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SYNTHESIS OF AN INTENSELY SWEET CHLORODEOXYSUCROSE: MECHANISM OF 4′-CHLORINATION OF SUCROSE BY SULPHURYL CHLORIDE

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ABSTRACT

Reaction of 6-*O*-acetylsucrose[1] with sulphuryl chloride in chloroform–pyridine affords, after dechlorosulphation and acetylation, a mixture of two isomeric 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-hexulofuranosides (**6** and **7**) and 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3,4-di-*O*-acetyl-1,6-dichloro-1,6-dideoxy-β-D-fructofuranoside (**4**). Chlorination of C-4, C-1′, and C-6′ occurs by direct displacement of the initially formed chlorosulphonyloxy groups by chloride ions, but displacement of the 4′-chlorosulphate is sterically hindered. The introduction of a 4′-chloro substituent involves ring opening of intermediate 3′,4′-epoxides by chloride ions, the *ribo*-epoxide producing the *sorbo*-isomer **6** and the *lyxo*-epoxide giving the *fructo*-isomer **7**. The proposed mechanism is supported by the formation of 4-chloro-4-deoxyfructofuranosides when 3′,4′-*lyxo*-hexulofuranosides are treated with sulphuryl chloride under the same conditions.

INTRODUCTION

The introduction of chlorine substituents at certain positions of the sucrose molecule has a profound effect upon the sweetness of the disaccharide which may be increased by several hundred times[2–4]. Studies of the structure–sweetness activity relationship in these chlorodeoxy derivatives[3] suggested that the chlorine substituents at C-4 of the glucopyranosyl unit and C-1 and C-6 of the fructofuranosyl unit are essential for the intense sweetness. However, these studies have been limited to compounds having a chlorine substituent at one or more of the C-4,6,1′,2′,6′ positions. 4′-Chloro-4′-deoxy derivatives have so far not been reported and the synthesis of such compounds is now described.

Recent studies[5] hinted that direct 4′-chlorination of sucrose may be effected using sulphuryl chloride. 4′-Chloro-4′-deoxy derivatives have been reported[5], but in low yields. Moreover, the method caused chemical modifications at other positions. An alternative and more efficient method for 4′-chlorination of sucrose and the synthesis of 4-chloro-4-deoxy-α-D-galactopyranosyl 1,4,6-trichloro-1,4,6-trideoxy-

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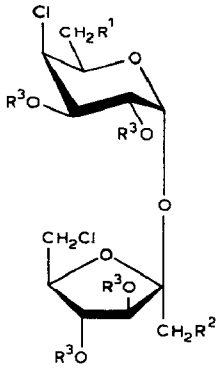
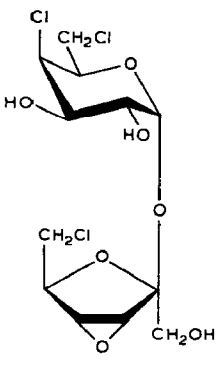
β-D-hexulofuranosides are now reported.

RESULTS AND DISCUSSION

The reactions of sulphuryl chloride with carbohydrates have been widely studied[6,7]. Sucrose generally gives complex mixtures but, under controlled conditions, 6′-chloro, 6,6′-dichloro, and 4,6,6′-trichloro derivatives could be obtained in good yields[5,8,9]. Direct C-1′-chlorination of sucrose is difficult because this position is hindered and is adjacent to the anomeric group. However, when sucrose was treated with 14 mol of sulphuryl chloride in a minimal proportion of pyridine, initially at −50° and then at 50°, in the absence of air, C-1′-chlorination occurred smoothly to produce 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 1,6-dichloro-1,6-dideoxy-β-D-fructofuranoside (**1**, 45%), 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 3,4-anhydro-6-chloro-6-deoxy-β-D-*ribo*-hexulofuranoside (**2**, 22%), and 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 6-chloro-6-deoxy-β-D-fructofuranoside (**3**, 11%). The structures of these compounds were assigned on the basis of their n.m.r. and mass-spectral data and, for **1** and **3**, by comparison with authentic samples. The ^{1}H-n.m.r. spectrum of trichloroacetylated **2** contained three high-field NH singlets indicating the presence of three hydroxyl groups in **2**. The pattern of the H-3′,4′ resonances and their chemical shifts were typical of protons attached to an oxirane ring which was fused to a larger ring[5,10–12]. The $J_{3',4'}$ (2.5 Hz) and $J_{4',5'}$ (1.0 Hz) values were similar to those for a 3′,4′-*ribo*-epoxide of sucrose; the corresponding *lyxo*-epimer has[12] a $J_{4',5'}$ value of 0.5 Hz. Accordingly, the hexulofuranosyl ring in **2** was assigned the *ribo* configuration. The resonances due to H-1,2,3,4,5 were consistent with the hexopyranosyl ring having the expected *galacto* configuration.



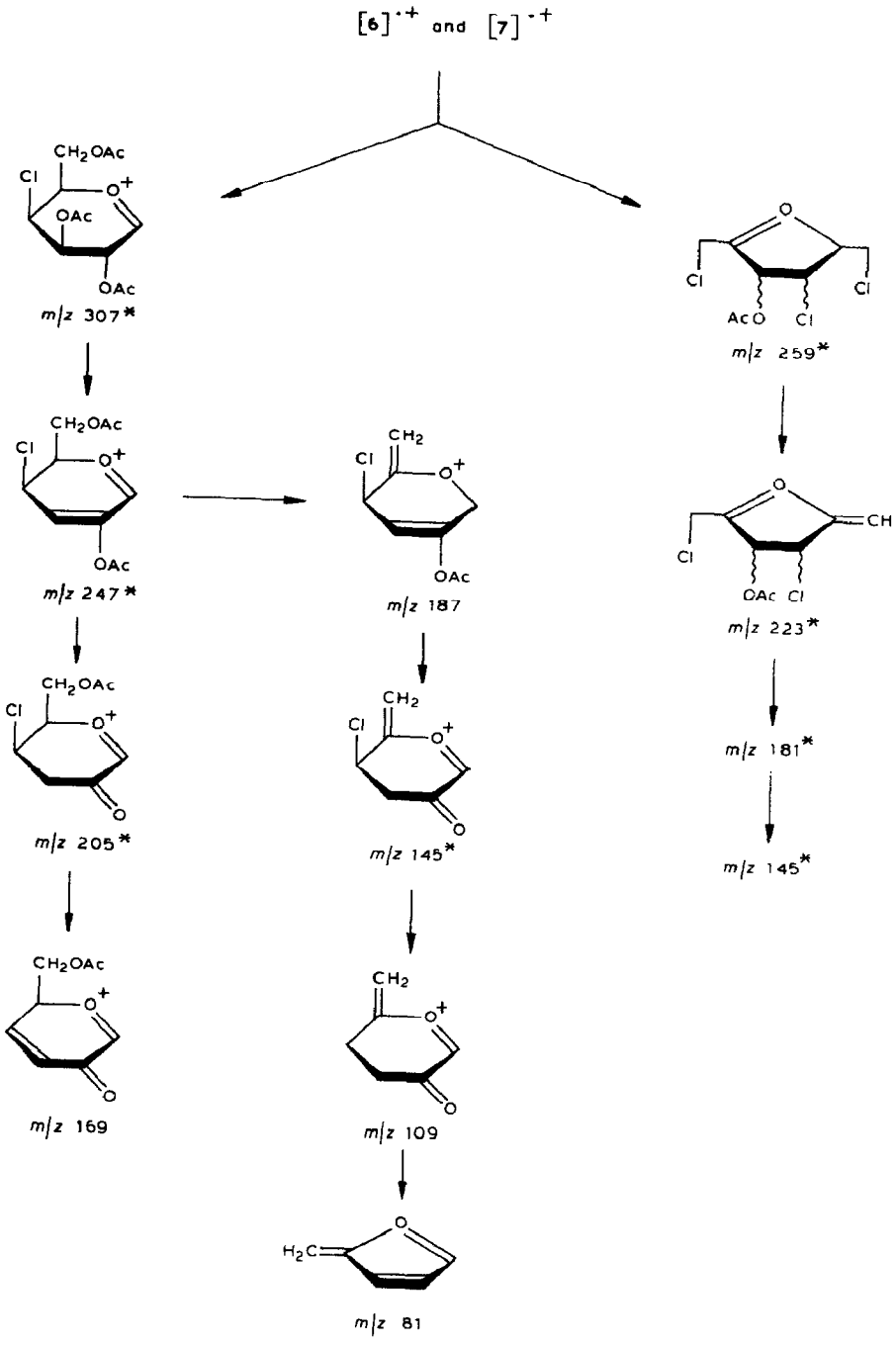
1 $R^1 = R^2 = Cl, R^3 = H$
3 $R^1 = Cl, R^2 = OH, R^3 = H$
4 $R^1 = OAc, R^2 = Cl, R^3 = Ac$
5 $R^1 = OH, R^2 = Cl, R^3 = H$



2

The formation of 4′-chloro-4′-deoxy derivatives has been reported from a reaction of sucrose with sulphuryl chloride but in very low yields, and they also contained a 2,3-cyclic sulphate. Ballard *et al.*[5] isolated 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 1,4,6-trichloro-1,3,4,6-tetradeoxy-β-D-*glycero*-hex-3-enofuranoside 2,3-sulphate (3%) and 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 1,4,6-trichloro-1,4,6-trideoxy-β-D-hexulofuranoside 2,3-sulphate (2%) after treating sucrose with sulphuryl chloride in pyridine at 50°. The formation of the 2,3-cyclic sulphate group was probably due to the large excess of pyridine used in the reaction[13]. Thus, it should be possible to use sulphuryl chloride to effect 4′-chlorination of sucrose without 2,3-sulphation. When 6-*O*-acetylsucrose[1] was treated with sulphuryl chloride in chloroform–pyridine (1:1) as described above, the product mixture, after dechlorosulphation, contained (t.l.c.) 3 major (fast) and several minor (slow) products. Prolonged heating at 50° decreased the proportion of the slowest moving compound and increased those of the two faster moving components. Chromatography of the acetylated mixture gave, as the slowest moving component, 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3,4-di-*O*-acetyl-1,6-dichloro-1,6-dideoxy-β-D-fructofuranoside (**4**, 11%). The two faster moving components (46%) had similar mobilities and could not be separated by chromatography. However, they gave two different (large) crystal forms (**A** and **B**) which could be separated by hand, purified by recrystallisation, and shown to be 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-sorbofuranoside (**6**) and 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-fructofuranoside (**7**), respectively, on the basis of their n.m.r., mass-spectral, and X-ray crystallographic data. The mass spectra of **6** and **7** were very similar and contained fragment ions corresponding to oxycarboniums at *m/z* 307 and 259. Accurate mass measurement indicated the former to be $C_{12}H_{16}ClO_7$ (*m/z* 307:309, 3:1 doublet) and the latter to be $C_8H_{10}Cl_3O_3$ (*m/z* 259:261:263:265, 27:27:9:1 quartet). Subsequent fragmentation occurred with loss of HCl, acetic acid, and ketene (Scheme 1).

The structure of the slightly faster moving compound **A** could not be obtained by X-ray diffraction since crystallisation produced twinned crystals. The ^{1}H-n.m.r. spectrum of **A** contained resonances due to H-1,2,3,4 that were consistent with the hexopyranosyl ring having the *galacto* configuration. The H-3′ signal of the hexulofuranosyl ring was at δ 5.63 ($J_{3',4'}$ 2.0 Hz) and that for H-4′ (δ 4.97, dd, $J_{4',5'}$ 9.0 Hz) was shifted upfield by ~1.2 p.p.m. That C-4′ carried a chlorine substituent was also indicated by the ^{13}C-n.m.r. spectral data of deacetylated **A** (**8**, Table I). An upfield shift of the C-4′ resonance of ~14 p.p.m. with respect to that for sucrose and ~15 p.p.m. with respect to that for 4-chloro-4-deoxy-α-D-galactopyranosyl 1,6-dichloro-1,6-dideoxy-β-D-fructofuranoside (**5**) was observed. The $J_{3',4'}$ and $J_{4',5'}$ values suggested H-3′,4′ to be *trans* and H-4′,5′ to be *cis*. The large $J_{4',5'}$ value is consistent with a nearly eclipsed arrangement of H-4′,5′, whereas the $J_{3',4'}$ value (2.0 Hz) corresponds to a dihedral angle of ~100° for H-3′,4′, suggesting that the hexulofuranosyl ring has the E_2 conformation. Hence, the chiralities of C-3′ and



Scheme 1. Fragmentation pattern of the 4,1′,4′,6′-tetrachloro-4-1′,4′,6′-tetradeoxy derivatives **6** and **7** (*mass based on ^{35}Cl).

TABLE I

^{13}C-N.M.R. CHEMICAL SHIFTS[a] (P.P.M.) FOR SOLUTIONS IN D_2O

Atom	*Sucrose*[b]	**5**	**8**	**9**
C-1	92.2	93.5	94.7	93.1
C-2	71.9	68.4	68.9	68.1
C-3	73.5	68.8	69.1	68.5
C-4	70.1	63.8	64.1	63.4
C-5	73.2	71.4	71.3	71.0
C-6	61.2	62.2	62.7	61.8
C-1′	63.3	45.6	44.3	44.3
C-2′	104.4	104.1	103.7	103.7
C-3′	77.4	76.9	74.2	77.7
C-4′	74.8	76.1	61.2	59.4
C-5′	82.2	81.9	80.9	82.5
C-6′	62.5	44.4	44.0	44.0

[a]P.p.m. downfield from DSS. [b]Ref. 31.

C-4′ were those of a sorbofuranoside. The compound could not have the tagatofuranose configuration since this would have a *cis,cis* arrangement of H-3′,4′,5′ and large $J_{3',4'}$ and $J_{4',5'}$ values would be expected. The structure **6** was, therefore, proposed for compound **A**.

The slightly slower moving compound **(B)** was also a tetrachloro derivative, and its mass spectrum indicated the presence of a hexopyranosyl ring with one chlorine substituent and a hexulofuranosyl ring with three chlorine substituents. The ^{1}H-n.m.r. spectrum of **B** contained resonances for H-1,2,3,4 that were consistent with the expected galactopyranose configuration. The resonance due to H-3′ (δ 5.61, $J_{3',4'}$ 5.5 Hz) of the hexulofuranosyl ring was typical for C-3′ carrying an acetoxyl group. The H-4′ signal (δ 5.00, t, $J_{4',5'}$ 4.0 Hz) was shifted upfield by ~0.4 p.p.m. relative to that of the corresponding proton in sucrose octa-acetate, indicating that the chlorine substituent was located at C-4′. This inference was also supported by the ^{13}C-n.m.r. spectrum of deacetylated **B** (**9**, Table I). The C-4′ resonance was observed to have shifted upfield by ~15 p.p.m. with respect to that for sucrose and by ~17 p.p.m. with respect to that for 4-chloro-4-deoxy-α-D-galactopyranosyl 1,6-dichloro-1,6-dideoxy-β-D-fructofuranoside (**5**). The ^{1}H-n.m.r. $J_{3',4'}$ and $J_{4',5'}$ values were clearly consistent with the fructofuranosyl configuration, and related data have been reported for other sucrose derivatives[8,14–24] and for 4′-chloro-4′-deoxysucrose hepta-acetate[25].

On the basis of the Karplus equation[26], the dihedral angles $\Phi_{3',4'}$ and $\Phi_{4',5'}$ of **B** were ~142° and ~133°, respectively, suggesting that the fructofuranosyl unit of compound **B** also has an E_2 or related skew conformation in which the hydroxymethyl group at C-2 and the 3- and 4-substituents were pseudo-equatorial. In such a conformation, which has been reported[24,27] also for methyl β-D-fructofuranoside, the anomeric substituent will be pseudo-axial, thereby satisfying the anomeric effect[28]. X-Ray diffraction measurement of a single crystal of the tetra-acetate gave

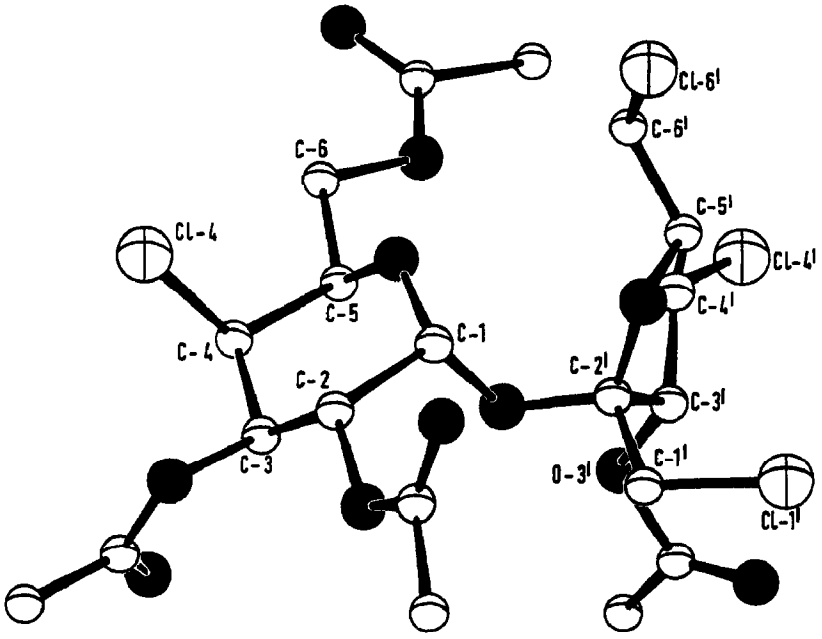
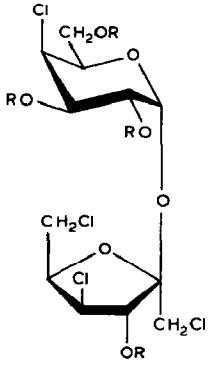


Fig. 1. Computer-generated view of 7 (B) which confirms the *fructo* configuration of the furanoid moiety.

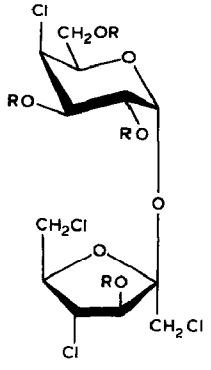
the co-ordinates from which a computer-generated view of the molecule clearly confirmed the *fructo* configuration of C-3′ and C-4′ (Fig. 1).

The formation of the tetrachloro derivatives **6** and **7** can be explained on the basis of previously reported data for reactions of sucrose and sulphuryl chloride and studies of nucleophilic reactions of sucrose 3′,4′-epoxides. With position 6 acetylated, the glucopyranosyl unit of sucrose reacts, as does methyl-6-*O*-acetyl-D-glucopyranoside[29], to give the 6-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl derivative independently of, but simultaneously with, the reactions of the hexulofuranose



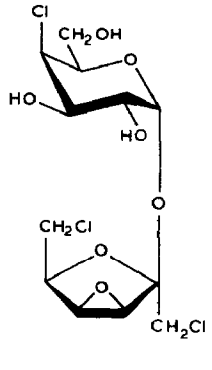
6 R = Ac

8 R = H



7 R = Ac

9 R = H



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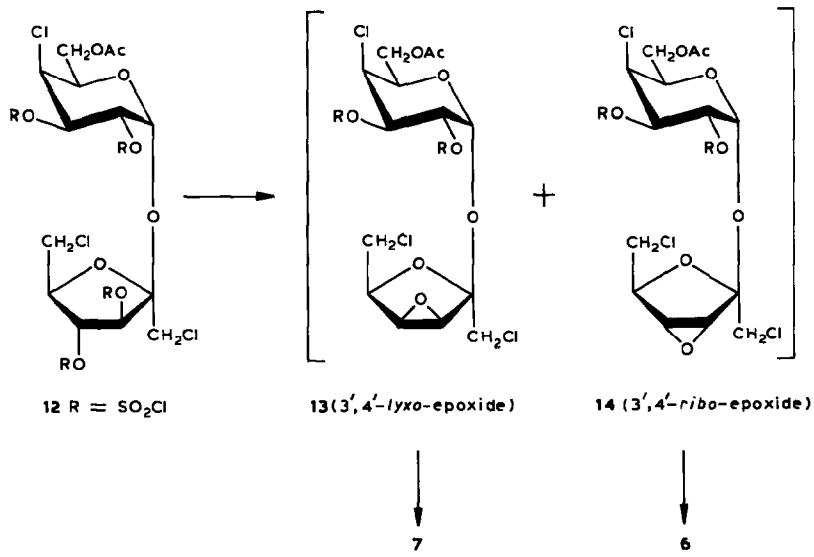
moiety. As with hexopyranosides, the fructofuranosyl portion is first completely chlorosulphated, and then undergoes displacement at C-1′ and C-6′ with the latter position being more reactive. Ballard *et al.*[5] suggested that the resulting 1′,6′-dichloro-3′,4′-bis(chlorosulphate) could then undergo either displacement of the 4′-chlorosulphate group to give 1′,4′,6′-trichloro-3′-chlorosulphate or epoxide formation. However, direct chlorination of C-4 in a D-fructofuranosyl derivative cannot be effected using sulphuryl chloride because of steric hindrance[30]. In the corresponding tagatofuranosyl derivative, there is no steric hindrance and 4-chlorination occurs readily[30]. Direct displacement of the 4′-chlorosulphate in **12** did not occur since no 4′-chloro-4′-deoxytagatofuranosyl derivative was isolated.

From studies of 3′,4′-epoxides of sucrose[12,25,31], 4′-chlorination most likely occurs *via* ring opening of a 3′,4′-epoxide, and, since two isomeric 4′-chloro-4′-deoxy derivatives were obtained, both the *lyxo*- and *ribo*-epoxides must have been involved. Treatment of sucrose 3′,4′-disulphonate with sodium methoxide produced[12] two isomeric 3′,4′-epoxides (*ribo*, minor; *lyxo*, major). The epoxides underwent[25] ring opening when treated with chloride ions to give mainly 4′-substituted products, due to steric and polar factors[32], the *lyxo*-epoxide giving the 4′-chloro-4′-deoxyfructofuranosyl derivative, whereas the *ribo*-epoxide gave the 4′-chloro-4′-deoxysorbofuranosyl derivative. Furthermore, the formation of epoxides from a vicinal *trans*-bis(chlorosulphate) has been observed with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside[13] and appears to be analogous to the formation of the same epoxide from the corresponding dimesylate[33] and ditosylate[34]. In addition, 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 3,4-anhydro-6-chloro-6-deoxy-β-D-*ribo*-hexulofuranoside (**2**) and 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 3,4-anhydro-1,6-dichloro-1,6-dideoxy-β-D-*ribo*-hexulofuranoside 2,3-sulphate[5] are formed during the reaction of sucrose and sulphuryl chloride. Therefore, **6** and **7** must



have arisen from the 1′,6′-dichloro-3′,4′-bis(chlorosulphate) intermediate **12** *via* the 3′,4′-*ribo*- (**13**) and -*lyxo*-epoxides (**14**) and then ring opening by chloride ions to produce the isomeric 1′,4′,6′-trichloro-1′,4′,6′-trideoxyhexulofuranosides. However, it is uncertain why the *sorbo* derivative was produced as the major product when the *lyxo*-epoxide should have been formed as the major product.

The proposed mechanism for the formation of the 4′-chloro-4′-deoxy derivatives was verified when reaction of 4-chloro-4-deoxy-α-D-galactopyranosyl 3,4-anhydro-1,6-dichloro-1,6-dideoxy-β-D-*lyxo*-hexulofuranoside[35] (**10**) with sulphuryl chloride gave **7** as the major product, after dechlorosulphation and re-acetylation. Furthermore, methyl 3,4-anhydro-1,6-di-*O*-benzoyl-β-D-tagatofuranoside[30] also gave a 4-chloro-4-deoxy derivative[36] which was characterised as the known methyl 4-deoxy-β-D-*threo*-hexulofuranoside[30], clearly indicating that 4-chlorination of the fructofuranosides by sulphuryl chloride takes place by ring opening of the 3′,4′-*lyxo*-epoxide.

Like some of the chlorinated analogues of sucrose[2,4], both the tetrachloro derivatives **8** and **9** were extremely sweet-tasting. Taste-panel testing indicated that the *sorbo* derivative **8** had a relative sweetness of only 200, whereas that of the *fructo* derivative **9** was about 2,200 times sweeter. As in many other instances[37], changes in configuration or conformation can cause very drastic changes in the taste. The structure-sweetness relationship of these compounds will be discussed elsewhere.

EXPERIMENTAL

All evaporations were carried out under reduced pressure at 45–55°. Optical rotations were determined on solutions in chloroform unless otherwise stated. Dry-column chromatography was performed on Kieselgel 7734 (Merck). Mass spectra were recorded on a Micromass 7035 spectrometer at 70 eV (ion source, 150–200°). ^{1}H-N.m.r. spectra were recorded at 220 MHz with a Varian HR-220 spectrometer, using Me_4Si as the internal standard. ^{13}C-N.m.r. spectra were determined on D_2O solutions with a Jeol JNM-FX90 instrument, using sodium 3-(trimethylsilyl)-1-propanesulphonate (DSS) as the internal standard.

Reaction of sucrose with sulphuryl chloride. — A solution of sucrose (12.0 g) in pyridine (18 mL) and chloroform (18 mL) was stirred vigorously at −50°, treated with freshly distilled sulphuryl chloride (42.5 mL, 15 mol) (dropwise), stirred for a further 2 h at −50°, and then allowed to slowly attain room temperature. The mixture was protected from moisture and kept at 50° for 24–48 h when t.l.c. (toluene–ethyl acetate, 3:1) revealed 3 major products. The mixture was poured into vigorously stirred ice-cold sulphuric acid (300 mL, 10%), stirred for 0.5 h, and extracted with dichloromethane. The extract was washed successively with water, saturated aqueous sodium hydrogencarbonate, and water, dried (Na_2SO_4), and concentrated. A solution of the syrupy residue in methanol (100 mL) was cooled (ice–salt bath), and treated with a few drops of 0.8% sodium iodide in methanol–water (1:1) (dechlorosulpha-

tion). The mixture was neutralised with sodium hydrogencarbonate, filtered, and concentrated. Column chromatography (dychloromethane–methanol, 15:1) of the syrupy residue gave, first, 4,6,1′,6′-tetrachloro-4,6,1′,6′-tetradeoxy-*galacto*-sucrose (1; 14.6 g, 45.3%), isolated as a syrup, $[\alpha]_D$ +79° (*c* 0.9, water); lit.[3] $[\alpha]_D$ +89° (methanol).

Eluted second was 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 3,4-anhydro-6-chloro-6-deoxy-β-D-*ribo*-hexulofuranoside (2; 1.5 g, 11.2%), m.p. 174–176° (dec.), $[\alpha]_D$ +105° (*c* 0.6, methanol) (Found; C, 38.4; H, 4.8; Cl, 27.9. $C_{12}H_{17}Cl_3O_7$ calc.: C, 37.9; H, 4.5; Cl, 28.1%). ^{1}H-N.m.r. data ($CDCl_3$–trichloroacetyl isocyanate): δ 4.33 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.81 (dd, 1 H, $J_{2,3}$ 8.5 Hz, H-2), 4.59 (t, 1 H, $J_{3,4}$ 3.0 Hz, H-3), 4.99 (dd, 1 H, $J_{4,5}$ 1.5 Hz, H-4), 5.4 (m, 2 H, H-5,5′), 6.4 (m, 4 H, H-6,6,6′,6′), 5.75 (d, 1 H, $J_{3',4'}$ 2.5 Hz, H-3′), 5.88 (dd, 1 H, $J_{4',5'}$ 1.0 Hz, H-4′), 7.20, 8.69, 8.92 (3 NH).

Eluted third was 4,6-dichloro-4,6-dideoxy-α-D-galactopyranosyl 6-chloro-6-deoxy-β-D-fructofuranoside (3; 3.1 g, 22.2%), m.p. 114–116°, $[\alpha]_D$ +87° (*c* 0.3, methanol); lit.[8] m.p. 115–116°, $[\alpha]_D$ +88° (methanol).

*2,3,6-Tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl-3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-sorbofuranoside* (6) *and -fructofuranoside* (7). — To a solution of sucrose 6-acetate (3 g) in pyridine (7.5 mL) and chloroform (7.5 mL) at −50° was added sulphuryl chloride (8.3 mL, 14 mol) dropwise during 1.5 h. The solution was stirred for a further 2 h at −50° and then slowly allowed to attain room temperature. The mixture was protected from moisture and kept at 45° for 24 h, when t.l.c. (butyl acetate–pyridine–water, 5:3:1) revealed two major products. The mixture was poured into vigorously stirred, ice-cold, aqueous 10% sulphuric acid (500 mL) and extracted with dichloromethane (3 × 100 mL). The combined extracts were washed successively with water, saturated aqueous sodium hydrogencarbonate, and water, and then concentrated to dryness. A solution of the syrupy product in methanol (100 mL) was stirred in an ice bath, and a few drops of 0.8% sodium iodide in water–methanol (1:1) were added. After stirring for 0.5 h, the solution was concentrated to dryness, and the residue was treated with pyridine (20 mL) and acetic anhydride (20 mL) at 45° for 45 min. The mixture was then poured into ice–water and extracted with dichloromethane, and the extract was dried ($MgSO_4$) and concentrated to dryness. Column chromatography (light petroleum–ethyl acetate, 1:1) of the syrupy residue gave incomplete separation. Column chromatography was repeated and the first-eluted (major) product (light petroleum–ethyl acetate, 4:1) contained a mixture of two compounds with similar polarities. Crystallisation of the mixture from ether gave two crystal forms that could be separated by hand when all the solvent had evaporated. Recrystallisation from ether–light petroleum of the slightly faster moving product (ether–light petroleum, 4:1) gave 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-sorbofuranoside (6; 1.4 g, 32%), m.p. 168–169°, $[\alpha]_D$ +86.5° (*c* 0.2) (Found: C, 40.9; H, 4.5; Cl, 24.3. $C_{20}H_{26}Cl_4O_{11}$ calc.: C, 41.1; H, 4.45; Cl, 24.3%). ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 5.62 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 4.95 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 5.40 (dd, 1 H, $J_{3,4}$ 3.5

Hz, H-3), 4.56 (m, 1 H, H-4), 5.63 (d, 1 H, $J_{3',4'}$ 2.0 Hz, H-3'), 4.79 (dd, 1 H, $J_{4',5'}$ 9.0 Hz, H-4'). Mass-spectral data [(a) and (a') 3:1 doublets (1 Cl) due to hexopyranosyl and ketofuranosyl cations; (b) 27:27:9:1 quartets (3 Cl), and (c) 9:6:1 triplet (2 Cl) due to ketofuranosyl cations]: *m/z* 307 (a), 259 (b), 247 (a), 223 (c), 211 (a), 205 (a), 187 (a), 181 (c), 145 (a,a'), 109.

The slower moving product (ether–light petroleum, 4:1) crystallised from methanol, to give 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3-*O*-acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-fructofuranoside (**7**; 0.6 g, 13.6%), m.p. 103–104°, $[\alpha]_D$ +75° (*c* 0.5, methanol) (Found: C, 40.9; H, 4.2; Cl, 23.8. $C_{20}H_{26}Cl_4O_{11}$ calc.: C, 41.1; H, 4.45; Cl, 24.3%). ^{1}H-N.m.r. data [$(CD_3)_2SO$]: δ 5.62 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.15 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 5.34 (dd, 1 H, $J_{3,4}$ 3.3 Hz, H-3), 4.83 (dd, 1 H, $J_{4,5}$ H-4), 4.62 (m, 2 H, H-5,5'), 4.02 (d, 1 H, $J_{1'a,1'b}$ 12.0 Hz, H-1'a), 3.82 (d, 1 H, H-1'b), 5.61 (d, 1 H, $J_{3',4'}$ 5.2 Hz, H-3'). 5.00 (t, 1 H, $J_{4',5'}$ 4.0 Hz, H-4'). Mass-spectral data: as for **6**.

The product eluted last crystallised from ethanol, to give 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranosyl 3,4-di-*O*-acetyl-1,6-dichloro-1,6-dideoxy-β-D-fructofuranoside (**4**; 0.5 g, 11.3%), identical with an authentic sample[8].

4-Chloro-4-deoxy-α-D-galactopyranosyl 1,4,6-trichloro-1,4,6-trideoxy-β-D-sorbofuranoside (**8**). — A methanolic solution of **6** (1.0 g in 15 mL) was treated with a catalytic amount of sodium methoxide at room temperature for 5 h. The solution was then deionised with Duolite MB 5113 mixed-bed resin and concentrated to give syrupy **8** (89%), $[\alpha]_D$ +71° (*c* 1.3, water) (Found: C, 34.5; H, 4.8; Cl, 34.2. $C_{12}H_{18}Cl_4O_7$ calc.: C, 34.6; H, 4.3; Cl, 34.1%).

4-Chloro-4-deoxy-α-D-galactopyranosyl 1,4,6-trichloro-1,4,6-trideoxy-β-D-fructofuranoside (**9**). — A methanolic solution of **7** (1.5 g in 25 mL) was treated with sodium methoxide as for **6**, to give **9** (0.65 g, 91.5%), m.p. 58–60° (from ether), $[\alpha]_D$ +72° (*c* 1, water) (Found: C, 35.05; H, 4.8; Cl, 34.2. $C_{12}H_{18}Cl_4O_7$ calc.: C, 34.6; H, 4.3; Cl, 34.1%).

Reaction of 4-chloro-4-deoxy-α-D-galactopyranosyl 3,4-anhydro-1,6-dichloro-1,6-dideoxy-β-D-lyxo-hexulofuranoside with sulphuryl chloride. — A solution of **10** in pyridine and chloroform was treated with sulphuryl chloride as described above, to give **7** as the major product (36%) after dechlorosulphation and acetylation.

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