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Chiral Titanium Coordination Assemblies: Robust Cooperative Self-Supported Catalysts for Asymmetric Ring Opening of *meso*-Epoxides with Aliphatic Amines

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Abstract: By utilizing the oxygen bridge in dimeric μ-oxo-titanium-salen complexes as an efficient cross-linkage, a series of robust chiral titanium coordination assemblies has been successfully fabricated with the ditopic bridging ligands derived from BINOL and salen derivatives *via* coordination polymerization, which are fully characterized by IR, elemental analysis, XRD and microscopic studies. Because of their insolubility in most organic solvents and water, these metal-organic assemblies can successfully function as robust self-supported chiral catalysts, allowing an asymmetric ring opening (ARO) of *meso*-epoxides with aliphatic amines. Remarkably, owing to the linkage effects and the cooperation of two kinds of chiral titanium moieties in the metal-organic assemblies, the self-supported chiral catalysts demonstrate extremely high stability. They not only show high tolerance towards various *meso*-epoxides and nucleophilic aliphatic amines, but also can be reused in more than 20 runs without obvious metal leaching and loss in yields and enantioselectivities. Furthermore, the self-supported catalyst accomplished a one-pot tandem olefin epoxidation and ARO of an epoxide sequence starting from the olefin, 30% hydrogen peroxide and benzylamine. In marked contrast, the reaction failed to work when using the two corresponding homogeneous catalysts under identical reaction conditions. Good yields and enantioselectivities were obtained by the robust self-supported catalyst, which clearly indicates the cooperative effects between two chiral moieties within the metal-organic assemblies. The two catalytic centers can perform their own duties without interference and this further supports our strategy for the self-supported catalyst design.

Keywords: asymmetric ring-opening reactions; linkage effect; self-supported catalysts; tandem reactions; titanium complexes

Introduction

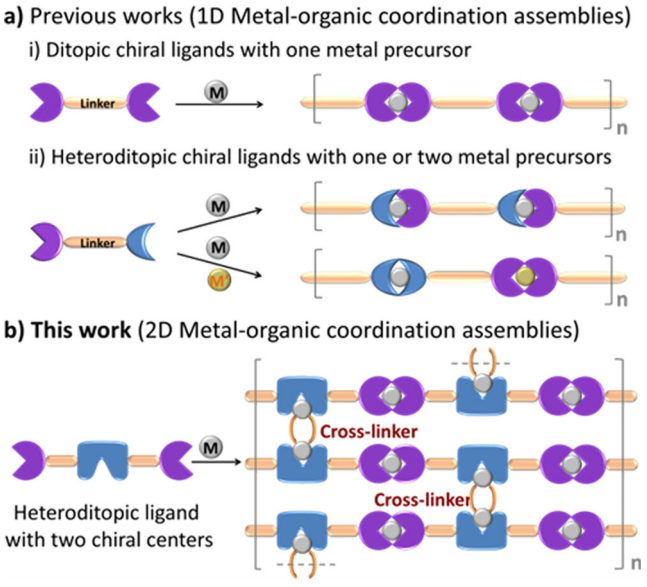
The past fifty years have witnessed tremendous advances in homogeneous transition metal-catalyzed asymmetric reactions;[1] however, only few of them have found utility in industry.[2] This is partly because of the high cost of luxury chiral ligands and noble metals, along with the contamination of products by the leaching of toxic metals.[3] Therefore, the design and development of new approaches for easy recovery and efficient recycling of chiral metal catalysts without metal leaching are highly desirable, but constitute a long-term challenge confronting synthetic chemists.[1b,4]

In order to tackle these problems, much attention has been devoted to immobilize the viable chiral homogeneous catalysts on inorganic solids or organic supports.[3,4] However, these conventional immobilization approaches with prefabricated supports often suffered from negative effects such as lower stability, reduced catalytic activity and/or selectivity as a result of the poor accessibility, random anchoring, or disturbed geometry of the active sites in the solid matrix. With the development of supramolecular chemistry, homochiral metal-organic assemblies that incorporate the chiral ligand and active metal site into their skeletons have emerged as an attractive platform to immobilize chiral catalysts.[5] However, few examples of the recovery and reuse of homochiral metal-organic assem-

blies have been documented, probably as a result of the vulnerability of the non-covalent metal-organic supramolecular assemblies that may compromise the chemical stability, especially, in the presence of strong nucleophiles or under basic conditions.[6]

In this context, a "self-supporting" approach developed recently to fabricate immobilized chiral catalysts *via* coordination assembly of ditopic chiral ligands with selected metal ions is especially noteworthy.[7] The catalytic active sites can preserve the structural features of their homogeneous catalyst counterparts, while being insoluble in common solvents by virtue of their higher structural dimensionality. Good to excellent enantioselectivities have already been observed in several enantioselective transformations, such as hydrogenation, oxidation, Michael addition by using the relevant chiral assemblies as self-supported catalysts, which were typically reused for several runs.[8] It is worth noting that most known self-supported catalysts are schematically one dimensional metal-organic assemblies *via* orthogonal coordination of one or two different metal ions with a single ditopic ligand (Scheme 1a), their stability and reusability still have ample room for improvement, especially in the presence of strong hetero-nucleophiles.

Following our recent interest in exploring the feasibility of metal-organic assemblies in catalysis and sensing,[9] we sought to develop two-dimensional self-supported chiral metal-organic assemblies through the cross-linking of 1D metal assemblies derived from ditopic chiral ligands, with the aim to enhance the structural robustness and hence the recyclability of the resulting catalyst (Scheme 1b). A rationally designed heteroditopic ligand with a suitable linker may first form a 1D metal assembly after metal coordination, which then undergoes cross-linking to form a two-dimensional network with enhanced stability. When the heteroditopic ligand contains two distinct types of chiral elements, the resulting 2D chiral metal-organic assemblies can provide us with an opportunity to investigate cooperative effects of two chiral elements, which may impact on the catalytic activity, enantioselectivity and reusability of the resulting catalysts. Furthermore, such a chiral network is embedded with two kinds of different site-isolated catalytic centers, which may also offer a possibility to realize one-pot sequential tandem reactions unattainable by the use of the corresponding monometallic homogeneous chiral catalysts. This is very attractive, as the development of multifunctional catalyst-promoted asymmetric one-pot sequential tandem reactions is of current interest. Also, how to prevent the quenching of different incompatible catalysts was one of the major challenges in this scenario.[10] Herein, we wish to report our newly developed chiral titanium coordination assemblies as powerful and recyclable catalysts for the highly enantioselective ring opening of *meso*-epoxides with amines, and their initial application toward a one-pot tandem epoxidation and aminolysis sequence.

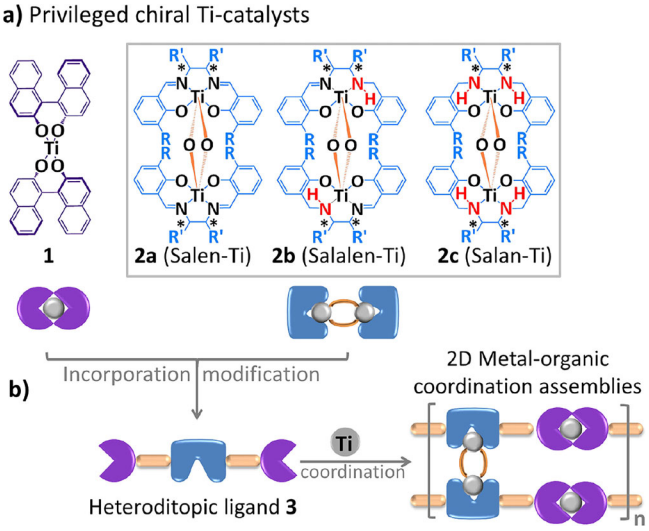


Scheme 1. Representative strategies to access a) 1D; and b) 2D self-supported chiral catalysts *via* coordination assembly.

Results and Discussion

Syntheses of Chiral Titanium Coordination Assemblies

Ti-BINOLate **1** and titanium salicylaldehydoethylenediamine (salen) complexes **2a** (Scheme 2a) are well-established privileged catalysts[11] in a number of important enantioselective transformations. Especially, both complexes are potent catalysts for asymmetric ring opening (ARO) reactions of epoxides using various carbo- or hetero-nucleophiles.[12] We would like to incorporate these two chiral elements to synthesize newly designed 2D self-supported catalysts, since Ti-salen complexes are known to be capable of forming a dimeric species through oxygen bridges (Scheme 2a),[13] which may function as a cross-linker to connect the initially formed 1D metal-organic assemblies to build up a more stable 2D matrix (Scheme 2b). The key to the development of such titanium coordination assemblies was to design chiral heteroditopic bridging ligands **3** which united both BINOL and salen moieties through a suitable linker. Therefore, by adjusting the linker of the heteroditopic ligands and the structure of each chiral element, it is possible to achieve the desired 2D assemblies with robust structures whilst keeping the catalytically active sites that recapitulate the structural features of their homogeneous catalyst counterparts. Delightfully,

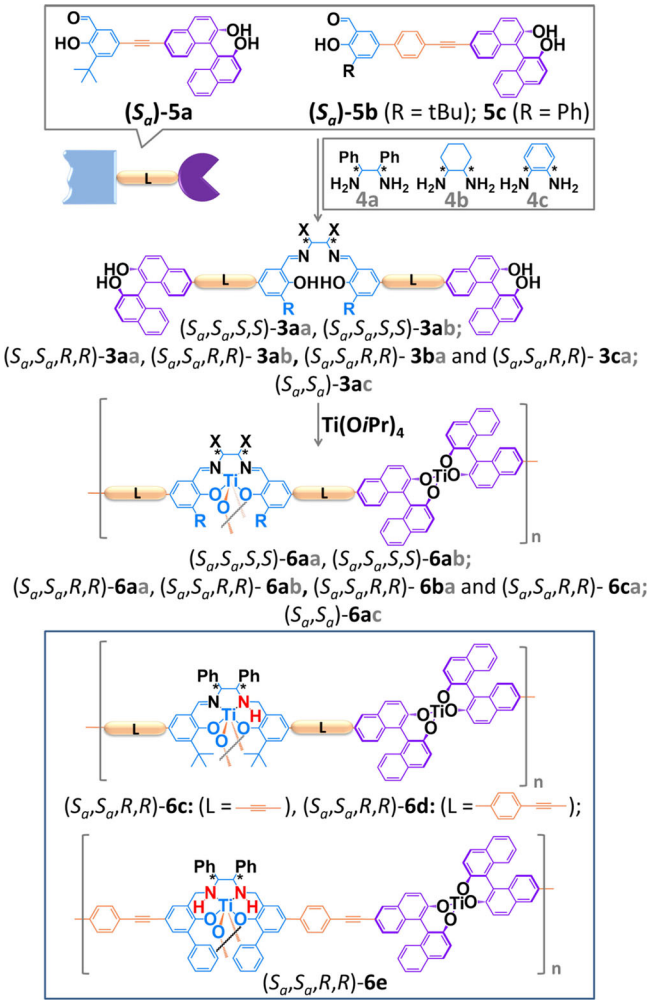


Scheme 2. a) Privileged Ti-complexes in the ARO reactions; b) the strategy to design 2D robust cross-linked titanium coordination assemblies containing two chiral centers derived from the privileged Ti-complexes.

chiral building block (S_a)-**5a** was readily accessible in good isolated yield *via* Pd-catalyzed Sonogashira coupling of the corresponding (S_a)-BINOL and the salicylic aldehyde derivative, and was further successfully transformed into a range of chiral heteroditopic ligands (S_a,S_a,*R*,*R*)- or (S_a,S_a,*S*,*S*)-**3aa** and **3ab** as well as (S_a,S_a)-**3ac** by condensation reactions with chiral 1,2-diphenylethane-1,2-diamine (**4a**), cyclohexane-1,2-diamine (**4b**) or benzene-1,2-diamine (**4c**), respectively (Scheme 2, for details see the Supporting Information, Scheme S6).

In order to explore the effects of linker length, chiral building block (S_a)-**5b** and relevant heteroditopic ligand (S_a,S_a,*R*,*R*)-**3ba** with an additional phenylene spacer were also synthesized by following a similar procedure. In addition, a chiral building block (S_a)-**5c** bearing a phenyl instead of *ortho*-substituent *t*-Bu group was synthesized to explore the steric effect of the group. In consideration of the findings that Ti complexes bearing salalen ligands (**2b**, with one imine and one amine functionality, Scheme 2a) and salan ligands (**2c**, with two amine functionalities, Scheme 2a) exhibit superior catalytic activity and enantioselectivity than their salen analogues (**2a**) in several homogeneous asymmetric transformations,[14] mono-reduced heteroditopic ligands (S_a,S_a,*R*,*R*)-**3c** and **d** with two kinds of acetylenic linkers and fully reduced salan ligand (S_a,S_a,*R*,*R*)-**3e** were also prepared (see the Supporting Information, Schemes S10 and S11).

With these chiral heteroditopic ligands in hand, a series of chiral titanium coordination assemblies was readily synthesized *via* metal coordination of chiral ligands **3** with Ti(O-*i*-Pr)$_4$ in a one-pot manner, followed by the addition of 40 equivalents of water (Scheme 3). Brick-red precipitates **6** were thereby obtained in quantitative yields after simply filtration, and were characterized by infrared spectroscopy and elemental analysis, which indicated the chemical compositions of the solids consistent with the expected structures. Scanning electron microscopy (SEM) images revealed that all coordination polymeric solids **6** consist of irregular micrometer-sized particles (Figure 1b), while powder X-ray diffraction (PXRD) patterns also confirmed the amorphous morphologies (see the Supporting Information, Figures S1–S18). After careful characterization, all newly prepared chiral titanium coordination assemblies **6** were found to be completely insoluble in water and various selected solvents, such as dichloromethane, chloroform, 1,4-dioxane, diethyl ether, tetrahydrofuran, toluene, benzene, xylene, and thus fulfil one of the requirements of heterogeneous catalysis.



Scheme 3. Synthesis of chiral titanium metal-organic assemblies **6**.

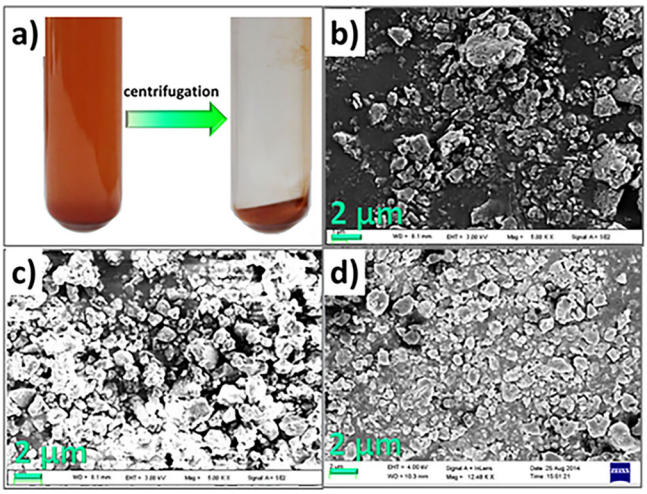
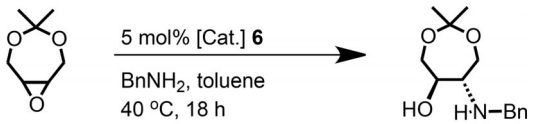


Figure 1. a) A suspension of the catalytic ARO reaction mixture with additional ether and the precipitates obtained after centrifugation; SEM morphologies of b) freshly prepared titanium coordination assemblies (S_a,S_a,*R*,*R*)-**6d** and the recovered polymeric catalysts after c) 6th run and d) 20th run.

Catalytic Activity of the Self-Supported Chiral Catalysts in ARO Reactions

In consideration that optically pure 2-aminobutane-1,3,4-triol (ABT) is an extremely versatile precursor to synthesize a number of biologically active molecules and drugs (e.g., phytosphingosine, statine and nelfinavir),[15] and could be simply accessible by deprotection of the products formed by aminolysis of the *meso*-epoxide 3,5,8-trioxabicyclo[5.1.0]octane (**7**) with the strong nucleophile benzylamine, therefore, the stability, catalytic activity and enantioselectivity of all newly developed chiral titanium coordination assemblies **6** were then investigated in this challenging and useful transformation (Table 1). Initially, 5 mol% solid (S_a,S_a,*R*,*R*)-**6aa** was used to optimize the reaction conditions. To our delight, a quantitative yield with good enantioselectivity of product **8** was observed (84% *ee*, entry 1), when the reaction was carried out with 1.05 equiv. benzylamine, 0.4 equiv. H_2O as additive in 0.5 mL toluene at 40 °C for 18 h. The reactions in other solvents under otherwise identical conditions afforded inferior outcomes (see the Supporting Information, Table S1). Since water often exhibits an important yet somewhat intriguing role in chiral Ti catalysis,[12a,d] the impact on the aminolysis in the presence of a certain amount of water was also investigated. However, deviations of the amount of water from 0.4 equiv. all resulted in inferior results (entries 2 and 3). When the reaction was carried at room temperature, only a trace amount of product **8** could be detected (see the Supporting Information, Table S1). The amount of benzylamine was also found to affect the reaction, only 81% yield was obtained with 1 equiv. amine, whereas, a slight lower *ee* value was observed when the amount of benzylamine was increased to 1.2 equiv. (see the Supporting Information, Table S1).

Table 1. Optimization of the reaction conditions.[a]



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Entry	[Cat.]	H_2O [mmol]	Yield [%][b]	*ee* [%]
1	(S_a,S_a,*R*,*R*)-**6aa**	0.4	99	84
2	(S_a,S_a,*R*,*R*)-**6aa**	1.0	97	78
3	(S_a,S_a,*R*,*R*)-**6aa**	0.2	91	67
4	(S_a,S_a,*S*,*S*)-**6aa**	0.4	99	63
5	(S_a,S_a,*R*,*R*)-**6ab**	0.4	91	59
6	(S_a,S_a,*S*,*S*)-**6ab**	0.4	93	43
7	(S_a,S_a)-**6ac**	0.4	85	77
8	(S_a,S_a)-**6bc**	0.4	80	72
9	(S_a,S_a)-**6cc**	0.4	83	79
10	(S_a,S_a,*R*,*R*)-**6ba**	0.4	99	90
11	(S_a,S_a,*R*,*R*)-**6ca**	0.4	99	85
12	(S_a,S_a,*R*,*R*)-**6c**	0.4	98	90
13	(S_a,S_a,*R*,*R*)-**6d**	0.4	99	91
14	(S_a,S_a,*R*,*R*)-**6e**	0.4	95	87
15	(*R*,*R*)-**2a**	0.4	20	13
16	(*R*,*R*)-**2b**	0.4	trace	–
17	(S_a,S_a,*R*,*R*)-**6f**	0.4	53	85
18	(*R*,*R*)-**9**	0.4	trace	–

[a] *Reaction conditions:* 1 mmol scale with 5 mol% catalyst **6**, 1.05 mmol $BnNH_2$, 0.4 mmol H_2O in 0.5 mL selected solvent at 40 °C for 18 h.
[b] Isolated yield.

With the optimized reaction conditions in hand, the catalytic activity and enantioselectivity of the rest Ti-containing metal-organic assemblies were then examined. Due to matching/mismatching of various steric and chiral units as well as the length of the linker, significant variations in catalytic activity and enantioselectivity of the reactions were observed. When solid (S_a,S_a,*S*,*S*)-**6aa** with the opposite chirality in the salen moiety was used, only a 63% *ee* value was found with product **8** (entry 4), which suggested that the cooperation of two kinds of chirality is crucial to achieve good enantioselectivity. Similar conclusions were drawn from the catalytic results obtained with the solids (S_a,S_a,*R*,*R*)-**6ab** and (S_a,S_a,*S*,*S*)-**6ab** derived from two enantiomers of cyclohexane-1,2-diamine, whereas, in contrast with their diphenylethane analogues, inferior outcomes were found in both cases (entries 5 and 6). Furthermore, catalysts (S_a,S_a)-**6ac**, (S_a,S_a)-**6bc** and (S_a,S_a)-**6cc**, which all contain chirality only in the BINOL moieties, also produced similar unsatisfactory results (Table 1, entries 7–9), clearly indicating that the solid (S_a,S_a,*R*,*R*)-**6aa** is a chiral cooperative cata-

lyst. To our delight, with the polymer (S_a,S_a,*R*,*R*)-**6ba** bearing a longer spacer, the *ee* value could be further enhanced to 90% (entry 10). When polymeric catalyst (S_a,S_a,*R*,*R*)-**6ca** with less-bulky phenyl substituents instead of *t*-Bu groups in the salen moiety was applied, a slightly inferior *ee* value was obtained (85% *ee*, entry 11). When the salalen analogues (S_a,S_a,*R*,*R*)-**6c** and (S_a,S_a,*R*,*R*)-**6d** were involved, thelonger linker also revealed a higher *ee* value (91% *ee vs.* 90% *ee*, entries 12 *vs.* 13). In comparison with its salen analogue, the fully reduced salan solid (S_a,S_a,*R*,*R*)-**6e** only gave a slightly higher *ee* value (87% *ee*, entry 14). In order to probe the true catalytic center of two Ti-containing fragments in these polymeric solids, homogeneous complexes **1** and **2** were also involved in the control test under the optimized reaction conditions. Homogeneous dimeric Ti-salen and Ti-salalen complexes (*R*,*R*)-**2a** and (*R*,*R*)-**2b** (R = *t*-Bu, R′ = Ph) gave much worse results (entries 15 and 16). The outcomes clearly highlighted that the Ti-BINOLate moiety not only functioned as "hinge" to support the titanium coordination assemblies, but also acted as true active catalytic sites for the ARO aminolysis transformation.

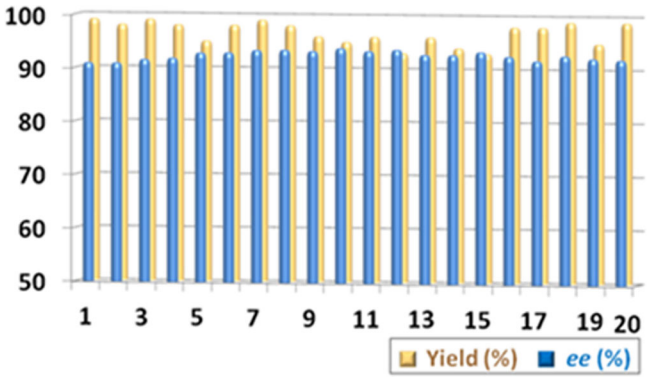


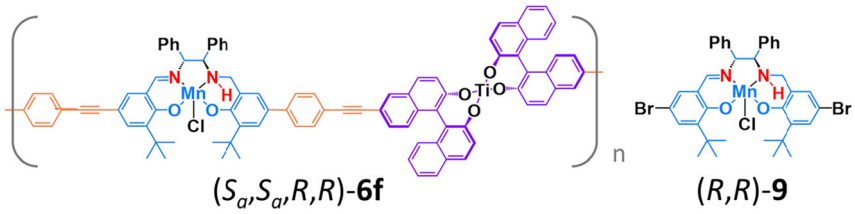
Figure 2. Recycling and reuse of the polymer catalyst (S_a,S_a,*R*,*R*)-**6d** in the catalytic ARO reaction of *meso*-epoxide **7** with benzylamine under the standard reaction conditions [each run was carried out on a 1 mmol scale with 5 mol% solid (S_a,S_a,*R*,*R*)-**6d**, 1.05 mmol $BnNH_2$, 0.4 mmol H_2O in 0.5 mL toluene at 40 °C for 18 h].

Reusability of the Self-Supported Chiral Catalysts

After completion of the ARO reaction, an aliquot of 8 mL ether was added to the reaction mixture, and the insoluble polymeric catalysts **6** were readily recovered quantitatively by centrifugation and decantation (Figure 1a). Consequently, the stability and reusability of the recovered (S_a,S_a,*R*,*R*)-**6** were then investigated. Upon completion of each run of aminolysis, the recovered catalyst was washed with ether and then recharged with the substrates, toluene and water for the next run under the standard reaction conditions. To our delight, catalyst (S_a,S_a,*R*,*R*)-**6d** could be reused for more than twenty cycles under the standard reaction conditions without significant loss in the yield and enantioselectivity (Figure 2). Interestingly, slightly increased *ee* values of the product were observed after the third cycle, which could be further enhanced to 94.1% *ee* at the 10th run. No obvious deterioration was found in the later runs (92.0–93.9% *ee*), which clearly indicated that the titanium coordination assemblies are relatively robust in the catalysis. In comparison with freshly prepared polymeric solids (S_a,S_a,*R*,*R*)-**6d**, similar irregular micrometer-sized particles were observed for the recovered catalyst samples after the 6th and 20th runs (Figure 1b *vs.* c and d). According to a previously reported procedure,[8b] inductively coupled plasma-atomic emission spectroscopy (ICP-AES) was applied to detect the possible metal leaching in the supernatant phase during the catalyst recycling experiments. Remarkably, after reaction completion, ether addition and filtration, no Ti species was detected in the filtrates (Supporting Information), which further attests to the superior thermal stability and robustness of these metallic-organic assemblies.

Linkage Effects

Consequently, we turned our attention to further explore the reasons for the good stability and enantioselectivity of these solid catalysts containing two types of chiral moieties. As expected, the oxygen (μ-oxo) bridge cross-linked dimeric Ti-salalen moieties between two neighboring 1D polymer chains may enhance the stability of the polymers. In order to further investigate this type of linkage effect, a hetero-bimetallic-organic assembly (S_a,S_a,*R*,*R*)-**6f** was therefore synthesized (Scheme 4). In consideration that there is no oxygen bridge formation within Mn-salalen complexes and no catalytic activity was observed with complex (*R*,*R*)-**2b** in the ARO reactions, ligand (S_a,S_a,*R*,*R*)-**3d** was first reacted with $Mn(OAc)_2$ and LiCl to form a bridging ditopic ligand containing the Mn-salalen core. Without isolation, the ditopic ligand successively coordinated with Ti(O-*i*-Pr)$_4$ in a one-pot manner and afford hetero-bimetallic assemblies (S_a,S_a,*R*,*R*)-**6f** in good yield (see the Supporting Information, Scheme S13). In light of the fact that hetero-bimetallic solid (S_a,S_a,*R*,*R*)-**6f** was also insoluble in the selected organic solvents, it was directly applied in the ARO reaction to test its catalytic efficiency and stability. However, despite the good enantioselectivity, only a low yield of product **8** was obtained (53% yield with 85% *ee*, entry 15). After reaction completion, centrifugation and decantation procedures were also applied to recover the catalyst, and only 50% (S_a,S_a,*R*,*R*)-**6 f** was recovered, which clearly indicated



Scheme 4. Hetero-bimetallic self-supported catalysts (S_a,S_a,R,R)-**6f** and related Mn-salalen complex (R,R)-**9**.

the stability of bimetallic assemblies dropped dramatically without the linkage of an oxygen bridge. ICP-AES analysis found there were Mn and Ti species in the filtrate after the hetero-bimetallic polymer recovery. Furthermore, when the recovered solid (S_a,S_a,R,R)-**6f** was reused for the second run, only a trace amount of product **8** was detected. In order to exclude the effect of Mn-salalen on enantioselectivity, Mn-salalen complex **9** (Scheme 4) was also synthesized[16] and examined in the ARO reaction as a homogeneous catalyst, and no reaction occurred even with elevated temperature and extended reaction time (entry 16). All these outcomes further supported the assumption that the oxygen-bridge linkage increased the robustness of titanium coordination assemblies.

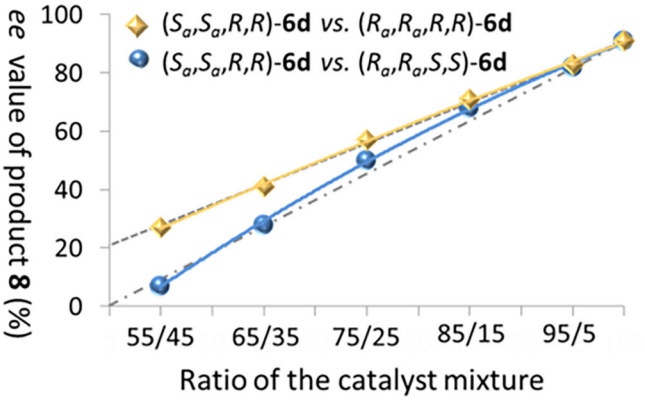


Figure 3. NLE study with the enantioisomers or diastereoisomrs of polymeric solids **6d** in the asymmetric ARO of epoxide **7** with benzylamine.

Cooperative Effects

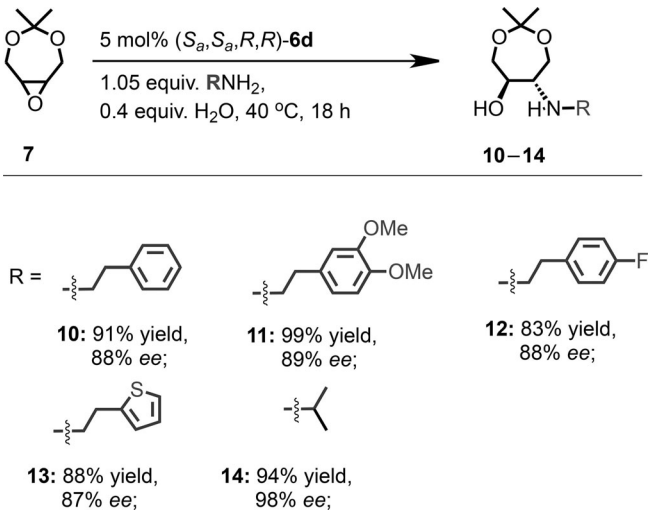
In the case of diastereomeric homochiral or heterochiral catalytic species, which are generated from the coordination of the metal ions with more than one chiral ligand with the same or opposite configurations, a non-linear effect (NLE) is always observed in a plethora of asymmetric reactions.[17] Although the exact reason for the observation of an NLE in enantioselective catalytic systems varies from case to case, an NLE effect constitutes a powerful tool to investigate the nature and the aggregation behavior of the catalytic protagonist involved in asymmetric reactions.[18] In consideration of thermodynamic stabilities and possible dynamic coordination/disassociation properties of titanium coordination assemblies, the NLE of the present heterogeneous ARO asymmetric catalysis was examined with the selected mixture of enantioisomers or diastereoisomers of (S_a,S_a,R,R)-**6d** under the optimized reaction conditions. Therefore, two other isomers (R_a,R_a,S,S)-**6d** and (R_a,R_a,R,R)-**6d** were synthesized for this purpose. Initially, a series of the mixture of enantiomeric solids (S_a,S_a,R,R)-**6d** and (R_a,R_a,S,S)-**6d** at different ratios was applied as heterogeneous catalyst. As shown in the Figure 3, unlike previous reports on homogeneous cases,[13a] only a slightly convex plot (blue line) was observed, which clearly demonstrated that there is no obvious NLE in the present heterogeneous catalytic system. This result again confirms that our titanium coordination assemblies are relatively robust, no apparent metal dissociation and reassembly takes place for the enantioisomers of polymeric solids under the reaction conditions.

In light of the fact that dimeric Ti-salen complex **2b** is ineffective for the ARO with amine, diastereoisomers (S_a,S_a,R,R)-**6d** and (R_a,R_a,R,R)-**6d**, which contain the same steric chiral configuration at the Ti-salen moiety but the opposite one at the Ti-BINOLate part, were selected for the further investigation. To our delight, a linear line plot (yellow line in Figure 3) was observed with the diastereoisomers on varying the ratio under the standard reaction conditions; however, the line did not cross the origin of the axis with an obvious intercept. Such a phenomenon revealed that although the Ti-salen moiety is not active to catalyze the ARO transformation, the chirality at salen still plays the crucial role. Only chiral cooperative titanium coordination assemblies achieved the best results, which is consistent with the results obtained with catalysts (S_a,S_a)-**6ac**, (S_a,S_a)-**6bc** and (S_a,S_a)-**6cc** in which no chiral center existed in the salen moieties (entries 7–9). One plausible explanation is that the rigid configuration of the central chiral salen strongly influenced the spatial orientation of two chiral BINOL terminals, which may be further fixed during the coordination assembly.

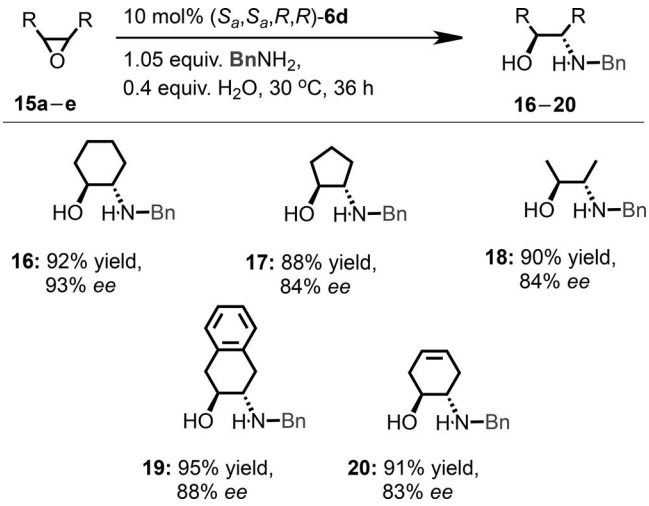
Substrates Scope with Other *meso*-Epoxides and Nucleophilic Aliphatic Amines

Although ABT is easily obtained after debenzylation of **8** with Pd/C and H_2, and plenty of substituted amino alcohols and bioactive molecules are therefore accessible after certain transformations,[15] we still attempted to investigate the stability and scope of the current self-supported catalytic system in the presence of other nucleophilic aliphatic amines. Especially, aliphatic amines are rarely successfully applied in the homogeneous desymmetrization of *meso* epoxides which is probably caused by possible deactivation of the Lewis acidic catalyst by its irreversible complex formation with the Lewis basic amine and/or with the generated amino alcohol.[19] To our delight, in the presence of 5 mol% (S_a,S_a,*R*,*R*)-**6d** under the standard reaction conditions, all selected aliphatic amines including heterocyclic substances reacted smoothly and produced the corresponding products **10**–**14** in good yields and enantioselectivities (Scheme 5), which further confirmed the stability and feasibility of the newly developed self-supported catalysts.

In addition, a series of *meso* epoxides **15a–e** was also selected to further to explore the catalytic efficiency of the solid catalyst (S_a,S_a,*R*,*R*)-**6d**. It has to be noted that the selected challenging *meso* epoxides including **15a** without chelating groups are scarcely applied in the ARO reactions due to their low reactivity.[12b] To our delight, in the presence of 10 mol% solid (S_a,S_a,*R*,*R*)-**6d**, 1.05 mmol $BnNH_2$, 0.4 mmol H_2O in 0.5 mL toluene at 30 °C for 36 h, these *meso* substrates were smoothly converted into desired the amino alcohols **16**–**20** with good to excellent yields and enantioselectivities (Scheme 6). Remarkably, in comparison with the known catalytic system for the ARO of **15a** with amine,[20] better results could be obtained with the solid catalyst (S_a,S_a,*R*,*R*)-**6d** under the identical reaction conditions. In the case of a *meso* epoxide containing olefin moiety, product **20** with the preserved double bond could be obtained in good yield and enantioselectivity, which was capable of undergoing further transformations.



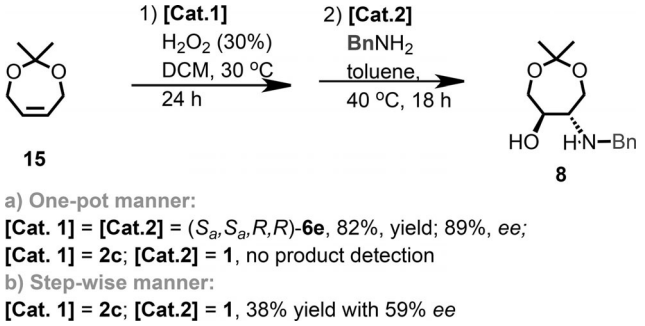
Scheme 5. ARO reactions of epoxide **7** with aliphatic amines using the polymer catalyst (S_a,S_a,*R*,*R*)-**6d**.



Scheme 6. ARO reactions of epoxide with benzylamine using the polymer catalyst (S_a,S_a,*R*,*R*)-**6d**.

The Feasibility of Self-Supported Chiral Catalysts in One-Pot Sequential Tandem Reactions

Finally, taking account that Ti-salalen and salan complexes are also known as highly efficient catalysts towards epoxidation reactions of olefins,[21] the feasibility of the self-supported catalysts **6** in directly amino alcohol syntheses from olefins in a one-pot manner was therefore tested (Scheme 7). After intensive investigation, solid (S_a,S_a,*R*,*R*)-**6e** was found to be effective catalyst for the transformation of olefin **15** to product **8** after sequential tandem epoxidation by H_2O_2 and ARO reaction with $BnNH_2$, and an 82% yield with 89% *ee* was obtained at a mild temperature



Scheme 7. Enantioselective catalytic transformation of olefin **15** to product **8** in a one-pot manner with self-supported catalyst (S_a,S_a,*R*,*R*)-**6e**.

within 24 h. In comparison, when homogeneous Ti-salen complex **2c** (R = R′ = Ph) and BINOLate-Ti complex **1** were applied under identical one-pot reaction conditions, no product was detected. When the epoxidation of olefin **15** catalyzed by Ti-salen complex **2c** with H_2O_2 as oxidant was first carried out, and the stirred solution of BINOLate-Ti complex **1** and $BnNH_2$ was added drop-wise into the above resulting mixture after epoxidation, still only a 38% yield with 59% *ee* was obtained for product **8**, which clearly highlighted the advantage and high stability of our newly developed self-supported catalyst.

Conclusions

In conclusion, by utilizing the oxygen-bridge in dimeric μ-oxo-Ti-salen complexes as an efficient cross-linker, we have successfully developed a novel series of chiral titanium coordination assemblies with the heteroditopic bridging ligands derived from BINOL and salen derivatives *via* coordination polymerization, which were fully characterized by IR, elemental analysis, XRD and microscopic studies. In light of their insolubility in most organic solvents and water, these titanium coordination assemblies were successfully applied as robust self-supported catalysts in the asymmetric ring opening (ARO) of *meso*-epoxides with amines, even tolerating various nucleophilic aliphatic amines. Remarkably, due to the linkage effects and the cooperation of two kinds of chiral Ti moieties in the metal-organic assemblies, along with excellent catalytic activity and enantioselectivity, the self-supported chiral catalysts demonstrated very high stability, and could be reused for more than 20 runs without obvious loss in the yield and enantioselectivity. With the assistance of ICP-AES, an NLE study as well as the control experiments involving the hetero-bimetallic analogue as a catalyst, the "oxygen-bridge" linkage effect in titanium coordination assemblies was found to enhance their robustness, and no apparent metal disassembly and reassembly took place during the reaction. In addition, although Ti-BINOLate moieties were confirmed as the active catalytic centers, the configuration of the salalen moiety, which was not directly responsible for the enantioselectivity, shown a strong cooperative effect on the ARO reactions. The unique structure of these titanium coordination assemblies also revealed an interesting feasibility in the direct amino alcohol syntheses from olefins in a one-pot manner, whereas, the corresponding homogeneous catalyst failed under identical reaction conditions, which further highlighted the advantage of the newly developed self-supported catalyst. Applications in other challenging asymmetric cascade reactions with these cooperative titanium coordination assemblies are still under the investigation in our laboratory.

Experimental Section

General Information

All commercial reagents were used directly without further purification, unless otherwise noted. ^{1}H, ^{13}C NMR spectra were recorded on Jeol ECA-400 and Bruker 400 DRX spectrometers. GC-MS spectra were recorded on Agilent technologies 1890A GC system and 5975C inert MSD with Triple-Axis Detector. ESI-MS were recorded on a Bruker micrOTOF II instrument. IR spectra were recorded on an AVATAR FT-IR 360 instrument. The enantioselectivity were determined by HPLC analyses with selected chiral columns. HPLC analyses were carried out on a JASCO 1580 liquid chromatograph with a JASCO CD-1595 detector and a JASCO 2089 liquid chromatograph with a JASCO 2075 detector. Powder XRD was recorded on a Bruker AXS D8. SEM spectra were recorded on a FEI Nova NanoSEM 450.

Synthesis of the Titanium Coordination Assemblies

For clarity, the detail synthetic procedures for ligands (S_a,S_a,*R*,*R*)-**3aa**, (S_a,S_a,*S*,*S*)-**3aa**, (S_a,S_a,*R*,*R*)-**3ba**, (S_a,S_a,*R*,*R*)-**3ab**, (S_a,S_a,*S*,*S*)-**3ab**, (S_a,S_a,*R*,*R*)-**3ca**, (S_a,S_a)-**3ac**, (S_a,S_a)-**3bc**, (S_a,S_a)-**3cc**, (S_a,S_a,*R*,*R*)-**3c**, (S_a,S_a,*R*,*R*)-**3d**, (R_a,R_a,*R*,*R*)-**3d**, (R_a,R_a,*S*,*S*)**3 d** and (S_a, S_a, *R*,*R*)-**3e** are presented in the Supporting Information.

General Procedure to Synthesize the Self-Supported Catalysts 6

Ti(O-*i*-Pr)$_4$ (1 mL, 0.5 M in CH_2Cl_2, 0.5 mmol) was added to a solution of ligand **3** (0.25 mmol) in CH_2Cl_2 (5 mL) under stirring at room temperature in a Schlenk tube. The orange solid appeared immediately upon addition of Ti(O-*i*-Pr)$_4$. After stirring for 4 h, 380 μL H_2O were added, the resulting mixture was stirred for another 12 h. The solvent in the mixture was removed under reduced pressure. The respective catalyst **6** was washed with diethyl ether and isolated as an orange solid in quantitative yield by filtration.

Polymer (S_a,S_a,*R*,*R*)-6aa: yield: 99%; orange solid; IR (KBr pellet): ν = 3432.97, 3059.79, 2955.16, 2348.88, 1617.75, 1540.5, 1497.37, 1457.25, 1435.37, 1405.83, 1384.7, 1359.64, 1341.17, 1277.2, 1242.27, 973.1, 819.72, 750.26, 726.03, 697.6, 575.21, 515.22 cm^{-1}; elemental analysis calcd. (%) for $(C_{80}H_{58}N_2O_8Ti_2{\cdot}CH_2Cl_2)_n$: C 71.75; H 4.46; N 2.07; found: C 71.32, H 4.74, N 2.04.

Polymer (S_a,S_a,*S*,*S*)-6aa: yield: 99%; orange solid; IR (KBr pellet): ν = 3432.96, 3059.78, 2348.86, 1617.74, 1540.5, 1497.36, 1435.37, 1405.81, 1384.74, 1359.61, 1341.16, 1277.20, 1242.26, 973.11, 819.71, 750.26, 726.00, 697.61, 575.20, 515.22 cm^{-1}; elemental analysis calcd. (%) for $(C_{80}H_{58}N_2O_8Ti_2{\cdot}CH_2Cl_2)_n$: C 71.75; H 4.46; N 2.07; found: C 71.28, H 4.78, N 2.05.

Polymer (S_a,S_a,*R*,*R*)-6ab: yield: 99%; orange solid; IR (KBr pellet): ν = 3447.41, 2348.83, 2949.98, 1684.77, 1653.88, 1647.44, 1617.54, 1559.55, 1541.27, 1458.13, 1278.42, 669.66; elemental analysis calcd. (%) for $(C_{72}H_{56}N_2O_8Ti_2{\cdot}3\,CH_2Cl_2)_n$: C 63.09, H 4.38, N 1.96; found: C 62.78, H 4.80, N 2.17.

Polymer (*S*$_a$,*S*$_a$,*S*,*S*)-6ab: yield: 96%; orange solid; IR (KBr pellet): ν = 3449.40, 2949.94, 1684.81, 1653.92, 1647.45, 1617.55, 1541.29, 1465.56, 1458.13, 1387.49, 1278.45, 669.21; elemental analysis calcd. (%) for $(C_{72}H_{56}N_2O_8Ti_2{\cdot}4\ CH_2Cl_2)_n$: C 60.35, H 4.26, N 1.85; found: C 60.11, H 4.65, N 1.99.

Polymer (*S*$_a$,*S*$_a$,*R*,*R*)-6ba: yield: 99%; orange solid; IR (KBr pellet): ν = 3444.63, 2954.09, 2348.97, 1614.33, 1462.46, 1384.47, 1342.26, 1243.74, 668.24, 526.18 cm^{-1}; elemental analysis calcd. (%) for $(C_{92}H_{66}N_2O_8Ti_2{\cdot}CH_2Cl_2)_n$: C 74.86; H 4.40; N 1.80; found: C 74.41, H 4.73, N 1.80.

Polymer (*S*$_a$,*S*$_a$,*R*,*R*)-6ca: yield: 99%, orange solid; IR (KBr pellet): ν = 3649.95, 3629.25, 3619.60, 3587.85, 3567.60, 3447.59, 1685.10, 1675.92, 1670.44, 1663.41, 1654.13, 1647.57, 1636.91, 1628.95, 1617.80, 1610.59, 1559.87, 1458.56, 1074.26, 669.13, 617.46, cm^{-1}; elemental analysis calcd. (%) for $(C_{96}H_{58}N_2O_8Ti_2{\cdot}CH_2Cl_2)_n$: C 75.25; H 3.91; N 1.81; found: C 74.66, H 3.93, N 1.79.

Polymer (*S*$_a$,*S*$_a$)-6ac: yield: 99%; orange solid; IR (KBr pellet): ν = 3418.97, 3056.57, 2960.73, 2909.81, 1618.96, 1583.02, 1532.11 1460.23, 1442.26, 1340.43, 1280.53, 1244.59, 1169.71, 972.04, 822.29, 753.41; elemental analysis calcd. (%) for $(C_{72}H_{56}N_2O_8Ti_2{\cdot}3\ CH_2Cl_2)_n$: C 60.59, H 3.88, N 1.86; found: C 59.75, H 4.11, N 1.94.

Polymer (*S*$_a$,*S*$_a$)-6bc: yield: 95%; orange solid; IR (KBr pellet): ν = 3428.07, 3049.26, 2948.33, 2929.81, 2902.44, 1628.44, 1590.52, 1532.11, 1248.80, 1238.22, 1153.85, 992.48, 936.72, 750.21; elemental analysis calcd. (%) for $(C_{84}H_{58}N_2O_8Ti_2{\cdot}2\ H_2O)_n$: C 74.45, H 4.61, N 2.07; found: C 74.17, H 5.03, N 1.96.

Polymer (*S*$_a$,*S*$_a$)-6cc: yield: 93%; orange solid; IR (KBr pellet): ν = 3436.90, 3044.27, 2909.81, 1639.20, 1581.71, 1529.82, 1433.82, 1399.23, 1280.51, 1241.29, 1120.93, 998.32, 954.16, 961.56, 754.49, 583.20; elemental analysis calcd. (%) for $(C_{88}H_{50}N_2O_8Ti_2{\cdot}2\ H_2O)_n$: C 75.76, H 3.90, N 2.01; found: C 75.44, H 4.25, N 1.99.

Polymer (*S*$_a$,*S*$_a$,*R*,*R*)-6c: yield: 99%; orange solid; IR (KBr pellet): ν = 3422.91, 2953.90, 2349.567, 1618.80, 1586.17, 1459.23, 1440.58, 1384.1, 1340.43, 1242.35, 1157.08, 1075.85, 1002.8, 974.63, 821.29, 749.91, 698.72, 576.44 cm^{-1}; elemental analysis calcd. (%) for $(C_{80}H_{60}N_2O_8Ti_2{\cdot}CH_2Cl_2)_n$: C 71.64, H 4.60, N 2.06; found: C 71.28, H 4.57, N 2.03.

Polymer (*S*$_a$,*S*$_a$,*R*,*R*)-6d: yield: 99%; orange solid; IR (KBr pellet): ν = 3448.92, 2348.83, 1618.66, 1459.75, 1242.00, 818.24, 579.63, cm^{-1}; elemental analysis calcd. (%) for $(C_{92}H_{68}N_2O_8Ti_2{\cdot}CH_2Cl_2)_n$: C 73.96; H 4.67; N 1.85; found: C 73.67, H 4.97, N 1.69.

Polymer (*R*$_a$,*R*$_a$,*R*,*R*)-6d: yield: 99%; orange solid; IR (KBr pellet): ν = 3448.92, 2353.31, 1626.00, 1617.34, 1430.80, 1421.09, 1209.61, 1103.45, 927.02, 880.34, 781.11, 774.00 579.63 cm^{-1}; elemental analysis calcd. (%) for $(C_{92}H_{68}N_2O_8Ti_2{\cdot}CH_2Cl_2)_n$: C 73.96; H 4.67; N 1.85; found: C 73.60, H 4.71, N 1.68.

Polymer (*R*$_a$,*R*$_a$,*S*,*S*)-6d: yield: 99%; orange solid; IR (KBr pellet): ν = 3448.90, 2348.85, 1618.66, 1617.34, 1430.82, 1242.00, 818.24, 579.63, cm^{-1}; elemental analysis calcd. (%) for $(C_{92}H_{68}N_2O_8Ti_2{\cdot}CH_2Cl_2)_n$: C 73.96; H 4.67; N 1.85; found: C 73.61, H 4.80, N 1.79.

Polymer (*S*$_a$,*S*$_a$,*R*,*R*)-6e: yield: 99%; orange solid; IR (KBr pellet): ν = 2537.19, 2350.21, 1626.01, 1619.44, 1427.82, 1421.09, 1439.25, 1209.62, 1102.44, 927.92, 878.24, 781.23, 773.92. cm^{-1}; elemental analysis calcd. (%) for $(C_{96}H_{64}N_2O_8Ti_2{\cdot}1.5\ CH_2Cl_2)_n$: C 73.34, H 4.23, N 1.75; found: C 72.95, H 4.19, N 1.72.

Synthesis of (*S*$_a$,*S*$_a$,*R*,*R*)-6f

To a hot solution of salen ligand (*S*$_a$,*S*$_a$,*R*,*R*)-**3ba** (139 mg, 0.1 mmol) in 2 mL of EtOH, $Mn(OAc)_2{\cdot}4H_2O$ (49 mg, 0.2 mmol) was added as a solid in one portion. The reaction mixture turned brown immediately. The mixture was heated to reflux for 30 min under an atmosphere of air and then cooled to room temperature. A solution of LiCl (0.212 g, 5.00 mmol) in EtOH (2 mL) was added, and the mixture was heated to reflux for an additional 30 min. Solvent was removed under vacuum and 5 mL DCM were added. To this dark brown solution, Ti(O-*i*-Pr)$_4$ (0.2 mL, 0.5 M in CH_2Cl_2, 0.1 mmol) was added. The brown solid appeared immediately upon adition of Ti(O-*i*-Pr)$_4$. After stirring for 4 h, 80 µL H_2O were added, the resulting mixture was stirred for another 12 h. The solvent in the mixture was removed under reduced pressure. The brown solid catalyst **6f** was washed with diethyl ether and isolated in quantitative yield by filtration. **(*S*$_a$,*S*$_a$,*R*,*R*)-6f:** yield: 99%; brown solid; IR (KBr pellet): ν = 3448.02, 2925.51, 2360.40, 2342.17, 1617.86, 1529.25, 1456.84, 1424.02, 1403.98, 1384.79, 1299.52, 1172.37, 1075.24, 735.12, 696.93, 668.77, 576.79, 421.98 cm^{-1}; elemental analysis calcd (%) for $(C_{92}H_{68}ClMnN_2O_6Ti\ {\cdot}3\ CH_2Cl_2)_n$: C 67.49; H 4.41; N 1.66; found: C 67.02, H 4.77, N 1.78.

Typical Procedure for Heterogeneous Ring-Opening Reactions and Catalyst Recycling

To a mixture containing the self-supported catalyst solid in dry toluene (0.5 mL), benzylamine (117 mg, 1.1 mmol) was added under a nitrogen atmosphere at room temperature. After stirring for 30 min, water (4 µL, 0.22 mmol), and substrate **7** (144 mg, 1.0 mmol) were successively injected into the solution, and the mixture was warmed up to 40 °C and stirred for 12 h. The solution was diluted with ethyl ether (8 mL) and centrifuged to recycle the catalyst for 3 times. The clear solution was separated and after concentration the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate/Et_3N = 2/1/0.15) to afford the amino alcohol product as a colorless sticky liquid. The remaining insoluble catalyst was dried under vacuum and reused in the next run. The *ee* values of **8**, **10**–**13**, and **15**–**19** were determined by HPLC analysis after di-acetylation with acetic anhydride (for details see the Supporting Information).

(5*R*,6*S*)-6-(Benzylamino)-2,2-dimethyl-1,3-dioxepan-5-ol (8):[12d] ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.42–7.28 (m, 5H), 3.98 (d, J = 13.2 Hz, 1H), 3.88–3.80 (m, 3H), 3.65–3.52 (m, 3H), 2.61 (td, J = 5.4, 1.6 Hz, 1H), 1.39 (s, 3H), 1.38 (s, 3H); MS (EI): m/z = 251.0, calcd. for $C_{14}H_{21}NO_3$: 251.2; $[\alpha]_D^{20}$: +56 (c 0.5, $CHCl_3$) for the compound with 93% *ee*.

(5*R*,6*S*)-2,2-Dimethyl-6-(phenethylamino)-1,3-dioxepan-5-ol (10):[1] ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.34–7.28 (m, 2H), 7.23 (dd, J = 7.1, 5.1 Hz, 3H), 3.73 (ddd, J = 14.3, 12.5, 2.1 Hz, 2H), 3.61–3.40 (m, 3H), 3.13–3.00 (m, 1H), 2.92–2.72 (m, 3H), 2.54 (td, J = 5.8, 2.0 Hz, 1H), 1.34 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$, 298 K): δ = 139.68, 128.63, 128.43, 126.19, 101.25, 71.74, 62.21, 61.96, 59.24, 48.44, 36.73, 24.60; HR-MS (ESI/TOF): m/z = 266.1751,

calcd. for $C_{15}H_{24}NO_3$ $[M+H]^+$: 266.1756; $[\alpha]_D^{20}$: +12 (*c* 0.5, $CHCl_3$) for the compound with 88% *ee*.

(5,6*S*)-6-[(3,4-Dimethoxyphenethyl)amino]-2,2-dimethyl-1,3-dioxepan-5-ol (11): ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 6.73 (d, *J* = 8.6 Hz, 1H), 6.68 (d, *J* = 6.3 Hz, 2H), 3.80 (s, 3H), 3.77 (s, 3H), 3.67 (dd, *J* = 12.4, 2.0 Hz, 1H), 3.60 (dd, *J* = 12.3, 2.1 Hz, 1H), 3.49 (dd, *J* = 12.3, 6.5 Hz, 1H), 3.45–3.33 (m, 2H), 2.93 (dt, *J* = 11.1, 7.2 Hz, 1H), 2.82–2.72 (m, 1H), 2.72–2.62 (m, 2H), 2.47 (dd, *J* = 5.8, 4.2 Hz, 1H), 1.26 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$, 298 K): δ = 148.80, 147.36, 132.23, 120.48, 111.86, 111.26, 101.15, 71.78, 62.25, 62.04, 59.25, 55.80, 55.71, 48.60, 36.22, 24.54; HR-MS (ESI/TOF): *m/z* = 326.1962, calcd. for $C_{17}H_{28}NO_5$ $[M+H]^+$: 326.1967; $[\alpha]_D^{20}$: +27 (*c* 0.5, $CHCl_3$) for the compound with 89% *ee*.

(5*R*,6*S*)-6-[(4-Fluorophenethyl)amino]-2,2-dimethyl-1,3-dioxepan-5-ol (12): ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.19–7.03 (m, 2H), 6.95 (t, *J* = 8.7 Hz, 2H), 3.77–3.60 (m, 2H), 3.57–3.35 (m, 3H), 2.98 (dt, *J* = 11.8, 7.8 Hz, 1H), 2.84–2.65 (m, 3H), 2.49 (dd, *J* = 7.6, 3.7 Hz, 1H), 1.30 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$, 298 K): δ = 135.35, 130.01, 129.94, 115.26, 115.05, 101.27, 71.79, 62.13, 61.87, 59.16, 48.50, 35.94, 24.59, 24.55; ^{19}F NMR (376 MHz, $CDCl_3$, 298 K): δ = −117.09; HR-MS (ESI/TOF): *m/z* = 284.1668, calcd. for $C_{15}H_{23}FNO_3$ $[M+H]^+$: 284.1662; $[\alpha]_D^{20}$: +11 (*c* 0.5, $CHCl_3$) for the compound with 88% *ee*.

(5*R*,6*S*)-2,2-Dimethyl-6-{[2-(thiophen-2-yl)ethyl]amino}-1,3-dioxepan-5-ol (13): ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.14 (d, *J* = 5.1 Hz, 1H), 6.94 (dd, *J* = 4.9, 3.5 Hz, 1H), 6.84 (d, *J* = 3.2 Hz, 1H), 3.79–3.68 (m, 2H), 3.56 (dd, *J* = 12.3, 6.4 Hz, 1H), 3.52–3.40 (m, 2H), 3.11–2.97 (m, 3H), 2.92–2.82 (m, 1H), 2.53 (dd, *J* = 7.7, 3.7 Hz, 1H), 1.34 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$, 298 K): δ = 142.30, 126.71, 124.98, 123.58, 101.27, 71.79, 62.17, 61.87, 59.34, 48.48, 30.97, 24.63, 24.57; HR-MS (ESI/TOF): *m/z* = 272.1315, calcd. for $C_{13}H_{22}NO_3S$ $[M+H]^+$: 272.1320; $[\alpha]_D^{20}$: +4 (*c* 0.5, $CHCl_3$) for the compound with 87% *ee*.

(5*R*,6*S*)-6-(Isopropylamino)-2,2-dimethyl-1,3-dioxepan-5-ol (14):[12d] ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 3.76 (td, *J* = 12.4, 2.0 Hz, 2H), 3.55 (dd, *J* = 12.3, 6.2 Hz, 1H), 3.46–3.32 (m, 2H), 2.93 (dt, *J* = 12.3, 6.2 Hz, 1H), 2.53 (dd, *J* = 7.4, 3.8 Hz, 1H), 1.32 (d, *J* = 7.4 Hz, 3H), 1.24 (s, 3H), 1.04 (dd, *J* = 13.1, 6.2 Hz, 6H); MS (EI): *m/z* = 203.0, calcd. for $C_{10}H_{21}NO_3$: 203.2; $[\alpha]_D^{20}$: +71 (*c* 1.0, $CHCl_3$) for the compound with 98% *ee*. The *ee* value was determined to be 98% by chiral GC (beta 120 column, 140 °C, 1.0 mL min^{-1}): t_1 = 13.1 min, t_2 = 13.7 min.

(1*S*,2*S*)-2-(Benzylamino)cyclohexan-1-ol (16):[22a] ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.39–7.32 (m, 4H), 7.26–7.20 (m, 1H), 3.98 (d, *J* = 12.9, 1H), 3.72 (d, *J* = 12.9, 1H), 3.28–3.11 (m, 1H), 2.38–2.25 (m, 1H), 2.23–2.13 (m, 1H), 2.11–2.01 (m, 1H), 1.84- 1.66 (m, 2H), 1.34–1.23 (m, 3H), 1.07–0.95 (m, 1H); MS (EI): *m/z* = 205.0, calcd. for $C_{13}H_{19}NO$: 205.1; $[\alpha]_D^{20}$: +30 (*c* 1.0, $CHCl_3$) for the compound with 93% *ee*.

(1*S*,2*S*)-2-(Benzylamino)cyclopentan-1-ol (17):[22a] ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.41–7.28 (m, 5H), 4.02–3.95 (m, 1H), 3.89 (d, *J* = 13.1 Hz, 1H), 3.79 (d, *J* = 13.0 Hz, 1H), 3.00–2.88 (m, 1H), 2.11–1.93 (m, 2H), 1.83–1.71 (m, 2H), 1.59–1.52 (m, 1H), 1.46–1.39 (m, 1H); MS (EI): *m/z* = 191.0, calcd. for $C_{12}H_{17}NO$: 191.1; $[\alpha]_D^{20}$: +22 (*c* 1.0, $CHCl_3$) for the compound with 84% *ee*.

(2*S*,3*S*)-3-(Benzylamino)butan-2-ol (18):[22b] ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.37–7.25 (m, 5H), 3.94 (d, *J* = 12.8, 1H), 3.70 (d, *J* = 12.8, 1H), 3.42–3.30 (m, 1H), 2.48–2.35 (m, 1H), 1.18 (d, *J* = 6.1, 3H), 1.11 (d, *J* = 6.4, 3H); MS (EI): *m/z* = 179.0, calcd. for $C_{11}H_{17}NO$: 179.1; $[\alpha]_D^{20}$: +17 (*c* 1.0, $CHCl_3$) for the compound with 84% *ee*.

(2*S*,3*S*)-3-(Benzylamino)-1,2,3,4-tetrahydronaphthalen-2-ol (19):[22c] ^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ = 7.39–7.28 (m, 5H), 7.20–7.08 (m, 4H), 4.11–3.98 (m, 1H), 3.84 (d, *J* = 12.9 Hz, 1H), 3.79–3.67 (m, 1H), 3.42–3.29 (m, 1H), 3.28–3.13 (m, 1H), 2.90–2.78 (m, 2H), 2.65–2.48 (m, 1H); MS (EI): *m/z* = 253.0, calcd. for $C_{17}H_{19}NO$: 253.1; $[\alpha]_D^{20}$: +19 (*c* 0.5, $CHCl_3$) for the compound with 88% *ee*.

(1*S*,6*S*)-6-(Benzylamino)cyclohex-3-en-1-ol (20):[22d] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.24 (m, 5H), 5.69–5.51 (m, 2H), 3.98 (d, *J* = 12.9 Hz, 1H), 3.76 (d, *J* = 12.9 Hz, 1H), 3.66–3.52 (m, 1H), 2.77–2.46 (m, 3H), 2.20–2.05 (m, 1H), 1.88–1.79 (m, 1H); MS (EI): *m/z* = 203.0, calcd. for $C_{13}H_{17}NO$: 203.1; $[\alpha]_D^{20}$: +9 (*c* 1.0, $CHCl_3$) for the compound with 83% *ee*.

Typical Procedure for Heterogeneous Ring-Opening Reactions and Catalyst Recycling

To a mixture containing self-supported catalyst (S_a,S_a,*R*,*R*)-**6e** in dry DCM (2 mL), 2,2-dimethyl-4,7-dihydro-1,3-dioxepine (128 mg, 1 mmol) and H_2O_2 (30%, 108 mg, 1.05 mmol) were added. The resulting mixture was stirred at 30 °C for 24 h until 2,2-dimethyl-4,7-dihydro-1,3-dioxepine could not be detected on GC-MS. The solvent was removed under vacuum. Toluene (0.5 mL) and benzylamine (117 mg, 1.1 mmol) was added under a nitrogen atmosphere at room temperature and the mixture was warmed up to 40 °C and stirred for 18 h. The solution was diluted with ethyl ether (8 mL) and centrifuged to recycle the catalyst for 3 times. The clear solution was separated and after concentration the residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate/Et_3N = 2/1/0.15) to afford the amino alcohol product as a colorless sticky liquid.

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