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Environment friendly protocol for enantioselective epoxidation of non-functionalized alkenes catalyzed by recyclable homochiral dimeric Mn(III) salen comp1exes with hydrogen peroxide and UHP adduct as oxidants

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Environment friendly oxidants e.g. H_2O_2 and anhydrous urea hydrogen peroxide adduct (UHP) epoxidize non-functionalized alkenes (epoxide yield 40–99%) with high enantioselectivity (up to 94% ee) in 4–15 h using two recyclable homochiral dimeric Mn(III) salen complexes in presence of PyN-oxide with the catalysts reusability several times when UHP was used as an oxidant.

1. Introduction

The use of environmentally benign and clean oxidation reaction remains an important aspect of chemical research. Although oxidation reactions constitute core technologies for converting bulk chemicals into useful higher value products [1] they are among the more problematic processes with regard to general usage. Even today most of the industrially practiced oxidation methods [2] lead to a significant amount of hazardous waste and therefore, a feasible alternative is highly desirable. To achieve this, oxidation technologies should include high atom efficiency, broad substrate scope, and usage of environment benign oxidation reagents, in combination with high catalyst stability, selectivity and productivity. By comparing different oxidation methods it is apparent that the oxidant used in the respective transformation defines the quality and applicability of the method. Clearly, molecular oxygen is the most ideal oxidant for a number of oxidation reactions [3]. However, mostly only one oxygen atom of an oxygen molecule is used productively for epoxidation (50% atom efficiency) [4–10], thus at least stoichiometric amounts of unwanted by-products are generated during the reactions. Apart from molecular oxygen, hydrogen peroxide is highly attractive oxidant because of its low cost, high oxygen contents and environment friendly nature as water is the sole by-product [11,12]. Owing to its characteristic physical properties H_2O_2 is particularly useful for liquid phase oxidations for the synthesis of fine chemicals, pharmaceuticals, agrochemicals and electronic materials. For the enatioselective epoxidation of non-functionalized alkenes Mn(III) salen complexes (Jacobsen–Katsuki) [13–15] have been most successful catalyst using various oxidants including H_2O_2 (aqueous, anhydrous). However, it has been established that the Mn(III) salen catalysts are unstable under prolonged exposure to oxidative condition and cannot be recovered and recycled [16]. Further, as chiral catalysts are very expensive, their stability as well as re-usability is an important concern using environmentally benign and clean oxidant. Herein, we report the catalytic enantioselective epoxidation of non-functionalized alkenes that uses aqueous H_2O_2 (30%) and UHP in the presence of recyclable homochiral dimeric Mn(III) salen complexes [17] with an aim to determine the extent of catalysts recovery and recycling.

The complexes **1** and **2** (1 mol%) catalyzed the epoxidation of styrene, indene and chromenes with 30% H_2O_2 and UHP in good yields (40–99%) in 4–15 h as shown in table 1 (figure 1). The catalytic activity (TOF) of complexes **1** and **2** was reasonably good for styrene (entries 1,2,13,14), 2,2-dimethylchromene (entries 7,8,19,20), 6-methoxy-2,2-dimethylchromene (entries 9,10,21,22) and 6-cyano-2,2-dimethylchromene (entries 11,12,23,24) with both the oxidants while indene showed good efficiency only with UHP (entries 15,16). However, the epoxidation reaction was slower with substrate spiro [cyclohexane-1,2′-[2H][1] chromene] (entries 5,6,17,18) with both the oxidants (figure 2). Moreover, complex **1** induced better enantioselectivity with bulkier alkenes (81–94%) except styrene whereas complex **2** gave higher ee (60–61%) with styrene. In all the catalytic runs,

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configuration of the dominant enantiomer of the product was the same as that of the catalyst.

It is pertinent to compare the efficiency of the catalyst **1** (2 mol% of Mn(III) salen unit) with the monomeric Jacobsen's complex (**X**) (2 mol%) for the epoxidation of 6-cyano-2,2-dimethylchromene in presence of PyNO under identical reaction conditions. When aqueous H_2O_2 was used as an oxidant, the catalyst **1** gave 61% conversion and 88% ee in 7 h (table 1, entry 11) while **X** gave 60% conversion and 66% ee in 9 h (table 1, entry 31). On the other hand when UHP was taken up as an oxidants, the epoxidation of 6-cyano-2,2-dimethylchromene with catalyst **1** gave 99% conversion and 95% ee in 5 h (table 1, entry 23) while **X** gave 95% conversion and 98% ee after 15 h (table 1, entry 32). These results clearly demonstrate that it is advantageous to use the dimeric catalyst **1** over the monomeric complex **X**. The possible reason for this advantage can be attributed to the co-operative interaction [17,18] between the two metal centers present in the dimeric catalysts that are not working in isolation. Further, the catalysts **1** and **2** were also found to be superior for most of the alkenes than previously reported $-CH_2-$ linked dimeric Mn(III) salen complex [19].

Manganese salts in combination with sodium bicarbonate has been reported [20,21] to catalyze the epoxidation of alkenes with aqueous hydrogen peroxide. Therefore, we thought that it would be appropriate to study the use of hydrogen peroxide and sodium bicarbonate combination with chiral dimeric catalyst **2** (2 mol%) using 6-cyano-2,2-dimethylchromene as representative substrate in different solvents at 2 °C. The catalytic reaction in dichloromethane, showed an epoxide conversion of 38% with 78% ee in 23 h (entry 30) whereas when acetonitrile was used as solvent the conversion of epoxide was 51% with 72% ee in 18 h (entry 29). Among the two solvents used the greater miscibility of acetonitrile with 30% H_2O_2 may be responsible for the relatively better activity shown by this catalytic system. Nevertheless, the use of sodium bicarbonate has not given any advantage over the use of pyridine N-oxide. Further, when the epoxidation reaction was carried out in the presence of ammonium acetate, the conversion to epoxide was excellent with UHP (entries 26, 28) than aqueous H_2O_2 (entries 25, 27).

Further, various O co-ordinating axial bases have also been reported to influence the activity and stability of the Mn(III) salen complexes during the epoxidation

Table 1
Product yield and ee data for epoxidation of non-functionalized alkenes catalyzed by complexes **1** and **2** in presence of PyNO as co-catalyst with hydrogen peroxide and UHP adduct as oxidants[a]

Catalyst	Entry	Substrate	% Yield[b]	Time (h)	Ee (%)[c]	TOF[d]$\times 10^{-3}$
1	1(13)	Styrene	40(50)	5(5)	37(41)[e]	2.22(2.77)
2	2(14)		60(50)	5(5)	60(61)[f]	3.33(2.77)
1	3(15)	Indene	50(58)	11(4)	81(94)[g]	1.26(4.02)
2	4(16)		65(56)	11(4)	76(65)[h]	1.64(3.88)
1	5(17)	Cy-Chromene	67(82)	13(13)	85(86)[i]	1.43(1.75)
2	6(18)		55(80)	15(15)	76(79)[j]	1.01(1.48)
1	7(19)	Chromene	75(99)	8(8)	87(81)[i]	2.60(3.43)
2	8(20)		71(99)	8(5)	84(80)[j]	2.46(5.50)
1	9(21)	MeO-Chromene	88(99)	6(5)	91(92)[i]	4.07(5.50)
2	10(22)		80(99)	8(6)	77(78)[j]	2.77(4.58)
1	11(23)	CN-Chromene	61(99)	7(5)	88(95)[i]	2.42(5.50)
2	12(24)		84(99)	9(4)	86(93)[j]	2.59(6.87)
1[k]	25(26)		70(99)	5(6)	78(72)[i]	3.88(4.58)
2[k]	27(28)		85(99)	7(5)	82(80)[j]	3.37(5.50)
2[l]	29		51	18	72[j]	0.79
2[m]	30		38	23	78[j]	0.46
X	31(32)		60(95)	9(15)	66(98)[i]	0.93(0.87)

[a] Reactions were carried out in CH_2Cl_2:MeOH (1.6 ml) with catalyst (0.025 mmol) substrate (2.5 mmol), PyNO as axial base (0.2 mmol), hydrogen peroxide and UHP adduct as an oxidants(3.0 mmol) at 2 °C. Value in parenthesis is given for UHP adduct as an oxidant.
[b] Determined on GC.
[c] By ^{1}H NMR using chiral shift reagent (+)Eu(hfc)$_3$/chiral capillary column GTA-type/chiral HPLC column OJ, OB.
[d] Turnover frequency is calculated by the expression [product]/[catalyst]$\times$time s^{-1}.
[e] Epoxide configuration *R*.
[f] Epoxide configuration *S*.
[g] Epoxide configuration 1*R*,2*S*.
[h] Epoxide configuration 1*S*,2*R*.
[i] Epoxide configuration 3*R*,4*R*.
[j] Epoxide configuration 3*S*,4*S*.
[k] All reaction parameter are identical to standard procedure and CH_3COONH_4 as co-catalyst.
[l] Sodium bicarbonate activated hydrogen peroxide, acetonitrile as solvent and catalyst 2 mol% at 2 °C.
[m] Sodium bicarbonate activated hydrogen peroxide, with CH_2Cl_2 as solvent and catalyst 2 mol% at 2 °C.

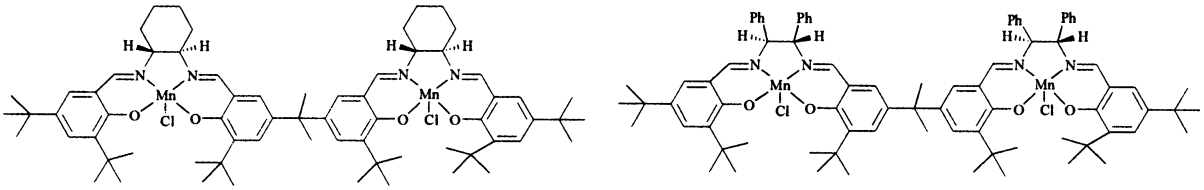

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Figure 1. Structures of catalysts **1** & **2**.

of non-functionalized alkenes using oxone, UHP and NaOCl as oxidants [22,18,19]. Hence, we studied the effect of axial bases namely, PyNO, 4-PhPyNO, 4-methyl morpholine N-oxide, (NMO) and dimethyl sulphoxide, (DMSO) in the epoxidation of styrene as model substrate using complex **2** (1 mol%) as catalyst with 30% hydrogen peroxide and an anhydrous UHP as oxidants. Water-soluble O co-ordinated axial bases such as PyNO and NMO showed higher activity (table 2, entries 33, 44) with aqueous H_2O_2 than with UHP (table 2, entries 34, 45), while 4-PhPyNO favors the use of UHP (table 2, entry 36), however, enantioselectivity remained unchanged. With either of the oxidants using *N*-methyl Imidazole/CH_3COONH_4 as axial base resulted in lower epoxide conversions along with appreciable degradation of the catalyst (entries 37, 38, 42, 43) whereas ee was unchanged with UHP (entries 43). In absence any co-catalyst, epoxidation of styrene does not proceed beyond a conversion of 2% (entry 39).

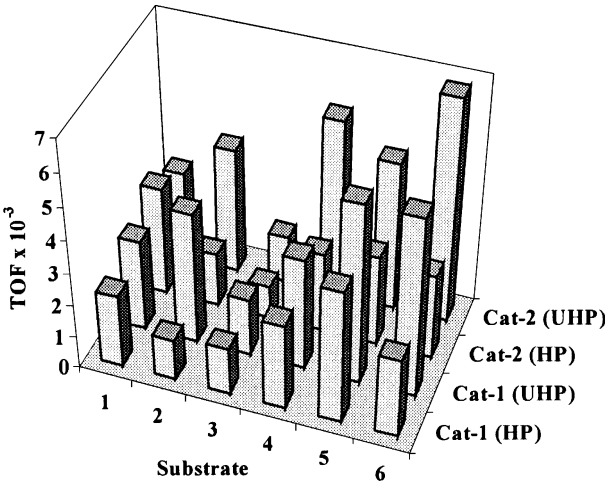

Figure 2. 3D view showing the TOF versus substrates (**1**) styrene, (**2**) indene, (**3**) cyclochromene, (**4**) chromene, (**5**) methoxy chromene, (**6**) cyanochromene for catalysts **1** and **2** with aqueous H_2O_2 (**HP**) and **UHP** as oxidants.

Recovery and recycling experiments were performed using complex **2** as catalyst for the epoxidation of 6-cyano-2,2-dimethylchromene with aqueous H_2O_2/UHP as an oxidant. We have observed that the dimeric catalyst is less soluble than the monomeric catalyst in the solvent system used in the catalytic runs. Taking advantage of the solubility difference, after completion of catalytic runs, the dimeric catalyst was precipitated from the reaction mixture by the addition of excess of hexane and was vacuum dried before re-use. However, in case of aqueous H_2O_2 after the first cycle, the precipitation resulted in pale yellow gummy solid that failed to catalyze epoxidation reaction in the recycle experiment. It may be due to the easily oxidizable imine and phenoxide moieties in the catalyst which were proposed to be responsible for the oxidative degradation of the catalyst during epoxidation [16]. Whereas, when UHP was used as an oxidant we were able to recover the catalyst by precipitation method and was used in the same manner as fresh catalyst in the epoxidation of 6-cyano-2,2-dimethylchromene using UHP as oxidant and PyNO as axial base (table 3). The catalyst **2** was recycled successfully up to three times with retention of the enantioselectivity. However, it took longer time to attain similar conversion in the second and subsequent catalytic run. This decreasing in the activity of the

Table 2
Conversion and enantiomeric excess for styrene-catalyzed by complex **2** in presence of the different axial bases with aqueous H_2O_2 and UHP as oxidants

Entry	Axial base	% Conversion	Time (h)	Ee (%)	TOF$\times 10^{-3}$
33(34)	PyNO	60(50)	5(5)	60(61)	3.33(2.77)
35(36)	4-PhPyNO	23(40)	5(5)	63(61)	1.27(2.22)
37(38)	*N*-methyl Imidazole	8(20)	4(5)	50(55)	0.55(1.11)
39	–	2	24	Nd	–
40(41)	DMSO	21(8)	12(5)	57(30)	0.48(0.44)
42(43)	CH_3COONH_4	10(10)	4(6)	49(60)	0.69(0.46)
44(45)	NMO	50(20)	6(6)	51(54)	2.31(0.93)

Results in parenthesis are for UHP.

Table 3
Recylability of catalyst **2** using UHP adduct as an oxidant and 6-cyano-2,2-dimethylchromene as a substrate

Run	Time (h)	%Conversion	Ee %
1	4	99	93
2	5	99	93
3	8	80	93

catalyst can be attributed to minor physical loss of the catalyst in post-epoxidation work up (table 3).

In conclusion, we have successfully used environmentally benign oxidants like UHP and aqueous H_2O_2 with the recyclable homochiral dimeric Mn(III) salen complexes **1** and **2** as catalysts for catalytic enantioselective epoxidation of non-functionalized alkenes with PyN-O as axial base. These complexes were recycled three times when anhydrous UHP adduct was used as oxidant, while in the case of aqueous H_2O_2 the catalyst could not be recycled after the first use.

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