단   신

올래핀 에폭시화 반응에 대한 옥사졸린 및 다이아민 리간드효과

朴祥佑 · 尹勝洙*
성균관대학교 자연과학부 화학과
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Effects of Bis-Oxazoline and Diamine Ligands in Olefin Epoxidation

Sang-Woo Park and Seung Soo Yoon*

Department of Chemistry, SungKyunKwan University, Suwon 440-746, Korea
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Epoxides are valuable intermediates in organic synthesis. Thus many efficient synthetic methods for epoxides have been developed.[1] Among those are catalytic olefin epoxidations by transition metal complexes.[2] Particularly, the titanium tartarate catalyzed epoxidation of allylic alcohols constitutes one of the most widely applied reactions in organic synthesis.[3] Furthermore, a number of highly promising new strategies for epoxidation catalysts have been developed successfully in the past few years, including salen[4]- and porphyrin[5]-based alkene epoxidation catalysts.

Metal-oxo species such as methyltrioxorhenium (MTO) and bis (acetylaceto) dioxomolybdenium (BADO) catalyzed olefin epoxidations have been studied for the long times. Monodentate nitrogen ligand such as pyridine and tertiary amines were found to accelerate MTO-catalyzed olefin epoxidation by H_2O_2.[6] Also, a variety of ligands including pyridine, bipyridine, α-hydroxy acid derivatives and simple aliphatic amine derivatives have been found to accelerate BADO-catalyzed olefin epoxidation by $tBuO_2H$.[7] However, there have been few systematic studies on effects of bidentate nitrogen ligand in these reactions. Here, to develope novel method for olefin epoxidation and expand the scope of alkene epoxidation catalysis, we describe novel bidentate nitrogen ligand-accelerated mode for methyltrioxorhenium (MTO)- and bis(acetylaceto) dioxomolybdenium (BADO)-catalyzed olefin epoxidation.

Novel bis-oxazoline ligand **3** was prepared as shown in *Scheme* 1.[8] An amide formation reaction of N-Boc-

(L)-aspartic acid dimethyl ester and (R)-phenylglycinol in the presence of NaCN provided bis amide of amino alcohol. Activation of hydroxy groups by tosylation and the subsequent intramolecular oxazoline formation reaction in the presence of DMAP provided novel bis-oxazoline ligand **3** with 19% yield.

Several olefin epoxidation reactions were conducted and the results are summarized in *Table* 1.

The results in *Table* 1 clearly demonstrate that bidentate nitrogen ligands accelerate greatly MTO- and BADO-
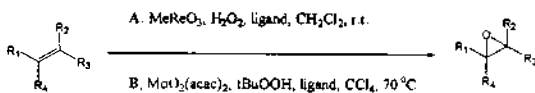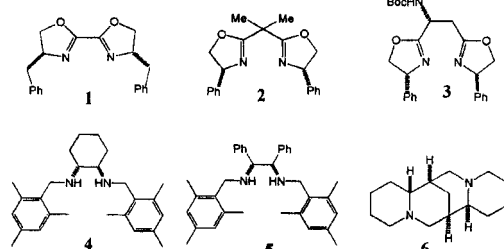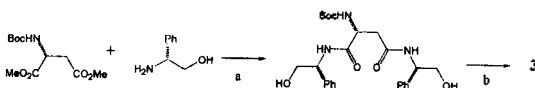

Fig. 1. Metal-oxide catalyzed Olefin Epoxidation and Structure of Ligands.

Scheme 1. Synthesis of Novel bis-oxazoline ligand **3**. (a) NaCN, MeOH, 45 °C. (b) TsCl, Et₃N in CH₂Cl₂ then DMAP.

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Table 1. Synthesis of epoxides by MTO- and BADO-catalyzed reactions in the presence of ligands (1-6)[a].

Entry	Olefin	yield (%)[c]					
		1	2	3	4	5	6
1[a]	PhCH=CH₂	89	80	87	NR[d]	NR	NR
2[a]	(Z)-PhCH=CHMe	21	98	97	NR	NR	NR
3[a]	(E)-PhCH=CHMe	12	20	95	NR	NR	NR
4[a]	(E)-PhCH=CHPh	32[e]	25[e]	50[e]	NR	NR	NR
5[a]	Vinyl cyclohexane			51			
6[b]	PhCH=CH₂	NR	NR	NR	94	65	NR
7[b]	(Z)-PhCH=CHMe	NR	NR	NR	93	55	NR
8[b]	(E)-PhCH=CHMe	NR	NR	NR	97	50	NR
9[b]	(E)-PhCH=CHPh	NR	NR	NR	50[e]	45[e]	NR
10[b]	Vinyl cyclohexane				53		

a: Method A, b: Method B, c: determined by GC except stilbene oxide, d: less than 5% yield, e: isolated yields.

catalyzed olefin epoxidations. In MTO-catalyzed olefin epoxidations, the added bis-oxazolines, 1-3 increased greatly the chemical yields of olefin epoxidation. Without bis-oxazolines, epoxides were not formed. Particularly, bis-oxazoline 3 has a profound effect in olefin epoxidations to provide the corresponding epoxide of aliphatic olefins as well as aromatic olefins with the 50-97% yields. This bis-oxazoline 3 increased not only the chemical yields of epoxides, but also the epoxidation rates greatly. For example, in the presence of 3, the olefin epoxidation completed within 2 hr. In BADO-catalyzed olefin epoxidations, the added diamines 4 and 5 play an important role in olefin epoxidation while bis-oxazolines have no effects in these reactions. Without diamine ligands, aliphatic olefins did not undergo epoxidations, whereas aromatic olefins gave the other oxidation products in large amounts. Particularly, diamine 4 has a profound effect in olefin epoxidations to provide the corresponding epoxide of aliphatic olefins as well as aromatic olefins with the 50~98% yields. It is interesting that not only certain class of ligands accelerated the specific metal-catalyzed olefin epoxidation, but also the yields of epoxide depended on the structure of ligands employed.

Although the exact mechanistic mode of the added ligands in these olefin epoxidation is not yet elucidated, it is clear that these ligands assist greatly the epoxidation reaction in terms of chemical yields and reaction rates. Furthermore, these ligands have the well defined chirality. It is reasoned that chiral centers of the ligands held close to the metal reaction center might assist chiral recognition of substrates such as simple olefins. Thus these
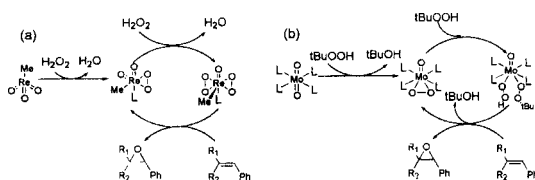
Scheme 2. The proposed mechanism of (a) MTO-catalyzed epoxidation and (b) BADO-catalyzed epoxidation.[6,7]

bidentate nitrogen ligands assisted-epoxidation might be the novel ligand-assisted, asymmetric epoxidation catalysis[10] for simple unfunctionalized olefins. To test this, enantioselectivities of the resulting epoxides were investigated using chiral gas chromatography. Until now, enantiomeric excess of styrene-derived epoxides are less than 10% ee. Further studies to understand the reaction mechanism and to improve enantioselectivities are in progress in this laboratory.

EXPERIMENTAL

Synthesis of 3. To a solution of 2.61 g of N-Boc-(L)-aspartic acid dimethyl ester (10 mmol) and 2.70 g of (S)-phenylglycinol (20 mmol) in 50 ml of MeOH was added 0.25 g of NaCN (5 mmol) at room temperature. The reaction mixture was kept stirring for 48 hr at 45°C. After the removal of all volitiles under reduced pressure, the crude mixture was washed with water.

To a solution of the resulting crude bis-amide in 30 ml of CH₂Cl₂ were added 4.2 g of TsCl (20 mmol), 3.42 ml of Et₃N (30 mmol) and 0.25 g of DMAP (2 mmol) at 0 °C. After stirring for 24 hr at room temperature, all volatiles were removed at reduced pressure. The residue

was purified by flash chromatography on silica gel using ethyl acetate : hexane=1:1 to give **3** as an amorphous white solid (0.84 g, 19.3 %): ^{1}H NMR (CDCl$_3$) δ 1.46 (s, 9H), 2.98 (m, 2H), 4.11 (m, 2H), 4.64 (m, 2H), 4.92 (dd, 2H, J=8.0, 4.5 Hz), 5.18 (m, 2H), 5.96 (d, 1H, J=8.5 Hz), 7.28 (m, 10H); ^{13}C NMR (CDCl$_3$) δ 22.24, 47.69, 52.21, 56.45, 66.22, 66.50, 75.51, 76.45, 127.31, 127.40, 127.46, 127.68, 129.34, 129.38, 129.49, 129.88, 155.8, 165.90, 168.09; IR (KBr) 2890, 1705, 1661, 1533, 1518, 1368, 1246, 1167 cm^{-1}; MS(FAB) m/z= 436(MH$^+$).

Typical procedure for the synthesis of epoxides. (1) Method A: To a CH$_2$Cl$_2$ solution of a solid MeReO$_3$ (0.0005 mmol, 0.5 mol %) and the corresponding ligand (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. A solid 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 yield except (E)-stilbene oxide. In the case of (E)-stilbene epoxidation, (E)-stilbene oxide was purified by column chromatography using silica gel and the yield was determined.

(2) Method B: Under nitrogen atmostphere, to a CCl$_4$ solution of the corresponding olefin (0.1 mmol) and the corresponding ligand (0.001 mmol) was added a solid MoO$_2$(acac)$_2$ (0.001 mmol). The mixture was stirred for 10 min at room temperature, and a decane solution of t-butyl hydroperoxide (0.5 mmol) was added. The mixture was heated to 70°C with stirring for 1 h, and cooled to 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 yield except (E)-stilbene

oxide. In the case of (E)-stilbene epoxidation, (E)-stilbene oxide was purified by column chromatography using silica gel and the yield was determined.

Determination of Yields and Enantioselectivities of epoxide. Gas chromatographic analysis of reaction products were performed on a Domam 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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