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Note

Transformation of lactose into its 3-epimer 4-*O*-β-D-galactopyranosyl-D-allopyranose*

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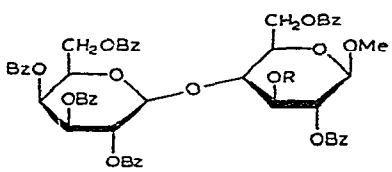
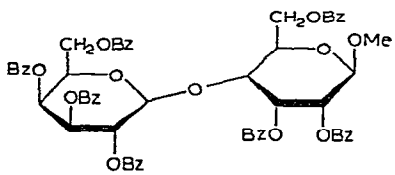
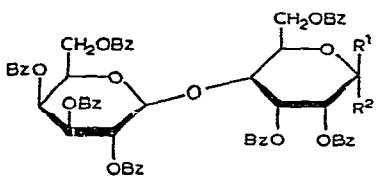
The monosaccharide allose rarely occurs in Nature[2], and has never been detected in a naturally occurring oligosaccharide. We have recently described the methyl glycoside of 4-*O*-α-D-glucopyranosyl-β-D-allopyranose[3], the 3-epimer of maltose, and also the *allo*-analogue of trehalose, α-D-allopyranosyl α-D-allopyranoside[4]. In the furtherance of our work on the chemical modification of lactose[1], we have synthesised the 3-epimer of lactose, namely, 4-*O*-β-D-galactopyranosyl-D-allose.



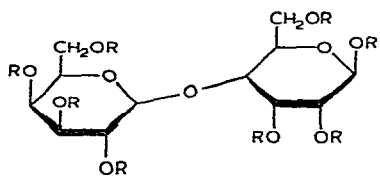
1 R = H
2 R = SO_2CH_3



3



4 R^1 = OAc, R^2 = H
5 R^1 = H, R^2 = OAc



6 R = H
7 R = Ac

*The chemistry of Cellobiose and Lactose: Part V. For Part IV, see Ref. 1.
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We have previously reported[5] that the selective hexa-*O*-benzoylation of methyl β-lactoside afforded the 2,6,2′,3′,4′,6′-hexabenzoate **1** in 33% yield. Mesylation of **1** gave the 3-mesylate **2** in 80% yield, which underwent displacement of the sulphonyloxy group when treated with sodium benzoate in hexamethylphosphoric triamide at 80° for 3 days. The resulting heptabenzoate **3** was isolated crystalline in 62% yield and the *allo* configuration of the "reducing" ring was confirmed by its 220-MHz ^{1}H-n.m.r. spectrum (Table I). In particular, the H-1 resonance for **3** was 0.41 p.p.m. to low field of that for the 3-mesylate **2**, indicating[5] the presence of an axial electronegative group at C-3. The *allo* configuration was further confirmed by the appearance of H-3 as a narrow triplet with splittings of 3 Hz, and H-2 and H-4 as double doublets (Table I).

Acetolysis of the heptabenzoate **3** with 1% sulphuric acid in acetic anhydride afforded a mixture of four components as indicated by t.l.c. The two faster-moving

TABLE I

FIRST-ORDER ^{1}H-N.M.R. PARAMETERS AT 220 MHz (τ AND Hz)

Compound	**2**	**3**	**4**	**5**	**7**
Solvent	C_6D_6	C_6D_6	$CDCl_3$	$CDCl_3$	$CDCl_3$
H-1	6.09 (d)	5.68 (d)	3.75 (d)	3.63 (d)	4.03 (d)
H-2	4.47 (dd)	4.30 (dd)	4.68 (dd)	4.68 (t)	5.16 (dd)
H-3	4.93 (t)	3.53 (t)	3.58 (t)	3.65 (t)	4.16 (t)
H-4	6.01 (t)	5.96 (dd)			6.18 (dd)
H-5		~5.65 (m)			5.82 (m)
H-6a	~5.36–6.2	5.13 (dd)	5.3–5.9	5.35–5.9	5.62–6.23
H-6b		5.32 (dd)			
H-1′	5.22 (d)	5.01 (d)	4.95 (d)	4.98 (d)	5.44 (d)
H-2′	3.76 (dd)	3.80 (t)	4.33 (dd)	4.37 (q)	4.83 (q)
H-3′	4.41 (dd)	4.37 (dd)	4.47 (dd)	4.53 (dd)	5.01 (dd)
H-4′	4.10 (d)	3.77 (m)	4.12 (d)	4.16 (d)	4.65 (d)
H-5′	6.43 (t)	6.22 (t)			
H-6′a	~5.36–6.2	5.44 (dd)	~5.3–5.9	5.35–5.9 (m)	5.62–6.23
H-6′b		5.82 (dd)			
OMe	6.96 (s)	6.83 (s)			
OMs	7.03 (s)		OAc 8.0 (s)	OAc 8.0 (s)	
$J_{1,2}$	8.2	8.2	8.4	4	9
$J_{2,3}$	9.6	3	3.6	4	3
$J_{3,4}$	9.6	3	3.6	4	3
$J_{4,5}$		10			
$J_{5,6a}$		2.2			
$J_{5,6b}$		6			
$J_{6a,6b}$		12			
$J_{1',2'}$	8	8	8	8	8
$J_{2',3'}$	10	9	10.4	10.4	10.8
$J_{3',4'}$	3.6		3.6	3.6	4
$J_{4',5'}$	~1		~1	~1	~1
$J_{5',6'a}$	6	~4.4			
$J_{5',6'b}$	7	~7			
$J_{6'a,6'b}$		12.4			

components were present in small proportions and were not isolated pure after chromatography. However, they were assumed to be products arising from acetolytic cleavage of the inter-glycosidic bond. The two major components were isolated in 21% and 9% yield and shown to be β- and α-1-acetates (**4** and **5**), respectively. A mixed fraction containing both anomers was also isolated (7% yield). The structures of the two 1-*O*-acetyl derivatives were readily assigned by their 220-MHz ^{1}H-n.m.r. spectra, which were largely first-order (Table I). In the β anomer, H-1 resonated at τ 3.75 with $J_{1,2}$ 8.4 Hz, whereas the α anomer resonated at τ 3.63 but had a small coupling (4 Hz). In both anomers, the resonances due to H-2,3,1′,2′,3′, and 4′ were readily recognised and were in full agreement with the structure assigned.

O-Debenzoylation of the mixture of α and β anomers (**5** and **4**; obtained above) gave the parent disaccharide 4-*O*-β-D-galactopyranosyl-D-allose (**6**), which was isolated crystalline in 50% yield. Acetylation of **6** with pyridine–acetic anhydride gave the β-octa-acetate **7** (70% yield), the structure of which was confirmed by its 220-MHz ^{1}H-n.m.r. spectrum (Table I).

EXPERIMENTAL

For general notes, see Ref. 1.

*Methyl 2,6-di-*O*-benzoyl-3-*O*-mesyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-*D*-galacto-pyranosyl)-β-*D*-glucopyranoside* (**2**). — A solution of the hexabenzoate[5] **1** (2 g) in anhydrous pyridine (15 ml) was cooled in an ice-bath, mesyl chloride (2 ml) was slowly added, and the solution was stored at 0° for 20 h. T.l.c. (chloroform–ethyl acetate, 15:1) then indicated completion of reaction. The mixture was poured into stirred ice–water, the brown precipitate was filtered off and washed well with water and ethanol, and a chloroform solution of the precipitate was decolorised with charcoal. Two recrystallisations of the product from chloroform–light petroleum gave the 3-mesylate **2** (1.7 g, 80%), m.p. 121–124°, $[\alpha]_D$ +67° (*c* 1, chloroform) (Found: C, 63.3; H, 4.83. $C_{56}H_{50}O_{19}S$ calc.: C, 63.5; H, 4.72%).

*Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-*D*-galactopyranosyl)-β-*D*-allopyranoside* (**3**). — A mixture of the 3-mesylate **2** (2 g), hexamethylphosphoric triamide, and sodium benzoate (2 g) was maintained at 105° (bath) for 3 days with stirring. The mixture was then cooled and poured into ice–water (~80 ml), and the resulting, white precipitate was filtered off, washed well with water, and air-dried. Recrystallisation from hot 2-propanol gave the analytically pure heptabenzoate **3** (1.3 g, 62%), m.p. 107–109°, $[\alpha]_D$ +33° (*c* 1, chloroform) (Found: C, 68.6; H, 5.00. $C_{62}H_{52}O_{18}$ calc.: C, 68.65; H, 4.79%).

*Acetolysis of methyl 4-*O*-β-*D*-galactopyranosyl-β-*D*-allopyranoside heptabenzoate* (**3**). — The heptabenzoate **3** (2 g) was dissolved in acetic anhydride (5 ml), the solution was cooled in an ice bath, and 1.5% sulphuric acid in acetic anhydride (15 ml) was slowly added. When the addition was complete, the mixture was kept at room temperature for 20 h and t.l.c. (chloroform–ethyl acetate, 25:1) then showed four

products, namely two slow-moving (major) and two fast-moving (minor) components. The mixture was poured into ice–water, and the precipitated solid was filtered off, and washed well with water and then with a little ethanol (4–5 ml).

Fractionation by dry-column chromatography[6] on silica gel, using dichloromethane–ethyl acetate (50:1) as eluant, first gave a small amount of a mixture of the two minor components which could not be purified and was discarded. Later fractions contained the faster-moving, major component which crystallised from chloroform–light petroleum to give 1-*O*-acetyl-2,3,6-tri-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-β-D-allopyranose (**4**; 0.42 g, 21%), m.p. 113–116°, $[\alpha]_D$ +33° (*c* 1, chloroform) (Found: C, 67.8; H, 4.42. $C_{63}H_{52}O_{19}$ calc.: C, 68.0; H, 4.67%).

Subsequent fractions contained both major components and were concentrated to dryness to give material (0.15 g, 7%) which was used for de-esterification (see below). Later fractions contained the slower-moving, major component which crystallised from chloroform–light petroleum to give 1-*O*-acetyl-2,3,6-tri-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-α-D-allopyranose (**5**) as a white, microcrystalline powder (0.18 g, 9%), m.p. 117–122°, $[\alpha]_D$ +51° (*c* 1, chloroform) (Found: C, 67.75; H, 4.51. $C_{63}H_{52}O_{19}$ calc.: C, 68.0; H, 4.67%).

4-O-β-D-*Galactopyranosyl*-D-*allose* (**6**). — The mixed fraction described above (0.15 g) was dissolved in methanol (8 ml), freshly prepared 0.4M methanolic sodium methoxide (0.5–1.0 ml) was added (pH ~10), and the mixture was stirred at room temperature for 2 days. T.l.c. (methanol–ethyl acetate–water, 2:3:3) then showed one product, and the mixture was neutralized with Amberlite IR-120 (H^+) resin and concentrated. The residue was crystallised from aqueous ethanol to give the disaccharide **6** (75 mg, 50%), m.p. 210–212°, $[\alpha]_D$ +49° (3 min) → +50.2° (30 min, constant value) (*c* 1, water) (Found: C, 42.1; H, 6.20. $C_{12}H_{22}O_{11}$ calc.: C, 42.1; H, 6.43%).

Acetylation of **6** with acetic anhydride–pyridine gave the octa-acetate **7** as white needles (70%), m.p. 104–106° (from ethanol), $[\alpha]_D$ +13° (*c* 1, chloroform) (Found: C, 49.5; H, 5.4. $C_{28}H_{38}O_{19}$ calc.: C, 49.55; H, 5.6%).

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