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THE FIRST REPLACEMENT OF A CHLOROSULPHONYLOXY GROUP BY CHLORINE AT C-2 IN METHYL α-D-GLUCOPYRANOSIDE AND SUCROSE DERIVATIVES*

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ABSTRACT

Treatment of methyl 3-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside 2-chlorosulphate (**2**), 3,4,6,3′,4′,6′-hexa-*O*-acetylsucrose 2,1′-bis(chlorosulphate), 3,4,6,3′,4′,6′-hexa-*O*-acetyl-1′-*O*-benzoylsucrose 2-chlorosulphate, and 3,4,3′,4′-tetra-*O*-acetyl-6,6′-dichloro-6,6′-dideoxysucrose 2,1′-bis(chlorosulphate) with lithium chloride in hexamethylphosphoric triamide gave the corresponding chlorodeoxy-*manno* derivatives. Treatment of the 2-chlorosulphate **2** with such nucleophilic reagents as lithium bromide, sodium azide, sodium chloride, and sodium benzoate in hexamethylphosphoric triamide gave the 2-hydroxy compound as a major product. Selective chlorination at C-1′ was achieved when 3,4,6,3′,4′,6′-hexa-*O*-acetylsucrose was treated with sulphuryl chloride in a mixture of pyridine and chloroform.

INTRODUCTION

The reaction of sulphuryl chloride with sugars gives products in which the primary hydroxyl groups are replaced by chlorine, and secondary hydroxyl groups are either esterified by cyclic sulphate or replaced by chlorine with inversion of configuration[2–7]. Throughout the series of glycosides studied, a common feature recognised was the inertness of HO-2 towards replacement. A similar lack of reactivity has also been observed in the replacement of the 2-sulphonic ester groups of methyl 4,6-*O*-benzylidene-2-*O*-mesyl-3-*O*-methyl-α-D-glucopyranoside and methyl 4,6-*O*-benzylidene-2-*O*-mesyl-3-*O*-methyl-α-D-mannopyranoside[8]. This has been ascribed to unfavourable alignments of dipoles in the transition state of the reaction[8,9].

We now describe the first example of the displacement of 2-chlorosulphate groups in methyl α-D-glucopyranoside and sucrose derivatives by chloride ion. No evidence was obtained to suggest that the replacement of the 2-chlorosulphate group by chloride proceeds either by an S_N2 process[6,7] or *via* a cyclic intermediate[10].

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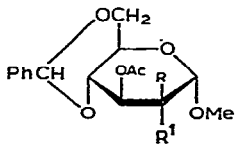
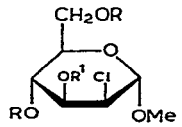
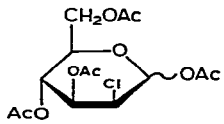
*Sucrochemistry: Part XXVII. For Part XXVI, see Ref. 1.

RESULTS AND DISCUSSION

Treatment of methyl 3-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside[11] (**1**) with sulphuryl chloride in a mixture of pyridine and chloroform at −75° gave the corresponding 2-chlorosulphate **2** in 60% yield. The reaction of **2** with lithium chloride in hexamethylphosphoric triamide at ~70° for 2.5 h gave, after chromotographic fractionation on silica gel, methyl 3-*O*-acetyl-4,6-*O*-benzylidene-2-chloro-2-deoxy-α-D-mannopyranoside (**3**) in 74% yield. In the ^{1}H-n.m.r. spectrum of **3**, discrete signals for H-1,2,3,4 and the benzylic methine protons were observed at τ 5.17, 5.48, 4.64, 5.85, and 4.45, respectively. These assignments were confirmed by spin-decoupling experiments. The derived, first-order coupling constants ($J_{1,2}$ 1.5, $J_{2,3}$ 3.5, $J_{3,4}$ 8.8, and $J_{4,5}$ 8.8 Hz) confirmed the $^4C_1$ conformation and the α-D-*manno* configuration for **3**. The mass spectrum of **3** contained a peak for the molecular ion at *m/e* 342, and subsequent fragmentation proceeded *via* h-fracture.







1 R = H, R^1 = OH
2 R = H, R^1 = OSO_2Cl
3 R = Cl, R^1 = H

4 R = H, R^1 = Ac
5 R = R^1 = Ac
6 R = R^1 = H

7

Treatment of **3** with aqueous acetic acid at 80° for 4 h gave, after chromatography on silica gel, the 4,6-dihydroxy compound **4** in 67% yield. In the ^{1}H-n.m.r. spectrum of **4**, the resonances due to H-1,2,3,4 appeared at τ 5.14, 5.57, 4.78, and 5.87, respectively. The first-order coupling constants ($J_{1,2}$ 1.5, $J_{2,3}$ 3.5, $J_{3,4}$ 9.5, and $J_{4,5}$ 9.5 Hz) were in agreement with the $^4C_1$ conformation and α-D-*manno* configuration for **4**. Addition of trichloroacetyl isocyanate to the n.m.r. solution of **4** in deuteriochloroform caused the appearance of two singlets at τ 1.36 and 1.41 due to imino protons, thereby suggesting the presence of two hydroxyl groups. The signals for H-4 were identified in the region of τ 4.48–4.71 by spin-decoupling experiments. This marked deshielding (1–2 p.p.m.) of H-4 revealed that one of the carbamate groups was located at C-4. The methylene protons (τ 5.45–5.60) were also deshielded (~1 p.p.m.), thereby suggesting that the other carbamate group was located at C-6. Conventional acetylation of **4** gave the triacetate **5**, whose structure was supported by ^{1}H-n.m.r. data. The resonances due to H-1 ($J_{1,2}$ 1.5 Hz) and H-2 ($J_{2,3}$ 3.0 Hz) appeared at τ 5.18 and 5.66, respectively. Although signals for H-3 and H-4 were not allocated, they were identified by spin-decoupling experiments in the region of τ 4.54–4.78. De-esterification of **5**, using a catalytic amount of sodium methoxide in methanol, gave methyl 2-chloro-2-deoxy-α-D-mannopyranoside (**6**).

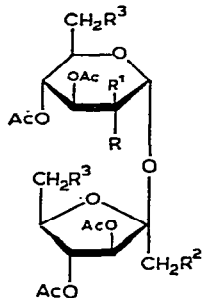
Acetolysis of **4**, using acetic acid, acetic anhydride, and conc. sulphuric acid, afforded the expected mixture of 1,3,4,6-tetra-*O*-acetyl-2-chloro-2-deoxy-α- and -β-D-

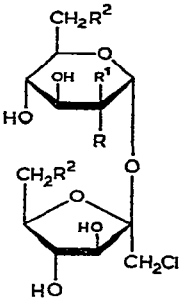
mannopyranose (**7**). The structure of **7** was supported by its ^{1}H-n.m.r. spectrum. A low-field doublet at τ 3.83 ($J_{1,2}$ 1.75 Hz) was assigned to H-1. The characteristic quartet due to H-2 was identified at τ 5.65. The absence of a signal due to a methyl group, and the presence of signals due to acetate protons, indicated that the acetolysis of **4** was complete.

Treatment of methyl 3-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside 2-chlorosulphate (**2**) with such nucleophilic reagents as lithium bromide, sodium azide, sodium benzoate, and sodium chloride in hexamethylphosphoric triamide gave the 2-hydroxy compound **1** as the major product. Little or no formation of the 2-chloride **3** was observed.

The reaction of 3,4,6,3′,4′,6′-hexa-*O*-acetylsucrose[12] with sulphuryl chloride, as described for **1**, followed by treatment with lithium chloride in hexamethylphosphoric triamide, gave 3,4,6-tri-*O*-acetyl-1-chloro-1-deoxy-β-D-fructofuranosyl 3,4,6-tri-*O*-acetyl-2-chloro-2-deoxy-α-D-mannopyranoside* (**8**) in 73% yield. The structure of **8** was supported by 100-MHz and 220-MHz ^{1}H-n.m.r., ^{13}C-n.m.r., and mass spectrometry. In the 100-MHz ^{1}H-n.m.r. spectrum, the individual protons were not identified. However, the general pattern of the spectrum was very different from those of sucrose derivatives. Most of the ring protons and the methylene protons of **8** appeared in three distinct groups: τ 4.30–4.65 (5 protons), 5.58–5.57 (7 protons), and 6.23–6.34 (2 protons). The 220-MHz ^{1}H-n.m.r. spectrum of **8** showed H-1,3,4,3′,4′ at τ 4.20, 4.31, 4.16, 4.24, and 4.35, respectively. The H-2 signals were identified in the region of τ 5.50–5.54 (*cf.* τ 5.02 in sucrose octa-acetate), indicating that one of the chlorine atoms was located at C-2. The signals due to methylene protons at C-1′ appeared as a typical quartet at τ 6.61 (*cf.* τ 5.63 and 5.72 in sucrose octa-acetate), thereby indicating that the second chlorine atom was located at C-1′. The first-order coupling constants ($J_{1,2}$ 2.0, $J_{2,3}$ 3.5, $J_{3,4}$ 9.0, and $J_{4,5}$ 9.0 Hz) were in complete agreement with the *manno* configuration and $^4C_1$ conformation for the hexopyranosyl ring in **8**. The structures of **8** and 1′,2-dichloro-1′,2-dideoxy-*manno*-sucrose (**9**) were supported by their ^{13}C-n.m.r. spectra. The tentative assignments for **8** and **9** given in Table I are based on earlier interpretations of the spectra of sucrose and sucrose octa-acetate. For this reason, the ^{13}C-chemical shift values of sucrose[13] and sucrose octa-acetate[14] are included. The signals for the anomeric carbon atoms in **9** were identified at the lower end of the spectrum, as expected, with C-2′ at the lowest field (104.1 p.p.m.). The chemical shift values (in p.p.m. downfield from Me_4Si) of most of the methine carbon atoms in **9** compared well with those of sucrose, except for the hydroxymethyl (-$^{13}CH_2O$-) group on C-2′. As expected[15,16], there was a drastic chemical shift (—17.6 p.p.m.) in the C-1′ resonance of **9** (with respect to sucrose) because of chlorination. The effect on the nearest neighbour carbon (C-2′), a so-called β-effect, was only 0.3 p.p.m. The signals for the other carbon atoms of the fructofuranosyl ring in **9** were virtually unaffected by the introduction of chlorine at C-1′. In the hexopyranosyl unit of **9**, the signals for C-1, C-2, and C-3 were altered

*This compound is trivially named as 1′,2-dichloro-1′,2-dideoxy-*manno*-sucrose hexa-acetate.





8 R = H, R^1 = R^2 = Cl, R^3 = OAc
10 R = R^3 = OAc, R^1 = H, R^2 = Cl
12 R = R^2 = OBz, R^1 = H, R^3 = OAc
13 R = OH, R^1 = H, R^2 = OBz, R^3 = OAc
14 R = OSO_2Cl, R^1 = H, R^2 = OBz, R^3 = OAc
15 R = H, R^1 = Cl, R^2 = OBz, R^3 = OAc
16 R = H, R^1 = R^2 = R^3 = Cl
18 R = R^2 = OSO_2Cl, R^1 = H, R^3 = Cl

9 R = H, R^1 = Cl, R^2 = OH
11 R = R^2 = OH, R^1 = H
17 R = H, R^1 = R^2 = Cl

TABLE I

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

Assignments[b]	*Chemical shift*[a] *of* ^{13}C *resonances*			
	Sucrose[c]	**9**[d]	*Sucrose octa-acetate*[e]	**8**[e]
C-2′	104.4	104.1	104.2	104.0
C-1	92.9	94.4	90.1	93.9
C-5′	82.2	82.7	79.3	78.7
C-3′	77.4	78.4	75.9	76.2
C-4′	74.8	75.0	75.2	73.8
C-3	73.5	67.1	70.4	65.4
C-5	73.2	74.7	69.8	70.0
C-4	70.1	69.8	68.6	69.4
C-2	71.9	63.0	68.4	62.5
C-1′	63.3	45.7	63.2	46.8
C-6′	62.5	63.0	63.0	62.1
C-6	61.2	61.3	61.9	58.5

[a]Chemical shifts are expressed in p.p.m. downfield from the ^{13}C resonance of tetramethylsilane. [b]Except for the general, anomeric carbon and primary (CH_2OH) carbon assignments, these are tentative. [c]Data from Ref. 1. [d]Measured in water. [e]Measured in $CDCl_3$.

because of chlorination at C-2. The replacement of HO-2 by chlorine, to give **9**, caused the expected shift of the signals for the α carbon atoms (63.0 p.p.m.) by 8.9 p.p.m. to higher field. β-Effects were observed on C-1 (+1.5 p.p.m.) and C-3 (−6.4 p.p.m.).

The ^{13}C-chemical shift values for **8** were in agreement with its structure. Chlorination effects at C-1′ (−16.9 p.p.m.) and at C-2 (−5.9 p.p.m.) were observed, with respect to sucrose octa-acetate. As in the case of **9**, β-effects at C-1 (+3.8 p.p.m.) and C-3 (−5.0 p.p.m.) were also observed. The structure of **8** was also supported by its mass spectrum, which showed an intense peak at *m/e* 307 (3:1 doublet) due to oxycarbonium ions. The subsequent fragmentation pattern showed ions at *m/e* 187 (3:1 doublet), 145 (3:1 doublet), and 109, due to the loss of two molecules of acetic acid, ketene, and hydrogen chloride, respectively.

Treatment of 3,4,6,3′,4′,6′-hexa-*O*-acetylsucrose[12] with sulphuryl chloride in a mixture of pyridine and chloroform at −70°, then at room temperature for 15 days, and finally at 40° for 4 days, followed by dechlorosulphation and conventional acetylation, gave 1′-chloro-1′-deoxysucrose hepta-acetate (**10**) in 30% yield. Little or no formation of 1′,2-dichloride (**8**) indicated that the 1′-chlorosulphate group is more reactive than that at C-2. Conventional de-esterification of **10** with methoxide in methanol afforded 1′-chloro-1′-deoxysucrose (**11**).

Treatment of 3,4,6,3′,4′,6′-hexa-*O*-acetylsucrose[12] with benzoyl chloride in a mixture of pyridine and chloroform at −50° gave a mixture of products that were isolated by column chromatography on silica gel. 2,1′-Di-*O*-benzoylsucrose hexa-acetate (**12**), 3,4,6,3′,4′,6′-hexa-*O*-acetyl-1′-*O*-benzoylsucrose (**13**), and the unreacted 3,4,6,3′,4′,6′-hexa-*O*-acetylsucrose were isolated in yields of 2, 38, and 48%, respectively. The structure of **12** was consistent with its ^{1}H-n.m.r. and mass spectra, and was not further investigated. The structure of **13** was confirmed by its ^{1}H-n.m.r. spectrum, which revealed a signal due to H-2 at τ 6.32. On addition of trichloroacetyl isocyanate to the n.m.r. solution in deuteriochloroform, the signal due to H-2 was deshielded and appeared at τ 5.05, thereby confirming the presence of a free hydroxyl group at C-2 in **13**.

Treatment of **13** with sulphuryl chloride in pyridine and chloroform at −75°, as described for **2**, gave the 2-chlorosulphate **14** in 91% yield. The structure of **14** was supported by its ^{1}H-n.m.r. spectrum. Treatment of **14** with lithium chloride in hexamethylphosphoric triamide at 80° for 24 h gave the 2-chloro-*manno* derivative **15** in 49% yield, as well as unreacted **14** (29%). The structure of **15** was supported by its 220-MHz, ^{1}H-n.m.r. spectrum. The mass spectrum of **15** revealed peaks at *m/e* 307 and 393, corresponding to mannopyranosyl (3:1 doublet) and fructofuranosyl cations, respectively.

The reaction of 3,4,3′,4′-tetra-*O*-acetyl-6,6′-dichloro-6,6′-dideoxysucrose[17] with sulphuryl chloride, as described for **2**, gave the corresponding 2,1′-bis(chlorosulphate) derivative in 80% yield. This was then treated with lithium chloride in hexamethylphosphoric triamide at 80° for 20 h, to give 2,6,1′,6′-tetrachloro-2,6,1′,6′-tetradeoxy-*manno*-sucrose tetra-acetate (**16**) in 85% yield. In the 100-MHz, ^{1}H-n.m.r. spectrum of **16**, the signals for the ring protons and the methylene protons appeared in three distinct groups, as in the case of **8**. The signals for H-1 and H-2 were identified by spin-decoupling experiments at τ 4.40 and 5.57, respectively. The appearance of the H-2 resonance at τ 5.57 (*cf.* τ 4.87 in sucrose octa-acetate) confirmed that one of

the chlorine atoms was located at C-2. The signals for the methylene protons were identified in the region of τ 6.10–6.51 (*cf.* τ 5.64–5.86 in sucrose octa-acetate), indicating that the remaining three chlorine atoms in **16** were located at C-6, C-1′, and C-6′. The first-order coupling constants ($J_{1,2}$ 2.0, $J_{2,3}$ 4.0 Hz) were in agreement with the structure of **16**, which was also supported by the mass spectrum [signal at *m/e* 283 (9:6:1, triplet) due to oxycarbonium ions].

Conventional de-esterification of **16** gave 2,6,1′,6′-tetrachloro-2,6,1′,6′-tetradeoxy-*manno*-sucrose (**17**).

Although no kinetic data are available at present on the displacement reaction of the 2-chlorosulphate group in **2**, 3,4,6,3′,4′,6′-hexa-*O*-acetylsucrose 2,1′-bis(chlorosulphate), or 3,4,3′,4′-tetra-*O*-acetyl-6,6′-dichloro-6,6′-dideoxysucrose 2,1′-bis(chlorosulphate), pertinent comments are possible. The replacement of chlorosulphate groups by chloride in sugars has been suggested to proceed either by an S_N2 process[6,7] or *via* a cyclic intermediate[10]. Considering electronic and steric factors, it appears unlikely that an S_N2 transition state would be formed at C-2 in the above-mentioned compounds. Further evidence against an S_N2 process is provided by the fact that replacement of 2-chlorosulphate in **2** occurs only with lithium chloride and not with other nucleophilic reagents such as lithium bromide, sodium chloride, sodium azide, and sodium benzoate. If the reaction were an intramolecular process and proceeded *via* a cyclic intermediate, it would be expected that heating **2** with hexamethylphosphoric triamide alone would give the 2-chloride **3**. However, the major product obtained from this reaction was the 2-hydroxy compound **1**. Little or no formation of **3** indicated that the reaction was not an intramolecular process.

EXPERIMENTAL

For details of general procedure, see Part XXIV[18].

Methyl 3-O-acetyl-4,6-O-benzylidene-α-D-glucopyranoside 2-chlorosulphate (**2**). — A solution of methyl 3-*O*-acetyl-4,6-*O*-benzylidene-α-D-glucopyranoside[10] (**1**) in chloroform (90 ml) and pyridine (30 ml) was treated with sulphuryl chloride (7.5 ml) at −75°, and then allowed to reach −40° during 45 min. The reaction mixture was poured into ice-cold sulphuric acid (10%, 500 ml) with vigorous shaking and then extracted with dichloromethane. The organic layer was washed successively with water, aqueous sodium hydrogen carbonate, and water, and dried (Na_2SO_4). The solution was concentrated to a syrup which was crystallised from ether–light petroleum, to give **2** (3.5 g, 60%), m.p. 115–117°, $[\alpha]_D$ +58.5° (*c* 1.02, chloroform); n.m.r. data: τ 4.88 (d, $J_{1,2}$ 3.8 Hz, H-1), 5.22 (q, $J_{2,3}$ 9.5 Hz, H-2), 4.35 (t, $J_{3,4}$ 9.5 Hz, H-3), 6.27 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.53 (s, PhC*H*), 6.54 (s, OMe), 7.92 (s, OAc), and 2.54–2.78 (aromatic protons).

Anal. Calc. for $C_{16}H_{19}ClO_9S$: C, 45.5; H, 4.5. Found: C, 45.6; H, 4.6.

Methyl 3-O-acetyl-4,6-O-benzylidene-2-chloro-2-deoxy-α-D-mannopyranoside (**3**). — A solution of **2** (15 g) in hexamethylphosphoric triamide (150 ml) was treated with lithium chloride (15 g) at ~70° for 2.5 h. The mixture was allowed to attain

ambient temperature and then poured into ice–water, the precipitate formed was filtered off and taken up in ether, and the solution was dried (Na_2SO_4) and concentrated. The syrupy residue was eluted from a column of silica gel (200 g) with ether–light petroleum (1:2), to afford **3** (9 g, 74%), $[\alpha]_D$ +3.6° (*c* 1.16, chloroform); n.m.r. (100 MHz) data: τ 5.17 (d, $J_{1,2}$ 1.5 Hz, H-1), 5.48 (q, $J_{2,3}$ 3.5 Hz, H-2), 4.64 (q, $J_{3,4}$ 8.8 Hz, H-3), 5.85 (t, $J_{4,5}$ 8.8 Hz, H-4), 4.46 (s, PhC*H*), 6.61 (OMe), 7.91 (OAc), and 2.50–2.76 (aromatic protons). Mass-spectral data [ions (a) correspond to 3:1 doublets due to one chlorine atom]: *m/e* 342 (a), 341 (a), 193 (a), 149, 133 (a), and 105 (a).

Anal. Calc. for $C_{16}H_{19}ClO_6$: C, 56.1; H, 5.6; Cl, 10.3. Found: C, 56.8; H, 5.9; Cl, 10.2.

*Methyl 3-*O*-acetyl-2-chloro-2-deoxy-*α*-*D*-mannopyranoside* (**4**). — A solution of **3** (8 g) in 60% aqueous acetic acid (150 ml) was heated at ~80° for 4 h. T.l.c. (ether–light petroleum, 5:1) showed a slow-moving, major product. The solution was concentrated by co-distillation with toluene, and the resulting syrup was eluted from a column of silica gel (200 g) with ether–light petroleum (4:1), to give **4** (4 g, 67%), m.p. 105–106° (from ether–light petroleum), $[\alpha]_D$ +27.7° (*c* 1.04, chloroform); n.m.r. (100 MHz) data: τ 5.14 (d, $J_{1,2}$ 1.5 Hz, H-1), 5.57 (q, $J_{2,3}$ 3.5 Hz, H-2), 4.78 (q, $J_{3,4}$ 9.5 Hz, H-3), 5.87 (t, $J_{4,5}$ 9.5 Hz, H-4), 6.06–6.38 (H-5,6), 6.56 (OMe), and 7.84 (OAc); after addition of trichloroacetyl isocyanate: τ 5.13 (d, $J_{1,2}$ 1.5 Hz, H-1), 4.48–4.71 (H-3,4), 5.45–5.60 (H-2,5,6), 6.54 (OMe), 7.90 (OAc), 1.36 (NH), and 1.41 (NH).

Anal. Calc. for $C_9H_{15}ClO_6$: C, 42.5; H, 5.9; Cl, 13.9. Found: C, 42.4; H, 5.9; Cl, 13.7.

*Methyl 3,4,6-tri-*O*-acetyl-2-chloro-2-deoxy-*α*-*D*-mannopyranoside* (**5**). — A solution of **4** (3 g) in pyridine (20 ml) was treated with acetic anhydride (3 ml) at room temperature for 24 h. T.l.c. (ether–light petroleum, 5:1) showed a fast-moving product. The solution was concentrated by co-distillation with toluene to give **5** (3.2 g, 80%) as a syrup, $[\alpha]_D$ +35.0° (*c* 1.13, chloroform); n.m.r. data: τ 5.18 (d, $J_{1,2}$ 1.5 Hz, H-1), 5.66 (q, $J_{2,3}$ 3.0 Hz, H-2), 4.54–4.78 (H-3,4), 6.06 (m, H-5), 5.84 (m, H-6), 6.62 (s, OMe), 7.95, 7.97, and 8.00 (3 s, 3 OAc).

Anal. Calc. for $C_{13}H_{19}ClO_8$: C, 46.1; H, 5.65; Cl, 10.5. Found: C, 46.6; H, 5.8; Cl, 9.8.

*Methyl 2-chloro-2-deoxy-*α*-*D*-mannopyranoside* (**6**). — A solution of **5** (1 g) in dry methanol (50 ml) was treated with a catalytic amount of sodium methoxide at room temperature for 24 h. T.l.c. (chloroform–methanol, 6:1) showed one product. The solution was deionised by shaking with Amberlyst-15(H^+) resin and concentrated to give **6** (0.57 g, 90%) as a syrup, $[\alpha]_D$ +59.9° (*c* 1.05, water).

Anal. Calc. for $C_7H_{13}ClO_5$: C, 39.5; H, 6.2; Cl, 16.7. Found: C, 40.6; H, 6.3; Cl, 15.6.

*1,3,4,6-Tetra-*O*-acetyl-2-chloro-2-deoxy-*D*-mannopyranose* (**7**). — Conc. sulphuric acid (2.5 ml) was added dropwise to a solution of **4** (3.6 g) in glacial acetic acid (100 ml) and acetic anhydride (7 ml) at 0°. The mixture was stored at room tempera-

ture for 5 days. T.l.c. (ether–light petroleum, 6:1) then showed one spot. The solution was diluted with dichloromethane, washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and concentrated, to give **7** (3.6 g, 70%) as a syrup, $[\alpha]_D$ +30.1° (*c* 1, chloroform); n.m.r. (100 MHz) data: τ 3.83 (d, $J_{1,2}$ 1.75 Hz, H-1), 5.65 (q, $J_{2,3}$ 3.0 Hz, H-2), 4.71 (q, $J_{3,4}$ 9.0 Hz, H-3), 4.56 (t, $J_{4,5}$ 9.0 Hz, H-4), 5.80–6.04 (3 H, H-5,6), 7.90, 7.95, 7.96, and 8.00 (12 H, 4 OAc).

Anal. Calc. for $C_{14}H_{19}ClO_9$: C, 45.9; H, 5.2; Cl, 9.7. Found: C, 46.6; H, 5.3; Cl, 9.3.

Reaction of **2** *with lithium bromide, sodium azide, sodium chloride, and sodium benzoate.* — In a typical reaction, **2** (1 g) was treated with the nucleophilic reagent (1 g) in hexamethylphosphoric triamide (15 ml) at ~70° for 6 h. The reaction mixture was worked up, as described for **3**. T.l.c. (ether–light petroleum, 5:1) showed that the reaction product was coincident with an authentic sample[11] of **1**. The ether extract was concentrated, to give crystalline **1** as the major product; n.m.r. (100 MHz) data: τ 5.21 (d, $J_{1,2}$ 3.5 Hz, H-1), 6.40 (q, $J_{2,3}$ 9.5 Hz, H-2), 4.68 (t, $J_{3,4}$ 9.5 Hz, H-3), 4.54 (s, PhC*H*), 2.54–2.78 (m, 5 H, C_6H_5), 6.56 (s, 3 H, OMe), and 7.90 (s, 3 H, OAc).

1′,2-Dichloro-1′,2-dideoxy-manno-*sucrose hexa-acetate* (**8**). — A solution of 3,4,6,3′,4′,6′-hexa-*O*-acetylsucrose[11] (5.4 g) in pyridine (27 ml) and chloroform (80 ml) was treated with sulphuryl chloride (6 ml) at −70° for 2 h. The reaction mixture was worked up at −40°, as described for **3**. The dichloromethane extract, which contained one product (t.l.c.; ether–light petroleum, 7:1), was concentrated to give a syrup (7 g), which was then treated with lithium chloride (5 g) in hexamethylphosphoric triamide (80 ml) at 80° for 20 h. The mixture was poured on to ice–water, and the precipitate was collected and washed thoroughly with water. A solution of the solid residue in ether was dried (Na_2SO_4), concentrated, and purified by elution through a column of silica gel with ether, to give **8** (4.2 g, 73%) as a syrup, $[\alpha]_D$ −17.2° (*c* 1.2, chloroform); n.m.r. (220 MHz, in deuteriobenzene) data: τ 4.20 (d, $J_{1,2}$ 2.0 Hz, H-1), 5.50–5.54 (m, H-2), 4.31 (q, $J_{2,3}$ 3.5, $J_{3,4}$ 9.0 Hz, H-3), 4.16 (t, $J_{4,5}$ 9.0 Hz, H-4), 6.61 (q, 2 H, H-1′), 4.24 (d, $J_{3',4'}$ 7.0 Hz, H-3′), and 4.35 (t, $J_{4',5'}$ 7.0 Hz, H-4′). Mass-spectral data [ions are 3:1 doublets due to 1 chlorine atom]: *m/e* 307, 187, and 145.

Anal. Calc. for $C_{24}H_{32}Cl_2O_{15}$: C, 45.7; H, 5.1; Cl, 11.2. Found: C, 45.8; H, 5.2; Cl, 11.5.

1′,2-Dichloro-1′,2-dideoxy-manno-*sucrose* (**9**). — A solution of **8** (2.3 g) in dry methanol (100 ml) was treated with a catalytic amount of sodium methoxide at room temperature for 4 h. T.l.c. (dichloromethane–methanol, 2.1) then showed one slow-moving product. The solution was deionised with Zerolite DM-F and concentrated by co-distillation with methanol, to give **9** (960 mg, 67%) as a syrup, $[\alpha]_D$ +23.1° (*c* 1, methanol).

Anal. Calc. for $C_{12}H_{20}Cl_2O_9$: C, 38.0; H, 5.3; Cl, 18.7. Found: C, 37.2; H, 5.2; Cl, 17.6.

1′-Chloro-1′-deoxysucrose hepta-acetate (**10**). — A solution of 3,4,6,3′,4′,6′-

hexa-*O*-acetylsucrose[11] (1.8 g) in pyridine (5 ml) and chloroform (25 ml) was treated with sulphuryl chloride (3 ml) at −70°. The mixture was stored at room temperature for 15 days, and then at 40° for 4 days. The mixture was concentrated, taken up in methanol (100 ml), and treated with sodium hydrogen carbonate (8 g) and sodium iodide (25 mg). The solid, inorganic residue was filtered off through "Hyflo", the filtrate was concentrated to dryness, and the residue was treated with acetic anhydride (2 ml) and pyridine (50 ml) at room temperature for 24 h. The solution was concentrated by co-distillation with toluene, and the resulting syrup was eluted from a column of silica gel (50 g) with ether–light petroleum (1:1), to afford **10** (600 mg, 30%), $[\alpha]_D$ +55.0° (*c* 1.2, chloroform); n.m.r. (100 MHz) data: τ 4.29 (d, $J_{1,2}$ 3.5 Hz, H-1), 5.11 (q, $J_{2,3}$ 10.0 Hz, H-2), 4.56 (t, $J_{3,4}$ 9.5 Hz, H-3), 4.94 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.32 (d, $J_{3',4'}$ 6.5 Hz, H-3'), 4.60 (t, $J_{4',5'}$ 6.5 Hz, H-4'), and 7.84–8.01 (7 OAc). Mass-spectral data: [(a) indicates ions due to hexopyranosyl cation, and (b) a 3:1 doublet (1 Cl) due to ketofuranosyl cation]: *m/e* 331 (a), 307 (b), 187 (b), 169 (a), 145 (b), and 109 (a).

Anal. Calc. for $C_{26}H_{35}ClO_{17}$: C, 47.7; H, 5.4; Cl, 5.4. Found: C, 47.5; H, 5.6; Cl, 5.7.

1'-Chloro-1'-deoxysucrose (**11**). — A solution of **10** (1 g) in dry methanol (10 ml) was treated with a catalytic amount of M sodium methoxide in methanol at room temperature for 5 h. T.l.c. (dichloromethane–methanol, 3:1) then showed a slow-moving product. The solution was deionised by shaking with Amberlyst-15(H^+) resin, filtered, concentrated, and purified by washing an aqueous solution with light petroleum. The aqueous layer was then concentrated and dried under vacuum, to give **11** (0.5 g, 89%), $[\alpha]_D$ +57.8° (*c* 0.7, water).

Anal. Calc. for $C_{12}H_{21}ClO_{10}$: C, 40.0; H, 5.9; Cl, 9.8. Found: C, 39.7; H, 6.1; Cl, 9.7.

*Reaction of 3,4,6,3',4',6'-hexa-*O*-acetylsucrose with benzoyl chloride.* — A solution of the title compound[11] (14.0 g) in pyridine (300 ml) and chloroform (150 ml) was cooled to −50°, and benzoyl chloride (9 ml) was added dropwise. The mixture was stirred at −50° for 2 h, and then poured into ice water. The product was extracted into dichloromethane (2 × 500 ml), which was washed successively with water, aqueous sodium hydrogen carbonate, and water. Concentration of the organic layer afforded a syrup that was eluted from a column of silica gel with ether–light petroleum 4:1, to give, initially, 2,1'-di-*O*-benzoylsucrose hexa-acetate (**12**; 0.35 g, 2%), $[\alpha]_D$ +67.6° (*c* 1, chloroform); n.m.r. ($CDCl_3$) data: τ 4.08 (d, $J_{1,2}$ 3.0 Hz, H-1), 4.88 (q, $J_{2,3}$ 9.5 Hz, H-2), 4.27 (t, $J_{3,4}$ 9.5 Hz, H-3), 4.81 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.46 (d, $J_{3',4'}$ 5.5 Hz, H-3'), 4.64 (t, $J_{4',5'}$ 5.5 Hz, H-4'), 1.90–2.80 (10 H, 2 Bz), and 7.89–8.10 (18 H, 6 OAc). Mass-spectral data: *m/e* 393, 273, 231, 169, and 105.

Anal. Calc. for $C_{38}H_{42}O_{19}$: C, 56.9; H, 5.3. Found: C, 57.2; H, 5.4.

Further elution of the column afforded 3,4,6,3',4',6'-hexa-*O*-acetyl-*1'-O*-benzoylsucrose (**13**; 6.2 g, 38%), $[\alpha]_D$ +67.8° (*c* 1.03, chloroform); n.m.r. data ($CDCl_3$): τ 4.41 (d, $J_{1,2}$ 3.0 Hz, H-1), 6.32 (q, $J_{2,3}$ 9.5 Hz, H-2), 4.81 (t, $J_{3,4}$ 9.5 Hz, H-3), 4.99 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.46 (d, $J_{3',4'}$ 5.5 Hz, H-3'), 4.50 (t, $J_{4',5'}$ 5.5 Hz,

H-4'), 1.94–2.67 (5 H, Bz), and 7.88–8.00 (18 H, 6 OAc); after addition of trichloroacetyl isocyanate to the n.m.r. sample: τ 4.29 (d, $J_{1,2}$ 3.0 Hz, H-1), 5.05 (q, $J_{2,3}$ 9.5 Hz, H-2), 4.62 (t, $J_{3,4}$ 9.5 Hz, H-3), 4.96 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.69 (d, $J_{3',4'}$ 5.5 Hz, H-3'), 4.77 (t, $J_{4',5'}$ 5.5 Hz, H-4'), 0.92 (s, 1 H, NH), 2.10–2.72 (5 H, Bz), and 7.90–8.06 (18 H, 6 OAc).

Anal. Calc. for $C_{31}H_{38}O_{18}$: C, 53.3; H, 5.5. Found: C, 52.9; H, 5.45.

Unreacted 3,4,6,3',4',6'-hexa-*O*-acetylsucrose (6.7 g, 48%) was obtained on washing the column with ether.

3,4,6,3',4',6'-Hexa-O-*acetyl-1'*-O-*benzoylsucrose 2-chlorosulphate* (**14**). — A solution of **13** (5.2 g) in a mixture of pyridine (25 ml) and chloroform (80 ml) was treated with sulphuryl chloride (6 ml) at −70° for 3 h. The reaction mixture was worked up at −40°, as described for compound **1**. The dichloromethane extract, which contained a single product (t.l.c.; ether–light petroleum, 4:1), was concentrated, to give **14** as a syrup (5.4 g, 91%), $[\alpha]_D$ +61.2° (*c* 1, chloroform); n.m.r. (100 MHz) data: τ 4.08 (d, $J_{1,2}$ 3.5 Hz, H-1), 5.19 (q, $J_{2,3}$ 9.5 Hz, H-2), 4.45 (t, $J_{3,4}$ 9.5 Hz, H-3), 4.87 (t, $J_{4,5}$ 9.5 Hz, H-4), 4.41 (d, $J_{3',4'}$ 5.5 Hz, H-3'), 4.62 (t, $J_{4',5'}$ 5.5 Hz, H-4'), 1.95–2.64 (5 H, Bz), and 7.88–7.97 (18 H, 6 OAc).

Anal. Calc. for $C_{31}H_{37}ClO_{20}S$: C, 46.7; H, 4.7; Cl, 4.45; S, 4.0. Found: C, 46.9; H, 4.7; Cl, 4.7; S, 5.0.

1'-O-*Benzoyl-2-chloro-2-deoxy*-manno-*sucrose hexa-acetate* (**15**). — Lithium chloride (5 g) was added to a solution of **14** (4.1 g) in hexamethylphosphoric triamide (80 ml), which was then stirred at 80° for 24 h. The reaction mixture was worked up as described in the preparation of **3**. Elution of the syrupy product from a column of silica gel (100 g) with ether–light petroleum (1:1) gave, in addition to unreacted **14** (1.2 g, 29%), **15** (1.7 g, 49%), $[\alpha]_D$ +7.6° (*c* 0.95, chloroform); n.m.r. (220 MHz) data: τ 4.08 (d, $J_{1,2}$ 2.0 Hz, H-1), 5.45 (q, $J_{2,3}$ 3.4 Hz, H-2), 4.23 (q, $J_{3,4}$ 9.5 Hz, H-3), 4.13 (q, $J_{4,5}$ 10.5 Hz, H-4), 4.28 (d, $J_{3',4'}$ 6.0 Hz, H-3'), 4.36 (t, $J_{4,5}$ 6.0 Hz, H-4'), 2.80–2.90 (m, 5 H, Bz); 8.14, 8.19, 8.29, 8.34, and 8.42 (18 H, 6 OAc). Mass-spectral data: [(a) indicates 3:1 doublet ions (1 Cl) due to the hexopyranosyl cations, and (b) indicates ions due to ketofuranosyl cations]: *m/e* 393 (b), 307 (a), 273 (b), 231 (b), 187 (a), 145 (a), and 109 (b).

Anal. Calc. for $C_{31}H_{37}ClO_{17}$: C, 51.9; H, 5.2; Cl, 4.9. Found: C, 52.0; H, 5.3; Cl, 4.9.

2,6,1',6'-Tetrachloro-2,6,1',6'-tetradeoxy-manno-*sucrose tetra-acetate* (**16**). — A solution of 3,4,3',4'-tetra-*O*-acetyl-6,6'-dichloro-6,6'-dideoxysucrose[15] (5 g) in pyridine (25 ml) and chloroform (75 ml) was treated with sulphuryl chloride (2.5 ml) at −75°. The reaction was worked up, as described for **2**, to give the 1',2-bis(chlorosulphate) **18** (5.4 g, 80%).

Compound **18** (4 g) was then treated with lithium chloride (4 g) in hexamethylphosphoric triamide (30 ml) at 80° for 20 h. The reaction mixture was worked up, as described for **8**, to give a syrup. Elution of the syrup from a column of silica gel (100 g), using ether–light petroleum (1:1), gave the 2,6,1',6'-tetrachloride **16** (2.7 g, 85%) as a syrup, $[\alpha]_D$ −16.7° (*c* 1, chloroform); n.m.r. data ($CDCl_3$): τ 4.40 (d,

$J_{1,2}$ 2.0 Hz, H-1), 5.57 (q, $J_{2,3}$ 4.0 Hz, H-2), 4.34–4.60 (m, 2 H, H-3',4'), 6.10–6.51 (6 H, H-6,1',6'), and 7.78–7.88 (12 H, 4 OAc). Mass-spectral data [ions are 9:6:1 triplets due to two chlorine atoms]: *m/e* 283, 223, and 163.

Anal. Calc. for $C_{20}H_{26}Cl_4O_{11}$: C, 41.1; H, 4.5; Cl, 24.3. Found: C, 42.1; H, 4.75; Cl, 24.1.

2,6,1',6'-Tetrachloro-2,6,1',6'-tetradeoxy-manno-*sucrose* (**17**). — A solution of **16** (1 g) in dry methanol was treated with a catalytic amount of sodium methoxide at room temperature for 20 h. The solution was deionised with Amberlyst-15(H^+) resin and concentrated, to afford **17** (0.64 g, 90%) as a syrup, $[\alpha]_D$ +22.4° (*c* 0.93, methanol).

Anal. Calc. for $C_{12}H_{18}Cl_4O_7$: C, 34.6; H, 4.4. Found: C, 35.2; H, 4.7.

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