Notes

Studies on Enantioselective Epoxidation of Styrene Derivatives with Transition Metal(W, Mo and Re)-Peroxo Complexes

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During the last decades, substantial progress has been made in the development of efficient asymmetric synthetic methods to obtain optically active compounds.[1] Enantioselcetive alkene epoxidation is an important reaction for the synthesis of optically active organic compounds.[2] Particularly, the titanium tartarate catalyzed enantioselective epoxidation of allylic alcohols constitutes one of the most widely applied reactions in asymmetric organic synthesis.[3] Furthermore, a number of highly promising new strategies for enantioselective epoxidation catalysts for unfunctionalized olefins have been developed successfully in the past few years, including salen[4]- and porphyrin[5]-based transition metal complexes. However, there still need to develope new enantioselective alkene epoxidation methods to offer greater synthetic flexibility to chemists.

Transition metal-peroxo species catalyzed alkene epoxidations have been studied for the long times. For example, polyoxo tungstate such as $PW_{12}O_{24}^{3-}$ has been found to catalyze the epoxidation of olefins in the presence of quarternary ammonium salts.[6] Also optically active molybdenum peroxo complexes catalyzed epoxidation of olefins was reported to provide the corresponding epoxides up to 50% chemical yield and 40% enantiomeric excess.[7] Furthemore, transition metal-oxo specie such as methyltrioxorhenium (MTO) has been found to catalyze olefin epoxidations using H_2O_2 as an oxidant.[8] However, there have been few systematic studies on enantioselectivity in transition metal-peroxo species catalyzed alkene epoxidations. Here, to develope novel method for enantioselective alkene epoxidation, we describe optically active transition metal-peroxo complexes catalyzed epoxidation of styrene derivatives.

Tungsten(VI) and molybdeum(VI) peroxo complexes were prepared by following the known procedures.[7] Several epoxidation reactions of styrene derivatives by tungsten(VI) and molybdeum(VI) peroxo complexes (**1**-**4**) in the presence of tBuOOH were conducted. The results are summarized in Table 1.

Data in Table 1 clearly show that tungsten and molybdeum peroxo complexes catalyze enantioselectively alkene epoxidation by tBuOOH. Although, in the case of styrene, chemical yields and enantioselectivities are quite low, metal peroxo complexes (**1**-**4**) were found to catalyze methylstyrene epoxidation to afford the corresponding epoxide in about 40-50 % yield and 30-80% ee. Particularly, tungsten peroxo complex **2** and molybdeum peroxo complex **4** were found to catalyze epoxidation of (E)-methylstyrene to afford the corresponding epoxide in 63% and 81% ee (41% and 49% yields), respectively. In the absence of **2** and **4**, alkenes did not undergo epoxidation. Also, there were significant solvent effects on epoxidations. For example, in CH_2Cl_2 and isooctane, alkenes did not undergo epoxidation in the presence of metal peroxo complexes and tBuOOH.

There are notable trends in data of Table 1. First, while molybdenum peroxo complexes (**3** and **4**) do not induce *cis-trans* isomerization in epoxidations, tungsten peroxo com-

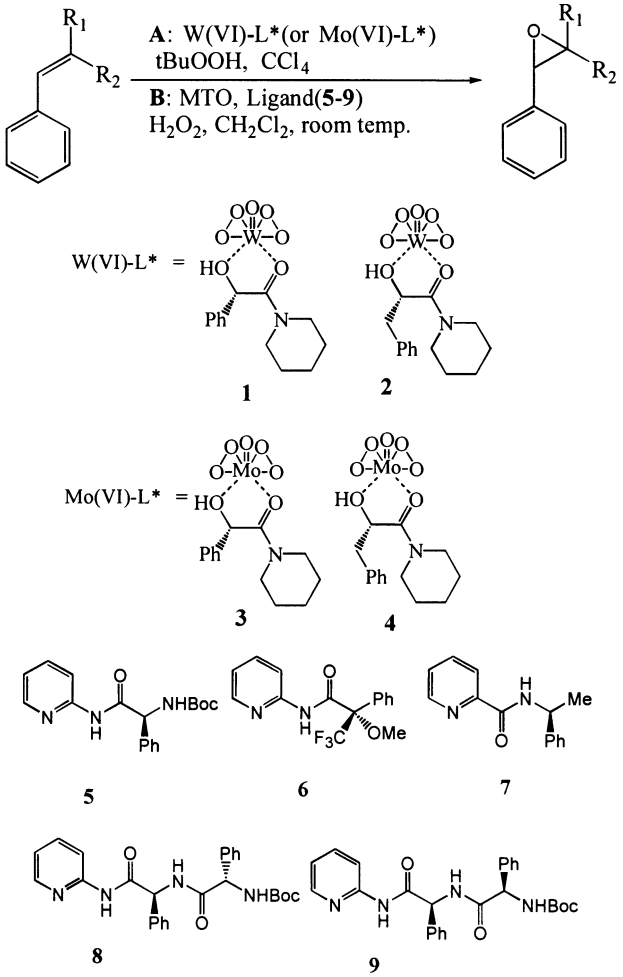

Figure 1. Transition Metal-peroxo Complexes Catalyzed Alkene Epoxidation and Structure of Ligands.

Table 1. Synthesis of Epoxides by Tungsten- and Molybdeum-Peroxo Complex Catalyzed Alkene Epoxidation

Entry	Alkene	Metal peroxo complex	Reaction Temp.	Reaction Time	Yield (%), Enantioselectivity (% ee)[c]
1	PhCH=CH_2	**1**	60 °C	5h	28, 7.0
2	(Z)-PhCH=CHMe	**1**	r.t.	15h	45 (10:1)[a], 30 (75)[b]
3	(E)-PhCH=CHMe	**1**	r.t.	72h	42, 40
4	PhCH=CH_2	**2**	60 °C	5h	29, 4.0
5	(Z)-PhCH=CHMe	**2**	r.t.	15h	45 (4:1)[a], 27 (83)[b]
6	(E)-PhCH=CHMe	**2**	r.t.	72h	41, 63
7	(Z)-PhCH=CHMe	**3**	r.t.	24h	42 (*cis* only)[a], 26
8	(E)-PhCH=CHMe	**3**	r.t.	24h	40, 40
9	(Z)-PhCH=CHMe	**4**	r.t.	72h	41 (*cis* only)[a], 40
10	(E)-PhCH=CHMe	**4**	r.t.	24h	49, 81

[a]ratio of *cis:trans* epoxides, [b]enantioselectivity of the isomerized *trans* epoxides, [c]absolute configuration of major enantiomers are (1*S*) for styrene derived epoxide, (1*S*, 2*R*) for *cis*-methylstyrene and (1*S*, 2*S*) for *trans*-methylstyrene. These are based on the comparison with authentic samples prepared by Jacobsen's method.[4]

plexes (**1** and **2**) provide about 10% and 20% *trans*-epoxide from *cis*-alkenes. Second, *trans*-alkenes are epoxidized more enantioselectively with metal peroxo complexes than *cis*-alkenes.[9] Thus *trans* and *cis* alkene are epoxidized with 40-81 % ee and 26-40 % ee, respectively. Third, molybdenum peroxo complexes (**3** and **4**) epoxidized alkens slightly more efficiently than tungsten peroxo complexes (**1** and **2**) in the terms of chemical yields and enantioselectivities.

Rhenium(VI) peroxo complexes were proposed as a reactive intermediate of pyridine-derived ligand assisted epoxidation of olefins by MTO and H_2O_2.[8] Thus it is reasonably expected that optically active rhenium(VI) peroxo complexes are formed by mixing MTO and the suitable optically pure ligands, and thus catalyzed olefin epoxidation enantioselectively. To explore this possibility, simple pyridine-derived ligands such as 2-picoline, 2-acetylaminopyridine and 2,6-diacetylaminopyridine assisted epoxidation of (Z)-methylstyrene by MTO and H_2O_2 were conducted. As shown entry 9-11 in Table 2, 2-acetylaminopyridine has found to accelerate epoxidation reaction. Based on these results, several pyridine-derived optically pure ligands (**5**-**9**) were prepared and alkene epoxidation reactions of styrene derivatives by MTO, ligands (**5**-**9**) and H_2O_2 were conducted. The results are summarized in Table 2.

Table 2. Synthesis of Epoxides by Ligand (**5**-**9**)-Accelerated Alkene Epoxidation by MTO

Entry	Alkene	Ligand	Yield (%), Enantioselectivity (% ee)
1	(Z)-PhCH=CHMe	**5**	50, 10
2	(E)-PhCH=CHMe	**5**	50, 0
3	(Z)-PhCH=CHMe	**6**	23, 0
4	(E)-PhCH=CHMe	**6**	27, 0
5	(Z)-PhCH=CHMe	**7**	15, 0
6	(E)-PhCH=CHMe	**7**	> 5.0, 0
7	(Z)-PhCH=CHMe	**8**	96.0, 0
8	(Z)-PhCH=CHMe	**9**	22.0, 0
9	(Z)-PhCH=CHMe	2-picoline	> 5.0, 0
10	(Z)-PhCH=CHMe	2-acetylaminopyridine	60.0, 0
11	(Z)-PhCH=CHMe	2,6-diacetylaminopyridine	> 5.0, 0

The results in Table 2 clearly demonstrate that ligands (**5**-**9**) accelerate MTO-catalyzed olefin epoxidations. In MTO-catalyzed olefin epoxidations, the added ligands (**5**-**9**) increased the chemical yields of olefin epoxidation. Without ligands (**5**-**9**), epoxides were not formed. Particularly, ligand **9** has a profound effect in olefin epoxidations to provide the corresponding epoxides of (Z)-methylstyrenes with the 96% yields. It is interesting that the yields of epoxide depend on the structure of ligands employed. However, enantioselectivities of the resulting epoxides were quite low. Until now, enantiomeric excess of styrene-derived epoxides are less than 10% ee. Presumably, in transition state, there is a relatively loose interactions between catalysts and substrates and thus the free-energy difference between the diastereomeric intermediates leading to asymmetric discrimination is not large enough.

Although the exact mechanistic mode of metal peroxo complexes in these alkene epoxidation[10] is not yet elucidated, it is clear that certain metal peroxo complexes such as **1**-**4** catalyze the epoxidation reaction with the moderate enantioselectivities. Further studies to understand the reaction mechanism and to improve enantioselectivities are in progress in this laboratory.

Experimental Section

Synthesis of W(VI) complexes. To a solution of 2.5 mL of 35% H_2O_2 was added 0.25 g of WO_3 (1.08 mmol). After stirring for 24 hr at 45 °C, the precipitates were filtered off. To the resulting filterate was added a solution of 1 equivalent of the corresponding ligand[11] in 1 mL of 1/1=MeOH/ H_2O at room temperature. After stirring for 24 hr at room temperature, the resulting solids were filtered. The residue was washed with ether and H_2O to give W(VI) complexe as an amorphous white solid (40-43%).

1: IR (KBr) 2940, 1599, 1451, 1272, 1070, 958, 879, 703 cm^{-1}; Anal. Calcd: C, 32.39; H, 3.34; N, 2.91. Found: C, 31.99; H, 3.67; N, 2.71.

2: IR (KBr) 2941, 1611, 1594, 1450, 1282, 1093, 956, 877,

751, 700 cm^{-1}; Anal. Calcd: C, 33.89; H, 3.66; N, 2.82. Found: 32.89; H, 3.57; N, 2.54.

Synthesis of Mo(VI) complexes. To a solution of 1 mL of 35% H_2O_2 was added 0.2 g of MoO_3 (1.39 mmol). After stirring for 24 hr at 45 °C, the precipitates were filtered off. To the resulting filterate was added a solution of 1 equivalent of the corresponding ligand in 1 mL of MeOH at room temperature. After stirring for 24 hr at room temperature, the resulting solids were filtered. The residue was washed with ether and H_2O to give Mo(VI) complexe as an amorphous white solid (36-38%).

3: IR (KBr) 3572, 3448, 2953, 1624, 1437, 958, 865, 713 cm^{-1}; Anal. Calcd: C, 39.61; H, 4.09; N, 3.55. Found: C, 38.93; H, 3.95; N, 3.77.

4: IR (KBr) 3449, 2935, 1611, 1450, 1087, 947, 910 cm^{-1}; Anal. Calcd: C, 41.19; H, 4.44; N, 3.43. Found: C, 41.21; H, 4.55; N, 3.25.

Typical procedure for the synthesis of epoxides. Method (A): To a CCl_4 solution of the corresponding olefin (0.1 mmol) was added the correspoding metal peroxo complex (0.01 mmol) under nitrogen atmostphere. The mixture was stirred for 10 min at room temperature, and a decane solution of t-butyl hydroperoxide (0.2 mmol) was added. The mixture was stirred and then added an aqueous $NaHCO_3$ solution. Organic materials were extracted with dichloromethane, and dried over $MgSO_4$. After passing through a short silica gel pad, a portion of solution was injected into GC to check the yield and enantioselectivities of the resulting epoxides.

Method (B): To a CH_2Cl_2 solution of a solid $MeReO_3$ (0.0005 mmol, 0.5 mol %) and the corresponding ligand[12] (0.01 mmol, 10 mol %) was added an aqueous solution of hydrogen peroxide (0.2 mmol). The mixture was stirred for 10 min at room temperature, and the corresponding olefin (0.1 mmol) was added. The mixture was stirred for 12 h at room temperature. An aqueous $NaHCO_3$ solution was then added. Organic materials were extracted with dichloromethane, and dried over $MgSO_4$. After passing through a short silica gel pad, a portion of solution was injected into GC to check the chemical yields and enantiomeric excesses of the corresponding epoxides.

Determination of chemical yields and enantioselectivities of epoxide. Gas chromatographic analysis of reaction products were performed on a Donam System 6200 gas chromatograph with a PEG-5 capillary Column (3 m, 0.25 mm diameter) and J & W γ-cyclodextrin Trifluoroacetyl capillary column (3 m; 0.25 mm diameter) using Hellium as carrier gas.

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11. Ligands for tungsten and molybdeun complexes were prepared by the standard DIC-promoted amide coupling reactions between (R)-Mandelic acid [or (R)-phenyllactic acid] and piperidine in the presence of HOBT. *See:* Bodanszky, M.; Bodanszky, A. *The Practice of Peptide Synthesis*; Springer-Verlag: Berline, 1984.
12. Ligands (**5**-**7**) were prepared by DIC-promoted amide bond formation reactions between 2-aminopyridine and N-Boc-(L)-phenylalanine for **5**, and between picolinic acid and (R)-2-phenylethylamine for **7** in the presence of HOBT, and acylation reaction between 2-aminopyridine and (R)-Mosher's acid chloride in the presence of triethylamine for **6**. Deprotection of Boc group of **5** by TFA, and subsequent DIC-promoted amide bond formation reactions with N-Boc-(R) and (S)-mandelic acid provided ligand **8** and **9**.