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SOME OBSERVATIONS ON THE SELECTIVE BENZOYLATION OF MALTOSE AND ITS DERIVATIVES

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ABSTRACT

Benzoylation of β-maltose monohydrate (**2**) with 10 mol. equiv. of benzoyl chloride in pyridine at −40° gave 1,2,6-tri-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl)-β-D-glucopyranose (**5**) in 87% yield, without the need for column chromatography. Similarly, benzoylation of **2** with 8 mol. equiv. of reagent afforded the octabenzoate **5**, and the 1,2,6,2′,3′,6′-hexabenzoate **11** in 3%, 79%, and 12% yield, respectively. Methyl 2,6,2′,3′,4′,6′-hexa-*O*-benzoyl-β-maltoside (**10**) was directly isolated as a crystalline monoethanolate in 83% yield, from the reaction mixture obtained by the benzoylation of methyl β-maltoside monohydrate (**8**) with 8.9 mol. equiv. of reagent. Benzoylation of **8** with 7 mol. equiv. of reagent produced **10** and the 2,6,2′,3′,6′-pentabenzoate **16** in 71% and 23% yield, respectively. The order of reactivity of the hydroxyl groups in methyl 4′,6′-*O*-benzylidene-β-maltoside towards benzoylation is HO-2, HO-6 > HO-2′ ≈ HO-3′ > HO-3. Benzoylation of methyl β-cellobioside (**33**) with 7.9 mol. equiv. of reagent gave the heptabenzoate and the 2,6,2′,3′,4′,6′-hexabenzoate **36** in 56% and 27% yield, respectively.Compounds **5**, **16**, and **36** were transformed into 4-*O*-α-D-glucopyranosyl-D-allopyranose, methyl 4-*O*-α-D-galactopyranosyl-β-D-allopyranoside, and methyl 4-*O*-β-D-glucopyranosyl-β-D-allopyranoside, respectively, by sequential sulfonylation, nucleophilic displacement, and *O*-debenzoylation.

INTRODUCTION

The low reactivity of HO-3 in maltose (**1**) and one of its derivatives towards acylation has been previously[1,4,5] reported. Acetylation of β-maltose monohydrate (2) with acetylpyridinium chloride in cold toluene gave[1] a mixture of the 1,2,6,2′,3′,4′,6′-heptaacetate **3** and the octaacetate **4** in the ratio of ~7:3. Under conditions of benzoylation similar to those under which cellobiose[2] and lactose[3] were completely converted into the corresponding octabenzoates, **1** afforded[4] a mixture of the 1,2,6,2′3′,4′,6′-heptabenzoate **5** and the octabenzoate **6** in the ratio of 11:9. Compounds **3** and **5** were

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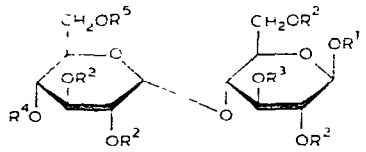
isolated in 71% and 54% yield, respectively, after column chromatography. A study of the selective benzoylation of 1,6-anhydro-4′,6′-*O*-benzylidene-β-maltose indicated that HO-3 has the lowest reactivity among the secondary hydroxyl groups[5]. Recently, Durette *et al.*[6,7] have shown the usefulness of **3** as a starting material for the introduction of a wide range of functional groups into a specific position of **1** and methyl β-maltoside (**7**).



1 $R^1 = R^2 = R^3 = R^4 = R^5 = H$
2 $R^1 = H \cdot H_2O, R^2 = R^3 = R^4 = R^5 = H$
3 $R^1 = R^2 = R^4 = R^5 = Ac, R^3 = H$
4 $R^1 = R^2 = R^3 = R^4 = R^5 = Ac$
5 $R^1 = R^2 = R^4 = R^5 = Bz, R^3 = H$
6 $R^1 = R^2 = R^3 = R^4 = R^5 = Bz$
7 $R^1 = Me, R^2 = R^3 = R^4 = R^5 = H$
8 $R^1 = Me \cdot H_2O, R^2 = R^3 = R^4 = R^5 = H$
9 $R^1 = R^2 = R^4 = R^5 = Bz, R^3 = Ms$
10 $R^1 = Me, R^2 = R^4 = R^5 = Bz, R^3 = H$
11 $R^1 = R^2 = R^5 = Bz, R^3 = R^4 = H$
12 $R^1 = R^2 = R^5 = Bz, R^3 = R^4 = Me$
13 $R^1 = R^2 = R^5 = Bz, R^3 = R^4 = Ac$
14 $R^1 = R^2 = R^5 = Bz, R^3 = R^4 = Ms$
15 $R^1 = Me, R^2 = R^5 = Bz, R^3 = R^4 = Ms$
16 $R^1 = Me, R^2 = R^5 = Bz, R^3 = R^4 = H$
17 $R^1 = Me, R^2 = R^3 = R^4 = R^5 = Bz$
18 $R^1 = Me, R^2 = Bz, R^3 = R^4 = R^5 = H$
19 $R^1 = Me, R^2 = Bz, R^3 = R^4 = R^5 = Ms$

We report here the partial benzoylation of β-maltose monohydrate[8] (**2**), methyl β-maltoside monohydrate[9] (**8**), and methyl 4′,6′-*O*-benzylidene-β-maltoside[10] (**26**) with a large proportion of benzoyl chloride in pyridine at low temperatures. Benzoylation of methyl β-cellobioside[9] (**33**) under conditions comparable to those of the benzoylation of **8** was also included for comparison. Furthermore, nucleophilic displacements of the sulfonyloxy derivatives that derived from partially esterified derivatives were investigated.

RESULTS AND DISCUSSION

The benzoylations were performed under two different sets of conditions (*A* and *B*, see Experimental). In experiments aimed at obtaining a high yield of the heptabenzoate **5**, the ratio of benzoyl chloride to **2** was varied under conditions *A*, and 10 mol. equiv. of the reagent was found to give the maximum yield. Thus, **5** was directly isolated in crystalline form in 87% yield from the reaction mixture, without resort to column chromatography, which is a marked improvement over the previous procedure[4], both for the high yield and ease of isolation.

Methanesulfonylation of **5** gave the crystalline 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-3-*O*-methylsulfonyl derivative **9** in 90% yield. Displacement of the sulfonyloxy group of **9** with sodium benzoate in *N,N,N′,N′,N″,N″*-hexamethylphosphoric triamide proceeded with considerable decomposition to give, in 41% yield, crystalline

4-*O*-α-D-glucopyranosyl-D-allopyranose octabenzoate (**20**) with inversion of configuration at C-3. *O*-Debenzoylation of **20** afforded 4-*O*-α-D-glucopyranosyl-D-allopyranose (**23**) as an amorphous solid. G.l.c. examination of the *O*-trimethylsilyl derivatives of the methanolyzate of **23** showed the presence of methyl α,β-D-glucopyranoside and methyl α,β-D-allopyranoside, which confirmed the structure of **23**.

Sequential treatment of **5** with hydrogen bromide in acetic acid and mercuric cyanide in methanol gave crystalline methyl 2,6,2′,3′,4′,6′-hexa-*O*-benzoyl-β-maltoside (**10**) in 76% yield. Both n.m.r. spectroscopy and elemental analysis established that **10** contained 1 mole of ethanol of crystallization.

Benzoylation of **2** with 8 mol. equiv. of benzoyl chloride under conditions *B* gave a mixture of three products (t.l.c.). Compound **5** was crystallized in 70% yield from this mixture, and column chromatography of the mother liquor afforded **6** and 1,2,6,2′,3′,6′-hexa-*O*-benzoyl-β-maltose (**11**) in 3% and 12% yield, respectively, together with another 9% of **5**. To determine the position of the free hydroxyl groups, **11** was methylated with diazomethane–boron trifluoride etherate[11] to give 1,2,6,2′,3′,6′-hexa-*O*-benzoyl-3,4′-di-*O*-methyl-β-maltose (**12**), which on *O*-debenzoylation and methanolysis, produced methyl 3-*O*-methyl- and 4-*O*-methyl-α,β-D-glucopyranoside that were identified by g.l.c. as the trimethylsilyl ethers. The n.m.r. spectrum of **11** in chloroform-*d* showed the H-1 resonance at τ 3.95 as a doublet with *J* 8.0 Hz, consistent with the β configuration at C-1.

Acetylation and methanesulfonylation of **11** gave the 3,4′-di-*O*-acetyl-1,2,6,2′,3′,6′-hexa-*O*-benzoyl (**13**) and 1,2,6,2′,3′,6′-hexa-*O*-benzoyl-3,4′-di-*O*-methylsulfonyl derivatives (**14**) in crystalline form, respectively. Similar sequential treatment of **14** with hydrogen bromide–acetic acid and mercuric cyanide–methanol, as applied to **5**, afforded crystalline methyl 2,6,2′,3′,6′-penta-*O*-benzoyl-3,4′-di-*O*-methylsulfonyl-β-maltoside (**15**).

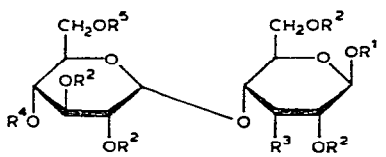
Benzoylation of the glycoside **8** with 8.9 mol. equiv. of benzoyl chloride under conditions *A* gave, as the major product, **10**, which was directly isolated as a crystalline monoethanolate in 83% yield from the reaction mixture and shown to be identical with that prepared from **5**.

Benzoylation of the glycoside **8** with 7 mol. equiv. of reagent under conditions *B* afforded a mixture of two products, no heptabenzoate **17** being detected on t.l.c. The hexabenzoate **10** crystallized as a monoethanolate in 63% yield from this mixture, and chromatographic fractionation of the mother liquor gave a further 8% of **10** and 23% of methyl 2,6,2′,3′,6′-penta-*O*-benzoyl-β-maltoside (**16**). Methanesulfonylation of **16** yielded **15** having physical constants in good agreement with those of the compound obtained from **14**, thus supporting the structural assignment of **16**.

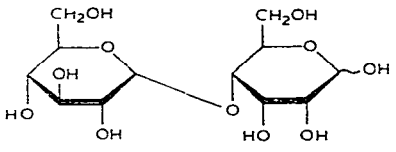
When treated with sodium benzoate in *N*,*N*,*N*′,*N*′,*N*″,*N*″-hexamethylphosphoric triamide, **15** underwent smooth replacement of the sulfonyloxy group to give, with inversion of configurations at C-3 and C-4′, methyl 4-*O*-α-D-galactopyranosyl-β-D-allopyranoside heptabenzoate (**24**) which was isolated as an amorphous powder in 73% yield, after column chromatography. This was *O*-debenzoylated to furnish crystalline methyl 4-*O*-α-D-galactopyranosyl-β-D-allopyranoside (**25**), the structure of

which was confirmed by methanolysis and g.l.c. examination of the trimethylsilyl derivatives of the methanolyzate.

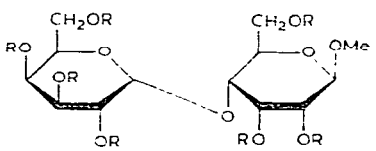
Interestingly, the introduction of a benzylidene group into **7** decreased the reactivity of the remaining hydroxyl groups towards benzoylation. Benzoylation with 10 mol. equiv. of reagent of the 4′,6′-*O*-benzylidene derivative **26** under conditions *B* gave the crystalline 2,6,2′,3′-tetrabenzoate **27** in 84% yield. The structure of **27** was established by its conversion into the known methyl 3-chloro-3-deoxy-4-*O*-(α-D-glucopyranosyl)-β-D-allopyranoside[6] (**22**), by treatment with sulfuryl chloride and pyridine in chloroform to afford crystalline methyl 2,6-di-*O*-benzoyl-3-chloro-3-deoxy-4-*O*-(2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-β-D-allopyranoside (**21**) which was successively debenzylidenated and *O*-debenzoylated to give **22**.



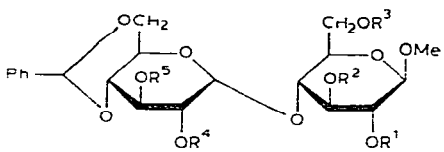
20 $R^1 = R^2 = R^4 = R^5 = Bz, R^3 = OBz$
21 $R^1 = Me, R^2 = Bz, R^3 = Cl, R^4, R^5 = PhCH$
22 $R^1 = Me, R^2 = R^4 = R^5 = H, R^3 = Cl$



23



24 R = Bz
25 R = H

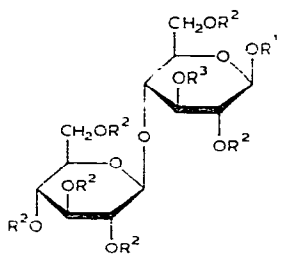


26 $R^1 = R^2 = R^3 = R^4 = R^5 = H$
27 $R^1 = R^2 = R^4 = R^5 = Bz, R^2 = H$
28 $R^1 = R^3 = R^4 = Bz, R^2 = R^5 = H$
29 $R^1 = R^3 = R^5 = Bz, R^2 = R^4 = H$
30 $R^1 = R^3 = R^4 = Bz, R^2 = R^5 = Me$
31 $R^1 = R^3 = R^5 = Bz, R^2 = R^4 = Me$
32 $R^1 = R^5 = H, R^2 = R^3 = R^4 = Bz$

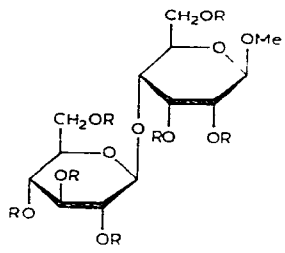
Treatment of **27** with aqueous acetic acid removed the benzylidene group to afford crystalline methyl 2,6,2′,3′-tetra-*O*-benzoyl-β-maltoside (**18**) which was converted by methanesulfonylation into the crystalline 2,6,2′,3′-tetra-*O*-benzoyl-3,4′,6′-tri-*O*-methylsulfonyl derivative **19**. Reaction of **19** with the benzoate ion in *N*,*N*,*N*′,*N*′,*N*″,*N*″-hexamethylphosphoric triamide gave, in 68% yield, **24**, identical with the compound prepared by a similar displacement of **15**.

When the benzylidene derivative **26** was treated with 10 mol. equiv. of benzoyl chloride under conditions *A*, t.l.c. indicated the presence of two components which

were isolated by column chromatography. The first-eluted component was obtained in 71% yield and identified as **27** by comparison with an authentic specimen obtained previously. The second fraction eluted from the column moved as a single component on t.l.c. in various solvent systems and was obtained in 22% yield as a crystalline compound having a double melting point. Elemental analysis indicated that it was a tribenzoyl derivative, which subsequently was shown to be a 1:1 mixture of the 2,6,2′-(**28**) and 2,6,3′-tribenzoates (**29**) by the following sequence of reactions: Methylation[11] resulted in the formation, in approximately equal amounts (t.l.c.), of two products that were fractionated on a column of silica gel. The faster-moving component was obtained in crystalline form in 43% yield and the structure of the 2,6,2′-tri-*O*-benzoyl-3,3′-di-*O*-methyl derivative **30** was assigned on the basis of *O*-debenzoylation and methanolysis, which gave methyl 3-*O*-methyl-α,β-D-glucopyranoside as the sole product (g.l.c.). The slower-moving component was isolated in crystalline form in 42% yield and proved to be the 2,6,3′-tri-*O*-benzoyl-3,2′-di-*O*-methyl derivative **31**. *O*-Debenzoylation of **31** followed by methanolysis gave methyl 2-*O*-methyl- and methyl 3-*O*-methyl-α,β-D-glucopyranoside, indicating that the two free hydroxyl groups in **29** were located at either C-3 and 2′ or C-2 and 3′. Further benzoylation with 2 mol. equiv. of reagent of the mixture of **28** and **29** under conditions *B* gave a high yield of **27**, precluding the possibility of the structure of the 3,6,2′-tribenzoate **32** for **29**. The formation of **28** and **29** in approximately equal amounts indicates that HO-2′ and -3′ in **26** are of equal reactivity. Although it is not possible to determine the reactivity order of HO-2 and HO-6 in **26** from this selective benzoylation, the reactivity sequence of the hydroxyl groups in **26** appears to be HO-2, HO-6 > HO-2′ ≈ HO-3′ > HO-3.



33 R^1 = Me, R^2 = R^3 = H
34 R^1 = Me, R^2 = R^3 = Bz
35 R^1 = R^2 = Bz, R^3 = H
36 R^1 = Me, R^2 = Bz, R^3 = H
37 R^1 = Me, R^2 = Bz, R^3 = Ms



38 R = Bz
39 R = H

Benzoylation of **33** with 7.9 mol. equiv. of the reagent under conditions *A* gave a complex mixture of two major and three minor components (t.l.c.). Only the two major compounds were isolated by column chromatography. One of them was obtained in crystalline form in 56% yield and was identified as the heptabenzoate **34**.

The second one, isolated crystalline in 27% yield, was found to be the 2,6,2′,3′,4′,6′-hexabenzoate **36** by comparison with the compound obtained by sequential treatment of 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-cellobiose[12] (**35**) with hydrogen bromide–acetic acid and mercuric cyanide–methanol. It is noteworthy that, under comparable conditions, **8** gave, as the major product, the hexabenzoate **10** having HO-3 free (83%).

Methanesulfonylation of **36** gave the crystalline 2,6,2′,3′,4′,6′-hexa-*O*-benzoyl-3-*O*-methylsulfonyl derivative **37** which was transformed into methyl 4-*O*-β-D-glucopyranosyl-β-D-allopyranoside heptabenzoate (**38**) in 68% yield by displacement with the benzoate ion in *N*,*N*,*N*′,*N*′,*N*″,*N*″-hexamethylphosphorotriamide. *O*-Debenzoylation of **38** furnished the 3-epimer of **33**, namely methyl 4-*O*-β-D-glucopyranosyl-β-D-allopyranoside (**39**) in crystalline form.

The very slow benzoylation of HO-3 in **1** was attributed to the presence of a strong, intramolecular hydrogen-bonding between HO-3 and HO-2′, caused by the close proximity of the two D-glucopyranose units[4]. Moreover, it was pointed out that, in (1→4)-linked disaccharides, the hydroxyl groups adjacent to the junction of the two glucopyranose rings (*i.e.*, HO-3, HO-2′, and HO-6) are subjected to the greatest steric interaction[7], and hence react sluggishly towards acylation[13,14]. However, the present experimental results indicate that, in **2** and **8**, HO-3 is the least reactive, followed by HO-4′. The low reactivity of HO-4′ cannot be accounted for by steric hindrance and it appears to be very similar to the low reactivity of HO-4 in methyl α-D-glucopyranoside[15] and in α-D-glucopyranose[16].

EXPERIMENTAL

General methods. — Melting points were determined with a Yanagimoto hot-stage microscope and are uncorrected. Optical rotations were measured with an Ohyo Denki automatic polarimeter, Model MP-1T. N.m.r. spectra were recorded in chloroform-*d* solution with a Varian A-60A spectrometer, and with tetramethylsilane as the internal standard. Gas-liquid chromatography was performed under the same conditions as described previously[17]. T.l.c. was performed on silica gel No 7731 (Merck); spots were detected by spraying a solution of 10% sulfuric acid, followed by heating. Column chromatography was performed on silica gel No 7734 (Merck). The following solvent systems (v/v) were used: (*A*) 9:1, (*B*) 19:1, and (*C*) 4:1 benzene–ethyl acetate. Solutions were evaporated at a temperature below 40° under reduced pressure.

General procedure for the selective benzoylation of **2**, **8**, **26**, *and* **33**. — *Method A.* The sugar was dissolved in anhydrous pyridine (40 ml/g of the sugar) and the solution was cooled to −40° with a carbon dioxide–acetone bath. Benzoyl chloride was added dropwise over a period of 20–30 min to the stirred solution, and the reaction mixture was further stirred for 1 h at −30°, 2 h at −20°, and then stored for 20 h at 0°.

Method B. After being processed as in conditions *A*, the mixture was allowed to reach room temperature, and then kept for 2 days.

Subsequently, the reaction mixture was treated with a small amount of ice and

concentrated to a mobile, thin syrup which was poured into ice–water, and the resulting precipitate was filtered off, washed extensively with water, and dried to give the crude product.

1,2,6-Tri-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl)-β-D-glucopyranose (**5**). — The product obtained by treatment of **2** (20 g) with benzoyl chloride (68.2 ml, 10 mol. equiv.) under conditions *A* was crystallized twice from acetone–methanol to give **5** (51.5 g, 87%), m.p. 141–142°, $[\alpha]_D^{24}$ +46.1° (*c* 1.2, chloroform); lit.[4]: m.p. 139–140° (acetone–methanol), $[\alpha]_D^{21}$ +47.0° (*c* 1.0, chloroform).

1,2,3-Tri-O-benzoyl-3-O-methylsulfonyl-4-O-(2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl)-β-D-glucopyranose (**9**). — A solution of **5** (1.5 g) in pyridine (7 ml) was cooled to −10°, treated with methanesulfonyl chloride (0.5 ml), and kept overnight at 0°. The solution was poured into ice–water, and the precipitate formed was filtered off, washed with water, and dried. Crystallization from ethanol afforded **9** (1.5 g, 90%), m.p. 156–157°, $[\alpha]_D^{24}$ +37.1° (*c* 1.0, chloroform); n.m.r. τ 7.05 (s, 3 H, OMs).

Anal. Calc. for $C_{62}H_{52}O_{20}S$: C, 64.80; H, 4.56; S, 2.79. Found: C, 64.68; H, 4.59; S, 2.60.

1,2,3,6-Tetra-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl)-β-D-allopyranose (**20**). — Compound **9** (1.2 g) was heated in *N,N,N',N',N'',N''*-hexamethylphosphoric triamide (10 ml) with sodium benzoate (1.2 g) for 20 h at 90°. The cooled mixture was poured into ice–water, and the precipitate that separated was collected by centrifugation and dissolved in chloroform. The solution was washed well with water, dried (Na_2SO_4), treated with charcoal, and evaporated to a syrup which crystallized from ethanol–acetone to give **20** (510 mg, 41%), m.p. 154–155°, $[\alpha]_D^{24}$ +45.2° (*c* 1.4, chloroform).

Anal. Calc. for $C_{68}H_{54}O_{19}$: C, 65.90; H, 4.63. Found: C, 65.62; H, 4.51.

4-O-α-D-Glucopyranosyl-D-allopyranose (**23**). — A solution of **20** (1 g) in dry chloroform (10 ml) was treated with methanolic M sodium methoxide (1 ml) in anhydrous methanol (10 ml), and the solution was kept for 3 h at room temperature. After neutralization with Amberlite IR-120 (H^+) ion-exchange resin, the solution was evaporated to dryness and the residue was thoroughly extracted with ether to give **23** (270 mg, 93%) as an amorphous solid, $[\alpha]_D^{24}$ +118.9° (equil., *c* 3.0, water).

Anal. Calc. for $C_{12}H_{22}O_{11}$: C, 42.11; H, 6.48. Found: C, 41.90; H, 6.64.

Methanolysis of **23** (30 mg; 1% methanolic HCl, 5 ml; reflux, 16 h) and g.l.c. of the resulting methyl glycosides as the *O*-trimethylsilyl derivatives gave peaks corresponding to methyl α,β-D-allopyranoside (8.7 and 9.6 min) and methyl α,β-D-glucopyranoside (13.8 and 15.2 min).

Methyl 2,6-di-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**10**). — (*a*). To a chilled solution of **5** (10 g) in acetic acid (45 ml) was added an acetic acid solution (40 ml) that had been saturated with HBr at 0°. The mixture was stirred for 1 h at room temperature and diluted with chloroform. The solution was washed successively with iced water, aqueous $NaHCO_3$ and water, dried ($MgSO_4$), and evaporated to give the α-D-glycosyl bromide. The bromide was dissolved in a

mixture of anhydrous methanol (15 ml) and dry benzene (80 ml) containing $Hg(CN)_2$ (3 g). The mixture was stirred for 4 h at room temperature and concentrated to a syrup which was dissolved in chloroform. The solution was filtered through a Celite pad, and the filtrate was washed extensively with water, dried (Na_2SO_4), and concentrated to dryness. Crystallization from ethanol gave **10** (7.3 g, 76%) as a monoethanolate, m.p. 114–115°, $[\alpha]_D^{24}$ +56.8° (*c* 1.2, chloroform); n.m.r. τ 6.53 (s, 3 H, OMe) and 8.82 (t, 3 H, CH_3 of ethanol).

Anal. Calc. for $C_{57}H_{54}O_{18}$: C, 66.66; H, 5.30. Found: C, 66.58; H, 5.37.

(*b*). The product obtained by treatment of **8** (5 g) with benzoyl chloride (13.8 ml, 8.9 mol. equiv.) under conditions *A* was crystallized from ethanol and recrystallized from the same solvent to give **10** (11.4 g, 83%) as a monoethanolate, m.p. and mixed m.p. 114–115°, $[\alpha]_D^{24}$ +56.0° (*c* 1.0, chloroform); the n.m.r. spectrum was identical with that obtained with method *a*.

Octamolar benzoylation of **2** *with 8 mol. equiv. of benzoyl chloride.* — Treatment of **2** with benzoyl chloride (25.9 ml) under conditions *B* gave a mixture which was shown by t.l.c. (Solvent *A*) to be composed of three benzoylated derivatives having R_F values of 0.78 (**6**), 0.58 (**5**), and 0.30 (**11**), respectively. Crystallization of the mixture from acetone–methanol afforded **5** (20.8 g, 70%), m.p. and mixed m.p. 141–142°, $[\alpha]_D^{24}$ +46.5° (*c* 1.5, chloroform).

The mother liquor of **5** was chromatographed on a column of silica gel (300 g) with Solvent *A*. The initial fraction from the column gave 1,2,3,6-tetra-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl)-β-D-glucopyranose (**6**) (1.1 g, 3%), m.p. 193–194° (acetone–methanol), $[\alpha]_D^{24}$ +67.7° (*c* 1.4, chloroform); lit.[4]: m.p. 190–192° (acetone–methanol), $[\alpha]_D^{21}$ +68.2° (*c* 1.0, chloroform).

The second fraction afforded an additional amount of **5** (2.8 g, 9%). Further elution of the column gave 1,2,6-tri-*O*-benzoyl-4-*O*-(2,3,6-tri-*O*-benzoyl-α-D-glucopyranosyl)-β-D-glucopyranose (**11**) (3.2 g, 12%) as an amorphous powder, $[\alpha]_D^{24}$ +58.4° (*c* 1.1, chloroform); n.m.r. τ 3.95 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1).

Anal. Calc. for $C_{54}H_{46}O_{17}$: C, 67.08; H, 4.80. Found: C, 66.90; H, 5.02.

1,2,6-Tri-O-benzoyl-3-O-methyl-4-O-(2,3,6-tri-O-benzoyl-4-O-methyl-α-D-glucopyranosyl)-β-D-glucopyranose (**12**). — Diazomethane in dichloromethane was gradually added to a cooled solution of **11** (800 mg) in dichloromethane (5 ml) containing BF_3 etherate (0.07 ml) until a pale-yellow color persisted. Polymethylene was filtered off, and the solution was washed successively with water, aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated. The residue was purified by elution from a column of silica gel (30 g) with Solvent *A* to give **12** (690 mg, 84%), m.p. 97–99° (ether–petroleum ether), $[\alpha]_D^{24}$ +73.1° (*c* 1.4, chloroform); n.m.r. τ 6.55 and 6.57 (s, 6 H, 2 OMe).

Anal. Calc. for $C_{56}H_{50}O_{17}$: C, 67.60; H, 5.07. Found: C, 67.48. H, 5.26.

O-Debenzoylation of **12** (50 mg), as described for **20**, followed by methanolysis of the resulting product under the same conditions as for **23**, and g.l.c. of the methanolyzate as the per(trimethylsilyl) ethers gave peaks corresponding to methyl

3-*O*-methyl-α,β-D-glucopyranoside (7.5 and 7.9 min) and methyl 4-*O*-methyl-α,β-D-glucopyranoside (8.4 and 9.6 min).

3-O-Acetyl-4-O-(4-O-acetyl-2,3,6-tri-O-benzoyl-α-D-glucopyranosyl)-1,2,6-tri-O-benzoyl-β-D-glucopyranose (**13**). — Conventional acetylation of **11** (130 mg) with 1:1 (v/v) acetic anhydride–pyridine (2 ml) overnight at 0° and isolation in the usual way gave **13** (123 mg, 87%), m.p. 178–179° (ethanol–chloroform), $[\alpha]_D^{24}$ +76.7° (*c* 1.3, chloroform); n.m.r. τ 8.10 (s, 6 H, 2 OAc).

Anal. Calc. for $C_{58}H_{50}O_{19}$: C, 66.28; H, 4.80. Found: C, 65.95; H, 4.98.

1,2,6-Tri-O-benzoyl-3-O-methylsulfonyl-4-O-(2,3,6-tri-O-benzoyl-4-O-methylsulfonyl-α-D-glucopyranosyl)-β-D-glucopyranose (**14**). — Methanesulfonylation of **11** (1 g), as described for the preparation of **9**, gave **14** (940 mg, 87%), m.p. 125–126° (ethanol–acetone), $[\alpha]_D^{24}$ +46.8° (*c* 1.0, chloroform); n.m.r. τ 7.09 and 7.13 (s, 6 H, 2 OMs).

Anal. Calc. for $C_{56}H_{50}O_{21}S_2$: C, 59.89; H, 4.49; S, 5.71. Found: C, 59.74; H, 4.57; S, 5.58.

Methyl 2,6-di-O-benzoyl-3-O-methylsulfonyl-4-O-(2,3,6-tri-O-benzoyl-4-O-methylsulfonyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**15**). — Sequential treatment of **14** (500 mg) in acetic acid (2 ml) with a saturated solution of HBr in acetic acid (2 ml), and then with methanol (1.5 ml) in benzene (7 ml) containing $Hg(CN)_2$ (130 mg), as described for the preparation of **10**, afforded **15** (340 mg, 74%), m.p. 109–110° (ethanol), $[\alpha]_D^{24}$ 82.6° (*c* 1.3, chloroform); n.m.r. τ 6.58 (s, 6 H, OMe), 7.13, and 7.15 (s, 6 H, 2 OMs).

Anal. Calc. for $C_{50}H_{48}O_{20}S_2$: C, 58.13; H, 4.68; S, 6.21. Found: C, 58.27; H, 4.63; S, 6.10.

Benzoylation of **8** *with 7 mol. equiv. of benzoyl chloride.* — Treatment of **8** (5 g) with benzoyl chloride (10.9 ml) under conditions *B* gave a product which was shown by t.l.c. (Solvent *A*) to contain two components having R_F values of 0.63 (**10**) and 0.33 (**16**). Crystallization of the product from ethanol afforded **10** (8.7 g, 63%) as a monoethanolate, m.p. and mixed m.p. 114–115° (from ethanol), $[\alpha]_D^{24}$ +57.0° (*c* 1.5, chloroform).

The mother liquor of **5** was fractionated on a column of silica gel (100 g) with Solvent *A*. The first fraction from the column gave a further amount of **10** (1.1 g, 8%). The next fraction gave methyl 2,6-di-*O*-benzoyl-4-*O*-(2,3,6-tri-*O*-benzoyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**16**) (2.7 g, 23%) as an amorphous solid, $[\alpha]_D^{24}$ +72.2° (*c* 1.3, chloroform).

Anal. Calc. for $C_{48}H_{44}O_{16}$: C, 65.75; H, 5.06. Found: C, 65.93; H, 5.10.

Methanesulfonylation of **16** (2.3 g), as described for the preparation of **9**, gave **15** (2.2 g, 81%), m.p. and mixed m.p. 109–110° (ethanol), $[\alpha]_D^{24}$ +81.5° (*c* 1.0, chloroform); the n.m.r. spectrum was identical with that of the compound obtained from **14**.

Methyl 2,3,6-tri-O-benzoyl-4-O-(2,3,4,6-tetra-O-benzoyl-α-D-galactopyranosyl)-β-D-allopyranoside (**24**). — A solution of **15** (1.5 g) in *N*,*N*,*N'*,*N'*,*N''*,*N''*-hexamethylphosphorotriamide (15 ml) containing sodium benzoate (1.5 g) was heated for 30 h

at 100°. The reaction mixture was processed as described for **20**, and the residue was purified by elution from a column of silica gel (50 g) with Solvent *B* to give **24** (1.1 g, 73%) as an amorphous powder, $[\alpha]_D^{24}$ +107.0° (*c* 1.0, chloroform).

Anal. Calc. for $C_{62}H_{52}O_{18}$: C, 68.63; H, 4.83. Found: C, 68.89; H, 4.78.

Methyl 4-O-α-D-galactopyranosyl-β-D-allopyranoside (**25**). — *O*-Debenzoylation of **24** (1 g), as described for **20**, gave **25** (260 mg, 79%), m.p. 215–216° (ethanol), $[\alpha]_D^{24}$ +112.3° (*c* 1.3, water).

Anal. Calc. for $C_{13}H_{24}O_{11}$: C, 43.82; H, 6.79. Found: C, 43.69; H, 6.88.

Methanolysis of **25**, under the same conditions as for **23**, and g.l.c. of the methanolyzate as the per(trimethylsilyl) ethers gave peaks corresponding to methyl α,β-D-allopyranoside (8.7 and 9.6 min) and methyl α,β-D-galactopyranoside (11.2 and 12.7 min).

Methyl 2,6-di-O-benzoyl-4-O-(2,3-di-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranosyl)-β-D-glucopyranoside (**27**). — The product obtained by treatment of **26** (3.5 g) with benzoyl chloride (9.2 ml, 10 mol. equiv.) under conditions *B* was crystallized from ethanol–chloroform to give **27** (5.7 g, 84%), m.p. 196–197°, $[\alpha]_D^{24}$ +53.3° (*c* 1.1, chloroform).

Anal. Calc. for $C_{48}H_{44}O_{15}$: C, 66.97; H, 5.15. Found: C, 66.85; H, 5.29.

Methyl 2,6-di-O-benzoyl-3-chloro-3-deoxy-4-O-(2,3-di-O-benzoyl-4,6-O-benzylidene-α-D-glucopyranosyl)-β-D-allopyranoside (**21**). — A solution of **27** (500 mg) in pyridine (1 ml) and chloroform (5 ml) was treated with $SOCl_2$ (0.5 ml) for 1 h at −30°. The mixture was gradually allowed to reach room temperature (within 1 h), kept for 1 h, and then diluted with chloroform. The solution was washed successively with cold M HCl, aqueous $NaHCO_3$, and water, dried (Na_2SO_4), and evaporated to give a crystalline mass which, on recrystallization from ethanol–chloroform, afforded **21** (430 mg, 84%), m.p. 214–215°, $[\alpha]_D^{24}$ +65.9° (*c* 1.2, chloroform).

Anal. Calc. for $C_{48}H_{43}ClO_{14}$: C, 65.57; H, 4.93; Cl, 4.03. Found: C, 65.67; H, 5.10; Cl, 4.16.

A solution of **21** (400 mg) in 60% acetic acid (6 ml) was heated for 20 min at 100°. The solvents were removed by codistillation with toluene. The residue was dried and *O*-debenzoylated, as for **20**, to give methyl 3-chloro-3-deoxy-4-*O*-(α-D-glucopyranosyl)-β-D-allopyranoside (**22**) (120 mg, 71%), m.p. 175–176° (95% ethanol), $[\alpha]_D^{24}$ +121.0° (*c* 1.0, methanol); lit.[6]: m.p. 178–179° (95% ethanol), $[\alpha]_D$ +120° (*c* 0.3, methanol).

Methyl 2,6-di-O-benzoyl-4-O-(2,3-di-O-benzoyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**18**). — A solution of **27** (3.5 g) in acetic acid (32 ml) was heated on a boiling-water bath, and water (20 ml) was added in small portions within a few min. After heating for 20 min, the solvents were removed by repeated codistillation with toluene to give a crystalline solid which, on recrystallization from ether–petroleum ether, afforded **18** (2.8 g, 90%), m.p. 183–184°, $[\alpha]_D^{24}$ +81.4° (*c* 1.2, chloroform).

Anal. Calc. for $C_{41}H_{40}O_{15}$: C, 63.73; H, 5.22. Found: C, 63.98; H, 5.11.

Methyl 2,6-di-O-benzoyl-4-O-(2,3-di-O-benzoyl-4,6-di-O-methylsulfonyl-α-D-glucopyranosyl)-3-O-methylsulfonyl-β-D-glucopyranoside (**19**). — Methanesulfonyl-

ation of **18** (2.4 g), as described previously, gave **19** (2.7 g, 87%), m.p. 110–112° (from ethanol), $[\alpha]_D^{24}$ +85.0° (*c* 1.0, chloroform); n.m.r. τ 6.97, 7.09, and 7.13 (s, 9 H, 3 OMs).

Anal. Calc. for $C_{44}H_{46}O_{21}S_3$: C, 52.48; H, 4.61; S, 9.55. Found: C, 52.58; H, 4.73; S, 9.47.

A solution of **19** (1.9 g) in *N,N,N',N',N'',N''*-hexamethylphosphoric triamide (20 ml) was heated with sodium benzoate (2 g) for 24 h at 100°. The reaction mixture was processed as described for **20**, and the residue was purified on a column of silica gel (80 g) with Solvent *B* to give **24** (1.4 g, 68%), $[\alpha]_D^{24}$ +108.1° (*c* 1.2, chloroform); the n.m.r. spectrum was identical with that of the compound prepared from **15**.

Benzoylation of **26** *with 10 mol. equiv. of benzoyl chloride.* — T.l.c. examination (Solvent *C*) of the product obtained by treatment of **26** (4 g) with benzoyl chloride (10.5 ml) under conditions *A* indicated the presence of two benzoylated derivatives having R_F values of 0.72 (**27**) and 0.33 (**28** and **29**). The mixture was fractionated on a column of silica gel (200 g) with Solvent *C*.

The first fraction eluted from the column gave **27** (5.5 g, 71%), m.p. and mixed m.p. 196–197° (ethanol–chloroform), $[\alpha]_D^{24}$ +54.0° (*c* 1.3, chloroform). The next fraction afforded a 1:1 mixture of methyl 2,6-di-*O*-benzoyl-4-*O*-(2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-β-D-glucopyranoside (**28**) and methyl 2,6-di-*O*-benzoyl-4-*O*-(3-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-β-D-glucopyranoside (**29**) (1.5 g, 22%), m.p. 178–181° and 213–216° (from ethanol), $[\alpha]_D^{24}$ 0° (*c* 3.0, chloroform).

Anal. Calc. for $C_{41}H_{40}O_{14}$: C, 65.07; H, 5.33. Found: C, 65.26; H, 5.25.

*Methyl 2,6-di-*O*-benzoyl-4-*O*-(2-*O*-benzoyl-3-*O*-methyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-3-*O*-methyl-β-D-glucopyranoside* (**30**) *and methyl 2,6-di-*O*-benzoyl-4-*O*-(3-*O*-benzoyl-2-*O*-methyl-4,6-*O*-benzylidene-α-D-glucopyranosyl)-3-*O*-methyl-β-D-glucopyranoside* (**31**). — Treatment of a mixture of **28** and **29** (1.4 g) with diazomethane–BF_3 etherate in dichloromethane, as described previously, gave a crystalline solid which was shown by t.l.c. (Solvent *A*) to contain two components having R_F values of 0.66 (**30**) and 0.40 (**31**). The mixture was chromatographed on silica gel (100 g) with Solvent *A*. The first component was crystallized from chloroform–ethanol to give **30** (630 mg, 43%), m.p. 209–210°, $[\alpha]_D^{24}$ +83.6° (*c* 1.1, chloroform); n.m.r. τ 4.48 (s, 1 H, benzylic-H), 6.43, 6.60, and 6.90 (s, 9 H, 3 OMe).

Anal. Calc. for $C_{43}H_{44}O_{14}$: C, 65.81; H, 5.65. Found: C, 65.89; H, 5.72.

O-Debenzoylation of **30** followed by methanolysis, as for **23**, and g.l.c. of the methanolyzate as the per(trimethylsilyl) ethers gave peaks corresponding to methyl 3-*O*-methyl-α,β-D-glucopyranoside (7.5 and 7.9 min).

The next-eluted component was crystallized from ethanol–chloroform to afford **31** (610 mg, 42%), m.p. 189–190°, $[\alpha]_D^{24}$ +61.4° (*c* 1.0, chloroform); n.m.r. τ 4.58 (s, 1 H, benzylic-H), 6.50, 6.53, and 6.57 (s, 9 H, 3 OMe).

Anal. Calc. for $C_{43}H_{44}O_{14}$: C, 65.81; H, 5.65. Found: C, 65.95; H, 5.57.

O-Debenzoylation of **31** followed by methanolysis, as for **23**, and g.l.c. of the methanolyzate as the per(trimethylsilyl) derivatives gave peaks corresponding to

methyl 3-*O*-methyl-α,β-D-glucopyranoside (7.5 and 7.9 min) and methyl 2-*O*-methyl-α,β-D-glucopyranoside (9.4 min).

Benzoylation of the mixture of **28** *and* **29**. — Treatment of the mixture of **28** and **29** (1.1 g) with benzoyl chloride (0.34 ml, 2 mol. equiv.) in pyridine (30 ml) under conditions *B* and isolation in the usual way gave **27** (1.1 g, 88%), m.p. and mixed m.p. 196–197° (ethanol–chloroform), $[\alpha]_D^{24}$ +54.5° (*c* 1.2, chloroform).

*Methyl 2,6-di-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-β-D-glucopyranoside* (**36**). — Sequential treatment of **35** (2 g) with a saturated solution of HBr in acetic acid (15 ml) in a mixture of acetic acid (5 ml) and chloroform (10 ml), and then with methanol (3 ml) in benzene (15 ml) containing $Hg(CN)_2$ (600 mg), as described previously, gave **36** (1.5 g, 82%), m.p. 220–221° (chloroform–ethanol), $[\alpha]_D^{24}$ −19.7° (*c* 1.5, chloroform); n.m.r. τ 6.61 (s, 3 H, OMe).

Anal. Calc. for $C_{55}H_{48}O_{17}$: C, 67.34; H, 4.93. Found: C, 67.52; H, 4.81.

Benzoylation of **33** *with 7.9 mol. equiv. of benzoyl chloride*. — The product obtained by treatment of **33** (2 g) with benzoyl chloride (5.1 ml) under conditions *A* was shown by t.l.c. (Solvent *A*) to be composed of two major components having R_F values of 0.65 (**34**) and 0.46 (**36**), and three minor components having R_F values of 0.29, 0.20, and 0.11, respectively. The mixture was fractionated on a column of silica gel (250 g) with Solvent *A*. The first fraction gave **34** (3.4 g, 56%), m.p. 177–179° (acetone–methanol), $[\alpha]_D^{24}$ −35.3° (*c* 1.5, chloroform).

Anal. Calc. for $C_{62}H_{52}O_{18}$: C, 68.63; H, 4.83. Found: C, 68.88; H, 4.93.

The second fraction afforded **36** (1.5 g, 27%), m.p. and mixed m.p. 220–221° (from chloroform–ethanol), $[\alpha]_D^{24}$ −19.3° (*c* 1.4, chloroform).

The isolation and structural elucidation of the three minor components were not performed.

*Methyl 2,6-di-*O*-benzoyl-3-*O*-methylsulfonyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-β-D-glucopyranoside* (**37**). — Methanesulfonylation of **36** (2 g), as described previously, gave **37** (2 g, 81%), m.p. 205–206° (dec.) (from chloroform–ethanol), $[\alpha]_D^{24}$ −31.4° (*c* 2.5, chloroform); n.m.r. τ 5.96 (s, 3 H, OMs).

Anal. Calc. for $C_{56}H_{50}O_{19}S$: C, 63.51; H, 4.76; S, 3.03. Found: C, 63.77; H, 4.61; S, 2.92.

*Methyl 2,3,6-tri-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl)-β-D-allopyranoside* (**38**). — A solution of **37** (1.9 g) in *N,N,N',N',N'',N''*-hexamethylphosphoric triamide (20 ml) containing sodium benzoate (2 g) was heated for 48 h at 100°. The reaction mixture was processed as described previously and the residue was purified by elution from a column of silica gel with Solvent *A* to give **38** (1.3 g, 68%) as a solid, softening at 105–110°, $[\alpha]_D^{24}$ −17.2° (*c* 1.9, chloroform).

Anal. Calc. for $C_{62}H_{52}O_{18}$: C, 68.63; H, 4.83. Found: C, 68.45; H, 4.90.

*Methyl 4-*O*-β-D-glucopyranosyl-β-D-allopyranoside* (**39**). — *O*-Debenzoylation of **38** (1.1 g), as described previously, afforded **39** (310 mg, 86%), m.p. 208–209° (from ethanol), $[\alpha]_D^{24}$ −17.7° (*c* 1.6, water).

Anal. Calc. for $C_{13}H_{24}O_{11}$: C, 43.82; H, 6.79. Found: C, 43.73; H, 6.92.

G.l.c. examination of the methanolyzate of **39** as the per(trimethylsilyl) ethers, as described previously, showed the presence of methyl α,β-D-glucopyranoside and methyl α,β-D-allopyranoside.

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