



Enantioselective epoxidation of non-functionalised alkenes catalysed by dimeric homochiral Mn(III) Salen complex using oxone as oxidant

Rukhsana Ilyas Kureshy*, Noor-ul Hasan Khan, Sayed Hasan Razi Abdi, Irshad Ahmed, Surendra Singh, Raksh Vir Jasra

Silicates and Catalysis Discipline, Central Salt and Marine Chemicals Research Institute, Gijubhai Badheka Marg, Bhavnagar 364002, Gujarat, India

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Abstract

Dimeric homochiral Mn(III) Salen complex **1** has been investigated as a catalyst for enantioselective epoxidation of indene, styrene, chromene and substituted chromenes in presence of pyridine *N*-oxide (PyN–O) using oxone (KHSO₅) as oxidant. Excellent conversions (>99%) were obtained with all alkenes except indene but high chiral induction (>99%) was obtained in case of nitro and cyano chromene by GC/¹H NMR using Eu(hfc)₃/HPLC. The system works well using 7 mol% catalyst loading with retention of enantioselectivity and catalyst that could be recycled up to three cycles.

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1. Introduction

The identification of new chiral epoxidation catalyst for the synthesis of the building blocks for pharmaceuticals and agrochemicals is of current interest [1]. In this respect, there is a need for stable catalysts to be designed for selective asymmetric epoxidation reactions, with high yields of the desired products. Mn(III) Salen complexes have been reported independently by Jacobsen and co-workers [2–4] and Katsuki and co-workers [5,6] as versatile catalysts for enantioselective epoxidation of non-functionalised alkenes under homogeneous conditions using several oxidants. However, the catalyst stability, product and

catalyst separation remains troublesome with these homogeneous systems. To overcome these problems one way is to increase of molecular weight the catalyst so that it has lower solubility in some of the non-polar organic solvents, facilitating product isolation and catalyst recovery, which in turn makes the post epoxidation work-up much convenient.

Further, among various oxidants used with Mn(III) Salen complexes [7–11], oxone is a strong, stable, cheap and non-chlorine single oxygen atom donor. We, therefore, decided to examine the utility of a dimeric Mn(III) complex [12,13] viz. 5,5-methylene di-[(*R,R*)-{*N*-(3-*tert*-butyl salicylidine)-*N'*-(3',5'-di-*tert*-butyl salicylidene)}-1,2-cyclohexanediaminato (2-) manganese(III) chloride] **1** for the enantioselective epoxidation of indene, styrene, chromene and substituted chromenes using oxone as an oxidant in presence of

* Corresponding author. Fax: +91-278-566970.
E-mail address: salt@csir.res.in (R.I. Kureshy).

pyridine *N*-oxide (PyN–O) as an axial base. The solubility of the complex **1** is less than its monomeric counter part, hence, it was easily precipitated out with hexane, separated from the product and reused.

2. Experimental

All the solvents used were purified by known procedure. The purity of the solvent, alkenes and analysis of the product epoxide was determined by GLC using Shimadzu GC-14B having FID detector and 2 m long, 3 mm i.d., 4 mm OD stainless steel column packed with SE30, (5% mesh size 60–80). GC column temperature was programmed from 70 to 150 °C with injection temperature 200 °C and nitrogen as a carrier gas with a flow rate of 30 ml/min. Synthetic standard of the product and/or tridecane as internal standard was used to determine yields by comparison of peak height and area. The enantiomeric excess (ee) for styrene epoxide was determined by GC using chiral capillary column GTA. For chromene and indene epoxides, ee's were determined by ¹H NMR using chiral shift reagent Eu(hfc)₃ as well as HPLC (Shimadzu SCL-10AVP) using Chiralcel OJ/OB.

2.1. Epoxidation of non-functionalised alkenes using catalyst (**1**)

Enantioselective epoxidation of indene, styrene, 2,2-dimethyl-2*H*-chromene (CR), 6-cyano-2,2-dimethyl-2*H*-chromene (CNCR), 6-nitro-2,2-dimethyl-2*H*-chromene (NO₂CR), 6-methoxy-2,2-dimethyl-2*H*-chromene (MeOCR) and spiro[cyclohexane-1,2'-[2*H*] [1]chromene (CyCR) [14] by the catalyst **1** was studied under homogeneous conditions with oxone as oxidant using following procedure: The catalyst, (0.028 mmol), styrene/indene/chromenes (0.4 mmol), *n*-tridecane (0.10 mmol) as GLC internal standard and PyN–O (0.4 mmol) as axial ligand were dissolved in CH₂Cl₂:CH₃CN (1.5:1.5 ml). The reaction was initiated by the addition of oxone (0.6 mmol) using phosphate buffer maintained at pH 11 in four equal portions. The reaction mixture was stirred at constant speed in an inert atmosphere at 2 °C. After an interval of 30 min, an aliquot was taken from the reaction mixture, quenched with dimethyl sulphide and analysed by GLC. Upon completion of the reaction, excess of

dimethyl sulphide and solid K₂CO₃ were added to the reaction mixture, filtered and then concentrated on rotary evaporator. The product was separated by short silica gel column (60–120 mesh) using hexane: dichloromethane as an eluent.

3. Results and discussion

The penta-coordinated homochiral dimeric complex **1** (Fig. 1) was prepared by the reported method [12,13] and was used as catalyst for epoxidation of alkenes with oxone as the oxidant at pH 11, in 1:1 dichloromethane and acetonitrile.

The results summarized in Table 1 show that high epoxide yields were obtained with all alkenes in 4–6 h, whereas excellent chiral induction (ee, >99%) was observed for cyano and nitro chromenes (entries 4 and 5). For other chromenes ee's ranged from 71–91% (Fig. 2). However, in case of styrene, the chiral induction was moderate (ee, 44%, entry 7).

To compare these results with that of monomeric Jacobsen catalyst, the epoxidation of CNCR was conducted under our standard reaction medium (1:1 acetonitrile: CH₂Cl₂) which gave poor epoxide yield (23%) after 13 h with 91% ee's. While, under similar reaction conditions the dimeric complex **1** with a loading of (7 mol%) yielded >99% epoxide with ee's >99% in 5 h (Table 1 entry 4). This remarkable improvement in the performance of dimeric complex **1** over monomeric complex suggests that the two catalytic centers are working in co-operation rather than in isolation.

Chiral Mn(III) Salen complexes are sensitive towards the choice of the solvent and it has been reported [15,16] that 15 mol% monomeric Jacobsen catalyst loading resulted in cyanochromene epoxide yield; 67%, ee's 85% in 15 min and yield 61%, ee's 19.8% in 12 h in acetonitrile and CH₂Cl₂ respectively.

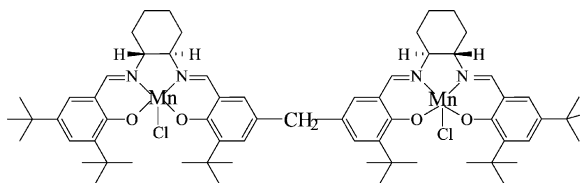
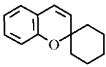
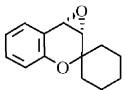
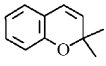
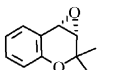
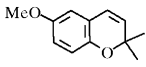
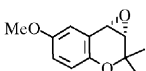
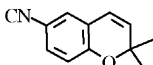
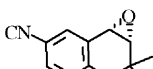
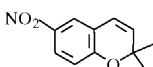
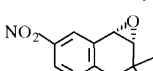

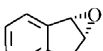




Fig. 1. Structure of the catalyst **1**.

Table 1

Data for enantioselective epoxidation of non-functionalised alkenes using the complex **1** with oxone in presence of PyN–O as proximal ligand

Entry	Substrate	Product	Conversion (%) ^a	Time (h)	ee (%) ^b	TOF ^c
1			>99	4.0	91	3.54
2			>99	5.0	71	2.82
3			>99	4.5	71	3.14
4			>99	5.0	>99	2.82
5			100	5.0	>99	2.82
6			95	6.0	78	2.26
7			>99	5.0	44 ^d	2.82

Reactions were carried out in CH₂Cl₂:CH₃CN (1.5:1.5 ml) with catalyst (0.028 mmol) substrate (0.4 mmol), *n*-tridecane (0.10 mmol), axial ligand (0.4 mmol), oxidant (0.6 mmol) at 2 °C.

^a Determined on GC.

^b By ¹H NMR using chiral shift reagent (+)Eu(hfc)₃, Configuration was determined by the ¹H NMR using chiral shift reagent/HPLC on Chiracel OJ, OB by comparison/analogy with an authentic CN-chromene oxide.

^c Turn over frequency = [mol of product]/[mol of catalyst] × time (s⁻¹).

^d Chiral capillary column GTA type.

In view of this, the effect of solvents using complex **1** as catalyst in the epoxidation of CNCR was studied (Table 2). The solvents like 1,4 dioxane and DMSO do not favor the reaction (entry 10, 11). While acetonitrile (miscible with water) which moderately dissolves complex **1** (entry 9) gave 40% conversion with 87%

ee's. On the other hand, the solvent dichloromethane (immiscible in water) dissolves complex **1** completely yielded 60% conversion with 85% ee's. Hence, a combination of CH₂Cl₂ and acetonitrile was used for all our studies, which turned out to be the right combination for the present epoxidation studies.

Also, axial bases have pronounced effect on the reactivity and selectivity of the enantioselective epoxidation reaction. It is known in the literature that in a biphasic reaction system axial bases have dual role to play (a) stabilizing the oxo intermediate and (b) transporting the oxidant into the organic phase. We therefore, studied the effect of axial bases on the epoxidation of CR as a model substrate in CH₂Cl₂–CH₃CN mixture (Table 3). In the present system where one of the solvent itself is working as a phase transfer

Table 2

Data for the enantioselective epoxidation of 6-CN 2,2 dimethyl chromene with catalyst **1** using different solvents

Entry	Solvent	Time (h)	Conversion (%)	ee (%)
8	CH ₂ Cl ₂	24	60	85
9	CH ₃ CN	24	40	87
10	DMSO	24	No reaction	–
11	1,4 Dioxane	24	5	ND

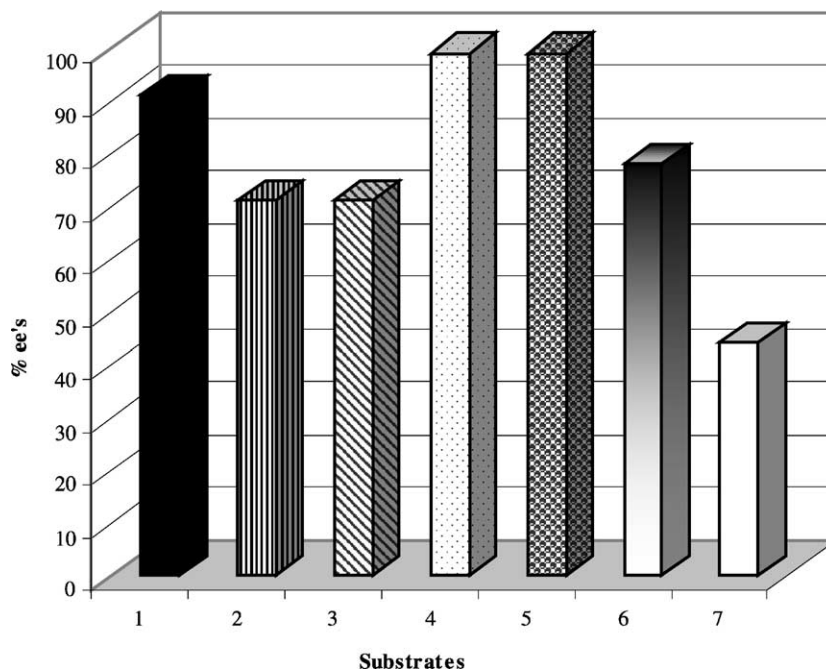


Fig. 2. 3D view showing the ee (%) vs. substrates (1) CyCR (cyclochromene), (2) CR (chromene), (3) MeOCR (methoxy chromene), (4) CNCR (cyanochromene), (5) NO₂CR (nitrochromene) (6) IND (indene), (7) STR (styrene).

agent, water insoluble axial base such as 4-phenyl pyridine N–O gave 65% conversion in 6 h (entry 12, Table 3) while using water soluble PyN–O as an axial base with the same complex **1** gave >99% conversion in 5 h (entry 2). Furthermore, when *N*-methyl morpholine-*N*-oxide (NMO) (entry 13) was used as axial base, the conversion was 40% in 12 h with comparable chiral induction but with *N*-methyl imidazole as an axial base, the conversion was low (entry 14) with ee's 50% and the findings are consistent with earlier reports on Mn(III) Salen catalysed enantioselective epoxidation [17].

Catalyst recycling studies were carried out after isolation of the catalyst from the reaction mixture by

Table 3

Data for the enantioselective epoxidation of 2,2-dimethyl chromene with catalyst **1** using different axial bases

Entry	Axial bases	Conversion (%)	Time (h)	ee (%)
12	4-PhPyNO	65	6	71
13	NMO	40	12	69
14	Imidazole	20	24	50

Table 4

Data for enantioselective epoxidation of 6-cyano 2,2-dimethyl chromene with recycled catalyst in presence of (PyN–O) as proximal ligand with oxone

Run	1	2	3
Conversion (%)	>99	80	69
ee (%)	>99	99	99
Time (h)	5	7	8

precipitation with hexane. The recovered catalyst was used three times under the similar reaction conditions. The data is given in Table 4. The activity of the recycled catalyst gradually decreased upon successive use possibly due to minor degradation and physical loss of the catalyst **1** under epoxidation condition with retention of ee's.

4. Conclusion

In conclusion, the homochiral dimeric chiral Mn(III) complex **1** worked very well with all non-functionalised alkenes and best chiral induction was

obtained with nitro- and cyano-chromene using oxone as oxidant in presence of PyN–O as axial base. The system works well using 7 mol% catalyst loading with retention of enantioselectivity and catalyst that could be recycled up to three cycles. The activity of the recycled catalyst gradually decreased upon successive use possibly due to minor degradation (physical loss) of the catalyst **1** under epoxidation condition.

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