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Note

Sucrochemistry
Part XIII[1]. Synthesis of 4,6-*O*-benzylidenesucrose

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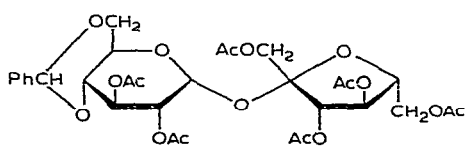
The importance of cyclic acetal derivatives of sugars as synthetic intermediates is well recognised, as is their value in conformational investigations[2]. Hitherto, cyclic acetal derivatives of sucrose have defied preparation, despite many attempts[3], and this is mainly due to the ready hydrolysis of the glycosidic bond. Basic conditions for acetalation of sucrose would, therefore, appear to be a necessary requirement. Previous studies[4] have shown that monosaccharide derivatives readily give benzylidene acetals when treated with benzylidene chloride or benzylidene bromide in pyridine, conditions under which sucrose would be expected to be stable. The first synthesis of the 4,6-*O*-benzylidene derivative of sucrose, using the above conditions[4], is now described.

Treatment of sucrose with benzylidene bromide in pyridine at 95°, followed by conventional acetylation with acetic anhydride, gave a mixture of products. Column chromatography of the reaction mixture gave 4,6-*O*-benzylidenesucrose hexa-acetate (**1**) in 35% yield. Attempts to use benzylidene chloride as the acetalating reagent were not successful.



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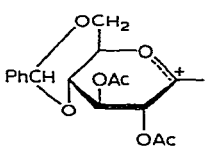
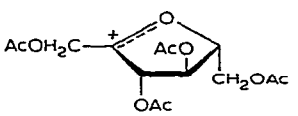


2 *m/e* 335

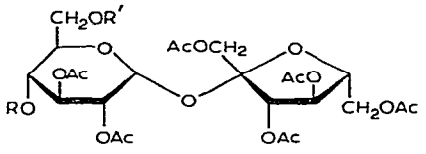


3 *m/e* 331

The structure of **1** was supported by p.m.r. spectral data. For a solution in deuteriochloroform, only the H-1 (τ 4.27) and H-2 (τ 5.1) signals could be interpreted on a first-order basis. However, when deuteriobenzene was used as solvent, discrete signals were observed for H-1, H-2, H-3, H-4, H-3′, H-4′, and the benzylic methine proton at τ 4.1, 4.96, 4.09, 6.51, 4.36, 4.55, and 4.73, respectively. These assignments were confirmed by spin-decoupling experiments. The derived, first-order coupling constants ($J_{1,2}$ 4.0, $J_{2,3}$ 10.0, $J_{3,4}$ 10.0, and $J_{4,5}$ 10.0 Hz) confirmed the $^4C_1$ con-

formation for the D-glucose moiety in **1**. The signal for the benzyl methine proton appeared at τ 4.74, which suggested the preferred chair conformation for the benzylidene ring in which the phenyl substituent was equatorial. Benzylidenation of methyl 2,3-di-*O*-methyl-α-D-glucopyranoside under similar reaction conditions has been reported previously[4] to give only the thermodynamically controlled product, *i.e.*, the 4,6-acetal having an equatorial phenyl group. The mass spectrum of **1** showed an ion at *m/e* 335, attributed to the hexopyranosyl cation **2**, and a relatively intense ion at *m/e* 331 due to the ketofuranosyl cation **3**.

The chemical proof of the structure of **1** was demonstrated by converting it into the known 4-*O*-methanesulphonylsucrose hepta-acetate[5] (**8**). 4,6-*O*-Benzylidenesucrose hexa-acetate (**1**), on treatment with aqueous acetic acid at 100° for 6 min, gave the sucrose hexa-acetate **4** as a syrup. The mass spectrum of **4** contained peaks at *m/e* 331 and 247 due to ketofuranosyl and hexopyranosyl cations, respectively. Treatment of **4** with chlorotriphenylmethane in pyridine at 60° afforded, after column chromatography, 6-*O*-tritylsucrose hexa-acetate **5**. In deuteriochloroform solution, **5** gave a complex p.m.r. spectrum and only signals due to H-1 and H-2 could be interpreted on a first-order basis. When the p.m.r. spectrum was recorded in deuteriobenzene, separate signals were observed for H-1, H-2, H-3, H-3′, and H-4′ at τ 4.1, 5.02, 4.25, 4.3, and 4.51, respectively. The presence of a free hydroxyl group at C-4 was indicated by the absence of the signal for H-4 in the region τ 4.5–5.4, where it usually occurs in acylated derivatives of sucrose. Addition of trichloroacetyl isocyanate to the solution in deuteriochloroform resulted in the appearance of a singlet at τ 1.59 due to the imino proton of the carbamate formed, thereby revealing the presence of a single hydroxyl group in **5**.



4 R = R′ = H
5 R = H, R′ = Tr
6 R = Ms, R′ = Tr
7 R = Ms, R′ = H
8 R = Ms, R′ = Ac

Treatment of **5** with methanesulphonyl chloride in pyridine gave 4-*O*-methanesulphonyl-6-*O*-tritylsucrose hexa-acetate (**6**). The appearance of a triplet at τ 5.04 in the p.m.r. spectrum of **6** suggested that the sulphonate group was located at C-4. Detritylation of **6**, using 45% hydrobromic acid in glacial acetic acid, gave 4-*O*-methanesulphonylsucrose hexa-acetate (**7**). The structure of **7** was supported by p.m.r. spectroscopy. Addition of trichloroacetyl isocyanate to the solution in deuteriochloroform indicated the appearance of a singlet at τ 0.69 due to the imino proton, thereby suggesting the presence of a single hydroxyl group. The mass spectrum of **7** showed peaks at *m/e* 331 and 325 due to ketofuranosyl and hexopyranosyl cations, respectively.

Treatment of **7** with acetic anhydride in pyridine gave the known 4-*O*-methanesulphonylsucrose hepta-acetate[5] (**8**). The mass spectrum of **8** indicated major frag-

ments at *m/e* 367 and 331 attributed to hexopyranosyl and ketofuranosyl cations, respectively.

EXPERIMENTAL

The general experimental data are as described in Part VI[6].

1',2,3,3',4',6'-Hexa-O-acetyl-4,6-O-benzylidenesucrose (**1**). — (*a*) A solution of sucrose (2.5 g) in dry pyridine (50 ml) was treated with benzylidene bromide (2.8 ml) at 85° for 1.5 h. After a further addition of benzylidene bromide (1 ml), the reaction mixture was heated at 95° for 0.5 h, treated with acetic anhydride (5 ml) at 0°, and then stored at room temperature for 5 h. The solution was poured into ice–water and extracted with dichloromethane, and the organic layer was washed with water and dried (Na_2SO_4). T.l.c. (ether–light petroleum, 4:1) showed a mixture of four products. The R_F of the slow-moving spot was identical with that of sucrose octa-acetate and the second fastest-moving component was the major product. The solution was concentrated and fractionated on a column of silica gel (200 g), using ether–light petroleum (1:1). Compound **1** (1.7 g, 35%), which crystallised in the tubes of the fraction collector, had m.p. 155–157°, $[\alpha]_D$ +44.3° (*c* 0.82, chloroform). N.m.r. data (*i*) in $CDCl_3$: τ 4.27 (*d*, 1 proton, $J_{1,2}$ 3.9, H-1), 5.1 (*q*, 1 proton, $J_{2,3}$ 10.0 Hz H-2), 2.42–2.68 (*m*, 5 protons, Ph), 7.74–7.94 (18 protons, 6 Ac); (*ii*) in C_6D_6: τ 4.1 (*d*, 1 proton, $J_{1,2}$ 3.9, H-1), 4.96 (*q*, 1 proton, $J_{2,3}$ 10.0 Hz, H-2), 4.09 (*t*, 1 proton, $J_{3,4}$ 10.0 Hz, H-3), 6.51 (*t*, 1 proton, $J_{4,5}$ 10.0 Hz, H-4), 4.36 (*d*, 1 proton, $J_{3',4'}$ 5.0 Hz, H-3'), 4.55 (*t*, 1 proton, $J_{4',5'}$ 5.0 Hz, H-4'), 4.73 (*s*, 1 proton, benzylic proton), 2.4–2.95 (*m*, 5 protons, Ph), 8.1, 8.14, 8.21, 8.25, 8.33, and 8.39 (*s*, 18 protons, 6Ac); mass-spectral data [(a) indicates ions arising only from **2** and (b) only from **3**]: *m/e* 335a, 331b, 275a, 233a, 211b, 169b, 127a, 109b, 105, 101, 43, 77 ($C_6H_5^+$), 91 ($C_7H_7^+$), 105 (C_6H_5–C^+=O), 106 ($C_6H_5CHO^+$), and 122 ($C_6H_5CO_2H^+$)

Anal. Calc. for $C_{31}H_{38}O_{17}$: C, 54.5; H, 5.6. Found: C, 54.3; H, 5.6.

(*b*) A solution of sucrose (2 g) in pyridine (50 ml) was treated with benzylidene bromide (2.5 ml) at 85° for 1 h. After a further addition of benzylidene bromide (1 ml), the reaction mixture was heated with stirring at 95° for 0.5 h. The reaction mixture was then acetylated and worked up as described previously to give a syrupy mixture. Compound **1** (1.1 g, 28%), which crystallised directly from the mixture on seeding, had m.p. and mixed m.p. 155–157° (from ether–light petroleum).

1',2,3,3',4',6'-Hexa-O-acetyl-6-O-tritylsucrose (**5**). — A solution of **1** (1.5 g) in glacial acetic acid (30 ml) was treated with water (15 ml) at 100° for 7–10 min. T.l.c. (ether) then showed a slow-moving product. The solution was concentrated by codistillation with toluene to give 1',2,3,3',4',6'-hexa-*O*-acetylsucrose (**4**) as a syrup (1 g, 80%), $[\alpha]_D$ +28.4° (*c* 0.9, chloroform); mass-spectral data [(a) indicates ions due to hexopyranosyl and (b) due to ketofuranosyl cations]: *m/e* 331b, 289b, 247a, 229b, 187a, 169b, 145a, 127b, 109b, and 101.

A solution of **4** (1.0 g) in pyridine (50 ml) was stirred with chlorotriphenylmethane (1.5 g) at 60° for 48 h. T.l.c. (ether–light petroleum, 4:1) then showed a fast-moving

product. The reaction mixture was diluted with dichloromethane, washed with aqueous sodium hydrogen carbonate, and water, and dried (Na_2SO_4). The solution was concentrated by codistillation with toluene to a syrup which, on elution from a column of silica gel (25 g) using ether–light petroleum (1:1), afforded **5** as a syrup (1.2 g, 85.3%), $[\alpha]_D$ +45.2° (*c* 1.02, chloroform). N.m.r. data (C_6D_6): τ 4.1 (*d*, 1 proton, $J_{1,2}$ 3.7 Hz, H-1), 5.0 (*q*, 1 proton, $J_{2,3}$ 10.0 Hz, H-2), 4.24 (*t*, 1 proton, $J_{3,4}$ 10.0 Hz, H-3), 6.4 (H-4), 4.3 (*d*, 1 proton, $J_{3',4'}$ 5.0 Hz, H-3'), 4.5 (*t*, 1 proton, $J_{4',5'}$ 5.0 Hz, H-4'), 2.3–2.5 and 2.75–3.05 (*m*, 15 protons, Tr), 7.2 (1 proton, OH), 8.07–8.4 (18 protons, 6Ac).

Anal. Calc. for $C_{43}H_{48}O_{17}$: C, 61.7; H, 5.7. Found: C, 61.6; H, 5.7.

*1',2,3,3',4',6'-Hexa-*O*-acetyl-4-*O*-methanesulphonyl-6-*O*-tritylsucrose* (**6**). — A solution of **5** (800 mg) in pyridine (20 ml) was treated with methanesulphonyl chloride (1.2 ml) at 0° and then stirred at room temperature for 48 h. To the cooled reaction mixture, water (1 ml) was added, and the solution was then left at room temperature for 30 min, diluted with dichloromethane, washed with water, and dried (Na_2SO_4). The solution was concentrated to a syrup which was crystallised from ether–light petroluem to give **6** (750 mg, 85.7%), m.p. 183–184°, $[\alpha]_D$ +55.1° (*c* 1.1, chloroform). N.m.r. data: τ 4.21 (*d*, 1 proton, $J_{1,2}$ 3.5 Hz, H-1), 5.12 (*q*, 1 proton, $J_{2,3}$ 10.2 Hz, H-2), 4.44 (*q*, 1 proton, $J_{3,4}$ 9.2 Hz, H-3), 5.04 (*t*, 1 proton, $J_{4,5}$ 9.2 Hz, H-4), 4.58 (*d*, 1 proton, $J_{3',4'}$ 5.0 Hz, H-3'), 4.67 (*t*, 1 proton, $J_{4',5'}$ 5.0 Hz, H-4'), 2.5–2.8 (*m*, 15 protons, Tr), 7.52 (*s*, 3 protons, Ms), 7.8–8.02 (18 protons, 6Ac).

Anal. Calc. for $C_{44}H_{50}O_{19}S$: C, 57.8; H, 5.5; S, 3.5. Found: C, 57.9; H, 5.5; S, 3.6.

*1',2,3,3',4',6'-Hexa-*O*-acetyl-4-*O*-methanesulphonylsucrose* (**7**). — A solution of **6** (500 mg) in dry dichloromethane (2.5 ml) and glacial acetic acid (3.5 ml) was treated with hydrobromic acid in glacial acetic acid (45%, 0.5 ml) at 0° for 5–8 min. The reaction mixture was diluted with dichloromethane and washed successively with aqueous sodium acetate, water, aqueous sodium hydrogen carbonate, and water. The solution was dried (Na_2SO_4) and concentrated to give a syrup which was purified by elution from a small column of silica gel, using ether–light petroleum (1:1), to give **7** (300 mg, 81.6%), $[\alpha]_D$ +54.5° (*c* 0.71, chloroform). N.m.r. data: τ 4.31 (*d*, 1 proton, $J_{1,2}$ 3.7 Hz, H-1), 5.2 (*q*, 1 proton, $J_{2,3}$ 10.2 Hz, H-2), 4.48 (*q*, 1 proton, $J_{3,4}$ 9.3 Hz, H-3), 5.25 (*t*, 1 proton, $J_{4,5}$ 9.3 Hz, H-4), 4.59 (*d*, 1 proton, $J_{3',4'}$ 5.75 H-3'), 4.6 (*t*, 1 proton, $J_{4',5'}$ 5.75 Hz, H-4'), 6.17 (1 proton, OH), 6.95 (*s*, 3 protons, Ms), 7.81–7.98 (18 protons, 6Ac). Mass-spectral data [(a) and (b) indicate ions due to hexopyranosyl and ketofuranosyl cations, respectively]: *m/e* 325a, 331b, 289b, 265a, 229b, 211b, 205a, 187b, 169b, 127b, and 109b.

Anal. Calc. for $C_{25}H_{36}O_{19}S$: C, 44.6; H, 5.4; S, 4.8. Found: C, 45.1; H, 5.4; S, 4.6.

Conventional treatment of **7** (500 mg) with acetic anhydride (2 ml) in pyridine (15 ml) at room temperature for 6 h gave 1',2,3,3',4',6,6'-hepta-*O*-acetyl-4-*O*-methanesulphonylsucrose[5] (**8**; 500 mg, 94%), m.p. and mixed m.p. 94–95° (from ethanol); the n.m.r. spectrum was identical with the standard sample. Mass-spectral

data [(a) and (b) indicate ions due to hexopyranosyl and ketofuranosyl cations, respectively]: *m/e* 367a, 331b, 307a, 271b, 247a, 211b, 205a, 169b, and 109b.

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