Asymmetric Oxidation of Sulfide to Sulfoxides on Ti-Containing Mesoporous Silica Catalysts with Hydrogen Peroxide in the Presence of Optically Active Tartaric Acid

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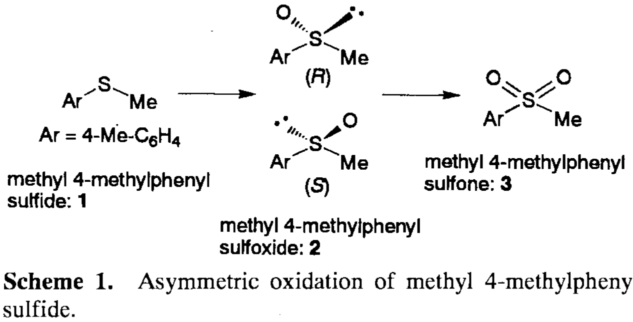
On Ti-containing MCM-41 prepared by a template ion-exchange method, sulfide could be asymmetrically oxidized to sulfoxides in the presence of optically active tartaric acid (54% yield and 30% ee). The oxidation was composed of the asymmetric induction to sulfoxides and the subsequent kinetic resolution of sulfoxides.

Heterogeneous asymmetric catalyses have eagerly been studied from three kinds of standpoints so far. First, the grafting or supporting of active homogeneous catalysts onto solid supports has a long history and many successful results. The second approach is the use of chiral surfaces of solid materials. The silk fiber[1] and quartz[2] have been employed to achieve the purpose. In particular the autocatalysis system on the quartz[2] has very recently given excellent ee values. The third effort is the preparation of chiral sites on achiral solid surface. In this case, several asymmetric hydrogenations have been achieved on metal surface modified with chiral organic molecules.[3] On the other hand, asymmetric reactions on porous oxides have just been realized. Hutchings et al.[4] have been reported asymmetric aziridination and epoxidation on metal ion-exchanged porous materials modified with chiral ligands which are known to be useful in homogeneous catalysis. However, there is still room for improvement in view of the leaching of active species from the solid catalysts, the variety of kinds of asymmetric reactions, and the stereoselectivity.



Scheme 1. Asymmetric oxidation of methyl 4-methylphenyl sulfide.

In the present study, asymmetric oxidation of sulfide (Scheme 1) was investigated, which consists of two consecutive reactions. In homogeneous catalysis, high enantioselectivity (99% ee) of sulfoxides has been attained by using Ti(O*i*Pr)$_4$ and diethyl (*R*, *R*)-tartarate.[5] In heterogeneous catalysis, there are a few reports on the sulfide oxidation. Titanium ion-containing MCM-41 (Ti-M41) prepared by a hydrothermal synthesis[6] or Ti-planted silica[7] has been reported to be active. The latter gave 13% ee in MeOH in the presence of (*R*,*R*)-tartaric acid, but leaching of Ti ions into the solution and the catalysis of resulting Ti ions were not negligible. Here we wish to report that Ti-M41 prepared by the template ion-exchange (TIE) method[8] was indeed active for the heterogeneous asymmetric oxidation.

The parent M41 or Ti-M41 was prepared by the reported manner[9] or the TIE method[8] using $(NH_4)_2[TiO(C_2O_4)_2]$. Ti-M41s showed Si/Ti ratios of 63 ± 4, pore diameters of 2.2 nm, and surface areas of 1,039 ± 15 $m^2\ g^{-1}$ and their regular structures were confirmed by XRD.

Methyl 4-methylphenyl sulfide or sulfoxides (1.0 mmol), Ti-M41 (0.050 mmol as Ti ion), 1,4-dibromobenzene (20 mg, internal standard), and chiral ligand (0 or 0.10 mmol) were put into a reaction vessel. After argon gas exchange, 7.0 cm^3 of solvent was poured into the vessel. The mixture was stirred at room temperature for 1 h and at reaction temperature for additional 1 h. The oxidation was started by introduction of oxidant and additional 3.0 cm^3 of solvent. A small part of the mixture (ca. 0.10 cm^3) was taken out from the reaction vessel at appropriate intervals and the reaction was stopped by addition of Na_2SO_3 and filtration. The sample was analyzed by a HPLC system with a Chiralcel OB column (Daicel) and a hexane–2-propanol flow.

Methyl 4-methylphenyl sulfide was oxidized by a H_2O_2 aqueous solution in CH_2Cl_2 in the presence of Ti-M41 and (*R*, *R*)-tartaric acid. The changes in concentrations of the reactant and the products and in the enantiomeric excess level of sulfoxides are shown in Figure 1 as a function of the reaction time.

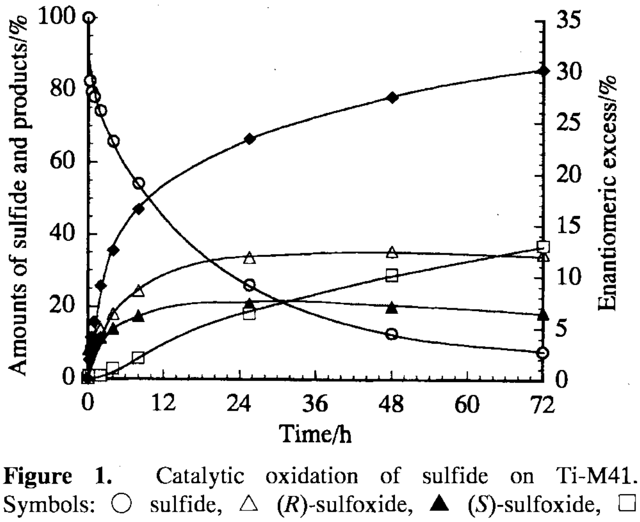


Figure 1. Catalytic oxidation of sulfide on Ti-M41. Symbols: ○ sulfide, △ (*R*)-sulfoxide, ▲ (*S*)-sulfoxide, □ sulfone, ◆ enantiomeric excess. Reaction conditions: methyl 4-methylphenyl sulfide, 1.0 mmol; Ti-M41, 240 mg; (*R*, *R*)-tartaric acid, 0.10 mmol; H_2O_2, 2.0 mmol; 1,4-dibromobenzene, 20 mg; CH_2Cl_2, 10 cm^3; 273 K.

The reaction mixture at 72 h contained 8% of sulfide, 54% of sulfoxides with 30% ee, and 37% of sulfone under the present reaction conditions. Asymmetric oxidation proceeded with (*R*)-isomer excess. The recycle use of Ti-M41 (7 times) confirmed that the present catalyst could be used repeatedly without any degradation.

The extent of enantiomeric excess gradually increased with the reaction time. Racemic mixture of methyl 4-methylphenyl sulfoxides was here oxidized under the same conditions. (*S*)-sulfoxide was consumed more rapidly than (*R*)-sulfoxide and the degree of enantiomeric excess reached to 43% ee at 72 h. A homogeneous catalyst[10] has been reported to show similar activity for the kinetic resolution of sulfoxides.

The kinetics of the asymmetric oxidation has been numerically analyzed by using following equations.

$$-d[\text{sulfide}]/dt = (k_{1R}+k_{1S})[\text{sulfide}][H_2O_2]$$

$$d[(R)\text{-sulfoxide}]/dt = k_{1R}[\text{sulfide}][H_2O_2] - k_{2R}[(R)\text{-sulfoxide}][H_2O_2]$$

$$d[(S)\text{-sulfoxide}]/dt = k_{1S}[\text{sulfide}][H_2O_2] - k_{2S}[(S)\text{-sulfoxide}][H_2O_2]$$

$$d[\text{sulfone}]/dt = k_{2R}[(R)\text{-sulfoxide}][H_2O_2] + k_{2S}[(S)\text{-sulfoxide}][H_2O_2]$$

where k_{1R} and k_{1S} are the rate constants of the formations of (*R*)- and (*S*)-sulfoxide, and k_{2R} and k_{2S} of the formations of sulfone from (*R*)- and (*S*)-sulfoxide, respectively. The ratio of k_{2R}/k_{2S} was determined to be 0.59 by using the data of the oxidation of racemic methyl 4-methylphenyl sulfoxides. Then the rate constants were calculated on the basis of the experimental data of Figure 1. The best-fitted results were obtained at k_{1R} = 0.19, k_{1S} = 0.13, k_{2R} = 0.083, and k_{2S} = 0.14 $dm^3 mol^{-1} h^{-1}$. The ratio of k_{1R}/k_{1S} was 1.5. It follows that first the present asymmetric oxidation is composed of the asymmetric induction to sulfoxide and the subsequent kinetic resolution of sulfoxides, and secondly both of the reactions proceed to yield the (*R*)-isomer preferentially.

The possibility of the homogeneous catalysis resulting from the dissolved Ti ions has been studied strictly. First, the filtrate after the first catalytic reaction did not show any activity for the further oxidation reaction. Secondly, the Ti contents in the filtrates were analyzed by a polarized Zeeman atomic absorption spectroscopy and were below the limitation of detection (ppb order). Thirdly, the Si/Ti ratios of Ti-M41s recovered after the reaction were in good agreement with those of fresh Ti-M41s within experimental errors. It can be concluded that there is no dissolved Ti ion in the solution and the observed asymmetric oxidation apparently proceeds on the surface of Ti-M41.

In Table 1, the chemical and optical yields of sulfoxides were compared under several reaction conditions. Entry 2 revealed that the catalysis indeed proceeds on Ti-M41. Without (*R,R*)-tartaric acid, there was no asymmetric oxidation (Entry 3). (*S,S*)-Tartaric acid gave almost the same results as those of (*R,R*)-tartaric acid with counter stereoselectivity (Entry 4). This clearly shows that the stereochemistry of the chiral ligands determines that of sulfoxide produced. On the other hand, neither combination of TBHP and (*R,R*)-tartaric acid (Entry 5) nor that of H_2O_2 and diethyl (*R,R*)-tartarate (Entry 6) gave high enantioselectivity. These are surprising in view of the fact that TBHP or diethyl (*R,R*)-tartarate are effective reagents in homogeneous asymmetric oxidations.[5,6,11] These would be attributable to the difference between the active sites on the surface and in the solution: It is the future problem to be solved.

Table 1. Asymmetric oxidation of methyl 4-methylphenyl sulfide under several reaction conditions.[a]

Ent.	Cat.	Chiral ligand[b]	Oxidant	Recovery or yield / %			% ee[c]
				1	**2**	**3**	
1	Ti-M41	(*R,R*)-TA	H_2O_2	8	54	37	30
2	none	(*R,R*)-TA	H_2O_2	96	3	1	3
3	Ti-M41	none	H_2O_2	32	56	13	0
4	Ti-M41	(*S,S*)-TA	H_2O_2	7	52	40	−28
5	Ti-M41	(*R,R*)-TA	TBHP	68	28	1	1
6	Ti-M41	(*R,R*)-DET	H_2O_2	34	54	11	1

[a]Reaction conditions: sulfide, 1.0 mmol; Ti-M41, 0 or 0.050 mmol as Ti; chiral ligand, 0 or 0.10 mmol; oxidant, 2.0 mmol; 1,4-dibromobenzene, 20 mg; CH_2Cl_2 10 cm^3; 273 K; 72 h. [b]TA = tartaric acid, DET = diethyl tartarate. [c]Positive and negative values mean (*R*)-isomer and (*S*)-isomer excesses, respectively.

The present results conclude that the combination of Ti-M41, optically active tartaric acid, and H_2O_2 is essential to the heterogeneous asymmetric oxidation.

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References and Notes

1 S. Akabori, S. Sakurai, Y. Izumi, and Y. Fujii, *Nature*, **178**, 323 (1956).

2 K. Soai, S. Osanai, K. Kadowaki, S. Yonekubo, T. Shibata, and I. Sato, *J. Am. Chem. Soc.* **121**, 11235 (1999).

3 Y. Izumi, M. Imaida, H. Fukawa, S. and Akabori, *Bull. Chem. Soc. Jpn.*, **36**, 21 (1963). Y. Orito, S. Imai, S. Niwa, and G. -H. Nguyen, *J. Synth. Org. Chem. Jpn.* **37**, 173 (1979).

4 C. Langham, P. Piaggio, D. Bethell, D. F. Lee, P. McMorn, P. C. B. Page, D. J. Willock, C. Sly, F. E. Hancock, F. King, and G. J. Hutchings, *Chem. Commun.* **1998**, 1601. P. Piaggio, P. McMorn, C. Langham, D. Bethell, P. C. B. Page, F. E. Hancock, and G. J. Hutchings, *New J. Chem.* **1998**, 1167.

5 J. -M. Brunel and H. B. Kagan, *Bull. Soc. Chim. Fr.* **133**, 1109 (1996).

6 A. Corma, M. Iglesias, and F. Sanchez, *Catal. Lett.* **39**, 153 (1996). A. M. Khenkin and R. Neumann, *Catal. Lett.* **68**, 109 (2000).

7 J. Fraile, J. Garcia, B. Lazaro, and J. Mayoral, *Chem. Commun.* **1998**, 1807.

8 M. Yonemitsu, Y. Tanaka, and M. Iwamoto, *Chem. Mater.* **9**, 2679 (1997). M. Yonemitsu, Y. Tanaka, and M. Iwamoto, *J. Catal.* **178**, 207 (1998).

9 T. Abe, Y. Tachibana, T. Uematsu, and M. Iwamoto, *J. Chem. Soc., Chem. Commun.* **1995**, 1617.

10 N. Komatsu, M. Hashizume, T. Sugita, and S. Uemura, *J. Org. Chem.* **58**, 4529, 7624 (1993).

11 P. Pitchen, E. Dunach, M. N. Deshmukh, and H. B. Kagan, *J. Am. Chem. Soc.* **106**, 8188 (1984).