CHAPTER II

EXPERIMENTAL

2.1 General procedure

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 Varian nuclear magnetic resonance spectrometer, model Mercury plus 400 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 chromatographic analysis was carried out on a Shimadzu gas chromatograph GC-14A instrument equipped with flame ionization detector with N_2 as a carrier gas. The column used for gas chromatograph was carbowax 20 m.

2.2 Chemical reagents

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

2.3 Synthesis of ligand

2.3.1 Synthesis of benzoylacetone [31]

Substituted acetophenone (1 mol-equiv) in dry benzene 50 mL and ethyl benzoate or ethyl benzoate derivatives (1 mol-equiv) in dry benzene 50 mL were added dropwise to a suspension of 60% NaH. The mixture was refluxed and monitored the progress of the reaction by TLC using 30% EtOAc/hexane as an eluent.

The reaction mixture was cooled down to room temperature, quenched with 10% HCl, extracted with EtOAc, washed with brine and dried over $MgSO_4$. After removal of the solvent, the residue was recrystallized from an appropriate solvent or purified by silica gel column chromatography.

2.4 Synthesis and characterization of catalysts

2.4.1 Synthesis of $Fe(BZA)_3$ [32]

Ferric chloride anhydrous 0.16 g (0.99 mmol) and benzoylacetone (BZA) 0.46 g (2.80 mmol) were dissolved in EtOH 50 mL. To this solution an aqueous solution (10 mL) of NaOAc 0.15 g was added. The mixture was left to stand overnight at room temperature to give dark solid. It was collected by filtration and recrystallized from hexane.

Tris-(benzoylacetonato)-Iron(III): $Fe(BZA)_3$: dark red solid (85%), mp 218-220 °C, IR (KBr, cm^{-1}): 1590, 1542, 1451, 1374, 1298, 1000, 954 and 710.

2.4.2 Synthesis of carboxylate complexes [33]

Fe(III)stearate, Fe(III)palmitate

Stearic acid (6.26 g, 22 mmol) was dissolved in dilute sodium hydroxide solution (0.88 g NaOH in 20 mL distilled water) at 80 °C. After the solution was stirred until homogeneous, selected transition metal salts (7.3 mmol) dissolved in 10 mL distilled water was added in one portion causing the precipitation. The mixture was allowed to stir for another 30 min, and then the precipitate was collected and dried *in vacuo*.

By using this methodology, palmitic acid (22 mmol) and naphthenic acid (22 mmol) were employed instead of stearic acid for synthesizing of Fe(III)palmitate and Fe(III)naphthenate, respectively.

Fe(III)stearate: orange solid (78%), m.p. 94-86 °C. IR (KBr, cm^{-1}): 2912, 2846, 1705, 1583, 1461 and 723.

Fe(III)palmitate: light orange solid (81%), m.p. 98-100 °C, IR (KBr, cm^{-1}): 2905, 2847, 1703, 1573, 1458 and 721.

2.4.3 Synthesis of $Fe(TFA)_3$ [34]

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: red powder 2.39 g, 98% yield, m.p. 107-110°C. IR (KBr, cm^{-1}): 1622 (s), 1209 (s), 1155 (s) and 730 (m) $cm\text{-}^{1}$.

2.4.4 Synthesis of $Fe(TCA)_3.1.5H_2O$ [35]

This complex was prepared employing the similar method to that described for $Fe(TFA)_3$ using trichloroacetic acid (13 g, 79 mmol) and anhydrous iron (III) chloride (1 g, 6.15 mmol).

Iron(III)trichloroacetate: brown solid 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%.

Other iron complexes including $Fe(naphthenate)_3$, Fe(porphyrin), $Fe(salen)_2O$, Fe(salen)Cl, $Fe(picolinate)_3$, $Fe(benzoate)_3$ and $Fe(4\text{-}nitrobenzoate)_3$ were kindly supplied by Ms. Theraporn Timthong [**36**].

2.5 Synthesis of authentic sample

2-Chloro-2-phenylethanol [37]

LiCl 3.4 g (20 mmol) was dissolved in DMF 20 mL, followed by the addition of styrene oxide 1.2 mL (10 mmol) and $Fe(TCA)_3.1.5H_2O$ 0.04 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.

2-Chloro-2-phenylethanol: yellow oil (7%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.85 (1H, dd, $J = 5.46, 2.71$ Hz), 3.19 (1H, dd, $J = 5.46, 3.90$ Hz), 3.90 (1H, t, $J = 3.18$ Hz) and 7.41-7.29 (5H, m).

2.6 Synthesis of starting materials

2.6.1 Synthesis of styrene oxide derivatives [38]

A general method for preparing authentic epoxides was performed following standard literature protocols, with purification being conducted by column chromatography (silica gel, appropriate eluent). A 300 mL three necked flask was added $NaHCO_3$ (3.55 g, 0.0423 mol), water (40 mL), acetone (4.90 mL), EtOAc (40 mL), and interested alkene (2.00 g, 0.0486 mol) and were stirred vigorously. An aqueous Oxone solution (Oxone 5.20 g, 0.00846 mol, water 36 mL) was added dropwise over 1 h at 20 to 25 °C. The reaction mixture was stirred for an additional 1 h. The organic layer was separated and washed with 20% (w/v) aqueous NaCl (20 mL) and then evaporated.

α-Methylstyrene oxide: colorless liquid (85%), R_f 0.47 (hexane:EtOAc 8:2); ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.73 (3H, s), 2.82 (1H, d, J = 5.44 Hz), 2.98 (1H, d, J = 5.43 Hz) and 7.23-7.42 (5H, m).

4-Chlorostyrene oxide: clear yellow liquid (62%), R_f 0.44 (hexane:EtOAc 8:2); ^{1}H-NMR ($CDCl_3$), δ (ppm): 2.79 (1H, m), 3.18 (1H, t, J = 4.12 Hz), 3.87 (1H, t, J = 3.79 Hz), 7.24 (2H, d, J = 8.45 Hz) and 7.35 (2H, d, J = 8.47 Hz).

4-Methylstyrene oxide: colorless liquid (65%), R_f 0.46 (hexane:EtOAc 8:2); ^{1}H-NMR ($CDCl_3$), δ (ppm): 2.35 (3H, s), 2.70 (1H, m), 2.95 (1H, d, J = 4.02), 3.80 (1H, t, J = 3.56 Hz) and 7.11-7.39 (4H, m).

4-Methoxystyrene oxide: clear pleasant yellow liquid (68%), R_f 0.42 (hexane:EtOAc 8:2); ^{1}H-NMR ($CDCl_3$), δ (ppm): 2.70 (1H, m), 2.8 (1H, t, J = 4.80 Hz), 3.82 (3H, s), 3.90 (1H, t, J = 3.46 Hz), 6.82 (2H, d, J = 8.61 Hz) and 7.04 (2H, d, J = 8.72 Hz).

β-Methylstyrene oxide: clear pleasant yellow liquid (71%), R_f 0.42 (hexane:EtOAc 8:2); ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.89 (3H, d, J = 6.47 Hz), 3.05 (1H, m), 3.58 (1H, s) and 7.26-7.37 (5H, m).

2.6.2 Synthesis of α,β-unsaturated ketone oxide and 1,1-diphenylethylene oxide [39]

A solution of 5.00 g (0.0225 mol) of unsaturated ketone in 100 mL. of methanol was treated with 10.0 mL of 30% hydrogen peroxide and 5.0 mL of 6 N aqueous NaOH at 15 °C over a period of 55 min. The temperature was held at 15-20

°C by cooling with ice bath. After addition, stirring was continued at 20-25 °C for 3 h. Water (100 mL) was added and the mixture was extracted three times with 150 mL of ether. The combined ether extracts were washed twice with 150 mL of H_2O, once with 150 mL of a 3% KI solution and dried over $MgSO_4$. The solvent was evaporated and the residue was distilled under aspirator pressure to give desired product.

Benzalacetophenone oxide: white solid (78%), R_f 0.46 (hexane:EtOAc 8:2); ^{1}H-NMR ($CDCl_3$), δ (ppm): 4.12 (1H, d, *J* = 1.72 Hz), 4.34 (1H, d, *J* = 1.83 Hz), 7.29 (5H, m), 7.53 (2H, t, *J* = 7.83 Hz), 7.66 (1H, t, *J* = 7.36 Hz) and 8.05 (2H, d, *J* = 7.24 Hz).

1,1-Diphenylethylene oxide: clear yellow oil (41%), 0.39 (hexane:EtOAc 8:2); ^{1}H-NMR ($CDCl_3$), δ (ppm): 3.21 (2H, s) and 7.30 (10, m).

2.6.3 Synthesis of anethole oxide [40]

19.25 g of anethole (0.13 mol, ~20mL) was dissolved in 200 mL of a 1:1 mixture of acetonitrile and methanol. 2 g of Na_2CO_3 was added and the mixture was stirred at room temperature with slow stirring. Within 10-15 min, 14.75 mL (0.13 mol) 30% H_2O_2 was added dropwise under stirring. Stirring was continued at room temp for 18-24 h. After the time has elapsed, the MeCN/MeOH was distilled off on a water bath. An oily epoxide suspension was remained. The crude epoxide was extracted with ether. The ether was washed with brine and dried over Na_2SO_4. After drying, the ether was distilled off on a water bath and the last traces of ether were removed in vacuum leaving the crude epoxide (clear yellow pleasant smelling oil) in the flask. To purify the crude epoxide, a slow vacuum distillation was used. The yellow crude epoxide was distilled at 13 mmHg and 15.4 g of water-clear, very pleasant smelling oil came over between 118-126 °C.

Anethole oxide: deep yellow oil (76%), ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.48 (3H, d, J = 5.18), 3.07 (1H, m), 3.83 (3H, s), 3.91 (1H, s), 6.91 (2H, d, *J* = 8.74 Hz) and 7.23 (2H, d, *J* = 8.79 Hz).

2.7 The general procedure for the rearrangement of epoxides

The solution of styrene oxide 0.12 mL (1 mmol) in THF (5 mL) containing $FeCl_3$ (0.05 mmol) in a round bottom flask was stirred at room temperature for 10 min. 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.

2.8 Study on the optimum conditions for the rearrangement of styrene oxide and other epoxides

2.8.1 Effect of the amount of iron complexes

The rearrangement of styrene oxide was carried out by $FeCl_3$ (anhydrous) or $Fe(acac)_3$ (0.05, 0.1, 0.3, 0.5, 1 and 2 mmol).

2.8.2 Effect of atmosphere

The rearrangement of styrene oxide was carried out under N_2, O_2 and air atmosphere using $FeCl_3$ or $Fe(acac)_3$ as a reagent.

2.8.3 Effect of time and temperature

The rearrangement of styrene oxide was performed according to the general procedure mentioned earlier using $FeCl_3$ or $Fe(acac)_3$ as a reagent, but different reaction temperatures (30°C, 70°C) and reaction times (10 min, 30 min, 1 h, 2 h) were varied.

2.8.4 Effect of types of iron complexes

The rearrangement of styrene oxide reaction was carried out employing $FeCl_3$ (anhydrous), $FeCl_3.6H_2O$, Fe(salen), Fe(salen)Cl, $Fe(acac)_3$, $Fe(TFA)_3$, $Fe(TCA)_3.1.5H_2O$, $Fe(palmitate)_3$, $Fe(stearate)_3$, $Fe(naphthenate)_3$, $Fe(behenate)_3$, $Fe(benzoate)_3$, $Fe(4\text{-}nitrobenzoate)_3$ and Ferrocene as a reagent.

2.8.5 Effect of solvent

The rearrangement of styrene oxide was carried out in the same manner as previously described but various solvents, namely acetonitrile, toluene dichloromethane, tetrahydrofuran, 1,4-dioxane, hexane, EtOAc and 1,2-dichloroethane were utilized.

2.8.6 Kinetics study on the rearrangement of styrene oxide by $Fe(acac)_3$

The general procedure for the rearrangement of stryrene oxide by $Fe(acac)_3$ was carried out. At different reaction time was proceeded, 7, 15, 30, 45, 60 and 120 mins. An aliquot from the reaction mixture was taken, worked up and analyzed by GC.

2.9 Competitive study on the rearrangement of epoxides

Following the general procedure, equimolar amount 1 mmol of styrene oxide, α-methylstyrene oxide, 4-chlorostyrene oxide, 4-methylstyrene oxide, 4-methoxystyrene oxide (1 mmol each) was used as a competitive substrate in the rearrangement of epoxides.

2.10 Rearrangement of various selected epoxides

Selected epoxides including cyclohexene oxide, 1-dodecene oxide, butylglycidyl ether, *tert*-butylglycidylether, α-methylstyrene oxide, β-methylstyrene oxide, *trans*-stilbene oxide, benzalacetophenone oxide, methyl *trans*-3-(4-methoxy phenyl)-glycidate, 1,1-diphenylethylene oxide and anethol oxide were subjected to this developed rearrangement system catalyzed by iron complexes. Other procedures were carried out as previously described.

2.11 General isolation procedure

After the reaction was completed (followed by TLC), the rearrangement product was separated as follows: the whole reaction mixture was extracted according to that described in the general procedure and all solvents were removed. The crude product was purified by silica gel column chromatography using a mixture of hexane-EtOAc as an eluent. The equivalent fractions monitored by TLC were combined and the solvents were completely evaporated.