

Mechanistic Studies and Applications of An Unusual (4+3) Cycloaddition

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The classical (4+3) cycloaddition is a ($4\pi + 2\pi$) reaction, isoelectronic with the Diels Alder reaction. The 2π electrons on a three atom fragment are typically carbocations. The most common of these are 2-oxyallyl cations which are stabilized by π -donation.

When we first considered the use of epoxy enolsilanes as dienophiles in the (4+3) cycloaddition, the main motivation was that this method could afford cycloadducts with additional functional groups, making them versatile intermediates for synthesis. When we continued our investigations, we found that the reaction was unexpectedly stereoselective with respect to the epoxide.

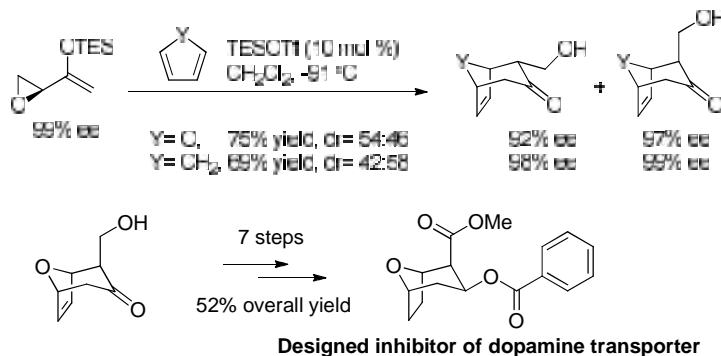
However, when the intermolecular (4+3) cycloadditions of enantiomerically pure epoxy enolsilanes and dienes were found to proceed with high conservation of ee, this was definitive proof that the mechanism does not involve the putative

oxyallylation as intermediate, and the reaction does not fit into the typical (4+3) cycloaddition paradigm.

It is clear that there is a higher degree of organization and stereochemical integrity than previously expected, but what is this chiral intermediate? Computational studies showed that the major dienophile is the activated epoxide, and not an allylcation, revealing that a nucleophile as weak as a diene can participate in backside attack of the activated species. Furthermore, we have also found that triflate can also participate as nucleophile, resulting in an observable inversion of stereochemistry.

This conservation of ee is also observed for the cycloadditions with aziridinyl enolsilanes, for the synthesis of optically pure bicyclic alkaloids.

Our mechanistic studies and how these reactions have been applied to synthetic problems will be presented.



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