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 ^{1}H 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.

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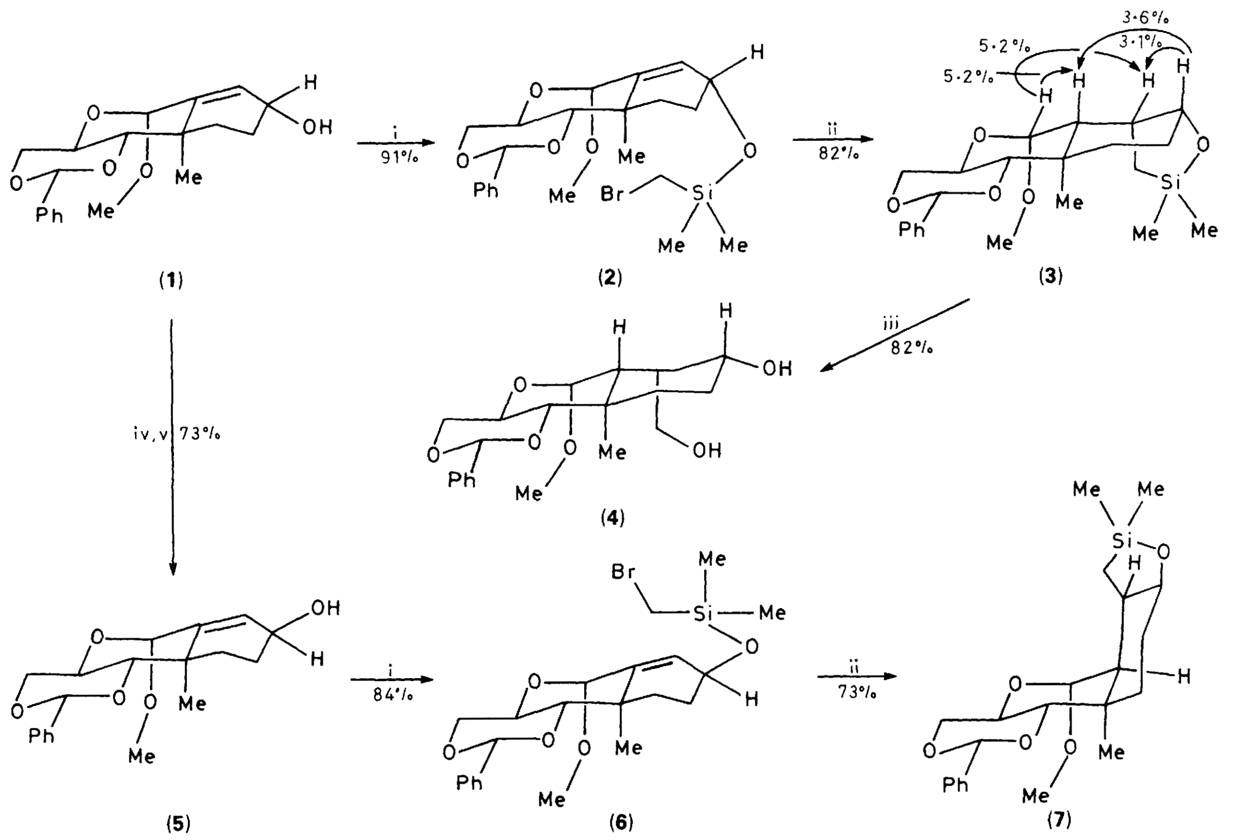
† All new compounds gave satisfactory spectroscopic data, and correct microanalytical figures or high resolution mass spectral data.



Scheme 1. *Reagents*: i, $ClSiMe_2CH_2Br$, 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**).

We acknowledge the S.E.R.C. for supporting this work and the assistance of Dr. D. R. Russell, Dr. J. Fawcett, and Lesley Sherry in the *X*-ray structure determination.

Received, 3rd October 1989; Com. 9/04201F

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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, μ = 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.