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Note

Identification of anhydrosucrose derivatives formed by Mitsunobu chlorination of sucrose*

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The Mitsunobu reaction applied to alcohols allows their conversion into their corresponding halides[3] with inversion of configuration[4]. The use of the triphenyl phosphine (TPP)–diethyl azodicarboxylate (DEAD) system for sucrose yields derivatives of "sucrose 3′,4′-epoxide" (α-D-glucopyranosyl 3,4-anhydro-β-D-tagatofuranoside[5]), and this type of epoxide was also observed in the synthesis of amino derivatives of sucrose[2]. Very recently, the formation of 3′,6′-anhydrosucrose as a by-product of the Mitsunobu dehydration of sucrose has been reported[6]; this prompted us to summarize similar results on the chlorination of sucrose using the same methodology as for the direct synthesis of chlorosucroses[7].

Treatment of sucrose (**1**) in *N*,*N*-dimethylformamide with 11 equivalents of the system diisopropyl azodicarboxylate–triphenylphosphine–zinc chloride–bis(pyridine) complex during 20 h gave, in 15% yield, the chlorosucrose epoxide **2** after acetylation. In contrast, the use of 22 equivalents of the reagent gave, after acetylation, 1′,4′:3′,6′-dianhydro-6-chloro-6-deoxysucrose (**3**) after 5 h of treatment. Only 16% of this dianhydrosucrose derivative has been isolated after complete transformation of **1**.

The ^{1}H-n.m.r. and ^{13}C-n.m.r. spectra of compounds **2** and **3** (see Tables I and II) are consistent with the values reported[5,6] for the non-chlorinated anhydro derivatives of sucrose. The chlorination of C-6 is clearly demonstrated by the upfield shift of the ^{13}C-n.m.r. signal for C-6 by 18 p.p.m. relative to the corresponding signal for the parent acetylated sucrose. The ^{1}H-n.m.r. data also show an upfield shift, for H-6a and H-6b, by 1 p.p.m. relative to the 6-*O*-acylated anhydrosucroses.

The formation of **3** involves nucleophilic displacement of both of the D-fructosyl primary hydroxyl groups by the secondary ones at C-3′ and C-4′. This observation confirmed the results[6] of Guthrie's group and shows the competition,

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TABLE I

^{1}H-N.M.R. DATA (350 MHz, C_6D_6) FOR COMPOUNDS **2** AND **3**

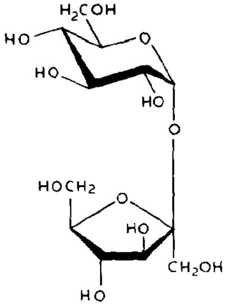
Compound	*Chemical shifts (δ scale)*													
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6a*	*H-6b*	*H-1'a*	*H-1'b*	*H-3'*	*H-4'*	*H-5'*	*H-6'a*	*H-6'b*
2	6.21	4.99	5.85	5.07	4.36	3.44	3.33	4.01	4.01	3.51	2.97	3.61	4.20	4.15
3	6.36	5.05	5.82	5.14	4.12	3.45	3.39	3.71	3.63	3.83	3.25	4.42	3.94	3.96
	J Values (Hz)													
	1,2	*2,3*	*3,4*	*4,5*	*5,6a*	*5,6b*	*6a,6b*	*1'a,1'b*	*3',4'*	*4',5'*	*5',6'a*	*5',6'b*	*6'a,6'b*	
2	3.8	10.3	9.4	10.3	2.6	7.5	12	0	3.0	0	6.0	4.8	11.8	
3	3.9	10.3	8.5	10.3	2.6	6.9	11.8	7.7	8.6	0	0	3.4	6.7	

TABLE II

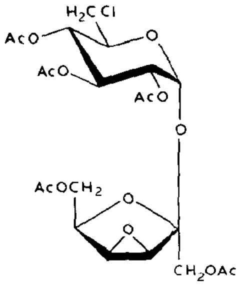
^{13}C-N.M.R. DATA (87.9 MHz, C_6D_6) FOR COMPOUNDS **2** AND 3

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1'*	*C-2'*	*C-3'*	*C-4'*	*C-5'*	*C-6'*
2	90.0	71.0	70.1	71.0	71.0	44.0	65.2	103.0	56.2	54.4	75.0	62.4
3	90.3	70.8	70.7	70.7	69.6	43.7	72.9[a]	110.5	82.8[b]	79.0[b]	76.9[b]	72.0[a]

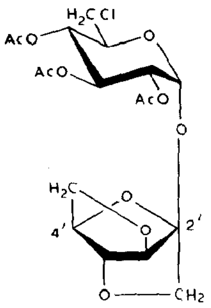
[a,b]Assignments may have to be reversed.



1



2



3

in sucrochemistry, between intramolecular dehydrations and nucleophilic substitutions under Mitsunobu conditions.

EXPERIMENTAL

General methods. — Optical rotations were measured with a Perkin–Elmer 241 polarimeter. ^{1}H-n.m.r. and ^{13}C-n.m.r. spectra were recorded for solutions in C_6D_6 (internal Me_4Si) with a CAMECA 350 instrument. Column chromatography was conducted on Kieselgel 60 (230–400 mesh, Merck).

2,3,4-Tri-O-acetyl-6-chloro-6-deoxy-α-D-glucopyranosyl 1,6-di-O-acetyl-3,4-anhydro-β-D-tagatofuranoside (**2**). — To an ice-cold solution of sucrose (0.5 g, 1.5 mmol), zinc chloride–bis(pyridine)[3] (2.5 g, 8.5 mmol), and triphenylphosphine (4.4 g, 16.8 mmol) in *N,N*-dimethylformamide (25 mL) was added dropwise, with stirring, diisopropyl azodicarboxylate (3.1 mL, 16.5 mmol). The mixture was then stirred for 20 h at room temperature, water (5 mL) was added to quench the reaction, and the solution was evaporated under diminished pressure. The resulting oil was partitioned between water and dichloromethane. The organic layer was extracted several times with water, the aqueous fractions were combined, and evaporated to dryness, and the residue was acetylated. After normal work-up, flash chromatography (ether) afforded **2** (0.120 g, 15%); $[\alpha]_D$ +65.6° (*c* 0.5, chloroform). For n.m.r. data, see Tables I and II.

Anal. Calc. for $C_{22}H_{29}ClO_{14}$: C, 47.79; H, 5.29. Found: C, 47.65; H, 5.41.

*1,4:3,6-Dianhydro-β-*D*-fructofuranosyl 2,3,4-tri-*O*-acetyl-6-chloro-6-deoxy-α-*D*-glucopyranoside* (**3**). — To an ice-cold solution of sucrose (0.5 g, 1.5 mmol), zinc chloride–bis(pyridine) (5 g, 17 mmol), and triphenylphosphine (8.8 g, 34 mmol) in *N,N*-dimethylformamide (25 mL) was added dropwise, with stirring, diisopropyl azodicarboxylate (6.2 mL, 34 mmol). The mixture was stirred for 5 h at room temperature, water (5 mL) was added, and the solution was evaporated; the residue was dissolved in pyridine and acetylated under the usual conditions. After normal work-up, flash chromatography (ether) gave **3** (0.115 g, 16.5%); $[\alpha]_D$ 104° (*c* 0.5, chloroform). For n.m.r. data, see Tables I and II.

Anal. Calc. for $C_{18}H_{23}ClO_{11}$: C, 47.96; H, 5.14. Found: C, 48.11; H, 5.30.

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