

STEREOSELECTIVITY IN FURFURYL CATION (4+3) CYCLOADDITIONS

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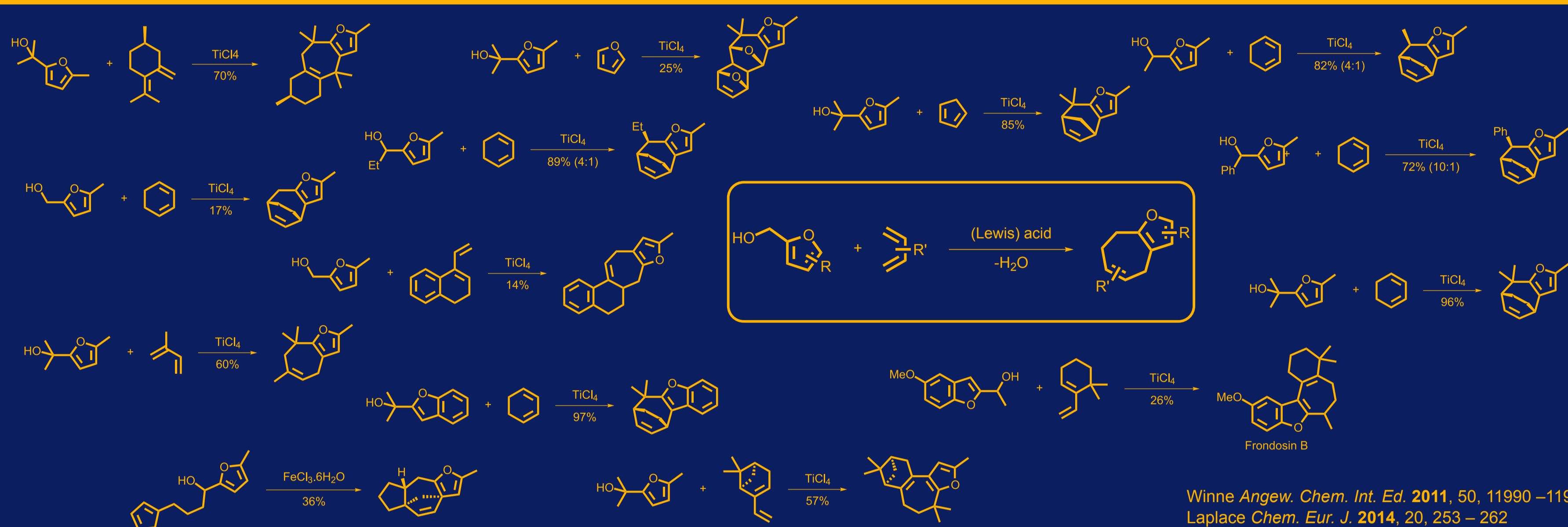
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1. Introduction

In 2009 Pattenden and Winne discovered a novel dehydrative (4+3)-cycloaddition reaction between furfuryl alcohols and conjugated 1,3-dienes. Since then this Lewis or Brønsted acid catalyzed reaction already led to a myriad of intriguing polycyclic structures of which some exhibit the cyclic core of natural products.

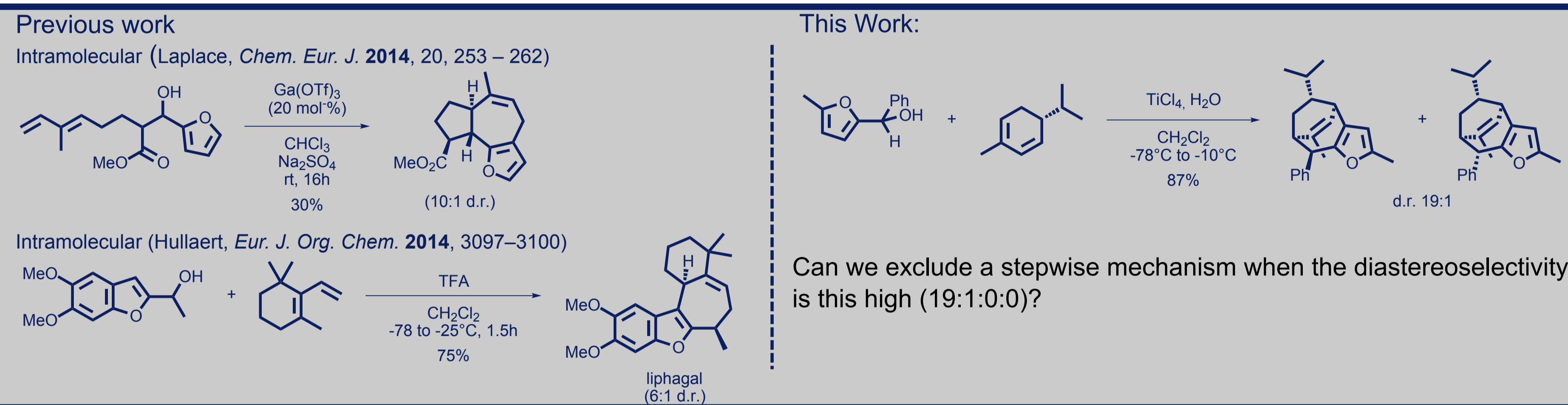
Until now the exact mechanism of this smooth cycloaddition reaction remained unresolved. Selectivities regarding stereochemistry have cast doubts on whether the reaction proceeds through a stepwise or concerted mechanism.

Based upon observations in the cycloaddition of furfuryl alcohols with phellandrene, we propose a mechanistic rationale for the regio- and stereoselectivity in this reaction.

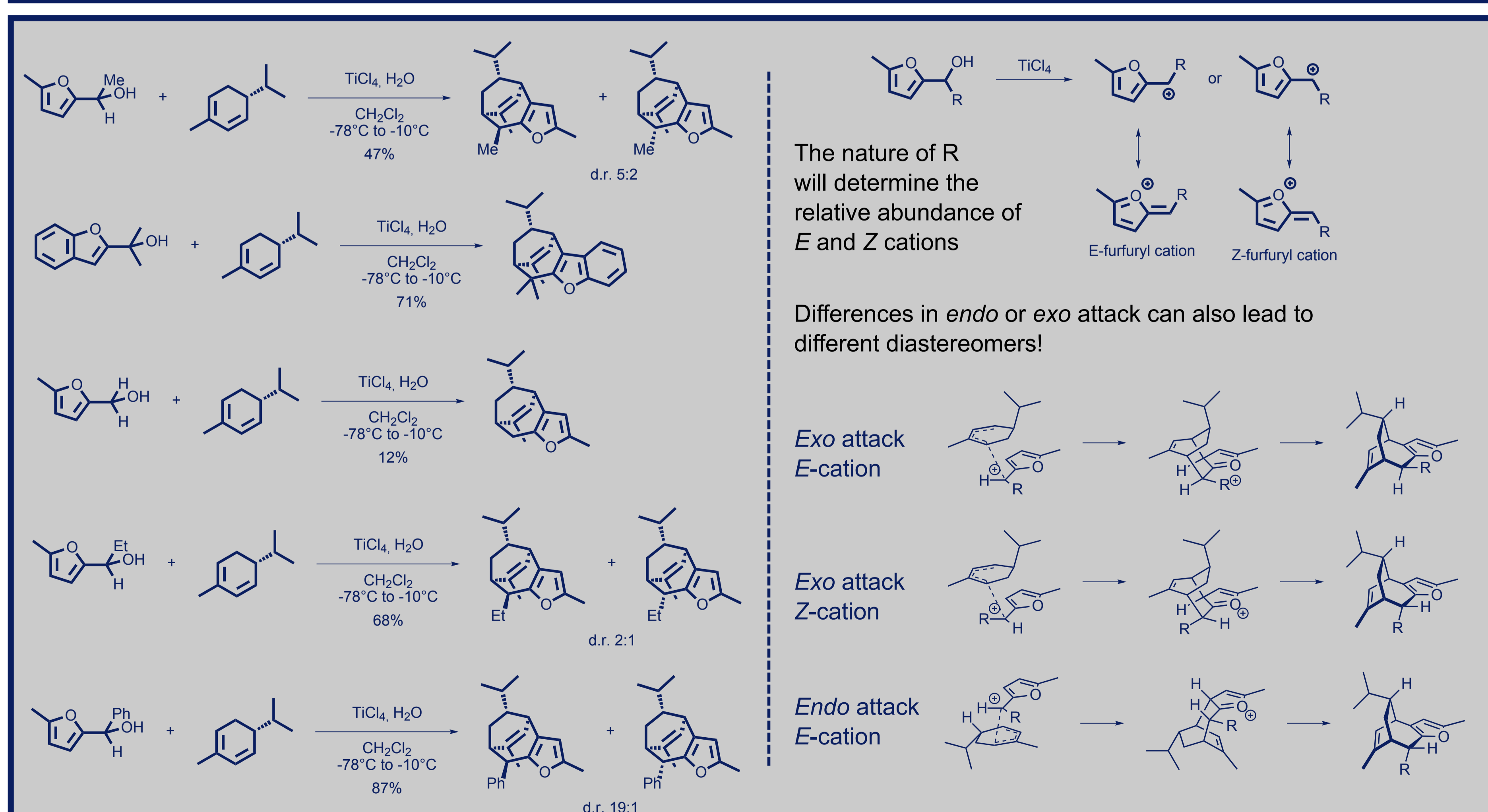
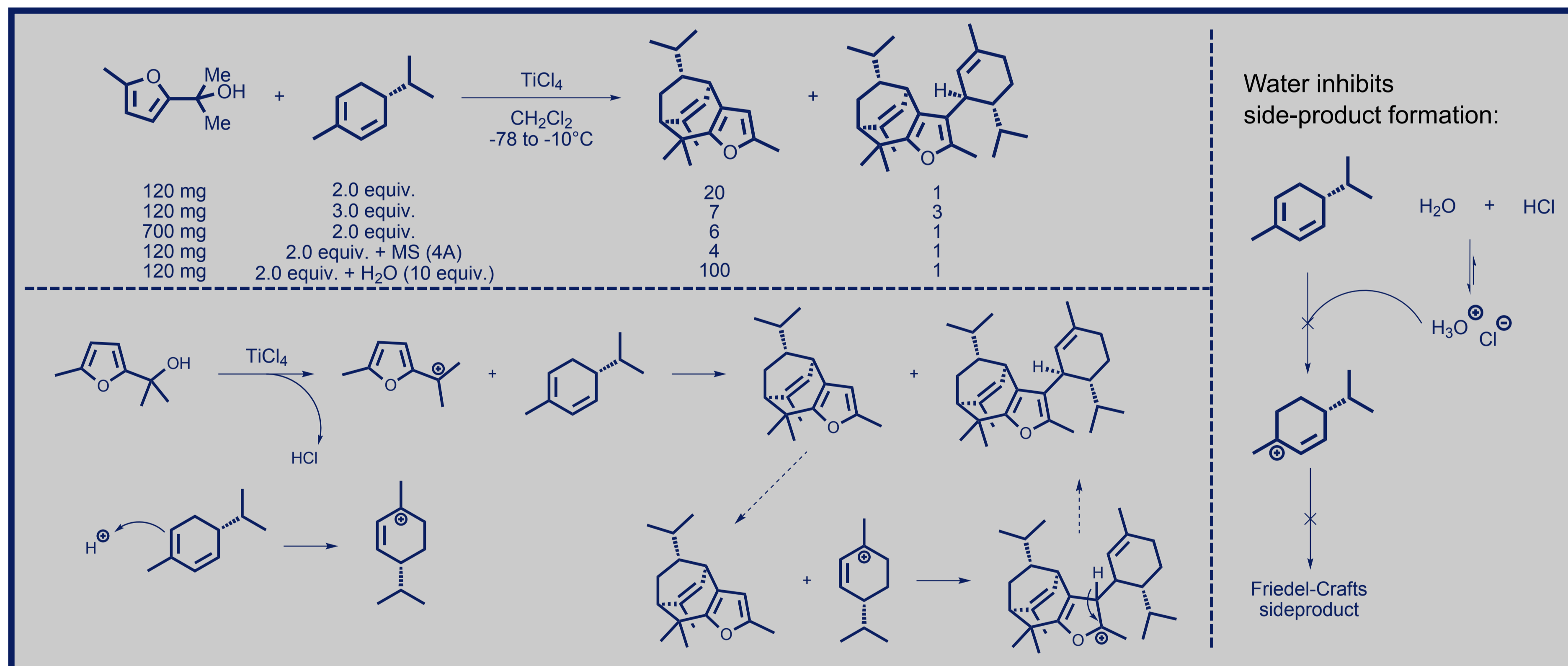


Winne *Angew. Chem. Int. Ed.* 2011, 50, 11990–11993
Laplace *Chem. Eur. J.* 2014, 20, 253–262
Laplace *Synlett* 2015, 26, 467–470

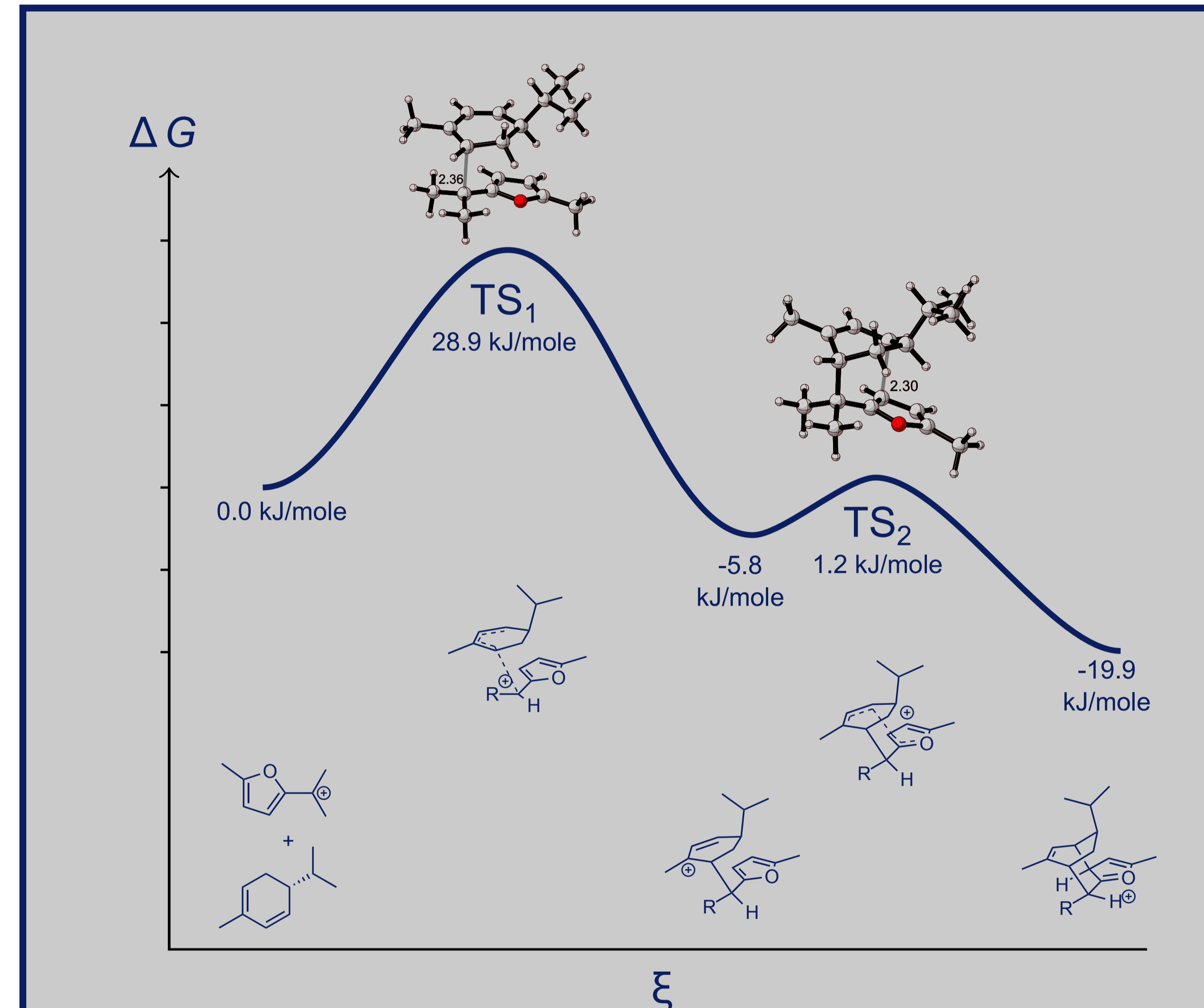
2. Stereoselective furfuryl cation (4+3) cycloadditions



3. Results

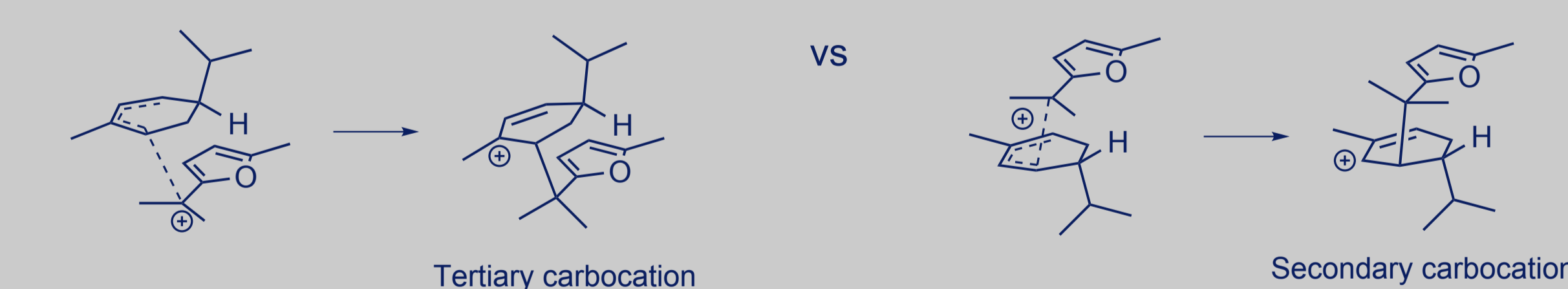


4. Transition State Model

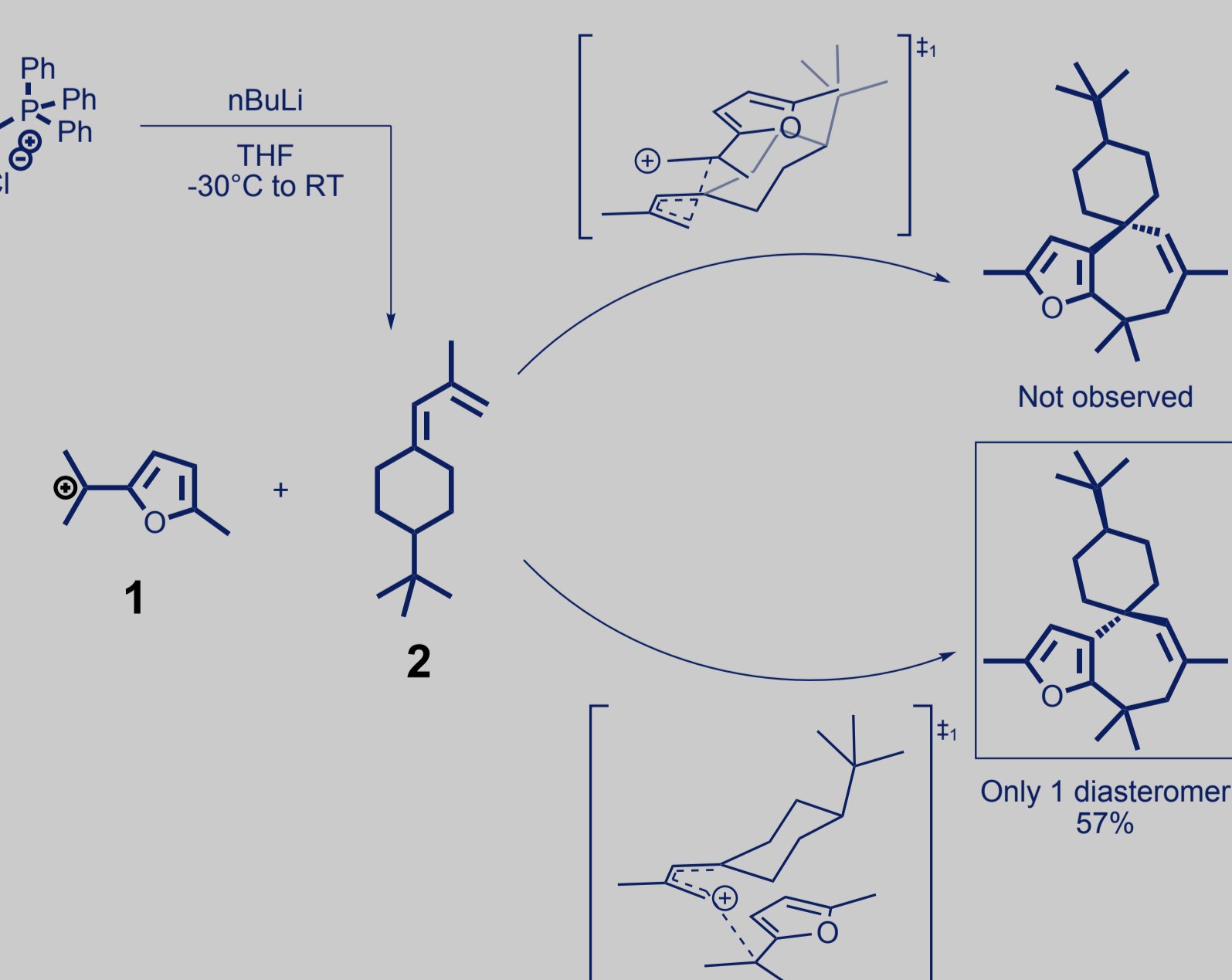


Calculations suggest a stepwise mechanism in which the first electrophilic attack is the rate determining step (RDS). The transition state of the RDS shows a high degree of preorganization which might explain why this reaction proceeds with such a high degree of stereoselectivity. In addition the model also suggests a preference for *exo* attack. This is usually seen in cationic cycloadditions since in this way, Coulombic repulsion of the partial positive charges is minimized.

The regioselectivity can be explained by the stability of the intermediate carbocation:



The cycloaddition between furfuryl cation 1 and diene 2 led to only one diastereomer which is indeed the product that can be expected when the RDS shows a high degree of preorganization.



6. Conclusions and perspectives

A transition state model for the (4+3)-cycloaddition was proposed. Based upon the reaction between furfuryl alcohols and phellandrene, a synthetic and computational effort was made to rationalize the observed stereo- and regioselectivities which were seen in these reactions. The reaction mechanism seems to involve a highly preorganized transition state in the rate determining step, explaining the found selectivities.

