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An Ionic Liquid immobilized Copper complex for catalytic epoxidation

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R. Dileep[a]* and B. J. Rudresha[b]

This article brings into focus on an *in situ* strategy of immobilization of a copper complex onto an ionic liquid support. A practical method of olefin and terpene epoxidation by immobilizing a copper complex and 1-ethyl-3-methylimidazolium hexafluorophosphate and using H_2O_2 as the terminal oxidant is developed. The advantageous properties of this catalytic system redefine an exceptionally clean environment for catalytic epoxidations.

Immobilization of transition metal Schiff-base complexes onto zeolitie, polymeric or clay matrices has been adopted to prepare heterogeneous catalysts. One of the prominent achievements in this field is the use of ionic liquids as homogeneous immobilization of organocatalysts in organic synthesis. [1, 2] Ionic liquid immobilized catalysts can induce organic reactions and such reactions are usually carried out in polar solvents, which can form a homogeneous system. After the reaction is complete, a less polar solvent, such as diethyl ether, is added and the IL immobilized catalyst can be easily separated from the organic phase due to solubility differences. As a result, the IL immobilized catalyst is regenerated and can be used for further reactions.

Olefins are one of the most important starting materials for organic synthesis and their oxidation leads to various value-added products such as epoxides, alcohols, aldehydes, ketones, and carboxylic acids. Hence these are important building blocks for the production of bulk and fine chemicals.[3] Epoxides are valuable and versatile intermediates in organic synthesis [4a-c] and useful starting materials for the preparation of industrial chemicals such as epoxy resins, surfactants, paints, adhesives, and surface coating agents. [4d-f] They can be efficiently obtained by metal-catalyzed oxidation of alkenes using a variety of oxidants such as oxygen, peroxides, hypochlorites, peracids etc. The catalyzed oxidations have the advantage of generating less waste by-products than the stoichiometric processes. [4d]

The term terpene used to refer to some hydrocarbons from turpentine, also called "resin of pine trees". This term is now more generally employed for all natural compounds composed by isoprene units. [7] The terpenes are oligomeres composed by isoprene units as monomer epoxides of terpenes are important starting materials with a wide variety of uses such as in flavors, fragrances, and pharmaceuticals. [5, 6] Pinene oxide is, for instance, a starting material for the synthesis of the sandalwood fragrance. Preparation of the oxidized terpenes under current industrial methods requires percarboxylic acids, which may leave an equimolar waste product after the reaction [5a, 6] Hydrogen peroxide (H_2O_2) is an ideal oxidant because water is the only side product and the atom efficiency is excellent. [7, 8] Although a number of metal-catalyzed H_2O_2 epoxidation reactions have been reported thus far [9, 10] the epoxidation of terpenes is still a challenging task due to their sensitivity toward acidic media. [5b, 10] Hence a catalytic system applicable to nearly neutral conditions without loss of activity at ambient temperature is necessary for the epoxidation of terpenes.

Pursuing the reactivity of copper complexes with a triphenylphosphine and a ligand derived from 2-hydrazinopyridine and salicylaldehyde and its 5-substituted derivatives is of our interest. We had reported earlier, the same complexes for the oxidation of a variety of alcohols. [11] Herein, the oxidation of selected olefins and some terpenes with H_2O_2 catalyzed by Copper complexes, 1-5, in ionic liquid, 6, under different reaction conditions is reported (Scheme 1). In this work, the advantageous properties of the Copper-H_2O_2 oxidation system and $[Emim]PF_6$ have been combined to give an exceptionally clean environment for catalytic oxidations. One major advantage of this system is that both peroxide and the catalyst are soluble in the ionic liquid. This gives an oxidation solution that is completely homogeneous. Based on the synthesized catalyst, an extremely effective and reusable oxidation system for the oxidation of olefins, performed in ionic liquid $[Emim]PF_6$ with a well-proportioned CH_2Cl_2 at room temperature is described.

Complexes **1-5** were tested for their catalytic activities on the epoxidation of some olefins (Table 1) under similar conditions as mentioned in the experimental. It was found that complexes **1, 2** and **5** gave a better result compare to complexes **3** and **4**. This may be due to the electronegative nature of the substituents in the complexes. Complex **1** gave the best result (conversion) followed by

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[a] *Department of Chemistry, GITAM University, Bengaluru campus, Doddaballapur, Bangalore North-561203, India.Email. dileepr@gitam.edu; dileep.618@gmail.com*

[b] *Department of Chemistry, Brindavan College of Engineering, Yelehanka, Bangalore- 560063, India*

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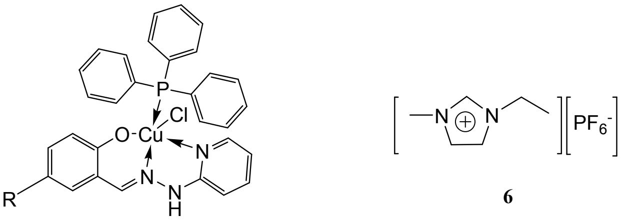
complexes **5** and **2**. Also, this may be due to the fact that the catalytic activity of complexes varies with the size of substituent. It was observed that the activity decreases with increase of bulkiness of the substituents. This may be due to steric hindrance caused by the substituent, which can affect the planarity of the ligand in the complexes.[12] Further the recycling of the catalyst-ionic liquid mixture was found to be easier with respect to **1**.



1-5

6

Scheme1. Structures of Copper complexes [R= -H **(1)**, -OCH$_3$ **(2)**, -Cl **(3)**, -Br **(4)**, -NO$_2$ **(5)**] and ionic liquid **(6)**

Table 1 Epoxidation of cyclic alkenes catalyzed by copper complexes **1-5** [a]

Entry	Substrate	Time (h)	Conversion (%)[b]				
			1	2	3	4	5
1	Cyclohexene	3	96	90	78	76	89
2	1-methylcyclohexene	3	89	87	65	67	80
3	Cyclohexen-1-yl benzene	3	92	87	54	49	82
4	Cyclohex-2en-1-ol	4	93	89	69	72	85
5	Styrene	3	97	91	78	71	81

[a] All the reactions were carried out at room temperature

[b] Epoxides were identified by using authentic samples for comparison**.**

Imidazole plays a crucial role in biological systems especially in metalloenzymes. [13] It is also used as solvent for many catalytic transformations involving metal complexes.[14, 15] Preliminary screening started with using a mixture of appropriate amounts of complex 1 and **Emim** in different solvents (Table 2). Styrene was chosen as the substrate for the epoxidation process using H$_2$O$_2$ as oxidant. No reaction was observed with water (Table 2, entry 1) and isopropyl alcohol (Table 2, entry 2) due to the high dielectric constants. With acetonitrile a little conversion of 24% was observed (Table 2, entry 3). High percentage conversions were observed with acetone (Table 2, entry 4) and dichloromethane (Table 2, entry 5). Between these two solvents, excellent conversions with good selectivity resulted by using dichloromethane as the co-solvent.

In the present experimental conditions, phosphoric acid acts as a co-catalyst. It is noteworthy that the selectivity of the reaction products decreased in absence of phosphoric acid (Table 3, entry 6). Also these reactions are effective at neutral pH. Most importantly, it is necessary to protect the epoxide from undergoing hydrolysis. This is done by the addition of NaOH for weakening the Brønsted acid reactivity. Without any pH alteration (without the addition of Sodium hydroxide) the yield of the epoxide was found to be very low (Table 3, entry 7).

Complex **1** was used as catalyst for the optimization of the reaction. Three different fractions of [**Emim**]PF$_6$ ionic liquid were chosen to make a kinetic study, which could clearly illustrates that the acceleration in the rate of the reaction results from the different mixed proportion. As shown in **Figure 1**, the reaction was almost complete within 30 hours in the mixed solvent [**Emim** (1 ml) + CH$_2$Cl$_2$ (1 ml)], however, there was no obvious rate acceleration effect in the mixed solvent [**Emim** (4 ml) + CH$_2$Cl$_2$ (1 ml)].

Table 2 Epoxidation of styrene[a] in [Emim]PF$_6$-H$_2$O$_2$ system

Entry	Solvent[b]	% Conversion	% Yield
1	Water	0	0
2	Isopropyl alcohol	0	0
3	Acetonitrile	24	12
4	Acetone	78	27
5	Dichloromethane	97	78

[a] all reactions were carried out with 1 mmol of Styrene with **8** mmol of catalyst 1, **2.6** equiv. of H$_2$O$_2$, **4** mmol H$_3$PO$_4$, pH adjusted to near neutral with NaOH solution

[b] The reaction was carried out with 1:1 Emim: Solvent.

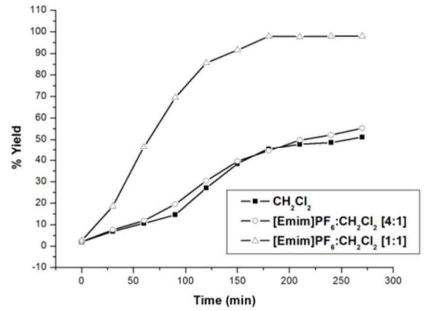


Figure 1 Study on the rate of the oxidation reaction of Styrene

The epoxidation of styrene with hydrogen peroxide was catalyzed by **1** was carried out in **6** to give styrene epoxide (**7**) and phenyl acetaldehyde (**8**) in 78.8% and 21.2% yield, respectively. The oxidation of cyclohexene (**9**) with hydrogen peroxide and **1** in **6** gave epoxycyclohexane (**10**), 2-cyclohexenol (**11**) and 2-cyclohexenone (**12**) in 87.6, 7.1, 5.3%, respectively (Scheme 2), but cyclooctene gave only epoxycyclooctane in 86% yield.

Styrene was used for the optimization of the reaction conditions in ionic liquid (Table 3). The initial study was carried out using styrene as substrate and 2 mmol of aqueous H$_2$O$_2$ at room temperature in the presence of 8 mmol of catalyst. The oxidation proceeded smoothly and 90% isolated yield of benzaldehyde was obtained with 99% conversion and 79% selectivity after one hour stirring.

The oxidation occurred only in poor yield by simply bubbling molecular oxygen through reaction mixture under similar reaction conditions (Table 3, entry 2). To evaluate the catalytic effect of catalyst, the oxidation of styrene was carried out under similar reaction conditions in the absence of catalyst and no conversion was observed (Table 3, entry 3). The reaction was complete at 60 minutes at room temperature (Table 3, entry 1). Further, when the oxidation of was carried out using less amount of the catalyst, the yield was low (Table 3, entry 4). Also the reaction was carried out by varying the oxidant concentration to get the optimum yield (Table 3, entry 5). The organic phase containing product was separated after the completion of the reaction leaving behind the catalyst immobilized in ionic liquid. The recovered brown oily ionic liquid containing **1** could be reused for further catalytic reactions.

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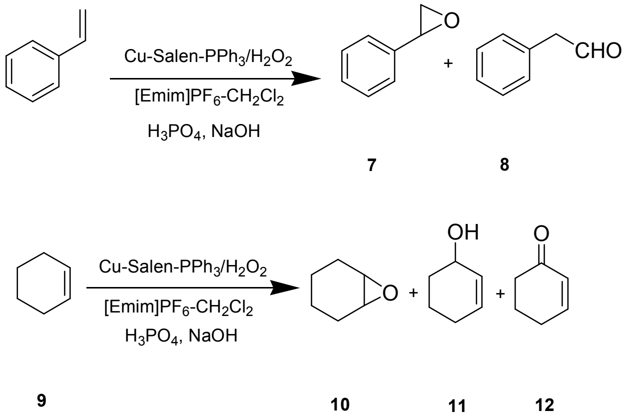

Scheme 2. The epoxidation of alkenes by hydrogen peroxide catalyzed by **1** immobilized in **6**

Table 3 Epoxidation of styrene[a] in [Emim]PF$_6$-H$_2$O$_2$ system

Entry	Reaction time (h)	% Conversion	% Yield
1	3	99	87
2[b]	10	<10	Nil
3[c]	10	NR[d]	Nil
4[e]	5	30	Nil
5[f]	5	73	9
6[g]	3	99	14
7[h]	3	23	8

[a] Unless otherwise indicated, all reactions were carried out with 1 mmol of Styrene with 8 mmol of catalyst 1, 2.6 equiv. of H$_2$O$_2$, 4 mmol H$_3$PO$_4$, pH adjusted to near neutral with NaOH solution.
[b] The reaction was carried out under oxygen instead of H$_2$O$_2$.
[c] Reaction without catalyst.
[d] NR: No reaction
[e] 1.5 mmol of catalyst.
[f] 1 mmol of H$_2$O$_2$.
[g] Reaction without H$_3$PO$_4$
[h] Reaction without NaOH

The results in Table 4 show that different olefinic substrates have been oxidized to epoxides, with good yields. In entry 3, to remove water completely from the system, molecular sieves were used for the reaction, and hence only the epoxide was obtained. One interesting fact is the poor conversion of 1-decene (entry 15). This may be due to the fact that 1-decene was almost insoluble in the ionic liquid and hence heterogeneity was present in the solution. Moreover after 36 h, we observed that the reaction mixture was still intensely yellow-brown, indicating that the catalyst is still active. Also the reaction mixture was stable in ionic media. The time required for the reaction is quite less. Remaining reactants and products are both easily removed from the reaction mixture via extraction with diethyl ether, which is immiscible with the ionic liquid used. This method of removing reactants and products is also advantageous because catalyst and the ionic liquid are insoluble in diethyl ether. Careful evaporation of the ether extracts gave the reactant–product mixture, which was then analyzed by GC and NMR spectra.

Table 5 shows the epoxidation of some terpenes. The reaction conditions were the same as that used for the epoxidation of alkenes, except for the temperature which was maintained at 25°C and the reaction time was 12- 15 hours. Because the epoxidation of terpenes is exothermic to a small extent, reaction temperature control was found critical for a better yield of the product.

Table 5 Epoxidation of some terpenes catalyzed by complex 1 [a]

Entry	Substrate	Time (h)	Conversion (%)	Yield[b] (%)
1	3-Carene	13	87	79
2	α-pinene	15	93	81
3	α -Terpinol	12	82	74
4	Limonene	12	86	74
5	Myrcene	14	82	75

[a] All the reactions were carried out at 25°C
[b] After distillation

It is noteworthy that the recycled copper catalyst **1** in ionic liquid **6** showed comparable activity even after 6–7 runs in the oxidation of styrene with hydrogen peroxide (Fig 2). However, the addition of excess oxidant to the reaction mixture resulted in the degradation of catalyst. However, it should be pointed out that ILs are not intrinsically "green". Most of them are as toxic as other organic solvents, whereas some demonstrate extreme toxicity. Recently, the issues of biodegradability and toxicity of ILs have become of primary interest. The toxicity of 1-alkyl-3- methyl Imidazolium ionic liquids increases with increase in the size of the alkyl group [16]. This is due to the fact that the ionic nature decreases as the bulkiness of the organic cation increases. Ionic liquids like **Emim** [PF$_6$] have a simple alkyl group which constitutes for a good ionic character and hence their toxicity levels are very low. Moreover the complete ionic liquid-catalyst mixture was recovered and reused.

Conclusions

In summary, the advantages of this oxidation system are: (i) hydrogen peroxide and catalyst are completely soluble in [Emim]PF$_6$, giving a homogeneous oxidation solution. (ii) Products are easily separated from the reaction solution by extraction with an immiscible solvent. We also hope to expand the use of this oxidation solution to substrates other than olefins, such as hydrocarbons, amines, Sulphides and other aromatic compounds.

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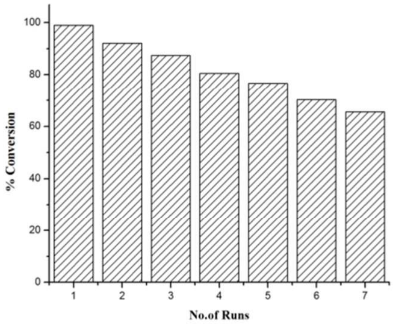

Fig 2 Effect of recycling on conversion

Table 4 Epoxidation of alkenes catalyzed by complex 1 [a]

Entry	Substrate	Time (h)	Conversion (%)	Selectivity (%)	
				Epoxide [b]	Others
1	Cyclohexene	3	96	87	12
2	1-methylcyclohexene	3	90	89	11
3	Cyclohexen-1-yl benzene	3	92	31	69[c]
4	Cyclohex-2en-1-ol	4	93	92	8[d]
5	Styrene	3	97	79	21[e]
6	2-chlorostyrene	3	86	76	24[f]
7	*Trans*-Stilbene	4.5	94	82	18
8	*Cis*-Stilbene	5	86	81	19
9	(E)-(2-(cyclohexa-2,4-dien-1-yl)prop-1-en-1-yl)benzene	4.5	91	89	11
10	(E)-prop-1-en-1-ylbenzene	4.5	92	88	12
11	Cyclododecatriene	6	89	65	35
12	Cyclooctene	3.5	89	86	14
13	Cyclooctadiene	3	88	87	13[g]
14	cyclopentene	5	97	90	10
15	1-decene	36	9	93	7

[a] All the reactions were carried out at room temperature
[b] Epoxides were identified by using authentic samples for comparison.
[c] Major product was a diol
[d] Major products were in the form of epoxyhexanol and epoxyhexanone
[e] Minor product was aldehyde
[f] Yield of ketone by-product
[g] Minor product was a monoepoxide

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An Ionic Liquid immobilized Copper complex for catalytic epoxidation

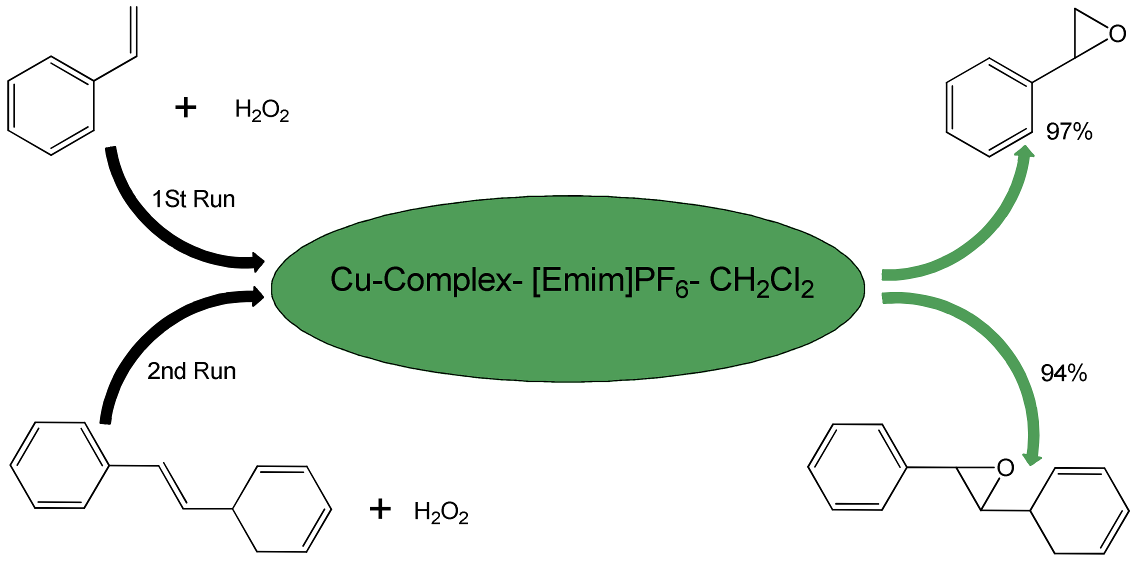
R. Dileep*[a] and B. J. Rudresha[b]

[a]*Department of Chemistry, GITAM University, Bengaluru campus, Doddaballapur, Bangalore North-561203, India*

[b] *Department of Chemistry, Brindavan College of Engineering, Yelehanka, Bangalore- 560063, India*

Graphical Abstract

A catalytic system consisting of Copper-Schiff base-triphenylphosphine complex and hydrogen peroxide was effective in the epoxidation of olefins and terpenes. The oxidation reactions were carried out in ethyl-methyl-imidazolium ionic liquid medium. The catalyst and the ionic liquid mixture was recycled and reused consistently for about 7 times.



*Corresponding author: *Department of Chemistry, GITAM University, Bengaluru campus, Doddaballapur, Bangalore North-561203, India Ph: +91 9880245273*

Email: dileepr@gitam.edu; dileep.618@gmail.com;