

Scheme 6. Reagents and conditions: a) Me_3Al (3 equiv), CH_2Cl_2 , -30°C ; b) our method.

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Asymmetric Epoxidation of Allyl Alcohol on Organic–Inorganic Hybrid Chiral Catalysts Grafted onto the Surface of Silica and in the Mesopores of MCM-41**

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Asymmetric epoxidation of allylic alcohols is an important reaction in synthetic organic chemistry.^[1] Sharpless and Katsuki^[2] have provided an excellent homogeneous catalytic

system for this reaction which consists of titanium tetraisopropoxide and a chiral dialkyl tartrate. Heterogeneous systems have tremendous advantages over homogeneous catalytic systems.^[3] One of the most attractive advantages is the easy separation of the product from the catalyst without tedious experimental work-up.

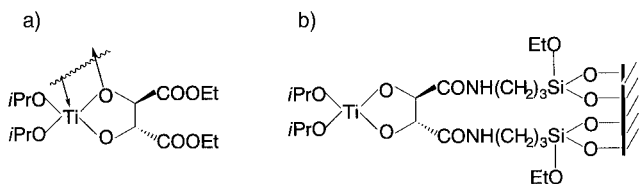
Different approaches have been used in the preparation of heterogeneous Sharpless-type catalytic systems for the asymmetric epoxidation of allylic alcohols. An early attempt to develop a polymer-supported system employed a single tartrate ester unit bound to a polystyrene resin;^[4a] in this case, the chiral induction was only modest (ca. 50–60% *ee*). Choudary et al.^[4b] reported the asymmetric epoxidation of allylic alcohols with a heterogeneous titanium-pillared montmorillonite catalyst in the presence of chiral tartrate ester. However, the preparation of the solids seems to be difficult to reproduce.^[5] Hormi and co-workers^[4c, 4d] synthesized insoluble branched/crosslinked poly(tartrate ester)s and investigated their use as optically active ligands in the heterogeneous asymmetric epoxidation of allylic alcohols with titanium tetraisopropoxide and *tert*-butyl hydroperoxide. These gel-type polymeric ligands swell during the catalytic reaction. Basset and co-workers^[4e] reported silica-supported tantalum catalysts for the enantioselective epoxidation of allylic alcohols in the presence of chiral tartrate derivatives. Their result is comparable to that obtained in the homogeneous Sharpless reaction. However, the organometallic tantalum compound used in the synthesis is not easy to prepare.^[6]

The preparation of organic–inorganic hybrid materials is of growing interest.^[7, 8] In contrast to organic polymers, organic–inorganic hybrid materials do not swell or dissolve in organic solvents, and have many advantages over most organic polymers because of their superior mechanical and thermal stabilities. Moreover, any leaching could be avoided as the organic moieties are covalently attached to the inorganic supports. For hybrid materials, the design and synthesis of chiral catalytic materials^[8] with high enantioselectivities are especially attractive.^[8c–e] Highly efficient and enantioselective transition metal complexes have been reported in the literature. The design and synthesis of chiral hybrids with activity and enantioselectivity similar to that of homogeneous catalysts remain a challenge. Few reports have appeared on the synthesis of organic–inorganic hybrid chiral materials and on their use as heterogeneous catalysts in enantioselective reactions.^[8c–e] We report herein the synthesis of organic–inorganic hybrid chiral materials by grafting a chiral tartaric acid derivative onto the surface of silica and in the mesopores of MCM-41 material (Scheme 1b), and provide the first example of their successful application in the heterogeneous asymmetric epoxidation of allyl alcohol. The catalytic systems resulted in enantiomer excesses up to 80%, which is as good as the homogeneous Sharpless system (Scheme 1a).

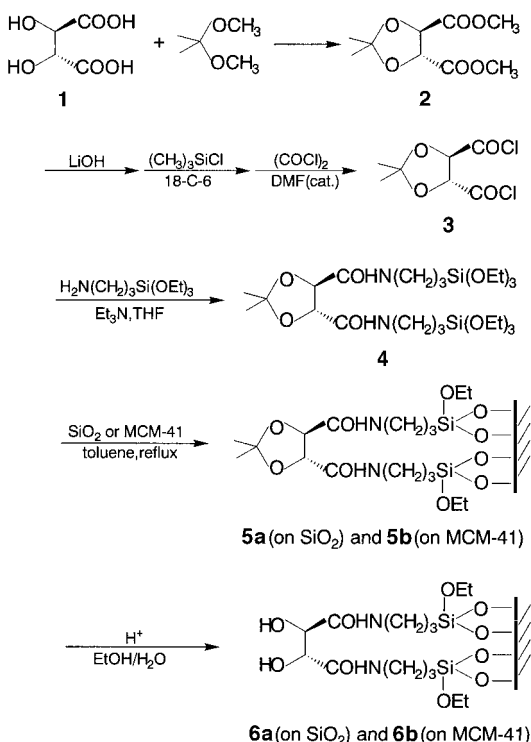
The chiral tartaric derivative was grafted onto inorganic supports in several steps, as outlined in Scheme 2. Tartaric acid (**1**) was converted into the protected tartaric acid dichloride **3**. Treatment of **3** with 3-aminopropyltriethoxysilane gave **4**, which was grafted onto SiO_2 and MCM-41 to afford **5a** and **5b**, respectively. Selective cleavage of the isopropylidene acetal removed the protecting groups and

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Scheme 1. a) Homogeneous chiral catalyst for the asymmetric epoxidation of allylic alcohols, proposed by Sharpless and Katsuki,^[2] which consists of $\text{Ti}(\text{O}i\text{Pr})_4$ and a chiral tartaric derivative (only half of the dimer is shown); b) heterogeneous chiral catalyst, prepared from organic-inorganic hybrid chiral material grafted onto the surface of silica and in the mesopores of MCM-41.



Scheme 2. The synthesis of organic-inorganic hybrid chiral materials on the surface of silica and in the mesopores of MCM-41.

gave the desired **6a** and **6b**, respectively. Although the selective cleavage of the isopropylidene acetal under homogeneous conditions is known, the selective removal of the protecting group grafted onto insoluble inorganic supports has not been reported. In our system, besides the protecting group, the tartaramide and the inorganic Si-O-Si bond can also be hydrolyzed under acidic conditions. The challenge is to selectively hydrolyze the protecting group, while keeping the tartaramide and inorganic Si-O-Si bond intact. If the conditions are too severe, the hybrid material may decompose. It was reported that the protecting group can be removed selectively when the substrate is dissolved and stirred in 90 % acetic acid at room temperature for about 40 h.^[9] Surprisingly, the cleavage of the isopropylidene acetal grafted onto inorganic supports required rather severe conditions and long reaction times. We found that the protecting group could not be removed even when the solid was stirred in 90 % acetic acid at 40 °C for 4 d. Neither could it be removed when the solid was stirred at 40 °C for 4 d in 95 % ethyl alcohol that had

been acidified to pH 4 with concentrated hydrochloric acid. When the pH value was decreased to 3 or below and the hydrolysis was carried out at 40 °C for 4 d, the protecting group could be removed.

The selective removal of the protecting group was confirmed by means of FT-IR and ^{13}C CP/MAS NMR spectroscopy (CP/MAS = cross polarization/magic-angle spinning). IR spectra of the hybrid materials were recorded before and after hydrolysis. The peak at 2889 cm^{-1} , associated with the protecting group, disappeared after hydrolysis, and the characteristic peak at 1666 cm^{-1} for the -CONH- stretching vibration still remained, which indicates the presence of the tartaramide. The ^{13}C NMR spectrum provided more direct evidence for the selective hydrolysis of the protecting group: the signal at $\delta = 113$, assigned to the quaternary carbon atom of the protecting group, remained unchanged when the hydrolysis was performed at $\text{pH} \geq 4$, but disappeared after the hydrolysis at $\text{pH} \leq 3$. Furthermore, the signal associated with the carbon atom attached to the protected hydroxy group shifted from $\delta = 78.3$ to 70.2 as a result of the removal of the protecting group (Figure 1).

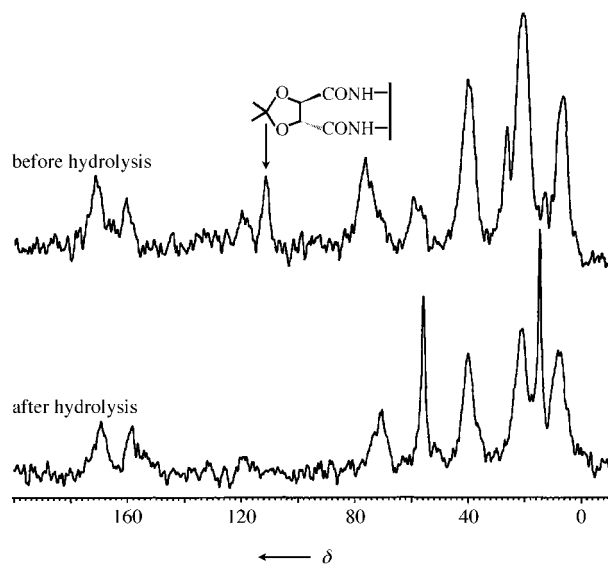
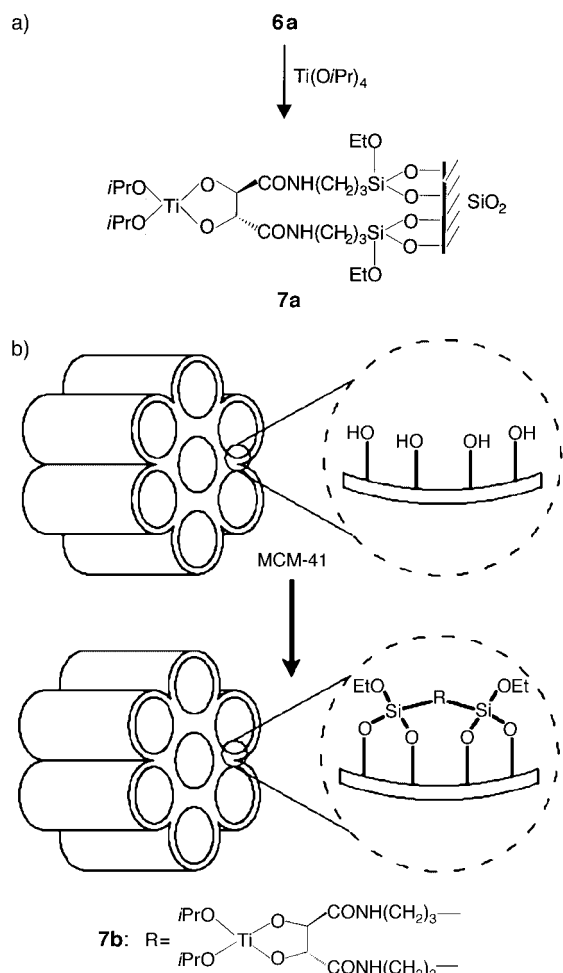


Figure 1. The ^{13}C CP/MAS NMR (400 MHz) of organic-inorganic hybrid chiral materials before and after hydrolysis.

Two kinds of organic-inorganic hybrid chiral materials that contain free hydroxy groups were obtained: on silica (**6a**) and in the mesopores of MCM-41 material (**6b**). The amount of tartaric acid derivative grafted onto the inorganic supports is about 0.5 mmol g^{-1} for **6a** and 0.6 mmol g^{-1} for **6b**, as estimated from elemental analysis data, taking into account mass % carbon and nitrogen.

The chiral catalysts **7a** and **7b** were synthesized directly by the reaction of titanium tetraisopropoxide with the organic-inorganic hybrid chiral materials **6a** and **6b**, respectively (Scheme 3). The synthetic catalysts were formed in situ and tested in the enantioselective epoxidation of allyl alcohol, and the results are presented in Table 1. The activity and enantioselectivity (Table 1, entry 2) are as good as those obtained from the homogeneous Sharpless reaction (Table 1,



Scheme 3. a) Heterogeneous chiral catalyst **7a**, synthesized in situ from **6a**. b) Heterogeneous chiral catalyst **7b**, synthesized in situ from **6b**.

Table 1. Asymmetric epoxidation of allyl alcohol on organic–inorganic hybrid chiral catalysts grafted onto the surface of silica and in the mesopores of MCM-41.

Entry	Catalyst ^[a]	Titanium/substrate ^[b]	Conversion ^[c]	TON	ee [%] ^[c,d]
1	TiP/DET ^[f]	5 %	76 %	15	83
2	7a	2 %	29 %	14	86
3	7b	2 %	22 %	11	84
4	7a	4 %	49 %	12	78
5	7b	4 %	43 %	10	80

[a] See Scheme 3. [b] Molar ratio. [c] Determined after reaction for 48 h at 0 °C by GC with *n*-nonane as internal standard. [d] Determined by means of GC on a chiral β -cyclodextrin column. [f] Ti(OiPr)₄ + L-diethyl tartrate.

entry 1). When the titanium/substrate ratio is increased from 2 to 4 %, the conversion is almost doubled. The increase in conversion is nearly proportional to the amount of titanium used in the epoxidation. The turnover number (TON) is nearly unchanged (Table 1, entry 4), which indicates that the activity and enantioselectivity may result from the monomeric titanium species complexed with the hybrid chiral material.

Chiral tartaric derivative grafted onto mesoporous MCM-41 shows similar results. However, the activity is lower than that of the catalyst grafted onto silica (Table 1, entry 3). This is probably a result of the slower diffusion of the substrate and the product in the mesopores of MCM-41. When the titanium/

substrate ratio is increased from 2 to 4 %, similar results are obtained. Again, the turnover number and the enantiomeric excess are nearly unchanged (Table 1, entry 5). This result indicates that all the titanium species are grafted onto the surface of silica or into the mesopores of MCM-41 in the form of a Sharpless-like complex. From Table 1, it is clear that the heterogeneous catalysts, synthesized from the monomeric titanium species complexed with the hybrid chiral material, show activity and enantioselectivity resembling that of the Sharpless catalyst. The result is in good agreement with our conceptual approach (Scheme 1): the environment surrounding the immobilized species is analogous to that of the homogeneous complex.

In summary, organic–inorganic hybrid chiral materials are synthesized by grafting a chiral tartaric acid derivative onto the surface of silica and in the mesopores of MCM-41, and the synthetic catalysts show enantioselectivities up to 80 % *ee* for the asymmetric epoxidation of allyl alcohol. This is the first example of the application of hybrid chiral materials in heterogeneous asymmetric epoxidation of allyl alcohol. For the chiral hybrids, the environment surrounding the immobilized species is analogous to that of homogeneous chiral complexes. The performance of the heterogeneous catalyst is also similar to the homogeneous Sharpless reaction. Our method could be a general approach to the synthesis of chiral heterogeneous catalysts. A further advantage of the system is that the product can be separated easily from the catalyst by simple filtration.

Experimental Section

2: Synthesized from L-tartaric acid (**1**) according to a literature procedure^[10]. $[\alpha]_D^{25} = -53.8^\circ$ (neat); lit. $[\alpha]_D^{20} = -54^\circ$ (neat).^[11] IR: $\tilde{\nu} = 2994, 2957, 1759, 1439, 1385, 1214, 1113, 859 \text{ cm}^{-1}$; $^1\text{H NMR}$ (400 MHz, CDCl₃): $\delta = 4.8$ (s, 2H; OCH), 3.8 (s, 6H; OCH₃), 1.5 (s, 6H; C(CH₃)₂).

3: Synthesized according to the procedure of Choi et al.^[12] as a light yellow solid (b.p. 52–54 °C/2 mmHg, [lit.]: 51–55 °C/2 mmHg).

4: 3-Aminopropyltriethoxysilane was treated with **3** in dry THF in the presence of Et₃N to afford **4** as a light yellow, viscous oil. IR: $\tilde{\nu} = 3320, 2973, 1672, 1531, 1443, 1385, 1078, 958, 782 \text{ cm}^{-1}$.

5a/5b: L-Tartaramide **4** was grafted onto MCM-41 material (3 g, S_{BET} : 747 m² g⁻¹, pore size: 33.6 Å) and silica (3 g, S_{BET} : 375 m² g⁻¹) to form **5a** and **5b**, respectively, according to a literature procedure.^[13] IR: $\tilde{\nu} = 2994, 2940, 2889, 1666, 1523, 1446, 1390, 804 \text{ cm}^{-1}$; $^{13}\text{C CP/MAS NMR}$ (400 MHz): $\delta = 172.1, 113.0, 78.3, 61.8, 43.0, 23.9, 9.9$.

6a or 6b: The white solid **5a or 5b** (3 g) was hydrolyzed at 40 °C for 4 days in 95 % ethyl alcohol (20 mL) that had been acidified to pH 3 with hydrochloric acid. IR: $\tilde{\nu} = 2940, 1666, 1523, 1446, 1390, 804 \text{ cm}^{-1}$; $^{13}\text{C CP/MAS NMR}$ (400 MHz): $\delta = 169.2, 70.2, 55.8, 39.9, 20.8, 14.8, 8.4$; elemental analysis: **6a:** C 8.56 %, H 1.58 %, N 1.55 %; **6b:** C 11.16 %, H 2.10 %, N 1.95 %.

Epoxidation: Titanium tetraisopropoxide, the hybrid chiral material **6a or 6b** (or L-(+)-diethyl tartrate; 1.5 equiv relative to titanium), and dry CH₂Cl₂ (20 mL) were added to a 50-mL Schlenk-type flask under an argon atmosphere. The mixture was cooled to 0 °C and stirred for 1 h. Allyl alcohol (10 mmol) and *n*-nonane (internal standard) were added. *tert*-Butyl hydroperoxide (20 mmol) was added dropwise with stirring. The mixture was stirred for 48 h at 0 °C. The reaction was stopped by removing the catalyst from the solution by filtration. Conversions, yields, and *ee* values were determined by means of gas chromatography on a chiral β -cyclodextrin column.

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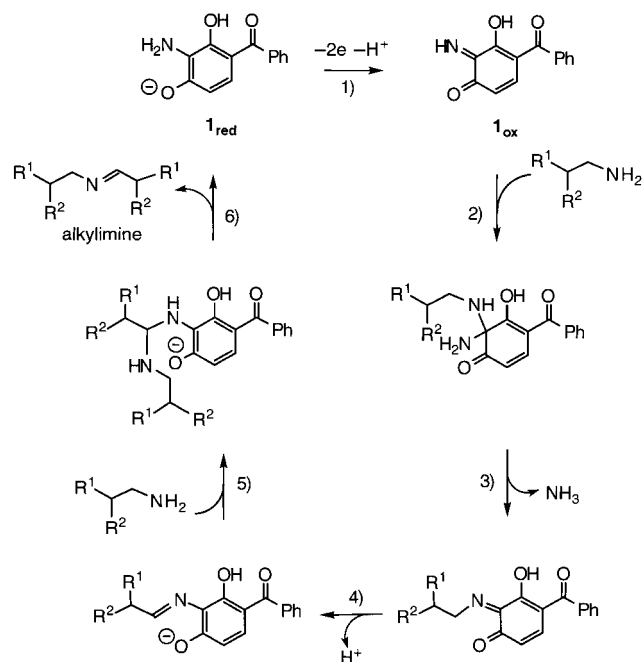
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Regiospecific Inverse-Electron-Demand Diels–Alder Reaction of Simultaneously Electrogenerated Diene and Dienophile: An Expeditious Route to Polyfunctionalized 1,4-Benzoxazine Derivatives

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Quinonoid systems are powerful intermediates for organic synthesis and constitute potential precursors to numerous naturally occurring substances.^[1] However, the synthesis of quinonoid entities, particularly *o*-quinones and *o*-azaquinones, which are usually unstable and very prone to polymerization, is not highly developed.^[2] The facile generation of *o*-quinone-type structures by the electrochemical oxidation of related *o*-quinols and their well-known ability to react with nucleophiles^[3] prompted us to investigate the reaction of highly reactive electrogenerated *o*-quinone species with amino alcohols, and we recently described the one-pot electrochemical synthesis of substituted 1,4-benzoxazine derivatives, a novel class of potent neuroprotective agents.^[4]

We also revealed a new mode of reactivity of these quinonoid systems,^[5] in which electrogenerated 3,4-azaquinone **1_{ox}** (Scheme 1) acts as an efficient catalyst for the



Scheme 1. Mechanism of catalytic oxidation of primary aliphatic amines mediated by electrogenerated model quinonoid cofactor **1_{ox}**.

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