Rearrangement of α-D-Glucopyranose 4-Sulphonates to 1,4-Anhydro-β-D-Galactopyranoses

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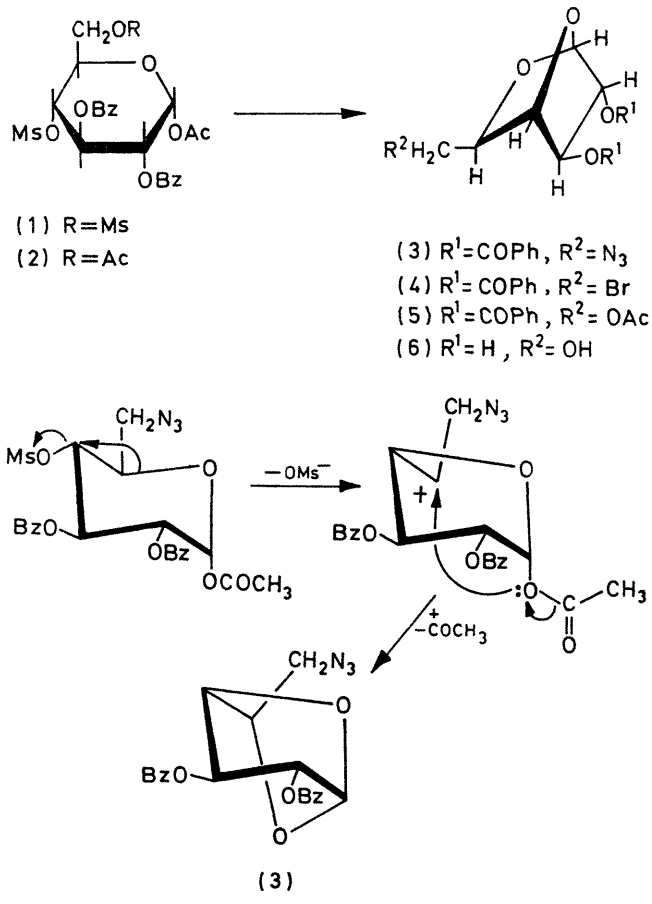
Summary α-D-Glucopyranose derivatives with a sulphonyl group at C-4 and an acetyl group at C-1 undergo rearrangement to 1,4-anhydro-β-D-galactopyranoses on treatment with sodium azide; the replacement of a terminal azide group by bromide on treatment with hydrogen bromide is reported.

4-SULPHONATES of methyl α-D-glucopyranoside readily undergo S_N2 displacement of the sulphonyloxy-groups by nucleophiles such as azide, benzoate, thiocyanate, *etc.*[1] However, when the azide replacement was applied to the 1-*O*-acetyl analogue, namely 1-*O*-acetyl-2,3-di-*O*-benzoyl-4,6-di-*O*-mesyl-α-D-glucopyranose (**1**) the expected 4,6-diazido-galactopyranose was not formed. Instead a mono-azide was isolated in *ca.* 50% yield which had no acetyl or mesyl groups. The ^{1}H n.m.r. spectrum suggested that a profound conformational and/or configurational change had occurred because the largest splitting in the observed multiplets for 1-H, 2-H, 3-H, and 4-H was only 2·5 Hz (Table).

^{1}H *N.m.r. parameters of* 1,4-*anhydro*-β-D-*galactopyranose derivatives*[a]

	(3)[b]	(4)[c]	(5)[b]
1-H	3·97d	3·86d	4·00d
2-H	4·79qu	5·07q	4·78qu
3-H	4·72d	4·45s	4·73d
4-H	5·16d	5·00q	5·09d
5-H	5·90t	5·59sp	5·9 cm
6a-H, 6b-H	6·77d	6·21t, 6·43q	
$J_{1,2}$	2·5	3·7	2·5
$J_{2,3}$	1·5	0	1·5
$J_{2,4}$	1·5	1·6	1·5
$J_{3,4}$	0	0	0
$J_{4,5}$	0	2·5	0
$J_{5,6a}$	6·0	8·6	—
$J_{5,6b}$	6·0	6·0	—
$J_{6a,6b}$	—	10·0	—

[a] s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, sp = septet, cm = complex multiplet; [b] in deuteriopyridine; [c] in deuteriochloroform.



SCHEME

The mono-azide reacted with hydrogen bromide in acetic acid with vigorous effervescence to give a bromine-containing product with no azide group. This reaction, we have found, is characteristic of a terminal azide group; full details will appear elsewhere. The mass spectrum of the bromide contained a peak at *m/e* 339 which corresponded to $C_{19}H_{15}O_6$, *i.e.* $[M - 94(CH_2Br)]$, showing that the bromide was a 6-bromo-anhydro-hexose dibenzoate. The ^1H n.m.r. spectrum suggested that it was a 1,4-anhydro-galactopyranose (**4**). The spectrum of the mono-azide anhydride was largely first-order and decoupling experiments enabled each resonance to be assigned to a ring hydrogen (Table). By analogy with the ^1H n.m.r. parameters of known 1,4-anhydro-hexopyranose derivatives, borneol,[3] and isoborneol[4] derivatives it was deduced that 2-H must be equatorial because of the finite value of $J_{1,2}$ (2·5). Had the 2-hydrogen been axial the dihedral angle between 2- and 1-H would have been 90° giving rise to a zero coupling. Likewise the zero values for $J_{3,4}$ and $J_{4,5}$ suggest that 3-H and 4-H must be axial. These data are in complete accord with the suggested structure (**3**). The spectra of the 6-bromide (**4**) and the 6-*O*-acetate (**5**) (see later) were similar except that the value for $J_{4,5}$ in (**4**) was 2·5 rather than zero.

To test the generality of this rearrangement, it was applied to 1,6-di-*O*-acetyl-2,3-di-*O*-benzoyl-4-*O*-mesyl-α-D-glucopyranose (**2**) and the corresponding 1,4-anhydride (**5**) was isolated in 67% yield. De-*O*-acylation of (**5**) afforded syrupy 1,4-anhydro-β-D-galactopyranose (**6**), which underwent hydrolysis to galactose in the presence of acid. Furthermore, it was simultaneously hydrolysed and oxidised with nitric acid to give mucic acid (galactaric acid).

A possible mechanism for the rearrangement is by a ring contraction involving cleavage of the C-5–5-O bond and elimination of the sulphonyloxy-group by the negatively charged 5-O, followed by attack of the C-5 carbonium ion by the 1-O and then loss of the 1-acetyl group as shown in the Scheme. This type of ring contraction has already been observed in displacement reactions of pyranoside 4-sulphonates in which direct displacement is inhibited by the presence of an axial substituent at C-2.[1,5,6] Furthermore, the migration of a 1-O on to C-5 of a hexofuranoside has also been observed.[1,5] Consequently the steps in the rearrangement are analogous to other rearrangements in carbohydrates, but it is difficult to explain the difference between the glycoside and the corresponding 1-*O*-acetyl derivative (**1**).

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