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Note

The preparation of 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 6-chloro-6-deoxy-β-D-fructofuranoside 1′,2,3,3′,4′-pentachlorosulphate

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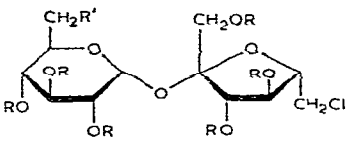
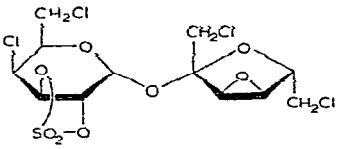
The reaction of sucrose with sulphuryl chloride was first studied by Jones and his co-workers[1] and extended by Hough and his co-workers[2]. Thus, reaction of sucrose with sulphuryl chloride (*a*) at −78°, followed by removal of the chlorosulphate groups, (*b*) at room temperature, and (*c*) at 50° resulted, after chromatography of the reaction mixtures, in the isolation of the following products: (*a*) **1** and **2**, (*b*) **4**, and (*c*) **4**, **5**, and **6**.



1 R′ = OH, R = H
2 R′ = Cl, R = H
3 R′ = Cl, R = Ac



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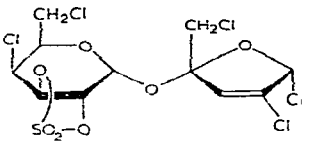

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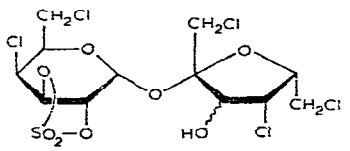

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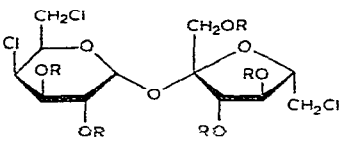


7 R = H
8 R = SO_2Cl
9 R = Ac

Recently, Hough *et al.*[3] have re-investigated this reaction in order to find optimal conditions for the direct preparation of di- and tri-chlorinated derivatives. Thus, reaction initially at −78° and then at −30 to −35° for 4 days afforded **3** in 15% yield after dechlorosulphation and acetylation of the reaction mixture, whereas a similar reaction at −5 to −10° for 16 h afforded **7** in 30% yield after dechlorosulphation. We now report on an improved chlorosulphation procedure, and the

direct isolation and characterization of a crystalline "trichlorosucrose pentachlorosulphate".

The reaction of carbohydrates with sulphuryl chloride is usually carried out by the dropwise addition of sulphuryl chloride to a cooled (−78°) solution or suspension of the carbohydrate in pyridine–chloroform[4]. Sucrose, which is sparingly soluble in this solvent system, tends to give low yields and a large number of products[2]. Increasing the volume of pyridine in order to increase the amount of sucrose in solution leads to conditions which favour the formation of undesirable cyclic sulphate derivatives. The formation of cyclic sulphates can be avoided if the temperature of the reaction is carefully controlled (usually below 0°) or if the pyridine–sulphuryl chloride ratio is maintained at 1.5–2 mol/mol. In an attempt to obtain improved yields, the sucrose–pyridine mixture was not diluted with chloroform. Instead, a solution of sulphuryl chloride in chloroform was added dropwise to the cooled (−78°) sucrose–pyridine mixture. The reaction was maintained below 0° for 4 h and finally allowed to stand at room temperature for 16 h, after which time t.l.c. revealed the presence of a single, major product (*B*) which was obtained crystalline and in 50% yield without recourse to chromatography.

B gave a positive test for chlorosulphate ester[5] and showed two characteristic, strong i.r. absorptions at 1407 and 1187 cm^{-1} for chlorosulphate ester[4]. Elemental analysis of *B* showed it to be a "trichlorosucrose pentachlorosulphate".

In the ^{1}H-n.m.r. spectrum of *B* (Table I), H-4 appears as a narrow, double doublet (τ 4.97) with coupling constants 2.7 and 1.3 Hz, indicating that the hexopyranosyl ring possesses the expected *galacto* configuration[6]. The H-2 and H-3 signals appear as a pair of overlapped doublets ($J_{1,2}$ 2.7 Hz; $J_{3,4}$ 2.7 Hz). The n.m.r. assignments for H-1,2,3,4 were confirmed by spin-decoupling experiments. In the ^{1}H-n.m.r. spectrum of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-dichlorosulphate (**10**) (Table I) and similar compounds[2,7,8] possessing the *galacto*

TABLE I

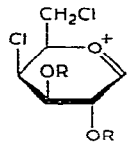
^{1}H-N.M.R. PARAMETERS[a]

Compound	**8**	**10**		**8**	**10**
H-1	3.70(d)	4.68–4.77(m)	$J_{1,2}$	2.7	3.0
H-2	4.68(d)	4.84(dd)	$J_{2,3}$	~0	9.5
H-3	4.64(d)	4.55(dd)	$J_{3,4}$	2.7	3.0
H-4	4.97(dd)	5.09(dd)	$J_{4,5}$	1.3	1.5
H-5	5.11–5.59(m)	5.66(cm)			
H-6a,b	6.24(d)	6.28(d)	$J_{5,6}$	~7.0	~6.7
H-1′a,b	5.11–5.59(m)		$J_{3',4'}$	1.0	
H-3′	4.31(d)		$J_{4',5'}$	7.0	
H-4′	4.27(q)				
H-5′	5.11–5.59(m)				
H-6′a,b	5.83–6.08(m)				

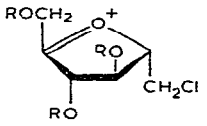
[a]First-order chemical shifts (τ values) and coupling constants at 60 MHz in $CDCl_3$. Key: d, doublet; dd, double doublet; q, quartet; m, multiplet; cm, complex multiplet.

configuration, H-2 and H-3 appear as a pair of strongly coupled, double doublets.

The mass spectrum of *B* showed two major ions at high mass, *m/e* 395 and 475, corresponding to ions *C* and *D* formed by the expected[2] cleavage of the interglycosidic bonds. Ion *C* was associated with three other ions at 397, 399, and 401, while *D* was associated with ions at 497, 499, and 501, each in the approximate ratios 20:26:13:3 indicative of the presence of four chlorine atoms in each ion. The mass spectrum of the derived acetate **9** showed ions at *m/e* 283 and 307, corresponding to ions *E* and *F* formed by the usual cleavage of the two glycosidic bonds. Ions *E* and *F* underwent further fragmentation as previously reported[3]. Thus, on the above evidence, *B* is assigned the structure 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 6-chloro-6-deoxy-β-D-fructofuranoside 1′,2,3,3′,4′-pentachlorosulphate (**8**).



C R = SO_2Cl (*m/e* 395)
E R = Ac (*m/e* 283)



D R = SO_2Cl (*m/e* 475)
F R = Ac (*m/e* 307)

Further confirmation of the structure of **8** was obtained from the derived dechlorosulphated product **7**, the physical constants of which were in agreement with those of 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 6-chloro-6-deoxy-β-D-fructofuranoside[3].

An attempt to synthesize the 1′,4,6′,6-tetrachloro-1′,4,6′,6-tetradeoxy derivative by effecting chloro substitution of the 1′-chlorosulphonyloxy group in **8** with pyridinium chloride in chloroform at 50° was not successful. The complex mixture of products obtained did not appear to contain any single, major product and was not further investigated.

EXPERIMENTAL

Evaporations were carried out at below 50° under diminished pressure. T.l.c. was performed with Silica Gel G as absorbent. The developed plates were sprayed with the aniline–pyridine reagent[5] for ester chlorosulphate, or with 10% ethanolic sulphuric acid, followed by charring on a hot plate. Optical rotations were measured with a Perkin–Elmer 141 polarimeter. N.m.r. spectra were measured on a Perkin–Elmer R-12 spectrometer. Mass spectra were determined with an A.E.I. MS-30 spectrometer at 70 eV. I.r. spectra were recorded on a Beckman I.R. 8 spectrophotometer.

4,6-Dichloro-4,6-dideoxy-α-D-galactopyranosyl 6-chloro-6-deoxy-β-D-fructofuranoside 1′,2,3,3′,4′-pentachlorosulphate (**8**). — Sulphuryl chloride (39 ml) in chloroform (100 ml) was added dropwise to a cooled (−78°), vigorously stirred solution of

sucrose (3 g) in pyridine (60 ml). After 2 h at −78°, the mixture was kept at 0° for a further 2 h, after which it was allowed to stand at room temperature for 16 h. The reaction mixture was poured into 10% sulphuric acid and worked up in the usual way to afford a pale-yellow syrup (4.6 g, 59%) which crystallised when triturated with ether. Recrystallisation from methanol afforded **8** as large crystals (3.85 g, 50%), m.p. 149–150°, $[\alpha]_D^{25}$ +77.3° (*c* 1.2, chloroform), ν_{max}^{KBr} 1407 and 1187 cm^{-1} (OSO_2Cl) (Found: C, 16.37; H, 1.53; S, 15.73; Cl, 32.35. $C_{12}H_{14}Cl_8O_{18}S_5$ calc.: C, 16.18; H, 1.57; S, 17.97; Cl, 31.91%). Mass spectrum [*a* indicates a 3:1 doublet (1 Cl), *b* a 9:6:1 triplet (2 Cl), *c* a 27:27:9:1 quartet (3 Cl), and *d* a 20:26:13:3 quartet (4 Cl)]: *m/e* 475*d* (5), 395*d* (14), 359*c* (10), 279*c* (45), 261*b* (52), 250*c* (18), 197*b* (22), 181*b* (30), 145 (16), 109 (8), 75 (32), 64 (88), 48 (46), 43 (52), and 36*a* (100).

Dechlorosulphation of **8** with sodium iodide in methanol, in the usual way[9], afforded **7** as a syrup, $[\alpha]_D^{25}$ +82.0° (*c* 0.6, methanol); lit.[3] m.p. 115–115°, $[\alpha]_D$ +88° (*c* 1.0, methanol). The infrared spectrum and t.l.c. mobility of **7** were identical with those of an authentic sample.

Acetylation of **7** with pyridine–acetic anhydride afforded the acetate **9** as a syrup, $[\alpha]_D^{25}$ +82.2° (*c* 3.1, methanol); lit.[3] $[\alpha]_D$ +90.3° (*c* 1.0, methanol). The infrared spectrum of **9** was identical with that of an authentic sample.

ACKNOWLEDGMENT

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