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THE SYNTHESIS OF CHLORODEOXYHEXOFURANOID DERIVATIVES*

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ABSTRACT

The reaction of 1,2-*O*-isopropylidene-α-D-glucofuranose with sulfuryl chloride at 0° and at 50° afforded 6-chloro-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose 3,5-bis(chlorosulfate) (**3**) and 5,6-dichloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose 3-chlorosulfate (**7**, not characterised), respectively. Dechlorosulfation of **3** afforded the hydroxy derivative, whereas treatment of **3** with pyridine gave the 3,5-(cyclic sulfate). Dechlorosulfation of **7** afforded 5,6-dichloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose which, on acid hydrolysis, was converted into 3,6-anhydro-5-chloro-5-deoxy-L-idofuranose. 5-Chloro-5-deoxy-α-L-idofuranosidurono-6,3-lactone and 5-chloro-5-deoxy-β-L-idofuranurono-6,3-lactone derivatives were also prepared.

INTRODUCTION

Interest in the synthesis of chlorodeoxy sugars using stereoselective chlorinating agents stems from the usefulness of these derivatives in the synthesis of amino and deoxy sugars, many of which are constituents of antibiotics, and from the pharmacological and biological activity of the chlorodeoxy sugars.

The sulfuryl chloride–pyridine reagent has been extensively applied[2] to hexopyranoid derivatives, but there are only a few examples of the use of the reagent with hexofuranoid[3–5] sugars. Jones *et al.*[6] reported on the reaction of sulfuryl chloride with some pentofuranosides. We now describe the synthesis of some chlorodeoxyhexofuranoid derivatives from sulfuryl chloride and glucofuranoid precursors.

RESULTS AND DISCUSSION

The reaction of sugars with sulfuryl chloride produces fully substituted derivatives containing both chlorodeoxy and chlorosulfonyloxy groups. The chlorodeoxy

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groups are probably produced *via* bimolecular substitution by chloride of favourably situated chlorosulfonyloxy groups in the fully chlorosulfated intermediates.

Treatment of 1,2-*O*-isopropylidene-α-D-glucofuranose (**1**) with sulfuryl chloride initially at ~ −40° and then at 0° gave, after 5 h, 87% of 6-chloro-6-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose 3,5-bis(chlorosulfate) (**3**). The intermediate tris-chlorosulfate (**2**) was not isolated. The product showed i.r. absorptions at 1407 and 1190 cm^{-1} characteristic of the chlorosulfate ester group. In the n.m.r. spectrum of **3** (Table I), the signal for H-5 was a low-field multiplet ($J_{4,5}$ 8.7, $J_{5,6}$ 2.9, $J_{5,6'}$ 2.9 Hz) and that for H-3 was a low-field doublet ($J_{3,4}$ 2.5 Hz). A comparison of the n.m.r. spectra of **3** and the dechlorosulfated derivative **4** shows that H-3 and H-5 are the protons most influenced by the chlorosulfonyloxy group, each resonating at ~1.2 p.p.m. lower field than in **4**. This is consistent with the presence of chlorosulfonyloxy groups at C-3,5, and therefore the chloro group is at C-6 in **3**.

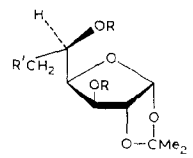
Dechlorosulfation of **3** with sodium iodide afforded 90% of the crystalline diol **4**, in the n.m.r. spectrum of which (Table I) only the resonances due to H-1,2,3

TABLE I

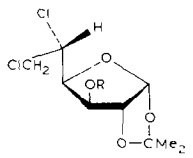
^{1}H-N.M.R. PARAMETERS[a]

Atom	**3**	**4**	**4**[b]	**5**	**6**	**8**	**8**[b]	**9**	**10**[b,c]
H-1	3.75(d)	4.09(d)	3.97(d)	4.06(d)	3.91(d)	3.95(d)	3.95(d)	4.02(d)	3.35(d)
H-2	4.73(d)	5.49(d)	5.22(d)	5.52(d)	5.28(d)	5.38(d)	5.23(d)	5.42(d)	4.68(d)
H-3	4.44(d)	5.63(d)	4.59(d)	4.63(d)	4.34(d)	5.47	4.60(d)	4.69(d)	5.02(s)
H-4	5.04(dd)	5.72	5.37(dd)	5.52(dd)	5.07(dd)	to	5.40(d)	5.45(d)	5.02(s)
H-5	4.55(m)	to	4.54(m)	4.63–4.93(m)	4.28(m)	5.65	5.35–5.70(m)	5.70(q)	5.38(d)
H-6	5.50(dd)	6.42	5.90(dd)	6.06(dd)	5.79(dd)	5.95	6.15(d)	6.10(dd)	5.67(dd)
H-6′	5.92(dd)		6.16(dd)	6.30(dd)	6.01(dd)	to 6.1	6.15(d)	6.31(dd)	5.92(d)
CMe_2	8.40	8.51	8.47	8.46	8.38	8.48	8.46	8.47	
	8.58	8.69	8.66	8.69	8.66	8.67	8.66	8.67	
OH		6.81				7.28			
OBz					1.74–2.74				
OAc				7.95				7.89	
NH			1.13				1.1		~0.67
			1.22						
$J_{1,2}$	3.7	3.7	3.7	3.5	3.7	4.0	4.0	4.0	4.7
$J_{3,4}$	2.5	2.0	2.7	2.9	2.7		2.7	3.4	~0
$J_{4,5}$	8.7		8.3	8.7	9.3		0	0	0
$J_{5,6}$	2.9		2.9	3.5	2.7		4.7	4.7	3.0
$J_{5,6'}$	2.9		5.1	4.7	3.1		4.7	4.7	0
$J_{6,6'}$	13.9		12.8	9.3	12.0			12.0	10.7

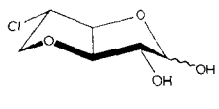
[a]First-order chemical shifts (τ values) and coupling constants at 60 MHz for solutions in $CDCl_3$. Key: d, doublet; dd, double doublet; q, quartet, m, multiplet; cm, complex multiplet. [b]After addition of trichloroacetyl isocyanate. [c]In CD_3COCD_3.



1 R′ = OH, R = H
2 R′ = OSO_2Cl, R = SO_2Cl
3 R′ = Cl, R = SO_2Cl
4 R′ = Cl, R = H
5 R′ = Cl, R = Ac
6 R′ = Cl, R = Bz



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



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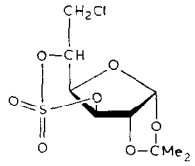

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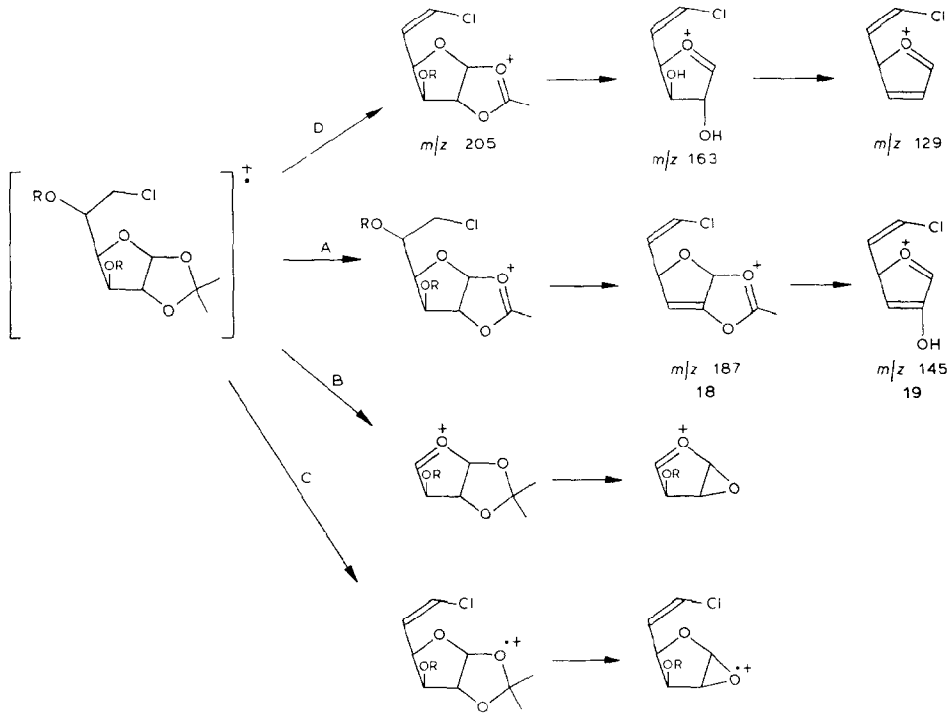
could be assigned. Reaction of **4** with trichloroacetyl isocyanate resulted in the appearance of singlets at τ 1.13 and 1.22 due to the NH groups of the resulting dicarbamate; H-3 and H-5 were deshielded by ~1 and ~1.2 p.p.m., respectively, thereby indicating the positions of the hydroxyl groups in **4**. Furthermore, the signal for H-4 could now be observed and was a double doublet at τ 5.37 ($J_{3,4}$ 2.7, $J_{4,5}$ 8.3 Hz).

Acid hydrolysis of **4** afforded 6-chloro-6-deoxy-D-glucose in good yield, and acetylation gave the diacetate **5**, previously[7] synthesised by the action of acetyl-



Scheme 1. Mass-spectral fragmentation of 3–6

salicyloyl chloride on **1**. The melting point of our sample was 11 higher than that previously reported[7], but the n.m.r. data and $[\alpha]_D$ value corresponded with the reported[7,8] data. Compound **4** was also converted into a crystalline dibenzoate (**6**).

The mass spectra of **3**–**6** exhibited the usual fragments derived from the 1,2-*O*-isopropylidene group. All spectra exhibited prominent [M 15] ions, but no molecular ions. Fragmentation of **3**–**6** proceeded mainly as depicted in Scheme 1, pathway A, involving the sequential loss of two HOR and ketene from the [M$^+$ - 15] ion to form fragments at *m/z* 187 (3:1 doublet) and 145 (3:1 doublet), respectively, and to a lesser extent according to pathway B in which the oxycarbonium ions formed by cleavage of the 4,5-bond undergo loss of acetone. Compounds **3** and **6** also showed minor fragments consistent with pathway C, and **4** fragmented to a minor extent *via* pathway D. The interpretation of the mass spectra was greatly facilitated by the presence of the chlorine "isotope clusters".

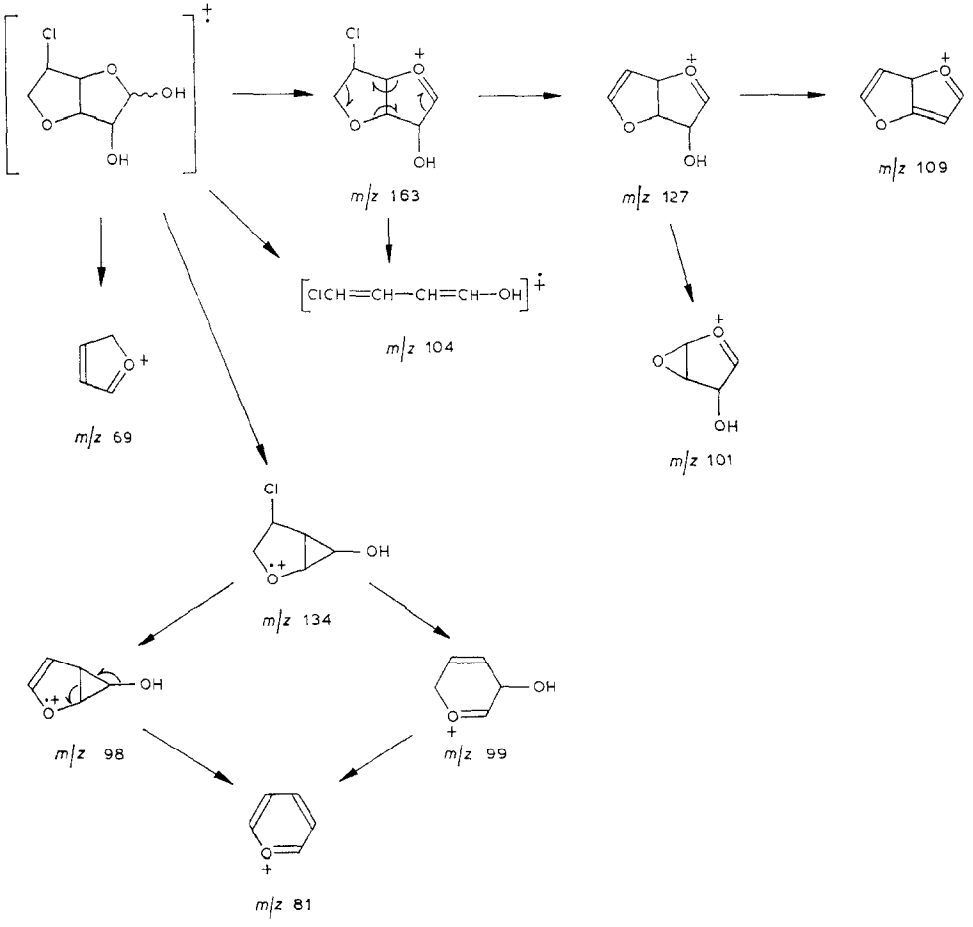
The reaction of **3** with cold pyridine for 2.5 h gave 54% of the six-membered cyclic sulfate **11** which, in addition to i.r. absorptions due to the isopropylidene group, showed strong absorptions at 1380 and 1190 cm^{-1}. This is in contrast to the five-membered cyclic sulfates produced from carbohydrates possessing vicinal chlorosulfonyloxy groups[5], which only show strong absorption at ~1400 cm^{-1}. The mass spectrum of **11** showed a prominent fragment at *m/z* 285 (3:1 doublet) corresponding to the [M$^+$ - 15] ion. Sequential loss of sulfuric acid and ketene gave fragments **18** and **19** (Scheme 1, pathway A), respectively, confirming that the sulfate group bridges positions 3 and 5 in **11**.

The reaction of **1** with sulfuryl chloride at ~ -40 as described above followed by a further 16 h at 50 afforded **7** as a syrup which was dechlorosulfated to yield crystalline 5,6-dichloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**8**). In the n.m.r. spectrum of **8** (Table I), the resonances due to H-3,4,5 overlapped. After reaction of **8** with trichloroacetyl isocyanate, the H-3 doublet was deshielded by ~0.9 p.p.m., indicating that the hydroxyl group in **8** was located at C-3 and that the second chloro group was therefore attached to C-5. The assigned L-*ido* configuration for **8** is consistent with the inversion of configuration that occurs when a chlorosulfonyloxy group is displaced by chloride ion and is supported by the appearance of the H-4 resonance as a doublet at τ 5.4 ($J_{3,4}$ 2.7, $J_{4,5}$ ~0 Hz). Whistler[9] reported the signal for H-4 to be a doublet at τ 5.42 ($J_{3,4}$ 3 Hz) in the n.m.r. spectrum of 6-*S*-acetyl-3-*O*-benzoyl-5-chloro-5-deoxy-1,2-*O*-isopropylidene-6-thio-β-L-idofuranose. Compound **8** decomposed slowly at room temperature, but was stable for several months when stored at 5°. The crystalline acetate **9** was stable at room temperature. The appearance of the H-4 resonance as a doublet at τ 5.45 ($J_{3,4}$ 3.3, $J_{4,5}$ ~0 Hz) in the n.m.r. spectrum of **9** is further evidence for the L-*ido* configuration for both **8** and **9**.

In contrast to **3**–**7**, **8** and **9** gave molecular ions of low intensity in their mass spectra in addition to prominent [M$^+$ - 15] fragments. Each compound fragmented mainly according to pathway A in Scheme 1, to give a prominent ion at *m/z* 181 (**20**)

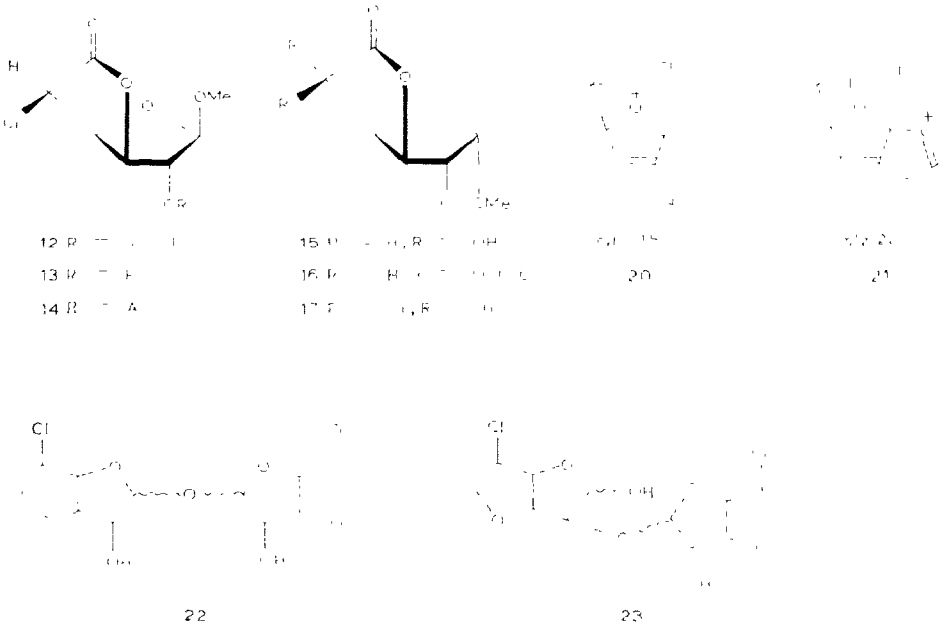
and a minor ion at *m/z* 223 (**21**). In addition, less-prominent fragments due to cleavage of the 4,5-bond were observed as for **3–6** (pathway B, Scheme 1).

Acid hydrolysis of **8** did not afford the expected 5,6-dichloro-5,6-dideoxy-L-idofuranose, but instead gave 80% of a crystalline chlorodeoxy derivative **10** ($C_6H_9ClO_4$) that reduced Fehling's solution, was oxidised by periodate, and mutarotated in aqueous solution. These data are consistent with the structure 3,6-anhydro-5-chloro-5-deoxy-L-idofuranose. A 3,5-anhydro-6-chloro-6-deoxy-D-glucofuranose structure for **10**, although possible, is not considered likely on steric grounds. The n.m.r. spectrum [$(CD_3)_2CO$] of **10** (Table I) was complex, consisting of overlapping signals of the α and β anomers. Reaction of **10** with trichloroacetyl isocyanate greatly simplified the spectrum, since only the dicarbamate of the α anomer was formed. The appearance of the H-4 resonance as a singlet at τ 5.02 ($J_{4,5}$ ~0 Hz) is in keeping with the L-*ido* configuration for **10**. In the mass spectrum of **10**, the most intense peak



Scheme 2 Mass-spectral fragmentation of 10

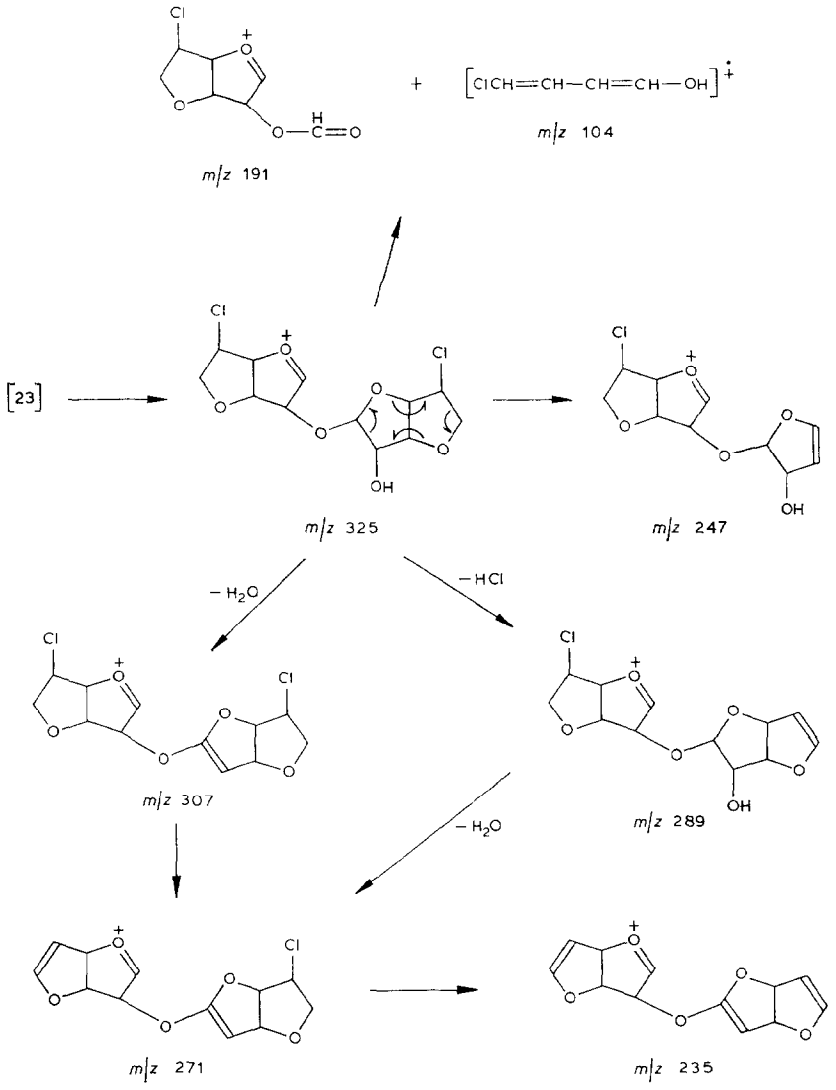
possessing a chlorine atom occurred at m/z 104 (31.6%) and is derived from either the M^+ or $[M^+ - 17]$ (m/z 163) ions as shown in Scheme 2. This type of fragmentation produces intense peaks in the mass spectra of methyl 3,6-anhydrofuranoses[11]. The fragments m/z 69 (base peak), 134 (1 Cl), and 99 constitute further proof of the 3,6-anhydro structure of **10**.



22 **23**

When the mass spectrum of **10** was recorded with the probe temperature above the m.p. (83°) of **10**, fragments of $m/z > 180$ were observed. The ion of greatest mass occurred at m/z 325 and is consistent with the dimerisation of **10** in the mass spectrometer; by appropriate selection of conditions, a spectrum of the dimers only could be obtained. Table II compares the relative abundance of the ions in the mass spectra of **10** and its dimer(s). The five possible dimers of **10** are represented by structures **22** and **23**. Only the two isomers represented by **23** could have given rise to the fragments of m/z 235–325 (Scheme 3). The fragmentation of isomers represented by **22** would be expected[3] to proceed *via* the cleavage of the interglycosidic bonds to afford a prominent oxycarbonium ion with m/z 163. The presence of this ion as the base peak in the mass spectrum of the dimer(s) is strong evidence for the presence of isomers of **22**.

The reaction of methyl β-D-glucofuranosidurono-6,3-lactone with sulfuryl chloride, initially at −70° and then at room temperature, afforded a crystalline chlorodeoxychlorosulfonyloxy derivative (**12**), dechlorosulfation of which afforded methyl 5-chloro-5-deoxy-α-L-idofuranosidurono-6,3-lactone (**13**), characterised as the crystalline acetate **14**. In the n.m.r. spectrum of **13** (Table III), the resonances of H-2 and HO-2 appeared as coupled doublets at τ 5.65 and 7.66, respectively ($J_{2,OH}$



Scheme 3 Mass-spectral fragmentation of 23

5 Hz). The OH signal disappeared and the H-2 doublet collapsed to a singlet on the addition of D_2O. The resonance of H-5 in **12–14** as singlets confirms the L-*ido* configuration and the presence of the chloro group at C-5 in these compounds. Irimajiri *et al.*[11] reported H-5 to resonate as a singlet (τ 5.7) for the bromo analogue of **13**. In the n.m.r. spectrum of **12** (Table III), the signal due to H-2 occurred at ~1 p.p.m. to lower field than in the spectrum of **13**. This is consistent with the presence of the chlorosulfonyloxy group at position 2 in **12**. The H-1 singlet and H-3 doublet, as expected, were also deshielded (~0.3 p.p.m.) in the spectrum of **12**.

TABLE II

RELATIVE ABUNDANCE OF THE IONS IN THE MASS SPECTRA OF **10** AND ITS DIMER(S)

m/z	*Relative abundance (%)*	
	Dimer(s)	**10**
325[b]	14.1	
307[b]	0.6	
289[a]	0.5	
271[a]	0.3	
247[a]	0.4	
235	1.4	
191[a]	1.3	
181[a]	2.8	
163[a]	100.0	2.5
151[a]	2.8	2.0
147[a]	12.6	
134[a]	5.6	2.5
127[a]	56.2	5.6
121[a]	22.4	7.1
109	25.1	2.5
104[a]	29.8	31.6
101	35.5	44.7
99	79.4	44.7
98	44.7	23.7
81	22.4	12.1
73	63.1	44.7
69	100.0	100.0
58	66.8	79.4

[a]3:1 doublets (1 Cl). [b]9:6:1 triplets (2 Cl).

TABLE III

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

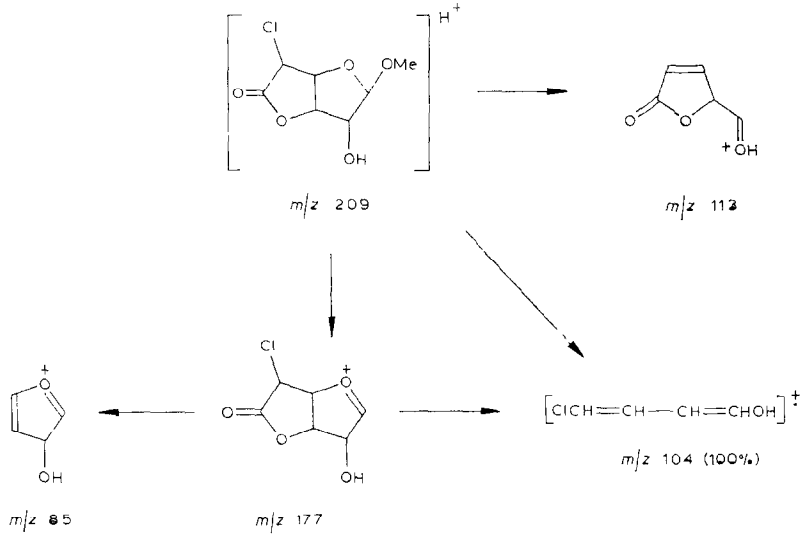
Atom	**12**[b]	**13**[b]	**14**[c]	**17**[c]
H-1	4.71(s)	5.04(s)	4.70(s)	4.03(d)
H-2	4.70(s)	5.65(d)	4.86(s)	5.14(d)
H-3	4.67(d)	4.99(d)	~4.90(d)	4.91(d)
H-4	4.86(d)	4.94(d)	~4.90(d)	5.12(d)
H-5	5.69(s)	5.75(s)	5.66(s)	5.73(s)
OCH_3	6.54	6.64	6.57	
OH		7.66(d)		
OAc			7.85	
CMe_2				8.48
				8.64
$J_{1,2}$				4.0
$J_{3,4}$	5.0	5.0	~3.3	3.0
$J_{4,5}$	0	0	0	0
$J_{2,OH}$		5.0		

[a]First-order chemical shifts (τ values) and coupling constants for solutions in $CDCl_3$. Key: as for Table I. [b]400 MHz. [c]60 MHz.

Treatment of 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone (**15**) with sulfuryl chloride afforded 80% of **17**; the intermediate chlorosulfate ester **16** was not isolated. The n.m.r. data (Table III) clearly establish the L-*ido* configuration for **17**. The reaction of 1,2-*O*-isopropylidene-5-*O*-toluene-*p*-sulfonyl-α-D-glucofuranurono-6,3-lactone with lithium bromide in *N*,*N*-dimethylformamide at 100° for 8 h afforded the L-*ido* and D-*gluco* bromo derivatives in approximately equimolar amounts[11]. Methanolysis of **17** in the presence of Amberlite IR-120 (H^+) resin afforded **13** in almost quantitative yield.

The replacement of the 5-chlorosulfonyloxy group by chloride in the glucose derivative **16** occurred at much lower temperature than with the glucofuranose derivative **3**. The greater reactivity of **16** is attributed to the stabilisation of the S_N transition-state by the participation of the lactone carbonyl group.

The mass spectra of **12**–**14** showed $[M + H]^+$ and $[M + H - 32]^+$ ions. The latter ion was the base peak in the mass spectrum of **14**. In addition to the fragments also formed from **13** (Scheme 4), the mass spectrum of **14** contained the acetylated counterparts of the ions *m/z* 209, 177, and 113. The prominent chlorinated fragment at *m/z* 104 is consistent with the *cis*-dioxapentalane system[10] in **13** and **14**. The mass spectrum of **12** differed in two main respects from those of **13** and **14**. Firstly, the ions at *m/z* 207, 191, 155, and 119 contain one hydrogen more than expected. Secondly, with the exception of the ion at *m/z* 119, the above-mentioned fragments possessed intact methoxyl groups.



Scheme 4 Mass-spectral fragmentation of 13

EXPERIMENTAL

General. — Unless otherwise stated, solutions were concentrated under diminished pressure below 40°. T.l.c. was performed on Silica Gel G with light petroleum–ether mixtures and detection with aniline–pyridine (for ester chlorosulfate[12]) or by charring with sulfuric acid. The term light petroleum refers to the fraction having b.p. 40–60°. Optical rotations were measured with a Perkin Elmer 141 polarimeter and i.r. spectra with a Beckman I.R. 8 spectrophotometer. ^{1}H-N.m.r. spectra (60 and 400 MHz, internal Me_4Si) were recorded with Perkin–Elmer R-12 and Bruker WH-400 spectrometers. Mass spectra (70 eV) were determined with an A.E.I. MS-30 Spectrometer.

6-Chloro-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose 3,5-bis(chlorosulfate) (**3**). — Sulfuryl chloride (15 mL) was added dropwise during 30 min to a vigorously stirred solution of **1** (10 g) in dry pyridine (24 mL) and dry chloroform (80 mL) at ~ −40°. After a further 2 h at ~ −40°, the mixture was allowed to attain 0°, maintained thereat for 2 h, diluted with chloroform, and worked-up as previously described. A solution of the resulting, orange syrup (18.3 g) in ether was decolourised (charcoal), and concentrated to afford a colourless, chromatographically pure syrup (17.3 g, 87%) that crystallised on storage. Recrystallisation from ether–light petroleum afforded **3** as long, flat needles, m.p. 56–57.5°, $[\alpha]_D$ −41° (*c* 1.9, chloroform); ν_{max}^{KBr} 1407 and 1190 cm^{-1} (OSO_2Cl). Mass spectrum: *m/z* 419 (3 Cl, 22.4%), 319 (2 Cl, 5.6), 261 (2 Cl, 7.9), 257 (1 Cl, 8.9), 199 (1 Cl, 4.5), 187 (1 Cl, 35.5), 129 (1 Cl, 4.5), 145 (1 Cl, 25.1), 85 (20.2), 64 (28.2), 59 (44.7), and 43 (100). (Found: C, 25.0; H, 2.93; Cl, 24.37; S, 14.24. $C_9H_{13}Cl_3O_9S_2$ calc.: C, 24.8; H, 2.99; Cl, 24.45; S, 14.7%).

6-Chloro-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (**4**). — A solution of **3** (9.5 g) in acetone–methanol (1:1, 250 mL) was dechlorosulfated[13] with methanolic 10% sodium iodide in the presence of excess of sodium hydrogencarbonate. Recrystallisation of the product from ether–light petroleum afforded **4** as needles (4.9 g, 94%), m.p. 78–79°, $[\alpha]_D$ −12° (*c* 1.6, chloroform); $\nu_{max}^{CHCl_3}$ 3500 cm^{-1} (OH). Mass spectrum: *m/z* 223 (1 Cl, 39.8%), 205 (1 Cl, 2.5), 187 (1 Cl, 12.6), 163 (1 Cl, 6.3), 159 (39.8), 145 (1 Cl, 56.1), 129 (1 Cl, 7.9), 127 (25), 101 (17.8), 85 (56.1), 73 (44.6), 59 (89.1), and 43 (100) (Found: C, 45.17; H, 6.33; Cl, 14.89. $C_9H_{15}ClO_5$ calc.: C, 45.28; H, 6.29; Cl, 14.88%).

3,5-Di-O-acetyl-6-chloro-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (**5**). — Conventional treatment of **4** (1.5 g) with pyridine (8 mL) and acetic anhydride (5 mL) at room temperature and recrystallisation of the product (1.64 g, 81%) from ether–light petroleum afforded **5** as needles, m.p. 128–129° (softens 118°), $[\alpha]_D$ ~0° (*c* 2.8, chloroform); lit.[7] m.p. 117–118°, $[\alpha]_D$ +4° (chloroform). Mass spectrum: *m/z* 307 (1 Cl, 2.5%), 201 (1.3), 187 (1 Cl, 3.0), 145 (1 Cl, 3.8), 143 (4.7), 101 (2.5), 85 (5.1), 59 (7.6), and 43 (100) (Found: C, 48.26; H, 5.87; Cl, 11.18. $C_{13}H_{19}ClO_7$ calc.: C, 48.37; H, 5.89; Cl, 11.08%).

3,5-Di-O-benzoyl-6-chloro-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (**6**). — Conventional treatment of **4** (1 g) with benzoyl chloride and pyridine at 0°, with

recrystallisation of the product from methanol, afforded **6** (1.7 g), m.p. 86–88°, $[\alpha]_D$ −129° (*c* 2.1, chloroform). Mass spectrum: *m/z* 431 (1 Cl, 17.8%), 266 (1 Cl, 5.6), 263 (7.9), 205 (11.2), 187 (1 Cl, 7.1), 145 (1 Cl, 4.5), 129 (4.0), 122 (4.0), 105 (100), 85 (4.5), 77 (35.5), 59 (6.3), and 43 (22.4) (Found: C, 61.96; H, 5.17; Cl, 8.86. $C_{23}H_{23}ClO_7$ calc.: C, 61.81; H, 5.15; Cl, 7.95%).

*6-Chloro-6-deoxy-*D*-glucose.* — To a solution of **4** (0.6 g) in water (10 mL) was added Amberlite IR-120 (H^+) resin (1 g), and the mixture was heated at ~100° for 0.5 h, filtered, and concentrated. Recrystallisation of the residue from ethanol–ether afforded 6-chloro-6-deoxy-D-glucose (0.42 g), m.p. 133–134°, $[\alpha]_D$ +103 (2 min) → +53° (150 min) (*c* 3.4, water); lit.[14] m.p. 135–136°, $[\alpha]_D$ +95.8 → +51° (18 h, water).

*6-Chloro-6-deoxy-1,2-*O*-isopropylidene-α-*D*-glucofuranose 3,5-sulfate* (**11**). — A solution of **3** (1.22 g) in pyridine at 0° was kept for 2.5 h, and then diluted with chloroform, washed successively with aqueous 10% sulfuric acid, water, saturated aqueous sodium hydrogencarbonate, and water, dried (Na_2SO_4), and concentrated. The brown, crystalline residue (0.66 g) contained (t.l.c.) a single, major component. A solution of the crystals in acetone was decolourised with charcoal and concentrated, and the residue was recrystallised from benzene to afford **11** (450 mg), m.p. 180–185°, $[\alpha]_D$ +23° (*c* 1.2, chloroform); ν_{max}^{KBr} 1380 and 1190 (cyclic sulfate), and 1100 and 1084 cm^{-1} (CMe_2). Mass spectrum: *m/z* 285 (1 Cl, 48.3%), 187 (1 Cl, 31.4), 145 (1 Cl, 57.6), 129 (7.6), 85 (16.1), 59 (50.9), and 43 (100) (Found: C, 36.38; H, 4.41; Cl, 12.37; S, 10.52. $C_9H_{13}ClO_7S$ calc.: C, 35.94; H, 4.33; Cl, 11.81; S, 10.65%).

*5,6-Dichloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-*L*-idofuranose* (**8**). — Compound **1** (10 g) was treated with sulfuryl chloride (15 mL), as described above, at room temperature for 4 h and then at 50° until t.l.c. revealed (~16 h) the presence of a single, major product. Work-up in the usual fashion afforded **7** as a syrup which was dechlorosulfated[13]. Recrystallisation of the product from ether–light petroleum afforded **8** as long, flat needles (8.2 g, 70%), m.p. 112–114°, $[\alpha]_D$ −19° (*c* 2.9, methanol). Mass spectrum: *m/z* 256 (2 Cl, 2.2%), 241 (2 Cl, 47.3), 223 (2 Cl, 1.6), 199 (2 Cl, 1.4), 205 (1 Cl, 2.5), 181 (2 Cl, 50.1), 163 (1 Cl, 8.9), 159 (12.6), 145 (1 Cl, 1.4), 105 (25.1), 101 (10.0), 85 (44.7), 83 (79.4), 59 (100), and 43 (100) (Found: C, 41.52; H, 5.36; Cl, 27.55. $C_9H_{14}Cl_2O_4$ calc.: C, 42.02; H, 5.45; Cl, 27.62%).

*3-*O*-Acetyl-5,6-dichloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-*L*-idofuranose* (**9**). — Conventional acetylation of **8** afforded **9** as thin needles, m.p. 93–94° (from ether–light petroleum), $[\alpha]_D$ +2° (*c* 0.94, chloroform). Mass spectrum: *m/z* 298 (2 Cl, 0.03%), 283 (2 Cl, 22.4), 241 (2 Cl, 0.7), 223 (2 Cl, 4.0), 205 (1 Cl, 0.6), 201 (2.5), 181 (2 Cl, 50.1), 143 (25.1), 141 (1.1), 129 (3.2), 101 (63.1), 85 (12.6), 59 (89.1), and 43 (100) (Found: C, 44.00; H, 5.39; Cl, 24.31. $C_{11}H_{16}Cl_2O_5$ calc.: C, 44.15; H, 5.35; Cl, 23.75%).

*Hydrolysis of 5,6-dichloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-*L*-idofuranose.* — A solution of **8** (1.0 g) in 0.5M sulfuric acid (10 mL) was kept at ~100° for 1 h, neutralised ($BaCO_3$), filtered, and concentrated. The chromatographically pure, syrupy residue (0.63 g, 89%) crystallised from chloroform, to give 3,6-anhydro-5-

chloro-5-deoxy-L-idofuranose (**10**), m.p. 81–83°, $[\alpha]_D$ +71.5 (3 min) → +49° (final) (*c* 1.3, water) (Found: C, 39.96; H, 5.07; Cl, 20.18. $C_6H_9ClO_4$ calc.: C, 39.89; H, 5.03; Cl, 19.67%).

Methyl 5-chloro-5-deoxy-α-L-idofuranosidurono-6,3-lactone 2-chlorosulfate (**12**). — Sulfuryl chloride (10 mL) was added dropwise during 30 min to a vigorously stirred solution of methyl β-D-glucofuranosidurono-6,3-lactone (10 g) in dry pyridine (16 mL) and dry chloroform (80 mL) at below −40°. The reaction was allowed to proceed essentially as described for the synthesis of **3**. Work-up in the usual way afforded a pale-yellow, crystalline mass (8.9 g, 55%) that was recrystallised from ether, to afford **12** as colourless needles, m.p. 102–104°, $[\alpha]_D$ −11° (*c* 1.5, chloroform); ν_{max}^{KBr} 1810 (C=O, lactone), 1415 and 1210 cm^{-1} (OSO_2Cl). Mass spectrum: *m/z* 307 (2 Cl, 1.8%), 275 (2 Cl, 7.9), 239 (1 Cl, 6.3), 207 (1 Cl, 25.1), 191 (1 Cl, 2.5), 185 (1 Cl, 5.0), 155 (1 Cl, 5.0), 147 (1 Cl, 6.3), 119 (1 Cl, 10), 85 (15.9), 83 (50.1), 91 (15.9), 73 (17.8), and 61 (100) (Found: C, 27.22; H, 2.62; S, 10.42; Cl, 22.75. $C_7H_8Cl_2O_7S$ calc.: C, 27.36; H, 2.61; S, 10.42; Cl, 23.13%).

Methyl 5-chloro-5-deoxy-α-L-idofuranosidurono-6,3-lactone (**13**). — Compound **12** (10 g) in acetone was dechlorosulfated, and recrystallisation of the product from chloroform–light petroleum afforded **13** as long needles (3.72 g, 55%), m.p. 137–139°, $[\alpha]_D$ −87° (*c* 1.5, chloroform); ν_{max}^{KBr} 3500 (OH) and 1780 cm^{-1} (C=O, lactone). Mass spectrum: *m/z* 209 (1 Cl, 2.0%), 177 (1 Cl, 10.0), 113 (50.1), 104 (1 Cl, 100), 91 (14.1), 85 (25.1), and 61 (44.7) (Found: C, 40.40; H, 4.31; Cl, 17.21. $C_6H_9ClO_5$ calc.: C, 40.29; H, 4.31; Cl, 17.03%).

Methyl 2-O-acetyl-5-chloro-5-deoxy-α-L-idofuranosidurono-6,3-lactone (**14**). — Conventional acetylation of **13** (167 mg) and crystallisation of the product (120 mg) from ether gave **14**, m.p. 95–96°, $[\alpha]_D$ −18° (*c* 0.44, chloroform). Mass spectrum: *m/z* 251 (1 Cl, 22.4%), 219 (1 Cl, 100), 183 (1 Cl, 5.3), 177 (1 Cl, 26.6), 155 (13.3), 141 (14.1), 115 (31.6), 113 (28.2), 111 (100), 104 (1 Cl, 50.1), 85 (39.8), 83 (25.1), and 61 (31.6) (Found: C, 43.10; H, 4.36; Cl, 14.01. $C_8H_{11}ClO_6$ calc. C, 43.13; H, 4.39; Cl, 14.17%).

5-Chloro-5-deoxy-1,2-O-isopropylidene-β-L-idofuranurono-6,3-lactone (**17**). — A solution of sulfuryl chloride (5 mL) in chloroform (10 mL) was added dropwise during 30 min to a stirred solution of **15** (10 g) in dry pyridine (8 mL) and dry chloroform (80 mL) at ~ −14°. After 2 h at −14° and 2 h at 0°, t.l.c. revealed a single product. Work-up in the usual way and recrystallisation of the product from ether–light petroleum afforded **17** (8.69 g, 80%), m.p. 137–139°, $[\alpha]_D$ +49° (*c* 1.5, chloroform); ν_{max}^{KBr} 1780 cm^{-1} (C=O, lactone). Mass spectrum: *m/z* 219 (1 Cl, 35.5%), 183 (7.0), 177 (1 Cl, 28.2), 141 (20.0), 113 (7.0), 101 (4.5), 85 (9.0), 83 (12.6), 58 (20), and 43 (100) (Found: C, 46.11; H, 4.93; Cl, 14.53. $C_9H_{11}ClO_5$ calc.: C, 46.06; H, 4.69; Cl, 15.14%).

Methanolysis of **17**. — A solution of **17** (100 mg) in dry methanol (10 mL) was boiled in the presence of Amberlite IR-120 (H^+) resin for 4 h, filtered, and concentrated, to give **13** in almost quantitative yield: m.p. and mixture m.p. (with **13** above) 136–137°.

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