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REACTIONS OF SUGAR CHLOROSULFATES

VII. SOME CONFORMATIONAL ASPECTS

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ABSTRACT

The reaction of sulfuryl chloride with several 1,6-anhydro-hexosans has yielded crystalline, fully chlorosulfated derivatives. Replacement of the chlorosulfate moieties by chlorodeoxy groups could not be achieved under the reaction conditions employed. This non-reactivity is discussed in terms of steric interactions in the transition state for substitution.

An examination of some chloro-substituted sugar chlorosulfates confirmed that an axial chlorodeoxy group in a glycopyranoside deactivates a neighboring equatorial chlorosulfate group and thus prevents further chlorodeoxy groups being introduced into such positions. Methyl α-D-altropyranoside, methyl α-L-rhamnopyranoside, methyl α-D-lyxopyranoside, L-rhamnose, and D-lyxose were reacted with sulfuryl chloride. The resulting products were those expected if these sugars reacted primarily in the C1 conformation.

INTRODUCTION

Previous work (1–5) has shown that the reaction of sulfuryl chloride with carbohydrates containing free hydroxyl groups gives derivatives containing both chlorodeoxy and chlorosulfate moieties, and that these products are formed via fully chlorosulfated derivatives. The chlorodeoxy groups are derived by the nucleophilic displacement (S_N2) of certain of the chlorosulfate groups by chloride ion. Kinetic studies carried out with model alkyl chlorosulfates have shown the remarkable facility with which the OSO_2Cl moiety can act as a leaving group (6).

It has been shown in the previous work carried out with hexopyranoses and hexopyranosides that the OSO_2Cl group at C-6 is the most reactive and is readily converted into a chlorodeoxy group. Preferential displacement at C-6 in hexopyranosides has been noted previously, for instance, with the tosyl derivatives (7).

Whether a secondary chlorosulfate group is replaced by the chloride ion depends on the conformation of the pyranoside of which it forms a part. Several steric factors have been demonstrated to affect adversely the replacement and may be summarized as: (*i*) 1,3-diaxial interactions to the approach of the chloride ion; (*ii*) deactivation of the C-2 position by anomeric chloro and methoxyl groups; and (*iii*) deactivation of an equatorial chlorosulfate ester group vicinal to an axial substituent which itself is resistant to substitution. The relevance of these factors to the synthesis of a fully chlorinated sugar glycoside was considered recently (8).

The present paper reports on a number of topics. For the first time, chlorosulfates of 1,6-anhydro-hexopyranoside derivatives have been investigated, with the view that the

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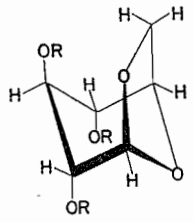
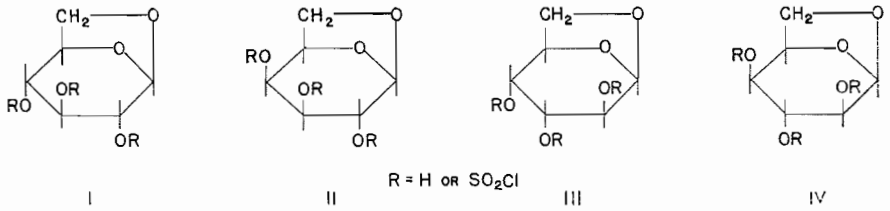
rigidity of these structures would impose stringent conditions on the substitution process. Secondly, a number of sugars have been examined in which chloro substituents were introduced into certain specific positions to learn more about steric and electronic effects in these substitution processes. Lastly, experiments have been performed with the aim of obtaining further information about the preferred conformation of certain sugars. Thus D-lyxose and D-altrose were considered by Reeves (9) to exist in both C1 and 1C conformations, but other workers (10, 11) have disagreed. It was considered that an examination of chlorosulfate substitution in these compounds might provide a chemical approach to this problem.

The Reaction of 1,6-Anhydro-hexosans

The following hexosans were studied: 1,6-anhydro-β-D-glucopyranose (I, R = H, or I*a*, R = H (conformational formula)), 1,6-anhydro-β-D-galactopyranose (II, R = H), 1,6-anhydro-β-D-altropyranose (III, R = H), and 1,6-anhydro-β-D-idopyranose (IV, R = H). The product obtained in each case was a crystalline 2,3,4-trichlorosulfate (I–IV, R = SO_2Cl). Treatment of the trichlorosulfates with pyridine hydrochloride in chloroform solution failed to introduce chlorodeoxy groups into the molecules under the conditions employed. Since substitution does not occur in any of the cases, it must be



Ia



R = H or SO_2Cl

I II III IV

concluded that the steric interactions are too great throughout or, of course, that the reaction conditions employed were not at an optimum. Another factor may contribute to the lower reactivity of the chlorosulfates of these bicyclic systems relative to that of the simple hexopyranosides, namely, that re-hybridization from sp^3 to sp^2 requisite for substitution (12) may be disfavored by the rigidity of this bicyclic system.

The Reaction of Some Substituted Methyl Glycopyranosides

When methyl α- and β-D-glucopyranosides were treated with sulfuryl chloride in pyridine, 4,6-dichloro-substituted derivatives were obtained which were resistant to further substitution (5). In the case of the methyl β-D-glycosidic derivative, in which the anomeric methoxyl group is equatorial, the resistance to further substitution was explained as being due to the deactivating effect of the axial chlorodeoxy group at C-4. It was decided in the current work to examine whether a chlorodeoxy group at C-3 would have the same deactivating effect. The known methyl 3-chloro-3-deoxy-β-D-allopyranoside

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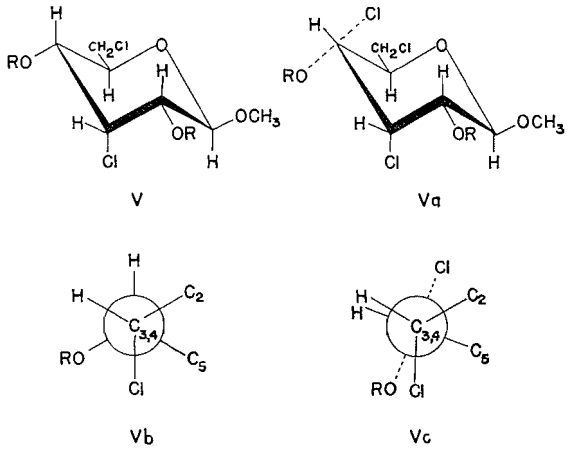
was prepared from methyl 4,6-*O*-benzylidene-β-D-glucopyranoside. The methyl 3-chloro-3-deoxy-β-D-allopyranoside (V) was then treated with sulfuryl chloride in the usual way. The product was a syrup which, on dechlorosulfation, gave a crystalline compound that was most probably methyl 3,6-dichloro-3,6-dideoxy-β-D-allopyranoside. Elemental analysis showed the formation of a dichlorodideoxy compound, and periodate oxidation results indicated that the chlorodeoxy groups were at the C-3 and C-6 positions. The D-allo configuration is assumed, since in all cases examined hitherto the chlorodeoxy groups were observed to be introduced with inversion (3–5).

The observation that no further substitution by chloride ion occurred under these standard conditions to form a trichlorotrideoxy derivative indicates a deactivating effect of the axial chloro group at C-3. This is further evidence that an axial substituent which cannot itself be replaced deactivates a vicinal, equatorial chlorosulfate ester group. A possible explanation for this is shown in formulae V–V*c*. To introduce a chlorodeoxy



group at C-4 by S_N2 reaction, the transition state V*a* would have to be formed (13). The end-on representation of V and V*a*, viewed along the C-3, C-4 axis, is shown in V*b* and V*c*, and it is seen that steric interaction in V*c* between the chlorodeoxy group on C-3 and the large chlorosulfate group on C-4 would strongly hinder S_N2 reaction at C-4.

The Reaction of Methyl α-L-Rhamnopyranoside and L-Rhamnose

Methyl α-L-rhamnopyranoside has the anomeric methoxyl group on C-1 and the hydroxyl group on C-2 axially oriented, since its preferred conformation is 1C (9). The product obtained from its reaction with sulfuryl chloride in pyridine was a crystalline trichlorosulfate, and no further substitution could be obtained even when it was heated in chloroform solution with pyridine hydrochloride. A chlorodeoxy group might perhaps be introduced into methyl α-L-rhamnopyranoside at C-2 since this chlorosulfate group is axially oriented, by analogy with cyclohexyl derivatives where it is known that axial substituents are displaced at a faster rate than corresponding equatorial substituents. The axial methoxyl group at C-1 would further hinder substitution at C-2.

To verify the latter effect, L-rhamnose itself was reacted with sulfuryl chloride and pyridine. The product from this reaction was a crystalline compound which analyzed as (β?)-L-rhamnosyl chloride 2,3,4-trichlorosulfate. Treatment of this trichlorosulfate with pyridine hydrochloride yielded a syrup which, after dechlorosulfation, had the R_f value and chlorine content expected for a dichlorodideoxy compound. A periodate oxidation

showed no uptake of reagent within 2 days, as expected for 2,4-dichloro-2,4,6-trideoxy-L-galactose which would result if it is assumed that inversion takes place in the normal manner when the chlorodeoxy groups are introduced. The only other possible structure which would not be affected by periodate is a 2,3-dichloro-2,3,6-trideoxy compound, but the formation of the compound is unlikely on the basis of previous results.

The Reactions of Methyl α-D-Altropyranoside, Methyl α-D-Lyxopyranoside, and D-Lyxose

Glycosides and free sugars in the D-altropyranose and D-lyxopyranose configurations have been reported as existing in the C1 and 1C conformations.

Methyl 6-chloro-6-deoxy-α-D-altropyranoside was obtained from methyl α-D-altropyranoside after it was reacted with sulfuryl chloride in pyridine followed by dechlorosulfation. This is the product that would be formed if the glycoside reacted in the C1 conformation, since in this conformation the C-2 and C-3 hydroxyl groups are axially oriented. In the 1C conformation the OR (R = H or SO_2Cl) group at C-4 would be axially oriented, as would be also the CH_2Cl group on C-5. Substitution of the axial chlorosulfate group at C-4 is therefore prevented by the neighboring axial CH_2Cl group.

Proof of the structure of the methyl 6-chloro-6-deoxy-α-D-altropyranoside was given by its elemental analysis and periodate oxidation. The periodate oxidation of this compound was somewhat unusual. The consumption of 2 moles of periodate and the release of 1 mole of formic acid were consistent with the chlorodeoxy group being on C-6. However, unlike the periodate oxidation of the corresponding gluco compound, the rate of production of formic acid was much less than half the uptake of periodate during the first 6 h of the oxidation, and it was not until the reaction had been proceeding for about 1 day that the number of moles of formic acid released became approximately half the number of moles of periodate consumed. If an internal hemiacetal is postulated as an intermediate, these results may be explained.

Methyl α-D-lyxopyranoside in the C1 conformation has the axial glycosidic methoxyl group at C-1 and also an axial substituent at C-2. This situation is directly analogous to the situation in methyl α-D-mannopyranoside and methyl α-L-rhamnopyranoside, which also have axial groups at C-1 and C-2. Methyl α-D-mannopyranoside was shown to yield methyl 6-chloro-6-deoxy-α-D-mannopyranoside 2,3,4-trichlorosulfate when reacted with sulfuryl chloride (5). It was found in the present study that the reaction between methyl α-D-lyxopyranoside and sulfuryl chloride yielded methyl α-D-lyxopyranoside 2,3,4-trichlorosulfate; no chlorodeoxy groups could be introduced by reacting the product further with pyridine hydrochloride. However, if methyl α-D-lyxopyranoside reacted in the 1C conformation, the product might well be the same, since in this conformation the C-3 and C-4 hydroxyl groups would be axial.

To extend the analogy with the manno conformation further, it was decided to examine the reaction of D-lyxose with the sulfuryl chloride – pyridine mixture. D-Mannose had been found to yield a 6-chloro-6-deoxy-trichlorosulfate which, when reacted with pyridine hydrochloride, gave a trichlorotrideoxy compound whose methyl glycoside was assigned the structure methyl 2,4,6-trichlorotrideoxy-β-D-galactopyranoside (compare with L-rhamnose) (5). D-Lyxose also gave a chloro-trichlorosulfate derivative when reacted with sulfuryl chloride, and reaction with pyridine hydrochloride followed by treatment with sodium iodide solution now gave a syrup which was shown by thin-layer chromatography and chlorine analysis to be a dichlorodideoxy sugar. Periodate oxidation showed no uptake of periodate after 48 h, so that the compound was probably 2,4-dichloro-2,4-dideoxy-L-arabinose if the sugar is assumed to react in the pyranose form. The other possibility,

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2,3-dichloro-2,3-dideoxy-D-ribose, is considered to be unlikely, since the D-ribose configuration is known to undergo readily further substitution at C-4 (14). This indicates that D-lyxopyranose reacts primarily in the C1 conformation, as does D-mannopyranose. If it were in the 1C conformation, there would be an axial chlorosulfate at both C-3 and C-4 and an equatorial chlorosulfate group at C-2. This situation would be unlikely to lead to further introduction of chlorodeoxy groups.

EXPERIMENTAL[2]

Thin-layer chromatograms were run by the ascending technique on glass plates which had been coated with silica gel G and dried at 150–160° for 2 h. The following solvent systems were used: (*a*) benzene–methanol (10:1), (*b*) benzene–methanol (20:1), (*c*) benzene–methanol (50:1), and (*d*) benzene–isopropanol (2:1). The sugars were detected on chromatograms by spraying them with sulfuric acid and subsequent heating of the plate in an oven at 110°.

Three general procedures were used. (A) Sulfuryl chloride[3] was added dropwise to the stirred pyridine–chloroform reaction mixtures, cooled in an acetone – solid carbon dioxide bath (approximately −70°), and maintained at this temperature for 2 h, after which time the mixtures were allowed to come to room temperature and held at that temperature for 1 to 2 h. The products were then isolated in the usual way (1–5). (B) The experiment was repeated, except that the mixture was left for 8–12 h before the products were isolated. (C) If thin-layer chromatography (t.l.c.) indicated that further reaction had taken place, then the product was heated with pyridine hydrochloride in dry chloroform to complete, as far as the configuration would allow, the formation of chlorodeoxy groups.

Tetra-*n*-butylammonium chloride could be used as an alternative source of chloride ions to effect displacement (see below).

The Preparation of 1,6-Anhydro Sugars

1,6-Anhydro-β-D-glucopyranose was obtained by the pyrolytic distillation of starch (15) but with the following modification. The dry starch was mixed with copper powder to improve heat transfer through the decomposing starch, and a layer of glass wool was placed above the charge to reduce frothing. The yield was about 40 g from 150 g of starch (26.8%).

1,6-Anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose was prepared from α-lactose monohydrate (16) except that copper powder was mixed with the charge to improve heat transfer through the decomposing lactose. 1,6-Anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose (10 g) was dissolved in water, and the solution was treated with 8 g of Amberlite IR-120 (H^+) resin for 1½ h on a water bath at 70° and then filtered. The product, after evaporation, was recrystallized from alcohol–water (80:20). The yield of 1,6-anhydro-D-galactopyranose, m.p. 220°, was practically quantitative.

1,6-Anhydro-β-D-altropyranose was prepared as follows. A solution of syrupy methyl α-D-altropyranoside (17) in 200 ml of 6% hydrochloric acid was refluxed for 2 h. The solution was neutralized with lead carbonate and filtered, and the lead ions were removed from the filtrate as lead sulfide. The filtered solution was then deionized to yield 10.5 g of syrup. The syrup (6 g) was separated on a cellulose column (63 × 5 cm). The eluting solvent was butan-1-ol half saturated with water. The first fraction was nonreducing in character, and crystallized as long, needle-shaped crystals upon evaporation of the solvent. The relative speed of movement on paper of D-altrose and 1,6-anhydro-β-D-altropyranose is not great but was sufficient to follow the separation without difficulty. In solvent system *e* (ethyl acetate – acetic acid – formic acid – water (18:3:1:4 by volume)) the R_{Rh} of D-altrose was 0.70, and of 1,6-anhydro-β-D-altropyranose 0.95. The yield of 1,6-anhydro-β-D-altropyranose was 2 g (63%), and of D-altrose 1.5 g (58%), characterized as the penta-acetate (17). The yields are based on a 53:47 ratio of anhydro compound to free sugar. 1,6-Anhydro-β-D-altropyranose analyzed as the anhydrous sugar.

Anal. Calcd. for $C_6H_{10}O_5$: C, 44.4; H, 6.22. Found: C, 44.4; H, 6.07.

No definite melting point has previously been reported for 1,6-anhydro-β-D-altropyranose. The melting point of the above sample was 133°, with slight preliminary sintering. It had $[\alpha]_D$ −210° (*c*, 1.0 in water). A sample of 1,6-anhydro-β-D-altropyranose was also obtained from Dr. N. K. Richtmyer; this had a melting point and a mixed melting point with the above sample of 133°. The infrared spectrographs of the two samples were also identical. Dr. Richtmyer's sample was believed to have been the monohydrate before it was stored.

1,6-Anhydro-β-D-glucopyranose 2,3,4-Trichlorosulfate

1,6-Anhydro-β-D-glucopyranose (2 g, 0.012 mole) in dry pyridine (8 ml, 0.099 mole) and dry chloroform (25 ml) was treated with sulfuryl chloride (5 ml, 0.061 mole) and the product isolated according to

[2]*For details see refs. 1–5.*

[3]*The amount of sulfuryl chloride used to make the chlorosulfate ester was 1.5 to 2 moles per hydroxyl group. The pyridine – sulfuryl chloride ratio was in the range 1.5 to 2 moles per mole.*

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procedure A. Recrystallization from chloroform–petrol gave colorless needles, 3.6 g (66%), m.p. 144–146°, $[\alpha]_D$ −17° (*c*, 1.0 in chloroform).

Anal. Calcd. for $C_6H_7Cl_3O_{11}S_3$: C, 15.7; H, 1.54; Cl, 23.2; S, 21.0. Found: C, 15.6; H, 1.66; Cl, 23.1; S, 21.3.

The product gave a positive test for chlorosulfate groups. The infrared spectrum exhibited very sharp peaks at 1 200 and 1 435 cm^{-1} characteristic of chlorosulfate groups (18).

A small amount of crystalline 1,6-anhydro-β-D-glucopyranose 2,3,4-trichlorosulfate was dissolved in methanol (5 ml), and barium carbonate (1 g) was added. One drop of *N* sodium iodide solution was added to dechlorosulfate the product; after 8 h the liquor was co-chromatographed against 1,6-anhydro-β-D-glucopyranose on a paper run in solvent *f* (butan-1-ol–ethanol–water (3:1:1 v/v/v)). The only sugar detected was 1,6-anhydro-β-D-glucopyranose.

The reaction between 1,6-anhydro-β-D-glucopyranose and sulfuryl chloride was carried out according to procedure B. The only chloroform-soluble product obtained was 1,6-anhydro-β-D-glucopyranose 2,3,4-trichlorosulfate.

1,6-Anhydro-β-D-glucopyranose 2,3,4-trichlorosulfate (2 g, 0.043 mole) in dry chloroform (20 ml) and pyridine hydrochloride (2 g, 0.012 mole) was treated according to procedure C. The white crystals so obtained (0.6 g (40.0%)) were found to be identical with the starting material. A small amount of a reducing product (0.012 g) was also obtained but could not be identified.

1,6-Anhydro-β-D-galactopyranose 2,3,4-Trichlorosulfate

1,6-Anhydro-β-D-galactopyranose (1.5 g, 0.0093 mole) in dry pyridine (6 ml, 0.075 mole) and dry chloroform was reacted with excess sulfuryl chloride (4 ml, 0.049 mole) (procedure A). The product was recrystallized from chloroform – petrol (b.p. 35–60°) to give colorless needles, 1.7 g (40%), m.p. 105–106°, $[\alpha]_D$ −27° (*c*, 1.0 in chloroform). The material gave a positive test for chlorosulfate groups and the infrared spectrum exhibited very sharp peaks at 1 418 and 1 183 cm^{-1} corresponding to OSO_2Cl groups (18).

Anal. Calcd. for $C_6H_7Cl_3O_{11}S_3$: C, 15.7; H, 1.54; S, 21.1; Cl, 23.2. Found: C, 15.4; H, 1.64; S, 20.8; Cl, 23.0.

Procedure B gave 1,6-anhydro-β-D-galactopyranose 2,3,4-trichlorosulfate in somewhat lower yield.

1,6-Anhydro-β-D-altropyranose 2,3,4-Trichlorosulfate

1,6-Anhydro-β-D-altropyranose (0.67 g, 0.0041 mole) in pyridine (3 ml, 0.038 mole) and dry chloroform (10 ml) was treated with an excess of sulfuryl chloride (2 ml, 0.025 mole) according to procedure A. The product was recrystallized from chloroform – petrol (b.p. 40–65°) as white needles, 0.74 g (40%), m.p. 143°, $[\alpha]_D^{25}$ −130° (*c*, 0.1 in chloroform). It gave a positive test for chlorosulfate groups and the infrared spectrum exhibited very sharp peaks corresponding to OSO_2Cl groups.

Anal. Calcd. for $C_6H_7Cl_3O_{11}S_3$: C, 15.7; H, 1.54; Cl, 23.2; S, 21.1. Found: C, 15.3; H, 1.4; Cl, 23.0; S, 21.0.

Procedure B gave 1,6-anhydro-β-D-altropyranose 2,3,4-trichlorosulfate in somewhat lower yield.

1,6-Anhydro-β-D-idopyranose 2,3,4-Trichlorosulfate[4]

1,6-Anhydro-β-D-idopyranose (1.01 g from 2.0 g of the triacetate) in pyridine (4.5 ml) and dry chloroform (12.0 ml) was converted into the trichlorosulfate by addition of sulfuryl chloride (2.2 ml) to the mixture (procedure A). The crystalline product had m.p. 164–165° and $[\alpha]_D$ −41° (*c*, 1.8 in methanol).

Anal. Calcd. for $C_6H_7Cl_3O_{11}S_3$: C, 15.7; H, 1.54; Cl, 23.2; S, 21.1. Found: C, 16.1; H, 1.83; Cl, 22.9; S, 21.1.

Procedure C gave starting material as the main product. Some small quantities of other unidentified sugar derivatives were also produced.

Methyl 3,6-Dichloro-3,6-dideoxy-β-D-allopyranoside

Methyl 3-chloro-3-deoxy-β-D-allopyranoside (1.4 g, 0.007 mole), prepared from methyl 4,6-*O*-benzylidene-β-D-glucopyranoside, in pyridine (6 ml, 0.0075 mole) and chloroform was treated with sulfuryl chloride according to procedure A. The product was a syrup (2 g (88%)) which solidified but could not be recrystallized. Dechlorosulfation with sodium iodide gave a crystalline product which, after two recrystallizations, was shown to be pure by t.l.c. in solvent *f* (as used for paper chromatography), R_f 0.59, yield 1.0 g (75%), $[\alpha]_D$ −45°, m.p. 145–156° with some decomposition.

Anal. Calcd. for $C_7H_{12}Cl_2O_4$: C, 36.4; H, 5.23; Cl, 30.7. Found: C, 36.6; H, 5.37; Cl, 30.5.

Periodate oxidation of the methyl 3,6-dichloro-3,6-dideoxy-β-D-allopyranoside, determined in the usual way (19, 20), showed no consumption of periodate during 24 h.

Methyl α-L-Rhamnopyranoside 2,3,4-Trichlorosulfate

Methyl α-L-rhamnopyranoside (31) (0.5 g, 0.003 mole) in anhydrous pyridine (3 ml, 0.038 mole) and dry chloroform (10 ml) was treated with sulfuryl chloride (2 ml, 0.025 mole) (procedure A). The crystalline product was recrystallized from chloroform–petrol, 0.9 g (64%), m.p. 112–113°, $[\alpha]_D$ −2° (*c*, 1.0 in chloroform). Infrared analysis and the aniline–pyridine spray test confirmed the presence of chlorosulfate groups.

[4]*This experiment was carried out by Mr. S. S. Ali.*

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Anal. Calcd. for $C_7H_{11}Cl_3O_{11}S_3$: C, 17.8; H, 2.3; Cl, 22.5; S, 20.0. Found: C, 18.1; H, 2.1; Cl, 22.5; S, 20.1.

A portion of the above crystals (0.5 g, 0.002 mole) in chloroform and anhydrous pyridine hydrochloride (0.5 g, 0.044 mole) was treated according to procedure C. The melting point (112–113°) of the product (0.3 g) was undepressed on admixture with the starting compound.

(β?)-L-Rhamnosyl Chloride 2,3,4-Trichlorosulfate

L-Rhamnose (8 g, 0.05 mole) (dehydrated by heating it at 50° in a vacuum oven for several hours) in pyridine (30 ml) and chloroform (85 ml) was treated with 17 ml of sulfuryl chloride (procedure A). The crystalline product was recrystallized from chloroform – petrol (b.p. 40–60°), 8.5 g (35%), m.p. 140°, $[\alpha]_D$ +57.8° (*c*, 0.1 in chloroform).

Anal. Calcd. for $C_6H_8Cl_4O_{10}S_3$: C, 15.1; H, 1.69; Cl, 29.7; S, 20.1. Found: C, 14.8; H, 1.69; Cl, 29.6; S, 20.5.

The trichlorosulfate (5 g) was dissolved in a minimum of dry chloroform which contained an excess of pyridine hydrochloride, and the solution was heated for 12 h. The product, after dechlorosulfation, contained a major component with R_f 0.67 (solvent *e*). It was purified by preparative thin-layer chromatography and then distilled. The syrupy product had $[\alpha]_D$ −45° (*c*, 1.0 in chloroform).

Anal. Calcd. for $C_6H_{10}Cl_2O_3$: Cl, 35.3. Found: Cl, 35.8.

Periodate oxidation of the dichlorodideoxy compound showed no consumption of periodate during 48 h.

Methyl 6-Chloro-6-deoxy-α-D-altropyranoside 2,3,4-Trichlorosulfate

Methyl α-D-altropyranoside (1 g, 0.0052 mole) in anhydrous pyridine (5 ml, 0.062 mole) and chloroform (20 ml) was treated with sulfuryl chloride (3 ml, 0.037 mole) (procedure A). The crystalline product was recrystallized from chloroform–petrol to give colorless prisms, 2.1 g (79.5%), m.p. 156°, $[\alpha]_D$ +99.2° (*c*, 0.97 in chloroform).

Anal. Calcd. for $C_7H_{10}Cl_4O_{11}S_3$: C, 16.5; H, 1.98; Cl, 27.9; S, 18.9. Found: C, 16.8; H, 2.04; Cl, 28.1; S, 19.0.

Methyl 6-Chloro-6-deoxy-α-D-altropyranoside

The above crystals (2 g) were dissolved in methanol and dechlorosulfated with sodium iodide as previously described. The colorless syrup (1 g (60%)) was shown by t.l.c. to be one component with R_f 0.25 in solvent *b*, $[\alpha]_D$ +101° (*c*, 0.92 in chloroform).

Anal. Calcd. for $C_7H_{13}ClO_5$: C, 39.5; H, 6.16; Cl, 16.7. Found: C, 39.3; H, 6.07; Cl, 16.7.

Periodate Oxidation of Methyl 6-Chloro-6-deoxy-α-D-altropyranoside

A sample of the glycoside (39 mg) was oxidized in the usual way (20). The results are shown in Table I.

TABLE I

Periodate oxidation of methyl 6-chloro-6-deoxy-α-D-altropyranoside

Time	Periodate uptake (moles per mole)	Formic acid released (mole per mole)
20 min	0.99	0.19
1 h	1.24	0.29
3 h	1.36	0.37
6½ h	1.53	0.58
10 h	1.65	0.66
23 h	1.91	0.91
34 h	1.94	0.97
48 h	1.95	0.97
96 h	1.95	0.97

Methyl α-D-Lyxopyranoside 2,3,4-Trichlorosulfate

Methyl α-D-lyxopyranoside (21) (2 g, 0.012 mole) in anhydrous pyridine (10 ml, 0.02 mole) and chloroform (25 ml) was treated with sulfuryl chloride (6 ml, 0.074 mole) (procedure A). The crystalline product was methyl α-D-lyxopyranoside 2,3,4-trichlorosulfate, 3.3 g (60%). It was recrystallized from chloroform – petrol (b.p. 35–60°). The colorless plates had m.p. 129–130° and $[\alpha]_D$ −7° (*c*, 1.0 in chloroform).

Anal. Calcd. for $C_6H_9Cl_3O_{11}S_3$: C, 15.8; H, 1.96; Cl, 23.1; S, 20.8. Found: C, 15.8; H, 1.98; Cl, 23.5; S, 20.6.

A portion of the crystals (1 g, 0.006 mole) obtained from the previous experiment was treated according to procedure C. The crystalline product, 0.52 g (52%), m.p. 129–130°, was indistinguishable from the starting material.

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D-Lyxosyl Chloride 2,3,4-Trichlorosulfate

D-Lyxose (2 g, 0.013 mole) in anhydrous pyridine (10 ml, 0.12 mole) and chloroform (25 ml) was treated with sulfuryl chloride (6 ml, 0.074 mole) according to procedure A and gave colorless crystals, 3 g (52%), m.p. 94–96°, $[\alpha]_D$ +20.4° (*c*, 1.0 in chloroform).

Anal. Calcd. for $C_5H_6Cl_4O_{10}S_3$: C, 13.0; H, 1.30; Cl, 30.6; S, 20.7. Found: C, 13.1; H, 1.37; Cl, 30.4; S, 20.6.

The Reaction of D-Lyxosyl Chloride 2,3,4-Trichlorosulfate with Pyridine Hydrochloride

The crystals (1.5 g, 0.003 mole) (above) in anhydrous chloroform and pyridine hydrochloride (1.3 g, 0.012 mole) gave (procedure C) a syrupy product containing several substances. A positive test for chlorosulfate groups was obtained. The syrup was dechlorosulfated with sodium iodide. A syrup was obtained which was shown by t.l.c. to contain one main substance, R_f 0.53 and R_{Rh} 2.5 in solvent *b*, and several minor substances. A small amount of the main substance was purified by t.l.c. followed by vacuum distillation. It had $[\alpha]_D$ +39.8°.

Anal. Calcd. for $C_5H_{10}Cl_2O_3$: Cl, 37.9. Found: Cl, 35.6.

Methyl 2-Chloro-2-deoxy-β-D-galactopyranoside[5]

Methyl 2-chloro-2-deoxy-β-D-galactopyranoside 2,3,4-triacetate (2.1 g, 0.007 mole), prepared from triacetyl D-galactal (22) in 19% yield according to the procedure of Lemieux and Fraser-Reid (23) except that silver carbonate was used in place of silver acetate, was dissolved in anhydrous methanol (25 ml) and cooled to 5°. It was de-*O*-acetylated catalytically with a cold, freshly prepared solution of sodium methoxide in the usual way. The methyl 2-chloro-2-deoxy-β-D-galactopyranoside, 0.95 g (72%), had m.p. 145–147° (mixed m.p. with a sample obtained from Dr. R. U. Lemieux 144–146°) and $[\alpha]_D$ +25° (*c*, 0.88 in water).

Methyl 2,3,4,6-Tetrachloro-2,3,4,6-tetradeoxy-β-D-alloside[5]

Methyl 2-chloro-2-deoxy-β-D-galactopyranoside (1.28 g, 0.006 mole) in pyridine (6 ml, 0.075 mole) and dry chloroform (24 ml) was treated with sulfuryl chloride (2.5 ml, 0.030 mole) (procedure A). The syrupy product (1 g) contained, as shown by t.l.c., one major component, R_f 0.94, and small amounts of two other components with R_f 0.83 and 0.75 (solvent *a*). Tests indicated that there was probably a small amount of material present containing the OSO_2Cl group. The syrup (1 g) in anhydrous chloroform and pyridine hydrochloride (0.5 g) was reacted according to procedure C and gave a syrupy product (0.85 g (54%)) which contained a single component, R_f 0.93 in solvent *a* and 0.62 in solvent *d* (t.l.c.). The volatile component was purified by vacuum distillation at 0.15 mm. The aniline–pyridine test for chlorosulfate groups was negative. The infrared spectrograph showed the absence of any hydroxyl peaks and confirmed the absence of any chlorosulfate groups.

Anal. Calcd. for $C_7H_{10}Cl_4O_2$: C, 31.4; H, 3.76; Cl, 52.9; OMe, 11.6. Found: C, 31.7; H, 3.7; Cl, 52.4; OMe, 11.9.

The Use of Tetra-n-butylammonium Chloride as a Source of Chloride Ions instead of Pyridine Hydrochloride

Methyl α-D-Glucopyranoside 2,3,4,6-Tetrachlorosulfate

Methyl α-D-glucopyranoside (10 g, 0.051 mole) was treated with sulfuryl chloride (26 ml, 0.32 mole) and pyridine in chloroform solution at −70° for 2 h. The mixture was allowed to warm up rapidly to −30° so that it became less viscous, while at this temperature an ice-cold 70% solution of sulfuric acid (500 ml) was added to the reaction mixture, with stirring. This modified method gave a considerably improved yield of the tetrachlorosulfate, 24 g (80%), m.p. 111–114°.

Methyl 4,6-Dichloro-4,6-dideoxy-α-D-galactopyranoside

The above material (2 g, 0.034 mole) in dry chloroform and anhydrous tetra-*n*-butylammonium chloride (2.06 g, 0.072 mole) was heated on a water bath at 50–60° for 5 h. From the chloroform solution was isolated a syrup which gave a positive test for chlorosulfate groups (aniline–pyridine test). The syrup was dechlorosulfated with sodium iodide to give a crystalline product, 0.70 g (85%), which, after recrystallization from chloroform–petrol, had m.p. 156–157°, undepressed on admixture with methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside (3, 4).

The previous experiment was repeated with a mole ratio of tetrachlorosulfate to tetra-*n*-butylammonium chloride of 1:4.4. The reaction was left for 24 h on the water bath at 50°. The only chloroform-soluble product obtained was methyl 4,6-dichloro-4,6-dideoxy-α-D-galactopyranoside 2,3-dichlorosulfate.

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[5]*A short account of these reactions has been given (8).*

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REFERENCES

1. P. D. Bragg, J. K. N. Jones, and J. C. Turner. Can. J. Chem. **37**, 1412 (1960).
2. J. K. N. Jones, M. B. Perry, and J. C. Turner. Can. J. Chem. **38**, 1122 (1960).
3. H. J. Jennings and J. K. N. Jones. Can. J. Chem. **40**, 1408 (1962).
4. H. J. Jennings and J. K. N. Jones. Can. J. Chem. **41**, 1151 (1963).
5. H. J. Jennings and J. K. N. Jones. Can. J. Chem. **43**, 2372 (1965).
6. E. Buncel and J. P. Millington. Proc. Chem. Soc. 406 (1964); Can. J. Chem. **43**, 547 (1965); **43**, 556 (1965).
7. J. W. H. Oldham and J. K. Rutherford. J. Am. Chem. Soc. **54**, 366 (1932).
8. A. G. Cottrell, E. Buncel, and J. K. N. Jones. Chem. Ind. London, 552 (1966).
9. R. E. Reeves. Advan. Carbohydrate Chem. **6**, 107 (1951).
10. G. R. Barker and D. F. Shaw. J. Chem. Soc. 584 (1959).
11. H. Spedding. Advan. Carbohydrate Chem. **19**, 23 (1964).
12. H. C. Brown. J. Chem. Soc. 1248 (1956).
13. E. L. Eliel. The stereochemistry of carbon compounds. McGraw-Hill Book Co., Inc., New York. 1962. Chap. 8. p. 225.
14. S. S. Ali and T. J. Mepham. Unpublished results.
15. R. B. Ward. Methods in carbohydrate chemistry. Vol. II. Academic Press, Inc., New York. 1962. p. 396.
16. R. M. Hann and C. S. Hudson. J. Am. Chem. Soc. **64**, 2435 (1942).
17. N. K. Richtmyer and C. S. Hudson. J. Am. Chem. Soc. **63**, 1727 (1941).
18. E. A. Robinson. Can. J. Chem. **39**, 247 (1961).
19. G. Neumüller and E. Vasseur. Arkiv Kemi, **5**, 235 (1953).
20. D. M. W. Anderson, C. T. Greenwood, and E. L. Hirst. J. Chem. Soc. 225 (1955).
21. F. P. Phelps and C. S. Hudson. J. Am. Chem. Soc. **48**, 503 (1926).
22. B. Helferich, E. N. Mulcahy, and H. Ziegler. Ber. **87**, 233 (1954).
23. R. U. Lemieux and B. Fraser-Reid. Can. J. Chem. **42**, 532 (1964).

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