Synthesis of Oligosaccharides by Cycloaddition. Part II.[1] Free and Protected *O*-Hexopyranosyl-(1 → 3)-D-glucoses with the α-D-*allo*-, α-D-*altro*-, α-L-*altro*-, β-L-*altro*-, and α-D-*galacto*-Configurations [2]

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O-α-D-Altropyranosyl-(1 → 3)-D-glucose (8), *O*-α-L-altropyranosyl-(1 → 3)-D-glucose, and *O*-β-L-altropyranosyl-(1 → 3)-D-glucose have been prepared from the products of cycloaddition of butyl glyoxylate to 3-*O*(buta-1,3-dienyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose. Configurational inversion in one step allowed the preparation of *O*-α-D-galactopyranosyl-(1 → 3)-D-glucose (27) and *O*-α-D-allopyranosyl-(1 → 3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (26).

In Part I [1] two of us suggested a new reaction sequence for disaccharide synthesis, which could be separated into three main steps: (i) synthesis of a dienyl ether of a monosaccharide, (ii) cycloaddition, and (iii) functionalization. The first two steps were carried out when *O*-(2,3,4-trideoxy-α-D-*glycero*-hex-2-enopyranosyl)-(1 → 3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (1) and its β-L-*glycero*- (9) and α-L-*glycero*- (13) analogues

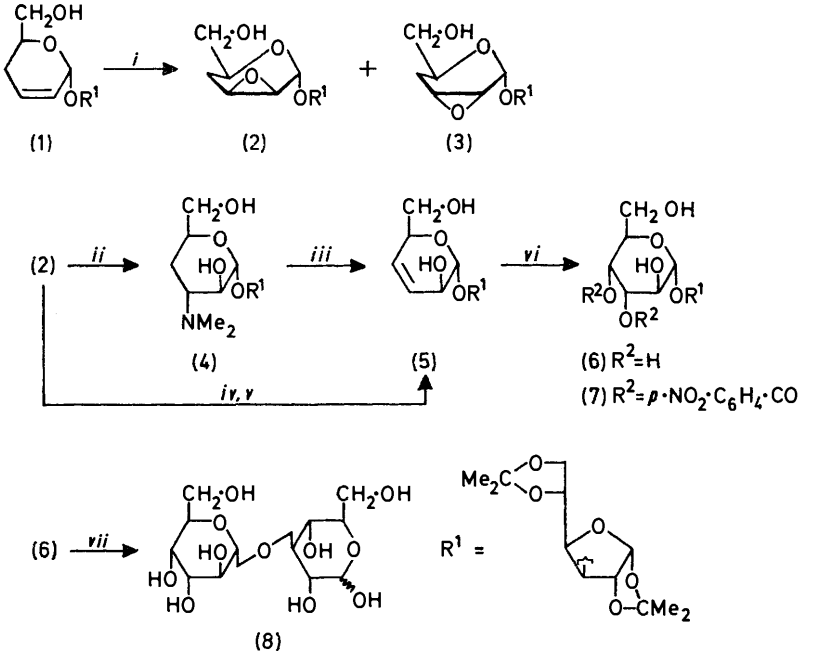
[1] Part I, S. David, J. Eustache, and A. Lubineau, *J.C.S. Perkin I*, 1974, 2274.

[2] Preliminary publication, S. David, A. Lubineau, and J. M. Vatèle, *J.C.S. Chem. Comm.*, 1975, 701.

were prepared in yields of 12.5, 27, and 25%, respectively, from ' diacetone-glucose.'[1] We now report the conversion of compounds (1), (9), and (13) into five completely functionalized, protected disaccharides (6), (12), (17), (25), and (26), four of which have been hydrolysed to the corresponding free disaccharides.

RESULTS

Simple, racemic analogues of compounds (1), (9), and (13) have previously been epoxidised[3] with benzonitrile–hydrogen peroxide. With the same reagent, compound (1) gave two epoxides, one as an amorphous solid (52%), and the other crystalline (8%). From the major epoxide, by the reactions outlined in Scheme 1, were obtained in succession a tertiary base, an allylic alcohol, and finally a partially protected disaccharide which must be



SCHEME 1 Reagents: i, PhCN–H_2O_2; ii, Me_2NH; iii, H_2O_2 (heating to 130 °C); iv, PhSeH; v, H_2O_2; vi, OsO_4; vii, H_2O–H^+

an α-D-hexopyranosyl derivative, since the reagents used have no effect on C-1 and C-5.† Structure (6) for this disaccharide was proved by acidic hydrolysis. One component of the reaction mixture was, as expected, D-glucose, and could be selectively destroyed in the medium by fermentation with yeast after adjustment of the pH. From the remaining solution, a crystalline dibenzyl dithioacetal could be prepared, with the same m.p. and optical rotation as an authentic specimen of D-altrose dibenzyl dithioacetal. The nature of the component sugars of the disaccharide (6) was confirmed by g.l.c. and paper chromatography. Mild, acidic hydrolysis of compound (6) gave the free disaccharide, *O*-(α-D-altropyranosyl)-(1 ⟶ 3)-D-glucose (8).

This settles the constitution of the allylic alcohol as (5), with the double bond at the same place as the *cis*-diol system in disaccharide (6). In the tertiary base, the nitrogen atom must be linked to either C-2 or C-3, and must be *trans* to the vicinal hydroxy-group. Since the Cope elimination led to the unsaturated alcohol (5), the nitrogen atom is linked to C-3, and the base thus has structure (4). Thus, the major, amorphous epoxide has the *lyxo*-configuration (2), and the minor, crystalline epoxide has the *ribo*-configuration (3).

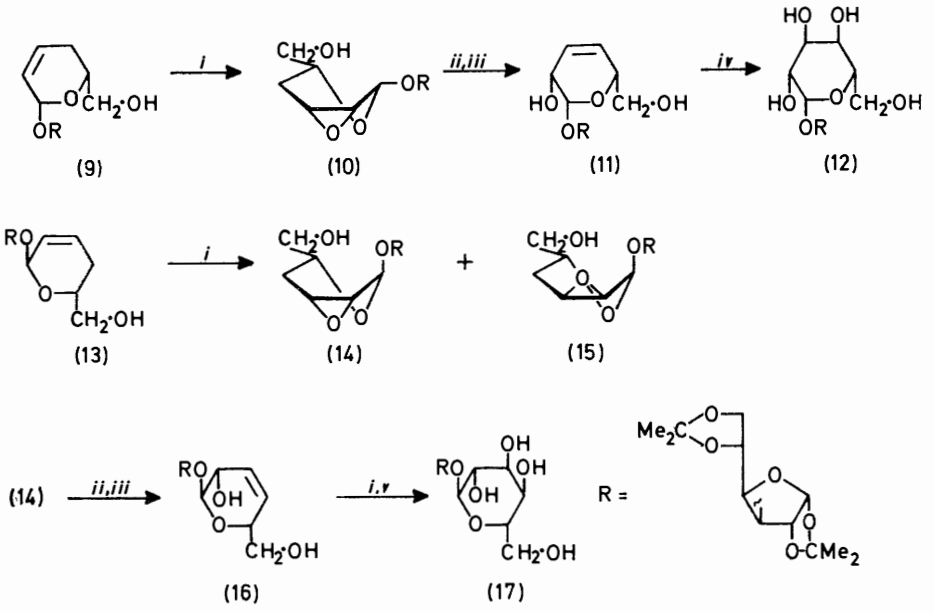
We have also found that the epoxide (2) can be converted into the alcohol (5) in one step, in better overall yield, by a thermal elimination reaction of the derived phenyl selenoxide. This new isomerisation procedure[4] is the synthetic method of choice for the preparation of such compounds.

The functionalisation of compound (9) was carried out in the same way (Scheme 2). Only one epoxide was obtained with benzonitrile–hydrogen peroxide. As it was difficult to separate the cycloadducts (1) and (9), we found it more convenient to epoxidise a mixture of the two. Epoxides (2), (3), and (10) were cleanly separated on a silica gel column. The same observation has been made previously for their simpler analogues.[3] This behaviour appears to be general in this series. The epoxide corresponding to compound (9) was isomerized to an alcohol, which was *cis*-hydroxylated to a protected disaccharide, which must be a β-L-hexopyranosyl derivative. The only component hexoses indicated by acidic hydrolysis were D-glucose and L-altrose. After removal of D-glucose from the medium as above a crystalline dibenzyl dithioacetal, enantiomeric with the

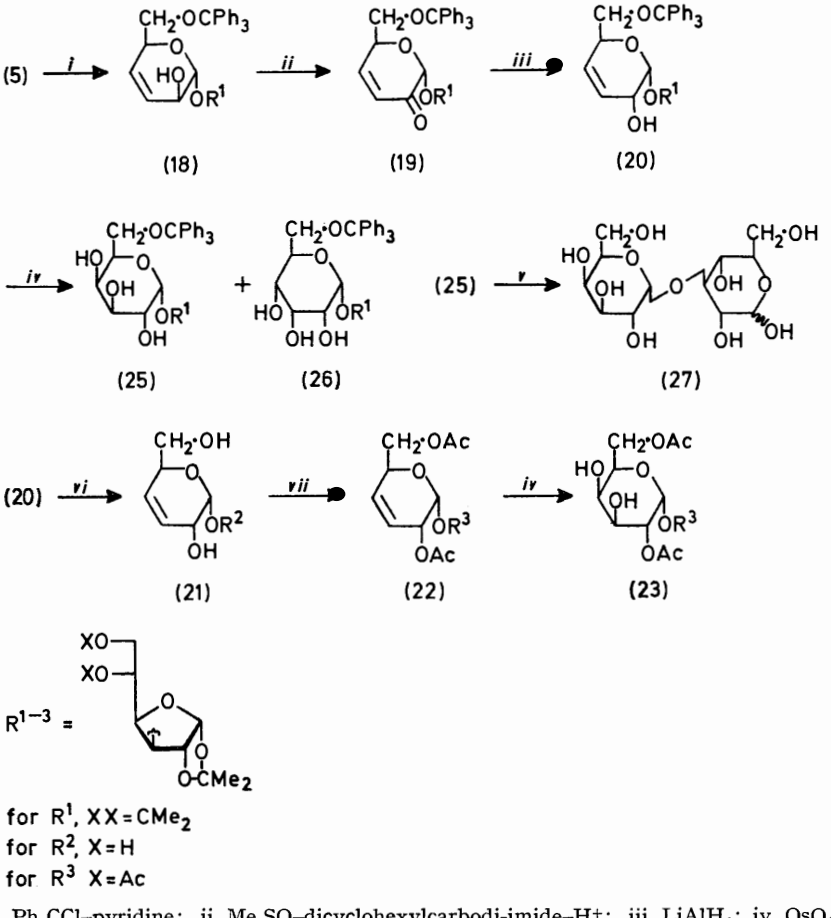
† Unless otherwise stated, the numbering refers to the newly built monosaccharide unit.

[3] A. Banaszek and A. Zamojski, *Roczniki Chem.*, 1971, **45**, 2089.

[4] K. B. Sharpless and R. F. Lauer, *J. Amer. Chem. Soc.*, 1973, **95**, 2697.



SCHEME 2 Reagents: i, $PhCN–H_2O_2$; ii, PhSeH; iii, H_2O_2; iv, OsO_4



SCHEME 3 Reagents: i, Ph_3CCl–pyridine; ii, Me_2SO–dicyclohexylcarbodi-imide–H^+; iii, $LiAlH_4$; iv, OsO_4; v, $H_2O–H^+$; vi, H_2O–AcOH; vii, Ac_2O–pyridine

altrose derivative described in the preceding section could be prepared from the remaining solution. Thus the protected disaccharide must have structure (12), the epoxide of compound (9) must be (10), and its isomerization product must be (11).

Epoxidation of compound (13) with benzonitrile–hydrogen peroxide gave two crystalline epoxides in markedly different yields (65 and 7%). The major one was converted in two steps into the protected disaccharide (17), which was identified as above. As before, after removal of D-glucose, crystalline L-altrose dibenzyl dithioacetal was isolated by derivatisation of the compounds remaining among the products of drastic hydrolysis. This proves that the configurations of the major epoxide, its isomeric allylic alcohol, and the minor epoxide are, respectively, L-*lyxo* (14), L-*threo* (16), and L-*ribo* (15) (Scheme 2).

To prepare a disaccharide with the more interesting D-*galacto*-configuration, it was necessary to invert the configuration at C-2. This was done in a classical way by an oxidation–reduction sequence (Scheme 3). The primary alcoholic function in the diol (5) was protected by tritylation, and oxidation of the trityl ether (18) under Pfitzner–Moffatt conditions gave the crystalline α,β-unsaturated ketone (19) in almost quantitative yield. Reduction of this ketone with lithium aluminium hydride proceeded as expected, mainly *trans* to the substituent at C-1, to give the new allylic alcohol (20), epimeric at C-2 with (18), in 75% yield. *cis*-Hydroxylation of the alcohol (20) gave a mixture of protected α-D-hexopyranosyl disaccharides. In the major one (54%), the presence of an α-D-galactopyranosyl unit was ascertained by g.l.c. of the products of drastic acidic hydrolysis. Moreover, milder acidic hydrolysis gave in 73% yield the known free disaccharide, *O*-(α-D-galactopyranosyl)-(1 → 3)-D-glucose, an amorphous powder, with the same optical rotation as the previously described compound.[5] Thus the main product of *cis*-hydroxylation has structure (25); the minor one (35%) should be the α-D-allopyranosyl derivative (26). This was confirmed by g.l.c. of the products of drastic acidic hydrolysis of compound (26). In a more efficient route to the *galacto*-disaccharide, the trityl ether (20) was hydrolysed to the unsaturated tetraol (21), which was then acetylated to give the tetra-acetate (22). *cis*-Hydroxylation then gave almost exclusively the crystalline *galacto*-protected disaccharide (23) in 80% (isolated) yield.

We considered that material with the D-*galacto*-configuration might also have been obtained by opening at C-3 of the D-*ribo*-epoxide (3). Treatment of the epoxide (3) with selenophenol gave two phenyl selenides in similar yields. In the n.m.r. spectra the signals of H-1 appeared at respectively δ 5.10 for the major (50%), less polar selenide, and 5.56 for the minor (35%), more polar selenide. It was considered that the deshielding of H-1 in the latter was due to the proximity of the phenyl ring; consequently, structure (29) was suggested for this, and structure (28) for the major, less polar selenide. Treatment of the selenide (28) with hydrogen peroxide and refluxing for 1 h in ethanol resulted in both elimination to the unsaturated diol (30) and ring closure back to the epoxide (3), to give an intractable mixture from which compound (30) could only be isolated in low yield. Similar treatment of the phenyl selenide (29) gave only the epoxide (3) and ' diacetone-glucose ', a product of cleavage of the glycosidic bond.

DISCUSSION

Addition of oxygen by benzonitrile–hydrogen peroxide to the dihydropyrans (1), (9), and (13) occurs mainly or exclusively *cis* to the hydroxymethyl side chain at C-5, in agreement with previous observations on simpler analogues.[3] The dihydropyran units of compounds (1) and (13) are enantiomeric, and they yield mixtures of epoxides with roughly the same ratio of *lyxo*- to *ribo*-derivatives, an indication that the chiral ' diacetone-glucose ' substituent on C-1 has little or no effect. The most stable conformations of the epoxides (2) and (3) are probably the half-chairs D-$^{O}H_{5}$, and for the epoxides (14) and (15) the half-chairs L-$^{5}H_{O}$, as in these conformations the side-chains and glycosidic oxygen atom respectively assume the very favourable pseudoequatorial and pseudoaxial dispositions. The conformation of epoxide (10) must also be the half-chair L-$^{5}H_{O}$, for there would be 1,3-diaxial interactions in the alternative L-$^{O}H_{5}$ conformation. In the n.m.r. spectra (solvent $CDCl_3$) the signals of H-1 of the epoxides (2) and (10) appear as singlets, and those of H-1 of the epoxides (3) and (15) as narrow doublets ($J_{1,2}$ 3.0 Hz).

The structures of the allylic alcohols obtained by isomerisation of compounds (2), (10), and (14) indicate that initial attack by the reagents dimethylamine or selenophenol has occurred at C-3. This corresponds to a *trans*-diaxial opening. The alternative, *trans*-diequatorial opening was not observed; even if it had escaped notice it must have been much less important. This orientation could be explained by the known difficulty of displacement of oxygen at C-2 of a sugar. On the other hand, *trans*-diaxial opening of the epoxide (3) by selenophenol, to give the ether (29), involves attack at C-2, an electronically disfavoured process, so that attack at C-3 can efficiently compete with it, leading to the phenyl selenide (28) in better yield. Both phenyl selenides undergo partial elimination on conversion into the phenyl selenoxide, with ring-closure back to the starting epoxide, a reaction which does not seem to have been recorded previously for this class of compounds.

Addition of osmium tetraoxide to the unsaturated sugars occurs essentially *trans* to the hydroxy or ester group at C-2, leading to the *altro*-configuration from compounds (5), (11), and (16) or to the *galacto*-configuration from compound (21), with, at most, only traces of an *allo*-isomer. Material with the *allo*-configuration was synthesised in good yield only from the trityl ether (20), an obvious consequence of the presence of a bulky substituent at C-5 *trans* to the C-2 hydroxy-group.

[5] R. U. Lemieux, K. James, and T. L. Nagabushan, *Canad. J. Chem.*, 1973, **51**, 42.

Nevertheless the yield was less than that of the *galacto*-derivative.

The molecular rotations $[M]_D^{20}$, of the disaccharides (17), (12), and (6) were −456, +7, and +170°, in fair agreement with the figures calculated as the sum of contributions from 'diacetone-glucose' and the corresponding methyl altropyranoside, *i.e.* −293, +53, and +196°.

Although we are still in the exploratory stages of this new method of disaccharide synthesis, we record here some preliminary observations. The overall yield of the functionalization sequence is *ca.* 40%, and only drops to 25% in the case of configurational inversion at C-2. Thus the usefulness of the method depends mainly on the availability of such starting materials as (1), (3), and (13), that is, on the steric course, as yet unpredictable, of the cycloaddition. From the dienyl ether of 'diacetone-glucose,' we obtained [1] mainly compounds with L-configuration at C-5, so that the disaccharides (12) and (17) are now easily available, as presumably would also be derivatives of L-galactopyranose (a sugar not uncommon in nature). On the other hand, as functions are introduced stepwise in the non-reducing unit, classical glycosidation might be performed at one, or several intermediate steps, providing an efficient route to higher oligosaccharides.

EXPERIMENTAL

General Methods.—These were as described in ref. 6. In addition, relative mobilities on paper chromatograms (R_{Glc}, *etc.*) were determined with the mobile phase butanol–pyridine–water–acetic acid, (6 : 4 : 3 : 1), at 20 °C; a 2.5% solution of aniline hydrogen phthalate in butanol was used as spray reagent.

General Procedure for Epoxidation.—To a solution of the unsaturated disaccharide (10 mmol) in methanol (20 ml), sodium hydrogen carbonate (3 g), benzonitrile (4.5 ml), and aqueous 30% hydrogen peroxide (4.5 ml) were added, and the suspension was stirred for 4 days at room temperature. T.l.c. (ether) then indicated the absence of the starting material. After filtration, the clear solution was evaporated to dryness, and the residue further processed as described below.

Epoxidation in this way of a mixture of compounds (1) and (9) was not complete after 4 days, so more benzonitrile (1 ml) and hydrogen peroxide (1 ml) were added, and the mixture was stirred again overnight. In this case, ether was added to the suspension to precipitate most of the benzamide before filtration.

O-(2,3-*Anhydro*-4-*deoxy*-α-D-lyxo-*hexopyranosyl*)- (2) *and* O-(2,3-*Anhydro*-4-*deoxy*-α-D-ribo-*hexopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (3).—The crude mixture of epoxides from compound (1) (1.74 g) was chromatographed on silica gel (ether) to give first the *epoxide* (2) (0.95 g, 52%) as an amorphous, distillable powder, b.p. 160° at 0.01 mmHg; $[\alpha]_D^{20}$ +16.4° (*c* 0.9 in CH_2Cl_2) (Found: C, 55.1; H, 7.1; O, 37.7. $C_{18}H_{28}O_9$ requires C, 55.7; H, 7.3; O, 37.1%), and then the *epoxide* (3) (0.145 g, 8%), m.p. 144° (from methanol–cyclohexane); $[\alpha]_D^{20}$ +18.5° (*c* 0.97 in CH_2Cl_2) (Found: C, 55.5; H, 7.1; O, 36.9%).

O-(2,3-*Anhydro*-4-*deoxy*-β-L-lyxo-*hexopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (10).—Chromatography on silica gel (in 2-isopropoxypropane–methanol, 94 : 6) of the crude mixture of epoxides from a 1 : 1 mixture of compounds (1) and (9) (3.53 g) first gave the epoxide (2) (1.31 g, 36%), then a mixture of the epoxide (3) and benzamide, and finally the *epoxide* (10) (1.22 g, 35%), m.p. 142—143° (from methanol–ether); $[\alpha]_D^{20}$ +4.2° (*c* 1 in CH_2Cl_2) (Found: C, 55.4; H, 7.05; O, 37.2%). The epoxide (3) was obtained pure by chromatography on silica gel (in ether–methanol, 99 : 1) (yield 0.25 g, 7%).

O-(2,3-*Anhydro*-4-*deoxy*-α-L-lyxo-*hexopyranosyl*)- (14) *and* O-(2,3-*Anhydro*-4-*deoxy*-α-L-ribo-*hexopyranosyl*)-(1 ⟶ 3)-1,2 : 5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (15).—Chromatography on silica gel (ether) of the crude mixture of epoxides from compound (13) (1.01 g) first gave the *epoxide* (14) (0.68 g, 65%), m.p. 160° (from methanol–ether); $[\alpha]_D^{20}$ −72.4° (*c* 1 in CH_2Cl_2) (Found: C, 55.4; H, 7.15; O, 36.9%). The next fraction was a mixture of the epoxide (15) and benzamide. A second chromatography of this fraction on silica gel (chloroform–ether–toluene–methanol, 40 : 35 : 20 : 5) allowed separation of the *epoxide* (15) (74 mg, 7%), m.p. 158—159° (from ether); $[\alpha]_D^{20}$ −74.9° (*c* 0.9 in CH_2Cl_2) (Found: C, 55.5; H, 7.0; O, 37.1%).

General Procedure for Epoxide Isomerisation.—Sodium borohydride (1.4 mmol) was added to a solution of diphenyldiselenide (0.675 mmol) in anhydrous ethanol (4 ml) and the mixture was kept under dry nitrogen. When the solution had become colourless, the epoxide (1 mmol), dissolved in anhydrous ethanol (4 ml) was added, and the mixture was stirred for 90 min at room temperature. Aqueous 30% hydrogen peroxide (1.4 ml) was then added, and the solution was heated at reflux for 30 min and then diluted with water. The alcohol was removed by evaporation and the solution was extracted with chloroform.

O-(3,4-*Dideoxy*-α-D-threo-*hex*-3-*enopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (5).—Crystallisation ot the chloroform extract obtained after isomerisation of the epoxide (2) (0.95 g) gave *compound* (5) (0.7 g, 74%), m.p. 153° (from methanol–ether); $[\alpha]_D^{20}$ +60° (*c* 0.8 in CH_2Cl_2) (Found: C, 56.0; H, 7.2. $C_{18}H_{28}O_9$ requires C, 55.7; H, 7.3%).

O-(3,4-*Dideoxy*-β-L-threo-*hex*-3-*enopyranosyl*)-(1 ⟶ 3)-1,2 : 5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (11).—Crystallisation of the chloroform extract obtained after isomerisation of the epoxide (10) (1.4 g) gave *compound* (11) (0.92 g, 66%), m.p. 156—157° (from methanol–ether); $[\alpha]_D^{20}$ −6.4° (*c* 0.9 in CH_2Cl_2) (Found: C, 56.0; H, 7.2%). Chromatography of the mother liquors on silica gel (in chloroform–methanol, 94 : 6) gave a further crop of compound (11) (85 mg; total 72%).

O-(3,4-*Dideoxy*-α-L-threo-*hex*-3-*enopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (16).—Chromatography on silica gel (in ether–methanol, 98 : 2) of the chloroform extract obtained after isomerisation of the epoxide (14) (0.39 g) gave *compound* (16) as a whitish, hygroscopic foam (0.28 g, 72%); $[\alpha]_D^{20}$ −97.5° (*c* 0.45 in CH_2Cl_2) (Found: C, 55.6; H, 7.3; O, 37.1%).

O-(3,4-*Dideoxy*-3-*dimethylamino*-α-D-arabino-*hexopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (4).—A solution of the epoxide (2) (1 g) in aqueous 66% dimethylamine (10 ml) was kept for 16 h at room temperature. Evaporation to dryness then gave the *amine* (4) as an amorphous powder (1.11 g, 99%), homogeneous by t.l.c. (in ether–methanol, 9 : 1); $[\alpha]_D^{20}$ +21.6° (*c* 1.1 in

[6] S. David, C. A. Johnson, and A. Veyrières, *Carbohydrate Res.*, 1973, **28**, 121.

CH_2Cl_2) (Found: C, 55.15; H, 8.05; N, 3.1; O, 33.3 $C_{20}H_{35}NO$ requires C, 55.4; H, 8.1; N, 3.2; O, 33.2%).

A solution of the amine (4) (0.82 g) in a mixture of aqueous 10% hydrogen peroxide (12 ml) and acetone (30 ml) was kept at room temperature for 40 h; t.l.c. (chloroform–methanol–ammonia, 80 : 18 : 2) then indicated the absence of the starting material. The solution was evaporated to dryness and the highly hygroscopic residue (presumably the *N*-oxide) was heated *in vacuo* (0.01 mmHg) at 130 °C for 15 min. Chromatography on silica gel (in ether–methanol, 9 : 1) then gave the *allylic alcohol* (5) (0.41 g, 48%), m.p. 153° (in methanol–ether), identical with a sample prepared as above.

General Procedure for cis-*Hydroxylation.*—A 10% solution of osmium tetraoxide in pyridine (2.54 ml) was added to a solution of the allylic alcohol (1 mmol) in pyridine (1 ml). Some heat was evolved and the solution was stirred for 5 h at room temperature. A solution of sodium disulphite (0.36 g) in 1 : 3 pyridine–water (3.6 ml) was added. After 30 min, the solution was evaporated to dryness, and the residue was extracted with chloroform.

O-(α-D-*Altrosyl*)-(1 ⟶ 3)-1,2 : 5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (6).—The gum obtained from compound (5) (0.6 g) was chromatographed on silica gel (in chloroform–methanol, 85 : 15) to give the *protected disaccharide* (6), as an amorphous powder (0.61 g, 93%); $[\alpha]_D^{20}$ +40.2° (*c* 1.4 in $CHCl_3$) (Found: C, 51.0; H, 6.8; O, 41.7. $C_{18}H_{30}O_{11}$ requires C, 51.2; H, 7.2; O, 41.7%).

O-(β-L-*Altrosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (12).—The gum obtained from compound (11) (427 mg) was chromatographed on silica gel (in chloroform–methanol, 85 : 15) to give the *protected disaccharide* (12) as an amorphous powder (416 mg, 90.5%); $[\alpha]_D^{20}$ +1.7° (*c* 0.7 in CH_2Cl_2) (Found: C, 50.8; H, 7.2; O, 41.5%).

O-(α-L-*Altrosyl*)-(1 ⟶ 3)-1,2 : 5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (17).—The gum obtained from compound (16) (163 mg) was chromatographed on silica gel (in chloroform–methanol), to give the *protected disaccharide* (17) (157 mg, 89%); $[\alpha]_D^{20}$ −108° (*c* 0.6 in $CHCl_3$) (Found: C, 50.7; H, 7.3%).

O-(6-O-*Trityl*-α-D-*galactopyranosyl*)- (25) *and* O-(6-O-*Trityl*-α-D-*allopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (26).—The chloroform extract from treatment of compound (20) (195 mg) was chromatographed on silica gel (in 2-isopropoxypropane–methanol, 9 : 1), to give first the *protected* galacto-*disaccharide* (25) as an amorphous powder (0.11 g, 54%); $[\alpha]_D^{20}$ +24° (*c* 0.7 in CH_2Cl_2) (Found: C, 66.9; H, 6.9; O, 26.2. $C_{37}H_{44}O_{11}$ requires C, 66.9; H, 6.7; O, 26.5%), then the *protected* allo-*disaccharide* (26), an amorphous powder (70 mg, 34%); $[\alpha]_D^{20}$ + 28.8° (*c* 0.4 in CH_2Cl_2) (Found: C, 66.8; H, 6.8; O, 26.6%).

O-(2,6-*Di*-O-*acetyl*-α-D-*galactopyranosyl*)-(1 ⟶ 3)-5,6-*di*-O-*acetyl*-1,2-O-*isopropylidene*-α-D-*glucofuranose* (23).—From compound (22) (237 mg), after chromatographic purification on silica gel (in chloroform–methanol, 9 : 1) the *protected disaccharide* (23) was obtained as a crystalline solid (198 mg, 80%), m.p. 103—105° (from ether); $[\alpha]_D^{20}$ +86° (*c* 0.35 in CH_2Cl_2) (Found: C, 50.0; H, 6.3; O, 43.3. $C_{23}H_{34}O_{15}$ requires C, 50.2; H, 6.2; O, 43.6%). Traces (*ca.* 5%) of the *allo*-isomer (24) were obtained as the next fraction.

O-(α-D-*Altropyranosyl*)-(1 ⟶ 3)-D-*glucose* (8).—A 1% solution of water in trifluoroacetic acid (0.6 ml) was added to a solution of compound (6) (0.27 g) in chloroform (4 ml). The mixture was kept for 2 h at room temperature and then evaporated to dryness. Water was added to the residue, and the aqueous solution was neutralised with ammonia and evaporated to dryness. Chromatography of the residue on silica gel (in ethyl acetate–propan-2-ol–water, 3 : 3 : 2) first gave O-(α-D-*altrosyl*)-(1 ⟶ 3)-1,2-O-*isopropylidene*-α-D-*glucofuranose*, and afterwards, the disaccharide (8), both contaminated with inorganic material. Chromatography of an aqueous solution of this last fraction on Dowex-50 (H^+) (5 ml) and then Amberlite IR-45(OH^-) (5 ml), followed by freeze-drying of the effluent, gave the *disaccharide* (8) as an amorphous powder (0.135 g, 61%), R_{Glc} 0.78); $[\alpha]_D^{20}$ +114° (*c* 1 in H_2O) (Found: C, 41.7; H, 6.4; O, 51.2. $C_{12}H_{22}O_{11}$ requires C, 42.1; H, 6.5; O, 51.4%).

Similar hydrolyses led to O-(α-L-altropyranosyl)-(1 ⟶ 3)-D-glucose {R_{Glc} 0.83; $[\alpha]_D^{20}$ −27.8° (*c* 0.5 in H_2O)} and O-(β-L-altropyranosyl)-(1 ⟶ 3)-D-glucose {R_{Glc} 0.80; $[\alpha]_D^{20}$ +42.3° (*c* 0.6 in H_2O)}.

General Procedure for Acidic Hydrolysis of Protected Disaccharides to their Component Sugars.—A solution of the protected disaccharide (0.2 g) in aqueous 0.6M-sulphuric acid (10 ml) was heated at 100 °C for 90 min, cooled to room temperature, neutralised with barium carbonate, and filtered. Paper chromatography (ethyl acetate–pyridine–water, 3 : 3 : 2) of the filtered solution indicated the presence of two compounds with the same R_F values as D-altrose and D-glucose. The volume of liquid was adjusted to 10 ml, and the pH adjusted to 5 with 1M-citrate buffer (0.3 ml). Glucose was removed from the solution by stirring for 3 h at room temperature in the presence of baker's yeast (dry weight 45 mg). After centrifugation, the supernatant was evaporated to dryness, and the residue was stirred for 16 h with concentrated hydrochloric acid (1 ml) and toluene-α-thiol (1 ml). Addition of ice precipitated a gum which was collected and dissolved in hot ethanol. This ethanolic solution was poured into hot water. The dibenzyl dithioacetal crystallised on cooling. Thus were obtained: (i) [from compound (6)] D-altrose dibenzyl dithioacetal, m.p. and mixed m.p. 120—121°; $[\alpha]_D^{20}$ +38.0° (*c* 0.75 in pyridine) {lit.,[7] m.p. 119—120° $[\alpha]_D^{20}$ +38.0° (*c* 0.75 in pyridine)}; (ii) [from compounds (12) and (17)] L-altrose dibenzyl dithioacetal, m.p. 120—121° $[\alpha]_D^{20}$ −38.7° (*c* 0.5 in pyridine).

O-(3,4-*Dideoxy*-6-O-*trityl*-α-D-threo-*hex*-3-*enopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (18).—A solution of compound (5) (0.7 g, 1.8 mmol) and chlorotriphenylmethane (834 mg, 3.2 mmol) in pyridine (8 ml) was kept at 80 °C for 7 h, and then evaporated to dryness. The chloroform extract of the residue was chromatographed on silica gel (in ether–petroleum, 1.5 : 1) to give the *trityl ether* (18) (1.01 g, 88%) as an amorphous powder; $[\alpha]_D^{20}$ −16° (*c* 0.75 in CH_2Cl_2) (Found: C, 70.1; H, 6.8; O, 22.9. $C_{37}H_{42}O_9$ requires C, 70.5; H, 6.7; O, 22.8%).

O-(3,4-*Dideoxy*-6-O-*trityl*-α-D-glycero-*hex*-3-*enopyranos*-2-*ulosyl*-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (19).—To a solution of the trityl ether (18) (360 mg, 0.57 mmol) in dimethyl sulphoxide were added dicyclohexylcarbodi-imide (410 mg, 2,3 mmol) and a solution of pyridine (1% v/v) and trifluoroacetic acid (0.5% v/v) in benzene (4 ml). The mixture was stirred for 7 h at room temperature, then ether was added, and the suspension filtered. The ethereal filtrate was washed (H_2O), dried ($MgSO_4$), and evaporated. Chromatography of the residue on silica gel

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(in ether–petroleum, 1 : 1) gave the crystalline ketone (19) (335 mg, 93.5%), m.p. 94—95°, $[\alpha]_D^{20}$ −38 °(*c* 0.68 in CH_2Cl_2), $\nu_{max.}$ (KBr) 1 711 cm^{-1} (CO), δ ($CDCl_3$) 5.29 (1 H, s, H-1), 5.93 (1 H, d, $J_{1,2}$ 3.7 Hz, H-1′), 6.2 (1 H, q, $J_{3,4}$ 11 Hz, H-4), 7.1 (1 H, q, H-3), and 7.2—7.7 (trityl H) (Found: C, 70.4; H, 6.5; O, 22.7. $C_{37}H_{40}O_9$ requires C, 70.7; H, 6.4; O, 22.9%).

O-(3,4-*Dideoxy*-6-O-*trityl*-α-D-erythro-*hex*-3-*enopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (20).—A solution of the ketone (19) (850 mg) in dry ether (40 ml) was added dropwise to a stirred solution of lithium aluminium hydride (70 mg) in dry ether (30 ml). The mixture was kept for 90 min at room temperature, then cooled to 0 °C, and ice and water were added. The ethereal layer was removed and evaporated to dryness. Chromatography of the residue on silica gel (in ether–petroleum, 1.5 : 1) first gave the *alcohol* (20) as an amorphous powder (644 mg, 75%); $[\alpha]_D^{20}$ −45.5° (*c* 0.6 in CH_2Cl_2) (Found: C, 70.7; H, 6.8; O, 23.1. $C_{37}H_{42}O_9$ requires C, 70.5; H, 6.7; O, 22.8%), then the epimeric alcohol (18) (59 mg, 7%).

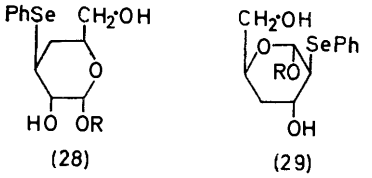
O-(3,4-*Dideoxy*-α-D-erythro-*hex*-3-*enopyranosyl*)-(1 ⟶ 3)-1,2-O-*isopropylidene*-α-D-*glucofuranose* (21).—The trityl ether (20) (434 mg) was dissolved in acetic acid (12 ml), water (8 ml) was added, and the solution was kept for 2 h at 45 °C. Acetic acid was removed by several co-evaporations with water, triphenylmethanol was removed by filtration, and the filtrate was evaporated to dryness. Chromatography of the residue on silica gel (in ether–methanol, 9 : 1) gave the free primary alcohol (21) as a gum (181 mg, 78%), homogeneous by t.l.c. (in ether–methanol, 9 : 1); $[\alpha]_D^{20}$ +102° (*c* 0.4 in CH_2Cl_2) (Found: C, 51.5; H, 7.1; O, 41.1 $C_{15}H_{24}O_9$ requires C, 51.7; H, 6.9; O, 41.3%).

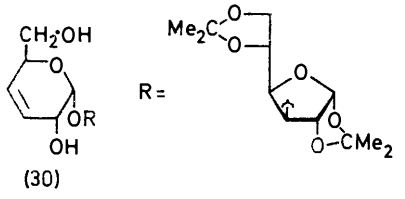
The 2,6-*di*-O-*acetyl derivative* (22), obtained with pyridine–acetic anhydride, and purified by chromatography on silica gel (in ether–petroleum, 3 : 1), was an oil (92.5%); $[\alpha]_D^{20}$ −32.6° (*c* 0.6 in CH_2Cl_2) (Found: C, 53.3; H, 6.4; O, 40.3. $C_{23}H_{32}O_{13}$ requires C, 53.5; H, 6.25; O, 40.3%).

O-(α-D-*Galactopyranosyl*)-(1 ⟶ 3)-D-*glucose* (27).—A solution of the trityl ether (25) (203 mg) in trifluoroacetic acid (1.8 ml) and water (0.2 ml) was kept for 15 min at room temperature, then evaporated, and the residue was chromatographed on silica gel (in ethyl acetate–propan-2-ol–water, 3 : 3 : 2) to give the *disaccharide* (27) as an amorphous powder (74 mg, 73%), $[\alpha]_D^{20}$ +154° (*c* 0.7 in H_2O), R_{Glc} 0.60; $R_{lactose}$ 1.28 {lit.,[5] $[\alpha]_D^{22}$ +159° (*c* 1.0 in H_2O)}.

Hydrolyses of the Protected Disaccharides (23).—(26) *to their Component Sugars*.—The protected disaccharide was mixed with M-sulphuric acid and kept for 1 h at 100 °C. The solution was neutralised ($BaCO_3$), filtered, and evaporated to dryness, and the residue was co-evaporated several times with pyridine. A portion (10 mg) of the residue was dissolved in pyridine (1 ml), hexamethyldisilazane (0.2 ml) was added, followed by chlorotrimethylsilane (0.1 ml), and the solution was examined by g.l.c. (SE 30 column operating at 150 °C). Authentic samples of sugars used for comparison were also kept for 1 h at 100 °C in M-sulphuric acid, and the solutions were processed as above. This is necessary because of the partial conversion of D-allose and D-altrose into their 1,6-anhydrides in aqueous acid. After this treatment, peaks were observed with the following retention times: glucose 14.4 and 23.8 min; galactose 11.7, 13.4, and 16.4 min; allose 11.7 and 12.8 min; altrose 9.6 and 12.2 min.

O-(3,4-*Dideoxy*-3-*phenylseleno*-α-D-xylo-*hexopyranosyl*)-(28) *and* O-(2,4-*Dideoxy*-2-*phenylseleno*-α-D-arabino-*hexopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (29).—Sodium borohydride (60 mg) was added to a solution of diphenyl diselenide (220 mg) in ethanol (5 ml) under dry nitrogen, followed by the epoxide (3)





(0.6 g) in ethanol (20 ml). The mixture was kept at 60 °C for 3 h; t.l.c. (ether) then indicated the disappearance of the starting material. Water was added to the cooled solution, which was extracted with chloroform. Chromatography of the dried ($MgSO_4$) extract on silica gel (ether) first gave the *selenide* (28) as an amorphous powder (0.27 g, 50%), $[\alpha]_D^{20}$ +85.7° (*c* 0.36 in CH_2Cl_2), δ ($CDCl_3$) 1.2—1.6 (12 H, m, 2 CMe_2), 1.7—2.3 (2 H, m, 2 H-4), 5.1 (1 H, s, H-1), 5.99 (1 H, d, $J_{1,2}$ 4 Hz, H-1′), and 7.3—7.8 (5 H, m, Ph) (Found: C, 52.7; H, 6.3; O, 26.1. $C_{24}H_{34}O_9Se$ requires C, 52.8; H, 6.3; O, 26.4%), and then the isomeric selenide (29), again an amorphous powder (180 mg, 34%), $[\alpha]_D^{20}$ −1.5° (*c* 0.6 in CH_2Cl_2), δ ($CDCl_3$) 1.2—1.6 (12 H, m, 2 CMe_2), 1.7—2.8 (2 H, m, 2 H-4), 5.56 (1 H, s, H-1), 5.95 (1 H, d, $J_{1,2}$ 4 Hz, H-1′), and 7.3—7.8 (5 H, m, Ph).

O-(3,6-*Dideoxy*-α-D-erythro-*hex*-3-*enopyranosyl*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (30).—A solution of the selenide (28) (250 mg) in ethanol (10 ml) to which had been added 30% hydrogen peroxide (1 ml) and sodium hydrogen carbonate (50 mg) was boiled at reflux for 1 h; t.l.c. (in 2-isopropoxypropane–propan-2-ol, 94 : 6) then showed the disappearance of the starting material, and the appearance of two new compounds of similar mobility, the more polar being the epoxide (3), as shown by t.l.c. in several solvent systems. These compounds, extracted with chloroform from the dilute, alcoholic solution (120 mg) were separated with difficulty by chromatography on silica gel (in 2-isopropoxypropane–propan-2-ol, 94 : 6). The allylic *alcohol* (30) was obtained as a crystalline solid (20 mg), m.p. 139—141° (hexane), $[\alpha]_D^{20}$ −5.7° (*c* 0.5 in CH_2Cl_2) (Found: C, 55.4; H, 7.2. $C_{18}H_{28}O_9$ requires C, 55.7; H, 7.3%).

Similar treatment of the selenide (29) led to the epoxide (3) and 1,2 : 5,6-di-*O*-isopropylidene-α-D-glucofuranose as the only products which could be detected by t.l.c. (in 2-isopropoxypropane–methanol, 94 : 6) after charring with concentrated sulphuric acid. Isolation and comparison with authentic specimens confirmed their identity.

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