Heterogeneous asymmetric epoxidation of alkenes catalysed by a polymer-bound (pyrrolidine salen)manganese(III) complex

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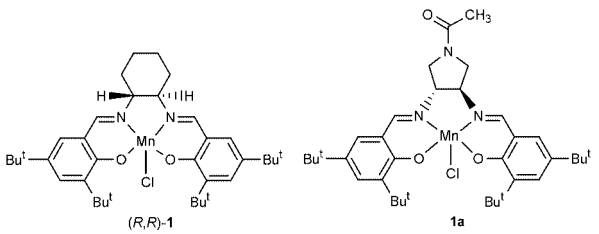
Excellent enantioselectivity (*e.g.* 92% ee for 2,2-dimethylchromene) has been achieved in heterogeneous asymmetric epoxidation using a polymer-bound (pyrrolidine salen)-manganese(III) complex; however, this polymeric catalyst underwent partial decomposition under epoxidation conditions.

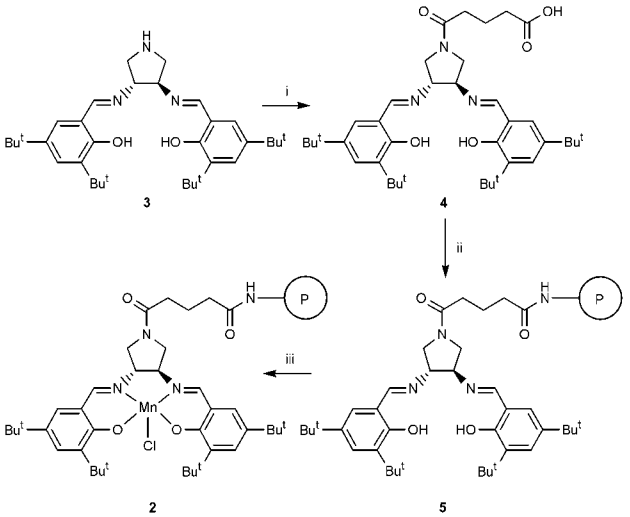
Catalytic asymmetric epoxidation of alkenes presents a powerful strategy for the synthesis of enantiomerically enriched epoxides. Among several catalytic methods, the asymmetric epoxidation of unfuntionalised alkenes catalysed by chiral salen manganese complexes, *e.g.* the compound **1** developed by Jacobsen *et al*. is one of the most relevant methods.[1]



Recently, several attempts to build heterogeneous systems by the covalent attachment of Jacobsen-type catalysts to insoluble solid supports have been made.[2,3] Facilitation of catalyst separation, catalyst reuse and an increase in stability of the catalyst [*e.g.* minimisation of the possibility of formation of inactive μ-oxo-manganese(IV) species[4]] are the main objectives of such research. However, the results obtained so far are rather disappointing. This is perhaps not surprising since most of approaches have been focussed on copolymerisation of bis-styryl derivatives of chiral salen ligands.[2a–f] Such systems may show steric restriction for complex formation. Recently, Sherrington and coworkers[2g] have reported a series of polymer supported chiral (salen)Mn complexes, where the chiral catalytic unit was immobilised in a pendant fashion by only one of its aromatic rings to polymer supports to minimise local steric restriction. In one case, a very high ee (91%) was achieved in the epoxidation of 1-phenylcyclohexene, although the yield of the corresponding epoxide was relatively low (49%).

We now report the synthesis and application of a polymer-bound chiral (pyrrolidine salen)manganese(III) complex **2**, in which the (pyrrolidine salen)Mn moiety is attached by a single flexible linkage *via* the N-atom of the pyrrolidine moiety to the polymer support.

The dark brown polymeric complex **2** was prepared as shown in Scheme 1 by the reaction of NovaSyn® TG amino resin LL[5] with the chiral pyrrolidine salen derivative **4**, followed by treatment with $Mn(OAc)_2 \cdot 4H_2O$ in the presence of an excess of NaCl. In order to remove soluble (salen)Mn species which could interfere with the catalysis, the polymeric catalyst **2** was extracted in a Soxhlet device with MeOH for 24 h. Manganese analysis of **2** indicated that 0.11 mmol g^{-1} of the (salen)Mn complex was incorporated. The chiral pyrrolidine salen derivative **4** was readily prepared in 86% yield by the reaction of **3**[6] with glutaric anhydride in the presence of triethylamine and DMAP (CH_2Cl_2, 12 h, room temp.). To compare the catalytic efficiency in homogeneous and heterogeneous reactions, the homogeneous analogue **1a** was also prepared by a similar procedure.



Scheme 1 *Reagents and conditions*: i, glutaric anhydride, NEt_3, DMAP, CH_2Cl_2, room temp., 12 h; ii, NovaSyn® TG amino resin LL (ref. 5), 1-hydroxybenzotriazole hydrate, $NEtPr^i_2$, 1.3-diisopropylcarbodiimide, DMF–CH_2Cl_2, room temp., 15 h; iii, $Mn(OAc)_2 \cdot 4H_2O$, EtOH–toluene, 85 °C, air, 12 h, then NaCl(aq).

Catalytic asymmetric epoxidations were carried out in the presence of 4 mol% of catalyst using NaOCl–PPNO (4-phenylpyridine *N*-oxide) or MCPBA–NMO as the oxidant system. The conditions were typical of those reported in the use of the soluble Jacobsen catalyst **1**[7] and the results obtained are shown in Table 1.

As a control experiment, we first investigated the catalytic efficiency (activity and enantioselectivity) of the monomeric analogue **1a** of the polymeric catalyst **2**. We were pleased to find that this catalyst was nearly as effective as Jacobsen's catalyst **1** (Table 1, entries 1 and 2). This result means that the chiral pyrrolidine salen moiety appears to be an appropriate chiral scaffold for the asymmetric epoxidation catalyst. With these results in hand, we turned to studying polymer-bound catalyst **2**. As shown in Table 1, the polymer-bound catalyst **2** exhibited quite satisfactory results, although the activity and enantioselectivity were still slightly lower than those obtained with its homogeneous analogue **1a**. In general, the reaction with MCPBA as the oxidant proceeded much faster than with NaOCl and afforded higher ee values. For example, the epoxidation of 2,2-dimethylchromene with MCPBA was completed in 1.5 h, affording the corresponding oxide with very high ee (92% ee, entry 4). On the other hand, the same reaction with NaOCl,

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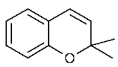
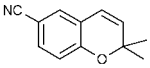
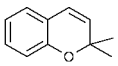
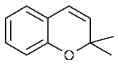
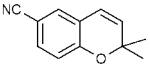
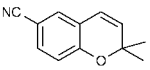
Table 1 Asymmetric epoxidation of alkenes catalysed by polymer-bound chiral (salen)Mn^{III} complex **2** or its homogeneous analogue **1a**[a]

Entry	Catalyst	Substrate	Oxidant system	t/h	Yield (%)[b]	ee (%)[c]
1	**6**		NaOCl –PPNO	4	90	95
2	**6**		NaOCl –PPNO	5	96	90
3	**2**		NaOCl –PPNO	24	84	87
4	**2**		MCPBA –NMO	1.5	85	92
5	**2**		NaOCl –PPNO	50	82	87
6	**2**		MCPBA –NMO	1.5	72	86
7	**2**		NaOCl –PPNO	24	82	78
8	**2**		MCPBA –NMO	2	76	68

[a] See footnote†. [b] Isolated yields. [c] Determined by chiral GC or chiral HPLC: see footnote† and ref. 7(*b*); major enantiomers: (3*R*,4*R*)-3,4-epoxy-2,2-dimethylchroman, (3*R*,4*R*)-3,4-epoxy-6-cyano-2,2-dimethylchroman and (1*R*,2*S*)-1-phenylcyclohexene oxide.

which was carried out under two-phase conditions, required 24 h for a comparable degree of conversion and gave the epoxide with 87% ee (entry 3). The polymeric catalyst **2** could be simply recovered by filtration so enabling catalyst recycling. However, the polymer-bound catalyst **2** underwent partial decomposition under epoxidation condition. The initially dark brown resin was more or less decolourised after the reaction. When MCPBA was used as oxidant, much more severe decolourisation was observed than when NaOCl was used. This result is in accord with results of Skarzewski *et al*., who also observed a fairly high resistance to degradation when NaOCl is used as an oxidant for salen complexes with *tert*-butyl groups at the 5- and 5′-positions.[8] This tendency of salen manganese catalysts to undergo decomposition under epoxidation conditions could limit successful recycling of immobilised catalyst.[9]

In summary, we have prepared a promising class of polymer-bound catalyst for heterogeneous asymmetric epoxidation of alkenes. Our results showed that polymeric catalyst **2** showed a comparable degree of enantioselectivity (92% ee for 2,2-dimethylchromene) in asymmetric epoxidation of alkenes to that obtained with its homogeneous analogue **1a**. However, the activity and enantioselectivity of the polymeric catalyst **2** are highly dependent on epoxidation conditions, and, moreover, the degree of decomposition of catalyst also seems to be highly influenced by oxidation conditions. Therefore, to carry out heterogeneous asymmetric epoxidation successfully, not only the design of supported catalysts, but also the selection of appropriate oxidation conditions are very important. More detailed studies concerning the optimisation of both catalyst structure (to increase activity and enantioselectivity by modifying the spacer length and resin morphology, *etc*.) and reaction conditions (to minimise catalyst decomposition) are currently in progress.

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Notes and references

† Asymmetric epoxidation using polymer-bound catalyst **2**.

Using NaOCl as the oxidant: resin beads of **2** (202 mg) were stirred in CH_2Cl_2 (2 mL) for 1 h. Alkene (0.54 mmol) and 4-phenylpyridine *N*-oxide (18.5 mg, 0.108 mmol) were then added and the mixture was cooled to 0 °C. To this mixture buffered NaOCl (0.81 mmol, pH = 11.3) was added and the reaction was stirred at 0 °C. At the end of the reaction, the suspension was filtered off and resin beads were washed with CH_2Cl_2. The filtrate was washed with brine and dried ($MgSO_4$). After removal of the solvent under reduced pressure, the residue was purified by column chromatography.

Using MCPBA as the oxidant: resin beads of **2** (202 mg) were poured into a solution containing 2.7 mmol (316 mg) of *N*-methylmorpholine *N*-oxide dissolved in CH_2Cl_2 (4 mL). Alkene (0.54 mmol) was then added and the mixture was cooled to −78 °C. Solid MCPBA (1.08 mmol, 186 mg) was then added as a solid in four roughly equal portions over a 2 min period. The reaction mixture was stirred at −78 °C and the progress of the reaction was monitored by TLC. At the end of the reaction, the suspension was filtered off and resin beads were washed with CH_2Cl_2. The filtrate was washed with 1 M NaOH, brine and dried. After removal of the solvent under reduced pressure, the residue was purified by column chromatography.

The ee values of products were determined by chiral HPLC or chiral GC: For 3,4-epoxy-2,2-dimethylchroman: Daicel Chiralpak AD, propan-2-ol–hexane (5:95), 0.8 mL min^{-1}; 9.30 min (3*R*,4*R*), 10.63 min (3*S*,4*S*); for 3,4-epoxy-6-cyano-2,2-dimethylchroman: Daicel Chiralcel OJ, propan-2-ol–hexane (30:70), 1 mL min^{-1}; 13.95 min (3*R*,4*R*), 26.88 min (3*S*,4*S*); for 1-phenylcyclohexene oxide: see ref. 7(*b*).

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8 J. Skarzewski, G. Gupta and A. Vogt, *J. Mol. Catal. A: Chem.*, 1995, **103**, L63.

9 Very recently, the degradation of Mn-loaded polymeric salen ligands under epoxidation conditions was also noted by Angelino *et al.* [see ref. 2(*i*)].

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