Asymmetric Allylic Oxidation Catalyzed by Copper(I) Complexes of Chiral (Iminophosphoranyl)ferrocenes

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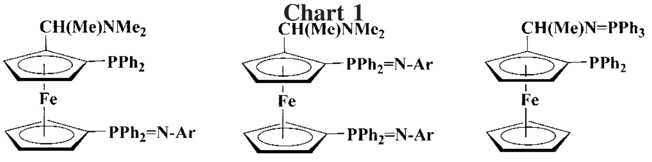
Received September 20, 2007

Summary: The chiral (iminophosphoranyl)ferrocenes **1−3** *are highly versatile ligands in Cu-catalyzed asymmetric allylic oxidation of a series of cyclic olefins with tert-butyl perbenzoate, achieving almost complete enantioselectivity (up to 99% ee) in a reasonably short period of time (36 h).*

Asymmetric allylic oxidation of olefins with peresters to chiral allylic esters catalyzed by chiral copper complexes has now been well-established.[1,2] As such, there are now known a great number of copper catalysts incorporating chiral sp[2] nitrogen donors such as bis-oxazoline,[3] tris-oxazoline,[4] and pybox ligands.[5] Despite some progress made so far, however, a major concern that still remains is how to keep a balance between high enantioselectivity and high reactivity (shorter reaction time). In some cases, for instance, enantioselectivity as high as 99% ee has been achieved, yet only at the cost of very poor reactivity (reaction time 8–17 days).[3f] In this regard, it is worth mentioning that Singh has recently demonstrated that the overall catalytic performance can be greatly enhanced by a unique combination of ligand, substrate, and reagent.[6] Enantioselectivity up to 98% ee has thus been achieved for the first time without losing the reactivity of the catalysts.

We have recently reported the synthesis of the chiral (iminophosphoranyl)ferrocenes **1−3** (Chart 1) and demonstrated that they can serve as a new class of practical ligands for Pd-catalyzed allylic alkylation of allyl acetates and Rh-catalyzed hydrogenation of some olefinic acids.[7,8] In particular, these new ligands have exhibited exceptionally high enantioselectivity (up to 99% ee) in the Rh- or Ir-catalyzed hydrogenation of nonfunctionalized, highly substituted olefins.[9] More recently, Ru-catalyzed asymmetric cyclopropanations of various olefins have also been carried out successfully to achieve high diastereoselectivity (up to 95/5 dr in favor of the cis isomer) as well as enantioselectivity (up to 99% ee).[10]

Chart 1

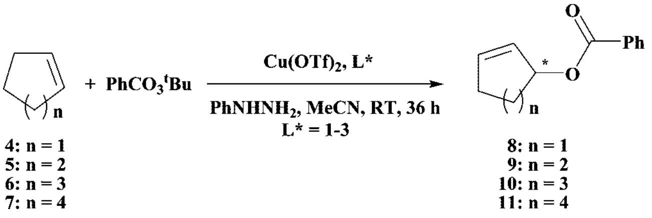


1: Ar = 2,6-Me$_2$-C$_6$H$_3$

2a: Ar = 2,6-Me$_2$-C$_6$H$_3$
2b: Ar = 2,6-^{i}Pr$_2$-C$_6$H$_3$

3

Scheme 1



One might anticipate that these ligands act as tightly binding chelates and thus be capable of stabilizing metal centers involved in catalytic cycles, even in rather low oxidation states.[11,12] Furthermore, as sterically demanding and robust chelates, they are supposed to accomplish quite high asymmetric induction in other reactions as well. We now wish to report a successful expansion of **1−3** as ligand in Cu-catalyzed asymmetric allylic oxidation of a series of cyclic olefins and 1,5-cyclooctadiene.

In the first set of experiments to benchmark the potential of our ligands, we performed allylic oxidation of cyclic olefins with *tert*-butyl perbenzoate (Scheme 1). A typical experimental procedure, as described in the literature, is as follows:[13] the active Cu(I) catalyst was generated in situ on reduction of the complex formed between Cu(OTf)$_2$ (5.0 mol %) and the ligand

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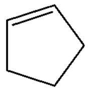
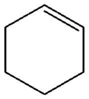
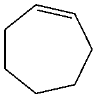
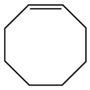
10.1021/om700935m CCC: $40.75

Table 1. Asymmetric Allylic Oxidation of Cyclic Alkenes

Entry	Olefin	Ligand	Yield (%)[a]	ee (%)[b]
1		**1**	38	81
2		**2a**	52	86
3		**2b**	43	97
4		**3**	54	98
5		**1**	41	97
6		**2a**	63	98
7		**2b**	75	97
8		**3**	79	96
9		**1**	34	96
10		**2a**	26	97
11		**2b**	38	92
12		**3**	85	97
13		**1**	52	84
14		**2a**	60	87
15		**2b**	66	88
16		**3**	48	91

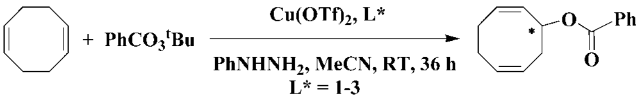
[a] Isolated yield based on the amount of *tert*-butyl perbenzoate used. [b] Determined by analytical chiral HPLC.

(6.0 mol %) with $PhNHNH_2$ (6.0 mol %) in MeCN (5.0 mL) under a nitrogen atmosphere. To the resulting mixture, after 1 h of stirring, were added *tert*-butyl perbenzoate (1.0 mmol) and cyclic alkene in excess (5.0 mmol). The reaction mixture was further stirred for 36 h at room temperature, after which time the product was isolated by flash chromatography. The enantiomeric excess was determined by analytical chiral HPLC or GC, and the absolute configuration of the product was assigned as *S* on the basis of a comparison of the optical rotations with literature values.[11]

Table 1 shows dramatically that the ligands **1**−**3** form very effective catalysts in situ to achieve excellent enantioselectivity (up to 98% ee) with varying chemical yields (medium to high). To the best of our knowledge, enantiomeric excesses reported in Table 1 may rank among the highest in the literature. Even more encouraging is the observation that the enantiomeric excess is virtually independent of the nature of both the olefin and the ligand, contrary to the observations made by others.[6] Nevertheless, catalytic performance in terms of enantioselectivity can be maximized by a proper combination of the ligand (**1**, **2**, or **3**) and the olefin substrate (entries 1–4 and 13–16). When a comparison is made among four olefins, cyclooctene exhibits the lowest enantiomeric excesses (entries 13–16).

As for the chemical yield, on the other hand, the roles of both the ligand and the olefin substrate seem to be a little more considerable. Thus, among various combinations of the ligand and the substrate, ligand **3** is the preferred choice as far as the reactions of cyclopentene, cycloohexene, and cycloheptene are concerned (entries 4, 8, and 12). The reaction of cyclooctene, however, gives the lowest yield with **3** (entry 16).

Table 2. Asymmetric Allylic Oxidation of 1,5-Cyclooctadiene



entry	ligand	yield (%)[a]	ee (%)[b]
1	**1**	92	98
2	**2a**	98	48
3	**2b**	96	99
4	**3**	99	99

[a] Isolated yield based on *tert*-butyl perbenzoate. [b] Determined by analytical chiral GC.

Motivated by the encouraging observations given in Table 1, we further pursued the allylic oxidation of a less reactive substrate such as 1,5-cyclooctadiene under the same set of experimental conditions (Scheme 1), and the results are given in Table 2. Indeed, the results are extraordinary, exhibiting perfect enantioselectivity (>99% ee) as well as complete conversion (>99%) regardless of the type of the ligand. These observations are remarkable in that only a few reports are available for the oxidation of this substrate. The low enantiomeric excess (48% ee) obtained with **2a** (entry 2) seems to be exceptional, resisting any reasonable explanation at the present moment.

In conclusion, we have investigated the enantioselective allylic oxidation of cyclopentene, cyclohexene, cycloheptene, cyclooctene, and cyclooctadiene with *tert*-butyl perbenzoate catalyzed by Cu complexes of some chiral (iminophosphoranyl)ferrocenes (**1**−**3**). Ligands **1**−**3** form very versatile catalysts to achieve excellent enantioselectivity (up to 98% ee) as well as high chemical yields (up to 85%) from the reaction of the cycloalkenes in a reasonably short period of time (36 h). Even more remarkably, perfect enantioselectivity (>99% ee) and complete conversion (>99%) have been observed, for the first time, from the reaction of cyclooctadiene.

Acknowledgment. T.-J.K. gratefully acknowledges financial support from The Advanced Medical Technology Cluster for Diagnosis and Prediction at KNU from MOCIE, ROK. Spectral measurements were performed by the KBSI.

Supporting Information Available: Text giving general experimental procedures and characterization data for cyclooctene and COD. This material is available free of charge via the Internet at http://pubs.acs.org.

OM700935M