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

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Abstract: A new strategy for the heterogenization of chiral titanium complexes was developed by the in situ assembly of bridged multitopic BINOL ligands with $[Ti(OiPr)_4]$ without using a support. The assembled heterogeneous catalysts (self-supported) showed excellent enantioselectivity in both the carbonyl–ene reaction of α-methylstyrene with ethyl glyoxylate (up to 98% *ee*) and the oxidation of sulfides (up to >99% *ee*). The catalytic performance of these heterogeneous catalytic systems was comparable or even superior to that attained with their homogeneous counterparts. The spacers between the two BINOL units of the ligands in the assembled catalysts had significant impact on the enantioselectivity of the carbonyl–ene reaction. This demonstrates the importance of the supramolecular structures of the assemblies on their catalytic behavior. In the catalysis of sulfoxidation, the self-supported heterogeneous titanium catalysts were highly stable and could be readily recycled and reused for over one month (at least eight cycles) without significant loss of activity and enantioselectivity (up to >99.9% *ee*). The features of these self-supported catalysts, such as facile preparation, robust chiral structure of solid-state catalysts, high density of the catalytically active units in the solids, as well as easy recovery and simple recycling, are particularly important in developing methods for the synthesis of optically active compounds in industrial processes.

Keywords: carbonyl–ene reaction · heterogeneous catalysis · immobilization · oxidation · titanium

Introduction

The asymmetric catalysis of organic reactions to provide enantiomerically enriched products is central to modern synthetic and pharmaceutical chemistry.[1] The development of chiral catalysts for the enantioselective reactions is a fundamental aspect in asymmetric catalysis.[2] Homogeneous asymmetric catalysis has the advantages of high enantioselectivity and catalytic activity in various asymmetric transformations under mild reaction conditions. The catalyst loadings employed in most cases have been in the range of 5–10 mol%,[2] which is impractical due to the high costs of noble chiral catalysts and difficulties associated with their recovery and reuse.[3] The heterogenization of the homogeneous catalysts provides a convenient approach to catalyst separation and recycling.[4] Immobilization of the homogeneous asymmetric catalyst is commonly achieved by the utilization of inorganic materials, organic polymers, or membranes as supports through either covalent bonding or noncovalent anchoring.[5] However, the catalysts immobilized by these approaches often display reduced enantioselectivity or activity relative to their homogeneous counterparts.

Metal–organic self-assembled frameworks exhibit permanent porosity and absorption capacity for organic guest molecules.[6] The design and synthesis of chiral metal–organic frameworks (chiral zeolite) may, therefore, provide a new strategy for asymmetric heterogeneous catalysis, as the chiral ligand can spontaneously form a chiral environment and the metal ion may act as the catalytically active center. Such molecular assemblies would have the advantage of both robust chiral frameworks and high density of the catalytically active units. Seo and co-workers demonstrated the enantioselective catalytic activity of a homochiral metal–organic porous material composed of tartaric acid-derived ligands and Zn ions for transesterification, despite low enantioselectivity (~8% *ee*).[7] More recently, Lin and co-workers reported the heterogenization of Noyori's catalyst with a zirconium phosphonate framework, which promotes the asymmetric hydrogenation of aromatic ketones with remarkably

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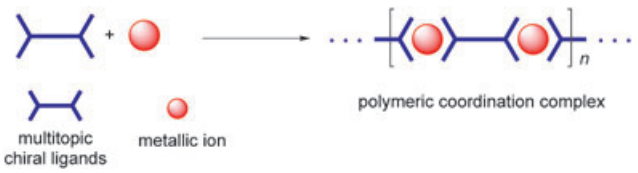
high activity, enantioselectivity, and reusability.[8] Sasai and our group independently reported a new strategy for the immobilization of homogeneous catalysts. This involved using homochiral metal–organic coordination polymers, formed by the self-assembly of chiral multitopic ligands and catalytically active metal ions, as "self-supported" chiral catalysts.[9] The application of the assembled titanium catalysts to the asymmetric carbonyl–ene reaction exhibited high activity and enantioselectivity.[9b] In particular, the self-supported heterogeneous titanium catalysts were highly stable and could be readily recycled and reused for over one month without significant loss of activity and enantioselectivity (up to >99.9% *ee*) in the catalysis of asymmetric sulfoxidation. Here, we report the heterogenization of titanium catalysts with a self-supporting strategy for the heterogeneous enantioselective carbonyl–ene reaction and the oxidation of sulfides.

Results and Discussion

The principle of chiral catalyst immobilization: In the classical immobilization of homogeneous catalysts with organic polymers,[4,5] the chiral ligands or the catalytically active units are usually anchored randomly onto irregular polymers, or are incorporated into the main polymer chain, as highlighted by Dai.[10] Although these strategies have yielded some success,[4,5] the polymeric ligands must be prepared before the active metallic species is uploaded, and the procedures for their syntheses are usually somewhat tedious. In contrast, the assembly of chiral multitopic ligands with catalytically active metal ions can afford coordination polymers (or oligomers) conveniently, without the use of support (Scheme 1).

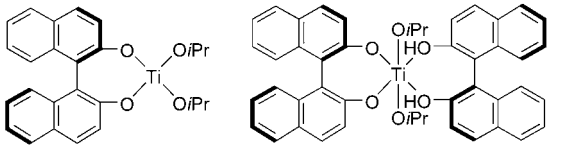


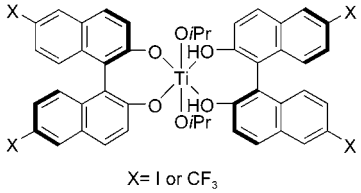
Scheme 1. Schematic representation of the self-supporting strategy for the immobilization of chiral catalysts.

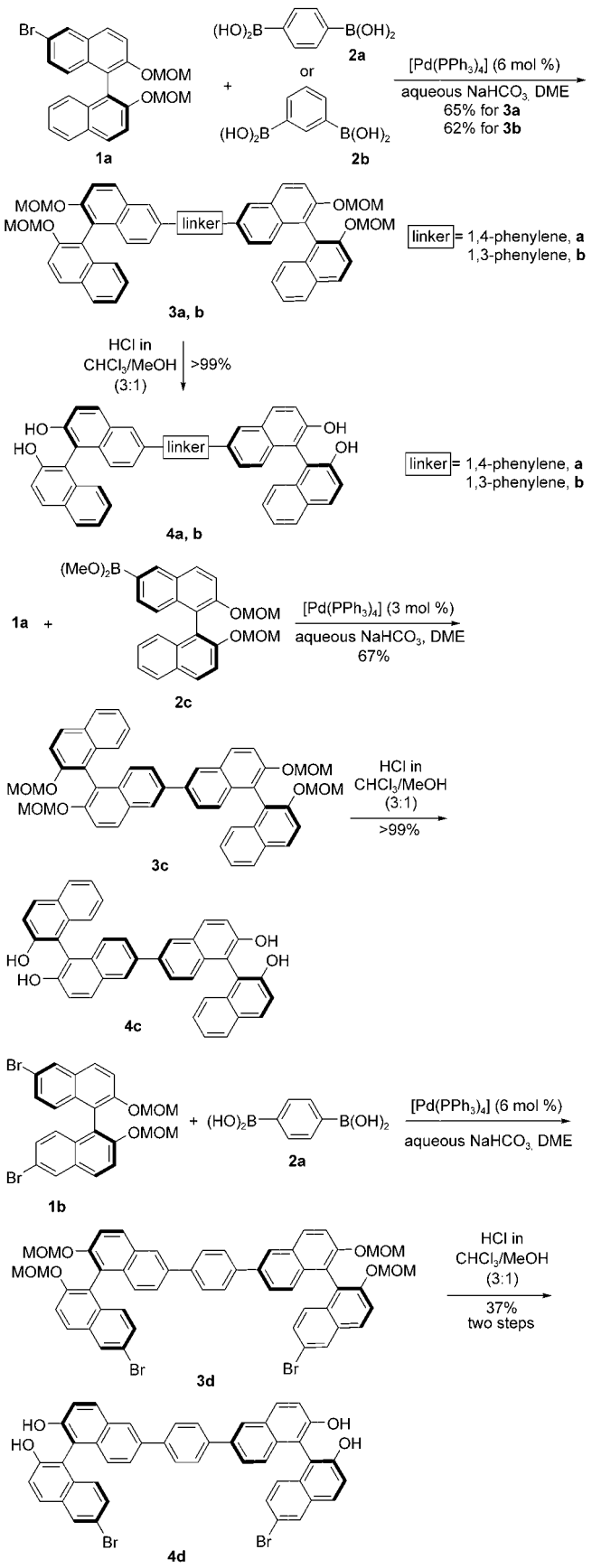
The resultant coordination polymers (or oligomers) often display low solubility in common organic solvents, which provides an excellent opportunity for performing asymmetric catalysis heterogeneously. This mode of chiral catalyst immobilization was called a self-supporting strategy.[9c,10] Accordingly, the key issue for the generation of self-supported chiral catalysts is the design and synthesis of multitopic ligands. The bridging linker of the ligand should be rigid to avoid the intramolecular interaction of two chiral units and to guarantee the formation of intermolecular coordination polymers.

Synthesis of multitopic BINOL ligands: To demonstrate the feasibility of our strategy, four bridged BINOL ligands were designed (**4a**–**d**), in which the spacers were assembled at the 6-position of the 1,1′-binaphthyl backbone to avoid the intramolecular interaction of two chiral units. The synthesis of **4a**–**d** was quite straightforward (Scheme 2). Suzuki coupling[11] reactions of (*S*)-6-bromo-2,2′-dimethoxymethoxy-1,1′-binaphthyl (**1a**) with 1,4- or 1,3-phenlene diboric acid (**2a**–**b**) in ethylene glycol dimethyl ether (DME), under the catalysis of [Pd(PPh$_3$)$_4$], afforded **3a** and **3b** in 62 and 67% yields, respectively. The acidic deprotection of methoxymethoxy (MOM) groups of **3a**–**b** furnished the expected bridged BINOL ligands **4a** and **4b** in >99% yields. The synthesis of **4c** was accomplished by the coupling of **1a** with (*S*)-6-(MeO)$_2$B-2,2′-dimethoxymethoxy-1,1′-binaphthyl (**2c**), followed by acidic deprotection of the methoxymethyl groups. The Suzuki coupling of (*S*)-6,6′-dibromo-2,2′-dimethoxymethoxy-1,1′-binaphthyl (**1b**) with 1,4-phenlene diboric acid **2a** afforded **3d**, which was then hydrolyzed under acidic conditions to give **4d** in 37% overall yield.

Self-supported titanium catalysts for enantioselective carbonyl–ene reactions: The asymmetric carbonyl–ene reaction is an important means of C–C bond formation in organic synthesis.[12] Among various chiral Lewis acids, such as Al, Ti, Ni, Pt, Pd, Yb, and Cu metallic complexes, titanium complexes of BINOL derivatives are among the most widely used for asymmetric carbonyl–ene reactions.[12–14] According to Mikami's asymmetric activation concept, an enantiopure [(*R*)-BINOL-Ti(O*i*Pr)$_2$] (10 mol%) catalyst could be activated by the further addition of (*R*)-BINOL(H$_2$), affording the product of the carbonyl–ene reaction in higher enantioselectivity (96.8% *ee* vs 94.5% *ee*).[14] Results of a kinetic study showed that the reaction catalyzed by the [(*R*)-BINOL-Ti(O*i*Pr)$_2$-(*R*)-BINOL(H$_2$)] complex was 25.6 times faster than that catalyzed by [(*R*)-BINOL-Ti(O*i*Pr)$_2$].[14a] We have demonstrated that the catalysts prepared by the homocombination of (*R*)-6,6′-I$_2$-BINOL with Ti(O*i*Pr)$_4$, or by the heterocombination of (*R*)-6,6′-I$_2$-BINOL and (*R*)-6,6′-(CF$_3$)$_2$-BINOL with [Ti(O*i*Pr)$_4$], show exceptionally high efficiencies for the carbonyl–ene reaction under nearly solvent-free

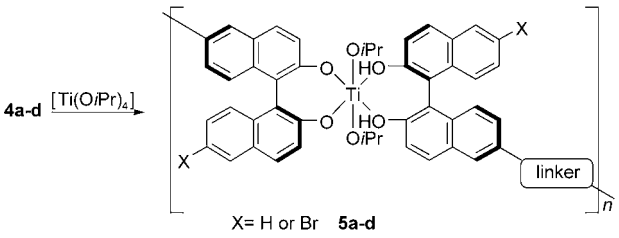






Scheme 2. Synthesis of bridged multitopic BINOL ligands **4a–d**.

conditions, affording α-hydroxy ester derivatives in good yields and excellent enantioselectivities.[15] These phenomena facilitated the design of assembled catalysts for this reaction by the assembly of bridged BINOL ligands with [Ti(O*i*Pr)$_4$] (Scheme 3).



Scheme 3. Heterogenization of BINOL-Ti catalysts by using the self-supporting strategy for the enantioselective carbonyl–ene reaction.

The catalysts **5a–d** were prepared by mixing ligands **4a–d** with [Ti(O*i*Pr)$_4$] (molar ratio 1:1) in CH_2Cl_2. The mixtures were stirred at room temperature for 4 h and then the solvent was removed under reduced pressure. The resultant solids were washed with diethyl ether three times and then dried in a vacuum. Elemental analyses showed that the composition of the resulting solids was consistent with the expected structures of **5a–d**. These solids had very poor solubility in the reaction system (Figure 1a and b). SEM images showed that they were composed of micrometer-sized particles (Figure 1c), and powder X-ray diffraction (PXD) patterns indicated that they were noncrystalline solids (see Supporting Information).

Catalysts **5a–d** were then submitted to the carbonyl–ene reaction of α-methylstyrene (**6**) with ethyl glyoxylate (**7**) in toluene, diethyl ether, or in the absence of solvent. The catalyst loading employed in the reaction was 1 mol%. As shown in Table 1, the carbonyl–ene reaction proceeded smoothly at room temperature under the catalysis of **5a** to give α-hydroxy ester (*S*)-**8** in 91% yield and 94.4% *ee* (entry 1). Lowering the reaction temperature to 0°C caused a decrease in reactivity with a slight improvement of the enantioselectivity (entry 2 vs entry 1). The addition of 4 Å molecular sieve (MS) had no significant impact on catalysis in terms of both enantioselectivity and reactivity of the reaction (entries 4 and 5 vs entries 1 and 2). The reaction could also be conducted under solvent-free conditions by using **5a** to afford the product (*S*)-**8** in 75% yield with 94% *ee* (entry 6). By contrast, the catalyst **5b**, prepared from ligand **4b** with a 1,3-phenylene spacer, showed poor catalytic activity and enantioselectivity under the same experimental conditions (entries 7 and 8). This implies that changing the linker moieties of the ligands probably alters the supramolecular structure of the assemblies. Interestingly, the catalyst **5c** obtained from a simple dimer of BINOL (**4c**) showed enhanced enantioselectivity and dramatically increased catalytic activity, giving product (*S*)-**8** in >99% yield and 96% *ee* (entry 9). Similarly, neither the addition of

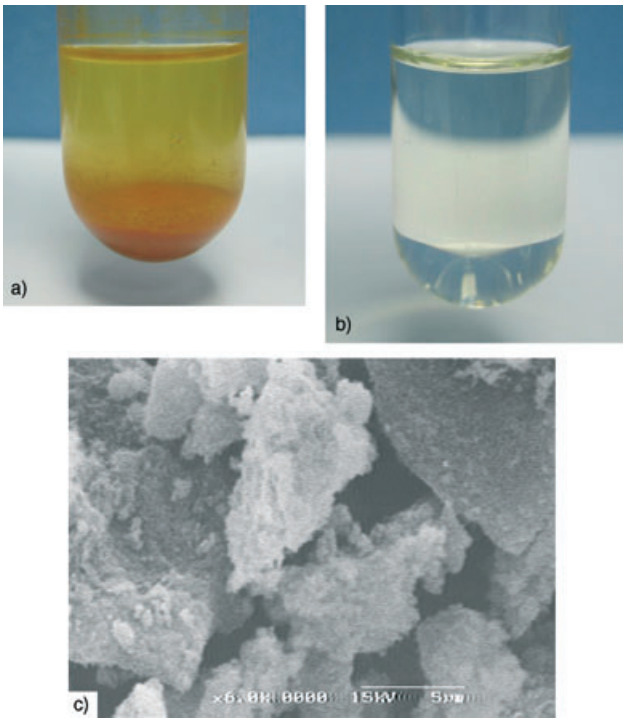
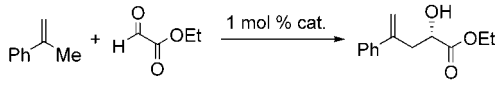


Figure 1. a) Self-supported chiral titanium catalyst **5a** (orange solids) in diethyl ether containing substrates **6** and **7**. b) The liquid phase obtained after catalyst recovery by filtration. c) SEM image of the self-supported titanium catalyst **5a**. The scale bar represents 5 μm.

Table 1. Enantioselective catalysis of carbonyl–ene reactions with the assembled catalysts **5a–d**.[a]



6 **7** **8**

Entry	Catalyst	Solvent	4 Å MS[b]	Stirring	Temp. [°C]	Time [h]	Yield [%][c]	*ee* [%][d]
1	**5a**	toluene	–	+	RT	48	91	94
2	**5a**	toluene	–	+	0	120	85	95
3	**5a**	toluene	–	–	0	120	96	95
4	**5a**	toluene	+	+	RT	120	93	92
5	**5a**	toluene	+	+	0	120	65	92
6	**5a**	free	–	–	0	120	75	94
7	**5b**	toluene	–	+	RT	48	32	9
8	**5b**	toluene	–	+	0	120	9	24
9	**5c**	toluene	–	+	RT	30	99	96
10	**5c**	toluene	–	+	0	96	95	91
11	**5c**	toluene	+	+	RT	96	85	92
12	**5c**	toluene	+	+	0	96	90	95
13	**5c**	free	–	+	0	96	90	92
14	**5c**	diethyl ether	–	+	RT	120	99	95
15	**5d**	toluene	–	+	RT	96	99	95
16	**5d**	toluene	–	+	0	96	99	98
17	**5d**	toluene	–	+	−10	96	99	98
18	**5d**	diethyl ether	–	+	RT	96	99	97

[a] The reaction was performed by using 3.0 M of **6** with the ratio of **6**/**7**/**5** = 1:2:0.01 on a 1.25 mmol scale. [b] 15 mg of 4 Å MS (dried in vacuo at 400 °C for 8 h) was added. [c] Isolated yield. [d] The *ee* was determined by performing HPLC using a Chiralcel OJ column, and the absolute configuration was assigned to be *S* by comparing their optical rotations with literature data.[15]

4 Å MS nor a reduction in the reaction temperature had advantage over the reaction at room temperature in the absence of 4 Å MS. Again, the reaction in solvent-free conditions could proceed smoothly under the catalysis of **5c**, affording the product in slightly decreased yield and enantioselectivity (entry 13). The solids of the catalyst **5c** were found to be gradually dissolved in the reaction mixture under solvent-free conditions, which suggests that the nature of the reaction in this case was homogenous.

As we reported previously,[15] the introduction of an electron-withdrawing substituent to the backbone of BINOL could significantly improve catalytic activity, due to the increase in Lewis acidity of titanium(IV) complexes. Accordingly, the assembled titanium catalyst, composed of ligands **4d** and having bromo substituents at the 6-positions of bridged BINOL, was examined for the catalysis of the carbonyl–ene reaction. As expected, the reaction promoted by catalyst **5d** always afforded the product in high yields (99 %) with excellent enantioselectivities (95–98 % *ee*) under various conditions (entries 15–18). Diethyl ether was an optimal solvent for running the heterogeneous catalysis of **5d**, due to the latter's lower solubility in this solvent (entry 18). On the basis of these results, the recovery and recycling of this type of self-supported titanium catalyst was conducted by using the catalyst **5d** in diethyl ether. After the reaction was complete, simple filtration of the reaction mixture enabled separation of the solid-state catalyst from the product-containing solution. The separated solids were recharged with diethyl ether and substrates in preparation for the next run. As shown in Table 2, the catalyst **5d** could be used for five cycles in the carbonyl–ene reaction. Clearly, both the activity and enantioselectivity of catalysis dropped gradually with each recycling step. This is probably due to the partial decomposition of the assemblies during catalysis, and as a result, the active titanium(IV) species may leach into the solution phase of the reaction mixture. Indeed, in the course of catalysis, the reaction mixture developed a pale yellow color.

Table 2. Recovery and reuse of the heterogeneous catalyst **5d** for the carbonyl–ene reaction of **6** with **7**.[a]

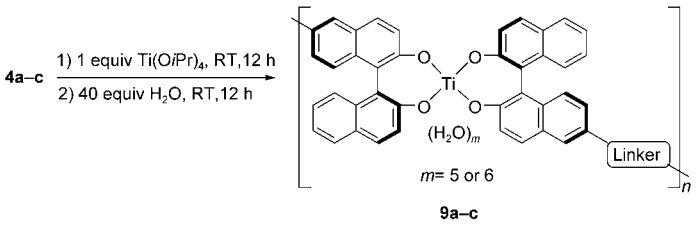
Run	Time [h]	Yield [%][b]	*ee* [%]
1	96	87	97
2	96	85	94
3	96	75	84
4	96	73	76
5	120	70	70

[a] The reaction was performed at a substrate concentration of 1.0 M with the ratio of **6**/**7**/**5d** = 1:1:0.01 in diethyl ether.[12] [b] Isolated yield.

Self-supported titanium catalysts for enantioselective sulfoxidation: Optically active sulfoxides are important chiral auxiliaries in organic synthesis, and valuable intermediates in the syntheses of pharmaceuticals and biologically active

compounds.[16] The asymmetric oxidation of sulfides in the presence of various chiral catalysts,[16a,17] such as Ti,[18] Mn,[19] V,[20] Nb,[21] W,[22] Zr[23] and Fe[24] complexes, is one of the most convenient routes for obtaining sulfoxides. The use of titanium complexes based on C_2-symmetric diol ligands has been key to achieving the homogeneous catalytic, asymmetric oxidation of prochiral sulfides.[18] Although various homogeneous enantioselective catalyses of oxidation of sulfides have been successful, little attention has been paid to the heterogeneous processes.[20i,22,25] As described above, the assembled titanium catalysts **5a–d** have been successfully applied to the catalysis of the asymmetric carbonyl–ene reaction. However, under some experimental conditions, the pale yellow color observed in the liquid phase of the reaction mixture suggested possible leaching of the heterogeneous active species into the solution phase during catalysis. Here, we demonstrate the development of truly heterogeneous self-supported titanium catalysts for the enantioselective oxidation of aryl alkyl sulfides. The catalysts developed for asymmetric sulfoxidation were highly stable and could be recycled at least eight times without loss of enantioselectivity, affording the corresponding optically active sulfoxides with up to >99.9% *ee*.

Kagan and Uemura have shown that the addition of water in the titanium catalyst systems is crucial for the catalysis of sulfide oxidation.[18a–c] The preparation of heterogeneous catalysts **9a–c** was similar to that of **5a–d**, except for the addition of water in the former (Scheme 4). The reaction of



Scheme 4. Heterogenization of BINOL-Ti catalysts by using the self-supporting strategy for enantioselective sulfoxidation.

bridged BINOL ligands **4a–c** with [Ti(O*i*Pr)$_4$] (1:1 molar ratio) was conducted in CCl_4 (12 h), followed by addition of H_2O (40 equiv relative to ligand). The mixture was stirred for an additional 12 h to afford the self-supported catalysts **9a–c** as orange or red solids. These solids were collected by filtration and washed with CCl_4 to remove the trace amount of soluble, low-molecular-weight species. As exemplified by catalyst **9a** in Figure 2a and b, these polymeric solids were completely insoluble in CCl_4, and accordingly, fulfilled one of the basic prerequisites for heterogeneous catalysis. Elemental analyses showed that the composition of the resulting solids was consistent with the expected structures of **9a–c** containing five or six molecules of water. SEM images revealed that these solids were composed of micrometer-sized particles (Figure 2c), and powder X-ray diffraction (PXD)

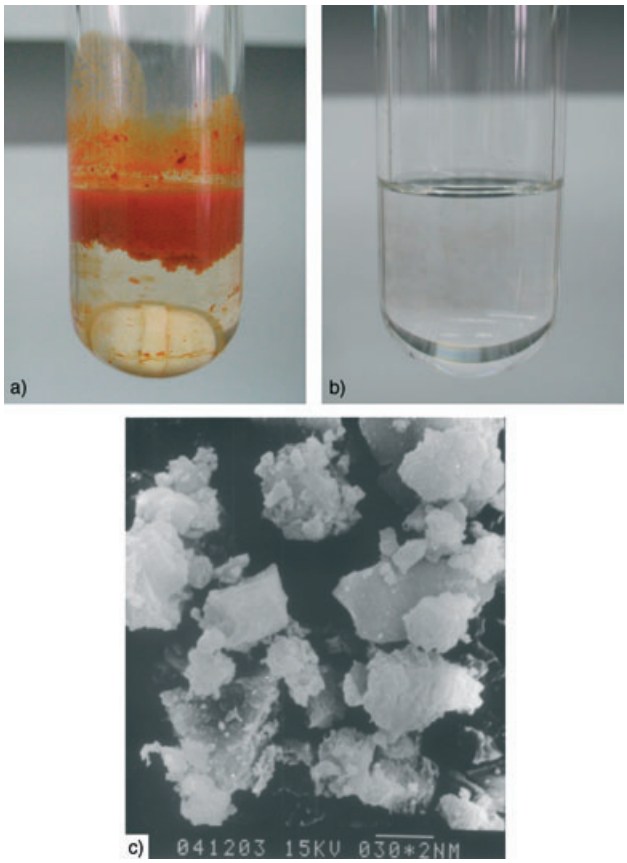
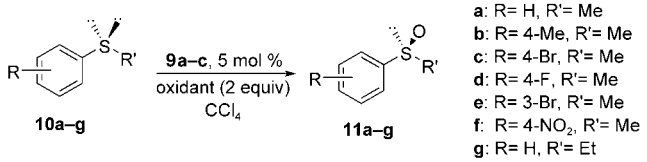


Figure 2. a) Self-supported chiral titanium catalyst **9a** (orange solids) in CCl_4 containing substrate **10a**. b) The liquid phase obtained after catalyst recovery by filtration. c) SEM image of the self-supported titanium catalyst **9a**. The scale bar represents 3 μm.

patterns indicated that they were noncrystalline solids (see Supporting Information).

The self-supported heterogeneous catalysts **9a–c** were then tested in the enantioselective oxidation of sulfides **10a–i** (Table 3), and CCl_4 was chosen as the solvent after a preliminary examination of the solvent effect. The reaction was conducted at room temperature by using 5 mol% of catalysts **9a–c**. The impact of oxidants on the reactivity and enantioselectivity of catalysis was investigated initially with thioanisole **10a** as the substrate. As shown in Table 3, the decane solution of *tert*-butyl hydroperoxide (TBHP, 5–6 M in decane) was superior to its aqueous solution (70% solution in water) in terms of enantioselectivity (entry 2 versus entry 1). However, the oxidation of **10a** with hydrogen peroxide (H_2O_2, 30% aqueous solution) as oxidant in the presence of **9a** drastically decreased the enantioselectivity of the reaction (entry 3, 31.1% *ee*), even though the reaction could proceed smoothly with complete conversion of sulfide **10a**. This was probably caused by the partial decomposition of the catalyst in the presence of a large excess of water in the reaction system. By using less explosive and less reactive cumene hydroperoxide (CMHP, 80% in cumene) as oxidant instead of TBHP, excellent enantioselectivity (99.2% *ee*) was achieved with 38% yield (entry 4). A catalyst prepared

Table 3. Enantioselective oxidation of sulfides catalyzed by self-supported catalysts **9a–c**.[a]



Entry	Substrate	Catalyst	Oxidant	Yield [%][b]	*ee*[c] [%] (configuration)[d]
1	**10a**	**9a**	TBHP[e]	68.8	74.5 (*S*)
2	**10a**	**9a**	TBHP[f]	32.9	97.5 (*S*)
3	**10a**	**9a**	H_2O_2[g]	32.8	31.1 (*S*)
4	**10a**	**9a**	CMHP	38.6	99.2 (*S*)
5	**10a**	**9a**[h]	CMHP	35.7	87.7 (*S*)
6	**10a**	**9b**	CMHP	37.8	99.5 (*S*)
7	**10a**	**9c**	CMHP	37.1	98.7 (*S*)
8	**10b**	**9a**	CMHP	36.6	>99.9 (*S*)
9	**10b**	**9b**	CMHP	41.5	99.8 (*S*)
10	**10b**	**9c**	CMHP	41.5	99.1 (*S*)
11	**10c**	**9a**	CMHP	30.7	>99.9 (*S*)
12	**10c**	**9b**	CMHP	30.1	99.8 (*S*)
13	**10c**	**9c**	CMHP	31.0	>99.9 (*S*)
14	**10d**	**9a**	CMHP	41.0	98.6 (*S*)
15	**10d**	**9b**	CMHP	38.5	96.4 (*S*)
16	**10d**	**9c**	CMHP	44.9	97.0 (*S*)
17	**10e**	**9a**	CMHP	32.9	>99.9 (*S*)
18	**10e**	**9b**	CMHP	36.5	>99.9 (*S*)
19	**10e**	**9c**	CMHP	34.7	>99.9 (*S*)
20[i]	**10f**	**9b**	CMHP	20.5	89.1 (*S*)
21	**10g**	**9a**	CMHP	36.3	75.5 (*S*)
22[j]	**10a**	**9a**	CMHP	45.7	99.9 (*S*)

[a] Unless otherwise stated, all of the reactions were performed at 25°C with 2 equivalents of oxidant in CCl_4 for 72 h. [b] Isolated yields of products. [c] Determined by performing HPLC using a Chiralcel column. [d] Absolute configurations were determined by comparison of their optical rotations with literature data.[20h,27] [e] 70% solution in water. [f] 5–6 M in decane. [g] 30% aqueous H_2O_2, reaction time 36 h. [h] Without addition of H_2O in the preparation of catalyst. [i] Reaction time 60 h. [j] The reaction was run for 24 h at 0°C, then for 48 h at 25°C.

from **4a** in the absence of water, under conditions otherwise identical to those mentioned above, displayed lower enantioselectivity (87.7%, entry 5), demonstrating the critical effect of water during catalyst preparation on the enantioselectivity of catalysis. Under the optimized conditions, catalysts **9b** and **9c** were also highly effective in the oxidation of **10a**, affording **11a** in 37–38% yield with 99.5% *ee* (entry 6) and 98.7% *ee* (entry 7), respectively. The enantioselectivity of the heterogeneous sulfoxidation was extremely high, although the yield of the product was only low to moderate. This might be attributable to the kinetic resolution in the further oxidation of sulfoxide to sulfone, which may enrich the enantiopurity of the primary oxidation product and simultaneously decrease sulfoxide yields, as reported in the literature.[18c,j,26] To confirm this speculation, the kinetic resolution of racemic phenyl methyl sulfoxide by using heterogeneous catalysts **9a–c** was investigated under the experimental conditions mentioned above. As shown in Table 4, at 25°C and after 24 h of reaction, the selectivity factor *S*, a measure of the effectiveness of a kinetic resolution process under a particular set of conditions,[28] was calculated to be

Table 4. Kinetic resolution of racemic phenyl methyl sulfoxides by using heterogeneous titanium catalysts **9a–c** with CMHP as the oxidant in CCl_4.[a]

Entry	Catalyst	Yield [%][b]	*ee* [%][c]	*S* [d]
1	**9a**	46.3	65.0 (*S*)	6.76
2	**9b**	48.0	64.0 (*S*)	7.33
3	**9c**	44.8	69.9 (*S*)	7.34

[a] Unless otherwise stated, all of the reactions were performed at 25°C with 1 equivalent of oxidant in CCl_4 for 24 h. [b] Isolated yields. [c] The enantiomeric excess was determined by performing HPLC using a Chiralcel OD column and the absolute configuration was determined by comparison of optical rotations with literature data. [d] The selectivity factor was calculated according to the equation reported by Kagan et al.[28]

6.76–7.34, which was comparable to the values obtained through an analogous homogeneous process reported recently by Chan.[18j]

Encouraged by our preliminary results described above, we next investigated the heterogeneous catalysis of the enantioselective oxidation of a variety of aryl alkyl sulfides by using catalysts **9a–c** with CMHP as oxidant. As shown in Table 3, the oxidation of both *para*-substituted (entries 8–16) and *meta*-substituted (entries 17–19) aryl methyl sulfides **10b–e** afforded very high enantioselectivities (from 96.4 to >99.9% *ee*) in about 40% yields. Notably, in the oxidation of the *para*-nitro-substituted substrate **10f** (entry 20), although the enantioselectivity (89.1%) was inferior to that for other substrates, it is still higher than the highest value reported thus far for Ti-catalyzed homogeneous asymmetric sulfoxidation of the same substrate.[29] In particular, the heterogeneous catalyst **9b** demonstrated significant improvement in enantioselectivity for the oxidation of **10f**, relative to that achieved by the homogeneous BINOL/Ti/H_2O catalyst under otherwise identical conditions.[30] The increase in steric bulk of the alkyl group in the substrate (**10g**) resulted in a moderate enantioselectivity (75.5% *ee*, entry 21). By following Chan's modified homogeneous procedure,[18j] the yield of this heterogeneous catalysis of sulfoxidation could be improved to some extent (45.7%), with same level of enantioselectivity (99.9%, entry 22).

The heterogeneous nature of the above catalytic systems was further confirmed by using the supernatant of **9a** in CCl_4 for the catalysis of sulfoxidation of **10a** under the same conditions. The isolated product was racemic, similar to that obtained from the control experiment in the absence of 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 titanium (<0.1 ppm) was leached into the organic solution, which again supported the heterogeneous nature of the present system.

The facile recovery and remarkable stability are two other features exhibited by this type of heterogeneous catalyst. After the reaction was complete, simple filtration in open air enabled the separation of the solid-state catalyst from the product-containing solution. The separated solids were recharged with CCl_4, substrate, and oxidant for the next run. As shown in Table 5, the catalyst **9a** could be used

Table 5. Recycling and reuse of the heterogeneous catalyst **9a** in the enantioselective oxidation of thioanisole (**10a**).[a]

Run	Time [h]	Yield [%][b]	*ee* [%][c]
1	72	38.6	98.2
2	72	34.3	99.1
3	72	42.1	99.2
4	72	38.5	99.2
5	96	29.3	99.0
6	96	37.8	99.1
7	96	32.1	>99.9
8	96	33.6	99.1

[a] All of the reactions were performed at 25 °C with 2 equivalents of CMHP (80% in cumene) in CCl_4. [b] Isolated yields. [c] Determined by performing HPLC using a Chiralcel OD column.

for at least eight cycles in the sulfoxidation of thioanisole without any loss of enantioselectivity. Moreover, no significant deterioration in activity of the recovered catalyst was observed after eight runs that covered a period of more than one month. Again, the titanium leaching during recycling of the catalysts was determined to be negligible (less than 0.1 ppm by ICP).

Conclusion

We have developed a new strategy for the heterogenization of titanium catalysts by the in situ assembly of bridged multitopic BINOL ligands and $[Ti(OiPr)_4]$, in the absence of support. The assembled heterogeneous catalysts showed excellent enantioselectivity in both the carbonyl–ene reaction of α-methylstyrene with ethyl glyoxylate and the oxidation of sulfides. The results achieved in these heterogeneous catalytic systems were comparable or even superior to those attained by using their homogeneous counterparts. The linkers between the two BINOL units of the ligands had a significant impact on the enantioselectivity of the carbonyl–ene reaction, which demonstrates the importance of the supramolecular structures of the assemblies on their catalytic behavior. Particularly, in the catalysis of asymmetric sulfoxidation, the self-supported heterogeneous titanium catalysts were highly stable and could be readily recycled and reused for over one month with no apparent loss of activity and enantioselectivity (up to >99.9% *ee*). This represents a remarkable example of the heterogeneous catalysis of enantioselective reactions by using titanium catalysts. The features of self-supported catalysts, such as facile preparation, robust chiral structure of solid-state catalysts, high density of the catalytically active units in the solids, as well as easy recovery and simple recycling, are particularly important in developing methods for the synthesis of optically active compounds in industrial processes. The strategy described here indicates a possible new direction in the design of chiral catalysts for asymmetric synthesis. Ongoing work includes investigations of an extended range of substrates, particularly those of pharmaceutical importance, and further optimization of the reaction medium and oxidants.

Experimental Section

General considerations: NMR spectra were recorded by using a Varian Mercury 300 spectrometer. Chemical shifts are reported in ppm relative to an internal standard: tetramethylsilane (0 ppm) for ^1H NMR and deuteriocholorform (77.0 ppm) for ^{13}C NMR spectra. EI (70 ev) and ESI mass spectra were obtained by using HP5989 A and Mariner LC-TOF spectrometers, respectively. HRMS spectra were recorded by using either a Kratos Concept instrument, a Q-Tof micro instrument or an APEX-III 7.0 TESLA FTMS. Elemental analysis was preformed by using an Elemental VARIO EL apparatus. Optical rotations were measured by using a Perkin–Elmer 341 automatic polarimeter. Infrared spectra were obtained by using a BIO-RAD FTS-185 Fourier transform spectrometer in KBr pellets. Scanning electron micrographs were obtained by using a Hitachi S-2150 scanning electron microscope. Powder X-ray diffraction (PXD) was performed by using a D8 Discover GADDS. Liquid chromatographic analyses were conducted by using a JASCO 1580 system. All experiments sensitive to moisture or air were conducted under an argon atmosphere by using standard Schlenk techniques. Commercial reagents were used as received without further purification, unless otherwise noted. Dichloromethane, chloroform and tetrachloromethane were freshly distilled from calcium hydride and THF, diethyl ether and toluene from sodium benzophenone ketyl.

(*S*)-6-Bromo-2,2′-bismethoxmethoxy-1,1′-binaphthyl (1a): (*S*)-6-Bromo-1,1′-bi-2-naphthol[31] was added to a suspension of NaH (1.40 g, 60% in mineral oil, 35 mmol) in THF (30 mL), and the mixture was stirred at room temperature for 30 min. Methoxymethylchloride (1.30 mL, 17.5 mmol) was added dropwise to the reaction system and the mixture was stirred for an additional 2 h. The reaction was carefully quenched with methanol/H_2O (3:1) and the resultant solution was extracted with diethyl ether (40 mL×3). The combined organic phase was washed sequentially with saturated aqueous $NaHCO_3$ (30 mL), water (30 mL), and brine (30 mL). The organic phase was dried over Na_2SO_4 and then concentrated. The residue was purified by performing column chromatography on silica gel with hexane/ethyl acetate (20:1) as eluent to afford **1a** in 97% yield as a white solid. M.p. 78–79 °C; $[\alpha]_D^{20}=-58.8$ ($c=1.00$ in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): $\delta=8.03$ (d, $J=2.1$ Hz, 1H), 7.96 (d, $J=8.7$ Hz, 1H), 7.84–7.89 (m, 2H), 7.60 (d, $J=9.3$ Hz, 1H), 7.57 (d, $J=7.8$ Hz, 1H), 7.23–7.35 (m, 3H), 7.10 (d, $J=8.4$ Hz, 1H), 7.03 (d, $J=9.3$ Hz, 1H), 5.07–5.11 (m, 2H), 4.96–4.99 (m, 2H), 3.15 (s, 3H), 3.14 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=153.2$, 152.8, 133.9, 132.7, 131.0, 130.4, 130.1, 120.0, 129.9, 129.2, 128.6, 127.6, 127.1, 125.1, 124.6, 120.7, 119.9, 118.3, 117.6, 117.2, 94.6, 94.5, 56.0, 55.9 ppm; FTIR (KBr pellet): $\tilde{\nu}=3053$, 2956, 2901, 1622, 1585, 1493, 1238, 1148, 1014, 923, 811, 749 cm^{-1}; MS (MALDI-TOF): m/z: 475.1 $[M+H]^+$; elemental analysis calcd (%) for $C_{24}H_{21}O_4Br_2$: C 63.59, H 4.67; found: C 63.78, H 4.45.

Synthesis of 3a: Compound **1a** (1.0 g, 2.2 mmol), $[Pd(PPh_3)_4]$ (0.153 g, 0.132 mmol), and DME (10 mL) were added to a 50 mL three-necked flask. The mixture was degassed and stirred for 30 min, and then 1,4-phenylene-diboronic acid (**2a**) (0.166 g, 1 mmol) and degassed aqueous $NaHCO_3$ (1.0 M, 6.5 mL, 6.5 mmol) were added. The resulting mixture was refluxed for 24 h until the starting material was almost consumed, as monitored by performing TLC (hexane/ethyl acetate = 3:1). After cooling to room temperature, the reaction mixture was passed through a pad of Celite and the filtrate was extracted with ethyl acetate (10 mL×3). The combined organic phase was washed with brine and dried over Na_2SO_4. After removal of the solvent under vacuum, the residue was purified by subjecting it to flash column chromatography on silica gel with hexane/ethyl acetate (5:1) as eluent to afford **3a** in 65% yield as a white solid. M.p. 176–177 °C; $[\alpha]_D^{20}=-22.9$ ($c=1.00$ in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): $\delta=8.15$ (s, 2H), 7.97–8.02 (m, 4H), 7.90 (d, $J=8.4$ Hz, 2H), 7.78 (s, 4H), 7.54–7.64 (m, 6H), 7.34–7.38 (m, 2H), 7.23–7.27 (m, 6H), 5.11–5.14 (m, 4H), 5.00–5.04 (m, 4H), 3.20 (s, 6H), 3.17 ppm (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=152.7$, 152.6, 139.6, 136.0, 133.9, 133.2, 130.1, 129.8, 129.7, 129.4, 127.9, 127.4, 126.3, 126.1, 125.7, 125.5, 125.4, 124.0, 121.1, 121.0, 117.5, 117.1, 95.0, 55.7 ppm; FTIR (KBr pellet): $\tilde{\nu}=$ 2923, 1593, 1494, 1345, 1240, 1197, 1149, 1072, 1014, 958, 920, 806, 748, 692 cm^{-1}; MS (MALDI-TOF): m/z: 823.9 $[M+H]^+$; HRMS (MALDI-

DHB): *m/z* calcd for $C_{54}H_{47}O_8$ $[M+H]^+$: 823.3266; found: 823.3242; elemental analysis calcd (%) for $C_{48}H_{42}O_8$: C 77.19, H 5.67; found: C 76.92, H 5.79.

Synthesis of 3b: By following the same procedure as for the preparation of **3a**, **3b** was obtained as a white solid in 62% yield. M.p. 184–185°C; $[\alpha]_D^{20}=-37.3$ ($c=1.00$ in $CHCl_3$); ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta=$ 8.34 (s, 2H), 8.01–8.13 (m, 5H), 7.93 (d, $J=7.5$ Hz, 2H), 7.55–7.71 (m, 9H), 7.31–7.36 (m, 2H), 7.21–7.26 (m, 2H), 6.95–7.02 (m, 4H), 5.04–5.14 (m, 8H), 3.05 ppm (d, $J=5.4$ Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$ 152.8, 152.6, 141.5, 136.6, 133.9, 133.2, 130.0, 129.8, 129.6, 129.4, 129.2, 127.8, 126.3, 126.1, 125.9, 125.8, 125.4, 124.0, 121.1, 117.6, 117.2, 95.1, 95.0, 55.7 ppm; FTIR (KBr pellet): $\tilde{\nu}=$2924, 1622, 1592, 1506, 1336, 1239, 1197, 1149, 1073, 1031, 1015, 921, 806, 749, 693 cm^{-1}; MS (MALDI-TOF): *m/z*: 845.5 $[M+Na]^+$; HRMS (MALDI-DHB): *m/z* calcd for $C_{54}H_{47}O_8$ $[M+Na]^+$: 845.3085; found: 845.3090.

Synthesis of 3c: *n*BuLi (9 mL, 1.6 M in hexane, 14.4 mmol) was added slowly to a solution of **1a** (3.3 g, 7.3 mmol) in THF (60 mL) at −78°C. After stirring for 2 h, the mixture was added to a solution of $B(OMe)_3$ (5.5 mL, 47.67 mmol) in THF (20 mL) at −78°C. The resulting mixture was allowed to warm to room temperature and then stirred at room temperature overnight. The reaction mixture was quenched with water (20 mL) at 0°C and then extracted with ethyl acetate (30 mL×3). The combined organic phase was dried on anhydrous Na_2SO_4, filtered, and concentrated to afford a solid of **2c** in 53% yield. Compound **2c** was used directly for next step of the coupling reaction without further purification. $[Pd(PPh_3)_4]$ (150 mg, 0.13 mmol) was added to a solution of **2c** (0.89 g, 2.1 mmol) in DME (150 mL), and the mixture was degassed and stirred for 30 min. Compound **1a** (1.04 g, 2.3 mmol) and degassed aqueous $NaHCO_3$ (1 M, 30 mL, 30 mmol) were then added. The resulting mixture was refluxed for 16 h until the staring material was almost consumed (monitored by performing TLC, hexane/ethyl acetate = 5:1). After cooling to room temperature, the reaction mixture was passed through a pad of Celite and the filtrate was extracted with ethyl acetate (30 mL×3). The combined organic phase was washed with saturated aqueous $NaHCO_3$, water, and brine, and then dried over Na_2SO_4. After removal of the solvent under vacuum, the residue was purified by performing flash column chromatography on silica gel with hexane/ethyl acetate (5:1) as eluent to afford **3c** as a white solid in 67% yield. M.p. 187–188°C; $[\alpha]_D^{20}=-28.4$ ($c=1.00$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$8.15 (s, 2H), 7.87–8.03 (m, 6H), 7.58–7.62 (m, 6H), 7.34–7.38 (m, 2H), 7.19–7.26 (m, 6H), 5.09–5.12 (m, 4H), 4.98–5.02 (m, 4H), 3.16–3.20 ppm (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$152.7, 152.6, 136.4, 134.0, 133.1, 130.1, 129.8, 129.6, 129.4, 127.8, 126.3, 126.1, 126.0, 125.7, 125.5, 124.1, 121.1, 117.6, 117.2, 95.2, 95.1, 55.83, 55.80 ppm; FTIR (KBr pellet): $\tilde{\nu}=$2953, 1621, 1591, 1505, 1470, 1328, 1243, 1198, 1151, 1070, 1039, 1015, 921, 820, 749, 690 cm^{-1}; EIMS (70 ev): *m/z*: 746 $[M]^+$; HRMS (MALDI-DHB): *m/z* calcd for $C_{48}H_{43}O_8$ $[M+H]^+$: 747.2952; found: 747.2966.

Synthesis of 4a: Aqueous HCl (6 M, 0.5 mL) was added to a solution of **3a** (450 mg, 0.61 mmol) in chloroform (15 mL) and methanol (3 mL). The resulting solution was refluxed for 6 h until the conversion of **3a** was complete. The solution was then cooled to room temperature, and saturated aqueous $NaHCO_3$ solution was added to neutralize the reaction mixture. The resulting mixture was then extracted with ethyl acetate (30 mL×3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated to give the crude product, which was further purified by performing flash chromatography on silica gel (hexane/ethyl acetate = 2:1) to afford **4a** as a white solid (390 mg, >99% yield). M.p. 192–193°C; $[\alpha]_D^{20}=+133.4$ ($c=1.00$ in $CHCl_3$); ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta=$9.30 (s, 2H), 9.24 (s, 2H), 8.19 (s, 2H), 7.93 (d, $J=9.3$ Hz, 2H), 7.80–7.86 (m, 8H), 7.55 (d, $J=9.0$ Hz, 2H), 7.29–7.34 (m, 4H), 7.14–7.24 (m, 4H), 6.94–7.01 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$152.8, 152.7, 139.6, 136.1, 133.4, 132.6, 131.5, 131.3, 129.6, 129.3, 128.3, 127.6, 127.4, 126.8, 126.1, 124.8, 124.1, 124.0, 118.2, 117.7, 110.9, 110.8 ppm; FTIR (KBr pellet): $\tilde{\nu}=$3501, 3056, 1700, 1620, 1597, 1498, 1383, 1344, 1253, 1214, 1145, 1042, 931, 819, 749, 610 cm^{-1}; ESI-MS: *m/z*: 647 $[M+H]^+$; HRMS (MALDI-DHB): *m/z* calcd for $C_{46}H_{30}NaO_4$ $[M+Na]^+$: 669.2036; found: 669.2047; elemental analysis calcd (%) for $C_{44}H_{26}O_4$: C 84.19, H 4.59; found: C 84.26, H 4.74.

Synthesis of 4b: By following the same procedure as for the preparation of **4a**, **4b** was obtained as a white solid in >99% yield. M.p. 206–207°C; $[\alpha]_D^{20}=+118.2$ ($c=1.00$ in $CHCl_3$); ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta=$ 9.29 (s, 2H), 9.23 (s, 2H), 8.22 (s, 2H), 8.00 (s, 1H), 7.93 (d, $J=9.0$ Hz, 2H), 7.81–7.85 (m, 4H), 7.49–7.66 (m, 5H), 7.28–7.34 (m, 4H), 7.13–7.23 (m, 4H), 6.94–7.01 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$152.9, 152.7, 141.5, 136.7, 133.4, 132.7, 131.6, 131.4, 129.6, 129.4, 128.4, 127.5, 127.1, 126.4, 126.3, 126.2, 124.9, 124.2, 124.0, 118.3, 117.8, 111.0, 110.9 ppm; FTIR (KBr pellet): $\tilde{\nu}=$3501, 3055, 1704, 1620, 1595, 1506, 1465, 1384, 1342, 1270, 1215, 1145, 1041, 943, 884, 815, 749, 690 cm^{-1}; ESI-MS *m/z*: 647.0 $[M+H]^+$; HRMS (MALDI-DHB): *m/z* calcd for $C_{46}H_{31}O_4$ $[M+H]^+$: 647.2217; found: 647.2203.

Synthesis of 4c: By following the same procedure as for the deprotection of MOM, described in the synthesis of **4a**, **4c** was obtained as a white solid in >99% yield. M.p. 195–196°C; $[\alpha]_D^{20}=+136.2$ ($c=1.00$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=$8.16 (s, 2H), 7.98–8.06 (m, 4H), 7.91 (d, $J=8.1$ Hz, 2H), 7.63–7.66 (m, 2H), 7.19–7.43 (m, 12H), 5.11 ppm (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$152.8, 152.7, 136.4, 133.4, 132.6, 131.6, 131.4, 129.7, 129.4, 128.4, 127.5, 127.1, 126.4, 124.9, 124.2, 124.0, 118.3, 117.8, 110.9, 110.7 ppm; FTIR (KBr pellet): $\tilde{\nu}=$3497, 2923, 1702, 1620, 1595, 1507, 1465, 1383, 1341, 1273, 1214, 1145, 1041, 928, 818, 749, 667 cm^{-1}; EIMS (70 ev): *m/z*: 570 $[M]^+$; HRMS (MALDI-DHB): *m/z* calcd for $C_{40}H_{27}O_4$ $[M+H]^+$: 571.1904; found: 571.1917.

Synthesis of 4d: (*S*)-6,6′-Dibromo-2,2′-dimethoxymethoxy-1,1′-binaphthyl (**1b**)[32] (4.00 g, 7.5 mmol), $[Pd(PPh_3)_4]$ (0.17 g, 0.15 mmol), and DME (125 mL) were added to a 250 mL three-necked flask. The mixture was degassed and stirred for 30 min, then 1,4-phenylenediboronic acid (**2a**) (0.42 g, 2.5 mmol) and degassed aqueous $NaHCO_3$ (1 M, 20 mL) were added. The resulting mixture was refluxed for 24 h and the reaction process was monitored by conducting TLC (eluent: hexane/ethyl acetate = 4:1). After cooling to room temperature, the reaction mixture was passed through a pad of Celite, and the filtrate was extracted with ethyl acetate (40 mL×3). The combined organic phase was washed with saturated aqueous $NaHCO_3$, water, and brine, and then dried over anhydrous Na_2SO_4. After removal of the solvent under vacuum, the residue was purified by subjecting it to flash column chromatography on silica gel with hexane/ethyl acetate (5:1) as eluent to afford crude **3d** as a white solid (0.90 g). Because the purification of this compound proved to be difficult, **3d** was submitted directly to acidic hydrolysis. Aqueous HCl (6 M, 0.6 mL) was added to a solution of the above crude product in chloroform (25 mL) and methanol (5 mL). The mixture was refluxed for 6 h until the staring material was completely converted (monitored by performing TLC, hexane/ethyl acetate = 2:1). The solution was cooled to room temperature and neutralized by the addition of saturated aqueous $NaHCO_3$ solution. The resulting mixture was then extracted with ethyl acetate (30 mL×3). The combined organic phase was washed with saturated $NaHCO_3$, water, and brine. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was submitted to column chromatography on silica gel (hexane/ethyl acetate = 2:1) to afford **4d** as a white solid (0.72 g, 37.0% overall yield for two steps). M.p. 211–212°C; $[\alpha]_D^{20}=+198.4$ ($c=1.00$ in $CHCl_3$); ^{1}H NMR (300 MHz, [D$_6$]DMSO): $\delta=$9.48 (s, 2H), 9.40 (s, 2H), 8.22 (s, 2H), 8.13 (s, 2H), 7.97 (d, $J=9.0$ Hz, 2H), 7.88 (d, $J=8.7$ Hz, 2H), 7.83 (s, 4H), 7.62–7.58 (m, 2H), 7.39–7.30 (m, 6H), 7.0 (d, $J=9.3$ Hz, 2H), 6.92 ppm (d, $J=9.0$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=$152.8, 152.6, 139.4, 136.1, 132.4, 131.9, 131.7, 130.6, 130.3, 130.2, 129.5, 127.5, 126.9, 126.1, 126.0, 124.6, 118.8, 118.2, 117.7, 111.2, 110.3 ppm; FTIR (KBr pellet): $\tilde{\nu}=$3506, 1702, 1588, 1497, 1381, 1345, 1252, 1215, 1146, 930, 880, 815, 670, 420 cm^{-1}; MS (MALDI-DHB): *m/z*: 803.0 $[M+H]^+$; HRMS (MALDI-DHB): *m/z* calcd for $C_{46}H_{29}O_4Br_2$ $[M+H]^+$: 803.0427; found: 803.0436.

General procedure for the preparation of catalysts 5a–d: $[Ti(OiPr)_4]$ (25 μL, 0.5 M in CH_2Cl_2, 0.0125 mmol) was added to a solution of ligand **4a** (8.1 mg, 0.0125 mmol) in $CHCl_3$ (0.2 mL) under stirring at room temperature in a Schlenk tube. The orange solid appeared immediately upon addition of $[Ti(OiPr)_4]$. After stirring for 4 h, the solvent in the mixture was removed under reduced pressure. The orange solid catalyst **5a** was

washed with diethyl ether and isolated in >95% yield by filtration. Data for **5a**: FTIR (KBr pellet): $\tilde{\nu}$=3517, 3056, 1619, 1595, 1500, 1459, 1338, 1239, 1146, 1078, 975, 819, 783, 749, 619 cm^{-1}; elemental analysis cald (%) for $(C_{52}H_{42}O_6Ti{\cdot}CH_2Cl_2)_n$: C 71.07, H 4.95; found: C 70.45, H 4.27.

By following the same procedure as for the preparation of **5a**, **5b–d** were obtained from **4b**, **4c**, and **4d**, respectively, in >99% yield. The SEM images and PXD patterns of **5a–d** are included in the Supporting Information.

5b: FTIR (KBr pellet): $\tilde{\nu}$=3512, 3052, 1619, 1587, 1500, 1460, 1337, 1238, 1145, 1078, 974, 816, 791, 749, 604 cm^{-1}; elemental analysis calcd (%) for $(C_{52}H_{42}O_6Ti{\cdot}0.5\,CH_2Cl_2)_n$: C 73.90, H 5.08; found: C 73.26, H 4.78.

5c: FTIR (KBr pellet): $\tilde{\nu}$=3517, 3055, 1619, 1584, 1500, 1459, 1336, 1265, 1239, 1145, 1079, 975, 820, 785, 749, 602 cm^{-1}; elemental analysis calcd (%) for $(C_{46}H_{38}O_6Ti{\cdot}0.5\,CH_2Cl_2)_n$: C 71.87, H 5.06; found: C 72.25, H 4.37.

5d: FTIR (KBr pellet): $\tilde{\nu}$=3523, 2969, 1586, 1487, 1462, 1336, 1238, 1148, 1068, 998, 972, 936, 879, 815, 684, 624 cm^{-1}; elemental analysis calcd (%) for $(C_{52}H_{40}Br_2O_6Ti{\cdot}0.5\,CH_2Cl_2)_n$: C 62.37, H 4.09; found: C 62.15, H 4.04.

Typical procedure for heterogeneous carbonyl–ene reactions and catalyst recycling: Anhydrous toluene (50 μL), α-methylstyrene (**6**) (165 μL, 1.25 mmol), and freshly distilled ethyl glyoxylate (**7**) (200 μL, 2.5 mmol) were added to a Schlenk tube containing the catalyst **5a** prepared above. After the heterogeneous mixture was stirred at room temperature for a specific period shown in Table 1, freshly distilled anhydrous ethyl ether (1 mL) was added and stirred for several minutes. The clear supernatant was removed by using a syringe and the catalyst remained at the bottom of the tube. This operation was repeated three times. The remaining insoluble catalyst was recharged with solvent, freshly distilled ethyl glyoxylate, and α-methylstyrene for the next run. The combined ethyl ether solution was concentrated and purified by performing flash chromatography on silica (ethyl acetate/hexane=1:5) to afford the carbonyl–ene product **8**;[15] $[\alpha]_D^{20}$=+21.8 (c=1.00 in $CHCl_3$), 95% *ee* with *S* configuration of major enantiomer; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.44–7.28 (m, 5H), 5.40 (s, 1H), 5.21 (s, 1H), 4.30–4.24 (m, 1H), 4.15–4.00 (m, 2H), 3.07 (dd, J=4.5, 13.5 Hz, 1H), 2.84 (dd, J=8.1, 13.5 Hz, 1H), 2.73 (d, J=6.30 Hz, 1H), 1.24 ppm (t, J=7.2 Hz, 3H); FTIR (neat): $\tilde{\nu}$=3475, 3084, 3058, 2984, 2939, 1737, 1630, 1496, 1446, 1372, 1267, 1210, 1114, 1030, 905, 780 cm^{-1}; EIMS (70 ev): m/z: 220 $[M]^+$. The enantiomeric excess of **8** was determined by performing HPLC using a Chiralcel OJ column: eluent, hexane/2-propanol (97:3); flow rate, 1 mL min^{-1}; UV detection at λ=254 nm; t_R=18.68 min (major), 29.36 min (minor).

General procedure for the preparation of catalysts 9a–c: [Ti(O*i*Pr)$_4$] solution in CH_2Cl_2 (0.5 M, 50 μL, 0.025 mmol) was added dropwise to a solution of ligand **4a** (16.5 mg, 0.025 mmol) in CCl_4 (3 mL), and the red solids appeared immediately. The mixture was stirred at room temperature for 12 h, followed by addition of water (18 μL, 1 mmol). The resultant suspension was stirred for an additional 12 h, the red solids (**9a**) were collected in almost quantitative yield by filtration and washed twice with CCl_4 (1 mL). Data for **9a**: FTIR (KBr pellet): $\tilde{\nu}$=3509, 3053, 1587, 1459, 1338, 1238, 1078, 975, 819, 785 cm^{-1}; elemental analysis calcd (%) for $(C_{46}H_{26}O_4Ti{\cdot}5\,H_2O)_n$: C 70.78, H 4.61; found: C 71.03, H 4.28.

By following the same procedure as for the preparation of **9a**, **9b**, and **9c** were obtained from **4b** and **4c**, respectively, in >99% yield. The SEM images and PXD patterns of **9a–c** are included in the Supporting Information.

9b: FTIR (KBr pellet): $\tilde{\nu}$=3522, 3056, 1587, 1463, 1338, 1240, 1079, 975, 819, 791 cm^{-1}; elemental analysis calcd (%) for $(C_{46}H_{26}O_4Ti{\cdot}6\,H_2O)_n$: C 69.17, H 4.76; found: C 69.31, H 4.19.

9c: FTIR (KBr pellet): $\tilde{\nu}$=3518, 3055, 1585, 1459, 1336, 1239, 1078, 975, 819, 783 cm^{-1}; elemental analysis calcd (%) for $(C_{40}H_{22}O_4Ti{\cdot}6\,H_2O)_n$: C 66.48, H 4.70; found: C 66.56, H 4.09.

Typical experimental procedure for heterogeneous asymmetric sulfoxidation and catalyst recycling: CCl_4 (3 mL) and thioanisole (0.5 mmol) were added to the solid-state catalyst **9a** obtained above. The mixture was stirred for 15 min before CMHP (80% in cumene, 180 μL, 1 mmol) was added dropwise at 0°C, and the heterogeneous mixture was stirred at room temperature for 72 h. After the isolation of the solids by filtration, the insoluble catalyst was recharged with CCl_4 (3 mL), substrates (0.5 mmol), and oxidant (1 mmol) for the next run. The filtrate was concentrated and the residue was submitted to column chromatography on silica gel using hexane/ethyl acetate (1:1) as eluent to give the sulfoxide (*S*)-**11a** as colorless oil in 38% yield; $[\alpha]_D^{20}$=−133.5 (c=1.1, acetone) (in reference [27]; $[\alpha]_D^{20}$=+135 (c=1, acetone), (*R*)-enantiomer, 99.2% *ee*); ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.74 (s, 3H), 7.52–7.55 (m, 3H), 7.64–7.68 ppm (m, 2H); EIMS: m/z (%): 140 (100) $[M]^+$, 125 (98), 97 (58), 77 (45), 51 (63). The *ee* value was determined by performing HPLC (Waters 515–2487) using a Chiralcel OD column: UV detection at λ=254 nm; 20°C; hexane/*i*PrOH, 9:1; flow rate, 1.0 mL min^{-1}; t_{R1}=12.4 min (minor isomer), t_{R2}=15.6 min (major isomer).

(*S*)-**11b**:[24f] $[\alpha]_D^{20}$=−185.8 (c=1.08, acetone), >99.9% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.42 (s, 3H), 2.71 (s, 3H), 7.32–7.35 (d, 2H, J=7.8 Hz), 7.53–7.56 ppm (d, J=7.8 Hz, 2H); EIMS: m/z (%): 154 (83) $[M]^+$, 139 (100).

(*S*)-**11c**:[24f] $[\alpha]_D^{20}$=−151.1 (c=0.43, acetone), >99.9% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.74 (s, 3H), 7.53–7.55 (d, J=8.4 Hz, 2H), 7.67–7.70 ppm (d, J=8.4 Hz, 2H); EIMS: m/z (%): 220 (66) $[M+1]^+$, 218 (65) $[M-1]^+$, 205 (100), 203 (98).

(*S*)-**11d**:[20h] $[\alpha]_D^{20}$=−129.6 (c=1.5, acetone), 98.6% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.72 (s, 3H), 7.20–7.26 (m, 2H), 7.63–7.68 ppm (m, 2H); EIMS: m/z (%): 158 (60) $[M]^+$, 143 (100), 115 (1), 95 (36), 75 (39).

(*S*)-**11e**:[20h] $[\alpha]_D^{20}$=−110.4 (c=1.33, acetone), >99.9% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.74 (s, 3H), 7.40–7.43 (m, 1H), 7.53–7.54 (m, 1H), 7.62 (m, 1H), 7.80–7.81 ppm (m, 1H); EIMS: m/z (%): 220 (81) $[M+1]^+$, 218 (81) $[M-1]^+$, 205 (93), 203 (96).

(*S*)-**11f**:[24f] $[\alpha]_D^{20}$=−126.5 (c=1.2, acetone), 89.1% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$): δ=2.79 (s, 3H), 7.82–7.85 (m, 2H), 8.38–8.40 ppm (m, 2H); EIMS: m/z (%): 185 (100) $[M]^+$, 170 (29), 140 (11).

(*S*)-**11g**:[24f] $[\alpha]_D^{20}$=−97.1 (c=1.3, acetone), 75.5% *ee*; ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.19–1.24 (t, J=7.5 Hz, 3H), 2.75–2.96 (m, 2H), 7.51–7.65 ppm (m, 5H); EIMS: m/z (%): 154 (20) $[M]^+$, 126 (54), 97 (15), 78 (100), 51 (32).

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complexes was not very successful (references [18d] and [18g]). Only 13% *ee* and 9% yield were obtained in the kinetic resolution of racemic sulfoxide **11f** by using homogeneous BINOL/Ti/H_2O catalyst (reference [26]).

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