Stereoselective Dienyl Ether Syntheses from Malonaldehyde *trans*-Enol Ethers: (*E*)-Buta-1,3-dienyl, and (*E,Z*)- and (*E,E*)-4-Chlorobuta-1,3-dienyl Ethers of a Protected Sugar; Conversion of the Latter into Functionalized Chiral Disaccharide Precursors

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Condensation of the enol tosylate of malonaldehyde with the sodium alcoholate NaOR derived from ' diacetone glucose ' gave in 92% yield the almost pure *trans*-enol ether RO–CH=CH–CHO (1). This could be readily condensed with suitable Wittig phosphoranes to give either the buta-1,3-dienyl ether (2) (87% yield; more than 90% *trans*), or a mixture of 4-chlorobuta-1,3-dienyl ethers (85%) of ' diacetone glucose; ' the main components were the (*E,Z*)-diene (5) (45%) and the (*E,E*)-diene (4) (45%). Cycloaddition of diethyl mesoxalate to the diene (4) gave a mixture of two 3-chloro-2,2-bisethoxycarbonyl-3,6-dihydro-2*H*-pyran-6-yl ethers, the (3*S*,6*S*)-derivative (6) (69%) and the (3*R*,6*R*)-derivative (7) (19%). Free-radical reduction of these chlorides (6) and (7) with tributylstannane led to mainly rearranged products: the 2,2-bisethoxycarbonyl-5,6-dihydro-2*H*-pyran-6-yl ethers, (6*S*) (9) and (6*R*) (11). In the same way, nucleophilic substitution of the chloride (6) with azide led to the (5*S*)-5-azido-derivative (12) of the dihydropyran (9). Catalytic reduction of the double bond and the azido-group in (12), followed by *N*-acetylation, gave the saturated (*S*)-acetamido derivative (13), which could be de-ethoxycarbonylated to give two disaccharides with a 2-acetamido-2-deoxyhexopyranosyl non-reducing unit. We consider that the above overall sequence of reactions is a useful extension of the cycloaddition method of disaccharide synthesis.

CYCLOADDITION of glyoxylic esters to buta-1,3-dienyl ethers of protected monosaccharides, which we have already used extensively in a new synthesis of disaccharides,[1] is normally very sluggish with the *cis*-isomers at ordinary pressures. Although this inconvenience may be circumvented by the use of the more reactive dienophile, diethyl mesoxalate,[2] a better synthesis of *trans*-buta-1,3-dienyl ethers seemed desirable, so as to avoid the waste of the sometimes expensive protected sugar moiety. Clearly, such a synthesis would also be of interest outside the carbohydrate field. The classical method of preparation of buta-1,3-dienyl ethers is the pyrolysis in the presence of catalysts of the trialkoxybutanes CH_3–CHOR–CH_2–$CH(OR)_2$ which gives mixtures containing up to 88% of *trans*-diene.[3] However, this can hardly be considered as a general route to the ethers of costly or sensitive alcohols. Base-induced elimination of alcohol or phenol from 1,4-bis-ethers RO–CH_2–CH=CH–CH_2OR has been reported [4] to give in one case 87% *trans*-compound, but in such reactions the yield from ROH obviously cannot exceed 50%. Addition of butadiyne to alcohols proceeds under relatively mild conditions to give *cis–trans*-mixtures of enynyl ethers which can be hydrogenated to buta-1,3-dienyl ethers.[5] However the proportions of *trans*-dienes are those of the addition product, and vary from 40 to 75%. A mixture containing *ca.* 40% *trans*-diene was obtained by the Wittig condensation with acrylaldehyde of a sugar-derived phosphorane, but this was not readily prepared.[5a]

We now report the preparation of the *trans*-malonaldehyde monoenol ether of a protected sugar (1). A Wittig reaction with methylenetriphenylphosphorane then gave, in excellent yield, a mixture containing more than 90% *trans*-buta-1,3-dienyl ether (2). The (*E,E*)- and (*E,Z*)-4-chlorobuta-1,3-dienyl ethers, (4) and (5) were obtained from the same aldehyde, and converted by cycloaddition into versatile intermediates in oligosaccharide synthesis.

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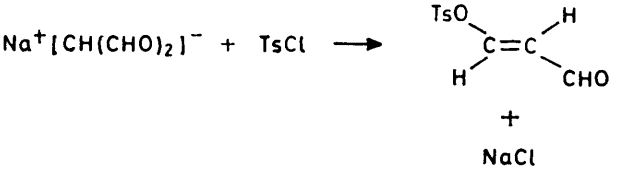
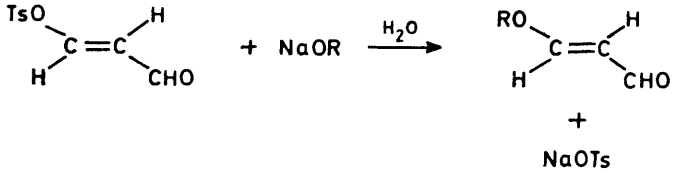
DISCUSSION

The synthesis of 3-alkoxy-acrylaldehydes from alcoholates does not appear to have been recorded so far. Although we report only the preparation of the derivative of ' diacetone glucose,' the method described can obviously be extended to a wide range of alcohols. The necessary intermediate, 3-tosyloxyacrylaldehyde was obtained in solution by cautious addition of the sodium salt of malonaldehyde to a solution of toluene-*p*-sulphonyl chloride in oxolan:



The reaction was apparently complete in a few minutes at room temperature in the presence of 18-crown-6 (0.7 mol %) but was extremely sluggish in its absence. The ^{1}H n.m.r. spectrum of this solution confirmed the presence of 3-tosyloxyacrylaldehyde, mainly or exclusively the *trans*-isomer, $J_{2,3}$ 12.5 Hz. Cooling gave a crystalline precipitate, but this decomposed with evolution of heat on attempted filtration. Concentration of the solution also led to decomposition, with concomitant acidification. For these reasons, further reactions with 3-tosylacrylaldehyde had to be conducted *in situ*.

The displacement of tosylate by alcoholate could be achieved only under the following somewhat unusual conditions: 2 equiv. of tosylate were necessary. Consecutive addition to the oxolan solution of sodium hydride (2 equiv.) and diacetone glucose (1 equiv.) gave the alcoholate, which however, did not react under these

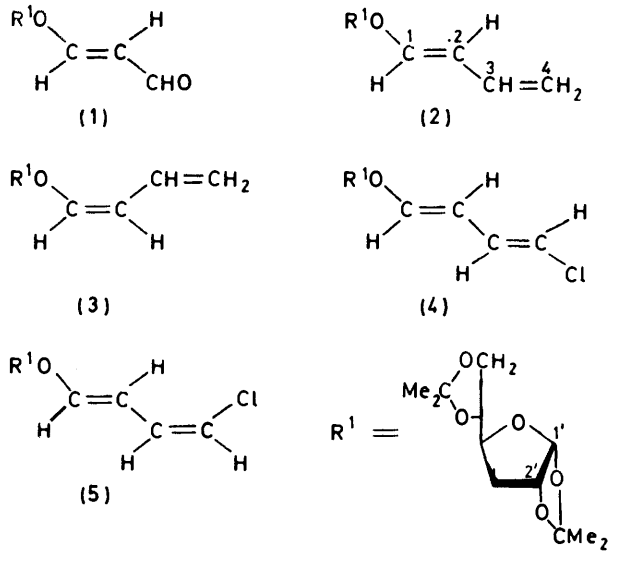


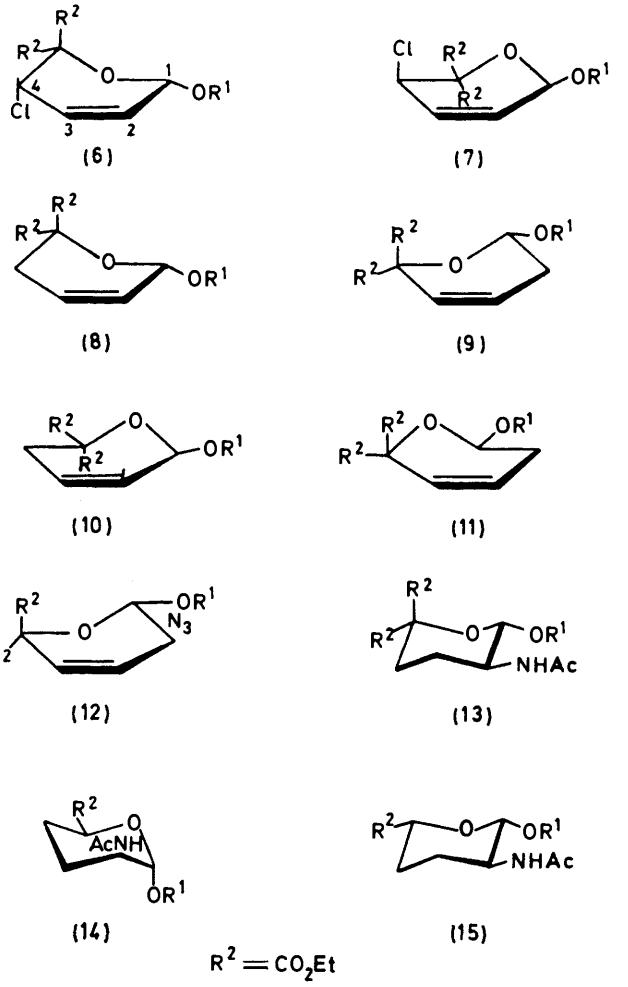
conditions. A vigorous reaction occurred only on addition of a solution of 2 equiv. of water in oxolan.

Quick processing, including short-column chromatography, gave the enol ether (1) in 92% yield (from the alcohol) as an oil which was too unstable for the determination of its composition. The ^{1}H n.m.r. spectrum again was that of a practically pure *trans* derivative ($J_{2.3}$ 12.5 Hz) although a weak signal at δ 7.18 might be attributed to 3-H of a *cis*-isomer, present in amounts too small to estimate. The overall retention of configuration in this substitution could be explained by a Michael-type addition of the alcoholate to the C=C bond of 3-tosyloxyacrylaldehyde followed by tosylate elimination to the *trans*-derivative. The necessity for water, however, is not so readily explained. Perfectly dry reagents show no reaction even after long periods. Addition of water before the sugar, or replacement of sodium hydride by powdered potassium hydroxide, led to no substitution. Finally we found that ' diacetone glucose ' does not add to prop-2-ynal under the conditions of our reaction.

The new readily available *trans*-acrylaldehyde derivative (1) appeared to be an attractive precursor of dienyl ethers with a 1,2-*trans*-double bond. In fact, condensation with methylenetriphenylphosphorane gave in 87% yield (of isolated material) a mixture of the known [5a] buta-1,3-dienyl ethers ‡ (2) and (3) containing more than 90% *trans*-isomer. Partial isomerization to *cis*-intermediates during the Wittig reaction seemed probable, but was not rigorously proved.

In the same way, condensation of the aldehyde (1) with chloromethylenetriphenylphosphorane gave in 85% yield a mixture containing 90% of isomers with the 1,2-*trans*-configuration, the (*E*,*E*)-diene (4) (45%) and the (*E*,*Z*)-diene (5) (45%). Again there is some evidence of partial isomerization in the process. The mixture of (4) and (5) could not be separated at that stage, but the pure *E*,*Z*-component (5) could be isolated at the following step because of its inertness in cycloaddition, as a crystalline solid. Then its ^{1}H n.m.r. spectrum could be recorded ($J_{1.2}$ 12, $J_{3.4}$ 5.2 Hz), and substraction from the spectrum of the (4)–(5) mixture gave the spectrum of the (*E*,*E*)-diene (4) ($J_{1.2}$ 12, $J_{2.3}$ 11.5 Hz), as there is practically no overlap of signals at 250 MHz. This is apparently the first recorded synthesis of 4-chlorobuta-1,3-dienyl ethers. The method is obviously a general one.





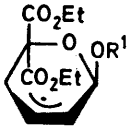
We have already pointed out the potential interest of functionalized dienes for oligosaccharide synthesis by the cycloaddition method.[1] A study of the usefulness of the diene (4) in this respect was undertaken. When the above mixture was heated for 10 h at 100 °C with diethyl

‡ The numbering scheme indicated on formulae (2) and (6) and in R^1 will be used throughout, except in the titles of sections in the Experimental section, when compounds (6)—(12) will be named as pyran derivatives.

mesoxalate (chosen as a dienophile for the sake of simplicity) only the *E,E*-component reacted. The cycloaddition to this diene at 100 °C proceeded three times more slowly than to the non-chlorinated analogue (2). Chromatographic separation first gave a mixture from which the unreactive *Z,E*-component could be obtained as a pure crystalline solid. The next two fractions were the dihydropyrans (6) and (7), in 69 and 19% respective yields when calculated from the amount of (*E,E*)-diene originally present. The given constitutions (6) and (7) rest on the following evidence: the adducts did not show the typical lability of pyranosyl chlorides, an indication that the oxygen of the dienophile had linked itself to C-1 of the diene. The *cis*-disposition of 1-O and 4-Cl was expected from the known course of cycloaddition. The ^{1}H n.m.r. spectra at 250 MHz were very similar, in agreement with the enantiomeric nature of the dihydropyran moieties. The proposed interpretations were confirmed by double irradiation at the frequencies of 1-H and 4-H. The conformations of the bonds to 1-H and 4-H, as respectively pseudoaxial and pseudoequatorial, were indicated by the coupling constants, $J_{1.2} = J_{1.3} = 1.2$ Hz and $J_{3.4}$ *ca.* 6 Hz (*cf.* ref. 6). The *S*-configuration of adduct (6) at C-1 was proved by tributylstannane reduction to the known [5a] dihydropyran (8), $[\alpha]_D^{20}$ −39°. Conversely the adduct (7) was reduced to the known [5] dihydropyran (10), m.p. 77 °C, $[\alpha]_D^{20}$ +24°, with the *R*-configuration at C-1. By adopting the D-^5H_O and L-$^OH_5$ conformations, the adducts (6) and (7) avoid unfavourable 1,3-diaxial interactions.

However, compounds (8) and (10) were only minor products in the above reductions, the main ones being the rearranged isomers (9) and (11) (*ca.* 65%). In the ^{1}H n.m.r. spectrum of (9), $[\alpha]_D^{20}$ −8°, on irradiation of the easily located methylene signal, the doublet of doublets due to 1-H collapsed to a singlet, and the signals of the olefinic protons to doublets, a proof that the methylene group is between C-1 and the double bond. All this could be repeated with the dextrorotatory isomer (11), $[\alpha]_D^{20}$ +17°, which had almost the same ^{1}H n.m.r. spectrum as (9).

It is now established that the first step in tributylstannane reduction is the removal of a chlorine atom to



(16)

give a free radical, which then withdraws a hydrogen atom from tributylstannane, leading to the final, reduced product.[7] In our case the intermediate will be an ambident, allylic radical (16).

The ratio of the yields of rearranged to 'normal' product, *ca.* 4 : 1 may be taken as a measure of relative reactivities at C-2 and C-4. Prediction would have been ambiguous, as both ends of the allylic radical are linked to a carbon atom substituted by electron-withdrawing groups.

Nucleophilic substitution of the chloro-derivative (6) with sodium azide in dimethyl sulphoxide solution also gave, in 56% yield, a rearranged product (12). The ^{1}H n.m.r. signal of 1-H is now a doublet, with a 4.4 Hz spacing, which rules out any coupling with the olefinic protons. The suggested attributions were confirmed by irradiation at the 4-H frequency. Exchange of azide [8] between C-2 and C-4 in 'S_N2'' reactions of 2-*O*-mesylates [9] in similar pyranoside systems, always to the advantage of C-2, have been recorded previously.

Catalytic reduction over platinum dioxide, followed by acetylation, gave a hexopyranoside (13) showing the anomeric proton signal as a doublet, $J_{1,2}$ 7 Hz; thus the nitrogen and anomeric oxygen are in *trans*-diequatorial mutual relationship in a $^1C_4$ conformation. This, again, avoids unfavourable 1,3-diaxial interactions of 'diacetone glucose' with one ethoxycarbonyl group.

The water–sodium chloride catalysed de-ethoxycarbonylation gave mainly (59%), the 1,5-*trans*-(α-D-) hexopyranose, as previously found with similar diesters.[2] This adopted the more stable D-$^4C_1$ chair conformation (14) ($J_{1.2}$ 2.2 Hz) with equatorial ethoxycarbonyl group and axial anomeric oxygen. On the other hand the minor decarboxylation product, the β-L-hexopyranoside (15) (12%) adopted the $^1C_4$ chair conformation, despite its unfavourable anomeric effect, to avoid 1,3-diaxial interactions.

Some general comments on these novel cycloadditions may be made. Substitution by chlorine at C-4 led to some deactivation: the chlorinated (*E,E*)-dienyl ether (4) reacted three times more slowly at 100 °C with diethyl mesoxalate than its unsubstituted analogue (2). Although the (*Z*)-dienyl ether (3) is still less reactive, good yields of adduct were obtained in 36 h at 100 °C, whereas the chlorinated (*Z,E*)-dienyl ether (5) did not react at all, even under forcing conditions at ordinary pressure. It has been found previously [1] that the introduction of a 4-benzyloxy-group into the dienyl ether leads to a substantial proportion of attack at C-4 by the carbonyl oxygen of the dienophile. There is no such decrease of regioselectivity with the 4-chloro-dienyl ethers, the two isolated adducts (6) and (7) resulting from exclusive attack at C-1, to give disaccharide-like compounds. Finally from the point of view of stereoselectivity, the 4-chloro-dienyl ether (4) behaves like all the dienyl ethers derived from 'diacetone glucose' which we have studied so far: there is predominant attack on the so-called 'negative face' of the diene,[5b] to give an adduct with the *S*-configuration at C-1, so that once more the preferred face seems to depend mainly on the configuration near the sugar, not on more remote parts of the diene.

It seems that the now readily available compounds (6)—(14) might be useful intermediates in carbohydrate chemistry.

EXPERIMENTAL

All the reported chromatographic separations were performed with silica gel columns. ^{1}H N.m.r. spectra were recorded at 250 MHz for samples dissolved in $CDCl_3$, in the presence of Me_4Si as internal reference, unless otherwise stated. In their interpretation, hydrogen atoms are numbered as in formulae (2) and (6) and in R^1.

trans-3-(1,2:5,6-*di*-O-*Isopropylidene*-α-D-*glucofuranos*-3-*yl*)*acrylaldehyde* (1).—Sodio-malonaldehyde (10.4 g, 0.11 mol) was added in 15 portions, at 1 min intervals, to a solution of tosyl chloride (15.2 g, 0.08 mol) and 18-crown-6 (0.16 g) in dry oxolan (60 ml). The mixture was then kept for 10 min; t.l.c. (chloroform–ether–light petroleum, 1 : 1 : 1) indicated the presence of a new, more polar component as a spot visible under u.v. light, which became yellow on heating. Sodium hydride (80%; 3 g, 0.1 mol) and a solution of diacetone glucose (10.4 g, 40 mmol) in oxolan (30 ml) were then added in succession. and after 10 min a solution of water (2 ml) in oxolan (30 ml) was slowly added, with vigorous stirring, while the temperature was kept below 20 °C with a cold water-bath. After another 10 min, t.l.c. indicated the presence of only one u.v.-absorbing component less polar than diacetone glucose. If the reaction was then not complete, more small portions (0.1 g) of sodium hydride were added. The mixture was filtered over a Celite bed, the solid was washed with oxolan, and the combined liquids were evaporated to dryness. Chromatography through a short column (same eluant as above) gave the unstable, substituted acrylaldehyde (1) (11.59 g, 92%), δ 9.36 (1 H, d, $J_{1,2}$ 8 Hz, CHO), 7.33 (1 H, d, $J_{2,3}$ 12.5 Hz, 3-H), 5.90 (1 H, d, $J_{1',2'}$ 3.7 Hz, 1'-H), 5.73 (1 H, dd, 2-H), and 4.58 (1 H, d, 2'-H).

The 90-MHz ^{1}H n.m.r. spectrum of 3-tosylacrylaldehyde could be recorded from its oxolan solution after filtration over a Celite bed; δ (oxolan) 9.47 (1 H, d, $J_{1,2}$ 8 Hz, CHO), 7.83 (2 H, Ar), 7.64 (1 H, d, $J_{2,3}$ 12.5 Hz, 3-H), 7.42 (2 H, Ar), 5.89 (1 H, dd, 2-H), and 2.43 (3 H, s, CH_3).

3-O-(*Buta*-1,3-*dienyl*)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose*, (2) *and* (3).—A solution of the aldehyde (1) (743 mg, 2.36 mmol) in toluene (5 ml) was first dried overnight over 4 Å molecular sieves, and then slowly added to a solution of methylenephosphorane (prepared in the usual way from 3 mmol of each reagent) in oxolan (15 ml), kept at −80 °C. The mixture was allowed to warm to room temperature (30 min), and kept at that temperature for 20 min with constant stirring. Chromatography (ether–light petroleum, 1 : 1) then gave the (*E*)-dienyl ether (2), mixed with less than 10% *Z*-isomer (3) (642 mg, 87%); the ^{1}H n.m.r. spectrum was identical with that of a sample of compound (2) prepared according to ref. 5*a*, except for some low-intensity signals corresponding to the (*Z*)-diene (3), δ 5.97 (1-H) and 4.57 (2-H) (Found: C, 61.9; H, 7.7; O, 30.2. Calc. for $C_{16}H_{24}O_6$: C, 61.5; H, 7.7; O, 30.7%).

3-O-(4-*Chlorobuta*-1,3-*dienyl*)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose*, E,E- *and* Z,E-*Isomers*, (4) *and* (5).—A solution of chloromethylenetriphenylphosphorane in oxolan (20 ml) was prepared from 11.5 mmol each of chloromethyltriphenylphosphonium chloride and phenyl-lithium, and cooled to 0 °C. To this was added a solution of the aldehyde (1) (2.80 g, 8.9 mmol) in oxolan (20 ml), dried as above. The mixture was allowed to warm to room temperature, kept for 20 min, filtered over a Celite bed, and evaporated to dryness. Chromatography (ether–light petroleum, 1 : 3) gave a 1 : 1 mixture of *chloro-dienes* (4) and (5) (2.63 g, 85%), b.p. 125—130 °C at 0.01 mmHg; δ for the (*E,E*)-diene (4): 6.50 (1 H, d, $J_{1,2}$ 12 Hz, 1-H), 6.28 (1 H, pseudo t, $J_{2,3}$ 11.5 Hz, $J_{3,4}$ 12.5 Hz, 3-H), 5.98 (1 H, d, 4-H), and 5.62 (1 H, dd, 2-H) (Found: C, 55.3; H, 6.6; Cl, 10.5; O, 27.5. $C_{16}H_{23}ClO_6$ requires C, 55.4; H, 6.6; Cl, 10.2; O, 27.7%).

Cycloaddition of the Chlorodienyl Ether Mixture with Diethyl Mesoxalate.—The mixture of chlorodienyl ethers 9.54 g, 27.5 mmol) was heated with diethyl mesoxalate (4.02 g, 23 mmol) for 10 h at 100 °C, under N_2, in the presence of 4 Å molecular sieves and cooled to room temperature. Chromatography (dichloromethane–light petroleum–acetone, 20 : 10 : 1) then gave three fractions, *A*, *B*, and *C*, of increasing polarity.

3-O-[(Z,E)-4-*Chlorobuta*-1,3-*dienyl*]-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (5).—From fraction *A* (5.3 g) the (E,Z)-*diene* (5) could be obtained as a crystalline solid (3.6 g), m.p. 84—86 °C (ether–light petroleum), $[\alpha]_D^{20}$ −20° (*c* 0.7 in CH_2Cl_2), δ 6.62 (1 H, d, $J_{1,2}$ 12 H, 1-H), 6.16 (1 H, dd, $J_{3,4}$ 5.2, $J_{2,3}$ 11.1 Hz, 3-H), 6.04 (1 H, pseudo t, 2-H), and 5.81 (1 H, d, 4-H) (Found: C, 54.9; H, 6.6; Cl, 10.9; O, 27.3. $C_{16}H_{13}ClO_6$ requires C, 55.4; H, 6.6; Cl, 10.2; O, 27.7%).

The ^{1}H n.m.r. spectrum of the mother-liquors indicated that they contained no (*E,E*)-diene (4).

3-O-[(3S,6S)-3-*Chloro*-2,2-*bisethoxycarbonyl*-3,6-*dihydro*-2H-*pyran*-6-*yl*]-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (6).—Fraction *B* (4.43 g) was the *dihydropyran* (6), obtained in 69% yield [from the (*E,E*)-diene (4) originally present in the mixture], b.p. 180 °C at 0.01 mmHg, $[\alpha]_D^{20}$ +105° (*c* 0.7 in CH_2Cl_2), δ($CDCl_3$) 6.18 (1 H, m, $J_{3,4}$ 6.5, $J_{2,3}$ 10, $J_{1,3}$ 1.2 Hz, 3-H), 5.90 (1 H, d, $J_{1',2'}$ 3.7 Hz, 1'-H), 5.80 (1 H, dd, $J_{1,2}$ 1.2 Hz, 2-H), 5.42 (1 H, br s, 1-H), 5.06 (1 H, dd, $J_{1,4}$ 1.6 Hz, 4-H), and 4.97 (1 H, d, 2'-H) (Found: C, 53.0; H, 6.4; O, 34.2. $C_{23}H_{33}ClO_{11}$ requires C, 53.0; H, 6.3; O, 33.8%).

3-O-[(3R,6R)-3-*Chloro*-2,2-*bisethoxycarbonyl*-3,6-*dihydro*-2H-*pyran*-6-*yl*]-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (7).—Fraction *C* (1.26 g) was the *dihydropyran* (7) [19% yield from the (*E,E*)-diene originally present in the mixture], m.p. 138 °C (ether), $[\alpha]_D^{20}$ −123° (*c* 0.7 in CH_2Cl_2), δ($CDCl_3$) 6.32 (1 H, m, $J_{3,4}$ 5.5, $J_{2,3}$ 10, $J_{1,3}$ 1.2 Hz, 3-H), 5.92 (1 H, d, $J_{1',2'}$ 3.7 Hz, 1'-H), 5.82 (1 H, dd, $J_{1,2}$ 1.2 Hz, 2-H), 5.64 (1 H, s, with fine structure, 1-H), 5.10 (1 H, dd, $J_{1,4}$ 1.6 Hz, 4-H), and 4.92 (1 H, d, 2'-H) (Found: C, 53.0; H, 6.4; O, 33.4. $C_{23}H_{33}ClO_{11}$ requires C, 53.0; H, 6.4; O, 33.8%).

3-O-[(6S)-2,2-*Bisethoxycarbonyl*-5,6-*dihydro*-2H-*pyran*-6-*yl*]-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (9).—A solution of the chloro-derivative (6) (1.31 g, 2.52 mmol), αα'-azoisobutyronitrile (10 mg) and tributylstannane (1.15 ml) in toluene (30 ml) was heated at reflux for 15 min under N_2. Chromatography (toluene–ether–light petroleum, 4 : 1 : 1) first gave the dihydropyran (9) (0.84 g, 69%), $[\alpha]_D^{20}$ −8° (*c* 7.5 in CH_2Cl_2), δ($CDCl_3$) 6.04 (1 H, dm, 4-H), 5.96 (1 H, dt, $J_{3,4}$ 10, $J_{2a,3} = J_{2b,3} = 3.5$ Hz, 3-H), 5.81 (1 H, d, $J_{1',2'}$ 3.5 Hz, 1'-H), 5.30 (1 H, dd, $J_{1,2a}$ 5.2, $J_{1,2b}$ 3.5 Hz, 1-H), 4.70 (1 H, d, 2'-H), and 2.28 (2 H, m, 2a-H, 2b-H) (Found: C, 56.4; H, 7.0; O, 35.9. $C_{23}H_{34}O_{11}$ requires C, 56.8; H, 7.0; O, 36.2%).

The next fraction was the known dihydropyran (8) (160 mg, 13%), $[\alpha]_D^{20}$ −39° (*c* 1.2 in CH_2Cl_2); the ^{1}H n.m.r. spectrum was identical with that of a sample prepared according to ref. 2 (lit.,[2] $[\alpha]_D^{20}$ −45°).

3-O-[6R-2,2-*Bisethoxycarbonyl*-5,6-*dihydro*-2H-*pyran*-6-*yl*]-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (11).—The

chloro-derivative (7) (0.54 g, 1.04 mmol) was reduced in the same manner as compound (6). Chromatography (ether–light petroleum, 1 : 1) first gave the known dihydropyran (10) (71 mg, 14%), m.p. 76—77 °C, $[\alpha]_D^{20}$ +24° (*c* 0.8 in CH_2Cl_2); the ^1H n.m.r. spectrum was identical with that of a sample prepared according to ref. 2 (lit.,[2] m.p. 66.5—68 °C, $[\alpha]_D^{20}$ +24°).

The next fraction was the *dihydropyran* (11) (0.3 g, 59%), m.p. 69—70 °C (cyclohexane), $[\alpha]_D^{20}$ +17° (*c* 1 in CH_2Cl_2); δ($CDCl_3$) 6.06 (1 H, dm, $J_{3,4}$ 10 Hz, 4-H), 5.94 (1 H, dt, $J_{2a,3} = J_{2b,3} = 3.5$ Hz, 3-H), 5.90 (1 H, d, $J_{1',2'}$ 3.5 Hz, 1'-H), 5.10 (1 H, dd, $J_{1,2a}$ 6, $J_{1,2b}$ 4.5 Hz, 1-H), 4.60 (1 H, d, 2'-H), and 2.20 (2 H, m, 2a-H, 2b-H) (Found: C, 56.5; H, 7.15; O, 36.6. $C_{23}H_{34}O_{11}$ requires C, 56.8; H, 7.0; O, 36.2%).

3-O-[(5S,6S)-5-*Azido*-2,2-*bisethoxycarbonyl*-5,6-*dihydro*-2H-*pyran*-6-*yl*]-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (12).—A solution of the chloro-derivative (6) (0.65 g, 1.25 mmol) and sodium azide (0.4 g) in dimethyl sulphoxide (5 ml) was heated at 100 °C for 2 h. Then t.l.c. (ether–light petroleum, 1 : 1) indicated the formation of two new compounds, and the less polar, major one was separated by column chromatography with the same eluant. This was the *azido-derivative* (12) (374 mg, 56%), b.p. 180 °C at 0.01 mmHg, $[\alpha]_D^{20}$ +55° (*c* 0.8 in CH_2Cl_2), δ($CDCl_3$) 6.36 (1 H, dd, $J_{3,4}$ 10, $J_{2,4}$ 1.6 Hz, 4-H), 5.93 (1 H, dd, $J_{2,3}$ 3.6 Hz, 3-H), 5.84 (1 H, d, $J_{1',2'}$ 3.6 Hz, 1'-H), 5.24 (1 H, d, $J_{1,2}$ 4.4 Hz, 1-H), 4.70 (1-H, d, 2'-H), and 3.75 (1 H, m, 2-H) (Found: C, 52.6; H, 6.6; N, 8.25; O, 33.7. $C_{23}H_{33}N_3O_{11}$ requires C, 52.4; H, 6.3; N, 8.0; O, 33.4%).

3-O-[(2S,3S)-3-*Acetamido*-6,6-*bisethoxycarbonyltetrahydro*-*pyran*-2-*yl*]-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose* (13).—A solution of the azido-derivative (12) (0.48 g, 0.9 mmol) in methanol (20 ml) in the presence of platinum dioxide (0.35 g) was shaken for 16 h in hydrogen. The solution was then filtered, and acetic anhydride (1 ml) was added. After 1 h, volatile material was removed by three co-evaporations with toluene. The *acetamido-derivative* (13) was obtained as a gum (0.45 g, 91%), b.p. 210 °C at 0.01 mmHg, $[\alpha]_D^{20}$ +20° (*c* 1 in CH_2Cl_2), δ($CDCl_3$) 6.12 (1 H, d, $J_{2,NH}$ 6 Hz, NH), 5.84 (1 H, d, $J_{1',2'}$ 3.5 Hz, 1'-H), 4.85 (1 H, d, $J_{1,2}$ 7 Hz, 1-H), 4.72 (1 H, d, 2'-H), 1.95 (3 H, s, NAc), and 2—2.5 (4 H, $2CH_2$) (Found: C, 54.8; H, 7.3; N, 2.4. $C_{24}H_{39}NO_{12}$ requires C, 55.0; H, 7.2; N, 2.6%).

O-(*Ethyl* 2-*acetamido*-3,4-*dideoxy*-α-D-threo- *and* β-L-erythro-*hexopyranosyluronate*)-(1 ⟶ 3)-1,2:5,6-*di*-O-*isopropylidene*-α-D-*glucofuranose*, (14) *and* (15).—A solution of compound (13) (0.28 g, 0.5 mmol), water (0.01 ml), and sodium chloride (0.1 g) in hexamethylphosphoramide (2 ml) was heated at 180 °C for 2 h. T.l.c. (toluene–chloroform–acetone, 1 : 1 : 3) indicated the formation of two new components. Column chromatography (toluene–dichloromethane–acetone, 2 : 1 : 1) first gave compound (15) (30 mg, 12%), m.p. 168—171 °C, $[\alpha]_D^{20}$ +30° (*c* 0.3 in CH_2Cl_2), δ($CDCl_3$) 6.18 (1 H, d, $J_{2,NH}$ 5 Hz, NH), 5.87 (1 H, d, $J_{1',2'}$ 3.5 Hz, 1'-H), 4.84 (1 H, d, 2'-H), and 4.34 (1 H, d, $J_{1,2}$ 8.5 Hz, 1-H).

The next fraction was *compound* (14) (144 mg, 59%), obtained as a glass, b.p. 200 °C at 0.01 mmHg, $[\alpha]_D^{20}$ +24° (*c* 1 in CH_2Cl_2), δ($CDCl_3$) 6.06 (1 H, d, $J_{2,NH}$ 8 Hz, NH), 5.84 (1 H, d, $J_{1',2'}$ 3.5 Hz, 1'-H), 5.02 (1 H, d, $J_{1,2}$ 2.2 Hz, 1-H), and 4.62 (1 H, d, 2'-H) (Found: C, 55.2; H, 7.3; N, 2.8. $C_{22}H_{35}NO_{10}$ requires C, 55.8; H, 7.4; N, 3.0%).

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