Carbohydrate Research, 83 (1980) 138–141
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

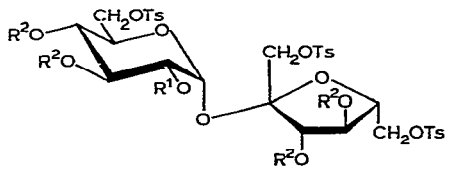
Note

Selective tetratosylation of sucrose: isolation of the 2,6,1′,6′-tetrasulphonate*

JOHN M. BALLARD, LESLIE HOUGH, SHASHI P. PHADNIS, AND ANTHONY C. RICHARDSON
Department of Chemistry, Queen Elizabeth College (University of London), London W8 7AH (Great Britain)

(Received September 20th, 1979; accepted for publication, October 1st, 1979)

The selective tosylation of sucrose using one[1], two[2], three[3], and four[4] molar equivalents of tosyl chloride in pyridine has resulted in the isolation of the 6,6′-ditosylate and the 6,1′,6′-tritosylate in preparative quantities after chromatography. The use of mesitylenesulphonyl chloride and 2,4,6-tri-isopropylbenzenesulphonyl chloride have been recommended for these selective reactions, since the corresponding 6,1′,6′-trisulphonates have been isolated without recourse to chromatography[5–7]. A recent examination of the tritosylation of sucrose by Ball *et al.*[7] has revealed the formation, *inter alia*, of the 2,6,6′-tritosylate, which was isolated by h.p.l.c. in low yield. We have isolated the corresponding trimesitylenesulphonate as a minor product from the reaction of sucrose with three molar equivalents of mesitylenesulphonyl chloride[8]. In a brief report, Long[4] stated that sucrose yielded a chromatographically homogeneous tetratosylate of undefined structure and we now report that this compound is the 2,6,1′,6′-tetra-ester **1**.



1 R^1 = Ts, R^2 = H
2 R^1 = Ts, R^2 = Ac
3 R^1 = R^2 = H
4 R^1 = R^2 = Bz

The reaction of sucrose at ~0° with 4 molar equivalents of tosyl chloride, followed by chromatography of the product mixture, afforded 33% of the 6,1′,6′-

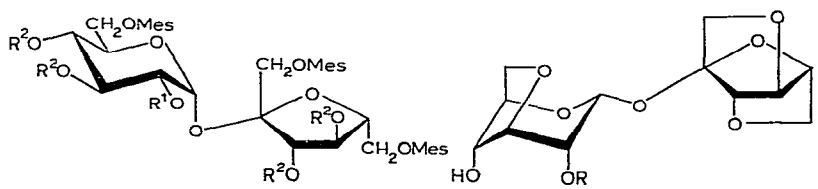
*Sucrochemistry, Part XXIX. For Part XXVIII, see R. Khan, C. L. Bhardwaj, K. S. Mufti, and M. R. Jenner, *Carbohydr. Res.*, 78 (1980) 185–189.

0008-6215/80/0000–0000/$ 02.25,

tritosylate **3**, which was characterised as its pentabenzoate **4**, and a crude mixture containing **1** and at least three other components of similar mobility. Further chromatography of this mixture gave 32% of pure, but amorphous, **1**. The other components of the mixture were not obtained homogeneous and were not investigated further.

The mass spectrum of the crystalline tetra-acetate (**2**) of **1** indicated that each monosaccharide unit carried two tosyl groups, since an intense ion was observed at *m/e* 555 ($Ac_2Ts_2Glcp^+$ and $Ac_2Ts_2Fruf^+$) which arose from cleavage of either of the two glycosidic linkages in **2**. Furthermore, a comparison of the ^{1}H-n.m.r. spectra of **2** and sucrose octa-acetate[9] revealed that, of the methine resonances, only that due to H-2 showed a marked upfield shift (0.57 p.p.m.), which was consistent with the presence of a tosyl group at that position. Thus, **1** had only one tosylate at a secondary position (position 2) and was therefore the 2,6,1′,6′-tetratosylate.

Treatment of **1** or **2** with base afforded a trianhydrotosylate **9**, which had a ^{1}H-n.m.r. spectrum very similar to that[5,10] of 3,6:1′,4′:3′,6′-trianhydrosucrose (**10**). Only two of the resonances were free from overlap, namely, a doublet at δ 6.21 ($J_{1,2}$ 3 Hz) due to H-1 and a triplet at δ 4.97 with splittings of ~3 Hz. Irradiation of the triplet resonance caused the H-1 doublet to collapse to a singlet, indicating that the triplet was due to H-2. The position of the H-2 resonance indicated that the 2-tosylate substituent was still intact and that the trianhydride was 3,6:1′,4′:3′,6′-trianhydro-2-*O*-tosylsucrose (**9**). The low yield (~20%) of **9** suggested that other anhydrides also may have been formed, and several other compounds could be detected by t.l.c.



5 $R^1 = R^2 = H$
6 $R^1 = Ts$, $R^2 = H$
7 $R^1 = Ts$, $R^2 = Ac$
8 $R^1 = Ts$, $R^2 = Bz$

9 R = Ts
10 R = H

The structure of **9** was further substantiated by its synthesis from 6,1′,6′-tri-*O*-mesitylenesulphonyl-2-*O*-tosylsucrose (**6**), which, in turn, was conveniently prepared in 53% yield by monotosylation of 6,1′,6′-tri-*O*-mesitylenesulphonylsucrose[5-7] (**5**); the ^{1}H-n.m.r. spectrum of **6** was consistent with the presence of the 2-tosylate, in particular the positions (δ 4.57) of the H-2 resonance for its derived tetra-acetate **7** and tetrabenzoate **8**. Treatment of **6** with sodium methoxide afforded 21% of the 2-tosyltrianhydride **9**.

EXPERIMENTAL

Selective, tetramolar tosylation of sucrose. — A solution of tosyl chloride (7.64 g, 40 mmol) in pyridine (25 ml) was added dropwise to a solution of sucrose (3.42 g, 10 mmol) in pyridine (210 ml) maintained at −10°. The mixture was kept at 0° for 72 h, and then treated with water (5 ml) and concentrated to dryness. A solution of the residue in chloroform was shaken with dilute hydrochloric acid, saturated, aqueous sodium hydrogencarbonate, and water, dried ($MgSO_4$), and concentrated to dryness. T.l.c. (chloroform–ethanol, 8:1) of the residue indicated two major components, the slower-moving of which had mobility identical with that of 6,1′,6′-tri-*O*-tosylsucrose **3**.

Chromatography of the mixture on a dry-packed[11] column of silica gel (Merck 7734) with chloroform–ethanol (8:1) afforded, first, a mixture (5.8 g, 60%) containing the faster-moving component together with several other minor components of similar mobility. This fraction was then subjected to further fractionation on silica gel with chloroform–ethanol (20:1) as eluent. Initially, a mixture was obtained (1.8 g), which contained three minor components and the 2,6,1′,6′-tetratosylate **1**, followed by fractions containing only **1**, which was obtained as a syrup (3.0 g, 32%), $[\alpha]_D$ +43° (*c* 0.3, chloroform) (Found: C, 50.3; H, 5.3; S, 13.1. $C_{40}H_{46}O_{19}S_4$ calc.: C, 50.1; H, 4.8; S, 13.4).

The slower-moving component from the original mixture was isolated as a syrup (2.4 g, 33%), and characterised as the 6,1′,6′-tritosylate **3** by conversion into the pentabenzoate **4** (80%) using benzoyl chloride–pyridine; m.p. 95–97° (ethanol), $[\alpha]_D$ +23° (*c* 0.4, chloroform); lit.[10] m.p. 87–90°, $[\alpha]_D$ +19°.

Conventional treatment of **1** with pyridine–acetic anhydride gave the tetra-acetate **2** (85%), m.p. 71–74° (from ethanol), $[\alpha]_D$ +63° (*c* 0.5, chloroform) (Found: C, 50.9; H, 4.9; S, 10.9. $C_{48}H_{54}O_{23}S_4$ calc.: C, 51.15; H, 4.8; S, 11.35). ^{1}H-N.m.r. data ($CDCl_3$, 100 MHz): δ 5.44 (d, 1 H, $J_{3',4'}$ 7.5 Hz, H-3′), 5.27 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.24 (t, 1 H, $J_{4',5'}$ 7.5 Hz, H-4′), 5.19 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 4.83 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.30 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2), 2.45 (s, 12 H, 4 *Me*Ar), 2.05 (s, 6 H, 2 Ac), 1.90 (s, 3 H, Ac), and 1.75 (s, 3 H, Ac).

6,1′,6′-Tri-O-mesitylenesulphonyl-2-O-tosylsucrose (**6**). — To an ice-cold solution of 6,1′,6′-tri-*O*-mesitylenesulphonylsucrose[5–7] (**5**; 4.7 g, 5.3 mmol) in pyridine (20 ml) was slowly added tosyl chloride (1.1 g, 5.8 mmol) in small portions. The solution was then stored at 0–5° for 72 h, when t.l.c. indicated that one major product had been formed, together with several minor products. The mixture of products was extracted in the usual way with chloroform, and then subjected to chromatography on silica gel. Elution with chloroform–acetone (6:1) gave some faster-moving, minor components, which were not further investigated. The major product **6** was eluted with chloroform–acetone (4:1) and isolated as a syrup (2.5 g, 53%), $[\alpha]_D$ +26° (*c* 1, methanol) (Found: C, 52.9; H, 5.7; S, 12.1. $C_{46}H_{58}O_{19}S_4$ calc.: C, 53.0; H, 5.6; S, 12.3).

The syrupy tetra-acetate (**7**) of **6** had $[\alpha]_D$ +52° (*c* 1, chloroform) (Found:

C, 53.4; H, 5.5; S, 10.4. $C_{54}H_{66}O_{23}S_4$ calc.: C, 53.55; H, 5.45; S, 10.6). ^{1}H-N.m.r. data (C_6D_6): δ 6.6–7.75 (10 H, aromatic protons), 5.76 (d, 1 H, $J_{3',4'}$ 7.0 Hz, H-3'), 5.58 (t, 1 H, $J_{3,4} = J_{2,3} = 10$ Hz, H-3), 5.53 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.35 (t, 1 H, $J_{4',5'}$ 7 Hz, H-4'), 5.06 (t, 1 H, $J_{4,5}$ 10 Hz, H-4), 4.57 (dd, 1 H, H-2), 3.8–4.5 (8 H, 3 CH_2, H-5,5'), 1.53, 1.64 (2), 1.73, 1.92 (2), 1.94, 2.03, 2.67 (2), 2.73 (2), and 2.77 (2) (9 s, 42 H, 14 Me, Ar*Me*, OAc).

The tetrabenzoate (**8**) of **6** was an amorphous solid, $[\alpha]_D$ +3° (*c* 1, chloroform) (Found: C, 61.6; H, 5.1; S, 8.4. $C_{74}H_{74}O_{23}S_4$ calc.: C, 60.9; H, 5.1; S, 8.8). ^{1}H-N.m.r. data ($CDCl_3$): δ 6.8–8.2 (30 H, aromatic protons), 5.96 (d, 1 H, $J_{3',4'}$ 8 Hz, H-3'), 5.62 (t, 1 H, $J_{2,3} = J_{3,4} = 10$ Hz, H-3), 5.55 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.52 (1 H, $J_{4',5'}$ 8 Hz, H-4'), 5.26 (t, 1 H, $J_{4,5}$ 10 Hz, H-4), 4.56 (dd, 1 H, H-2), 3.8–4.5 (m, 8 H, 3 CH_2, H-5,5'), 2.16, 2.20, 2.26, 2.33, 2.49 (2), 2.64 (2), and 2.70 (2) (7s, 30 H, 10 Ar*Me*).

3,6:1',4':3',6'-Trianhydro-2-O-tosylsucrose (**9**). — (*a*) A solution of **1** (3.6 g) in methanolic M sodium methoxide (35 ml) was heated under reflux for 30 min, and then cooled, neutralised with Zerolite mixed-bed ion-exchange resin, filtered, and concentrated to dryness. The syrupy residue crystallised, but contained several components (t.l.c.). Recrystallisation from ethanol gave **9** (0.33 g, 20%), m.p. 130–133°, $[\alpha]_D$ +98° (*c* 0.5, chloroform) (Found: C, 51.5; H, 5.1; S, 7.3. $C_{19}H_{22}O_{10}S$ calc.: C, 51.6; H, 5.0; S, 7.2).

When the reaction was repeated on **2**, **9** was obtained in diminished yield (7%). ^{1}H-N.m.r. data (C_5D_5N): δ 7.9 (d, 2 H, aromatic protons), 7.16 (2 H, aromatic protons), 6.21 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1), 4.97 (bt, 1 H, $J_{2,3}$ ~2.5, $J_{2,4}$ ~1 Hz, H-2), 4.20–4.64 (m, 6 H, H-3,3',4,4',5,5'), 3.8–4.0 (m, 4 H, H-6a,6b,6'a,6'b), 3.78 (d, 1 H, $J_{1'a,1'b}$ 7.5 Hz, H-1'a), and 3.62 (d, 1 H, H-1'b).

(*b*) The above reaction was repeated with **6**, except that **9** was isolated (21%) by column chromatography on silica gel with chloroform–methanol (10:1); **9** had m.p. 137° (from ethanol), $[\alpha]_D$ +100° (*c* 1, chloroform).

REFERENCES

1 I. Jezo, *Chem. Zvesti*, 25 (1971) 364.
2 R. U. Lemieux and J. P. Barrette, *Can. J. Chem.*, 38 (1960) 656–662.
3 C. H. Bolton, L. Hough, and R. Khan, *Carbohydr. Res.*, 21 (1972) 133–143.
4 V. Kollonitsch, *Sucrose Chemicals*, International Sugar Research Foundation Inc., 1970, p. 75.
5 L. Hough, S. P. Phadnis, and E. Tarelli, *Carbohydr. Res.*, 44 (1975) c12–c13.
6 R. G. Almquist and E. J. Reist, *J. Carbohydr. Nucleos. Nucleot.*, 1 (1974) 461–468.
7 D. H. Ball, F. H. Bissett, and R. C. Chalk, *Carbohydr. Res.*, 55 (1977) 149–163.
8 S. P. Phadnis, Ph.D. Thesis, University of London, 1976.
9 W. W. Binkley, D. Horton, and N. S. Bhacca, *Carbohydr. Res.*, 10 (1969) 245–258.
10 R. Khan, *Carbohydr. Res.*, 22 (1972) 441–445.
11 L. Hough, A. K. Palmer, and A. C. Richardson, *J. Chem. Soc., Perkin Trans. 1*, (1972) 2513–2517.