

ASYMMETRIC MICHAEL-ADDITIONS CATALYZED BY ENVIRONMENTALLY BENIGN HETEROGENEOUS CHIRAL 1,2-DIAMINE DERIVATIVES

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Abstract

Asymmetric Michael additions of isobutyraldehyde to maleimides catalyzed by optically pure diamines and their sulfonamides were investigated to develop heterogeneous chiral catalysts for these reactions. Chiral solid materials were prepared by covalent bonding of the diamines on different functionalized organic and inorganic supports. The heterogeneous catalyst prepared by bonding optically pure 1,2-diphenylethane-1,2-diamine to polystyrene support was highly enantioselective, giving results approaching those obtained using soluble sulfonamide derivatives. The catalysts could be recycled a few times, retaining their activity followed by a small decrease in conversion, while still producing high – up to 97% – enantiomeric excess. These materials are the first efficient recyclable catalysts used in the enantioselective Michael-addition of aldehydes to maleimides.

Introduction

Asymmetric Michael-additions are among the most often-used stereospecific reactions for coupling organic molecules, widely applied for preparing optically pure fine chemicals. Succinimide derivatives may be obtained by the enantioselective addition of nucleophiles, such as aldehydes, to maleimides [1]. These reactions are efficiently catalyzed by chiral diamines and their derivatives, among which cyclohexane-1,2-diamines, 1,2-diphenylethylene-1,2-diamines, their sulfonamides and thiocarbamides are well-functioning chiral catalysts [2-4].

Until now heterogeneous chiral catalysts have not been used in these reactions, although these environmentally friendly, recyclable materials can serve as good alternatives for their soluble counterparts. A detailed study is of paramount importance for selecting the proper support, catalyst structure and the linker for the immobilization of these organocatalysts in order to obtain heterogeneous, recyclable catalysts. In our previous study, the Michael-additions of aldehydes to maleimides were carried out with commercial chiral catalysts in homogeneous media. Based on the results of this study we aimed to attempt the immobilization of the selected chiral 1,2-diamine catalyst using an appropriate linker over various inorganic and organic supports. Our goal was to develop a highly efficient, reusable heterogeneous chiral catalyst for the asymmetric Michael-addition of isobutyraldehyde to *N*-benzylmaleimide.

Experimental

The heterogeneous catalysts are prepared by coupling reactions in Merrifield flasks. The success of the immobilization process of the chiral compound was checked by FT-IR spectroscopy. We have immobilized optically pure cyclohexane-1,2-diamines or 1,2-diphenylethane-1,2-diamines using linkers having acidic, H-bond donor character, such as sulfonamide, thiocarbamide or squaramide groups over silica or polystyrene resin supports. In a typical reaction, the given amount of catalyst was introduced into a glass vial followed by the addition of the solvent and the reactants. The slurry was stirred magnetically or agitated in a shaker for the given reaction time, diluted with the solvent and the product solution was separated. Products resulted in the Michael-additions were analyzed by GC-MSD and GC-

FID using a chiral capillary column. Larger scale experiments were also carried out, the resulted products were purified by column chromatography for determination of the yields. The pure compounds were characterized by ^1H - and ^{13}C -NMR spectroscopy.

Results and discussion

Immobilization of chiral organocatalysts on insoluble supports is a convenient method to prepare enantioselective heterogeneous chiral catalysts. According to results obtained in homogeneously catalyzed reactions using optically pure 1,2-diamine-derived sulfonamides, anchoring 1,2-diamines by sulfonamide linkers on solid materials may results in efficient chiral catalysts. As has been shown in our previous research, the presence of the formed hydrogen donor group improves the orientation of the molecule in the transition state.

The addition of isobutanal to *N*-benzylmaleimide was selected as a test reaction for studying the influence of the chiral catalyst structure. Several inorganic and organic materials are available commercially, which may be used as supports. Applying such materials we have prepared chiral solids both from optically pure cyclohexane-1,2-diamines and 1,2-diphenylethane-1,2-diamines, respectively. The success of the immobilization process of the chiral compounds was checked by FT-IR spectroscopy.

The method used in the preparation of one of the heterogeneous catalyst is shown in Figure 1. Selected results obtained by reusing this catalyst are also shown in Figure 1. The recyclability of the enantioselective catalysts obtained using the polymeric support was also examined.

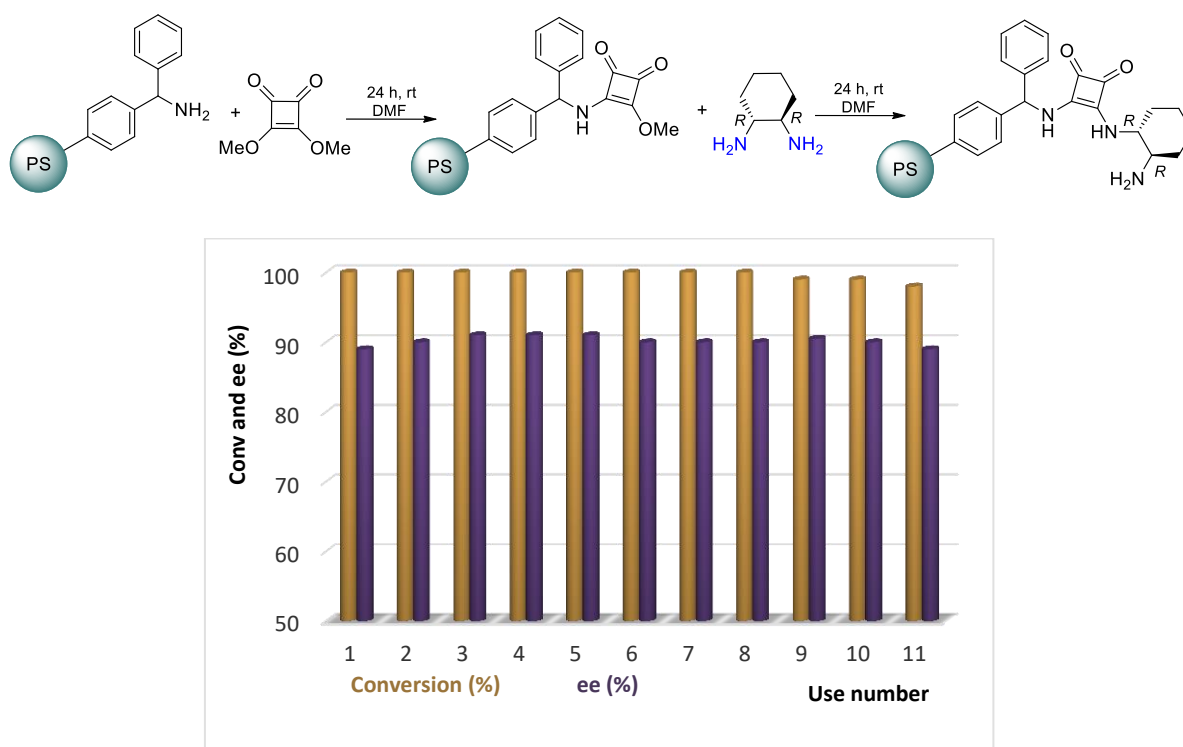


Figure 1. Chiral solid catalysts prepared by immobilization of optically pure 1,2-cyclohexanediamine through squaramide linker and its recyclability.

As shown in Figure 2, the silica-supported catalysts gave lower enantioselectivities and partially lost their activity upon reuse, which we ascribed to the unfavorable effect of the support's surface acidic sites. On the contrary, the chiral catalysts immobilized on polystyrene resins approached the performances of the soluble catalysts, affording the same conversion and only a slight decrease in the enantioselectivity. Moreover, the enantiodiscrimination

ability of the catalyst was kept in a 2nd run. The small decrease in conversion may be attributed to the small amount of catalyst lost during manipulations. Good results were also obtained with catalysts immobilized on polystyrene resins via thiocarbamides groups (not shown in the figure).

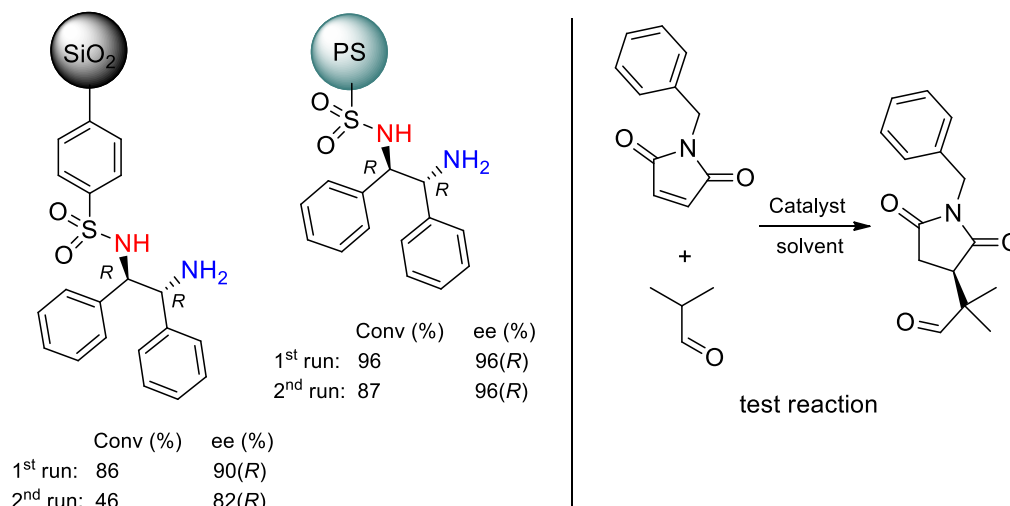


Figure 2. Selected heterogenized chiral catalysts and results obtained in the test reaction.

Conclusion

In our previous studies we have investigated in detail the effect of variations in the structure of the catalysts in homogeneous media. Based on these results we selected the proper catalyst, support and linker for the immobilization of the chiral catalyst to obtain heterogeneous chiral catalysts. These heterogeneous catalysts approached the performances of their soluble counterparts. The proper choice of the support allowed the reuse of the solid catalysts without enantioselectivity decrease. Finally, we note that the prepared heterogeneous catalysts are the first, which were designed for the asymmetric Michael-addition of aldehydes to maleimides. Results presented in this work are also promising starting-points of further efforts devoted to applying heterogeneous, environmentally friendly catalysts in the preparation of practically relevant chiral succinimide derivatives.

References

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