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Enantioselective oxidation of olefins catalyzed by chiral copper bis(oxazolinyl)pyridine complexes: a reassessment

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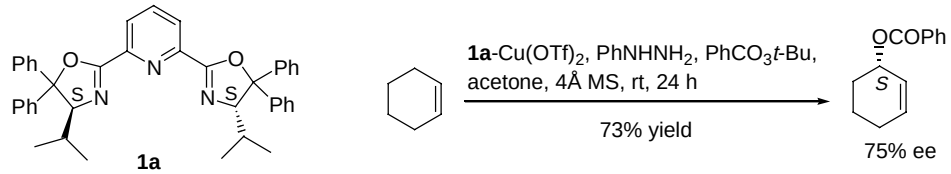
Abstract—Copper complexes of chiral tridentate pybox ligands synthesized using a modified procedure have been studied as catalysts for the enantioselective allylic oxidation of olefins. A variety of olefins have been used in this reaction. Using 5 mol% of a Cu(II) complex of the tridentate pybox ligand, phenylhydrazine, and *tert*-butyl perbenzoate as oxidant in acetone, optically active allylic benzoates were obtained up to 94% ee in few hours. It was also observed that the use of molecular sieves in the reaction did not alter the enantioselectivity. Temperature was found to be very crucial in rate of the enantioselective allylic oxidation of olefins. Using EPR spectra, it has been shown that the Cu(II) species is reduced to Cu(I) by phenylhydrazine and phenylhydrazone, but the reduction with the former is faster in comparison to the latter. It was concluded that the rate enhancement was not specific to the presence of phenylhydrazine or phenylhydrazone, but both were equally responsible provided acetone was used as a solvent.

1. Introduction

Enantioselective allylic oxidation of olefins catalyzed by chiral copper complexes continues to be an important area in asymmetric synthesis.[1,2] Early attempts with this reaction using copper complexes of (+)-α-ethyl camphorate,[3a] chiral Schiff bases,[3b] and L-amino acids[4] gave poor asymmetric induction (5–63% ee). Although important contributions were made in this area by Pfaltz,[5] Andrus,[6] Katsuki,[7] and Singh[8] using peresters and *t*-butyl peroxide[9] as oxidant with copper complexes of chiral bis and trisoxazoline ligands,[10] the longer reaction time was a universal problem with all these reports. The enantioselectivity using the oxazoline ligands had been reasonably good (60–93% ee), but the longer reaction time (up to a month) precluded broader use of these methods in applied synthesis. We later discovered that the use of phenylhydrazine with copper(II) complex of pyridine 2,6-bis(4′-isopropyl-5′,5′-diphenyloxazoline) **1a** (hence forth this is referred to as 'ip-pybox-diph' ligand) in acetone reduced reaction time to a great extent without affecting the enantioselectivity (Scheme 1).

The concept of using phenylhydrazine in the allylic oxidation of olefins catalyzed by chiral bipyridine–copper complexes has also been used by other researchers in this field.[11] The reaction was complete in few hours, but the asymmetric induction was moderate (55% ee in the case of cyclohexene and 75% ee in the case of cycloheptene).[11a] While working on this and related asymmetric reactions using the **1a**, we discovered some discrepancy in the physical data of this ligand. After some time, we could detect and solve the problem (vide infra). It was also discovered that the use of the 'ip-pybox-diph' ligand (**1a**)



Scheme 1.

Keywords: Enantioselective allylic oxidation; Olefins; Phenylhydrazine; Phenylhydrazone.
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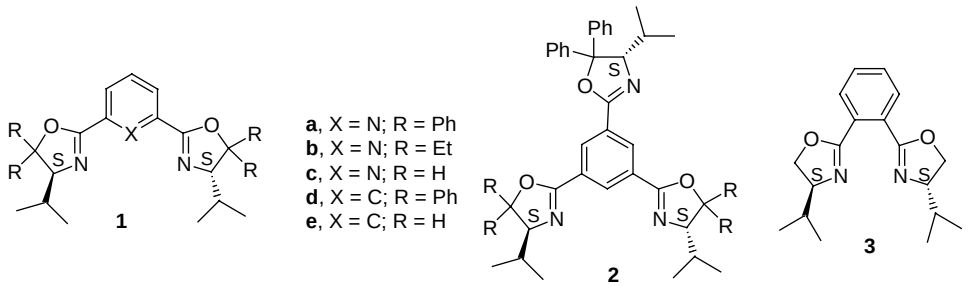
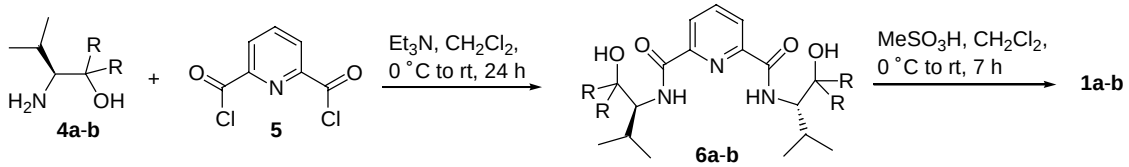
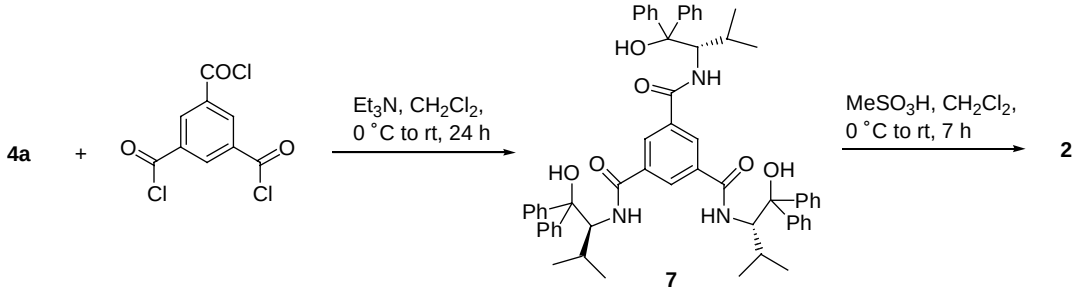


Figure 1.



Scheme 2.



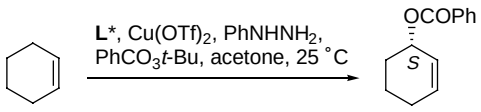
Scheme 3.

from a new procedure gave 93% ee as opposed to a 75% ee reported earlier in the enantioselective allylic oxidation of cyclohexene.[8b] To our delight, the reaction was complete in 1 h (67% yield, 91% ee) not 24 h (73% yield, 75% ee;). In view of this remarkable result, we extended our study further and report our full results in this paper.

It was planned to study the general role of phenylhydrazine in the enantioselective oxidation of olefins using the ligand **1a** (Fig. 1), which was prepared using a procedure previously reported.[12] During the synthesis of **1a**, it was observed that there is an overlapping spot with higher R_f seen on a silica gel tlc plate as an impurity. In a normal way, these were seen as a single spot under UV light, but the impurity becomes clear only when the tlc plate was seen under UV light after exposure to iodine vapour. The impurity could be removed only when the compound was recrystallized from ether. It was observed that the impurity could be minimized if the cyclization of **6a** with methanesulfonic acid was done at rt (Scheme 2). Ligand **1b** was prepared in the same fashion (Scheme 2). A new chiral ligand **2** was also prepared using the above procedure from (*S*)-diphenylvalinol **4a** and the corresponding acid chloride (Scheme 3).

In our initial study, 5 mol% complex of the newly prepared ligand (*S*)-**1a** and $Cu(OTf)_2$, in conjunction with phenylhydrazine, was found to be effective for the allylic oxidation of cyclohexene with *tert*-butyl perbenzoate in acetone. The reaction was complete in 1 h and the (*S*)-allylic benzoate was obtained in 67% yield and 91% ee (Table 1, entry 1). The ip-pybox-dieth ligand **1b** was equally efficient, but the enantioselectivity was slightly lower (85% ee). Under the identical condition, ligand **1c**[13] gave 65% ee (Table 1, entry 3). We could also reproduce Pfaltz's result where 71% ee was reported with this ligand in MeCN.[5] As reported earlier, ligand **1d**[8b] gave racemic product. Along the same line, it was expected that **1e** would not give any enantioselection

Table 1. Enantioselective allylic oxidation of cyclohexene with different ligands



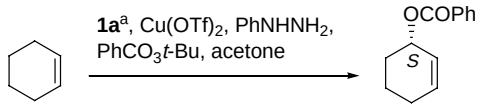
Entry	Ligand (**L***)[a]	Time (h)	Yield (%)	ee (%)
1	**1a**	01	67	91
2	**1b**	07	66	85
3	**1c**	18	85	65[b]
4	**1d**	02	50	00
5	**1e**	15	59	00
6	**2**	05	42	00
7	**3**	37	58	00

[a] 5 mol% of the chiral ligand was used.
[b] The **1c** is known (Ref. 5) to give 71% ee under other condition (**1c**–CuOTf, MeCN, 3 days).

and this was indeed the case (Table 1, entry 5). These results indicated that the pyridine nitrogen is important in chelation with copper in these systems. The results (Table 1, entries 6 and 7) from the ligands **2** and **3** support this hypothesis.

Having achieved good results in the above reaction at rt with ligand **1a**, the reaction at different temperature was studied with the hope to increase the enantioselectivity. The reaction was very sluggish at −20 °C and we could isolate only 3% of the product with the same level of enantioselectivity in 33 days (Table 2, entry 1). Although the reaction took a little longer time (11–29 h) for completion at 0 and 10 °C, the optical yield of the product was slightly better (up to 93% ee), although the chemical yield was similar (Table 2, entries 2 and 3). It was also observed that if the reaction was initiated at 0 °C and then warmed to rt, the optical activity of the product was similar (92% ee) but the reaction time was 20 h (Table 2, entry 4). Thus, it was concluded that 20–25 °C was the optimal temperature for this reaction. In order to see whether the reaction was moisture sensitive, the reaction was carried out in the presence of water (6 mol%) at 25 °C. To our delight, there was no erosion in chemical nor optical yield, however, the reaction time increased from 1 h (67% yield, 91% ee) to 11 h (74% yield, 90% ee) (Table 2, entry 6). In view of our earlier observation that 4 Å molecular sieves are beneficial to this reaction, its effect was also studied. To our surprise, it was found out that as such there was no effect of molecular sieves on chemical and optical yield of this reaction (Table 2, entry 7).

Table 2. Effect of temperature and additive on allylic oxidation



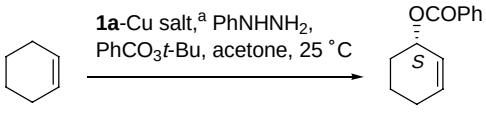
Entry	Additive	Temperature (°C)	Time	Yield (%)	ee (%)
1	Nil	−20	33 days	03	90
2	Nil	0	29 h	67	93
3	Nil	10	11 h	62	91
4	Nil	0 to 25	20 h	75	92
5	Nil	25	01 h	67	91
6	H_2O[b]	25	11 h	79	90
7	4 Å MS	25	04 h	74	91

[a] 5 mol% of the complex was used.
[b] 6 mol% of water added.

As established earlier by us, phenylhydrazine plays an important role in increasing the rate of the allylic oxidation of olefins with *tert*-butyl perbenzoate catalyzed by copper triflate in acetone.[8a] In order to ascertain its role with various Cu salt, the reaction was investigated in different solvents and the results are summarized in Table 3. We already know that the high enantioselectivity is obtained by a complex of **1a** with Cu(I) species and not by Cu(II). Thus, **1a**–CuOTf complex gave 91% ee and the reaction took 39 h for completion in acetone (Table 3, entry 2). In the presence of phenylhydrazine, the same reaction was complete in only 9 h without affecting the enantioselectivity (Table 3, entry 1). If the Cu(I) species was prepared in situ by reduction of **1a**–$Cu(OTf)_2$ with phenylhydrazine in acetone, the reaction was complete in 1 h with 91% ee (Table 3, entry 12). On changing the solvent to acetonitrile using Cu(I) complex and phenylhydrazine, the reaction time was not affected as it took 11–13 days to reach completion with slightly lower optical yield (Table 3, entries 7 and 8). As observed above, if a complex of **1a**–$Cu(OTf)_2$ and phenylhydrazine were used in acetonitrile, where Cu(I) species were prepared in situ by reduction, the reaction time was reduced to 3–4 days without affecting the ee (Table 3, entry 9). A similar trend was observed in benzene, except the enantioselectivity was poor (Table 3, entries 10 and 11). Invariably, lower enantioselectivity (47–60% ee) was obtained when benzene was used as a solvent in this reaction. From the results listed in Table 3, it was concluded that the Cu(I) species prepared by reduction of **1a**–$Cu(OTf)_2$ with phenylhydrazine in acetone is more efficient than use of Cu(I) salt directly in allylic oxidation of olefins.

In order to determine the optimal amount of catalyst in the allylic oxidation of cyclohexene, the reaction was tried with varying amounts of the copper complex (Table 4). Initially, the reaction was tried with 10 mol% of the complex using 10 equiv of cyclohexene (Table 4, entry 1). The reaction was complete in 1 h with high yield (86%) and

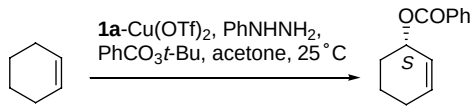
Table 3. Effect of solvent, $PhNHNH_2$, and Cu salt on the reaction



Entry	Solvent	$PhNHNH_2$	Cu salt	Time	Yield (%)	ee (%)
1	Acetone	Yes	CuOTf·PhH	09 h	73	91
2	Acetone	No	CuOTf·PhH	39 h	67	91
3	Acetone	Yes	$[Cu(MeCN)_4]PF_6$	11 h	62	92
4	Acetone	No	$[Cu(MeCN)_4]PF_6$	43 h	90	91
5	MeCN	Yes	CuOTf·PhH	11 days	79	89
6	MeCN	No	CuOTf·PhH	13 days	88	88
7	MeCN	Yes	$[Cu(MeCN)_4]PF_6$	10 days	75	86
8	MeCN	No	$[Cu(MeCN)_4]PF_6$	10 days	88	88
9	MeCN	Yes	$Cu(OTf)_2$	88 h	50	86
10	Benzene	Yes	$[Cu(MeCN)_4]PF_6$	22 h	59	60
11	Benzene	No	$[Cu(MeCN)_4]PF_6$	06 days	61	48
12	Acetone	Yes	$Cu(OTf)_2$	01 h	67	91

[a]5 mol% of the complex was used in the reaction.

Table 4. Effect of amount of the catalyst on the reaction[a]



Entry	**1a**–Cu(OTf)$_2$ (mol%)	Time (h)	Yield (%)	ee (%)
1	10	01	86	91
2	10	03	79	91[b]
3	05	01	67	91
4	05	11	56	91[c]
5	05	14	66	92[d]
6	2.5	08	82	91
7	01	39	91	91

[a] Usually 10 equiv of cyclohexene was used in all the reactions unless stated otherwise.
[b] 5 equiv of cyclohexene was used.
[c] 2 equiv of cyclohexene used.
[d] After disappearance of PhCO$_3$*t*-Bu, 1 equiv of this was added again.

enantioselectivity (91% ee). By reducing the amount of the catalyst to 5 mol%, there was no change in the reaction rate (Table 4, entry 3). On further reduction of the amount of the catalyst to 2.5 and 1 mol%, the similar chemical and optical yields were obtained, but the reaction time was 8 and 39 h, respectively (Table 4, entries 6 and 7). Normally, in all the above reactions, 10 equiv of olefins with respect to *tert*-butyl perbenzoate were used. By reducing the amount of olefin to 5 and 2 equiv, the reaction time was little increased slightly (3 and 11 h), but there was no change in the enantioselectivity (Table 4, entries 2 and 4). Since the reaction was monitored by the disappearance of the perester, an extra equivalent of the perester was added after a tlc indicated disappearance of the 1st equivalent of the perester, but there was no affect on the reaction (Table 4, entry 5).

Initially, phenylhydrazine was used in the reaction for reducing the Cu(II) complex of the ligand to Cu(I).[14] Since the rate enhancement was much higher when acetone was used as a solvent, it was assumed that phenylhydrazone might be responsible for enhancing the rate. It was further found that phenylhydrazine and phenylhydrazone were both reducing Cu(II) to Cu(I) species (green to dark brown), but the rate enhancement in the reaction could be mainly due to phenylhydrazone formed in situ from phenylhydrazine and acetone. In order to confirm and determine the extent of reduction, EPR spectra were run. EPR study of the complex **1a**–Cu(OTf)$_2$ with phenylhydrazine in acetone indicated that the reduction required 15 min (Fig. 2). For the same reduction, phenylhydrazone took 3 h (Fig. 3). So, it was concluded that phenylhydrazone also reduced Cu(II) to a Cu(I) species, but the reduction process was slower. This is also clear from the results shown in Table 5. The reaction was catalyzed by a Cu(II) complex containing chiral ligand **1a**, but the enantioselectivity was not good (Table 5, entry 1). By addition of phenylhydrazine, the reaction time was reduced from 7 days to 1 h and the enantioselectivity was enhanced from 62 to 91% (Table 5, entry 2).

Assuming that phenylhydrazone formed in situ in the above reaction was responsible for the rate enhancement in the reaction, it was used in place of phenylhydrazine. Thus, an equivalent amount (5–6 mol%)

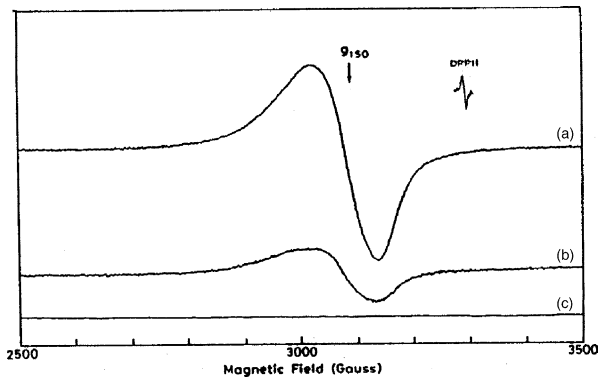


Figure 2. EPR spectrum study with phenylhydrazine in acetone. (a) EPR spectrum of **1a**–Cu(OTf)$_2$ in acetone at rt. (b) PhNHNH$_2$ was added immediately and EPR spectrum was run. (c) EPR spectrum was run after 15 min.

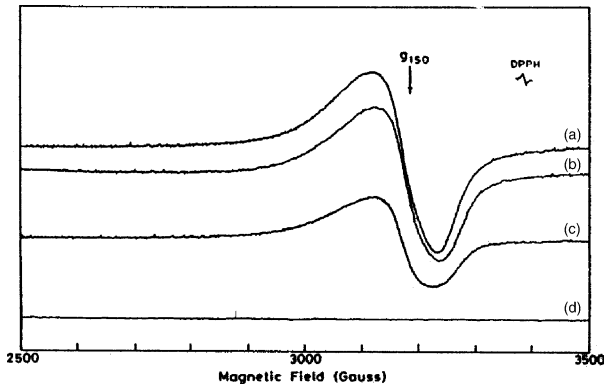
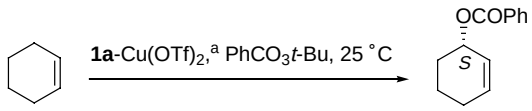
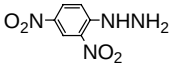
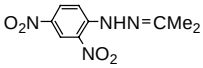


Figure 3. EPR spectrum study with phenylhydrazone in acetone. (a) EPR spectrum of **1a**–Cu(OTf)$_2$ in acetone at rt. (b) PhNHN=CMe$_2$ was added and EPR spectrum was run after 30 min. (c) EPR spectrum was run after 1.5 h. (d) EPR was run after 3 h.

of phenylhydrazone was added to **1a**–Cu(OTf)$_2$ and stirred for 0.5, 1, 2 and 3.5 h before adding cyclohexene and perester. As the reduction time of the Cu(II) complex was increased from 0.5 to 1 h, the time for completion of the reaction was reduced from 24 to 8 h and there was very little improvement in the enantioselectivity (Table 5, entries 3 and 4). However, there was not much difference on increasing the reduction time to 2–3.5 h (Table 5, entries 5 and 6). This was in accord with the above fact from EPR spectra that the reduction of the Cu(II) complex with phenylhydrazone was slower. Reaction in acetone indicated that phenylhydrazine and phenylhydrazone both were increasing the rate of the allylic oxidation reaction, but the former was more efficient (Table 5, entry 2; 1 h reaction time) than the latter (Table 5, entry 6; 3 h reaction time). However, on changing the solvent to acetonitrile, the reaction was slower in both cases (Table 5, entries 9 and 10) and there was no difference in the rate (reaction time 88 and 74 h). Thus, it was concluded that the rate enhancement was not specific to the presence of phenylhydrazine or phenylhydrazone, but both were equally responsible provided acetone was used as a solvent. 2,4-Dinitrophenylhydrazine and its corresponding hydrazone had no effect on the reaction rate (35 days). This observation is more obvious as the electron transfer rate will be much more slower due to the nitro-substitution.

Table 5. Effect of reducing agents on the reaction[a]

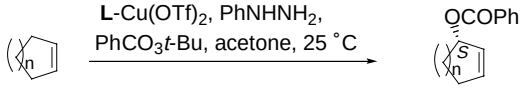


Entry	Reducing agent	Solvent	Time	yield (%)	ee (%)
1	Nil	Acetone	07 days	35	62
2	$PhNHNH_2$	Acetone	01 h	67	91
3	$PhNHN{=}CMe_2$	Acetone	24 h	64	89
4	$PhNHN{=}CMe_2$	Acetone	08 h	67	90[b]
5	$PhNHN{=}CMe_2$	Acetone	08 h	69	90[c]
6	$PhNHN{=}CMe_2$	Acetone	03 h	62	90[d]
7	$PhNHN{=}CMe_2$	CH_2Cl_2	18 h	75	66
8	$PhNHN{=}CMe_2$	Benzene	76 h	65	40
9	$PhNHNH_2$	Acetonitrile	88 h	50	86
10	$PhNHN{=}CMe_2$	Acetonitrile	74 h	51	89
11		Acetone	35 days	40	78
12		Acetone	35 days	41	66

[a] Normally the reaction mixture (RM) was stirred for 30 min after the addition of a reducing agent unless stated otherwise (viz. b,c, and d).
[b] The RM was stirred for 1 h.
[c] The RM was stirred for 2 h.
[d] The RM was stirred for 3.5 h.

Having established optimal conditions for enantioselective allylic oxidation of cyclohexene, the reaction was extended to other olefins with *tert*-butyl perbenzoate using chiral ligands **1a** and **1b**. The results are summarized in Table 6. Cyclopentene and cycloheptene gave a maximum of 70 and 86% ee, respectively. Although cyclooctene gave the highest enantioselectivity (94% ee), cyclooctadiene gave only 80% ee.

Table 6. Enantioselective allylic oxidation of different olefins with *tert*-butyl perbenzoate[a]

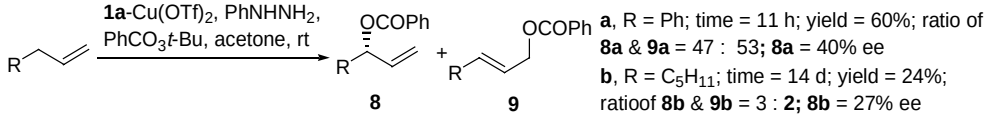


Entry	Olefin	L	Time	Yield (%)	ee (%)
1		**1a**	01 h	67	91
2		**1b**	07 h	66	85
3		**1a**	03 h	76	70
4		**1b**	24 h	58	65
5		**1a**	06 h	47	86
6		**1b**	48 h	37	60
7		**1a**	06 h	34	94
8		**1b**	06 d	46	71
9		**1a**	05 d	31	80
10		**1b**	05 d	40	71

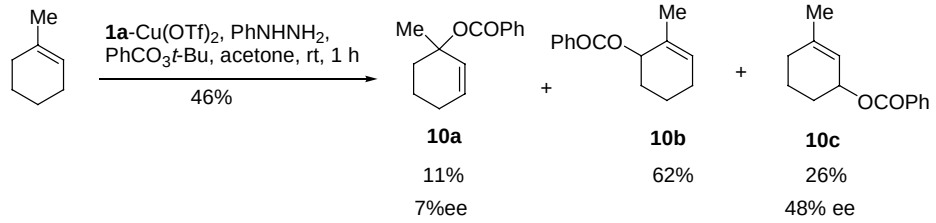
[a] The ee was determined by HPLC on chiral columns as mentioned in Section 2.

Although a high ee was obtained for cyclic olefins, acyclic olefins gave poor selectivity (Scheme 4). During the oxidation of allylic benzene, 60% yield of a mixture of benzoates (**8a** and **9a**) with a ratio of 47:53 were obtained. The optical purity of **8a** was 40%. 1-Octene gave a poor yield of products (**8b** and **9b**) in a ratio of 3:2. Enantioselectivity in this case was very poor (27% ee). The allylic oxidation was also attempted on 1-methylcyclohexene (Scheme 5). Under optimal conditions, 46% yield of a mixture of three products (**10a**, **10b**, and **10c**) was obtained. Among these, we could determine the enantioselectivity only in case of **10a** (7% ee) and **10c** (48% ee). Although **10b** was a major product, its enantiomeric excess could not be determined.

The transition state model based on π-stacking with the ligand **1a** has been proposed earlier for this reaction.[8b] The results detailed in this paper also support the transition state model proposed earlier. There is an enhancement of enantioselectivity from 65 to 91% from the ligand ip-pybox **1c** to ip-pybox-diph **1a** (Table 1, entries 1 and 3). This does suggest that the *gem*-diphenyl groups play an important role in stabilizing the transition state, and we feel that it is primarily due to π-stacking.[15] *gem*-Diethyl groups also enhanced the ee to 85% (Table 1, entry 2), but its effect is less than that of *gem*-diphenyl groups. The effect from



Scheme 4. Enantioselective allylic oxidation of acyclic olefins.



Scheme 5. Enantioselective oxidation of 1-methylcyclohexene.

diphenyl to diethyl groups in the chiral ligand is quite consistent in all the olefins studied (Table 6).

In conclusion, we have investigated enantioselective allylic oxidation of olefins with a copper complex of pybox ligands with *tert*-butyl perbenzoate. We have shown that the reaction time is reduced drastically by using phenylhydrazine in acetone as a solvent. It was also confirmed that phenylhydrazone formed in situ is also responsible for the same effect. It was concluded that the shorted reaction time was not specific to the presence of phenylhydrazine or phenylhydrazone, but both were equally responsible, provided acetone was used as a solvent. Under the optimal conditions using 'ip-pybox-diph' ligand (*S*,*S*)-**1a**, we were able to convert olefins into (*S*)-allylic benzoate in up to 94% ee.

2. Experimental

2.1. General methods

^{1}H NMR spectra were recorded on 400 MHz spectrometer. Chemical shifts are expressed in ppm downfield from TMS as internal standard, and coupling constants are reported in Hz. Routine monitoring of reactions were performed by TLC, using precoated silica gel TLC plates obtained by E-Merck. All the column chromatographic separations were done by using silica gel (Acme's, 60–120 mesh). Petroleum ether used was of boiling range 60–80 °C. Reactions that needed anhydrous conditions were run under the atmosphere of nitrogen or argon using flame-dried glassware. The organic extracts were dried over anhydrous sodium sulfate. Evaporations of solvents was performed at reduced pressure. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under nitrogen. Benzene, dichloromethane, acetonitrile and acetone were distilled from CaH_2.

2.1.1. *N*,*N*′-Bis[1′-(*S*)-isopropyl-2′2′-diphenyl-2′-hydroxyethyl]-2,6-pyridine-dicarboxamide (6a).[8b] This was prepared as per our procedure. But, the purification was done by column chromatography over silica gel followed by recrystallization from CH_2Cl_2/*n*-hexane. Yield 95%; mp 220–221 °C (lit.[8b] mp 110–111 °C); R_f 0.27 (1:2, EtOAc in petroleum ether); $[\alpha]_D^{25}$ −50.3 (*c* 1, $CHCl_3$) [lit.[8b] $[\alpha]_D^{25}$ −46.2 (*c* 1, $CHCl_3$)]. ^{1}H NMR (DMSO-d_6, 400 MHz) δ 0.83 (d, J=6.8 Hz, 6H), 1.08 (d, J=6.6 Hz, 6H), 1.81 (m, 2H), 2.49 (s, 2H, OH), 5.02 (d, J=10.7 Hz, 2H), 6.07(s, 2H, NH) 7.02 (t, J=7.3 Hz, 2H), 7.11–7.19 (m, 6H), 7.32 (t, J=7.6 Hz, 4H), 7.52–7.55 (m, 8H), 7.99–8.08 (m, 1H), 8.26 (d, J=10.7 Hz, 2H); MS (FAB, *m*/*z*) 642 (M^++1).

2.1.2. *N*,*N*′-Bis[1′-(*S*)-isopropyl-2′2′-diethyl-2′-hydroxyethyl]-2,6-pyridine-dicarboxamide (6b). This was prepared as per our procedure. But, the purification was done by column chromatography over silica gel followed by recrystallization from CH_2Cl_2/*n*-hexane. Yield 50%; mp 141–142 °C; R_f 0.37 (1:1, EtOAc in petroleum ether); $[\alpha]_D^{25}$ −8.2 (*c* 1, $CHCl_3$); [lit.[8a] $[\alpha]_D^{25}$ −3.6 (*c* 0.6, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.82 (d, J=7.6 Hz, 6H), 0.90 (d, J=7.6 Hz, 6H), 0.96 (d, J=6.8 Hz, 6H), 0.99 (d, J=6.8 Hz, 6H), 1.45–1.70 (m, 8H), 2.21 (m, 2H), 4.02 (dd, J=10.3, 1.9 Hz, 2H), 8.03 (t, J=7.8 Hz, 1H), 8.27 (d, J=10.0 Hz, 2H), 8.32 (d, J=7.8 Hz, 2H).

2.2. General procedure for cyclization of amido alcohols (6) to ip-Pybox-diph (1a) and ip-Pybox-dieth (1b)

Methanesulfonic acid (30 mmol) was added dropwise to a solution of amido alcohol **6** (5 mmol) in CH_2Cl_2 (120 mL) at 0 °C over a period of approximately 10 min and the reaction mixture was stirred for 7 h in the case of **1a** and 18 h in the case of **1b** and during the process the cooling bath warmed to rt (0 to 25 °C). It was diluted with CH_2Cl_2 (100 mL) and washed with aqueous $NaHCO_3$, water and brine. The organic layer was dried over anhydrous $NaSO_4$ and the solvent was evaporated in vacuo to afford **1** as off-white solid, which was purified by column chromatography and recrystallization.

2.2.1. 2,6-Bis[5′,5′-diphenyl-4′-(*S*)-isopropyloxazolin-2′-yl]pyridine (1a).[8] This was prepared from **6a** using a general procedure mentioned above and then recrystallized with Et_2O to afford the product **1a** as a white crystal: yield 65%; mp 161–163 °C (lit.[8b] mp 65–66 °C); R_f 0.37 (1:2, EtOAc in petroleum ether); $[\alpha]_D^{25}$ −386.2 (*c* 1.1, $CHCl_3$) [lit.[8b] $[\alpha]_D^{25}$ −233.0 (*c* 2.7, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.67 (d, J=6.6 Hz, 6H), 1.06 (d, J=6.8 Hz, 6H), 1.93 (m, 2H), 4.87 (d, J=4.6 Hz, 2H), 7.21–7.30 (m, 9H), 7.34–7.42 (m, 7H), 7.66 (d, J=6.1 Hz, 4H), 7.89 (t, J=6.0 Hz, 1H), 8.22 (d, J=7.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) 17.3, 21.9, 30.3, 80.5, 93.5, 125.6, 126.3, 127.0, 127.3, 127.7, 127.8, 128.3, 137.4, 140.5, 145.2, 147.2, 160.6; MS (FAB, *m*/*z*) 606 (M^++1).

2.2.2. 2,6-Bis[5′,5′-diethyl-4′-(*S*)-isopropyloxazolin-2′-yl]pyridine (1b).[8a] This was prepared from **6b** using the above general procedure: yield 85%; mp 82–84 °C; R_f 0.4 (2:3, EtOAc in petroleum ether); $[\alpha]_D^{25}$ −36.4 (*c* 1.1, $CHCl_3$) [lit.[8b] $[\alpha]_D^{25}$ −37.1 (*c* 1.4, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.95 (t, J=7.6 Hz, 6H), 1.02–1.06 (m, 12H), 1.16 (d, J=6.6 Hz, 6H) 1.70 (m, 4H), 1.86–2.0 (m, 6H), 3.74 (d, J=7.8 Hz, 2H), 7.82 (t, J=7.8 Hz, 1H), 8.03 (d, J=7.8 Hz, 2H).

2.2.3. *N*,*N*′,*N*″-Tris[1′-(*S*)-isopropyl-2′2′-diphenyl-2′-hydroxyethyl]-1,3,5-benzene-tricarboxamide (7). A solution of 1,3,5-benzenetricarboxylic chloride (4.8 mL, 1.0 M solution in CH_2Cl_2) was added slowly to a mixture of (*S*)-(−)-2-amino-3-methyl-1,1-diphenylbutan-1-ol **4a**[8] (3.63 g, 14.2 mmol), Et_3N (5 mL, 36 mmol) and CH_2Cl_2 (50 mL) at 0 °C over a period of 15 min and the mixture was stirred for 24 h (0 °C to rt). The reaction mixture was diluted with CH_2Cl_2 (50 mL) and washed with aqueous $NaHCO_3$, water, and brine. The organic layer was dried over anhydrous $NaSO_4$, and the solvent was evaporated in vacuo to afford white solid, which was purified by column chromatography over silica gel and recrystallised from CH_2Cl_2/hexane to get pure product **7** (3.10 g, yield 80%): mp 178–180 °C; R_f 0.22 (1:4, EtOAc in petroleum ether); $[\alpha]_D^{25}$ −82.0 (*c* 2, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (d, J=6.8 Hz, 9H), 0.97 (d, J=6.8 Hz, 9H), 1.96 (m, 3H), 6.74 (d, J=10 Hz, 3H), 7.09 (t, J=7.6 Hz, 3H), 7.19–7.26 (m, 11H), 7.35 (t, J=7.6 Hz, 6H), 7.51 (t, J=7.6 Hz, 13H), 7.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 18.0, 22.9, 29.1, 58.9, 76.7, 77.0, 77.3, 82.2, 125.2, 125.3, 126.9, 127.8, 128.3, 128.4, 135.4, 145.2, 146.0, 166.3. Anal. Calcd for $C_{60}H_{63}N_3O_6$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.0; H, 6.97; N, 4.48.

2.2.4. 1,3,5-Tris[5′,5′-diphenyl-4′-(*S*)-isopropyloxazolin-2′-yl]benzene (2). Methane sulfonic acid (571 μL, 8.8 mmol) was added dropwise to a solution of amido alcohol **7** (900 mg, 0.98 mmol) in CH_2Cl_2 (40 mL) at 0 °C over a period of 10 min and the mixture was stirred for 18 h (0 °C to rt). The reaction mixture was diluted with CH_2Cl_2 (30 mL) and washed with aqueous $NaHCO_3$, water and brine. The organic layer was dried over anhydrous $NaSO_4$ and the solvent was evaporated in vacuo to afford **2** as a off-white solid, which was purified by column chromatography (650 mg, yield 77%): mp 121–124 °C; R_f 0.56 (1:4, EtOAc in petroleum ether); $[\alpha]_D^{25}$ −376.3 (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.67 (d, J=6.6 Hz, 9H), 1.06 (d, J=6.6 Hz, 9H), 1.87 (m, 3H), 4.85 (d, J=4.6 Hz, 3H), 7.23–7.38 (m, 24H), 7.59 (d, J=7.6 Hz, 6H), 8.90 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) 17.1, 21.9, 30.5, 80.2, 93.2, 126.3, 127.0, 127.3, 127.7, 127.8, 128.3, 128.9, 130.6, 140.5, 145.2, 160.4. Anal. Calcd for $C_{60}H_{57}N_3O_3$: C, 83.01; H, 6.62; N, 4.84. Found: C, 82.90; H, 6.71; N, 4.76.

2.3. General procedure for enantioselective allylic oxidation of olefins with *tert*-butyl perbenzoate in the presence of $PhNHNH_2$ using a complex of chiral ligands and $Cu(OTf)_2$

A solution of a chiral ligand (0.06 mmol) and $Cu(OTf)_2$ (0.05 mmol) in appropriate solvent (4 mL) was stirred at appropriate temperature (see Tables) for 1 h. To this colored (green for **1a**; blue for **1b**, **1c**, **1d**, **1e**, and 3; colorless for **2**,) solution was added phenylhydrazine (6 μL, 0.06 mmol), and the mixture was stirred for 30 min. During this time, the color of the solution changed (dark brown for **1a** and **1b**; light brown for **1c**; yellow for **1d**, **1e**, and **3**; fluorescent orange for **2**) giving an indication for reduction of Cu(II) to Cu(I) species. Then, an olefin (2 mmol to 10 mmol depending upon the experiment) was added followed by a dropwise addition of a *tert*-butylperbenzoate (1 mmol) under N_2 atmosphere. After few minutes, the color of the solution changed (green for **1a**, **1b**, **1c**, **1d**, **1e**, and **3**; fluorescent reddish brown for **2**). The reaction mixture was left at rt until the reaction was complete (disappearance of perester by TLC) during which time the color of the reaction mixture again changed (dark brown for **1a** and **1b**; light brown for **1c**; green for **1d**; yellow for **1e** and **3**; fluorescent reddish brown for **2**). After the reaction was over, the solvent was removed in vacuo and the crude product was purified by column chromatography using silica gel.

2.4. General procedure for enantioselective allylic oxidation of cyclohexene with *tert*-butyl perbenzoate using a complex of chiral ligand (1a) and $(CuOTf)_2\cdot PhH$ or $[Cu(CH_3CN)_4]PF_6$

A solution of **1a** (0.06 mmol) and Cu(I) salt (0.05 mmol) in appropriate solvent (4 mL) was stirred at rt for 1 h. To this brown solution was added cyclohexene (10 mmol), and the mixture was stirred for 5 min. Then, *tert*-butyl perbenzoate (1 mmol) was added dropwise under N_2 atmosphere. After few minutes, the color of the solution turned green. The reaction mixture was left at rt until the reaction was complete (disappearance of perester by TLC) during which time the color of the reaction mixture turned dark brown again. After the reaction was over, the solvent was removed in vacuo and the crude product was purified by column chromatography using silica gel.

2.5. General procedure for enantioselective allylic oxidation of cyclohexene with *tert*-butyl perbenzoate using a complex of chiral ligand (1a) and $(CuOTf)_2\cdot PhH$ or $[Cu(CH_3CN)_4]PF_6$ in the presence of $PhNHNH_2$

A solution of a chiral ligand (0.06 mmol) and Cu(I) salt (0.05 mmol) in appropriate solvent (4 mL) was stirred at rt for 1 h. To this brown solution was added phenylhydrazine (6 μL, 0.06 mmol), and the mixture was stirred for 30 min. Then, an olefin (10 mmol) was added followed by a dropwise addition of a perester (1 mmol) under N_2 atmosphere. After few minutes, the color of the solution started changing towards green. The reaction mixture was left at rt until the reaction was complete (disappearance of perester by TLC) during which time the color of the reaction mixture turned dark brown again. After the reaction was over, the solvent was removed in vacuo and the crude product was purified by column chromatography using silica gel.

2.6. General procedure for enantioselective allylic oxidation of cyclohexene with *tert*-butyl perbenzoate using (1a)–$Cu(OTf)_2$ in the presence of hydrazones

A solution of a **1a** (0.06 mmol) and $Cu(OTf)_2$ (0.05 mmol) in appropriate solvent (4 mL) was stirred at rt for 1 h. To this green solution was added appropriate arylhydrazone (0.06 mmol), and the mixture was stirred for appropriate time (Table 5). During this time, the color of the solution changed (brown for phenylhydrazone and yellow for 2,4-dinitrophenylhydrazone) giving an indication for reduction of Cu(II) to Cu(I) species. Then, an olefin (10 mmol) was added followed by a dropwise addition of a perester (1 mmol) under N_2 atmosphere. After few minutes, the color of the solution turned green in the case of phenylhydrazone. The reaction mixture was left at rt until the reaction was complete (disappearance of perester by

TLC) during which time the color of the reaction mixture again changed to dark brown in the case of phenylhydrazone. After the reaction was over, the solvent was removed in vacuo and the crude product was purified by column chromatography using silica gel.

2.6.1. (*S*)-2-Cyclohexenyl-1-benzoate (Table 2, entry 2).[8b] It was obtained in a maximum of 93% ee. The optical purity was determined by HPLC on chiralpak AD-H column [hexane/2-propanol 99.7:0.3]; flow rate 0.5 mL/min; t_R=11.52 min (*R*), 12.63 min (*S*); $[\alpha]_D^{25}$ −167.2 (*c* 4.4, $CHCl_3$) [lit.[8b] (86% ee); $[\alpha]_D^{25}$ −157.0 (*c* 0.45, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.68–2.17 (m, 6H), 5.51 (m, 1H), 5.81–5.85 (m, 1H), 5.99–6.03 (m, 1H), 7.43 (t, *J*=7.8 Hz, 2H), 7.54 (t, *J*=7.3 Hz, 1H), 8.06 (dd, *J*=6.8, 1.3 Hz, 2H).

2.6.2. (*S*)-2-Cyclopentenyl-1-benzoate (Table 6, entry 11).[7b] It was obtained in a maximum of 70% ee. The optical purity was determined by HPLC on chiralcel OD column [hexane/2-propanol 99.9:0.1]; flow rate 0.5 mL/min; t_R=26.82 min (*S*), 32.35 min (*R*). $[\alpha]_D^{25}$ −136.2 (*c* 0.9, $CHCl_3$) [lit.[7b] (93% ee); $[\alpha]_D^{25}$ −179.0 (*c* 0.37, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.93–2.01 (m, 1H), 2.34–2.45 (m, 2H), 2.55–2.64 (m, 1H), 5.92–5.97 (m, 2H), 6.16 (p, 1H), 7.25–7.44 (m, 2H), 7.53 (tt, *J*=7.6, 1.2 Hz, 1H), 8.03 (m, 2H).

2.6.3. (*S*)-2-Cycloheptenyl-1-benzoate (Table 6, entry 14).[8b] It was obtained in a maximum of 86% ee. The optical purity was determined by HPLC on chiralpak AD-H column [hexane/2-propanol 99.7:0.3]; flow rate 0.5 mL/min; t_R=15.70 min (*R*), 16.37 min (*S*); $[\alpha]_D^{25}$ −57.8 (*c* 0.6, $CHCl_3$) [lit.[8b] (82% ee) $[\alpha]_D^{25}$ −38.2 (*c* 1, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.43–2.30 (m, 8H), 5.65 (d, *J*=9.8 Hz, 1H), 5.81–5.92 (m, 2H), 7.44 (t, *J*=7.8 Hz, 2H), 7.55 (t, *J*=7.3 Hz, 1H), 8.06 (d, *J*=7.3 Hz, 2H).

2.6.4. (*S*)-2-Cyclooctenyl-1-benzoate (Table 6, entry 17).[8b] It was obtained in a maximum of 94% ee. The optical purity was determined by HPLC on chiralpak AD-H column [hexane/2-propanol 99.7:0.3]; flow rate 0.5 mL/min; t_R=21.79 min (*S*), 12.63 min (*R*); $[\alpha]_D^{25}$ +86.5 (*c* 1.2, $CHCl_3$) [lit.[8b] (82% ee) $[\alpha]_D^{25}$ +72.6° (*c* 1.25, $CHCl_3$)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.43–1.75 (m, 7H), 2.04–2.40 (m, 3H), 5.60–5.75 (m, 2H), 5.87–5.92 (m, 1H), 7.43 (t, *J*=7.6 Hz, 2H), 7.54 (t, *J*=7.3 Hz, 1H), 8.05 (d, *J*=7.3 Hz, 2H).

2.6.5. (*S*)-2-Cyclooctadienyl benzoate (Table 6, entry 20).[16] It was obtained in a maximum of 80% ee. The optical purity was determined by HPLC on chiralpak AD-H column [hexane/2-propanol 99.7:0.3]; flow rate 0.5 mL/min; t_R=17.71 min (*S*), 19.01 min (*R*): $[\alpha]_D^{25}$ −132.0 (*c* 0.6, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.47–1.54 (m, 1H), 1.64–1.72 (m, 1H), 1.85–1.96 (m, 2H), 2.07 (m, 1H), 2.37 (m, 1H), 5.65 (m, 2H), 5.75–5.81 (m, 1H), 5.93–6.00 (m, 2H), 7.43 (t, *J*=7.8 Hz, 2H), 7.55 (t, *J*=7.6 Hz, 1H), 8.05 (d, *J*=8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) 21.6, 28.3, 30.0, 74.4, 125.8, 126.1, 128.2, 129.5, 130.7, 130.9, 132.8, 133.1, 165.8. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: 78.78; H, 7.21.

2.6.6. (*R*)-1-Phenyl-2-propenylbenzoate (8a).[6a] It was obtained in a maximum of 40% ee. The optical purity was determined by HPLC on chiralpak AD-H column [hexane/2-propanol 99.7:0.3]; flow rate 0.5 mL/min; t_R=13.28 min (*R*), 14.01 min (*S*). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.30 (td, *J*=10.5, 1.2 Hz, 1H), 5.40(td, *J*=17.3, 1.2 Hz, 1H), 6.13 (s, *J*=5.8 Hz, 1H), 6.52 (d, *J*=5.8 Hz, 1H), 7.29–7.47 (m, 8H), 8.10 (dd, *J*=8.3, 1.2 Hz, 2H).

2.6.7. (*S*)-1-Octenyl-3-benzoate (8b).[6a] It was obtained in a maximum of 27% ee. The optical purity was determined by HPLC on chiralcel OD column [hexane/2-propanol 99.9:0.1]; flow rate 0.5 mL/min; t_R=20.91 min (*R*), 22.78 min (*S*). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.88–1.84 (m, 11H), 5.20 (d, *J*=6.5 Hz, 1H), 5.32(d, *J*=17.0 Hz, 1H), 5.46–5.51 (m, 1H), 5.85–5.93 (m, 1H), 7.44 (t, *J*=7.3 Hz, 2H), 7.55 (t, *J*=7.3 Hz, 1H), 8.06 (d, *J*=8.3 Hz, 2H).

2.6.8. 1-Methyl-1-cyclohexen-3-yl benzoate (10c).[5,9] It was obtained in a maximum of 47.6% ee. The optical purity was determined by HPLC on chiralpak AD-H column [hexane/2-propanol 99.7:0.3]; flow rate 0.5 mL/min; t_R=11.71 min (minor), 12.19 min (major) δ 1.77 (s, 3H), 1.46–2.06 (m, 6H), 5.50 (bs, 1H), 5.60 (bs, 1H), 7.42 (t, *J*=7.6 Hz, 2H), 7.54 (t, *J*=7.3 Hz, 1H), 8.05 (d, *J*=7.3 Hz, 2H).

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