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Chemical interaction between the aglycon and the allyl group of 6-*O*-allylhexopyranoside derivatives

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ABSTRACT

The free radical derived from 1-*O*-allyl-2,6-anhydro-3,4,7,9-tetradeoxy-8-*O*-phenoxythiocarbonyl-D-*arabino*-non-3-en-5-ulose ethylene acetal (**4**), in the presence of tributyltin hydride, gave the direct product of reduction (**13**) and also products (**15**), derived following tandem cyclisation, which are structurally related to the trichothecenes. In addition, evidence was found which indicated that the initial radical reacted intramolecularly with the allyl group. To establish whether radicals in aglycons can react with the alkene groups of 6-allyl ethers of hexopyranosides, 2-bromoethyl 2,3,4-tri-*O*-acetyl-6-*O*-allyl-β-D-glucopyranoside (**19**) was treated with tributyltin hydride and a radical initiator. The 11-membered ring product 5′-hydroxypentyl 2,3,4-tri-*O*-acetyl-6,5′-anhydro-β-D-glucopyranoside (**21**) was isolated (15%, unoptimised) as well as the product of direct reductive debromination.

INTRODUCTION

Many intramolecular cyclisations involving the trapping of radicals by alkenes followed by hydrogen abstraction by the adduct radicals have been reported both in general organic chemistry[1–3] and in carbohydrate chemistry[4]. Ring formations caused by reaction of radicals on substituent groups with double bonds within sugar structures[5,6] ($S^{\cdot}-C^{C=C}$ closures[4]), the reverse processes[7,8] ($C^{\cdot}-S^{C=C}$), and cyclisations of carbohydrate carbon radicals onto alkene groups within the same carbon chain or extended carbon chain ($C^{\cdot}-C^{C=C}$)[9–11] are well known, but only few examples have been given of reactions between substituent radicals and multiple bonds on other substituent groups ($S^{\cdot}-S^{C=C}$)[12–14]. While it has been shown that reactions of the last group can be used to give 5-membered rings[12–14], the question of the trapping by alkene groups of distant radicals, and thus the formation of larger rings, has received little attention. We have encountered the chemical interaction between a radical on the aglycon of a 6-*O*-allylated hexopyra-

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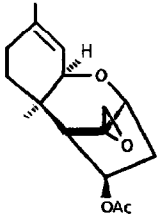
nosyl *C*-glycoside and the double bond of the allyl group, and have pursued this matter by investigating the fate of the radical derived by debromination of 2-bromoethyl 2,3,4-tri-*O*-acetyl-6-*O*-allyl-β-D-glucopyranoside.

In general organic chemistry, 5- and 6-membered ring formation by radical methods is now a major synthetic tool, but it has also been shown that large rings can be made with reasonable efficiency by radical trapping procedures. Thus, Porter et al.[15,16] produced the 15-membered cyclic (*R*)-(−)-muscone by a process which gave 40–45% yield in the ring closure step, and Hitchcock and Pattenden[17] made the 14-membered dimethyl ether of zearalenone (55% yield for the cyclisation step). In both cases, carbon radicals were trapped intramolecularly by the electron-deficient centres of enones.

RESULTS AND DISCUSSION

In the course of a study of a novel route to compounds having structures related to those of the trichothecenes, for example, trichodermin (**1**)[18], we found that the radical derived from the thionocarbonate **2** cyclised to give the 2-oxabicyclo[3.2.1]octane derivative **3**[19], and it became of interest to determine whether the radical formed after the cyclisation of the initial species could be intercepted by an unsaturated function bonded to C-6 (carbohydrate numbering). While a carbon-bonded substituent would be required at this position for formation of the trichothecene framework, a preliminary study was undertaken using compound **4** having an allyl ether group at C-6. The required ester (**4**) was made from the enone **6** (derived in one step from tetra-*O*-acetyl-1,5-anhydro-D-*arabino*-hex-1-enitol, **5**) by methoxymercuration followed by chloride exchange to give the mercurial **7**, reductive removal of the mercury to give **8**[19], deacetylation to the primary alcohol **9**, *O*-allylation to ether **10**, opening of the furanoid ring to the enone **11**, O-8 esterification to the thionocarbonate **12**, and acetalation to the ester acetal **4** (Scheme 1).



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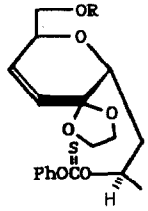
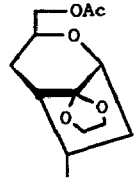


2 R = Ac

4 R = $CH_2CH{=}CH_2$



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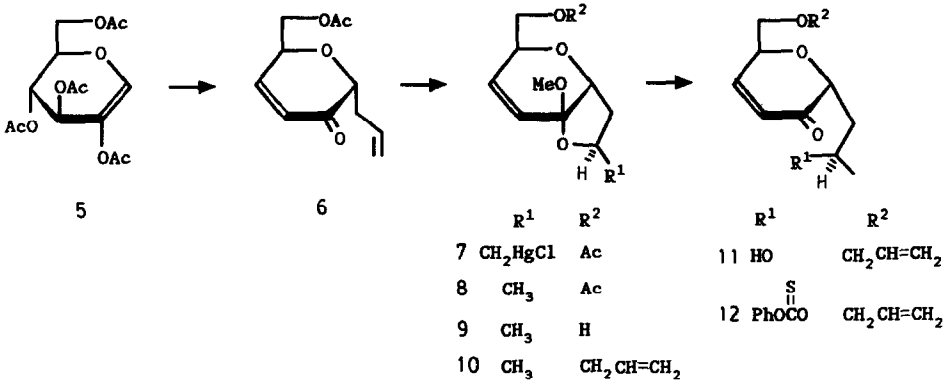
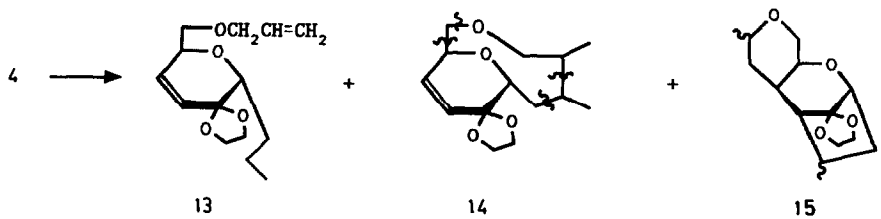
Initial attempted radical cyclisation of the thionocarbonate **4** gave two major products (gas chromatographic analysis) in the ratio 2:3, which were assigned structures **13** and **14**, respectively (Scheme 2), on the basis of their mass-spectral fragmentation patterns and the ^{13}C NMR spectrum of the mixture. The former



Scheme 1.

product of reductive de-esterification fragmented predominantly in the mass spectrometer by retro-Diels–Alder loss of butanal. Similarly, compound **14**, which was formed by trapping of the initial radical by the allyl ether group, cleaved by the retro-Diels–Alder mechanism, but the dienic portion, in this case, remained bonded to the butanal segment and subsequent cleavage occurred at the bonds indicated. There were six alkene carbon signals and three methyl resonances in the ^{13}C NMR spectrum of the mixture of **13** and **14**. It was concluded that, under the conditions used, the allyl group had reacted significantly with the intermediate derived from the thionocarbonate **4**.

A second radical cyclisation reaction was conducted on compound **4** under more dilute conditions selected to reduce the proportion of the direct reduction product **13**. In this case, seven products were detected by gas chromatography in the approximate percentage ratios 24:17:25:10:10:6:9 (order of elution), the first two being compounds **13** and **14**, respectively (retention times and mass spectra). From the similarity of their mass spectra, it was concluded that the four products eluted third to sixth (51% total) were stereoisomers of each other and also structural isomers of compounds **13** and **14**. They were assigned structure **15** on the following bases: (*i*) there were four isomers, which is consistent with the formation of new asymmetric centres at the two carbon atoms bearing methyl groups; (*ii*) they gave relatively strong molecular ions (*m/z* 254) in the mass spectrometer (indicating



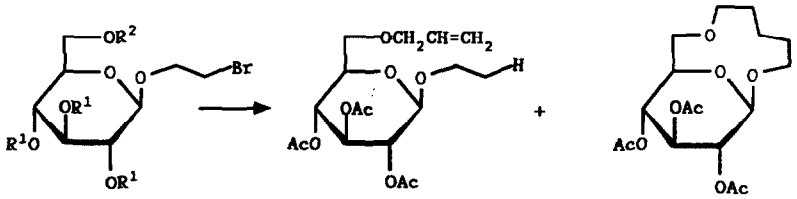
Scheme 2.

relatively stable structures; compounds **13** and **14** gave no such ions); (*iii*) there were no products of retro-Diels–Alder cleavage (indicating that the double bond of the dihydropyran ring of the starting material **4** had been saturated); (*iv*) there were only minor differences in the ^{13}C NMR alkene carbon resonances of the mixture of **13** and **14**, and of the seven-component mixture (indicating that the new products in the second experiment were not allyl ethers); and (*v*) there was an increase of approximately 18 in the number of resonances of unoxygenated sp^3-hybridised carbon atoms (indicating the production of saturated products). Although the mass spectra of compounds **15** could be interpreted to indicate the presence of allyl ethers, this ^{13}C NMR evidence is taken as definitive.

On the basis of these observations, it was concluded that the radical derived from **4** reacts, in the presence of excess of reagent, to give the product of direct reduction together with that formed following cyclisation with the allyl ether at C-6. Only when the concentration of tributyltin hydride is low and the initial radical's life time is relatively long does it cyclise and lead to the product **15** of tandem cyclisation. It is notable that no product of single cyclisation (akin to compound **3**) was observed, suggesting again that the allyl group was a potent radical trap. Therefore, it became of interest to examine, in more detail, the trapping of distant radicals by allyl groups and thereby the possible formation of large rings fused to carbohydrate molecules.

To this end, the 6-*O*-allyl bromoethyl glycoside **19** was prepared from 2-bromoethyl β-D-glucopyranoside (**16**) by selective tritylation using collidine as base (with pyridine, the solvent replaced the bromo substituent), followed by acetylation to give compound **17**, detritylation to **18**, and subsequent allylation using allyl trichloroacetimidate prepared by the method of Overman[20]. Treatment of the resulting allylated glycoside **19** by slow addition of tributyltin hydride and azobisisobutyronitrile (AIBN) to a solution in toluene gave the ethyl glycoside **20** formed by direct reductive debromination, and a second product in the ratio 6:1 (Scheme 3). A small sample of the latter was isolated by column chromatography and shown mainly by NMR methods to be the product **21** of endo-trapping of the intermediate radical by the allyl group. In particular, it contained three methylene groups not bonded to oxygen and three such groups which bore single oxygen substituents. There were no methyl groups present other than those of the acetates.

It is concluded that the allyl group can trap distant radicals and that, while only low yields of products were formed in this experiment, optimisation of reaction conditions to favour the cyclisation at the expense of direct reduction could lead to improvements. The isolation and characterisation of compounds **20** and **21** as the only products of the reaction of **19** suggest that the radical intermediate reacted directly in the two ways discussed and did not rearrange to the corresponding anomeric radical — as was possible given the relative ease of abstraction of axial anomeric hydrogen atoms[21–23]. Had such rearrangement occurred, the resulting intermediate would have been expected to abstract hydrogen from the reagent



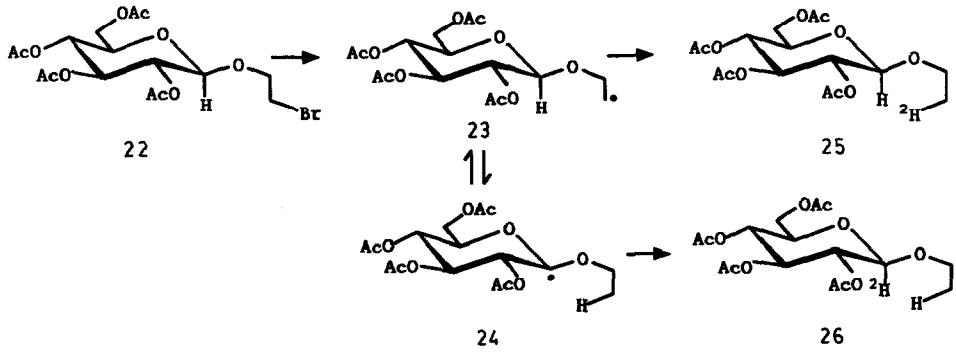
	R^1	R^2
16	H	H
17	Ac	Tr
18	Ac	H
19	Ac	$CH_2CH{=}CH_2$

20 21

Scheme 3.

from the axial direction[24,25] and hence also give the ethyl glycoside **20** as product. It therefore could have gone undetected.

To investigate whether this third reaction may have occurred, 2-bromoethyl tetra-*O*-acetyl-β-D-glucopyranoside (**22**) was treated with tributyltin deuteride, and the ethyl glycoside produced was examined by NMR methods to establish whether any deuterium had been incorporated at the anomeric centre (Scheme 4, compound **26**). The only signal in the ^2H NMR spectrum appeared at δ 1.10, indicating that the deuterium had been incorporated only into the methyl group and that none was present at the anomeric centre (expected[26] resonance δ 4.5). Additionally, the anomeric hydrogen appeared as a one-proton doublet in the ^1H NMR spectrum and the methyl hydrogens gave a two-proton triplet of triplets (J 7 and 1.8 Hz) as expected for the singly deuterated group of compound **25**. The possible rearrangement reaction of radical **23** to **24** therefore did not occur under the reaction conditions used.



22 23 25 24 26

Scheme 4.

EXPERIMENTAL

^1H NMR and ^{13}C NMR spectra were measured on $CDCl_3$ solutions, using a Bruker AC300E instrument. DEPT 135 experiments[27] and 2-dimensional proton–proton and carbon–proton correlations were used to assist with resonance assignments. Accurate mass measurements were determined by use of ammonia chemical ionisation on a VG70-250S instrument. Gas chromatography–mass spectrometry was carried out using a Hewlett–Packard HP 5995 system fitted with a split injector (20:1 split), a 12-m Hewlett–Packard HP-1 fused-silica column (0.2 mm i.d.; 0.33 μm film), and an open split interface to the mass spectrometer. GC operating conditions: injector temperature, 250°C; oven temperature held at 50 °C for 2 min, then raised at 6°C/min to 250°C; He carrier gas. Mass spectra were scanned repetitively for 25–650 amu at an ionising voltage of 70 eV.

Specific rotations were measured in $CHCl_3$ within the range 1–2%, using a Perkin–Elmer 241 polarimeter.

*Methyl 2,6-anhydro-3,4,7,9-tetradeoxy-β-*D*-arabino-non-3-en-5-ulo-5,8-furanoside* (**9**).—The acetate **8** (0.27 g), the synthesis of which is described elsewhere[19], was stirred in triethylamine, MeOH, and water (20 mL, 1:5:4) at 20°C for 3 h, after which the solvent was removed, with coevaporation with toluene, to give the alcohol **9** (0.195 g, 87%); $[\alpha]_D$ −65°. NMR data: ^1H δ 1.35 (d, 3 H, $J_{8,9}$ 6.2 Hz, H-9), 1.62 (ddd, 1 H, $J_{7a,7b}$ 13.3, $J_{7a,8}$ 6.3, $J_{6,7a}$ 2.7 Hz, H-7a), 2.15 (br s, 1 H, OH), 2.50 (ddd, 1 H, $J_{6,7b}$ 6.6, $J_{7b,8}$ 6.8 Hz, H-7b), 3.31 (s, 3 H, OMe), 3.58 (dd, 1 H, $J_{1a,2}$ 3.4, $J_{1a,1b}$ 11.9 Hz, H-1a), 3.78 (dd, 1 H, $J_{1b,2}$ 8.7 Hz, H-1b), 4.20 (dd, 1 H, H-6), 4.25–4.35 (m, 2 H, H-2,8), 5.90 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.7 Hz, H-3), 6.21 (dd, 1 H, $J_{2,4}$ 2.0 Hz, H-4); ^{13}C, δ 21.9 (C-9), 38.1 (C-7), 48.4 (OMe), 61.8 (C-1), 73.6, 74.3, 75.9 (C-2,6,8), 100.4 (C-5), 123.5, 128.5 (C-3,4). Mass spectrum: m/z, M^+. Calcd for $C_{10}H_{16}O_4$: 200.1053. Found: 200.1055.

*Methyl 1-*O*-allyl-2,6-anhydro-3,4,7,9-tetradeoxy-β-*D*-arabino-non-3-en-5-ulo-5,8-furanoside* (**10**).—The alcohol **9** (0.40 g) and allyl bromide (1 mL) were stirred in benzene (10 mL) with NaH (0.1 g) at 60°C for 16 h under N_2. Ethyl acetate (50 mL) was added, and the mixture was washed with water and dried ($MgSO_4$). Removal of the solvent gave an oil which was purified by radial chromatography to afford **10** (0.35 g, 87%); $[\alpha]_D$ −105°. NMR data: ^1H, δ 1.35 (d, 3 H, $J_{8,9}$ 6.2 Hz, H-9), 1.63 (ddd, 1 H, $J_{7a,7b}$ 13.3, $J_{7a,8}$ 6.0, $J_{6,7a}$ 2.3 Hz, H-7a), 2.50 (ddd, 1 H, $J_{6,7b}$ 6.5, $J_{7b,8}$ 7.6 Hz, H-7b), 3.30 (s, 3 H, OMe), 3.43 (dd, 1 H, $J_{1a,1b}$ 10.5, $J_{1a,2}$ 4.1 Hz, H-1a), 3.65 (dd, 1 H, $J_{1b,2}$ 7.7 Hz, H-1b), 4.00–4.05 (m, 2 H, $OCH_2CH{=}CH_2$), 4.20 (dd, 1 H, H-6), 4.2–4.45 (m, 2 H, H-2,8), 5.15–5.3 (m, 2 H, $OCH_2CH{=}CH_2$), 5.85–6.0 (m, 1 H, $OCH_2CH{=}CH$), 5.95 (dd, 1 H, $J_{3,4}$ 10.6, $J_{2,3}$ 3.5 Hz, H-3), 6.19 (dd, 1 H, $J_{2,4}$ 1.9 Hz, H-4); ^{13}C, δ 22.0 (C-9), 38.3 (C-7), 48.4 (OMe), 69.0, 72.3 (C-1, $OCH_2CH{=}CH_2$), 72.2, 74.4, 76.2 (C-2,6,8), 100.5 (C-5), 117.4 ($OCH_2CH{=}CH_2$), 122.9, 129.7 (C-3,4), 134.5 ($OCH_2CH{=}CH_2$), Mass spectrum: m/z, MH^+. Calcd for $C_{13}H_{21}O_4$: 241.1440. Found: 241.1457. $(M - OCH_3)^+$. Calcd for $C_{12}H_{17}O_3$: 209.1178. Found: 209.1184.

*1-O-Allyl-2,6-anhydro-3,4,7,9-tetradeoxy-*D-arabino-*non-3-en-5-ulose* (**11**).—The acetal **10** (0.35 g) was stirred with *p*-toluenesulfonic acid (0.27 g) at 20°C in CH_2Cl_2 (10 mL) and water (1.0 mL) for 1.5 h. Further CH_2Cl_2 (50 mL) was added, and the solution was washed with satd aq $NaHCO_3$ and water, and dried. Removal of the solvent gave **11** (0.32 g, 98%); $[\alpha]_D$ −89°. NMR data: ^{1}H, δ 1.26 (d, 3 H, $J_{8,9}$ 6.2 Hz, H-9), 1.84 (ddd, 1 H, $J_{7a,7b}$ 14.6, $J_{7a,8}$ 8.8, $J_{6,7a}$ 4.5 Hz, H-7a), 1.95 (ddd, 1 H, $J_{6,7b}$ 8.7, $J_{7b,8}$ 3.2 Hz, H-7b), 2.62 (d, 1 H, $J_{OH,8}$ 5.0 Hz, OH), 3.65 (dd, 1 H, $J_{1a,1b}$ 10.2, $J_{1a,2}$ 4.9 Hz, H-1a), 3.75 (d, 1 H, $J_{1b,2}$ 6.3 Hz, H-1b), 4.0–4.1 (m, 3 H, H-8, $OCH_2CH{=}CH_2$), 4.55–4.65 (m, 1 H, H-2), 4.61 (dd, 1 H, H-6), 5.20–5.35 (m, 2 H, $OCH_2CH{=}CH_2$), 5.85–6.0 (ddd, 1 H, $OCH_2CH{=}CH_2$), 6.16 (dd, 1 H, $J_{3,4}$ 10.5, $J_{2,4}$ 2.1 Hz, H-4), 7.02 (dd, 1 H, $J_{2,3}$ 2.9 Hz, H-3); ^{13}C, δ 23.4 (C-9), 37.9 (C-7), 64.7 (C-8), 69.7, 72.5 (C-1, $OCH_2CH{=}CH_2$), 70.0, 75.5 (C-2,6), 117.8 ($OCH_2CH{=}CH_2$), 127.0 (C-4), 134.0 ($OCH_2CH{=}CH_2$), 147.7 (C-3), 196.6 (C-5). Mass spectrum: m/z, MH^+. Calcd for $C_{12}H_{19}O_4$ 227.1283. Found: 227.1272.

*1-O-Allyl-2,6-anhydro-3,4,7,9-tetradeoxy-8-O-phenoxythiocarbonyl-*D-arabino-*non-3-en-5-ulose* (**12**).—The alcohol **11** (0.32 g), phenyl chlorothionocarbonate (0.27 g, 1.1 mol equiv), and pyridine (0.22 g, 2 mol equiv) were stirred in toluene (20 mL) for 7 h at 20°C. Ethyl acetate (50 mL) was added, and the solution was washed with aq $NaHCO_3$, dil HCl, and water, and dried ($MgSO_4$). Removal of the solvent and radial chromatographic purification gave **12** (0.35 g, 68%); $[\alpha]_D$ −91°. NMR data: ^{1}H, δ 1.49 (d, 3 H, $J_{8,9}$ 6.3 Hz, H-9), 1.99 (ddd, 1 H, $J_{7a,7b}$ 14.7, $J_{7a,8}$ 3.8, $J_{6,7a}$ 10.7 Hz, H-7a), 2.38 (ddd, 1 H, $J_{6,7b}$ 3.2, $J_{7b,8}$ 9.1 Hz, H-7b), 3.70 (dd, 1 H, $J_{1a,1b}$ 10.0, $J_{1a,2}$ 5.2 Hz, H-1a), 3.74 (dd, 1 H, $J_{1b,2}$ 5.2 Hz, H-1b), 4.0–4.05 (m, 2 H, $OCH_2CH{=}CH_2$), 4.55–4.65 (m, 1 H, H-2), 4.54 (dd, 1 H, H-6), 5.15–5.3 (m, 2 H, $OCH_2CH{=}CH_2$), 5.62 (m, 1 H, H-8), 5.87 (m, 1 H, $OCH_2CH{=}CH_2$), 6.17 (dd, 1 H, $J_{3,4}$ 10.5, $J_{2,4}$ 2.0 Hz, H-4), 7.05 (dd, 1 H, $J_{2,3}$ 2.9 Hz, H-3), 7.05–7.45 (m, 5 H, OPh); ^{13}C, δ 19.6 (C-9), 35.2 (C-7), 70.2, 74.4 (C-2,6), 70.5, 72.5 (C-1, $OCH_2CH{=}CH_2$), 78.3 (C-8), 117.6 ($OCH_2CH{=}CH_2$), 122.0, 126.5, 129.5, 153.3 (Ph), 126.6 (C-4), 134.1 ($OCH_2CH{=}CH_2$), 148.1 (C-3), 194.4, 195.4 (C-5, C=S). Mass spectrum: m/z, $(M + NH_4^+)$. Calcd for $C_{19}H_{26}NO_5S$: 380.1532. Found: 380.1536.

*1-O-Allyl-2-6-anhydro-3,4,7,9-tetradeoxy-8-O-phenoxythiocarbonyl-*D-arabino-*non-3-en-5-ulose ethylene acetal* (**4**).—The phenoxythiocarbonyl ester **12** (0.35 g) and ethane-1,2-diol (2 mL) were heated for 2 h in refluxing benzene (30 mL) containing *p*-toluenesulfonic acid (0.2 g) with azeotropic removal of water. Ethyl acetate (50 mL) was added, and the solution was washed with aq $NaHCO_3$ and water, and dried ($MgSO_4$). Removal of the solvent and purification by radial chromatography gave **4** (0.275 g, 70%); $[\alpha]_D$ −97°. NMR data: ^{1}H, δ 1.49 (d, 3 H, $J_{8,9}$ 6.2 Hz, H-9), 1.89 (ddd, 1 H, $J_{7a,7b}$ 14.5, $J_{7a,8}$ 3.5, $J_{6,7a}$ 10.8 Hz, H-7a), 2.10 (ddd, 1 H, $J_{6,7b}$ 1.5, $J_{7b,8}$ 9.4 Hz, H-7b), 3.53 (dd, 1 H, $J_{1a,1b}$ 9.8, $J_{1a,2}$ 5.6 Hz, H-1a), 3.63 (dd, 1 H, $J_{1b,2}$ 6.0 Hz, H-1b), 3.9–4.1 (m, 7 H, H-6, $OCH_2CH{=}CH_2$, OCH_2CH_2O) 4.40 (m, 1 H, H-2), 5.15–5.53 (m, 2 H, $OCH_2CH{=}CH_2$), 5.60 (m, 1 H, H-8), 5.82 (dd, 1 H, $J_{3,4}$ 10.6, $J_{2,3}$ 1.6 Hz, H-3), 5.87 (m, 1 H, $OCH_2CH{=}CH_2$),

6.02 (dd, 1 H, $J_{2,4}$ 2.5 Hz, H-4), 7.05–7.45 (m, 5 H, Ph); ^{13}C, δ 19.9 (C-9), 34.0 (C-7), 64.7, 65.2 (OCH_2CH_2O), 70.5, 72.4 (C-1, $OCH_2CH{=}CH_2$), 71.1, 71.2 (C-2,6), 79.3 (C-8), 101.8 (C-5), 117.3 ($OCH_2CH{=}CH_2$), 122.1, 126.4, 129.4, 153.3 (Ph), 126.7, 130.6 (C-3, C-4), 134.5 ($OCH_2CH{=}CH_2$), 194.4 (C=S). Mass spectrum: m/z, MH^+. Calcd for $C_{21}H_{27}O_6S$: 407.1528. Found: 407.1534.

Treatment of **4** *with tributyltin hydride.*—To the ester **4** (18 mg) in refluxing benzene (5 mL) were added slowly under N_2 over 6 h, tributyltin hydride (20 mg) and AIBN (2 mg) in the same solvent (1 mL). Heating was continued for 12 h, the solvent was removed, and the products (4 mg) were isolated by radial chromatography. Gas chromatographic examination showed the presence of mainly two compounds with retention times 19.2 and 19.5 min (also traces of compounds with retention times 19.8 and 20.3 min) in the ratio 2:3. The former (assigned structure **13**) showed no M^+ (m/z 254) but mainly $[M - CH_3CH_2CH_2CHO]^{+\cdot}$ (m/z 182) and $[M - CH_3CH_2CH_2CHO - CH_2CH_2]^+$ (m/z 138). The latter (assigned structure **14**) showed no M^+ (m/z 254) but mainly $[M - \dot{C}H_2CHO]^+$ (m/z 211), $[M - CH_3\dot{C}HCH_2CHO]^+$ (m/z 183), $[M - \dot{O}CH_2CH(CH_3)CH(CH_3)CH_2CHO]$ (m/z 125), $[M - \dot{C}H_2OCH_2CH(CH_3)CH(CH_3)CH_2CHO]^+$ m/z (112).

The reaction was repeated using ester **4** (21 mg), tributyltin hydride (50 mg) and AIBN (2 mg) in benzene (50 mL). Product (11 mg) was isolated; gas chromatographic retention times of the components were 19.2, 19.5, 19.8, 20.0, 20.3, 20.4, and 20.5 min. The third to the sixth of these all showed $M^{+\cdot}$ (m/z 254) and $[M - CH_3\dot{C}HCH_2]^{+\cdot}$ (m/z 196), $[M - CH_2{=}CHCH_2\dot{O}]^+$ (m/z 197), $[M - CH_2{=}CHCH_2\dot{O} - CH_2CH_2]^+$ (m/z 153), and $[M - CH_2{=}CHCH_2\dot{O}CH_2 - CHCH_2]^+$ (m/z 139), and were assigned structure **15**.

*2-Bromoethyl 2,3,4-tri-*O*-acetyl-6-*O*-triphenylmethyl-β-*D*-glucopyranoside* (**17**).—A solution of 2-bromoethyl β-D-glucopyranoside (**16**) made from the known tetra-acetate[28] (2.73 g, 9.5 mmol), triphenylmethyl chloride (3.98 g, 14.3 mmol), and 2,4,6-collidine (2.32 g, 19.0 mmol) in CH_2Cl_2 (80 mL) was stirred at 35°C for 24 h. The solution volume was then reduced to 25 mL, and pyridine (15 mL) and acetic anhydride (15 mL) were added. Stirring was continued at room temperature for 1.5 h. The reaction mixture was poured onto ice–water and after stirring for 1 h, the aqueous phase was extracted with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed (dil HCl), dried ($MgSO_4$), filtered, and evaporated. Compound **17** was isolated from the resulting syrup by column chromatography (light petroleum–EtOAc) and recrystallised (yield 5.11 g, 82%) from light petroleum–EtOAc; mp 162–163.5°C; $[\alpha]_D$ + 27.2°; NMR data: ^1H, δ 1.73, 1.99, 2.07 (9 H, 3 s, OAc), 3.11 (dd, 1 H, $J_{5,6a}$ 4.8, $J_{6a,6b}$ 10.5 Hz, H-6a), 3.27 (dd, 1 H, $J_{5,6b}$ 2.1 Hz, H-6b), 3.49–3.59 (m, 3 H, H-5, CH_2Br), 3.92 (dt, 1 H, J 7.0, 11.3, $J_{1,2}$ 7.7 Hz,

OCH_2), 4.17 (dt, 1 H, *J* 6.3 Hz, OCH_2), 4.57 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 5.03–5.20 (m, 3 H, H-2,3,4), 7.20–7.45 (m, 15 H, Ar); ^{13}C, δ 20.38, 20.65, 20.76 ($COCH_3$), 29.95 (CH_2Br), 61.93 (C-6), 68.71 (C-4), 69.63 (OCH_2) 71.31 (C-2), 73.01 (C-5), 73.54 (C-3), 86.67 ($OCPh_3$), 101.17 (C-1), 127.08, 127.84, 128.70 (aromatic CH), 143.56 (aromatic C) 168.93, 169.48, 170.36 ($COCH_3$). Anal. Calcd for $C_{33}H_{35}BrO_9$: C, 60.5; H, 5.4; Br, 12.2. Found: C, 60.7; H, 5.3; Br, 11.9.

*2-Bromoethyl 2,3,4-tri-*O*-acetyl-β-*D*-glucopyranoside* (**18**).—Compound **17** (4.80 g) was stirred in aq acetic acid (80 mL; 80%) at 40°C for 4 h. The acid was removed under reduced pressure, and toluene (3 × 25 mL) was mixed with the residue and evaporated. Compound **18** was isolated by column chromatography (light petroleum–EtOAc) and recrystallised (yield 2.27 g, 75%) from light petroleum EtOAc; mp 118–119 °C; $[\alpha]_D$ −14.6° (c 1.2); NMR data: 2.02, 2.06, 2.07 (3 s, 9 H, OAc), 2.38 (dd, 1 H, *J* 6.1 and 7.5 Hz, OH), 3.47 (t, 2 H, *J* 5.8 Hz, CH_2Br), 3.54 (ddd, 1 H, $J_{4,5}$ 9.7, $J_{5,6a}$ 4.6, $J_{5,6b}$ 2.0 Hz, H-5), 3.60–3.87 (m, 3 H, H-6a,6b, OCH_2), 4.18 (dt, 1 H, *J* 5.5 and 11.2 Hz, OCH_2), 4.61 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.99 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2), 5.04 (t, 1 H, *J* 9.7 Hz, H-4), 5.27 (t, 1 H, H-3); ^{13}C, δ 20.63, 20.63, 20.74 ($COCH_3$), 29.97 (CH_2Br), 61.21 (C-6), 68.70 (C-4), 69.73 (OCH_2), 71.27 (C-2), 72.56 (C-5), 74.27 (C-3), 100.95 (C-1), 169.44, 170.15, 170.23 ($COCH_3$). Anal. Calcd for $C_{14}H_{21}BrO_9$: C, 40.7; H, 5.1; Br, 19.3. Found: C, 41.2; H, 5.2; Br, 18.9.

*2-Bromoethyl 2,3,4-tri-*O*-acetyl-6-*O*-allyl-β-*D*-glucopyranoside* (**19**).—To a stirred solution of the primary alcohol **18** (1.0 g) and allyl trichloroacetimidate (0.98 g, 2 mol equiv) in 1:1 cyclohexane–CH_2Cl_2 (25 mL) was added triflic acid (0.10 mL). Stirring was continued at room temperature for 2 h, the mixture was filtered, and the filtrate was diluted with CH_2Cl_2. The CH_2Cl_2 solution was washed (satd $NaHCO_3$), dried ($MgSO_4$), and concentrated to a syrup. Compound **19** was isolated by column chromatography (light petroleum–EtOAc) and recrystallised (yield 0.80 g, 73%) from light petroleum–EtOAc; mp 97.5–99°C; $[\alpha]_D$ −7.0°; NMR data: ^1H, δ 2.01, 2.02, 2.07 (3 s, 9 H, OAc), 3.46 (dd, 2 H, *J* 5.9 and 7.7 Hz, CH_2Br), 3.53–3.55 (m, 2 H, H-6a,6b), 3.66 (m, 1 H, H-5), 3.82 (dt, 1 H, *J* 4.9 and 11.2 Hz, OCH_2CH_2Br), 3.98–4.01 (m, 2 H, $OCH_2CH{=}CH_2$), 4.17 (dt, 1 H, *J* 5.6 Hz, OCH_2CH_2Br), 4.56 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 5.00 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2), 5.04 (t, 1 H, $J_{3,4} = J_{4,5} = 9.6$ Hz, H-4), 5.22 (t, 1 H, H-3), 5.17–5.30 (2 H, m, $CH{=}CH_2$), 5.80–5.93 (1 H, m, $CH{=}CH_2$); ^{13}C, δ 20.65, 20.70, 20.77 ($COCH_3$), 30.00 (CH_2Br), 68.83 (C-6), 69.25 (C-4), 69.66 (OCH_2CH_2Br), 71.15 (C-2), 72.58 ($OCH_2CH{=}CH_2$), 72.72 (C-3), 73.40 (C-5), 100.88 (C-1), 117.55 ($CH{=}CH_2$), 134.19 ($CH{=}CH_2$), 169.44, 169.54, 170.32 ($COCH_3$). Anal. Calcd for $C_{17}H_{25}BrO_9$: C, 45.1; H, 5.6; Br, 17.6. Found C, 45.3; H, 5.6; Br, 17.3.

Treatment of **19** *with tributyltin hydride.*—A degassed solution of tributyltin hydride (106 mg, 0.36 mmol) and AIBN (5 mg, 0.03 mmol) in toluene (6 mL) was added, over 6 h, to a degassed solution of **19** (150 mg, 0.33 mmol) in refluxing dry toluene (40 mL). After 10 h heating, the toluene was removed under low pressure and the resulting residue taken up in acetonitrile (10 mL). The acetonitrile

solution was washed with light petroleum (3 × 10 mL) in order to remove most of the tin residues. Gas chromatographic analysis of the residue obtained on removal of the acetonitrile revealed two products present in the ratio 6:1. The product mixture was subjected to column chromatography (light petroleum–EtOAc) and the major component was isolated and recrystallised from light petroleum–EtOAc to give ethyl 2,3,4-tri-*O*-acetyl-6-*O*-allyl-β-D-glucopyranoside (**20**) (85 mg, 69%); mp 70.5–72°C; $[\alpha]_D$ −15.7°; NMR data: 1.20 (t, 3 H, *J* 7.1 Hz, OCH_2CH_3), 2.00, 2.01, 2.04 (3 s, 9 H, OAc), 3.53–3.55 (m, 2 H, H-6a,6b), 3.57–3.70 (m, 2 H, H-5, OCH_2CH_3), 3.91 (dq, 1 H, *J* 7.1 and 9.7 Hz, OCH_2CH_3), 4.00 (dd, 2 H, *J* 1.0 and 5.5, $OCH_2CH{=}CH_2$), 4.50 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.95 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2), 5.02 (t, 1 H, $J_{3,4} = J_{4,5} = 9.7$ Hz, H-4), 5.20 (t, 1 H, H-3), 5.16–5.29 (2 H, m, $CH{=}CH_2$), 5.80–5.93 (m, 1 H, $CH{=}CH_2$); ^{13}C, δ 15.02 (OCH_2CH_3), 20.60, 20.63, 20.63 ($COCH_3$), 65.43 (OCH_2CH_3), 69.15 (C-6), 69.57 (C-4), 71.54 (C-2), 72.55 ($OCH_2CH{=}CH_2$), 73.05 (C-3), 73.33 (C-5), 100.43 (C-1), 117.27 ($CH{=}CH_2$), 134.34 ($CH{=}CH_2$), 169.32, 169.52, 170.30 ($COCH_3$).

A small, chromatographically pure sample (1.8 mg) of the minor product, 5′-hydroxypentyl 2,3,4-tri-*O*-acetyl-6,5′-anhydro-β-D-glucopyranoside (**21**) had: $[\alpha]_D + 3.1 \pm 0.8°$; NMR data: ^1H, δ 1.26–1.36 (m, 2 H, H-3′), 1.56–1.73 (m, 4 H, H-2′,4′), 2.01, 2.01, 2.05 (3 s, 9 H, OAc), 3.46 (dd, 1 H, *J* 12.8 and 8.3 Hz, H-6a), 3.66 (dd, 1 H, *J* 1.8 Hz, H-6b), 3.48–3.71, 3.83–3.89, 4.05–4.11 (m, 5 H, H-5,1′,5′), 4.49 (d, 1 H, $J_{1,2}$ 6.9 Hz, H-1), 4.95–5.04 (m, 2 H, H-2,4), 5.19 (t, 1 H, $J_{2,3} = J_{3,4} = 8.6$ Hz, H-3); ^{13}C, δ 20.67 ($COCH_3$), 22.21, 29.24, 29.68 (C-2′,3′,4′), 69.37 (C-5), 69.90, 70.83, 72.96 (C-6,1′,5′), 72.53, 73.28, 75.44 (C-2,3,4), 101.77 (C-1). Mass spectrum: *m/z*, MH^+. Calcd for $C_{17}H_{27}O_9$: 375.1655. Found: 375.1671.

Treatment of 2-bromoethyl tetra-O-acetyl-β-D-glucopyranoside (**22**) *with tributyltin deuteride.*—A degassed solution of **22** (40 mg), tributyltin deuteride (28.2 mg, 1.1 mol equiv), and AIBN (3 mg) in benzene (97 mL) was heated under reflux for 17 h. The solvent was evaporated, and the residue was taken up in acetonitrile and washed several times with light petroleum. The residue remaining on removal of the acetonitrile was stirred in CCl_4 for 10 min. Further solvent evaporation afforded the product **25**, which was analysed by ^2H NMR spectroscopy ($CHCl_3$ solution, $^2H_6$-benzene internal standard): δ (referenced to $^2H_6$-benzene singlet set at 7.30 ppm) 1.10 (bs, OCH_2CH_2D).

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