CHAPTER II

EXPERIMENTAL

2.1 General procedure

Melting points were measured on Fisher-Johns melting point apparatus and are uncorrected.

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) and aluminium oxide 90 (70-230 mesh ASTM). Gas chromatography analysis was carried out on a Shimadzu Gas chromatograph GC-14A instrument equipped with flame ionization detector (FID) with nitrogen as a carrier gas. The column used for chromatography was a capillary column type of DB-wax (30 m x 0.250 mm).

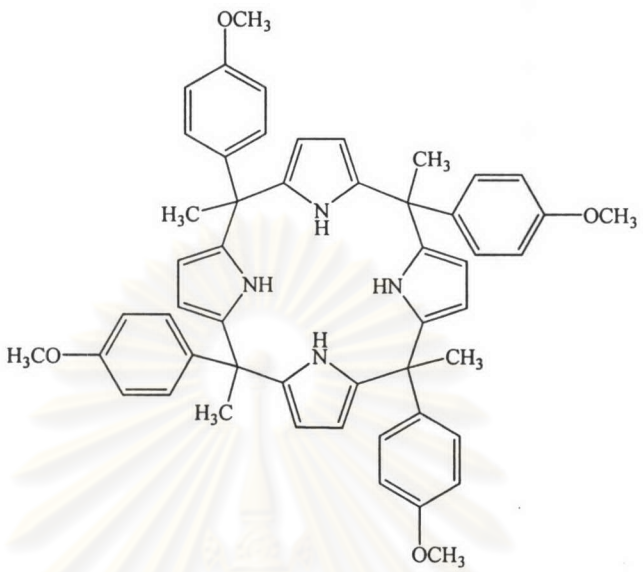
Spectrometers: the Fourier Transform-Infrared Spectra (FT-IR) were recorded on Nicolet Impact 410 FT-IR spectrometer. The ^{1}H and ^{13}C NMR spectra (both 1D and 2D) were performed in deuterated chloroform or dimethylsulfoxide-d_6 or otherwise stated with tetramethylsilane as an internal reference on Bruker Fourier Transform Nuclear Magnetic Resonance Spectrometer, model AC-F200 and a Joel, model JNM-A500 and a Bruker Avance 300 FT-NMR spectrometer. Mass spectrometry (MS) analysis was conducted on Fisson Instrument Model Trio 2000.

2.2 Chemical reagents

All solvents used in this research were purified by standard methodology except for those which were reagent grades. The reagents utilized for synthesizing the ligands, metal complexes and all alkenes were purchased from Fluka chemical company or otherwise stated and were used without further purification.

2.3 Syntheses

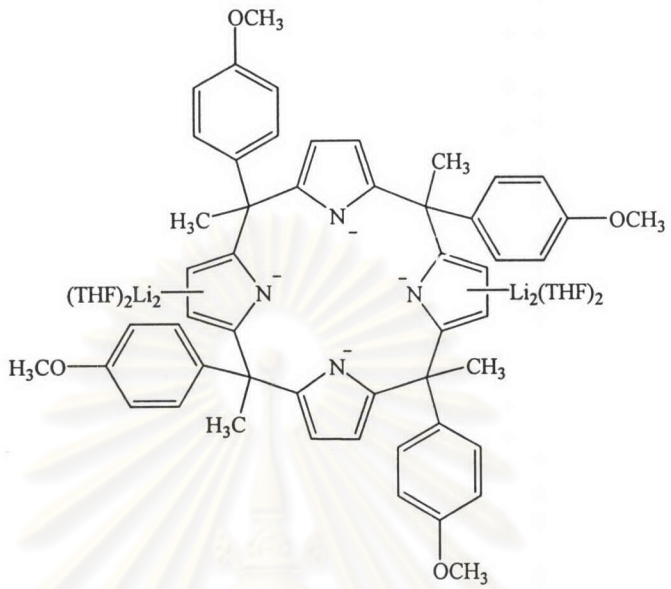
2.3.1 *meso*-Tetrakis(4-methoxyphenyl)-tetramethyl-calix[4]pyrrole[39, 40]



10

Ligand **10** was prepared by slowly adding methanesulfonic acid (7% mol) to a solution of 4-methoxyacetophenone 15.02 g (0.1 mol), pyrrole 7.0 mL (0.1 mol) and ethanol 50 mL. The mixture was allowed to reflux for 4 hours and then cooled. The brown solid was filtered off, washed with several portions of ethanol and dried at room temperature, the brown solid 19.82 g (99% yield) was obtained; m.p. 121-122 °C; R_f 0.43 (hexane:ethyl acetate 8:2); IR (KBr, cm^{-1}): 3431 (s), 2970 (s), 2832 (m), 1608 (s), 1456 (s), and 1250 (s); ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.53 (4H, s), 6.92-7.15 (8H, m), 6.50-6.85 (8H, m), 5.66-5.92 (8H, m), 3.78 (12H, m) and 1.85 (12H, s); ^{13}C-NMR ($CDCl_3$) δ (ppm): 157.5 (4C), 139.4 (4C), 136.8 (8C), 128.3 (8C), 113.0 (8C), 105.5 (8C), 55.0 (4C), 43.6 (4C) and 17.8 (4C).

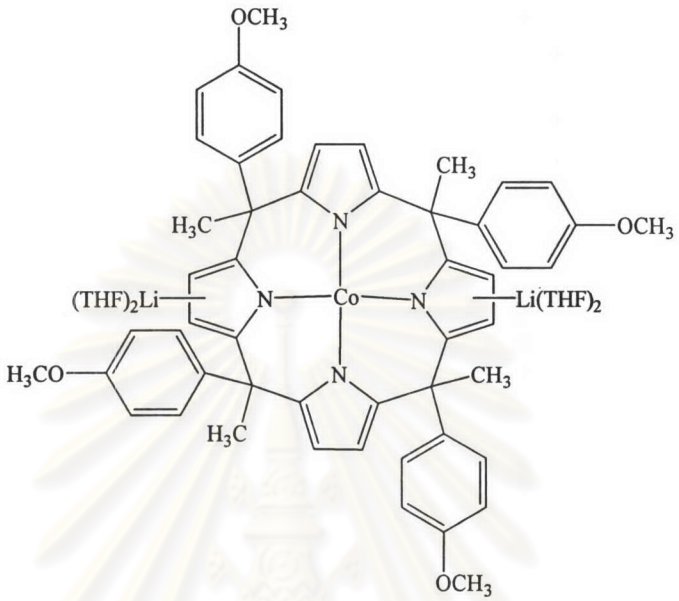
2.3.2 Lithium of *meso*-tetrakis(4-methoxyphenyl)-tetramethyl-calix[4] pyrrole tetraanion [41]



11

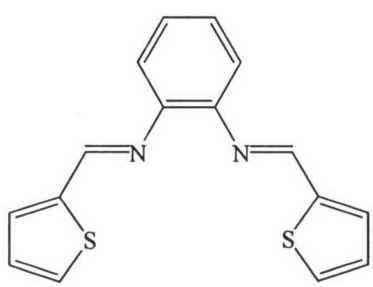
To a solution of **10** 5.57 g (7 mmol) in tetrahydrofuran (THF) 40 mL was added butyl lithium (BuLi) 2.27 mL (28 mmol). The reaction mixture was refluxed under stirring for 2 hours. The solvent was evaporated *in vacuo* and the residue was washed with dry hexane to afford the brown solid 5.67 g (76% yield); m.p. 112 °C ; R_f 0.45 (hexane:ethyl acetate 8:2); IR (KBr, cm^{-1}): 3090 (w), 2631 (w), 1607 (w), 1456 (m) and 1250 (m); ^{1}H-NMR ($CDCl_3$) δ (ppm): 6.93-7.15 (8H, m), 6.64-6.78 (8H, m), 5.78-5.90 (8H, m), 3.77 (12H, m), 4.68 (16H, br, THF), 1.86 (12H, s) and 1.75 (16H, br, THF).

2.3.3 Dilithium-tetrakis(tetrahydrofuran)-α,β,γ,δ-tetrakis-(4-methoxyphenyl)-tetramethyl-calix[4]pyrrole tetraanion Cobalt(II) complex: Cobalt(II) calix[4]pyrrole



Cobalt (II) chloride 0.79 g (3.3 mmol) and polyanion **11** 4.43 g (4 mmol) were dissloved in toluene 40 mL. The reaction mixture was stirred for 48 hours. After the reaction was completed, the brown solid was filtered off and washed with several portions of toluene. The filtrate was collected and kept in refrigerator for 24 hours. The solvent was evaporated *in vacuo* to give brown solid 3.99 g (87% yield); m.p. 116-117 °C, R_f 0.43 (hexane:ethyl acetate 8:2), IR (KBr, cm^{-1}): 2959 (w), 1724 (s), 1672 (m), 1597 (s) and 1254 (s).

2.3.4 *N, N'*-1,2-phenylene *bis* (2-thenylideneimine) (thiophen-*o*-phen)[42]



12

o-Phenylenediamine 2.7 g (0.05 mol) in ethanol 30 mL was added to thiophen-2-aldehyde 5.6 g (0.05 mol) to give a drak green solution which was then heated on steam-bath for 30 min, whereupon the color was changed to red. The reaction mixture was cooled and the clear red solution was decanted from a small amount of brown oil and filtered. The filtrate on standing overnight deposited yellow needles of Schiff's base 4.56 g (62% yield); m.p. 148-149 °C, R_f 0.68 (ethanol); IR (KBr, cm^{-1}): 3090-3050 (w), 2950 (w), 1630 (w) and 1225 (s); ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.83 (dd, J = 6.87, 1.83 Hz, 1H), 7.51 (dd, J = 5.03, 1.22 Hz, 1H), 7.47 (dd, J = 3.82, 1.22 Hz, 1H), 7.37 (dd, J = 7.32, 1.22 Hz, 1H), 7.29 (m, 2H), 7.23 (dd, J = 4.89, 1.23 Hz, 1H), 7.13 (t, J = 4.27 Hz, 1H), 6.94 (t, J = 4.43 Hz, 1H), 6.86 (dd, J = 3.36, 1.22 Hz, 1H), 5.70 (s, 2H); ^{13}C-NMR ($CDCl_3$) δ (ppm): 147.6, 143.0, 138.8, 135.8, 131.8, 128.9, 128.0, 127.9, 127.2, 125.4, 125.2, 123.3, 123.0, 119.9, 109.9 and 44.0

2.3.5 *N, N'*-1,2-phenylene *bis* (2-thenylideneimine) cobalt(II) complex: Co(II) thiophen-*o*-phen

An ethanolic solution (80 mL) of ligand **12** (10 mmol) was mixed with an aqueous solution (80 mL) of cobalt(II) chloride hexahydrate (10 mmol). Then a solution (42 mL) of $CH_3COONa.3H_2O$ (30 mmol) was added and refluxed for 2-3 hr. After that the solution was cooled down to room temperature and kept it for overnight to deposit green needles 2.13 g (60% yield); IR (KBr, cm^{-1}): 3073 (w), 2945 (w), 1563 (w) and 1221 (s).

Other cobalt(II) catalysts: cobalt(II) complexes of salophen **13**, saloa **14**, salen OMe **16**, salen* **17**, salophen OMe **18** and saltn **19** utilized in this work were kindly obtained from Mr. Jirasak Imurai. The identification of these well-characterized complexes could be visualized in ref 43.

2.4 Synthesis of authentic samples

To a solution of alkenes (9.7 mmol) in 50 mL of dry methylene chloride at 0°° C was added 70% *m*-CPBA acid (2.22 mmol) in 40 mL of dry methylene chloride over a period of 30 min. After the solution was stirred for 3-4 hours, the excess peracid was decomposed with 5 mL of 10% sodium sulfite solution and the dry methylene chloride solution was washed carefully with 100 mL of saturated sodium bicarbonate solution, the organic layer was separated, and the aqueous layer was

washed twice with dry methylene chloride. The organic layers were combined, washed with brine, dried and evaporated to yield the desired epoxide.

1-methylcyclohexene oxide: Colorless liquid, R_f 0.57 ($CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ (ppm): 2.95 (t, J = 3.51 Hz, 1H), 1.45-1.89 (m, 8H) and 1.29 (s, 3H)

α-methyl styrene oxide:[25] Colorless liquid, R_f 0.36 ($CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.23-7.42 (m, 5H), 2.98 (d, J = 5.4 Hz, 1H), 2.82 (d, J = 5.4 Hz, 1H) and 1.73 (s, 3H)

cis-stilbene oxide:[44] Colorless liquid, R_f 0.31 (hexane:$CHCl_3$ 8:2); ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.11-7.37 (m, 10H) and 4.37 (s, 2H)

trans-stilbene oxide:[44] White solid, m.p 69-70°C, R_f 0.36 (hexane:$CHCl_3$ 8:2); ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.24-7.40 (m, 10H) and 3.92 (s, 2H)

1,2-dihydronaphthalene oxide: Pale orange liquid, R_f 0.25 ($CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.24-7.58 (m, 4H), 4.23 (d, J = 3.52 Hz, 1H), 3.00 (m, 1H), 2.21-2.32 (m, 2H) and 2.03-2.08 (m, 2H)

2.5 Synthesis of starting materials

4-methoxy cinnamic acid[45-48]

Malonic acid 3.12 g (31 mmol) was dissolved in 6 mL of anhydrous pyridine, 4-methoxybenzaldehyde 3.54 g (26 mmol) and 0.26 mL of piperidine were added. The solution was refluxed approximately 1.5 hr, cooled to room temperature, then poured into a mixture of 16 g of ice, 8 mL of conc HCl and 26 mL of H_2O, precipitating the acid as a colorless solid. The product was filtered, wash with ice water and recrystallized with ethanol. The white mirror-like needle crystal (78% yield); m.p. 173-174°C, R_f 0.62 (ethanol); IR (KBr, cm^{-1}): 3650-3300, 1690, 1630, 1598, 1516, 1446, 1432, 1250, 1210 and 1175; ^{1}H-NMR (DMSO) δ (ppm): 7.64 (d, J = 15.87 Hz, 1H), 6.97-7.64 (m, 4H), 6.40 (d, J = 16.17 Hz, 1H) and 3.82 (s, 3H); ^{13}C-NMR (DMSO) δ (ppm): 168.2 (-COOH), 162.5, 130.6 (2x1C), 128.0, 115.2 (2x1C) (aromatic carbon), 145.3, 116.5 (olefinic carbons) and 67.2 (-OCH_3)

Synthesis ethylcinnamate derivatives

General Procedure[45]

Ethanol (0.01 mol) was dissolved in 10 mL of benzene and then substituted *trans*-cinnamic acid (0.01 mol) was added thereto. After that 0.3 mL of conc H_2SO_4 was added and the mixture was refluxed for 5 hours. The reaction mixture was concentrated to remove benzene and the residue was poured into 8 mL of ice water. The mixture was extracted three time with 10 mL of ether. The combined extracts were washed twice with 10 mL of H_2O, dried over Na_2SO_4, evaporated in vacuum and the residue was fractionally distilled to give the desired compound.

Trans-ethylcinnamate: Yellow oil (57% yield), R_f 0.78 (EtOAc); IR (KBr, cm^1): 1712, 1633, 1446, 1310 and 1267; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.68 (d, J = 15.83, 1H), 7.38-7.53 (m, 5H), 6.43 (d, J = 15.83 Hz, 1H), 4.26 (q, J = 7.04 Hz, 2H) and 1.33 (t, J = 7.04 Hz, 3H)

Trans-ethyl 4-methoxycinnamate: Colorless oil (69% yield), R_f 0.56 (ethanol); IR (KBr, cm^{-1}): 1703, 1625, 1602, 1513, 1287, 1248 and 1170; ^{1}H-NMR ($CDCl_3$) δ (ppm): 7.67 (d, J = 15.83 Hz, 1H), 7.51 (d, J = 8.21 Hz, 2H), 6.93 (d, J = 8.21 Hz, 2H), 6.34 (d, J = 15.83 Hz, 1H), 4.28 (q, J = 7.04 Hz, 2H), 3.87 (s, OCH_3) and 1.36 (t, J = 7.04 Hz, 3H)

2.6 The general procedure for the epoxidation of alkenes

Cobalt complex (0.05 mmol) was dissolved in acetonitrile (15 mL), followed by the addition of alkene (5 mmol) and 2-ethylbutyraldehyde (10 mmol) to a round bottom flask fitted with a balloon filled with oxygen. The mixture was stirred for 24 hours at room temperature. After the reaction was completed, 1 mL of the reaction mixture was taken and extracted with diethyl ether. The combined extracts were washed with saturated solution of $NaHCO_3$ and brine, respectively. 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.

2.7 Study on the optimum conditions for the epoxidation of cyclohexene and other alkenes

2.7.1 Effect of solvent

The epoxidation reaction was carried out in the same manner as previously described except for that toluene and a mixture of toluene and acetonitrile with various ratios were employed instead of acetonitrile.

2.7.2 Effect of the amount of 2-ethylbutyraldehyde

The epoxidation reaction was carried out in the same manner as previously described but the amount of 2-ethylbutyraldehyde was varied (10 and 20 mmol).

2.8 Comparative kinetic study of the epoxidation of alkenes catalyzed by cobalt complexes

The general epoxidation procedure utilizing cobalt(II) complexes of calix[4]pyrrole **10**, thiophen-*o*-phen **12**, salophen **13**, and saloa **14** as catalyst and cyclohexene as substrate were carried out. At different reaction times proceeded (3, 6, 9, 12, 15, 18, 21 and 24 hours), an aliquot (1.0 mL) of the reaction mixture was taken, worked up and analyzed by GC.

In addition, cobalt(II) complex of calix[4]pyrrole **10** catalyzed a variety of substrates including cyclohexene, 1-dodecene and 1-methylcyclohexene were also kinetically investigated.

2.9 Competitive study on the epoxidation of cyclohexene, 1-dodecene and 1-methylcyclohexene

Following the general epoxidation procedure, equimalar amount (5 mmol) of cyclohexene and 1-dodecene or cyclohexene and 1-methylcyclohexene were used as competitive substrate in the reaction. Other procedures were performed according to those described in Topic 2.6.

2.10 Epoxidation of various selected alkenes

Selected alkenes including 4-vinylcyclohexene, *cis*-4-hexen-1-ol, *trans*-2-hexen-1-ol, α-pinene, β-pinene, *trans*-ethylcinnamate, *trans*-ethyl 4-methoxycinna mate, α-methylstyrene and 1,2-dihydronaphthalene were subjected to this developed epoxidation reaction catalyzed by cobalt(II) complexes of calix[4]pyrrole **10**,

thiophen-*o*-phen **12**, salophen **13**, and saloa **14**. Other procedures were carried out as previously described.

2.11 Stereoselectivity study

The general epoxidation procedures using cobalt(II) complexes of calix[4]pyrrole **10** and thiophen-*o*-phen **12** as catalyst and *trans*-stilbene and *cis*-stilbene as substrates were carried out. An aliquot (1 mL) of the reaction mixture was taken, worked up and analyzed by ^{1}H-NMR.

2.12 General isolation procedure

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