine), to give **10a**, which was recrystallized from methanol–water (yield 0.19 g, 83%), and identified by mixed m.p., and n.m.r. spectrum.

*Preparation of authentic samples of 2,3:5,6-di-*O-*isopropylidene-*D-*mannofuranose* (**5**) *and 2,3-*O-*isopropylidene-*D-*mannofuranose* (**4**). — These compounds were prepared by modification of the methods described by Iwadare[5].

A suspension of **1** (10 g) and anhydrous copper(II) sulfate (10 g) in acetone (200 ml) was stirred vigorously. After 48 h, analysis by t.l.c. indicated that only a small proportion of the D-mannose had reacted, giving essentially one fast-migrating product (the products of kinetic reaction of D-mannose with alkyl vinyl ethers were undetectable). One drop of concentrated sulfuric acid was then added, and the suspension was stirred for an additional 48 h. Practically all of the starting material had then reacted. The suspension was filtered, and sodium carbonate (5 g) and water (10 ml) were added to the filtrate, which was then evaporated. The resultant syrup was extracted with dichloromethane (100 ml), and the extract was washed with aqueous sodium carbonate (3 × 5 ml), dried (sodium sulfate), and evaporated, to give **5** (8.6 g, 63%), which was recrystallized from hexane, m.p. 120–122°, $[\alpha]_D^{20}$ +12° (*c* 1.1, chloroform); {lit.[11] m.p. 122–123°, $[\alpha]_D$ +16° (ethanol)}. Its mass spectrum was in close accord with that described by DeJongh and Biemann[14], notably *m/e* 245 (57, $M^+ - Me\cdot$), 187 (11, $245 - Me_2CO$), 159 (1.3, $M^+ - 101$), 101 (62), and 43 (100).

A solution of compound **5** (5 g) in a citrate buffer solution, pH 4.0 (Pufferlösung pH 4.0, Merck; 100 ml) was heated for 2 h at 150°, cooled, and freeze-dried. The solid mass thus obtained was triturated with anhydrous methanol. The methanolic extract was evaporated, and the resulting syrup was chromatographed on silica gel (eluant, 4:1 ethyl acetate–methanol), to give **4** (0.9 g, 20%) which did not crystallize; $[\alpha]_D^{20}$ −3° (final, 48 h; *c* 1.0, water) {lit.[5] m.p. 80.5–82°, $[\alpha]_D^{15}$ −3.7° (40 h, water)}.

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