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PREPARATION AND CHARACTERIZATION OF 1,2,6,2′,3′,4′,6′-HEPTA-*O*-ACETYL-β-MALTOSE*

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ABSTRACT

Acetylation of a slurry of β-maltose monohydrate in cold toluene with acetylpyridinium chloride gave 1,2,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-maltose (**1**) in 70% yield, with octa-*O*-acetyl-β-maltose as a byproduct. Crystalline 3-*O*-methyl (**2**) and 3-*O*-phenylcarbamoyl (**3**) derivatives of **1** were readily obtained. A deacetylated sample of **2** was shown to yield 3-*O*-methyl-α,β-D-glucose and α,β-D-glucose after aqueous hydrolysis. To discriminate between the O-3 and O-3′ positions, a second portion of deacetylated **2** was reduced with sodium borohydride and the product methanolyzed, to yield 3-*O*-methyl-D-glucitol and methyl α,β-D-glucopyranoside; components of the methanolyzate were identified by g.l.c. Deacetylation and methanolysis of **3** gave methyl 3-*O*-phenylcarbamoyl-α,β-D-glucopyranoside (**5**), from which methyl 2,4,6-tri-*O*-benzoyl-3-*O*-phenylcarbamoyl-β-D-glucopyranoside (**6**) was isolated crystalline; synthesis of **6** from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose proved its structure.

INTRODUCTION

To increase the possibilities for industrial utilization of maltose (4-*O*-α-D-glucopyranosyl-D-glucopyranose), a current program of this laboratory is designed to expand the chemistry of this readily accessible sugar. In one phase of the work, chemical reactivities of the individual hydroxyl groups of maltose are being investigated. A distinctly lower relative reactivity has been found at the 3-hydroxyl group toward acetylation by acetylpyridinium chloride in toluene. A procedure for slow, heterogeneous acetylation was developed expressly to show reactivity differences between hydroxyl groups. Under identical conditions of reaction, both α- and β-D-glucose were fully acetylated in 95% yields.

Synthesis of the title compound (**1**) in 70% yield provides access to 3-*O*-substituted derivatives of maltose. Other heptaacetates of maltose that are known have free hydroxyl groups at C-1, C-6, and C-6′. These have been obtained by hydrolysis of

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acetylmaltosyl halides[1], by the action of piperidine on octa-*O*-acetyl-β-maltose[2], and by detritylation of the acetylated 6-trityl or 6′-trityl ethers of maltose[3,4].

The use of acetyl halides for the preparation of acetylglycosyl halides has been reviewed by Staněk and his colleagues[5]. Sugihara[6] summarized investigations before 1958, which showed high reactivities of the hydroxyl groups at C-6 and C-2 of D-glucose toward acylation. In 1967, Williams and Richardson[7] established a reactivity sequence for the secondary hydroxyl groups in methyl α-D-glucopyranoside, toward benzoyl chloride in pyridine, but the sequence that they found, namely, 2-OH > 3-OH > 4-OH, may not hold for other acylating systems or other hexosides.

Specificities that depend on the class of acylating agent employed were demonstrated by Jeanloz and Jeanloz[8]. They reported that methyl 4,6-*O*-benzylidene-α-D-glucopyranoside is selectively acylated at O-2 by carboxylic acid chlorides, and at O-3 by the corresponding anhydrides. In most cases, yields were modest, with various degrees of reagent discrimination.

Attempts to rationalize selective acylations in the monosaccharide series have involved a number of as yet incompletely evaluated parameters: the mechanism of acylation, the class of acylating reagent, the catalyst[9], the anomeric configuration, the steric environment of the hydroxyl groups, hydrogen bonding, the ring size, and the conformation of the molecule. Similar specificities doubtless apply to maltose and other disaccharides, but with the possible added complication of intramolecular hydrogen bonding between hydroxyl groups of adjoining saccharide molecules. From 3-dimensional X-ray diffraction data, Hybl *et al.*[10] showed hydrogen bonds between O-2 and O-3 of each contiguous pair of D-glucose residues in the cyclohexaamylose–potassium acetate complex, and the results were extrapolated to embrace helical V-amylose. From n.m.r. and i.r. spectral measurements, Casu *et al.*[11] deduced hydrogen-bonding between the 3-OH and 2′-OH groups in maltose, maltocyclodextrins, and amylose; and Chu and Jeffrey[12] found the same bonding in crystalline methyl β-maltoside monohydrate by X-ray diffraction data. Whether this bonding is responsible for the inhibited acetylation at 3-OH in maltose is being investigated by acetylation of other disaccharides alleged to be intramolecularly hydrogen-bonded.

RESULTS AND DISCUSSION

β-Maltose monohydrate was slurried in cold toluene, and acetylated slowly with acetylpyridinium chloride. Reaction variables of temperature, time, and reagent concentration were evaluated by thin-layer chromatographic estimation of compositional changes in the reaction mixtures. A 70% yield of the new heptaacetate (**1**) was obtained with the optimum procedure. The anomeric configuration remained unchanged during the acetylation. Finely divided maltose was required for maximum conversion. Purification of the product mixture required column chromatography on silica gel. The t.l.c. systems of Wolfrom and de Lederkremer[13] gave excellent separation of **1** and the byproduct, octa-*O*-acetyl-β-maltose.

The purified heptaacetate **1** was readily converted into octa-*O*-acetyl-β-maltose in cold pyridine–acetic anhydride. A control reaction on β-maltose monohydrate in

cold pyridine–acetic anhydride gave the same yield of octaacetate as **1**, and neither reaction product showed any α anomer by t.l.c. examination[14].

In chloroform-*d*, the heptaacetate **1** and octa-*O*-acetyl-β-maltose showed nearly identical low-field doublets for the anomeric proton (τ 4.36 and τ 4.25, respectively, with $J_{1,2}$ 8 Hz). Such deshielding of the anomeric proton is characteristic for a 1-acetate, and the location and large coupling constant indicate an axial orientation (β anomer)[15–17]. The integrated spectrum confirmed the presence of seven *C*-methyl (acetyl) groups in **1**, within the region assigned for equatorial *O*-acetyl groups (τ 7.93–8.01). No signals could be detected at the resonance of τ 7.82 reported[16] for axial *O*-acetyl groups, and since no other *C*-methyl resonances were observed, any ortho-ester forms are ruled out.

These findings agree with the β configuration that was also assigned by use of Hudson's rule and by the isolation of octa-*O*-acetyl-β-maltose after peracetylation of **1** in cold pyridine–acetic anhydride. The i.r. spectrum of **1** in a potassium bromide disc showed the expected strong absorption band (type 2b, 890 cm^{-1}). This band, supposedly specific for a β-D configuration in the D-aldopyranose acetate series[18], was accompanied by a weak band (type 2a, 844 cm^{-1}), allegedly indicating the presence of the α-D-(1→4) interglycose linkage.

The resonance of the hydroxyl proton was observed in methyl sulfoxide-d_6. For 2,3,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-maltose, the 1-OH signal appeared far downfield as a doublet (τ 2.42, $J_{1,OH}$ 6 Hz). Our heptaacetate, however, showed a different doublet for the hydroxyl proton (τ 4.30, *J* 7 Hz). Both doublets were eliminated by exchange with deuterium oxide. Although a position for the free hydroxyl group could not be assigned by n.m.r. spectroscopy alone, similar low-field resonances were found by Casu *et al.*[11] for the C-3 and C-2′ hydroxyl protons of β-maltose in methyl sulfoxide solution.

It was assumed that the hydroxyl group was not at C-2 when it was observed that **1** failed to mutarotate in aqueous pyridine or in acetic acid solution. Lemieux and Morgan[16] have shown that an analogous C-2-hydroxylated compound, 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose, readily "mutarotates" in aqueous acetic acid to give the anomers of 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose by acetyl migration.

Although the heptaacetate **1** was not crystallized, crystalline derivatives were obtained in high yield by methylation or by treatment with phenyl isocyanate.

Initial methylations by the procedure of Kuhn *et al.*[19] were complicated by acetyl migration before substitution. Similar problems had been reported by Angyal and Melrose[20]. The 3-methyl ether (**2**) was formed in a modified boron trifluoride–diazomethane[21,22] system. The n.m.r. spectrum of **2** at 100 MHz in chloroform-*d* showed the expected *O*-methyl resonance (τ 6.59), and the anomeric-proton doublet remained unchanged at τ 4.36, $J_{1,2}$ 8 Hz. Examination of the integrated spectrum confirmed the presence of a single *O*-methyl group and of seven *C*-methyl (acetyl) groups (τ 7.93–8.01). A comparison spectrum of the analogous 3-*O*-phenylcarbamoyl derivative (**3**) showed the anomeric proton doublet at τ 4.22 ($J_{1,2}$ 8 Hz), essentially identical with that for octa-*O*-acetyl-β-maltose.

The first step in our proof of structure was identification of the mono-*O*-methyl-D-glucose produced by deacetylation and hydrolysis of **2**. Gas–liquid chromatography (g.l.c.), with a liquid phase of Carbowax* 20M, greatly simplified identification. All samples were converted into their trimethylsilyl ethers[23] before injection. By co-injecting reference compounds with the hydrolyzate, and by referring to relative retention values (see Table I), the presence of 3-*O*-methyl-α,β-D-glucose and of α,β-D-glucose was established. No other products were observed.

TABLE I

RELATIVE RETENTION VALUES OF D-GLUCOSE DERIVATIVES[a]

Sample[b]	*Internal reference standards*[c]		
	α-D-Glucose, 150°	*Methyl β-D-glucoside, 160°*	*D-Glucitol, 160°*
3-*O*-Methyl-D-glucitol	0.85	0.47	0.86 (150°) 0.96 (160°)
D-Glucitol	[d]	0.49	
3-*O*-Methyl-α-D-glucose	0.76	0.44	
4-*O*-Methyl-α-D-glucose	0.90		
2-*O*-Methyl-α-D-glucose	1.08		
3-*O*-Methyl-β-D-glucose	1.25	0.72	
2-*O*-Methyl-β-D-glucose	1.50		
6-*O*-Methyl-α-D-glucose	1.52		
4-*O*-Methyl-β-D-glucose	1.67		
β-D-Glucose	1.82		
6-*O*-Methyl-β-D-glucose	1.85		

[a] t/t_{std} at designated temperature, as pertrimethylsilyl ethers. [b] The order of appearance for the 4-*O*-methyl-D-glucose anomers presumably follows that observed for known anomers available to us. In all, the α-D preceded the β-D. [c] With 19.5% Carbowax 20M on Chromosorb W. [d] Coincides with the standard. Peaks were separable on a column packing of Carbowax 20M on Gas-Chrom Q.

On a larger scale, purification on a Celite column was used to isolate 3-*O*-methyl-α,β-D-glucose in amounts sufficient for conversion into the phenylosazone. A mixed m.p. of the isolated phenylosazone with authentic 3-*O*-methyl-D-*arabino*-hexulose phenylosazone was undepressed.

To distinguish between substitutions at the O-3 and O-3′ positions of maltose, a second sample of the 3-*O*-methylmaltose heptaacetate (**2**) was deacetylated, the product was reduced with aqueous sodium borohydride, and the substituted alditol was refluxed in methanolic hydrogen chloride. After trimethylsilylation of the product, g.l.c. showed a mixture of 3-*O*-methyl-D-glucitol and methyl α,β-D-glucopyranoside, when co-injection of authentic reference compounds was again used.

Additional support for the structure 1,2,6,2′,3′,4′,6′-hepta-*O*-acetyl-β-maltose for **1** was gained by examination of its mono-*O*-phenylcarbamoyl derivative (**3**).

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Although alkaline procedures caused extensive wandering of the phenylcarbamoyl group, deacetylation in 2% methanolic hydrogen chloride[24] produced methyl 3-*O*-phenylcarbamoyl-α,β-D-glucopyranoside (**5**) as the sole monosubstituted product. After column purification, substance **5** could be converted into pure methyl 2,4,6-tri-*O*-benzoyl-3-*O*-phenylcarbamoyl-β-D-glucopyranoside (**6**). The β-D assignment was based on the use of Hudson's rule, and confirmed by n.m.r. (100 MHz in chloroform-*d*). The H-1 doublet (τ 5.29, $J_{1,2}$ 8 Hz) corresponded closely to that observed in a reference spectrum for methyl 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranoside (τ 5.21, $J_{1,2}$ 8 Hz). Assignment of **6** as the 3-*O*-phenylcarbamoyl derivative was confirmed by comparison of the m.p., specific rotation, and n.m.r. spectrum with those of an authentic, crystalline specimen prepared from 1,2:5,6-di-*O*-isopropylidene-3-*O*-phenylcarbamoyl-α-D-glucofuranose (**7**) by methanolysis and benzoylation.

EXPERIMENTAL

Melting points were determined with a Thomas–Hoover melting-point apparatus (Arthur H. Thomas Co., Philadelphia, Pa.) and are corrected. Optical rotations were measured with a Rudolph polarimeter in a 1-dm tube. I.r. spectra were recorded with a Perkin–Elmer Model 621 spectrophotometer, by the potassium bromide disc technique. N.m.r. spectra were measured at 100 MHz with a Varian HA-100 spectrometer. Tetramethylsilane was used as an internal standard in chloroform-*d* or methyl sulfoxide-d_6. Chemical shifts are given on the τ scale. An F & M research chromatograph, Model 810, was employed for g.l.c. The column was a 12-ft length of 1/4-in o.d. copper tubing, packed with 19.5% Carbowax 20M on Chromosorb W* (80–100 mesh). Operation was isothermal at 150°, with helium as the carrier gas, and flame ionization detection.

All samples were dissolved in pyridine and converted into their trimethylsilyl ethers approximately 18 h before injection. T.l.c. on Silica Gel G (E. Merck, Darmstadt, Germany) was performed without heat activation of the plates. Solvent proportions are on the v/v basis. For column chromatography, Baker Analyzed Silica Gel (J. T. Baker Chemical Co., Phillipsburg, N. J.) was used without pretreatment. Solutions were concentrated below 40° under diminished pressure. Pyridine was removed from organic phases by alternately washing with water and 5% aqueous cupric sulfate. Calcium hydride was used whenever rigorous drying of organic liquids was needed, and anhydrous sodium sulfate was used for drying solutions.

Acetylation of β-maltose monohydrate. — All solvents were anhydrous. The reaction temperature was kept below 5° at all times. β-Maltose monohydrate[25] (10 g, free from D-glucose and oligosaccharides) was finely powdered in a mortar and then transferred to the reaction vessel with 200 ml of toluene and 30 ml of pyridine. The stirred slurry was treated dropwise with 17.5 ml of acetyl chloride (98%) in 50 ml of toluene during 0.5 h. Maximum reaction required 60 h, at which time the pink slurry

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was filtered. The solids were rinsed twice with fresh toluene, and the combined filtrates were washed, dried, and evaporated to a syrup (17 g). T.l.c. examination with 1:1 ethyl acetate–benzene (A) or 200:7 benzene–methanol (B) disclosed only two components, octa-*O*-acetyl-*β*-maltose and **1**. For solvent A, the R_F values were 0.61 and 0.40, respectively. Unreacted maltose (0.5 g) was recovered from the filtered solids after several washes on the funnel with chloroform.

Any increases in temperature, time, or concentration of acetyl chloride caused a corresponding increase in the amount of octa-*O*-acetyl-*β*-maltose produced. Decrease in the reaction time or in the acetyl chloride or pyridine concentration lowered the conversion into acetylated products, with no increase in the ratio of **1** to octaacetate. Substitution of benzene for toluene gave the same results.

*1,2,6,2′,3′,4′,6′-Hepta-*O*-acetyl-β-maltose* (**1**). — A sample (6.1 g) of the syrup obtained above was purified on a column of silica gel packed, and irrigated, with solvent A. Of 6.0 g of product that was recovered, the octa-*O*-acetyl-*β*-maltose weighed 1.7 g (28%) and **1** weighed 4.3 g (71%). All attempts to crystallize **1** failed. Use of multiple-ascent t.l.c. with solvent B showed **1** to be a single anomer. The only exception noted was for acetylation of a slurry of anomerized maltose, which gave **1** in both anomeric forms. Distillation of **1** under diminished pressure was accompanied by decomposition. Purified **1** had $[\alpha]_D^{20}$ +87.5° (*c* 0.4, chloroform); n.m.r. data (chloroform-*d*): τ 4.36 (doublet, $J_{1,2}$ 8 Hz, H-1), τ 7.93–8.01 (seven acetyl groups); in methyl sulfoxide-d_6: τ 3.98 (doublet, $J_{1,2}$ 8 Hz, H-1), τ 4.30 (doublet, *J* 7 Hz, hydroxyl proton), τ 7.63–7.69 (seven acetyl groups).

Anal. Calc. for $C_{26}H_{36}O_{18}$: C, 49.06; H, 5.70; acetyl, 47.3. Found: C, 48.96; H, 5.95; acetyl[26], 46.6.

Peracetylation of **1**. — A 100-mg portion of **1** was dissolved in a cold solution of 1 ml of acetic anhydride in 3 ml of pyridine. The temperature was kept for 24 h below 5°, and was then allowed to rise to 25°. After a total of 72 h, 5 ml of methanol was added, and the solution was concentrated to a thin syrup. The syrup was dissolved in ethyl acetate, and the solution was freed of pyridine and acetic acid, dried, and reconcentrated. Multiple-ascent t.l.c. with solvent B showed no traces of *α*-maltose octaacetate or of **1**. Comparison with a standard showed **1** to have been completely converted into octa-*O*-acetyl-*β*-maltose.

Essentially the same results were obtained by acetylating *β*-maltose monohydrate in pyridine–acetic anhydride under the same conditions.

*1,2,6,2′,3′,4′,6′-Hepta-*O*-acetyl-3-*O*-methyl-β-maltose* (**2**). — A solution of 2.5 g of purified **1** in 25 ml of dichloromethane was chilled in an acetone–solid CO_2 bath. Prepared solutions of boron trifluoride (1.7 ml of BF_3 etherate diluted to 50 ml with dichloromethane) and diazomethane (0.42M, in dichloromethane) were chilled in a separate bath. Both solutions were kept at the bath temperature at all times. The reaction was initiated by adding 1 ml of the stock solution of BF_3 and 10 ml of the diazomethane solution to the solution of **1**. At 12-min intervals during 2 h, 1-ml portions of BF_3 solution and 20 ml of CH_2N_2 solution were alternately added until a total of 6 ml of BF_3 solution and 110 ml of CH_2N_2 solution had been added; the

mixture was then kept for 30 min, which was usually sufficient for discharge of all residual color. T.l.c. with solvent A showed an approximately 90% conversion into **2**. At this point, 5 ml of pyridine was added, and the solution was rapidly warmed to 25°. Polymethylene was removed by filtration, and the filtrate, washed to remove pyridine and other water-soluble substances, was added to a column of silica gel; elution with solvent A gave 2 g of product, readily crystallized from aqueous methanol. After being dried under vacuum, this hygroscopic compound had m.p. 115–116°, $[\alpha]_D^{20}$ +77.2° (*c* 1.1, chloroform); n.m.r. data (chloroform-*d*): τ 4.36 (doublet, $J_{1,2}$ 8 Hz, H-1), τ 6.59 (one OMe group), τ 7.93–8.01 (seven acetyl groups).

Anal. Calc. for $C_{27}H_{38}O_{18}$: C, 49.85; H, 5.89; OMe, 4.77. Found: C, 49.96; H, 5.85; OMe, 5.05.

Parallel attempts at methylation, essentially by the techniques of Kuhn and co-workers[19], were unsuccessful. Deacetylation and hydrolysis of the methylated products gave (as shown by t.l.c.) several mono-*O*-methyl-D-glucoses.

Gas–liquid chromatography. — Experimentation with standard mono-*O*-methyl-D-glucoses (2-*O*-, 3-*O*-, 4-*O*-, and 6-*O*-methyl isomers) showed that g.l.c. would afford ready identification of the mono-*O*-methyl-D-glucose(s) obtained by deacetylation and hydrolysis of **2**, either as the glycoside or as the reducing sugar. For each sample, a solution of 10–20 mg in 0.5 ml of pyridine was treated with 0.2 ml of hexamethyldisilazane and chlorotrimethylsilane. A reaction period of 18 h was used, to ensure complete trimethylsilylation. The relative retention times are listed in Tables I and II.

TABLE II

RELATIVE RETENTION VALUES OF METHYL D-GLUCOPYRANOSIDES AND DERIVATIVES[a]

Methyl D-*Glucopyranoside*[b]	*Internal reference standards*[c]		
	α-D-*Glucose*, *150°*	*Methyl* β-D-*glucoside*, *160°*	D-*Glucitol*, *160°*
3-*O*-methyl-α-	1.11	0.69	
3-*O*-methyl-β-	1.27		
4-*O*-methyl-α-	1.41		
2-*O*-methyl-α-	1.50		
4-*O*-methyl-β-	1.57		
α-	1.63	0.93	1.90
β-	1.76		2.05
2-*O*-methyl-β-	1.79		
6-*O*-methyl-α-	2.33	1.38 (150°)	
6-*O*-methyl-β-	2.54	1.50 (150°)	

[a] t/t_{std} at designated temperature, as pertrimethylsilyl ethers. [b] The order of anomer appearance for the 2-, 3-, and 6-*O*-methyl-D-glucosides presumably follows that observed for the known anomers available to us. In all, the α-D preceded the β-D. [c] With 19.5% Carbowax 20M on Chromosorb W.

Hydrolysis of **2**. — A 1.0-g portion of **2** in 15 ml of 0.05M barium methoxide was kept for 18 h at 0°. The syrup obtained after neutralization with Amberlite IR-50 resin and evaporation was dissolved in 20 ml of 0.25M hydrochloric acid, and the solution

was kept for 18 h at 100°. T.l.c. with 3:1 ethyl acetate–methanol (C) then showed only one mono-*O*-methyl-D-glucose.

A sample of the hydrolyzate was trimethylsilylated, and co-injected with a reference sample of pertrimethylsilylated *α*-D-glucose. Three product components were observed, having retention values equal to those for 3-*O*-methyl-*α*- and -*β*-D-glucose (0.76 and 1.25) and for *β*-D-glucose (1.82). When pertrimethylsilylated methyl *β*-D-glucopyranoside was used as the internal standard, a fourth component was observed; it was identified as *α*-D-glucose.

By contrast, examination of the hydrolyzate from the product from the silver oxide–*N*,*N*-dimethylformamide–methyl iodide system[19] showed a complex mixture of mono-*O*-methyl D-glucoses, and confirmed the earlier observations made by t.l.c.

Detection of 3-O-methyl-D-glucitol. — A solution of a 50-mg portion of deacetylated **2** in 5 ml of deionized water was chilled to 5°, and treated with 100 mg of sodium borohydride. After 24 h at room temperature, the solution was evaporated to a thick syrup which was mixed with 10 ml of methanol. After 1 h, 1 ml of concentrated hydrochloric acid was added, and the slurry was evaporated to dryness, with four re-treatments with methanol. The residue was mixed with 10 ml of fresh methanol and 0.3 ml of acetyl chloride, and the mixture was refluxed for 1 h, and kept for 24 h at room temperature. After evaporation and four additional retreatments with methanol, the solution was rendered neutral with ammonium hydroxide and evaporated twice more. The final residue was extracted with 2 ml of pyridine, and a 0.5-ml aliquot of the extract was converted into the trimethylsilyl ether as before. G.l.c. at 160° revealed that the hydrolyzate contained only 3-*O*-methyl-D-glucitol and methyl *α*,*β*-D-glucopyranoside. Authentic samples of methyl *β*-D-glucopyranoside, D-glucitol, and 3-*O*-methyl-D-glucitol[27] were prepared for comparison.

3-O-Methyl-D-arabino-hexulose phenylosazone. — The 3-*O*-methyl-*α*,*β*-D-glucose in the deacetylated hydrolyzate from **2** was freed of contaminants on a Celite column[28] irrigated with 2:5:5 (v/v) pyridine–ethyl acetate–water[29]. This column afforded 155 mg of chromatographically pure material, which was converted into the corresponding phenylosazone[30]. A mixed m.p. with authentic material was undepressed (at 172–175°).

1,2,6,2',3',4',6'-Hepta-O-acetyl-3-O-phenylcarbamoyl-β-maltose (**3**). — A crude product (11 g) from the slurry acetylation, containing approximately 70% of **1**, was dissolved in toluene (250 ml) and pyridine (10 ml). Phenyl isocyanate (10 ml) was added, and the solution was kept for 24 h at room temperature. The reaction was completed by heating for 15 min on a steam bath. Excess phenyl isocyanate was decomposed by addition of water, and the mixture was evaporated to dryness. The residue was extracted with 400 ml of chloroform, and the extract was filtered, and washed to remove pyridine. After the solution had been dried, it was again filtered (to remove the last traces of carbanilide). Chloroform was removed completely, and the product was dissolved in the minimal volume of ethyl ether. Crystallization was spontaneous, and **3** readily separated at room temperature; wt., 8.5 g. Recrystallization from abs. ethanol gave pure **3**, m.p. 174.5–175.5, $[\alpha]_D^{20}$ +58.7° (*c* 0.9, chloro-

form); n.m.r. data (chloroform-*d*): τ 4.22 (doublet, $J_{1,2}$ 8 Hz, H-1), τ 7.89–8.11 (seven acetyl groups).

Anal. Calc. for $C_{33}H_{41}NO_{19}$: C, 52.45; H, 5.47; N, 1.85. Found: C, 52.68; H, 5.81; N, 1.88.

2,3,6,2',3',4',6'-Hepta-O-acetyl-1-O-phenylcarbamoyl-β-maltose (**4**). — This compound was prepared for comparison with **3**. A 2.0-g sample of 2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-maltose was dissolved in 10 ml of pyridine, and 1 ml of phenyl isocyanate was added. After 1 h at 100°, the solution was processed as for **3**. After two recrystallizations from ethanol, the compound had m.p. 146–148°, $[\alpha]_D^{20}$ +60.1° (*c* 0.98, chloroform); n.m.r. data (chloroform-*d*): τ 4.21 (doublet, $J_{1,2}$ 8 Hz, H-1), τ 7.93–8.01 (seven acetyl groups).

Anal. Calc. for $C_{33}H_{41}NO_{19}$: C, 52.45; H, 5.47; N, 1.85. Found: C, 52.04; H, 5.55; N, 1.82.

Isolation of methyl 2,4,6-tri-O-benzoyl-3-O-phenylcarbamoyl-β-D-glucopyranoside (**6**). — A 4.0-g sample of **3** was deacetylated in 80 ml of anhydrous methanol mixed with 2.3 ml of 98% acetyl chloride. After 48 h at room temperature, the acid was neutralized with Amberlite IR-45 (OH^-) ion-exchange resin, the suspension was filtered, and the filtrate was evaporated to a syrup (2.3 g). T.l.c. with 9:1 ethyl acetate–ethanol (D) showed the presence of only one methyl glucoside monocarbanilate. Purification was accomplished on a column of silica gel, packed with ethyl acetate and irrigated with solvent D. The syrupy methyl 3-*O*-phenylcarbamoyl-α,β-D-glucopyranoside (**5**), weighing 1.1 g, was not examined further, but was converted directly into the tribenzoate, essentially as described in the next section. After isolation, the β-D anomer (**6**) crystallized readily from ethanol. After two recrystallizations, **6** had m.p. 160–161°, $[\alpha]_D^{20}$ +43.0° (*c* 1.0, in chloroform); n.m.r. data (chloroform-*d*): τ 5.29 (doublet $J_{1,2}$ 8 Hz, H-1), τ 6.51 (OMe).

Anal. Calc. for $C_{35}H_{31}NO_{10}$: C, 67.19; H, 4.99; N, 2.24. Found: C, 67.41; H, 5.22; N, 2.16.

Direct synthesis of methyl 2,4,6-tri-O-benzoyl-3-O-phenylcarbamoyl-β-D-glucopyranoside (**6**). — A solution of 3.5 g of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose and 2 ml of phenyl isocyanate in 25 ml of pyridine was heated for 45 min at 100°. Excess of isocyanate was decomposed with water, and the solution was evaporated to dryness. The residue was extracted with 250 ml of hot chloroform, and the extract was filtered, washed to remove pyridine, dried, and refiltered. Evaporation gave a syrup that was used without further examination.

The crude 1,2:5,6-di-*O*-isopropylidene-3-*O*-phenylcarbamoyl-α-D-glucofuranose (**7**) was dissolved in 80 ml of warm, 1:1 water–methanol, and the solution was treated with 1 ml of concentrated sulfuric acid. A 90-min period at reflux completed the hydrolysis; t.l.c. with 4:1 ethyl acetate–ethanol (E) was used to determine the progress of the reaction. After being processed, the sample was purified on a Celite column in the way described for 3-*O*-methyl-α,β-D-glucose. Efforts to crystallize 3-*O*-phenylcarbamoyl-α,β-D-glucose (**8**) have not yet been successful. Acetylation in cold pyridine–acetic anhydride gave crystalline 1,2,4,6-tetra-*O*-acetyl-3-*O*-phenylcarbamoyl-α-D-

glucopyranose (**9**); m.p. 199.5–200.5°, $[\alpha]_D^{20}$ + 61.1° (*c* 0.51, chloroform); n.m.r. data (chloroform-*d*): τ 3.65 (doublet, $J_{1,2}$ 4 Hz, H-1 of α-D anomer), τ 7.82 (one axial acetate group), τ 7.94–8.02 (three equatorial acetate groups).

Anal. Calc. for $C_{21}H_{25}NO_{11}$: C, 53.96; H, 5.39; N, 3.00. Found: C, 54.16; H, 5.53; N, 3.02.

A 2.0-g sample of **8** was dissolved in 100 ml of methanol, 1.5 ml of 98% acetyl chloride was added, and the mixture was refluxed for 3 h. T.l.c. with solvent D showed conversion into the methyl 3-*O*-phenylcarbamoyl-α,β-D-glucopyranosides (**5**). After isolation, purification on silica gel with solvent D removed all traces of byproducts.

A solution of pure **5** in 5 ml of pyridine and 30 ml of dichloromethane was cooled to below 5° in an ice bath, and 2.6 ml of benzoyl chloride in 15 ml of dichloromethane was added dropwise during 30 min. Stirring was continued for 18 h below 5° and for 4 h at 25°. Excess reagent was decomposed with water, and the solution was evaporated at 25° to a thin syrup which was dissolved in ethyl acetate; the solution was washed to remove pyridine and benzoic acid, and dried. As before, it crystallized readily from ethanol, to give **6** having m.p. 160–161°. A mixed m.p. with **6** isolated above was undepressed.

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