Remarkable matrix effect in polymer-supported Jacobsen's alkene epoxidation catalysts

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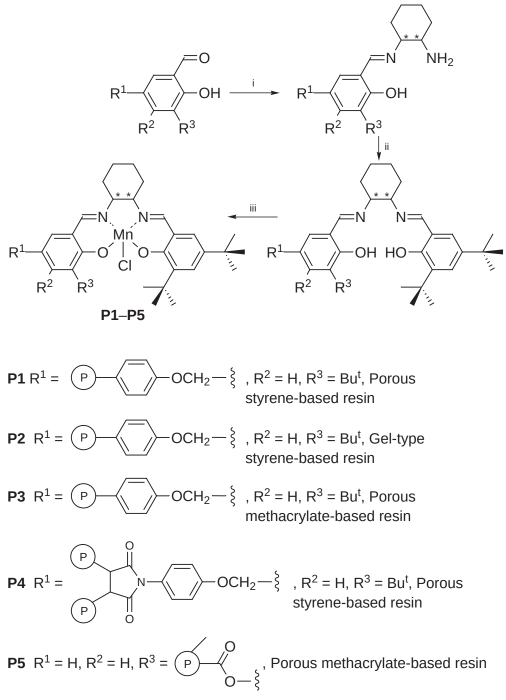
Adaptation of the polymer matrix has allowed high enantioselectivity to be achieved for the first time with a polymer-supported chiral Mn^{III}(salen) alkene epoxidation catalyst.

Previous attempts to immobilise Jacobsen's chiral Mn^{III}(salen) asymmetric alkene epoxidation catalyst[1,2] on polymer resins have focussed on copolymerisation of distyryl derivatives of chiral salen ligands, such that the Mn complex formed is essentially localised on a crosslink.[3,4] Perhaps not surprisingly the steric restriction of this system has led to disappointingly low levels of enantiocontrol in epoxidations. Our own first attempt to develop a polymer-supported system was also rather disappointing,[5] but encouraged us to believe that providing the following design criteria could be met, a highly active and selective heterogeneous catalyst should result: (i) the local molecular structure of the Mn complex should mimic precisely the optimum structure of Jacobsen's catalyst; (ii) the complex should be attached by a single flexible linkage to the polymer support to minimise local steric restriction; (iii) the catalyst should be attached to the polymer with sufficiently low loading to maximise site isolation of catalytic centres, hence minimising the possibility of inactive oxo-bridged dimer formation; and (iv) the morphology of the support should be such that no mass transfer limitation arises, with all active sites freely accessible. We now report on the synthesis and application of a number of polymer-supported analogues of Jacobsen's catalyst developed on the basis of the above criteria.

Polymer resin catalysts **P1**–**P5** were synthesised as shown in Scheme 1 to yield Mn complex loadings (calculated from Mn content determined by inductively coupled plasma absorption) of 0.35, 0.17, 0.08, 0.34 and 0.22 mmol g^{-1} respectively. The styrene-based resins used to prepare **P1** and **P2** employed *p*-acetoxystyrene as a functional co-monomer, commercial divinylbenzene (80% DVB grade) as the crosslinker, with styrene itself making up the co-monomer balance. The methacrylate-based resin forming the basis of **P3** likewise used *p*-acetoxystyrene as the functional co-monomer, ethane-1,2-diyl dimethacrylate as the crosslinker, and methyl methacrylate as the co-monomer balance. **P4** was derived from a resin prepared from *p*-hydroxyphenylmaleimide, divinylbenzene and styrene, while **P5** was synthesised from a resin made from 3-methacryloyoxy-2-hydroxybenzaldehyde,[7] ethane-1,2-diyl dimethacrylate and methyl methacrylate. Polymerisation compositions and resin parameters are shown in Table 1. The yields of high quality beads were good and along with subsequent chemical derivatisation confirmed good incorporation of each functional



Scheme 1 *Reagents and conditions*: i, (*R*,*R*)-1,2-diaminocyclohexane, CH_2Cl_2, room temp., 12 h; ii, 2,4-di-*tert*-butylsalicylaldehyde (ref. 6); iii, CH_2Cl_2, room temp., 12 h; vi, $Mn(OAc)_2\cdot4H_2O$, EtOH, air, reflux, 30 h, then LiCl.

Table 1 Synthesis of resin precursors to polymer catalysts **P1**–**P5**[a]

	Polymerisation conditions				Resin				
Precursor	Cross-linker/ mol%	Co-monomer (%)	Porogen	Monomer: porogen (v/v)	Yield of beads (%)	Bead diameter (% 200–500 μm)	Average pore radius/nm	Surface area/ m^2 g^{-1}	Morphology
P1	1.6[b]	32[c]	—	—	57	39	—	—	Gel-type
P2	24[b]	32[c]	2-Ethylhexan-1-ol	1:1	95	67	5.9[d]	31	Porous
P3	68[e]	13[c]	Toluene	1:1	84	58	0.9[d]	123[f]	Porous
P4	60[b]	20[g]	2-Ethylhexan-1-ol–DMF (7:3, v/v)	1:1	83	80	4.6[d]	227[f]	Porous
P5	30[e]	25[h]	2-Ethylhexan-1-ol–toluene (6:5, v/v)	1:1	73	60	6.5[i]	101[f]	Porous

[a] All polymers made by suspension polymerisation using procedures already reported (ref. 8). [b] DVB. [c] *p*-Acetoxystyrene. [d] from N_2 sorption, BJH method (ref. 9) (Micromeritics Accursorb 2100E). [e] Ethane-1,2-diyl dimethacrylate. [f] From N_2 sorption, BET method (ref. 10). [g] *p*-Hydroxyphenylmaleimide. [h] 3-Methacryloyloxy-2-hydroxybenzaldehyde. [i] Hg intrusion porosimetry (Micromeritics Autopore 9220).

Table 2 Asymmetric epoxidation of 1-phenylcyclohex-1-ene using MCPBA catalysed by polymer-supported chiral Mn^{III}(salen) complex[a]

		Epoxide		
Catalyst	Configuration	Yield (%)[b]	Ee (%)[c]	Configuration[d]
Soluble[e]	*S*,*S*	72	92	(+)-(*R*,*R*)
P1	*R*,*R*	36	61	(−)-(*S*,*S*)
P2	*R*,*R*	47	66	(−)-(*S*,*S*)
P3	*R*,*R*	49	91	(−)-(*S*,*S*)
P4	*R*,*R*	5	5	(−)-(*S*,*S*)
P5	*R*,*R*	5	~0	(−)-(*S*,*S*)

[a] See note †. [b] Determined by GC after 2 h using PhBr as internal standard. [c] Determined by HPLC using Diacel CHIRACEL OJ column (hexane–Pr^iOH, 90:10, as eluent). [d] Absolute configuration confirmed by polarimetry. [e] Jacobsen's catalyst used as supplied from Aldrich.

co-monomer. In the case of the precursors to resin catalysts **P1**–**P3** the acetoxy group was cleaved with NH_2NH_2 and the sodium salt of the liberated phenol reacted with 3-*tert*-butyl-5-chloromethyl-2-hydroxybenzaldehyde.[4] The sodium salt of the phenolic precursor to **P4** was similarly derivatised. In all cases the immobilised salicylaldehyde residues were further elaborated as in Scheme 1. Interim elemental microanalysis of beads at various stages of the catalyst synthesis, and model reactions using 5-bromo-2-hydroxybenzaldehyde instead of the di-*tert*-butyl analogue, confirmed the success of the stepwise synthesis of the catalysts, and indicated typically $\geqslant$90% of salen ligands to be attached pendantly (extensive details will be presented in due course in a full paper[11]). Interestingly the reactions can be monitored superficially by the succession of characteristic colour changes of the beads; acetoxy resin, white; phenolic resin, cream; phenoate resin, pale pink; salicylaldehyde resin, sandy yellow; mono-Schiff-base resin, yellow; salen resin, yellow; Jacobsen resin, dark brown.

Asymmetric epoxidations of 1-phenylcyclohex-1-ene were carried out in CH_2Cl_2 at 0 °C using MCPBA as the oxidant, and NMO as the activator. The conditions employed were typical of those reported in the use of the soluble catalyst.[6] The results obtained are shown in Table 2. In the case of polymer catalysts **P4** and **P5** both the yield and enantiomeric purity of the epoxide product are very low. With **P5** we believe this is so because attachment of the chiral Mn^{III}(salen) complex to the support is *via* the position *ortho* to the phenolic OH on one of the aromatic rings. The synthetic route to this species is facile, cost effective, and offers a highly structurally pure polymer catalyst. We had hoped the local steric restriction might reinforce the enantioselectivity. In practice this seems not to be so, and the local congestion seems so high as to inhibit any significant approach to the Mn centre, let alone an enantiocontrolled one. The poor performance of **P4** is less easily explained. The polymer matrix from which this is derived was synthesised using 60 mol% divinylbenzene crosslinker and 20 mol% *p*-hydroxyphenylmaleimide with a high level of porogen present (Table 1). The porosity characteristics suggest that mass transfer to the interior of this rather heavily crosslinked species should nevertheless be quite good. Since styrene and maleimide display a high tendency to form a 1:1 alternating copolymer structure, despite the modest loading of functional co-monomer, these residues may well therefore be in close proximity to each other in the matrix. Consequently bimolecular deactivating reactions between Mn centres might be encouraged. Since the phenylmaleimide residue is likely to be a rather rigid segment in the matrix backbone, both of these factors seem to have conspired to produce low catalytic activity and selectivity. The performance of the gel-type styrene-based resin **P1** is much better. The enantioselectivity achieved (61% ee) is as good as any previous data in the literature for polymer-supported species of this type, and far better than our earlier attempt with a gel-type resin.[5] In the latter case the polymer catalyst also displayed low activity, suggesting that deactivating dimerisation of the Mn^{III} centres was occurring. With catalyst **P1** the Mn loading level and morphological characteristics are not too different to our earlier gel-type species, but the attachment to the polymer matrix is quite different. Previously the linkage had been *via* an ether group at the position *meta* to the phenolic OH on one of the aromatic groups of the salen.[5] With **P1** the linkage is *via* an oxymethylene at the position *para* to the phenolic OH. Bearing in mind the sensitivity of these chiral salen ligands to the pattern and nature of the substitution on the aromatic rings, this simple change alone may well account for the improved catalytic performance of the gel-type species **P1**. Interestingly, catalyst **P2** is chemically similar to **P1** both in terms of the local structure in and around the catalytic centres, the Mn loading, and in terms of the longer range environment. It differs only in having a (macro)porous morphology rather than a gel-type one. Its dry porosimetry characteristics suggest mass transport should be quite good. Both the activity and enantioselectivity displayed by **P2** are very similar to those of **P1**, and suggest that further manipulations of the morphology of styrene-based resins may not alone offer significant improvement in catalyst activity and selectivity. Catalyst **P3** displays comparable activity to those of **P1** and **P2** under the conditions employed but is significantly more enantioselective ($>$90% ee). Indeed the enantiocontrol displayed mirrors that of the soluble catalyst. The experimental ee is significantly higher than that reported to date for any polymer-supported system, and suggests that contrary to earlier findings a practical polymer-supported Jacobsen's catalyst may well be achievable. **P3** is prepared from a heavily crosslinked (macro)porous resin and has rather low loading of Mn sites (0.08 mmol g^{-1}). The dry resin has a good surface area and the porogen employed (toluene) is known to generate rather small pores.[12] Probably of key significance however is that **P3** is derived from a methacrylate-based resin rather than a styrene-based one, although the immediate link to the polymer is *via* a styryl residue. We believe that such a matrix, although macroscopically rigid, has considerably improved local mobility relative to a styrene-based analogue, and of course is of significantly higher polarity. These two factors, coupled with the rather low loading of catalytic sites (0.08 mmol g^{-1}), seem to be key in allowing rapid catalysis and a stereochemical outcome that are essentially analogous to those found with the soluble catalyst.

Notes and references

† Asymmetric epoxidation procedure. Resin beads (0.13 mmol Mn) were poured into a solution containing NMO (15.79 mmol) dissolved in CH_2Cl_2 (25 ml) and evacuated (water pump) for *ca*. 1 min. Phenylcyclohex-1-ene (3.16 mmol) and PhBr (2.04 mmol) were then added and the mixture was cooled to 0 °C. MCPBA (6.32 mmol) was then added in four equal portions over a 2 min period.

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