The Preparation and Reactions of a New Glycoside: 2'-Chloroethyl β-D-Fructopyranoside

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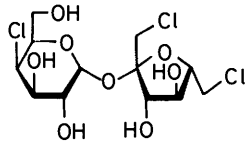
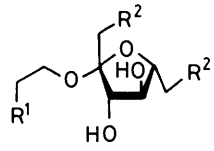
Reaction of D-fructose with 2-chloroethanol containing hydrogen chloride at room temperature afforded highly crystalline 2'-chloroethyl β-D-fructopyranoside (**4**) in >90% yield. The chloro substituent has been substituted by various nucleophilic anions (N_3^-, NCS^-, AcS^-, BzO^-) and reaction of the glycoside with base afforded the spiro-internal glycoside 1,2-*O*-ethylene-β-D-fructopyranose (**7**) in high yield. Tritylation of the glycoside (**4**) afforded the 1-*O*-trityl ether in about 50% yield whereas selective mesitylenesulphonylation gave the 1,4-disulphonate as the major product with the 1-sulphonate being isolated in only low yield. When the 1,4-disulphonate was treated with base the 4-sulphonyloxy group was selectively displaced to give the epoxide, which on more prolonged reaction afforded 4,5-anhydro-2,3-*O*-ethylene-1-*O*-mesitylenesulphonyl-β-D-fructopyranose (**31**) in high yield. Ring-opening of these epoxides by anions revealed that they proceeded in an *anti*-Furst–Plattner fashion. Reaction of the 2'-chloroethyl glycoside with triphenylphosphine and carbon tetrachloride gave 2'-chloroethyl 5-chloro-5-deoxy-α-L-sorbopyranoside in high yield.

Our discovery of the intense sweetness of certain chlorinated sucroses,[1] such as 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (**1**), suggested that the



(**1**)



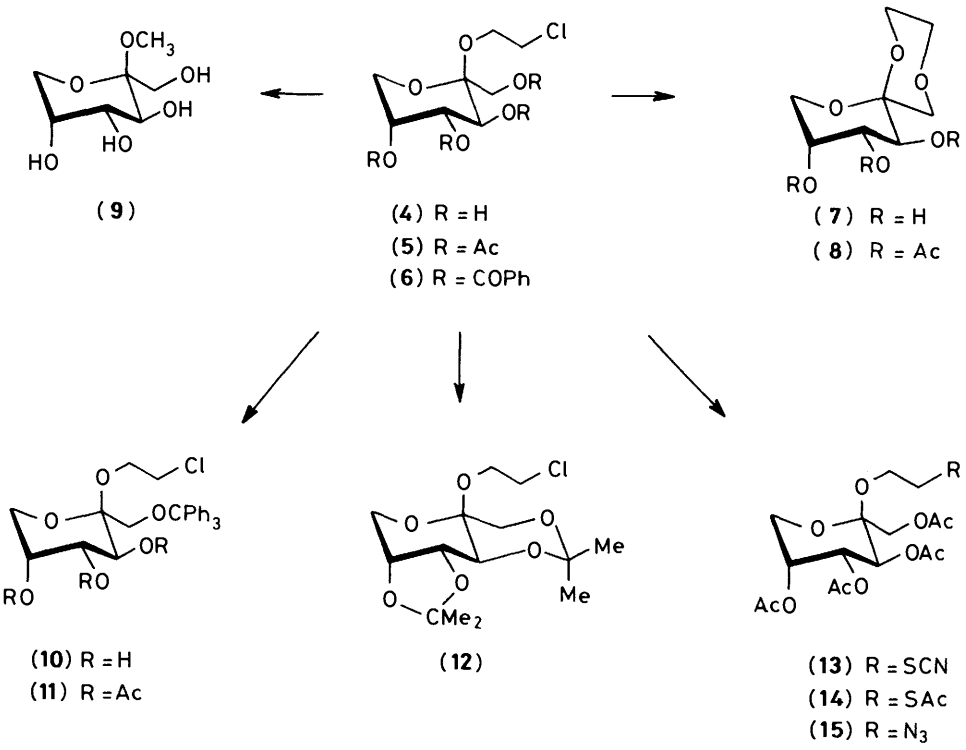
(**2**) R^1 = OH, R^2 = Cl
(**3**) R^1 = Cl, R^2 = OH

preparation of a series of related glucopyranosides and fructofuranosides would be worthwhile in order to probe the molecular elements responsible for the intense sweetness of these compounds. One such glycoside was 2'-hydroxyethyl 1,6-dichloro-1,6-dideoxy-β-D-fructofuranoside (**2**) which should be accessible from 2'-chloroethyl β-D-fructofuranoside (**3**) and it was in turn anticipated that compound (**3**) would be available by the direct reaction of fructose with 2-chloroethanol in the presence of an acid catalyst, since reaction of fructose with methanol containing 2.9% sulphuric acid at room temperature for 30 min afforded 84% of a mixture of the two methyl furanosides.[2] Consequently the ketose was treated with 2-chloroethanol containing about 1% hydrogen chloride at room temperature. The reaction mixture never became homogeneous but the heavy granular crystals of fructose disappeared to be replaced by a fine solid which was filtered off after 2 h to give 90% of 2'-chloroethyl β-D-fructopyranoside (**4**). The addition of further fructose to the filtrate afforded a further 93% yield of the glycoside (**4**) after an additional 2—4 h at room temperature and this procedure could be repeated at least five times with the same chloroethanol to give yields of compound (**4**) consistently in the 85—95% range so that the glycoside is available with great ease in large amounts.

The structure of the glycoside (**4**) was established by its n.m.r. spectrum and by its subsequent reactions. The glycoside afforded an amorphous tetra-*O*-acetate (**5**) and a crystalline tetra-*O*-benzoate (**6**), the ^{1}H n.m.r. spectrum of which clearly indicated that the product was a pyranoside since three ring-proton resonances were to low field of δ 5, indicating that there were three secondary benzoyloxy groups. The coupling constants $J_{3,4}$ (10.5 Hz), $J_{4,5}$ (3.3 Hz), $J_{5,6_{ax}}$ (1.2 Hz), and $J_{5,6_{eq}}$ (1.9 Hz) were in agreement with the glycoside existing in the $^2C_5$ conformation (Table 1). The β-anomeric configuration was established by comparison of its molecular rotation (−35 890°) with that of methyl β-D-fructopyranoside[3] (−33 562°) and also by the fact that the alternative α-anomer would almost certainly have existed in the $^5C_2$ conformation in which the glycosidic group occupies an axial position due to the favourable anomeric effect and with the hydroxymethyl group in an equatorial position.

The isolation of the pyranoside (**4**) was quite unexpected since the Fischer glycosidation procedure is kinetically controlled in the early stages of the reaction, and therefore favours furanosides when performed at room temperature for short periods.[4] Normally pyranosides are only formed when the reaction is carried out at higher temperatures for longer reaction times but in this case when the reaction mixture was heated to about 100 °C it became homogeneous and dark coloured, forming a complex mixture of products (as indicated by t.l.c.) of which the β-pyranoside (**4**) appeared only to be a minor component. The normal room-temperature reaction was difficult to study because of its heterogeneous nature, but at no stage did t.l.c. indicate the formation of any other product. In an attempt to see whether the reaction could be conducted homogeneously it was carried out in mixtures of 2-chloroethanol and ethanol (or methanol), but in spite of the fact that the glycoside (**4**) was almost insoluble in both ethanol and methanol only poor yields of (**4**) could be obtained, and even then only with high concentrations of chloroethanol. Use of sucrose rather than fructose in this reaction was also heterogeneous and gave compound (**4**) in yields of up to 70% but the reaction was much slower, taking at least 15 h. From these results it is tempting to speculate that the reaction may be taking place in the solid phase rather than in solution, leading to the somewhat unexpected reaction pathway.

Treatment of the glycoside (**4**) with either sodium methoxide or sodium hydroxide in ethanol afforded a crystalline chlorine-free product in 82% yield which was characterised as the spiro-anhydride (**7**). The ^{1}H n.m.r. spectrum of the derived crystalline tri-*O*-acetyl derivative (**8**) showed three low-field resonances below δ 5, which indicated that none of the three secondary hydroxy groups had become involved in anhydride ring

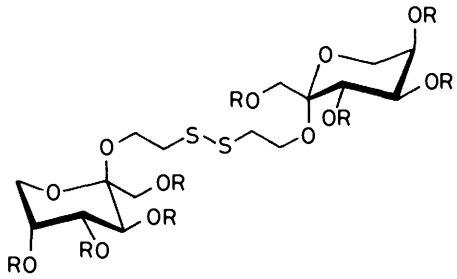


formation (Table 2). Therefore, the primary 1-OH group had displaced the chloro substituent rather than the secondary 3-OH. No other product could be detected in the reaction mixture.

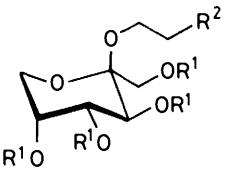
The only other glycoside of fructose readily available without the need for chromatography is the benzyl β-glycoside which was prepared by Purves and Hudson in about 25—30% yield.[3] They found that the methanolysis of this glycoside proceeded with remarkable selectivity to give methyl β-D-fructopyranoside (**9**) in 80% yield. It was therefore of interest to see whether this new glycoside behaved in the same way. Accordingly, compound (**4**) was stirred with methanolic hydrogen chloride at room temperature until complete dissolution occurred (6 h) after which the solution was neutralised and concentrated to dryness to give a 50% yield of pure crystalline ethyl β-D-fructopyranoside (**9**), making this now a readily available glycoside of fructose.

The tetra-*O*-acetyl derivative (**5**) of the chloroethyl glycoside (**4**) underwent ready displacement of the chlorine with a variety of nucleophilic anions. Thus reaction of compound (**5**) with potassium thiocyanate in boiling butanone afforded the 2′-thiocyanatoethyl β-D-fructopyranoside (**13**) in 84% yield as a syrup. Conventional *O*-deacetylation with sodium methoxide resulted in the formation of a product which crystallised directly from the reaction mixture. The i.r. spectrum indicated the absence of thiocyanate and ester groups and the absence of a thiol group was indicated by the nitroprusside test. However, the product exhibited a weak u.v. absorption at $\lambda_{max.}$ 244 nm (ε 396) which was characteristic of an aliphatic disulphide,[5] suggesting that the first formed thiol had undergone atmospheric oxidation to give 1,6-di-(β-D-fructopyranosyloxy)-3,4-dithiahexane (**16**). Acetylation of the product afforded the syrupy octa-acetate (**17**), the ^1H and ^{13}C n.m.r. spectra of which indicated that both fructopyranoside rings were magnetically equivalent (Table 1).

Similarly, when the 2′-chloroethyl glycoside tetra-acetate (**5**) was treated with potassium thioacetate in butanone it afforded the 2′-thioacetyl derivative (**14**) in 80% yield and with sodium azide in *N*,*N*-dimethylformamide (DMF) it gave the 2′-azide



(**16**) R = H
(**17**) R = Ac



(**18**) R^1 = H, R^2 = N_3
(**19**) R^1 = H, R^2 = OH
(**20**) R^1 = COPh, R^2 = OCOPh

(**15**) in 84% yield, deacetylation of which gave 2′-azidoethyl β-D-fructopyranoside (**18**) in quantitative yield. When the tetra-*O*-benzoyl derivative (**6**) of 2′-chloroethyl fructopyranoside was heated with sodium benzoate in DMF, the chlorine was replaced by a benzoyloxy group to give the penta-*O*-benzoate (**20**) in quantitative yield, which upon *O*-debenzoylation gave 2-(β-D-fructopyranosyloxy)ethanol (**19**) in near quantitative yield.

The selective chemical modification of fructose has never been an easy task due to the lack of readily available blocked derivatives, particularly glycosides. As a result of the ready

Table 1. ^{1}H N.m.r. data (δ, *J*/Hz) for ketopyranosides

Compound	(5)[a]	(6)[b]	(11)[c]	(13)[c]	(14)[c]	(15)[d]	(17)[c]	(20)[b]	(22)[a]	(24)[c]	(26)[c]	(28)[c]	(30)[c]	(31)[c]	(33)[c]	(39)[c]
1-H_a	4.41(d)	4.81(d)	3.62(d)	4.36(d)	4.49(d)	4.41(d)	4.54(d)	4.86(d)	4.08(d)	4.11(d)	4.15(d)	4.05(d)	4.06(d)	4.29(d)	4.14(d)	4.31(d)
1-H_b	4.02(d)	4.35(d)	3.06(d)	4.01(d)	4.09(d)	4.07(d)	4.17(d)	4.37(d)	4.00(d)	4.03(d)	4.08(d)	3.97(d)	3.96(d)	3.93(d)	4.02(d)	3.90(d)
3-H	5.89(d)	6.36(d)	6.34(d)	5.88(d)	5.91(d)	5.91(d)	5.96(d)	6.36(d)	5.92(d)	5.89(dd)	5.86(dd)	2.73(d)	~2.60(m)	3.61(d)	5.71(d)	5.36(d)
4-H	5.66(dd)	5.93(dd)	5.68(dd)	5.58(dd)	5.66(dd)	5.64(dd)	5.74(dd)	5.94(dd)	5.35(dd)	5.31(dd)	5.66(dd)	2.93(m)	2.96(m)	3.02(m)	3.77(dd)	5.80(t)
5-H	5.47(m)	5.83(m)	5.56(m)	5.49(m)	5.50(m)	5.50(m)	5.51(m)	5.79(m)	5.27(m)	5.30(m)	5.43(m)	4.77(m)	4.80(m)	2.67(m)	5.00(m)	3.70—
6-H_{ax}	3.72(dd)	4.36(dd)	3.79(dd)	3.50(s)	3.73(d)	3.48(dd)	3.80(m)	4.26(dd)	3.60(dd)	3.53(dd)	3.66(dd)	3.78(dd)	3.78(dd)	3.83(dd)	3.49(dd)	
6-H_{eq}	3.47(dd)	4.11(dd)	3.64(dd)	3.49(s)	3.51(d)		3.58(dd)	4.08(dd)	3.46(dd)	3.42(dd)	3.35(dd)	3.30(dd)	3.36(m)	3.59(d)	3.38(dd)	3.48
1′-$H'_{a,b}$	3.20(m)	4.01(m)	3.08(m)	3.09(m)	3.29(m)	2.99(t)	3.52(m)	4.07(m)	3.16(m)	3.15(ddd)	3.23(m)				3.15(m)	2.86—
2′-$H'_{a,b}$	3.06(m)	3.82(m)		2.02(m)	2.85(t)	2.59(t)	2.62(m)	4.67(m)	2.90(m)	2.90(td)	3.03(m)				3.83(ddd)	3.16
$J_{1_a,1_b}$	11.9	11.8	9.2	11.9	11.8	11.9	11.9	11.8	10.7	10.8	9.8	10.6	10.6	10.6	10.8	11.8
$J_{3,4}$	10.7	10.5	10.7	10.6	10.7	10.6	10.7	10.5	9.9	11.3	10.6	2.0		0.4	10.7	9.9
$J_{4,5}$	3.4	3.3	3.2		3.4	3.4	3.5	3.3	3.7	3.6	3.2	~1.0		~4.0	3.3	9.7
$J_{5,6_{ax}}$	1.5	1.2	1.0		1.5		1.5	1.0	1.1	1.0	1.2	1.8	1.8	1.4	1.7	~2.5
$J_{5,6_{eq}}$	1.8	1.9	1.9		1.8		1.7	1.9	1.8	1.5	1.7	1.1		0	1.5	~2.5
$J_{6_{ax},6_{eq}}$	13.1	13.2	13.0		13.1		13.0	13.9	13.2	13.3	13.1	12.9	12.8	13.3	13.1	

[a] At 250 MHz in [$^2H_6$]benzene. [b] 200 MHz in $CDCl_3$. [c] 200 MHz in [$^2H_6$]benzene. [d] 250 MHz in $CDCl_3$.

Table 2. N.m.r. data (δ, *J*/Hz) for fused bicyclic compounds

Compound	(8)[a]	(35)[b]	(37)[a]
1-H_a	3.81(d)	4.25(d)	4.14(s)
1-H_b	3.47(d)	4.21(d)	
3-H	5.49(m)	3.49(d)	3.45(d)
4-H	5.88(dd)	5.62(t)	5.57(dd)
5-H	5.41(m)	2.79(ddd)	3.62(ddd)
6-H_{ax}	3.47(dd)	3.44(dd)	3.71(dd)
6-H_{eq}	3.37(dd)	3.21(dd)	3.30(dd)
1′-H_{ax}	3.59(ddd)	3.79(td)	2.14(td)
1′-H_{eq}	3.01(br.d)	2.82(ddd)	3.00(m)
2′-H_{ax}	3.30(m)	3.26(td)	3.15(td)
2′-H_{eq}		3.08(dd)	2.25(ddd)
$J_{1_a,1_b}$	11.8	10.2	
$J_{3,4}$	10.7	9.5	8.3
$J_{4,5}$	3.3	9.5	9.7
$J_{5,6_{ax}}$	1.8	10.8	10.3
$J_{5,6_{eq}}$	1.5	5.2	4.4
$J_{6_{ax},6_{eq}}$	12.8	11.4	11.8
$J_{1'_{ax},1'_{eq}}$	10.9	12.0	10.0
$J_{1'_{ax},2'_{ax}}$	8.6	12.0	10.0
$J_{1'_{ax},2'_{eq}}$	6.3	3.9	4.4
$J_{1'_{eq},2'_{ax}}$	4.0	3.5	3.5
$J_{1'_{eq},2'_{eq}}$	1.5	2.4	3.0
$J_{2'_{ax},2'_{eq}}$		12.0	12.5

[a] At 250 MHz in [$^2H_6$]benzene. [b] 400 MHz in [$^2H_6$]benzene.

availability of compound (**4**) it was decided to explore the selective blocking and displacement of hydroxy groups as a prelude to utilisation of this substrate as a starting material in synthesis.

Tritylation of the glycoside (**4**) was slow, but a 49% yield of the crystalline 1-*O*-trityl ether (**10**) could be obtained using a large excess of trityl chloride at room temperature; the structure of the ether was indicated by the ^1H n.m.r. spectrum of the derived syrupy tri-*O*-acetyl derivative (**11**) (Table 1).

The reaction of the glycoside (**4**) with 2,2-dimethoxypropane in DMF containing toluene-*p*-sulphonic acid (PTSA) afforded a di-*O*-isopropylidene derivative shown to be the 1,3:4,5-isomer (**12**). Its ^{13}C n.m.r. spectrum indicated two isopropylidene acetal ring carbons which resonated at δ_C 108.91 and 100.14 p.p.m., indicating a five- and a six-membered ring respectively. Furthermore the chemical shifts of the methyl carbons at δ_C 26.1 and 28.4 (five-membered ring) and 28.95 and 18.5 (six-membered ring) were also consistent with structure (**12**) according to the rules proposed by Buchanan *et al.*[6] The coupling constants derived from the ^1H n.m.r. spectrum of compound (**12**), namely, $J_{3,4}$ (8.4 Hz) and $J_{4,5}$ (5.6 Hz), were indicative of distortion of the pyranoside ring towards a $^2HC_0$ conformation (Experimental section). The rather poor yield of the di-isopropylidene derivative (40%) was probably due to the acid lability of the glycoside (**4**) which was surprisingly acid-sensitive for a pyranoside. The glycoside had a half-life of about 19 min at room temperature in molar hydrochloric acid, a value comparable with that of sucrose. Contrary to popular belief it seems likely that sucrose is readily hydrolysed not because it is a furanoside but because it is a glycoside of a ketose, which hydrolyses *via* the tertiary oxycarbonium ion. The formation of such an intermediate seems not to be affected by ring size, so that fructofuranosides and fructopyranosides hydrolyse at comparable rates, a fact originally established by Purves and Hudson[3] in the 1930s but not widely appreciated.

Selective sulphonylation of the 2′-chloroethyl glycoside (**4**) with either toluene-*p*-sulphonyl chloride or mesyl chloride was complex and under a variety of different conditions no major products could be detected by t.l.c. However, selective esterification of the glycoside (**4**) with mesitylenesulphonyl chloride was much more promising and was best accomplished with 4 mol equiv. of the reagent which gave a mixture in which three products predominated. Column chromatography of the mixture afforded the more mobile compound in 51% yield which was shown to be the 1,4-di-*O*-sulphonate (**21**). The other two products were eluted together in about 20% yield and appeared to be a mixture of monosulphonates, from which one was isolated by crystallisation in 6% yield and characterised as the 1-*O*-sulphonate (**25**); the other isomer could not be isolated pure but was probably the 4-*O*-sulphonate.

The structure of the monosulphonate (**25**) was obvious from a comparison of the ^1H n.m.r. spectrum of the derived tri-*O*-acetate (**26**) with that of the acetylated parent glycoside (**5**). The chemical shifts of 3-H, 4-H, and 5-H were virtually identical, indicating that the *O*-sulphonyl group, which is usually less deshielding than an *O*-acetyl group, could not be located on a secondary hydroxy group and was therefore at the 1-position. A comparison of the ^1H n.m.r. spectrum of the derived di-*O*-acetyl derivative (**22**) of the disulphonate (**21**) with that of the triacetate (**26**) indicated that the signal due to 4-H had shifted substantially upfield by 0.31 p.p.m., whereas those for 3-H and 5-H had shifted slightly downfield (0.06 p.p.m.) and upfield (0.16 p.p.m.) respectively. These shifts clearly indicated that the sulphonyl groups were located at O-1 and O-4 and this conclusion was supported by the subsequent reactions of compound (**21**).

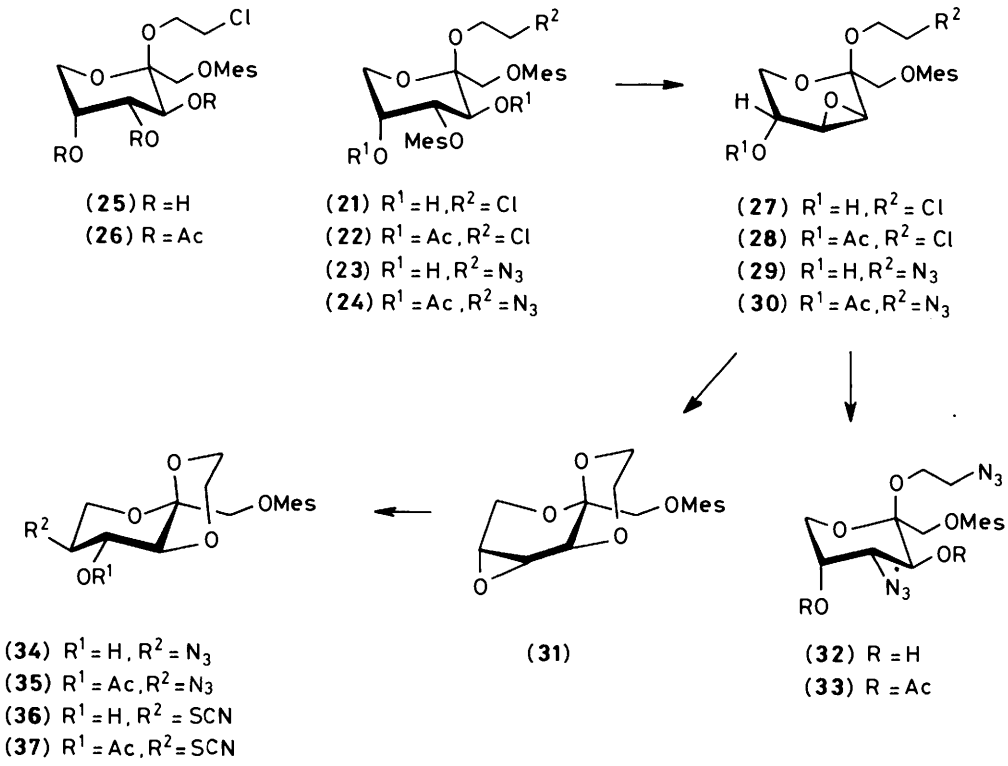
The lack of reactivity of the primary hydroxy group towards sulphonylation was not entirely unexpected since the 1-hydroxy group is of the neopentyl type and is sterically hindered particularly towards such a hindered reagent as mesitylenesulphonyl chloride. Similar lack of reactivity of the 1-hydroxy group of the fructosyl moiety in sucrose derivatives towards acylation and sulphonylation has been noted,[7] such that it is markedly less reactive than the other two primary hydroxy groups.

Similarly, selective mesitylenesulphonylation of the 2′-azidoethyl glycoside (**18**) afforded the 1,4-disulphonate (**23**) in 50% yield. The structure of the product (**23**) was established by comparison of the ^1H n.m.r. spectrum of the derived di-*O*-acetyl derivative (**24**) with that of (**22**) (Table 1).

When the 1,4-disulphonate (**21**) was treated with sodium methoxide it was transformed very rapidly (5 min) into a slower moving product (**27**) (t.l.c.) which was isolated from the reaction mixture in 75% yield. The ^1H n.m.r. spectrum of the derived acetyl derivative indicated that it contained a single *O*-acetyl group and only one mesitylenesulphonyl substituent. The 1-H_a and 1-H_b resonances formed a AB-quartet at δ *ca.* 4, indicating that the 1-*O*-mesitylenesulphonyl group was unaffected. Consequently the acetylated product was assigned as 2′-chloroethyl 5-*O*-acetyl-3,4-anhydro-1-*O*-mesitylenesulphonyl-β-D-tagatopyranoside (**28**).

When the reaction was allowed to proceed for 3 h the epoxide (**27**) was slowly transformed into a more mobile product on t.l.c. which was isolated crystalline in 76% yield. The product did not contain chlorine and the n.m.r. spectrum indicated that the 1-*O*-sulphonate group was still intact, but the i.r. spectrum indicated the lack of a hydroxy group. In view of the well known ability of epoxide rings to migrate when situated *trans* to a hydroxy group, the product was formulated as 4,5-anhydro-2,3-*O*-ethylene-1-*O*-mesitylenesulphonyl-β-D-fructopyranose (**31**) formed by migration of the epoxide ring to the 4,5-position followed by internal nucleophilic displacement of the chlorine atom by the 3-hydroxy group.

When 2′-azidoethyl 1,4-di-*O*-mesitylenesulphonyl-β-D-fructopyranoside (**23**) was treated very briefly with base the 3,4-epoxide (**29**) was formed which was isolated as its 5-*O*-acetyl derivative (**30**) in 78% yield. The ^1H n.m.r. spectrum of



(25) R = H
(26) R = Ac

(21) R^1 = H, R^2 = Cl
(22) R^1 = Ac, R^2 = Cl
(23) R^1 = H, R^2 = N_3
(24) R^1 = Ac, R^2 = N_3

(27) R^1 = H, R^2 = Cl
(28) R^1 = Ac, R^2 = Cl
(29) R^1 = H, R^2 = N_3
(30) R^1 = Ac, R^2 = N_3

(34) R^1 = H, R^2 = N_3
(35) R^1 = Ac, R^2 = N_3
(36) R^1 = H, R^2 = SCN
(37) R^1 = Ac, R^2 = SCN

(31)

(32) R = H
(33) R = Ac

Mes = 2,4,6-$Me_3C_6H_2SO_2$–

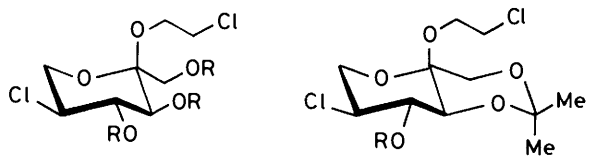
compound (**30**) was very similar to that of (**28**) thus confirming the structure of the compound.

Ring-opening of the 3,4-epoxide (**27**) with azide was highly stereospecific and afforded the *anti*-Furst–Plattner product, namely, 2′-azidoethyl 4-azido-4-deoxy-1-*O*-mesitylenesulphonyl-β-D-fructopyranoside (**32**) in an isolated yield of 86%, formed by concomitant displacement of the chloro group by azide. It is, however, noteworthy that the 1-*O*-mesitylenesulphonyl group remained unaffected by these conditions and appears to have a rather low reactivity towards displacement reactions, as expected from similar studies on sucrose derivatives.[8] The ring-opening of the epoxide (**27**) by attack at C-4 rather than C-3 was not entirely unexpected since it is known that nucleophilic attack by anions at positions adjacent to the anomeric centre are unfavourable due to dipolar repulsions[9] and also displacements at C-3 in ketoses are similar to displacements in the neopentyl system, which are also known to be unfavourable due to steric constraints. Hence it appears that compound (**27**) must react *via* the $^0HC_6$ conformation. The ^{1}H n.m.r. spectrum of the di-*O*-acetyl derivative (**33**) at 200 MHz showed two low-field resonances which were clearly not mutually coupled and therefore must be due to 3-H (doublet) and 5-H (narrow multiplet). The 4-H resonance appeared at higher field as a double doublet (Table 1).

Ring-opening of the 4,5-epoxide (**31**) with azide also proceeded in the *anti*-Furst–Plattner manner with high stereospecificity to give 5-azido-5-deoxy-2,3-*O*-ethylene-1-*O*-mesitylenesulphonyl-α-L-sorbopyranose (**34**) in 91% yield. The structural assignment of compound (**34**) was based on the 400 MHz ^{1}H n.m.r. spectrum of the derived *O*-acetyl derivative (**35**) which was almost completely first-order (Table 2). The resonance due to the ring proton adjacent to the *O*-acetyl group was the only resonance below δ 4.2 and appeared as a triplet with couplings of about 10 Hz, indicative of two axial–axial couplings consistent only with the 5-azide (**35**). Similarly the epoxide (**31**) reacted with potassium thiocyanate in ethanol to give the 5-thiocyanate (**36**) in 48% yield, the *O*-acetyl derivative of which had a similar n.m.r. spectrum to that of the azide (**35**), confirming that it was the 5-thiocyanate (**37**) (Table 2).

The reason for this very marked discrimination between the 4- and 5-position for nucleophilic attack is not clear and requires further study because in both of the half-chair conformations of the epoxide (**31**) the nucleophile must approach from an *endo* position with respect to the bicyclic ring system and in both cases the transition states seem comparable.

Selective chlorination of the glycoside (**4**) at C-1 was attempted with triphenylphosphine and carbon tetrachloride in pyridine, a 'cocktail' which has been reported as selective for primary hydroxy groups[10] and has been used for the conversion of 2,3:4,5-di-*O*-isopropylidene-D-fructopyranose into the 1-chloro-1-deoxy derivative.[11] The glycoside reacted smoothly with the reagent to give, after *O*-acetylation, a single crystalline product (**39**) in 85% yield. The ^{1}H n.m.r. spectrum of the product indicated the presence of the three acetyl groups with only 3-H (doublet) and 4-H (triplet) resonating at low field below δ 5 as two strongly coupled resonances. The values of the coupling constants, $J_{3,4}$ (9.7 Hz) and $J_{4,5}$ (9.7 Hz), confirmed the *sorbo* configuration. *O*-Deacetylation of compound (**39**) afforded 2′-chloroethyl 5-chloro-5-deoxy-α-L-sorbopyranoside (**38**) as a crystalline product in 92% yield and acetalation of



(38) R = H
(39) R = Ac

(40) R = H
(41) R = Ac

compound (**38**) with 2,2-dimethoxypropane in the presence of PTSA afforded a crystalline 1,3-*O*-isopropylidene derivative, (**40**), in 82% yield. The ^{1}H n.m.r. spectrum of the derived acetyl derivative (**41**) indicated that the *O*-acetyl group was attached to O-4 and hence the isopropylidene group was located at 1,3. The ^{13}C n.m.r. chemical shift of the isopropylidene acetal carbon (δ_C 100.9 p.p.m.), when considered alongside those of the methyl carbons (δ_C 18.58 and 28.61 p.p.m.), indicated a dioxane ring, thus confirming the structure of compound (**40**).

Experimental

Unless otherwise stated optical rotations were determined at a concentration of about 1% in chloroform solution at room temperature (18—23 °C) in 1 dm tubes on a Perkin-Elmer 141 automatic polarimeter. ^{1}H N.m.r. spectra were recorded on either a Bruker WH-400 (400 MHz), a Bruker WM-250 (250 MHz), or on a Nicolet NT-200 (200 MHz) instrument and ^{13}C n.m.r. spectra were recorded on a Bruker WP-60 spectrometer operating at 15.08 MHz. In all cases tetramethylsilane was used as internal standard. Mass spectra were determined on a Kratos MS-25 spectrometer by electron impact at 70 eV. M.p.s were measured on a Kofler hot-stage and are uncorrected. Reactions were monitored by t.l.c. on silica gel ready coated on aluminium sheet (Merck 5554) and spots were visualised by spraying with 1% β-naphthol in conc. sulphuric acid–ethanol (1:20). Column chromatography was carried out either conventionally on silica gel G (Merck 7734) or in some cases by 'flash chromatography' on silica gel G (Merck 9385) at a pressure of 10 p.s.i. Acetylations and benzoylations were carried out by dissolution of the compound in pyridine (3—10 ml per mmol) followed by the addition of an excess of either acetic anhydride or benzoyl chloride as appropriate. The reaction mixture was then processed by decomposition with ice–water and extraction into chloroform. The chloroform layer was then washed successively with water, 10% hydrochloric acid, and saturated aqueous sodium hydrogen carbonate and finally dried ($MgSO_4$) and evaporated to dryness. Pyridine was dried over KOH pellets and DMF over molecular sieve 4A. Light petroleum refers to the fraction boiling in the range 40—60 °C.

2′-Chloroethyl β-D-*Fructopyranoside* (**4**).—Powdered D-fructose (50 g) was added to 2-chloroethanol (400 ml) containing 1.3% hydrogen chloride [obtained by the prior addition of acetyl chloride (10 ml)]. The mixture was stirred for 2 h at room temperature during which time the heavy granular crystals of the ketose were transformed into a thick, soup-like, finely divided suspension of the product. The glycoside was filtered off and washed well with ethanol and then with ether, *but the original filtrate of chloroethanol was not allowed to mix with the washings.* The *glycoside* (**4**) (60.7 g, 90%) was sufficiently pure for subsequent reactions but could be recrystallised from water (*CARE*—a neutral pH must be maintained), m.p. 146—147 °C; $[\alpha]_D$ − 148° (*c* 1 in water) (Found: C, 39.45; H, 6.25. $C_8H_{15}ClO_6$ requires C, 39.6; H, 6.2%); *m/z* 213 and 211 ($M - CH_2OH$, 0.7 and 1.9% respectively), and 163 ($M - OCH_2CH_2Cl$, 0.6).

The original mother liquor of the above reaction mixture was then stirred with a further amount D-fructose (50 g) for 2—4 h to give a further crop (63 g, 90%) of the glycoside (**4**). This process could be repeated at least five times with yields of at least 85%.

Acetylation of compound (**4**) afforded the *tetra*-O-*acetate* (**5**) as an amorphous solid (97%), m.p. 54—56 °C; $[\alpha]_D$ −140.7° (Found: C, 46.55; H, 5.6. $C_{16}H_{23}ClO_{10}$ requires C, 46.8; H, 5.6%); *m/z* 339 and 337 ($M - CH_2OAc$, 0.7 and 2.1%), and 331 ($M - OCH_2CH_2Cl$, 0.4).

Benzoylation of compound (**4**) afforded the crystalline *tetrabenzoate* (**6**) in 96% yield, m.p. 103—104 °C (from ethanol); $[\alpha]_D$ −177.5° (Found: C, 65.1; H, 4.75. $C_{36}H_{31}ClO_{10}$ requires C, 65.6; H, 4.7%).

1,2-O-*Ethylene*-β-D-*fructopyranose* (**7**).—A solution of the glycoside (**4**) (20 g) in either 1M-sodium methoxide or 1M-ethanolic sodium hydroxide (150 ml) was heated under reflux for 10—15 min, when t.l.c. [chloroform–methanol (2:1)] indicated that the reaction was complete to give a slower-moving product. The reaction mixture was cooled, neutralised by Amberlite IR-120 (H^+) resin, and then evaporation to dryness. The orange-coloured syrup was decolourised with charcoal and after evaporation to dryness the syrup was crystallised from propan-2-ol to give the *spiro-bicycle* (**7**) (13.5 g, 82%), m.p. 131.5—132.5 °C; $[\alpha]_D$ −143° (*c* 1 in methanol) (Found: C, 46.95; H, 6.7. $C_8H_{14}O_6$ requires C, 46.6; H, 6.8%); *m/z* 207 ($M^+ + 1$, 0.5%), 206 (M^+, 0.8), 176 ($M - CH_2O$, 1.2), 175 (3.2), 149 (1.7), 148 ($M - CH_2O - C_2H_4$, 1), and 145 (2.2).

Acetylation of the triol (**7**) afforded 3,4,5-*tri*-O-*acetyl*-1,2-O-*ethylene*-β-D-*fructopyranose* (**8**) in 90% yield, m.p. 177—178.5 °C (from ethanol); $[\alpha]_D$ −136° (Found: C, 50.4; H, 6.0. $C_{14}H_{20}O_9$ requires C, 50.6; H, 6.0%).

Methyl β-D-*Fructopyranoside* (**9**).—To a stirred suspension of 2′-chloroethyl β-D-fructopyranoside (**4**) (2 g) in methanol (30 ml) was added acetyl chloride (0.3 ml). The mixture was kept at room temperature until the glycoside had dissolved (about 6 h) and was then neutralised with lead carbonate, filtered, and the filtrate was evaporated to dryness to give a crystalline solid which was recrystallised from ethanol to give the methyl glycoside (**9**) (0.8 g, 50%), m.p. 118—120 °C (lit.,[3] 120 °C); $[\alpha]_D$ −171.3° (*c* 1 in water) (lit.,[5] −173°) (Found: C, 43.0; H, 7.75. Calc. for $C_7H_{14}O_6$: C, 43.3; H, 7.2%); *m/z* 163 (M − OMe and/or $M - CH_2OH$, 21%).

2′-Chloroethyl 1-O-*Trityl*-β-D-*fructopyranoside* (**10**).—Trityl chloride (23 g, 82.4 mmol) was added portionwise to a stirred suspension of 2′-chloroethyl fructopyranoside (**4**) (5 g, 20.6 mmol) in pyridine (100 ml). After 5 days at room temperature the reaction mixture contained one major product and a few minor components as indicated by t.l.c. [chloroform–methanol (10:1)]. The reaction mixture was poured into ice–water and the product was isolated by extraction into chloroform. The extract was then successively washed well with dil. hydrochloric acid and water and then dried ($MgSO_4$) and evaporated to dryness to give a syrup which was subjected to column chromatography. Initial elution with chloroform–light petroleum (1:2) removed the triphenylmethanol and subsequent elution with chloroform–methanol (40:1) gave the crystalline *trityl ether* (**10**) (4.9 g, 49%), m.p. 180—181 °C (from ethanol); $[\alpha]_D$ −62.3° (Found: C, 66.85; H, 6.05. $C_{27}H_{29}ClO_6$ requires C, 66.85; H, 6.0%).

The derived triacetate (**11**) was obtained as a syrup in quantitative yield, $[\alpha]_D$ −30°.

2′-Chloroethyl 1,3:4,5-*Di*-O-*isopropylidene*-β-D-*fructopyranoside* (**12**).—2,2-Dimethoxypropane (40 ml) was slowly added to a stirred suspension of compound (**4**) (10 g) in DMF (100 ml) containing PTSA (50 mg) and molecular sieves (Type 3A). The mixture was stirred at room temperature for 4 h, when t.l.c. [ether–light petroleum (1:1)] indicated the formation of a major faster moving product. The reaction mixture was neutralised with Amberlite IR-45(OH^-) resin and the solvent was removed under reduced pressure to afford a syrup which was purified by column chromatography [ether–light petroleum (2:1) as eluant] to give the *di*-O-*isopropylidene derivative* (**12**) (5.3 g, 40%), m.p. 81—82.5 °C (from ethanol); $[\alpha]_D$ −130° (Found: C, 51.95; H, 6.85. $C_{14}H_{23}ClO_6$ requires C, 52.1; H, 7.15%); *m/z* 309 and 307 (M − Me, 1.1 and 3.6%), 252 and 250

(5.8 and 17.9), 243 (M − OCH_2CH_2Cl, 3.2) and 236 and 234 (M − CH_2O − Me_2CO, 0.9 and 2.9); δ_H (200 MHz; C_6H_6) 4.51 (1 H, dd, $J_{3,4}$ 8.4, $J_{4,5}$ 5.6 Hz, 4-H), 4.01 (1 H, d, 3-H), 3.97 (1 H, dd, $J_{5,6a}$ 2.5, $J_{5,6e}$ < 1 Hz, 5-H), 3.90 (2 H, m, 6-H_2), 3.66 (1 H, d, $J_{1a,1e}$ 12.7 Hz, 1-H_e), 3.51 (1 H, d, 1-H_a), 3.1—3.5 (4 H, m, CH_2CH_2Cl), 1.53 (3 H, s, Me), 1.47 (3 H, s, Me), 1.26 (3 H, s, Me), and 1.22 (3 H, s, Me); δ_C ($CDCl_3$) 108.9 and 100.14 (CMe_2), 92.69 (C-2), 73.58, 73.56, and 72.61 (C-3, -4, and -5), 66.11 (C-6), 61.55 and 61.25 (C-1 and -1′), 42.88 (C-2′), and 28.95, 28.40, 26.10, and 18.47 (CMe_2).

2′-Thiocyanatoethyl 1,3,4,5-*Tetra*-O-*acetyl*-β-D-*fructopyranoside* (**13**).—A solution of 2′-chloroethyl 1,3,4,5-tetra-*O*-acetyl-β-D-fructopyranoside (**5**) (5.0 g) and potassium thiocyanate (6 g) in butanone (100 ml) was heated under reflux for 16 h, after which t.l.c. indicated the complete conversion of the chloride (**5**) into a single slower moving product. The reaction mixture was evaporated to dryness and the brown residue was purified by column chromatography with ether–light petroleum (5:4) as eluant. The *thiocyanate* (**13**) was obtained as a syrup (4.6 g, 84%), $[\alpha]_D$ −127° (Found C, 46.6; H, 5.0; N, 3.0. $C_{17}H_{23}NO_{10}S$ requires C, 47.1; H, 5.3; N, 3.25%).

1,6-*Di*-(β-D-*fructopyranosyloxy*)-3,4-*dithiahexane* (**16**).—A solution of the above thiocyanate (**13**) (2 g) in methanol (20 ml) was treated with 1M-sodium methoxide (2 ml.) After 30 min the precipitated *disulphide* (**16**) was filtered off (0.94 g, 85%), m.p. 204—207 °C (from aqueous methanol); $[\alpha]_D$ −221° (*c* 0.5 in water) (Found: C, 39.95; H, 6.05; S, 13.2. $C_{16}H_{30}O_{12}S_2$ requires C, 40.15; H, 6.3; S, 13.4%).

Acetylation afforded the syrupy *octa-acetate* (**17**) (89%), $[\alpha]_D$ −175° (Found: C, 46.85; H, 5.25. $C_{32}H_{46}O_{20}S_2$ requires C, 47.15; H, 5.65%); δ_C ($CDCl_3$) 99.17 (C-2), 69.00, 68.27, and 67.69 (C-3, -4, and -5), 62.86, 62.18, and 60.33 (C-1, -1′, and -6) and 38.64 (C-2′).

2′-(Acetylthio)ethyl 1,3,4,5-*Tetra*-O-*acetyl*-β-D-*fructopyranoside* (**14**).—A solution of the tetra-*O*-acetyl derivative (**5**) (5 g) and potassium thioacetate (8 g) in butanone (100 ml) was heated under reflux for 18 h and then evaporated to dryness. The product was then purified by column chromatography using ether–light petroleum (1:1) as eluant to give the *thioacetate* (**14**) (4.4 g, 80%) as a syrup, $[\alpha]_D$ −65° (Found: C, 48.55; H, 6.0. $C_{18}H_{26}O_{11}S$ requires C, 48.0; H, 5.8%).

2′-Azidoethyl 1,3,4,5-*Tetra*-O-*acetyl*-β-D-*fructopyranoside* (**15**). —The 2′-chloroethyl glycoside (**5**) (10 g) and sodium azide (10 g) in DMF were heated at 90 °C for 18 h, when t.l.c. [ether–light petroleum (4:1)] indicated the presence of a single slower moving product. The reaction mixture was then poured into water and the mixture was extracted several times with ether. The combined extracts were then dried ($MgSO_4$) and evaporated to dryness to give the crystalline *2′-azidoethyl glycoside* (**15**) (8.5 g, 84%), m.p. 59—60 °C (from ethanol); $[\alpha]_D$ −133° (Found: C, 45.7; H, 5.5; N, 10.1. $C_{16}H_{23}N_3O_{10}$ requires C, 46.05; H, 5.5; N, 10.1%); *m/z* 344 (M − CH_2OAc, 1.9%) and 331 (M − $OCH_2CH_2N_3$, 0.6).

Deacetylation of compound (**15**) gave *2′-azidoethyl* β-D-*fructopyranoside* (**18**) in 92% yield, m.p. 156—158 °C (from aqueous methanol); $[\alpha]_D$ −103° (*c* 1 in water) (Found: C, 38.65; H, 5.95; N, 16.8. $C_8H_{15}N_3O_6$ requires C, 38.55; H, 6.0; N, 16.85%); *m/z* 218 (M − CH_2OH, 24.7%) and 163 (M − $OCH_2CH_2N_3$, 7.6).

2′-Benzoyloxyethyl 1,3,4,5-*Tetra*-O-*benzoyl*-β-D-*fructopyranoside* (**20**).—A solution of the tetrabenzoate (**6**) (20 g) and sodium benzoate (20 g) in DMF (150 ml) was heated at 100—110 °C for 16 h, when t.l.c. [ether–light petroleum (1:2)] indicated that the reaction was complete and that a single slower moving product had been formed. When the reaction mixture was poured into water, the *pentabenzoate* (**20**) crystallised out (22.2 g, 96%), m.p. 125—126 °C (from ethanol); $[\alpha]_D$ −171° (Found: C, 69.2; H, 4.9. $C_{43}H_{36}O_{12}$ requires C, 69.35; H, 4.85%).

Conventional *O*-debenzoylation of compound (**20**) yielded *2′-hydroxyethyl* β-D-*fructopyranoside* (**19**) in 90% yield, m.p. 149—151 °C (from methanol); $[\alpha]_D$ −144° (*c* in water) (Found: C, 42.9; H, 7.15. $C_8H_{16}O_7$ requires C, 42.85; H, 7.15%); *m/z* 193 (M − CH_2OH, 26.1%) and 163 (M − OCH_2CH_2OH, 6.5).

Selective Mesitylenesulphonylation of 2′-Chloroethyl β-D-*Fructopyranoside* (**4**).—To an ice-cold suspension of compound (**4**) (10 g, 41.2 mmol) in pyridine (110 ml) was added dropwise a solution of mesitylenesulphonyl chloride (36 g, 164.8 mmol) in pyridine (40 ml) at 0—5 °C. The reaction mixture was stored at room temperature for 4 days, after which t.l.c. [chloroform–acetone (10:1)] indicated a complex reaction mixture in which three products appeared to predominate. The reaction mixture was then poured into ice–water and the products were extracted with chloroform in the usual way. Evaporation of the extract gave a syrup which was fractionated by column chromatography. Initial elution with chloroform–acetone (100:1) afforded *2′-chloroethyl* 1,4-*di*-O-*mesitylenesulphonyl*-β-D-*fructopyranoside* (**21**) as a crystalline solid (12.8 g, 51%), m.p. 73—76 °C (from ethanol); $[\alpha]_D$ −66° (Found: C, 51.65; H, 6.1. $C_{26}H_{35}ClO_{10}S_2$ requires C, 51.45; H, 5.75%).

Acetylation of the diol (**21**) afforded the *diacetate* (**22**) in 87% yield, m.p. 121—123 °C (from ethanol); $[\alpha]_D$ −85° (Found: C, 52.15; H, 5.75. $C_{30}H_{39}ClO_{12}S_2$ requires C, 52.15; H, 5.65%).

Further elution of the column with chloroform–methanol (40:1) gave a mixture of the other two products (3.5 g), fractional crystallisation of which from ethanol afforded *2′-chloroethyl* 1-O-*mesitylenesulphonyl*-β-D-*fructopyranoside* (**25**) (1.0 g, 6%), m.p. 125—127 °C (decomp.); $[\alpha]_D$ −72° (Found: C, 48.25; H, 5.8. $C_{17}H_{25}ClO_8S$ requires C, 48.05; H, 5.9%).

Acetylation of the triol (**25**) afforded the *triacetate* (**26**) as a syrup, $[\alpha]_D$ −74° (Found: C, 50.7; H, 5.15. $C_{23}H_{31}ClO_{11}S$ requires C, 50.15; H, 5.65%).

2′-Azidoethyl 1,4-*Di*-O-*mesitylenesulphonyl*-β-D-*fructopyranoside* (**23**).—To an ice-cold suspension of the tetraol (**18**) (10 g, 40.2 mmol) in pyridine (110 ml) was added dropwise a solution of mesitylenesulphonyl chloride (35.5 g, 161.8 mmol) in pyridine (40 ml). The reaction mixture was maintained at 0—5 °C for 4 days after which t.l.c. [chloroform–acetone (10:1)] indicated the presence of one major product and several minor components. The reaction mixture was then processed as for the preparation of compound (**21**) above and the *disulphonate* (**23**) was obtained after column chromatography [chloroform–acetone (100:1) as eluant] (12.2 g, 50%), m.p. 55—57 °C (from methanol); $[\alpha]_D$ −53° (Found: C, 50.5; H, 5.7; N, 6.7. $C_{26}H_{35}N_3O_{10}S_2$ requires C, 50.9; H, 5.7; N, 6.85%).

Acetylation of the diol (**23**) afforded the *diacetate* (**24**), m.p. 65—67 °C (from ethanol); $[\alpha]_D$ −74° (Found: C, 51.65; H, 5.75; N, 5.85. $C_{30}H_{39}N_3O_{12}S_2$ requires C, 51.65; H, 5.6; N, 6.0%); *m/z* 611 (M − $OCH_2CH_2N_3$, 2.5%) and 484 (M − CH_2OMes, 2).

2′-Chloroethyl 3,4-*Anhydro*-1-O-*mesitylenesulphonyl*-β-D-*tagatopyranoside* (**27**).—A solution of the 1,4-dimesitylene sulphonate (**21**) (5.0 g) in 0.5M-sodium methoxide (40 ml) was heated under reflux for 5 min, after which t.l.c. [ethyl acetate–light petroleum (2:3)] indicated that all the starting material had reacted to give a major slower moving product. The reaction mixture was cooled, neutralised with Amberlite IR-120(H^+) resin, and evaporated to dryness. The crude product was purified by column chromatography [ethyl acetate–light

petroleum (1:6) as eluant] to give the 3,4-*epoxide* (**27**) (2.6 g, 75%), m.p. 99—100 °C (from ethanol); $[\alpha]_D$ −34° (Found: C, 50.1; H, 5.65. $C_{17}H_{23}ClO_7S$ requires C, 50.2; H, 5.65%); *m/z* 327 (*M* − OCH_2CH_2Cl, 0.5%) and 195 and 193 (*M* − CH_2OMes, 6.3 and 16.9).

Acetylation of compound (**27**) afforded the 5-O-*acetate* (**28**), m.p. 134.5—136.5 °C (from ethanol); $[\alpha]_D$ −17° (Found: C, 50.6; H, 5.5. $C_{19}H_{25}ClO_8S$ requires C, 50.85; H, 5.6%).

4,5-*Anhydro*-2,3-O-*ethylene*-1-O-*mesitylenesulphonyl*-β-D-*fructopyranose* (**31**).—A solution of 2′-chloroethyl 1,4-di-*O*-mesitylenesulphonyl-β-D-fructopyranoside (**21**) (6.5 g) in 1M-methanolic sodium methoxide (50 ml) was heated under reflux for 3 h, when t.l.c. [chloroform–acetone (10:1)] indicated the formation of mainly one component and the absence of the tagatopyranoside (**27**). The reaction mixture was cooled and then neutralised with Amberlite IR-120 (H^+) resin and evaporated to dryness. The solid residue was extracted with chloroform (2 × 50 ml) and the combined extracts were evaporated to give the *epoxide* (**31**) (3.2g, 76%), m.p. 119—120 °C (from ethanol); $[\alpha]_D$ −34° (Found: C, 54.95; H, 5.95; S, 8.75. $C_{17}H_{22}O_7S$ requires C, 55.15; H, 5.95; S, 8.65%); *m/z* 157 (*M* − CH_2OMes, 5.3%).

2′-*Azidoethyl* 5-O-*Acetyl*-3,4-*anhydro*-1-O-*mesitylenesulphonyl*-β-D-*tagatopyranoside* (**30**).—A solution of the 2′-azido-1,4-di-*O*-sulphonate (**23**) (2 g) in 0.5M-methanolic sodium methoxide (20 ml) was heated under reflux for 5 min, when t.l.c. [chloroform–acetone (10:1)] indicated that the reaction was complete with the formation of a slower moving product. The reaction mixture was processed as described for the preparation of compound (**31**) above and the crude solid residue obtained, compound (**29**), was acetylated with pyridine (5 ml) and acetic anhydride (2 ml). The reaction mixture was then poured into water, and the crystalline *epoxide* (**30**) was filtered off and recrystallised from ethanol (1.1 g, 78%), m.p. 53—55 °C; $[\alpha]_D$ + 2° (Found: C, 50.35; H, 5.4; N, 9.2. $C_{19}H_{25}N_3O_8S$ requires C, 50.1; H, 5.5; N, 9.25%).

2′-*Azidoethyl* 4-*Azido*-4-*deoxy*-1-O-*mesitylenesulphonyl*-β-D-*fructopyranoside* (**32**).—A stirred suspension of the 2′-chloroethyl 3,4-epoxide (**27**) (2 g), sodium azide (1.5 g), and ammonium chloride (0.5 g) in a mixture of ethanol (17 ml) and water (3 ml) was heated under reflux for 5 days, when t.l.c. [chloroform–acetone (10:1)] indicated the formation of a slower moving product and traces of starting material. The reaction mixture was cooled and evaporated to dryness and the residue was extracted with chloroform. The extract was then passed through a silica gel column and eluted with chloroform to give the *diazide* (**32**) as a syrup (1.9 g, 86%), $[\alpha]_D$ −36° (Found: C, 44.25; H, 5.25; N, 18.5. $C_{17}H_{24}N_6O_7S$ requires C, 44.75; H, 5.25; N, 18.4%.

Acetylation of the diol (**32**) afforded the *diacetate* (**33**) as a syrup, $[\alpha]_D$ −75° (Found: C, 46.95; H, 5.4; N, 15.95. $C_{21}H_{28}N_6O_9S$ requires C, 46.65; H, 5.2; N, 15.55%.

5-*Azido*-5-*deoxy*-2,3-O-*ethylene*-1-O-*mesitylenesulphonyl*-α-L-*sorbopyranose* (**34**).—A mixture of the 4,5-epoxide (**31**) (5 g), sodium azide (3.5 g), and ammonium chloride (1.2 g) in a mixture of ethanol (45 ml) and water (5 ml) was heated under reflux for 16 h, after which t.l.c. indicated the formation of a slower moving product. The reaction mixture was cooled and filtered, the filtrate was evaporated to dryness, and the residue was fractionated by column chromatography using ethyl acetate–light petroleum (1:4) as eluant. The *azide* (**34**) was obtained as a syrup (5.1 g, 91%), $[\alpha]_D$ −30° (Found: C, 50.25; H, 6.15; N, 9.5. $C_{17}H_{23}N_3O_7S$ requires C, 49.4; H, 5.6; N, 10.2%).

Acetylation of compound (**34**) afforded the *acetyl derivative* (**35**) as a crystalline solid, m.p. 95—96 °C (from ethanol); $[\alpha]_D$ −48° (Found: C, 49.95; H, 5.7; N, 9.2. $C_{19}H_{25}N_3O_8S$ requires C, 50.1; H, 5.5; N, 9.25%).

5-S-*Cyano*-2,3-O-*Ethylene*-1-O-*mesitylenesulphonyl*-5-*thio*-α-L-*sorbopyranose* (**36**).—A mixture of ethanol (20 ml) and water (5 ml) containing the 4,5-epoxide (**31**) (2 g), ammonium chloride (0.5 g), and potassium thiocyanate (2.6 g) was heated under reflux for 8 h, when t.l.c. indicated the formation of one major product and a little starting material. The reaction mixture was filtered, the filtrate was evaporated to dryness, and the crude solid residue was subjected to column chromatography [ethyl acetate–light petroleum (1:3) as eluant]. The *thiocyanate* (**36**) was obtained as a white solid (1.0 g, 43%), m.p. 156—158 °C, which could not be recrystallised, $[\alpha]_D$ +46° (Found: C, 50.8; H, 5.1; N, 2.8. $C_{18}H_{23}NO_7S_2$ requires C, 50.4; H, 5.35; N, 3.25%).

Acetylation afforded the *monoacetate* (**37**), m.p. 112—114 °C (from ethanol); $[\alpha]_D$ +12 (Found: C, 50.75; H, 5.3; N, 3.3. $C_{20}H_{25}NO_8S_2$ requires C, 50.95; H, 5.3; N, 3.0).

2′-*Chloroethyl* 1,3,4-*tri*-O-*acetyl*-5-*chloro*-5-*deoxy*-α-L-*sorbopyranoside* (**39**).—To an ice-cold solution of the 2′-chloroethyl fructoside (**4**) (10 g) in pyridine (220 ml) was added triphenylphosphine (38 g) followed by the dropwise addition of a solution of carbon tetrachloride (15 ml) in pyridine (30 ml). During the addition the temperature of the reaction mixture was maintained at 0 °C, and when the addition was complete the temperature of the reaction mixture was raised to 85 °C for 1 h. T.l.c. [chloroform–methanol (4:1)] then indicated that the reaction was complete and that a faster moving product had been formed. The reaction mixture was then cooled and the excess of the reagent was decomposed by the addition of methanol (100 ml). The reaction mixture was evaporated to dryness and the product was acetylated with pyridine (100 ml) and acetic anhydride (25 ml) at room temperature for 4 h. The mixture was then poured into ice–water and the product was extracted into chloroform in the usual way. The resulting syrup was then fractionated by column chromatography with ethyl acetate–light petroleum (1:1) as eluant to give the 5-*chloride* (**39**) (13.5 g, 85%), m.p. 98—99 °C (from ethanol); $[\alpha]_D$ −21° (Found: C, 43.2; H, 5.0. $C_{14}H_{20}Cl_2O_8$ requires C, 43.4; H, 5.2%).

O-Deacetylation of the triacetate (**39**) in methanol with a catalytic amount of sodium methoxide afforded 2′-chloroethyl 5-chloro-5-deoxy-α-L-sorbopyranoside (**38**) in 92% yield, m.p. 100—102 °C (decomp.) (from ethanol); $[\alpha]_D$ −66° (Found: C 36.5; H, 5.4. $C_8H_{14}Cl_2O_5$ requires C, 36.8; H, 5.35%); *m/z* 233, 231, and 229 (*M* − CH_2OH, 50, 31, and 5% respectively) and 183 and 181 (*M* − CH_2CH_2Cl, 13 and 5% respectively).

2′-*Chloroethyl* 5-*Chloro*-5-*deoxy*-1,3-O-*isopropylidene*-α-L-*sorbopyranoside* (**40**).—A mixture of the 5-chlorosorboside (**38**) (5 g), PTSA (20 mg), and 2,2-dimethoxypropane (50 ml) was heated under reflux for 1 h, after which t.l.c. indicated the formation of a faster moving product. When the reaction mixture was cooled the product crystallised out and was filtered off. The mother liquors were then neutralised by the addition of a little Amberlite IR-120(H^+) resin and concentrated to dryness to give a syrup which crystallised from ethanol to give a further yield of product. The combined yield of the *isopropylidene derivative* (**40**) was 4.8 g (82%), m.p. 148—150 °C (decomp.); $[\alpha]_D$ −58° (Found: C, 43.7; H, 6.15. $C_{11}H_{18}Cl_2O_5$ requires C, 43.85; H, 6.0%); *m/z* 289, 287, and 285 (*M* − Me, 0.9, 5.8, and 8.8%) and 223 and 221 (*M* − OCH_2CH_2Cl, 2.0 and 5.5).

Acetylation of compound (**40**) afforded 2′-*chloroethyl* 4-O-*acetyl*-5-*chloro*-5-*deoxy*-1,3-O-*isopropylidene*-α-L-*sorbopyranoside* (**41**) in 93% yield, m.p. 80—81 °C (from ether–light petroleum); $[\alpha]_D$ −64° (Found: C, 45.7; H, 5.35. $C_{13}H_{20}Cl_2O_6$

requires C, 45.5; H, 5.85%); δ_C 100.93 (CMe_2), 93.76 (C-2), 73.9 and 71.2 (C-3 and -4), 63.60, 61.58, and 61.39 (C-1, -1′, and -6), 54.81 (C-5), 42.14 (C-2′), and 28.61 and 18.48 (CMe_2).

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