

# Asymmetric ring opening of *meso*-epoxides catalyzed by the chiral phosphine oxide BINAPO

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**Abstract**—The enantioselective ring opening of *meso*-epoxides with tetrachlorosilane in the presence of diisopropylethylamine using chiral phosphine oxide BINAPO as the catalyst affords the corresponding chlorohydrins in high enantioselectivities of up to 90% ee. © 2005 Elsevier Ltd. All rights reserved.

## 1. Introduction

Metal-free catalytic reactions, organocatalysis, have recently attracted considerable attention because of their environmentally benign nature.<sup>1</sup> Although phosphine oxides have strong electron-donor properties and form complexes with various acceptors,<sup>2</sup> less attention has been paid to chiral phosphine oxides<sup>3</sup> in the field of asymmetric synthesis except for their utility as synthetic intermediates in the preparation of chiral phosphine ligands. Quite recently, Kobayashi et al. reported on the enantioselective allylation of imines promoted by the chiral phosphine oxide BINAPO, which afforded the corresponding homoallyl amines in high enantioselectivity.<sup>4</sup> We reported on the enantioselective allylation of aldehydes promoted by substoichiometric amounts of BINAPO, which represented the first example of the use of a chiral phosphine oxide as a catalyst.<sup>5</sup> As part of our ongoing program directed at the development of asymmetric organocatalysis,<sup>6</sup> we herein report on an enantioselective ring opening reaction of *meso*-epoxides catalyzed by BINAPO.

The asymmetric ring opening of *meso*-epoxides<sup>7,8</sup> is a versatile method for preparing optically active chlorohydrins. Among the various catalysts reported for this type of reaction, Lewis bases such as phosphoramides<sup>9</sup> and *N*-oxides<sup>6d,10</sup> have been reported to be effective

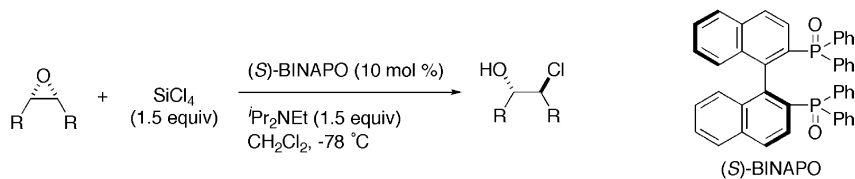
catalysts for the ring opening of epoxides with tetrachlorosilane.

## 2. Results and discussion

We initially investigated the ring opening of *meso*-stilbene oxide with a solution of tetrachlorosilane in dichloromethane using 10 mol % BINAPO at  $-78$  °C. The reaction proceeded smoothly to afford the corresponding chlorohydrin in high yield. However, the enantioselectivity of the reaction was not satisfactory (95% yield, 59% ee). After considerable screening of the reaction conditions, we found that the addition of diisopropylethylamine caused a dramatic increase in enantioselectivity (94% yield, 90% ee).<sup>11</sup> Sterically less hindered amines gave products in less selectivity (triethylamine: 82% ee, pyridine: 11% ee), which may be due to the coordination of nitrogen to silicon to provide a racemic product in part.<sup>12–15</sup>

Some selected data for the asymmetric ring opening of epoxides are summarized in Table 1. Although the epoxides derived from butenediol, pyrrolidine and dihydrofuran gave low selectivities (entries 2–4), epoxides derived from six- and eight-membered cycloalkenes gave moderate enantioselectivities (entries 5 and 6), the highest selectivities reported for the asymmetric synthesis of cyclic chlorohydrins. The present reaction represents the first example of the use of a chiral phosphine oxide as a catalyst in the asymmetric opening of epoxides.

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**Table 1.** Asymmetric ring opening of *meso*-epoxide catalyzed by chiral phosphine oxide (*S*)-BINAPO

Entry	Epoxide	Time (h)	Yield <sup>a</sup> (%)	ee <sup>b</sup> (%) (confgn) <sup>c</sup>	$[\alpha]_D^{25}$
1	R = Ph	4	94	90 ( <i>S,S</i> )	+19.7 ( <i>c</i> 1.0, EtOH)
2	R = CH <sub>2</sub> OCH <sub>2</sub> Ph	12	97	31 ( <i>S,S</i> )	+1.0 ( <i>c</i> 1.0, EtOH)
3	R, R = -CH <sub>2</sub> NTsCH <sub>2</sub> -	1	95	34	+1.2 ( <i>c</i> 1.0, CHCl <sub>3</sub> )
4 <sup>d</sup>	R, R = -CH <sub>2</sub> OCH <sub>2</sub> -	1	73	39	+43.3 ( <i>c</i> 1.3, CHCl <sub>3</sub> )
5 <sup>d</sup>	R, R = -(CH <sub>2</sub> ) <sub>4</sub> -	1	81	71	+67.3 ( <i>c</i> 1.0, CHCl <sub>3</sub> )
6 <sup>d</sup>	R, R = -(CH <sub>2</sub> ) <sub>6</sub> -	72	81	50	+42.9 ( <i>c</i> 1.0, CHCl <sub>3</sub> )

<sup>a</sup> Isolated yields.<sup>b</sup> Determined by chiral HPLC analysis.<sup>c</sup> Assigned by comparison to the literature values<sup>9</sup> of optical rotations.<sup>d</sup> Isolated as the 4-nitrobenzoate.

In summary, the effectiveness of BINAPO as a catalyst for the enantioselective ring opening of *meso*-epoxide with tetrachlorosilane has been demonstrated. Studies on the design of chiral phosphine oxides to further enhance enantioselectivity are currently in progress.

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- Typical procedure: To a stirred solution of (*S*)-BINAPO (16.6 mg, 10 mol %), *cis*-stilbene oxide (50 mg) and diisopropylethylamine (0.065 mL, 1.5 equiv) in dichloromethane (1 mL) was added 1M tetrachlorosilane in dichloromethane (0.38 mL, 1.5 equiv) at –78 °C under an argon atmosphere. The mixture was stirred at the same temperature for 4 h. After quenching the reaction with aqueous satd sodium bicarbonate (2 mL), the aqueous layer was treated with aqueous potassium fluoride/potassium dihydrogenphosphate and extracted with ethyl acetate (30 mL × 3). The organic layer was washed with brine (20 mL), dried over sodium sulfate and concentrated. The crude material was purified by column chromatography (silica gel, 5 g, hexane–AcOEt = 10:1) to give 2-chloro-1,2-diphenylethanol (56 mg, 94%). HPLC (AD-H, hexane–2-propanol = 29:1): *t*<sub>R</sub> (1*R*,2*R*)-(–)-isomer, 22.0 min (5%); (1*S*,2*S*)-(+)-isomer, 24.0 min (95%).
- 1.5 equiv of diisopropylethylamine was sufficient for achieving optimum chemical and optical yields. It is reasonable to assume that diisopropylethylamine traps the hydrogen chloride produced through the adventitious hydrolysis of tetrachlorosilane which reacts directly with the epoxide to form a chlorohydrin in a nonstereoselective process.
- The use of trichloromethylsilane as a chloride ion source gave the racemic chlorohydrin in 84% yield, while chlorotrimethylsilane gave the product in 13% yield.
- Dichloromethane was found to be the solvent of choice (propionitrile: 83% yield, 74% ee; toluene: 70% yield, 25% ee; THF: 56% yield, 90% ee). A reaction in THF gave 2-(4-chlorobutoxy)-1,2-diphenylethanol in 29% yield as a by-product.
- Derivatives of BINAPO gave lower selectivities than BINAPO itself (*p*-Tol-BINAPO: 96% yield, 82% ee; *m*-Xyl-BINAPO: 98% yield, 30% ee).