The Chemistry of Maltose. Part III.[1] Introduction of Azido- and Amino-substituents at Specific Positions of Methyl β-Maltoside

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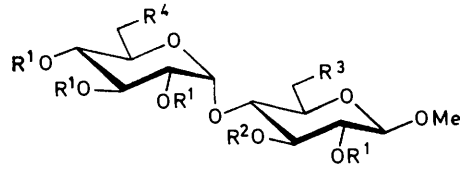
A variety of sulphonate ester derivatives of methyl β-maltoside have been prepared (6-, 6′-, 4′-, 6,6′-, 3,6′-, and 3,6,6′-). All these sulphonates undergo displacement with azide anion, with inversion of configuration at chiral centres, to give the corresponding azides, which in most cases have been reduced to the corresponding amines.

ALTHOUGH several disaccharides, such as maltose, lactose, cellobiose, *etc.*, are readily available, apart from our studies with trehalose [2] and sucrose,[3] there has been no systematic study of their chemistry. In particular, the possibility of exploiting these disaccharides as starting materials for the synthesis of less readily available disaccharides is attractive, since the establishment of the interglycosidic linkage by classical procedures is often difficult and low-yielding, particularly for α-linked disaccharides. Our interest in maltose arose from its relationship to the group of nucleoside antibiotics comprising amicetin, plicacetin, and bamicetin,[4] which are nucleosides of disaccharides with the same skeletal and interglycosidic linkage as maltose;



(1) $R^1 = R^2 = H$, $R^3 = R^4 = OH$
(2) $R^1 = H$, $R^2 = Ms$, $R^3 = R^4 = OH$
(3) $R^1 = Ac$, $R^2 = Ms$, $R^3 = OAc$, $R^4 = OCPh_3$
(4) $R^1 = Ac$, $R^2 = Ms$, $R^3 = R^4 = OCPh_3$
(5) $R^1 = Ac$, $R^2 = Ms$, $R^3 = OAc$, $R^4 = OH$
(6) $R^1 = Ac$, $R^2 = Ms$, $R^3 = OAc$, $R^4 = OMs$
(7) $R^1 = Ac$, $R^2 = Ms$, $R^3 = R^4 = OH$
(8) $R^1 = Ac$, $R^2 = Ms$, $R^3 = R^4 = OTs$
(9) $R^1 = R^2 = Ac$, $R^3 = OAc$, $R^4 = OCPh_3$
(10) $R^1 = R^2 = Ac$, $R^3 = OAc$, $R^4 = OH$
(11) $R^1 = R^2 = Ac$, $R^3 = OAc$, $R^4 = OMs$
(12) $R^1 = R^2 = Ac$, $R^3 = OAc$, $R^4 = N_3$
(13) $R^1 = R^2 = Ac$, $R^3 = OAc$, $R^4 = NHAc$
(14) $R^1 = R^2 = Ac$, $R^3 = OH$, $R^4 = OAc$
(15) $R^1 = R^2 = Ac$, $R^3 = OTs$, $R^4 = OAc$
(16) $R^1 = R^2 = Ac$, $R^3 = N_3$, $R^4 = OAc$
(17) $R^1 = R^2 = Ac$, $R^3 = R^4 = OTs$
(18) $R^1 = R^2 = Ac$, $R^3 = R^4 = N_3$
(19) $R^1 = R^2 = Ac$, $R^3 = R^4 = NHAc$

the latter could therefore serve as a convenient starting point for the total synthesis of these antibiotics. We describe here the synthesis of several sulphonic esters of methyl β-maltoside (1) and their conversion into azido- and acetamido-derivatives.

The 3,6′-disulphonate and 3,6,6′-trisulphonate esters were synthesised from methyl 3-*O*-mesyl-β-maltoside (2).[1] Treatment of (2) with 1·5 equiv. of chlorotriphenylmethane, followed by acetylation, afforded, after chromatographic fractionation, the 6′-trityl ether (3) in 47% yield together with some of the 6,6′-ditritylate (4).[1] The structure of the monoether was based on the ^1H n.m.r. spectral parameters (Tables 1 and 2) and upon the known greater reactivity of the 6′-hydroxy-group. Thus, Wolfrom and Koizumi [5] have reported that the selective tritylation of β-maltose afforded a 31% yield of the 6′-tritylate and only 3% of the 6-tritylate. Similarly, selective tritylation of benzyl β-maltoside afforded mainly the 6′-tritylate,[6] and selective tosylation of methyl β-maltoside (1) yielded both the 6′ and 6-tosylates in the ratio 18 : 1, respectively.[7] The large difference in the relative reactivities of the two primary hydroxy-groups in maltose derivatives has been ascribed to the non-identical stereoelectronic environment at these two positions,[8] and molecular models of the favoured conformation of maltose [9] and its methyl glycoside [10] indicate that the 2′-, 3-, and 6-hydroxy-groups will be subject to the greatest steric interaction. It has already been established that the 3-hydroxy-group is the most resistant to acylation by acid chlorides.[1,11] In the ^1H n.m.r. spectrum of (3), as observed for the di-*O*-trityl ether (4),[1] one of the acetyl resonances occurred at abnormally high field (τ 8·30). It appears that the strong shielding effect observed in both (3) and (4) emanates from the 6′-trityloxy-group and the high field resonance is most likely to be that due to a proximate acetyl group, namely that at C-4′, the methyl group of which must lie within the shielding cone of one of the benzene rings of the trityloxy-group.

De-*O*-tritylation of (3) by brief treatment with hydrogen bromide in acetic acid at low temperature gave methyl 2,2′,3′,4′,6-penta-*O*-acetyl-3-*O*-mesyl-β-maltoside (5) which was converted directly into the 3,6′-dimesylate (6) in the usual way. The possibility of 4′ ⟶ 6′ acetyl migration, which sometimes occurs in de-*O*-tritylation,[12] was excluded by comparison of the n.m.r. spectral parameters of (6) with those of methyl

[1] Part II, P. L. Durette, L. Hough, and A. C. Richardson, preceding paper.
[2] A. C. Richardson and E. Tarelli, *J.C.S. Perkin I*, 1973, 1520. and preceding parts of the series.
[3] J. M. Ballard, L. Hough, A. C. Richardson, and P. H. Fairclough, *J.C.S. Perkin I*, 1973, 1524, and further parts of the series.
[4] R. J. Suhadolnik, 'Nucleoside Antibiotics,' Wiley-Interscience, New York, 1970, pp. 203—217.
[5] M. L. Wolfrom and K. Koizumi, *J. Org. Chem.*, 1967, **32**, 656.
[6] B. Helferich and W. Speicher, *Annalen*, 1953, **579**, 106.
[7] R. T. Sleeter and H. B. Sinclair, *J. Org. Chem.*, 1970, **35**, 3804.
[8] G. G. S. Dutton and K. N. Slessor, *Canad. J. Chem.*, 1966, **44**, 1069.
[9] G. J. Quigley, A. Sarko, and R. H. Marchessault, *J. Amer. Chem. Soc.*, 1970, **92**, 5834.
[10] S. S. C. Chu and G. A. Jeffrey, *Acta Cryst.*, 1967, **23**, 1038.
[11] W. E. Dick, jun., B. G. Baker, and J. E. Hodge, *Carbohydrate Res.*, 1968, **6**, 52.
[12] L. Hough and A. C. Richardson, in 'Rodd's Chemistry of Carbon Compounds,' vol. 1F, Elsevier, Amsterdam, 1967, p. 382.

β-maltoside hepta-acetate.[1] As observed previously with peracetylated maltose derivatives,[1] replacement of an acetoxy-group with a mesyloxy-group results in an upfield shift of the methine proton resonance by *ca.* 0·3 p.p.m. No such upfield shift in the H-4 resonance was observed (Table 1).

configuration at C-3 was indicated by the ^{1}H n.m.r. spectral data (Tables 1 and 2), in particular by the values (*ca.* 3 Hz) of the coupling constants $J_{2,3}$ and $J_{3,4}$. The chemical shifts observed (Table 1) were very similar to those of methyl 3-azido-3-deoxy-4-*O*-(α-D-glucopyranosyl)-β-D-allopyranoside hexa-acetate,[1] except for

TABLE 1

^{1}H N.m.r. parameters; first-order chemical shifts (τ values) at, unless otherwise stated, 220 MHz

	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, NAc
(3) *a,b*	5·61d	5·01t	5·10t	5·97t	6·34m	5·43dd	5·62dd	4·53d	4·95dd	4·68t	4·82t	6·05m	6·77m	6·98	6·55	6·98	7·89, 7·91, 8·04, 8·09, 8·30
(6) *a*	5·55d	5·06t	5·10t	6·01t	6·31m	5·43dd	5·66dd	4·56d	5·01dd	4·59t	4·97t	5·87sx	5·76m		6·53	6·92 6·94	7·89, 7·91, 7·96, 8·01
(9) *a,b*	5·54d	5·11t	*c*	5·90t	6·32m	5·51dd	5·79dd	4·49d	5·02dd	*c*	*c*	6·10m	6·70m	6·99dd	6·52		7·93, 7·96, 8·01, 8·17, 8·31
(10) *d,e*	5·87d	5·06t	4·71t	6·10t	6·98sx	5·66dd		4·55d	5·11dd	4·33t	4·91t				6·79		8·05, 8·12, 8·21, 8·27, 8·31
(11) *e*	5·56d	5·20t	4·76t	6·01t	6·33m	5·54dd		4·61d	5·17dd	4·65t	4·97t	5·97m	*ca.* 6·0m		6·51	6·93	7·87, 7·94, 7·97, 7·99
(12) *e,f*	5·82d	4·92t	4·60t	6·02t	7·03sx	5·52dd	5·84dd	4·46d	4·97dd	4·20t	4·84t	*ca.* 5·9m	6·86m		6·78		8·02, 8·17, 8·22, 8·26, 8·34
(13) *a,g*	5·57d	5·19t	4·77t	6·07t	6·33m	5·53dd	5·81dd	4·68d	5·20dd	4·67t	5·16t	6·17m	5·52m		6·52		7·84, 7·95, 7·96, 7·98, 8·00, 8·01
(14) *a,e*	5·53d	5·20t	4·71t	5·85t				4·55d	5·18dd	4·62t	4·98t		5·70dd		6·50		7·91, 7·97, 7·99, 8·01
(15) *a,e,h*	5·67d	5·35t	4·83t	6·06t				4·63d	5·17dd	4·65t	4·96t				6·66		7·91, 7·96, 7·99, 8·00, 8·03
(16) *d,e*	5·87d	4·99t	4·69t	6·20t	7·29sx	7·03m		4·52d	5·01dd	4·23t	4·74t	6·02m	5·54dd	5·70dd	6·81		8·09, 8·20, 8·28, 8·31
(17) *d,e,i*	6·05d	5·28t	4·80t	6·36t	7·35sx		5·44dd	4·66d	5·18dd	4·21t	4·61t	5·67sx	5·88m		6·97		8·06, 8·12, 8·21, 8·31
(18) *a*	5·52d	5·15t	4·75t	5·98t	6·33m	6·38dd	6·52dd	4·59d	5·19dd	4·69t	5·03t	6·16m	6·58dd	6·68dd	6·50		7·98, 8·01
(19) *d,j*	5·90d			6·35t	6·17oc			4·34d		4·35t		5·8m			6·74		8·06, 8·09, 8·19, 8·21, 8·27, 8·33
(20) *a*	5·24—5·33m		5·65t	6·12dd	*k*	5·54dd	5·83dd	4·70d	5·13dd	4·58t	4·96t	*k*	6·61dd	6·71dd	6·52		7·86, 7·90, 7·92, 7·98, 8·01
(21) *a,l*								4·97d	*ca.* 5·2dd	4·51t	5·11t		6·44m	6·80m	6·55		7·76, 7·91, 7·94, 7·97, 7·99
(22) *a,e*	5·22m		5·62t	*m*	*m*	*m*	*m*	4·66d	5·16dd	4·60t	5·00t	*m*	*m*	*m*	6·50		7·86, 7·92, 7·97, 8·00
(24) *a,e*	5·56d	5·20t	4·76t	6·01t				4·61d	5·18dd	4·60t	5·25t				6·53	6·98	7·87, 7·89, 7·93, 7·96, 7·99, 8·01
(25) *f*	5·89d	4·99t	4·67t	6·24t	7·04m	5·57dd	5·95dd	4·49d	4·56dd	4·39dd	6·22dd	5·70sx		5·85dd	6·84		8·05, 8·20, 8·24, 8·26, 8·28, 8·33
(26) *a*	4·52 *n*	5·42 *n*	5·20 *n*	6·54 *n*	5·25 *n*	6·02dd	6·22dd	4·71d	5·16dd	4·46t	4·93t	5·58sx	5·75—5·90m				7·82, 7·92, 7·94, 7·95, 7·98, 8·00

a In [^{2}H]chloroform. *b* $OCPh_3$ 2·54—2·81. *c* H-3, H-3′, H-4′ 4·60—4·74m. *d* In [^{2}H]chloroform–[$^2H_6$]benzene. *e* At 100 MHz. *f* In [$^2H_6$]benzene. *g* NH 3·91t. *h* $ArCH_3$ 7·56, Ar 2·19d, 2·66d. *i* $ArCH_3$ 8·28, Ar 2·10q, 3·15q. *j* NH 3·87t. *k* H-5,H-5′ 5·98—6·08m. *l* NH 3·65d, 3·80t. *m* H-4,H-5,H-5′ 5·97—6·21m; H-6a,H-6b, H-6′a,H-6′b 6·40—6·69m. *n* Broad singlet due to vicinal and long-range W couplings.

TABLE 2

First-order coupling constants (Hz) *a*

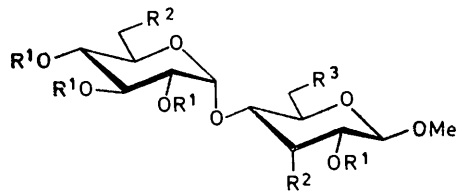
	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4}$	$J_{4',5'}$	$J_{5',6'a}$	$J_{5',6'b}$	$J_{6'a,6'b}$
(3)	7·0	7·9	8·8	8·6	2·3	3·5	−12·4	3·9	10·6	9·6	9·9		4·5	−10·5
(6)	6·8	7·0	8·9	8·4	2·6	4·0	−12·1	4·2	10·5	10·1	9·5			
(9)	8·0	9·4	9·4	9·0	2·5	3·5	−12·1	3·9	9·7	*ca.* 9·5	*ca.* 9·5	1·5	3·5	−10·6
(10)	7·5	9·3	8·9	8·9	2·8		−11·8	3·7	10·8	9·7	9·5			
(11)	7·7	9·5	9·4	9·0	2·9		−12·3	3·6	10·9	9·9	10·0			
(12)	7·5	8·6	9·0	9·5	2·9	4·6	−12·3	3·8	10·3	9·4	10·1			
(13)	7·7	9·1	9·0	9·0	2·2	4·5	−12·4	3·7	10·8	9·5	9·1			
(14)	7·8	9·2	9·1	9·3				4·0	10·2	9·7	9·5	4·0		−12·5
(15)	7·6	9·1	8·5	9·4				4·0	10·2	9·5	9·5			
(16)	7·7	9·1	8·7	9·3				3·6	10·3	9·6	9·9	4·4	2·5	−12·3
(17)	7·9	9·3	9·0	9·3		3·5	−11·6	4·2	10·4	9·5	9·8			
(18)	7·9	9·5	9·0	9·0	2·5	5·1	−13·3	4·2	10·5	9·6	9·5	2·8	5·1	−13·5
(19) *b*	7·8		8·5	8·5				3·2	10·1	9·8				
(20)		3·0	3·0	9·2	2·2	3·8	−12·2	3·8	10·5	9·6	9·9	2·9	5·4	−13·5
(21) *c*								3·5	10·2	9·6	*ca.* 9·5			
(22)		*ca.* 3	*ca.* 3					3·7	10·1	9·2	9·6			
(24)	7·5	8·9	8·8	9·4				3·9	10·2	9·2	10·1			
(25)	8·0	9·2	9·0	9·1	2·4	5·0	−12·5	4·0	10·8	3·5	1·4		6·0	−12·3
(26)					1·3	5·8	−7·7	4·0	10·4	9·5	9·5			

a For conditions refer to Table 1. *b* J_{NH,CH_2} 5·0 Hz. *c* J_{NH,CH_2} 8·5, J_{NH,CH_2} 5·0 Hz.

Nucleophilic displacement of the two sulphonate groups was readily achieved with sodium azide in hexamethylphosphoric triamide to give methyl 3-azido-4-*O*-(6-azido-6-deoxy-α-D-glucopyranosyl)-3-deoxy-β-D-allopyranoside penta-acetate (20). T.l.c. indicated the formation of an intermediate, presumably the 6′-azido-3-*O*-mesylate, which was not isolated. Inversion of the signals due to the 6′-methylene protons which were moved upfield [Δ(H-6′a) 0·89; Δ(H-6′b) 0·75 p.p.m.] owing to the less deshielding nature of the azido-group. Catalytic hydrogenation of the diazide (20), followed by acetylation, afforded the 3,3′-diacetamido-derivative (21) in high overall yield.

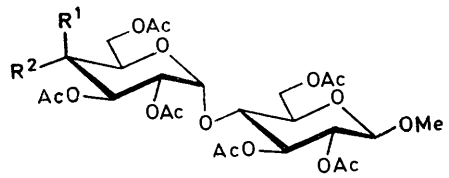
As previously reported,[1] the 3-*O*-mesyl-6,6′-di-*O*

trityl-maltoside (4) may be obtained from (2) in 51% yield. De-*O*-tritylation of (4) afforded the 6,6′-diol (7), which was treated directly with tosyl chloride to give the 3-*O*-mesyl-6,6′-di-*O*-tosylate (8) in 79% overall yield. Subsequently we have found that this compound



(20) R^1 = Ac, R^2 = N_3, R^3 = OAc
(21) R^1 = Ac, R^2 = NHAc, R^2 = OAc
(22) R^1 = Ac, R^2 = R^3 = N_3

can be prepared more conveniently by selective tetra-*O*-acetylation [13] of methyl 6,6′-di-*O*-tosyl-β-maltoside [14] followed by mesylation of the 3-hydroxy-group to give (8) in high overall yield. Treatment of the trisulphonate with sodium azide in hexamethylphosphoric triamide resulted in the displacement of all three sulphonate groups to give methyl 3,6-diazido-4-*O*-(6-azido-6-deoxy-α-D-glucopyranosyl)-3,6-dideoxy-β-D-allopyranoside tetra-acetate (22). The *allo*-configuration of the reducing ring was indicated by the n.m.r. parameters (Tables 1 and 2).

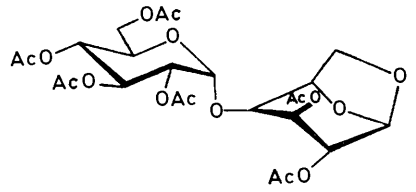


(23) R^1 = H, R^2 = OH
(24) R^1 = H, R^2 = OMs
(25) R^1 = N_3, R^2 = H

The introduction of sulphonate groups at C-4′ and C-6′ of methyl β-maltoside (1) was accomplished *via* the 6′-tritylate (9), which was readily prepared by selective tritylation of the glycoside (1). De-*O*-tritylation of (9) with hydrogen bromide in acetic acid gave the crystalline 2,2′,3,3′,4′,6-hexa-acetate (10) in 86% yield, which was converted into the 6′-mesylate (11) in the usual way. Migration of the 4′-acetyl group of (10) to the 6′-position was induced by treatment of (10) with a trace of alkali. The isomerised hexa-acetate (23) was obtained as a syrup, which on mesylation gave the 4′-*O*-mesylate (24) in 59% overall yield from (10). Comparison of the n.m.r. spectral parameters (Table 1) of (11) and (24) with those of methyl β-maltoside hepta-acetate [1] indicated that (24) had a mesyloxy-group at C-4′, since the H-4′ resonance appeared *ca.* 0·3 p.p.m. to higher field than the H-4′ resonances of both (11) and the hepta-acetate.[1]

[13] E. Tarelli, unpublished results.
[14] M. L. Wolfrom, Y.-L. Hung, P. Chakravarty, G. U. Yuen, and D. Horton, *J. Org. Chem.*, 1966, **31**, 2227.
[15] G. Birch and A. C. Richardson, *J. Chem. Soc.* (*C*), 1970, 749; for a discussion of the dependence of vicinal proton–proton spin couplings on the configuration of electronegative substituents see P. L. Durette and D. Horton, *Org. Magnetic Resonance*, 1971, **3**, 417.

The synthesis of the corresponding 6′-tosylate by selective tosylation of (1) has been described.[7] Although this present procedure involves two additional steps the overall yield (33%) is considerably higher than by the direct procedure.



(26)

Replacement of both the 6′-sulphonate (11) and the 4′-sulphonate (24) with azide anion afforded the azides (12) and (25), respectively, in high yields. In the case of the 4′-azide (25), the inversion of configuration at C-4′ was clearly shown by the n.m.r. parameters (Tables 1 and 2). In particular, the high-field quartet at τ 6·22 with splittings of 3·5 and 1·4 Hz was diagnostic of a galactopyranoside [15] with the less deshielding azido-group at C-4′. In the case of the 6′-azide (12) catalytic reduction afforded the 6′-amine, characterised as the 6′-acetamido-derivative (13).

The introduction of a sulphonate group at C-6 was accomplished from 1,6-anhydro-β-maltose (maltosan) hexa-acetate (26).[16,17] The ^{1}H n.m.r. parameters (Tables 1 and 2) of (26) recorded at 220 MHz indicated that the 1,6-anhydro-ring adopts the $^1C_4$ conformation [18] in spite of the axial glycosyloxy-group at C-4. Treatment of the 1,6-anhydride (26) with titanium tetrachloride [17] and treatment of the resulting glycosyl chloride with mercury(II) acetate in methanol afforded, in 7% overall yield, the methyl β-maltoside hexa-acetate (14) with the 6-hydroxy-group free, which then gave the 6-tosylate (15). Reaction of (15) with sodium azide in the usual way afforded the 6-azido-6-deoxymaltoside (16).

Finally, the synthesis of 6,6′-azido- and 6,6′-amino-derivatives was achieved from the known [7] methyl 6,6′-di-*O*-tosyl-β-maltoside penta-acetate (17), which readily underwent displacement with azide anion to give the 6,6′-diazide (18) in 94% yield. Subsequent catalytic reduction followed by acetylation afforded the 6,6′-diacetamido-maltoside (19).

EXPERIMENTAL

For general notes see ref. 1.

Methyl 2,6-Di-O-acetyl-3-O-methylsulphonyl-4-O-(2,3,4-tri-O-acetyl-6-O-triphenylmethyl-α-D-glucopyranosyl)-β-D-glucopyranoside (3).—A solution of methyl 3-*O*-mesyl-β-maltoside [1] (2) (10 g) and chlorotriphenylmethane (9·5 g) in dry pyridine (60 ml) was stirred in the absence of moisture at room temperature for 48 h, then cooled in an ice-bath. A mixture of acetic anhydride (50 ml) and pyridine (40 ml) was added and the reaction mixture was kept at ice temperature for 3 h and then at room temperature for a further 36 h. The mixture was then poured into ice–water and the

[16] P. Karrer and L. Kamienski, *Helv. Chem. Acta*, 1932, **15**, 739.
[17] L. Asp and B. Lindberg, *Acta Chem. Scand.*, 1952, **6**, 941.
[18] L. D. Hall and L. Hough, *Proc. Chem. Soc.*, 1962, 382.

precipitate was filtered off, dried by suction, dissolved in a minimal volume of dichloromethane and chromatographed on silica gel with ether–dichloromethane (1 : 19) as eluant. The first fractions contained the ditritylate [1] (4). The fractions containing the slower-moving monoether were combined and concentrated to a crystalline residue which was recrystallised from 95% ethanol to give the *trityl ether* (9·6 g, 47%), m.p. 100—103°, $[\alpha]_D$ +74° (*c* 1) (Found: C, 58·3; H, 5·7; S, 3·6. $C_{43}H_{50}O_{18}S$ requires C, 58·2; H, 5·7; S, 3·6%).

Methyl 2,6-*Di*-O-*acetyl*-3-O-*methylsulphonyl*-4-O-(2,3,4-*tri*-O-*acetyl*-6-O-*methylsulphonyl*-α-D-*glucopyranosyl*)-α-D-*glucopyranoside* (6).—A solution of the 6′-tritylate (3) (2·6 g) in acetic acid (8 ml) was cooled in an ice-bath and treated with hydrogen bromide in acetic acid (45% w/v; 1·5 ml) which had been similarly precooled. The mixture was then shaken vigorously for 60 s and quickly filtered with the filtrate passing into ice–water (50 ml). The filter pad was washed with ice–water and the combined filtrates were extracted with dichloromethane (3 × 50 ml). The extracts were concentrated to dryness and the residual acetic acid was removed by co-evaporation with toluene to give the syrupy penta-acetate (5), which was not further characterised but immediately mesylated with pyridine (10 ml) and mesyl chloride (3 ml). The resulting syrupy product was contaminated with triphenylmethanol, which was removed by chromatography on silica gel [ether–dichloromethane (1 : 5) as eluant]. The slower-moving *disulphonate* (1·5 g, 72%) was obtained as an amorphous solid which precipitated from a cooled solution in propan-2-ol; $[\alpha]_D$ +53° (*c* 1) (Found: C, 41·8; H, 5·4; S, 8·6. $C_{25}H_{38}O_{20}S_2$ requires C, 41·6; H, 5·3; S, 8·9%).

Methyl 2,6-*Di*-O-*acetyl*-3-*azido*-3-*deoxy*-4-O-(2,3,4-*tri*-O-*acetyl*-6-*azido*-6-*deoxy*-α-D-*glucopyranosyl*)-β-D-*allopyranoside* (20).—The disulphonate (6) (1·9 g) was dissolved in dry hexamethylphosphoric triamide (15 ml) and sodium azide (1·5 g) was added. The mixture was heated at 110° for 18 h, then cooled, and since t.l.c. indicated that some de-*O*-acetylation had occurred, a mixture of acetic anhydride (2 ml) and pyridine (3 ml) was added and the mixture was set aside for 24 h. The solid which precipitated upon pouring into water was collected, decolourised in dichloromethane with a little charcoal, and recrystallised from ethanol to give the *diazide* (1·4 g, 86%), m.p. 158—160°, $[\alpha]_D$ +69° (*c* 0·7) (Found: C, 44·7; H, 5·1; N, 14·0. $C_{23}H_{32}N_6O_{14}$ requires C, 44·8; H, 5·2; N, 13·6%).

Hydrogenation of the diazide over 5% palladium–charcoal in ethyl acetate–methanol (1 : 4), followed by acetylation (acetic anhydride–pyridine) afforded an amorphous solid which was precipitated from propan-2-ol with light petroleum, $[\alpha]_D$ +46° (*c* 1·5) (Found: C, 49·2; H, 6·3; N, 4·4. $C_{27}H_{40}N_2O_{16}$ requires C, 50·0; H, 6·2; N, 4·3%).

Methyl 2-O-*Acetyl*-3-O-*methylsulphonyl*-6-O-p-*tolylsulphonyl*-4-O-(2,3,4-*tri*-O-*acetyl*-6-O-p-*tolylsulphonyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (8).—A solution of methyl 2-*O*-acetyl-3-*O*-methylsulphonyl-6-*O*-triphenylmethyl-4-*O*-(2,3,4-tri-*O*-acetyl-6-*O*-triphenylmethyl-α-D-glucopyranosyl)-β-D-glucopyranoside [1] (4) (2·1 g) was detritylated with hydrogen bromide in acetic acid as already described. The product was dried and dissolved in dry pyridine (10 ml), and tosyl chloride (2·5 g) was added. The mixture was then kept at room temperature for 24 h and poured into ice–water. The precipitated oil was extracted with dichloromethane (3 × 30 ml); the extract was washed with 10% sulphuric acid, saturated sodium hydrogen carbonate solution, and then with water, and dried ($MgSO_4$). Evaporation afforded a glass which crystallised from methanol. Recrystallisation from methanol afforded the *trisulphonate* (1·4 g, 79%), m.p. 184—184·5°, $[\alpha]_D$ +55° (*c* 0·8) (Found: C, 47·6; H, 4·7; S, 10·5. $C_{36}H_{46}O_{21}S_3$ requires C, 47·5; H, 5·1; S, 10·6%).

Methyl 2-O-*Acetyl*-3,6-*diazido*-3,6-*dideoxy*-4-O-(2,3,4-*tri*-O-*acetyl*-6-*azido*-6-*deoxy*-α-D-*glucopyranosyl*)-β-D-*allopyranoside* (22).—The trisulphonate (8) (1·1 g) was dissolved in dry hexamethylphosphoric triamide (15 ml) and heated at 120° for 24 h with sodium azide (2 g). T.l.c. suggested that some deacetylation had occurred. Consequently a mixture of acetic anhydride (1 ml) and pyridine (2 ml) was added to the cooled mixture, which was then kept at room temperature overnight. On pouring into ice–water an oil precipitated which was extracted into ether. The extract was evaporated to dryness and residual pyridine was removed by co-distillation with toluene. The residual syrup was purified by silica gel chromatography [ether–dichloromethane (1 : 10) as eluant]. The fractions containing the product were evaporated to give the amorphous solid triazide (0·45 g, 63%). A good elemental analysis could not be obtained, but the ^1H n.m.r. spectrum indicated that the compound was pure and was in agreement with the proposed structure (Tables 1 and 2).

Methyl 2,3,6-*Tri*-O-*acetyl*-4-O-(2,3,4-*tri*-O-*acetyl*-6-O-*triphenylmethyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (9).—A mixture of methyl β-maltoside [19] (1) (10 g) (dried over P_4O_{10} at 100°), chlorotriphenylmethane (17·2 g), and dry pyridine (60 ml) was stirred, in the absence of moisture, at room temperature for 72 h, then cooled in an ice-bath, treated with acetic anhydride (50 ml) and pyridine (40 ml), and stirred for a further 3 h at 0° and then at room temperature for 36 h. Addition of ice–water and extraction of the precipitate into dichloromethane afforded a crude product which was purified by silica gel chromatography [ether–dichloromethane (1 : 19) as eluant]. The first fractions contained triphenylmethanol and a middle fraction contained the 6,6′-*ditritylate* (2·6 g, 9%), obtained as an amorphous solid from 95% ethanol, $[\alpha]_D$ +55° (*c* 1) (Found: C, 69·9; H, 6·0. $C_{61}H_{62}O_{16}$ requires C, 69·7; H, 6·0%).

The final fractions contained the 6′-*tritylate* (9·8 g, 41%), m.p. 165—168° (from 95% ethanol), $[\alpha]_D$ +88° (*c* 2) (Found: C, 62·1; H, 6·2. $C_{44}H_{50}O_{17}$ requires C, 62·1; H, 5·9%).

Methyl 2,3,6-*Tri*-O-*acetyl*-4-O-(2,3,4-*tri*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (10).—The 6′-tritylate (9) (9 g) was detritylated as described previously. The product crystallised without the need for chromatography to give the *hexa-acetate* (5·5 g, 86%), m.p. 187—190° (from ethanol), $[\alpha]_D$ +49° (*c* 0·7) (Found: C, 49·4; H, 5·9. $C_{25}H_{36}O_{17}$ requires C, 49·3; H, 6·0%).

Methyl 2,3,6-*Tri*-O-*acetyl*-4-O-(2,3,4-*tri*-O-*acetyl*-6-O-*methylsulphonyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (11).—To a cooled solution of the hexa-acetate (10) (2·1 g) in dry pyridine (10 ml) was added mesyl chloride (1·5 ml); the mixture was stirred at 0° for a further 1 h and then poured into ice–water. The precipitate was filtered off, decolourised with charcoal (dichloromethane), and recrystallised from ethanol to give the *sulphonate* (2·2 g, 94%), m.p. 154·5—156° (change in crystalline form), 164—166°, $[\alpha]_D$ +58° (*c* 0·5) (Found: C, 45·7; H, 5·5; S, 4·3. $C_{26}H_{38}O_{19}S$ requires C, 45·5; H, 5·6; S, 4·7%).

[19] P. L. Durette, L. Hough, and A. C. Richardson, *Carbohydrate Res.*, 1973, in the Press.

Methyl 2,3,6-*Tri*-O-*acetyl*-4-O-(2,3,4-*tri*-O-*acetyl*-6-*azido*-6-*deoxy*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (12).—The sulphonate (11) (1·6 g) was dissolved in *NN*-dimethylformamide (15 ml) and heated with sodium azide (1·5 g) for 5 h at 85°. The cooled mixture was then poured into water and the precipitate filtered off and recrystallised from methanol to give the *azide* (1·3 g, 87%), m.p. 145—146°, $[\alpha]_D$ +68° (*c* 1) (Found: C, 47·6; H, 5·5; N, 6·6. $C_{25}H_{35}N_3O_{16}$ requires C, 47·4; H, 5·6; N, 6·6%).

Catalytic reduction of the azide over 5% palladium–charcoal in ethyl acetate–methanol (1 : 2), followed by acetylation (acetic anhydride–pyridine), afforded the 6′-*acetamido-maltoside* (13) (90%), m.p. 94·5—96° (from ethanol–light petroleum), $[\alpha]_D$ +51° (*c* 1) (Found: C, 49·7; H, 5·8; N, 2·4. $C_{27}H_{39}NO_{17}$ requires C, 49·9; H, 6·1; N, 2·2%).

Methyl 2,3,6-*Tri*-O-*acetyl*-4-O-(2,3,6-*tri*-O-*acetyl*-4-O-*methylsulphonyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (24).—To a solution of the hexa-acetate (10) (1·8 g) in ethanol (11 ml) was added aqueous 0·1N-sodium hydroxide (0·3 ml); the solution was stored at room temperature for 6 h, and then neutralised by dropwise addition of acetic acid. The solution was concentrated to dryness and the residue fractionated between water and dichloromethane (4 × 25 ml). The combined organic extracts were evaporated to dryness and any residual acetic acid was removed by co-distillation with toluene. The resulting syrup failed to crystallise and was mesylated in pyridine (8 ml) with mesyl chloride (1 ml). On pouring the mixture into ice–water a precipitate formed which was filtered off and purified by silica gel chromatography [ether–dichloromethane (1 : 5)]. The chromatographically pure *mesylate* (1·2 g, 59%) was obtained as a glass, $[\alpha]_D$ +44° (*c* 0·3) (Found: C, 45·2; H, 5·5; S, 4·8. $C_{26}H_{38}O_{19}S$ requires C, 45·5; H, 5·6; S, 4·7%).

Methyl 2,3,6-*Tri*-O-*acetyl*-4-O-(2,3,6-*tri*-O-*acetyl*-4-*azido*-4-*deoxy*-α-D-*galactopyranosyl*)-β-D-*glucopyranoside* (25).—The 4-sulphonate (24) (0·7 g) was heated in hexamethylphosphoric triamide (8 ml) with sodium azide (1 g) for 3 h at 100°; the mixture was then cooled and poured into water. The resulting precipitate was filtered off, washed well with water, and then decolourised with charcoal in dichloromethane. Recrystallisation from ethanol gave the 4′-*azide* (0·5 g, 77%), m.p. 106—108°, $[\alpha]_D$ +21° (*c* 0·4) (Found: C, 46·6; H, 5·4; N, 6·9. $C_{25}H_{35}N_3O_{16},0{\cdot}5H_2O$ requires C, 46·7; H, 5·6; N, 6·5%), $\nu_{max.}$ 1640 cm^{-1} (H_2O).

Methyl 2,3-*Di*-O-*acetyl*-6-*azido*-6-*deoxy*-4-O-(2,3,4,6-*tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (16).—To a solution of 2,3-di-*O*-acetyl-1,6-anhydro-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranose (26) (25 g) [17] in anhydrous chloroform (300 ml) and ethanol (5 ml), was added titanium tetrachloride (40 g). The mixture was heated under reflux for 48 h, cooled, and then poured into ice–water (1 l). The organic layer was separated and washed with water (4 × 250 ml), dried ($MgSO_4$), and evaporated. The resulting syrupy glycosyl chloride was dried thoroughly and then dissolved in anhydrous benzene (100 ml) to which were added anhydrous calcium sulphate (10 g), dried mercury(II) acetate (10 g), and dry methanol (15 ml). The mixture was stirred at room temperature for 24 h and then filtered through a pad of Hyflo Supercel. The filtrate was diluted with 1,2-dichloromethane (100 ml) and the solution washed three times with water, then dried and evaporated. T.l.c. indicated the presence of the hexa-acetate (14) together with some unchanged starting material and a slower-moving minor component. Chromatographic fractionation on silica gel with ether–dichloromethane (1 : 5) afforded the hexa-acetate (14) as a glass (see Tables 1 and 2 for n.m.r. spectral parameters); yield 1·9 g (7%).

A sample (1·6 g) of the foregoing syrup in pyridine (5 ml) was treated with tosyl chloride (0·75 g). The mixture was stirred at room temperature overnight and then processed in the usual way to give the tosylate (15) as a glass which was chromatographically pure (see Tables 1 and 2 for n.m.r. spectral parameters).

The foregoing sulphonate (15) (1·2 g) was heated with sodium azide (1 g) in *NN*-dimethylformamide (10 ml) for 4 h at 85°. The product was precipitated by pouring the mixture into water and then purified by silica gel chromatography (ether–dichloromethane, 1 : 5). The *azide* was obtained initially as a glass which crystallised from methanol; yield 0·72 g (72%), m.p. 107—110°, $[\alpha]_D$ +73° (*c* 0·5) (Found: C, 47·5; H, 5·5; N, 6·6. $C_{25}H_{35}N_3O_{16}$ requires C, 47·4; H, 5·6; N, 6·6%).

Methyl 2,3-*Di*-O-*acetyl*-6-*azido*-6-*deoxy*-4-O-(2,3,4-*tri*-O-*acetyl*-6-*azido*-6-*deoxy*-α-D-*glucopyranosyl*)-β-D-*glucopyranoside* (18).—A mixture of methyl 2,3-di-*O*-acetyl-6-*O*-*p*-tolylsulphonyl-4-*O*-(2,3,4-tri-*O*-acetyl-6-*O*-*p*-tolylsulphonyl-α-D-glucopyranosyl)-β-D-glucopyranoside (17) [7] (1·5 g), *NN*-dimethylformamide (15 ml), and sodium azide (1·5 g) was heated, with stirring, at 85° for 4 h and then poured into ice–water. The precipitated solid was recrystallised twice from ethanol to give the *diazide* (0·99 g, 94%), m.p. 149—150·5°, $[\alpha]_D$ +75° (*c* 1) (Found: C, 45·1; H, 5·4; N, 13·3. $C_{23}H_{32}N_6O_{14}$ requires C, 44·8; H, 5·2; N, 13·6%).

Hydrogenation of the diazide followed by acetylation was conducted as before except that the final product was separated from a faster-moving component by silica gel chromatography [ethyl acetate–methanol (10 : 1)]. The *diacetamido-derivative* (84%) was obtained as an amorphous solid by precipitation from propan-2-ol with light petroleum; $[\alpha]_D$ +46° (*c* 2) (Found: C, 49·4; H, 6·6; N, 4·1. $C_{27}H_{40}N_2O_{16}$ requires C, 50·0; H, 6·2; N, 4·3%).

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