Hessisches Kompetenzzentrum
für Hochleistungsrechnen

Bidentate Lewis-Acid Catalysed Diels-Alder Reactions



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Introduction

Novel methods to access complex molecular structures open new avenues for applications in medical as well as material sciences. That is the reason why we investigate inverse electron-demand Diels-Alder (IEDDA) reactions of phthalazine. Starting from simple reactants like aldehydes, amines and phthalazine, complex structures can be generated within one step executing such IEDDA. But, phthalazine is an unreactive species in this context. Therefore, it has to be activated, for example by a Lewis-acid catalyst, like dimethyl-9,10-diboraanthracene (DBA). One major aspect of such reactions is the energy gap between the LUMO (lowest unoccupied molecule orbital) of phthalazine and the HOMO (highest occupied molecule orbital) of the dienophile. The orbital energies of phthalazine are lowered by bidentate coordination to the Lewis-acid catalyst, which enables the reaction. Currently, we focus on the development of chiral bidentate Lewis-acids to execute these transformations in an enantiomeric fashion since chirality plays a crucial role, especially in the context of biological active compounds. In this process, the 3D structure of the phthalazine-catalyst complex is of particular interest.

Methods

Both, energy gaps and geometries can be calculated by computational chemistry. We design chiral Lewis-acids and apply computational chemistry to modulate the binding behaviour of these candidates to phthalazine. Sterics in addition to non-covalent interactions determine the favourable conformation of the phthalazine-catalyst complex and control the orientation of

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the incoming dienophile. Thus, the major enantiomer of the *ortho*-quinodimethane intermediates should be converted into the desired enantiomeric product.

Results

The most promising catalyst candidates are based on the 9,10-diboraanthracene scaffold, which is functionalized with various chiral substituents. We developed synthesis strategies to prepare them and already synthesised some of them.

Outlook

At the moment we concentrate on the synthesis and characterisation of these bidentate Lewis-acids. In parallel we apply them to IEDDA reactions and investigate the enantiomeric excess of the products.

Publications

Reference

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