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Note

A reinvestigation of the reaction of β-maltose octaacetate with phosphorus pentachloride

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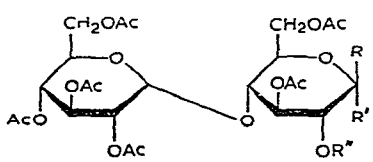
The reaction of β-maltose octaacetate (**1**) with phosphorus pentachloride was first reported by Brigl and Mistele[1] to give a crystalline tetrachloro derivative which was assumed to be 2′,3,3′,4′,6,6′-hexa-*O*-acetyl-2-*O*-trichloroacetylmaltosyl chloride, but the structure including the configuration at C-1 was not well ascertained Koeppen[2] extended this reaction to the preparation of 1,2′,3,3′,4′,6,6′-hepta-*O*-acetyl-β-maltose (**6**), however, the isolation of any intermediary compounds involved in this series of reactions was not described In our previous study[3], the reaction of β-maltotriose hendecaacetate with phosphorus pentachloride gave the expected 2′,2″, 3,3′,3″,4″,6,6′,6″-nona-*O*-acetyl-2-*O*-trichloroacetyl-β-maltotriosyl chloride in 42% yield, which was then successfully converted into 1,2′,2″,3,3′,3″,4″,6,6′,6″-deca-*O*-acetyl-β-maltotriose, and methyl α-and β-maltotriosides, in these preparations, all the intermediates were isolated in crystalline form and fully characterized These results prompted a reinvestigation of the reaction of **1** with phosphorus pentachloride



1 R = OAc, R′ = H R″ = Ac
2 R = Cl, R′ = H R″ = $COCCl_3$
3 R = H, R = Cl, R″ = $COCCl_3$
4 R = Cl, R = R″ = H
5 R = R″ = H R = Cl
6 R = OAc, R′ = R″ = H
7 R = R″ = H, R′ = OMe
8 R = OMe, R = R″ = H
9 R = OMe, R = H, R″ = Ac
10 R = OMe R′ = H R″ = Ms

Treatment of **1** with 5 molar equivalents of phosphorus pentachloride, in the presence of carbon tetrachloride, under reflux for 3 h gave a mixture that was fractionated by column chromatography on silica gel to afford, in 58% yield, the crystalline 2-trichloroacetyl, β-chloride derivative **2** having physical constants in good

agreement with those reported by Brigl and Mistele[1] The n m r spectrum of **2** in benzene-d_6 showed a doublet at τ 4 31 for the anomeric proton with $J_{1,2}$ 9.0 Hz, consistent with a β-D-anomeric configuration. The structure of **2** was corroborated by anomerization and conversion into the known β-heptaacetate[2] **6** Compound **2** could not be anomerized with titanium tetrachloride[4] in chloroform, but inversion at C-1 was achieved with tetramethylammonium chloride[5] in acetonitrile to give the corresponding α-chloride **3** in crystalline form Selective removal of the trichloroacetyl group of **2** afforded the crystalline β-chloride **4** having a free hydroxyl group at C-2 which was smoothly anomerized with titanium tetrachloride to yield the crystalline α-anomer **5** This compound was also obtained by the ammonolysis of **3** Subsequent treatment of **5** with mercuric acetate in acetic acid gave crystalline **6** in overall yields (based on **1**) of 37% and 39% *via* **3** and **4**, respectively, the physical properties of **6** agree with those given by Koeppen[2] These results not only prove the identity of the tetrachloro derivatives of maltose isolated in the work of Brigl and Mistele[1] and in the present study, but also confirm the structure **2** of this compound.

Previous work[3] suggested that methyl 2',3,3',4',6,6'-hexa-*O*-acetyl-α- and β-maltosides (**7** and **8**) might be obtained by methanolysis of the β- and α-chlorides **4** and **5**, respectively Treatment of **4** with methanol in the presence of pyridine and silver nitrate[6] gave, in 83% yield, a crystalline product that was homogeneous on t l c in various solvent systems However, the n m r spectrum of the product in benzene-d_6 indicated that it was a mixture of **7** and **8** in the ratio 6 1, as deduced from the ratio of the intensity of the methoxyl proton signals at τ 6 73 (β) and τ 6 96 (α) Repeated recrystallization of the mixture did not change the ratio of the α- and β-anomers Furthermore, an attempt to separate **7** from **8**, either by column chromatography or by t l c, failed This is in contrast with the result obtained with methyl 2',2",3,3',3",4",6,6',6"-nona-*O*-acetyl-α-maltotrioside[3] which is readily isolated in pure crystalline form from the reaction product with methanol by fractional crystallization Treatment of **5** with methanol under the same conditions furnished, in 81% yield, pure, crystalline **8** which on acetylation gave the known methyl β-maltoside heptaacetate[7] (**9**) Methanesulfonylation of **8** gave methyl 2',3,3',4',6,6'-hexa-*O*-acetyl-2-*O*-methylsulfonyl-β-maltoside (**10**) in crystalline form

EXPERIMENTAL

General experimental specifications were the same as those described previously[3].

3,6-Di-O-*acetyl-4*-O-(*2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-*2*-O-*trichloroacetyl*-β-D-*glucopyranosyl chloride* (**2**) — The β-octaacetate **1** (15 g) was thoroughly mixed with phosphorus pentachloride (23 g, 0 11 mol), and dry carbon tetrachloride (8 ml) was added The mixture was heated under reflux for 3 h with exclusion of moisture T l c (2·1, v/v, benzene–ethyl acetate) showed the presence of one major and several slower-moving, minor products. No starting material was detected The volatile by-products were evaporated under reduced pressure until the bath temper-

ature had risen to about 60°. The residue was extracted with ether (2 × 250 ml), and the extracts were successively washed with cold water, aqueous sodium hydrogen carbonate and water, and dried ($MgSO_4$) The solution was evaporated to a syrup which was fractionated on a column of silica gel (300 g) with 2 1 (v/v) benzene–ethyl acetate. The first fractions crystallized from ether to give **2** (9.7 g, 58%), m p 133–134°, $[\alpha]_D^{25}$ +57 3° (*c* 2 2, benzene), lit [1] m p. 132–133°, $[\alpha]_D^{15}$ +58 7° (benzene), n m r data (benzene-d_6). τ 4 31 (d, 1 H, $J_{1,2}$ 9 0 Hz, H-1)

Anal Calc for $C_{26}H_{32}Cl_4O_{17}$ C, 41.18, H, 4 25, Cl, 18 70 Found· C, 41 10; H, 4 33, Cl, 18 88

3,6-Di-O-*acetyl-4*-O-(*2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-*2*-O-*trichloroacetyl*-α-D-*glucopyranosyl chloride* (**3**) — A solution of **2** (3 4 g) in acetonitrile (80 ml) was stirred with tetramethylammonium chloride (480 mg) overnight at 80°. The mixture was concentrated to a syrup which was extracted with chloroform The solution was washed with water, dried (Na_2SO_4), and evaporated to a syrup which crystallized from ether to afford **3** (3 g, 88%), m p 124–125°, $[\alpha]_D^{25}$ +142 1° (*c* 1 5, chloroform), n m r. data (chloroform-*d*) τ 3 68 (d, 1 H, $J_{1,2}$ 3 5 Hz, H-1)

Anal Calc for $C_{26}H_{32}Cl_4O_{17}$ C, 41 18, H, 4 25, Cl, 18 70. Found. C, 41 05; H, 4 38; Cl. 18 77

3,6-Di-O-*acetyl-4*-O-(*2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranosyl chloride* (**4**) — Compound **2** (4 g) was finely powdered and rapidly dissolved at 0° in ether (100 ml) that had been saturated with ammonia The mixture was vigorously stirred for 20 min, and the crystals formed were collected and recrystallized from ether–ethyl acetate to yield **4** (2 9 g, 90%), m p 143–144°, $[\alpha]_D^{25}$ +80 5° (*c* 1 1, benzene); n m r data (benzene-d_6)· τ 4 29 (d, $J_{1,2}$ 9 0 Hz, H-1)

Anal Calc for $C_{24}H_{33}ClO_{16}$. C, 47 03, H, 5 43, Cl, 5 78 Found C, 46 90, H, 5 56, Cl, 5 67.

3,6-Di-O-*acetyl-4*-O-(*2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-α-D-*glucopyranosyl chloride* (**5**) — (*a*) Compound **3** (1.1 g) was treated at 0°, as described for **2**, in ether (25 ml) saturated with ammonia to give **5** (950 mg, 86%), m.p 72–73° (from ether–ethyl acetate), $[\alpha]_D^{26}$ +162 2° (*c* 1 2, chloroform), n m r data (chloroform-*d*) τ 3 88 (d, 1 H, $J_{1,2}$ 3 8 Hz, H-1)

Anal Calc for $C_{24}H_{33}ClO_{16}$ C, 47 03, H, 5 43; Cl, 5 78 Found C, 47 11, H, 5 36; Cl, 5 89

(*b*) Compound **4** (2 g) was treated with titanium tetrachloride (12 ml) in chloroform (80 ml), according to the procedure of Wolfrom *et al* [4], to afford **5** (1 78 g, 89%), m p and mixed m p 72–73 5° (from ether–ethyl acetate), $[\alpha]_D^{20}$ +161 8° (*c* 1 0, chloroform), the n m r spectrum was identical with that of the compound prepared following procedure (*a*)

1,3,6-Tri-O-*acetyl-4*-O-(*2,3,4,6-tetra*-O-*acetyl*-α-D-*glucopyranosyl*)-β-D-*glucopyranose* (**6**) — Compound **5** (1 g) was treated with a solution of mercuric acetate (1 g) in acetic acid (10 ml) for 5 h at room temperature The solution was diluted with chloroform, washed with water, dried (Na_2SO_4), and evaporated to a crystalline mass which was recrystallized from ethanol to give **6** (1 04 g, 85%), m p. 168–169°, $[\alpha]_D^{22}$

+85 9° (*c* 1 5, chloroform), lit [2] m p 166 5–168 5°, $[\alpha]_D^{25}$ +86 7° (*c* 2 6, chloroform), n m r data (dimethyl sulfoxide-d_6) τ 4 38 (d, 1 H, $J_{2\ 2-OH}$ 5 0 Hz, exchangeable with D_2O, OH-2) and 4 44 (d, 1 H, $J_{1,2}$ 8 0 Hz, H-1)

Treatment of **4** *with methanol* — A solution of **4** (2 5 g) in anhydrous methanol (60 ml) containing pyridine (0 73 ml) and silver nitrate (762 mg) was boiled for 2 h under reflux The mixture was filtered and the filtrate was concentrated to dryness The residue was dissolved in chloroform and the solution was washed with water, dried (Na_2SO_4), and evaporated to a syrup which crystallized from ether to give a crystalline mixture of methyl 3,6-di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-α- and β-D-glucopyranoside (**7** and **8**) (2 06 g, 83%), m p 81–82°, $[\alpha]_D^{28}$ +141 1° (*c* 1 5, chloroform), t l c R_F 0 51 (ethyl acetate–benzene 2 1, v/v), the n m r data (benzene-d_6) τ 6 73 (s, OMe of **8**) and 6 96 (s, OMe of **7**) (ratio of peaks at τ 6 73 and τ 6 96, 1 6) Six recrystallizations of the mixture from ether did not change the melting point and the ratio of **7** to **8**

Anal Calc for $C_{25}H_{36}O_{17}$ C, 49 34, H, 5 96 Found C, 49 25, H, 6 03

*Methyl 3,6-di-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside* (**8**). — A solution of **5** (2 g) in dry methanol (50 ml) containing pyridine (0 3 ml) and silver nitrate (610 mg) was boiled for 2 h under reflux Isolation, as just described, and crystallization of the resulting product from ethanol gave **8** (1 61 g, 81%), m p 157–158°, $[\alpha]_D^{23}$ +85 3° (*c* 1 5, chloroform), n m r data (benzene-d_6) τ 6 73 (s, 3 H, OMe)

Anal Calc for $C_{25}H_{36}O_{17}$ C 49 34, H 5 96 Found C 49 39, H, 5 90

Conventional acetylation of **8** (650 mg) with acetic anhydride (7 ml) and pyridine (8 ml) at room temperature afforded methyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**9**) (612 mg, 88%), m p 131–132° (from ethanol), $[\alpha]_D^{25}$ +53 6° (*c* 2 8, chloroform), lit [7] m p 123–124°, $[\alpha]_D^{20}$ +53 5° (*c* 3 1, chloroform)

Conventional methanesulfonylation of **8** (400 mg) with methanesulfonyl chloride (0 3 ml) and pyridine (3 ml) at 0° gave methyl 3,6-di-*O*-acetyl-2-*O*-methylsulfonyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**10**) (388 mg, 86%), m p 132–133° (from ethanol), $[\alpha]_D^{26}$ +61 0° (*c* 1 3, chloroform), n m r data (chloroform-*d*) τ 6 45 (s, 3 H OMe) and 6 96 (s 3 H, $MeSO_2$)

Anal Calc for $C_{26}H_{38}O_{19}S$ C, 45 48, H, 5 58, S, 4 67 Found C, 45 55, H, 5 49, S, 4 58

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