Carbohydrate Research, 65 (1978) 109–113

Note

Synthesis and reactions of 4,6-acetals of sucrose*

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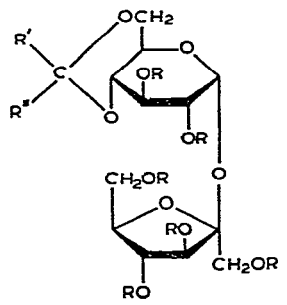
(Received August 24th, 1977; accepted for publication, October 3rd, 1977)

A significant development in the field of cyclic acetal derivatives of sucrose resulted from an investigation of the reaction of sucrose with 2,2-dimethoxypropane in *N*,*N*-dimethylformamide containing toluene-*p*-sulphonic acid[2,3] (reagent *A*).

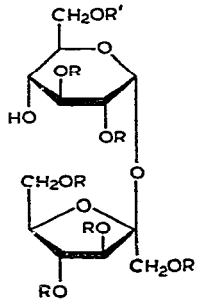
When the reaction was performed at room temperature, followed by acetylation and chromatographic fractionation, it gave, in addition to 1′,2:4,6-di-*O*-isopropylidenesucrose tetra-acetate[3] (15%), 4,6-*O*-isopropylidenesucrose hexa-acetate (**1**, 55%). The ^{1}H-n.m.r. spectrum of **1** showed two peaks at τ 8.55 and 8.63 due to the isopropylidene group. The H-4 signal appeared at τ 6.31 (*cf.* τ 4.7–5.6 for acetylated derivatives of sucrose), indicating that C-4 was involved in the cyclic acetal linkage. The structure of **1** was proved by converting it into the 4,6-diol **2** by treatment with aqueous acetic acid at 100° for 10 min, and thence into the known[4] 2,3,1′,3′,4′,6′-hexa-*O*-acetyl-6-*O*-tritylsucrose (**3**). In the ^{1}H-n.m.r. spectrum of **2**, the absence of resonances due to H-4 in the region τ 4.7–5.6 indicated the presence of a hydroxyl group at C-4. Addition of trichloroacetyl isocyanate to the solution of **2** in deuteriochloroform resulted in the appearance in the spectrum of two singlets at τ 0.5 and 1.12 due to imino protons, thereby indicating the presence of two hydroxyl groups in **2**. The resonance due to H-4 was shifted to τ 5.51, thereby confirming the presence of one of the hydroxyl groups at C-4. The location of the second hydroxyl group at C-6 was ascertained when treatment with trityl chloride and pyridine at 60° for 48 h gave **3**.

Treatment of sucrose with reagent *A* followed by conventional benzoylation gave crystalline 4,6-*O*-isopropylidenesucrose hexabenzoate (**4**, 30%), the structure of which was supported by its ^{1}H-n.m.r. spectrum. Zemplén deacetylation of **1** followed by benzoylation also gave **4**. Treatment of **4** with boiling, aqueous acetic acid in acetone gave the crystalline hexabenzoate **5** (90%), the ^{1}H-n.m.r. spectrum of which contained resonances due to H-1,2,3,3′,4′, as expected, in the region τ 4.0–4.73. Since there were no signals for H-4 in the region τ 4.5–5.0, HO-4 was unsubstituted. On addition of trichloroacetyl isocyanate to a solution of **5** in deuteriochloroform, two

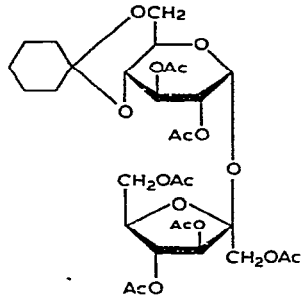
*Sucrochemistry: Part XXV. For Part XXIV, see Ref. 1.



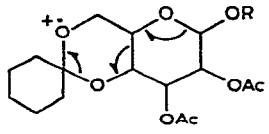
1 R = Ac, R′ = R″ = Me
4 R = Bz, R′ = R″ = Me
9 R = Ac, R′ = H, R″ = Ph



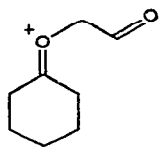
2 R = Ac, R′ = H
3 R = Ac, R′ = Tr
5 R = Bz, R′ = H



6



7 *m/e* 674
R = 1,3,4,6-tetra-*O*-acetyl-β-D-fructofuranosyl



8 *m/e* 141

singlets appeared at τ 0.6 and 1.65, thus confirming the presence of two hydroxyl groups.

The reaction of methyl α-D-glucopyranoside with cyclohexanone dimethyl acetal (reagent *B*) gives methyl 2,3:4,6-di-*O*-cyclohexylidene-α-D-glucopyranoside, methyl 4,6-*O*-cyclohexylidene-α-D-glucopyranoside, and the starting material, in yields of 2, 78, and 17%, respectively. Treatment of sucrose with reagent *B*, followed by acetylation and chromatography on silica gel, gave 4,6-*O*-cyclohexylidenesucrose hexa-acetate (**6**, 34%), together with sucrose octa-acetate. In the ^{1}H-n.m.r. spectrum of **6**, the resonance due to H-4 appeared at a relatively high-field position (τ ~5.8) which indicated that C-4 was involved in the acetal linkage. Resonances due to ten cyclohexylidene-ring protons appeared in the region of τ 8.4–8.8. The mass spectrum of **6** contained a peak for the molecular ion **7** at *m/e* 674 (10% of base peak at *m/e* 43), which indicated that, in addition to the usual localised ionisation of the glycosidic oxygen, ionisation also occurred at one of the acetal oxygen atoms. Therefore, it should be possible for *h*-fracture to occur, and this view was supported by the intense peak at *m/e* 141 attributed to the oxycarbonium ion **8** at *m/e* 141. A similar fragmentation pattern for cyclic acetals of alditols has been described[6]. De-acetalation of **6** with boiling, aqueous acetic acid gave the expected 4,6-diol **2**.

The reaction of sucrose with α,α-dibromotoluene in pyridine[4] (reagent *C*) gives 4,6-*O*-benzylidenesucrose hexa-acetate (**9**, 35%). In order to develop a cheaper route

to **9**, the reaction of sucrose with reagent *C* was investigated. After 2 h at room temperature, followed by conventional acetylation and chromatography, **9** was isolated in 35% yield. The mass spectrum of **9** showed a molecular ion peak at *m/e* 682, and an intense peak at *m/e* 149 which was probably due to the *h*-fracture fragmentation pattern.

EXPERIMENTAL

For details of the general procedures, see Part XXIV[1].

4,6-O-Isopropylidenesucrose hexa-acetate (**1**). — A solution of sucrose (5 g) in *N,N*-dimethylformamide (200 ml) was stirred with 2,2-dimethoxypropane (20 ml) and toluene-*p*-sulphonic acid (150 mg) at room temperature for 1.25 h, and then neutralised by stirring for 15 min with Amberlite IR-45 (HO^-) resin, filtered, and concentrated under reduced pressure at 60–70°. The resulting syrup was treated with acetic anhydride (20 ml) and pyridine (150 ml) at room temperature for 16 h. The mixture was then concentrated by codistillation with toluene, and the residue was eluted from a column of silica gel (150 g) with ether–light petroleum (2:1) to give **1** (5.9 g, 55%), as a syrup, $[\alpha]_D$ +46° (*c* 0.2, chloroform). N.m.r. data ($CDCl_3$): τ 4.36 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.18 (q, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.64 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-3), 4.55–4.8 (2 H, H-3′,4′), 7.68–7.98 (m, 18 H, 6 Ac), and 8.46–8.86 (6 H, 2 Me). Mass-spectral data [(a) indicates hexopyranosyl and (b) ketofuranosyl cations]: *m/e* 619 (M − 15), 331(b), 287(a), 227 (a), 211(b), 169(b), and 109(b).

Anal. Calc. for $C_{27}H_{38}O_{17}$: C, 51.1; H, 6.0. Found: C, 52.1; H, 6.0.

2,3,1′,3′,4′,6′-Hexa-O-acetylsucrose (**2**). — A solution of **1** (2 g) in 60% aqueous acetic acid (50 ml) was kept at 80° for 10 min. T.l.c. (ether) then showed a slow-moving product. The solution was concentrated by codistillation with toluene to give **2** (1.7 g, 91.8%). N.m.r. data ($CDCl_3$): τ 4.39 (d, 1 H, $J_{1,2}$ 4.0 Hz, H-1), 5.26 (q, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.68 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-3), 4.60 (d, 1 H, $J_{3',4'}$ 5.0 Hz, H-3′), 4.36 (t, 1 H, $J_{4',5'}$ 5.0 Hz, H-4′), and 7.82–7.94 (18 H, 6 Ac). The optical rotation and mass-spectral data of **2** were indistinguishable from those previously reported[4].

Conventional treatment of **2** (1.0 g) with trityl chloride in pyridine at 60° for 24 h gave, after chromatography, 2,3,1′,3′,4′,6′-hexa-*O*-acetyl-6-*O*-tritylsucrose[4] (**3**) as a syrup (1.2 g, 85%). The ^{1}H-n.m.r. spectrum of **3** was indistinguishable from that of a standard sample[4].

4,6-O-Isopropylidenesucrose hexabenzoate (**4**). — (*a*) Sucrose (10 g) was acetalated with *N,N*-dimethylformamide (200 ml), 2,2-dimethoxypropane (40 ml), and toluene-*p*-sulphonic acid (300 mg), as described above. The syrupy residue was treated with benzoyl chloride (40 ml) and pyridine (300 ml) at 0°. The mixture was stored at room temperature for 24 h, and then worked-up in the conventional manner to give **4** (8.8 g, 30%), m.p. 168–170° (from ethanol), $[\alpha]_D$ +46° (*c* 1, chloroform). N.m.r. data ($CDCl_3$): τ 4.04 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.74 (q, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.13 (t, 1 H, $J_{3,4}$ 10.0 Hz, H-3), 3.85–4.05 (m, 2 H, H-3′,4′), 1.78–2.94 (m, 30 H, 6 Bz), 8.55 and 8.67 (2 s, 6 H, 2 Me).

Anal. Calc. for $C_{57}H_{50}O_{17}$: C, 68.0; H, 5.0. Found: C, 67.8; H, 4.9.

(*b*) A solution of **1** (1 g) in dry methanol (20 ml) was treated with a catalytic amount of M sodium methoxide at 0°, and then stored at room temperature for 24 h. T.l.c. (dichloromethane–methanol, 4:1) showed a major product. The solution was concentrated to dryness and the residue was treated with benzoyl chloride (3 ml) and pyridine (25 ml) initially at 0° and then at room temperature for 24 h. The reaction mixture was worked-up in the usual manner to give **4** (1.3 g, 82%), m.p. and mixture m.p. 168–170° (from ethanol).

2,3,1',3',4',6'-Hexa-O-benzoylsucrose (**5**). — A mixture of **4** (3 g), glacial acetic acid (100 ml), acetone (15 ml), and water (28 ml) was kept at 90° for 1.5 h. T.l.c. (ether) then showed a slow-moving product. The solution was concentrated by codistillation with toluene to give **5** (2.6 g, 90%), m.p. 124–125° (from ether–light petroleum), $[\alpha]_D$ +59° (*c* 1, chloroform). N.m.r. data ($CDCl_3$): τ 4.03 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.72 (q, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.0 (d, 1 H, $J_{3',4'}$ 6.5 Hz, H-3'), 4.07 (t, 1 H, $J_{4',5'}$ 6.5 Hz, H-4'), 1.85–3.0 (m, 30 H, 6 Bz), 6.81 and 7.5 (2 H, 2 OH).

Anal. Calc. for $C_{54}H_{46}O_{17}$: C, 67.1; H, 4.8. Found: C, 67.1; H, 4.7.

4,6-O-Cyclohexylidenesucrose hexa-acetate (**6**). — A solution of sucrose (10 g) in *N,N*-dimethylformamide (200 ml) was stirred with cyclohexanone dimethyl acetal (10 ml) in the presence of toluene-*p*-sulphonic acid (150 mg) at room temperature for 2 h. The mixture was worked-up and the product was acetylated, as described in the preparation of **1**, to give a syrupy residue which, on elution from a column of silica gel with ether–light petroleum (2:1), afforded **6** (6.7 g, 34%), $[\alpha]_D$ +51° (*c* 1.2, chloroform). N.m.r. data ($CDCl_3$): τ 4.39 (d, 1 H, $J_{1,2}$ 3.8 Hz, H-1), 5.19 (q, 1 H, $J_{2,3}$ 10.0 Hz, H-2), 4.66 (q, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 4.58 (d, 1 H, $J_{3',4'}$ 6.0 Hz, H-3'), 4.61 (t, 1 H, $J_{4',5'}$ 6.0 Hz, H-4'), and 8.4–8.8 (10 H, C_6H_{10}). Mass-spectral data [(a) indicates hexopyranosyl and (b) ketofuranosyl cations]: 674, 327(a), 331(b), 267(b), 211(b), 169(b), 141(a), 109(b), and 43.

Anal. Calc. for $C_{30}H_{42}O_{17}$: C, 53.4; H, 6.3. Found: C, 54.5; H, 6.4.

4,6-O-Benzylidenesucrose hexa-acetate (**9**). — A solution of sucrose (10 g) in *N,N*-dimethylformamide (200 ml) was treated with benzaldehyde dimethyl acetal (20 ml) in the presence of toluene-*p*-sulphonic acid (150 mg) at room temperature for 2 h. The reaction mixture was neutralised with Amberlite IR-45 (HO^-) resin and then concentrated by codistillation with toluene. The syrupy residue was treated with acetic anhydride (20 ml) and pyridine (100 ml) at room temperature for 16 h. The solution was concentrated by codistillation with toluene to give **9** (7 g, 35%), m.p. 160–161° (from ether), $[\alpha]_D$ +45° (*c* 1, chloroform); lit.[4], m.p. 155–157°, $[\alpha]_D$ +44.3° (*c* 0.8, chloroform). The ^{1}H-n.m.r. and mass spectra of **9** were indistinguishable from those of a standard sample[4].

ACKNOWLEDGMENTS

We thank Professor A. J. Vlitos, Chief Executive of the Tate and Lyle Research Centre, for his interest and support, and Dr. K. J. Parker for helpful discussions.

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