The Chemistry of Maltose. Part II.[1] Chemical Modifications at the Reducing Unit

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Chemical transformations of the reducing unit of maltose have been accomplished by routes starting from the known 1,2,2',3',4',6,6'-hepta-acetate. In particular, the syntheses of 3-chloro-3-deoxy-, 3-azido-3-deoxy-, 2,3-anhydro-, 3,6-anhydro-, and 3-oxo-α-1,4-linked disaccharides are described. The 2,3-anhydride, which has the *allo*-configuration in the reducing ring, reacted with hydrogen bromide to give the 3-bromo-3-deoxy-maltose derivative by specific diequatorial ring opening. Methyl 4-*O*-(α-D-glucopyranosyl)-β-D-*ribo*-hex-3-ulopyranoside hexa-acetate underwent ready epimerisation to give the 2-axial epimer.

We have embarked [1] on a programme aimed at the chemical modification of maltose; in particular we hope to convert it into analogues of amicetin, bamicetin, and plicacetin, nucleoside antibiotics of a maltose-type disaccharide.[2]

Dick *et al.*[3] have reported the selective acetylation of β-maltose (1) monohydrate with acetyl chloride in pyridine–toluene to give a mixture of the 1,2,2',3',4',6,6'-hepta-acetate (2) and the octa-acetate (3) in the ratio *ca.* 7 : 3, respectively. The hepta-acetate (2) was isolated as a glass in 70% yield after chromatography. The very slow acetylation of the 3-hydroxy-group has been attributed to the presence of a strong intramolecular hydrogen bond between the 3- and the 2'-hydroxy-groups, which has been observed in the crystal structures of maltose monohydrate [4] and methyl β-maltoside monohydrate [5] and has been postulated for maltose in dimethyl sulphoxide solution from i.r. and n.m.r. spectral evidence.[6] Although we acknowledge that there is a correlation between the lack of reactivity of the 3-hydroxy-group and its hydrogen bonding to the 2'-hydroxy-group, we believe that the reason for its lack of reactivity may be more profound since it has been established in other cases that intramolecular hydrogen bonding *enhances* the rate of acylation by acid chlorides.[7] In agreement with this, a similar lack of reactivity of the 3-hydroxy-group has been observed for the β-1,4-linked disaccharide lactose,[8] which has been shown to adopt preferentially a conformation in which hydrogen bonding between the 2'- and 3-hydroxy-groups is not possible.[9]

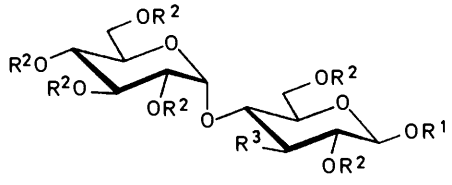
The corresponding maltose heptabenzoate (4) has also been prepared by an analogous reaction,[10] but in view of the lower yield reported (54%) we considered the hepta-acetate (2) [3] more convenient for further transformations.

In the light of a consideration of the steric and polar factors influencing the feasibility of S_N2 reactions,[11]

[1] Part I, P. L. Durette, L. Hough, and A. C. Richardson, *Carbohydrate Res.*, in the press.
[2] R. J. Suhadolnik, 'Nucleoside Antibiotics,' Wiley-Interscience, New York, 1970, pp. 203—217.
[3] W. E. Dick, jun., B. G. Baker, and J. E. Hodge, *Carbohydrate Res.*, 1968, **6**, 52.
[4] G. J. Quigley, A. Sarko, and R. H. Marchessault, *J. Amer. Chem. Soc.*, 1970, **92**, 5834.
[5] S. S. C. Chu and G. A. Jeffrey, *Acta Cryst.*, 1967, **23**, 1038.
[6] B. Casu, M. Reggiani, G. G. Gallo, and A. Vigevani, *Tetrahedron*, 1966, **22**, 3061.
[7] K. W. Buck, J. M. Duxbury, A. B. Foster, A. R. Perry, and J. M. Webber, *Carbohydrate Res.*, 1966, **2**, 122.
[8] I. M. Vazquez, I. M. E. Thiel, and J. O. Deferrari, *Carbohydrate Res.*, 1973, **26**, 351.
[9] C. A. Beevers and H. N. Hansen, *Acta Cryst.*, 1971, **B27**, 1323.
[10] I. M. E. Thiel, J. O. Deferrari, and R. A. Cadenas, *Annalen*, 1969, **723**, 192.
[11] A. C. Richardson, *Carbohydrate Res.*, 1969, **10**, 395.

displacements should occur readily at C-3 in suitable derivatives of the β-hepta-acetate (2) regardless of the chirality at C-3. Hence it should be possible to effect a double inversion at C-3 of maltose resulting in overall retention of configuration. The most appropriate method was considered to be that of Jones *et al.*[12] in which replacement of the hydroxy-group by a chloro-substituent with inversion of configuration by reaction with sulphuryl chloride is followed by displacement of the chloro-substituent by an S_N2 reaction with an appropriate nucleophilic anion.

Treatment of the hepta-acetate (2) with sulphuryl chloride afforded a highly crystalline chloro-derivative (12) in 84% yield. The inversion of configuration at C-3 was indicated by the ^{1}H n.m.r. data (Tables 1 and 2), particularly by the H-4 resonance at τ 5·95 which appeared as a quartet ($J_{3,4}$ 2·5, $J_{4,5}$ 9 Hz). The H-1 and H-5 resonances appeared at lower field (0·35 p.p.m. for H-1) than the corresponding resonances of β-maltose

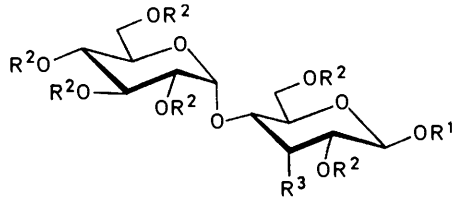


(1) $R^1 = R^2 = H$, $R^3 = OH$
(2) $R^1 = R^2 = Ac$, $R^3 = OH$
(3) $R^1 = R^2 = Ac$, $R^3 = OAc$
(4) $R^1 = R^2 = Bz$, $R^3 = OH$
(5) $R^1 = Me$, $R^2 = Ac$, $R^3 = OH$
(6) $R^1 = Me$, $R^2 = Ac$, $R^3 = OAc$
(7) $R^1 = Me$, $R^2 = Ac$, $R^3 = N_3$
(8) $R^1 = R^2 = Ac$, $R^3 = OMs$
(9) $R^1 = Me$, $R^2 = Ac$, $R^3 = OMs$
(10) $R^1 = Me$, $R^2 = H$, $R^3 = OMs$
(11) $R^1 = Me$, $R^2 = Ac$, $R^3 = Br$

octa-acetate (3), as a result of deshielding by the *syn*-axial chloro-substituent at C-3. Other than a slight upfield shift (0·15 p.p.m.) for H-1′, the chemical shifts and spin–spin coupling constants for the non-reducing ring protons were similar to those observed for β-maltose octa-acetate (3).[13]

De-*O*-acetylation of (12) by the Zemplén method gave the crystalline disaccharide 3-chloro-3-deoxy-4-*O*-(α-D-glucopyranosyl)-D-allopyranose (13). Attempts at displacement of the chloro-group in (12) by azide anion in both *NN*-dimethylformamide and hexamethylphosphoric triamide at elevated temperatures proceeded with extensive decomposition, probably initiated by deacetylation at C-1 (see later). Hence, methyl glycoside formation was deemed necessary prior to nucleophilic displacement. Therefore the 3-chloro-hepta-acetate (12) was treated in sequence with hydrogen bromide in acetic acid and mercury(II) acetate in methanol, conditions which were adequate for the formation of methyl β-maltoside hepta-acetate (6) from maltose octa-acetate (3).[1] However, elemental analytical data for the highly crystalline product indicated that it was a hexa-acetate of the 3-chloro-disaccharide.

The ^{1}H n.m.r. spectrum of the product indicated that the acetyl group at C-1 had been lost [the H-1 doublet ($J_{1,2}$ 7·0 Hz) had moved upfield by 0·92 p.p.m. in comparison with the spectrum of (12)]. Hence, the hexa-acetate was identified as 2,6-di-*O*-acetyl-3-chloro-3-deoxy-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-allopyranose (15), which could be obtained directly in 73% yield by the reaction of the chloro-hepta-acetate (12) with mercury(II) acetate in methanol. Clearly this reagent could be useful for the selective removal of the anomeric acetyl group in sugar acetates. Acetylation of the hexa-acetate (15) afforded the β-hepta-acetate (12). Presumably (12) failed to react with hydrogen bromide, under the reaction conditions employed, to give the α-glycosyl bromide (22) because of the severe *syn*-diaxial interaction between the 3-Cl and the 1-Br in the α-anomer.



(12) $R^1 = R^2 = Ac$, $R^3 = Cl$
(13) $R^1 = R^2 = H$, $R^3 = Cl$
(14) $R^1 = Me$, $R^2 = Ac$, $R^3 = Cl$
(15) $R^1 = H$, $R^2 = Ac$, $R^3 = Cl$
(16) $R^1 = Me$, $R^2 = H$, $R^3 = Cl$
(17) $R^1 = Me$, $R^2 = OAc$, $R^3 = N_3$
(18) $R^1 = Me$, $R^2 = OAc$, $R^3 = NHAc$
(19) $R^1 = Me$, $R^2 = OAc$, $R^3 = OBz$
(20) $R^1 = Me$, $R^2 = H$, $R^3 = OH$
(21) $R^1 = Me$, $R^2 = Ac$, $R^3 = OAc$

The desired methyl 3-chloro-maltoside (14) could be prepared in high yield by an alternative procedure. Thus, treatment of maltose 1,2,2′,3′,4′,6,6′-hepta-acetate (2) in sequence with hydrogen bromide in acetic acid and mercury(II) acetate in methanol afforded crystalline methyl 2,2′,3′,4′,6,6′-hexa-*O*-acetyl-β-maltoside (5) in 76% yield. That no acetyl migration took place during this sequence of reactions was indicated by the n.m.r. spectral data for (5); the H-3 resonance appeared as a wide triplet ($J_{2,3} = J_{3,4} = 9{\cdot}4$ Hz) at *ca.* 1·6 p.p.m. to higher field of the corresponding resonance in methyl β-maltoside hepta-acetate (6) in accord with H-3 being attached to the carbon atom bearing the less deshielding hydroxy-group. The resonances due to the other ring protons of the reducing ring were also moved upfield with respect to the corresponding resonances in (6), but to a smaller extent. Reaction of (5) with sulphuryl chloride then afforded crystalline methyl 3-chloro-3-deoxy-4-*O*-(α-D-glucopyranosyl)-β-D-allopyranoside hexa-acetate (14) in 86% yield. Subsequently it was

[12] B. T. Lawton, W. A. Szarek, and J. K. N. Jones, *Carbohydrate Res.*, 1970, **15**, 397, and references cited therein.

[13] B. Casu, M. Reggiani, G. G. Gallo, and A. Vigevani, *Carbohydrate Res.*, 1970, **12**, 157; G. Keilich, E. Siefert, and H. Friebolin, *Org. Magnetic Resonance*, 1971, **3**, 31.

TABLE 1

First-order chemical shifts (τ values) at 220 MHz in [^{2}H]chloroform, unless otherwise stated [a]

Compd.	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	H-1′	H-2′	H-3′	H-4′	H-5′	H-6′a	H-6′b	OMe	OMs	OAc and NAc
(2)	**4·40d**	5·10t	*b*	**6·17t**	*b*	**5·55** [e]	*b*	**4·66d**	**5·06dd**	4·61t	**4·96t**	*b*	*b*	*b*			7·90, 7·93, 7·96, 7·98, 8·00
(3)	4·26**d**	5·02t	4·71t	5·96t	6·16m	5·55dd	5·71dd	4·59d	5·14dd	4·64t	4·94t	6·06m	5·76dd	5·96dd			7·88, 7·91, 7·96, 7·99, 8·02
(5)	5·66d	5·24t	6·35t	6·22t	*ca.* 6·4m	5·49dd	5·82dd	4·61d	5·02dd	4·57t	4·94t	*ca.* 5·9m	5·74dd	5·94dd	6·53		7·89, 7·90, 7·92, 7·96, 7·98, 8·00
(6)	5·55d	5·17t	4·74t	5·98t	6·31oc	5·50dd	5·76dd	4·58d	5·14t	4·63t	4·94t	6·04m	5·74dd	5·96dd	6·53		7·87, 7·91, 7·97, 7·99, 8·02
(7)	**5·64d**	5·08t	**6·44t**	6·33t	6·4m	5·49dd	5·79dd	4·56d	5·02t	4·57t	4·92t	*ca.* 5·9m	5·75dd	*ca.* 5·9dd	6·52		7·86, 7·90, 7·91, 7·97, 7·98
(8)	**4·28**d	4·88t	5·05t	5·98t	6·17m	5·47dd	5·69dd	4·59d	5·00t	4·62t	4·94t	5·99m	5·77dd	5·95dd		6·90	7·88, 7·89, 7·90, 7·98, 8·01
(9)	5·56m	5·03—5·11m		5·97t	6·30sx	5·41dd	5·69dd	4·55d	4·95t	4·60t	4·92t	*d*	5·75dd	*d*	6·53	6·94	7·88, 7·91, 7·98, 8·01
(11)	5·72d	4·93t	5·94t	6·07t	6·37oc	5·50dd	5·74dd	4·42d	4·94t	4·59t	4·92t	5·80—5·96m			6·54		7·89, 7·90, 7·93, 7·98, 8·00
(12)	**3·91d**	*e*	*e*	5·95dd	*e*	5·53 [e]	*e*	4·74d		4·57t	4·93t	6·07oc	*e*	5·94dd			7·89, 7·90, 7·95, 7·98, 8·00
(14)	5·19**d**	5·26dd	5·19t	5·96dd	5·81sx	5·47dd	5·75dd	4·75d	5·15t	4·55t	4·93t	6·03oc	5·73dd	5·94dd	6·49		7·86, 7·89, 7·91, 7·95, 7·98, 8·00
(15) [f]	4·83d							4·74d	5·18t	4·56t	4·95t						7·85, 7·89, 7·91, 7·95, 7·98, 8·00
(17)	5·29m		5·66m	6·13dd	*g*	5·51dd	5·82dd	4·71d	5·10t	4·54t	4·91t	*g*	5·72dd	5·96dd	6·51		7·86, 7·91, 7·99, 8·00
(18) [f,h,i]			5·0m					5·32d	4·25t	4·78t					6·84		7·80, 8·14, 8·19, 8·28, 8·34
(19) [j]	5·20m		4·03m	6·07dd	*k*	5·41dd	*k*	4·81d	5·09t	4·72t	4·98t	*k*	*k*	*k*	6·48		7·86, 7·89, 8·00, 8·02, 8·09, 8·61
(21)	5·30—5·39m		4·39m	6·14dd	*l*	5·51 [e]	5·79dd	4·92d	5·07t	4·67t	4·96t	*l*	*l*	*l*	6·51		7·85, 7·89, 7·91, 7·98, 7·99, 8·03
(21) [h]	5·34d	5·05dd	4·34t	6·57dd	*ca.* 5·9m	5·52dd	5·92dd	5·37d	4·95t	4·36t	4·71t	6·13m	5·63dd	5·78dd	6·75		8·03, 8·04, 8·21, 8·27, 8·28, 8·35 8·39
(23)	5·27s	5·20d	*m*	6·10m	*m*	5·68d	6·10dd	4·80d	5·12t	4·46t	4·92t	*m*	5·80m		6·56		7·82, 7·92, 7·96, 7·97, 8·00
(24) [n]	5·61d	*ca.* 5·1m	5·09t	5·71t	*o*	6·33 [e]	*o*	4·70d	4·88t	4·83t	4·92t	*o*	6·91 [e]	7·36dd	6·45	6·86	7·84, 7·95, 8·06, 8·33
(26) [p]	5·25s			5·52dd				4·31d	5·15t	4·68t	4·89t		*ca.* 6·9dd	7·50dd	6·37		7·96, 8·02, 8·32
(27) [f]	5·25s	*q*	*q*	*q*	*q*	*q*	*q*	4·48d	5·13t	4·54t	4·94t		*q*	*q*	6·49		7·91, 7·92, 7·98, 7·99
(30) [f]	5·45d	4·89dd		5·55dd	6·23sx			4·72d	5·09t	4·56t	4·94t				6·44		7·84, 7·86, 7·91, 7·98, 8·00
(31) [f]	5·33d	4·55d						4·29d	5·03t	4·56t	4·92t				6·52		7·88, 7·91, 7·98, 8·00

[a] The ring protons in the non-reducing ring are given primed numbers; sx = sextet, oc = octet. [b] H-3, H-6b, H-5′, H-6′a at 5·74—6·05m; H-5, H-6′b at 6·27—6·4m. [c] Broadened doublet. [d] H-5′, H-6′b at 5·91—6·03m. [e] H-2, H-3, H-2′ at 5·11—5·20m; H-5, H-6*b*, H-6′a at 5·68—5·83m. [f] At 100 MHz. [g] H-5, H-5′ at 5·93—6·04m. [h] In [^{2}H$_6$]benzene. [i] NH at 3·64d. [j] OBz at 1·94—2·55m. [k] H-5, H-6b, H-6′a at 5·71—5·80m; H-5′, H-6′b at 5·9—6·0m. [l] H-5, H-5′, H-6′a, H-6′b at 5·82—6·11m. [m] H-3, H-5, H-5′ at 5·49—5·62m. [n] $OCPh_3$ at 2·61—3·02m. [o] H-5, H-6b, H-5′ at 6·49—6·61m. [p] $OCPh_3$ at 2·61—2·89. [q] H-2, H-3, H-5 at 6·27—6·67; H-4, H-6a, H-6*b*, H-5′, H-6′a, H-6′b at 5·57—6·04m.

TABLE 2

First-order coupling constants (Hz) for [^{2}H]chloroform solutions, unless otherwise stated

Compound	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'a}$	$J_{5',6'b}$	$J_{6'a,6'b}$
(2)	8·4	9·5	9·0	8·1			−12·2	3·5	10·5	10·0	9·9			
(3)	8·2	9·0	8·8	8·8	2·3	4·1	−12·0	4·0	10·6	9·7	10·0	3·7	2·4	−12·1
(5)	7·9	9·4	9·4	8·3	1·4	4·5	−12·3	3·9	10·5	9·8	9·8	4·0	2·1	−12·1
(6)	7·9	8·9	9·0	9·6	2·7	4·4	−12·4	4·0	10·5	10·0	9·9	4·0	2·1	−12·4
(7)	8·0	9·5	9·8	8·7	1·3	4·5	−12·2	3·9	10·5	9·8	9·5	4·7	2·0	−12·5
(8)	7·9	8·9	8·0	9·7	2·2	4·0	−12·4	4·1	10·9	10·0	9·8	4·5	2·3	−12·2
(9)	7·4	8·5	8·7	9·4	2·8	4·0	−12·3	4·0	10·5	9·3	10·2	4·2		−12·8
(11)	7·7	10·0	9·0	9·0	1·9	4·2	−12·1	3·9	9·7	9·4	10·1			
(12)	7·6		2·5	*ca.* 9			−11·5	3·7	10·1	9·4	9·9		2·5	−11·5
(14)	7·9	2·9	3·0	9·0	2·5	4·5	−11·8	3·9	10·4	9·7	9·8	4·4	1·9	−12·5
(15)	7·0							3·7	10·2	9·5	9·7			
(17)		*ca.* 3	3·2	9·4	2·5	4·3	−12·2	3·8	10·3	9·9	9·7	4·5	2·0	−12·4
(18) [a,b]								3·2	9·5	9·5	9·8			
(19)		*ca.* 3	*ca.* 3	*ca.* 9	5·0		−13·0	3·4	10·0	10·0	9·7			
(21)		*ca.* 3	3·0	9·2		5·0	−12·5	3·7	10·4	10·0	9·7			
(21) [a]	8·1	3·0	2·9	9·9	2·0	4·7	−12·3	3·8	10·6	10·0	9·7	4·1	2·0	−12·4
(23)	<0·5	3·6			<1	2·6	−10·1	3·7	10·2	9·5	10·4	3·5		
(24)	7·7	9·0	8·3	8·9			−10·5	3·9	*ca.* 9	*ca.* 9	*ca.* 9		3·6	−10·5
(26)	<0·5		1·3	9·2				3·8	10·4	9·5	9·4		2·7	−10·6
(27)	<0·5							4·0	10·2	9·8	9·6			
(30) [c]	8·1			10·0				3·6	10·3	9·4	9·4			
(31)	2·6							3·5	10·1	9·4	9·3			

[a] In [^{2}H$_6$]benzene. [b] $J_{NH,CH}$ 8·2 Hz. [c] $J_{2,4}$ 1·4 Hz.

found that the required product (14) could be made without the isolation of the intermediates (2) and (5). Thus sequential treatment of maltose monohydrate (1) with acetyl chloride–pyridine, hydrogen bromide–acetic acid, methanol–mercury(II) acetate, and sulphuryl chloride–pyridine afforded (14) in an overall yield of 43% without the need for chromatography at any stage. The structure of (14) was confirmed by its ^{1}H n.m.r. spectrum which was largely first-order (Tables 1 and 2). The coupling constants $J_{1,2}$ (7·9), $J_{2,3}$ (2·9), $J_{3,4}$ (3·0), and $J_{4,5}$ (9·0 Hz) indicated that the reducing unit was an allopyranosyl ring ($^4C_1$ conformation) and the downfield shifts of the H-1 and H-5 signals (0·36 and 0·50 p.p.m., respectively) in comparison with methyl β-maltoside hepta-acetate (6) were indicative of an axial 3-Cl.

Deacetylation of (14) afforded the free glycoside (16) crystalline in 92% yield. As anticipated the chloro-substituent of (14) was also susceptible to nucleophilic displacement and reacted with azide ion with inversion of configuration to give methyl 3-azido-3-deoxy-β-maltoside hexa-acetate (7) in 81% yield. The *gluco*-configuration of the reducing unit was confirmed by the n.m.r. spectral parameters; $J_{1,2}$ 8·0, $J_{2,3}$ 9·5, $J_{3,4}$ 9·8, and $J_{4,5}$ 8·7 Hz. Furthermore the H-3 resonance appeared at 1·70 p.p.m. to high field of the corresponding resonance of methyl β-maltoside hepta-acetate (6), indicative of the presence of the less deshielding azido group at C-3. Comparison of the n.m.r. spectrum of (7) with that of (6) indicates that, besides the H-3 resonance, the H-4 resonance is the only one affected by the change in the nature of the C-3 substituent (an upfield shift of 0·35 p.p.m.), which suggests that it lies within the shielding cone of the anisotropic azide group.

The preparation of the epimeric methyl 2,6-di-*O*-acetyl-3-azido-3-deoxy-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-allopyranoside (17) was also accomplished from β-maltose hepta-acetate (2). Mesylation of (2) afforded the 3-mesylate (8) in near quantitative yield, which was converted into the corresponding methyl glycoside (9) in the usual manner. Comparison of the ^{1}H n.m.r. spectrum of the 3-mesylate (8) with that of β-maltose octa-acetate (3) showed only one divergence, a 0·34 p.p.m. upfield shift of the H-3 resonance (Table 1), indicative of the location of the mesyl group at C-3.

As was observed in the case of (12), extensive decomposition took place when the 3-*O*-mesyl-hepta-acetate (8) was treated with sodium azide in *NN*-dimethylformamide, but the corresponding methyl β-glycoside (9) underwent smooth displacements in hexamethylphosphoric triamide with both sodium azide and sodium benzoate to give, with inversion of configuration at C-3, the 3-azido- and 3-*O*-benzoyl derivatives, (17) and (19) respectively, in high yields. The configuration at C-3 was indicated by the n.m.r. parameters (Tables 1 and 2); in both cases $J_{2,3}$ and $J_{3,4}$ were near 3 Hz. Catalytic hydrogenation of the 3-azide (17) followed by acetylation afforded methyl 3-acetamido-2,6-di-*O*-acetyl-3-deoxy-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-allopyranoside (18).

In the ^{1}H n.m.r. spectrum of the 3-benzoate (19), one of the acetyl resonances appeared at abnormally high field (τ 8·61) in [^{2}H]chloroform. This resonance was tentatively assigned to the 2′-acetyl group, the protons of which can be envisaged (on the basis of molecular models) as lying in the shielding region of the benzene ring of the 3-*O*-benzoyl group when the molecule exists in a conformation similar to that adopted by maltose and its methyl glycoside [4-6] (in which the 3′- and 2-hydroxy-groups are close enough to form a strong hydrogen bond). That the signal probably does not arise from the vicinal 2-acetyl group was suggested by previous work on the effect of aroyloxy-groups at C-1 of pyranoses on the chemical shift of the neighbouring 2-acetoxy-group.[14] In these studies no significant shift was detected, which was attributed to the steric difficulty of aligning all of the acetyl protons simultaneously in the shielding region above the aromatic ring.

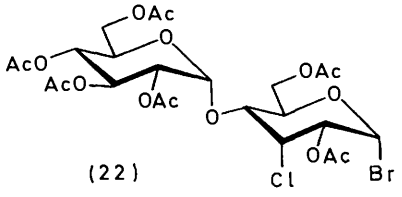
Deacylation of (19) afforded methyl 4-*O*-(α-D-glucopyranosyl)-β-D-allopyranoside (20) as a syrup, which was characterised as the hepta-acetate (21). A comparison of the n.m.r. spectrum of (21) with that of methyl β-maltoside hepta-acetate (6) indicated a downfield shift of the H-1 resonance, undoubtedly due to the *syn*-axial relationship with the 3-acetoxy-substituent. In accord with Lemieux's empirical rules concerning the influence of configuration on the chemical shifts of methine ring protons in sugar acetates,[15] the equatorial H-3 resonance appeared at lower field (0·35 p.p.m.) than that of the axial H-3 in (6). However, the occurrence of the H-2 and H-4 resonances of (21) at higher fields than those of the corresponding protons in (6) (*ca.* 0·16 p.p.m.) appears to be an exception to these rules. Of the resonances in the non-reducing ring, only the H-1′ resonance was affected by the changes in the other ring, being shifted to higher field by 0·34 p.p.m. This shift suggests that the 1′-proton in the maltoside hepta-acetate (6) must lie within the deshielding region of the 3-acetoxy-group.

The ready availability of the methyl β-maltoside 3-mesylate (9) prompted us to investigate its conversion into a 2,3-epoxide, since such derivatives are versatile synthetic intermediates.[16] However, treatment of the mesylate (9) with boiling methanolic sodium methoxide, followed by reacetylation, afforded only the 3,6-anhydride (23), which obviously arose by initial formation of the 2,3-epoxide (25) followed by ring-opening at C-3 due to attack of the 6-hydroxy-group (probably as the alkoxide). This rearrangement of an epoxide to a 3,6-anhydro-derivative has many precedents in carbohydrate chemistry [17] although it had been hoped that the

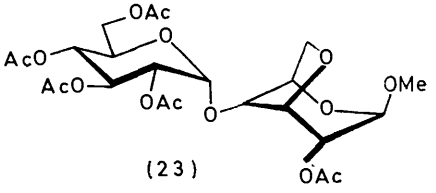
[14] N. Pravdić and D. Keglević, *Carbohydrate Res.*, 1970, **12**, 193; P. L. Durette and D. Horton, *ibid.*, 1971, **18**, 389.
[15] R. U. Lemieux and J. D. Stevens, *Canad. J. Chem.*, 1965, **43**, 2059.
[16] J. G. Buchanan and H. Z. Sable, *Selective Organic Transformations*, 1972, **2**, 1.
[17] A. B. Foster, M. Stacey, and S. V. Vardheim, *Acta Chem. Scand.*, 1958, **12**, 1819; R. D. Guthrie in 'The Carbohydrates,' eds. W. Pigman and D. Horton, Academic Press, New York, 1972, vol. 1A, p. 423.

necessity for the large C-4 substituent to become axial would retard the reaction. The ^{1}H n.m.r. spectrum of (23) showed $J_{1,2}$ *ca.* 1 Hz indicating that the reducing ring adopted a $^1C_4$ conformation (calc. $J_{1,3}$ 1—3 Hz) rather than the only other alternative, the $B_{1,4}$ conformation (calc. $J_{1,2}$ 7—10 Hz), in spite of the *syn*-diaxial interaction between the 1-methoxy-group and the anhydro-bridge.

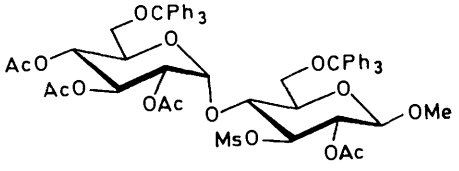
To circumvent the formation of the 3,6-anhydride the 6- and 6′-hydroxy-groups were blocked by tritylation. Methyl 3-*O*-mesyl-β-maltoside hexa-acetate (9) was carefully de-*O*-acetylated with a catalytic amount of sodium methoxide in methanol. The resulting crystalline mesylate (10) was then tritylated with 2·4 mol. equiv. of chlorotriphenylmethane in pyridine and the product was acetylated to give the 6,6′-di-*O*-trityl ether as the tetra-acetate (24) in 51% yield, after chromatography to remove the slower moving mono-ether (described in the following paper). The structure of the



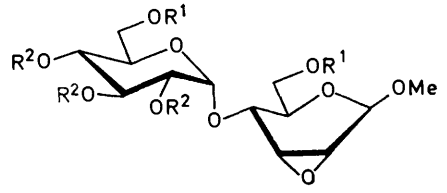
(22)



(23)



(24)



(25) $R^1 = R^2 = H$
(26) $R^1 = CPh_3, R^2 = Ac$
(27) $R^1 = R^2 = Ac$

ditritylate (24) was indicated by its ^{1}H n.m.r. parameters; integration indicated the presence of two trityl groups and the chemical shifts of the methine protons (H-2, H-2′, H-3′, and H-4′) were indicative of adjacent acetoxy-groups (Table 1). One of the acetyl methyl groups resonated at the abnormally high field of τ 8·33, most probably owing to the 4′-acetoxy-group lying in the shielding cone of one of the aromatic rings of the 6′-trityl group.[18] Treatment of a boiling methanolic solution of the ditritylate (24) with sodium methoxide afforded, after acetylation, the desired 2,3-epoxide as the triacetate (26). The structure of the epoxide (26) was demonstrated by its ^{1}H n.m.r. spectrum, in which H-1 appeared as a singlet, indicating that the *epi*-ring proton at C-2 and H-1 were *trans*-disposed.[19] The H-4 resonance occurred as a double doublet as a result of a small coupling (1·3 Hz) to H-3 and a large ' diaxial ' coupling (9·2 Hz) to H-5. The observed spin couplings are in accord with the generalisation that protons attached to an *epi*-ring fused to a six-membered ring are weakly coupled to vicinal *trans*-protons and more strongly coupled to *cis*-protons.[19]

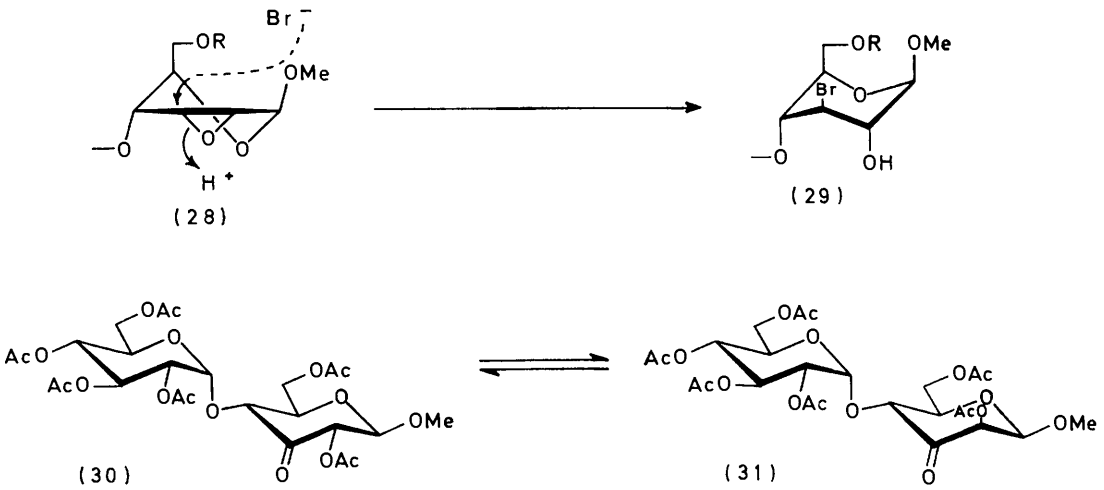
Attempted detritylation of (26) by a brief contact with hydrogen bromide in acetic acid (2 min), followed by acetylation, afforded a product in which the anhydro-ring had been ruptured to give a bromo-derivative. The ^{1}H n.m.r. parameters (Tables 1 and 2), in particular the coupling constants ($J_{1,2}$ 7·7, $J_{2,3}$ 10·0, $J_{3,4}$ 9·0, $J_{4,5}$ 9·0 Hz) showed conclusively that the product was the 3-bromo-3-deoxy-maltoside (11), which must have arisen from ' diequatorial ' ring-opening by attack at C-3 by the bromide anion. If such a reaction had S_N2 character, then the epoxide would have had to react *via* the ^5H_O conformation (28) so that the 2- and 3-substituents would be held antiperiplanar in the first-formed $^1C_4$ conformation (29). However, the approach of the bromide anion to the rear of C-3 would be severely hindered by the axial group at C-5 and the *quasi*-axial group at C-1 (β-*trans*-axial effect [11]), so this mechanism would be highly unlikely. It is possible that the reaction proceeds by an S_N1 mechanism which would be initiated by protonation of the epoxide oxygen atom followed by heterolysis of the C(3)–O bond to give the C-3 carbonium ion, probably with the underside protected by the newly formed hydroxy-group (*cf.* ion pair). Attack at the less hindered upper-face of the ring would give the observed product (11). The electron-withdrawing effect of the anomeric group would make the 2-carbonium ion less stable than the 3-carbonium ion, accounting for the absence of 2-bromo-products.

The 6,6′-ditritylate (26) was successfully detritylated without rupture of the epoxide ring by treatment with acetic acid; acetylation then gave the penta-acetate (27) of the epoxide.

[18] D. Horton, J. B. Hughes, J. S. Jewell, K. D. Philips, and W. N. Turner, *J. Org. Chem.*, 1967, **32**, 1073.

[19] D. H. Buss, L. Hough, L. D. Hall, and J. F. Manville, *Tetrahedron*, 1965, **21**, 69; L. Hough, P. A. Munroe, and A. C. Richardson, *J. Chem. Soc.* (*C*), 1971, 1090.

Oxo-analogues of methyl β-maltoside were of interest as synthetic intermediates, particularly for the synthesis of branched derivatives. Only one such analogue is known, namely, 4-O-(α-D-*ribo*-hex-3-ulosyl)-D-glucose, which is produced by the enzymic oxidation of maltose with growing intact cells of *Agrobacterium tumefaciens*, a plant tumour-inducing bacterium.[20] The ketose is of biochemical interest since it inhibits the uptake of sucrose by resting cells of *A. tumefaciens*[21] and is hydrolysed by an α-3-ketoglucosidase isolated from sonic extracts of *A. tumefaciens* IAM-1525.[22]



Accordingly, we have investigated the oxidation of methyl β-maltoside 2,2',3',4',6,6'-hexa-acetate (5). We found that ruthenium tetraoxide was the most efficient oxidant for this reaction and afforded the required 3-ketone (30) crystalline in 84% yield after chromatography. Its structure was indicated by its ^{1}H n.m.r. spectrum: H-1 resonated as a doublet ($J_{1,2}$ 8·1 Hz) and H-2 as a quartet because of a long-range coupling to H-4 (1·4 Hz). Long-range coupling between protons across a carbonyl group had been observed in cyclohexanone systems [23] and in glycopyranosiduloses.[24] Such coupling is only significant when the protons have a symmetrical relationship [25] (*i.e.* diaxial or diequatorial).

During initial attempts to crystallise the oxo-glycoside (30) it was observed that in ethanolic solution at room temperature it was slowly transformed into another compound. The proportion of this new component gradually increased over 7 days, after which the two components were present in approximately equal amounts. Chromatographic fractionation of the mixture afforded the unknown component in 42% yield. Elemental analysis and its ^{1}H n.m.r. spectrum indicated that this compound was isomeric with (30) and that the compounds differed only in the configuration at C-2. Thus H-1 and H-2 resonated as narrow doublets ($J_{1,2}$ 2·6 Hz), indicating that they were *syn*-clinal, and the absence of significant long-range coupling between H-2 and H-4 was indicative of a non-symmetrical arrangement of these protons.[24,25] On the basis of this evidence the compound was assigned structure (31). That the two pyranosiduloses were in thermodynamic equilibrium with one another was shown by the fact that (31) in pyridine solution was transformed partially into its 2-epimer (30).

The epimerisation of an equatorial acetoxy-group to an axial position was surprising, particularly since similar equilibria at positions adjacent to carbonyl groups, involving azido- and acetamido-groups, have always shown a preference for equatorial positions.[26] This observation may be rationalised on the basis of studies on the conformational equilibrium of 3-acetoxytetrahydropyran,[27] which revealed that the conformer with the 3-acetoxy-group axial was present to a much greater extent than would have been predicted on steric grounds alone. In some solvents the 3-axial form was the predominating species. An explanation in terms of dipole–dipole interactions between the 3-substituent and the dipole associated with the ring oxygen atom has been presented.[27] It was also considered that the steric and polar forces that control the position of the conformational equilibria in 2-halogenocyclohexanones,[28] such that an axial halogeno-group is preferred, might also play a role in the stabilisation of (31). However,

[20] S. Fukui and R. M. Hochster, *Canad. J. Biochem. Physiol.*, 1963, **41**, 2363.
[21] S. Fukui and R. M. Hochster, *Canad. J. Biochem. Physiol.*, 1964, **42**, 1023.
[22] K. Hayano and S. Fukui, *J. Bacteriol.*, 1970, **101**, 692.
[23] Y. Osawa and M. Neeman, *J. Amer. Chem. Soc.*, 1963, **85**, 2856; E. W. Garbisch, jun., *Chem. and Ind.*, 1964, 1715; P. Laszlo and J. I. Musher, *Bull. Soc. chim. France*, 1964, 2558; B. Lacoume, *ibid.*, 1967, 3496.
[24] P. M. Collins, D. Gardiner, S. Kumar, and W. G. Overend, *J.C.S. Perkin I*, 1972, 2596.
[25] L. M. Jackman and S. Sternhell, 'Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford, 1969, p. 338.
[26] B. R. Baker and D. H. Buss, *J. Org. Chem.*, 1965, **30**, 2304, 2308; Y. Ali and A. C. Richardson, *Carbohydrate Res.*, 1967, **5**, 441; M. Matsui, M. Saito, M. Okada, and M. Ishidate, *Chem. and Pharm. Bull. (Japan)*, 1968, **16**, 1294.
[27] C. B. Anderson, D. T. Sepp, M. P. Geis, and A. A. Roberts, *Chem. and Ind.*, 1968, 1805.
[28] J. Cantacuzene, R. Jantzen, and D. Ricard, *Tetrahedron*, 1972, **28**, 717, and references cited therein.

in view of the observation that 2-acetoxycyclohexanone exists predominantly in the conformation with the acetoxy-group equatorial,[29] such an effect must be small.

EXPERIMENTAL

All evaporations were performed below 50° under diminished pressure. M.p.s were determined on a Kofler hot-stage apparatus. Unless otherwise stated, specific rotations were measured for solutions in chloroform on a Perkin-Elmer 141 automatic polarimeter [1 dm narrow bore polarimeter tube at ambient temperature (24—27°)]. I.r. spectra were determined with a Perkin-Elmer 137 spectrophotometer and ^{1}H n.m.r. spectra with either a Varian HA-100 or HR-220 spectrometer. T.l.c. was performed on 0·25 mm layers of silica gel G activated at 120°, with 5% sulphuric acid in ethanol as indicator. Column chromatography was performed on silica gel (7734; Merck), with a 30 : 1 ratio of adsorbent to mixture. Light petroleum of boiling range 40—60° was used throughout.

1,2,6-*Tri*-O-*acetyl*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranose* (2).—This was prepared according to the method of Dick *et al.*[3] by acetylation of β-maltose monohydrate (Koch-Light Laboratories Ltd.) with acetyl chloride in pyridine–toluene. A mixture of the hepta-acetate and the octa-acetate (3) was obtained, which in certain cases (indicated) was used directly. The pure hepta-acetate, when required, was obtained by silica gel chromatography with ether–dichloromethane (1 : 7) as eluant. As previously reported,[3] the hepta-acetate was amorphous, being obtained as a glass by evaporation of an ethereal solution.

1,2,6-*Tri*-O-*acetyl*-3-*chloro*-3-*deoxy*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*allopyranose* (12).—A stirred solution of the hepta-acetate (2) (1·5 g) in dry chloroform (15 ml) and pyridine (2 ml) was cooled to about −70° and treated dropwise with sulphuryl chloride (1 ml). The mixture was maintained at this temperature for 2 h and then allowed to warm to room temperature. After a further 18 h the mixture was diluted with chloroform (30 ml) and the solution washed successively with 3N-hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and water, dried ($MgSO_4$), and concentrated to dryness. The resulting syrup was purified by column chromatography on silica gel with ether–dichloromethane (1 : 3) as eluant. The 3-*chloro-derivative* (1·3 g, 84%) had m.p. 154—157° (from ethanol), $[\alpha]_D$ +96° (*c* 1·2) (Found: C, 47·9; H, 5·4; Cl, 5·4. $C_{26}H_{35}ClO_{17}$ requires C, 47·7; H, 5·4; Cl, 5·4%).

3-*Chloro*-3-*deoxy*-4-O-(α-D-*glucopyranosyl*)-β-D-*allopyranose* (13).—A solution of (12) (1·1 g) in dry methanol (10 ml) was treated with methanolic 0·1N-sodium methoxide (0·6 ml). The solution was kept at room temperature overnight, then neutralised with a little Amberlite IR-120(H) resin, filtered, and evaporated to a syrup which crystallised from 95% ethanol to give the *chloro-disaccharide* (0·55 g, 91%), m.p. 121—130° (decomp.), $[\alpha]_D$ +155° (*c* 1 in H_2O) (Found: C, 39·9; H, 5·8; Cl, 9·9. $C_{12}H_{21}ClO_{10}$ requires C, 40·0; H, 5·9; Cl, 9·8%).

2,6-*Di*-O-*acetyl*-3-*chloro*-3-*deoxy*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*allopyranose* (15).—To a solution of (12) (0·5 g) in dry benzene (10 ml) were added dry mercury(II) acetate (0·2 g) and anhydrous methanol (2 ml). The mixture was stirred at room temperature overnight, after which t.l.c. (ether–dichloromethane, 1 : 3) indicated the absence of starting material and the presence of a slower-moving product. The mixture was then filtered through a pad of Hyflo Supercel and the filtrate washed twice with water, dried ($MgSO_4$), and concentrated to a solid residue. This was shown by t.l.c. to be composed of a major product and two slower-moving minor contaminants, which were removed by silica gel chromatography [ether–dichloromethane (1 : 2)]. The *hexa-acetate* (0·34 g, 73%), recrystallised from ethanol, had m.p. 188—193°, $[\alpha]_D$ +115° (*c* 1·6) (Found: C, 46·8; H, 5·3; Cl, 5·8. $C_{24}H_{33}ClO_{16}$ requires C, 47·0; H, 5·4; Cl, 5·8%).

Acetylation of the hexa-acetate with acetic anhydride–pyridine afforded exclusively the β-hepta-acetate (12).

Methyl 2,6-*Di*-O-*acetyl*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (5).—A solution of the hepta-acetate (2) (3 g) in dichloromethane (25 ml) was cooled (0—5°) and treated with hydrogen bromide in acetic acid (45% w/v; 6 ml). The stirred mixture was kept at 0° for 30 min and then diluted with ice-cold dichloromethane (30 ml); the resulting mixture was washed with ice–water, then with saturated sodium hydrogen carbonate, and again with ice–water, dried ($MgSO_4$), and evaporated to dryness, giving the α-glycosyl bromide as a glass. To a solution of the bromide in dry benzene (20 ml) were added anhydrous calcium sulphate (3 g), mercury(II) acetate (2 g), and dry methanol (3 ml). The mixture was stirred overnight at room temperature, then filtered through Hyflo Supercel, and diluted with 1,2-dichloroethane. The solution was washed well with water, dried ($MgSO_4$), and evaporated to an amorphous glass which crystallised from ethanol to give the *methyl glycoside* (2·2 g, 76%), m.p. 75—77°, $[\alpha]_D$ +61° (*c* 1) (Found: C, 49·1; H, 5·8. $C_{25}H_{36}O_{17}$ requires C, 49·3; H, 6·0%).

Methyl 2,6-*Di*-O-*acetyl*-3-*chloro*-3-*deoxy*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*allopyranoside* (14).—(*a*) A solution of (5) (2·1 g) in anhydrous pyridine (3 ml) and dry chloroform (20 ml) was treated with sulphuryl chloride (1·5 ml) as described above. The product was purified by silica gel chromatography with ether–dichloromethane (1 : 5) as mobile phase to give the 3-*chloro-glycoside* (1·8 g, 86%), m.p. 182—184° (from ethanol), $[\alpha]_D$ +89° (*c* 0·8) (Found: C, 48·2; H, 5·6; Cl, 5·4. $C_{25}H_{35}ClO_{16}$ requires C, 47·9; H, 5·6; Cl, 5·7%).

(*b*) The mixture of (2) and (3) resulting from the selective acetylation of β-maltose (9 g) (see before) was treated in sequence with hydrogen bromide in acetic acid (45% w/v) and mercury(II) acetate in benzene–methanol as described for the preparation of (5). The resulting crude product was then treated with sulphuryl chloride (4·5 ml) as in (*a*) and processed in the usual way to give the chloro-compound in 43% overall yield from (1) [identical with the product obtained in (*a*)].

Methyl 3-*Chloro*-3-*deoxy*-4-O-(α-D-*glucopyranosyl*)-β-D-*allopyranoside* (16).—A solution of (14) in warm, dry methanol (15 ml) was mixed with methanolic 0·1N-sodium methoxide (0·5 ml) and kept overnight at room temperature. After neutralisation [Amberlite IR-120(H)], evaporation afforded the *product* (0·72 g, 92%), m.p. 178—179° (crystallised from 95% ethanol and dried over P_4O_{10} *in vacuo* at 50°), $[\alpha]_D$ +120° (*c* 0·3 in MeOH) (Found: C, 41·9; H, 6·1; Cl, 9·2. $C_{13}H_{23}ClO_{10}$ requires C, 41·7; H, 6·2; Cl, 9·5%).

1,2,6-*Tri*-O-*acetyl*-3-O-*methylsulphonyl*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-α-D-*glucopyranose* (8).—To a

[29] P. L. Durette, H. Höhne, and H. Paulsen, unpublished results; M. J. T. Robinson, *Pure Appl. Chem.*, 1971, **25**, 635.

cooled solution of maltose hepta-acetate (2) (1·5 g) in pyridine (5 ml) was added mesyl chloride (1 ml). The mixture was kept at 0° with stirring for 2 h, then poured into ice–water and the resulting white precipitate was filtered off and recrystallised twice from dichloromethane–ethanol to give the *sulphonate* (1·6 g, 95%), m.p. 152—153°, $[\alpha]_D$ +65° (*c* 2) (Found: C, 45·7; H, 5·4; S, 4·5. $C_{27}H_{38}O_{20}S$ requires C, 45·4; H, 5·4; S, 4·5%).

The sulphonate could be obtained more readily if the mixture of (2) and (3) resulting from the acetylation of β-maltose was used rather than the pure hepta-acetate. The required product was obtained in 57% yield from β-maltose monohydrate and was isolated from the crude product by crystallisation from ethanol–dichloromethane. The recrystallisation was carried out by dissolution of the mixture in boiling dichloromethane followed by addition of ethanol. When most of the dichloromethane had boiled away the product crystallised upon cooling.

Methyl 2,6-*Di*-O-*acetyl*-3-O-*methylsulphonyl*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (9).—The 3-sulphonate (8) (3·5 g) was treated sequentially with hydrogen bromide in acetic acid and mercury(II) acetate in benzene–methanol as for the preparation of (5). The *glycoside* (2·4 g, 69%), had m.p. 73—76° (from methanol), $[\alpha]_D$ +56° (*c* 1·3) (Found: C, 45·5; H, 5·7; S, 4·7. $C_{26}H_{38}O_{19}S$ requires C, 45·5; H, 5·6; S, 4·7%).

De-*O*-acetylation of (9) (2·2 g) was effected in the same way as for (14), with a catalytic amount of sodium methoxide, to give *methyl* 4-O-(α-D-*glucopyranosyl*)-3-O-*methylsulphonyl*-β-D-*glucopyranoside* (10) (1·3 g, 92%), m.p. 105—109° (from 95% ethanol), $[\alpha]_D$ +41° (*c* 0·4 in MeOH) (Found: C, 39·1; H, 5·7; S, 6·8. $C_{14}H_{26}O_{13}S$ requires C, 38·7; H, 6·0; S, 7·4%).

Methyl 2,6-*Di*-O-*acetyl*-3-*azido*-3-*deoxy*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (7).—The 3-chloro-glycoside (14) (0·9 g) was heated in dry *NN*-dimethylformamide (10 ml) with sodium azide (1 g) at 120° for 24 h. The precise reaction time was difficult to assess because the product and starting material had similar t.l.c. mobilities in a variety of solvents. However, since t.l.c. indicated that some de-*O*-acetylation had occurred during the course of the reaction, a mixture of acetic anhydride (1·5 ml) and pyridine (3 ml) was added to the cooled mixture to effect re-acetylation. After 24 h at room temperature the mixture was poured into ice–water and the resulting precipitate was extracted with ether (3 × 25 ml). The combined extracts were evaporated to dryness and the pyridine was removed by repeated co-distillation with toluene. The resulting syrup crystallised from ethanol and a further recrystallisation afforded the pure *azide* (0·74 g, 81%), m.p. 86—89°, $[\alpha]_D$ +30° (*c* 0·4) (Found: C, 47·3; H, 5·5; N, 6·4. $C_{25}H_{35}N_3O_{16}$ requires C, 47·4; H, 5·6; N, 6·6%).

Methyl 2,6-*Di*-O-*acetyl*-3-*azido*-3-*deoxy*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*allopyranoside* (17).—The 3-mesylate (9) (1 g) was heated in dry hexamethylphosphoric triamide (10 ml) with sodium azide (1 g) at 95° for 24 h. The cooled mixture was then poured into water and the precipitated solid filtered off and washed well with water and then dissolved in dichloromethane. The solution was washed with water, dried ($MgSO_4$), and evaporated to a syrup which crystallised from methanol to give the *azide* (0·81 g, 88%), m.p. 102—104° (from methanol), $[\alpha]_D$ +51° (*c* 0·7) (Found: C, 47·4; H, 5·5; N, 6·5. $C_{25}H_{35}N_3O_{16}$ requires C, 47·4; H, 5·6; N, 6·6%).

Methyl 3-*Acetamido*-2,6-*di*-O-*acetyl*-3-*deoxy*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*allopyranoside* (18).—The 3-azido-allopyranoside (17) (0·77 g) was dissolved in ethyl acetate (10 ml) and methanol (20 ml) and hydrogenated at 50 lb in^{-2} over 5% palladium–charcoal (0·1 g) for 24 h. The mixture was then filtered and evaporated to a syrup which was acetylated with acetic anhydride–pyridine. The mixture was then evaporated to dryness and the pyridine removed by co-distillation with toluene and finally with carbon tetrachloride. The residue was then dissolved in the minimal volume of ethyl acetate and introduced onto a column of silica gel, which was then eluted with ethyl acetate–methanol (30 : 1). Traces of a faster moving material, probably unchanged starting material, were followed by the *acetamido-glycoside* (0·71 g, 90%), obtained as an amorphous solid by precipitation from propan-2-ol with light petroleum, $[\alpha]_D$ +49° (*c* 2) (Found: C, 49·6; H, 5·7; N, 2·4. $C_{27}H_{39}NO_{17}$ requires C, 49·9; H, 6·1; N, 2·2%).

Methyl 2,6-*Di*-O-*acetyl*-3-O-*benzoyl*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*allopyranoside* (19).—A solution of the 3-sulphonate (9) (2 g) in hexamethylphosphoric triamide (15 ml) was heated with sodium benzoate (2 g) at 90° for 24 h, after which time t.l.c. indicated that the reaction was complete. The cooled mixture was then poured into water, and the precipitated solid was filtered off and washed well with water. A solution of the solid in dichloromethane was shaken with a mixture of charcoal and anhydrous magnesium sulphate, filtered, and then evaporated to a syrup which crystallised from propan-2-ol. Recrystallisation from 95% ethanol gave the 3-O-*benzoate* (1·7 g, 80%), m.p. 75—78°, $[\alpha]_D$ +30° (*c* 0·7) (Found: C, 54·0; H, 5·5. $C_{32}H_{40}O_{18}$ requires C, 53·9; H, 5·7%).

Methyl 2,3,6-*Tri*-O-*acetyl*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*allopyranoside* (21).—A solution of the 3-*O*-benzoate (19) (1·2 g) in dry methanol (10 ml) was treated with methanolic 0·1N-sodium methoxide (0·6 ml) and the solution was kept at room temperature overnight. After neutralisation [Amberlite IR-120(H)] the solution was evaporated to dryness to give syrupy (20) which was then acetylated with acetic anhydride–pyridine. The syrup so obtained was passed through a short column of silica gel with ether–dichloromethane (1 : 6) as eluant to remove some residual methyl benzoate, which appeared in the early fractions. The fractions containing the *hepta-acetate* were evaporated to dryness; yield 0·97 g (89%), m.p. 72—74° (from ethanol), $[\alpha]_D$ +49° (*c* 0·6) (Found: C, 49·6; H, 5·8. $C_{27}H_{38}O_{18}$ requires C, 49·8; H, 5·9%).

Methyl 2,6-*Di*-O-*acetyl*-3,6-*anhydro*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (23).—A solution of the 3-mesyl-maltoside (9) (1·1 g) in warm dry methanol (15 ml) was treated with methanolic N-sodium methoxide (15 ml). The solution was heated under reflux for 2 h, and then neutralised [Amberlite IR-120(H)] and evaporated to dryness. The resulting syrup was acetylated with acetic anhydride–pyridine to give the 3,6-*anhydride* (0·68 g, 78%), m.p. 159—165° (from ethanol), $[\alpha]_D$ +29° (*c* 1) (Found: C, 50·5; H, 5·8. $C_{23}H_{32}O_{15}$ requires C, 50·4; H, 5·9%).

Methyl 2-O-*Acetyl*-3-O-*methylsulphonyl*-4-O-(2,3,4-*tri*-O-*acetyl*-6-O-*triphenylmethyl*-α-D-*glucopyranosyl*)-6-O-*triphenylmethyl*-β-D-*glucopyranoside* (24).—A mixture of methyl 3-*O*-mesyl-β-maltoside (10) (6 g) and chlorotriphenylmethane (9·2 g, 2·4 equiv) was dissolved in anhydrous pyridine (36 ml) and the solution was kept at room

temperature for 24 h and then at 65° for 48 h. It was then cooled to 0° and treated with acetic anhydride (30 ml) and pyridine (25 ml); the mixture was kept at room temperature for 36 h then poured into ice–water and stirred for 4 h. The resulting precipitate was filtered off, dried on a Buchner funnel, and chromatographed on silica gel with ether–dichloromethane (1 : 19) as eluant. The initial fractions contained triphenylmethanol and the later fractions the *ditritylate* (7·7 g, 51%), m.p. 118—122° (from 95% ethanol), $[\alpha]_D$ +51° (*c* 1·7) (Found: C, 66·1; H, 5·8; S, 2·8. $C_{60}H_{62}O_{17}S$ requires C, 66·3; H, 5·8; S, 3·0%).

Methyl 2,3-*Anhydro*-4-O-(2,3,4-*tri*-O-*acetyl*-6-O-*triphenylmethyl*-α-D-*glucopyranosyl*)-6-O-*triphenylmethyl*-β-D-*allopyranoside* (26).—To a solution of the 3-*O*-mesylate (24) (6·5 g) in hot anhydrous methanol (30 ml) was added methanolic N-sodium methoxide (25 ml), and the solution was heated under reflux for 2 h; t.l.c. then indicated that the starting material had been completely converted into a slower moving substance. The cooled mixture was then neutralised [Amberlite IR-120(H)], concentrated to dryness and acetylated with acetic anhydride–pyridine. The product which separated on addition of ice–water was extracted with dichloromethane (3 × 30 ml). The combined extracts were then evaporated to dryness and the pyridine was removed by several co-distillations with toluene and finally with carbon tetrachloride. The resulting syrup was dissolved in hot 95% ethanol and precipitated as an amorphous solid on cooling to give the *epoxide* (4·1 g, 72%), m.p. 117—120° (softening), $[\alpha]_D$ +120° (*c* 1) (Found: C, 72·2; H, 5·9. $C_{57}H_{56}O_{13}$ requires C, 72·1; H, 6·0%).

Methyl 6-O-*Acetyl*-2,3-*anhydro*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*allopyranoside* (27).—A solution of the epoxide (26) (1·7 g) in acetic acid (20 ml) and water (5 ml) was heated at 100° (bath) for 3 h, then cooled. The precipitated triphenylmethanol was filtered off, and the filtrate was concentrated to dryness. Traces of acetic acid were removed by co-distillation with toluene, and the residue was acetylated with pyridine–acetic anhydride to give the penta-*O*-acetyl-epoxide as a glass (0·71 g, 72%) which failed to crystallise. The structure of this compound was supported by its ^1H n.m.r. spectrum (Tables 1 and 2).

Methyl 2,6-*Di*-O-*acetyl*-3-*bromo*-3-*deoxy*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (11).—A solution of (26) (1 g) in acetic acid (4 ml) was cooled in an ice-bath and treated with hydrogen bromide in acetic acid (45% w/v; 1 ml). The mixture was shaken for 2 min and then filtered, with the filtrate passing directly into ice–water (25 ml). The filter was washed with water and the combined filtrate was extracted with dichloromethane (5 × 20 ml). The combined, dried ($MgSO_4$) extracts were evaporated to dryness and freed from residual acetic acid by co-distillation with toluene. The residue was then acetylated with acetic anhydride (2 ml) and pyridine (3 ml) and processed in the usual manner to give the *bromo-maltoside* (0·6 g, 85%), m.p. 85—88° (change in crystalline form), 154·5—156° (from ethanol), $[\alpha]_D$ +48° (*c* 0·6) (Found: C, 44·5; H, 5·4; Br, 11·4. $C_{25}H_{35}BrO_{16}$ requires C, 44·7; H, 5·3; Br, 11·9%).

Methyl 2,6-*Di*-O-*acetyl*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-ribo-*hex*-3-*ulopyranoside* (30).—Ruthenium tetraoxide was prepared by stirring hydrated ruthenium dioxide (0·96 g) with a mixture of aqueous 10% sodium periodate (20 ml) and carbon tetrachloride (50 ml), according to the procedure of Horton and Just.[30] The carbon tetrachloride layer, containing the tetraoxide, was then added to a solution of the methyl hexa-*O*-acetyl-β-maltoside (5) (2 g) in carbon tetrachloride (10 ml). The mixture was kept at room temperature for 24 h and propan-2-ol was added to decompose the excess of oxidant. The mixture was then filtered through a pad of Hyflo Supercel to remove the precipitated ruthenium dioxide, and the filtrate was concentrated to dryness. T.l.c. indicated the presence of a major product and small amounts of slower moving impurities which were removed by chromatography on silica gel [ether–dichloromethane (1 : 3)]. The *ketone* (1·7 g, 84%) was obtained as a glass which crystallised from diethyl ether; m.p. 112—113·5°, $[\alpha]_D$ +109° (*c* 0·7) (Found: C, 49·5; H, 5·5. $C_{25}H_{34}O_{17}$ requires C, 49·5; H, 5·7%).

Methyl 2,6-*Di*-O-*acetyl*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-arabino-*hex*-3-*ulopyranoside* (31).—An ethanolic solution of the 3-uloside (30) (1·5 g) was kept at room temperature. T.l.c. showed the progressive formation of a slower-moving component and after 7 days the components were in the ratio of *ca.* 1 : 1. The solutions was evaporated to dryness and fractionated on a column of silica gel with ether–dichloromethane (1 : 8) as eluant. The first fractions contained starting material and later fractions yielded the slower-moving component as a syrup which crystallised from ether–light petroleum to give the epimerised *ketone* (0·63 g, 42%), m.p. 75—78°, $[\alpha]_D$ +28° (*c* 0·2) (Found: C, 49·9; H, 5·9. $C_{25}H_{34}O_{17}$ requires C, 49·5; H, 5·7%).

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[30] D. Horton and E. K. Just, *Carbohydrate Res.*, 1969, **9**, 129.