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SYNTHESIS OF 6,1′,6′-TRI-*O*-(MESITYLENESULFONYL)SUCROSE, FURTHER EXAMINATION OF "TRI-*O*-TOSYLSUCROSE", AND THE CHEMISTRY OF 3,6:1′,4′:3′,6′-TRIANHYDROSUCROSE*†

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ABSTRACT

Selective trimolar mesitylenesulfonylation of sucrose resulted in the formation of a highly crystalline trimesitylenesulfonate (**1**), which was isolated in greater than 50% yield without recourse to chromatography. As anticipated, the sulfonyl groups in **1** were located at the primary positions, as treatment with alkali afforded 3,6:1′,4′:3′,6′-trianhydrosucrose (**4**) in high yield. Fractionation of "tri-*O*-tosylsucrose" by high-pressure liquid chromatography effected separation of the minor isomer from the known, preponderant 6,1′,6′-isomer **3**. ^{13}C-N.m.r. spectroscopy indicated that the minor isomer was 2,6,6′-tri-*O*-*p*-tolylsulfonylsucrose (**2**). The trianhydride **4** was found to be dimorphous and was further characterized as the diacetate (**5**), the dibenzoate (**6**), the di-*p*-toluenesulfonate (**7**), and the dimethyl ether (**8**). Considerable differences in the reactivities toward acylation and etherification of the two axial hydroxyl groups in **4** permitted the preparation, in good yields, of the 4-acetate (**9**) and of the 4-methyl ether (**12**). Several derivatives of methyl 3,6-anhydro-α-D-glucopyranoside (**13**) were prepared for comparison with corresponding derivatives of **4**, and the hydroxyl groups in **13** also showed differences in reactivities analogous with those of **4**.

INTRODUCTION

Since publication[3] in 1950 of a preparation of "tri-*O*-tosylsucrose", selective sulfonylation of sucrose, as an economical method for the preparation of potentially useful, polyfunctional derivatives, has attracted much attention. Progress towards this objective has been somewhat disappointing, and some results have proved to be controversial. Initial attempts[4] to establish the structure and homogeneity of "tri-*O*-tosylsucrose" by methylation analysis were strongly criticized[5]; and X-ray crystallographic analysis[6,7] of the trianhydrosucrose obtained from crystalline 6,1′,6′-tri-*O*-*p*-tolylsulfonylsucrose pentaacetate raised the possibility that the structure previously

*Dedicated to the memory of Prof. J. K. N. Jones, F.R.S.

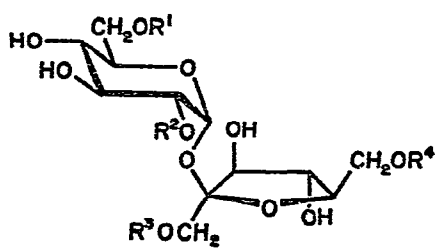
†Part IV in the series "Selective Sulfonylation of Carbohydrates". For a preliminary report, see ref. 1. For part III of this series, see ref. 2.

deduced for a trianhydrosucrose[8,9], was incorrect. The early work was hampered by chromatographic techniques that were inadequate for this class of compounds, but thin-layer chromatography had a great impact in this area. For example, t.l.c. indicates at least a dozen different products from a "tri-*O*-tosylsucrose" preparation. High-pressure liquid chromatography (h.p.l.c.) now facilitates rapid analytical or preparative separations of such mixtures, and is proving to be of wide application, especially in investigations of selective substitution. The other major deterrents to progress in this area were the rather poor yields and the lack of crystallinity of the products. These two factors combined to necessitate the use of chromatography for the preparation of homogeneous products[5,10]. Although 6,6'-di-*O*-*p*-tolylsulfonylsucrose is crystalline[5], column chromatography must still be utilized for its isolation[5,11].

In retrospect, it is somewhat suprising that the use of other sulfonylating reagents was not examined earlier. The present investigation was prompted by the work of Creasey and Guthrie[12], who described some advantages in the use of a "bulky" sulfonyl halide, mesitylenesulfonyl chloride, for selective sulfonylations of polyhydroxy compounds. Since our initial report[1], notes on the use of 2,4,6-triisopropylbenzenesulfonyl chloride[13] and of mesitylenesulfonyl chloride[14] for the preparation of sucrose trisulfonates have appeared*.

DISCUSSION

Trimolar sulfonylation of sucrose with mesitylenesulfonyl chloride in pyridine, followed by conventional processing of the mixture, gave a syrupy mixture of chloroform-soluble products. Dilution with ethyl acetate resulted in rapid crystallization of the trimesitylenesulfonate **1** in >50% yield. This product was suitable for



1 $R^1 = R^3 = R^4$ = mesitylenesulfonyl, R^2 = H

2 $R^1 = R^2 = R^4$ = *p*-toluenesulfonyl, R^3 = H

3 $R^1 = R^3 = R^4$ = *p*-toluenesulfonyl, R^2 = H

*The pentaacetate of **1** has also been prepared; R. D. Guthrie and M. W. Wright, unpublished work (M. W. Wright, D. Phil. Thesis, University of Sussex, 1972).

most subsequent reactions, and minor contaminants were readily removed by recrystallization from ethanol. The ^{13}C-n.m.r. spectrum of **1** is shown in Fig. 1. The absence of signals for hydroxymethyl carbon atoms, which resonate in the 61–63 p.p.m. range, indicated that sulfonylation had occurred, as expected, at the three primary positions. Analysis of the total reaction product by h.p.l.c. (using conditions that separated the tri-*p*-toluenesulfonates **2** and **3**) gave no indication for the presence of an isomeric trimesitylenesulfonate.

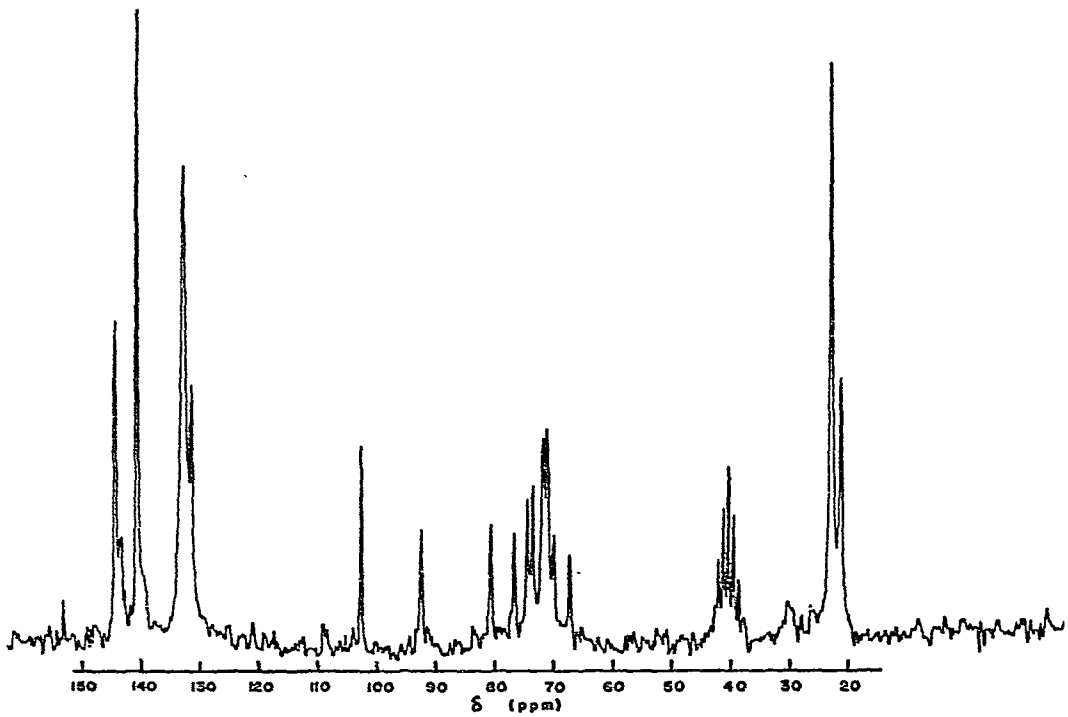


Fig. 1. The ^{13}C-n.m.r. spectrum of the trimesitylenesulfonate **1** in Me_2SO-d_6.

The chloroform-soluble products from a trimolar *p*-toluenesulfonylation of sucrose were fractionated by h.p.l.c. in two stages. In the first, a mixture of two tri-*p*-toluenesulfonates, free from higher- and lower-substituted sulfonates, was obtained. Subsequently, this mixture was completely separated by using a longer column. The partial ^{13}C-n.m.r. spectra of these compounds, showing only the signals due to the sucrose carbon atoms, are shown in Fig. 2. The spectrum (B) of the major isomer, 6,1′,6′-tri-*O*-*p*-tolylsulfonylsucrose (**3**), was almost identical with the corresponding regions in the spectra of **1** and of 6,1′,6′-tri-*O*-(2,4,6-triisopropylbenzenesulfonyl)-sucrose[13].

It has been established[5,11] that the 6 and 6′ hydroxyl groups in sucrose are somewhat more readily sulfonylated than that at the 1′ position; and, among the

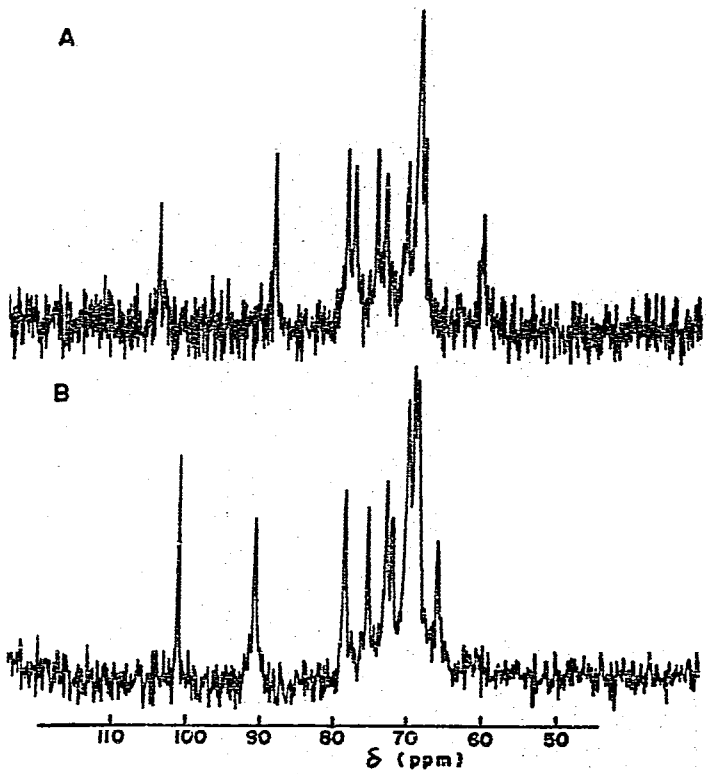
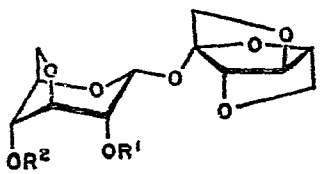
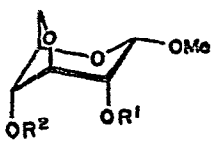


Fig. 2. Partial ^{13}C-n.m.r. spectra of tri-*O*-*p*-tolylsulfonylsucrose isomers in acetone-d_6: A, the 2,6,6′-isomer; B, the 6,1′,6′-isomer.

secondary hydroxyl groups in the α-glucopyranoside ring, that at C-2 is the most reactive toward sulfonylation[15,16]. The most probable structure for the minor isomer therefore seemed to be 2,6,6′-tri-*O*-*p*-tolylsulfonylsucrose (**2**), and the ^{13}C-n.m.r. spectrum (Fig. 2A) supports this assignment. It has been found that sulfonylation[17,18] (and sulfation[19]) of aliphatic hydroxyl groups causes downfield shifts of 6–13 p.p.m. at the α-carbon atoms and *upfield* shifts of 2–3 p.p.m. at β-carbon atoms. In Fig. 2B, the signal for C-2′ at 101.0 p.p.m. is ~3 p.p.m. upfield of the corresponding resonance in Fig. 2A. This difference indicates that the hydroxyl group at C-1′ of the minor isomer is not sulfonylated, and that the signal at 61 p.p.m. in Fig. 2A is that of C-1′. The resonance for the anomeric carbon atom of the glucose ring (namely C-1) is observed at 88.5 p.p.m. in Fig. 2A, and this is 2 p.p.m. upfield from the corresponding resonance in Fig. 2B. This shift indicates that the hydroxyl group at C-2 is sulfonylated in the minor isomer, and this isomer is therefore the 2,6,6′-trisulfonate **2**. Treatment of **3** with alkali afforded the 3,6:1′,4′:3′,6′-trianhydride **4**, but, under similar conditions, compound **2** gave a complex mixture of products that was not further examined.

A solution of the trimesitylenesulfonate **1** in M sodium methoxide was boiled for 30 min under reflux and, after removal of methanol, the residue was acetylated with pyridine and acetic anhydride. These are the conditions used by Lemieux and Barrette[5] for the preparation (in 77% yield from **3**) of the diacetate of a trianhydrosucrose. The yield from **1** was 81%, no evidence for an isomeric product was indicated by t.l.c., and the physical constants were in excellent agreement with those previously reported[5]. It may be significant that the diacetate **5** was obtained[13] in only 17% yield from tri-*O*-(2,4,6-triisopropylbenzenesulfonyl)sucrose, even after boiling in M sodium methoxide for 5.5 h. Displacement of the 2,4,6-triisopropylbenzenesulfonyloxy groups appears to be more difficult than analogous displacements in **1** or **3**.





4 $R^1 = R^2 = H$
5 $R^1 = R^2 = Ac$
6 $R^1 = R^2 = Bz$
7 $R^1 = R^2 = Ts$
8 $R^1 = R^2 = Me$
9 $R^1 = H$, $R^2 = Ac$
10 $R^1 = H$, $R^2 = Bz$
11 $R^1 = Bz$, $R^2 = H$
12 $R^1 = H$, $R^2 = Me$

13 $R^1 = R^2 = H$
14 $R^1 = R^2 = Ac$
15 $R^1 = R^2 = Bz$
16 $R^1 = R^2 = Me$
17 $R^1 = H$, $R^2 = Ac$
18 $R^1 = H$, $R^2 = Me$

Catalytic deacetylation of **5** afforded 3,6:1′,4′:3′,6′-trianhydrosucrose (**4**) in high yield, with physical constants in good agreement with those reported previously[6,10]. Recrystallization of **4** gave a product melting ~30° lower, and this value was in reasonable agreement with that obtained by Lemieux and Barrette[5]. As re-acetylation gave the same diacetate, **5**, and as no difference between the two forms could be detected by ^{13}C or ^1H-n.m.r. spectroscopy, the trianhydride appears to crystallize in two isomorphic forms, and there seems little doubt that the compound obtained by Lemieux and Barrette was 3,6:1′,4′:3′,6′-trianhydrosucrose (**4**). The dibenzoate **6**, the di-*p*-toluenesulfonate **7**, and the dimethyl ether **8** were all obtained crystalline, although melting points, even after repeated recrystallizations, were broad and rather unsatisfactory in this series of compounds. Physical constants for **8** were in fair agreement with those previously reported[9].

TABLE I

^{13}C-N.M.R. CHEMICAL SHIFTS FOR TRIANHYDROSUCROSE DERIVATIVES

Compound	*Chemical shifts on the δ scale*[a]											
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1′*	*C-2′*	*C-3′*	*C-4′*	*C-5′*	*C-6′*
3,6:1′,4′:3′,6′-Trianhydrosucrose (4)	94.5	74.4	74.5	75.9	79.8	72.2	76.8	114.0	86.2	82.4	79.8	75.9
2,4-Di-*O*-acetyl-3,6:1′,4′:3′,6′-trianhydrosucrose (5)	92.5	71.9	73.2	74.4	77.3	71.3	76.4	113.6	85.8	82.1	79.8	75.8
4-*O*-Acetyl-3,6:1′,4′:3′,6′-trianhydrosucrose (9)	94.3	73.2	74.7	75.0	76.9	71.4	76.6	113.7	85.9	82.1	79.7	75.7
3,6:1′,4′:3′,6′-Trianhydro-2,4-di-*O*-benzoylsucrose (6)	93.1	73.0	74.1	75.0	77.4	71.8	76.6	113.8	85.9	82.2	80.0	75.9
3,6:1′,4′:3′,6′-Trianhydro-4-*O*-benzoylsucrose (10)	94.4	73.3	75.3	75.3	77.1	71.8	76.7	113.8	85.9	82.2	79.8	75.8
3,6:1′,4′:3′,6′-Trianhydro-2-*O*-benzoylsucrose (11)	93.0	73.7	74.6	75.1	79.8	71.8	76.5	113.7	85.9	82.2	79.7	75.9
3,6:1′,4′:3′,6′-Trianhydro-2,4-di-*O*-*p*-tolysulfonylsucrose (7)	91.5	77.1	74.3	76.7	76.9	71.6	76.1	113.3	85.8	82.0	79.6	75.8
3,6:1′,4′:3′,6′-Trianhydro-2,4-di-*O*-methylsucrose (8)	94.5	82.5	74.8	82.5	76.6	71.4	76.6	113.4	85.6	81.9	79.5	75.4
3,6:1′,4′:3′,6′-Trianhydro-4-*O*-methylsucrose (12)	94.8	74.2	75.2	84.1	75.8	72.0	76.7	113.7	85.7	82.2	79.8	75.8

[a]Chemical shifts, measured downfield from external Me_4Si, are taken from proton noise-decoupled spectra of solutions in $CDCl_3$. $\delta_{CDCl_3} = 80.5$ p.p.m.

Selective acetylation of **4** with acetic anhydride in pyridine gave, in high yield, a crystalline monoacetate that was shown by ^{1}H-n.m.r. spectroscopy to be the 4-acetate **9**. Selective benzoylation with benzoyl chloride–pyridine was less specific; both monobenzoates were formed and were separated by h.p.l.c. The 2-benzoate **11** was the preponderant isomer but interestingly, attempts to recrystallize **11** resulted in mixtures of **11** and the 4-benzoate **10**. Intramolecular benzoyl-migration thus occurs readily between the 1,3-diaxial hydroxyl groups. In view of the even greater propensity for acetyl groups to migrate, it seems likely that the C-2 hydroxyl group is more readily acylated and that the high yield of **9** is a consequence of acetyl migration.

If these esterifications involve rate-determining attack by the alcohol on an acylpyridinium salt, the higher reactivity of C-2 could be due to an intramolecular hydrogen-bond between O-2 and O-4 that involves the proton from the C-2 hydroxyl group[20].

These preliminary results appear to justify a more-systematic study to elucidate the reaction mechanisms involved. Several derivatives (**14**–**16**) of methyl 3,6-anhydro-α-D-glucopyranoside (**13**) were prepared to aid in spectral assignments of the corresponding trianhydrosucrose derivatives, and it was also found that selective acetylation of **13** was analogous with that of **4**. The 4-*O*-acetyl derivative **17** was formed in good yield and its structure was established by ^{1}H-n.m.r. spectral analysis and by conversion into the known methyl 4-*O*-acetyl-3,6-anhydro-2-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside[21].

Selective methylation of **13** with silver oxide–methyl iodide–acetone is known[22] to give the 4-methyl ether **18**. Under the same conditions, **4** behaved analogously and

TABLE II

^{13}C-N.M.R. CHEMICAL SHIFTS FOR DERIVATIVES OF METHYL 3,6-ANHYDRO-α-D-GLUCOPYRANOSIDE

Compound	*Chemical shifts on the δ scale*[a]						
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*O-1-Me*
Methyl 3,6-anhydro-α-D-glucopyranoside (**13**)	101.8	74.4	74.0	75.8	79.1	72.4	60.5
Methyl 2,4-di-*O*-acetyl-3,6-anhydro-α-D-glucopyranoside (**14**)	100.3	71.7	73.4	74.6	77.0	71.7	61.3
Methyl 4-*O*-acetyl-3,6-anhydro-α-D-glucopyranoside (**17**)	101.3	73.1	74.7	75.3	76.7	71.9	60.8
Methyl 3,6-anhydro-2,4-di-*O*-benzoyl-α-D-glucopyranoside (**15**)	100.5	72.3	74.0	75.1	77.0	72.0	61.2
Methyl 3,6-anhydro-2,4-di-*O*-methyl-α-D-glucopyranoside (**16**)	101.8	81.9	74.5	82.4	75.7	71.6	60.1 (61.3)
Methyl 3,6-anhydro-4-*O*-methyl-α-D-glucopyranoside (**18**)	102.2	73.8	75.1	83.8	75.1	72.2	60.5 (61.4)

[a]See footnote for Table I.

TABLE III

^{1}H-N.M.R. SPECTRAL DATA[a] FOR DERIVATIVES OF TRIANHYDROSUCROSE AND METHYL 3,6-ANHYDRO-α-D-GLUCOPYRANOSIDE

Compound	*Chemical shifts in τ values (First order couplings in parentheses)*[a]								
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6a, 6b*	*H-1'a,1'b*	*H-3',4',5'*	*H-6'a,6'b*
3,6:1',4':3',6'-Trianhydrosucrose (4)	4.16d ($J_{1,2}$ 2.5)	~6.0m	———			5.3–6.1m			———
2,4-Di-*O*-acetyl-3,6:1',4':3',6'-trianhydrosucrose (5)	4.03d ($J_{1,2}$ 3)	4.89m	~5.5m	5.31m	~5.5m	5.75, 6.05m[b] (J_{AB} 11)	6.05, 6.17ABq (J_{AB} 8)	5.4–5.6m	5.94, 6.06ABq (J_{AB} 9)
4-*O*-Acetyl-3,6:1',4':3',6'-trianhydrosucrose (9)	4.12d ($J_{1,2}$ 3)	~6.1m	~5.5m	5.15dd ($J_{3,4}$ 5, $J_{4,5}$ 3)	~5.5m	——— 5.7–6.1m ———		5.4–5.6m	5.7–6.1m
3,6:1',4':3',6'-Trianhydro-2,4-di-*O*-benzoylsucrose (6)	3.84d ($J_{1,2}$ 3.5)	4.67t ($J_{2,3}$ 3.5)	———	5.04m ———	5.23t ($J_{5,6b}$ 3)	5.61, 5.89m[b] (J_{AB} 11)	6.11, 6.23ABq (J_{AB} 8)	5.4–5.6m	5.88, 6.04ABq (J_{AB} 9)
3,6:1',4':3',6'-Trianhydro-4-*O*-benzoylsucrose (10)	4.06d ($J_{1,2}$ 3.5)	~6.1m	~5.3m	4.92dd	~5.4m	——— 5.6–6.1m ———		5.4–5.6m	5.8–6.1m
3,6:1',4':3',6'-Trianhydro-2,4-di-*O*-*p*-tolylsulfonyl-sucrose (7)	4.18d ($J_{1,2}$ 3)	———		5.3–5.8m	———	5.80, 6.07m[b] (J_{AB} 10)	6.37, 6.61ABq (J_{AB} 8)	5.4–5.6m	6.08s
3,6:1',4':3',6'-Trianhydro-2,4-di-*O*-methyl-sucrose (8)	4.10d ($J_{1,2}$ 3)	~6.6m	~5.6m	~5.5m	6.36m	——— 5.7–6.2m ———		5.4–5.6m	5.7–6.2m
3,6:1',4':3',6'-Trianhydro-4-*O*-methylsucrose (12)	4.16d ($J_{1,2}$ 3)	~6.2m	———			5.3–6.2m			———

(*Table continued on p. 157*)

TABLE III (*continued*)

Compound	*Chemical shifts in τ values (First order couplings in parentheses)*[a]								
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6a,*	*H-1'a,1'b*	*H-3',4',5'*	*H-6a,6'b*
Methyl 3,6-anhydro-α-D-glucopyranoside (13)	5.09d ($J_{1,2}$ 3)	6.05m	~5.7m	~5.9m	~5.7m	5.88, 6.04m[b] (J_{AB} 10, $J_{5,6b}$ 3)			
Methyl 2,4-di-*O*-acetyl-3,6-anhydro-α-D-gluco-pyranoside (14)	5.00d ($J_{1,2}$ 3)	4.91m	~5.4m	5.28dd ($J_{3,4}$ 5, $J_{4,5}$ 2.5)	5.45m	5.78, 6.00m[b] (J_{AB} 10.5 $J_{5,6b}$ 2.5)			
Methyl 4-*O*-acetyl-3,6-anhydro-α-D-gluco-pyranoside (17)	5.05d ($J_{1,2}$ 3)	6.15m	5.44t ($J_{2,3}$ 5, $J_{3,4}$ 5)	5.12m	~5.5m	5.81, 6.00m[b] (J_{AB} 11, $J_{5,6b}$ 2.5)			
Methyl 3,6-anhydro-2,4-di-*O*-benzoyl-α-D-gluco-pyranoside (15)	4.83d ($J_{1,2}$ 3.5)	4.64m ($J_{2,3}$ 4.5)	5.14t ($J_{3,4}$ 4.5)	4.97dd ($J_{4,5}$ 2.5)	5.26t ($J_{5,6b}$ 2.5)	5.69, 5.89m[b] (J_{AB} 11)			
Methyl 3,6-anhydro-2,4-di-*O*-methyl-α-D-gluco-pyranoside (16)	5.03d ($J_{1,2}$ 3)	~6.6m	~5.6m	~6.4m	~6.5m	5.83, 6.08m[b] (J_{AB} 10.5, $J_{5,6b}$ 3)			
Methyl 3,6-anhydro-4-*O*-methyl-α-D-gluco-pyranoside (18)	5.06d ($J_{1,2}$ 3)	~6.2m	5.62t ($J_{2,3}$ 5, $J_{3,4}$ 5)	~6.1m	5.48m	5.77, 6.03m[b] (J_{AB} 10, $J_{5,6b}$ 3)			

[a]All values are for solutions in chloroform-*d*; apparent first-order couplings are given in Hz; peak multiplicities: d, doublet; dd, doublet of doublets; m, multiplet; ABq, AB quartet; s, singlet. [b]The AB portion of an ABX system; calculated couplings and chemical shifts are given; in all cases examined, the upfield, exo-proton (6b) is coupled to H-5, the other proton (6a) is not (compare ref. 26).

crystalline 3,6:1′,4′:3′,6′-trianhydro-4-*O*-methylsucrose (**12**) was obtained. When these methylations were monitored by t.l.c., it was found in each instance that monomethylation was complete in less than 2 h, whereas introduction of the second methyl group required several days. A hydrogen bond of the type already discussed would facilitate removal of a proton from the 4-hydroxyl group and may well explain the pronounced differences in reactivities observed under these conditions.

^{13}C-N.m.r. spectral data for the trianhydrosucrose derivatives and for the methyl 3,6-anhydro-α-D-glucopyranoside derivatives are given in Tables I and II respectively. Assignments were facilitated by single-frequency, off-resonance decoupling and by selective, single-frequency, heteronuclear-decoupling techniques[23,24]. The ^{1}H-n.m.r. data for these compounds are summarized in Table III.

EXPERIMENTAL

General methods. — Solutions were concentrated under diminished pressure below 50°. Melting points were determined in glass capillaries with a Thomas–Hoover apparatus and optical rotations were measured with a Thorn-NPL automatic polarimeter equipped with a yellow (sodium) filter and a Bendix Model DR-1 digital readout unit. ^{1}H-N.m.r. spectra were recorded at 100 MHz with a Varian HA-100 spectrometer operating in the frequency-sweep mode with tetramethylsilane as the internal reference. ^{13}C-N.m.r. spectra were obtained on the same instrument equipped with a Digilab FTS/NMR-3HC system using 8-mm sample tubes. High-pressure liquid chromatography (h.p.l.c.) was performed on a Waters Associates ALC-100 chromatograph equipped with a Model 6000 Solvent-Delivery System, a differential-refractometer detector (sensitivity 1×10^{-7} r.i. units) and a fixed-wavelength (254 nm) u.v. detector. Ascending t.l.c. was performed on Silica Gel GF, and developed plates were examined under u.v. light (where appropriate) and then sprayed successively with 1% ethanolic 1-naphthol and with sulfuric acid and then heated. Open-column chromatography was performed on silica gel (70–325 mesh ASTM; E. Merck A.G. Darmstadt, Germany: distributed by Brinkmann Instruments, Inc.)

6,1′,6′-Tri-O-mesitylenesulfonylsucrose (**1**). — A solution of sucrose (34.2 g, 0.1 mol) in dry pyridine (1 liter) was stirred and cooled to −20°. A solution of mesitylenesulfonyl chloride (72.2 g, 0.33 mol) in pyridine (400 ml) was added slowly during 2 h and the temperature was maintained at about −20°. The mixture was stored for 3 days in a freezer (−18°), for 3 days in a refrigerator (4°) and then for 2 days at room temperature. T.l.c. (chloroform–2-propanol, 9:1) then indicated no further change in the products. Most of the pyridine was then evaporated off and the residual syrup was diluted with chloroform. The solution was washed successively with water (twice), cold M sulfuric acid, water, and cold sodium hydrogencarbonate solution. Concentration of the dried (sodium sulfate) solution gave a syrup that was diluted with ethyl acetate (~400 ml). The trimesitylenesulfonate (50 g, 56%), which crystalized readily, contained small amounts of slower- and faster-moving compounds.

Recrystallization from ethanol gave pure **1** having m.p. 131–132°, $[\alpha]_D^{26}$ +42.5° (*c* 2, acetone).

Anal. Calc. for $C_{39}H_{52}O_{17}S_3$: C, 52.69; H, 5.90; S, 10.82. Found: C, 52.37; H, 5.99; S, 10.75.

Trimolar tosylation of sucrose. — A solution of sucrose (3.42 g, 10 mmol) in dry pyridine (90 ml) was stirred and cooled to −20°. Recrystallized *p*-toluenesulfonyl chloride (6.3 g, 33 mmol) in pyridine (20 ml) was added dropwise during 2 h. The mixture was stored for 5 days at 0°, after which time t.l.c. (9:1 chloroform–2-propanol) indicated no further change in the products. Most of the pyridine was removed by evaporation, the residual syrup was taken up in chloroform, and the solution was washed successively with cold M sulfuric acid, sodium hydrogencarbonate solution, and water. Concentration of the dried (sodium sulfate) solution gave a syrup (9.6 g). A portion (25%) of this mixture, dissolved in 9:1 chloroform–2-propanol (4 ml) was fractionated, in two runs, by h.p.l.c. on a 4 ft × 3/8 in. Porasil A column with 9:1 chloroform–2-propanol as the mobile phase and a flow rate of 8 ml/min. This operation afforded a mixture of two isomeric tri-*O*-tosylsucroses (0.77 g, 38%), which were subsequently separated in two runs by using the same conditions but with two 4 ft × 3/8 in. Porasil A columns in series.

Isomer A (0.14 g) was the faster-moving, minor component and was identified by ^{13}C-n.m.r. spectroscopy as the 2,6,6′-isomer (**2**) (see Fig. 2).

Isomer B (0.53 g), the slower-moving, major component was the previously characterized 6,1′,6′-isomer (**3**). Treatment with sodium methoxide [as described next for the preparation of 3,6:1′,4′:3′,6′-trianhydrosucrose (**4**) from **1**], followed by deacetylation, gave the same trianhydride **4**, as shown by ^{13}C-n.m.r. spectroscopy.

2,4-Di-O-acetyl-3,6:1′,4′:3′,6′-trianhydrosucrose (**5**). — A solution of **1** (17.8 g, 20 mmol) in M methanolic sodium methoxide (200 ml) was boiled for 30 min under reflux. Evaporation afforded a partially crystalline residue that was taken up in pyridine (50 ml) and re-evaporated to remove residual methanol. The residue was stirred with pyridine (150 ml), and acetic anhydride (75 ml) was added slowly with intermittent cooling. The mixture was kept overnight at room temperature, after which time, two-dimensional t.l.c., first in ether (to effect separation of the products from pyridine, acetic anhydride, and pyridinium acetate) and then in ethyl acetate, indicated complete acetylation. Water was added to decompose the excess of acetic anhydride and dissolve salts, and the solution was evaporated. The residue was taken up in water and the solution was extracted 4 times with chloroform. Evaporation of the dried (sodium sulfate) extracts afforded a crystalline solid that was recrystallized from ethanol to give **5** (6.0 g, 81%) m.p. 178–182°. After a second recrystallization from ethanol, it had m.p. 180–183°, $[\alpha]_D^{28}$ +129° (*c* 2.0, chloroform). Lemieux and Barrette[5] recorded m.p. 181.5–182.5°, $[\alpha]_D$ +128.6° (*c* 1.8, chloroform) for the diacetate of "trianhydrosucrose II". For n.m.r. data, see Tables I and III.

3,6:1′,4′:3′,6′-Trianhydrosucrose (**4**). — To a solution of **5** (4.0 g) in warm methanol (100 ml) was added M methanolic sodium methoxide (0.1 ml). After 2 days at room temperature, the product had crystallized; yield 2.7 g (87%), m.p. 190.5–

191.5° $[\alpha]_D^{30}$ +130° (*c* 1.0, chloroform), $[\alpha]_D^{25}$ +104° (*c* 1.0, water). Recorded values[8,9] for "trianhydrosucrose II" are m.p. 163–164.5°, $[\alpha]_D$ +117° (*c* 0.92, chloroform); $[\alpha]_D$ +117° (*c* 0.9, water). R. Khan[10] reported m.p. 194–196°, $[\alpha]_D$ +95° (*c* 2.4, water), in good agreement with values first reported by N. W. Isaacs *et al.*[6]. For n.m.r. data, see Tables I and III.

In subsequent preparations of **4**, and during attempts to raise the m.p. of the foregoing preparation, a crystalline product having m.p. 158–162° was obtained. No difference between the two crystalline forms could be detected by ^{13}C or ^1H n.m.r. spectroscopy, and re-acetylation gave a crystalline diacetate, identical (m.p., mixture m.p. and n.m.r. spectroscopy) with **5**.

*3,6:1′,4′:3′,6′-Trianhydro-2,4-di-*O*-benzoylsucrose* (**6**). — To a solution of **4** (0.29 g, 1 mmol) in dry pyridine (5 ml) was added benzoyl chloride (0.5 ml). After 2 h at room temperature, t.l.c. (ethyl acetate) indicated complete conversion of **4** into a single product. Water was added to decompose the excess of benzoyl chloride, and to dissolve pyridinium chloride, and the solution was poured into stirred ice–water. The precipitated dibenzoate (**6**) was collected by filtration, washed with water, and recrystallized from ethanol; yield 0.47 g (96%), m.p. 185–187°. Further recrystallization from ethanol afforded an analytical sample, m.p. 177–190°, $[\alpha]_D^{28}$ +46° (*c* 2.0, chloroform). For n.m.r. data, see Tables I and III.

Anal. Calc. for $C_{26}H_{24}O_{10}$: C, 62.90; H, 4.87. Found: C, 62.65; H, 4.91.

*3,6:1′,4′:3′,6′-Trianhydro-2,4-di-*O-p-*tolylsulfonylsucrose* (**7**). — To a solution of **4** (0.29 g, 1 mmol) in dry pyridine (10 ml) was added *p*-toluenesulfonyl chloride (0.57 g, 3 mmol) and the solution was stored at room temperature. After 3 days, t.l.c. (ethyl acetate) indicated almost complete sulfonylation. Water was added to decompose the excess of sulfonyl chloride, and the solution was poured into ice–water. The precipitated di-*p*-toluenesulfonate (**7**) was collected by filtration and recrystallized from ethanol; yield 0.48 g (80%), m.p. 137–142° (dec.). Three further recrystallizations from methanol (once) and ethanol (twice) gave an analytical sample having m.p. 148–151° (dec.) $[\alpha]_D^{32}$ +75.5° (*c* 1.13, chloroform) (lit.[9] m.p. 164.5–166°). For n.m.r. data, see Tables I and III.

Anal. Calc. for $C_{26}H_{28}O_{12}S_2$: C, 52.34; H, 4.73; S, 10.75. Found: C, 51.95; H, 4.87; S, 10.57.

*3,6:1′,4′:3′,6′-Trianhydro-2,4-di-*O*-methylsucrose* (**8**). — Silver oxide was added to a solution of **4** (0.29 g, 1 mmol) in methyl iodide, and the suspension was boiled under reflux. Several additions of silver oxide were made during 6 days, after which time, t.l.c. (ethyl acetate) indicated one main product (slower moving than **4**). Silver salts were filtered off and extracted several times with boiling chloroform. Evaporation of the combined extracts gave a syrup that crystallized. Recrystallization from ethanol gave **8** (0.20 g, 63%), m.p. 160–166°. Three further recrystallizations from ethanol gave an analytical sample having m.p. 170–178°, $[\alpha]_D^{31}$ +150° (*c* 1.9, chloroform) [lit.[9] m.p. 179–181°, $[\alpha]_D^{24}$ +140° (*c* 1.9, chloroform)]. For n.m.r. data, see Tables I and III.

Anal. Calc. for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 52.93; H, 6.37.

Selective acetylation of **4**. — To a stirred solution of **4** (0.58 g, 2 mmol) in dry pyridine (10 ml), cooled to about −20°, was added acetic anhydride (0.21 ml, 2.2 mmol). The solution was kept for 2 days at −20°, for 2 days at 5°, and for 2 days at room temperature. Evaporation afforded a syrup that was fractionated on a column of silica gel (45 g) eluted first with ether and then with 2:1 ether–ethyl acetate.

Fraction *A* (0.06 g) was mainly the diacetate **5**.

Fraction *B* (0.53 g) was different from **4** and **5** and appeared to be a monoacetate. This fraction crystallized, and recrystallization from ethanol gave a product having m.p. 160–165° (unchanged by further recrystallization), $[\alpha]_D^{26}$ +108° (*c* 1.03, chloroform). The n.m.r. data (Tables I and III) indicated that this product was the 4-acetate **9**.

Anal. Calc. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49. Found: C, 50.77; H, 5.58.

Fraction *C* (0.08 g) was mainly starting trianhydride **4**.

Selective benzoylation of **4**. — To a stirred solution of **4** (0.58 g, 2 mmol) in dry pyridine (10 ml), cooled to about −20°, was added benzoyl chloride (0.25 ml, 2.2 mmol). The solution was allowed to warm to room temperature during ~4 h. Evaporation afforded a syrup that was fractionated on silica gel (50 g) with ether as eluent.

Fraction *A* (0.10 g) was the dibenzoate **6**.

Fraction *B* (0.31 g) was a mixture of **6** and a slightly slower-moving compound. A portion (0.25 g) in chloroform (2 ml) was fractionated by h.p.l.c. on a column of Porasil A (4 ft × 3/8 in.) with 19:1 chloroform–2-propanol as the mobile phase and a flow rate of 2 ml/min. A complete separation of the two components was achieved in 30 min. *Fraction* B_1 (0.14 g) was the dibenzoate **6** and *fraction* B_2 (0.11 g) crystallized and was identified by ^1H n.m.r. (Table III) as the 4-benzoate **10**. Recrystallization from ethanol afforded material having m.p. 141–142° (unchanged by further recrystallization), $[\alpha]_D^{25}$ +87° (*c* 1.0, chloroform). For n.m.r. data, see Tables I and III.

Anal. Calc. for $C_{19}H_{20}O_9$: C, 58.16; H, 5.14. Found: C, 58.02; H, 5.09.

Fraction *C* (0.30 g) crystallized and appeared by ^1H n.m.r. to be the 2-benzoate **11**. Attempts to recrystallize this material led to mixtures of **10** and **11** because of facile intramolecular migration of the benzoyl group, and this compound was therefore not completely characterized. For n.m.r. data, see Tables I and III.

Selective methylation of **4**. — A solution of **4** (0.50 g) in acetone and methyl iodide was boiled under reflux with silver oxide. After 2 h, t.l.c. (9:1 chloroform–2-propanol) indicated the absence of **4** and the formation of one product. The mixture was filtered, silver residues were extracted with acetone (three times), and the combined extracts were evaporated to a syrup that crystallized. Recrystallization from ethanol gave the monomethyl ether **12** (0.32 g, 61%), m.p. 125–129° (unchanged by further recrystallization), $[\alpha]_D^{31}$ +107° (*c* 1.0, chloroform). For n.m.r. data, see Tables I and III.

Anal. Calc. for $C_{13}H_{18}O_8$: C, 51.66; H, 6.00. Found: C, 51.50; H, 6.05.

*Preparation of derivatives of methyl 3,6-anhydro-α-*D*-glucopyranoside.* — The following known compounds were prepared by standard procedures for spectral

analysis and comparison with the corresponding trianhydrosucrose derivatives. Methyl 3,6-anhydro-α-D-glucopyranoside[22] (**13**), m.p. 107–108.5°, $[\alpha]_D^{31}$ +51° (*c* 1.2, water); methyl 2,4-di-*O*-acetyl-3,6-anhydro-α-D-glucopyranoside[21] (**14**), m.p. 134.5–136°, $[\alpha]_D^{29}$ +106° (*c* 1.0, chloroform); methyl 3,6-anhydro-2,4-di-*O*-methyl-α-D-glucopyranoside[22] (**16**), $[\alpha]_D^{30}$ +48° (*c* 1.0, water); and methyl 3,6-anhydro-4-*O*-methyl-α-D-glucopyranoside[22] (**18**) m.p. 148–152°, $[\alpha]_D^{31}$ +22° (*c* 1.2, water).

Methyl 3,6-anhydro-2,4-di-O-benzoyl-α-D-glucopyranoside (**15**). — To a solution of **13** (0.70 g) in pyridine (20 ml) was added benzoyl chloride (2 ml) and the solution was kept overnight at room temperature. Water was added to dissolve pyridinium chloride and decompose the excess of benzoyl chloride, and the solution was poured into stirred ice–water. The precipitate was collected by filtration, washed with water, and crystallized from ethanol to give **15** (0.60 g) m.p. 70–73° (unchanged by further recrystallization), $[\alpha]_D^{30}$ +19.3° (*c* 1.4, chloroform). For n.m.r. data, see Tables II and III.

Anal. Calc. for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24. Found: C, 65.43; H, 5.37.

Selective acetylation of **13**. — A solution of **13** (0.70 g, 4 mmol) in dry pyridine (20 ml) was cooled to −20°. Acetic anhydride (0.42 ml, 4.5 mmol) was added dropwise to the stirred solution and the mixture was stored overnight (17 h) at −20° and then for 1 day at 5°. T.l.c. (ether or ethyl acetate) indicated a mixture, the major component of which had an R_F value intermediate between those of **13** and the diacetate **14**. Evaporation afforded a syrup that was fractionated on silica gel (50 g), with ether as eluent.

Fraction *A* (0.38 g) was a mixture of **14**, the major product, and a third component.

Fraction *B* (0.31 g) was the major product. This fraction crystallized, and recrystallization from ether afforded pure material having m.p. 98–99° (unchanged by further recrystallization), $[\alpha]_D^{27}$ +49° (*c* 1.35, chloroform). The n.m.r. data (Tables I and III) indicated that this was the 4-acetate **17**.

Anal. Calc. for $C_9H_{14}O_6$: C, 49.54; H, 6.47. Found: C, 49.13; H, 6.52.

Treatment of **17** with *p*-toluenesulfonyl chloride in pyridine resulted in slow sulfonylation, which was complete after 1 week. Pyridine was removed by evaporation and the residue was chromatographed on silica gel. The product crystallized and, after recrystallization from ethanol, had m.p. 161–161.5°, $[\alpha]_D^{29}$ +73° (*c* 0.92, chloroform). Wolfrom *et al.*[21] gave m.p. 162°, $[\alpha]_D^{21}$ +70° (*c* 1, chloroform) for methyl 4-*O*-acetyl-3,6-anhydro-2-*O*-*p*-tolysulfonyl-α-D-glucopyranoside.

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