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Tether-directed synthesis of highly substituted oxasilacycles *via* an intramolecular allylation employing allylsilanes

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Abstract

Background: Using a silyl tether to unite an aldehyde electrophile and allylsilane nucleophile into a single molecule allows a subsequent Lewis-acid-mediated allylation to proceed in an intramolecular sense and therefore receive all the benefits associated with such processes. However, with the ability to cleave the tether *post* allylation, a product that is the result of a net intermolecular reaction can be obtained. In the present study, four diastereoisomeric β-silyloxy-α-methyl aldehydes, which contain an allylsilane tethered through the β-carbinol centre, have been prepared, in order to probe how the relative configuration of the two stereogenic centres affects the efficiency and selectivity of the intramolecular allylation.

Results: *Syn*-aldehydes, ***syn*-4a** and ***syn*-4b**, both react poorly, affording all four possible diastereoisomeric oxasilacycle products. In contrast, the *anti* aldehydes ***anti*-4a** and ***anti*-4b** react analogously to substrates that lack substitution at the α-site, affording only two of the four possible allylation products.

Conclusion: The outcome of the reaction with *anti*-aldehydes is in accord with reaction proceeding through a chair-like transition state (T.S.). In these systems, the sense of 1,3-stereoinduction can be rationalised by the aldehyde electrophile adopting a pseudoaxial orientation, which will minimise dipole-dipole interactions in the T.S. The 1,4-stereoinduction in these substrates is modest and seems to be modulated by the R substituent in the starting material. In the case of the *syn*-substrates, cyclisation through a chair T.S. is unlikely as this would require the methyl substituent α to the reacting carbonyl group to adopt an unfavourable pseudoaxial position. It is therefore proposed that these substrates react through poorly-defined T.S.s and consequently exhibit essentially no stereoselectivity.

Background

*Intra*molecular reactions offer distinct advantages over their *inter*molecular counterparts providing the tethering unit, which connects the reacting functionalities, is neither too long such that the reaction resembles an intermolecular process, nor too short, in which case geometrical constraints can physically prevent the reaction. When these conditions on the tether are satisfied, however, the proximity of the reacting partners, combined with a reduction in the degrees of freedom in the system, render the intramolecular reaction more entropically and kinetically favourable. This can result in a more stereo-, regio- and chemoselective process, which is often reflected in an increased yield of the desired product.