

## Asymmetric catalysis with “planar-chiral” heterocycles\*

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*Abstract:* Planar-chiral heterocycles serve as effective enantioselective nucleophilic catalysts and as useful ligands for asymmetric metal-catalyzed processes.

### INTRODUCTION

Although many useful organic reactions, such as the acylation of alcohols and the rearrangement of *O*-acylated enolates, are catalyzed by nucleophiles, relatively little work has been devoted to the discovery of asymmetric variants of these processes. In light of this opportunity, in 1995 we decided to initiate a program directed at the development of enantioselective nucleophilic catalysts.

Because of its versatility as a nucleophilic catalyst, 4-(dimethylamino)pyridine (DMAP) represented a particularly inviting starting point for our studies. We felt that a reasonable strategy for desymmetrizing achiral DMAP and related nucleophilic catalysts would be to  $\pi$ -complex the heterocycle to a metal ( $ML_n$ ) and to incorporate a substituent (R) in the 2-position of the ring (for example, see Fig. 1). Practical considerations led us to focus specifically on two families of complexes, planar-chiral DMAP derivatives and azaferrocenes (Fig. 2) [1].

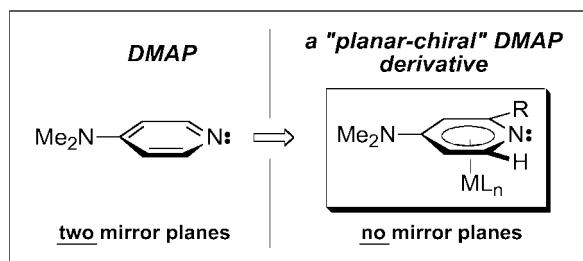


Fig. 1 Desymmetrization of DMAP.

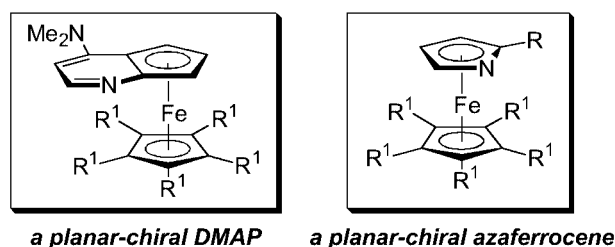


Fig. 2 Targeted planar-chiral nucleophilic catalysts.

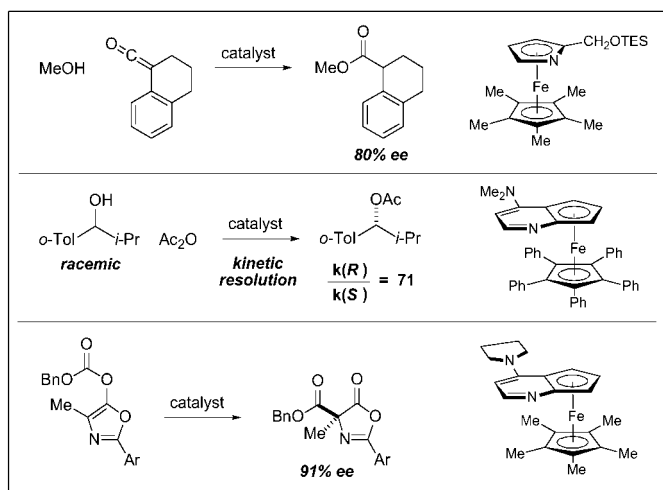
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## ENANTIOSELECTIVE NUCLEOPHILIC CATALYSIS

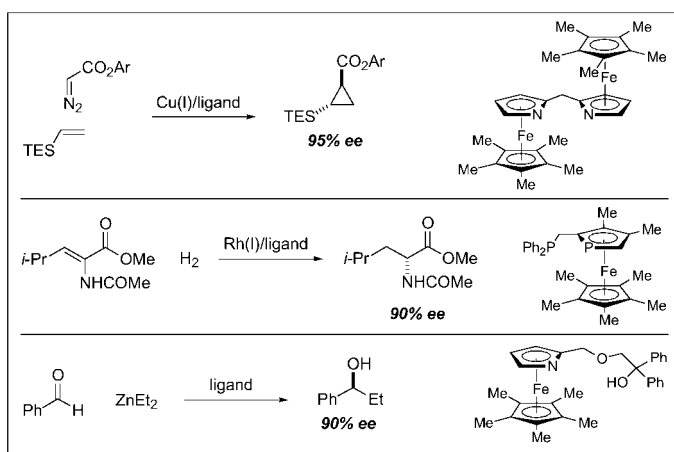
These two families of nucleophilic catalysts have indeed proved to be effective for a number of different reactions (Fig. 3) [2]. Thus, planar-chiral heterocycles catalyze useful processes such as the enantioselective addition of alcohols to ketenes, the kinetic resolution of secondary alcohols, and the enantioselective rearrangement of *O*-acylated enolates.

## CHIRAL LIGANDS

More recently, we have pursued the notion that the same features that make planar-chiral heterocycles effective as chiral nucleophilic catalysts could also enable them to be effective as chiral ligands for metals. We have been pleased to discover that planar-chiral nitrogen and phosphorus heterocycles furnish good enantioselectivity in a range of interesting reactions, including the Cu(I)-catalyzed cyclopropanation of olefins, the Rh(I)-catalyzed hydrogenation of dehydroaminoacids, and the addition of organo-zinc reagents to aldehydes (Fig. 4) [3].



**Fig. 3** Enantioselective nucleophilic catalysis with planar-chiral heterocycles.



**Fig. 4** Planar-chiral heterocycles as chiral ligands.

## CONCLUSION

During the past five years, we have designed, synthesized, and developed applications of several families of planar-chiral heterocycles. These versatile complexes have found utility both as enantioselective nucleophilic catalysts and as chiral ligands for metals. Currently, we are exploring additional applications of planar-chiral heterocycles in these two roles, as well as pursuing their possible use in other roles (e.g., as chiral Brønsted acid/base catalysts).

## REFERENCES

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