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ALLYLIC SUBSTITUTIONS IN TRI-*O*-BENZYL-GLYCALS, 4,6-*O*-BENZYLIDENE-GLYCALS AND RELATED COMPOUNDS*†

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ABSTRACT

3,4,6-Tri-*O*-benzyl-D-glucal and the benzyl 4,6-di-*O*-benzyl-2,3-dideoxy-hex-2-enopyranosides react with sodium azide in acetonitrile under boron trifluoride catalysis to yield mixtures of 3-azido-glycals and 2,3-unsaturated glycosyl azides. Similar reactions with derivatives of 4,6-*O*-benzylidene-D-allal and -glucal and with related 2,3-unsaturated analogues gave only azido-glycals. The mechanism of these reactions is discussed and compared with reactions of the tri-*O*-acetyl-glycals and related systems.

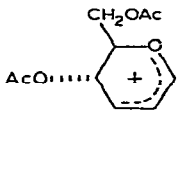
INTRODUCTION

In the preceding paper[1] we reported that the boron trifluoride-catalyzed reaction of various acetylated unsaturated sugars with sodium azide in acetonitrile led to mixtures of 4,6-di-*O*-acetyl-3-azido-3-deoxy-glycals and 4,6-di-*O*-acetyl-2,3-dideoxy-hex-2-enopyranosyl azides. Although an SN1′ mechanism with nucleophilic attack solely at C-1 of an ion of the type **1** was strongly implicated, a definite mechanistic assignment was precluded by the observation that the products rearranged under the conditions of reaction. Furthermore, in the reactions of the glycals, the possibility of an initial SNi′ rearrangement preceding nucleophilic attack could not be eliminated. The suggestion that **1** is the common intermediate in these reactions may be criticized in that the existence of an alternative ionic structure **2** has been unequivocally demonstrated[2] in the solvolysis of 3,4,6-tri-*O*-acetyl-D-glucal in liquid hydrogen fluoride at −70°. In order to explore the mechanism of these and related reactions, we have investigated the behaviour of other unsaturated sugars under the azidolysis conditions previously described[1].

RESULTS AND DISCUSSION

As observed with the tri-*O*-acetyl analogue, 3,4,6-tri-*O*-benzyl-D-glucal (**3**) reacted with sodium azide in acetonitrile under boron trifluoride catalysis. Repeated

*Dedicated to Professor Stephen J. Angyal on the occasion of his retirement.
†Part II of the series "Allylic Nucleophilic Substitution Reactions in Sugars". For Part I, see preceding paper.



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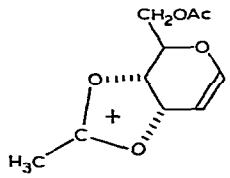

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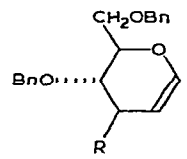
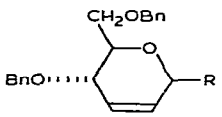
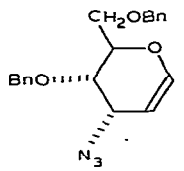


3 R = OBn
4 R = N_3

Bn = Benzyl



5 R = N_3
6 R = OBn



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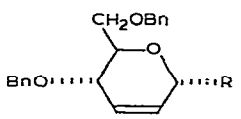


8 R = N_3
9 R = OBn

chromatography resolved the product-mixture into three fractions, of which the i.r. spectra indicated that two contained azido sugars. The ^{13}C-n.m.r. and 270-MHz ^{1}H-n.m.r. spectra of the chromatographically most-mobile fraction were consistent with a mixture of 3-azido-4,6-di-*O*-benzyl-3-deoxy-D-glucal (**4**) and 4,6-di-*O*-benzyl-2,3-dideoxy-*β*-D-*erythro*-hex-2-enopyranosyl azide (**5**).

Unlike the corresponding spectrum of the di-*O*-acetyl analogues[1], signals in the 270-MHz ^{1}H-n.m.r. spectrum corresponding to **5** were not sufficiently resolved for determination of the various coupling-constants. Structural assignment was therefore based on the products from the benzylation of 3-azido-3-deoxy-D-glucal[1], namely a mixture of **4** and a compound indistinguishable by ^{13}C-n.m.r. and t.l.c. from that assigned as **5**.

The mixture of **4** and **5** was chromatographically inseparable, but samples enriched in either isomer underwent re-equilibration to an 89:11 mixture of **4** and **5** at 25°. No epimerization occurred during 3 months at room temperature.

The ^{13}C-n.m.r. and 270-MHz ^{1}H-n.m.r. spectra of the second fraction eluted by chromatography of the mixture were consistent with a mixture of 3-azido-4,6-di-*O*-benzyl-3-deoxy-D-allal (**7**) and 4,6-di-*O*-benzyl-2,3-dideoxy-*α*-D-*erythro*-hex-2-enopyranosyl azide (**8**). Again, the coupling constants of **8** could not be deduced from the 270-MHz ^{1}H-n.m.r. spectrum, and assignment was based on the products of benzylation of a mixture[1] of 3-azido-3-deoxy-D-allal and 2,3-dideoxy-*α*-D-*erythro*-hex-2-enopyranosyl azide. At equilibrium the mixture had the composition **7**:**8** = 82:18. Because a wide enough range of concentrations in mixtures enriched in either isomer could not be obtained, optical rotations could not be calculated by the method described in the previous paper[1]. The overall ratio of the products from the azidolysis of **3** was calculated from the 270-MHz ^{1}H-n.m.r. spectrum of the mixture (Table I). This calculation was based on the equilibrium mole-fraction of each isomer derived from the ^{1}H-n.m.r. spectra of both pairs of interconverting isomers. The ratio of

β-face : α-face products (**4** + **5**) : (**7** + **8**) thus obtained (~3 : 7) was different from that reported by Heyns and Hohlweg[3] (1 : 4) for a similar reaction. Their value was also derived from a ^{1}H-n.m.r. spectrum of the product-mixture, but these authors did not report detection of **5** or **8**. Further, although their overall yield (48%) suggests the formation of other products or the incomplete conversion of starting material, no mention of either was made.

The remaining fraction from the chromatographic resolution of the mixture did not contain azide (i.r. spectrum). The ^{13}C-n.m.r. and ^{1}H-n.m.r. spectra were identical with those of the product-mixture obtained when **3** was treated with boron trifluoride–diethyl etherate in ether in the manner described by Descotes and Martin[4]. This product-mixture had two components, the major of which was identified as benzyl 4,6-di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**9**) from its ^{13}C-n.m.r. spectrum. The second compound present in both samples (but *not* reported by Descotes and Martin[4]) was identified as the β anomer (**6**) on the basis of the similarity of, but expected differences from, the ^{13}C-n.m.r. and ^{1}H-n.m.r. spectra of **9**. The mixture of **6** and **9** could not be completely resolved by chromatography.

The same sensitivity of the yield towards variations in the reaction conditions was observed in the azidolysis of **3** as found with the analogous acetate[1]. Optimum yields (88%) were obtained when 30 equiv. of boron trifluoride–diethyl etherate were added in three aliquots, but substantial amounts of **6** and **9** remained on isolation. A fourth aliquot of catalyst caused considerable decomposition.

A mixture of **6** and **9** also underwent azidolysis under these conditions, giving a mixture of **4**, **5**, **7**, and **8** in the same ratio as that obtained from **3** (Table I). Again, the reaction could not be forced to completion.

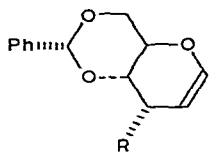
3-*O*-Acetyl-4,6-*O*-benzylidene-D-allal (**10**) reacted in part with sodium azide in acetonitrile under boron trifluoride–diethyl etherate catalysis. Separation of the products from unreacted starting material was best effected by initial treatment with sodium methoxide, followed by p.l.c., which afforded three compounds, one of which was readily identified as 4,6-*O*-benzylidene-D-allal (**11**).

TABLE I

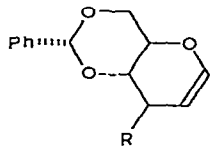
EQUILIBRIUM PRODUCT-RATIOS (±2%) FOR COMPOUNDS **4**, **5**, **7**, AND **8** (BY ^{1}H-N.M.R. SPECTROSCOPY)

Substrate	*Equiv. of* NaN_3	*Equiv. of* $BF_3 \cdot Et_2O$	*Percent yields*		
			4	**7**	(**5** + **8**)[a]
3	5	30	28	56	16
(**6** + **9**)	5	30	28	57	15
(**4** + **5**)	5	30	30	54	16
(**7** + **8**)	5	30	25	60	16
(**4** + **5**)[b]			89		11[c]
(**7** + **8**)[b]				82	18

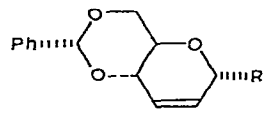
[a]Ratio of **5**:**8** may be determined from equilibrium values[b]. [b]Equilibrium values. [c]**5** only. [d]**8** only.



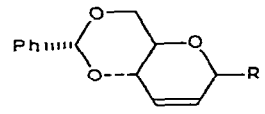
10 R = OAc
11 R = OH
12 R = N_3
13 R = OMe
14 R = NHAc



15 R = N_3
16 R = OH
17 R = OAc
18 R = OMe
19 R = NHAc



20 R = N_3
21 R = OMe
22 R = OAc



23 R = N_3
24 R = OAc
25 R = OMe

Both of the remaining compounds were crystalline and each contained an azido group (i.r.). The ^{1}H-n.m.r. spectrum of the major product was consistent with that expected for 3-azido-4,6-*O*-benzylidene-3-deoxy-D-allal (**12**), as was the ^{13}C-n.m.r. spectrum.

Examination of the ^{1}H-n.m.r. spectrum of the minor product revealed a doublet of doublets at δ 6.41 ($^3J_{1,2}$ 6.0, $^4J_{1,3}$ 2.0 Hz) and at δ 4.70 ($^3J_{2,3}$ 1.8 Hz) characteristic of H-1 and H-2 of a glucal. This, and the ^{13}C-n.m.r. spectrum, led to the assignment of a 3-azido-4,6-*O*-benzylidene-3-deoxy-D-glucal structure (**15**).

When the azidolysis of **10** was performed rapidly, with processing at 4°, the ^{1}H-n.m.r. spectrum of the mixture exhibited resonances consistent with those expected for a 2,3-dideoxy-unsaturated hexose, but evaporation of the solvent gave a crystalline residue, and only **12** and **15**, together with unreacted starting material, were obtained after p.l.c. Alternatively, when this same mixture was immediately deacetylated and resolved by p.l.c., a hitherto undetected band was visible. Extraction with cold acetone afforded a mixture of **12** and a 2,3-unsaturated sugar (^{1}H-n.m.r.). A second chromatography again resolved this mixture into two distinct bands, but extraction as before afforded a mixture of the same compounds in approximately the same proportions. Evaporation of the solvent and inoculation with a seed crystal of **12** resulted in the complete conversion of the 2,3-unsaturated compound into **12**.

In view of the stereospecific isomerizations of the various glycosyl azides previously described[1], this behaviour was attributed to the presence in the original mixture of 4,6-*O*-benzylidene-2,3-dideoxy-α- and -β-D-*erythro*-hex-2-enopyranosyl azides (**20** and **23**, respectively). Contrary to Heyns and Hohlweg's statements[3], these compounds apparently underwent an irreversible isomerization to the glycals **12** and **15**, respectively (and see later).

As was observed in the reactions previously described[1], the yield from the azidolysis of **10** was critically dependent on the reaction conditions. In particular, the use of more than 18 equiv. of catalyst resulted in substantial decomposition and the formation of benzaldehyde.

Other suitable substrates having a 4,6-*O*-benzylidene group were difficult to find. The azidolysis of 3-*O*-acetyl-4,6-*O*-benzylidene-D-glucal (**17**) surprisingly resulted in no reaction, even at 50°. Starting material was recovered unchanged. The isomeric hex-2-enoses (**22/24**) are unknown. Attempts to prepare them by the acid-catalyzed rearrangement of the allal (**10**) (compare ref. 5), or by an acid-catalyzed rearrangement of **10** with sodium acetate in acetonitrile, were unsuccessful. However, the successful azidolysis[1] of ethyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside prompted an investigation into the possibility of using the known methyl 4,6-*O*-benzylidene-2,3-dideoxy-α- and -β-D-*erythro*-hex-2-enopyranosides (**21** and **25**, respectively) as substrates.

Treatment of either **21** or **25** with sodium azide and boron trifluoride–diethyl etherate (3 × 6 equiv.) in acetonitrile gave the 3-azido-glycals **12** and **15**, but again the reactions were incomplete. Attempts to force the reaction to completion by the use of additional catalyst resulted in substantial decomposition. After p.l.c., the fraction corresponding to unreacted starting material was found in both instances to be a mixture of both **21** and **25**, the relative proportions of which could not be estimated by ^{1}H-n.m.r. Measurements of optical rotation indicated a mole fraction of **25** of 0.40 ±0.05, but as this value could not consistently be reproduced, it was not possible to determine with certainty whether or not the recovered glycoside fractions from the azidolysis of **21** and **25** were identical.

A reaction with either of the glycosides **21** or **25** that was prematurely quenched and processed rapidly at 4° afforded mixtures in which the azido-glycals **12** and **15** were not detectable by t.l.c. or by ^{1}H-n.m.r., but attempted isolation of the products gave only the 3-azido-glycals. These results are consistent with attack by azide at C-1, followed by an irreversible rearrangement to give the glycals **12** and **15**.

As these findings are in direct conflict with those reported by Heyns and Hohlweg[3], the α-glycoside (**21**) was subjected to azidolysis under the conditions reported by them. Again, the glycosyl azides **20** and **23** were the initial products, and these underwent rearrangement to the glycals **12** and **15** as previously described. We cannot account for the discrepancy between our results and those of Heyns and Hohlweg[3], in particular, the claim that **20** failed to isomerize on heating in nitrobenzene at 170°.

Two other substrates chosen were the isomeric 4,6-*O*-benzylidene-3-*O*-methyl-D-allal (**13**) and -D-glucal (**18**). The allal **13** reacted under the azidolysis conditions described for **21** and **25**. Again, the only azide-containing sugars isolated were the azido-glycals **12** and **15**. In addition to these and unreacted starting material, a third compound was also isolated that was identified as the α-glycoside **21**. No trace of the β-glycoside **25** was detected, but the proportion of glycosidic material produced in the reaction was at best 14%, and small amounts of **25** would have evaded detection.

TABLE II

EQUILIBRIUM PRODUCT-RATIOS (±2%) FOR COMPOUNDS **12** AND **15**[a]

Substrate	**12** (%)	**15** (%)
10	81	19
12	100	
13	85	15
15		100
21	83	17
25	83	17

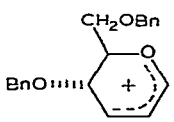
[a] 5 equiv. of NaN_3, 18 equiv. of $BF_3 \cdot Et_2O$.

Like its 3-*O*-acetyl analogue **17**, the glucal (**18**) did not undergo azidolysis, even at 50°. The product ratios obtained from the azidolysis of **10**, **21**, **25**, and **13** are presented in Table II.

Both **12** and **15** were readily reduced by lithium aluminium hydride in ether. The resulting, crystalline amines were unstable and could not be characterized, but acetylation afforded 3-acetamido-4,6-*O*-benzylidene-3-deoxy-D-allal (**14**) and -D-glucal (**19**), respectively.

The various mechanistic considerations discussed for the analogous acetates[1] are also applicable to the azidolysis of the tri-*O*-benzyl unsaturated sugars **3**, **6**, and **9**. Again, the similarities in the product ratios from these reactions imply a common intermediate, although mixtures of **4** and **5** or of **7** and **8** partially epimerized under the azidolysis conditions. However, as with the analogous acetates, the product ratios obtained from these epimerizations were in both instances removed from the value corresponding to the thermodynamic equilibrium, in the direction of the starting material (Table I). In the absence of sodium azide, solutions of either mixture underwent deep-seated decomposition upon addition of boron trifluoride–diethyl etherate, leading to black tars.

By analogy with the acetates[1], the common intermediate in the azidolysis of the benzyl ethers is probably the free carbonium ion **26**. Because such an ion as **2** cannot be formed in this system, this type of anchimeric assistance by a C-4 acyloxy



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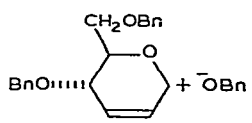

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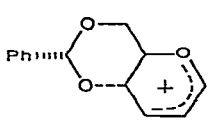

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group is ruled out for these reactions. As **6** and **9** did not undergo SNi′ isomerization to the isomeric glycals upon treatment with boron trifluoride–diethyl etherate in acetonitrile, the route to **26** from these glycosides was by evidently simple ionization of the anomeric benzyloxy group.

In the case of **3**, the recovery of **6** and **9** from the azidolysis mixture, together with the complete absence of **3** in the mixture upon purification, provided evidence that an SNi′ rearrangement of **3** to the glycosides **6** and **9** was important in this instance. Furthermore, the formation of *both* anomers suggests two possible mechanisms for this rearrangement. It was not stereospecific, and therefore proceeded by ionization of the C-3 benzyloxy group to give the ion **26** (or a loose ion-pair having the same geometry), which was then competitively attacked at C-1 by either the available azidotrifluoroborate[1] or benzyloxytrifluoroborate. Alternatively, the SNi rearrangement may have been stereospecific, to give exclusively **6**, which subsequently anomerized.

A close correspondence exists between the results for the azidolysis of the tri-*O*-benzyl compounds **3**, **6**, and **9**, and those for the 4,6-benzylidene sugars **10**, **13**, **21**, and **25**. However, as the products from the latter reactions did not epimerize under the conditions used, the assignment of a rate-determining SN1′ (or SN1) mechanism was free of complications. In consideration of the previous findings for the analogous acetates and benzyl ethers, the common intermediate in these reactions was either a free carbonium ion **28** or a very similar, loose ion-pair.

In the case of **10**, no initial isomerization to the hex-2-enoses **22** and **24** was detected, but this may have arisen from an increase in the reactivity of the latter compounds with respect to the allal **10**, which would result in their preferential reaction with available azidotrifluoroborate ion. The increased reactivity of the 1,4,6-tri-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-enopyranoses with respect to 3,4,6-tri-*O*-acetyl-D-glucal and -D-allal has already been described[1].

The 3-*O*-methyl-allal **13** underwent azidolysis by a mechanism similar to that of **3**, with an SNi′ isomerization to the glycosides **21** and **25** preceding or competing with attack by azide.

The *trans*-fused, 4,6-*O*-benzylidene ring introduces severe restraints on the conformational freedom of unsaturated sugars: glycals can no longer undergo conformational inversion and are restricted to the $^4H_5$ conformation: hex-2-enoses are similarly restricted to the $^4H_0$ conformation.

The favoured geometry for the rupture of the allylic bond is attained in six-membered rings when the leaving group is in the *quasi*-axial orientation[6]. Because of the conformational restraints introduced by the *trans*-4,6-*O*-benzylidene ring, the glucals **17** and **18** cannot achieve the $^5H_4$ conformation having the allylic substituent *quasi*-axially disposed. The corresponding allal derivatives **10** and **13**, in which the leaving-group is in such an orientation in the ground state, reacted at a rate comparable to that of the glycosides **21** and **25**.

TABLE III

^{13}C-N.M.R. DATA (CHLOROFORM-*d*)

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*Other*
4	146.1	98.3	60.8	74.7	77.4	68.2	74.7, 73.7 (benzyl CH_2)
7	147.4	95.9	53.5	73.4	73.4	68.4	73.6, 72.0 (benzyl CH_2)
12	146.6	97.6	53.1	77.4	64.9	68.6	101.8 (acetal)
15	145.5	99.6	57.4	78.5	68.3	68.9	101.5 (acetal)

[a]Excluding aromatic carbon atoms.

EXPERIMENTAL

General methods. — See preceding paper[1]. For ^{13}C-n.m.r. data, see Table III.

General procedure for the reaction of unsaturated sugars with sodium azide in acetonitrile under boron trifluoride–diethyl ether catalysis. — The sugar (1 mmol) and sodium azide (5 mmol) were stirred in acetonitrile (50 mL) for 0.5 h at room temperature, and boron trifluoride–diethyl etherate (x mL) was added in y aliquots at 0.5-h intervals. After a further 0.5 h, solid anhydrous sodium carbonate was added and the mixture stirred for 2 h. The mixture was filtered and the solvent evaporated (40°) from the filtrate. The residue was partitioned between dichloromethane (40 mL) and saturated sodium carbonate solution (20 mL), and the organic phase washed with water and dried. Evaporation of the solvent afforded mixtures of the various product-azides, together (in some instances) with unreacted starting-material or isomers of the starting material. The respective experimental data for individual substrates are given next:

(*a*) *3,4,6-Tri-*O*-benzyl-*D*-glucal*[7] (**3**): $x = 0.75$, $y = 3$, yield 88% (see Table I) (based on reacted starting material), together with benzyl 4,6-di-*O*-benzyl-2,3-dideoxy-α-β-D-*erythro*-hex-2-enopyranoside (**9**) and **6** (4%). Separation of the products was effected as follows. The syrupy mixture was chromatographed (p.l.c., toluene–ethyl acetate, 19:1, three developments) to give four bands of which the least mobile was found to be a mixture of compounds **6** and **9**. The most mobile band was rechromatographed (p.l.c., toluene–ethyl acetate, 39:1, fifteen developments) to give two bands. The more mobile band was extracted to give a mixture of 3-azido-4,6-di-*O*-benzyl-3-deoxy-D-glucal (**4**) and 4,6-di-*O*-benzyl-2,3-dideoxy-β-D-*erythro*-hex-2-enopyranosyl azide (**5**) in the ratio of 89:11; ν_{max}^{neat} 2110 (N_3) and 1645 cm^{-1} (–C=C–O); ^{1}H-n.m.r.: δ 7.30–7.42 (m, 10 H, benzyl aromatic protons), 6.48 (dd, 1 H, $J_{1,2}$ 6.0, $J_{1,3}$ 2.3 Hz, H-1), 4.50–4.97 (m, 5 H, H-2 and benzyl CH_2), and 4.01–4.27 (m, 5 H, H-3,4,5,6,6′).

Anal. Calc. for $C_{20}H_{21}N_3O_5$: C, 68.4; H, 6.0; N, 12.0. Found: C, 68.6; H, 6.2; N, 11.8.

The third band (from the original chromatography) was extracted and re-

chromatographed (p.l.c., toluene–ethyl acetate, 39:1, fifteen developments) to give three bands of which the least mobile was extracted and found to be a mixture of 3-azido-4,6-di-*O*-benzyl-3-deoxy-D-allal (**7**) and 4,6-di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl azide (**8**) in the ratio of 82:18; ν_{max}^{film} 2100 (N_3), 1642 (–C=C–O–), and 1250 cm^{-1} (–C–O–C); ^{1}H-n.m.r.: δ 7.25–7.50 (m, 10 H, benzyl aromatic protons), 6.52 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.50–4.95 (m, 5 H, H-2 and benzyl CH_2), and 3.70–4.27 (m, 5 H, H-3,4,5,6,6′); *m/e* 351.158, M^+ requires 351.158.

All of the remaining bands in the three chromatographic developments were mixtures of compounds **4**, **5**, **7**, and **8**, and these were combined and re-chromatographed as before.

(*b*) *Benzyl 4,6-di-*O*-benzyl-2,3-dideoxy-α,β-*D*-*erythro*-hex-2-enopyranoside*[4] (**9** + **6**): $x = 0.75$, $y = 3$, yield 83% (see Table I) (based on reacted starting-material), together with 5% of unreacted **6** and **9**. Separation was effected as described in (*a*).

(*c*) *3-Azido-4,6-di-*O*-benzyl-3-deoxy-D-glucal* (**4**) *and 4,6-di-*O*-benzyl-2,3-dideoxy-β-D-erythro-hex-2-enopyranosyl azide* (**5**): $x = 0.75$, $y = 3$, yield 40% (see Table I).

(*d*) *3-Azido-4,6-di-*O*-benzyl-3-deoxy-D-allal* (**7**) *and 4,6-di-*O*-benzyl-2,3-dideoxy-α-D-erythro-hex-2-enopyranosyl azide* (**8**): $x = 0.65$, $y = 3$, yield 76% (see Table I).

(*e*) *3-O-Acetyl-4,6-O-benzylidene-D-allal*[8] (**10**): $x = 0.45$, $y = 3$, yield 79% (based on reacted starting material), together with 5% of unreacted **10**. The products were separated as follows. The residue was dissolved in methanol (50 mL) and treated with sodium (5 mg) for 16 h at room temperature. The solution was made neutral with solid carbon dioxide and the solvent evaporated to give a solid that was partitioned between water (200 mL) and dichloromethane (50 mL). The organic phase was washed with water, dried, and the solvent removed. Chromatography (p.l.c., acetone–hexane, 1:9, five developments) resolved the mixture into four fractions to give (in increasing order of mobility) 4,6-*O*-benzylidene-D-allal (**11**; 25 mg, corresponding to 30 mg of unreacted starting material), m.p. 84–85°, $[\alpha]_D^{25}$ +209° (*c* 1.25) (lit.[9] m.p. 84–85°, $[\alpha]_D^{25}$ +209.5°); a mixture of 3-azido-4,6-*O*-benzylidene-3-deoxy-D-allal (**12**) and 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-eno-pyranosyl azide (**20**) (315 mg, 44%); and 3-azido-4,6-*O*-benzylidene-3-deoxy-D-glucal (**15**; 72 mg, 15%). The mixture of **12** and **20** constituted the second and third most-mobile bands, and was converted into pure crystalline **12** upon evaporation of the solvent.

3-Azido-4,6-*O*-benzylidene-3-deoxy-D-allal (**12**) had m.p. 77.5° (from ether–hexane), $[\alpha]_D^{22}$ +219° (*c* 1.08); ν_{max}^{Nujol} 2110 (N_3) and 1640 cm^{-1} (–C=C–O); ^{1}H-n.m.r.: δ 7.12–7.67 (m, 5 H, aromatic protons), 6.39 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 5.57 (s, 1 H, H-7), 4.80 (t, 1 H, $J_{2,3}$ 6.0 Hz, H-2), and 3.70–4.57 (m, 5 H, H-3,4,5, 6ax,6eq).

Anal. Calc. for $C_{13}H_{13}N_3O_3$: C, 60.2; H, 5.05. Found: C, 60.4; H, 5.1.

3-Azido-4,6-*O*-benzylidene-3-deoxy-D-glucal (**15**) had m.p. 80° (from aqueous 2-propanol), $[\alpha]_D^{22}$ −112° (*c* 1.07); ν_{max}^{Nujol} 2105 (N_3) and 1642 cm^{-1} (C=C–O–);

^{1}H-n.m.r.: δ 7.28–7.64 (m, 5 H, aromatic protons), 6.41 (dd, 1 H, $J_{1,2}$ 6.0, $J_{1,3}$ 2.0 Hz, H-1), 6.65 (s, 1 H, H-7), 4.70 (dd, 1 H, $J_{2,3}$ 1.8 Hz, H-2), 4.11–4.50 (m, 2 H, H-3,6eq), and 3.70–4.10 (m, 3 H, H-4,5,6ax).

Anal. Calc. for $C_{13}H_{13}N_3O_3$: C, 60.2; H, 5.05. Found: C, 59.9; H, 5.3.

(*f*) *Methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-*D-erythro-*hex-2-enopyranoside*[10] (**21**): $x = 0.45$, $y = 3$, yield 61% (based on reacted starting material), together with 41% of **21** and **25**. The products were separated as follows. The residue was chromatographed (p.l.c., toluene–ethyl acetate, 19:1, five developments) to give two bands which were extracted. The less mobile band contained a mixture of **21** and **25** (102 mg, 41%). The more mobile band was re-chromatographed (p.l.c., acetone–hexane, 1:9, three developments) to give two bands which were extracted. The upper band contained 3-azido-4,6-*O*-benzylidene-3-deoxy-D-glucal (**15**, 16 mg) and the lower one, 3-azido-4,6-*O*-benzylidene-3-deoxy-D-allal (**12**, 74.5 mg).

(*g*) *Methyl 4,6-*O*-benzylidene-2,3-dideoxy-β-*D-erythro-*hex-2-enopyranoside*[11] (**25**): $x = 0.45$, $y = 3$, yield 36% (based on reacted starting material), together with a mixture of **12** and **15** (21%), and a product (9%) of lower R_F value, which was not identified. The products were separated as in (*e*).

(*h*) *4,6-*O*-Benzylidene-3-*O*-methyl-*D-*allal*[12] (**13**): $x = 0.45$, $y = 3$, yield 48% (based on reacted starting material), together with 34% of unreacted **13**, and methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**21**, 10%). The products were separated as follows. The residue was chromatographed (p.l.c., hexane–toluene–ethyl acetate, 10:10:1, two developments) to give three bands which were extracted. The least mobile band was identified as unreacted starting-material, m.p. 69.5–70°, $[\alpha]_D^{22}$ +181° (lit.[12] m.p. 69–70°, $[\alpha]_D$ +181.7°). The middle band was recrystallized from ether–hexane to afford colourless needles of **21**, m.p. 115–116°, $[\alpha]_D^{20}$ +132° (lit.[10] m.p. 117–118°, $[\alpha]_D^{22}$ +124°). A second chromatography of the most mobile fraction (p.l.c., acetone–hexane, 1:9, three developments) afforded 3-azido-4,6-*O*-benzylidene-D-glucal (**15**, 10.3 mg), and the isomeric azido-allal (**12**, 58.6 mg).

(*i*) *3-Azido-4,6-*O*-benzylidene-3-deoxy-*D-*allal* (**12**): $x = 0.45$, $y = 3$; yield of isolated starting material, 93%.

(*j*) *3-Azido-4,6-*O*-benzylidene-3-deoxy-*D-*glucal* (**15**): $x = 0.45$, $y = 3$; yield of isolated starting material, 92%.

(*k*) *3-*O*-Acetyl-4,6-*O*-benzylidene-*D-*glucal*[9] (**17**): $x = 0.45$, $y = 3$; yield of unreacted starting material, 94%.

(*l*) *4,6-*O*-Benzylidene-3-*O*-methyl-*D-*glucal*[12] (**18**): $x = 0.45$, $y = 3$; yield of unreacted starting material, 91%.

*Benzylation of 3-azido-3-deoxy-*D*-glucal.* — A mixture of 3-azido-3-deoxy-D-glucal[1] (170 mg) and silver oxide (0.5 g) in *N*,*N*-dimethylformamide (10 mL) was treated with α-bromotoluene (0.5 mL) and stirred for 24 h at room temperature. A second portion of silver oxide (0.2 g) was added, and stirring continued for a further 24 h, after which time the solids were removed by filtration. Processing afforded a syrup that was chromatographed (p.l.c., acetone–hexane, 1:5, two developments)

to give a mixture of 3-azido-4,6-di-*O*-benzyl-3-deoxy-D-glucal (**4**) and 4,6-di-*O*-benzyl-2,3-dideoxy-*β*-*erythro*-hex-2-enopyranosyl azide (**5**) (256 mg, 76%), indistinguishable from that obtained as already described.

*Benzylation of 3-azido-3-deoxy-*D*-allal.* — A mixture[1] of 3-azido-3-deoxy-D-allal and 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl azide (170 mg, greatly enriched in the former isomer) was treated with silver oxide and α-bromotoluene in *N*,*N*-dimethylformamide as described for the glucal isomer. Chromatography (as before) yielded a mixture of 3-azido-4,6-di-*O*-benzyl-3-deoxy-D-allal (**7**) and 4,6-di-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl azide (**8**) (182 mg, 52%), indistinguishable from that already obtained.

*3-Acetamido-4,6-*O*-benzylidene-3-deoxy-*D*-allal* (**14**). — A mixture of 3-azido-4,6-*O*-benzylidene-3-deoxy-D-allal (**12**, 200 mg) and lithium aluminium hydride (150 mg) was boiled under reflux in ether (50 mL) for 0.5 h. The excess of hydride was then made neutral with methanol, the solids were filtered through Celite, washed with methanol, and the solvent was evaporated. The residue was dissolved in pyridine (10 mL) and treated with acetic anhydride (1.0 mL) for 16 h at room temperature. Isolation afforded a crystalline residue (192 mg, 90%) that was recrystallized from ether to afford **14** as colourless needles, m.p. 140–141°, $[\alpha]_D^{22}$ +159° (*c* 1.15); ^{1}H-n.m.r.: δ 7.22–7.60 (m, 5 H, aromatic protons), 6.69 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 6.27 (bd, 1 H, $J_{3,H}$ 8.0 Hz, NH), 5.58 (s, 1 H, H-7), 5.00 (t, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 4.70 (m, 1 H, H-3), 3.65–4.50 (m, 4 H, H-4,5,6ax,6eq), and 1.91 (s, 3 H, *N*-acetyl).

Anal. Calc. for $C_{15}H_{17}NO_4$: C, 65.4; H, 6.2; N, 5.1. Found: C, 65.4; H, 6.3; N, 5.0.

*3-Acetamido-4,6-*O*-benzylidene-3-deoxy-*D*-glucal* (**19**). — 3-Azido-4,6-*O*-benzylidene-3-deoxy-D-glucal (**15**, 195 mg) was reduced with lithium aluminium hydride and then acetylated as described for **12**, to give a crystalline solid (172 mg, 83%) that was recrystallized from acetone–ethyl acetate to give **19** as colourless needles, m.p. 248–250° (dec.), $[\alpha]_D^{20}$ −70.0° (*c* 0.30); ^{1}H-n.m.r.: δ 7.22–7.60 (m, 5 H, aromatic protons), 6.42 (dd, 1 H, $J_{1,2}$ 6.0, $J_{1,3}$ 1.9 Hz, H-1), 5.65 (s, 1 H, H-7), 4.57 (dd, 1 H, $J_{2,3}$ 1.8 Hz, H-2), 4.28 (m, 1 H, H-3), 3.30–4.18 (m, 5 H, H-4,5,6ax,6eq, NH), and 1.83 (s, 3 H, *N*-acetyl).

Anal. Calc. for $C_{15}H_{17}NO_4$: C, 65.4; H, 6.2; N, 5.1. Found: C, 65.1; H, 6.4; N, 5.0.

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