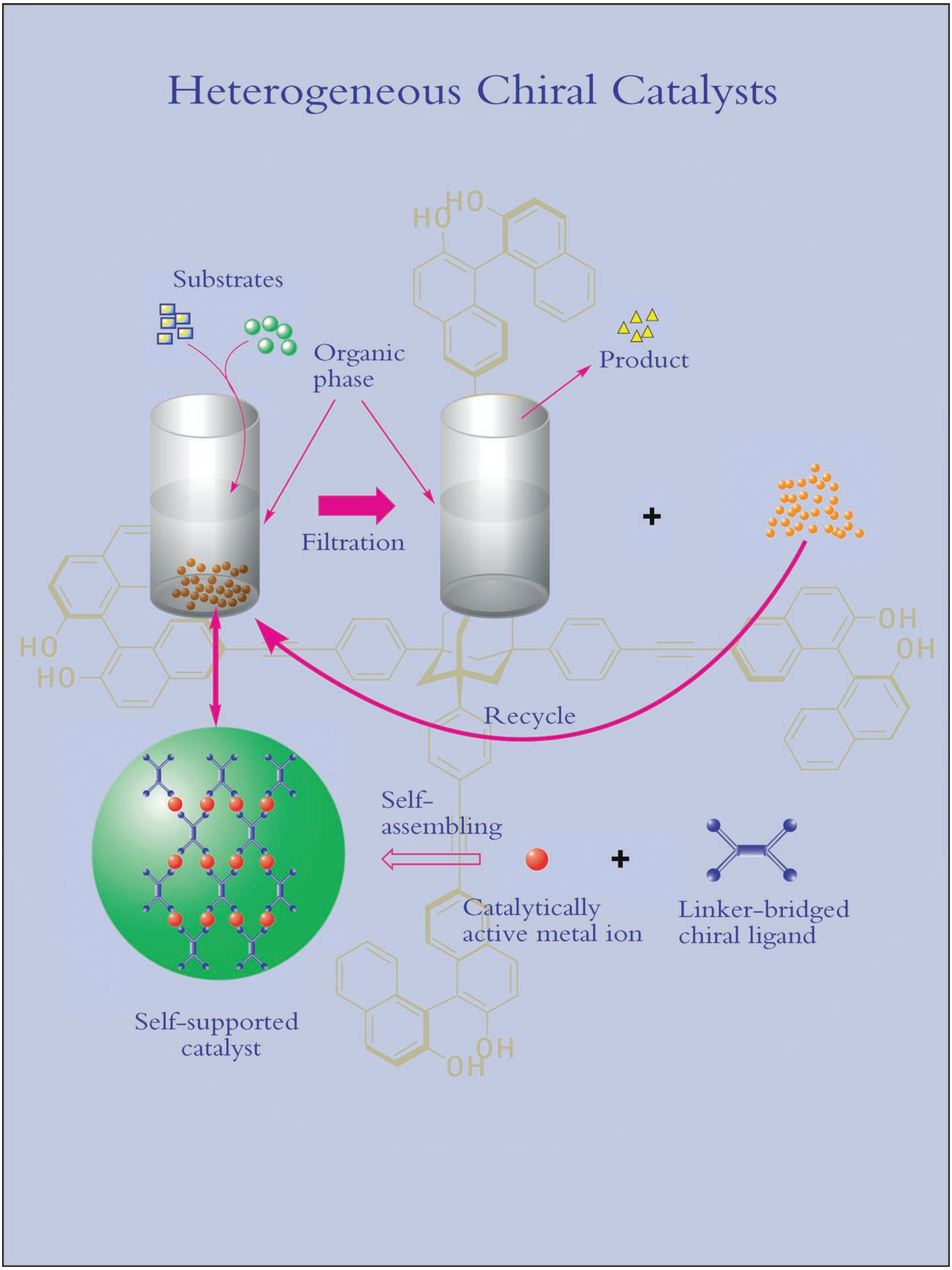
Heterogeneous Chiral Catalysts
Substrates
Organic phase
Product
Filtration
+
Recycle
Self-assembling
+
Catalytically active metal ion
Linker-bridged chiral ligand
Self-supported catalyst
HO
HO
OH
OH

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Self-Supported Chiral Catalysts for Heterogeneous Enantioselective Reactions

Kuiling Ding,* Zheng Wang, Xingwang Wang, Yuxue Liang, and Xisheng Wang[a]

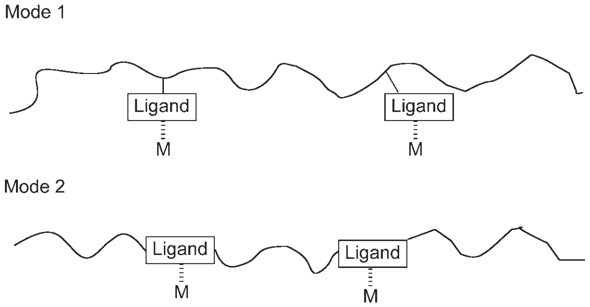
Abstract: The development of heterogeneous chiral catalysts for enantioselective reactions is highly desirable in order to overcome some drawbacks of homogeneous catalysts. Different from the conventional approaches by using various types of supports or biphasic systems for the recovery and reuse of homogeneous catalysts, a conceptually new strategy for heterogenization of homogeneous chiral catalysts, that is, a "self-supporting" approach, has been developed to use homochiral metal–organic coordination polymers generated by the self-assembly of chiral multitopic ligands with metal ions, and thus obviates the use of any support. In this concept article, the success of this "self-supporting" strategy will be exemplified in heterogeneous catalysis of asymmetric carbonyl–ene, sulfoxidation, epoxidation, and asymmetric hydrogenation reactions.

Keywords: asymmetric catalysis • C–C coupling • heterogeneous catalysis • hydrogenation • oxidation • self-assembly

Introduction

Asymmetric catalysis of organic reactions to provide enantiomerically enriched products is of central importance to modern synthetic and pharmaceutical chemistry.[1] Although homogeneous asymmetric catalysis has the advantages of high enantioselectivity and catalytic activity in a variety of asymmetric transformations under mild reaction conditions,[1] the high catalyst loadings (usually 1–10 mol%) and the difficulties associated with recovery and the reuse of expensive chiral catalysts severely hampers its practical applications. In addition, sometimes the metal contaminants can leach from the homogeneous catalysts into the products; this contamination is particularly unacceptable for pharmaceutical production. As one of the most promising solutions to these problems, immobilization of homogeneous chiral catalysts for asymmetric catalysis has attracted a great deal of recent interest.[2]

For the immobilization of homogeneous catalysts, many approaches have been employed, including the use of inorganic materials, organic polymers, dendrimers, or membranes as supports, as well as the use of ionic liquid and other biphasic systems.[2] Despite the fact that some successes have been achieved in this field, the catalysts immobilized by these approaches often display reduced enantioselectivity or activity in the catalysis in comparison with their homogeneous counterparts. In the conventional immobilization of homogeneous catalysts by using organic polymers, the chiral ligands or the catalytically active units are usually anchored randomly onto irregular polymers (mode 1, Scheme 1),[2] or are incorporated into the main chain of the polymers (mode 2, Scheme 1),[3] as highlighted by Dai.[4] Although these strategies have yielded some successes, the polymeric



Scheme 1. Schematic representation of the classical methods for immobilization of chiral catalysts using organic polymers as the supports. Mode 1: Pendent ligands by anchoring on a polymer, through a polymer reaction. Mode 2: Ligand on the backbone, through copolymerization.

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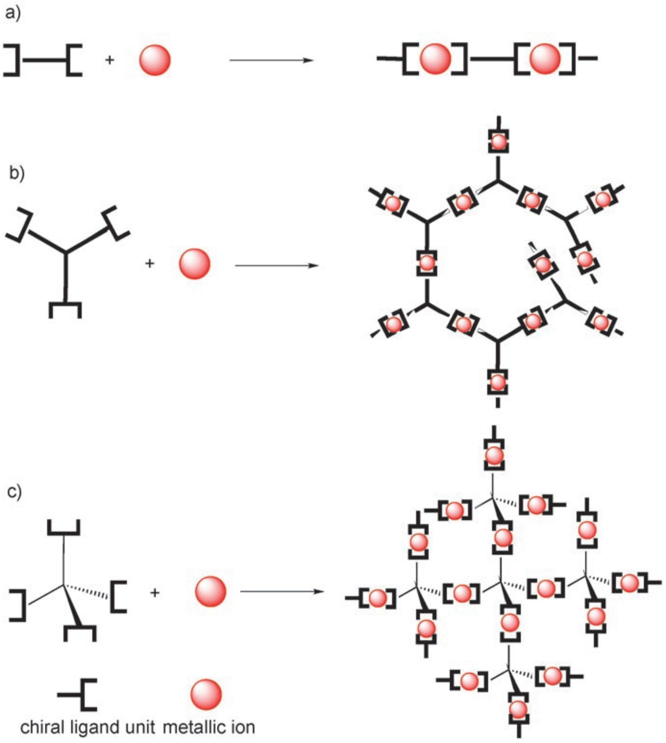
ligands must be prepared before the active metallic species is loaded, and the procedures for their syntheses are usually somewhat tedious. In the present account, we present a conceptually new strategy, that is, a "self-supporting" approach, for the immobilization of homogeneous catalysts through assembly of chiral multitopic ligands and metal ions without the use of any support. The success of this strategy will be exemplified in heterogeneous asymmetric carbonyl–ene, sulfoxidation, epoxidation, and asymmetric hydrogenation reactions.

The Principle for the Generation of Self-Supported Heterogeneous Chiral Catalysts for Asymmetric Catalysis

Since the 1990s, the design and synthesis of metal–organic coordination polymers or metal–organic frameworks (MOF) as functional materials have been an interesting and rapidly growing research area in material sciences.[5] These materials are usually prepared by the reactions of multitopic ligands with metal ions in solution through molecular self-assembly, and sometimes possess cavities, pores, or channels capable of adsorption and inclusion of guest molecules and ions, like natural materials such as clays and zeolites. By adjusting the size and geometry of the organic ligand as well as the coordination preference of the metal species, one can, in principle, control the size and the shape of the formed pores in the resulting frameworks. Accordingly, the structural and functional information of the components can be conveniently expressed in a specific target material through building block carriers. Among the variety of promising applications of these assemblies, the most attractive one may lie in the area of heterogeneous catalysis because these assemblies often display poor solubility in common organic solvents, and both the catalytic activity and the selectivity might be tuned by the pore matrices and chemical functionality of the cavities through metal and ligand diversity.

The use of nonchiral metal–organic assemblies as the heterogeneous catalysts for organic transformations has been demonstrated by several groups in oxidation, hydrogenation, cyanosilylation, Diels–Alder, and polymerization reactions.[6] In parallel, homochiral metal–organic coordination polymers formed by self-assembling of enantiopure chiral multitopic ligand with catalytically active metal ions should be applicable as a new type of heterogeneous chiral catalysts for asymmetric transformations. Since the stereochemical features of the chiral ligands will be retained in the coordination polymers by virtue of the mild synthesis, it can be expected that the chiral multitopic ligand would spontaneously form a chiral environment inside the cavities or on the surface of the solids for enantioselective control of the reaction, and the metal ion may act as the catalytically active center (Scheme 2). On the basis of the fact that the polymeric chiral catalyst obviates any extra support in the heterogenous catalysis, the use of chiral metal–ligand assemblies can be considered as a "self-supporting strategy".[4,7] However, despite the apparent feasibility of this rationale, the use of homochiral metal–organic assembly for the applications in asymmetric catalysis did not meet with success until the beginning of this century.



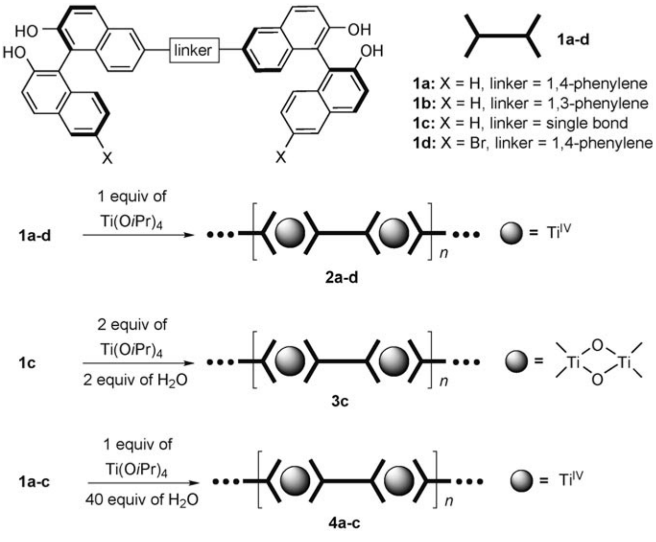
Scheme 2. Schematic representation of the "self-supporting" strategy for heterogenization of chiral catalysts through the reactions of a) one-dimensional, b) two-dimensional and c) three-dimensional multitopic chiral ligands with metallic ions.

In 2000, Kim and co-workers demonstrated the application of assembled, homochiral, microporous metal–organic material in enantioselective heterogeneous catalysis.[8] Although the enantiomeric excess in the product of transesterification was rather low (~8%), this work constituted the first example of asymmetric catalysis with a well-defined homochiral metal–organic assembly as the heterogeneous catalyst, and triggered the further interest in the research of this unexplored field.[9,10] It should be noted that although numerous coordination polymers have been developed over the past two decades,[5] only sporadic successful applications in catalytic transformations can be found in the literature,[6] even fewer for catalytic enantioselective reactions. The inherent reason for this limitation might be attributed to the fact that most coordination polymers prepared thus far have coordinatively saturated metal centers, which precludes their involvement in the catalytic transformation.[5a]

Since the metal centers in the homochiral metal–organic assembly play the dual roles as the structural binders (Scheme 2) as well as the catalytically active sites, it is essential that they should be capable of simultaneously bonding with at least two ligand moieties (same or different), and still have vacant or labile sites available for substrate and/or reagent coordination and activation. In the course of our studies on the combinatorial approach to the discovery of chiral catalysts for asymmetric reactions, a variety of highly efficient and enantioselective catalysts have been developed on the basis of a two-component ligand modification strategy for the generation of a chiral catalyst library.[11] The common feature of the catalysts discovered by this approach is the incorporation of either two homo- or two heteroligands in the active catalysts. This feature of homogeneous catalysts provides an excellent opportunity for generation of heterogeneous catalysts through self-supporting strategy shown in Scheme 2. One can easily imagine that if the component chiral ligands with known excellent asymmetric induction for a target reaction are bridged with a specific spacer, the reaction of the bridged multitopic ligands with the catalytically active metal species would spontaneously form metal–organic coordination polymers through assembly. In such a case, the high activity and enantioselectivity of the formed metal–organic coordination polymers can be expected by judicious choice of the bridged chiral ligand and metal species. In the following text, we will summarize our results on heterogenization of homogeneous chiral catalysts for asymmetric catalysis on the basis of this concept.

Self-Supported Heterogeneous Titanium Catalysts for Enantioselective Carbonyl–Ene and Sulfoxidation Reactions

Th asymmetric carbonyl–ene reaction is an important approach to C–C bond formation in organic synthesis,[12] for which the titanium complexes of 1,1′-bi-2-naphthol (binol) derivatives are among the most widely used chiral Lewis acidic catalysts. According to Mikami's asymmetric activation concept,[13] an enantiopure [Ti{(*R*)-binol}(O*i*Pr)$_2$] catalyst could be further evolved for this reaction by addition of another equivalent of (*R*)-binol(H$_2$), affording the product in higher enantioselectivity.[13c] The results of kinetic study showed that the reaction catalyzed by the [Ti{(*R*)-binol}(O*i*Pr)$_2$]/(*R*)-binol complex was 25.6 times faster than that catalyzed by [Ti{(*R*)-binol}(O*i*Pr)$_2$] alone.[13c] We have demonstrated that the catalysts prepared by the homocombination of two equivalents of (*R*)-6,6′-I$_2$-binol with Ti(O*i*Pr)$_4$ or by the heterocombination of one equivalent of (*R*)-6,6′-I$_2$-binol and one equivalent of (*R*)-6,6′-(CF$_3$)$_2$-binol with Ti(O*i*Pr)$_4$ show exceptionally high efficiency for the carbonyl–ene reaction between ethyl glyoxylate and a variety of olefins under nearly solvent-free conditions, affording α-hydroxy ester derivatives in good yields and excellent enantioselectivities.[14] These observations provided the rational basis for the design of assembled catalysts for this reaction by reaction of bridged binol ligands with Ti(O*i*Pr)$_4$.

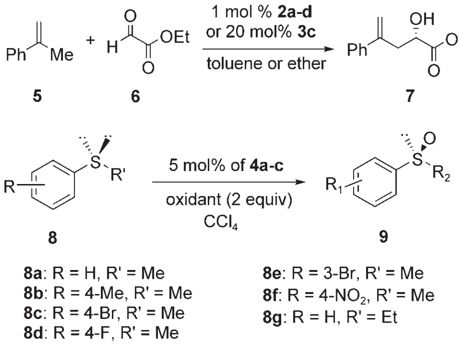


Scheme 3. Generation of self-supported chiral titanium catalysts for carbonyl–ene reaction and sulfoxidation.

Sasai[7a] and our group[7b,15] independently reported the heterogenization of chiral titanium complexes by in situ assembly of bridged multitopic binol ligands with Ti(O*i*Pr)$_4$ (Scheme 3), and the assembled heterogeneous catalysts were found to show excellent enantioselectivity (up to 98 % *ee*) in carbonyl–ene reaction of α-methylstyrene with ethyl glyoxylate. Consistent with the activities exhibited by the discrete Ti–binolate catalysts for the same reaction under the homogeneous conditions, the ratio of the binol unit to Ti(O*i*Pr)$_4$ employed in the preparation of the coordination polymers was found to be critical for their catalytic activity.[7a,b,15] The heterogeneous catalyst **2c** obtained by employing a 2:1 molar ratio of binol unit to Ti(O*i*Pr)$_4$ is evidently more active and enantioselective than the catalyst **3c** prepared with a 1:1 molar ratio of binol unit to Ti(O*i*Pr)$_4$ (entry 3 versus 7, Table 1). The spacers between two binol units of the ligands in the assembled catalysts showed significant impact on the enantioselectivity of the carbonyl–ene reaction. For example, catalysts **2a** and **2b**, prepared and tested under the same conditions with the only difference lying in their spacer moieties, displayed dramatically different performance in terms of both catalytic activity and enantioselectivity (entry 1 versus 2, Table 1). This fact suggests that a change in the linker moieties of the ligands may alter the supramolecular structures of the assemblies, and as a result, impact the activity and/or enantioselectivity of the catalysis. Consistent with one of our previous reports,[14] the introduction of an electron-withdrawing substituent to the backbone of binol, such as ligand **1d**, resulted in the improvement of the catalytic activity due to the increase of Lewis acidity of the Ti^{IV} complexes, affording the product in very high yield (99 %) with excellent enantioselectivities (up to 98 % *ee*, entry 5).[15]

The recovery and recycling of this type of self-supported titanium catalyst was examined with catalyst **2d** in diethyl ether. Upon completion of the reaction, simple filtration of the reaction mixture realized the separation of the solid-state catalyst from the product-containing solution. The separated solids were recharged with diethyl ether and substrates for the next run. Similar to the observation with catalyst **3c** reported by Sasai,[7a] catalyst **2d** could be used for

Table 1. Self-supported Ti catalysts for the enantioselective carbonyl–ene reaction[a] and sulfoxidation.[b]



Entry	Substrate	Catalyst [mol %]	Solvent	T [°C]	t [h]	Yield [%]	*ee* [%]
1	**5** + **6**	**2a** (1)	toluene	0	120	85	95
2	**5** + **6**	**2b** (1)	toluene	0	120	9	24
3	**5** + **6**	**2c** (1)	toluene	RT	30	99	96
4	**5** + **6**	**2d** (1)	toluene	RT	96	99	95
5	**5** + **6**	**2d** (1)	toluene	0	96	99	98
6	**5** + **6**	**2d** (1)	diethyl ether	RT	96	99	97
7	**5** + **6**	**3c** (20)	diethyl ether	RT	98	88	88
8	**8a**	**4a** (5)	CCl_4	RT	72	38	99.2
9	**8a**	**4b** (5)	CCl_4	RT	72	38	99.5
10	**8a**	**4c** (5)	CCl_4	RT	72	37	98.7
11	**8b**	**4b** (5)	CCl_4	RT	72	41	99.8
12	**8c**	**4c** (5)	CCl_4	RT	72	31	>99.9
13	**8d**	**4a** (5)	CCl_4	RT	72	41	98.6
14	**8e**	**4b** (5)	CCl_4	RT	72	36	>99.9
15	**8f**	**4b** (5)	CCl_4	RT	60	20	89.1
16	**8g**	**4a** (5)	CCl_4	RT	72	36	75.5

[a] Catalyst **2d** could be recycled on the carbonyl–ene reaction of α-methylstyrene (**5**) with ethyl glyoxylate (**6**) five times, affording **7** with 87–70 % yield and 97–70 % *ee*. [b] Catalyst **4a** could be recycled on the sulfoxidation of **8a** eight times, affording **9a** with 29–42 % yield and 98.2→99.9 % *ee*.

five cycles in the carbonyl–ene reaction with gradually deteriorated activity (from 87 to 70 % yield) and enantioselectivity (from 97 to 70 % *ee*). This is probably due to the partial decomposition of the assemblies during the catalysis, and as a result, some amount of the active Ti^{IV} species may be leached into the solution phase of the reaction mixture during the catalysis and lost in the catalyst recovery.[15]

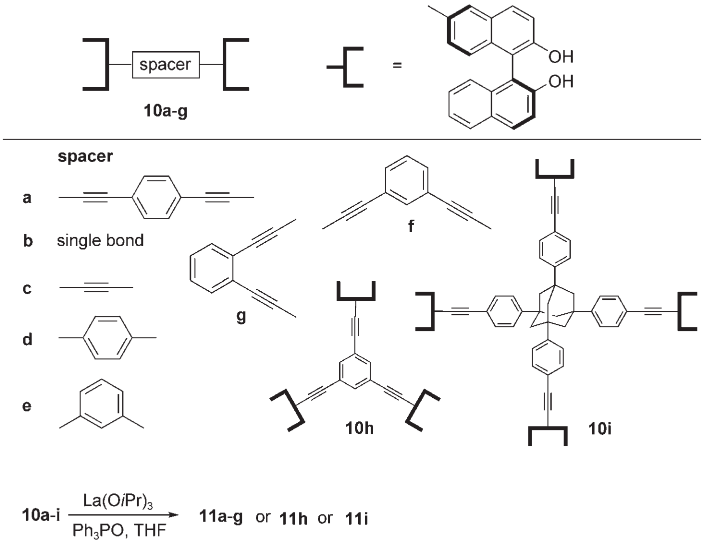
The heterogeneous Kagan–Uemura type[16] catalysts **4a**–**c** for asymmetric sulfoxidation of sulfides were prepared in a similar manner, that is, by the reaction of bridged binol ligands **1a**–**c** with $Ti(O\mathit{i}Pr)_4$ (1:1 molar ratio) followed by addition of H_2O (40 equiv relative to ligand). Different from that observed in carbonyl–ene reaction, **4a**–**c** were found to be completely insoluble in CCl_4.[15] The heterogeneous enantioselective oxidation of a variety of aryl alkyl sulfides was then investigated by using catalysts **4a**–**c** with cumene hydroperoxide (CMHP) as the oxidant. As shown in Table 1, the oxidation of both *para*- or *meta*-substituted aryl methyl sulfides **8a**–**e** afforded chiral sulfoxides **9a**–**e** with very high enantioselectivities (from 96.4 to >99.9 % *ee*) in moderate yields (ca. 40 %). The heterogeneous nature of the above catalyst systems was confirmed by using the supernatant of **4a** in CCl_4 for the catalysis of sulfoxidation of thioanisole (**8a**) under the same conditions. The isolated product (**9a**) was racemic, similar to that obtained from the control experiment without using any catalyst under otherwise identical conditions. The inductively coupled plasma (ICP) spectroscopic analyses of the liquid phase after filtration of the insoluble catalysts indicated that no detectable Ti (<0.1 ppm) was leached into the organic solution; this fact further supports the heterogeneous nature of the present system. The facile recovery and remarkable stability of this type of heterogeneous catalyst was exemplified by the oxidation of thioanisole (**8a**) by using catalyst **4a**. This catalyst was reused for eight cycles that covered a period of more than one month without any loss of enantioselectivity (99.0→99.9 % *ee*) or evident deterioration of activity (38–33 % yield).

In addition to the heterogeneous Ti catalysts for carbonyl–ene reactions, Sasai and coworkers also reported that the heterogeneous Al-bridged polymers (ALB) prepared by the reaction of $LiAlH_4$ with bisbinol ligands were efficient catalysts for enantioselective Michael addition of dibenzyl malonate to 2-cyclohexenone, affording the corresponding adduct with the results (86 % yield, 96 % *ee*) comparable to those obtained with a homogeneous catalyst (100 % yield, 97 % *ee*).[7a] The heterogeneous ALB catalyst could be recycled for four times with slight drop of activity (88–59 % yield) and enantioselectivity (96–77 % *ee*).

Heterogenization of Shibasaki's Binol/La^{III} Catalyst for Enantioselective Epoxidation of α,β-Unsaturated Ketones by Using Multitopic Binol Ligands: the Impact of Bridging Spacers

As can be envisioned from Scheme 2, in the use of self-supporting strategy for the heterogenization of homogeneous chiral catalysts, the stereochemical characteristics of the multitopic ligands should in principle have substantial impact on the microstructures of the resulting homochiral metal–organic polymers, and thus may exert a profound influence on the enantioselectivity and activity of the catalysis in a given reaction.

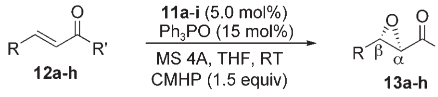
Such effects of bridging spacers in the multitopic ligands have been investigated in the heterogenization of Shibasaki's lanthanum catalyst[17] for the enantioselective catalysis of epoxidation of α,β-unsaturated ketones.[18] As shown in Scheme 4, four types of multitopic ligands (**10a–i**) containing different bridging linkers, including linear (**10a–d**), angular (**10e–g**), trigonal-planar (**10h**), and tetrahedral (**10i**) spacers, were designed to investigate the impact of the spatial arrangement of chiral units ((*S*)-binol) on the catalytic properties of their assemblies with the lanthanum ion. The heterogeneous catalysts (**11a–i**) were prepared by dropwise addition of a solution of the corresponding multitopic ligand (**10a–i**) and triphenylphosphine oxide in THF to a solution of La(O*i*Pr)$_3$ in THF under argon atmosphere. The application of the heterogeneous catalysts **11a–i** in the epoxidation of chalcone **12a** (Table 2) demonstrated that the influence of structure of the spacer on the enantioselectivity of the catalysis was dramatic. For the ligands with a linear spacer (**10a–d**), extending the length of the linker between two chiral units generally had a beneficial effect on the enantioselectivity (entries 1–4). However, the reduction of the extension angles of the spacers (**10e**, **10g**) was clearly unfavorable for the enantioselectivity (entry 5 versus 4, 6 and entry 7 versus 1). The catalysts composed of planar tritopic **10h** and tetrahedral tetratopic **10i** ligands with longer spacers also demonstrated high activity and enantioselectivity of the heterogeneous epoxidation (entries 8 and 9). Given the modular nature of the multitopic ligands, it can be expected that both the reactivity and enantioselectivity may be fine-tuned by judicious choice of the spacer part of the ligands.



Scheme 4. Multitopic ligands **10a–i** employed for the generation of heterogeneous lanthanum catalysts **11a–i**.

Under the optimized reaction conditions, the enantioselective epoxidation of several α,β-unsaturated ketones **12a–h** was then carried out in the presence of catalyst **11a** with CMHP as oxidant (Table 2). The reactions proceeded efficiently to give corresponding epoxides in excellent yields (91–99 %) and high enantioselectivities (84.9–97.6 % *ee*). The remarkable advantage of the present self-supported heterogeneous catalysts over their homogeneous counterparts was again exemplified by the facile recovery and recycle of **11a** in the catalysis of the epoxidation of chalcone **12a**. As outlined in the footnote of Table 2, **11a** can be recycled and reused for at least six cycles without significant loss of enantioselectivity and activity. Moreover, the lanthanum leaching in each run during the recycling of the catalyst was determined to be less than 0.4 ppm by ICP. The heterogeneous nature of the above catalyst system has been further confirmed by the fact that the supernatant of **11a** in THF did not exhibit any catalytic activity for the epoxidation under the same experimental conditions.

Table 2. Enantioselective epoxidation of α,β-unsaturated ketones with heterogenized Shibasaki's catalysts (**11a–i**).



R = Ph, R' = Ph (**a**)
R = 4-F-Ph, R' = Ph (**b**)
R = 4-Cl-Ph, R' = Ph (**c**)
R = 4-Br-Ph, R' = Ph (**d**)
R = 4-NO$_2$-Ph, R' = Ph (**e**)
R = 4-NC-Ph, R' = Ph (**f**)
R = Ph, R' = 4-MeO-Ph (**g**)
R = *i*-Pr, R' = Ph (**h**)

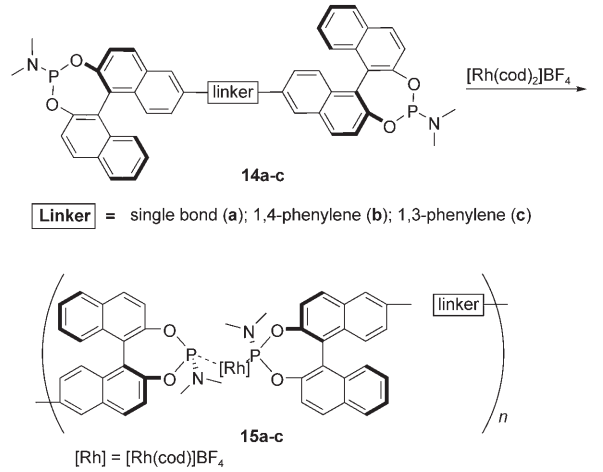
Entry	Catalyst [mol %]	Substrate	*t* [h]	Yield [%]	*ee* [%]
1[a]	**11a**	**12a**	0.5	99	97.6
2	**11b**	**12a**	0.5	99	83.7
3	**11c**	**12a**	0.5	99	82.9
4	**11d**	**12a**	0.5	99	95.5
5	**11e**	**12a**	0.5	99	93.3
6	**11f**	**12a**	0.5	99	95.1
7	**11g**	**12a**	0.5	99	84.2
8	**11h**	**12a**	0.5	99	91.5
9	**11i**	**12a**	0.5	99	95.0
10	**11a**	**12b**	0.5	99	96.2
11	**11a**	**12c**	0.5	99	96.0
12	**11a**	**12d**	0.5	99	95.6
13	**11a**	**12e**	1.0	95	95.7
14	**11a**	**12f**	1.0	99	94.3
15	**11a**	**12g**	0.5	99	95.0
16	**11a**	**12h**	3.0	91	84.9

[a] Catalyst **11a** could be recycled on the epoxidation of **12a** SIX times, affording **13a** with 99–83 % yield and 96.5–93.2 % *ee.*

Self-Supported Mono-Phos/Rh^{I} Catalysts for Enantioselective Hydrogenation Reactions

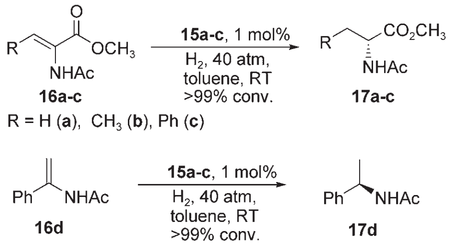
The use of monodentate phosphorous ligands in Rh-catalyzed enantioselective hydrogenation of olefin derivatives represents one of the breakthroughs in the area of asymmetric hydrogenation,[19] for which the generally accepted mechanism is that the catalytically active species has a composition of 2:1 molar ratio of monodentate phosphorous ligands to Rh^{I} metal ion. One can easily imagine that if two or more monodentate phosphorous ligand motifs are covalently bridged with some rigid spacer at the backbone of the ligand, homochiral metal–ligand coordination polymers can be conveniently constructed by the reaction of the corresponding multitopic phosphorus ligands with Rh^I precursor.

As expected, the reaction of Feringa's MonoPhos ligands bridged with a linker (**14a–c**) with the catalyst precursor [Rh(cod)]BF$_4$ (cod = cyclooctadiene) in a dichloromethane/toluene mixed solvent resulted immediately in the formation of orange solids (Scheme 5), which were confirmed to be completely insoluble in toluene.[7c] As shown in Table 3, the application of the self-supported Rh^I catalysts (**15a–c**) in the asymmetric hydrogenation of some representative substrates including β-aryl- or alkyl-substituted dehydro-α-amino acid (**16a–c**) and enamide (**16d**) derivatives afforded a variety of amino acid (**17a–c**) and secondary amine (**17d**) derivatives with high yields and enantioselectivities, which are comparable to the cases of homogeneous catalysis at the same level of catalyst loading. Particularly, the self-supported catalysts demonstrated remarkably improved enantioselectivity (95–97% *ee*) in the hydrogenation of the enamide derivative in comparison with the cases that make use of a MonoPhos/Rh homogeneous catalyst (88% *ee*). The heterogeneous nature of the catalysis was also confirmed by the inactivity of the supernatants of these self-supported catalysts for the hydrogenation. The ICP spectroscopic analysis indicated that no detectable rhodium was leached into the solution phase and the concentration of phosphorus in solution was less than 3 ppm for each round of hydrogenation; these facts further confirmed the heterogeneous nature of the present systems. The catalysts could be readily recycled and reused for at least seven runs without significant loss of activity and enantioselectivity.[7c] Very recently, Wong and co-workers designed a beautiful ditopic chiral "linear" monodentate phosphoramidite ligand with a biphenylene backbone for the generation of self-assembled oligomeric or polymeric Rh catalysts. The solid catalyst demonstrated excellent enantioselectivities (97–99% *ee*) in the hydrogenation of a variety of dehydro-α-amino acid derivatives.[20]



Scheme 5. Heterogenization of Feringa's catalyst by self-supporting strategy.

Table 3. Enantioselective hydrogenation of olefin derivatives (**16a–d**) under the catalysis of self-supported catalysts **15a–c**.



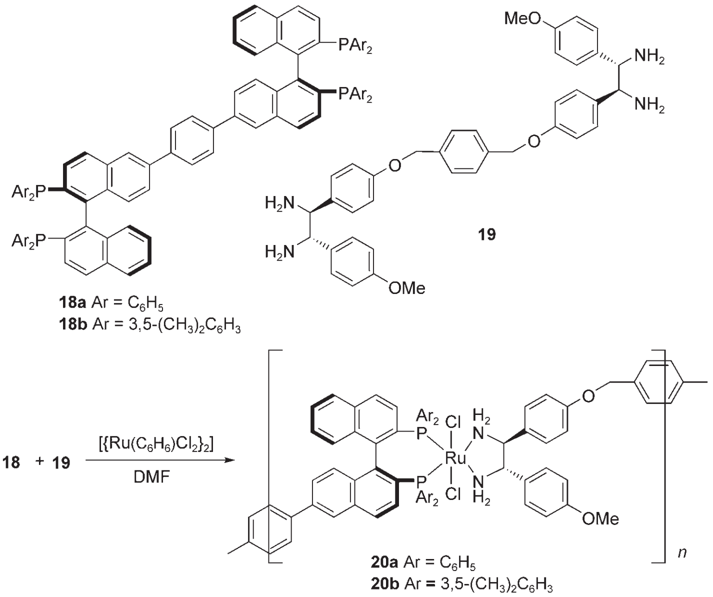
Entry	Catalyst	Substrate	*ee* [%]
1	**15a**	**16a**	95.8
2	**15a**	**16b**	95.7
3	**15a**	**16c**	96.6
4	**15a**	**16d**	97.3
5	**15b**	**16a**	94.3
6	**15b**	**16b**	94.9
7	**15b**	**16c**	94.7
8	**15b**	**16d**	96.8
9[a]	**15c**	**16a**	95.0
10	**15c**	**16b**	95.9
11	**15c**	**16c**	96.2
12	**15c**	**16d**	95.9

[a] Catalyst **15c** could be recycled on the hydrogenation of **16a** seven times with >99% conversion and 95.0–89.5% *ee*.

Programmed Assembly of Two Different Ligands with Metal Ions: Generation of Self-Supported Noyori-Type Catalysts for Heterogeneous Asymmetric Hydrogenation of Ketones

As mentioned above, the heterogenization of the chiral catalysts by using a self-supporting strategy through the homocombination of multitopic chiral ligands with metallic ions is very convenient. On the other hand, the assembly of polymeric or oligomeric homochiral catalyst by heterocombination of two different multitopic chiral ligands (L^1 and L^2) with metal ions (M) is a very challenging task, since a complex multispecies system (e.g., [M(L^1)$_2$], [M(L^2)$_2$], [ML^{1}L^2], etc.) would be easily envisioned when the three reacting components were mixed together. Thus, specific formation of a heteroligand combination complex [ML^{1}L^2] would require that the structural and coordination information stored in the ligands and metallic ion, respectively, must be sufficiently strong to dictate their coordinating organization and thus direct the assembly process in a programmed way. In this respect, the structural feature of Noyori's catalyst,[21] [RuCl$_2${(*R*)-binap}{(*R*,*R*)-dpen}] (binap: 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl; dpen: 1,2-diphenylethylenediamine), can provide an excellent opportunity for generation of self-supported catalysts by the programmed assembly[22] of a [ML^{1}L$_2$] type of coordination polymer.

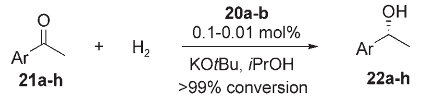
As shown in Scheme 6, both bridged binap **18** and diamine **19** were designed to possess a 1,4-phenylene or a 1,4-phenylenebismethoxy linkers, which were assembled at 6-position of the corresponding 1,1′-binaphthyl backbone or at



Scheme 6. Generation of self-supported Noyori's catalyst by programmed assembly.

4′-position of (*S*,*S*)-dpen derivative, respectively, in order to avoid the intramolecular interaction of two chiral units. The self-supported catalysts (**20a**,**b**) were prepared by reacting bridged binap ligands (**18a**,**b**) with [{Ru(C_6H_6)Cl_2}$_2$] in DMF at 100 °C, followed by the treatment of the resulting reddish brown solution with one equivalent of bridged dpen **19** at room temperature. As shown in Table 4, the application of the self-supported catalyst **20** in the catalysis of the asymmetric hydrogenation of acetophenone (**21a**) indicated that catalyst **20b** was highly efficient and enantioselective, affording 1-phenylethanol in quantitative yield with 97.4 % *ee*, which is slightly higher than those obtained with its homogeneous counterparts (95.5–96.4 % *ee*).[22] Moreover, the catalyst loading for **20b** can be further reduced to 0.01 mol% without significant deterioration of yield or enantioselectivity (entry 10). The turnover frequency (TOF) under these circumstances was calculated to be ~500 h^{-1}, illustrating the high activity of the assembled solid catalyst. The supernatant of catalyst **20b** in 2-propanol did not show any catalytic activity in the hydrogenation of acetophenone, indicating the heterogeneous nature of catalysis. Furthermore, catalysis with **20b** was extended to the hydrogenation of a series of aromatic ketones (**21a**–**h**), affording the corresponding secondary alcohols (**22a**–**h**) with excellent enantioselectivities (entries 3–9). The self-supported catalyst **20b** could be reused for seven cycles of hydrogenation without evident loss of enantioselectivity and catalytic activity.[22]

Table 4. Enantioselective hydrogenation of aromatic ketones (**21a**–**h**) under the catalysis of self-supported Noyori-type catalysts **20a**–**b**.



Ar = Ph (**a**), 1-naphthyl (**b**), 2-naphthyl (**c**), 4′-F-Ph (**d**), 4′-Cl-Ph (**e**), 4′-Br-Ph (**f**), 4′-Me-Ph (**g**), 4′-MeO-Ph (**h**)

Entry	Catalyst [%]	Substrate	*ee* [%]
1	**20a** (0.1)	**21a**	78.2 (*R*)
2[a]	**20b** (0.1)	**21a**	97.4 (*R*)
3	**20b** (0.1)	**21b**	98.1 (*R*)
4	**20b** (0.1)	**21c**	94.5 (*R*)
5	**20b** (0.1)	**21d**	96.2 (*R*)
6	**20b** (0.1)	**21e**	96.9 (*R*)
7	**20b** (0.1)	**21f**	97.2 (*R*)
8	**20b** (0.1)	**21g**	97.5 (*R*)
9	**20b** (0.1)	**21h**	96.2 (*R*)
10	**20b** (0.01)	**21a**	95.2 (*R*)

[a] Catalyst **20b** could be recycled on the hydrogenation of **21a** seven times with 97→99 % conversion and 97.4–95.4 % *ee*.

Conclusion and Outlook

In summary, we have demonstrated a conceptually new strategy, that is, a "self-supporting" approach, for the immobilization of homogeneous catalysts through self-assembly of chiral multitopic ligands and metal ions without the use of any support. On the basis of this strategy, the chiral multitopic ligand can spontaneously form chiral environment inside the cavities of or on the surface of the solids for enantioselective control of the reaction, and the metal ions act as the catalytically active centers. The success of this strategy has been demonstrated in heterogeneous catalysis of asymmetric carbonyl–ene, sulfoxidation, epoxidation, and asymmetric hydrogenation reactions. In addition to the simple recovery and convenient recycle commonly associated with heterogeneous catalysts, such kinds of homochiral metal–organic assemblies may also exhibit advantages of facile preparation, robust chiral structures, and excellent enantioselectivities. These remarkable features, coupled with the versatile methods for rational design and synthesis of the multitopic chiral ligand, suggest a considerable scope of application of this "self-supporting" strategy in the development of new, efficient, and practical catalysts for heterogeneous asymmetric catalysis.

This emerging field calls for the principles of supramolecular chemistry, coordination chemistry, and catalysis in the design and generation of robust heterogeneous catalysts. Although some remarkable achievements have been attained recently, a variety of challenges still remain, among which the most demanding one is the detailed structural elucidation of the self-supported catalysts. Although several analytical techniques such as elemental analysis, solid-state NMR spectroscopy, IR spectroscopy, powder X-ray diffraction analysis and scanning electronic microscopy (SEM) have been employed for the characterization of the assembled heterogeneous catalysts, the usually noncrystalline nature of these solids precludes the possibility of a more detailed study by using single-crystal X-ray diffraction. This lack of structural information renders mechanistic probing extremely difficult. In this respect, design of structurally well-defined and catalytically active homochiral metal–organic coordination polymers is highly desirable to facilitate the understanding the microenvironment of the assemblies and identifying their mechanism of action on a molecular level. This is particularly useful for the rational design of the new generation of the heterogeneous chiral metal–organic polymeric catalysts. Moreover, the construction of the structurally diverse multitopic ligands through covalent bonding is still somewhat tedious at the moment. The future development might be directed to the use of noncovalent interactions (such as hydrogen or coordination bonds)[23] for linking chiral motifs together in order to simplify the procedure for the construction of multitopic ligands. This concept is also expected to extend to much broader scope of organic transformations, such as nonchiral catalysis or polymerization processes, and materials science. We hope that the concept in this account for the heterogenization of homogeneous catalysts may provide a new approach to bridge the gap between homogeneous and heterogeneous asymmetric catalysis and stimulate further research on the development of practical processes for industrial syntheses of optically active products.

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[1] For examples, see: a) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, Wiley-Interscience, New York, **1994**; b) *Catalytic Asymmetric Synthesis*, 2nd ed. (Ed.: I. Ojima), Wiley-VCH, New York, **2000**; c) *Comprehensive Asymmetric Catalysis, Vols. I–III* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**; d) *Lewis Acids in Organic Synthesis* (Ed.: H. Yamamoto), Wiley-VCH, Weinheim, **2001**.

[2] For comprehensive reviews, see: a) *Chiral Catalyst Immobilization and Recycling*, (Eds.: D. E. de Vos, I. F. Vankelecom, P. A. Jacobs), Wiley-VCH, Weinheim, **2000**; b) C. E. Song, S. Lee, *Chem. Rev.* **2002**, *102*, 3495–3524; c) Q. Fan, Y.-M. Li, A. S. C. Chan, *Chem. Rev.* **2002**, *102*, 3385–3466; d) D. E. de Vos, M. Dams, B. F. Sels, P. A. Jacobs, *Chem. Rev.* **2002**, *102*, 3615–3640.

[3] For examples: a) Q. H. Fan, C. Y. Ren, C. H. Yeung, W. H. Hu, A. S. C. Chan, *J. Am. Chem. Soc.* **1999**, *121*, 7407–7408; b) R. ter Halle, B. Colasson, E. Schulz, M. Spagnol, M. Lemaire, *Tetrahedron Lett.* **2000**, *41*, 643–646; c) L. Pu, *Chem. Eur. J.* **1999**, *5*, 2227–2232.

[4] For a highlight, see: L.-X. Dai. *Angew. Chem.* **2004**, *116*, 5846–5850; *Angew. Chem. Int. Ed.* **2004**, *43*, 5726–5729.

[5] a) B. J. Holliday, C. A. Mirkin, *Angew. Chem.* **2001**, *113*, 2076–2097; *Angew. Chem. Int. Ed.* **2001**, *40*, 2022–2043; b) S. Kitagawa, R. Kitaura, S. Noro, *Angew. Chem.* **2004**, *116*, 2388–2430; *Angew. Chem. Int. Ed.* **2004**, *43*, 2334–2375; c) O. M. Yaghi, M. O'Keeffe, N. W. Ockwig, H. K. Chae, M. Eddaoudi, J. Kim, *Nature*, **2003**, *423*, 705–714; d) S. R. Seidel, P. J. Stang, *Acc. Chem. Res.* **2002**, *35*, 972–983.

[6] a) T. Sawaki, T. Dewa, Y. Aoyama, *J. Am. Chem. Soc.* **1998**, *120*, 8539–8540; b) T. Sawaki and Y. Aoyama, *J. Am. Chem. Soc.* **1999**, *121*, 4793–4798; c) M. Fujita, Y.-J. Kwon, S. Washizu, K. Ogura, *J. Am. Chem. Soc.* **1994**, *116*, 1151–1152; d) O. Ohmori, M. Fujita, *Chem. Commun.* **2004**, 1586–1587; e) J. M. Tanski, P. T. Wolczanski, *Inorg. Chem.* **2001**, *40*, 2026–2033; f) B. Gomez-Lor, E. Gutierrez-Puebla, M. Iglesias, M. A. Monge, C. Ruiz-Valero, N. Snejko, *Inorg. Chem.* **2002**, *41*, 2429–2432; g) R. Tannenbaum, *Chem. Mater.* **1994**, *6*, 550–555; h) R. Tannenbaum, *J. Mol. Catal. A* **1996**, *107*, 207–215; i) I. Feinstein-Jaffe, A. Efraty, *J. Mol. Catal.* **1987**, *40*, 1–7; j) S. Naito, T. Tanibe, E. Saito, T. Miyao, W. Mori, *Chem. Lett.* **2001**, 1178–1179; k) B. G. Xing, M.-F. Choi, B. Xu, *Chem. Eur. J.* **2002**, *8*, 5028–5032; l) S. J. Hong, J. Y. Ryu, J. Y. Lee, C. Kim, S.-J. Kim, Y. Kim, *Dalton Trans.* **2004**, 2697–2701; m) L.-G. Qiu, A.-J. Xie, L.-D. Zhan, *Adv. Mater.* **2005**, *17*, 689–692; n) S. J. Hong, J. S. Seo, J. Y. Ryu, J. H. Lee, C. Kim, S. J. Kim, Y. Kim, A. J. Lough, *J. Mol. Struct.* **2005**, *751*, 22–28.

[7] a) S. Takizawa, H. Somei, D. Jayaprakash, H. Sasai, *Angew. Chem.* **2003**, *115*, 5889–5892; *Angew. Chem. Int. Ed.* **2003**, *42*, 5711–5714; b) H. Guo, X. Wang, K. Ding, *Tetrahedron Lett.* **2004**, *45*, 2009–2012; c) X. Wang, K. Ding, *J. Am. Chem. Soc.* **2004**, *126*, 10524–10525.

[8] J. S. Seo, D. Whang, H. Lee, S. I. Jun, J. Oh, Y. J. Jeon, K. Kim, *Nature* **2000**, *404*, 982–986.

[9] a) O. R. Evans, H. L. Ngo, W. Lin, *J. Am. Chem. Soc.* **2001**, *123*, 10395–10396; b) H. L. Ngo, A. G. Hu, W. Lin, *J. Mol. Catal. A* **2004**, *215*, 177–186.

[10] For the heterogenization of Noyori's catalyst by in situ formation of chiral porous hybrid solids, see: a) A. Hu, H. L. Ngo, W. Lin, *J. Am. Chem. Soc.* **2003**, *125*, 11490–11491; b) A. Hu, H. L. Ngo, W. Lin, *Angew. Chem.* **2003**, *115*, 6182–6185; *Angew. Chem. Int. Ed.* **2003**, *42*, 6000–6003.

[11] For comprehensive reviews, see: a) K. Ding, *Pure Appl. Chem.* **2005**, *77*, 1251–1257; b) K. Ding, H. Du, Y. Yuan, J. Long, *Chem. Eur. J.* **2004**, *10*, 2872–2884; c) M. T. Reetz. *Angew. Chem.* **2001**, *113*, 292–320; *Angew. Chem. Int. Ed.* **2001**, *40*, 284–310; d) M. Tsukamoto, H. B. Kagan, *Adv. Synth. Catal.* **2002**, *344*, 453–463; e) C. Gennari, U. Piarulli, *Chem. Rev.* **2003**, *103*, 3071–3100.

[12] For reviews on enantioselective carbonyl–ene reactions: a) K. Mikami, M. Shimizu, *Chem. Rev.* **1992**, *92*, 1021–1050; b) K. Mikami, M. Terada, In *Comprehensive Asymmetric Catalysis, Vol. III* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer, Berlin, **1999**, Chapter 32; c) L. C. Dias, *Curr. Org. Chem.* **2000**, *4*, 305–342.

[13] a) K. Mikami, M. Terada, T. Korenaga, Y. Matsumoto, M. Ueki, R. Angelaud, *Angew. Chem.* **2000**, *112*, 3676–3701; *Angew. Chem. Int. Ed.* **2000**, *39*, 3532–3556; b) K. Mikami, M. Terada, T. Korenaga, Y. Matsumoto, S. Matsukawa, *Acc. Chem. Res.* **2000**, *33*, 391–401; c) K. Mikami, S. Matsukawa, *Nature* **1997**, *385*, 613–615.

[14] Y. Yuan, X. Zhang, K. Ding, *Angew. Chem.* **2003**, *115*, 5636–5638; *Angew. Chem. Int. Ed.* **2003**, *42*, 5478–5480.

[15] X. Wang, X. Wang, H. Guo, Z. Wang, K. Ding, *Chem. Eur. J.* **2005**, *11*, 4078–4088.

[16] For early examples, see: a) S. H. Zhao, O. Samuel, H. B. Kagan, *Org. Synth.* **1989**, *68*, 49–54; b) J. M. Brunel, H. B. Kagan, *Synlett* **1996**, 404–406; c) N. Komatsu, M. Hashizume, T. Sugita, S. Uemura, *J. Org. Chem.* **1993**, *58*, 4529–4533; for a recent example, see: d) X. Jia, X. Li, L. Xu, Y. Li, Q. Shi, T.-L. Au-Yeung, C. Yip, X. Yao, A. S. C. Chan, *Adv. Synth. Catal.* **2004**, *346*, 723–726.

[17] For early examples, see: a) M. Bougauchi, S. Watanabe, T. Arai, H. Sasai, M. Shibasaki, *J. Am. Chem. Soc.* **1997**, *119*, 2329–2330; b) K. Daikai, M. Kamaura, J. Inanaga, *Tetrahedron Lett.* **1998**, *39*, 7321–7322; for recently examples, see: c) T. Kinoshita, S. Okada, S. R. Park, S. Matsunaga, M. Shibasaki, *Angew. Chem.* **2003**, *115*, 4828–4832; *Angew. Chem. Int. Ed.* **2003**, *42*, 4680–4684; d) S. Matsunaga, T. Kinoshita, S. Okada, S. Harada, M. Shibasaki, *J. Am. Chem. Soc.* **2004**, *126*, 7559–7570; e) R. Chen, C. Qian, J. G. de Vries, *Tetrahedron* **2001**, *57*, 9837–9842; f) R. Kino, K. Daikai, T. Kawanami, J. Inanaga, *Org. Biomol. Chem.* **2004**, *2*, 1822–1824.

[18] X. Wang, L. Shi, M. Li, K. Ding, *Angew. Chem.* **2005**, *117*, 6520–6524; *Angew. Chem. Int. Ed.* **2005**, *44*, 6362–6366.

[19] For a highlight, see: a) I. V. Komarov, A. Börner, *Angew. Chem.* **2001**, *113*, 1237–1240; *Angew. Chem. Int. Ed.* **2001**, *40*, 1197–1200; for leading references, see: b) F. Guillen, J. C. Fiaud, *Tetrahedron Lett.* **1999**, *40*, 2939–2942; c) M. T. Reetz, G. Mehler, *Angew. Chem.* **2000**, *112*, 4047–4049; *Angew. Chem. Int. Ed.* **2000**, *39*, 3889–3890; d) M. van den Berg, A. J. Minnaard, E. P. Schudde, J. van Esch, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *J. Am. Chem. Soc.*

2000, *122*, 11539–11540; e) C. Claver, E. Fernandez, A. Gillon, K. Heslop, D. J. Hyett, A. Martorell, A. G. Orpen, P. G. Pringle, *Chem. Commun.* **2000**, 961–962. For recent examples, see: f) D. Peña, A. J. Minnaard, J. G. de Vries, B. L. Feringa, *J. Am. Chem. Soc.* **2002**, *124*, 14552–14553; g) R. Hoen, J. A. F. Boogers, H. Bernsmann, A. J. Minnaard, A. Meetsman, T. D. Tiemersma-Wegman, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *Angew. Chem.* **2005**, *117*, 4281–4284; *Angew. Chem. Int. Ed.* **2005**, *44*, 4209–4212; h) M. van den Berg, R. M. Haak, A. J. Minnaard, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *Adv. Synth. Catal.* **2002**, *344*, 1003–1007; i) D. Peña, A. J. Minnaard, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries, L. B. Feringa, *Org. Biomol. Chem.* **2003**, *1*, 1087–1089; j) M. van den Berg, A. J. Minnaard, R. M. Haak, M. Leeman, E. P. Schudde, A. Meetsma, B. L. Feringa, A. H. M. de Vries, C. E. P. Maljaars, C. E. Willans, D. Hyett, J. A. F. Boogers, H. J. W. Henderickx, J. G. de Vries, *Adv. Synth. Catal.* **2003**, *345*, 308–323; k) R. Hoen, J. A. F. Boogers, H. Bernsmann, A. J. Minnaard, A. Meetsman, T. D. Tiemersma-Wegman, A. H. M. de Vries, J. G. de Vries, B. L. Feringa, *Angew. Chem.* **2005**, *117*, 4281–4284; *Angew. Chem. Int. Ed.* **2005**, *44*, 4209–4212; l) A. Duursma, R. Hoen, J. Schuppan, R. Hulst, A. J. Minnaard, B. L. Feringa, *Org. Lett.* **2003**, *5*, 3111–3113; m) R. Hoen, M. van den Berg, H. Bernsmann, A. J. Minnaard, J. G. de Vries, B. L. Feringa, *Org. Lett.* **2004**, *6*, 1433–1436; n) L. Lefort, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries, *Org. Lett.* **2004**, *6*, 1733–1735; o) C. Monti, C. Gennari, U. Piarulli, J. G. de Fries, A. H. M. de Vries, L. Lefort, *Chem. Eur. J.* **2005**, *11*, 6701–6717; p) Y. Fu, J.-H. Xie, A.-G. Hu, H. Zhou, L.-X. Wang, Q.-L. Zhou, *Chem. Commun.* **2002**, 480–481; q) A.-G. Hu, Y. Fu, J.-H. Xie, H. Zhou, L.-X. Wang, Q.-L. Zhou, *Angew. Chem.* **2002**, *114*, 2454–2456; *Angew. Chem. Int. Ed.* **2002**, *41*, 2348–2350; r) S. Wu, W. Zhang, Z. Zhang, X. Zhang, *Org. Lett.* **2004**, *6*, 3565–3567; s) M. T. Reetz, J.-A. Ma, R. Goddard, *Angew. Chem.* **2005**, *117*, 416–419; *Angew. Chem. Int. Ed.* **2005**, *44*, 412–415; t) M. T. Reetz, T. Sell, A. Meiswinkel, G. Mehler, *Angew. Chem.* **2003**, *115*, 814–817; *Angew. Chem. Int. Ed.* **2003**, *42*, 790–793; u) M. T. Reetz, A. Meiswinkel, G. Mehler, K. Angermund, M. Graf, W. Thiel, R. Mynott, D. G. Blackmond, *J. Am. Chem. Soc.* **2005**, *127*, 10305–10313; v) M. T. Reetz, X.-G. Li, *Angew. Chem.* **2005**, *117*, 3019–3021; *Angew. Chem. Int. Ed*, **2005**, *44*, 2959–2962; w) Y. Liu, K. Ding, *J. Am. Chem. Soc.* **2005**, *127*, 10488–10489.

[20] H.-Y. Peng, C.-K. Lam, T. C. W. Mak, Z. Cai, W.-T. Ma, Y.-X. Li, H. N. C. Wong, *J. Am. Chem. Soc.* **2005**, *127*, 9603–9611.

[21] a) T. Ohkuma, H. Ooka, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 10417–10418; b) C. A. Sandoval, T. Ohkuma, K. Kuniz, R. Noyori, *J. Am. Chem. Soc.* **2003**, *125*, 13490–13503.

[22] Y. Liang, Q. Jing, X. Li, L. Shi, K. Ding, *J. Am. Chem. Soc.* **2005**, *127*, 7694–7695.

[23] a) J. -M. Lehn. *Supramolecular Chemistry: Concepts and Perspectives*, Wiley-VCH, Weinheim, **1995**; b) *Molecular Self-Assembly-Organic versus Inorganic Approaches, Vol. 96* (Ed.: M. Fujita), Springer, Berlin, **2000**; c) S. Leininger, B. Olenyuk, P. J. Stang. *Chem. Rev.* **2000**, *100*, 853–908; d) L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.* **2001**, *101*, 4071–4097; e) C. Schmuck, W. Wienand, *Angew. Chem.* **2001**, *113*, 4493–4499; *Angew. Chem. Int. Ed.* **2001**, *40*, 4363–4369; f) W. Gerhardt, M. Crne, M. Weck, *Chem. Eur. J.* **2004**, *10*, 6213–6221; g) J. M. Lehn, *Science* **2002**, *295*, 2400–2403. Recently, Lin and co-workers used homochiral metal–organic coordination frameworks constructed by coordination bonds as porous polymeric ligands in conjunction with Ti^{IV} as a heterogeneous catalyst for highly enantioselective diethylzinc addition to aromatic aldehydes, see: h) C. D. Wu, A. Hu, L. Zhang, W. B. Lin, *J. Am. Chem. Soc.* **2005**, *127*, 8940–8941.