One-step Synthesis of Glycosidic Spiroketals from 2,3-Epoxybutyl Glycoside Derivatives

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The *cis*-epoxides **12** and **13**, made by epoxidation of (*Z*)-4'-hydroxbut-2'-enyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside, have been converted into the corresponding 4'-iodides which, on treatment with tributyltin hydride under UV light, gave the crystalline spiroketal **21** (68%, from the iodide **14** derived from **12**) and four analogous isomeric products (from the iodide **16** derived from **13**). The differences in the selectivities of the reactions are attributed to hydrogen bonding in intermediate anomeric radicals. In both cases, 4'-oxobutyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside **24** was produced as a by-product.

Our interests in the use of carbohydrates as starting materials for the synthesis of compounds of significance in medicinal chemistry,[1] and in the application of free radical synthetic methods,[2–4] has led us to investigate a new approach to D-glucose-based spiroketals. Here we report on a direct procedure for converting 2',3'-epoxy-4'-iodobutyl glycopyranoside tetraacetates into spiroketals of the 1,6-dioxaspiro[4.5]decane category.

Spiroketals occur naturally in an extensive range of species—plants, marine organisms, insects, micro-organisms—and have a wide variety of biological activities. Their chemical and pharmacological exploration has therefore received appreciable attention, and considerable effort has been devoted to their syntheses.[5,6] As insect pheromones they occur as simple spiroketals, but they also arise in elaborate forms as components of complex, potently bioactive microbiological metabolites such as the milbemycins, the avermectins and monensin. Those members which bear oxygen-bonded ring substituents have been targets of syntheses from carbohydrates, 1,6-anhydro-β-D-glucopyranose for example having been used to obtain the relevant components of the milbemycins,[7] and the spiroketal parts of the avermectins have, likewise, been made from carbohydrate precursors.[8,9]

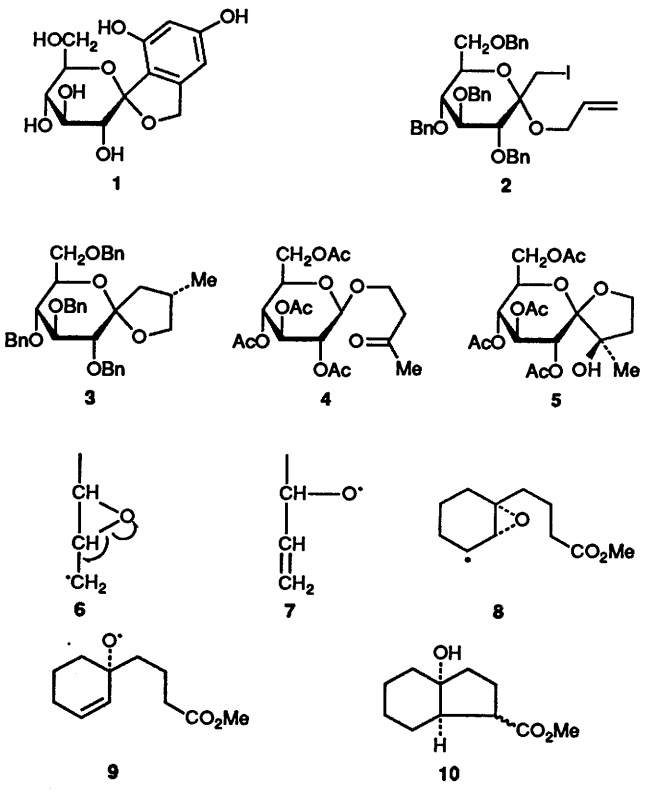
Containing complete D-glucopyranosyl moieties (*e.g.* **1**) within their structures, the spiroketal components of the papulacandin family of antifungal agents are readily accessible from glucose,[10] as are related benz-fused compounds,[11] and recently Redlich and co-workers, who have previously synthesised several spiroketal insect pheromones from D-glucose,[12] reported the production of spiro compounds comprising two hexopyranose units which share a common anomeric carbon atom.[13] Such 1,6-dioxaspiro[5.5]undecane compounds are bicyclic anhydrides of undec-6-uloses.

Most of the procedures used for making spiroketals from carbohydrates have centred on the synthesis of ketones (with the carbonyl groups at the anomeric centres of chain-extended ketoses) often by use of carbanionic attack at the carbonyl groups of aldonolactones. One synthesis, however, relied on the oxidative coupling of the anomeric centre and a hydroxy group in the 'aglycone' of a *C*-glycosidic compound.[8] Related coupling between the anomeric centre and a carbon atom of the aglycone of an *O*-glycoside is now reported.

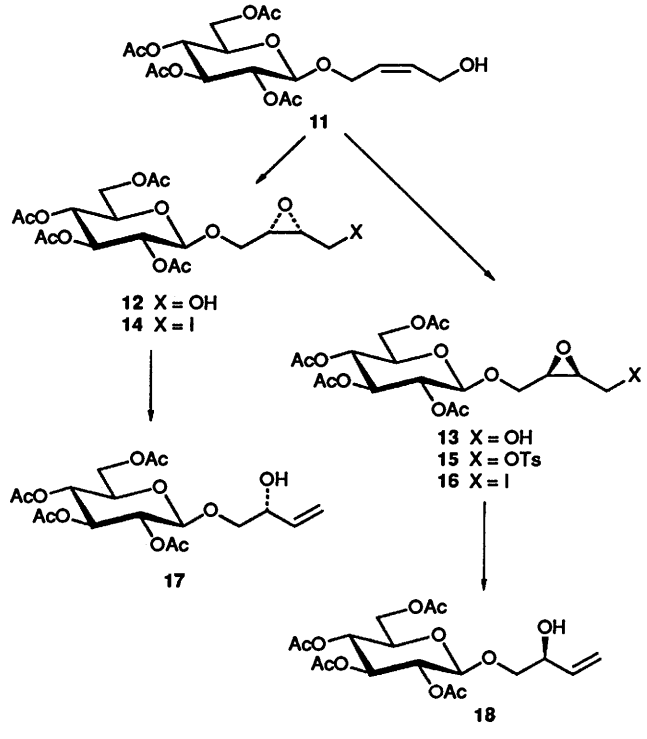
Free radical procedures have opened new opportunities for the synthesis of spiroketals from carbohydrates as illustrated by Haudrechy and Sinay who treated the *exo*-alkene derived by use of Tebbe's reagent from tetra-*O*-benzyl-D-glucono-1,5-lactone with allyl alcohol and *N*-iodosuccinimide to give the allyl 1-deoxy-1-iodoketoside **2**. On treatment with tributyltin hydride in the presence of catalytic amounts of azoisobutyronitrile (AIBN) this cyclised to the spiro compound **3** in 77% yield.[14] Earlier, however, Descotes and co-workers had shown that related compounds result from UV irradiation of 3-oxoalkyl glycosides, the reactions involving Norrish type II photocyclisations (*e.g.* **4** ⟶ **5**).[15,16] Glycosides, *e.g.* β-glucopyranosides, with equatorial aglycones—and thus more readily abstracted axial anomeric hydrogen atoms—reacted relatively quickly,[15–19] and since glucopyranos-1-yl radicals are trapped preferentially in the axial mode,[17,19–21] the reaction products also had equatorial oxygen substituents following kinetically controlled coupling of the anomeric radicals with the aglycone *C*-radicals. By application of this approach to a phenyl β-D-glucopyranoside having a carbonyl group at the *ortho*-position of the aromatic ring Descotes *et al.* made β-bonded benz-substituted spiroketals and hence, following acid-catalysed anomerisation, α-linked compounds related to compound **1** but having the aromatic rings fused 2,3- rather than 3,4- to the tetrahydrofuran rings.[22]

A related method for synthesising spiroketals from sugars should apply if anomeric hydrogen atoms are abstracted intramolecularly in the presence of alkene functions in the aglycones. With this in mind we therefore investigated the use of glycosides having aglycones containing epoxide rings and an adjacent group from which *C*-radicals can readily be produced since such species rearrange to allyloxy radicals (**6** ⟶ **7**).[23] In the case of the glycosides these could act both as abstractors of anomeric hydrogen atoms and traps for the radicals so formed. Previous use of an analogous strategy involved the generation of the radical **8** (derived from a hydroxy group *via* the thionoimidazolide) which underwent epoxide ring opening to give the oxygen radical **9**. This abstracted the activated hydrogen atom adjacent to the carbonyl group to give a radical which added in normal fashion to the alkene group to give a 3:1 mixture of the *cis*-fused epimers **10**.[24] A similar procedure has used a 3,4-epoxyalkene and activation by addition of a tributyltin radical at C-1.[25]

The starting material for the required iodides was the known (*Z*)-4'-hydroxybut-2-enyl tetra-*O*-acetyl-β-D-glucopyranoside **11** which had been epoxidised by Stick and co-workers by use of *m*-chloroperbenzoic acid to give a crystalline mixture (67%) of the two possible epoxides (**12** and **13**) in equal proportions.[26] They then used Sharpless asymmetric epoxidation to give, by use of (−)-diethyl tartrate, a 9:1 mixture of **13** and **12**. (+)-Diethyl tartrate afforded **12** containing 2% of **13**. In our hands *m*-chloroperbenzoic acid also gave a 1:1 mixture of **12** and **13** in 95% yield (magnesium monoperoxyphthalate gave 89%; **12**:**13**, 2:3), and fractional crystallisation allowed the isolation in 38% of epoxide **13** containing < 1% of the isomer, while epoxide **12**



was obtained in 43% yield contaminated with 8% of **13** (Scheme 1). Although a pure sample of **12** was obtained in low melting, crystalline form, the bulk fraction could not be crystallised. In the earlier publication[26] compounds **12** and **13** were assigned the illustrated configurations on the basis of Sharpless' quadrant rule,[27] and evidence given below accords with these assignments. However, Stick *et al.* described them as (2′*R*,3′*S*) and (2′*S*,3′*R*), respectively,[26] while we, following the guidance of Hanson,[28] believe then to be (2′*S*, 3′*R*) and (2′*R*,3′*S*), respectively.



Scheme 1

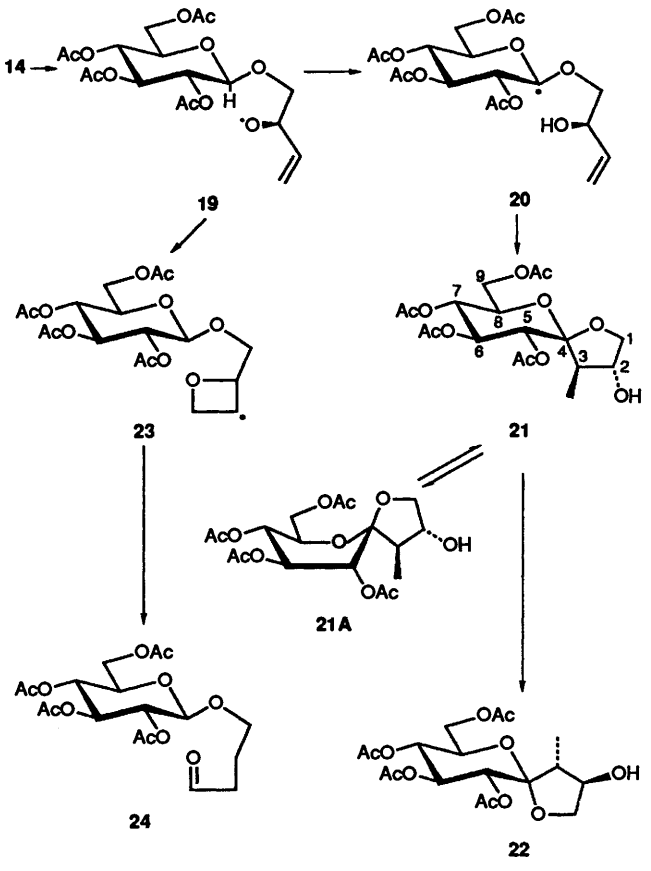
The toluene-*p*-sulfonate **15** of epoxide **13**, on treatment with sodium iodide, did not give the corresponding iodide, but was instead converted into the hydroxyalkene **18** (Scheme 1). For the preparation of the iodoepoxides **14** and **16** the method of Garegg and Samuelsson, which uses iodine in the presence of triphenylphosphine and imidazole, was found suitable.[29] These compounds, on treatment with sodium iodide in refluxing 1,2-dimethoxyethane, also underwent epoxide ring opening to give, respectively, the allylic alcohols **17** and **18** in good yields following, presumably, nucleophilic attack at the iodine atoms. These are the tetra-*O*-acetyl-β-D-glucopyranosides of (*R*)- and (*S*)-but-1-ene-3,4-diol, respectively, and since these alcohols have been reported to have $[\alpha]_D$ values of $+40$[30] and -43.6,[31] respectively, an estimate of the expected specific rotations of **17** and **18** can be made from the assumption that they would be very similar to those of equimolar solutions of methyl tetra-*O*-acetyl-β-D-glucopyranoside and (*R*)- and (*S*)-but-1-ene-3,4-diol, *i.e.* -6 and -30, respectively (taking + and -42 as the mean $[\alpha]_D$ value of the diols). Observed values of -13 and -24 support the assignments made by Stick *et al.*[26]

Treatment of iodoepoxide **14** with tributyltin hydride in benzene under UV irradiation and without heating led to the isolation of crystalline **21** in 68% yield. A methyl group bonded to a methine carbon atom and a quaternary ketal carbon atom were detected by ^{13}C NMR spectroscopy, and the ^1H NMR spectrum revealed that the anomeric proton had been removed, indicating that epoxide ring opening had occurred to give radical **19** and that bonding of the anomeric centre to C-3′ had taken place by way of the derived anomeric radical **20** (Scheme 2). The product was therefore a 1,4-anhydronon-4-ulopyranose derivative (and is numbered accordingly). Since ring opening had occurred at C-3′ of **14** the configuration at C-2 of **21** was unaltered and that at C-3 was assigned (*R*) following recognition of strong nuclear Overhauser interaction between the protons of the methyl group and 6-H. No correlation was observed with 8-H as would be expected for the C-3 epimer of **21**. A small correlation was also observed between the methyl group protons and 5-H which suggests that the compound assumes in part the boat conformation **21A**, and a $J_{5,6}$ value of 7.1 Hz is consistent with this and with the finding that the pyranoid ring of closely related spiroketals adopt this boat conformation both in solution[15] and in the crystal.[32]

The configuration at the ketal centre of **21** was assumed to be unaltered during the cyclisation process since anomeric radicals lead to products of axial addition on hydrogen abstraction.[20,21] In similar studies Descotes *et al.* produced analogous products with the β-configuration which anomerised to the thermodynamically favoured α-analogues on treatment with acid.[15,16,22] In similar manner, β-ketal **21** isomerised completely to the α-linked **22** (β-anomer remaining $<1\%$) on such treatment, $[\alpha]_D$ changed from -19 to $+38$, 6-H was deshielded (0.18 ppm), and 7-H and C-4 were shielded (0.35 and 2.0 ppm, respectively). All of these changes are consistent with a β ⟶ α anomerisation, Descotes' analogous changes for the anomerisation of **5** being: -16 ⟶ $+55$ and $+0.63$, -0.25 and -2.4 ppm, respectively.[16]

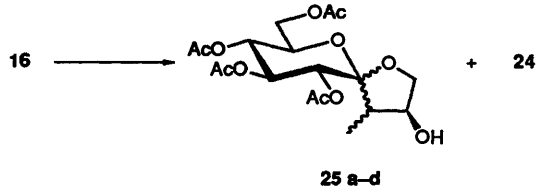
As well as **21** in the products of cyclisation of **14** two other spiroketals were detected in small amounts and an unexpected by-product, isolated in 8% yield, was 4′-oxobutyl tetra-*O*-acetyl-β-D-glucopyranoside **24**.

Reaction of the isomeric iodoepoxide **16** with tributyltin hydride, under the same conditions as were used for **14** or thermally, resulted in the isolation of an unresolved mixture of four isomeric spiroepoxides **25** (52%, proportions 1.0:2.4:1.3:1.5) and, again, small proportions of 4′-oxobutyl tetra-*O*-acetyl-β-D-glucopyranoside **24** were formed (Scheme 3). ^{13}C NMR spectroscopy of the main products revealed four ketal carbon signals and four methyl ^{13}C resonances which correlated in a



Scheme 2

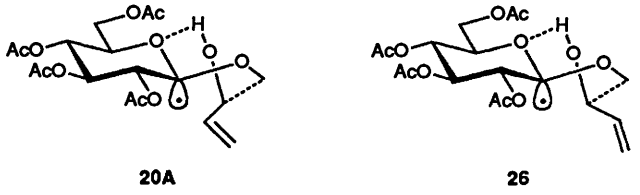
^{1}H-^{13}C COSY experiment with four ^{1}H *C*-methyl doublets. A significant feature of the ^{1}H NMR spectrum was the presence of two triplets (*J* 9.5, 9.2) at δ 5.42 and 5.56 which were downfield from the other ring proton resonances and from that of 6-H of **21** (δ 5.29). These are consistent with the presence of two α-linked spiroketals (*cf.* 6-H of the α-**22**, δ 5.47). Benzoylation of the mixed isomeric spiroketals gave four monobenzoates confirming that the former were monohydroxylated.



Scheme 3

To determine whether the much greater selectivity observed in the ring closure of iodoepoxide **14** was due to markedly different relative reactivities of **14** and **16**, an equimolar mixture of them was subjected to cyclisation using 0.5 equiv. of tributyltin hydride. The heights of the seven observed ketal ^{13}C NMR resonances (one major and two minor from **14** and four from **16**) allowed the conclusion that compound **14**, which reacted much the more selectively, also reacted 1.4 times more readily than did **16**. The observation that the latter gave significant proportions of α-spiroketals is evidence that its reaction by way of the anomeric radical and attack at C-3′ to give the products of normal axial addition is impeded. It appears that intramolecular hydrogen bonding could be responsible for the marked differences observed.

Hydrogen bonding between the ring oxygen atom and the hydroxy group in the favoured anomeric radical **20** derived from **14** assists in keeping C-3′ adjacent to C-1 with the alkene group preferentially in the *exo*-orientation **20A** and accounts for the observed selective reaction and for the configuration at C-3 of **21**. In the case of the epimeric radical derived from **16**, however, such hydrogen bonding does not allow approach of the axial radical to C-3′ **26**. An equatorial anomeric radical, on the other hand, can gain such approach—hence the appearance of α-linked spiroketals in the products.



The production of the aldehydic by-product **24** in the reactions of both iodoepoxides can be accounted for by the intermediacy of the oxetane radical **23** and its rearrangement.

Experimental

Except where noted, NMR spectra were measured in deuteriochloroform with tetramethylsilane as internal reference, and by use of a Bruker AC300E instrument. For COSY and NOESY experiments standard Bruker-supplied pulse sequences were used with results displayed in the magnitude mode. ^{13}C signal assignments were performed using ^{13}C–^{1}H COSY methods. For determining multiplicities of ^{13}C signals standard Bruker-supplied DEPT pulse sequences were used. *J* Values are given in Hz.

Optical rotations were determined for chloroform solutions (0.6–1.6 g/100 cm^3) with a Perkin-Elmer 241 automatic polarimeter; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}.

M.p.s were measured by use of a Reichert Jung Thermover hot-stage apparatus and are uncorrected. Radial chromatography was performed on a Harrison Research Chromatotron model 7924T using silica gel 60 PF_{254} (with $CaSO_4$ binder) coated plates. Silica gel 60 (0.96–0.04 mm) was used for column chromatography. Light petroleum refers to the fraction boiling in the range 60–80 °C.

(2′R,3′S)- and (2′S,3′R)-*2′,3′-Epoxy-4′-hydroxybutyl 2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosides* **13** *and* **12**.—(a) *By use of m-chloroperbenzoic acid.* The but-2-enyl glycoside **11**[26] (1.00 g, 2.39 mmol) and *m*-chloroperbenzoic acid (80%; 0.77 g, 3.6 mmol) were stirred in dry chloroform (20 cm^3) at 38 °C for 16 h. Dichloromethane (30 cm^3) was added and the solution was washed successively with saturated aq. $NaHCO_3$ and water and dried ($MgSO_4$). Removal of the solvent gave a syrup (0.99 g, 95%) comprising epoxides **12** and **13** in equal proportions (determined from the relative intensities of the epoxide carbon signals in the ^{13}C NMR spectrum). Crystallisation and recrystallisation (light petroleum–ethyl acetate) selectively afforded the (2′R,3′S)-*epoxy alcohol* **13** (0.40 g, 38%, containing <1% **12**), m.p. 137.5–138.5 °C (lit.,[26] 133–134 °C for mixture of **13** and **12**, 9:1), $[\alpha]_D$ −11.3 (lit.,[26] −9.8 for mixture of **13** and **12**, 9:1) (Found: C, 49.8; H, 6.0. $C_{18}H_{26}O_{12}$ requires C, 49.8; H, 6.0%); δ_H 2.01, 2.03, 2.06, 2.09 (12 H, 4 s, OAc), 3.19–3.28 (2 H, m, 2′- and 3′-H) 3.71–3.80 (4 H, m, 4′-H_2, 1′- and 5-H), 4.05 (1 H, dd, *J* 5.5 and 11.6, 1′-H), 4.16 (1 H, dd, $J_{5,6}$ 2.4, $J_{6,6'}$ 12.3, 6-H), 4.27 (1 H, dd, $J_{5,6'}$ 4.8, 6-H′), 4.59 (1 H, d, $J_{1,2}$ 7.9, 1-H), 5.00 (1 H, dd, $J_{2,3}$ 9.4, 2-H), 5.09 (1 H, t, $J_{3,4} = J_{4,5}$ 9.4, 4-H) and 5.21 (1 H, t, 3-H); δ_C 20.57, 20.57, 20.65, 20.71 (CH_3CO), 54.19, 55.97 (C-2′,3′), 60.28 (C-4′), 61.92 (C-6), 67.37 (C-1′), 68.41 (C-4), 71.24 (C-2), 72.02 (C-5), 72.74 (C-3), 100.49 (C-1), 169.41, 169.51, 170.23 and 170.68 (CH_3CO).

The 2′S,3′R-*epoxide* **12** was mainly recovered from the

crystallisation mother liquors as a syrup containing 8% **13**, $[\alpha]_D$ −14.0 (lit.,[26] −14.1 for mixture of **12** and **13**, 98:2). A small sample obtained crystalline (light petroleum–ethyl acetate) contained < 1% **13** and had m.p. 54–55 °C, $[\alpha]_D$ −17 (Found: C, 47.8; H, 5.9. $C_{18}H_{26}O_{12}\cdot H_2O$ requires C, 47.7; H, 6.2%); δ_H 2.01, 2.03, 2.07, 2.09 (12 H, 4 s, OAc), 3.18–3.26 (2H, m, 2'- and 3'-H), 3.73 (1 H, ddd, $J_{5,6}$ 2.6, $J_{5,6'}$ 4.5 and $J_{4,5}$ 9.8, 5-H), 3.77 (2 H, d, J 4.8, 4'-H_2), 3.82 (1 H, dd, J 6.1 and 11.6, 1'-H), 3.96 (1 H, dd, J 4.5, 1'-H), 4.16 (1 H, dd, $J_{6,6'}$ 12.3, 6-H), 4.25 (1 H, dd, 6-H'), 4.64 (1 H, d, $J_{1,2}$ 7.9, 1-H), 5.00 (1 H, d, $J_{2,3}$ 9.5, 2-H), 5.09 (1 H, t, 4-H) and 5.22 (1 H, t, 3-H); δ_C 20.58, 20.67, 20.71, 21.61 (CH_3CO), 54.66, 55.58 (C-2', 3'), 60.27 (C-4'), 61.87 (C-6), 67.30 (C-1'), 68.42 (C-4), 71.24 (C-2), 71.98 (C-5), 72.71 (C-3), 100.44 (C-1), 169.43, 169.54, 170.23 and 170.71 (CH_3CO).

(b) *By use of magnesium monoperoxyphthalate hexahydrate* (*MMPP*). Compound **11** (12.9 g, 30.7 mmol) and MMPP (80%; 14.3 g 23.1 mmol) were stirred in isopropyl alcohol (200 cm^3) at 45 °C for 20 h. The mixture was filtered through Celite and the solvent evaporated. The residue was taken up in dichloromethane and washed successively with saturated aq. NaCl and water and dried ($MgSO_4$) and the solvent evaporated to afford the two epoxide isomers **12** and **13** in the approximate proportions 3:2 (11.9 g, 89%).

(2'R,3'S)-2',3'-*Epoxy*-4'-O-(p-*tolylsulfonyloxy*)*butyl* 2,3,4,6-*Tetra*-O-*acetyl*-β-D-*glucopyranoside* **15**.—Compound **13** (100 mg, 0.23 mmol), tosyl chloride (90 mg, 0.47 mmol), 2,4,6-collidine (55 mg, 0.46 mmol) and 4-(dimethylamino)pyridine (28 mg, 0.23 mmol) were stirred in dry dichloromethane (5 cm^3) together with Drierite (20 mg) at 20 °C for 36 h. The mixture was filtered and the filtrate diluted with dichloromethane (20 cm^3), washed successively with dilute HCl and aq. $NaHCO_3$, dried ($MgSO_4$) and evaporated. Radial chromatography and crystallisation from light petroleum–ethyl acetate afforded the *title tosylate* (98 mg, 73%), m.p. 97–98 °C, $[\alpha]_D$ −2.3 (Found: C, 51.0; H, 5.5; S, 5.5. $C_{25}H_{32}O_{14}S$ requires C, 51.0; H, 5.5; S, 5.5%); δ_H 2.00, 2.03, 2.04, 2.08 (12 H, 4 s, OAc), 2.46 (3 H, s, Me), 3.15–3.27 (2 H, m, 2'- and 3'-H), 3.69–3.75 (1 H, m, 5-H), 3.75 (1 H, dd, J 3.4 and 11.8, 1'-H), 3.91 (1 H, dd, J 4.2, 1'-H), 4.08–4.29 (4 H, m, 4'-H_2, 6-H_2), 4.53 (1 H, d, $J_{1,2}$ 7.9, 1-H), 4.95 (1 H, dd, $J_{2,3}$ 9.1, 2-H), 5.07 (1 H, dd, $J_{3,4}$ 9.4, $J_{4,5}$ 9.7, 4-H), 5.20 (1 H, t, 3-H) and 7.38 and 7.82 (4 H, 2 d, J 8.0, Ar); δ_C 20.57, 20.57, 20.61, 20.70 (CH_3CO), 21.67 (Me), 52.95, 54.07 (C-2', 3'), 61.81 (C-6), 66.88 (C-1'), 67.77 (C-4'), 68.29 (C-4), 71.12 (C-2), 72.05 (C-5), 72.77 (C-3), 100.59 (C-1), 120.01, 130.02, 132.80, 145.25 (Ar), 169.33, 169.38, 170.17 and 170.60 (CH_3CO).

(2'S)-2'-*Hydroxybut*-3'-*enyl* 2,3,4,6-*Tetra*-O-*acetyl*-β-D-*glucopyranoside* **18**.—To a solution of the tosyl derivative **15** (92 mg, 0.16 mmol), anhydrous sodium iodide (47 mg, 0.32 mmol) and AIBN (3 mg) in refluxing dimethoxyethane (DME) (5 cm^3), was added over 10 h, a solution of tributyltin hydride (92 mg, 0.32 mmol) in DME (5 cm^3). After 12 h the solvent was removed and the resulting yellow residue was taken up in acetonitrile (10 cm^3). The acetonitrile solution was filtered and washed several times with light petroleum. The syrup remaining on evaporation of the acetonitrile was dissolved in dichloromethane (10 cm^3) and stirred with an equal volume of saturated aq. $NaHCO_3$. To the stirred emulsion was added, dropwise, saturated aq. $Na_2S_2O_3$ until no iodine colour remained. The organic phase was then washed with water, dried ($MgSO_4$), filtered and concentrated to a colourless syrup. Radial chromatography and crystallisation from light petroleum–ethyl acetate gave the but-3-enyl glycoside (49 mg, 75%), m.p. 81.0–82.5 °C, $[\alpha]_D$ −24.0 (Found: C, 51.7; H, 6.2. $C_{18}H_{26}O_{11}$ requires C, 51.7; H, 6.3%); δ_H 2.01, 2.03, 2.05, 2.10 (12 H, 4 s, OAc), 3.64 (1 H, dd, J 7.7 and 10.9, 1'-H), 3.77 (2 H, m, 5-H and 1'-H), 4.17 (1 H, dd, $J_{6,6'}$ 12.3, $J_{5,6}$ 2.9, 6-H), 4.23 (1 H, dd, $J_{5,6'}$ 5.1, 6-H'), 4.28–4.34 (1 H, m, 2'-H), 4.58 (1 H, d, $J_{1,2}$ 7.9, 1-H), 5.01 (1 H, d, $J_{2,3}$ 9.5, 2-H), 5.08 (1 H, t, $J_{3,4} = J_{4,5}$ 9.5, 4-H), 5.22 (1 H, t, 3-H), 5.21 (1 H, dd, J 10.6, 4'-H), 5.37 (1 H, dt, J 1.5 and 17.2, 4'-H) and 5.80 (1 H, ddd, J 5.0, 3'-H); δ_C 20.56, 20.65 (CH_3CO), 62.00 (C-6), 68.46 (C-4), 71.32 (C-2), 71.38 (C-2'), 71.98 (C-5), 72.69 (C-3), 75.47 (C-1'), 101.42 (C-1), 116.75 (C-4'), 135.89 (C-3'), 169.39, 170.20 and 170.63 (CH_3CO).

(2'R,3'R)-2',3'-*Epoxy*-4'-*iodobutyl* 2,3,4,6-*Tetra*-O-*acetyl*-β-D-*glucopyranoside* **16**.—A solution of the epoxy alcohol **13** (200 mg, 0.46 mmol), triphenylphosphine (144 mg, 0.55 mmol), imidazole (76 mg, 1.10 mmol) and iodine (128 mg, 0.51 mmol) in dry toluene (15 cm^3), was stirred at 47 °C for 1.5 h. After the solution had cooled, an equal volume of saturated aq. $NaHCO_3$ solution was added and the two phases were stirred for 10 min. Saturated aq. $Na_2S_2O_3$ was added dropwise until the toluene phase was devoid of iodine. It was then washed with water, dried ($MgSO_4$) and evaporated to a yellow residue. Radial chromatography and crystallisation from light petroleum–ethyl acetate afforded the *title iodide* (178 mg, 72%), m.p. 83.0–84.5 °C, $[\alpha]_D$ −45.8 (Found: C, 39.9; H, 4.7; I, 23.1. $C_{18}H_{25}IO_{11}$ requires C, 39.7; H, 4.6; I, 23.3%); δ_H 2.01, 2.03, 2.06, 2.10 (12 H, 4 s, OAc), 3.01 (1 H, dd, J 7.2 and 9.5, 4'-H), 3.27–3.42 (3 H, m, 2'-, 3'-, 4'-H), 3.75 (1 H, ddd, $J_{5,6}$ 2.4, $J_{5,6'}$ 4.8 $J_{4,5}$ 9.9, 5-H), 3.83 (1 H, dd, J 4.7 and 11.8, 1'-H), 3.91 (1 H, dd, J 5.5, 1'-H), 4.16 (1 H, dd $J_{6,6'}$ 12.3, 6-H), 4.28 (1 H, dd, 6-H'), 4.60 (1 H, d, $J_{1,2}$ 7.9, 1-H), 5.03 (1 H, dd, $J_{2,3}$ 9.4, 2-H), 5.10 (1 H, t, $J_{3,4}$ 9.7, 4-H) and 5.22 (1 H, t, 3-H); δ_C 0.28 (C-4'), 20.60–20.77 (CH_3CO), 56.37, 57.29 (C-2', 3'), 61.78 (C-6), 66.30 (C-1'), 68.23 (C-4), 71.09 (C-2), 71.96 (C-5), 72.23 (C-3), 100.54 (C-1), 169.32, 169.40, 170.26 and 170.66 (CH_3CO).

(2'S,3'S)-2',3'-*Epoxy*-4'-*iodobutyl* 2,3,4,6-*Tetra*-O-*acetyl*-β-D-*glucopyranoside* **14**.—This iodide was obtained from the epoxy alcohol **12** (1.83 g, 4.2 mmol) by the method employed for the synthesis of compound **16**. The iodinated product **14** (1.78 g, 78%), recrystallised from light petroleum–ethyl acetate, had m.p. 96.5–98.0 °C, $[\alpha]_D$ +19.2 (Found: C, 39.8; H, 4.7; I, 23.3. $C_{18}H_{25}IO_{11}$ requires C, 39.7; H, 4.6; I, 23.3%); δ_H 2.01, 2.03, 2.06, 2.10 (12 H, 4 s, OAc), 3.02 (1 H, dd, J 7.4 and 9.9, 4'-H), 3.27–3.39 (3 H, m, 2'-, 3'-, 4'-H), 3.65 (1 H, dd, J 6.6 and 11.9, 1'-H), 3.73 (1 H, ddd, $J_{5,6}$ 2.6, $J_{5,6'}$ 4.6, $J_{4,5'}$ 9.9, 5-H), 4.07 (1 H, dd, J 3.8, 1'-H), 4.18 (1 H, dd, $J_{6,6'}$ 12.3, 6-H), 4.25 (1 H, dd, 6-H'), 4.65 (1 H, d, $J_{1,2}$ 7.9, 1-H), 5.02 (1 H, dd, $J_{2,3}$ 9.5, 2-H), 5.10 (1 H, t, 4-H) and 5.22 (1 H, t, 3-H); δ_C 0.16 (C-4'), 20.58, 20.58, 20.71, 20.77 (CH_3CO), 55.86, 57.81, (C-2', 3'), 61.87 (C-6), 66.44 (C-1'), 68.37 (C-4), 71.20 (C-2), 72.01 (C-5), 72.80 (C-3), 100.39 (C-1), 169.37, 169.37, 170.20 and 170.58 (CH_3CO).

(2'R)-2'-*Hydroxybut*-3-*enyl* 2,3,4,6-*Tetra*-O-*acetyl*-β-D-*glucopyranoside* **17**.—A solution of iodide **14** (200 mg, 0.37 mmol) and sodium iodide (135 mg, 0.93 mmol) in DME (10 cm^3) was heated under reflux, with stirring, for 12 h. The solvent was evaporated and the residue taken up in dichloromethane. The dichloromethane solution was washed successively with aq. $Na_2S_2O_3$, aq. $NaHCO_3$ and water, dried ($MgSO_4$) and the solvent was removed. The *product* **17**, was isolated as a syrup by radial chromatography (light petroleum–ethyl acetate), (96.4 mg, 63%), $[\alpha]_D$ −13.5 (Found: C, 51.5; H, 6.0. $C_{18}H_{26}O_{11}$ requires C, 51.7; H, 6.3%); δ_H 2.01, 2.03, 2.05, 2.09 (12 H, 4 s, OAc), 3.53 (1 H, dd, J 7.8 and 10.3, 1'-H), 3.73 (1 H, ddd, $J_{5,6}$ 2.5, $J_{5,6'}$ 5.1 and $J_{4,5}$ 9.8, 5-H), 3.88 (1 H, dd, J 1'-H), 4.16 (1 H, dd, $J_{6,6'}$ 12.2, 6-H), 4.25 (1 H, dd, 6-H'), 4.27–4.35 (1 H, m, 2'-H), 4.57 (1 H, d, $J_{1,2}$ 8.0, 1-H), 5.01 (1 H, dd, $J_{2,3}$ 9.4, 2-H), 5.07 (1 H, t, 4-H), 5.22 (1 H, t, 3-H), 5.21 (1 H, d, $J_{3',4'}$ 9.7, 4'-H), 5.35 (1 H, d, $J_{3',4'}$ 17.2, 4'-H) and 5.81 (1 H, ddd, J 5.4, 10.6 and 16.7, 3'-H); δ_C 20.58, 20.68 (CH_3CO), 61.99 (C-6), 68.45 (C-4), 71.43 (C-2),

C-2'), 71.98 (C-5), 72.69 (C-3), 74.62 (C-1'), 101.43 (C-1), 116.73 (C-4'), 135.82 (C-3'), 169.41, 169.49, 170.21 and 170.63 (CH_3CO).

Treatment of the Iodo Derivative **14** *with Tributyltin Hydride.*—A de-gassed solution of tributyltin hydride (640 mg, 2.21 mmol) and AIBN (3 mg) in benzene (24 cm^3) was added to a stirred de-gassed solution of the iodo derivative **14** (1.0 g, 1.84 mmol) in dry benzene (40 cm^3) over 8 h and under UV irradiation. Stirring was continued under UV irradiation for a further 12 h. The benzene was evaporated under low pressure and the resulting residue taken up in acetonitrile. The acetonitrile solution was washed several times with light petroleum and the residue obtained on removal of the acetonitrile was subjected to column chromatography (light petroleum–ethyl acetate) to give 1,4-*anhydro*-3-*deoxy*-3-C-*methyl*-5,6,7,9-*tetra*-O-*acetyl*-β-D-erythro-L-ido-*non*-4-*ulopyranose* **21** (from light petroleum–ethyl acetate) (5.20 mg, 68%), m.p. 135–136 °C, $[\alpha]_D$ −19.0 (Found: C, 51.9; H, 6.5. $C_{18}H_{26}O_{11}$ requires C, 51.7; H, 6.3%); δ_H 1.33 (3 H, d, *J* 7.5 CH_3), 1.89 (1 H, d, *J* 7.0, OH), 2.02, 2.03, 2.08, 2.10 (12 H, 4 s, OAc), 2.48 (1 H, dq, *J* 5.5 and 7.5, 3-H), 3.85 (1 H, dd, *J* 9.4, $J_{1,2}$ 2.8, 1-H), 3.90 (1 H, ddd, $J_{8,9}$ 2.7, $J_{8,9'}$ 4.5 and $J_{7,8}$ 9.5, 8-H), 4.09 (1 H, dd, $J_{9,9'}$ 12.1, 9-H), 4.12 (1 H, dd, $J_{1',2}$ 4.5 1-H'), 4.21 (1 H, dd, 9-H'), 4.37–4.47 (1 H, m, 2-H), 5.15 (1 H, d, $J_{5,6}$ 7.1, 5-H) and 5.26–5.37 (2 H, m, 6-H and 7-H); δ_C 10.57 (Me), 20.69, 20.69, 20.78, 20.83 (CH_3CO), 47.00 (C-3), 62.83 (C-9), 68.77 (C-7), 70.34 (C-8), 72.41 (C-6), 72.80 (C-5), 73.52 (C-1), 74.29 (C-2), 108.19 (C-4), 168.91, 169.52, 170.23 and 170.72 (CH_3CO).

Also isolated and crystallised (light petroleum–ethyl acetate) was 4-oxobutyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside **24** (61 mg, 8%); m.p. 100.5–101.5 °C, $[\alpha]_D$ −18.3; ν_{max}/cm^{-1} 1750 (CO); δ_H 1.88–1.95 (2 H, m, 2'-H_2), 2.01, 2.03, 2.06, 2.10 (12 H, 4 s, OAc), 2.52 (2 H, dt, *J* 1.2 and 7.0, 3'-H_2), 3.55 (1 H, ddd, *J* 5.4, 7.2 and 12.5, 1'-H), 3.69 (1 H, ddd, $J_{5,6}$ 2.5, $J_{5,6'}$ 4.8, $J_{4,5}$ 9.9, 5-H), 3.91 (1 H, dt, *J* 6.0, 1'-H), 4.14 (1 H, dd, $J_{6,6'}$ 12.3, 6-H), 4.26 (1 H, dd, 6-H'), 4.48 (1 H, d, $J_{1,2}$ 7.9, 1-H), 4.98 (1 H, dd, $J_{2,3}$ 9.5, 2-H), 5.08 (1 H, t, $J_{3,4}$ 9.7, 4-H), 5.20 (1 H, t, $J_{2,3}$ 9.7, 3-H) and 9.75 (1 H, t, *J* 1.2, 4'-H); δ_C 20.59, 20.65, 20.71 (CH_3CO), 22.27 (C-3'), 40.39 (C-2'), 61.97 (C-6), 68.50 (C-4), 68.75 (C-1'), 71.30 (C-2), 71.90 (C-5), 72.86 (C-3), 100.73 (C-1), 169.40, 170.25, 170.65 (CH_3CO) and 201.72 (C-4').

Epimerisation of Spiroglycoside **21**.—Boron trifluoride–diethyl ether (138 mg, 1.0 mmol) was added to a stirred solution of spiroglycoside **21** (80 mg, 0.2 mmol) in chloroform (5 cm^3) and the mixture was heated to 50 °C for 6 h. Dichloromethane (20 cm^3) was added and the solution was washed with saturated aq. $NaHCO_3$ and dried ($MgSO_4$). Removal of the solvent gave 1,4-anhydro-3-deoxy-3-*C*-methyl-5,6,7,9-tetra-*O*-acetyl-α-D-*erythro*-L-*ido*-non-4-ulopyranose **22**, isolated as a syrup by column chromatography (light petroleum–ethyl acetate; 62 mg, 77%); $[\alpha]_D$ +37.8; δ_H 1.13 (3 H, d, *J* 7.1, CH_3), 1.94 (1 H, dq, $J_{2,3}$ 5.2 and 7.1, 3-H), 1.99, 2.04, 2.06, 2.08 (12 H, 4 s, OAc), 2.72 (1 H, d, *J* 11.6, OH), 3.96–4.03 (2 H, m, 9-H and 1-H), 4.09–4.22 (3 H, m, 1', 2 and 8-H), 4.28 (1 H, dd, $J_{8,9}$ 2.4, $J_{9,9'}$ 11.9, 9-H'), 4.99 (1 H, dd, *J* 9.4 and 10.1, 7-H), 5.12 (1 H, d, $J_{5,6}$ 10.0, 5-H) and 5.47 (1 H, t, *J* 9.6, 6-H); δ_C 6.52 (Me), 20.58, 20.65 (CH_3CO), 42.21 (C-3), 62.24 (C-9), 67.80 (C-5), 68.16 (C-8), 68.92 (C-7), 71.68 (C-6), 73.19 (C-2), 77.30 (C-1), 106.22 (C-4), 169.66, 169.88, 169.93 and 170.59 (CH_3CO).

Treatment of the Iodo Derivative **16** *with Tributyltin Hydride.*—(a) *UV initiation.* A de-gassed solution of tributyltin hydride (320 mg, 1.10 mmol) and AIBN (2 mg) in benzene (12 cm^3) was added to a stirred, de-gassed solution of the iodo derivative **16** (0.5 g, 0.92 mmol) in dry benzene (20 cm^3) over 4 h with stirring under UV irradiation. Stirring was continued under UV irradiation for a further 18 h, the benzene was removed and the resulting residue was taken up in acetonitrile. The acetonitrile solution was washed several times with light petroleum. The residue obtained on removal of the acetonitrile phase was subjected to column chromatography (light petroleum–ethyl acetate) and gave a mixture of the four spiroglycoside isomers, **25** (196 mg, 52%), which gave an elongated (single spot on TLC; δ_H 0.95 (d, *J* 7.3, CH_3), 1.01 (d, *J* 7.6, CH_3), 1.17 (d, *J* 7.0, CH_3), 1.20 (d, *J* 7.0, CH_3), 5.02–5.25 (m, 5-, 6-, 7-H), 5.42 (t, *J* 9.5, 6-H) and 5.56 (t, *J* 9.2, 6-H); δ_C 8.17, 8.26, 8.54, 13.47 (Me) (intensities 1.0:2.4:1.3:1.5), 45.68 (× 2), 47.71 and 48.83 (C-3), 105.7, 106.69, 107.14 and 109.31 (C-4). Also isolated was the aldehyde **24** (27 mg, 7%).

(b) *Thermal initiation.* A de-gassed solution of tributyltin hydride (64 mg, 0.22 mmol) and AIBN (1 mg) in benzene (4 cm^3) was added to a de-gassed solution of compound **16** (100 mg, 0.18 mmol) in refluxing dry benzene (4 cm^3) over 6 h, and the heating was continued for a further 2 h. The benzene was evaporated and the resulting residue taken up in diethyl ether (10 cm^3). DBU (34 mg, 0.26 mmol) was added to the stirred ether solution, followed dropwise by a solution of iodine in diethyl ether (0.1 mol dm^{-3}), until the iodine colour persisted.[33] The ether solution was filtered through a bed of silica gel and the silica washed with ether. The combined ether washings were concentrated and the residue subjected to column chromatography (light petroleum–ethyl acetate) to give the four spiro isomers **25** (26.5 mg, 35%) and the aldehyde **(24)** (6 mg, 8%).

Benzoylation of the Mixed Spiroglucosides.—To a stirred, cooled (ice bath) solution of the mixed spiroglucosides **25** (25 mg, 60 μmol) in 2:1 dichloromethane–pyridine (3 cm^3), was added benzoyl chloride (85 mg, 0.6 mmol). Stirring was continued at low temperature for 0.5 h, and then at room temperature for 2.5 h. Several portions of toluene were added to the residue and evaporated to aid removal of the acetic acid. The products, appearing as a single spot on TLC, were isolated by radial chromatography (light petroleum–ethyl acetate) (26 mg, 87%); δ_C 8.36, 8.72, 8.77, 14.08 (CH_3), 44.67, 45.03, 46.20, 47.12 ($CHCH_3$), 104.84, 106.08, 107.62, 107.93 (C-4) and 128.51–133.71 (Ar).

Treatment of the Iodides **14** *and* **16** (1:1) *with* 0.5 *Molar Equivalents of Tributyltin Hydride.*—A de-gassed solution of tributyltin hydride (27 mg, 0.09 mmol) and AIBN (1 mg) in benzene (2 cm^3) was added to a stirred, de-gassed solution of the iodides **14** and **16** (50 mg of each, 0.18 mmol) in dry benzene (5 cm^3), over 4 h under UV irradiation. Stirring was continued under UV irradiation for a further 6 h. The benzene was evaporated and the resulting residue taken up in acetonitrile. The acetonitrile solution was washed several times with light petroleum. The acetonitrile was removed and the residue analysed by ^{13}C NMR spectroscopy. The chemical shifts of C-4 of the spirocyclised products (with the respective epoxy iodide precursors and relative intensities) were: δ_C 105.2 (**14**, 5.6), 105.7 (**16**, 3.7), 106.4 (**14**, 12.2), 106.7 (**16**, 8.2), 107.2 (**16**, 18.4), 108.2 (**14**, 40.7) and 109.3 (**16**, 11.2).

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