Polystyrene and polymethacrylate resin-supported Jacobsen's alkene epoxidation catalyst

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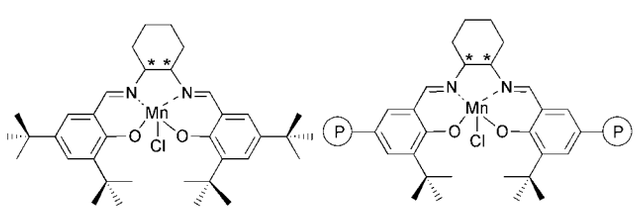
Polystyrene and polymethacrylate-based resin supported Jacobsen's chiral Mn salen complexes have been prepared. The resins are of defined molecular structure and morphology, and the complexes have been attached primarily in a pendant fashion. The loadings of Mn(III) are in the range ~0.08–0.35 mmol g^{-1} to maximise the likelihood of site-isolation. The polymer-supported complexes have been used as enantioselective catalysts in the epoxidation of 1,2-dihydronaphthalene, indene, 1-phenylcyclohex-1-ene and 1-phenyl-3,4-dihydronaphthalene using *m*-chloroperbenzoic acid as the oxidant and 4-methylmorpholine *N*-oxide as the co-oxidant. Though the activities of the polymer catalysts are reduced relative to the soluble homogeneous analogue, the catalysts are sufficiently active to be useful. The corresponding reduction in enantioselectivity is more significant, and is both substrate and polymer resin dependent. However, in the case of 1-phenylcyclohex-1-ene and a macroporous polymethacrylate-based resin the enantioselectivity is equivalent to that of the soluble complex (91–92% ee). This is the first report of a polymer-supported analogue of Jacobsen's catalyst being as selective as the homogeneous species. The catalysis data is discussed in detail in the context of the design of the polymer-supported system, and the existing data already available in the literature.

Attempts have also been made to recycle the polymer catalysts with and without re-loading of Mn. In fact the level of leaching of Mn is very low, but the catalysts show a very rapid fall off in both activity and selectivity in the first and second cycles. Overall therefore it seems that the intrinsic stability of the chiral Mn(II) salen complex itself is too low to allow viable recycling, and the development of other more stable supported chiral metal salen complexes for use in other enantioselective reactions seems a better future option.

Introduction

The exponential growth in the use of polymer-supported methodology in combinatorial chemistry and parallel synthesis attests to the tremendous advantages offered by such solid phase strategies.[1] The most positive factors are associated with ease of manipulation, work-up and product isolation, such that various levels of automation can be implemented, in turn leading to more rapid throughput in synthesis.[2] So successful has been the approach in lead compound discovery programmes in the pharmaceutical industry, that already a similar strategy has been adopted in the search for new catalysts and materials.[3] Interestingly, however, as the area matures rapidly, the major disadvantage of the methodology, namely the inability to achieve a sophisticated molecular structural analysis at each stage in a supported stepwise synthesis, is encouraging many practitioners to consider adopting an inverse strategy in which the target molecule is assembled in solution, using solid supported reagents, catalysts and scavengers.[4] The latter approach still offers all the advantages of automation and fast throughput, but also allows purification and conventional molecular structural analysis to be performed readily at all stages of a complex synthesis. Recently Ley and his co-workers[5] have demonstrated just how powerful this multi-step solid phase reagent/catalyst/scavenger approach can be. Key targets in terms of heterogenised supported reactive species for use in this strategy are the wealth of highly active and selective soluble transition metal complex based catalysts which have emerged in recent years. Not surprisingly therefore soluble asymmetric catalysts are a pivotal sub-group in this respect.[6] It is also not surprising that some of the world's leading organic synthetic groups are now themselves very active in developing effective supported reagents and catalysts.[7,8]

Jacobsen's soluble chiral Mn(III) salen asymmetric alkene epoxidation catalyst,[9] (**1a**), is particularly active and enantio-



1a **1b**

selective in the context of unfunctionalised *cis* internal alkenes, and has found significant use in target synthesis. There has therefore been considerable activity in trying to produce an equally active and selective heterogeneous analogue of this. Many groups have approached this employing zeolite and other inorganic species as the support[10,11,12] and indeed *via* physical trapping within a polysiloxane membrane.[13] Usually enantiocontrol is reduced relative to that found with the soluble catalyst, but progress is good, with the polysiloxane membrane reported to be very attractive.

There have also been some attempts to immobilise this catalyst system on polymer resins.[14,15,16,17] As with other supports, though active catalysts have been produced, to date they have usually been of low enantioselectivity. We have already made a preliminary disclosure of how the performance of these polymer-supported species can be considerably improved by appropriate choice of support, linker and ligand structure[18] and we now present a more detailed report.

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Table 1 Synthesis of resin beads **4a–c** and **7d**[a]

	Polymerisation feed				Resin product					
Resin	Cross-linker/ mol%	Functional comonomer/ mol%	Porogen	Monomer : porogen/v/v	Yield of beads (%)	Diameter 200–500 μm (%)	Surface[i] area/ $m^2\ g^{-1}$	Pore radius/nm	Swelling[l] factor (%)	Theoretical OAc content/ mmol g^{-1}
4a	1.6[b]	32[d,f]	—	—	57	39	—	—	340	2.60
4b	24[b]	32[d,f]	2-Ethyl-hexan-1-ol	1 : 1	95	67	31	5.9[j]	110	2.47
4c	68[c]	13[d,g]	Toluene	1 : 1	84	58	123	0.9[j]	50	1.22
7d	30[c]	25[e,g]	(6 : 5 v/v)[h]	1 : 1	73	60	101 —	6.5[k]	30	1.62[m]

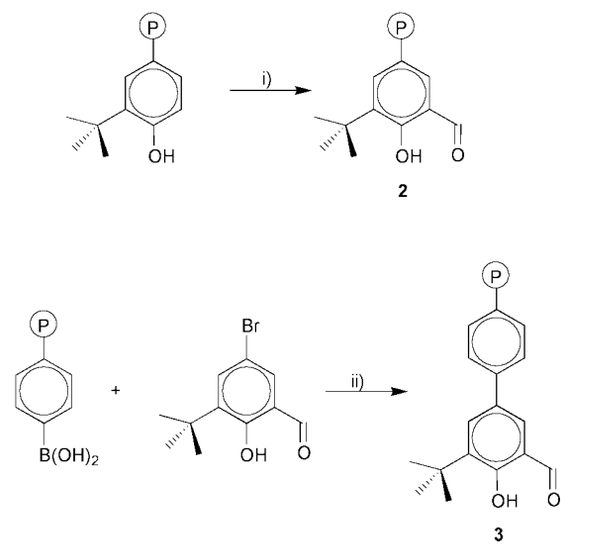
[a] Suspension polymerisation.[22,23] [b] Divinylbenzene. [c] Ethylene glycol dimethacrylate. [d] *p*-Acetoxystyrene. [e] Monomer (**8**). [f] Styrene make-up. [g] Methyl methacrylate make-up. [h] 2-Ethylhexan-1-ol–toluene. [i] N_2 sorption, BET method.[32] [j] N_2 sorption, BJH method.[33] [k] Hg intrusion porosimetry. [l] $[(V_f - V_i)/V_i] \times 100$ in CH_2Cl_2. [m] Salicylaldehyde content.

Results and discussion

Defining of objective

The early attempts to immobilise analogues of Jacobsen's catalyst on polymers used structurally and morphologically poorly defined crosslinked polymers in which the chiral ligand was introduced *via* copolymerisation of distyryl derivatives of the chiral salen species.[14,15] This route was adopted presumably because synthesis of non-symmetrically substituted salen ligands is extremely difficult, *i.e.* simple monostyryl precursors are not readily accessible. The effect of using distyryl derivatives of the chiral salen ligand is to localise the catalytic centre on the crosslink of the polymer matrix (**1b**) and this would be expected to offer the worst prospects in terms of macroscopic access to such sites and also in terms of local mobility of the catalyst complex. Since there is some evidence that bent transition states or intermediates may be involved in the catalytic cycle,[19] allowing maximum local freedom and facile longer range access to catalytic sites seem to be essential prerequisites for achieving catalytic activity and selectivity equivalent to or better than the soluble catalyst. Though the earlier polymer-supported species were of reasonable chemical activity, perhaps not surprisingly their enantioselectivity was in general significantly lower than that of the soluble species. Our own first attempt to produce an immobilised analogue in which the chiral salen ligand was attached to the polymer specifically in a pendant fashion[20] was similar to the strategy reported by Angelino and Laibinis.[17] Both groups faced the difficulty of developing an efficient route to the pendant immobilisation of the favoured Jacobsen's structure (**1a**), and both compromised by omitting the *ortho*-Bu′ on the aromatic ring of the salen ligand which is tethered to the polymer. Furthermore both groups utilised only styrene-based resins, and while we synthesised both gel-type and macroporous species with defined morphologies, the US group used only a commercially available gel-type Merrifield precursor resin. Once again, though heterogeneous catalysts with good activity were obtained, the level of enantioselectivity was disappointing.

Nevertheless these results encouraged us to believe that, providing the following design criteria could be met, a highly active and selective 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 at sufficiently low loading to maximise site isolation of catalytic centres and hence minimise the possibility of inactive oxo-bridge dimer formation; iv) the polarity of the resin should be such as to provide the optimum microenvironment for the catalyst; and v) the morphology of the support should be such that no mass transfer limitation arises, with all active sites freely accessible.

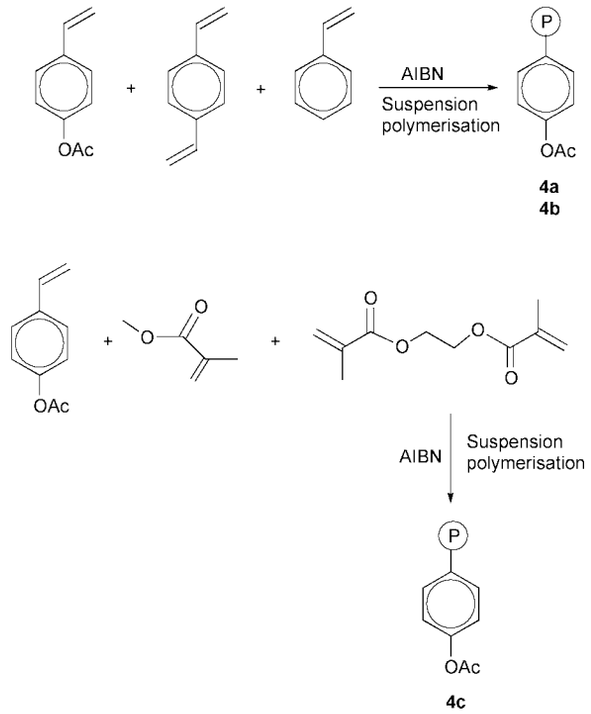


Scheme 1 Early routes examined in the synthesis of *o*-Bu′-substituted salicylaldehyde containing resins. i) $SnCl_4$, H_2CO, lutidine; ii) $Pd(PPh_3)_4$, K_2CO_3.

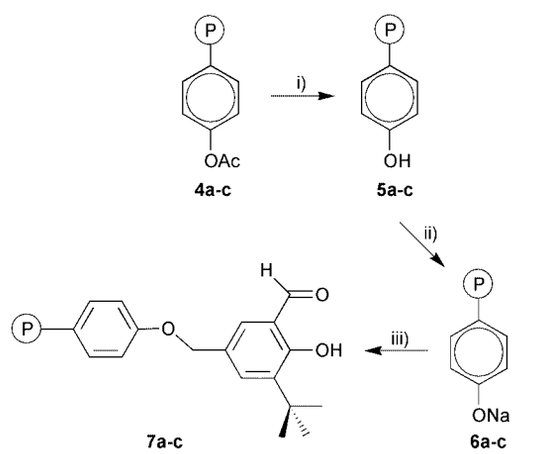
Synthesis of *o*-Bu′ substituted salicylaldehyde-containing resins (4a–c)

Two routes that were explored initially are summarised in Scheme 1 and despite great efforts both of these proved problematical in terms of achieving clean derivatisations.[21] Though we, like many others, routinely employ chloromethylated polystyrene resins as a convenient starting point for immobilisation procedures we have described the synthesis and exploitation of *p*-acetoxystyrene derived resins[22] in this context. It occurred to us that forming the nucleophile on the resin offered us a novel opportunity in this instance as well. Accordingly poly(*p*-acetoxystyrene-*co*-styrene-*co*-divinylbenzene) resins **4a** and **4b** and poly(*p*-acetoxystyrene-*co*-methyl methacrylate-*co*-ethylene glycol dimethacrylate) resin **4c** (Scheme 2) were produced in good yield (60–95%) by our published suspension polymerisation procedure.[22,23] Resin **4a** is a lightly crosslinked (1.6 mol%) gel-type species while **4b**,**c** are macroporous and more heavily crosslinked to allow this morphology to be generated. The physical characteristics of the various resins are summarised in Table 1. As anticipated using the precipitating porogen 2-ethylhexan-1-ol with a moderate level of crosslinker (24 mol%) produced a resin (**4b**) with rather low surface area, 30 $m^2\ g^{-1}$, and a medium pore size, while a higher level of crosslinker (68 mol%) and a solvating porogen, toluene, in the case of resin **4c** generates higher surface area (125 $m^2\ g^{-1}$) with concomitantly smaller pores.

Structural characterisation of the subsequent elaborations of **4a–c** was difficult since the steps shown in Scheme 3 do not



Scheme 2 Synthesis of *p*-acetoxystyrene derived resins **4a**–**c**.



Scheme 3 Synthesis of salicylaldehyde-containing resins **7a**–**c**. i) NH_2NH_2, dioxane, 80 °C, 48 h; ii) NaOH (4 M), 80 °C, 48 h; iii) 3-Bu′-5-chloromethyl-2-hydroxybenzaldehyde, CH_2Cl_2, 40 °C, 48 h.

involve exchange of any heteroatoms (to allow use of elemental microanalysis) on the resin, and since **4b**,**c** are rather heavily crosslinked gel-phase magic angle ^{1}H NMR analysis is not useful. Only FTIR spectra offered a qualitative guide.

Deprotection of **4a**–**c** to generate **5a**–**c** (Scheme 3) carried out in dioxane using a large excess of hydrazine hydrate seemed satisfactory. In the FTIR spectrum a new band at 3413 cm^{-1} (phenol) and loss of a band at 1779 cm^{-1} (C=O) were diagnostic. Deprotonation to generate phenolate residues produced pale pink coloured **6a**–**c** and was achieved with ethanolic NaOH. The coupling of 3-*tert*-butyl-5-chloromethyl-2-hydroxybenzaldehyde to **6a**–**c** was carried out at 40 °C (48 h), and after work-up all three resins, **7a**–**c**, displayed a significant C=O vibration in their FTIR spectra (1680 cm^{-1}) characteristic of the salicylaldehyde group. The presence of the latter was confirmed when the pale yellow beads became dark orange–red when tested with Brady's reagent. Furthermore no Cl was detected by elemental microanalysis of **7a**–**c** confirming that the salicylaldehyde residues present were indeed covalently bound to the resins, and not simply physically trapped as the chloromethyl precursor.

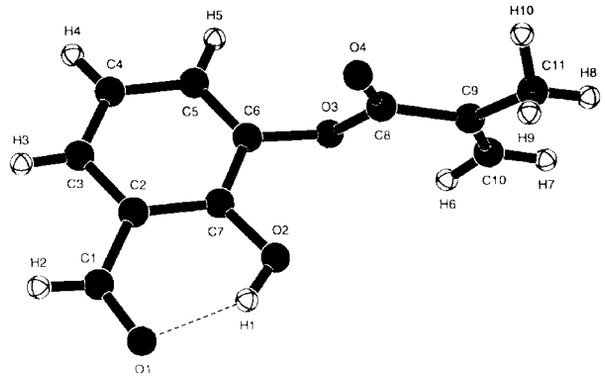
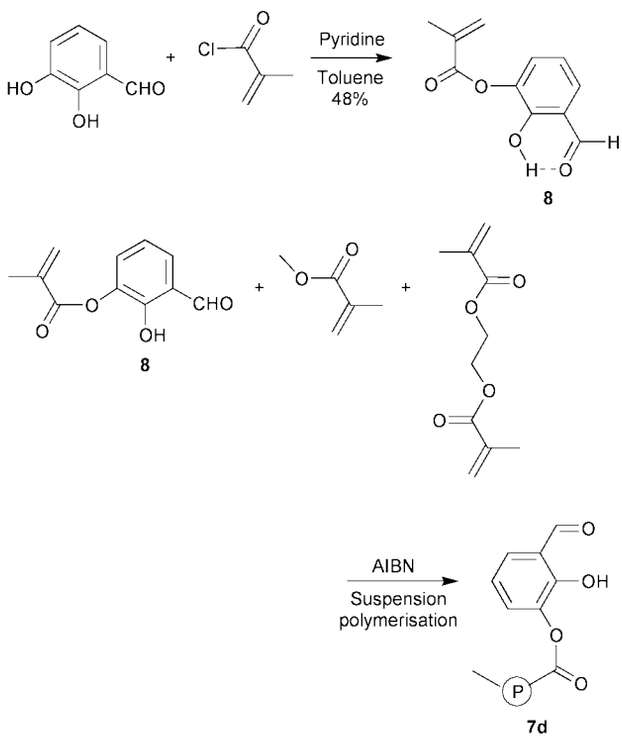


Fig. 1 X-Ray crystal structure of salicylaldehyde-containing methacrylate monomer **8**.



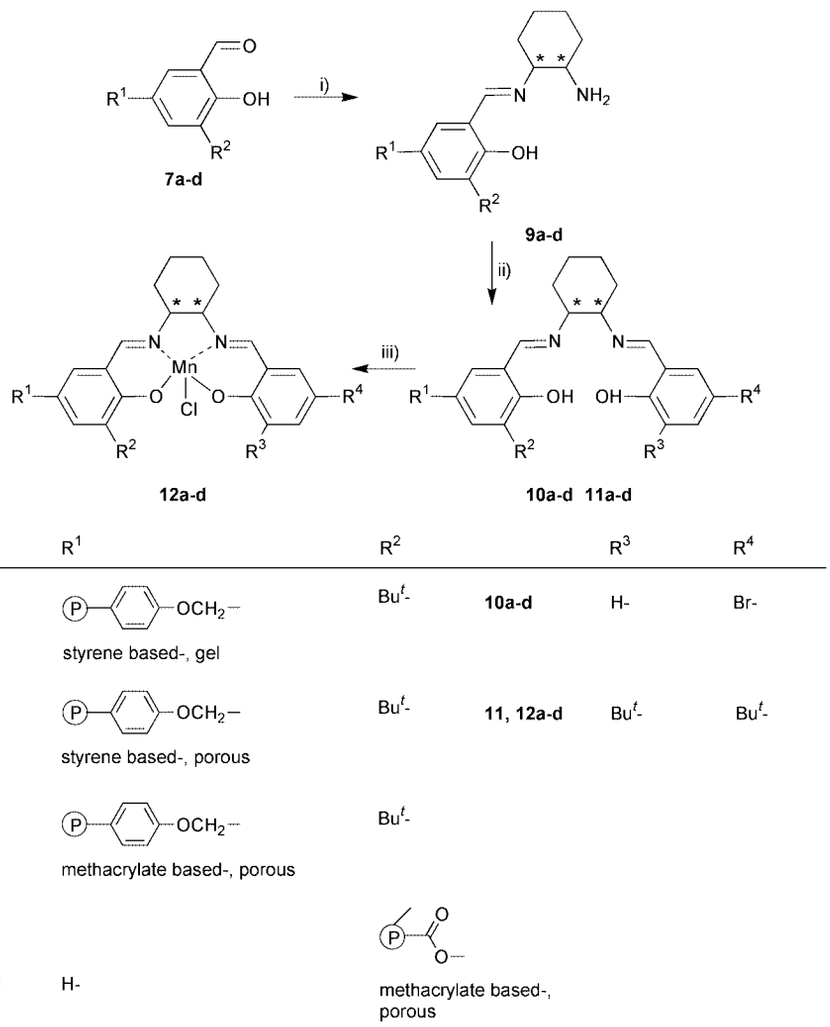
Scheme 4 Synthesis of salicylaldehyde-containing resin **7d**.

Synthesis of *o*-attached salicylaldehyde methacrylate resin, 7d

The route to this resin is shown in Scheme 4. 2-Hydroxy-3-methacryloyloxybenzaldehyde **8** was obtained selectively in 48% yield along with unreacted 2,3-dihydroxybenzaldehyde starting material which was recovered for re-use. The crystal structure of **8** (Fig. 1) shows the intramolecular hydrogen bond between the C=O group and its adjacent OH group which seems to play a protecting role during methacryloylation. As a result the latter is very regioselective in yielding monomer **8**. Co-polymerisation of the latter with methyl methacrylate and ethylene glycol dimethacrylate employing 2-ethylhexan-1-ol–toluene as porogen yielded the macroporous resin **7d**. The physical characteristics of the latter are summarised in Table 1. The surface area is moderate, 100 m^2 g^{-1}, and the average pore size comparable to that of **4b**. An FTIR spectrum indicated the presence of the salicylaldehyde residue (C=O 1650–80 cm^{-1}) and this was confirmed by a positive Brady's reagent test when the beige beads (**7d**) became dark orange very rapidly.

Synthesis of chiral Mn salen-containing resins 12a–d

The synthetic route adopted is shown in Scheme 5. The expectation was that by keeping the loading of salicylaldehyde



	R^1	R^2		R^3	R^4
7,9-12a	P–OCH_2– styrene based-, gel	Bu^t-	**10a-d**	H-	Br-
7,9-12b	P–OCH_2– styrene based-, porous	Bu^t-	**11, 12a-d**	Bu^t-	Bu^t-
7,9-12c	P–OCH_2– methacrylate based-, porous	Bu^t-			
7,9-12d	H-	P–C(=O)–O– methacrylate based-, porous			

Scheme 5 Synthesis of salen-containing resins **10a–d**, **11a–d** and Mn(III) salen containing resins **12a–d**. i) (*R*,*R*)-1.2-diaminocyclohexane, CH_2Cl_2, rt, 12 h; ii) 4-bromosalicylaldehyde (for **10a–d**) and 2,4-di-Bu^t-salicylaldehyde (for **11a–d**), CH_2Cl_2, rt, 12 h; iii) $Mn(OAc)_2{\cdot}4H_2O$, ethanol, air, reflux 30 h, LiCl added.

residues in resins **7a–d** low, reaction with a pure enantiomer of *trans*-1,2-diaminocyclohexane would generate selectively the monoamino monoimine structures in **9a–d** (Scheme 5). Failure of this site-isolation strategy would allow the thermodynamically more stable bisimine (*i.e.* salen) to be formed, simultaneously immobilising any derived Mn complex on a polymer crosslink (**1b**). In order to allow some measure of quantification of the level of site-isolation achieved, a group of model resins (**10a–d**) was synthesised using 5-bromosalicylaldehyde (Scheme 5) in the final coupling reaction yielding a mono-*p*-brominated salen with the halogen present as a convenient analytical handle.

By reacting the salicylaldehyde resins **7a–d** with excess chiral diamine it was also hoped to encourage formation of the monoimines **9a–d**. The pale yellow resins **7a–d** rapidly turned deep yellow characteristic of many Schiff bases. This was confirmed by the FTIR spectra displaying the imine vibration band at 1640 cm^{-1}. The appearance of a new $-NH_2$ vibration (3300 cm^{-1}) could not be distinguished clearly because of the existing broad phenolic band (3400 cm^{-1}). Elemental microanalytical data (N%) allowed for the first time some indication of the level of the desired functionalisation achieved (Table 2). Since the absolute values of N% are low the loading data quoted should be taken only as a guide. Resins **9a–c** were produced by a 4 step chemical modification of acetoxy functions, and it is reasonable to assume that most salicylaldehyde residues in **7a–c** introduced in the sequence will be located in the more accessible regions of the resins. Deprotection of the phenol moiety (step 1) and deprotonation (step 2) would be expected to be rather efficient (Scheme 3), as indeed would be imine formation (step 1, Scheme 4). The experimentally determined imine contents of **9a–c** (Table 2), all of which fall short of the theoretically predicted values assuming efficient incorporation of *p*-acetoxystyrene during resin synthesis, almost certainly therefore reflect the efficiency of the salicylaldehyde attachment (step 3, Scheme 3). The situation with resin **9d** is somewhat different. In this case the salicylaldehyde residues are introduced *via* comonomer **8** during polymerisation and there is no evidence that this copolymerisation is inefficient (Scheme 4). The low conversion to imine relative to theory in this case is more likely to be associated with poor access to some of the salicylaldehyde groups, and hence **9d** very likely contains a relatively high level of these unreacted groups.

Calculation of the imine content from the experimental N% data also assumes that site isolation has been effective. The model resins **10a–d** give some indication of this. The N% allows estimation of the total salen content (including any crosslinking units (**1b**)) and the Br% allows estimation specifically of the pendant salen ligand content. Again the absolute experimental values for N% and Br% are low and must be treated with care. However, the data in Table 3 seem rather self-consistent, indeed rewarding, and suggest very strongly that a high proportion of pendant salen groups have been achieved in **10a–c** with the level of crosslinking species being ≤10%. The analytical data for **10d** were too low to form any firm conclusions but superficially it seems that most salen groups are present as crosslinks (**13**) and site isolation has failed. Since the targeted level of salen functionality was

Table 2 Synthesis of mono-Schiff base-containing resins **9a**–**d** and (*R*,*R*)-salen-containing resins **11a**–**d**

	Resin **9a**–**d**					Resin **11a**–**d**		
			Imine content/mmol g^{-1}					
Starting resin	Code	N% found (calc[a])	Found[b]	Calc	Conversion (%)	Code	N% found (calc)	Salen content[b]/ mmol g^{-1}
7a	**9a**	1.5 (4.5)	0.53	1.62	33	**11a**	1.2 (3.3)	0.43
7b	**9b**	1.2 (4.3)	0.43	1.54	28	**11b**	0.9 (3.2)	0.31
7c	**9c**	0.3 (2.6)	0.11	0.94	11	**11c**	0.5 (2.2)	0.18
7d	**9d**	0.6 (3.9)	0.23	1.50	15	**11d**	0.3 (3.0)	0.10

[a] Based on original functional monomer feed. [b] Deduced from N% found.

Table 3 Synthesis of brominated salen-containing resins **10a**–**d**

	Resin **10a**–**d**					
Starting resin	Code	N% found (calc)	Br% found (calc)	Total[a]/ mmol g^{-1}	Salen content Pendant[b]/ mmol g^{-1}	% Pendant
9a	**10a**	1.1 (3.5)	3.0 (10.0)	0.40	0.37	93
9b	**10b**	1.8 (3.4)	4.8 (9.6)	0.64	0.60	94
9c	**10c**	0.6 (2.2)	1.5 (6.4)	0.21	0.19	90
9d	**10d**	0.4 (3.1)	Trace (9.0)	0.14	~0	~0

[a] Deduced from N% found. [b] Deduced from Br% found.

Table 4 Synthesis of (*R*,*R*)-Mn(III) salen-containing resins **12a**–**d**

	Resin **12a**–**d**							
				Mn salen content (mmol g^{-1})				
Starting resin	Code	N% found (calc)	Cl% found (calc)	From N%[a]	From Cl%[a]	From Mn%[b]	Mol%[c] Mn salen	Swelling[d] factor (%)
9a	**12a**	0.9 (3.0)	0.9 (3.8)	0.33	0.25	0.35	~10	70
9b	**12b**	0.6 (2.9)	0.6 (3.7)	0.21	0.16	0.17	~5	50
9c	**12c**	0.4 (2.0)	1.9 (2.6)	0.15	0.51	0.08	~1.5	40
9d	**12d**	0.3 (2.7)	0.3 (3.4)	0.12	0.09	0.22	~5.5	20

[a] Elemental microanalytical data. [b] Inductively coupled plasma AA. [c] Estimate of % polymer segments carrying Mn salen complex. [d] $[(V_f - V_i)/V_i] \times 100$ in dichloromethane.

similar to that in the other resins this seems unlikely, and the analytical data is probably insecure.

The resin-supported chiral salen ligands **11a**–**d** destined to form the basis of the immobilised catalysts **12a**–**d** (Scheme 5) were produced from **9a**–**d** by condensation with 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde. This contained no convenient analytical handle and so evaluation of **11a**–**d** was based only on N% content and FTIR spectra. The latter displayed the anticipated imine stretch (1635 cm^{-1}) and the N% content was found to fall relative to **9a**–**d** (Table 2) as expected from the mass increase on completing the salen skeleton. The corresponding salen loadings are shown in Table 2 and the conversions in this step seem very good.

Resin-supported Jacobsen's catalysts, 12a–d

The deep yellow salen resins **11a**–**d** were converted to the corresponding Mn(III) complexes by refluxing in air in the presence of Mn(II) acetate and LiCl.[24] The beads turned dark red–brown in colour. FTIR spectra indicated the presence of C=N (1660 cm^{-1}) and C–O (1170 cm^{-1}) vibrations characteristic of the Mn salen complex.[25] The analytical data in Table 4 show the N%, Cl% and Mn%, and the catalyst loading (mmol g^{-1}) calculated from these data. Bearing in mind the low absolute levels of N and Cl present, the data are reasonably self-consistent. The high sensitivity of the Mn analyses probably provides the most accurate indication of the metal complex content, with the apparent shortfall in N% and Cl% in for example **12d** simply arising from experimental error. The final metal complex contents 0.08–0.35 mmol g^{-1} were satisfying and well within the targeted figure judged suitable for catalytic application.

Despite the shortcomings in analytical data it does seem that a satisfactory route to pendantly immobilised analogues of the optimum Jacobsen's Mn(III) salen complex has been achieved. Although not quantitative, the remarkable and predictable colour changes which occur in the resins at each stage of the stepwise assembly attest to the success of the synthesis and not the least add to the enjoyment of this work.[26]

Asymmetric alkene epoxidation

To achieve high enantioselectivity coupled with high conversion it is important to follow the protocols described in the literature when utilising Jacobsen's catalyst. The co-oxidant 4-methylmorpholine *N*-oxide used in excess is believed to interact with *m*-chloroperbenzoic acid effectively quenching the latter as a direct (uncatalysed) non-asymmetric oxidant of alkenes. The co-oxidant also appears to coordinate to the unsaturated Mn(III) species emerging from a first catalytic cycle and prevents this reacting with active Mn(V) oxo species to produce catalytically inactive μ-oxo-Mn(IV) dimer.[19] While the latter dimerisation should be considerably reduced with site isolated immobilised complexes, nevertheless maintaining the balance of co-oxidant and oxidant was judged to be prudent.

Table 5 Asymmetric epoxidation of alkenes[a] catalysed by homogeneous and polymer-supported Jacobsen's chiral Mn salen complex

			Epoxide		
Entry	Substrate[b]	Catalyst[c]	Yield (%)[d]	Ee (%)	Configuration[g]
1	A	(*S*,*S*)-soluble	92	80[e]	(−)-(*1S,2R*)
2	A	(*R*,*R*)-**12a**	61	6[e]	(+)-(*1R,2S*)
3	A	(*R*,*R*)-**12b**	67	16[e]	(+)-(*1R,2S*)
4	A	(*R*,*R*)-**12c**	65	26[e]	(+)-(*1R,2S*)
5	B	(*S*,*S*)-soluble	80	85[e]	(+)-(*1S,2R*)
6	B	(*R*,*R*)-**12a**	51	28[e]	(−)-(*1R,2S*)
7	B	(*R*,*R*)-**12b**	72	33[e]	(−)-(*1R,2S*)
8	C	(*S*,*S*)-soluble	50	89[f]	—[h]
9	C	(*R*,*R*)-**12b**	51	7[f]	—[h]

[a] NMO 5 equiv., *m*-CPBA 2 equiv., CH_2Cl_2. [b] A = 1,2-dihydronaphthalene, B = indene, C = 1-phenyl-3,4-dihydronaphthalene. [c] 0.04 equiv. [d] 0 °C, 2 h, GC analysis. [e] HPLC Diacel CHIRACEL OB, hexane–propan-2-ol (95 : 5). [f] HPLC Diacel CHIRACEL OJ, hexane–propan-2-ol (90 : 10). [g] Absolute configuration confirmed by polarimetry. [h] Not determined.

Table 6 Asymmetric epoxidation of 1-phenylcyclohex-1-ene[a] catalysed by homogeneous and polymer-supported Jacobsen's chiral Mn salen complex

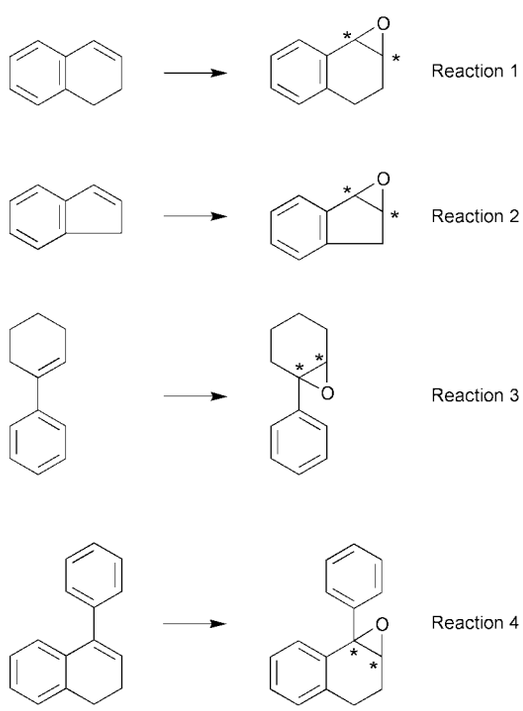
	Catalyst				Epoxide		
Entry	Structure	Equiv.	Temperature/°C	Time/h	Yield (%)[b]	Ee (%)[c]	Configuration[d]
1	(*S*,*S*)-soluble	0.04	0	2	72	92	(+)-(*1R,2R*)
2	(*R*,*R*)-**12a**	0.04	0	2	36	61	(−)-(*1S,2S*)
3	(*R*,*R*)-**12b**	0.04	0	2	47	66	(−)-(*1S,2S*)
4	(*R*,*R*)-**12b**	0.04	−32	16	52	72	(−)-(*1S,2S*)
5	(*R*,*R*)-**12b**	0.04	−78 to −45	16	0	—	—
6	(*R*,*R*)-**12b**	0.08	0	2	61	71	(−)-(*1S,2S*)
7	(*R*,*R*)-**12b**	1	0	2	29	40	(−)-(*1S,2S*)
8	(*R*,*R*)-**12c**	0.04	0	2	49	91	(−)-(*1S,2S*)
9	(*R*,*R*)-**12d**	0.04	0	48	5	~0	—
10	(*R*,*R*)-**12d**	0.08	0	2	33	~0	—

[a] NMO 5 equiv., *m*-CPBA 2 equiv., CH_2Cl_2. [b] GC analysis. [c] HPLC Diacel CHIRACEL OJ, hexane–propan-2-ol (90 : 10). [d] Absolute configuration confirmed by polarimetry.

Accordingly therefore a blank reaction was performed using the same conditions as described when a polymer catalyst was employed—in this instance in the absence of catalyst. 1-Phenylcyclohex-1-ene was the alkene examined, and GC analysis of a reaction mixture held at 0 °C for 48 h showed no conversion. The mixture was warmed to room temperature for a further 48 h again with no reaction apparent. Finally even after 12 h at 40 °C no loss of alkene was detected. A second blank reaction was also performed using the same reaction conditions and salen-containing resin **11c** with no Mn present. This was to ensure that the partition of co-oxidant and oxidant between the liquid phase and the resin phase was such that no significant imbalance occurred. If for example 4-methylmorpholine *N*-oxide was heavily preferentially sorbed into the resin relative to the *m*-chloroperbenzoic acid, then the latter might be able to act in an uncatalysed non-asymmetric alkene epoxidation in the liquid phase. In the event again no reaction was detected in this test and so selective sorption effects were deemed to be absent.

Catalyst activity and enantioselectivity

The four resins **12a**–**d** were examined as catalysts in the enantioselective epoxidation of 1,2-dihydronaphthalene, indene, 1-phenylcyclohex-1-ene and 1-phenyl-3,4-dihydronaphthalene (Scheme 6) using conditions typical of those reported in the use of soluble catalysts.[27] Although reactions were run for 2 h in fact epoxidations generally proceeded rapidly, and after ~30 min most reactions had reached a plateau in the conversion (Fig. 2). The results are shown in Tables 5 and 6. The resin catalysts carry the (*R*,*R*) analogue of Jacobsen's catalyst. The results of control reactions are also reported for soluble (*S*,*S*) Jacobsen's catalyst. Using standard conditions



Scheme 6 Asymmetric epoxidation of *cis* cyclic alkenes catalysed by Jacobsen's chiral Mn salen complex; NMO co-oxidant, *m*-CPBA oxidant.

(4 mol% Mn, 0 °C, 2 h) the four alkenes were converted in 92, 85, 89 and 72% yield respectively to their epoxides. Essentially no by-products were seen and the corresponding

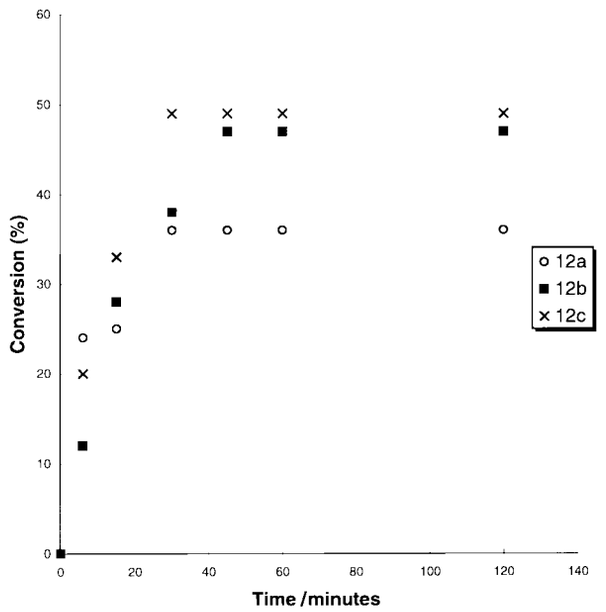


Fig. 2 Epoxidation of 1-phenylcyclohex-1-ene catalysed by resin Mn salen complexes **12a**–**c** (0 °C, 10 ml CH_2Cl_2, see Table 8).

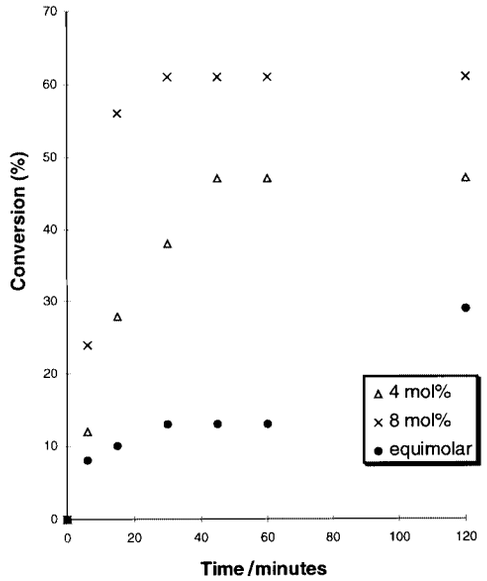


Fig. 3 Effect of level of catalyst **12b** used in epoxidation of 1-phenylcyclohex-1-ene (0 °C, 10 ml CH_2Cl_2, see Table 8).

enantioselectivities were 80, 85, 89, 92% ee. (*Note* higher values than these were obtained in synthesising epoxide standards by adjusting the conditions slightly.) The configuration of each product was as expected from the literature results. Using the same reaction conditions resin catalysts **12a**–**c** gave somewhat lower conversions of 1,2-dihydronaphthalene but more disappointingly substantially lower levels of induction (entries 2–4, Table 5). The picture is similar for **12a**,**b** used with indene (entries 6 and 7, Table 5), and in the case of 1-phenyl-3,4-dihydronaphthalene with **12b** the product epoxide is almost racemic.[28] Much more encouragingly, however, catalysts **12a**–**c** with 1-phenylcyclohex-1-ene gave modest yields 36, 47 and 49% and reasonable to good enantioselectivities 61, 66, 91% ee respectively (entries 2, 3 and 8, Table 6). Indeed the latter figure is the best yet achieved with a polymer-supported analogue of Jacobsen's catalyst and represents enantiocontrol as good as the soluble catalyst.

Clearly there is a strong substrate dependence in the context of enantioselectivity and this is difficult to rationalise. Obviously the trisubstituted alkene 1-phenylcyclohex-1-ene is oxidized very selectively relative to the two disubstituted species 1,2-dihydronaphthalene and indene, but the pattern is not consistent since the trisubstituted 1-phenyl-3,4-dihydronaphthalene is a relatively poor substrate. More results with the latter are really required however to confirm this picture.

It is also clear that there is strong dependence of enantioselectivity on the structure of the resin catalyst. In general enantiocontrol increases consistently in series **12a**, **12b**, **12c**. **12a** is a gel-type styrenic resin with a loading ~0.35 mmol Mn g^{-1}, **12b** is a macroporous styrenic with a similar loading and **12c** is a macroporous methacrylate with a significantly lower loading ~0.08 mmol Mn g^{-1}. The latter is much the best catalyst although again more data is needed to confirm this. The difference in performance does not arise from a simple factor such as difference in accessibility of solvents and reagents at the macroscopic level, since despite their different morphologies catalysts **12a**–**c** sorb rather similar levels of dichloromethane (Table 4). The effect is more subtle than this. The results do seem to suggest however, that further manipulation of the loading and morphology of styrene-based resins are unlikely to yield heterogeneous catalysts with selectivity much improved on the structurally well defined species **12a** and **12b**. In the case of **12c** the improved performance could be associated with the lower loading and hence better site isolation (Table 4) but may also be related to the more flexible polymer backbone and polar microenvironment offered by this methacrylate-based resin. Further manipulation of polar resins like this one may well prove to be a fruitful way forward with this and related metal complex catalysts tolerant to the presence of ester groups.

In this context catalyst **12d** proved very disappointing. It is indeed methacrylate-based but in this case attachment to the resin matrix is *via* the position *ortho* to the phenolic OH on one of the aromatic rings; in this respect the linker to the resin functions superficially like a bulky Bu^t-group. The synthetic route to this species is facile, cost effective, and offers a highly structurally pure polymer catalyst. Indeed we had hoped that the local steric restriction offered by the proximity of the polymer backbone might reinforce the enantioselectivity. In practice this seems not to be so, and the local congestion seems so high as to reduce catalytic activity and indeed eliminate all enantiocontrol (entry 9, Table 6).

Effect of temperature and catalyst mol%

In attempt to improve the level of enantiocontrol the effect of reducing the reaction temperature was examined using **12b** with 1-phenylcyclohex-1-ene keeping the level of catalyst as before (4 mol% Mn). The results appear in Table 6. Between −78 and −45 °C catalytic activity was totally suppressed (entry 5, no conversion, 16 h). This may reflect not only the normal Arrhenius response of the rate controlling step, but it may also arise from the slowing down of local polymer molecular motions. At −32 °C the catalyst did start to turnover delivering a 52% yield in 16 h (entry 4, Table 6). Under these conditions the level of asymmetric induction also improved to 72% ee and further optimisation might be achievable.

A series of epoxidations were also performed using **12b** and 1-phenylcyclohex-1-ene varying the level of catalyst employed keeping other parameters the same. The results are shown in Fig. 3 and the derived quantitative data shown in Table 6 (entries 3, 6 and 7). In doubling the catalyst level to 8 mol% both the yield and enantioselectivity rise, the latter being equivalent to that found when the reaction is run at −32 °C. With double the number of catalytic sites, statistically each individual site is likely to be used less often. This suggests that the level of asymmetric induction delivered early in the lifetime of an active site is higher than later in its lifetime, and this is in accord with results reported with soluble catalysts.[27,29] However, rather strangely when **12b** was used on an equimolar basis to the alkene (*i.e.* in generating a stoichiometric oxidation *reagent*)

Table 7 Recycling of resin catalysts in asymmetric epoxidation[a] of 1-phenylcyclohex-1-ene

Entry	Catalyst[b]	Mn content/mmol g^{-1} (comments)	Run	Time/h	Epoxide		Mn leaching (%)
					Yield (%)[c]	Ee (%)[d]	
1	(*R*,*R*)-**12a**	0.35 (initial load)	1	2	36	61	0.01
2	(*R*,*R*)-**12a**	0.35 (not re-loaded)	2	3	15	46	[e]
3	(*R*,*R*)-**12b**	0.17 (initial load)	1	2	47	66	0.03
4	(*R*,*R*)-**12b**	0.17 (not re-loaded)	2	3	35	43	[e]
5	(*R*,*R*)-**12b**	0.35 (re-loaded as initially)	3	3	18	25	[e]
6	(*R*,*R*)-**12c**	0.08 (initial load)	1	2	49	91	0.03
7	(*R*,*R*)-**12c**	0.08 (not re-loaded	2	3	17	54	[e]

[a] NMO 5 equiv., *m*-CPBA 2 equiv., CH_2Cl_2, 0 °C. [b] 0.04 equiv. [c] GC analysis. [d] HPLC Diacel CHIRACEL OJ, hexane–propan-2-ol (90 : 10); absolute configuration confirmed by polarimetry. [e] Not determined.

both the yield and enantioselectivity were reduced (entry 7, Table 6). This may imply that two (or more) alkene molecules are involved at a given metal centre during the catalytic cycle but there is no evidence from kinetic studies in the literature that this might be so.

Recycling and stability studies

One key factor in the drive to develop heterogeneous analogues of soluble metal complex catalysts is to improve the use of the latter by allowing facile recovery for re-use or re-cycling. The work of Angelino and Laibinis[17] appears to be the only case where this issue has been addressed seriously in the context of polymer-immobilised Jacobsen catalyst analogues.

Catalyst resin beads **12a**–**c** which had already been used once to epoxidise 1-phenylcyclohex-1-ene were recycled. The samples of **12a** and **12b** were extracted with dichloromethane in a Soxhlet (12 h), whereas the sample of **12c** was simply thoroughly rinsed with this solvent. After drying to constant weight each catalyst was re-used under strictly identical conditions to the first run. In all cases both catalytic activity and enantioselectivity fall considerably (Fig. 4, Table 7). The Mn contents of resins **12a**–**c** were identical before and after run 1, and analysis of the aqueous phase from the work-up of each first reaction confirmed negligible leaching of Mn (~0.01–0.03% of the original Mn was detected). The decline of performance of each catalyst in run 2 therefore cannot be attributed to loss of Mn from the resins, but must be due to degradation or deactivation of the active metal complex without metal loss and/or to morphological and accessibility changes in the resins. Confirmation that Mn leaching is not the key factor was obtained by re-loading resins **12a** and **12b** with more Mn after their second catalytic run. In each case the Mn content of the resin rose significantly, possibly indicating the formation of bimetallic species. When resin **12b** was used as a catalyst for a third run both the catalytic activity and enantioselectivity dropped even further.

The recycling results concur with the findings reported by Angelino and Laibinis[17] who have tried hard to characterise the molecular structural changes occurring when their polymer-immobilised catalyst was used in epoxidations. They are also in agreement with the results reported for Jacobsen's catalyst immobilised on inorganic supports[11,12] and indeed with the reports of the instability of the soluble catalyst itself.[12,30] It seems therefore that the more optimistic results of recycling experiments recorded earlier, accompanied by no substantiating data, were more a representation of expectation rather than experimentation.[14,15,16]

Conclusions

Application of a number of key design criteria in synthesising polymer-supported analogues of Jacobsen's chiral Mn salen alkene epoxidation catalyst has allowed a macroporous methacrylate-based resin system to be produced displaying for the first time enantioselectivity as high as the soluble complex. However, the selectivity is both substrate and polymer structure dependent. Recycling experiments have shown overall that the likelihood of producing a re-usable polymer-supported analogue of Jacobsen's chiral Mn salen complex is very low, and the demanding syntheses of structurally well-defined supported chiral salen ligands may be more profitably used in forming other more stable metal complexes for exploitation in other reactions.[8,31]

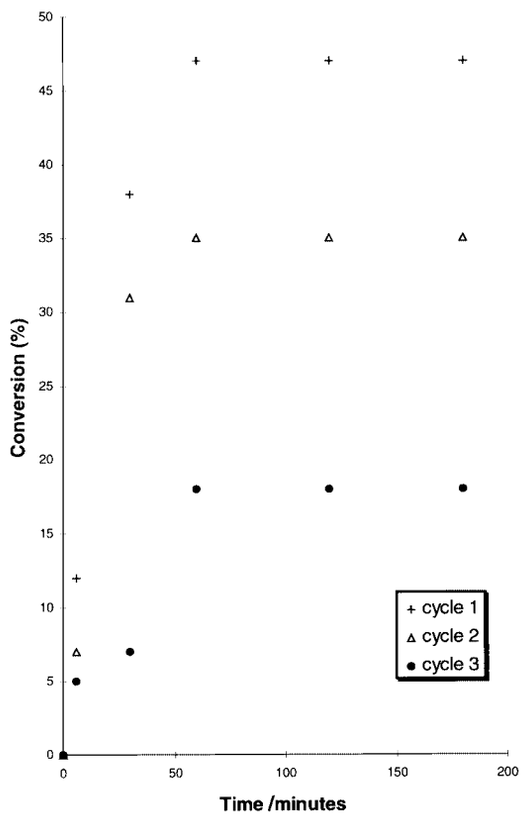


Fig. 4 Recycling of resin catalyst **12b** in the epoxidation of 1-phenylcyclohex-1-ene (0 °C, 10 ml CH_2Cl_2, see Tables 7 and 8).

Experimental

Materials

Resin syntheses. *p*-Acetoxystyrene, styrene, ethylene glycol dimethacrylate, divinylbenzene (80% grade), methyl methacrylate, hydrazine hydrate (55%) and 2-ethylhexan-1-ol were from the Aldrich Chem. Co. Toluene and azobisisobutyronitrile were from B.D.H.

Ligand syntheses. (±)-*trans*-1,2-Diaminocyclohexane, 2-*tert*-butylphenol, 2,4-di-*tert*-butylphenol, 2,3-dihydroxybenz-

aldehyde, 5-bromosalicylaldehyde, L-(*R*,*R*)-tartaric acid, tin(IV) tetrachloride, paraformaldehyde and methacryloyl chloride were from the Aldrich Chem. Co.

Alkenes. Indene, 1-phenylcyclohex-1-ene, 1,2-dihydronaphthalene and 1-phenyl-3,4-dihydronaphthalene were from the Aldrich Chem. Co.

Catalysts/oxidants. Mn(II) acetate tetrahydrate, ((*S*,*S*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)cyclohexane-1,2-diamino)-Mn(III) chloride, *m*-chloroperbenzoic acid (86%), and 4-methylmorpholine *N*-oxide were from the Aldrich Chem. Co.

All the above key materials were >95% unless indicated and were used as supplied. Other materials were laboratory grade species from UK suppliers.

Instrumentation and techniques

Analyses. ^{1}H NMR spectra were recorded at 250 MHz on a Bruker WM 250 spectrometer with Me_4Si as an internal standard. FTIR spectra were recorded on a Matson or Nicolet 400^D spectrometer running 10 scans at a resolution of 4 cm^{-1}. Elemental microanalyses were provided by the Microanalytical Service at the University of Strathclyde with an error of ±0.3% for C, H and N, and ±0.5% for Cl and Br. Manganese analyses of solutions of digested (cHCl, 600 °C, 4 h) resins were performed using the inductively coupled plasma technique with a detection limit of ±0.002 ppm. These analyses were carried out by the service at the University of Paisley.

Melting points were measured using a IA 9100 apparatus. Mass spectra were recorded on a instrument in the Pharmacy Department at the University of Strathclyde. X-Ray crystal structure determination was carried out in the X-ray laboratory in the Department of Pure and Applied Chemistry of the University of Strathclyde. Optical rotations were measured on a Perkin-Elmer 241 polarimeter operating with a sodium lamp and are given in 10^{-1} deg cm^2 g^{-1}.

Mercury intrusion porosimetry was performed using a Micromeritics Autopore 9220 instrument. Nitrogen adsorption isotherms were generated using a Micromeritics Accusorb 2100 E apparatus and the resultant data were subjected to a Brunauer, Emmett and Teller[32] or Barrett, Joyner and Halenda[33] treatment. The solvent up-take of each resin was measured using a known mass of resin (~1 g) in a measuring cylinder (15 ml). The volume of settled bed was noted (V_i). Dichloromethane was then added until the liquid level remained ~1 cm above the level of the beads. The system was capped and left to equilibrate for 2 h. The excess solvent was carefully pipetted out and the new swollen volume of the beads noted (V_f). The solvent up-take was calculated as $[(V_f - V_i)/V_i] \times 100\%$ (Tables 1 and 4).

Suspension polymerisations and resin modifications. Spherical particulate polymer resins were produced by suspension polymerisation employing a parallel-sided baffled glass vessel (250 ml) fitted with a metal stirrer carrying two impellers driven downward by an overhead stirrer. Details of this and our suspension polymerisation procedure (including the aqueous phase composition) have been published before.[23]

A similar rector was used in the chemical modification of resins, this time employing a glass stirrer and Teflon® baffles, again with overhead stirring.

Monitoring of reactions. Thin layer chromatography was carried out using Camlab silica plates impregnated with fluorescent indicator UV_{254} and analysed using a Minenalight UVGL-25 lamp or developed using DNP (Brady's reagent).

Gas chromatography monitoring was performed using a HRGC 5300 Mega Series fitted with a BPX5 column. To follow the conversion of dihydronaphthalene and indene, the following program was used: 80 °C min^{-1} for 1 min then 25 °C min^{-1} up to 180 °C. Responses appeared as follows: bromobenzene at 1.56 min, dihydronaphthalene at 3.48 min, indene at 2.63 min, 1,2-epoxy-1,2,3,4-tetrahydronaphthalene at 5.18 min and 1,2-epoxyindane at 4.0 min. To monitor the epoxidation of 1-phenylcyclohex-1-ene, the following program was used: 90 °C min^{-1} for 1 min then 45 °C min^{-1} up to 260 °C. Responses appeared as follows: bromobenzene at 1.56 min, 1-phenylcyclohex-1-ene at 4.09 min and 1,2-epoxy-1-phenylcyclohexane at 4.34 min. To monitor the epoxidation of 1-phenyl-3,4-dihydronaphthalene, the following program was used: 90 °C min^{-1} for 1 min then 45 °C min^{-1} up to 300 °C. Responses appeared as follows: bromobenzene at 1.53 min, 1-phenyl-3,4-dihydronaphthalene at 6.68 min and 1,2-epoxy-1-phenyl-1,2,3,4-tetrahydronaphthalene at 7.33 min.

High performance chiral liquid chromatography was carried out using instrumentation from Applied Chromatography Systems. A Diacel CHIRACEL OB column employing hexane–propan-2-ol (95 : 5) as eluent was used to determine the enantiomeric excess (% ee) of 1,2-epoxy-1,2,3,4-tetrahydronaphthalene and 1,2-epoxyindane. The flow rate was 0.5 ml min^{-1} and the responses appeared as follows: 1,2-epoxy-1,2,3,4-tetrahydronaphthalene at 34 and 42 min; 1,2-epoxyindane at 39 and 54 min. A Diacel CHIRACEL OJ column employing hexane–propan-2-ol (90 : 10) as eluent was used to determine the enantiomeric excess of 1,2-epoxy-1-phenylcyclohexane and 1,2-epoxy-1-phenyl-1,2,3,4-tetrahydronaphthalene. The flow rate was 0.5 ml min^{-1} and the responses appeared as follow: 1,2-epoxy-1-phenylcyclohexane at 17 and 19 min; 1,2-epoxy-1-phenyl-1,2,3,4-tetrahydronaphthalene at 20 and 25 min.

Syntheses

1. Low molecular weight compounds. *(1R,2R)-(+)-Diaminocyclohexane L-tartrate.* (±)-*trans*-Diaminocyclohexane (45 g, 394 mmol) and L-(*R*,*R*)-tartaric acid (29.6 g, 197 mmol) were dissolved in boiling water (80 ml). The solution was allowed to cool to 80 °C before slowly adding boiling ethanol (40 ml). The homogeneous solution generated shiny white crystals upon slow cooling to room temperature. These were collected by filtration and recrystallised twice from ethanol (32.7 g, 63%). $[a]_D^{20} = +12.4$ (*c*, 2 in H_2O) (Aldrich, 99% ee, $[a]_D^{20} = +12.5$ (*c*, 4 in H_2O)); Anal. Found (Calc.) %: C 45.4 (45.45), H 7.2 (7.6), N 10.7 (10.6).

3,5-Di-tert-butyl-2-hydroxybenzaldehyde.[24] At room temperature, tin(IV) tetrachloride (2.84 ml, 24.2 mmol) was added to a solution of 2,4-di-*tert*-butylphenol (50.0 g, 242 mmol) and tri-*n*-butylamine (18.0 g, 97 mmol) in freshly distilled toluene (100 ml) under a nitrogen atmosphere. After the addition was complete the mixture was stirred at room temperature for a further 30 min. Paraformaldehyde (16.0 g, 533 mmol) was then introduced and the resulting yellowish solution was heated to 100 °C for 12 h. The reaction mixture was allowed to cool down to room temperature, poured into water (100 ml) and acidified with 2 M HCl until pH 1. The solution was extracted with dichloromethane (3 × 30 ml). The organic layer was washed with brine (30 ml), dried over $MgSO_4$, concentrated and purified *via* flash chromatography (SiO_2, petroleum ether–dichloromethane = 1 : 1) to generate shiny yellow crystals (25.4 g, 45%). Mp 52–56 °C (lit. 53–56 °C[24]); ^{1}H NMR (250 MHz; $CDCl_3$) δ_H ppm 1.44 (9 H, s, C(C*H*$_3$)$_3$), 1.49 (9 H, s, C(C*H*$_3$)$_3$), 7.36 (1 H, d, *J* 2.4 Hz, Ar*H*), 7.60 (1 H, d, *J* 2.4 Hz, Ar*H*), 8.85 (1 H, s, C*H*O), 11.65 (1 H, s, O*H*); FTIR ($CHCl_3$) ν_{max}/cm^{-1} 1651 (C=O); Anal. Found (Calc.) %: C 76.5 (76.9), H 9.0 (9.5).

3-tert-Butyl-2-hydroxybenzaldehyde.[24] At room temperature, tin(IV) tetrachloride (0.4 ml, 3.33 mmol) was added to a solution of 2-*tert*-butylphenol (5.0 g, 3.33 mmol) and 2,6-dimethylpyridine (2.5 g, 13.3 mmol) in freshly distilled toluene (30 ml) under a nitrogen atmosphere. After the addition was complete, the mixture was stirred at room temperature for a

further 20 min. Paraformaldehyde (2.2 g, 33.3 mmol) was introduced and the resulting yellowish solution was heated to 100 °C for 10 h. The reaction mixture was allowed to cool down to room temperature, poured into water (100 ml) and acidified using HCl (2 M) until pH 2. The solution was then extracted with dichloromethane (3 × 30 ml). The organic layer was washed with brine (30 ml), dried over $MgSO_4$, concentrated and purified *via* flash chromatography (SiO_2, petroleum ether–dichloromethane = 2 : 1) to generate a yellow liquid (5.1 g, 85%). ^{1}H NMR (250 MHz; $CDCl_3$) δ_H ppm 1.51 (9 H, s, C(C*H*$_3$)$_3$), 7.00 (1 H, overlapping dd, *J* 7.6 Hz, Ar*H*), 7.49 (1 H, dd, *J* 7.8 and 1.6 Hz, Ar*H*), 7.63 (1 H, dd, *J* 7.6 and 1.6 Hz, Ar*H*), 9.99 (1 H, s, C*H*O), 11.88 (1 H, s, O*H*); FTIR ($CHCl_3$) ν_{max}/cm^{-1} 2959 (OH), 1651 (CHO); MH^+ Found (Calc. for $C_{11}H_{14}O_2$) 178.0990 (178.2304); Anal. Found (Calc.) %: C 74.2 (74.1), H 8.0 (7.9).

3-tert-Butyl-5-chloromethyl-2-hydroxybenzaldehyde.[15] A mixture of 3-*tert*-butyl-2-hydroxybenzaldehyde (2.7 g, 15.2 mmol), paraformaldehyde (1.0 g, 33.3 mmol) and tetrabutylammonium bromide (0.47 g, 1.46 mmol) in cHCl (11 ml) was vigorously stirred at 40 °C for three days. The mixture was extracted using ethyl acetate (5 × 15 ml), washed cautiously with 5% $NaHCO_3$ (2 × 10 ml), then brine (2 × 10 ml), dried over $MgSO_4$, and then concentrated to leave a yellow crystalline solid (3.4 g, 99%) (lit. viscous oil).[15] ^{1}H NMR (250 MHz; $CDCl_3$) δ_H ppm 1.46 (9 H, s, C(C*H*$_3$)$_3$), 4.60 (2 H, s, C*H*$_2$), 7.45 (1 H, d, *J* 2.3 Hz, Ar*H*), 7.54 (1 H, d, *J* 2.2 Hz, Ar*H*), 9.88 (1 H, s, C*H*O), 11.88 (1 H, s, O*H*); FTIR (nujol) ν_{max}/cm^{-1} 2959 (OH), 1660 (CHO), 698 (CCl); Mp 62.2–62.9 °C; MH^+ Found (Calc. for $C_{12}H_{15}O_2Cl$) 226.0719 (226.7023); Anal. Found (Calc.) %: C 63.5 (63.6), H 6.2 (6.7), Cl 15.6 (15.6).

*2-Hydroxy-3-(methacryloyloxy)benzaldehyde (**8**) (Scheme 4).* A stirred solution of 2,3-dihydroxybenzaldehyde (2.0 g, 14.5 mmol), pyridine (1.8 ml, 21.5 mmol) and toluene (30 ml) was heated at 40 °C. Methacryloyl chloride (1.6 ml, 16 mmol) was added and the system was heated to 110 °C for 6 h. TLC indicated the formation of a new product (R_f = 0.94) together with unreacted 2,3-dihydroxybenzaldehyde. The mixture cooled down and distilled water (30 ml) was added. The organic layer was washed with HCl (2 M, 10 ml) and distilled water (30 ml). The aqueous phase was extracted twice with dichloromethane (30 ml). The combined organic phases were dried over $MgSO_4$, concentrated and purified by flash chromatography (SiO_2, dichloromethane) to give product (**8**) as pale yellow crystals (0.90 g, 48%). Mp 80–82 °C; ^{1}H NMR (250 MHz; $CDCl_3$) δ_H ppm 2.51 (3 H, s, CC*H*$_3$), 5.80 (1 H, d, *J* 4.5 Hz, C*H*HC), 6.40 (1 H, d, *J* 4.1 Hz, CH*H*C), 7.01 (1 H, t, *J* 7.9 Hz, Ar*H*), 7.36 (1 H, dd, *J* 7.4 and 1.7 Hz, Ar*H*), 7.75 (1 H, dd, *J* 7.7 and 1.6 Hz, Ar*H*), 9.89 (1 H, s, C*H*O), 11.14 (1 H, s, O*H*); FTIR ($CHCl_3$) ν_{max}/cm^{-1} 1740 (CO), 1661 (CHO); MH^+ Found (Calc. for $C_{11}H_{10}O_4$) 206.0547 (206.1980); Anal. Found (Calc.) %: C 63.5 (64.1), H 4.9 (4.9).

Single crystals of compound **8** suitable for X-ray diffraction analysis were selected directly from the analytical sample.

*Crystal structure determination of compound **8**†.* Crystal data: $C_{11}H_{10}O_4$, M = 206.20, triclinic, a = 6.667(2), b = 7.607(3), c = 10.567(4) Å, α = 73.34(3), β = 86.35(3), γ = 75.58(3)°, U = 497.2(3) Å^3, T = 123 K, space group $P\bar{1}$, Z = 2, μ(Mo-K$_\alpha$) = 0.105 mm^{-1}, 2371 reflections measured, 2179 unique (R_{int} = 0.0097) of which 1840 observed with $I > 2\sigma(I)$ were used in final refinement on F to R = 0.0333 for 177 parameters. (R for all data = 0.0440). Hydrogen atoms were refined isotropically and all other atoms were refined anisotropically.

2. Enantiomerically pure epoxide standards

The (*1R,2R*) epoxide of 1-phenylcyclohex-1-ene, the (*1S,2R*) epoxide of 1,2-dihydronaphthalene and the (*1S,2R*) epoxide of indene were obtained in high purity (C, H%; ^{1}H NMR) by asymmetric epoxidation of the respective alkenes using (*S,S*)-Jacobsen's catalyst and *m*-chloroperbenzoic acid–4-methylmorpholine *N*-oxide as oxidant. The optical purity was 98% ee by chiral HPLC and the absolute configurations were confirmed by polarimetry.[34,35] These species were used as GC and chiral HPLC standards.

In contrast attempts to prepare a pure enantiomer of the epoxide of 1-phenyl-3,4-dihydronaphthalene by a similar route were unsuccessful. The chemical purity (C, H%; ^{1}H NMR) could not be improved sufficiently to allow absolute configurational assignment, but the material was useful as a GC marker.

3. Resins

Precursor *p*-acetoxystyrene-derived resins **4a**–**c** (Scheme 2) were prepared by suspension polymerisation[22,23] employing respectively the following organic phase compositions:

4a: *p*-acetoxystyrene (15.6 g, 96.1 mmol, 32 mol%), styrene (20.7 g, 198.3 mmol, 66 mol%), divinylbenzene (80% grade) (0.79 g, 6.1 mmol, 2.0 mol%), AIBN (1.5 g).

4b: *p*-acetoxystyrene (8.0 g, 49.3 mmol, 32 mol%), styrene (6.0 g, 57.6 mmol, 38 mol%), divinylbenzene (80% grade) (6.0 g, 46.1 mmol, 30 mol%), 2-ethylhexan-1-ol (20 ml), AIBN (0.8 g).

4c: *p*-acetoxystyrene (1.62 g, 10.0 mmol, 13 mol%), methyl methacrylate (1.53 g, 15.0 mmol, 19 mol%), ethylene glycol dimethacrylate (5.05 g, 53.0 mmol, 68 mol%), toluene (7 ml), AIBN (0.5 g).

Suspension polymerisations were carried out at 80 °C for 6 h. After cooling, the resultant beads were collected by filtration, washed copiously with water and acetone, and finally extracted in a Soxhlet with acetone for 24 h before being vacuum dried (55 °C/10 mmHg) for 24 h. Aggregated particles and fines were removed by sieving, and the physical characteristics of the resins are summarised in Table 1.

Precursor resin **7d** (Scheme 4) was similarly prepared by suspension polymerisation the salicylaldehyde moiety being introduced by use of the monomer, 2-hydroxy-3-methacryloyloxybenzaldehyde **8**. The organic phase composition was: **8** (5.3 g, 25.5 mmol, 25 mol%), methyl methacrylate (4.5 g, 45.0 mmol, 45 mol%), ethylene glycol dimethacrylate (6.0 g, 30.0 mmol, 30 mol%), 2-ethylhexan-1-ol (6 ml), toluene (5 ml), AIBN (0.8 g). The isolated dried beads turned rapidly from a beige to an intense orange on treatment with 2,4-dinitrophenylhydrazine. The characteristics of the product are also summarised in Table 1.

4. Chemical modification of precursor resins

Resins **4a**–**c** were elaborated as shown in Schemes 3 and 5. Resin (**7d**) was elaborated as shown in Scheme 5.

*Formation of resins **5a**–**c*** is exemplified with **5a**: Resin **4a** (10.0 g, 2.6 mmol -OAc g^{-1} (theo)) was swollen in dioxane (100 ml) for 30 min. Hydrazine hydrate (4 ml, 128.4 mmol) was then added at room temperature and the mixture heated to 80 °C for 48 h. The cream coloured beads were filtered off, washed successively with water (400 ml), dioxane (40 ml) and ethanol (40 ml), and then extracted in a Soxhlet with dioxane for 24 h. Whereas the gel-type species **5a** was vacuum dried (55 °C/10 mmHg) for 24 h, the macroporous species **5b** and **5c** were freeze dried for 24 h. No analysis of free phenol content was made but FTIR (KBr) spectra showed the appearance of ArOH (3420 cm^{-1}) and the disappearance of -OCOCH$_3$ (1761 cm^{-1}). Theoretical phenol contents are: **5a** 2.96, **5b** 2.87 and **5c** 1.29 mmol g^{-1}.

*Conversion to phenolate resins **6a**–**c*** is exemplified with **6a**: Resin **5a** (8.2 g, 2.96 mmol) was added to methanolic NaOH solution (4 M, 20 ml) and shaken vigorously at room temperature for 48 h. The beads were collected, rinsed with methanol, and then extracted with the same solvent using a Soxhlet for

† CCDC reference number 207/440. See http://www.rsc.org/suppdata/p1/b0/b002118k/ for crystallographic files in .cif format.

Table 8 Reaction compositions used in asymmetric alkene epoxidations

Alkene			4-Methylmorpholine/ *N*-oxide		*m*-Chloroperbenzoic acid		Bromobenzene[a]		Mn content in resin catalyst/ mmol
Type	Mass/g	mmol	Mass/g	mmol	Mass/g	mmol	Mass/g	mmol	
Indene	0.5	4.3	2.25	19.2	1.33	7.71	0.35	2.23	0.15
3,4-Tetra-hydronaphthalene	0.5	3.8	2.80	21.5	1.48	8.58	0.40	2.55	0.17
1-Phenylcyclohex-1-ene	0.5	3.2	1.85	15.8	1.09	6.32	0.32	2.04	0.13
1-Phenyl-3,4-tetra-hydronaphthalene	0.5	2.4	1.42	12.1	0.84	4.84	0.30	1.91	0.10

[a] GC internal standard.

48 h. The samples were dried as before. Again no definitive analytical data are available but all samples became pink coloured and the theoretical phenolate contents are: **6a** 2.68, **6b** 2.60 and **6c** 1.25 mmol g^{-1}.

*Attachment of salicylaldehyde residues to form resins **7a–c*** is exemplified with **7a**: Resin **6a** (8.0 g, 2.68 mmol phenolate g^{-1} (theo)) was added to a solution of 3-*tert*-butyl-5-chloromethyl-2-hydroxybenzaldehyde (6.9 g, 30.6 mmol) in dichloromethane (5 ml). The mixture was mechanically stirred at 40 °C for 48 h. The beads were filtered off, washed and then extracted with acetone in a Soxhlet for 24 h. The samples were dried as before. No definitive analytical data are available but FTIR (KBr) spectra show the appearance of -CHO (1651 cm^{-1}) and treatment of the pale yellow coloured beads with 2,4-dinitrophenylhydrazone converts them to a dark reddish-orange. No Cl content was detected in any of the samples. The theoretical aldehyde contents are: **7a** 1.88, **7b** 1.81 and **7c** 1.03 mmol g^{-1}.

*Synthesis of the amino-imine-containing resins **9a–d*** (Scheme 6) is exemplified with **9a**: (*1R,2R*)-(+)-1,2-Diaminocyclohexane L-tartrate (5.3 g, 20.2 mmol) was dissolved in distilled water (50 ml) and potassium carbonate (5.6 g, 40.4 mmol) added. The solution was shaken vigorously then extracted with dichloromethane (3 × 5 ml). The organic solution was separated and resin **7a** (1.8 g, 1.88 mmol -CHO g^{-1} (theo)) added. The suspension was shaken vigorously overnight and the beads recovered by filtration, washed with dichloromethane and then extracted with the same solvent using a Soxhlet for 24 h. Each sample of yellow coloured beads was dried as previously described. FTIR (KBr) spectra showed the presence of -OH/-NH_2 (3400 cm^{-1}) and -C=N- (1640–45 cm^{-1}). For **9c** and **9d** the -C=O stretch at 1730–1735 cm^{-1} was also a strong feature. At this stage in the synthesis %N allows confirmation of the transformations achieved and these data are summarised in Table 2.

*Synthesis of the brominated salen-containing resins **10a–d*** is exemplified with **10a**: Resin **9a** (100 mg, 0.53 mmol NH_2 g^{-1}) was added to 4-bromosalicylaldehyde (100 mg, 0.49 mmol) in dichloromethane (2 ml). The suspension was shaken vigorously at room temperature for 3 days. The yellow coloured beads were filtered off, rinsed with dichloromethane and then extracted with this solvent using a Soxhlet for 24 h, when the washings were clear. Each sample was then freeze dried. The FTIR (KBr) showed the presence of -C=N- (1640 cm^{-1}) and -C=O (1725–35 cm^{-1}) in the case of **10d** and **10c**. The elemental microanalytical data (N and Br) are summarised in Table 3.

*Synthesis of the salen-containing resins **11a–d*** is exemplified with **11a**: Resin **9a** (2.3 g, 0.53 mmol NH_2 g^{-1}) was added to a solution of 3,5-di-*tert*-butylsalicylaldehyde (1.7 g, 7.3 mmol) in dichloromethane (5 ml). The suspension was shaken vigorously at room temperature for three days and the resins isolated, cleaned and dried as described for **10a**. The anticipated bands were present in the respective FTIR (KBr) spectra, and the %N data are recorded in Table 2.

*Synthesis of Mn(salen)-containing resins **12a–d*** is exemplified with **12a**: Resin **11a** (2.1 g, 0.43 mmol salen g^{-1}) was added to Mn(II) acetate tetrahydrate (3.7 g, 51.1 mmol Mn) in ethanol (25 ml) and the solution refluxed for 4 h with gentle mechanical stirring. Solid lithium chloride (0.85 g, 20 mmol) was added and the mixture stirred at room temperature for a further 2 h. The beads were filtered off, rinsed with water and ethanol before being extracted with ethanol and then dichloromethane in a Soxhlet, each for 3 days. Resin **12a** was vacuum dried (55 °C/10 mmHg) for 24 h, whereas **12b–d** were freeze-dried for 12 h. In each case the product beads were dark red–brown in colour. The FTIR (KBr) spectra showed the expected bands and elemental analytical data (%N, Cl and Mn) are summarised in Table 4.

5. Asymmetric alkene epoxidations using polymer-supported chiral Mn(salen) species 12a–d

The general procedure was as follows: a sample of resin **12a–d** was added to a solution containing 4-methylmorpholine *N*-oxide dissolved in dichloromethane (25 ml) and the solution degassed under vacuum (water pump) for 1 min. The alkene and bromobenzene (internal standard) were then added and the system was cooled down to the required temperature with a small overhead stirrer. *m*-Chloroperbenzoic acid was added in four equal portions over a five minute period. The progress of the reaction was monitored by GC for 2 h. The beads were then removed by filtration and rinsed with dichloromethane. The organic phase was poured into NaOH (25 ml, 1 M). The aqueous phase was extracted twice using dichloromethane (10 ml). The combined organic layers were washed with brine (25 ml), dried over $MgSO_4$ and concentrated under vacuum. The product was isolated from the GC standard and the starting material by flash column chromatography (SiO_2, petroleum ether and then methylene chloride) and was identified from its ^1H NMR spectrum. The enantiomeric excess (% ee) was determined by HPLC. In some cases the aqueous phase residue was assayed for Mn content by inductively coupled plasma analysis to assess possible leaching.

Although each alkene substrate was examined under broadly comparable conditions the precise reaction compositions varied a little and are specified in Table 8.

In recycling experiments after the first catalytic run resin beads were recovered by careful filtration and washed (or extracted in some cases) with dichloromethane for 12 h. Each sample was air dried for 12 h before being re-used as a catalyst employing the same proportions of regents and alkene. In some cases (see Table 7) Mn was re-loaded onto re-cycled resins using the same synthetic procedure and purification method as previously employed.

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