Acetalation of Sucrose by Acetal Exchange with Concomitant Fission of the Glycosidic Bond. Some New Acetals of D-Glucose and Methyl α-D Fructofuranoside

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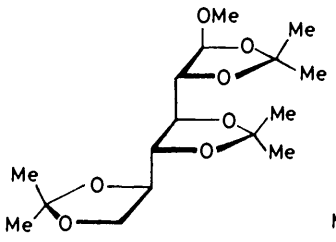
Prolonged reaction of sucrose with 2,2-dimethoxypropane in *NN*-dimethylformamide in the presence of toluene-*p*-sulphonic acid (0.3% w/v) afforded, after acetylation, methyl 4,6-di-*O*-acetyl-1,3-*O*-isopropylidene-α-D-fructofuranoside together with four acetals of D-glucose, namely, (1*S*)-1-methoxy-1,2:3,4:5,6-tri-*O*-isopropylidene-D-glucitol, 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose, 3-*O*-acetyl-1,2:4,6-di-*O*-isopropylidene-α-D-glucopyranose, and 1,2,3-tri-*O*-acetyl-4,6-*O*-isopropylidene-α,β-D-glucopyranose. The mechanism of formation of these compounds is discussed. Several derivatives of methyl α- and β-D-fructofuranosides have been prepared from methyl 1,3-*O*-isopropylidene-α-D-fructofuranoside.

CONVENTIONAL synthesis of acetals of sucrose has been frustrated by fission of the glycosidic bond and formation of acetals of D-glucose and D-fructose.[1] However, acetal exchange using a catalytic amount of toluene-*p*-sulphonic acid with acetals such as 2,2-dimethoxypropane,[2] 1,1-dimethoxycyclohexane,[3] and α,α-dimethoxytoluene [3] have yielded the 4,6-*O*- and 1′,2:4,6-di-*O*-acetals of sucrose in good overall yields. The use of 2-methoxypropene has afforded the same derivatives [4] and reaction of sucrose with α,α-dibromotoluene in pyridine has afforded the 4,6-*O*-benzylidene derivative in good yield.[5]

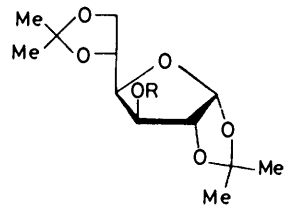
Whilst the acetal exchange procedure requires lesser amounts of acid catalyst, it also differs from direct acetalation (using aldehydes and ketones) inasmuch as it appears to be kinetically controlled, whereas the direct method is thermodynamically controlled. In the case of acetal exchange with 2,2-dimethoxypropane the most accessible hydroxy-groups (*e.g.* the primary hydroxy-groups) react preferentially, so that, with sucrose, the initial product is probably the 1′,6,6′-tri-*O*-(1-methoxy-1-methylethyl) ether. Subsequent cyclisation to give the 4,6-acetal ring is facile, whereas formation of the eight-membered 1′,2-acetal ring occurs less readily, and the 6′-*O*-(1-methoxy-1-methylethyl) group does not have a conveniently placed hydroxy-group with which to cyclise. Any remaining 1-methoxy-1-methylethyl groups, which are highly acid labile, would probably be lost on work-up. We have studied the acetal exchange under more forcing conditions (*e.g.* higher temperatures, higher acid concentrations, *etc.*) in the hope that a more highly substituted sucrose acetal would be formed, such as the 1′,2:4,6:3′6′-triacetal. Although we have no indication that higher acetals are formed, we noted that the use of higher concentrations of acid catalyst resulted in interglycosidic bond fission and the formation of several hitherto unknown acetals of D-glucose and methyl α-D-fructofuranoside.

Thus, treatment of sucrose with 2,2-dimethoxypropane and toluene-*p*-sulphonic acid (0.3% w/v) in *NN*-dimethylformamide resulted initially in the formation of the mono- and di-acetals of sucrose, but these were slowly consumed to give several chromatographically more mobile components. After *ca.* 36 h at room temperature, the crude reaction product was processed and acetylated to give a mixture which was fractionated on silica gel to give, in order of elution, five components (A)—(E).

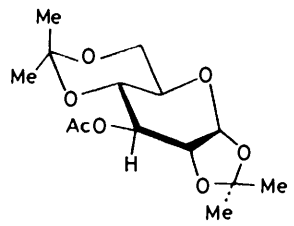
Component (A) was obtained in 6% yield as a syrup and its ^{1}H n.m.r. spectrum (Table 1) indicated that it contained three isopropylidene groups and one methoxy-group (δ 3.28). Hydrolysis of component (A) with dilute aqueous acid afforded only glucose, identified chromatographically, and the mass spectrum of component (A), in displaying an intense ion at *m/e* 317 (*M* − 15), indicated that it was a simple monosaccharide derivative. However, the need to accommodate three isopropylidene groups and a methoxy-group suggested that the compound contained either two cyclic isopropylidene groups and a 1-methoxy-1-methylethyl group attached to a glucopyranose or glucofuranose unit, or three cyclic acetal groups and a 1-*O*-



(1)



(2) R = C(OMe)Me$_2$
(3) R = Ac
(4) R = H



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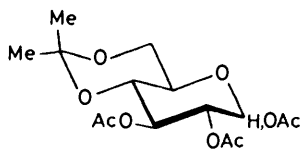


(6)

methyl group attached to glucose in the acyclic modification, as in compound (1). A 5,6-*O*-isopropylidene group was indicated in the mass spectrum by the presence of a prominent fragment at *m/e* 101 which results from the cleavage of C(4)–C(5).[6] However, the ^{1}H n.m.r. spectral data of component (1) (Table 1) were considerably at variance with those expected for 1,2:5,6-di-*O*-isopropylidene-3-*O*-(1-methoxy-1-methylethyl)-α-D-glucofuranose (2), particularly the coupling $J_{2,3}$ (2 Hz) which is usually zero in related compounds such as (3). Hence the acyclic triacetal structure (1) was assigned to component (A) and this was borne out by its mass spectrum in which fragments arising from the cleavage of the bonds of C(1)–OMe (*m/e* 301), C(2)–C(3) (131 and 201), and C(4)–C(5) (231 and 101) were observed. Additionally, the ^{13}C n.m.r. spectral data (Table 2) were in agreement with the three isopropylidene groups being five-membered, since the three quaternary acetal carbons resonated in the region δ_C 109.8—111.3 p.p.m., whereas six-membered isopropylidene rings give rise to quaternary carbon resonances in the region of δ_C 100 p.p.m.[7] Compound (1) along with its diastereoisomer, has been obtained from the reaction of the diacetal (4) with acidified methanolic acetone.[8]

The second eluted component (B) was obtained in 12.5% yield and was characterized as 3-*O*-acetyl-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (3) by direct comparison (see Tables 1 and 2 for the spectral data).

TABLE 1

^{1}H N.m.r. spectral data for the glucose acetals (δ and Hz)

	Compound				
	(1) [a,b]	(3) [a,b]	(5) [a]	(6) [a,c]	
				α-Anomer [d]	β-Anomer [d]
1-H	5.25(d) [e]	5.70(d)	5.42(d) [e]	6.27(d)	5.76(d)
2-H	4.47(dd) [e]	4.26(d)	3.95(t) [e]	5.11(dd)	5.10(dd)
3-H	4.09(dd) [e]	5.56(d)	5.52(dd) [e]	5.43(t)	5.22(t)
4-H		4.45(dd)	3.73(t)	3.54(t)	3.51(t)
5-H		4.30(m)	4.05(m)		
6a-H		4.11(dd)	3.91(dd)		
6b-H		3.96(dd)	3.63(t)		
$J_{1,2}$	3.5	3.5	4.7	4.0	8.0
$J_{2,3}$	2.0	0.0	4.5	10.0	9.0
$J_{3,4}$	7.5	3.0	8.5	9.5	9.5
$J_{4,5}$		8.0	9.0	9.5	10.0
$J_{5,6a}$		4.5	5.5		
$J_{5,6b}$		6.0	10.0		
$J_{6a,6b}$		8.5	10.5		

[a] At 220 MHz. [b] In C_6D_6. [c] In $CDCl_3$. [d] Spectrum run on a mixture of the two anomers. [e] Assignment verified by spin decoupling.

Further elution of the column afforded a highly crystalline component (C) which was isomeric with component (B) in that its n.m.r. spectra indicated the presence of two isopropylidene groups and one *O*-acetyl substituent. The 220 MHz ^{1}H n.m.r. spectrum of component (C) was first-order and the individual resonances were assigned by spin decoupling (Table 1) which showed that the *O*-acetyl group must be located at *O*-3, since the 3-H resonance was to lower field of all other resonances. This suggested that component (C) was the previously unknown 3-*O*-acetyl-1,2:4,6-di-*O*-isopropylidene-α-D-glucopyranose (5), which is the acetylated pyranose analogue of the ubiquitous 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (4) and has not pre-

TABLE 2

Tentative assignments of ^{13}C n.m.r. chemical shifts (in p.p.m. relative to $SiMe_4$ at 15.08 MHz)

	Compound									
	(1) [a]	(3) [a]	(5) [a]	(6) [a]		(8) [a]	(7) [b]	(14) [c]	(18) [c]	(19) [b]
				α-Anomer	β-Anomer					
C-1	104.4	105.1	97.5	89.8	92.3	62.2	62.3	58.9	60.9	62.3
C-2	82.1	79.7	76.6	69.3	70.1	102.6	103.7	109.2	104.8	104.1
C-3	77.4	76.1	73.6	71.5	72.3	81.3	82.8	81.1	78.0	82.6
C-4	77.4	83.4	63.6	66.1	68.1	79.1	78.4	78.3	76.1	79.7
C-5	80.0	72.5	70.9	71.0	71.5	79.1	86.3	84.2	82.3	85.6
C-6	67.9	67.1	62.2	61.8	62.0	64.2	63.2	62.3	63.7	45.3
OMe	55.3					48.5	48.4	49.3	50.0	
O–C–O [d]	111.3	112.1	108.4	99.9	99.9	99.2	99.5			99.5
	110.0									
	109.8	109.2	99.6							
C*Me* [d]	27.4	26.8	28.89							
	27.3	26.2	27.43			27.01	27.08			27.14
	27.0	25.2	26.52			20.31	21.36			21.23
	26.8	25.2	18.91							
	25.4									

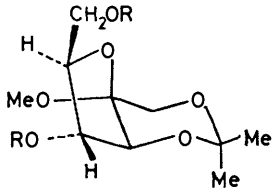
[a] In $CDCl_3$. [b] In D_2O. [c] In $(CD_3)_2CO$. [d] Isopropylidene group.

viously been encountered in the numerous studies of the acetonation of D-glucose. A comparison of the ^{1}H n.m.r. spectral data of compound (5) with those of 3-*O*-acetyl-1,2:4,6-di-*O*-benzylidene-α-D-glucopyranose revealed that the coupling constants for the two compounds were virtually identical. As noted by Coxon,[9] the observed coupling constants indicate considerable distortion of the pyranose ring which adopts the $^4HC_5$ conformation, as in compound (5). The ^{13}C n.m.r. parameters (Table 2) further indicated that one isopropylidene ring was six-membered and that the other was five-membered, since the quaternary acetal carbons resonated at δ_C 108.4 and 99.6 p.p.m., in agreement with the figures quoted by Buchanan *et al.*[7] Furthermore, the separations of the pairs of acetal methyl resonances ($\Delta\delta_C$ 9.98 and 0.91 p.p.m.) indicated a six- and five-membered isopropylidene ring, respectively.[7]

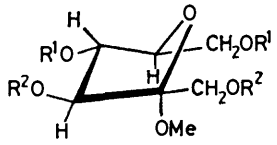
The next eluted component (D) was obtained in 16% yield and the ^{1}H n.m.r. spectrum indicated that it was a mixture of the α- and β-anomers of a monoisopropylidene triacetate, which could not be separated chromatographically. The resonances due to 1-, 2-, and 3-H of each anomer were easily identified at chemical shifts below δ *ca.* 5 p.p.m., which indicates that *O*-acetyl groups were present at these positions, and the observed coupling constants were in accord with a pyranose ring structure. Therefore component (D) was identified as 1,2,3-tri-*O*-acetyl-4,6-*O*-isopropylidene-α,β-D-glucopyranose (6), and the presence of the 6-membered acetal ring was confirmed by the chemical shift (δ_C 99.9 p.p.m.) of the quaternary acetal carbon of the isopropylidene group, and the separation of the methyl carbon resonances ($\Delta\delta_C$ 9.92 p.p.m.).[7] The β-anomer of this compound has previously been reported by Hasegawa and Fletcher [10] and by Wolfrom *et al.*[11]

The next eluted component (E) was the major product of the reaction and was obtained in 36% yield as a syrup. Its n.m.r. spectra revealed that it was a monoisopropylidene derivative containing one methoxy-group and two *O*-acetyl substituents. Its 220 MHz ^{1}H n.m.r. spectrum was largely first-order and interpretable only in terms of the fructofuranoside (8). The lowest field resonance was the 4-H doublet at δ 4.90 ($J_{4,5}$ 4, $J_{3,4}$ 0 Hz) and the next lowest field resonance was that due to 6a- and 6b-H which suggests that the two *O*-acetyl groups were located at the 4- and 6-positions. The 3-H resonance appeared as a singlet at δ 4.10. In the ^{13}C n.m.r. spectrum of compound (8) the acetal carbon of the isopropylidene group resonated at δ_C 99.2 p.p.m. and the separation of the resonances due to the two methyl carbons was 6.70 p.p.m. which is indicative of a six-membered isopropylidene ring, although the smaller than usual separation of the two methyl carbons might be indicative of a deformed chair conformation of the six-membered ring. These facts show that component (E) is methyl 4,6-di-*O*-acetyl-1,3-*O*-isopropylidene-α-D-fructofuranoside (8) and that the anomeric configuration is limited to alpha by the nature of the fused ring system. Examination of molecular models of compound (8) indicates that the 3- and 4-hydrogens subtend a dihedral angle of *ca.* 90° and therefore the zero coupling of $J_{3,4}$ is expected.

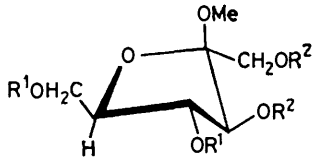
The fructofuranoside (8) was previously unknown, although Guthrie and Jenkins [12] have obtained it independently in an analogous manner. Furthermore, Horton and his co-workers have recently described the



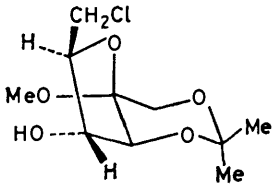
(7) R = H
(8) R = Ac
(9) R = Bz
(10) R = Ms



(11) R^1 = Bz, R^2 = H
(12) R^1 = Bz, R^2 = Ac
(13) R^1 = R^2 = Ac
(14) R^1 = R^2 = H



(15) R^1 = Bz, R^2 = H
(16) R^1 = Bz, R^2 = Ac
(17) R^1 = R^2 = Ac
(18) R^1 = R^2 = H



(19)

TABLE 3

^{1}H N.m.r. spectral data for the fructofuranosides (δ and Hz)

	Compound							
	(8) [a,d]	(9) [b,d]	(10) [c,d]	(11) [c,e]	(12) [b,d]	(13) [c,d]	(15) [c,e]	(17) [a,f]
1a-H	3.93(s)	3.92(s)	3.91(s)		4.47(d)	4.40(d)	3.72(d)	4.38(d)
1b-H					4.18(d)	4.10(d)	3.48(d)	4.29(d)
3-H	4.10(s)	4.28(s)	4.25(s)		5.53(d)	5.28(d)	4.64(d)	5.74(d)
4-H	4.90(d)	5.32(d)	4.78(d)	5.41(dd)	5.34(dd)	4.93(dd)	5.60(t)	5.62(dd)
5-H	4.18(m)	4.44(dt)		4.38d(t)	4.52(cm)			
6a-H	4.45(dd)	4.75(cm			4.69(cm)	4.1—4.5(cm)		
6b-H	4.28(dd)							
$J_{1a,1b}$					14.0	12.3	12.5	12.0
$J_{3,4}$	0	0	0	1.7	1.5	1.8	7.5	*ca.* 6
$J_{4,5}$	4.0	4.0	3.7	5.0	4.7	4.7	7.5	*ca.* 6
$J_{5,6a}$	4.5	4.5		*ca.* 5			5.0	
$J_{5,6b}$	6.5	9.5		*ca.* 9			7.5	
$J_{6a,6b}$	11.5						12.0	

[a] At 220 MHz. [b] At 100 MHz. [c] At 90 MHz. [d] In $CDCl_3$. [e] In $(CD_3)_2SO$. [f] In C_6D_6.

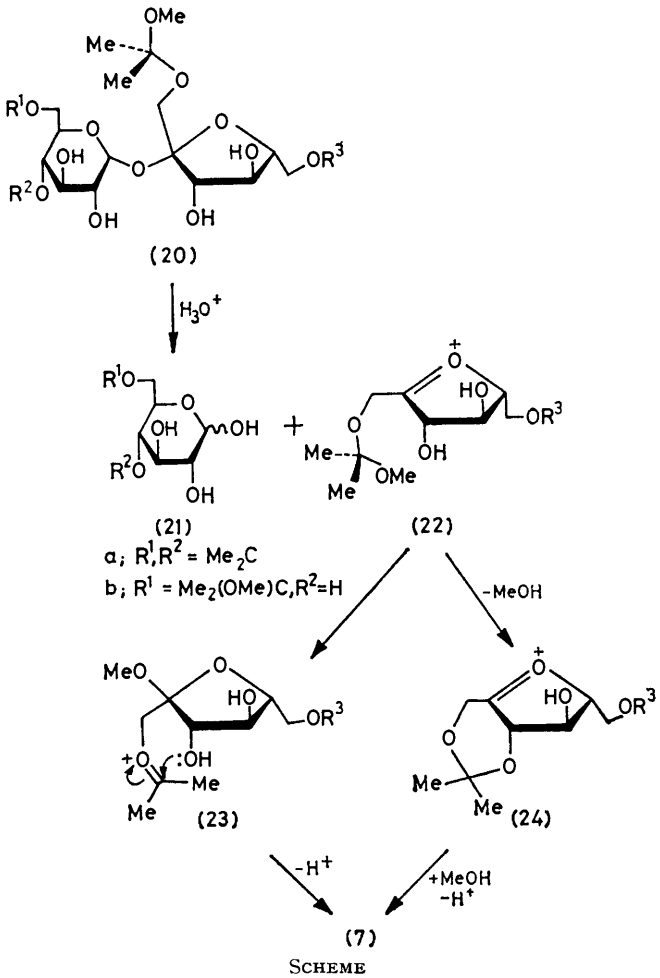
free sugar 1,3-*O*-isopropylidene-α-D-fructofuranose obtained from the kinetic acetalation of fructose with 2-methoxypropene.[13]

When we attempted the preparation of the acetal directly from the reaction of D-fructose with 2,2-dimethoxypropane under the same conditions, a complex mixture of products was obtained which, after acetylation, appeared to contain the methyl fructoside (8) as a minor product only.

The 1,3-acetal (8) was further characterised by de-*O*-acetylation to compound (7) followed by either benzoylation or mesylation to give the respective diesters (9) and (10) which were both non-crystalline, but have n.m.r. spectral data similar to the diacetate (8) (Tables 2 and 3). Mild acid-catalysed methanolysis of the dibenzoate (9) resulted in loss of the isopropylidene group and partial anomerisation of the anomeric centre. When the reaction was conducted at −5 °C, anomerisation was less marked and syrupy methyl 4,6-di-*O*-benzoyl-α-D-fructofuranoside (11) was obtained in 70% yield together with 18% of the crystalline β-anomer (15). However, when the reaction was conducted at reflux for *ca.* 1.5 min, the α- and β-anomers were obtained in yields of 32 and 59%, respectively, which shows that the β-anomer is thermodynamically the more stable. The coupling constants $J_{3,4}$ and $J_{4,5}$ are substantially different for each anomer (Table 3) and indicate that the α- and β-fructofuranosides adopt different conformations, a fact which we have previously noted for similar compounds.[14] The most favoured conformation for each is that in which the aglycone occupies a pseudo-axial configuration due to the anomeric effect and, in the β-anomer, this can be achieved in the E_2-conformation (15) or a related skew in which the hydroxymethyl group at C-2 and the 3- and 4-substituents assume pseudo-equatorial positions. The observed coupling constants fit this conformation well. The α-anomer, on the other hand, probably assumes the E^0 conformation (11) or a related skew in which C-1 and C-6 are held in pseudo-equatorial configurations.

De-*O*-benzoylation of each anomer afforded the respective syrupy methyl fructofuranosides (14) and (18), the optical rotations of which closely agree with those reported by Bethell and Ferrier.[15] Additionally, the ^{13}C n.m.r. chemical shifts (Table 2) of each anomer agreed with the published data.[16] The fructofuranosides (14) and (18) were then converted into their syrupy tetra-acetates (13) and (17) which, surprisingly, do not appear to have been previously reported. The ^{1}H n.m.r. spectral data suggest that these too adopt E^0 and E_2 conformations, similar to compounds (11) and (15) above, respectively.

Finally, the reaction of methyl 1,3-*O*-isopropylidene-



SCHEME

α-D-fructofuranoside (7) with sulphuryl chloride proceeded smoothly to give the 6-chloro-derivative (19) in 66% yield; the position of the chlorine atom is shown by the large upfield shift of the C-6 resonance in the ^{13}C n.m.r. spectrum of compound (19) (Table 2).

The origin of the monosaccharide acetals derived from sucrose is of considerable interest because most of them have not previously been encountered by direct acetalation of fructose and glucose. The fructofuranoside (7) probably arises from a 1′-*O*-(1-methoxy-1-methylethyl) derivative, such as compound (20), in which R^1, R^2 is either $Me_2(OMe)C$, H or $Me_2C<$ and R^3 is H or $Me_2(OMe)C$. Fission of the β-fructofuranoside linkage would then give the fructofuranosyl oxycarbonium ion (22) which would rearrange to compound (23) by migration of the methoxy-group to C-2, followed by ring closure to give the 1,3-*O*-isopropylidene derivative (7) or *vice versa* by way of compound (24) (Scheme). This could explain why (7) is not formed to the same extent from fructose under these conditions, since fructose exists mainly in the pyranose modification. The formation of the glucose acetals could be explained by further reaction of 4,6-*O*-isopropylidene-D-glucopyranose (21a) or 6-*O*-(1-methoxy-1-methylethyl)-D-glucose (21b) with 2,2-dimethoxypropane.

EXPERIMENTAL

T.l.c. was carried out on silica-gel-coated plastic film (Schleicher and Schull, LS 254) and the separated compounds were detected either under u.v. light (for benzoates, *etc.*) or by an α-naphthol spray and heat. Column chromatography was conducted on silica-gel G (Merck 7734). Optical rotations were measured at *ca.* 20 °C in a 1 dm cell using a Perkin-Elmer Model 141 automatic polarimeter. Mass spectra were recorded at 70 eV on either an A.E.I. MS-30 or a Kratos MS-25 spectrometer. Melting points were determined on a Kofler microscope hotstage and are uncorrected. ^1H and ^{13}C N.m.r. spectral data are given in Tables 1—3.

*Reaction of Sucrose with 2,2-Dimethoxypropane in the presence of Toluene-*p*-sulphonic Acid.*—A mixture of sucrose (10 g, 29.2 mmol), toluene-*p*-sulphonic acid (0.75 g; 0.3% w/v), and dry *NN*-dimethylformamide (200 ml) was stirred at room temperature for 0.5 h and 2,2-dimethoxypropane (52 ml, 410 mmol) was then added to the resulting solution. Stirring was continued for 36 h, when t.l.c. (chloroform–methanol, 6 : 1) showed the presence of one major and several minor products. The reaction mixture was neutralized [Amberlite IR-45(OH)] and concentrated to a syrup which was dissolved in dry pyridine (150 ml) and treated with acetic anhydride (50 ml). The mixture was kept for 18 h at room temperature, then concentrated to dryness by co-distillation with toluene, and fractionated on a dry-packed [17] column of silica gel. Elution with light petroleum–diethyl ether (6 : 1) gave 5 components (A—E). The first eluted component (A) was identified as (1*S*)-*methoxy*-1,2:3,4:5,6-*tri*-O-*isopropylidene*-D-*glucitol* (1) (0.58 g, 6%), $[\alpha]_D$ +56° (*c* 1, chloroform) (lit.,[8] $[\alpha]_D$ +76.6°) (Found: C, 57.65; H, 8.25. Calc. for $C_{16}H_{28}O_7$: C, 57.83; H, 8.43%); *m/e* 317 (67%) (*M* − Me), 301 (11) (*M* − OMe), 259 (48), 231 (15), 201 (14.6), 173 (28.6), 143 (75), 141 (28), 131 (4.4), 101 (40), and 43 (100).

The second eluted component (B) was identified as 3-O-*acetyl*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (3) (1.1 g, 12.5%), m.p. and mixed m.p. 62.5 °C, $[\alpha]_D$ −30.3° (*c* 1, chloroform) (lit.,[18] m.p. 62—63 °C, $[\alpha]_D$ −31°) (Found: C, 55.45; H, 7.15. $C_{14}H_{22}O_7$ requires C, 55.63; H, 7.3%).

Component (C) was identified as the crystalline 3-O-*acetyl*-1,2:4,6-*di*-O-*isopropylidene*-α-D-*glucopyranose* (5) (0.8 g, 9%), m.p. 150—151 °C, $[\alpha]_D$ +52.7° (*c* 1, chloroform) (Found: C, 55.85; H, 7.45. $C_{14}H_{22}O_7$ requires C, 55.63; H, 7.3%); *m/e* 303 (7.2%) (*M* + 1), 287 (62) (*M* − Me), 245 (32), 229 (24.6), 227 (10.1), 201 (30), 169 (47), 143 (100), 127 (29.7), and 43 (75).

The fourth component (D) was characterised as 1,2,3-*tri*-O-*acetyl*-4,6-O-*isopropylidene*-α,β-D-*glucopyranose* (6) (1.62 g, 16%), m.p. 120—121 °C, $[\alpha]_D$ +16.3° (*c* 1, chloroform) (Found: C, 51.65; H, 6.45. $C_{15}H_{22}O_9$ requires C, 52.0; H, 6.36%).

The final eluted component (E) was *methyl* 4,6-*di*-O-*acetyl*-1,3-O-*isopropylidene*-α-D-*fructofuranoside* (8) (3.35 g, 36%), $[\alpha]_D$ +35.5° (*c* 1, chloroform) (Found: C, 52.75; H, 6.8. $C_{14}H_{22}O_8$ requires C, 52.83; H, 6.92); *m/e* 303 (3.6%) (*M* − Me), 287 (36) (*M* − OMe), 245 (1.9) (*M* − CH_2OAc), 186 (20.2), 171 (4.5), 158 (3.9), 145 (2.5), 130 (19.8), 115 (10.2), 111 (27.3), 101 (9.9), and 43 (100).

Methyl 1,3-O-*Isopropylidene*-α-D-*fructofuranoside* (7).—The diacetate (8) (12.5 g) was suspended in methanol (50 ml) and treated with M-sodium methoxide (15 ml). After 24 h the reaction mixture was deionised [Amberlite IR-120(H)], concentrated to dryness, and purified by column chromatography with chloroform–methanol (10 : 1) as eluant to give the syrupy acetal (7) (8.5 g, 92%), $[\alpha]_D$ +42.5° (*c* 1, methanol) (Found: C, 51.55; H, 7.55. $C_{10}H_{18}O_6$ requires C, 51.3; H, 7.7%).

Methyl 1,3-O-*Isopropylidene*-4,6-*di*-O-*mesyl*-α-D-*fructofuranoside* (10).—Methanesulphonyl chloride (2 ml, 26 mmol) was added as drops to a cold solution of compound (7) (1.5 g, 6.4 mmol) in anhydrous pyridine (50 ml) and, after 18 h at room temperature, t.l.c. (chloroform–methanol, 10 : 1) revealed the formation of a single, faster-moving product. The reaction mixture was then poured into ice–water, extracted with chloroform, and concentrated to a syrup which was purified by elution from a small column of silica gel with chloroform to give the syrupy *dimesylate* (10) (2.3 g, 92%), $[\alpha]_D$ +37° (*c* 1, chloroform) (Found: C, 36.75; H, 5.55; S, 16.25. $C_{12}H_{22}O_{10}S_2$ requires C, 36.92; H, 5.64; S, 16.4%).

Methyl 4,6-*Di*-O-*benzoyl*-1,3-O-*isopropylidene*-α-D-*fructofuranoside* (9).—An ice-cold solution of the diol (7) (7.8 g, 33.3 mmol) in anhydrous pyridine (100 ml) was treated slowly with benzoyl chloride (14 ml, 121 mmol). The reaction was complete after 16 h at room temperature (t.l.c., light petroleum–diethyl ether, 1 : 1). The mixture was then decomposed with ice–water, extracted with chloroform, concentrated, and purified by elution from a silica-gel column with light petroleum–diethyl ether (3 : 1) to give the syrupy *dibenzoate* (9) (13.4 g; 91%), $[\alpha]_D$ +29.5° (*c* 1, chloroform) (Found: C, 65.1; H, 6.0. $C_{24}H_{26}O_8$ requires C, 65.16; H, 5.9%).

Methyl 4,6-*Di*-O-*benzoyl*-α-D-*fructofuranoside* (11) *and its* β-*Anomer* (15).—To a solution of the dibenzoate (9) (3 g) in dichloromethane (60 ml) was added methanol, containing 1% hydrogen chloride (20 ml). The solution was then stored at −5 °C for 24 h, when t.l.c. (chloroform–methanol, 9 : 1) revealed the presence of two products, of which the faster-moving was the major component. The reaction mixture was then neutralised (lead carbonate), filtered, evaporated,

and applied to a column of silica gel. Elution with chloroform afforded the *diol* (11) (1.9 g, 70%), $[\alpha]_D$ +103° (*c* 1, chloroform) (Found: C, 62.55; H, 5.65. $C_{21}H_{22}O_8$ requires C, 62.7; H, 5.47%).

Further elution of the column gave a syrup, which crystallised from ethanol to give *methyl* 4,6-*di*-O-*benzoyl*-β-D-*fructofuranoside* (15) (0.48 g, 17.5%), m.p. 134 °C, $[\alpha]_D$ −49.5° (*c* 1, methanol) (Found: C, 62.85; H, 5.35. $C_{21}H_{22}O_8$ requires C, 62.7; H, 5.47%).

When the same reaction was conducted at reflux temperature for *ca.* 1.5 min, the products (11) and (15) were obtained in 31 and 59% yields, respectively.

Methyl 1,3-*Di*-O-*acetyl*-4,6-*di*-O-*benzoyl*-α-D-*fructofuranoside* (12).—A solution of the diol (11) (0.5 g) in dry pyridine (20 ml) was treated with acetic anhydride (5 ml) at room temperature for 14 h after which t.l.c. (diethyl ether–light petroleum, 3 : 1) indicated completion of the reaction. The reaction mixture was worked up in the usual manner to give the syrupy *tetra-ester* (12) (0.55 g, 91%), $[\alpha]_D$ +51.7° (*c* 1, chloroform) (Found: C, 61.65; H, 5.55. $C_{25}H_{26}O_{10}$ requires C, 61.73; H, 5.35%).

Methyl 1,3-*Di*-O-*acetyl*-4,6-*di*-O-*benzoyl*-β-D-*fructofuranoside* (16).—The diol (15) (0.4 g) was acetylated in the usual way (pyridine and acetic anhydride) to yield the syrupy *tetra-ester* (16) (0.43 g, 89%), $[\alpha]_D$ −35.7° (*c* 1, chloroform) (Found: C, 61.95; H, 5.55. $C_{25}H_{26}O_{10}$ requires C, 61.73; H, 5.35%).

Methyl α-D-*Fructofuranoside* (14).—A solution of the dibenzoate (11) (2.5 g) in methanol (25 ml) was treated with 1M sodium methoxide (10 ml) for 30 h, when t.l.c. (chloroform–methanol, 3 : 1) revealed completion of the reaction. The reaction mixture was then deionised [Amberlite IR-120(H)], evaporated to dryness, and purified on a silica-gel column using chloroform–methanol (7 : 1) as eluant to give the syrupy compound (14) (1.05 g, 87%), $[\alpha]_D$ +89.5° (*c* 1, water) (lit.,[15] $[\alpha]_D$ +87°) (Found: C, 43.1; H, 7.35. Calc. for $C_7H_{14}O_6$: C, 43.3; H, 7.22%).

Methyl β-D-*Fructofuranoside* (18).—Debenzoylation of compound (15) (2.3 g) was carried out as described above to give the syrupy glycoside (18) (1 g; 91%), $[\alpha]_D$ −47.5° (*c* 1, water) (lit.,[15] $[\alpha]_D$ −49°) (Found: C, 42.95; H, 7.43. Calc. for $C_7H_{14}O_6$: C, 43.3; H, 7.22%).

Methyl 1,3,4,6-*Tetra*-O-*acetyl*-α-D-*fructofuranoside* (13).—Acetylation of compound (14) (0.3 g) was performed in the usual manner (pyridine and acetic anhydride, overnight) to give the syrupy *tetra-acetate* (13) (0.5 g, 89%), $[\alpha]_D$ +89.7° (*c* 1, chloroform) (Found: C, 49.6; H, 6.15. $C_{15}H_{22}O_{10}$ requires C, 49.72; H, 6.07%).

Methyl 1,3,4,6-*Tetra*-O-*acetyl*-β-D-*fructofuranoside* (17).—Acetylation of compound (18) (0.35 g) was carried out in the usual way to give the syrupy *tetra-acetate* (17) (0.56 g, 86%), $[\alpha]_D$ −13.3° (*c* 1, chloroform) (Found: C, 49.55; H, 6.15. $C_{15}H_{22}O_{10}$ requires C, 49.72; H, 6.07%).

Methyl 6-*Chloro*-6-*deoxy*-1,3-O-*isopropylidene*-α-D-*fructofuranoside* (19).—Sulphuryl chloride (0.85 ml, 10.5 mmol) was added as drops to a solution of the 4,6-diol (7) (1.25 g, 5.35 mmol) in chloroform (30 ml) and dry pyridine (30 ml) at −25 °C. The reaction mixture was maintained at the same temperature for 0.5 h, then allowed to warm to room temperature. After 18 h, t.l.c. (chloroform–methanol, 12 : 1) showed the presence of two products. The reaction mixture was then poured into a stirred suspension of sodium carbonate (1.5 g) in methanol (40 ml) containing a catalytic amount of sodium iodide (dechlorosulphation). After 0.5 h the mixture was filtered through Hyflo-supercel, concentrated, and purified by column chromatography. Elution with chloroform–methanol (20 : 1) gave the syrupy 6-*chloride* (19) (0.89 g, 66%), $[\alpha]_D$ +31.3° (*c* 1, chloroform) (Found: C, 47.45; H, 6.65; Cl, 14.15. $C_{10}H_{17}ClO_5$ requires C, 47.52; H, 6.73; Cl, 14.06%).

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