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Note

Sucrochemistry

Part XIV[1]. Further studies of the partial *O*-deacetylation of sucrose octa-acetate

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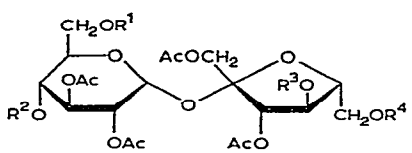
We have previously described the isolation of sucrose 1′,2,3,3′,4,4′,6-hepta-acetate (**1**) in 9% yield from the mixture of products obtained by the selective *O*-deacetylation of sucrose octa-acetate (**2**) with alumina[2]. Further investigation of the reaction mixture has revealed a mixture of four hepta-acetates, including **1**, in addition to much (70–80%) unchanged sucrose octa-acetate (**2**). The unknown components, designated *A*, *B*, and *C*, in order of decreasing chromatographic mobility, were separated by extensive chromatography, which afforded *B* and *C* as chromatographically homogeneous syrups in yields of 2.7 and 6%, respectively. *A*, which was present only in small quantities and could not be obtained pure, was not further investigated.



1 $R^1=R^2=R^3=Ac$, $R^4=H$
2 $R^1=R^2=R^3=R^4=Ac$
3 $R^1=R^3=R^4=Ac$, $R^2=H$
4 $R^1=R^3=R^4=Ac$, $R^2=CONHCOCCl_3$
5 $R^1=R^3=R^4=Ac$, $R^2=COCD_3$
6 $R^1=Tr$, $R^2=R^3=R^4=Ac$
7 $R^1=R^3=R^4=Ac$, $R^2=Ms$
8 $R^1=R^2=R^4=Ac$, $R^3=H$
9 $R^1=R^2=R^4=Ac$, $R^3=CONHCOCCl_3$
10 $R^1=R^2=R^4=Ac$, $R^3=COCD_3$

The structure of *B* was indicated by comparison of its ^1H n.m.r. parameters with those[3] of sucrose octa-acetate (**2**). The characteristic H-4 resonance at τ 4.93 for **2** was absent from the corresponding region of the spectrum of *B*, but was observed at higher field (τ 6.48) as a broadened triplet, suggesting that the lone hydroxyl group

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was present at C-4 as in **3**. This was substantiated by the addition of trichloroacetyl isocyanate to the n.m.r. solution, which formed the appropriate carbamate **4** *in situ*[4]. The O*H* resonance at τ 6.76 then disappeared, the H-4 resonance was deshielded by ~1.5 p.p.m., and an N-*H* resonance appeared at τ 1.23. The modified n.m.r. spectrum closely resembled that of sucrose octa-acetate[3] (**2**). Treatment of *B* with hexadeuterioacetic anhydride afforded the 4-*O*-trideuterioacetyl derivative **5**, which possessed the same n.m.r. spectrum as sucrose octa-acetate (**2**) except for the absence of the acetyl resonance at τ 7.96, which had been assigned previously to the 4-*O*-acetyl group by Otake *et al.*[5], thus confirming that *B* was the 1′,2,3,3′,4′,6,6′-hepta-acetate **3**.

An unequivocal synthesis of **3** was achieved from 6-*O*-tritylsucrose hepta-acetate (**6**) by detritylation under conditions favourable for migration of the 4-*O*-acetyl group to the 6-position[5,7]. The resulting product gave an n.m.r. spectrum superimposable or that of *B*, and it afforded a crystalline methanesulphonate[8] (**7**) identical with that derived from *B*.

TABLE I

FIRST-ORDER CHEMICAL SHIFTS (τ values) AND COUPLING CONSTANTS AT 100 MHZ IN CHLOROFORM-*d*

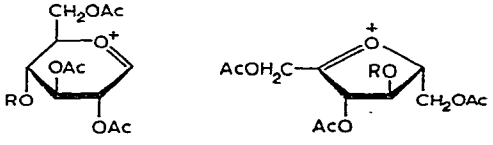
Compound	**3**[a]	**4**[a,b]	**8**[a]	**9**[a,b]
H-1	4.39 d	4.29 d	4.34 d	4.30 d
H-2	5.22 dd	5.14 dd	5.13 dd	5.13 dd
H-3	4.65 t	4.48 t	4.57 t	4.56 t
H-4	6.48 t	4.93 t	4.97 t	4.92 t
H-3′	4.55 d	4.60 m	4.77 d	4.45–4.7 m
H-4′	4.67 t			
OH	6.76 m		6.47 d	
NH		1.23 s		1.28 s
$J_{1,2}$	3.5	3.6	3.5	3.5
$J_{2,3}$	10.3	10.3	10.0	10.2
$J_{3,4}$	~9	9.3	9.5	~10
$J_{4,5}$	~9	~9	~9	~9
$J_{3',4'}$	~6		7.5	
$J_{4',5'}$	~6			

[a]The resonances due to H-5,5′,6,6′ appeared as a complex, overlapped multiplet in the region τ 5.5–6.0. [b]Spectrum measured after the addition of excess trichloroacetyl isocyanate to a solution of the corresponding hydroxy compound.

The ^{1}H n.m.r. spectrum of *C*, unlike that of sucrose octa-acetate (**2**), was largely first-order and free of overlap in the region τ 4.3–5.2. The resonances due to H-1, H-2, H-3, and H-4 were readily recognised from their chemical shifts and splitting patterns[3], which suggested that the D-glucopyranosyl ring was fully acetylated. Apart from these signals, the only other resonance in this section of the spectrum was a doublet at τ 4.66 (splitting 7.5 Hz) which could only be due to H-3′. The

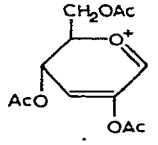
resonance due to H-4′ overlapped those due to the primary protons and H-5,5′, which formed a complex multiplet at τ 5.6–6.0. However, on addition of trichloroacetyl isocyanate to the n.m.r. solution, the carbamate **9** was formed and a single resonance (H-4′) was deshielded from the region τ 5.6–6.0 to *ca.* 4.6, giving rise to considerable second-order character for that part of the spectrum, which made it difficult to analyse. Nevertheless, this shift proved conclusively that *C* was the 1′,2,3,3′,4,6,6′-hepta-acetate **8**, which was further characterised as the 4′-trideuterioacetate **10** by treatment with hexadeuterioacetic anhydride.

The mass spectra of the two deuterated sucrose octa-acetates, **5** and **10**, were of interest since they should throw some light on the fragmentation pathway of sucrose octa-acetate and related compounds. The major, initial fragmentation in most non-reducing disaccharides appears to be the cleavage of the glycosidic bonds to give the two cyclic oxycarbonium ions[9,10]. For sucrose derivatives, the cyclic oxycarbonium ion derived from the D-fructosyl unit, *i.e.* **13**, seems to preponderate, probably because it is tertiary[11], but subsequent fragmentation pathways for **13** are not known. The mass spectra of **5** and **10** showed that the oxycarbonium ion formed from the D-fructosyl moieties, **13** and **14**, respectively, preponderated over those from the D-glucopyranosyl unit, although the ratios were not as high as previously encountered in other sucrose derivatives (1.15 and 1.3, respectively). For **5**, the ion from the D-glucose residue **12** underwent loss of acetic acid (*m/e* 334→274, ratio 16:1), whereas loss of trideuterioacetic acid (*m/e* 334→271) was not observed. Surprisingly, the loss of acetic acid from the D-fructosyl oxycarbonium ion **13** (*m/e* 331→271) was also not observed. Similarly, for **10**, no loss of acetic or trideuterioacetic acid was observed from the D-fructosyl unit carbonium ion **14** (*m/e* 334→374, *m/e* 334→331, respectively). These results indicate that the D-fructosyl carbonium ion **13** does not fragment by the loss of the elements of acetic acid to give the ion **16** in the same way as the D-glucosyl oxycarbonium ion gives the ion **15**.



11 R = Ac (*m/e* 331)
12 R = $COCD_3$ (*m/e* 334)

13 R = Ac (*m/e* 331)
14 R = $COCD_3$ (*m/e* 334)



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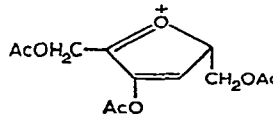

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It is, perhaps, surprising that the selective *O*-deacetylation of the octa-acetate **2** should occur at secondary positions as well as at the primary 6′-position. However, it is well known[6,7] that facile 4→6 acetyl migrations occur in hexopyranosides with a vacant primary hydroxyl group, as in the synthesis of **3**; consequently, it is tempting to speculate that the 4- and 4′-hydroxy derivatives **3** and **8** arise from the 6- and 6′-hydroxy derivatives, respectively.

EXPERIMENTAL

Partial de-esterification of sucrose octa-acetate (**2**). — A solution of sucrose octa-acetate (30 g) in chloroform (435 ml) was poured on to a column of dry alumina (Laporte Type H, 700 g) and allowed to stay in contact with the alumina for 44 h. The column was then eluted with ethyl acetate, which gave a mixture of starting material and sucrose hepta-acetates (25.7 g) in a ratio of ~4:1, as indicated by t.l.c. The mixture was subjected to an initial fractionation on a column (40 × 5 cm) of silica gel with ethyl acetate–light petroleum (2:1) as eluant. The first fractions contained sucrose octa-acetate (7.1 g), and subsequent fractions contained mixtures of the octa- and hepta-acetates, which were combined and evaporated to a syrup (13.2 g). T.l.c. of the mixture (chloroform–methanol, 50:1, three developments) indicated the presence of the octa-acetate **2**, the 1′,2,3,3′,4,4′,6-hepta-acetate[2] **1** (R_F *ca.* 0.8), and three isomeric hepta-acetates designated *A*, *B*, and *C*, with approximate R_F values of 0.75, 0.70, and 0.63, respectively. The mixture was then further fractionated on a column (80 × 5 cm) of silica gel with chloroform–methanol (500:1) as eluant, collecting 10-ml fractions. The first fractions contained a mixture of **2**, **1**, *A*, and *B* (8.5 g).

Subsequent fractions contained component *B* as a syrup (0.8 g, 2.7%), which was identified as sucrose 1′,2,3,3′,4′,6,6′-hepta-acetate **3**, $[\alpha]_D$ +46.3° (*c* 0.5, chloroform) (Found: C, 49.0; H, 5.9. $C_{26}H_{36}O_{18}$ calc.: C, 49.0; H, 5.7%).

Treatment of **3** (0.24 g) with hexadeuterioacetic anhydride (0.6 g) in pyridine (1 ml) gave, after concentration to dryness and recrystallisation of the residue from aqueous ethanol, 4-*O*-(trideuterioacetyl)sucrose hepta-acetate **5** (0.22 g, 86%), m.p. 84–87°, Mass spectrum: *m/e* 334 (**12**, 13%), 331 (**13**, 17%), 274 (0.8%), 211 (49%), 169 (76%), 109 (56%), 43 (100%).

Esterification of **3** (0.17 g) with mesyl chloride (0.2 g) in pyridine (4 ml) gave, after the usual work-up, the 4-methanesulphonate **7** (0.14 g, 76%), m.p. 87–89° (from aqueous ethanol), $[\alpha]_D$ +48.8° (*c* 0.2, chloroform); lit.[7] m.p. 94–95°, $[\alpha]_D$ +25.2° (Found: C, 45.6; H, 5.7; S, 4.4. $C_{27}H_{38}O_{20}S$ calc.: C, 45.4; H, 5.3; S, 4.5%).

After the elution of *B* from the column, fractions containing pure *C* were obtained and evaporated to dryness to give the syrupy 1′,2,3,3′,4,6,6′-hepta-acetate **8** (1.8 g, 6%), $[\alpha]_D$ +54.3° (*c* 0.4, chloroform) (Found: C, 49.4; H, 5.9%).

Treatment of **8** (0.22 g) with hexadeuterioacetic anhydride (0.36 g) in pyridine (1 ml), as described above, afforded 4′-*O*-(trideuterioacetyl)sucrose hepta-acetate (**10**), m.p. 85–88° (from aqueous ethanol). Mass spectrum: *m/e* 334 (18%), 331 (15%), 271 (1.4%), 211 (52%), 169 (80%), 109 (55%), 43 (100%).

Detritylation of 6-O-*tritylsucrose hepta-acetate.* — A solution of the 6-trityl-ether **6** (12.2 g) in chloroform (50 ml) was treated with hydrogen bromide in acetic acid (25 ml, 45% w/v). The mixture was stirred at room temperature for 30 min and then diluted with ice–water, and the chloroform layer was separated. The aqueous layer was extracted several times with chloroform. The combined chloroform layer and extracts were washed with saturated, aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and concentrated to dryness to give a syrup (12 g). Exami-

nation of the syrup by t.l.c. revealed it to be a mixture of trityl bromide (characteristic yellow colour with 4% ethanolic sulphuric acid) and two slower-moving carbohydrate components. Fractionation of the mixture by elution from silica gel with ethyl acetate–light petroleum (1:1) afforded trityl bromide, followed by the faster-moving carbohydrate component (1 g, 11%), $[\alpha]_D$ +43.4° (*c* 0.3), which was not adequately characterised but was assumed to be the 1′,2,3,3′,4,4′,6′-hepta-acetate.

Later fractions contained the 1′,2,3,3′,4′,6,6′-hepta-acetate **3**, isolated as a syrup (5.0 g, 55%), $[\alpha]_D$ +48° (*c* 0.9), which was shown to be identical (n.m.r. and t.l.c.) with *B* described above.

Esterification of **3** (0.4 g) with mesyl chloride (0.4 g) in pyridine (10 ml), in the usual way, afforded the 4-methanesulphonate **7** (0.36 g, 85%), m.p. 85–88° (from aqueous ethanol), $[\alpha]_D$ +49° (*c* 0.4) (Found: C, 45.5; H, 5.2; S, 5.0. $C_{27}H_{38}O_{20}S$ calc.: C, 45.4; H, 5.3; S, 4.5%).

The sulphonate **7** was identical (i.r., t.l.c.) with that derived from the mesylation of *B*.

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