

# CATALYTIC ENANTIOSELECTIVE ALLYLIC OXIDATION OF OLEFINS

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Asymmetric version of allylic oxidation of olefins to allylic esters is an important transformation. The reaction is performed usually using peresters in the presence of a metal catalyst in a chiral environment. Copper catalyst was mainly used by most of the people. Development in this area has been summarized here in a chronological manner. Initially, a modest asymmetric induction in this reaction was achieved by using a variety of chiral amino acids. Lately, a variety of chiral ligands have been introduced to obtain high enantiomeric excess (up to 93% ee) in the allylic oxidation of a variety of cyclic olefins. One of the drawbacks of the reaction was longer time ranging from a week to a month for completion. This shortcoming was overcome to some extent by using phenylhydrazine/phenylhydrazone in the reaction mixture. The reason for enhancement in rate of the reaction is not yet clear, but the reaction can now be completed within a day or two without losing enantioselectivity. Despite so much progress in this area, the reaction is restricted only to cyclic olefins. Acyclic olefins do not give high asymmetric induction.

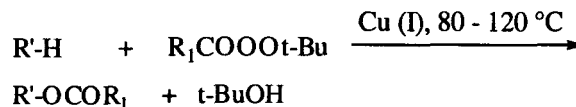
**Key Words:** Kharasch Reaction; Enantioselective; Allylic Oxidation; Olefins; Allylic Esters; Copper Complexes

## 1 Introduction

Allylic oxidation of olefins to allylic esters/alcohols/carbonyls is one of the most studied reactions in organic chemistry. These transformations have been achieved by a variety of metals such as Hg(II)<sup>1a</sup>, Tl(III)<sup>1b</sup>, Pd(II)<sup>1c</sup>, Pb(IV)<sup>1b</sup>, Se(IV)<sup>1d</sup>, Cr(IV)<sup>1e</sup>, Mn(III)<sup>1f</sup>, Co(III)<sup>1f</sup>, Ce(IV)<sup>1f</sup>, Co(II)<sup>1g</sup>, Cu(I)/Cu(II)<sup>2</sup>, etc.<sup>3</sup> The functionalization at the allylic carbon atom takes place due to the special nature of the allylic C-H bond. Asymmetric version of this reaction can, in principle, be achieved by incorporating chiral nonracemic ligands in a rational way to a metal center. However, only copper has been effective for inducing chirality in the reaction<sup>4</sup>. In this article we have described enantioselective allylic oxidation of olefins in a chronological manner. In order to have a better understanding of the reaction, we have also described mechanistic part of the reaction in brief.

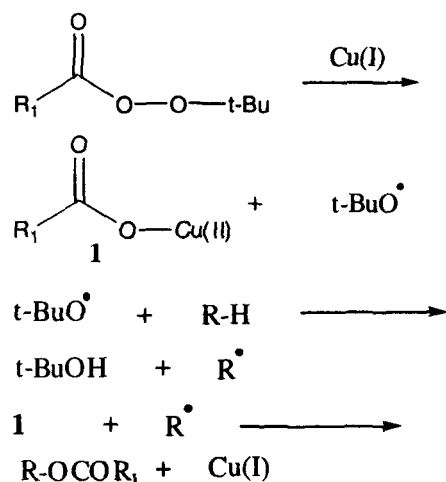
## 2 Mechanism

A substrate containing activated hydrogen reacts with an organic peroxyester in the presence of a catalytic amount of metal salt (Cu or Co) to give esters. This reaction is popularly known as Kharasch reaction<sup>2</sup> (Scheme I).



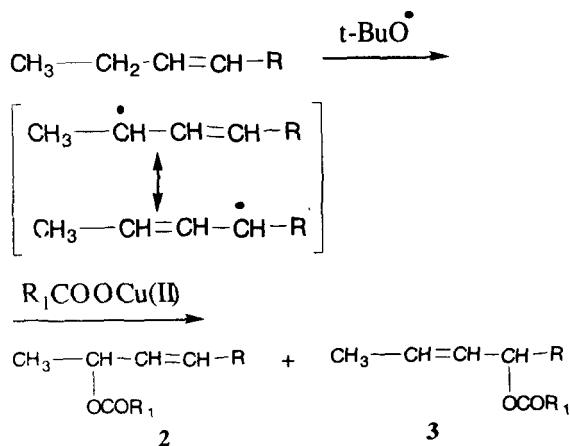
**Scheme I**

The facile decomposition of *tert*-butyl perbenzoate in the presence of copper salt made it possible to be utilized as synthetic reagent. The use of *tert*-butyl hydroperoxide in the presence of a carboxylic acid has been an alternative oxidant. The use of copper ion has two-fold effects. Firstly, it increases the rate of decomposition of peroxyester. Secondly, it is the deciding factor for the composition of the end products, and in many cases, the products observed may differ from those of uncatalyzed reaction. The reaction mechanism involves three important steps. In the first step, there is a homolytic cleavage of the perester oxygen-oxygen bond by Cu(I) to generate benzoate anion and *tert*-butoxy radical. In the process, Cu(I) is oxidized to Cu(II) which reacts with benzoate anion to form Cu(II) benzoate **1**<sup>5</sup>. In the next step, *tert*-butoxy radical abstracts the active hydrogen from the substrate to produce an alkyl radical<sup>6</sup>. This radical then reacts with **1** to form the peroxyester, while Cu(II) is back to its original state, which again enters the catalytic cycle (Scheme II)<sup>7</sup>.



Scheme II

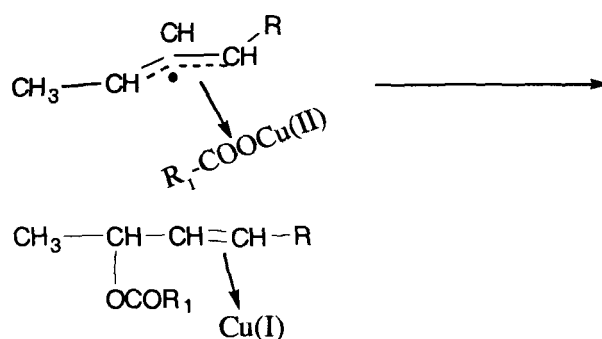
Of particular theoretical and practical interests are the reactions of *t*-butyl perbenzoate with allylic systems. Thus, the direct functionalization of olefins exploiting the special nature of the allylic C-H bond occurs to bring about allylic oxidation reaction. Radical reactions with allylic compounds usually result in a mixture of isomeric products<sup>2a</sup>. This is because the substrate radical may be represented by two contributing resonance structures. Consequently, hydrogen abstraction at an allylic carbon can result in either unrearranged product **2** or rearranged product **3** as shown in Scheme III.



Scheme III

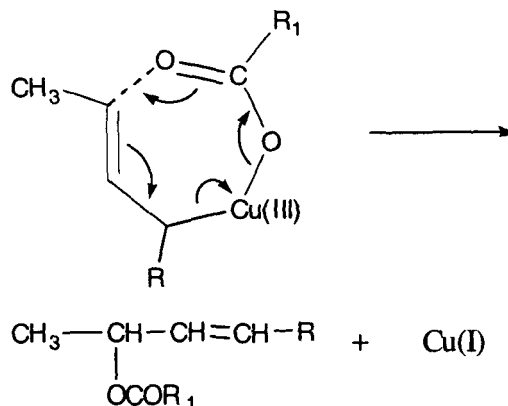
One of the remarkable features of these reactions is that under most conditions, the reaction of *t*-butyl perbenzoate and allylic compounds gives the thermodynamically least stable isomer **2** in considerable preference to the most stable isomer **3**<sup>2,8</sup>. So, terminal olefins were found to react with *tert*-butyl peresters in the presence of a copper salt catalyst yielding the unrearranged secondary allylic esters in major amount.

This fact provided evidence against the involvement of conventional free radical or carbonium ion intermediates, which generally resulted in isomerization of the allylic system. This suggests that the displacement of the allylic hydrogen by the benzoyloxy group probably occurs in a concerted manner. So, there are two alternative proposals for this concerted mechanism<sup>9</sup>. Firstly, there may be the specific interaction between the species **1** and the organic radical. The driving force for the selective formation of terminal olefin is provided by the incipient Cu(I)-alkene interaction which is more favoured by a terminal rather than an internal double bond (Scheme IV).



Scheme IV

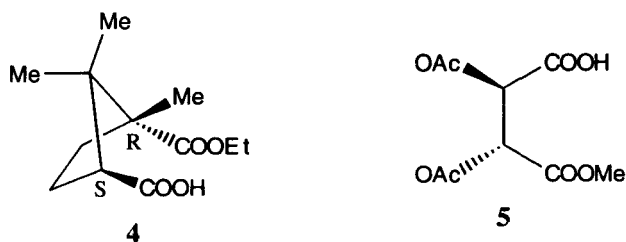
The second proposal suggested an organocopper intermediate, involving a Cu(III) species in a pericyclic reaction. The rapid addition of Cu(II) to the allyl radical takes place to generate Cu(III) benzoate with the bound allyl fragment<sup>7</sup>. A bond between Cu(II) and a radical would be consistent with the paramagnetic nature of Cu(II). In view of a number of evidences in favour of the intermediacy of Cu(III) species in the formation of allylic esters<sup>9,10</sup>, second proposal was found to be the most accepted one (Scheme V).



Scheme V

### 3 Asymmetric Version of Allylic Oxidation of Olefins

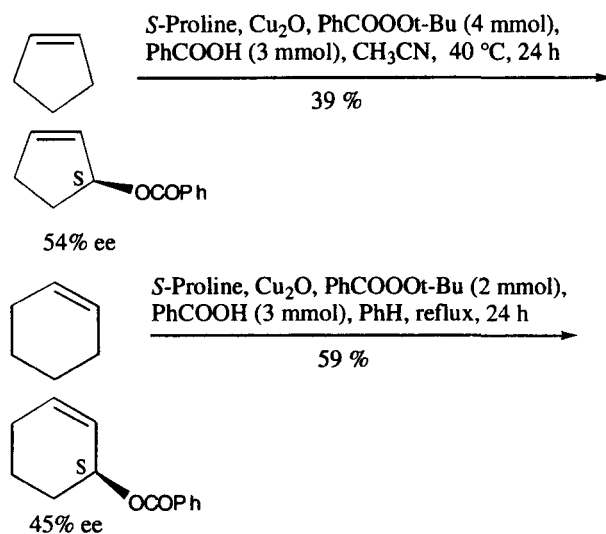
In 1965, D B Denney and coworkers<sup>11</sup> reported the first asymmetric allylic oxidation using Kharasch reaction. They used stoichiometric amount of chiral copper complexes of (+)- $\alpha$ -ethyl camphorate **4** and di-O-acetyl tartaric acid half-methyl ester **5** and carried out the reactions of different alkenes with *t*-butylhydroperoxide as oxidant. They achieved a maximum diastereomeric excess of 6-7%.



After a decade in 1977, a report<sup>12</sup> appeared in which oxidation of olefins was carried out with *t*-butyl perbenzoate using catalytic amount of optically active Cu-complex of a Schiff base or an amino acid in the presence of acetic acid. 2-Cyclohexenyl acetate with  $[\alpha]_D = -23.7^\circ$  was produced in 16-17% enantiomeric excess. This was the first catalytic enantioselective allylic oxidation reaction.

In 1991, Muzart<sup>13a</sup> carried out the asymmetric allylic oxidation of cyclohexene using a catalytic amount of amino acids as chiral promoters. Among all the amino acids, *S*-proline turned out to be the best. He tried the reaction in two different conditions. In the first condition 'A', Muzart used *t*-butyl hydroperoxide as the oxidant with acetic acid in benzene. In the second condition 'B', acetonitrile was used as a solvent. In both the cases,  $\text{Cu}(\text{OAc})_2$  was used as a copper salt. Under the condition 'A', heating was required for the product formation and it was observed that in order to get maximum asymmetric induction during the reaction, at least 4 equivalents of an amino acid per  $\text{Cu}(\text{OAc})_2$  was necessary. In this way a maximum of 28% ee for (*S*)-2-cyclohexenyl acetate was estimated during the oxidation of cyclohexene. On the other hand, under the condition 'B', 30% ee was obtained using slightly more than the stoichiometric amount of chiral ligand (1.3 equivalent with respect to Cu). They obtained the same sense of asymmetric induction, as reported by Araki<sup>12</sup>, which supports the similarity between the mechanisms of acyloxylation carried out with  $\text{RCO}_3t\text{-Bu-Cu}$  and  $\text{RCO}_2\text{H-}t\text{-BuOOH-}$

Cu. The detailed study of his work was disclosed in 1995, in which they used  $\text{Cu}_2\text{O}$  along with various structural analogs of (*S*)-proline as chiral catalysts<sup>13b,c</sup>. They tried the reactions under different conditions and the best results obtained are summarized in scheme VI.

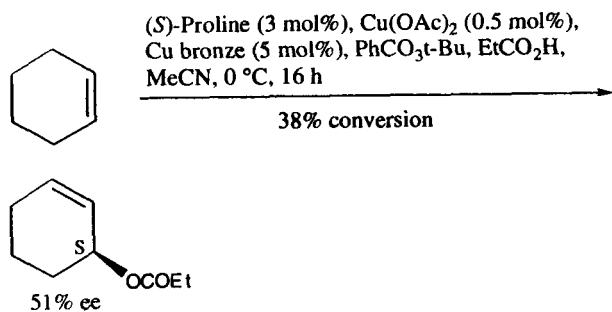


Scheme VI

So, under the conditions mentioned in the scheme VI, they obtained a maximum of 54% ee for (*S*)-2-cyclopentenyl-1-benzoate and 45% ee for (*S*)-2-cyclohexenyl-1-benzoate. Other cyclic alkenes gave poor yield (27 - 34% yield) and poor enantioselectivity (cycloheptene 23% ee; cis-cyclooctene 4% ee) during their oxidation to allylic benzoates. Two acyclic olefins such as 1-octene and allylbenzene were also used as substrates for allylic oxidation studies. In the case of 1-octene, a mixture of normal and rearranged products (4:1 ratio; 23% yield) was reported and optical purity of the chiral compound was only 9%. Allyl benzene, on allylic oxidation, gave a mixture of normal and rearranged products (ratio 65 : 35) in 77% yield, but there was no chiral induction in the reaction. The solvents for allylic oxidation had to be aprotic, nonoxidizable and with suitable boiling temperature. The authors, in their studies showed the absence of any correlation between solvent polarity and enantioselectivity of the process. Besides acetonitrile and benzene, solvents like dichloroethane and sulfolane served good purpose. Invariably, acetonitrile gave better asymmetric induction compared to other solvents. The only exception was cyclohexene where benzene was superior (45% ee) to  $\text{CH}_3\text{CN}$  (39% ee). Among the different chiral promoters, they found (*S*) or (*R*)-

proline to give the maximum ees. While the (*S*)-proline gave (*S*)- enantiomer of the allyl benzoate, (*S*)-*N*-methyl proline gave (*R*)-isomer of the allyl benzoate. They also varied the carboxylic acid used for the reaction, and the data they obtained did not show any clear dependence between the enantioselectivity and the nature of the R<sub>1</sub> group, except a weak increase in ee for aliphatic acids relative to aromatic ones. The best ee of 52% was obtained on using (CH<sub>3</sub>)<sub>3</sub>CCOOH in the case of cyclohexene. They also showed the dependency of enantioselectivity with nature of oxidant. It was found to decrease slightly in the following manner: *tert*-butylhydroperoxide~*tert*-butyl perbenzoate > cumylhydroperoxide. They used more than 2 equivalents of a chiral amino acid in comparison with Cu<sub>2</sub>O and suspected that CuL<sub>2</sub> (L = amino acid) species is involved in the reaction. This was based on two observations: (i) development of deep blue colour of the reaction mixture (UV, λ<sub>max</sub> = 610 nm); (ii) use of di-(*S*)-prolinato-Cu(II) as a catalyst in the above reaction gave the same result as it was obtained from Cu<sub>2</sub>O/(*S*)-proline<sup>13b</sup>. It was found that the co-ordination of the copper ion with amino acids remained unchanged during the whole reaction<sup>13d</sup>.

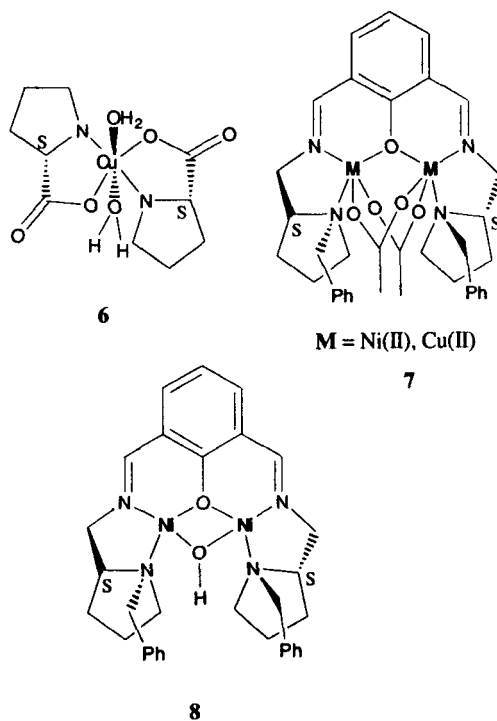
In the same year, Feringa *et al.*<sup>14a</sup> reported similar work by using several chiral Cu(II) complexes of cyclic amino acids to catalyze the enantioselective allylic oxidation of cyclohexene to cyclohexenyl propionate. They reported that enhanced enantioselectivity (51% ee) was obtained for this reaction when copper bronze was also used and the reaction was done in a solvent mixture of propionic acid and acetonitrile (Scheme VII).



Scheme VII

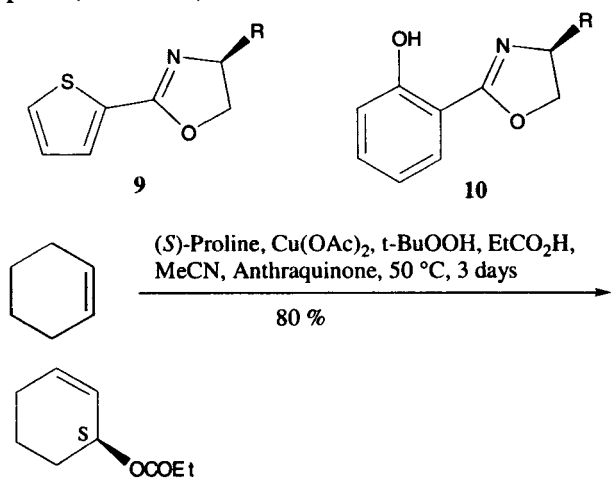
The influence of the variation of a number of parameters was studied. Acetic acid in place of propionic acid gave only 35% ee in the above reaction. The use of CuOTf, Cu(OTf)<sub>2</sub> and CuCN instead of Cu(OAc)<sub>2</sub> lowered the enantioselectivity. When Zn

was used instead of Cu bronze, 58% ee was achieved highlighting the role of metal as reducing agent in the catalytic cycle. The maximum enantioselectivity upto 61% ee was obtained on the use of 1,1-dimethyl propyl peroxyvaloate [*t*-BuCO<sub>3</sub>-C(Me<sub>2</sub>)Et] instead of *t*-butyl peroxybenzoate. Among different cyclic aminoacids as chiral ligands, (*S*)-proline turned out to be the best. Substitution at α-position of proline lowered the enantioselectivity. Also, the variation of the ring size decreased the enantioselectivity in the following order: (*S*)-proline > (*S*)-azetidine-2-carboxylic acid > (*S*)-pipercoline-2-carboxylic acid. The results obtained suggested the involvement of a chiral copper-proline complex. Structurally well defined bis-aquo-bis-(*S*)-prolinato-Cu(II) **6** gave similar results indicating the involvement of the same type of complex. In preliminary experiments, chiral dinuclear Ni(II) and Cu(II) complexes **7** and **8** were used in the oxidation of cyclohexene and allylbenzene with *tert*-butyl peroxyacetate (or -propionate), but only upto 10% ee was reported under the best condition.



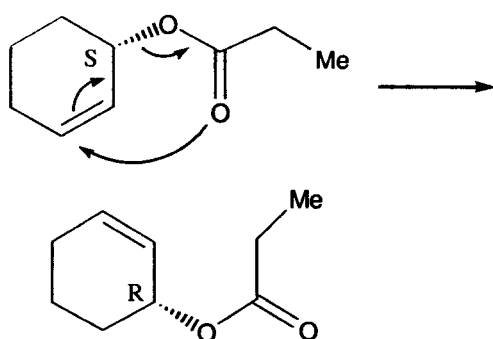
Enantioselectivity was improved by using 4 equivalents of anthraquinone with respect to Cupric acetate from 45 to 60%, but only when *t*-butyl hydroperoxide was used as oxidant (Scheme VIII)<sup>14b</sup>. With *t*-butyl perbenzoate, no significant change was observed. Although the role of anthraquinone is not very clear, they have proposed that it possibly acts as a cooxidant by activating *t*-butyl hydroperoxide or as

an oxidant for low valent copper species. Chiral ligands such as **9** and **10** were also synthesized and used for the above reaction, but the enantioselectivity was very poor (5-10% ee).



**Scheme VIII**

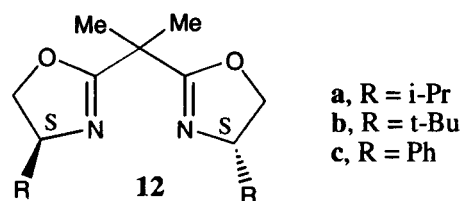
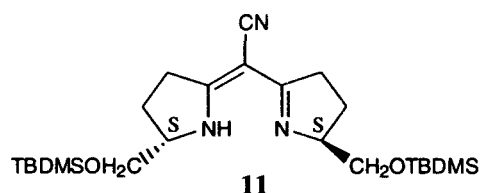
In order to examine the stability of the product in the reaction mixture under the above condition, enantiomerically enriched (*S*)-2-cyclohexenyl-1-propionate (59% ee) was added to the allylic oxidation mixture of cyclopentene. After the reaction was complete, the (*S*)-2-cyclohexenyl-1-propionate was recovered in 51% ee. With this observation, Feringa proposed that there was some thermal racemisation via a Claisen-type rearrangement as shown in the Scheme IX.



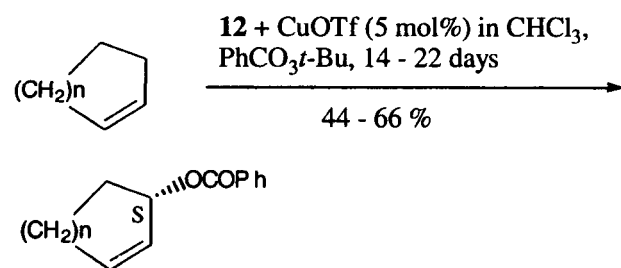
**Scheme IX**

Pfaltz *et al.*<sup>15</sup>, Andrus *et al.*<sup>16a</sup>, Katsuki *et al.*<sup>17a</sup> independently reported around the same time the use of copper complexes of chiral semicorrin and oxazoline type ligands<sup>18</sup> in the enantioselective allylic oxidation of olefins. Pfaltz in connection with his work on chiral semicorrin-Cu complexes for enantioselective cyclopropanation of olefins found that enantiomeric excess of 65-75% could be obtained with a

stoichiometric amount of Cu(I) complex of the semicorrin ligand **11** for the reaction of cyclohexene with *tert*-butyl perbenzoate. The analogous catalytic reaction showed significant decrease in enantioselectivity. This prompted them to try bisoxazoline type ligands **12** for the same purpose<sup>15</sup>. Copper complexes of these ligands have been used earlier in the asymmetric cyclopropanation reactions<sup>19</sup> by Masamune and Evans independently.



The Cu(I) complexes, prepared *in situ* from CuOTf or [Cu<sup>I</sup>(MeCN)<sub>4</sub>]PF<sub>6</sub> and bisoxazolines **12**, showed good catalytic activity for allylic oxidation of cyclic olefins such as cyclopentene, cyclohexene, and cycloheptene using *tert*-butyl perbenzoate as oxidant (Scheme X).

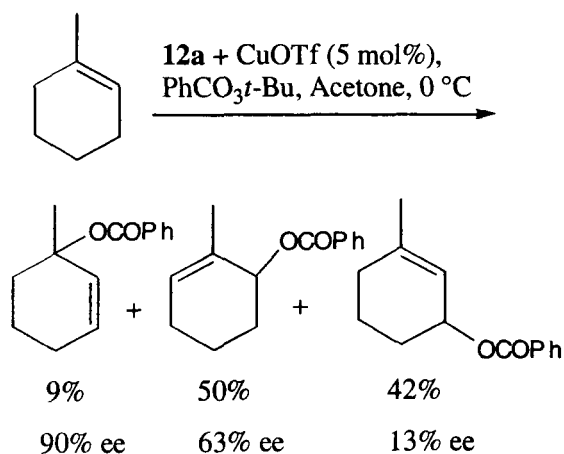


n	Ligands	Solvents	Temp.	%ee
1	<b>12a</b>	Acetone	-20 °C	82%
1	<b>12b</b>	CH <sub>3</sub> CN	-20 °C	84%
2	<b>12b</b>	CH <sub>3</sub> CN	7 °C	77%
3	<b>12a</b>	CH <sub>3</sub> CN	7 °C	82%

**Scheme X**

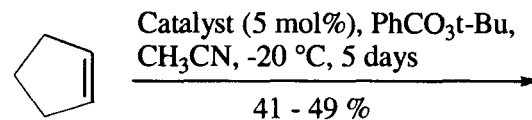
They reported a maximum of 82% ee in the allylic oxidation of cyclopentene and cycloheptene to their corresponding (*S*)-allylic benzoates using the ligand **12a**. In the case of cyclohexene, the ligand **12b** gave a maximum of 77% ee. Depending upon a substrate

and the specific ligand, either acetone or acetonitrile proved to be the solvent of choice. The reaction in acetone was generally faster than in acetonitrile. It is mentioned qualitatively that an analogous catalyst prepared from  $\text{Cu}(\text{OTf})_2$  is less reactive and less selective. The reaction was also extended to 1-methyl cyclohexene, which gave a mixture of three regioisomers and the results are shown in Scheme XI. The methyl group was not oxidized under these conditions.

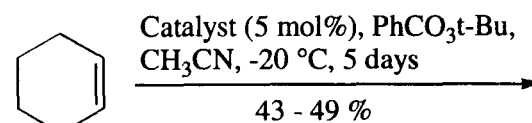


Andrus *et al.*<sup>16a</sup> published their results on allylic oxidation of olefins using chiral bisoxazoline-copper complexes **13**, **14** and **15**. The best results for allylic oxidation with the above complexes have been summarized in Scheme XII. Selectivity for cyclopentene was best (81% ee) using the catalyst **15**. With cyclohexene the highest selectivity, 80% ee was obtained using **13** as a catalyst. It is reported that cyclooctene reacted at a much slower rate and with very poor selectivity (13% ee with **13**; 0% ee with **14**). Acyclic olefins were found to react with good yields in acetonitrile at 5°C but the enantioselectivities were

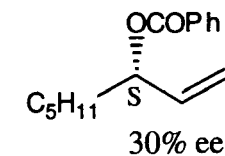
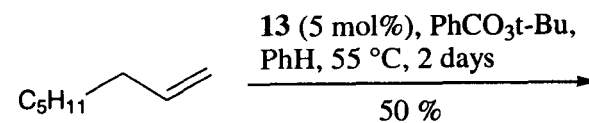
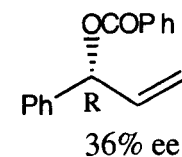
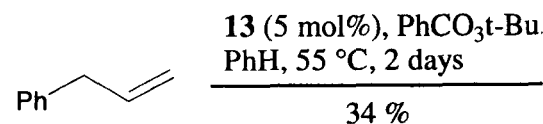
zero. However, at higher temperatures in benzene the enantioselectivities were raised to 36 and 30% ee for allylbenzene and 1-octene, respectively (Scheme XII).



Catalysts	%ee
<b>13</b>	70
<b>14</b>	42
<b>15</b>	81

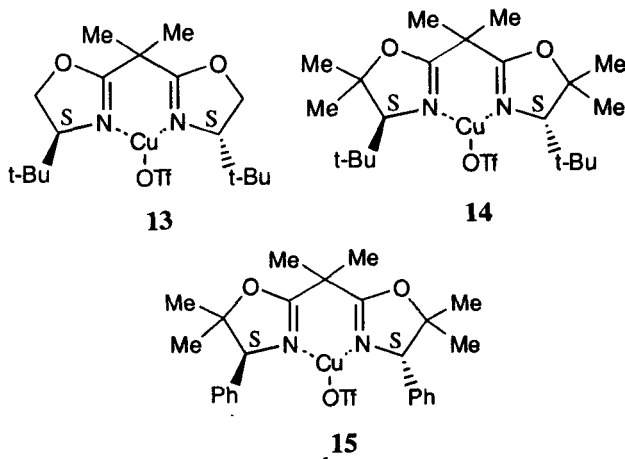


Catalysts	%ee
<b>13</b>	80
<b>14</b>	67
<b>15</b>	47

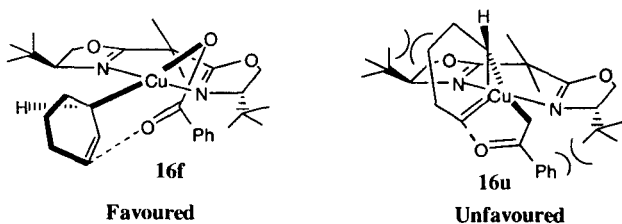


**Scheme XII**

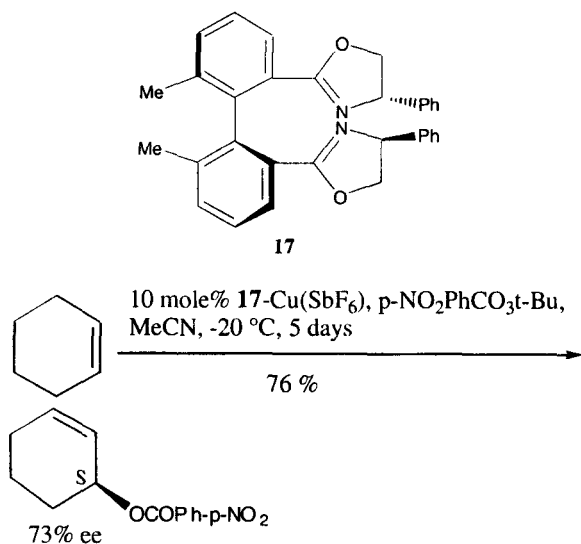
Recently Andrus and co-workers published full details of their work where they have studied a variety of peresters in the allylic oxidation of olefins, but no improvement was made in the asymmetric induction of the reaction<sup>16b</sup>. The following model has been proposed by the authors to account for the stereoinduction in the above reactions.



In the favoured transition state (**16f**), the allyl and benzoate groups are linked to Cu in such a way so as to minimize the interaction with the flanking *tert*-butyl groups of the ligand. The Cu(III) intermediate thus adopted a distorted square planar geometry placing the allyl and benzoate groups above or below the plane of the copper bisoxazoline ring. Then, the rearrangement takes place with the benzoate being delivered to the olefins. The authors further proposed that the lower selectivity for the acyclic olefins was due to an extra degree of freedom for rotation which exposes the other face of the olefin.

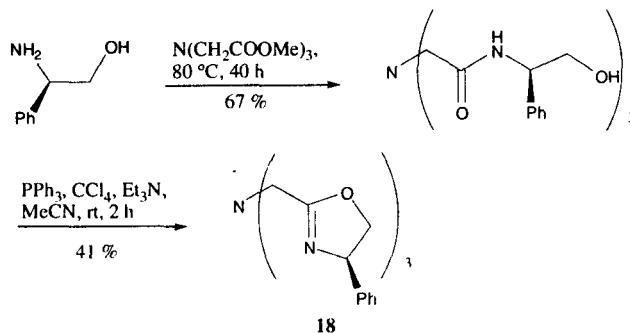


They further synthesized a new  $C_2$  symmetric bis(oxazoline) ligand **17** and used it for allylic oxidation reaction<sup>16c</sup>. The Cu(I) complex of this ligand gave 73% ee in the allylic oxidation of cyclohexene under the above condition (Scheme XIII).



**Scheme XIII**

Katsuki and coworkers reported a novel Cu(II)-tris(oxazoline) complex as a catalyst for enantioselective allylic oxidation of olefins<sup>17</sup>. The tris(oxazoline) type ligand such as **18** was synthesized from an easily available nitrilotriacetic acid trimethylester and phenyl glycinol in two steps (Scheme XIV). Using this scheme, they synthesized a variety of chiral ligands by changing the  $\alpha$ -amino alcohols.

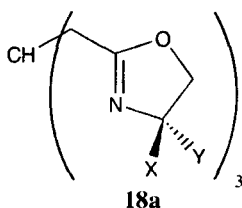


**Scheme XIV**

In a preliminary study, 1:1 complex of the chiral ligand **18** with a variety of metal salts such as Fe(ClO<sub>4</sub>)<sub>2</sub>, FeCl<sub>2</sub>, Fe(ClO<sub>4</sub>)<sub>2</sub>, CuOTf, and Cu(OTf)<sub>2</sub> was made *in situ*. The Fe complex did not show any catalytic activity. Both the copper complexes [CuOTf-**18** and Cu(OTf)<sub>2</sub>-**18**] catalyzed the allylic oxidation reaction, but the latter one induced higher asymmetric induction (74% ee, 68% yield) than the former (66% ee, 67% yield) with cyclopentene and *tert*-butyl perbenzoate in acetone at rt. Allylic oxidation of cyclopentene with benzoyl peroxide and the 18-Cu(OTf)<sub>2</sub> complex gave a mixture of allylic benzoate (68% ee and 21% yield) and a saturated benzoate (15% yield). Using *tert*-butyl hydroperoxide as an oxidant, 2-cyclopentene-1-ol (13% ee, 29% yield) and 2-cyclopentene-1-one (6% yield) were obtained. Generally the reaction proceeded well in polar solvents, but no clear relationship was observed between ee and polarity of the solvents. Acetone was found to be the best in terms of ee and yield amongst the solvents studied. Ethyl acetate showed slightly diminished enantioselectivity as compared to acetone. Ee of the reaction increased as the reaction temperature was decreased.

It was further reported that the ee of the product slightly decreased, as the reaction time became longer. The optical purity of cyclopentenyl benzoate decreased from 75% to 65% ee when it was exposed to Cu(OTf)<sub>2</sub>-**18** complex in acetone (5 mol % to benzoate) for 60 h at rt. Like, Feringa's observation (*vide supra*), they also predicted that there was racemisation of the allylic benzoate during the reaction condition. To suppress the racemization, they examined the effect of several additives such as H<sub>2</sub>O and 4 Å molecular sieves. When 1 equivalent of water (with respect to Cu ion) was added to the reaction mixture, the reaction did not take place. Like Singh and coworkers (*vide infra*), Katsuki also observed that the

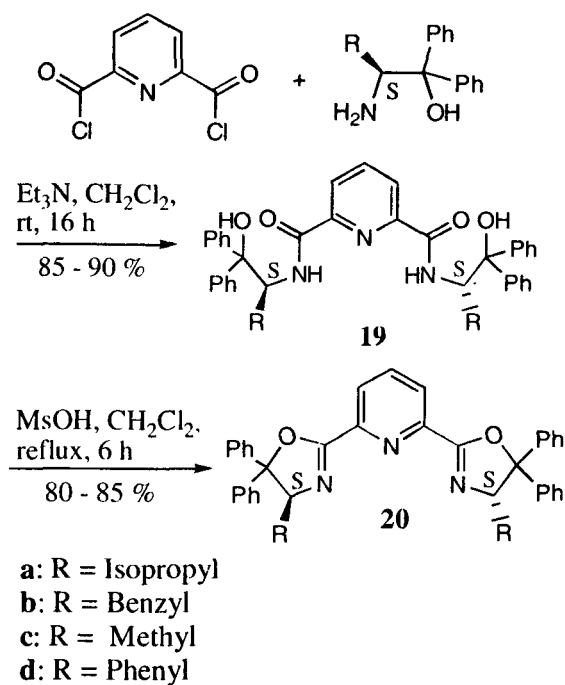
rate of reaction, ee and yield of the product increased by the addition of 4 Å molecular sieves to the reaction mixture<sup>17b</sup>. At -20 °C cyclopentene gave a maximum of 93% ee and 30% yield of allylic ester with **18**-Cu(OTf)<sub>2</sub> complex in acetone and 4 Å mol. sieves. All other ligands turned were inferior to ligand **18**. It was also found that there was not much effect in the ee, when the R<sub>1</sub> group of the perester was changed. However, *tert*-butyl *p*-nitro perbenzoate did not show any reaction. A maximum of 93% ee for cyclopentenyl benzoate (-20 °C, 200 h, 30% yield), 72% ee for cyclohexenyl benzoate (-20 °C, 255 h, 4% yield), 60% ee for cycloheptenyl benzoate (rt, 90 h, 5% yield) and 64% ee for cyclooctenyl benzoate (rt, 50 h, 11% yield) with **18a**-Cu(OTf)<sub>2</sub> complex (5 mol %) and *tert*-butyl perbenzoate in acetone with 4 Å mol. sieves was obtained. An acyclic olefin such as 1-octene gave only 23% ee at rt.



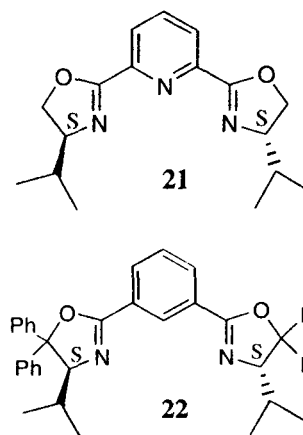
Katsuki extended the work further and synthesized some new C<sub>3</sub> symmetric tris(oxazoline) ligands **18a**<sup>17a,b,c</sup>. The reaction with this type of ligands was slow and ees were low compared with **18** as the chiral ligand. The enantioselectivity, however, could be increased by running the reaction in nonpolar solvents. This was unlike of other oxazoline ligands. The other interesting feature was that the sense of enantioselection by this new ligand **18a** was opposite to that by **18**. They also studied allylic oxidation of dicyclopentadiene and reported upto 87% ee<sup>17d</sup>.

In 1996, Singh and coworkers reported that a copper complex of ip-pybox-diph ligand **20a**<sup>20</sup> is quite suitable as a catalyst for the enantioselective allylic oxidation of olefins with perester<sup>21a, 22</sup>. This kind of pybox ligand such as **21** has been developed by Professor Nishiyama and used extensively for other kind of reactions by him and others<sup>23</sup>. The ligands **20a-d** were synthesized in two steps, viz., by coupling of 2,6-dipicoyl chloride and (*S*)-diphenylamino alcohol followed by intramolecular condensation of **19** with methanesulfonic acid (Scheme XV).

The allylic oxidation of olefins with *t*-butyl perbenzoate in the presence of a catalytic amount of complex prepared from chiral ligands **20** and a variety



Scheme XV

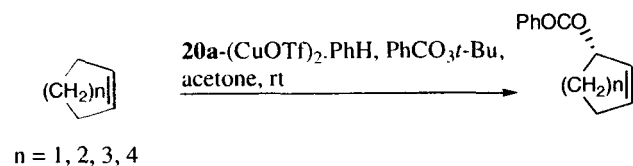


of copper salts has been extensively studied by Singh and coworkers<sup>22</sup>. It was reported that only a Cu(I) triflate complex gave reasonably higher asymmetric induction in the reaction. It is also reported that phenyl hydrazine in acetone has dramatic effect on increase in rate of the reaction (Table I). They have also proved that it was phenyl hydrazone and not phenyl hydrazine, formed *in situ*, was responsible for increase in rate of the reaction. They also confirmed by epr studies that the reduction of Cu(II) to Cu(I) species took place by phenylhydrazone, but the rate of the reduction was slower than by phenyl hydrazine<sup>24</sup>. The exact reason for increase in the rate is not very clear, but the results would be useful for further development in this area.



Table I

Effect of Phenylhydrazine on Catalytic Enantioselective Allylic oxidation of Olefins with Chiral **20a**-(CuOTf) Complex<sup>a</sup>



Entry	Olefins	Ph NHNH <sub>2</sub>	Time <sup>b</sup>	%Yield <sup>c</sup>	%ee <sup>d</sup>
1		No	48h	90	51
2		Yes	03h	62	54
3		No	06d	87	73
4		Yes	05h	78	70
5		No	6.5d	63	71
6		Yes	06h	35	72
7		No	30d	28	80
8		Yes	24h	26	81

<sup>a</sup>The reaction was done at rt, which here refers to 18-20°C. <sup>b</sup>h for hours and d for days. <sup>c</sup> Isolated yield. <sup>d</sup> Determined by HPLC on chiral columns and by 400 MHz<sup>1</sup>H NMR spectrum of a Mosher ester of the corresponding alcohol.

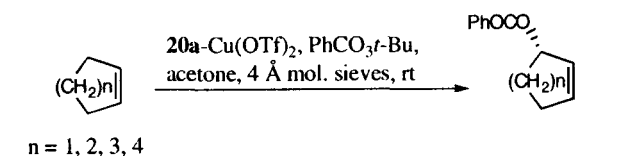
The effect of 4 Å molecular sieves along with phenyl hydrazine or phenyl hydrazone has been studied. The molecular sieves increased the enantioselectivity at the cost of reaction time. For example, 86% ee has been reported in case of cyclohexene with **20a**-CuOTf in the presence of 4 Å, but the reaction time was 21 days. However, on addition of phenyl hydrazine to the same mixture, the time was reduced to 10 h, but the enantioselectivity was also reduced to 70 % ee. Singh and coworkers have reported optimum conditions for the above reaction by using **20a**-Cu(OTf)<sub>2</sub>, phenyl hydrazine, 4 Å and running the reaction in acetone. Under these conditions, they have reported more than 81% ee in the allylic oxidation of cycloheptene and cyclooctene (Table II). Other substituents such as benzyl, methyl, and phenyl at the chiral centre of the ligand **20** gave lower enantioselectivity in the allylic oxidation reaction.

The absence of any asymmetric induction with ligand **22** indicated that the pyridine *N* was essential for chirality transfer in the catalytic allylic oxidation reaction of olefins.

In view of Singh and Katsuki's findings that Cu(II) complexes also catalyze the reaction equally well, the mechanism of the allylic oxidation reaction becomes even more complicated. In that case, it can be assumed

Table II

Catalytic Enantioselective Allylic oxidation of Olefins with Chiral **20a**-Cu(I) Complex Reduced in situ from **20a**-Cu(OTf)<sub>2</sub> by Phenylhydrazine<sup>a</sup>

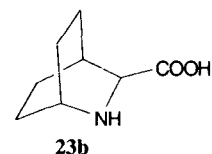
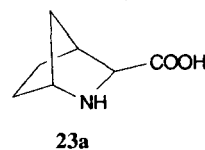


Entry	Olefins	Time <sup>b</sup>	%Yield <sup>c</sup>	%ee <sup>d</sup>
1		04h	80	60
2		24h	73	75
3		24h	42	82
4		72h	28	81

<sup>a</sup>The reaction was done at rt, which here refers to 28-30°C. <sup>b</sup>h for hours. <sup>c</sup> Isolated yield. <sup>d</sup> Determined by HPLC on chiral columns and by 400 MHz<sup>1</sup>H NMR spectrum of a Mosher ester of the corresponding alcohol.

that the reaction proceeds *via* the Scheme IV. Knowing the complex nature of redox chemistry of copper, the possibility of an intermediate shown in the Scheme V also can not be ignored (*vide supra*).

Andersson and co-workers have reported unnatural bicyclic α-amino acid **23**-copper complex for enantioselective allylic oxidation of olefins<sup>25</sup>. When they treated the ligand **23a**, Cu(OAc)<sub>2</sub>, copper bronze and benzoic acid in benzene with cyclohexene and *tert*-butyl perbenzoate, they obtained 64% ee and 40% yield for 2-cyclohexenyl-1-benzoate after two days. When the concentration of the catalyst was increased from 5 to 10 mol %, the yield was increased to 63% but there was not much change in the enantioselectivity (64% to 65%). Lowering the temperature to 5 °C, the ee was reduced to 60% and the yield was 25% in 21 days. Under the best condition cyclopentene gave 2-cyclopentenyl-1-benzoate in 55% yield (60% ee, 2 days). Under the same condition *L*-proline was found to be inferior to the new ligand **23a**. The ligand **23b** was not satisfactory for inducing asymmetric induction in the reaction (15% ee for cyclohexenyl-1-benzoate and 11% ee for cyclo-pentenyl -1-benzoate).



Fahmi used a complex of chiral dinucleating ligands **24-27** (Fig. 1) and  $\text{Cu}(\text{CH}_3\text{CN})_4\text{PF}_6$  as a catalyst for enantioselective allylic oxidation of cyclohexene<sup>26</sup>. He prepared the Cu(I) complex *in situ* in acetonitrile and used it with *tert*-butyl perbenzoate for allylic oxidation of cyclohexene at room temperature. Cyclohexenyl benzoate was obtained in yields ranging from 30-92% and with enantioselectivities upto 32%. He observed that the yield and enantioselectivity were strongly influenced by the copper to ligand ratio suggesting that structurally different catalytically active species for different ratios. He also isolated a minor imide product **28** in 16% yield during the above allylic oxidation reaction. It was postulated that insertion of coordinated acetonitrile was a competing process in the above reaction.

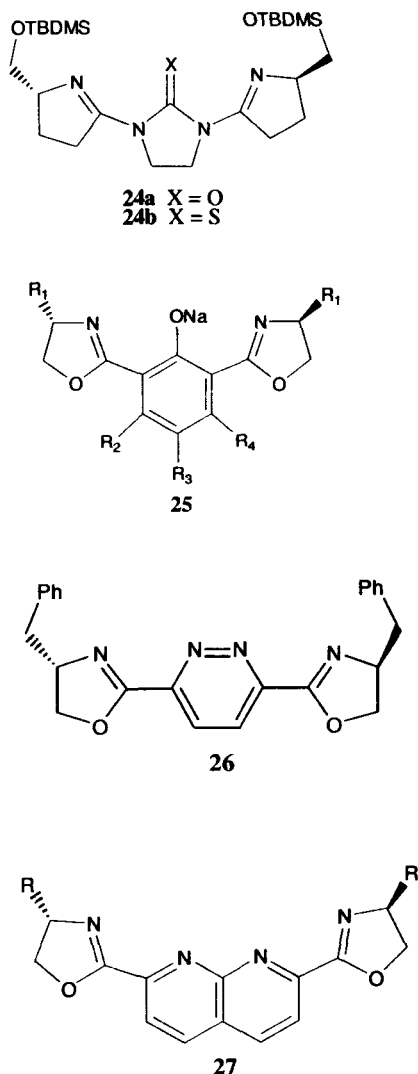
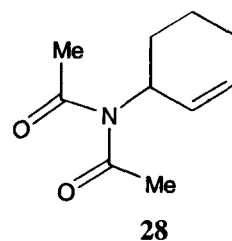
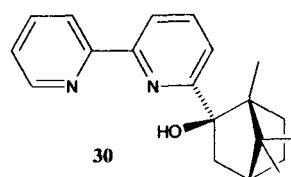
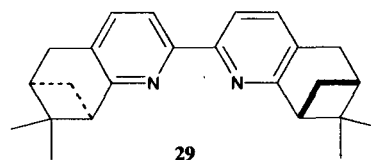


Fig. 1



Recently, bipyridine type chiral ligands such as **29** and **30** were used for allylic oxidation of olefins, but the enantioselectivity reported was moderate<sup>27</sup>. Asymmetric peroxidation of olefins has also been reported for allylic and benzylic compounds to provide allylic peresters by using *t*-butyl hydroperoxide as oxidant and Cu(I) complex of bis(oxazoline) complexes. A maximum of 84% ee has been reported for this transformation<sup>28</sup>.



#### 4 Conclusion

In conclusion, the authors have described development in the area of enantioselective allylic oxidation of olefins in a chronological manner. Although reasonably high optical yield has been obtained in the allylic oxidation of cyclic olefins, very little success has been achieved in case of acyclic olefins. This warrants for more work in this area. Design of new kind of chiral ligands is needed so that high ees can be obtained in all types of olefins<sup>29</sup>. Role of phenylhydrazone to increase the rate of the reaction needs to be looked and analyzed.

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