# Synthesis and Characterization of a Polymer-Supported Salen Ligand for Enantioselective Epoxidation

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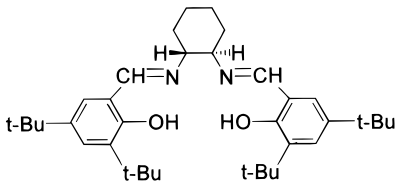
ABSTRACT: We report the synthesis of a covalently linked salen complex onto the surface of a 98 vol % styrene/2 vol % divinylbenzene polymeric support. The solid-phase method allows manipulation of the substituents on the salen complex in a more versatile manner than can be done for the homogeneous ligand and the production of a support for catalysis that guarantees accessibility to the supported active sites. The ligand was constructed in a stagewise manner that allows the possibility for combinatorial syntheses. Immobilized salen complex **1** was formed by the sequential treatment of the resin with 2,4,6-trihydroxybenzaldehyde, a chiral *trans*-1,2-diaminocyclohexane, and 3,5-di-*tert*-butylsalicylaldehyde. After loading the immobilized ligand with Mn, the support effected the enantioselective epoxidation of 1,2-dihydronaphthalene, *cis*-*β*-methylstyrene, and styrene as test olefins with enantiomeric excesses of 46%, 79% (*cis*-epoxide), and 9%, respectively, using aqueous sodium hypochlorite as the oxidant. The heterogeneous catalyst also showed a selectivity toward the formation of the trans-epoxide in the case of *cis*-*β*-methylstyrene. The heterogeneous system allows ease of separation and recycle, albeit with diminished enantioselectivity in reuse.

## Introduction

Enantioselective catalysis provides an efficient pathway for the preparation of chiral synthetic intermediates such as epoxides and aziridines.[1] These chiral species are versatile intermediates in organic synthesis and are widely exploited for the production of chiral pharmaceuticals.[2] The traditional methods for the production of a single enantiomer are often highly inefficient as they involve the use of expensive, optically pure reagents or the tedious separation of the two enantiomers from a racemic mixture through the use of resolving agents.[3] As alternatives, homogeneous enantioselective catalysts offer improved selectivity; however, they are frequently expensive and must also be separated from the reaction mixture. Heterogeneous catalysts offer the practical advantages of simplifying the separation and isolation of products, especially on a commercial scale, while permitting easy recovery of the supported catalyst for its potential regeneration and recycle.

In this paper, we describe the construction of covalently attached salen complexes within a polymeric support for use in the asymmetric epoxidation of olefins. These salen complexes are analogues of the [*N*,*N*′-bis-(3,5-di-*tert*-butylsalicylidene)]−(1,2-diaminocyclohexane) complex reported by the Jacobsen group[1,4] for the enantioselective epoxidation of alkenes. We selected




this salen complex as a model for our heterogeneous system on the basis of its synthetic scope, its resiliency to various reaction conditions, and its useful enantioselectivity in the epoxidation of olefins. In addition, the homogeneous salen framework has demonstrated exceptional versatility as the incorporation of transition metal ions produces complexes that perform asymmetric epoxidations,[1,4,5] aziridinations,[6] cyclopropanations,[7] and hydroxylations,[8] and can kinetically resolve racemic epoxides.[9]

Earlier work on supported salen complexes involved its immobilization within zeolites[11] and polymer membranes.[12] In these cases, the homogeneous catalyst was synthesized within the host material and produced a salen ligand that was sterically confined within the rigid support structure. Covalent attachment of the salen complex would offer a more robust system for recycle and separations. To accomplish this goal, covalent attachment of salen complexes onto a polymer support could be performed by either of two methods: (i) by polymerization or copolymerization of monomers that contain the preformed complex and polymerizable moieties, or (ii) by chemical modification of accessible functional groups on a preformed polymer. A few studies have used the first methodology to incorporate a homogeneous salen ligand with pendant vinyl groups covalently into a polymerized matrix.[13] A problem with this strategy is the formation of inaccessible catalytic sites within the polymer. Here we rely on surface modification strategies to produce covalently attached salen complexes on a polymer by the latter route.

In this approach (Scheme 1), the first building block for the salen complex is attached via a covalent bond to pendant chloromethyl groups on the surface of a commercially available polymer resin particle. The addition of successive organic building blocks is repeated in a stepwise manner to produce the desired salen complex on the polymer surface. This solid-phase synthesis of the salen complex allows easy separation of the salen intermediates from the various reagents needed for each step. This method is akin to that used in solid-phase peptide synthesis as the salen complex is constructed on the surface of a porous polymer in a stepwise manner.[14] However, unlike peptide synthesis, the completed salen ligand is not cleaved from the surface, as the final product is the supported complex.

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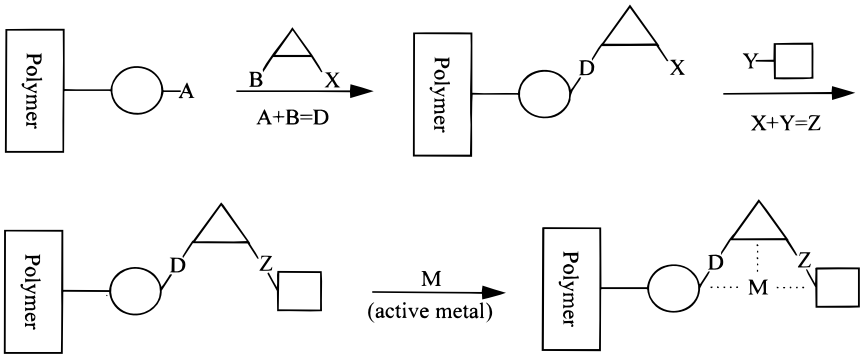
**Scheme 1. Generalized Methodology for Ligand Construction**



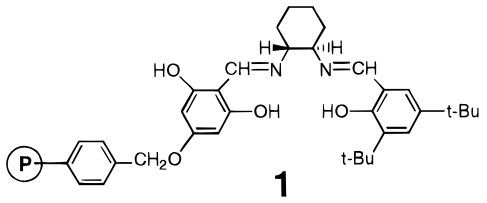

The principal advantage of this methodology is that it allows the ligand to be synthesized in a sterically unhindered manner. For successful stagewise construction of the salen complex, the sites for reaction must be readily accessible by the organic building blocks that produce the ligand. Because of this requirement, these surface sites should also be accessible to the metal being loaded, as well as the olefins and oxidant involved in the epoxidation reactions. This degree of accessibility is particularly important for enantioselective catalysts, such as the salen complex, as the approach paths to the metal center are vital in establishing stereoselectivity.[16] The accessibility should also yield a higher percentage of reactive centers for catalysis than do immobilization strategies based on copolymerization using reactive monomers of the salen complex.

This stepwise methodology also provides a salen complex which is synthesized in a controlled manner. The salen complex can be selectively tuned by manipulating the substituents on the building blocks for the salen complex and can prepare asymmetric salen complexes on the polymer support in a straightforward manner. The preparation of such complexes is synthetically tedious because the traditional synthesis of the salen complex occurs by reaction of the central component of the ligand with two equivalent moieties to produce a symmetric product.[1] The reaction of two different moieties with the central component in a homogeneous reaction produces both symmetric and asymmetric ligands. Therefore, the ability to control the asymmetry of the catalyst and the placement of substituents by the solid-phase route (Scheme 1) allow a greater ability to modify the electronic and steric properties of the chiral catalyst and allow examination of their effect on the reactivity and selectivity of this catalyst class.[17] This ability may offer the potential to examine the mechanism of oxygen transfer from the catalyst to olefin, particularly the approach path of the olefins to the coordinated metal center. Variations to substituents on the phenyl rings of an asymmetric ligand could be related to changes in the reactivity and selectivity of the catalyst in a manner previously limited with symmetric substitutions. Therefore, this systematic approach also provides a versatile method for immobilizing complexes that are not easily produced by homogeneous methods.

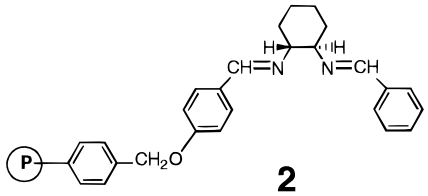
The present work focuses on the synthesis of the salen and provides a demonstration of their catalytic ability. In our investigation, we synthesized the salen complex on a styrene/divinylbenzene polymer matrix. Manganese, which is a highly effective catalyst for alkene epoxidation,[18] was loaded onto the supported salen ligand and catalyzed the reaction between the olefin and oxidant. With this system, the asymmetric catalytic epoxidation of 1,2-dihydronaphthalene, styrene, and *cis*-$\beta$-methylstyrene proceeded with moderate enantioselectivities. As a first generation, the results demonstrate the utility of this strategy for producing supported analogues of homogeneous salen-based enantioselective catalysts and the use of such systems for performing epoxidation reactions.

## Results and Discussion

**Synthesis of the Supported Metal Complexes.** We synthesized two different polymer-bound salen ligands by a common reaction pathway. These salen complexes (**1** and **2**) differ by two hydroxyl groups in the central region of the salen ligand that chelates the metal center. The hydroxyl groups provide the tetradentate chelation required for the incorporation of metals such as Mn[1,4,5] for asymmetric epoxidation and Cr[9] and Co[10] for the kinetic resolution of terminal epoxides. The other ligand (**2**) provides the bidentate chelating environment required for metals such as Cu that catalyze the aziridination of olefins[6] and was primarily used as a model compound in establishing the synthetic methodology.



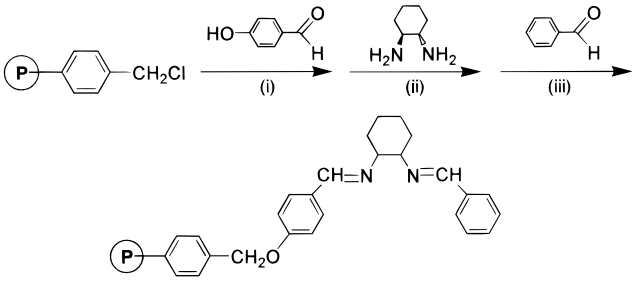

**1**




**2**

We constructed these supported ligands in a sequential manner; Scheme 2 presents the procedure for the heterogeneous synthesis of **2** on the polymer support. The pendant chloromethyl groups on the surface of Merrifield-type peptide resins (98 vol % styrene/2 vol % divinylbenzene) provided reactive sites for generating an ether linkage to a hydroxybenzaldehyde. In the synthesis of **1**, the use of 2,4,6-trihydroxybenzaldehyde guaranteed that the attached species would contain a

**Scheme 2. Methodology for Synthesis of the Polymer-Supported Salen Complex**[a]




[a] Reaction conditions: Commercially available Merrifield peptide resin was used as the support. (i) 4-Hydroxybenzaldehyde, $K_2CO_3$, and 18-Crown-6 in 1,4-dioxane; refluxed for 24 h at 95 °C. (ii) *trans*-1,2-Diaminocyclohexane in 1,4-dioxane; refluxed for 24 h at 95 °C. (iii) Benzaldehyde in 1,4-dioxane; refluxed for 24 h at 95 °C. Following each stage, the resin was dried under vacuum for 24 h at 60 °C.

free hydroxyl group adjacent to the aldehyde regardless of which phenol group reacted with the resin; the free hydroxyl group is needed for tetradentate coordination of the metal center. The resulting resin was then reacted with resolved *trans*-1,2-diaminocyclohexane (either the L or D enantiomer depending on the desired chirality of the catalyst) to generate part of the diimine bridge of the salen ligand. For ligand **2**, the second imine bond was formed by reacting benzaldehyde with the free amine. Ligand **1** was constructed by reacting the generated free amine with 3,5-di-*tert*-butylsalicylaldehyde to produce a salen ligand that mimicked the local steric environment present in highly enantioselective salen epoxidation catalysts.[1,4,5]

For each reaction involved in the synthesis of **2**, we used 1,4-dioxane as solvent. For the case of **1,** *N*,*N*-dimethylformamide substituted for 1,4-dioxane in the initial step involving 2,4,6-trihydroxybenzaldehyde for reasons of better solubility. Ethanol is typically used in the synthesis of the homogeneous complex; however, the styrene/divinylbenzene polymer support is hydrophobic, and the use of ethanol did not result in any significant reaction on the polymer surface. The selection of 1,4-dioxane as solvent was based on its use in reactions between hydroxybenzaldehyde derivatives and benzyl halides[19] and its ability to swell the polymer resin. We hypothesized that the swelling by this solvent could increase access by the reagents to reactive sites within the polymer matrix. A drawback in the use of 1,4-dioxane in the heterogeneous synthesis was a need to use resolved 1,2-diaminocyclohexane in a free and uncomplexed state. The diamine is resolved by forming a diastereomeric complex with enantiomerically pure tartaric acid (either L or D). For the homogeneous

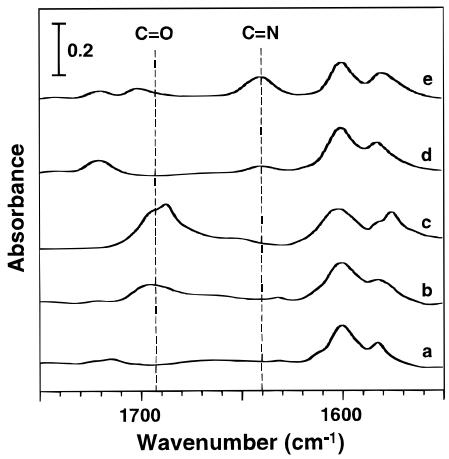



**Figure 1.** Infrared spectra for the stagewise synthesis of the anchored salen complex onto Merrifield resin (chloromethylated polymer of 98 vol % styrene and 2 vol % divinylbenzene): (a) Merrifield resin; (b) a + 4-hydroxybenzaldehyde; (c) benzyl chloride + 4-hydroxybenzaldehyde; (d) b + (±)-*trans*-1,2-diaminocyclohexane; and (e) d + benzaldehyde. The approximate position of the aldehydic carbonyl and imine stretching vibrations are 1694 and 1640 $cm^{-1}$, respectively. The additional peak observed at 1720 $cm^{-1}$ is an overtone band characteristic of the phenyl ring. The spectra have been offset vertically for clarity. The peaks between 1580 and 1610 $cm^{-1}$ are aromatic stretching modes due to the polystyrene support.

synthesis of the catalyst, this diastereomeric complex is soluble in the reaction solvent (ethanol with 15 vol % water) and used directly.[1c] As the complex was not soluble in 1,4-dioxane, we separated the tartrate from the amine−acid complex before reaction with a concentrated KOH solution[21] and used the free, resolved 1,2-diaminocyclohexane, which is soluble in 1,4-dioxane.

To complete the synthesis of the supported enantioselective catalyst, the constructed ligand (**1**) was loaded with Mn by reaction with $Mn(OAc)_2 \cdot 4H_2O$ in the presence of tetra-*n*-butylammonium chloride to generate the active Mn(III) cationic complex.

**IR Analysis.** The principal evidence for construction of ligands **1** and **2** onto the polymer support is the appearance and loss of IR peaks that correspond to the introduction or transformation of distinct functional groups at each stage in the synthesis of the salen ligand. Table 1 provides the key IR peaks for both the heterogeneous ligands and their homogeneous counterparts. Figure 1 shows the spectra for the intermediates prepared in the synthesis of ligand **2** along with the spectrum for the Merrifield peptide resin used in our experiments (Figure 1a). The peaks in the spectra from 1580 to 1620 $cm^{-1}$ are assigned to the aromatic stretching modes of the polystyrene-based support and served

**Table 1. Infrared Peak Assignments for Salen Ligands**

| | IR peak assignment ($cm^{-1}$) | | | |
|---|---|---|---|---|
| functional group | ligand **1** | homogeneous analogue[a] | ligand **2** | homogeneous analogue[a] |
| aldehyde carbonyl | 1678 | 1678[b] | 1694 | 1690[e] |
| imine | 1629 | 1630[c] | 1640 | |
| diimine | 1627 | 1632[d] | 1640 | 1642[f] |
| *tert*-butyl (C−H) | 2965, 2870 | 2964, 2872[d] | 2966, 2871[g] | 2964, 2872[d] |

[a] Products were confirmed using $^1H$ NMR. [b] From the reaction product of benzyl chloride + 2,4,6-trihydroxybenzaldehyde. [c] Literature reference[12b] for single imine bond between 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde and (±)-trans-1,2-diaminocyclohexane. [d] From the reaction product of 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde (2 equiv) + (±)-trans-1,2-diaminocyclohexane (1 equiv). [e] From the reaction product of benzyl chloride + 4-hydroxybenzaldehyde. [f] From the reaction product of 4-hydroxybenzaldehyde (2 equiv) + (±)-trans-1,2-diaminocyclohexane (1 equiv). [g] Results from the use of 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde as a spectroscopic tag.

as an internal standard for comparing spectra. Upon reaction between the resin and 4-hydroxybenzaldehyde, the spectrum (Figure 1b) shows a new peak at 1694 $cm^{-1}$ that corresponds to the carbonyl stretching vibration of the aldehyde. The assignment of this peak is supported by the IR spectrum for the product of the homogeneous model reaction between benzyl chloride and 4-hydroxybenzaldehyde (Figure 1c). Further evidence for the reaction on the resin is noted by a decrease in the intensity of the peak at 1265 $cm^{-1}$ (not shown) that corresponds to the H−C−Cl wagging modes of the original chloromethylated resin.

The subsequent reaction of the aldehyde with an amine group of the diaminocyclohexane produces a peak at 1640 $cm^{-1}$ (Figure 1d) that corresponds to the imine (C═N) stretching vibration. In Figure 1d, the disappearance of the aldehydic carbonyl peak at 1694 $cm^{-1}$ is further evidence of this reaction and its completeness on the resin surface. For comparison, the IR spectrum of a model compound produced by the homogeneous reaction between 4-hydroxybenzaldehyde and the diamine showed an imine stretching vibration at 1642 $cm^{-1}$. The reaction of this resin with benzaldehyde to terminate the ligand yields an approximate doubling of the imine peak (Figure 1e), indicating the formation of the second imine linkage. Complementary experiments were conducted to terminate the ligand with a substituted benzaldehyde to provide independent spectroscopic verification that the second aldehyde was successfully linked to the support. For this purpose, we reacted 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde with the polymer-bound diamine product and used the *tert*-butyl groups as spectroscopic tags for the reaction. Upon subtraction of the spectrum for the precursor resin from that of this reaction, peaks at 2870 and 2965 $cm^{-1}$ were observed in the C−H stretching regions that correspond to the methyl symmetric and asymmetric vibrations of the *tert*-butyl groups, respectively. The imine stretching peak for the product with this benzaldehyde appeared at 1631 $cm^{-1}$. In the reaction with the 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde, the spectrum also contained a small peak at 1696 $cm^{-1}$. Due to the presence of a hydroxyl group on the salicylaldehyde moiety, reaction may occur between this compound and unreacted chloromethyl groups on the polymer surface as for the attachment of the hydroxybenzaldehydes in the initial stage of the complex synthesis. We believe that the small peak observed at 1696 $cm^{-1}$ is most likely due to aldehyde groups on the polymer from this side reaction. The species generated from this reaction are not expected to complex Mn ions or generate catalytically reactive sites.

The IR spectra for the synthesis of **1** followed the same general stepwise spectral changes as with **2**. Due to the additional substituents on 2,4,6-trihydroxybenzaldehyde, the spectrum after the first step in the reaction sequence was not as clear as that for the product from 4-hydroxybenzaldehyde in the synthesis of **1**. In particular, a broad doublet of peaks at 1632 and 1678 $cm^{-1}$ was observed for the resin after reaction with 2,4,6-trihydroxybenzaldehyde. We observed these same peaks for the product of the homogeneous reaction between benzyl chloride and 2,4,6-trihydroxybenzaldehyde (Table 1).

The reaction between the anchored trihydroxybenzaldehyde and free diamine yielded a peak at 1629 $cm^{-1}$ which was assigned to an imine. The complete loss of the aldehydic carbonyl peak at 1678 $cm^{-1}$ provided further evidence of the surface reaction and its completeness. We confirmed the peak assignment for the imine by comparison with the IR spectrum for the homogeneous reaction between the product of benzyl chloride and 2,4,6-trihydroxybenzaldehyde with 0.5 equiv of the diamine (Table 1). The ligand-capping reaction on the polymer with 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde yielded the formation of additional imine groups as evidenced by the increased intensity of the C═N stretching mode at 1627 $cm^{-1}$. As with ligand **2**, the position of the imine peak after reaction with 3,5-di-*tert*-butyl-2-hydroxybenzaldehyde occurred at a lower wavenumber than for the initial imine linkage. The spectrum for the supported trihydroxybenzaldehyde ligand also contained peaks at 2870 and 2965 $cm^{-1}$ for the methyl vibrations of the *tert*-butyl groups.

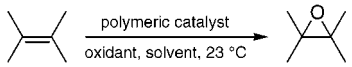
The reaction between the 2,4,6-trihydroxybenzaldehyde and the polymer could proceed to form an ether linkage that is either ortho or para to the aldehyde moiety. To examine whether an ether linkage located ortho to the aldehyde might sterically prevent construction of the complete ligand, we performed control experiments using the polymer resin and 2-hydroxybenzaldehyde. The IR spectrum for this reaction product was similar to that for **2** and demonstrated possible reaction by the ortho substituents on the 2,4,6-trihydroxybenzaldehyde with the polymer resin. Reaction of the supported salicylaldehyde with 1,2-diaminocyclohexane exhibited complete conversion of the aldehydes to imines by IR. This observation suggests that attachment of 2,4,6-trihydroxybenzaldhyde to the polymer by an ortho hydroxyl group would allow formation of the complete inner ligand structure on the polymer (as shown for **1**) with the position of complexation being the other exterior hydroxyl group.

In developing the reaction sequence, control experiments were conducted to ensure that the reactants added at each stage reacted only at the linkage site provided by the previous reaction in the ligand synthesis. This process was accomplished by omitting a step in the ligand synthesis and investigating whether the subsequent step produced any changes in the IR spectra of the resin. For the exposure of the chloromethylated resin to the diamine, we observed no change in the IR spectrum from that of the precursor spectrum. With the terminal benzaldehydes, we observed a small peak at 1696 $cm^{-1}$ when the benzaldehyde contained hydroxyl groups. As indicated earlier, we hypothesize that this absorption is a result of reaction at the surface with the chloromethyl groups.

Ligand **1** was loaded with manganese ions to examine the utility of the supported salen ligands for enantioselective catalysis. The supported metal complex was prepared by refluxing the resin with $Mn(OAc)_2 \cdot 4H_2O$ in DMF and rinsing it first with [*n*-$Bu_4N$]Cl in 1,4-dioxane and then a dioxane/water mixture to remove excess Mn. This procedure is analogous to the homogeneous process used by Jacobsen[1] with the difference being the use of 1,4-dioxane to aid in swelling the polymer in the rinse step and the substitution of [*n*-$Bu_4N$]Cl for NaCl as a more soluble chlorine donor.

**Stability and Loading of the Supported Salen Ligands.** The utility of a heterogeneous catalyst is based partly on the stability of the ligand and the extent to which the ligand can be loaded onto the support. We

**Table 2. Heterogeneous Epoxidation of Olefins Catalyzed by Polymeric Catalyst 1**




| olefin | solvent | oxidant | time (h) | conversion (%) | yield (%)[a] | ee (%)[b] |
|---|---|---|---|---|---|---|
| dihydronaphthalene | $CH_3CN$ | NaOCl | 2 | 99 | 56 | 7 |
| dihydronaphthalene | $CH_2Cl_2$ | NaOCl | 20 | 100 | 42 | 46 |
| *cis*-$\beta$-methylstyrene | $CH_2Cl_2$ | NaOCl | 20 | 93 | 2/27[c] | 79/12[d] |
| styrene | $CH_2Cl_2$ | NaOCl | 20 | 23 | 7 | 9 |

[a] Yields were determined using capillary GC by integration of product peaks against an internal quantitative standard (chlorobenzene). [b] Ee's determined by chiral GC. Product assignments performed by comparison of elution order with authentic samples prepared using the (*S*,*S*) form of Jacobsen's catalyst. [c] Reported yields are for *cis*/*trans*-epoxides, respectively. [d] Ee's refer to cis/trans enantiomers, where the trans enantiomers were resolved using $^1$H NMR in the presence of Eu(hfc).

evaluated the stability of ligands **1** and **2** using IR spectroscopy to determine the resilience of the linkages between the complex and the support (polymer). These studies allow the occurrence of fractures by the linkages in the salen ligand during their use or the entrapment of reactants within the polymer matrix during their synthesis to be investigated.

In these experiments, we sonicated the product after each stage of the synthesis for 1 h at room temperature in toluene and refluxed it for 24 h in both 1,4-dioxane or toluene (each is a swelling solvent for the polymer). For each of the polymer systems, the aromatic stretching peaks between 1570 and 1610 $cm^{-1}$ from the styrene/divinylbenzene support provided an internal standard and were used for comparing the spectra of the supported ligands. We normalized the peak areas for key ligand functionalities (aldehydic carbonyl and imine) to that of the internal standard (aromatic stretching peaks) and compared the relative intensities of the ligand absorptions before and after exposure to the above conditions. In general, we observed intensity changes of $<5\%$ by the procedures, suggesting that the supported salen complexes have relatively good stability under the synthetic conditions and under much greater stresses such as sonication.

We used elemental analysis to determine the loading level of ligand **1** on the resin and the reaction yields in its synthesis. The Merrifield resin originally contained 2.0 mequiv of Cl/g of resin, and analysis of the chlorine content after the initial stage of reaction suggests approximately 55% conversion[20] in this step. From an analysis of the nitrogen composition for the final ligand structure, a loading of 0.65 mequiv of ligand/g of resin was estimated. Finally, Mn analysis of the loaded ligand structure indicated that each gram of resin contained 0.13 mequiv of the active complex with coordinated Mn within the salen ligands. For comparison, heterogeneous analogues of Jacobsen's catalyst that were synthesized by incorporating a vinyl-substituted salen complex into the polymerization mixture are reported to contain approximately 0.6 mequiv of active ligand/g of polymer.[13] An important difference between these systems is that the former loading level represents accessible ligands on the polymer surface, whereas the latter include incorporated ligands within the bulk polymer that may not be active or accessible for reaction.

The loading levels produced by our stepwise synthesis may be increased by altering the loading procedure[20] or by increasing the specific surface area of the polymer used for constructing the ligand. In this work, we used commercially available peptide resins based on their ease of accessibility and supply; however, such resins typically have low specific surface areas.[14,15] As a support for peptide synthesis, these resin properties are viewed as advantageous in offering greater accessibility to immobilized species. However, these specific surface areas and loadings of the polymer support should be amenable to improvements by tailoring the structure and composition of the polymer through its synthesis.

**Catalytic Activity of the Supported Catalyst.** As a proposed asymmetric catalyst, the standard by which the heterogeneous system is measured is ultimately its ability to produce one enantiomer over the other as noted by an enantiomeric excess (ee). To this end, ligand **1** was loaded with $Mn^{II}$ and evaluated as an asymmetric catalyst for the enantioselective epoxidation of 1,2-dihydronaphthalene (DHN), *cis*-$\beta$-methylstyrene, and styrene using an aqueous solution of sodium hypochlorite (NaOCl) as oxidant. We used reaction conditions that were analogous to those for the homogeneous catalytic reaction. Additionally, 4-phenylpyridine *N*-oxide, which has been shown to enhance ee's slightly for the homogeneous case,[25] was used in these reactions.

For enantioselective epoxidation, DHN and *cis*-$\beta$-methylstyrene typically provide high enantioselectivities in the homogeneous case and provide practical tests to the effectiveness of the polymeric catalyst **1**. In the homogeneous case, these olefins give ee's ranging from 70 to 98% depending on the substituents on the catalyst structure.[1,23] Thus, if the polymeric catalyst is to show any degree of enantioselectivity, the results should be observable with these olefins. *cis*-$\beta$-Methylstyrene also provides a good test as to whether the heterogeneous catalyst is cis selective in the formation of the resulting epoxide as is the homogeneous catalyst.[28] Finally, styrene provides a test case of a terminal olefin.

Reactions were conducted using ligand **1** with the (*S*,*S*) configuration corresponding to a resolved D-*trans*-1,2-diaminocyclohexane in the ligand. The epoxidation results for DHN indicated differences in the ee depending on the solvent. The ee varied from 7 to 46% as the solvent was switched from $CH_3CN$ to $CH_2Cl_2$ (Table 2). This trend mirrors the homogeneous case where the ee varies from 37 to 82%. The principal explanation for this difference is that $CH_3CN$ is readily miscible with the aqueous oxidant (NaOCl), and the oxidant is active toward production of the racemate thereby lowering the ee of the reaction. In contrast, $CH_2Cl_2$ is immiscible with the aqueous oxidant solution and competition between racemate formation from the oxidant alone is less than oxo transfer aided by the enantioselective catalyst.

The epoxidation of *cis*-$\beta$-methylstyrene using $CH_2Cl_2$/NaOCl provided an ee of 79% for the *cis*-epoxide. In contrast with the homogeneous case where the catalyst is cis selective,[28] the dominant product of the heterogeneous reaction is the trans product. This result indicates a rotation of the carbon−carbon bond before

formation of the second carbon−oxygen bond of the epoxide. The enantioselectivity of the *trans*-epoxide was 12% (Table 2), but its much lower value is not surprising in that the homogeneous salen catalyst is less enantioselective for the *trans*-epoxide than the *cis*-epoxide.[1b,e] As for the possible reasons for the observed trans selectivity, the asymmetry of the heterogeneous catalyst or microenvironment effects caused by the polymer may play a role.

The trans selectivity for the epoxidation of *cis*-*β*-methylstyrene may explain the low ee (9%) with styrene (Table 2). Terminal olefins epoxidize with lower enantioselectivity (50−60%) in $CH_2Cl_2$/NaOCl than more highly substituted olefins.[1b,24] This result is due to an enantiomeric "leakage" pathway.[26] In the case of *cis*-*β*-methylstyrene, a rotation about the carbon−carbon bond before its collapse forms the *trans*-epoxide. The analogous rotation and collapse for styrene would produce the competing enantiomer and reduce the observed ee. This ee for the case of styrene is higher than some values (<2%[13d]) and less than others (16%[13f]) that have been reported for immobilized salen complexes on polymers using pendant vinyl groups. However, a comparative trans selectivity for a disubstituted olefin such as *cis*-*β*-methylstyrene had not been tested in these cases as to offer a possible reason for the reduced ee values.

We examined the ability to separate and recycle the polymer-supported catalyst by a simple filtration process. When resin which has been in contact with olefin and oxidant under typical reaction conditions for 40 h was subsequently filtered on filter paper, rinsed, and dried under vacuum for reuse, the catalyst exhibited catalytic activity and enantioselectivity for the epoxidations when added to a fresh reaction mixture. This procedure was repeated three times (each involving exposure to the reaction conditions for 40 h) with each subsequent use of the catalyst demonstrating activity and enantioselectivity albeit at diminishing levels from the use of the initially prepared material. This recovery and recycle is notable as the homogeneous catalyst deactivates in the oxidant by a dimerization process.[27] The demonstration of recycle provides evidence for the site isolation of the supported Mn−salen complexes. The diminished activity of the catalyst after each cycle is partly due to the extended reaction times used to test the catalyst and establish enantioselective performance. The prolonged exposure (40 h) to oxidant may be causing cleavage of the salen complex (possibly at an ether linkage) and the lower activity, we expect that reduced reaction times would improve the performance of the recycled catalysts.

As with other heterogeneous systems, the level of enantioselectivity resulting from our system is lower than those reported for epoxidation of these test olefins by the homogeneous catalyst under similar reaction conditions.[1,23] We note that the observed ee's with DHN and *cis*-*β*-methylstyrene and the developed catalyst (46 and 79%) are higher than those reported for polymer-based salen ligands incorporated using pendant vinyl groups (37 and 62%, respectively).[13f] An advantage of the present strategy is that it offers the possibility for further straightforward optimization of the ligand structure because of its stepwise synthetic approach.

## Conclusions

The sequential reactions between a chloromethylated polymer (Merrifield's resin) and a hydroxybenzaldehyde, diaminocyclohexane, and a second aldehyde can be used to produce immobilized salen ligands on a polymer support. These ligands can be prepared for inclusion of metal ions such as $Mn^{II}$ and be used for the asymmetric epoxidation of olefins. In particular, demonstrated epoxidations converted 1,2-dihydronaphthalene with 46% ee, *cis*-*β*-methylstyrene with 79% ee for the *cis*-epoxide, and styrene with 9% ee using NaOCl(aq) as the oxidant. The catalyst can be easily separated and recycled. However, its performance diminished by prolonged exposure to the oxidant. Work is currently underway to optimize the ee's from the catalyst system and to enhance the stability of the ligand.

## Experimental Section

**Materials.** Solvents and chemicals were obtained from Aldrich and used as received unless specified otherwise. (±)-*trans*-1,2-diaminocyclohexane was resolved using a procedure similar to that reported by Galsbol.[21]

**Instrumentation and Analyses.** Infrared spectra were recorded in transmission mode using a Bio Rad FTS 175 spectrometer. Elemental analyses were performed by Quantitative Technologies, Inc. Conversions, yields, and enantiomeric excesses for catalytic epoxidations were determined by gas chromatography using a Hewlett-Packard HP6890 series gas chromatograph (fid detector) with a *β*-Dex 120 chiral phase capillary column (Supelco, Inc.; 30 m × 0.25 mm i.d., 0.25 *μ*m film). Chlorobenzene was used as a quantitative internal standard. For the *trans*-epoxide of *cis*-*β*-methylstyrene, Eu(hfc)$_3$ was used to obtain the enantiomeric excess by $^1$H NMR.[29] Specific surface areas were determined using a Quantachrome Autosorb-1 automatic volumetric sorption analyzer.

**Supported 4-Hydroxybenzaldehyde (3).** A mixture of Merrifield resin (0.515 g, 2.0 mmol Cl/g), 4-hydroxybenzaldehyde (0.243 g, 2.0 mmol), potassium carbonate (0.136 g, 1.0 mmol), and 18-crown-6 (0.036 g, 0.14 mmol) in anhydrous 1,4-dioxane (20 mL) was heated at reflux under $N_2$ for 24 h. The product resin was collected by gravity filtration and washed thoroughly with 1,4-dioxane (50 mL) and warm distilled water (20 mL). After drying in air for 12 h, the collected resin was dried under reduced pressure for 24 h at 60 °C. IR (KBr): 1694 (C═O), 1601 (aromatic), 1265 (*ω*-H−C−Cl) cm$^{-1}$.

**Supported 2,4,6-Trihydroxybenzaldehyde (4).** A mixture of Merrifield resin (8.11 g, 2.0 mmol Cl/g), 2,4,6-hydroxybenzaldehyde (5.0 g, 32.4 mmol), potassium hydroxide (7.2 g, 128.3 mmol), and 18-crown-6 (0.42 g, 1.59 mmol) in anhydrous DMF (135 mL) was heated at 95 °C under $N_2$ for 24 h. The product resin was collected by gravity filtration and washed thoroughly with DMF (150 mL) and warm distilled water (150 mL). After drying in air for 12 h, the collected resin was dried under reduced pressure for 24 h at 60 °C. IR (KBr): 1678 (C═O), 1632 (OH), 1601 (aromatic), 1265 (*ω*-H−C−Cl) cm$^{-1}$.

**Supported *N*-[4-Hydroxybenzylidene]-1,2-diaminocyclohexane (5) and Supported *N*-[2,4,6-Trihydroxybenzylidene]-1,2-diaminocyclohexane (6).** (1*S*,2*S*)-1,2-Diaminocyclohexane (0.306 mL, 2.55 mmol) and anhydrous pyridine (0.412 mL, 5.1 mmol) were added sequentially to a mixture of ***3*** (0.156 g) in 5 mL of anhydrous 1,4-dioxane. The mixture was stirred at reflux for 24 h. The mixture was gravity filtered, and the collected resin was washed with 1,4-dioxane (20 mL) and dried for 12 h in air and for 24 h under reduced pressure at 60 °C. This general procedure was also followed for the reaction of the diaminocyclohexane with **4**. For **5**, IR (KBr): 1640 (C═N), 1601 (aromatic) cm$^{-1}$. For **6**, IR (KBr): 1654 (OH), 1629 (C═N), 1601 (aromatic) cm$^{-1}$. Anal. Calcd (100% conversion): C, 74.90; H, 7.17; N, 6.10; Cl, 0.0. Found: C, 59.51; H, 6.29; N, 4.16; Cl, 0.10.

**Supported *N*-[4-Hydroxybenzylidene]-*N*′-[benzylidene]-1,2-diaminocyclohexane.** A common procedure was used for reaction between the supported *N*-substituted diamines and the terminal benzaldehydes. The benzaldehyde (0.74 mmol) was added to a mixture of 83.7 mg of supported *N*-[4-hydroxybenzylidene]-1,2-diaminocyclohexane (**5** or **6**) and 5 mL

of 1,4-dioxane. The mixture was stirred and refluxed for 24 h. Gravity filtration yielded the product which was rinsed with 20 mL of 1,4-dioxane, dried for 12 h in air, and dried for 24 h at 60 °C under reduced pressure. For the reaction between **5** and benzaldehyde, IR (KBr): 1640 (C═N), 1601 (aromatic) $cm^{-1}$. Anal. Calcd (100% conversion): C, 86.12; H, 6.70; N, 3.84; Cl, 0.0. Found: C, 83.90; H, 7.31; N, 1.82; Cl, 3.30. For the reaction between **5** and 3,5-di-*tert*-butylsalicylaldehyde, IR (KBr): 2966, 2871 (*tert*-butyl), 1696 (C═O), 1647 (OH), 1631 (C═N), 1601 (aromatic) $cm^{-1}$. For the reaction between **6** and 3,5-di-*tert*-butylsalicylaldehyde, IR (KBr): 2965, 2870 (*tert*-butyl), 1696 (C═O), 1653 (OH), 1627 (C═N), 1601 (aromatic) $cm^{-1}$.

**Loading of Polymer-Supported Ligand (1) with Mn.** This procedure is a modification of that reported by Jacobsen et al.[1c] Anhydrous DMF (230 mL) and $Mn(OAc)_2 \cdot 4H_2O$ (1.48 g, 6.0 mmol) were added to ligand **1** (3.0 g, 0.60 mequiv of ligand/g) in a two-neck, 250-mL round-bottom flask. The mixture was refluxed and stirred for 8 h while air was sparged through the system. The resin was collected by gravity filtration and dried in air. This resin was combined with 230 mL of 1,4-dioxane (a swelling solvent for the polymer) and tetra-*n*-butylammonium chloride (2.52 g, 9.1 mmol). The mixture was stirred and refluxed for 12 h, and the above procedure of filtration and drying was repeated. The collected resin was refluxed in 230 mL of a 90/10 vol % mixture of 1,4-dioxane and water for 8 h. The catalyst was then Soxhleted with acetonitrile for 48 h and rinsed with hot toluene. After filtration and air-drying, the resin was dried for 24 h at 60 °C under reduced pressure. This final product was used in subsequent epoxidation reactions. Calcd (100% conversion): C, 76.81; H, 5.97; N, 3.44; Cl, 4.24; Mn, 6.57. Found: C, 80.61; H, 7.32; N, 1.69; Cl, 1.18; Mn, 0.71.

**Representative Reaction: Heterogeneous Ligand (1)-Catalyzed Epoxidation of Dihydronaphthalene.** A solution of dihydronaphthalene (0.157 mL, 1.2 mmol), dichloromethane (9.65 mL), and chlorobenzene as internal standard (24.1 $\mu$L, 0.237 mmol) was cooled to 2 °C, 4-phenylpyridine *N*-oxide (0.053 g, 3.0 mmol) and supported ligand **1** (0.600 g, 0.129 mequiv of Mn/g) was added to the mixture, and the oxidant (10.9 mL of 0.55 M NaOCl in $H_2O$)[14a] which was also equilibrated to 2 °C was subsequently added. The reaction was continuously stirred. Aliquots (0.05 mL) of the reaction mixture were periodically removed to monitor the reaction via GC using a chiral phase capillary column. The samples were filtered through a pad of alumina before injection into the GC. Typical GC conditions were 1.3 mL/min at constant flow, 250 °C inlet temperature, and a temperature program for a 120 °C isotherm for 35 min.

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**Supporting Information Available:** Procedures for the synthesis of homogeneous analogues of the supported salen intermediates (2 pages). See any current masthead page for ordering and Internet access instructions.

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