MECHANISTIC INSIGHTS INTO THE SILYL-PRINS REACTION

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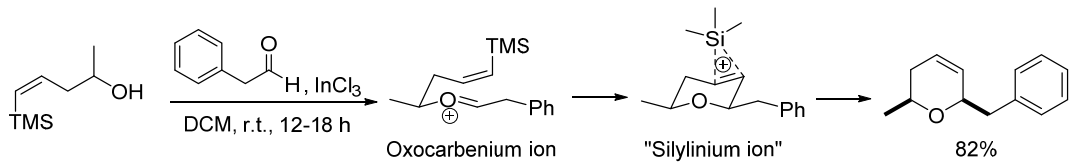
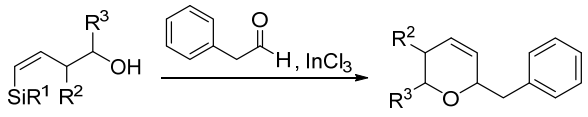
Heterocycles are a key structural motif found in the majority of pharmaceuticals and natural products. The Prins and silyl-Prins reactions are an effective way of forming various oxygen, nitrogen and sulphur heterocycles, with many examples being offered towards the synthesis of a wide range of biologically relevant molecules.

Our work has focused on elucidating the mechanism of these reactions using a mixture of computational and experimental methods, in order to gain an insight into the reactive intermediates and transition states involved and offer potential developments and novel applications of the Prins and silyl-Prins cyclisation.

Based on the known reaction between (*Z*)-4-(TMS)-4-penten-2-ol and phenylacetaldehyde [1] and our existing mechanistic work on the Prins cyclisation [2], we have carried out the first computational study of the silyl-Prins reaction to offer a full reaction pathway. The reaction proceeds *via* an oxocarbenium ion intermediate which undergoes direct cationic cyclisation to a "silylinium" ion, whereby non-vertical silicon hyperconjugation stabilizes the carbocation to release the dihydropyran product.



Furthermore, we have investigated the influence of different silyl groups on carbocation stability in the silyl-Prins reaction, by examining the silicon hyperconjugation offered by each group. This has led us towards the aim of synthesizing fluorinated dihydropyrans, whereby the destabilizing effect of the fluorine atoms on the carbocationic species may be overcome by the beta-silicon effect.



R^1 = Me_3, Et_3, $^iPr_3$, $^tBuMe_2$, $^tBuPh_2$
R^2 = H_2, F, F_2, Me, Me_2
R^3 = H_2, alkyl, aryl

[1] A. P. Dobbs and S. Martinović, *Tetrahedron Lett.*, 2002, **43**, 7055-7057

[2] L. C. Evans, A. P. Dobbs and J. Pang, *in preparation*, 2019