Silica gel anchored chiral Mn(III)salen complexes for enantioselective epoxidation of unfunctionalised olefins

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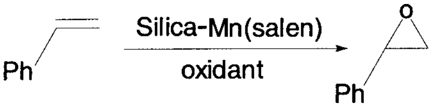
Received 16 May 2001; accepted 18 July 2001

Heterogeneous Mn(III) chiral salen complexes are prepared through covalent attachment of salen ligand on silica gel *via* chloropropyl spacer and subsequent complexation with manganese. The complexes are well characterized by IR, UV/VIS, TGA and elemental analysis. Epoxidation of unfunctionalised prochiral olefins by Mn(III) chiral salen complexes using iodosobenzene and *m*-CPBA as the terminal oxidants and NMO as a co-oxidant was achieved with good yields albeit low enantiomeric excess.

KEY WORDS: asymmetric epoxidation; Mn(III)salen complex; olefins; heterogeneous catalysis

1. Introduction

Design and synthesis of chiral metal complexes as catalysts for asymmetric epoxidation of unfunctionalised olefins is of topical interest in synthetic chemistry, as the epoxides formed are very useful synthetic intermediates for chiral bioactive molecules or as end products having biological activity such as gypsy moth insect pheromones [1]. The advent and successful employment of various chiral Mn(III)salen complexes in asymmetric epoxidation of unfunctionalised olefins devised by Jacobsen and Katsuki's groups has greatly enhanced the progress in the asymmetric epoxidation of simple olefins conjugated with alkenyl, alkynyl or aryl groups with high enantioselectivity [2,3]. The high enantioselectivity achieved here is ascribed to the directed path of the prochiral olefin to the metal centre, while other possible approaching paths are blocked by the introduction of bulky substituents on salen ligands.



A number of groups tried to immobilise salen complexes on various supports, as the heterogeneous catalysts offer the advantages of easy recovery, separation and reuse. These approaches are: (a) non-covalent immobilisation in zeolites, clays or siloxane membranes [4], (b) covalent grafting onto inorganic supports such as silica or MCM-41 [5–8], (c) copolymerisation of a functionalised salen monomer into an organic polymer [9], and (d) attachment or build-up of a salen structure to a preformed polymer [10]. Pozzi and coworkers have described an interesting fluorous biphase system (FBS) [11] to recover the catalyst. They showed that a salen catalyst containing perfluorinated alkyl chains could be utilised for effective enantioselective epoxidation reactions carried out under biphasic (fluorous/organic) conditions. Although the catalyst could be readily recovered from the fluorous layer by phase separation techniques, reasonable enantioselectivities were obtained for one substrate only.

Silica support has high thermal and mechanical stability over polymers and covalent attachment of the chiral catalyst on silica proved to be the best method of immobilisation. In continuation of our interest on immobilised Mn-salen catalysts [12], we report here the synthesis of silica gel anchored chiral Mn(III)salen complexes through covalent attachment of salen ligand on silica gel *via* chloropropyl spacer and subsequent complexation with manganese for catalytic enantioselective epoxidation of olefins using iodosylbenzene and *m*-CPBA as oxidants.

2. Experimental

2.1. Preparation of catalysts

2.1.1. Synthesis of catalyst **1**

The chiral salen was synthesised from a known dimesylate [13] prepared in three steps from natural tartaric acid.

3,4-diazido-1-benzylpyrrolidene. To a dimesylate compound (3.49 g, 10 mmol) in dry dimethylformamide (15 ml), sodium azide (1.95 g, 30 mmol) was added slowly. The reaction mixture was allowed to reflux at 100 °C for 24 h. The reaction was monitored by TLC. After completion of the reaction, it was cooled to room temperature and extracted with ether. The ethereal extract was washed with water and ensured the removal of dimethylformamide. The organic phase was dried over anhydrous sodium sulfate and evaporated under reduced pressure to get 3,4-diazido-l-benzylpyrrolidine. The product was purified by column chromatography on silica gel using 5% ethyl acetate–hexane as an eluant to give

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pure diazide (1.7 g, 70% yield). $[\alpha]_D^{24} = -85$ (c 1 MeOH); IR (film) 2922, 2802 and 2099 cm^{-1}; ^{1}H NMR (200 MHz, $CDC1_3$) 7.32 (s, 5H, ArH), 3.89 (t, 2H, 3-H, 4-H), 3.68 (m, 2H, $PhCH_2$–, diastereotopic), 3.00 (m, 2H, 2-H, 5-H), 2.63 (dd, 2H, 2-H, 5-H).

3,4-diamino-l-benzylpyrrolidine. To a solution of diazide (2.43 g, 10 mmol) in 20 ml methanol, MCM-Pd (0.125 g, 0.023 mmol) was added [14]. The mixture was hydrogenated at 27 °C and atmospheric pressure for 2 h. The catalyst was then removed by filtration and the filtrate was evaporated under vacuum to afford diamine as a colourless syrup $[\alpha]_D^{24} = -14$ (c 1 MeOH); ^{1}H NMR (200 MHz, $CDC1_3$) 7.29 (s, 5H, ArH), 3.57 and 3.63 (m, AB system, 2H, $PhCH_2$–, diastereotopic, $J = 12.3$ Hz), 2.90 and 3.05 (2m, 2 × 2H, 2-H, 5-H), 2.15–2.35 (m, 2H, 3-H, 4-H), 1.63 (br s, 4H, $-NH_2$); IR (film) 3349, 3027, 2912, 2794 and 1602 cm^{-1}.

Schiff base. 3,4-diamino-l-benzylpyrrolidine (0.955 g, 5 mmol) and 2-*tert*-butyl-4-methylsalicylaldehyde (1.92 g, 10 mmol) in 50 ml absolute ethanol were refluxed for 9 h to obtain a Schiff base (2.425 g, 90% yield). M.p. 69 °C; $[\alpha]_D^{24} = -437$ (c 1 CH_2C1_2); ^{1}H NMR (200 MHz, $CDCl_3$) 13.30 (s, 2H), 8.2 (s, 2H), 7.30 (m, 5H), 7.15 (s, 2H), 6.81 (s, 2H), 3.96 (dd, 2H), 3.70 (d, 2H), 3.11 (dd, 2H), 2.90 (dd, 2H), 2.23 (s, 6H), 1.42 (s, 18H); IR (KBr) 2958, 2869, 1643 and 1567 cm^{-1}. Anal. calcd. for $C_{35}H_{45}N_3O_2$: C 77.86, H 8.40, N 7.79. Found: C 77.85, H 8.42, N 7.78.

The Schiff base (1.078 g, 2 mmol) was dissolved in hot absolute ethanol (20 ml) and solid $Mn(OAc)_2 \cdot 4H_2O$ (1.47 g, 6 mmol) was added in one portion and the solution was refluxed for 1 h. Then LiCl (0.252 g, 6 mmol) was added and the mixture was heated to reflux for an additional 0.5 h under air. Cooling the mixture to 0 °C afforded Mn(III)salen complex **1** as dark brown crystals, which was washed thoroughly with water and isolated by filtration (1.08 g, 86% yield). IR (KBr) 2953, 1607 and 1534 cm^{-1}. Anal. calcd. for $C_{35}H_{43}ClMnN_3O_2$: C 66.88, H 6.89, Cl 5.64, Mn 8.74, N 6.68. Found: C 66.85, H 6.88, Cl 5.63, Mn 8.72, N 6.71.

*2.1.2. Synthesis of catalyst **2***

Palladium on carbon (10% w/w, 0.55 g, 0.26 mmol) was added to a solution of (R,R)-3,4-diazido-l-benzylpyrrolidene (1.5 g, 6.17 mmol) in ethanol/trifluoroacetic acid (20 ml, 4 : 1). The suspension was stirred under hydrogen atmosphere for 16 h, filtered through celite and concentrated under vacuum. The crude residue was dissolved in ethanol/water (50 ml, 9 : 1) and neutralised with potassium carbonate (3.00 g, 21.71 mmol). Neat 2-*tert*-butyl-4-methylsalicylaldehyde (2.6 g, 13.59 mmol) was added at once and the reaction was refluxed for 2 h. The reaction mixture was then poured into 100 ml brine and extracted with dichloromethane (3 × 50 ml). The organic phases were combined and washed with brine (50 ml), dried over sodium sulfate and concentrated. The product was purified by column chromatography (ethylacetate/hexane, 1 : 1) to give a foamy yellow compound. To this ligand (1 mmol), chloropropyl silica (1 g, 0.7 mmol of Cl), tributylamine (0.370 g, 2 mmol) and toluene (20 ml) were added, stirred under reflux for 24 h, filtered and washed with toluene to give silica anchored Schiff base (0.13 mmol/g). IR (KBr) 1640 (C=N), 1568 cm^{-1} (aromatic).

The silica anchored Schiff base (1 g, 0.13 mmol) in EtOH (10 ml) was heated to 90 °C. $Mn(OAc)_2 \cdot 4H_2O$ (0.095 g, 0.39 mmol) was then added and stirred for 12 h. At this juncture, LiCl (0.016 g, 0.39 mmol) was added and the mixture was refluxed for an additional 0.5 h under air. The reaction mixture was then filtered and washed with water, acetone and finally dichloromethane to give the brown coloured catalyst, **2**. Elemental analysis indicates that 0.12 mmol/g of Mn was incorporated.

*2.1.3. Synthesis of catalyst **3***

Chloropropyl silica (1 g, 0.7 mmol of Cl) and (R,R)-1,2-diaminocyclohexane (0.342 g, 3 mmol) in toluene (10 ml) were refluxed for 12 h. The reaction mixture was filtered and washed with toluene to obtain diaminocyclohexyl propyl silica, which, in turn was treated with 2-*tert*-butyl-4-methylsalicylaldehyde (1.344 g, 0.7 mmol) in toluene under reflux for 12 h. It was filtered and washed with toluene to afford the Schiff base (1 g, 0.41 mmol) which on subsequent complexation with Mn, gives catalyst **3**. Elemental analysis indicates that 0.18 mmol/g of Mn was incorporated.

*2.1.4. Synthesis of catalyst **4***

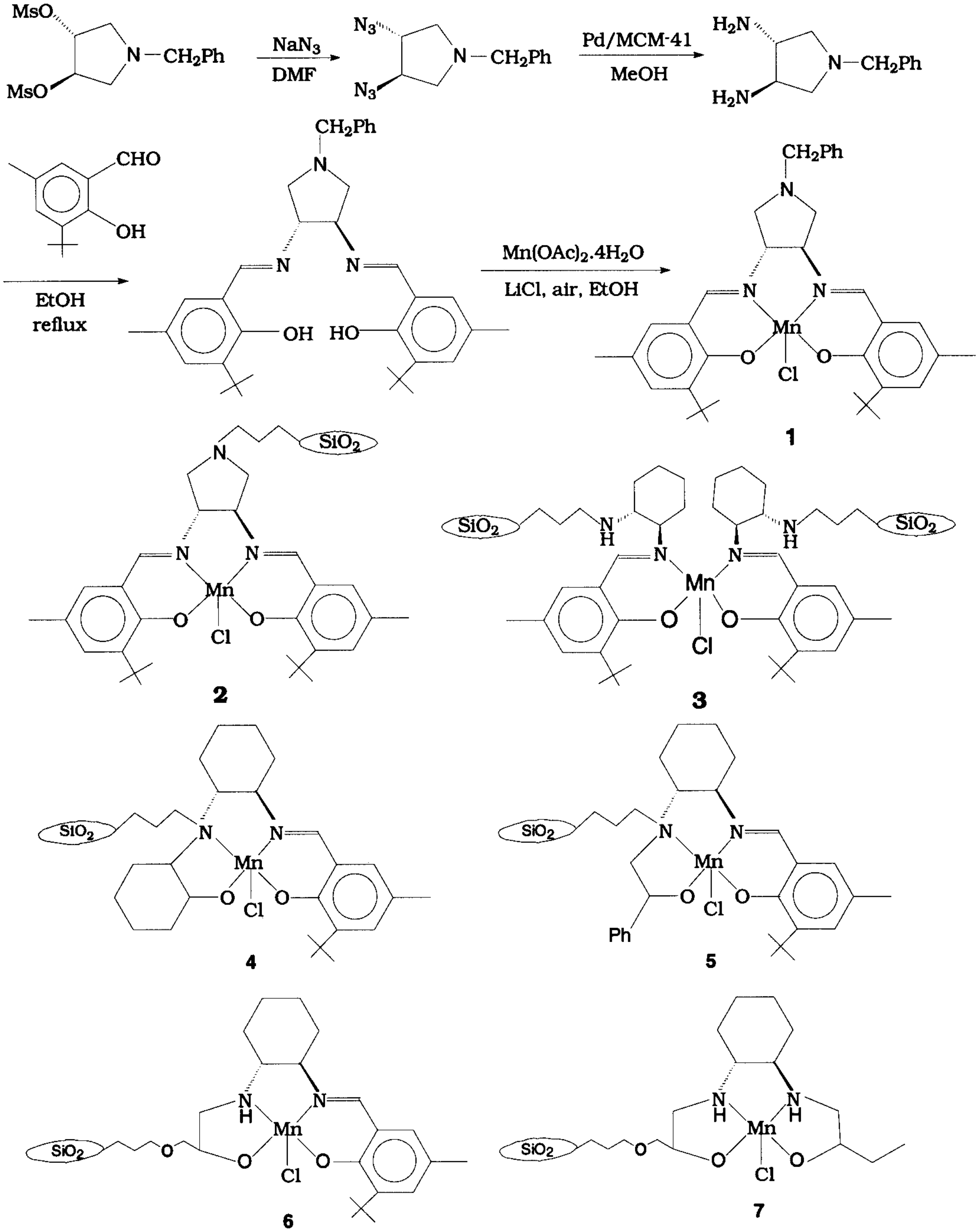
A mixture containing the silica anchored Schiff base (1 g, 0.41 mmol) and cyclohexene epoxide (0.040 g, 0.41 mmol) in ethanol (10 ml) was stirred under reflux for 12 h. Complexation with Mn affords catalyst **4**. Elemental analysis indicates that 0.36 mmol/g of Mn was incorporated.

*2.1.5. Synthesis of catalyst **5***

A mixture containing the silica anchored Schiff base (1 g, 0.41 mmol) and (R)-styrene epoxide (0.049 g, 0.41 mmol) in ethanol (10 ml) was stirred under reflux for 12 h. Complexation with Mn affords catalyst **5**. Elemental analysis indicates that 0.35 mmol/g of Mn was incorporated.

*2.1.6. Synthesis of catalyst **6***

3-glycidyloxypropyltrimethoxysilane (2.36 g, 10 mmol) and (R,R)-1,2-diaminocyclohexane (1.14 g, 10 mmol) in toluene were stirred under reflux for 12 h. 5 g of silica gel (200 mesh) was added to this solution and stirred under reflux for another 24 h. The solid was filtered off and washed with toluene and acetone to give silica anchored diamino alcohol (0.35 mmol/g), which is subsequently converted to a Schiff base which upon complexation with Mn gives catalyst **6**. Elemental analysis indicates that 0.31 mmol/g of Mn was incorporated.



Scheme 1.

2.1.7. Synthesis of catalyst 7

A mixture containing silica anchored diamino alcohol (1 g, 0.35 mmol) and 1,2 epoxybutane (0.025 g, 0.35 mmol) in EtOH (10 ml) was stirred at 60 °C for 12 h, which on complexation with Mn gives catalyst **7**. Elemental analysis indicates that 0.29 mmol/g of Mn was incorporated.

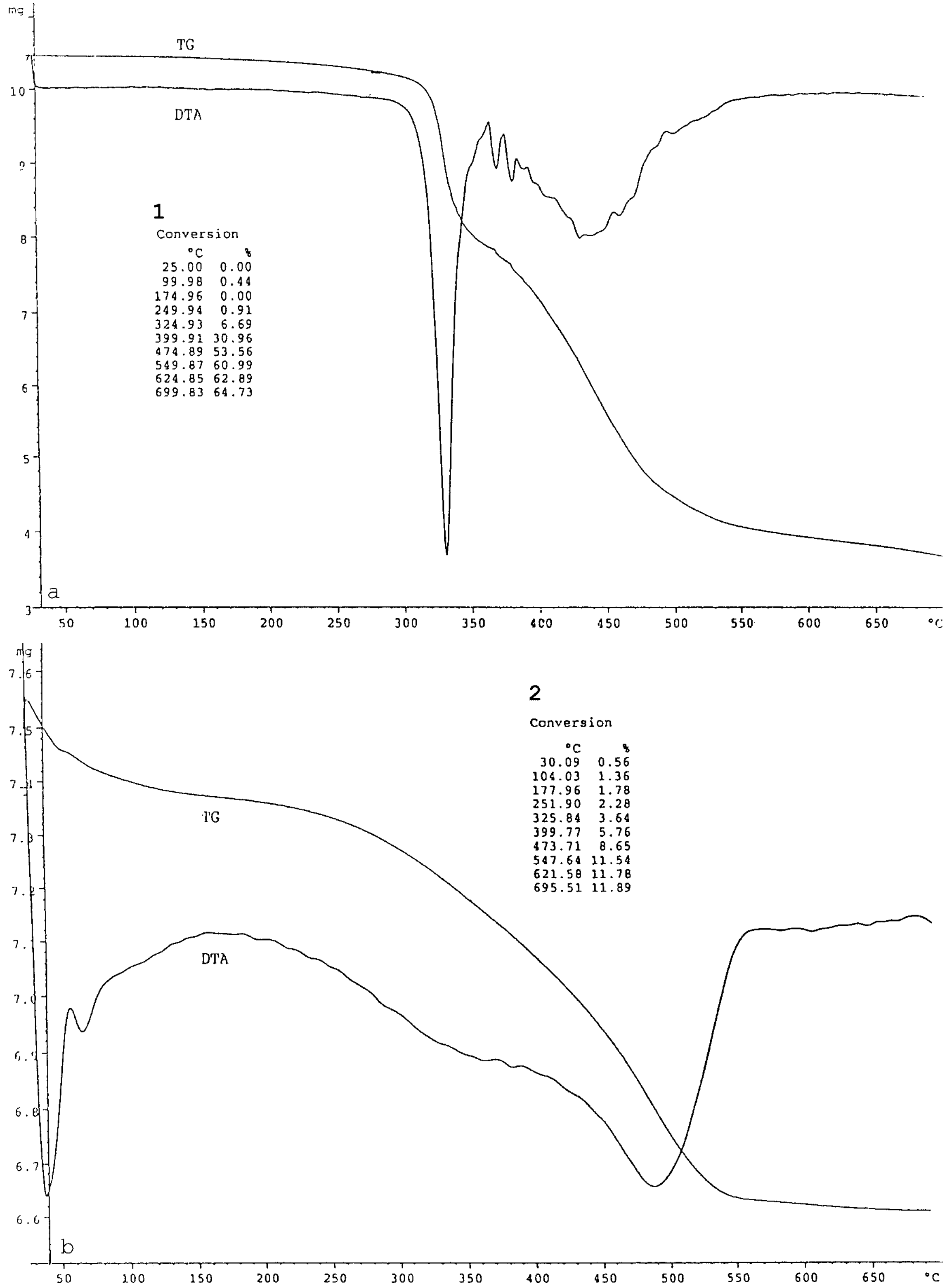
2.2. General procedure for enantioselective epoxidation of olefins

2.2.1. Using PhIO as the oxidant

To a mixture containing 5 mol% of the catalyst and PhIO (0.472 g, 2 mmol) in CH_3CN (6 ml), N-methylmorpholine N-oxide (0.067 g, 0.5 mmol) and olefin (1 mmol) were added. The reaction was stirred at 0 °C and monitored by TLC. After completion of the reaction, the catalyst was filtered and washed with dichloromethane. After removing the solvent, the crude material was column chromatographed on silica gel to afford the corresponding epoxide.

2.2.2. Using m-CPBA as the oxidant

To a mixture containing 5 mol% of the catalyst in CH_2Cl_2 (10 ml), N-methylmorpholine N-oxide (0.648 g, 4.8 mmol) and olefin (1 mmol) were added. *m*-CPBA (0.330 g, 1.92 mmol) was then added in four equal portions



1

Conversion

°C	%
25.00	0.00
99.98	0.44
174.96	0.00
249.94	0.91
324.93	6.69
399.91	30.96
474.89	53.56
549.87	60.99
624.85	62.89
699.83	64.73

2

Conversion

°C	%
30.09	0.56
104.03	1.36
177.96	1.78
251.90	2.28
325.84	3.64
399.77	5.76
473.71	8.65
547.64	11.54
621.58	11.78
695.51	11.89

Figure 1. TG-DTA curves of (a) catalyst **1** and (b) catalyst **2**.

over a 2 min period. The reaction was stirred at 0 °C and monitored by TLC. After completion of the reaction, the catalyst was filtered and washed with dichloromethane. After removing the solvent, the crude material was column chromatographed on silica gel to afford the corresponding epoxide.

3. Results and discussion

3.1. Characterisation of catalysts

The prepared catalysts were characterised by IR, UV and TGA. The anchoring and loading of the ligands on silica was confirmed by performing elemental analysis at different stages.

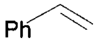
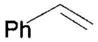
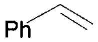
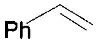
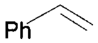
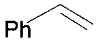
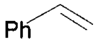
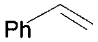
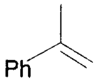
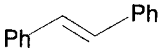
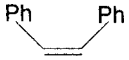
The anchoring of the complexes was checked by combined TG-DTA measurements. The decomposition behaviour of the free complex **1** and anchored complex **2** has been compared in order to understand the effect of anchoring (figure 1). The free complex decomposes during heating to 500 °C in several well-defined steps. This behaviour indicates that the complex **1** decomposes in a relatively well-defined manner and releases defined fragments, which readily burn off. An exothermic weight loss of 31% appears at temperatures below 400 °C. From the weight loss, we tentatively assign these steps to the successive cleavage of the *tert*-butyl and methyl groups. Above this temperature, the remaining ∼30% organic moieties are decomposed up to 500 °C with a non-volatile residue of 39%.

The anchored complex **2** shows somewhat different decomposition behaviour due to covalent bonding. The combined TG-DTA curves of silica anchored complex **2** show less defined steps of weight loss and maxima peak. A broad exothermic DTA peak is observed between 300 and 550 °C. Decomposition of the complex is complete at 550 °C. The shift of the onset temperature of decomposition of the anchored complex **2** in comparison with free complex **1** is attributed to covalent bonding of the complex onto the silica gel support. The efficiency of the complexation method is illustrated by UV-VIS diffuse reflectance spectroscopy. The absorption spectra of the silica anchored complex **2** shows similar bands to that of the corresponding complex **1** in dichloromethane solution ($\lambda = 268$, 338 and 462 nm). The heterogeneous complexes **3–7** also show similar bands indicating that there is no change in co-ordination.

3.2. Epoxidation of olefins

The prepared catalysts **1–7** were screened for epoxidation of olefins according to standard Jacobsen procedure. We chose iodosobenzene or *m*-CPBA as the terminal oxidants and NMO as a co-oxidant. The *m*-CPBA oxidant gave improved yield and ee. *m*-CPBA is able to perform the epoxidation of styrene to racemic epoxide in the absence of Mn(salen) and NMO. In the absence of NMO, *m*-CPBA epoxidation of styrene in the presence of Mn(salen) produced racemic epoxide. However, in the presence of excess NMO, *m*-CPBA forms a 1 : 1 salt, which is unreactive towards olefins but appears to oxidise the Mn(salen) catalysts with high efficiency which in turn gives chiral epoxides [15]. There is no effect of immobilisation on ee. However, the heterogeneous catalyst **2** shows less activity than its homogeneous counterpart **1** (table 1, entries 1 and 2). The C_2 symmetric heterogeneous catalysts **2** and **3** and the unsymmetrical chiral salen complexes **4–7** were tested for epoxidation of olefins. The catalysts **1–3** gave the epoxides with good yields, albeit poor enantiomeric excess. Similarly, epoxidation of α-methylstyrene, *trans*-stilbene and *cis*-stilbene using catalyst **2** gave the epoxides with good yield. However, no asymmetric induction was observed with catalysts **4–7**, which may be due to the electronic factors. These catalysts

Table 1
Asymmetric epoxidation of olefins with Mn(III)salen type catalysts.

Entry	Olefin	Catalyst	Oxidant	Time (h)	Yield[a] (%)	ee[b] (%)
1		**1**	*m*-CPBA	1	98	16
2		**2**	*m*-CPBA	4	92(79,67)[c]	15(15,13)[c]
3		**3**	*m*-CPBA	4	80	7
4		**4**	*m*-CPBA	4	85	–
5		**5**	*m*-CPBA	4	82	–
6		**6**	*m*-CPBA	4	64	–
7		**7**	*m*-CPBA	4	22	–
8		**2**	PhIO	24	80	9
9		**2**	*m*-CPBA	1	93	20
10		**2**	*m*-CPBA	1	62	14
11		**2**	*m*-CPBA	1	78(29 : 71)[d]	36[e]

[a] Isolated yield of epoxide.

[b] Enantiomeric excess is determined by chiral HPLC analysis.

[c] Numbers in parentheses refer to the 2nd and 3rd runs with used catalyst, respectively.

[d] Product is a mixture of *cis*- and *trans*-epoxides. Numbers in parentheses are a ratio of *cis*- and *trans*-epoxides.

[e] ee of *trans*-epoxide.

have amino alcohol ligands instead of Schiff base ligands thus indicating that the amino alcohol ligands are inferior to Schiff base ligands for asymmetric induction in the epoxidation reactions. The catalysts are recyclable with reduced activity. For example, catalyst **2** gave the styrene epoxide with 92, 79 and 67% yields and 15, 15 and 13% ee's for the 1st, 2nd and 3rd runs, respectively (entry 2). The loss of activity observed in the reused catalyst may be attributed to the degradation of the salen complex during the reaction [16]. *Trans*-stilbene gives a *trans*-epoxide, whereas *cis*-stilbene gives a mixture of *cis*- and *trans*-epoxides in the ratio of 29 : 71. The ee of *trans*-epoxide obtained from *cis*-stilbene is higher than the one obtained from *trans*-stilbene.

In conclusion, we have prepared silica anchored catalysts by covalent bonding for heterogeneous asymmetric epoxidation of alkenes. The bonding and formation of metal complex on silica was confirmed by elemental analysis, IR and UV-VIS. Our results showed that the silica anchored catalyst **2** exhibited a comparable activity and enantioselectivity in asymmetric epoxidation of alkenes to that of analogous homogeneous complex **1**.

Acknowledgement

NSC thanks the Council of Scientific and Industrial Research, India, for the award of a research fellowship.

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