Catalytic asymmetric epoxidation of unfunctionalized olefins by supported Cu(II)-amino acid complexes

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Polymer-supported Cu(II) complexes with L-phenyl alanine and L-valine were used as chiral catalysts for asymmetric epoxidation of nonfunctionalized straight-chain terminal olefins *viz*. 1-octene, 1-hexene, 2-methyl-1-pentene and 4-methyl-1-pentene using *m*-chloroperbenzoic acid (*m*-CPBA) as oxidant giving high conversions and selectivity. Enantiomeric yields, though moderate, are comparable with the best-reported ees using homogeneous catalysts. All catalysts displayed good recycling efficiency. Variations in percent ee have been discussed on the basis of the structural geometry of the supported catalysts and the trajectory of the olefin approach to the active oxo-intermediate.

KEY WORDS: Cu-amino acid complexes; polymer-supported catalyst; asymmetric epoxidation; 1-octene; recycling.

1. Introduction

The preparation of polymer-supported catalysts containing main-chain or pendant chirality represents one of the most interesting applications of polymers in organic chemistry [1–3]. Accordingly, much effort has been directed toward the development of immobilized chiral auxiliaries for asymmetric processes [4–6]. The design and development of catalysts that can lead to enantioselectivity in the epoxidation of unfunctionalized terminal olefins constitutes a major challenge in asymmetric synthesis [7–9]. Though considerable success has been achieved in the asymmetric epoxidation of specific substrates such as styrene or *cis*/*trans* alkenes using homogeneous chiral porphyrins and salen complexes as amply demonstrated by Collman, Jacobsen and others [10–14], no notable success has been reported in the epoxidation of simple straight-chain aliphatic terminal olefins [15,16].

Recent literature search revealed interesting applications of naturally occurring amino acids in asymmetric reactions [17,18]. Poly(amino acids) such as poly (leucine) and poly (alanine) have been shown to efficiently catalyze the asymmetric epoxidation of α, β-unsaturated ketones under basic conditions in the absence of a metal [19–21]. Of particular interest have been the recent examples on asymmetric cyclopropanation using supported C_2-symmetric Cu(II)-amino acid complexes [22]. Comparison of activities for unsupported and polymer-supported amino acids (figure 1, structure I) indicated poor enantioselectivity for this reaction (ee 0–4%). A possible explanation for low ees lies in the use of relatively long spacer groups to link two amino acid fragments resulting in catalytically inactive Cu-amide (–NH–CO–) species. Evidently, no further work has appeared on these catalyst systems. Using a simple synthetic strategy, we have, in a recent study [23], shown that amino acids linked directly to a poly(styrene-divinylbenzene) back bone were capable of forming a chelate with metal ions (structure II) and subsequently exhibited catalytic activity in the oxidation of olefins in the presence of *tert*-butyl hydroperoxide as a terminal oxidant under mild conditions.

In the present work, we have examined the complexes of Cu(II) with polymer-anchored amino acids in the asymmetric epoxidation of aliphatic terminal olefins using *m*-chloroperbenzoic acid. Some critical factors influencing enantioselectivity as well as results of catalyst recycle have been discussed.

2. Experimental

Asymmetric epoxidation of straight-chain unfunctionalized terminal olefins were carried out using Cu-supported catalysts as per the following general procedure:

Alkene (1 mmol), methylene dichloride (15 mL) and supported catalyst (100 mg, 0.45 mmol Cu/g resin) were charged into a 50-mL round-bottomed flask. Then, *m*-CPBA (2 mmol) was slowly added in five equal portions over a period of 30 min. The reaction mixture was stirred for 10 h at 25 °C. At the end of the reaction, the catalyst was separated by filtration, and the filtrate was washed with 1 N NaOH (10 mL) followed by distilled

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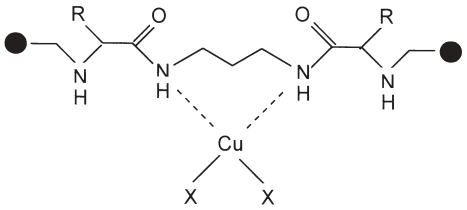
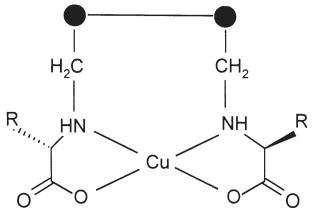


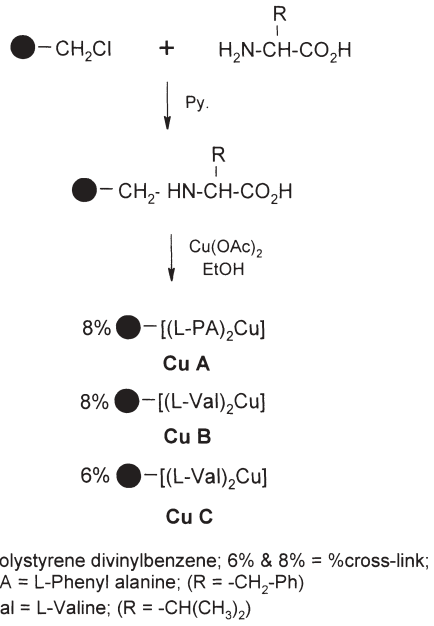
Structure I



R = -CHMe$_2$; -CH$_2$Ph;

Structure II

Figure 1. Supported amino acid Cu complexes.



Scheme 1. Synthesis of polymer-supported Cu(II) amino acid complexes.

water. The epoxide was finally extracted in methylene dichloride and dried over anhydrous sodium sulphate. This extract was analyzed by GC using a chiral capillary column (Chiraldex ATA, 30 m) to determine the percent optical yield.

3. Results

L-phenyl alanine and L-valine anchored to cross-linked chloromethylated poly(styrene-divinyl benzene) resin were prepared as previously described [23]. The reaction of amino-acid-anchored resin and $Cu(OAc)_2$ in an ethanolic medium gave catalysts **Cu A**–**Cu C** as depicted in scheme 1.

Catalysts **Cu A**–**Cu C** were initially screened for the asymmetric epoxidation of 1-octene in the presence of *m*-CPBA at various temperatures in methylene dichloride as solvent (table 1). Asymmetric olefin epoxidation are known to be highly sensitive to the reaction temperature [24]. In our experiments, irrespective of the nature of optically active amino acid, very high conversions (94–98%) and epoxide selectivity (90–94%) were obtained with all the Cu catalysts within the temperature range of 6 °C–40 °C (entry 1–8, table 1). Interestingly, however, the enantioselectivity was considerably reduced at a lower temperature (entry 1,4,7). In order to understand the substrate steric effect on enantiomeric excess, a series of aliphatic olefins such as 1-hexene (1-C_6), 2-methyl-1-pentene (2MP1) and 4-methyl-1-pentene (4MP1) were epoxidized at room temperature using **Cu A**. Results in table 2 again indicated excellent conversion and selectivity. There were, however, noticeable differences in ees with branched olefins compared to straight-chain terminal olefins. The reactivity pattern with this catalyst followed the order 4MP1 < 2MP1 $\approx$ 1-C_6 < 1-C_8. Maximum percent ee was obtained at 25 °C and remains largely unaffected up to 40 °C (entries 2,3,5,6, table 1). Neither the cross-link density of the polymer backbone (6% *versus* 8%) nor the nature of amino acid (L-valine versus L-phenyl alanine) had any major influence on the enantioselectivity.

For catalytic recycling experiments, 1-octene was employed as a model substrate with **Cu A** (table 3). Even after three cycles, the catalyst exhibited high conversions (96–98%) while enantioselectivity was slightly lowered with successive recycling steps.

Table 1
Enantioselective epoxidation of 1-octene catalyzed by polymer-supported Cu complexes

Entry	Catalyst	Temp. °C	Convn. (%)	Epoxide selectivity (%)	ee (%)[a]
1	**Cu A**	6	96	94	17
2		25	98	94	32
3		40	98	92	30
4	**Cu B**	6	96	93	18
5		25	98	92	30
6		40	98	92	29
7	**Cu C**	6	94	94	16
8		25	97	92	32
9		40	98	92	29

[a] Determined by GC using Chiraldex ATA capillary column.

Table 2
Asymmetric epoxidation of terminal olefins with Cu A at 25 °C

Entry	Substrate	Convn. (%)	Epoxide selectivity (%)	ee (%)[a]
1	1-octene	98	94	32
2	1-hexene	97	93	26
3	2-methyl-1-pentene	98	94	22
4	4-methyl-1-pentene	96	90	18

[a]Determined by GC using Chiraldex ATA capillary column.

4. Discussion

4.1. Activity

Catalytic asymmetric epoxidation of alkenes has been extensively investigated primarily focusing on metallo-salen (N_2O_2 ligand) as the model catalyst [7,24–26]. The only other exception to this class of ligand is the chiral β-ketoiminato complex (N_2O_2 core) reported by Mukaiyama [27,28]. The present amino acid complexes resemble the Schiff-base structural motif by way of bidentate chelation to Cu through the N_2O_2 donor set, though the ring size in the latter is essentially smaller and compact. While metallo-salens were shown to be highly active in the low temperature asymmetric epoxidation of unfunctionalized olefins such as styrene and *cis*-β-methyl styrene with *m*-CPBA as oxygen donor, they were not effective for simple terminal olefins like 1-hexene or 1-octene [13,29]. The lower enantiofacial selectivity with terminal olefins was ascribed to a special type of "enantiomeric leakage" mechanism. The Cu catalysts described in this work adopt a nearly planar geometry around the central metal and are probably spatially better configured in incorporating stereogenic centers closer to the metal. This feature may facilitate the interaction between the catalytically active species and the substrate olefin. Such a hypothesis gains credence from the fact that when branched olefins such as 4MP1 were epoxidized, ees were considerably reduced (table 2, entry 3 and 4) compared to straight-chain olefins 1-C_6 or 1-C_8. In all of our experiments, the enantioselectivity decreased significantly with lowering temperature. This behavior is ascribed to poor diffusibility of the substrate at reduced temperature on account of agglomeration of reactive sites on the polymer matrix. However, the reaction conducted at 25 °C exhibited better enantioselectivity for all the Cu catalysts (table 1, entry 2,5,8). The observed ees of ~32% are by far the highest achieved so far with non-Schiff-base polymer-anchored catalysts [15,16]. This is also reflected by the turn over numbers (TON) for our system (~20, 10 h), which was better than the reported values for Ni-Schiff–base complexes (~30–40, 24 h) [15]. Interestingly, though two different amino acids were anchored to the polymer, they displayed identical reactivity pattern. Similarly, the variation in cross-link density (6% versus 8%) also did not influence the percent ee to any noticeable extent.

Table 3
Recycling of **Cu A** in asymmetric epoxidation of 1-octene at 25 °C

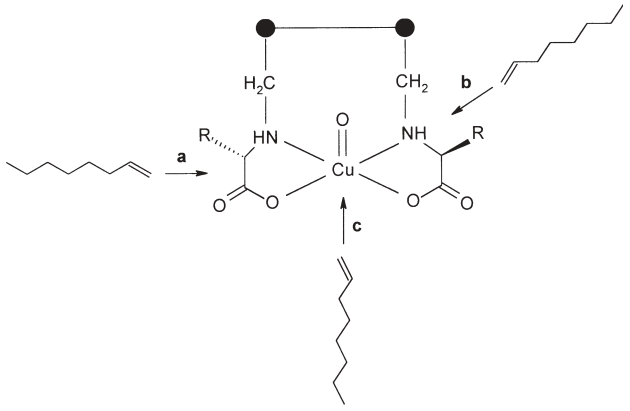
Cycle no.	Convn. (%)	Epoxide selectivity (%)	ee (%)
1	98	94	32
2	98	92	30
3	96	91	27
4	97	90	22

4.2. Mechanism

The observed enantioselectivity with the present supported catalysts can be rationalized using a simple mechanistic model suggested by Jacobsen [13,24,30], which includes three critical factors like (i) catalyst structure; (ii) structure of olefin and its trajectory of approach toward the catalyst and (iii) nature of active species. With regard to the catalyst structure, the amino acid complexes can be assumed to be similar to the planar Schiff-base Cu complex core (figure 1, structure II).

The incoming olefin can attack the metal–oxo bond in one of the three possible directions, *viz*. side-on, inclined (along the Cu–N bond axis) or a perpendicular (to the Cu–N_2O_2 plane) trajectory (scheme 2).

Orientation of the olefin along pathway **a** and **b** is expected to result in greater steric repulsion owing to the smaller size of the amino acid chelate as compared to the Schiff-base complexes. The only favorable pathway for the olefin seems to be along pathway **c**, which is in tune with the model suggested by Houk and coworkers [31] wherein the enantioselection was viewed as being provided by the chiral environment set up by transmission through the salen ligand of the effect of stereogenic carbons. Thus the observed percent ee for 1-alkenes in our case, though moderate, cannot be rationalized by either pathway **a** or **b**. Indirect evidence in support of



Scheme 2. Possible olefin trajectory to the metal–oxo bond.

pathway **c** of the olefin approach was obtained in the asymmetric epoxidation of styrene with **Cu A**. To our surprise, only about 4% ee was observed under identical conditions. The bulky aryl substituent may pose steric constraints compared to the straight-chain 1-alkenes leading to the observed differences in enantioselectivity. This also holds true for substituted 1-alkenes like 2-methyl-1-pentene and 4-methyl-1-pentene.

Further work is in progress to gain insight into the mechanism of asymmetric induction with this catalyst system.

4.3. Recycling

For a truly effective polymer-supported catalyst, it is essential that the recovery be simple and efficient and that the recovered catalyst retains its activity through multiple cycles [32]. Our recycling experiments with **Cu A** clearly showed that epoxide conversions were unaffected up to four cycles. The ees were somewhat lowered probably owing to leaching of the active center from the surface of resin. The extent of this leaching was, however, less than 14%. The results indicate that swelling properties of the polymer as well as overall loading of metal complex can significantly influence the reaction of the olefin with the catalytically active species.

5. Conclusion

Polymer-supported L-valine and L-phenyl alanine complexes of Cu(II) were investigated as catalysts for the enantioselective epoxidation of 1-octene, 1-hexene, 2-methyl-1-pentene and 4-methyl-1-pentene in the presence of *m*-CPBA as oxidant. High conversions and moderate enantioselectivity were observed for this group of substrates. Nevertheless, the ees are comparable to those reported with the most active homogeneous metal Schiff-base complexes. The reaction is sensitive to temperature and the observed enantioinduction can be interpreted in terms of the trajectory of the olefin approach to the active catalyst. The design and synthesis of well-characterized amino acid complexes may provide a new class of catalysts for asymmetric reactions.

Acknowledgments

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