

Increased Reaction Rates and Enantioselectivity of Asymmetric Reactions in Ionic Liquids

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Introduction

The use of ionic liquids as a medium for homogeneous catalysis has several benefits associated over conventional solvents including improved catalyst stability, facile product separation and an increase in activity and selectivity.¹ In addition, due to their low volatility and immiscibility with non-polar organic solvents, ionic liquids have been extensively investigated for immobilization and subsequent recycle of the dissolved catalysts. In this regard, there has recently been an increasing number of reports utilizing ionic liquids in asymmetric catalysis. However, in general, the reactions in ionic liquids have not shown significant advantages in terms of enantioselectivity (ee). Moreover, the ionic liquids are mainly used as a co-solvent with molecular solvents where the ionic medium is used to increase the recyclability of the catalyst.

This study compares the use of ionic liquids and molecular solvents for the Lewis acid catalysed enantioselective Diels-Alder and carbonyl-ene reaction (Figure 1). Herein, a series of enantiopure Cu(II) and Pt(II) complexes have been used and compared with respect to recyclability, reaction rate, enantioselectivity and ease of reaction conditions.

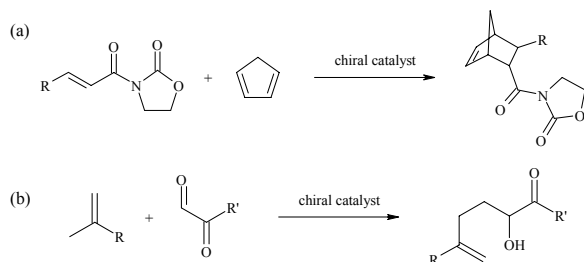


Figure 1. Schematic of (a) asymmetric Diels-Alder and (b) carbonyl-ene reactions examined in this study.

Materials and Methods

All manipulations involving air-sensitive materials were carried out using standard Schlenk line techniques under an atmosphere of nitrogen or argon in oven-dried glassware. All molecular solvents were distilled prior to use. 1-Ethyl-3-methylimidazolium

bis{(trifluoromethyl)sulfonyl}imide ([emim][NTf₂]) was prepared following the method of Bonhôte *et al.* from the corresponding bromide salt.² The ionic liquid used in the study was found to contain 10.1 ppm bromide by suppressed ion chromatography analysis and 0.06 wt% water by Karl Fisher analysis. Cu(II) bis(oxazoline) catalysts and Pt(II) NUPHOS diphosphine complexes were prepared according to published methods.^{3,4} Analytical high performance liquid chromatography (HPLC) was performed on an Agilent 110 Series HPLC equipped with a variable wavelength detector using a Daicel Chiralcel OD-H column. Enantiomeric excess was calculated from the HPLC profile.

Results and Discussion

Enantiopure Lewis acid complexes of conformationally flexible acyclic and monocyclic NUPHOS diphosphines, δ - and λ -[(NUPHOS)Pt(OTf)₂], were found to efficiently catalyse the Diels-Alder and carbonyl-ene reactions, shown in Figure 1, in both ionic liquids and molecular solvents. However, in the ionic liquid significant enhancements in the ee, as well as reaction rate, were achieved compared with the organic media. The increase in ee is in part due to the reduction in the rate of catalyst racemization in the ionic liquid compared with the organic solvent, as evidenced by gradual erosion in ee with time in dichloromethane and supported by NMR studies. However, the ionic liquid also has an inherent effect on the catalyst-reactant orientation as rigid BINAP based catalysts also showed an increased ee, albeit smaller than for the conformationally flexible NUPHOS complexes. Similarly, the copper bis(oxazoline) complexes showed much higher rates and ee's for the Diels-Alder reaction in ionic liquid compared with dichloromethane at room temperature. In this case, the increased rates has enabled catalyst loadings as low as 0.5 mol% to give complete conversions within 2 min whilst retaining the same level of enantioselectivity in the ionic liquid.

For both catalyst systems efficient recycling of the ionic liquid-catalyst system has been observed with little loss in rate or ee found over 10 reactions. Although, there is little leaching of the Pt(II) catalyst, significant *ligand* leaching in the case of the copper bis(oxazoline) complexes was found. This was reduced to undetectable levels by covalently tethering the bis(oxazoline) to the imidazolium cation. No decrease in the activity or ee of the catalyst was found on forming the cationic ligand.

Significance

Ionic liquids have been shown to enhance the enantioselectivity for a number of reactions without the need for a co-solvent or low temperatures as is often needed for molecular solvents. Excellent recycling of the ionic liquid-catalyst system has been shown and very low catalyst loadings may be employed which are not possible in conventional media.

References

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