Supporting Information for

Liquid-Phase Synthesis of Chiral Tartrate Ligand Library for Enantioselective Sharpless Epoxidation of Allylic Alcohols

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The supporting information contains:

1. General procedures.
3. The preparation of anhydrous tert-butyl hydroperoxide (TBHP) in isoctane and molarity determination of anhydrous TBHP/isoctane.
4. General determination methods of ee values: (1) General preparation and GC analysis of the derived acetates. (2) General preparation and $^1$H NMR analysis of Mosher esters. (3) General preparation and $^1$H NMR shift analysis of the derived acetates with Eu(hfc)$_3$.
5. Absolute configuration.
7. General procedure for the catalytic asymmetric epoxidation.
8. $^1$H NMR of ligands L1-L15.
9. $^1$H NMR and $^{13}$C NMR of the epoxide products E1-E7.
General Procedures. $^1$H NMR spectra were recorded on a Bruker DRX300 at 25 °C. Chemical shifts were expressed in ppm with TMS as an internal standard ($\delta = 0$ ppm) for $^1$H NMR. Optical rotations were measured with a HORIBA SEPA-200 automatic polarimeter. IR spectra were obtained on a Shimazu IR-435 spectrometer. Melting points were determined on a Yanagimoto apparatus and were uncorrected. Gas chromatographic analyses were conducted on a Model SP-6800A Gas Chromatograph. All the experiments that were sensitive to moisture were carried out under nitrogen atmosphere. Commercial reagents were used as received without further purification unless otherwise noted.

Material. Pellet, powdered 3 Å molecular sieves (MS) and powered 4 Å molecular sieves (MS) were activated by heating in a vacuum oven at 350 °C and 0.1 mmHg pressure for 5 h. Dichloro methane was distilled over the CaH₂.

The Preparation of Anhydrous tert-Butyl Hydroperoxide (TBHP) in Isooctane and Molarity Determination of Anhydrous TBHP/isooctane. The preparation and molarity determination of anhydrous TBHP/isooctane were carried out according to the procedure described by Sharpless et al.¹² The TBHP is dangerous, and please see the notes about the treatment of TBHP shown by Sharpless et al.¹²

General Preparation and GC Analysis of the Derived Acetates. This method was suitable for the analysis of (2S, 3S-trans)-3-propyloxiranemethanol, (2S, 3S-trans)-3-methyloxiranemethanol and (2S, 3R-cis)-3-ethylxiranemethanol.

The enantiomers of the three alcohols could not directly be resolved on the self-prepared chiral gas capillary columns, but the acetates of all three alcohols could be well resolved. Therefore all three...
alcohols were derived as their acetate using acetyl chloride before test. A mixture of 18 mg (0.15 mmol, 1.0 equiv) of 4-dimethylaminopyridine (DMAP) and 0.10 mL of triethylamine in 0.5 mL of dichloromethane was treated with 0.15 mmol of the epoxide product. Immediately, 11.5 μL of acetyl chloride was added. The solution became warm and turned orange. Reactions were generally complete in a few minutes and some solid appeared. In order to remove the impurities, the reaction mixture was concentrated and the residue was passed through a pad of silica gel using ethyl acetate-hexane (1:5) as the eluent.

The acetates of (2S, 3S-trans)-3-propyloxiranemethanol and (2S, 3S-trans)-3-methylxiranemethanol were analyzed on the chiral capillary column whose chiral stationary phase was 2,6-di-O-benzyl-3-O-heptanonyl-β-cyclodextrin. The acetate of (2S, 3R-cis)-3-ethylxiranemethanol was analyzed on the chiral capillary column whose chiral stationary phase was 2,3-di-O-benzyl-6-O-octanoyl-β-cyclodextrin.

The acetates that had been prepared by the above-mentioned procedure were dissolved in 0.5 mL of acetone. 0.5 μL of the acetone solution was used when the GC analyses of acetates were carried out.

**General Preparation and ^1^H NMR Analysis of Mosher Esters.** This method was used for the determination of the enantiomeric excess (ee%) of (2S, 3S-trans)-3-heptyloxiranemethanol, (2S, 3S-trans)-3-phenyloxiranemethanol, (2S, 3R-cis)-3-propyloxiranemethanol, and (2S, 3R-cis)-3-ethylxiranemethanol. The detailed procedure described by Sharpless et al.\(^{12}\) was followed to determine the ee values of those epoxide products.

**General Preparation and ^1^H NMR Shift Analysis of the Derived Acetates with Eu(hfc)\(_3\).** This method was suitable for (2S, 3S-trans)-3-methyl-3-(4-methyl-3-pentenyl)xiranemethanol, and the
detailed procedure is the same as the procedure developed by Sharpless et al.\textsuperscript{12}

**Absolute Configuration.** Absolute configuration was determined by comparison of the observed rotation by polarimetry with the literature value.

**General Workup Procedure.**

The workup procedure developed by Sharpless et al\textsuperscript{12} for the epoxidation of allylic alcohols was followed with modifications. The epoxy alcohol was isolated in all of the epoxidation reactions using one of the following two workups (A and B). After the epoxidation reaction completed, the CH\textsubscript{2}Cl\textsubscript{2} was removed by distillation under reduced pressure at 25 °C, then added diethyl ether to the resulting mixture to precipitate the tartrate at −10 °C - −20 °C under vigorous stirring conditions, and filtered under reduced pressure to obtain white solid with slight yellow which was tartrate ligand, the recovery of ligand >98%. The filtrate was treated with two different procedures. According to the workup method of the filtrates, the entire workup procedure was divided into Workup A and Workup B:

**Workup A:**

A mixture of 8.25 g (0.03 mol) of ferrous sulfate heptahydrate and 2.5 g (0.0015 mol) of tartaric acid in 25 mL of distilled water was cooled to about 0 °C. The filtrate was allowed to warm to about 0 °C, and then was slowly poured into a beaker containing the precooled stirring ferrous sulfate solution. During or after the addition process, external cooling was not necessary. The two-phase mixture was stirred for 20 min and then transferred into a separatory funnel. The two phases were separated and the aqueous phase was extracted with three 20 mL of diethyl ether. The combined organic phases were treated with 0.3 mL of a precooled (0 °C) solution of 30% NaOH (w/v) in saturated brine. The mixture was stirred for 20 min, and then filtered under reduced pressure. The filtrate was dried on anhydrous
sodium sulfate, filtered, and concentrated to give the crude product.

The preparation of 30% NaOH in saturated brine: the solution was obtained by mixing 0.5 g of NaCl, 3 g of NaOH and 9 mL of distilled water.

**Workup B:**

0.3 mL of a precooled (0 °C) solution of 30% NaOH (w/v) in saturated brine was added into the filtrate whose temperature had increased to 0 °C and then stirred for 20 min. 5 g of anhydrous sodium sulfate was added to the mixture and continued to stir for 10 min, and then the mixture was filtered under reduced pressure. The filtrate was dried on anhydrous sodium sulfate, filtered and concentrated. The equal volume of toluene was added into the concentrated mixture. The TBHP was removed by azeotropic distillation with toluene under reduced pressure, and the residual toluene was removed under the same condition to give the crude product.

**General Procedure for the Catalytic Asymmetric Epoxidation**

The procedure developed by Sharpless et al.\(^\text{12}\) for the epoxidation of allylic alcohols was followed with small modifications. To an oven-dried 250 mL of four-necked flask equipped with a magnetic stirrer, a thermometer, a pressure equalizing addition funnel, nitrogen inlet and bubbler, was added 4 Å powered, activated molecular sieves (MS) and dried CH₂Cl₂. The mixture was cooled to −20 °C. Tartrate ligand and Ti(O-i-Pr)₄ were added sequentially with stirring. The reaction mixture was stirred at −20 °C as TBHP solution in isoctane was added through the addition funnel at moderate rate (about 5 min). The resulting mixture was stirred at −20 °C for 1-2 h. The allylic alcohol dissolved in dried CH₂Cl₂ was added dropwise through the same funnel in 15 min at about −20 °C. The mixture was stirred for additional 8 h or 24 h. After the epoxidation reaction completed, the CH₂Cl₂ was
removed by distillation under reduced pressure at 25 °C, then diethyl ether was added to the resulting mixture to precipitate the tartrate at −10 °C - −20 °C under vigorous stirring conditions. The mixture was filtered under reduced pressure to give white solid with slight yellow which was tartrate ligand, and the recovery of ligand was >98%. The filtrate was treated by Workup A or Workup B to afford the crude product.