

Enantioselective Photooxidation of a Sulfide by a Chiral Ruthenium(II) Complex Immobilized on a Montmorillonite Clay Surface: The Role of Weak Interactions in Asymmetric Induction

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The present work pursued a possibility that enantioselectivity was achieved through weak intermolecular interactions between a catalyst and a substrate. For that purpose, we studied the photooxidation of α -ethylbenzyl phenyl sulfide catalyzed by a polypyridyl ruthenium(II) complex as a chiral photosensitizer. No covalent bonding was formed between a catalyst and a substrate, because the complexes used ($[\text{Ru}(\text{phen})_3]^{2+}$ or $[\text{Ru}(\text{bpy})_3]^{2+}$) were coordinatively saturated. Enantiomer excess (ee) was attained to be 30% when a chiral photosensitizer was immobilized on montmorillonite clay. It was even improved to 43% in the presence of an additional chiral auxiliary, dibenzoyl-D(+)-tartaric acid. Notably, no enantioselectivity was achieved when the reaction took place in homogeneous solutions. The ab initio calculations were performed on the stability of an associate composed of a catalyst (metal complex) and a product (sulfoxide) to obtain a clue to reaction mechanisms. The calculations suggest that chiral discrimination is achieved even through noncovalent interactions between a substrate and a chiral sensitizer when the attacking direction by a substrate toward a catalyst is limited sterically on a solid surface.

Introduction

Asymmetric catalysts have been a topic of extensive interest in organic syntheses. Homogeneous catalytic systems are a mainstream for the stereochemical control during reactions. For example, a number of molecular catalysts employ chiral organometallic complexes with symmetrical ligands such as BINAP, salen, or bis(oxazoline) (both with C_2 symmetry).^{1,2} In these cases, steric control is achieved under the stereochemical influence of a ligand over a substrate within a coordination sphere. Attack onto a substrate is confined in one direction among several possible pathways. Despite their high enantioselectivities and turnover numbers, however, they have practical problems such as the expensiveness of catalysts, the low efficiency of recoveries, and the limitation for large-scale applications.

One of the solutions to these problems is the immobilization of a chiral catalyst onto a solid surface. This leads to an advantage of the versatile separation of the catalyst from a solution as well as the avoidance of effluxes of poisonous metals.³ Only a few heterogeneous asymmetric catalyses have been reported so far as a practical use probably because of difficulties in the preparations of suitable solid supports for a catalyst.^{4,5} A wide range of materials have been attempted as a support, covering zeolites, mesoporous silicas, and layered silicates.^{6–11} These attempts take a strategy to immobilize the catalysts that are already known to exhibit high asymmetric catalytic activities in homogeneous systems.

Among layered inorganic materials, a clay mineral has attracted a great deal of attention due to its network structure with cation-exchange properties.^{12,13} Adsorbed cations exist at high density under steric control by a two-dimensional phyllosilicate sheet. In this study, we intended to examine a possibility whether enantioselectivity in chemical reactions was achieved through weak interactions such as dipole-charge, hydrogen bonding, π - π , and van der Waals interactions between a substrate and a catalyst. For that purpose, steric constraint was imposed by immobilizing a catalyst on a solid surface. The photooxidation of a sulfide (or α -ethylbenzyl phenyl sulfide) was studied on the surface of montmorillonite clay. As a chiral director, a chiral metal complex, $[\text{Ru}(\text{bpy})_3]^{2+}$ (bpy = 2,2'-bipyridine) or $[\text{Ru}(\text{phen})_3]^{2+}$ (phen = 1,10-phenanthroline), was immobilized on smectite by ion-exchanging. Application of smectite as a solid support for asymmetric syntheses has been motivated by our previous finding that a column packed with smectite modified by these catalysts is efficient in resolving a wide variety of organic racemic mixtures.¹⁴

Experimental Section

Preparation of Materials. α -Ethylbenzyl phenyl sulfide was a gift from Prof. K. Kobayashi (University of Tokyo).¹⁵ $[\text{Ru}(\text{bpy})_3]\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ was purchased commercially (Merck Co.). $[\text{Ru}(\text{phen})_3]\text{Cl}_2$ was prepared by reacting potassium aquapentachlororuthenium(III) (Sigma-Aldrich Co.) with 1,10-phenanthroline monohydrate in dimethylformamide. Reduction was performed with phosphinic acid (Wako Pure Chemical Ind. Ltd). Optical resolution of $[\text{Ru}(\text{phen})_3]^{2+}$ was carried out by adding bis[(+)-tartratodiantimonate(III) dipotassium trihydrate (denoted by $\text{K}_2\text{-(SbOtart)} \cdot 3\text{H}_2\text{O}$ (Kanto Chemical Co., Inc.) to its racemic mixture. An insoluble salt, $\Lambda\text{-}[\text{Ru}(\text{phen})_3](\text{SbOtart}) \cdot 6\text{H}_2\text{O}$, was

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filtered and transformed into a perchlorate salt by use of anion-exchange resin (Dowex Co.). The resolution of $[\text{Ru}(\text{bpy})_3]\text{Cl}_2$ and $[\text{Ni}(\text{phen})_3]\text{Cl}_2$ was performed in the same way.¹⁶ The absolute configurations of these complexes were assigned from their CD spectra according to the literature.^{17,18}

Procedures of Homogeneous Oxidation in the Dark. A stock solution of a sulfide (2.5×10^{-4} M) was prepared by dissolving 23 mg of the sulfide into 400 mL of $\text{H}_2\text{O}/\text{MeOH}$ ($v/v = 1$). Next, 2.3 mg of sodium periodate (Kanto Chemical Co., Inc.) was added to 40 mL of the stock solution. After it was stirred at room temperature for 12 h, the solution was evaporated. The residue was dispersed in water and extracted with chloroform. This extract was evaporated again and dissolved in 3 mL of methanol and analyzed by HPLC, the details of which are described below.

Procedures of Homogeneous Photooxidation. Λ - $[\text{Ru}(\text{bpy})_3](\text{ClO}_4)_2$ (6 mg) was added to 40 mL of the sulfide stock solution (2.5×10^{-4} M, $\text{H}_2\text{O}/\text{MeOH}$ ($v/v = 1$)). The solution was irradiated with a halogen lamp (300 W, Cabin, JCD 100 V/300 WL) through a monochromic filter (450 ± 10 nm, Andover Corp.) under stirring at room temperature for 18 h. The mixture was evaporated and dispersed in water and extracted with chloroform. After the chloroform solution was evaporated, the residue was dissolved in methanol. The product was analyzed chromatographically in the same way as in the dark reactions.

Procedures of Heterogeneous Photooxidation. 40 mL of either Λ - $[\text{Ru}(\text{phen})_3](\text{ClO}_4)_2$ or Λ - $[\text{Ru}(\text{bpy})_3](\text{ClO}_4)_2$ (1.4×10^{-4} M) was mixed with 17.5 mg of sodium montmorillonite (Kunimine Co., Inc.). The dispersion was shaken vigorously and left at room temperature for 24 h. After it was centrifuged at 5000 rpm for 40 min, the UV/vis spectrum of the supernatant was measured (UV-160A, Shimadzu), confirming that the whole of the added metal complex was adsorbed by montmorillonite clay. The precipitate was dispersed again in 40 mL of the sulfide stock solution (2.5×10^{-4} M, $\text{H}_2\text{O}/\text{MeOH}$ ($v/v = 1$)). The dispersion was shaken vigorously and left at room temperature for 24 h. It was centrifuged at 5000 rpm for 40 min (6500, Kubota). From the UV/vis absorption of the supernatant, about 50% of sulfide was adsorbed by an adduct of montmorillonite and a metal complex. The precipitate of a ternary adduct consisting of montmorillonite, a metal complex, and a sulfide was dispersed in 40 mL of water in an open Pyrex tube and irradiated with a halogen lamp through a monochromic filter under stirring at room temperature for 24 h. The mixture was centrifuged at 5000 rpm for 40 min. The precipitate was dispersed in 40 mL of chloroform and filtrated to remove an adduct of montmorillonite/metal complex. The chloroform filtrate was dried in a vacuum, and the residue was dissolved in 500 μL of methanol and analyzed by HPLC.

In the case of nickel complexes, all procedures were performed at 2 °C to avoid racemization. Chiral auxiliaries were added before irradiation as the following solutions: sodium-D-(+)-tartrate (Wako Pure Chemical Ind. Ltd) in pure water and diethyl-L-(+)-tartrate (Wako Pure Chemical Ind. Ltd.) and dibenzoyl-D-(+)-tartaric acid (Fluka Chemie AG) in a $\text{MeOH}/\text{H}_2\text{O}$ ($v/v = 3$) mixture, respectively.

Chromatographic Analyses. Purification of an oxidation product was performed by high performance liquid chromatography (HPLC) using an HPLC system (980series, JASCO, Japan). 100 μL of methanol solution was loaded and eluted with methanol on a C18 silica-based column (CAPCELL PAK C18 AQ, Shiseido Co., Ltd.) at a flow rate of 0.40 mL min^{-1} . Detection was made spectrophotometrically at 252 nm, which corresponded to a peak due to a sulfoxide. The eluent was

collected and concentrated to 50 μL . The analyses of enantiomeric distribution were performed on a chiral column (Cera-mospher chiral RU-1, Shiseido Co., Ltd.) by use of methanol as an eluent at a flow rate of 0.40 mL min^{-1} .

Identification of Chemical Species and Their Absolute Configurations. An FT-IR spectrum of an eluted fraction in HPLC was measured with an FT-IR-460plus instrument (JASCO, Japan). Their ^1H NMR spectra were measured in CDCl_3 with a JNM-EX270 instrument (JEOL, Japan). Their CD spectra were measured in chloroform with a J-720 spectropolarimeter (JASCO, Japan). The ORD spectrum of the sulfide isomer was measured in chloroform at 589 nm (sodium D-line) with a DIP-140 Digital polarimeter (JASCO, Japan). These measurements were performed to identify the absolute configuration of sulfides and sulfoxides.

Actinometry. The intensity of an incident light was determined by chemical actinometry.^{19,20} Potassium tris(oxalato)-ferrate(III) trihydrate (Strem Chemicals) was used. Light intensity was obtained by reducing Fe(III) to Fe(II) in which the quantum yield of potassium ferrioxalate was known. The amount of produced Fe(II) was determined by measuring the absorbance at 510 nm as a phenanthroline complex with a UV/vis spectrometer at every 15 min ($\epsilon_{510} = 1.11 \times 10^4$).

X-ray Diffraction Measurements. 500 μL of an aqueous dispersion of a reactant in heterogeneous oxidation was cast onto a glass plate (Matsunami, Japan) and dried under air. Its XRD pattern was measured with a RINT 2000 (RIGAKU, Japan) using $\text{Cu K}\alpha$ radiation. The sampling step and counting time were 0.02 and 1.5 s, respectively.

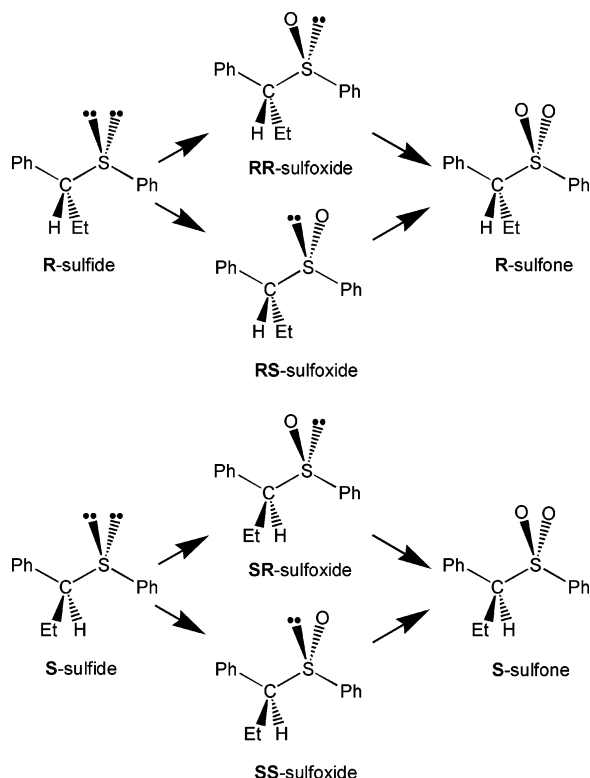
Calculation Details

Ab initio molecular orbital calculations were performed using the Gaussian 03 program.²¹ In the presence of Δ - $[\text{Ru}(\text{phen})_3]^{2+}$, the association structure of the metal complex and a sulfoxide (product) was geometrically optimized. Four isomers of sulfoxide (*RR*, *SS*, *RS*, and *SR*) and Δ - $[\text{M}(\text{phen})_3]^{2+}$ were geometrically optimized at the DFT (density functional theory) calculation using B3LYP functional in combination with 3-21G** basis function.²² Two representative configurations were assumed as an initial state. In one case, a sulfoxide was placed along the C_2 axis of the metal complex, and, in the other case, a sulfoxide was placed along the C_3 axis of the complex. The central metal ion of a complex was assumed to be Mg(II) instead of Ru(II). The total energies were compared among four types of sulfoxide isomers.

Results

The present substrate (α -ethylbenzyl phenyl sulfide) and its oxidized products (sulfoxides) were both stable up to at least 60 °C with no racemization. The substrate (sulfide) has an enantiomeric pair, and the products have two enantiomeric pairs in diastereomeric relations (Scheme 1). Both enantioselectivity and diastereoselectivity were investigated to elucidate the mechanisms of oxidation.

Determination of the Absolute Configurations of Sulfoxides. A racemic mixture of the sulfide was resolved by the HPLC on a chiral column as shown in Figure 1. The absolute configuration of a resolved sulfide was assigned from the sign of ORD at 589 nm according to the previous report.^{23–25} Each enantiomer was oxidized to sulfoxides with NaIO_4 . When the sulfoxides obtained from the *R*-sulfide were eluted on a chiral column at a flow rate of 0.40 mL min^{-1} , they gave the peaks at 27.5 and 36.0 min, while the sulfoxides obtained from the *S*-sulfide gave the peaks at 25.0 and 41.3 min. The ^1H NMR

SCHEME 1: Asymmetric Oxidation of α -Ethylbenzyl Phenyl Sulfide

spectra of the first two fractions (25.0 and 27.5 min) showed the peaks at 6.90, 6.92, and 7.22 ppm, which were assigned to the *RS* and *SR* diastereomers, respectively, according to the previous report.²⁶ The ^1H NMR spectra of the last two fractions (36.0 and 41.3 min) showed the peaks at 6.85, 7.09, and 7.18 ppm, which were assigned to the *RR* and *SS* diastereomers, respectively. From their CD spectra, the first two (25.0 and 27.5 min) and the last two peaks (36.0 and 41.3 min) were confirmed to be enantiomeric antipodes, respectively. As a conclusion, the absolute configuration of a sulfoxide at each peak of the chromatogram on a chiral column was assigned to *SR* (25.0 min), *RS* (27.5 min), *RR* (36.0 min), and *SS* (41.3 min) at a flow rate of 0.40 mL min^{-1} , respectively.

Homogeneous Oxidation by NaIO_4 without Chiral Sources. The sulfide was oxidized by NaIO_4 in $\text{H}_2\text{O}/\text{MeOH}$ ($v/v = 1$) under stirring for 12 h at room temperature. The product was extracted with chloroform. After the residue was dissolved in methanol, the solution was analyzed by HPLC on a C18 silica-based column using methanol as an eluent. A main peak was observed at 8.2 min at a flow rate of 0.40 mL min^{-1} . The FT-IR spectra of the fraction showed the absorption band at 1038 cm^{-1} , which was assigned to the S–O stretching vibration of a

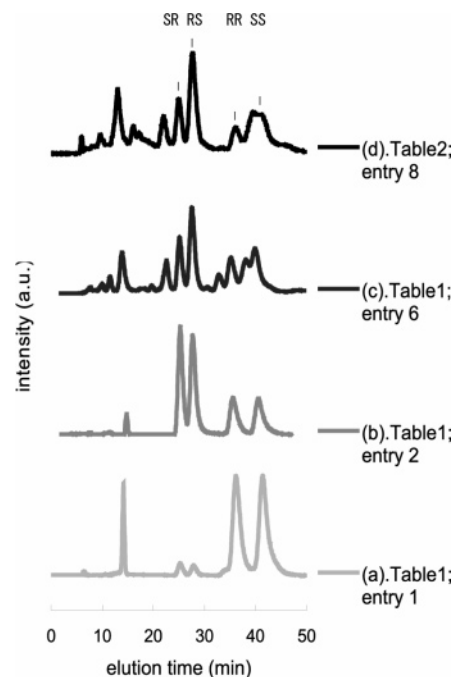


Figure 1. Chromatogram for the separation of the sulfoxide isomers on a chiral column (eluent = methanol; flow rate = 0.40 mL min^{-1} ; loaded amount = $50\text{ }\mu\text{L}$; wavelength = 252 nm).

sulfoxide. The fraction was analyzed further on a chiral clay-based column. As shown in Figure 1a, four peaks were observed at 25.0, 27.5, 36.0, and 41.3 min at a flow rate of 0.40 mL min^{-1} . As stated in the preceding section, the former two peaks (25.0 and 27.5 min) were assigned to *SR*- and *RS*-diastereomers and the latter two peaks (36.0 and 41.3 min) to *RR*- and *SS*-diastereomers, respectively. Comparing the area of each peak, the ratio of (*SR* + *RS*):(*RR* + *SS*) was obtained to be 6:94 (Table 1; entry 1). There was no stereoselectivity observed, or the ratio of *RR*:*SS* or *SR*:*RS* was unity within an experimental error.

Homogeneous Photooxidation by a Chiral Ruthenium Complex as a Photosensitizer. The sulfide was oxidized with $\Lambda\text{-}[\text{Ru}(\text{bpy})_3](\text{ClO}_4)_2$ as a photosensitizer in $\text{H}_2\text{O}/\text{MeOH}$ ($v/v = 1$) under irradiation with a halogen lamp for 12 h at room temperature. Light intensity was estimated to be $1.4 \times 10^{-6}\text{ einsteins s}^{-1}$ by chemical actinometry.^{19,20} The HPLC analyses on a C18 silica-based column showed that the sulfoxide was produced at 100% yield. The HPLC results on a chiral column are shown in Figure 1b. According to it, the diastereomeric selectivity was reversed from that for the dark reaction, or the ratio of (*SR* + *RS*):(*RR* + *SS*) was 64:36, while the enantiomeric ratio of *SR*:*RS* or *RR*:*SS* was unity within an experimental error (entry 2 in Table 1). Thus, no stereoselectivity was attained in a homogeneous reaction, although a chiral Ru(II) complex was used.

TABLE 1: Diastereomeric and Enantiomeric Selectivities of α -Ethylbenzyl Phenyl Sulfides in Homogeneous and Heterogeneous Oxidations

entry	complex	support	oxidation	ee (%) ^a		diastereomer ratio (<i>SR</i> + <i>RS</i>):(<i>RR</i> + <i>SS</i>)
				<i>SR</i> : <i>RS</i>	<i>RR</i> : <i>SS</i>	
1			NaIO_4	0	0	6:94
2	$\Lambda\text{-}[\text{Ru}(\text{bpy})_3]^{2+}$		light	−2	0	64:36
3	$\Lambda\text{-}[\text{Ru}(\text{bpy})_3]^{2+}$	montmorillonite	light	5	11	67:33
4	$\Delta\text{-}[\text{Ru}(\text{bpy})_3]^{2+}$	montmorillonite	light	−9	−9	71:29
5	$\Lambda\text{-}[\text{Ru}(\text{phen})_3]^{2+}$	montmorillonite	light	13	11	62:38
6	$\Delta\text{-}[\text{Ru}(\text{phen})_3]^{2+}$	montmorillonite	light	−30	−29	53:47

^a Each ee (enantiomer excess) is defined as (*SR* − *RS*)/(*SR* + *RS*) or (*RR* − *SS*)/(*RR* + *SS*) for *SR*:*RS* or *RR*:*SS* as obtained from the HPLC peak areas, respectively.

TABLE 2: Stereoselectivities of α -Ethylbenzyl Phenyl Sulfide in Various Heterogeneous Oxidations

entry	heterogeneous catalyst	altered condition ^a	ee (%) ^b		diastereomer ratio (SR + RS):(RR + SS)
			SR:RS	RR:SS	
1	Δ -[Ru(phen) ₃] ²⁺ /montmorillonite	reused catalyst	-23		
2	Δ -[Ru(phen) ₃] ²⁺ /montmorillonite	re-reused catalyst	-34		
3	Δ -[Ru(phen) ₃] ²⁺ /montmorillonite	100% CEC loading of Ru(II) complex	-26	30	56:44
4	Δ -[Ru(phen) ₃] ²⁺ /montmorillonite	at 4 °C	-33	-36	51:49
5	Δ -[Ni(phen) ₃] ²⁺ /montmorillonite	oxidation by NaIO ₄ , at 4 °C	-12		58:42
6	Δ -[Ru(phen) ₃] ²⁺ /montmorillonite	sodium-D-(+)-tartrate added, at 4 °C	-30	-30	45:55
7	Δ -[Ru(phen) ₃] ²⁺ /montmorillonite	diethyl-L-(+)-tartrate added, at 4 °C	15		69:31
8	Δ -[Ru(phen) ₃] ²⁺ /montmorillonite	dibenzoyl-D-(+)-tartaric acid added, at 4 °C	-43		66:34

^a The experimental conditions were altered from the corresponding ones in Table 1. Entry 6: 50% CEC loading of Ru(II) complex, fresh catalyst, at room temperature, photooxidation, and no other chiral auxiliary added. ^b Each ee (enantiomer excess) is defined as (SR - RS)/(SR + RS) or (RR - SS)/(RR + SS) for SR:RS or RR:SS as obtained from the HPLC peak areas, respectively.

Heterogeneous Photooxidation by a Chiral Metal Complex Immobilized on a Montmorillonite Clay Surface. Chiral [Ru(bpy)₃]²⁺ or [Ru(phen)₃]²⁺ was immobilized to montmorillonite clay by ion-exchanging up to the loading of 50% of CEC. An obtained adduct was dispersed in an H₂O/MeOH (v/v = 1) solution of sulfide. The mixture was shaken vigorously and left for 24 h under the dark condition. Thereafter, the mixture was centrifuged and the residue was dispersed in water again. The dispersion was irradiated under stirring for 24 h at room temperature.

The product was extracted with chloroform and dried in vacuo. The residue was dissolved in methanol and analyzed by HPLC on a C18 silica-based column. As a result, for Δ -[Ru(bpy)₃]²⁺, the ratio of (SR + RS):(RR + SS) isomers was 71:29, which was closer to the homogeneous reaction catalyzed by the same photosensitizer than to the dark reaction (Table 1, entry 4). Notably, the RS isomer was produced more than the SR isomer at 9% ee, while the SS isomer was produced more than the RR isomer at 9% ee. When the results were compared to the homogeneous reactions, the enantioselective reaction was achieved only when the chiral ruthenium complex was immobilized on montmorillonite clay. In the case of Λ -[Ru(bpy)₃]²⁺, enantioselectivity was reversed as expected (Table 1, entry 3), confirming that the observed enantioselectivity originated from the chirality of a photosensitizer. In the case of Λ -[Ru(phen)₃]²⁺ and Δ -[Ru(phen)₃]²⁺, even higher enantioselectivity was observed (Table 1, entries 5 and 6). The RS/SR selectivity attained 29% ee when Δ -[Ru(phen)₃]²⁺ was used as a photosensitizer.

Several additional peaks were observed in 0–20 min in a chromatogram on a chiral column (Figure 1c). The fractions collected for these peaks showed the absorption between 220 and 260 nm that corresponded to the aryl groups. Similar products were obtained also when a solution of a sulfide was irradiated in the presence of montmorillonite alone. Thus, we concluded that these compounds were produced by the catalytic activity of montmorillonite clay. No enantioselectivity was observed in the oxidation of a sulfide by montmorillonite clay alone.

Further experiments were carried out by changing the reaction conditions. Table 2 shows the summary of the results. (i) In the case of Δ -[Ru(phen)₃]²⁺, a clay–metal complex adduct was recovered and reused under the same conditions repeatedly. Although the catalyst gave similar enantioselectivity and diastereoselectivity, the amount of the byproducts increased on reusing the same catalyst (Table 2, entries 1 and 2). Presumably, montmorillonite clay particles were fragmented at each run, resulting in the increase of the number of hydroxyl groups at the edges of a sheet. These sites might be active in the catalytic decomposition of the sulfide. (ii) When the loading of a

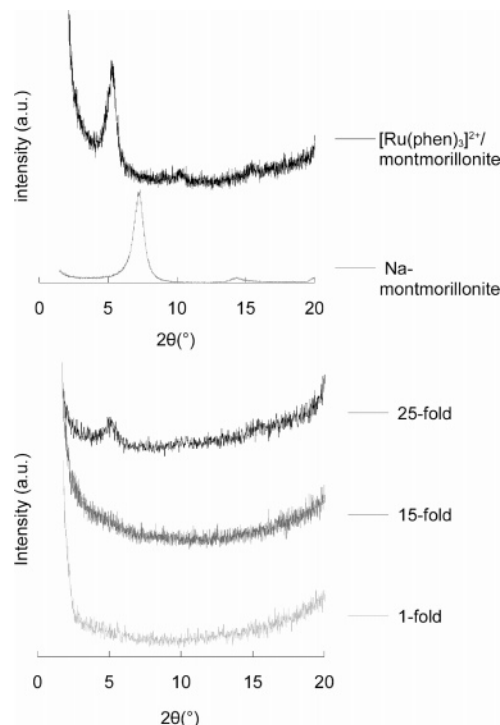


Figure 2. XRD patterns of montmorillonite clay modified with Ru(II) complex: (a) dried samples; (b) aqueous suspensions concentrated to the different degrees as indicated in the figure.

photosensitizer (Λ -[Ru(phen)₃]²⁺ or Δ -[Ru(phen)₃]²⁺) increased from 50% to 100%, no appreciable difference was observed in both enantioselectivities and diastereoselectivities (Table 2, entry 3). It was suggested therefore that the adsorbed Ru(II) complexes always formed a cluster at these loadings. A sulfide might be associated with such clustered metal complexes on a montmorillonite clay surface. (iii) When temperature was lowered from room temperature to 4 °C, no effect was observed both in diastereomeric and in enantiomeric selectivity (Table 2, entry 4). (iv) Dark oxidation by NaIO₄ was attempted for a montmorillonite clay system by using enantiomeric [Ni(phen)₃]²⁺ as a chiral director. The Ni(II) complex did not act as a photosensitizer. When NaIO₄ was added to an aqueous dispersion of an adduct of montmorillonite clay, Δ -[Ni(phen)₃]²⁺ and a sulfide at 4 °C, the obtained enantioselectivity was lower than in photooxidation (Table 2, entry 5). It implied that, in photooxidation, the oxidation of a sulfide took place close to a montmorillonite clay surface, leading to the effective steric constraint by the complex. To the contrary, the oxidation of a sulfide by IO₄⁻ took place distant from a montmorillonite clay surface, because the oxidant was negatively charged so that it was repelled from a negative montmorillonite clay particle.

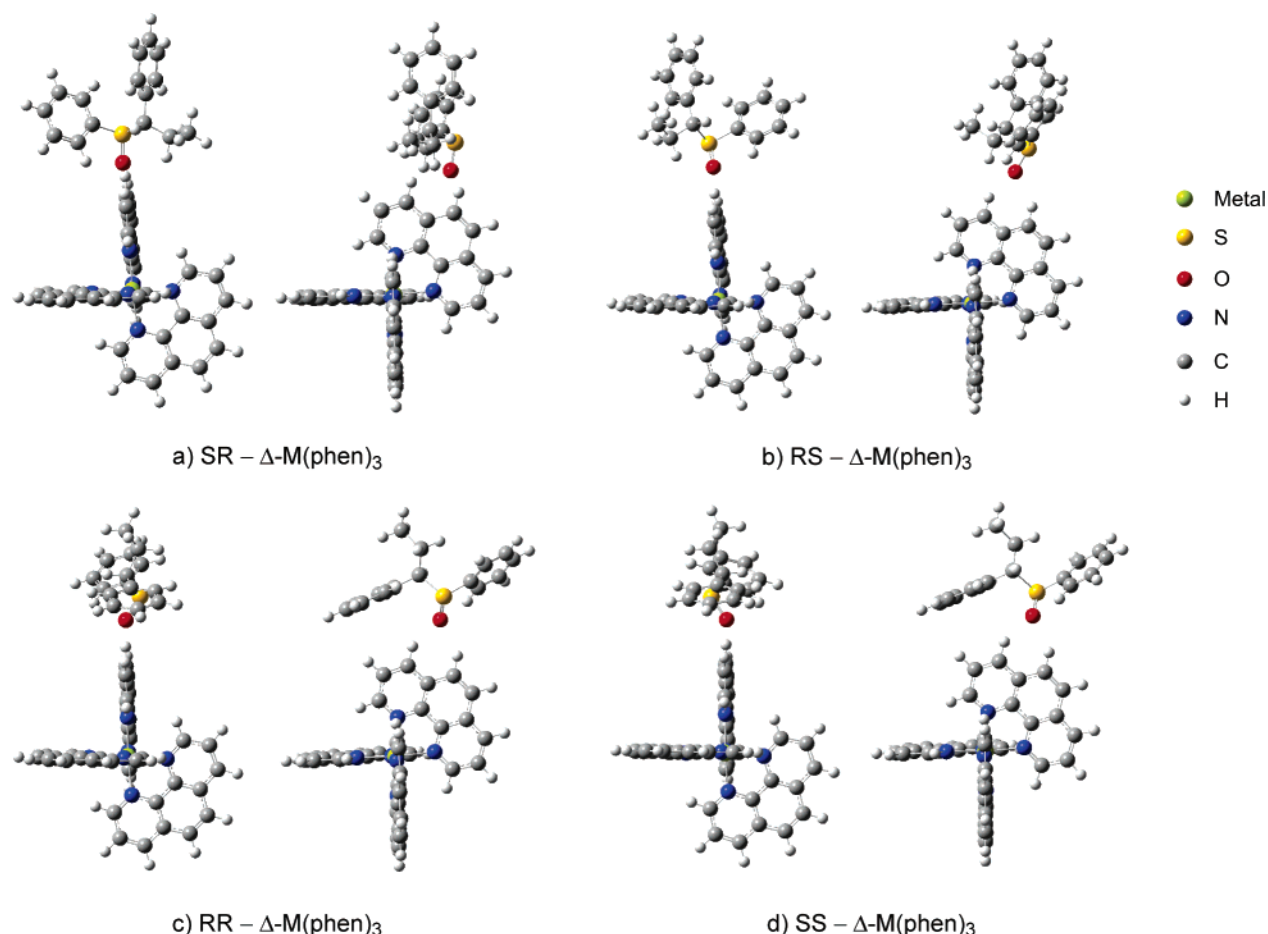


Figure 3. Optimized structures of sulfoxide/ Δ -Ru(II) complex associates for the C_2 association mode. The left and right pictures in each figure correspond to the ones projected along the directions as indicated by arrows L and R in Figure 4.

It was previously reported that a chiral auxiliary had an effect of enhancing enantioselectivity by a catalyst through weak interactions with a substrate.²⁷ The facts motivated us to attempt chiral molecules as an assisting reagent. For that purpose, sodium-D(+)-tartrate or diethyl-L(+)-tartrate or dibenzoyl-D-(+)-tartaric acid was added to an aqueous dispersion of a ternary adduct of montmorillonite clay, Δ - or Δ -[Ru(phen)₃]²⁺ and a sulfide. There was no remarkable change in the case of sodium-D(+)-tartrate and diethyl-L(+)-tartrate (Table 2, entries 6 and 7). In the case of dibenzoyl-D(+)-tartaric acid, however, the enantioselectivity of SR/RS sulfoxide isomers increased to 43% ee in the case of Δ -[Ru(phen)₃]²⁺ (Table 2, entry 8; Figure 1d). The results indicated that the weak π - π interaction between the aryl groups of Δ -[Ru(phen)₃]²⁺ and dibenzoyl-D(+)-tartaric acid was effective in increasing steric constraint to the approaching path by a sulfide.

Structural Analyses of Heterogeneous Catalysts. XRD measurements were performed on a dried sample of an adduct of montmorillonite/ Δ -[Ru(phen)₃]²⁺. The interlayer distance was determined to be 1.7 nm from the (001) diffraction at $2\theta = 5^\circ$ (Figure 2a, upper curve). Subtracting 0.9 nm as a layer thickness from this value, the height of an interlayer space was estimated to be 0.8 nm, which was nearly equal to the molecular height of Δ -[Ru(phen)₃]²⁺ along its C_3 axis. Thus, a sulfide was unable to approach [Ru(phen)₃]²⁺ along its C_3 axis when the Ru(II) complex was intercalated between montmorillonite clay layers. The XRD measurements were also performed on the following samples (Figure 2b): an original aqueous dispersion (lowest), 15-fold (middle), and 25-fold (upper) concentrated samples. The diffraction peak (0.5 nm) at $2\theta = 5^\circ$ was absent for the initial

sample, weak for the 15-fold concentrated sample, and clearly seen for the 25-fold concentrated sample, respectively. For the last sample, the stacking number of montmorillonite clay sheets was estimated to be less than five from the half-width of 1.4° of the (001) peak on the basis of Scherrer's equation.²⁸ From these results, a used montmorillonite clay was exfoliated to a single layer in an aqueous dispersion. Based on this, the present photooxidation reaction occurred on an external surface of montmorillonite clay but not in the interlayer spaces.

Theoretical Analyses of Mechanisms of Enantioselective Reactions. Theoretical calculation was performed by the ab initio method to elucidate the reaction mechanisms of sulfide oxidation. Attention was focused on the comparison between theory and experiments on diastereoselectivity and enantioselectivity.

The stability of an associate between a catalyst (metal complex) and a reaction product (sulfoxide) was studied in the case of Δ -[M(phen)₃]²⁺. The following two modes of associations were assumed as below:

(1) *Association along the C_2 Direction of a Complex.* A sulfoxide was placed along the C_2 direction of the complex. As a result, a sulfide was found to form a hydrogen bond through an oxygen atom with two hydrogen atoms at the fifth and sixth positions of a phenanthroline ligand (Figure 3a–d). The structures at the left- and right-hand side of each associate in Figure 3 were drawn when it was seen in the directions indicated by arrows L and R shown in Figure 4, respectively. Table 3 gives the optimized energy difference in the four isomers of a sulfoxide. The RS - and SR -isomers were more stable than the SS - and RR -isomers by about 10 kJ mol⁻¹. When it is supposed

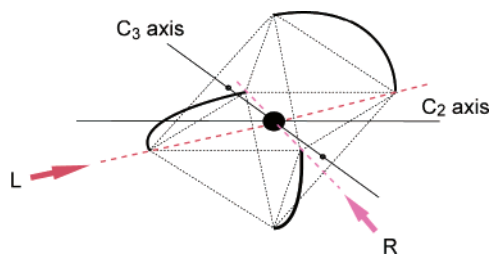


Figure 4. The direction of the projection of a metal complex/sulfide associate as shown in Figures 3 and 5. Arrows L and R indicate the direction for the left and right pictures in these figures.

TABLE 3: Relative Energy Difference among Sulfoxide Isomers in Optimized Structures of Sulfoxide/ Δ -Ru(II) Complex Associates in the C_2 Association Mode or the C_3 Mode

sulfoxide isomers	C_2 association mode ΔE (kJ mol $^{-1}$) ^a	C_3 association mode ΔE (kJ mol $^{-1}$)
<i>SR</i>	1.44	4.17
<i>RS</i>	0	0
<i>RR</i>	10.08	14.80
<i>SS</i>	9.57	6.50

^a ΔE is the association energy measured from the system with the lowest total energy.

that selectivity is determined dominantly by the stability of an associate of a catalyst and a product, the calculated results (Table 3) are in accord with the experimentally observed diastereoselectivity ($(SR + RS) > (RR + SS)$) in a homogeneous reaction. Moreover, the calculations predict only the small energy difference (<1.5 kJ mol $^{-1}$) between the enantiomers (*RS* vs *SR* or *SS* vs *RR*), which is in accord with the fact that no enantioselectivity was achieved in a homogeneous system.

(2) *Association along the C_3 Direction of a Complex.* [Ru(phen) $_3$] $^{2+}$ and [Ru(bpy) $_3$] $^{2+}$ are known to be adsorbed on a montmorillonite clay surface with their C_3 axes perpendicularly.^{29–31} To simulate these situations, the position of the central

metal(II) ion of a chiral complex was fixed during the optimization of an associate of a sulfoxide and a metal complex. Under this configuration, a sulfoxide approached along the C_3 direction of Δ -[M(phen) $_3$] $^{2+}$. Figure 5a–d shows the optimized structures for such an associate of a metal complex and either one of four isomers of a sulfoxide. According to the calculation results given in Table 3, the order of the stability of an associate was obtained to be $RS > SR > SS > RR$. Based on the same assumption as above, the results agree well with both of the diastereomeric and enantiomeric selectivities ($RS > SR \gg SS > RR$) as experimentally observed in the heterogeneous experiments (Table 1, entry 8). Notably, the total energy of an *RS* isomer/Ru(II) complex associate in C_2 mode was calculated to be more stable by -22.2 kJ mol $^{-1}$ than that of the same associate in C_3 mode. This indicates that the C_2 mode association should be achieved if there is no constraint on selecting a route of an approach toward a Ru(II) complex or it corresponds to the global minimum state.

Discussion

The present study aimed at an asymmetric synthesis in heterogeneous systems under the control of noncovalent interactions. As a result, it has been demonstrated that the photooxidation of α -ethylbenzyl phenyl sulfide proceeded in a stereoselective way by a chiral ruthenium(II) complex only when the catalysts were immobilized on montmorillonite clay. Although neither a covalent nor a coordinating bond was formed between a catalyst and a substrate, high diastereoselectivity and moderate enantioselectivity were accomplished as summarized in Table 1.

In contrast with the systems involving strong interactions such as covalent and coordinating bonds, it was difficult to apply conventional spectroscopic methods such as NMR and XRD to elucidate a mechanism experimentally. To overcome the difficulty, theoretical calculations were performed as a help to get a clue to the reaction mechanisms. The calculation results

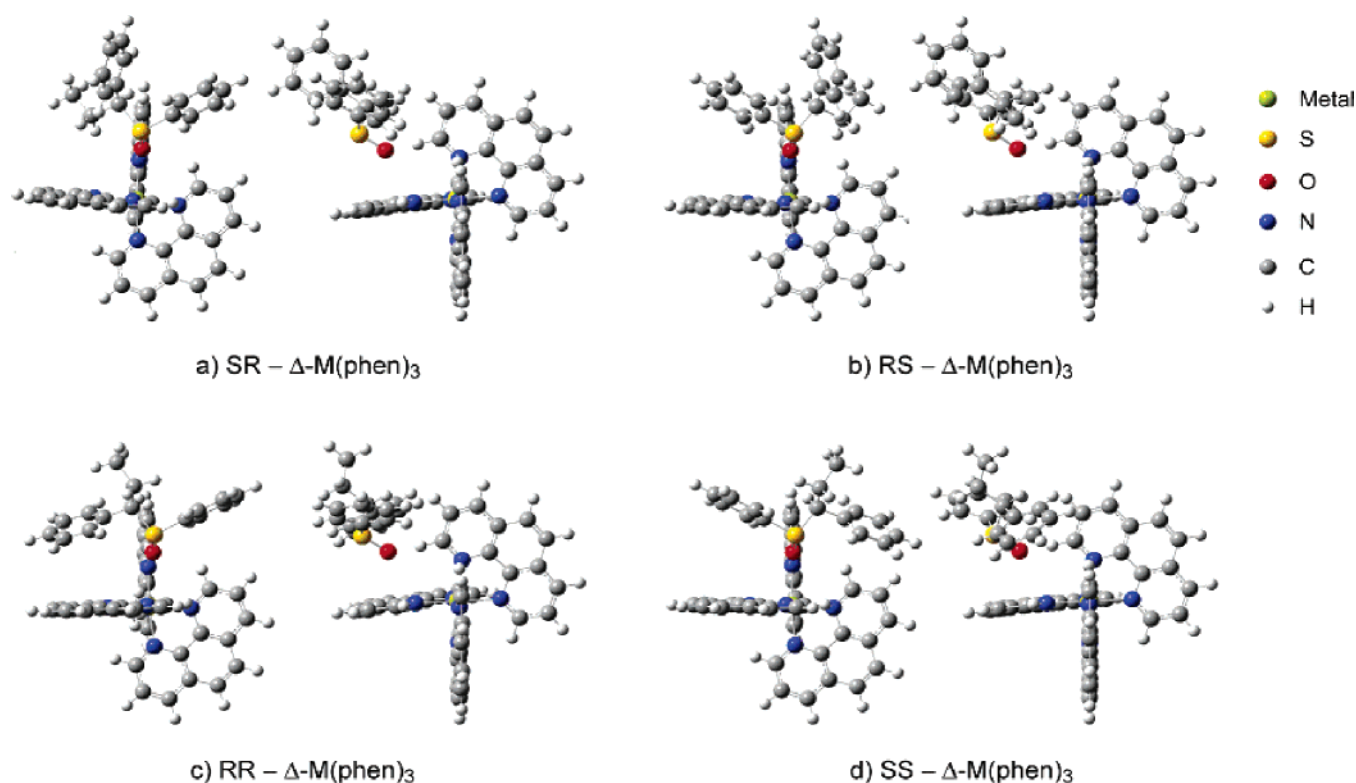


Figure 5. Optimized structures of sulfoxide/ Δ -Ru(II) complex associates: the C_3 association mode.

are summarized in Table 3. Although the calculations were far from the complete simulation of real systems (e.g., no participation of solvents and no tracking along a reaction coordinate), the predicted selectivity focused on the stability of a catalyst (metal complex) and a product (a sulfoxide) seems to give us a valuable view of this problem.

The above results lead us to a view that, in homogeneous reactions, a sulfide approaches along the C_2 direction to reach the most stable state, or the global minimum, while, in heterogeneous reactions, a sulfide approaches along the C_3 direction to reach a state with the local minimum. In the latter case (or the heterogeneous reactions), the system was unable to attain a state with the global minimum energy due to the blockage of the C_2 route. The inhibition of the route along the C_2 direction was thought to be an essential factor in the appearance of enantioselectivity in oxidation of a sulfide (Figures 3 and 4 and Table 3). In supporting this mechanism, the previous XRD results showed that the modified montmorillonite clay was exfoliated to at least a few sheets. Under these situations, an adsorbed Ru(II) complex was mostly on an external surface so that the approach along its C_3 direction was possible (Figure 2).

The theoretical investigation to overcome the experimental difficulty has led us to a model that the association mode of the substrate toward the Ru(II) complex is quite different between the homogeneous and heterogeneous systems (Figures 3 and 4). On the basis of this model, the following experimental approaches are suggested to confirm the proposed reaction mechanisms. The most important features of the proposed associates between a sulfoxide and a Ru(II) complex are that the sulfoxide is located more closely to the Ru(II) complex on a clay surface than in a homogeneous solution. Accordingly, the ethyl group in the sulfoxide, for example, is nearly above one of the phenanthroline ligands on a clay surface, while it is far away from the ligand. These differences would be detected if the chemical shifts due to the ethyl groups in NMR spectra are compared between the homogeneous and heterogeneous systems. In the former system, the usual solution NMR is applicable for an associate of a substrate and a Ru(II) complex, while the solid-state NMR spectroscopy should be applied in the latter system.

The following mechanisms are proposed for the present oxygenation reactions:

- (1) photoexcitation of a Ru(II) complex, $[\text{Ru}(\text{phen})_3]^{2+} + h\nu \rightarrow [\text{Ru}(\text{phen})_3]^{2+*}$;
- (2) generation of a Ru(II) complex by O_2 , $[\text{Ru}(\text{phen})_3]^{2+*} + \text{O}_2 \rightarrow [\text{Ru}(\text{phen})_3]^{3+} + \text{O}_2^-$;
- (3) two-electron oxidation of a sulfide by a Ru(III) complex, $-\text{S}- + 2[\text{Ru}(\text{phen})_3]^{3+} \rightarrow -\text{S}^{2+} + 2[\text{Ru}(\text{phen})_3]^{2+}$; and
- (4) generation of a sulfoxide by reaction with a water molecule, $-\text{S}^{2+} + \text{H}_2\text{O} \rightarrow -\text{SO}- + 2\text{H}^+$.

The above mechanisms were previously postulated on the previous experimental facts that both oxygen and water molecules were necessary for the production of a sulfoxide.^{29b}

Enantioselectivity was improved further by adding another chiral source. About 50% ee was achieved by adding dibenzoyl-D(+)-tartaric acid (Table 2). No appreciable change of the stereoselectivity was observed in case of sodium-D(+)-tartrate and diethyl-L(+)-tartrate. When this fact is viewed on the basis of the above postulate, it seems reasonable to expect that the aryl groups of dibenzoyl-D(+)-tartaric acid may disturb the $\pi-\pi$ interaction between the sulfide and the complex, but the nonaromatic other two may not affect it.

The present results are compared to the previous attempts on the elucidation of asymmetric syntheses with the help of various kinds of molecular associations. TADDOL, a chiral alcohol, achieved a high enantioselectivity, for example, in the Diels–Alder reactions in homogeneous systems.³² In this case, the steric constraint by hydrogen bonding is thought to be responsible for the achievement of enantioselection. In another case, stereoselective reactions on inorganic crystalline surface seemed to be controlled by weak interactions.³³ Such an example is seen in the case of the asymmetric synthesis of pyrimidyl alkanol by use of a powdered chiral crystal of quartz.³⁴ These examples show that even a weak interaction achieves stereoselectivity under the proper steric control. To improve the enantioselectivity of the present systems, a more effective additive should be developed according to the molecular design based on the theoretical simulation concerning the possible association structure of a catalyst and a substrate.

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