

The Stereochemistry of the Stork Silyl Methylene Radical Cyclisation in an Annulated Sugar Derivative

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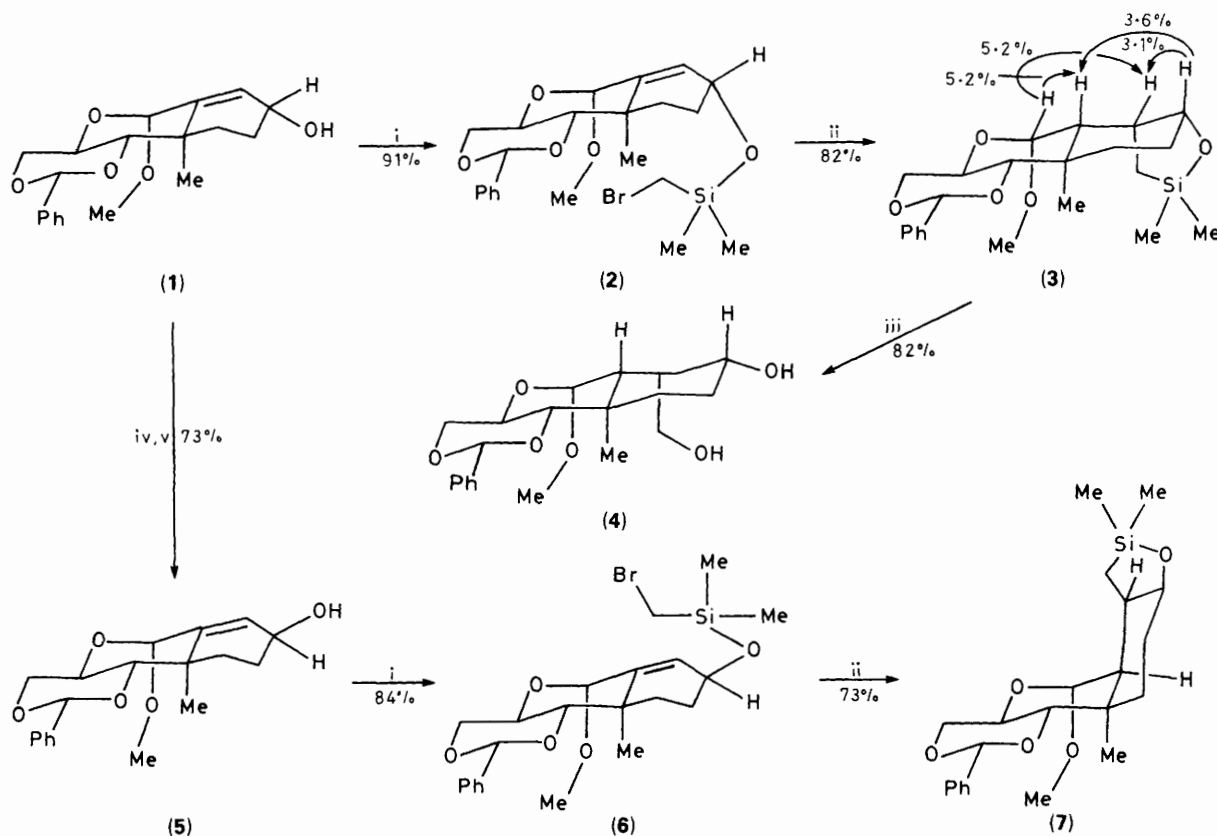
Annulated sugar derivatives with α - and β -allylic alcohol groups have been subjected to the Stork silyl methylene radical cyclisation reaction, in both cases, *trans*-addition of the radical occurred to produce a new fused ring system.

There is considerable current interest in the synthetic applications of radical chemistry.¹ One of the most original contributions to this area involves the conversion of an allylic alcohol to a fused ring system *via* a cyclisation of a silyl methylene radical.² As part of a synthetic strategy we have carried out this reaction on two allylic alcohols derived from the product of a Robinson annulation on a glucose methyl ketone.³ Several possible reaction pathways were in theory open to the molecule, however in both cases *trans*-addition of the radical and a hydrogen atom took place.

The first example is shown in Scheme 1, where the alcohol (**1**)[†] was produced by the *L*-Selectride reduction of the

corresponding ketone.³ Reaction of (bromomethyl)chlorodimethylsilane produced the silyl ether (**2**) which underwent a radical cyclisation reaction on treatment with tributyltin hydride to give the tetracyclic structure (**3**) as a white crystalline solid m.p. 155–157 °C, the ¹H NMR spectrum and the observed nuclear Overhauser effect (NOE) experiments shown on the formula of (**3**) were entirely consistent with the structure assigned to (**3**). Treatment with KF and hydrogen peroxide produced the diol (**4**) in 82% yield. These results are entirely in accord with expectations from the literature.² Our synthetic route required a different stereochemical outcome of the radical cyclisation reaction and one way to achieve this would be to invert the alcohol (**1**) and for it to undergo a *cis* radical cyclisation. We needed to know if the stereochemical constraints on the ring system would cause it to undergo such a *cis* radical cyclisation.

[†] All new compounds gave satisfactory spectroscopic data, and correct microanalytical figures or high resolution mass spectral data.



Scheme 1. Reagents: *i*, $\text{ClSiMe}_2\text{CH}_2\text{Br}$, Et_3N ; *ii*, Bu_3SnH , azoisobutyronitrile (AIBN); *iii*, H_2O_2 , KF ; *iv*, PPh_3 , diethylazodicarboxylate, PhCO_2H ; *v*, K_2CO_3 , MeOH .

The second part of Scheme 1 describes the inversion of the α -alcohol (1) using the Mitsunobu procedure,⁴ followed by hydrolysis which leads to the β -alcohol (5). Conversion to the silyl ether proceeded under the normal conditions to give the β -bromosilane (6). Radical cyclisation occurred on treatment with tributyltin hydride to produce the tetracyclic structure (7) m.p. 142–145 °C, where the radical and the hydrogen atom have again added *trans*, despite the fact that this results in the formation of two *cis* ring fusions. The structure of (7) was confirmed by an *X*-ray crystal structure.[‡]

In conclusion we have proved that the Stork radical cyclisation reaction occurs with the *trans* stereochemistry in

two epimeric sugar derivatives despite the fact that this leads to the doubly *cis* fused tetracyclic ring system (7).

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[‡] *Crystal data*: orthorhombic, space group $P2_12_12_1$, $a = 18.851$, $b = 15.767$, $c = 7.547$ Å, $Z = 4$, $\mu = 0.96$ cm⁻¹; λ (Mo- K_α) = 0.7107 Å, $F(000) = 872$, final R 0.085. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.