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Polymer-Supported (Salen)Mn Catalysts for Asymmetric Epoxidation: A Comparison between Soluble and Insoluble Matrices

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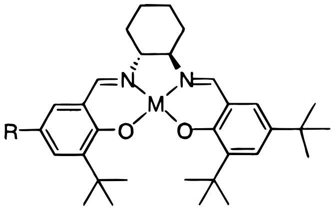
Abstract: This paper describes the synthesis of both soluble and insoluble polymer-supported chiral (salen)-Mn complexes and their use in asymmetric epoxidation reactions. These studies were undertaken to establish whether high enantioselectivities could be achieved with a polymer-bound catalyst and if the complexes could be recovered and reused for multiple cycles. Poly(ethylene glycol) monomethyl ether (MeO-PEG) and non-cross-linked polystyrene (NCPS) were used as soluble supports while *J*anda*J*el and Merrifield resins served as insoluble supports. Each polymer was linked to the salen catalyst through a glutarate spacer. The soluble catalysts were recovered by precipitation with a suitable solvent while the insoluble catalysts were simply filtered from the reaction mixture. Three olefins were utilized as epoxidation substrates: styrene, *cis*-*β*-methylstyrene, and dihydronaphthalene. Best results were obtained with *cis*-*β*-methylstyrene as the enantioselectivity obtained with each polymer-bound catalyst (86−90%) was equivalent to that achieved with the analogous commercially available, solution-phase (salen)Mn catalyst **1** (88%). The soluble polymer-supported catalysts **5** and **6** could be used twice before a decline in yield and enantioselectivity was observed and the *J*anda*J*el attached catalyst **7** could be used for three cycles in some cases. The Merrifield-bound catalyst **8** was found to lose activity with each use. This work presents the most effective (salen)Mn catalyst that has been attached to gel-type resin to date and may have practical applications in high-throughput organic chemistry.

Introduction

The growth of both polymer-supported chemistry and asymmetric catalysis has been tremendous in the past decade.[1,2] This is not surprising considering the industrial need for diverse libraries of enantiomerically pure compounds for lead identification in the drug discovery process. Homogeneous catalysis often provides the best results in achieving high levels of enantioselectivity whereas heterogeneous catalysis offers the advantages of simplified product purification and the potential for catalyst recycling. Clearly, heterogeneous catalysts which can provide high enantioselectivity would be an important development with potential applications in industrial and high-throughput organic chemistry.

The Jacobsen epoxidation[3] has recently emerged as a powerful method for the asymmetric oxidation of unfunctionalized olefins. The best results are usually achieved with cis-disubstituted alkenes. This reaction is catalyzed by structurally simple Mn(III)−salen complexes and has been optimized in terms of the catalyst structure and choice of stoichiometric oxidants and other additives.[3b] The steric and electronic properties of the salen framework, composed of two salicylaldehyde units and a chiral diamine, can be tuned by altering the substituents on either portion. Both enantiomers of the most general catalyst **1** (Figure 1) are commercially available.



1; R = *t*Bu, M = MnCl
2; R = OH, M = H,H

Figure 1. Typical salen complexes.

Soon after the development of this reaction, a number of reports appeared describing efforts to incorporate the salen ligand into a heterogeneous support as a means to recycle the chiral catalyst. These approaches can be roughly grouped into four categories: (1) noncovalent immobilization in zeolites, clays, or siloxane membranes,[4] (2) grafting onto inorganic supports such as silica or MCM-41,[5] (3) copolymerization of a functionalized salen monomer into an organic polymer,[6] and

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(4) attachment or build-up of a salen structure to a preformed polymer.[7] The inclusion of a salen structure within a rigid membrane (approach 1) has been moderately successful for asymmetric epoxidations. Drawbacks of this strategy include leaching of the complexes from the membrane and lower conversions to epoxide products. The use of inorganic supports (approach 2) has produced varied results, giving promising enantioselectivity for a narrow range of substrates in some cases and poor selectivity, conversion, and recyclability in others. Dhal[6a,b] and Salvadori[6c,d] used the third approach wherein a salen monomer containing pendant vinyl groups was copolymerized with either ethylene glycol dimethacrylate or styrene/divinylbenzene, respectively, to yield polymers where the manganese centers were localized at cross-links. These catalysts provided adequate yields of epoxide products and could be recycled for multiple uses but showed very poor enantioselectivity. This probably resulted from inaccessibility of the substrate to the sterically crowded catalytic centers at the cross-links. Sherrington[7a,b] and Laibinis[7c,d] have developed a strategy where a pendant salen structure is built in a stepwise manner onto a preformed polymer (approach 4). Good results for one substrate were achieved with a methacrylate resin[7a] while styrene/divinylbenzene resins[7b−d] were less successful as supports. The ability to recycle these supported catalysts, however, was either not described or found to be severely limited. Pozzi and co-workers have described an interesting approach to a recoverable, though not polymer-supported, epoxidation catalyst by taking advantage of the relatively new phase-separation and immobilization technique known as FBS (Fluorous Biphase Systems).[8] They showed that a salen catalyst containing perfluorinated alkyl chains could be utilized for 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 just one substrate.

In related work, Jacobsen has described the synthesis of polystyrene-bound chiral Co(salen) complexes and their application to the hydrolytic kinetic resolution of racemic epoxides.[9] This catalyst proved to be highly effective and excellent enantioselectivities of ring-opened products were observed. In this study it was desirable to use high-loading supports since the ring-opening reactions are believed to occur from a cooperative effect of two separate catalytic units. This stands in contrast to the Mn(salen)-catalyzed epoxidation where site isolation of the catalytic centers is believed to be imperative. This limits the formation of μ-oxo-Mn(IV) dimers, a potential deactivation pathway resulting from the reaction of a Mn(III) and a Mn(V)═O species.[10] Accordingly, we expected that low loading polymers would provide the greatest opportunity to achieve maximum reactivity and selectivity. Therefore, using approach 4, we attached a salen ligand containing an appropriate linker to a low loading preformed polymer. This convergent strategy stands in contrast to the previously described linear, stepwise construction of the ligand on the polymer[7] as it reduces the number of transformations that are carried out on the polymer and should result in more homogeneous catalysts. The immediate goals of our studies were (1) to evaluate the effect of a distribution of polymer supports on the enantioselectivity of alkene epoxidation and (2) to determine the extent to which any effective polymer-bound catalysts can be recycled for repeated use. The results of these efforts are described herein.

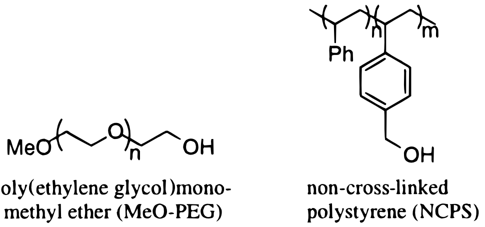

Figure 2. Functionalized soluble polymers.

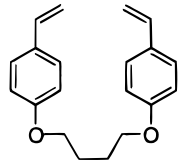

Figure 3. Cross-linker **3** used in the preparation of *J*anda*J*el.

Results and Discussion

A. The Effect of the Polymer Support on Enantioselectivity. To get a clear picture of the effect the polymer support has on the enantioselectivity of the Jacobsen epoxidation reaction, a variety of commercially available or readily prepared functionalized polymers were examined. Poly(ethylene glycol) monomethyl ether (MeO-PEG) and non-cross-linked polystyrene (NCPS) provide examples of soluble supports with broad solubility profiles.[11] They are each soluble in CH_2Cl_2, THF, EtOAc, and DMF but can be precipitated from ether (MeO-PEG) or methanol (NCPS). Furthermore, MeO-PEG is commercially available in a wide range of molecular weights while functionalized NCPS is prepared by the radical polymerization of styrene and hydroxymethylstyrene.[12] We expected that a soluble polymer-supported salen complex would be an effective catalyst since it is believed that nonbonded interactions between the catalyst and approaching olefinic substrate are critical in determining enantioselectivity.[3b] Heterogenization of one of these components (generally the catalyst) could therefore be expected to result in diminished enantiomeric excess (ee) of the product epoxide. The validity of this reasoning has been demonstrated by us in a closely related catalytic asymmetric transformation.[13]

As a complement to the soluble polymer approach, two insoluble polymers were also investigated as supports for the (salen)Mn catalyst. The *J*anda*J*el[14] resins have been recently developed in our group and are designed specifically for use in synthetic organic chemistry.[15] Well-defined hydroxyl functionalized beads were prepared from the suspension copolymerization[16] of styrene, hydroxymethylstyrene, and the flexible tetrahydrofuran-based cross-linker **3**.[17] This gel-type resin exhibits swelling properties which are superior to those of the

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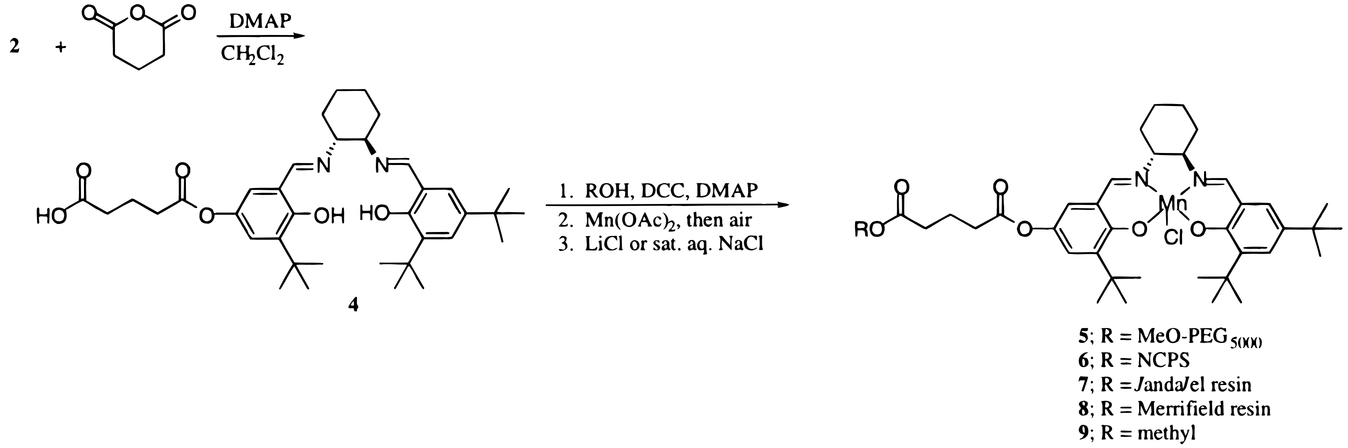
[14] *J*anda*J*el is a registered trademark of Aldrich Chemical Co.

[15] Toy, P. H.; Janda, K. D. *Tetrahedron Lett.* **1999**, *40*, 6329.

[16] Wilson, M. E.; Paech, K.; Zhou, W. J.; Kurth, M. J. *J. Org. Chem.* **1998**, *63*, 5094.

Scheme 1. Synthesis of Polymer-Bound (Salen)Mn Complexes

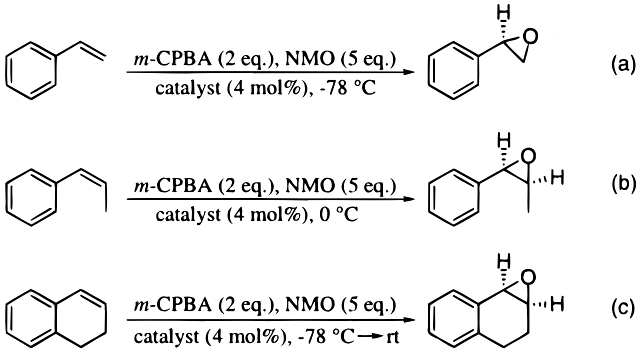


common commercially available Merrifield and Tentagel resins.[15] We hoped that the increased swelling of JandaJel would result in better solvation of the reaction complex and would therefore minimize any loss of enantioselectivity resulting from heterogenization of the catalyst. Finally, hydroxymethyl Merrifield resin, which contains a rigid divinylbenzene cross-linker, was utilized to determine how the nature of the cross-linking agent influenced the reactivity of the resin-bound catalyst.

For simple access to these polymer-supported catalysts, a suitable salen precursor that could be easily and efficiently attached to a hydroxyl functionality was required and salen derivative **4** containing a glutaric acid linker was chosen. We anticipated that the five carbon spacer provided by this linking group would place the catalyst sufficiently away from the polymer backbone to allow unimpeded access of the olefinic substrate to the metal center. Compound **4** was prepared by reaction of the known unsymmetrical salen ligand **2**[9a] with glutaric anhydride and DMAP. Attachment of each of the four polymeric supports to **4** was then accomplished using dicyclohexylcarbodiimide (DCC) coupling conditions to provide the polymer-bound ligands. Insertion of manganese was performed as previously described by Jacobsen to give catalysts **5**−**8**.[18] Interestingly, the color change of the polymers with each derivatization provided a qualitative means for assessing the success or failure of each reaction. All of the polymers are white solids and their color changes to yellow after ligand attachment and dark brown after metal insertion. The loading level of each of the polymer-bound catalysts was determined by elemental analysis of manganese and/or nitrogen content and ranged from 0.08 to 0.75 mmol/g. Finally, the soluble catalyst **9** was prepared to evaluate the effect of replacing the *tert*-butyl group found in commercial Jacobsen catalyst **1** with the glutarate linker.

Jacobsen has described a number of different oxidation systems that are effective for carrying out the epoxidation.[3b] We chose to utilize conditions which employ *m*-chloroperbenzoic acid (*m*-CPBA) as the oxidant and *N*-methylmorpholine-*N*-oxide (NMO) as an additive since this combination has been shown to produce the highest enantioselectivities.[19] The epoxidation of three alkenes, styrene, *cis*-*β*-methylstyrene, and dihydronaphthalene, was studied and the specific conditions for each as well as the configuration of the major enantiomer of the product epoxide is shown in Scheme 2. It should be noted that the unsymmetrical salen ligand **2** was prepared from (*R*,*R*)-*trans*-1,2-diaminocyclohexane and that each of the polymer-supported catalysts produced the same enantiomer in excess as the commercial (*R*,*R*)-salen catalyst **1**.[20]

Scheme 2. Reaction Conditions for the Epoxidation of (a) Styrene, (b) *cis*-*β*-Methylstyrene, and (c) Dihydronaphthalene



The results from the epoxidation of these substrates with the polymer-supported catalysts, the commercial catalyst **1**, and the modified catalyst **9** are shown in Table 1. It is noteworthy that most of the reactions were complete in 15 min or less even at low temperatures and only reactions involving Merrifield-bound catalyst **8** required as much as 1 h to proceed to completion. It is also interesting to note that, in general, the insoluble catalysts gave equivalent ee as the soluble catalysts. The best substrate proved to be *cis*-*β*-methylstyrene since the enantioselectivities obtained with all of the catalysts differed by only a few percent.[21] In fact, the soluble polymer-bound catalysts were even slightly better than the commercial catalyst **1**. In all cases the isolated yield of the epoxide products was high.

To determine any matrix effects on the rate of reaction, the kinetics of the epoxidation of *cis*-*β*-methylstyrene catalyzed by **7** and **9** were compared. We chose to examine JandaJel catalyst **7** since it provided the best results of the insoluble polymer catalysts. Catalyst **9** contains the same glutarate linker and differs from **7** only in that it is not bound to a polymer support. Thus, any effects of the polymer on the reaction kinetics should be

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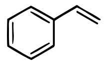
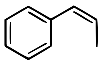
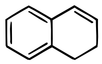
(20) This was determined for styrene oxide by comparing the retention times of the synthetic epoxide enantiomers on a gas chromatography chiral column with authentic chiral epoxide samples. The absolute configurations of the major enantiomer for the other two substrates were deduced by analogy.

(21) All ee values for *cis*-*β*-methylstyrene refer to the *cis*-epoxide which was generally favored by 6−7:1 over the trans diastereomer.

Table 1. Epoxidation Results for Different (Salen)Mn Catalysts

substrate						
catalyst	ee (%)[a]	yield (%)[b]	ee (%)[c]	yield (%)[b]	ee (%)[a]	yield (%)[b]
1	57	84	88	82	85	80
5	52	82	88	79	76	70
6	51	76	90	79	73	69
7	51	81	88	77	79	71
8	35	61	86	75	78	69
9	52	82	87	80	84	75

[a] ee determined by ^{1}H NMR in the presence of the chiral shift reagent, Eu(hfc)$_3$. [b] Isolated yield. [c] ee of the *cis*-epoxide as determined by GC analysis using a Chiraldex G-TA chiral column.

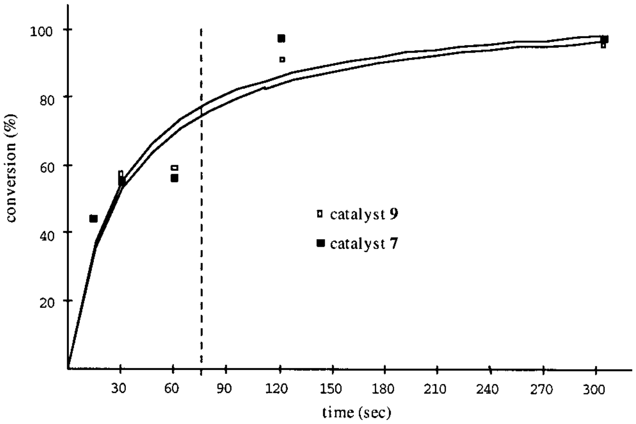
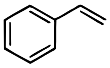
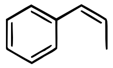


Figure 4. Rates of epoxidation catalyzed by salen complexes **7** and **9**: 1 equiv *m*-CPBA added at time = 0 and 1 equiv added at time = 70 s as indicated by the hashed line.

Table 2. Effect of Catalyst **7** Loading on Enantioselectivity

substrate		
loading (mmol/g)[a]	ee (%)[b]	ee (%)[c]
0.10	51	88
0.29	51	88
0.38	51	88
0.52	51	88
0.75	51	88

[a] The values for catalyst loading were determined by elemental analysis for manganese content. [b] ee determined by ^{1}H NMR in the presence of the chiral shift reagent, Eu(hfc)$_3$. [c] ee of the *cis*-epoxide as determined by GC analysis using a Chiraldex G-TA chiral column.

manifested in this comparison. Aliquots of each reaction were taken at various time intervals and the conversion (as measured against an internal standard, dodecane) and ee were measured. In each case the ee was found to remain constant throughout the course of the reaction. In these experiments it was critical that the *m*-CPBA be added in two portions (1 equiv at time = 0 s, 1 equiv at time = 70 s) to ensure maximum conversion. Addition of all of the *m*-CPBA at time = 0 s resulted in a 20% decrease in conversion. Greater than 50% conversion to products was achieved after only 30 s for both reactions and maximum conversion occurred within 5 min. This indicates that the insoluble nature of catalyst **7** does not adversely affect the rate of epoxidation.

As noted previously, it has been postulated that a low concentration of catalytic sites would provide the best opportunity for high conversion and enantioselectivity by limiting the formation of inactive catalyst dimers. The earlier literature examples of Merrifield resin-bound (salen)Mn catalysts had loadings ranging from 0.15 to 0.65 mmol/g and did not provide high ee of the epoxidation products.[7] To evaluate the importance of the loading level, we prepared a series of *J*anda*J*el-bound catalysts with loading capacities ranging from 0.10 to 0.75 mmol/g.[22] As illustrated in Table 2, the loading level of catalyst **7** had no effect on the enantioselectivity of the product epoxide. This indicates that the extent to which dimer formation occurs is not dependent on the catalyst loading. This may be a consequence of the excellent swelling properties of the resin which can serve to isolate the catalytic centers of even the highest loading polymers.

These results represent some of the most effective (salen)-Mn catalysts to date which are attached to readily available polymeric supports. Previous efforts to attach salen complexes to styrene/divinylbenzene polymers may have suffered from lower enantioselectivities as a result of the lack of any bulky *tert*-butyl substituents on one-half of the salen framework.[7b−d] Our complexes have a glutarate linked polymer in place of one *tert*-butyl group and this does not appear to significantly compromise the enantioselectivity of the catalyst. In fact, the glutarate linker appears to be critical in positioning the catalyst away from the polymer to allow a clear approach for the olefin toward the metal.

B. Recyclability of the Polymer-Supported Catalysts. For a truly effective polymer-supported catalyst, it is critical that recovery be simple and efficient and that the recovered catalyst retain its activity through multiple cycles. It has been established that the commercial catalyst **1** is unstable to prolonged oxidative conditions and cannot be recycled.[23] Laibinis has reported that supported (salen)Mn complexes are also susceptible to decomposition; however, these reactions were carried out at room temperature for prolonged times (20 h).[7c,d] We hoped that the short reaction times and low temperatures used in our studies would prevent or at least slow catalyst degradation. As each of the tested catalysts displayed adequate selectivity, attention was next turned to examining their recovery and reuse.

The PEG-bound catalyst **5** was recovered by dropwise addition of the reaction mixture into a stirred solution of cold ether. The precipitate, which included NMO and chlorobenzoic acid in addition to the polymer-bound catalyst, was filtered and dried. This mixture could be used in a second epoxidation reaction with no appreciable loss of enantioselectivity for the epoxidation of styrene and *cis*-β-methylstyrene (Table 3). After the first recycle, however, precipitation resulted in a gummy, difficult-to-handle solid that gave poor results in further reactions. The recovery of the NCPS-bound catalyst **6** was accomplished as follows: (1) evaporation of the reaction solvent to leave a crude residue that was taken up in a minimum amount of THF and (2) dropwise addition of this solution to a stirring solution of cold methanol. This procedure was much cleaner than that for the PEG-bound catalyst as the solid precipitate contained only the supported catalyst while NMO and other reaction byproducts remained in solution. After filtration and drying, the recycled catalyst was used in a second run with no

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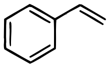
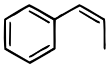
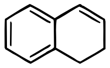
[22] The highest possible loading for our system is 1.36 mmol/g, which corresponds to the inverse of the molecular weight of one functionalized monomer unit.

[23] Zhao, S. H.; Ortiz, P. R.; Keys, B. A.; Davenport, K. G. *Tetrahedron Lett.* **1996**, *37*, 2725.

Table 3. Studies on the Recyclability of the Polymer-Bound Catalysts

substrate				
catalyst	run	ee (%)[a]	ee (%)[b]	ee (%)[a]
1		57	88	84
5	1	52	88	76
	2	51	87	64
	3	12	17	15
6	1	51	90	73
	2	51	87	56
	3	11	15	12
7	1	51	88	79
	2	50	86	69
	3	50	80	20
8	1	35	87	78
	2	22	77	66
	3	10	55	15

[a] ee determined by ^1H NMR in the presence of the chiral shift reagent, Eu(hfc)$_3$. [b] ee of the *cis*-epoxide as determined by GC analysis using a Chiraldex G-TA chiral column.

change in results. Unfortunately, any further attempt to precipitate and recycle the catalyst again gave poor results. With each of the soluble polymer-bound catalysts, a color change from dark brown to a lighter shade of brown was observed with each successive use. This likely results from leaching of manganese caused by oxidative degradation of the salen ligand, a problem that has been documented by others with insoluble supported catalysts.[7c,d]

With limited success in recycling the soluble polymer-bound catalysts, we hoped the insoluble supports would provide a more robust environment for the salen framework. Recovery of both the *J*anda*J*el- and Merrifield resin-bound catalyst beads was easily accomplished by filtration of the reaction mixture. The *J*anda*J*el-derived catalyst **7** could be used three times in the epoxidation of styrene and *cis*-β-methylstyrene without a significant drop in selectivity. Further attempts to use the catalyst, however, resulted in poor conversion and enantioselectivity of the epoxide product. The Merrifield-bound catalyst **8** lost activity with each use and was essentially ineffective by the third recycle. It is not entirely clear why the *J*anda*J*el-bound catalyst **7** was slightly more robust than **8** but this may be a consequence of microenvironment effects imparted by the resin. As observed in the soluble polymer examples, the brown color of the insoluble catalysts faded with repeated use, possibly resulting from the loss of manganese. Indeed, elemental analysis of the *J*anda*J*el-bound catalyst after three uses indicated a 35% decrease in manganese content. Attempts to reload the metal into the ligand were unsuccessful and this lends further support to the prospect that the ligand undergoes decomposition under the reaction conditions.[24]

Conclusion

We have described the synthesis and evaluation of soluble and insoluble polymer-supported (salen)Mn complexes for use in asymmetric epoxidation reactions. The enantioselectivities derived from the soluble and *J*anda*J*el polymeric catalysts were nearly equivalent to those for the commercial catalyst **1**; however, only the *J*anda*J*el-bound complex **7** could be used for as many as three cycles. Apparently, oxidative decomposition over repeated use gradually renders the catalyst inactive, as has been noted previously.[7c,d] This inability to recycle the catalysts indefinitely appears to be a fundamental limitation of salen-based oxidation catalysts which is difficult to overcome without sacrificing enantioselectivity. Nevertheless, the *J*anda*J*el-bound catalyst described herein provides the highest ee to date for epoxidation catalysts attached to gel-type resins and may find utility in high-throughput organic synthesis since they simplify product purification.

Experimental Section

General. Methylene chloride was dried over CaH$_2$. Poly(ethylene glycol) monomethyl ether (MeO-PEG, MW = 5000) and (*R*,*R*)-Jacobsen catalyst **1** were purchased from Aldrich and hydroxymethyl Merrifield resin (0.67 mmol/g) was purchased from Novabiochem. The *m*-CPBA was dried and recrystallized from CH$_2$Cl$_2$ prior to use. All other solvents and chemicals were obtained from commercial sources and were used without further purification. NMR spectra were recorded on Bruker AC-250, AMX-400, and DRX-500 spectrometers.

Preparation of Hydroxymethyl-NCPS. Argon was bubbled vigorously through a solution containing styrene (39.45 g, 379 mmol), hydroxymethylstyrene (0.56 g, 4.2 mmol), and toluene (140 mL). After 30 min, bubbling was discontinued and AIBN (0.29 g, 1.8 mmol) was added. The mixture was heated at 90 °C for 24 h. The solvent was removed and the residue was heated at 50 °C under high vacuum for 30 min. The crude material was dissolved in 50 mL of THF and added dropwise to a cold (~5 °C) vigorously stirring solution of methanol (1 L). The white precipitate was filtered and dried to give 19.0 g (48%) of polymer with a loading of 0.13 mmol/g as determined by ^1H NMR.

Preparation of Hydroxymethyl-Functionalized *J*anda*J*el. A solution of acacia gum (6.0 g) and NaCl (3.75 g) in water (150 mL) was placed in a 150 mL flanged reaction vessel equipped with a floating magnetic stirrer and deoxygenated by purging with N$_2$. A solution of hydroxymethylstyrene (0.20 g, 1.5 mmol), styrene (10.2 mL, 89.2 mmol), cross-linker **3**[17] (0.53 g, 1.81 mmol), and benzoyl peroxide (0.15 g) in chlorobenzene (10 mL) was injected into the rapidly stirred aqueous solution. This mixture was heated at 85 °C for 16 h. The crude polymer was collected by filtration and rinsed sequentially with water, methanol, THF, ether, and hexanes. The beads were dried in vacuo and a loading of 0.13 mmol/g was determined by UV analysis following Fmoc derivatization and cleavage. Higher loading resins were prepared by increasing the proportion of hydroxymethylstyrene in the mixture of monomers.

Preparation of Salen Glutarate (mono-ester) 4. Glutaric anhydride (137 mg, 1.2 mmol) was added to a solution containing unsymmetrical salen **2** (506 mg, 1 mmol) and DMAP (146 mg, 1.2 mmol) in CH$_2$Cl$_2$ (5 mL). The mixture was stirred for 15 h at room temperature and then concentrated under reduced pressure. The crude oil was purified by silica gel chromatography (CH$_2$Cl$_2$/methanol = 95/5) to give **4** (390 mg, 63%) as a yellow foam; ^1H NMR (400 MHz, CDCl$_3$) δ 1.27 (s, 9H), 1.38 (s, 9H), 1.40 (s, 9H), 1.75−2.06 (m, 10H), 2.49 (t, 2H, $J = 7.3$ Hz), 2.60 (t, 2H, $J = 7.3$ Hz), 3.33 (br s, 2H), 6.76 (d, 1H, $J = 2.9$ Hz), 6.92 (d, 1H, $J = 2.9$ Hz), 6.98 (d, 1H, $J = 2.2$ Hz), 7.31 (d, 1H, $J = 2.2$ Hz), 8.24 (s, 1H), and 8.31 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 24.2, 29.1, 29.4, 31.4, 33.1, 33.2, 34.0, 34.8, 34.9, 72.1, 72.4, 117.7, 118.2, 121.3, 122.7, 125.9, 126.9, 136.3, 138.6, 139.4, 141.3, 157.9, 158.2, 164.6, 165.8, and 171.9; HRMS calcd for [C$_{37}$H$_{52}$N$_2$O$_6$ + H$^+$] 621.3898, found 621.3881.

General Procedure for the Preparation of the Soluble (Salen)-Mn Catalysts 5 and 6. Dicyclohexylcarbodiimide (2.1 equiv) was added to a solution of the soluble polymer (1 equiv), salen **4** (2 equiv), and DMAP (0.5 equiv) in CH$_2$Cl$_2$ (40 mL/mmol polymer). The reaction mixture was stirred at room temperature for 24 h and then filtered through a pad of Celite to remove the urea byproduct. The filtrate was concentrated and then added dropwise to a stirring solution of 150 mL of cold ether (MeO-PEG-bound ligand) or methanol (NCPS-bound ligand). The yellow precipitate was filtered and dried in vacuo.

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[24] To further analyze the degradation of this system, a control experiment was run in which the reaction mixture, after filtration of the polymeric catalyst, was reused without the addition of fresh catalyst. Further formation of epoxide products would indicate that the salen catalyst was cleaved intact from the resin while the absence of additional epoxide formation would be indicative of manganese leaching and/or ligand decomposition. It was found that recycling of the crude reaction did not lead to the formation of additional epoxide product.

A solution of the polymer-bound ligand (1 equiv) in DMF (40 mL/mmol) was heated to 90 °C. $Mn(OAc)_2 \cdot 4H_2O$ (3 equiv) in water was then added at which point the yellow solution turned dark brown. After 30 min, air was bubbled into the solution and after an additional 30 min, LiCl (3 equiv) was added to the mixture which was then cooled to room temperature over 2 h. The solution was concentrated to dryness, taken up in CH_2Cl_2, and filtered. The filtrate was concentrated to ∼5 mL and added dropwise to an ether solution to precipitate **5** or a methanol solution to precipitate **6**. The resulting brown solids were filtered and dried. Elemental analysis indicated a Mn content of 0.86% for **5** and 0.46% for **6** corresponding to loadings of 0.16 and 0.08 mmol/g, respectively.

General Procedure for the Preparation of Insoluble (Salen)Mn Catalysts 7 and 8. DCC (2.1 equiv) was added to a solution of the insoluble resin (1 equiv), salen **4** (2 equiv), and DMAP (0.5 equiv) in CH_2Cl_2 (15 mL/g of resin). The reaction mixture was vigorously stirred at room temperature for 24 h and filtered through a medium frit. The collected solid was washed sequentially with water, methanol, CH_2Cl_2, ether, and hexanes to give yellow beads.

A solution containing the polymer-bound ligand (1 equiv) in DMF (20 mL/g of resin) was heated to 90 °C. $Mn(OAc)_2 \cdot 4H_2O$ (3 equiv) in water was then added at which point the solution turned a dark brown color. After 30 min, air was bubbled into the solution and after an additional 30 min, saturated aqueous NaCl (3 mL/g of resin) was added to the mixture which was then cooled to room temperature over 2 h. The solution was filtered through a medium frit and the collected solid was washed with water, methanol, CH_2Cl_2, ether, and hexanes to give dark brown beads. Elemental analysis indicated a nitrogen content of 0.27% for **7** and a Mn content of 1.48% for **8**, corresponding to loadings of 0.10 and 0.27 mmol/g, respectively.

Preparation of Salen Methyl Glutarate 9. 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) (23 mg, 0.12 mmol) was added to a solution containing methanol (3 μL, 0.066 mmol), salen **4** (36 mg, 0.058 mmol), and DMAP (8 mg, 0.066 mmol) in CH_2Cl_2 (3 mL). The mixture was stirred for 16 h at room temperature and then poured into water (5 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by silica gel chromatography (EtOAc/hexane = 1/4) to provide the expected methyl ester (26 mg, 72%) as a yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 1.24 (s, 9H), 1.38 (s, 9H), 1.40 (s, 9H), 1.73−1.95 (m, 8H), 2.02−2.07 (m, 2H), 2.44 (t, 2H, $J = 7.3$ Hz), 2.58 (t, 2H, $J = 7.3$ Hz), 3.33 (m, 2H), 3.69 (s, 3H), 6.76 (d, 1H, $J = 2.6$ Hz), 6.92 (d, 1H, $J = 2.6$ Hz), 6.98 (d, 1H, $J = 2.0$ Hz), 7.31 (d, 1H, $J = 2.0$ Hz), 8.23 (s, 1H), and 8.30 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 24.2, 29.1, 29.4, 31.4, 32.9, 33.0, 33.1, 33.2, 34.0, 34.8, 34.9, 51.7, 72.2, 72.4, 117.7, 118.2, 121.3, 122.8, 126.0, 127.0, 136.4, 138.6, 140.0, 141.4, 157.9, 158.1, 164.7, 165.9, 171.9, and 173.3; HRMS calcd for $[C_{35}H_{54}N_2O_6 + H^+]$ 635.4055, found 635.4060.

A solution containing the above salen ligand (25 mg, 0.039 mmol) in DMF (5 mL) was heated to 90 °C. $Mn(OAc)_2 \cdot 4H_2O$ (29 mg, 0.12 mmol) in water (2 mL) was added at which point the reaction turned dark brown. After 30 min, air was bubbled into the solution and after an additional 30 min, saturated aqueous NaCl (1 mL) was added and the mixture was cooled to room temperature over 2 h. The solvent was removed under reduced pressure and the crude residue was taken up in CH_2Cl_2 and washed with brine. The organic layer was washed with water, dried over Na_2SO_4, concentrated, and dried in vacuo to provide **9** (25 mg, 89%) as a black solid.

General Procedure for Epoxidation Reactions.[19] A solution containing the alkene (1 mmol), NMO (5 mmol), and the (salen)Mn catalyst (0.04 mmol) in CH_2Cl_2 (6 mL) was cooled to the desired temperature (see Scheme 2). *m*-CPBA (2 mmol) was added in three equal portions over 2 min and the reaction progress was monitored by TLC. Recovery of catalyst **5** was accomplished by dropwise addition of the reaction to a stirring solution of cold ether (150 mL) and filtration. Recovery of **6** was accomplished by evaporation of the reaction solvent and addition of 4 mL of THF to the crude material followed by its dropwise addition to a stirring solution of cold methanol (150 mL) and filtration. Recovery of **7** and **8** was accomplished by filtration of the reaction mixture. In each case, the filtrate, which contained the product epoxide, was washed with 1 N NaOH and brine. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure to give a crude product that was further purified by passage through a short plug of silica gel. The ee for epoxides derived from styrene and dihydronaphthalene was determined by ^1H NMR in the presence of the chiral shift reagent Eu(hfc)$_3$. The ee for the *cis*-epoxide derived from *cis*-β-methylstyrene was determined by GC using a commercial chiral column (Chiraldex G-TA, 100 °C isothermal, $t_R = 3.3_{min}$ and 4.7_{maj} min).

General Procedure for Time-Course Study. The same procedure as outlined above was followed with the exception that *m*-CPBA (2 equiv) was added in two equal portions at time = 0 and 70 s to the reaction which also contained dodecane (1 equiv) as an internal standard. Aliquots (25 μL) taken at time intervals of 0, 15, 30, 60, 120, and 300 s were quenched into a solution containing 200 μL of 1 N NaOH and 200 μL of ether. After thorough shaking, 50 μL of the organic layer was added to 200 μL of an ether solution containing a small amount of $MgSO_4$. A 50 μL sample of this mixture was then diluted with 100 μL of ether and analyzed by GC for conversion to epoxide products and ee (*cis*-epoxide only).

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