

Chiral Metal–Organic Assemblies—A New Approach to Immobilizing Homogeneous Asymmetric Catalysts

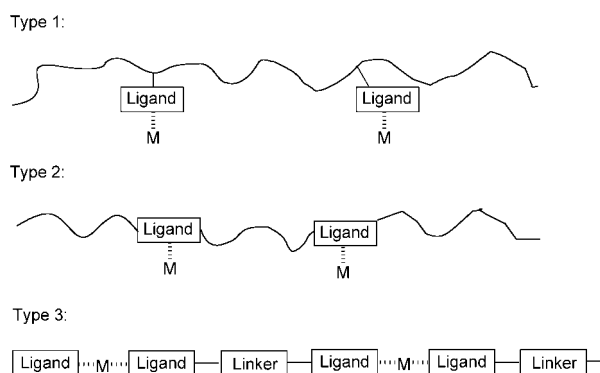
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Homogeneous asymmetric catalysis has the advantages of high enantioselectivity and catalytic activity for a variety of asymmetric transformations conducted under relatively mild reaction conditions.^[1] However, since the catalyst loadings employed in most cases have ranged from 1 to 10 mol %, homogeneous methods remain impractical due to the high cost of the chiral noble metal catalysts and the difficulty of their recovery and reuse.^[2] The other problem with homogeneous catalysis stems from the trace contaminants leached from the catalysts in the products, which is particularly unacceptable for pharmaceutical production. The immobilization of homogeneous catalysts should resolve the problems of recovering and recycling.^[3,4] Many approaches have been employed with this aim, including using inorganic materials, organic polymers, dendrimers, and membranes as supports, as well as conducting the reactions in ionic liquid and biphasic systems.^[3,4]

In the classical immobilization with organic polymers,^[3,4] the chiral ligands or the catalytically active units are anchored randomly onto irregular polymers (Type 1, Scheme 1). The resulting immobilized catalysts often display reduced enantioselectivity and less efficiency than their homogeneous counterparts. The incorporation of chiral ligands on the main chain of the polymers



Scheme 1. Three types of polymer-immobilized chiral catalysts.

Type 1: Pendant ligands anchored on a polymer; prepared by polymer reaction. Type 2: Ligands on the backbone; prepared by copolymerization. Type 3: Ligand and metal on the backbone; prepared by coordination.

is another approach (Type 2, Scheme 1). Here, the chiral ligand unit is copolymerized with a specific linker.^[5] Although the use of chiral polymers for asymmetric catalysis has a long history,^[3] successful examples were realized at the end of last century by incorporating the rigid binaphthyl skeleton in the main chain. For example, Chan and Fan et al. incorporated the binap skeleton (binap = 2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl) into a polyester chain,^[6] and Lemaire et al. used a polyamide to copolymerize with the binap skeleton.^[7] On the other hand, the backbone of the catalyst developed by Pu and co-workers was a wholly rigid aromatic system, comprising a large portion of the binaphthyl skeleton.^[5] All of these catalysts showed excellent enantioselectivity. Moreover, Chan and Fan et al. also showed that the leaching of metal from the polymer-supported catalyst is almost negligible (< 16 ppb).^[6] This strategy is indeed successful,^[8] but it is necessary to

synthesize the polymeric ligands beforehand.

Very recently, the third type of polymer-immobilized chiral catalyst (Type 3, Scheme 1) was described.^[9] Several examples showed very high enantioselectivity and efficiency.^[10–12] This type of catalyst is called a metal–ligand polymer^[13] for the sake of simplicity and in the context of asymmetric catalysis.

The concept is to transform a ligand from a homogeneous catalysts which has one coordination site into a ligand with two or more coordination sites and then react it with metal species to ensure the self-assembly of the metal–ligand polymer (or oligomer).

Recent extensive research on the design and synthesis of metal–organic frameworks has led to the increasing numbers of such metal–organic assemblies. Accordingly, many novel metal–organic assemblies with high stability, organic functionality, and porosity have been reported in the last decade. The research groups led by Lehn,^[14] Yaghi,^[15] Stang,^[16] and Fujita,^[17] among others^[18] have significantly forwarded the development of this challenging area and have demonstrated that these metal–organic assemblies based on discrete or infinite networks with well-defined coordination geometries and functions can be rationally designed and synthesized by the combination of organic bridging ligands and metal ions. Aoyama and co-

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workers have demonstrated the catalytic properties of nonchiral metal–organic materials for Diels–Alder reactions.^[19] With a few exceptions,^[20] homochiral metal–ligand polymers have not been tested for applications in asymmetric catalysis up to the beginning of this century. In any case, the design and synthesis of chiral metal–organic frameworks or polymers might provide a new strategy for asymmetric heterogeneous catalysis, because the chiral bridging ligand can spontaneously form a chiral environment inside the cavities of the materials or on the surface of the solids for enantioselective control of the reaction, and the metal ion acts as the catalytically active center. These solid-state metal–organic materials usually have extremely low solubility in the reaction medium even when other supports are not used and thus fulfill one of the basic prerequisites of heterogeneous catalysis. Accordingly, the use of chiral metal–ligand assemblies can be considered as a “self-supported” strategy^[21] for the heterogenization of homogeneous catalysts in enantioselective reactions. This type of chiral metal–organic assembly would not only have the advantages of heterogeneous catalysts, such as easy recovery and convenient recycling, but also of facile preparation and robust chiral frameworks, as well as high density of the catalytically active units.

Kim and co-workers first demonstrated the application of a homochiral metal–organic porous material to enantioselective separation and catalysis in 2000.^[9] The homochiral open-framework solid having the formula of $[\text{Zn}_3(\mu_3\text{-O})(\text{1-H})_6]\cdot 12\text{H}_2\text{O}$ (**2**) was prepared by the reaction of Zn^{2+} with the enantiopure chiral building block **1** derived from D-tartaric acid (Scheme 2). Although the enantiomeric excess in the product of transesterification was rather low ($\approx 8\%$ ee), the enantioselectivity was unprecedented because this asymmetric induction was observed for a reaction promoted by a modular porous material. This creative work triggered interest in using self-supported metal–organic systems to immobilize homogeneous catalysts.^[22]

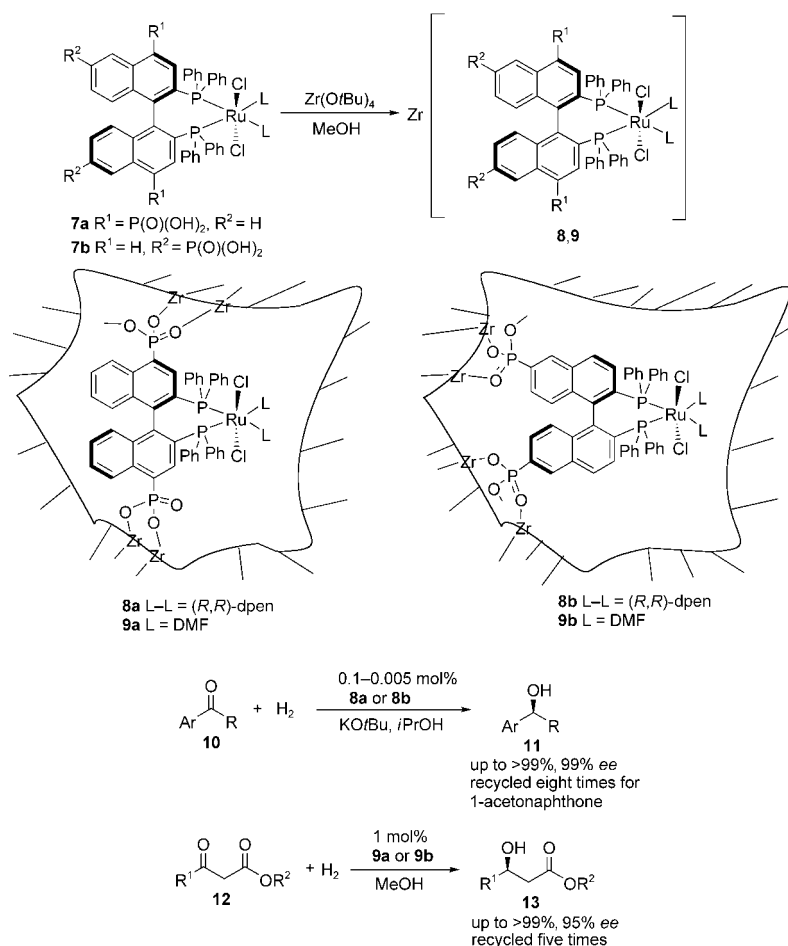
The success of asymmetric catalysis with this kind of metal–ligand polymer was realized only very recently. Lin and co-workers reported that the heteroge-



Scheme 2. Chiral metal–organic porous materials for the enantioselective transesterification of **3** with racemic **4**.

nization of Noyori’s catalysts could be achieved by in situ formation of chiral porous hybrid solids such as **8** and **9** through the reaction of zirconium *tert*-butoxide with chiral bisphosphine/Ru complexes functionalized with phosphonic acid groups (**7**) (Scheme 3).^[10a]

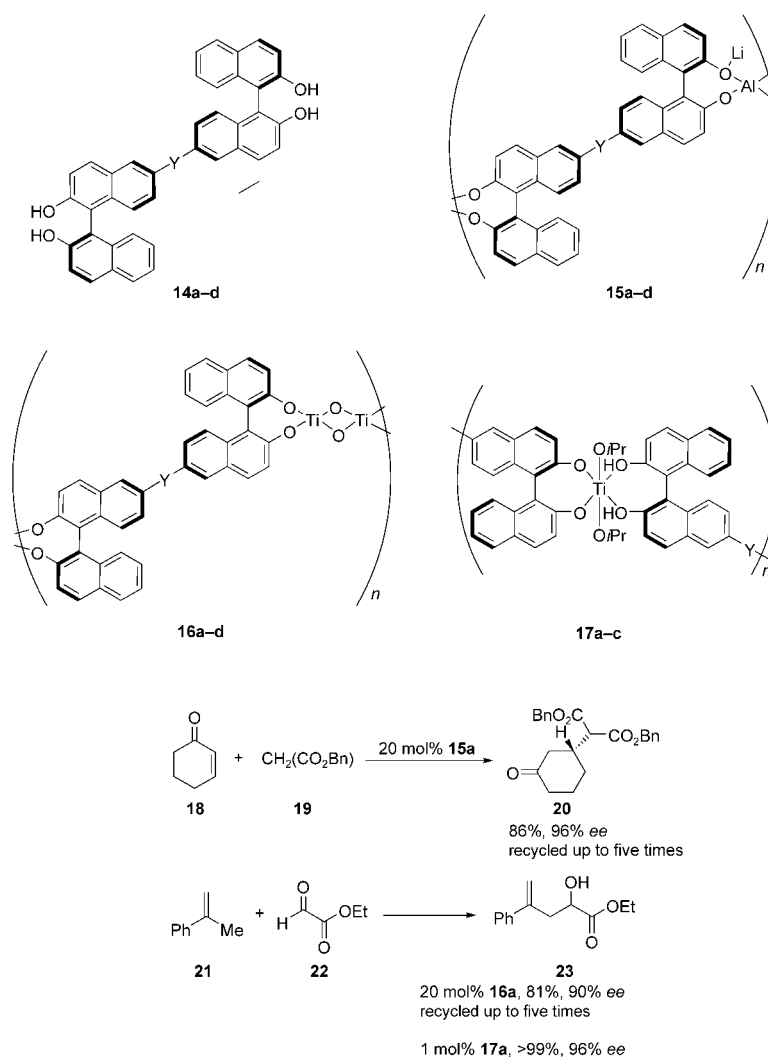
Nitrogen adsorption measurements demonstrated that these hybrid solids are highly porous with rather wide pore-size distributions. The total BET surface areas of the solids range from 328 to 475 m^2g^{-1} with microporous surface areas of 60–161 m^2g^{-1} and pore volumes



Scheme 3. Chiral metal–ligand polymer in the catalysis of enantioselective hydrogenation of ketones.

of $0.53\text{--}1.02\text{ cm}^3\text{ g}^{-1}$. The heterogenized catalysts **8a** and **8b** exhibited exceptionally high activity and enantioselectivity in the hydrogenation of aromatic ketones. With 0.1 mol % of catalyst **8a**, the conversion of the substrates was quantitative and the enantioselectivity approached 99% *ee*. Particularly, the catalyst loading can be reduced to 0.005 mol % without significant loss of the enantioselectivity. Remarkably, these binap-derived porous Zr phosphonates provide enantioselectivity superior to that of the parent homogeneous counterpart, the binap/RuCl₂/dppe system developed by Noyori et al.^[23] The other two catalyst systems, **9a** and **9b**, were also used for the asymmetric hydrogenation of a series of β -keto esters. Under optimized conditions, the hydrogenation with 1 mol % of **9b** afforded the corresponding β -hydroxy esters in quantitative yield and good to excellent enantioselectivities.^[10b] For the asymmetric hydrogenation of methyl acetoacetate the catalyst **9b** could be recycled five times without significant loss of enantioselectivity. Catalysts **8a** and **9b** showed better catalytic activity and enantioselectivity than catalysts **8b** and **9a**, respectively, which demonstrates the importance of the position of the linker on the backbone of binap in the formation of the microporous catalyst.

Almost at the same time, the research groups led by Sasai^[11] and Ding^[12] independently reported an alternative approach to generating chiral metal-organic coordination polymers for enantioselective catalysis. As shown in Scheme 4, the rigid chiral ligands having two 1,1'-2,2'-binaphthol (binol) units react with metal ions, resulting in the spontaneous formation of assembled metal-organic polymers in which the metal ions not only play the role of the bridging linker, but also act as the catalytically active sites. Moreover, the chirality of the binol units in the ligands can provide the asymmetric environment around the catalytically active centers in the polymers. These assembled metal-organic coordination polymers are insoluble in common organic solvents. This offers an excellent opportunity for running heterogeneous catalysis with these "self-supported" cata-



Scheme 4. Self-supported chiral metal-ligand polymer as catalyst in Michael addition and carbonyl-ene reactions. Bn = benzyl. Y = single bond (a); 1,4-phenylene (b); 1,3-phenylene (c); 1,2-phenylene (d).

lysts. The metal-ligand polymer of the Sasai and Ding groups is somewhat different from that of Lin et al. In the latter, the catalytic metal center, Ru, is situated as a pendant group on the Zr-linked backbone,^[10] while the catalytically active metal of Sasai, Ding, et al. is located on the backbone of the polymer.^[11,12]

The success of this strategy was demonstrated in asymmetric Michael additions^[11] and carbonyl-ene reactions.^[11,12] The heterogeneous Al-bridged polymers **15** prepared by the reaction of LiAlH₄ with bis(binol) ligands **14** was employed in the enantioselective Michael addition of dibenzyl malonate (**19**) to 2-cyclohexenone (**18**) in THF. Adduct **20** was obtained with results comparable to those obtained with a homogeneous

Al-Li-bis(binaphthoxide) (ALB) catalyst (100% yield, 97% *ee*). After the reaction was complete, catalyst **15a** could be recovered conveniently and reused at least three times with a slight decrease of enantioselectivity (from 96% *ee* for the first run to 85% *ee* for the third run). Similarly, the heterogeneous Ti-bridged catalysts (**16** and **17**) prepared by the reaction of ligands **14** with Ti(OiPr)₄ (**14**:Ti = 1:2 or 1:1) gave excellent enantioselectivity (up to 96.5% *ee*) in the carbonyl-ene reaction of **21** with **22**.^[11,12] The reusability of this type of catalyst (**16a**) in the carbonyl-ene reaction was also demonstrated by Sasai et al. After being reused five times the Ti-bridged polymer exhibited consistent catalytic selectivity, affording **23** with an *ee* value of 88% at a catalyst

loading of 20 mol%. It seems that catalyst **17a** prepared with **14**:Ti = 1:1 (1 mol%, up to 99% yield and 96% ee) possesses higher activity and enantioselectivity than **16a** prepared with **14**:Ti = 1:2 in the presence of 1 equiv of H₂O (20 mol%, up to 72% yield and 92% ee). This phenomenon probably arises from the activating effect of additional binol unit in **17a**.^[24] In both the Michael addition and carbonyl-ene reaction, the linkers between two binol units in the ligands have significant impact on the enantioselectivity of the assembled catalysts prepared from them. The heterogeneous catalysts derived from **15a,b** and **17a,b**, in the pairs of the phenolic hydroxy groups are situated at opposite sites in the symmetric, multidentate ligands, gave the Michael adduct or carbonyl-ene adduct with higher enantioselectivity than that attained with the catalysts from ligands **15c,d** and **17c**, respectively. The dramatic influence of the linking spacer on the enantioselectivities of the reactions reflects that the linkers between two binol units of the ligands probably significantly alter the supramolecular structure of the assemblies in the catalysts. Therefore, the frameworks of assembled catalysts can be optimized by the rational design of chiral ligands to improve the catalytic activity and enantioselectivity of the “self-supported” catalyst.

Obviously, the “metal–ligand polymer” strategy for the immobilization of homogeneous catalysts developed by the Lin,^[10] Sasai,^[11] and Ding groups^[12] represents a significant breakthrough in the heterogeneous asymmetric catalysis, since it satisfies many requirements for the immobilized catalysts. Their performance is comparable to or better than that of the parent catalysts, they are easy to separate and reuse, and there is minimum leaching of the catalyst. Furthermore, the metal–ligand polymer was prepared by an in situ self-assembling process, a really simple manipulation. This strategy might provide a new direction in asymmetric catalysis, particularly for the development of practical syntheses of optically active compounds. Meanwhile, the use of chiral “metal–ligand” assemblies for chiral recognition

and separation may be another exciting area in chiral chemistry.^[25]

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