

## Catalytic Asymmetric Oxidation of Sulfides to Sulfoxides Using *R*-(+)-Binaphthol

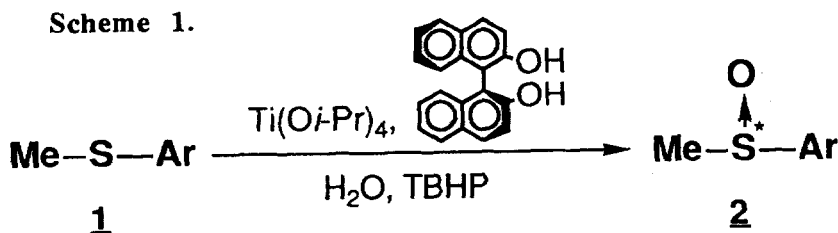
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**Abstract:** An asymmetric oxidation system using *R*-(+)-binaphthol as a chiral auxiliary catalyzes the oxidation of sulfides to chiral sulfoxides in good enantiomeric excess (up to 73% e.e.) and in a high chemical yield.

Although the chiral binaphthol derivatives have been used as an effective chiral auxiliary in many asymmetric reactions because of its extraordinary chiral recognition properties,<sup>1</sup> they were almost uneffective ligands for Sharpless epoxidation.<sup>2</sup> It has been described that the ester or amide oxygens were required at both ends of a diol ligand for a good enantioselectivity to be obtained in the epoxidation. Recently, however, several successful reports using binaphthol were published on catalytic asymmetric C-C bond forming reactions such as aldol,<sup>1a,3</sup> Diels-Alder<sup>1a,4</sup>, and ene reactions<sup>5</sup>. These success prompted us to investigate the possibility of binaphthol as a chiral ligand for some asymmetric oxidations. Eventually we found that the oxidation of sulfides to sulfoxides proceeded catalytically and often more enantioselectively than Kagan's catalytic method<sup>6</sup> using diethyl tartrate as a chiral source.

A typical procedure is as follows. To a solution of *R*-(+)-binaphthol (0.10 mmol) in 2 ml dry toluene were added dropwise  $\text{Ti}(\text{O}i\text{-Pr})_4$  (0.05 mmol) and  $\text{H}_2\text{O}$  (1.0 mmol) at room temperature under a nitrogen atmosphere. After stirring for 1 h, methyl *p*-tolyl sulfide (0.5 mmol) was added and then the mixture was cooled



**1** :  $\text{Ti}(\text{O}i\text{-Pr})_4$  : *R*-(+)-binaphthol :  $\text{H}_2\text{O}$  : TBHP = 1 : 0.1 : 0.2 : 2 : 2

to  $-20^{\circ}\text{C}$ . A solution of 5.4 N *tert*-butyl hydroperoxide (TBHP) in toluene (1.0 mmol) was added and the mixture was stirred for 45 h with GLC monitoring. The resulting methyl *p*-tolyl sulfoxide (88% yield) was isolated by column chromatography (silica gel, ether) and the e.e. (73%) was determined by HPLC using Daicel Chiralcel OB column, its configuration being revealed to be *R*<sup>7</sup>. Although optimization of binaphthol / Ti ratio for this catalytic reaction was not carried out in detail, the change of the ratio of 2/1 to 1/1 and 4/1, all other conditions maintained, resulted in a decrease of e.e. to 59 and 58 %, respectively. The reaction temperature did not affect so much the e.e. value as well as the chemical yield in the range of  $-25 \sim 0^{\circ}\text{C}$ .

On the other hand, the amount of water added had a large effect upon the e.e. value. Thus, the correlation between the amount of water added and e.e. value of the obtained sulfoxide is shown in the Fig. 1. As shown in the figure, a high e.e. was obtained when 0.5 - 3.0 eq. of  $\text{H}_2\text{O}$  to the sulfide was added, while a clear decrease of e.e. was observed when less than 0.5 eq. or more than 3.0 eq. of  $\text{H}_2\text{O}$  was used. In the absence of added  $\text{H}_2\text{O}$  only low e.e. was obtained.

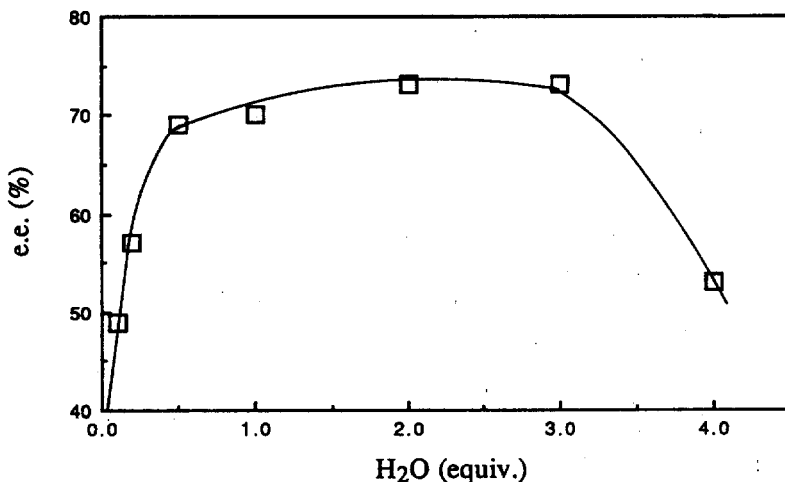


Fig. 1. Effect of the amount of added  $\text{H}_2\text{O}$  upon the e.e. value in the catalytic asymmetric oxidation of methyl *p*-tolyl sulfide

Representative results of oxidation of several sulfides under various reaction conditions were summarized in the Table 1. The solvent showed a marked effect upon both the e.e. value and the chemical yield. The use of either aromatic solvents or  $\text{CCl}_4$  gave a high e.e. value and a high yield, the toluene being revealed to be the solvent of choice for this oxidation. A low e.e. value and a high yield were obtained in several chlorinated solvent other than  $\text{CCl}_4$ , while a high e.e. value and a low yield were observed in ether solvents. It is worth noting that  $\text{CH}_2\text{Cl}_2$ , which is the optimum solvent for Sharpless type reactions such as epoxidation<sup>2</sup> and sulfide oxidation<sup>8</sup>, was not suitable for this catalytic reaction. All the sulfoxides obtained had *R* configuration, but the configuration of the obtained methyl 2-naphthyl sulfoxide was not determined.

Table 1. Catalytic Asymmetric Oxidation of Sulfides to Sulfoxides<sup>a</sup>

Run	Ar	Solvent	React.time (h)	Yield <sup>b</sup> (%)	e.e. <sup>c</sup> (config.) <sup>d</sup> (%)
1	<i>p</i> -tolyl	toluene	4.5	8.8	73 ( <i>R</i> )
2 <sup>e</sup>	<i>p</i> -tolyl	toluene	4.4	9.4	70 ( <i>R</i> )
3 <sup>f</sup>	<i>p</i> -tolyl	toluene	2.0	7.7	59 ( <i>R</i> )
4 <sup>g</sup>	<i>p</i> -tolyl	toluene	4.4	8.4	58 ( <i>R</i> )
5	<i>p</i> -tolyl	CH <sub>2</sub> Cl <sub>2</sub>	1.9	8.4	16 ( <i>R</i> )
6	<i>p</i> -tolyl	CHCl <sub>3</sub>	1.9	7.4	23 ( <i>R</i> )
7	<i>p</i> -tolyl	CCl <sub>4</sub>	2.8	7.6	67 ( <i>R</i> )
8 <sup>e</sup>	<i>p</i> -tolyl	CCl <sub>4</sub>	4.9	7.8	65 ( <i>R</i> )
9	<i>p</i> -tolyl	ClCH <sub>2</sub> CH <sub>2</sub> Cl	2.8	8.6	25 ( <i>R</i> )
10	<i>p</i> -tolyl	THF	7.1	4.6	72 ( <i>R</i> )
11	<i>p</i> -tolyl	diethyl ether	7.1	3.2	57 ( <i>R</i> )
12	<i>p</i> -tolyl	<i>o</i> -xylene	4.8	8.8	61 ( <i>R</i> )
13	<i>p</i> -tolyl	cumene	4.8	8.6	57 ( <i>R</i> )
14	Ph	toluene	4.8	8.6	63 ( <i>R</i> )
15	Ph	CCl <sub>4</sub>	4.8	8.0	65 ( <i>R</i> )
16	2-naphthyl	toluene	6.6	6.7	5.6
17	2-naphthyl	CCl <sub>4</sub>	6.6	7.3	5.1

<sup>a</sup> Sulfide (0.5 mmol), Ti(O*i*-Pr)<sub>4</sub> (0.05 mmol), (*R*)-binaphthol (0.10 mmol), H<sub>2</sub>O (1.0 mmol), TBHP (1.0 mmol) at -20°C unless otherwise mentioned.

<sup>b</sup> Isolated yield. <sup>c</sup> Determined by HPLC using a Daicel Chiralcel OB column.

<sup>d</sup> Determined by optical rotation. <sup>e</sup> 1 Equiv. of H<sub>2</sub>O (0.5 mmol) was added instead of 2 equiv. <sup>f</sup> (*R*)-Binaphthol (0.05 mmol); (*R*)-binaphthol/Ti(O*i*-Pr)<sub>4</sub> =1/1. <sup>g</sup> (*R*)-Binaphthol (0.20 mmol); (*R*)-binaphthol/Ti(O*i*-Pr)<sub>4</sub>=4/1.

Although the exact nature of asymmetric catalysis of this reaction is not yet clear, we presume the presence of a mononuclear titanium with two binaphthol ligands as a catalyst, which is different from a binuclear titanium complex proposed in Sharpless epoxidation<sup>2</sup> using diethyltartrate as a chiral ligand, because the higher e.e. values were obtained when binaphthol / Ti = 2/1. The complex might be present in a more rigid state in non-polar solvents such as CCl<sub>4</sub> and toluene than in polar ones, leading to a high e.e. value of the oxidation product. Ethers might fill the vacant coordination site of titanium and deactivate the catalyst, thus longer reaction time was needed and the yield of the sulfoxide was low. As to the role of water added we do not have any reasonable explanation yet, although it is quite plausible that water affects the structure of a titanium complex and the rate of its formation.

As a summary we found that the chiral binaphthol works as an effective chiral ligand, which does not need any carbonyl oxygens, in this catalytic oxidation reaction of sulfides to sulfoxides. We are now applying this catalytic system to other oxidation reactions, particularly, asymmetric selenoxide elimination<sup>9</sup> developed by us.

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