CHAPTER II

EXPERIMENTAL

2.1 General procedure

The FT-IR spectra were recorded on a Nicolet fourier transform infrared spectrophotometer model Impact 410. Solid samples were incorporated to potassium bromide to form a pellet. The ^{1}H and ^{13}C NMR spectra were obtained in deuterated chloroform ($CDCl_3$) solution, or deuterated dimethylsulfoxide (DMSO-d_6) with tetramethylsilane (TMS) as an internal reference on the Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 NMR spectrometer which operated at 399.84 MHz for ^{1}H and 100.54 MHz for ^{13}C nuclei. The chemical shifts (δ) are assigned by comparison with residue solvent protons.

Chromatography: Thin layer chromatography (TLC) was carried out on aluminium sheets precoated with silica gel (Merck's, Kieselgel 60 PF_{254}). Column chromatography was performed on silica gel (Merck's, Kieselgel 60 G). Gas chromatography analysis was carried out on a Shimadzu gas chromatograph GC-9A instrument equipped with flame ionization detector with N_2 as a carrier gas. The column used for gas chromatography was carbowax 20 m. Chiral gas chromatography analysis was carried out on HP 6890 gas chromatograph. The column used was 10% BSiMe in PS 255, 15.029 m.

Atomic absorption analysis was carried out on a Perkin Elmer AAnalyst 100 atomic absorption spectrometer.

2.2 Chemicals

All solvents used in this research were purified by standard methodology except for those which were reagent grades. The reagents used for synthesizing metal salen complexes, metal carboxylate complexes and all epoxides were purchased from Fluka chemical company and were used without further purification.

2.3 Synthesis and characterization of catalysts

Metal salen complexes

Metal salen complexes: $[Cr(III)(salen)(H_2O)_2]Cl$, Co(II) salen, VO(IV) salen, Ni(II)salen, Cu(II)salen, Mn(II)salen, and Fe(II)salen utilized in this work were kindly obtained from Mr. Jirasak Imurai. The identification of these well-characterized complexes could be visualized in ref 28.

Metal carboxylate complexes

$Fe(TFA)_3$[23]

An excess of trifluoroacetic acid (5 mL, 44 mmol) was added to anhydrous iron(III)chloride (1 g, 6.15 mmol) in a round-bottomed flask under nitrogen atmosphere and the resulting mixture was stirred magnetically and refluxed for 48 h. The product was washed with *n*-hexane and filtered. The resulting red cake was collected and dried at 70°C for 3 h. Iron(III)trifluoroacetate was gained as a red powder 2.39 g, 98% yield, m.p. 107-110°C (lit[23] 110°C).

IR(KBr): 1622 (s), 1209 (s), 1155 (s) and 730 (m) cm^{-1}

$Fe(TCA)_3 \cdot 1.5H_2O$

This complex was prepared employing the similar method to that described for $Fe(TFA)_3$ by using trichloroacetic acid (13 g, 79 mmol) and anhydrous iron (III) chloride (1 g, 6.15 mmol). The brown solid of $Fe(TCA)_3 \cdot 1.5H_2O$ was obtained in 2.59 g, 83% yield, m.p. 215°C.

IR (KBr): 1664 (s), 1396 (s) and 847 (m) cm^{-1}. AA analysis found Fe^{3+}: 9.75%, calculated for $Fe(TCA)_3.1.5H_2O$: 9.79%.

Fe(picolinate)$_3$, Fe(4-nitrobenzoate)$_3$, Fe(2,4-dinitrobenzoate)$_3$ and Fe(benzoate)$_3$

Carboxylic acid 22 mmol was dissolved in dilute sodium hydroxide solution (0.88 g NaOH in 20 mL distilled water) at 80°C. After stirring solution until homogeneity, iron (III) trichloride anhydrous (1.18 g, 7.3 mmol) dissolved in 10 mL distilled water was added in one portion causing the precipitation which was collected and dried *in vacuo.*

Fe(picolinate)$_3$: 2.25 g, 73% yield, m.p. >300°C, IR(KBr): 1604 (s), 1344 (s) and 1083 (m) cm^{-1}.

Fe(benzoate)$_3$: 2.48 g, 81% yield, m.p. 290-300°C, IR(KBr): 1603 (s), 1567 (s) and 1178 (m) cm^{-1}.

Fe(4-nitrobenzoate)$_3$: 3.60 g, 89% yield, m.p. >300°C, IR(KBr): 1696 (s), 1527 (s) and 1102 (m) cm^{-1}.

Fe(2,4-dinitrobenzoate)$_3$: 3.79 g, 78% yield, m.p. >300°C, IR(KBr): 1608 (w), 1536 (s) and 1352 (s) cm^{-1}.

Cr(benzoate)$_3$ and Cr(4-nitrobenzoate)$_3$[29]

These complexes were prepared employing the similar method to that described for Fe(carboxylate)$_3$ by using carboxylic acid 22 mmol and chromium(III) trichloride hexahydrate (1.94 g, 7.3 mmol). The precipitate was collected and dried *in vacuo*. Metal carboxylate complexes: Cr(stearate)$_3$ and Cr(behenate)$_3$ utilized in this work were kindly donated from Mr. Nut Songsangcharoen. The identification of these well-characterized complexes could be reached in ref 29.

Cr(benzoate)$_3$: 2.42 g, 80% yield, m.p. 288-295°C, IR(KBr): 1603 (s), 1567(s) and 1178 (m) cm^{-1}.

Cr(4-nitrobenzoate)$_3$: 3.49 g, 87% yield, m.p. >300°C, IR(KBr): 1696 (s), 1527 (s) and 1102 (m) cm^{-1}.

Cr(Alanine)$_3$[30]

Alanine 0.18 g (2 mmol) was dissolved in water 5 mL. 6 M NaOH 3 mL was then added to the alanine solution. $CrCl_3.6H_2O$ 0.23 g (1 mmol) was dissolved in water 5 mL and added to the alanine solution. The reaction was stirred at room temperature for a few minutes to gain the complex which was precipitated out from the reaction. The product was washed three times with acetone and dried *in vacuo*. The purple solid 0.20 g, 64% yield, m.p. 280-288°C was obtained. -

IR(KBr): 3400 (w), 1598 (m), 1501 (m), 1321 (s) and 758 (w) cm^{-1}.

2.4 Preparation of authentic samples

2-Methoxy-2-phenylethanol

Styrene oxide 1.2 mL (10 mmol) was dissolved in 30 mL of methanol, $Fe(TCA)_3.1.5H_2O$ 0.0454 g (0.1 mmol) was added. The reaction was stirred under ambient conditions for 24 h. The reaction mixture was extracted three times with 25 mL of ether. The combined extracts were washed twice with 25 mL of H_2O, dried over anhydrous Na_2SO_4, evaporated in vacuum and the residue was isolated by silica gel column chromatography eluting with hexane: ethyl acetate (6:1). The product was colorless oil; 1.43 g, 94% yield, IR (KBr): 3441 (w), 2817 (m), 1106 (s) and 1029 (m) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.40-7.29 (5H, m), 4.34 (1H, dd, J = 8.58, 3.90 Hz), 3.71 (1H, dd, J = 11.68, 8.43 Hz), 3.64 (1H, dd, J = 11.65, 3.88 Hz) and 3.34 (3H, s).

2-Methoxy-1-phenylethanol [31]

Styrene oxide 1.2 mL (10 mmol) was dissolved in 30 mL of MeONa/MeOH. The reaction was stirred at room temperature for 24 h. The mixture was extracted with diethyl ether. The combined extracts were washed with H_2O. The organic layer was dried over anhydrous Na_2SO_4, evaporated in vacuum and the residue was separated by silica gel column chromatography eluting with hexane: ethyl acetate (6:1) to give the desired compound 1.18 g, 78% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.43-7.29 (5H, m), 4.93 (1H, dd, J = 8.58, 3.90 Hz), 3.64 (1H, dd, J = 11.68, 3.80 Hz), 3.58 (1H, dd, J = 9.79, 3.09 Hz) and 3.45 (3H, s).

2-Ethoxy-2-phenylethanol, 2-propoxy-2-phenylethanol, 2-isopropoxy-2-phenylethanol and 2-butoxy-2-phenylethanol

$Fe(TCA)_3.1.5H_2O$ 0.0454 g (0.1 mmol) was dissolved in alcohol (ethanol, *n*-propanol, *i*-propanol or *n*-butanol, 30 mL), followed by the addition of styrene oxide 1.2 mL (10 mmol). The reaction was stirred at room temperature for 24 h. The mixture was extracted with diethyl ether and H_2O. The organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuum. The residue was separated by column chromatography using hexane: ethyl acetate (6:1) as an eluent to furnish colorless liquid as the desired product.

2-ethoxy-2-phenylethanol: 1.21 g, 73% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.36-7.26 (5H, m), 4.42 (1H, dd, J = 8.78, 3.51 Hz), 3.69-3.57 (2H, m), 3.42 (2H, q, J = 7.00 Hz) and 1.22 (3H, t, J = 7.03 Hz).

2-propoxy-2-phenylethanol: 0.28 g, 16% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.41-7.29 (5H, m), 4.43 (1H, dd, J = 7.80, 3.90 Hz), 3.69 (2H, dd, J = 11.62, 3.88 Hz), 3.40 (2H, t, J = 6.88 Hz), 1.65 (2H, sextet, J = 7.17 Hz) and 0.96 (3H, t, J = 7.41 Hz).

2-isopropoxy-2-phenylethanol: 0.34 g, 19% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.43-7.30 (5H, m), 4.57 (1H, dd, J = 7.99, 4.47 Hz), 3.67-6.59 (3H, m), 1.23 (3H, d, J = 6.24 Hz) and 1.16 (3H, d, J = 6.24 Hz).

2-butoxy-2-phenylethanol: 0.15 g, 8% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.43-7.22 (5H, m), 4.47 (1H, dd, J = 8.50, 3.83 Hz), 3.79-3.68 (2H, m), 3.42 (2H, t, J = 6.88 Hz), 1.68-1.55 (2H, m), 1.40 (2H, sextet, J = 7.25 Hz) and 0.90 (3H, t, J = 7.37 Hz).

2-Azido-2-phenylethanol

To a dichloromethane solution (30 mL) of $Fe(TCA)_3.1.5H_2O$ 0.0454 g (0.1 mmol), styrene oxide 0.6 mL (5 mmol) and trimethylsilyl azide 2.6 mL (20 mmol) was added. The mixture was refluxed for 4 h. The solution was extracted with diethyl ether and then H_2O. The organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuum. The residue was separated by silica gel column chromatography using hexane: ethyl acetate (6:1) as an eluent. The product as brown oil 0.12 g, 15% yield was obtained. IR (KBr): 3416 (w), 2104 (s), 905 (s) and 738 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.67-7.51 (5H, m), 4.69 (1H, t, J = 6.24 Hz) and 3.75 (2H, d, J = 7.80 Hz).

2-Phenyl-2-phenylsulfanyl ethanol

Styrene oxide 1.2 mL (10 mmol) was dissolved in thiophenol 5 mL (50 mmol), followed by the addition of $Fe(TCA)_3.1.5H_2O$ 0.0454 g (0.1 mmol) into the reaction and refluxed for 8 h. The mixture was extracted with diethyl ether and H_2O. The organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuum. The residue was isolated by silica gel column chromatography with hexane:

ethyl acetate (6:1) as an eluent to yield dark brown oil 1.52 g, 66% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.38-7.11 (10H, m), 4.37-4.17 (1H, m) and 3.99-3.74 (2H, m).

2-Chloro-2-phenylethanol

Lithium chloride 3.4 g (20 mmol) was dissolved in DMF 20 mL, followed by the addition of styrene oxide 1.2 mL (10 mmol) and $Fe(TCA)_3.1.5H_2O$ 0.0454 g (0.1 mmol) to the solution. The reaction was refluxed for 8 h. The mixture was extracted with diethyl ether and H_2O. The organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuum. The residue was separated by silica gel column chromatography using hexane as an eluent. The product obtained was yellow oil 0.11 g, 7% yield. ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.41-7.29 (5H, m), 3.90 (1H, t, J = 3.18 Hz), 3.19 (1H, dd, J = 5.46, 3.90 Hz) and 2.85 (1H, dd, J = 5.46, 2.71 Hz).

2-Methoxy-1-dodecanol, 1-methoxy-2-dodecanol, 2-methoxy-1-cyclohexa-nol, butyl (2-hydroxy-1-methoxypropyl) ether, *tert*-butyl(2-hydroxy-1-methoxypropyl) ether, sobrerol dimethyl ether and 1,7,7-trimethyl-6-*exo*-methoxy bicyclo[2.2.1]-heptan-2-*endo*-ol

$Fe(TCA)_3.1.5H_2O$ 0.0454 g (0.1 mmol) was dissolved in methanol 30 mL, followed by the addtion of epoxide 10 mmol (1-dodecene oxide, cyclohexene oxide, butyl glycidyl ether, *tert*-butyl glycidyl ether and α-pinene oxide, respectively) to the solution. The mixture was refluxed for 8 h. The solution was extracted with diethyl ether and H_2O. The organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuum. The residue was isolated by silica gel column chromatography with hexane: ethyl acetate (6:1) as an eluent.

2-methoxy-1-dodecanol: 0.95 g, 44% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.70 (1H, dd, J = 11.14, 2.93 Hz), 3.52 (1H, dd, J = 11.72, 6.44 Hz), 3.44 (3H, s), 3.38-3.23 (1H, m), 1.68-1.44 (2H, m), 1.40-1.22 (16H, m) and 0.92 (3H, t, J = 6.73 Hz).

1-methoxy-2-dodecanol: 0.82 g, 38% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.88-3.75 (1H, m), 3.45 (1H, d, J = 2.93 Hz), 3.52 (1H, t, J = 8.20), 3.44 (3H, s), 1.48-1.44 (2H, m), 1.38-1.23 (16H, m), and 0.90 (3H, t, J = 6.76 Hz).

2-methoxy-1-cyclohexanol: 1.01 g, 78% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.33 (3H, s), 3.16-3.14 (1H, m), 2.98-2.88 (1H, m), 2.19-1.96 (2H, m), 1.80-1.58 (2H, m), 1.37-1.00 (4H, m).

butyl (2-hydroxy-1-methoxypropyl) ether: 0.23 g, 15% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.91-3.87 (1H, m), 3.57-3.54 (4H, m), 3.41 (3H, s), 1.59 (2H, quin, J = 7.03 Hz), 1.32 (2H, sextet, J = 7.62 Hz) and 0.86 (3H, t, J = 7.32 Hz).

tert-butyl (2-hydroxy-1-methoxypropyl) ether: 0.25 g, 17% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 3.80 (1H, s), 3.50-3.31 (2H, m), 3.39 (3H, s) and 1.20 (9H, s).

sobrerol dimethyl ether[32]: 0.55 g, 28% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 5.62 (1H, br s), 3.53 (1H, br s), 3.42 (3H, s), 3.21 (3H, s), 2.17 (1H, dd, J =13.26, 1.56 Hz), 2.03-1.95 (2H, m), 1.79 (3H, br s), 1.74-1.70 (2H, m), 1.15 (3H, s) and 1.13 (3H, s).

1,7,7-trimethyl-6-*exo*-methoxy bicyclo[2.2.1]-heptan-2-*endo*-ol[32]: 0.57 g, 31% yield, ^{1}H-NMR ($CDCl_3$) δ (ppm): 4.10 (1H, br m), 3.86 (1H, d, J = 9.36 Hz), 3.37 (3H, s), 2.49-2.43 (1H, m), 2.35-2.27 (1H, m), 1.80-1.77 (1H, m), 1.38 (1H, dd, J = 13.26, 3.12 Hz), 1.26 (1H, dd, J = 13.26, 3.90 Hz), 1.09 (3H, s), 0.87 (3H, s) and 0.86 (3H, s).

2.5 Study on the optimum conditions for styrene oxide ring opening

2.5.1 General procedure

The solution of styrene oxide 0.12 mL (1 mmol) in methanol (3 mL) containing a catalyst (0.05 mmol) in a round bottom flask was stirred for 10 min at room temperature. After the specific time or the reaction was completed (followed by TLC), 1 mL of the reaction mixture was taken and extracted twice with diethyl ether. The combined extracts were washed with distilled water. The organic layer was dried over anhydrous Na_2SO_4 and analyzed by GC with the addition of an exact amount of an appropriate internal standard.

The ring opening reaction was carried out in the same manner as described above, $FeCl_3$ (anhydrous), $FeCl_2$ (anhydrous), $FeCl_3.6H_2O$, $FeCl_3/SiO_2$, $FeSO_4.7H_2O$, Fe(salen), $Fe(acac)_3$, $Fe(TFA)_3$, $Fe(TCA)_3.1.5H_2O$, $Fe(palmitate)_3$, $Fe(stearate)_3$, $Fe(naphthenate)_3$, $Fe(behenate)_3$, $Fe(benzoate)_3$, $Fe(4\text{-nitrobenzoate})_3$, Ferrocene, $Fe(2,4\text{-dinitrobenzoate})_3$, Cr(salen)Cl, $Co(OAc)_2.4H_2O$, $CoCl_2.6H_2O$, $Co(palmitate)_2$, $Co(stearate)_2$, $Co(naphthenate)_2$, Co(salen)OMe, Co(salop),

Co(salen)(pyridine)$_4$, Co(salen)*, Co(salth) or Co(sal)-*m*-phen were used as a catalyst.

2.5.2 Effect of metal salen and metal carboxylate complexes

The ring opening reaction was carried out in the same manner as described above employing eight metal salen complexes: Fe(salen), Fe(salen)Cl, Co(salen), Cu (salen), Cr(salen)Cl, Ni(salen), VO(salen), Mn(salen) or ten metal carboxylate complexes: Fe(benzoate)$_3$, Fe(4-nitrobenzoate)$_3$, Fe(2,4-dinitrobenzoate)$_3$, Fe(picolinate)$_3$, Cr(stearate)$_3$, Cr(behenate)$_3$, Cr(alanine)$_3$, Cr(benzoate)$_3$ or Cr(4-nitrobenzoate)$_3$ as a catalyst instead of $FeCl_3$ (anhydrous).

2.5.3 Effect of time and temperature

The styrene oxide ring opening reaction was performed according to the general procedure mentioned earlier using Cr(salen)Cl or Fe(4-nitrobenzoate)$_3$ as a catalyst, but different reaction temperatures (30°C, 70°C) and reaction times (10 min, 30 min, 1 h, 2 h, 4 h, 6 h, 24 h) were varied.

2.5.4 Effect of the amount of methanol

The styrene oxide ring opening reaction was carried out according to the general procedure, but the amount of methanol was changed to 5, 20, 50 and 100 mmol.

2.5.5 Effect of solvent

The styrene oxide ring opening reaction was carried out in the same manner as previously described but various solvents, namely acetonitrile, dichloromethane, tetrahydrofuran, *N,N'*- dimethylformamide and ethyl acetate were utilized.

2.6 Effect of nucleophile for styrene oxide ring opening

2.6.1 Oxygen nucleophile

Alcohol group

The general procedure using styrene oxide and Fe(TCA)$_3$.1.5H_2O as starting material and catalyst, respectively at reflux dichloromethane temperature for 2 hours

was conducted. But different alcohols: ethanol, *n*–propanol, isopropanol and *n*-butanol were employed instead of methanol.

***Iso*-propanol as nucleophile**

The general procedure using styrene oxide *iso*-propanol and dichloromethane as reagent, nucleophile and solvent, respectively was carried out at different reaction times (2, 6, 10 and 24 h), temperatures (30 and 40°C), catalysts ($Fe(TCA)_3.1.5H_2O$, Fe(2,4-dinitrobenzoate)$_3$, Co(salen) and Cr(salen)Cl) and amount of catalyst (0, 0.01, 0.05, 0.10, 0.30 and 0.50 mmol).

2.6.2 Other nucleophiles

Nitrogen nucleophile

The reaction was carried out using reaction condition described for styrene oxide ring opening with an alcohol, but different nucleophiles: diethylamine, triethylamine and trimethylsilyl azide were employed instead of methanol.

Sulfur nucleophile

The styrene oxide ring opening reaction was carried out as described in general procedure using thiophenol as a nucleophile. Different types of catalysts: $Fe(TCA)_3.1.5H_2O$, Fe(2,4-dinitrobenzoate)$_3$, Co(salen) and Cr(salen)Cl were varied.

Halogen nucleophile

The styrene oxide ring opening reaction was performed according to the general procedure using lithium chloride as a nucleophile, but different solvents were varied (CH_2Cl_2, CH_3CN:CH_2Cl_2 (7:3) and DMF:CH_2Cl_2 (5:12)).

2.7 Rearrangement of styrene oxide

$Fe(TCA)_3.1.5H_2O$ 0.54 g (1 mmol) was dissolved in tetrahydrofuran 3 mL and stirred until homogeneous. Styrene oxide 0.12 mL (1 mmol) in tetrahydrofuran 2 mL was added to the reaction mixture and stirred under nitrogen atmosphere at room temperature for 15 min.

2.8 Preliminary study on asymmetric ring opening of styrene oxide

The ring opening reaction was carried out according to the general procedure, but (*R*)-styrene oxide was employed instead of racemic styrene oxide.

2.9 Other epoxides

1-dodecene oxide

The general procedure of ring opening reaction using 1-dodecene oxide, methanol and $Fe(TCA)_3.1.5H_2O$ as starting material, nucleophile and catalyst, respectively was carried out at difference reaction times (1, 2, 4 and 8 h), reaction temperatures (30, 40 and 80°C) and solvents (CH_3CN, CH_2Cl_2, THF and DMF).

cyclohexene oxide

The reaction was carried out cyclohexene oxide as the substrate under the reaction conditions described in the general procedure but difference reaction times (2, 4 and 8 h) and reaction temperature (30 and 40°C) were varied.

butyl glycidyl ether and *tert*-butyl glycidyl ether

The butyl glycidyl ether and *tert*-butyl glycidyl ether ring opening reaction was carried out in the same manner as previously described, but the reaction times (2, 4 and 8 h) and reaction temperature (30 and 40°C) were varied.

α-pinene oxide

The ring opening reaction was carried out according the general procedure but α-pinene oxide was employed instead of styrene oxide.

2.10 Competitive study on the ring opening reaction of epoxides

Following the general procedure, equimolar amount 1 mmol of styrene oxide, 1-dodecene oxide, cyclohexene oxide, butyl glycidyl ether and *tert*-butyl glycidyl ether were used as a competitive substrate in the epoxide ring opening reaction.