

## CHAPTER II

### EXPERIMENTAL SECTION

#### 2.1 General Procedure

##### 2.1.1 Materials

All reagents were either reagent or analytical grade, purchased from Fluka (Switzerland) or Merck (Germany) and used without further purification. Commercial grade solvents such as acetone, ethyl acetate, hexane were distilled prior to use. Chromatographic separations were performed on silica gel column (kieselgel 60, 63-200  $\mu\text{m}$  Merck). Thin layer chromatography (TLC) were carried out using silica gel plates (kieselgel 60 F<sub>254</sub>, 1 mm, Merck. Unless specified otherwise, all reactions were carried out under nitrogen. The products were characterized by <sup>1</sup>H-NMR spectroscopy, <sup>13</sup>C-NMR spectroscopy and IR spectroscopy. The salen complexes were characterized by elemental analysis, IR spectroscopy and matrix assisted laser desorption ionization ion trap mass spectroscopy. All the spectra are presented in the appendix section at the end of this thesis.

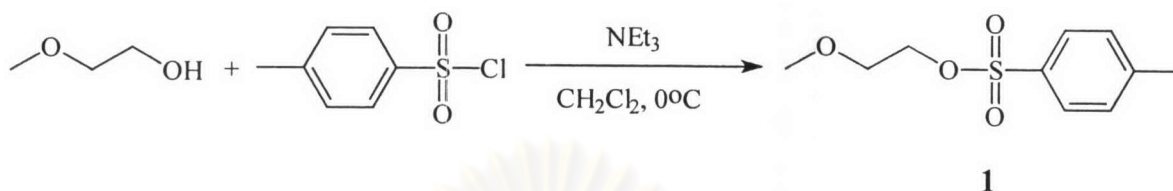
##### 2.1.2 Analytical Instruments

The <sup>1</sup>H-NMR spectra and <sup>13</sup>C-NMR spectra were recorded on a Bruker ACF 200 nuclear magnetic resonance spectrometer operating at 200 MHz (<sup>1</sup>H) and 50 MHz (<sup>13</sup>C). Chemical shifts were reported using a residual chloroform signal as an internal reference. FTIR spectra were registered on a Nicolet Impact 410 fourier transform infrared spectrometer. Gas chromatographic analyzes were conducted on a Shimadzu GC-14A chromatograph equipped with a 30-m long and 0.25-mm. o.d. Carbowax column. The mass spectra were acquired on an Esquire3000plus\_01012.

## 2.2 Synthesis of chiral salens containing ethylene glycol chains

### 2.2.1 Preparation of (*R,R*)-*N,N'*-bis(3-*t*-butyl-5-(2-methoxyethoxy)salicylidine)-1,2-cyclohexanediamine (4)

#### 2.2.1.1 Preparation of ethylene glycol monomethyl tosylate (1)

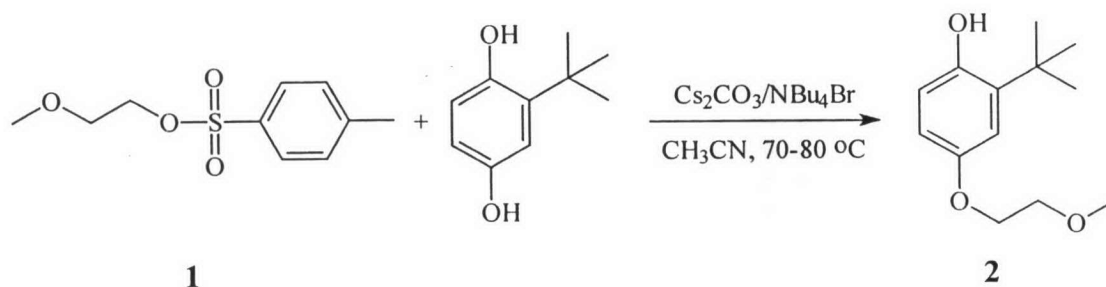


In a 250 mL round-bottomed flask equipped with a magnetic bar and an addition funnel, ethylene glycol monomethyl ether (7.06 g, 92.8 mmol) and triethylamine (16 mL) were dissolved in dichloromethane (20 mL). The solution was stirred and cool to 0°C for 15 minutes. A solution of 4-toluenesulfonyl chloride (17.57 g, 92.2 mmol) in dichloromethane (25 mL) was added dropwise into this solution. The funnel was rinsed with dichloromethane (5 mL). The mixture was allowed to warm to room temperature and stirred for 15 hours. The mixture was filtered and the salt was washed with dichloromethane. The combined filtrate was extracted with HCl (2 M, 30 mL) and water (2 x 25 mL). The organic layer was separated, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and filtered. The filtrate was evaporated to give the product as viscous pale yellow liquid (15.42 g, 73 %). This product was pure enough for the next synthesis without further purification.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) : δ 2.40 (3H, ArCH<sub>3</sub>, s), 3.27 (3H, OCH<sub>3</sub>, s), 3.55 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.8 Hz), 4.12 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.8 Hz), 7.31 (2H, ArH, d, *J* = 8.0 Hz), 7.77 (2H, ArH, d, *J* = 8.0 Hz)

<sup>13</sup>C-NMR (CDCl<sub>3</sub>) : δ 22 (ArCH<sub>3</sub>), 58 (OCH<sub>3</sub>), 68 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 71 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 127, 129, 133, 145 (Ar)

### 2.2.1.2 Preparation of 2-*t*-butyl-4-(2-methoxyethoxy)phenol (2)



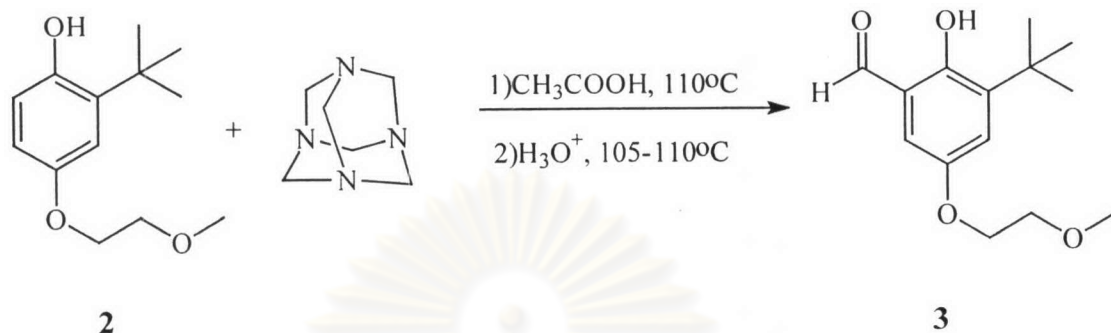
In a 100 mL round-bottomed flask equipped with a magnetic bar and a reflux condenser, *t*-butylhydroquinone (2.25 g, 13.5 mmol), ethylene glycol monomethyl ether tosylate, **1** (2.81 g, 12.2 mmol), cesium carbonate (3.93 g, 12.1 mmol) and tetrabutylammonium bromide (0.39 g, 1.2 mmol) were mixed in acetonitrile (30 mL). The mixture was refluxed for 2 days and then allowed to cool to room temperature. HCl (2 M, 30 mL) was added into the mixture and the resulting mixture was poured into separatory funnel. The brown organic layer was separated. The aqueous layer was extracted with dichloromethane (2 x 25 mL). The combined organic layer was dried over anhydrous  $\text{Na}_2\text{SO}_4$  and filtered. The solvent was removed by rotary evaporator. The residue was eluted through a silica gel column by hexane/ethyl acetate (100:0 to 90:10). The product was collected and the solvent was removed to give a viscous dark brown liquid (1.11 g, 41%).

**$^1\text{H-NMR}$  ( $\text{CDCl}_3$ ):**  $\delta$  1.35 (9H,  $\text{C}(\text{CH}_3)_3$ , s), 3.44 (3H,  $\text{OCH}_3$ , s), 3.72 (2H,  $\text{ArOCH}_2\text{CH}_2\text{O}$ , t,  $J = 4.5$  Hz), 4.04 (2H,  $\text{ArOCH}_2\text{CH}_2\text{O}$ , t,  $J = 4.5$  Hz), 4.95 (1H,  $\text{ArOH}$ , br), 6.57 (2H,  $\text{ArH}$ , d,  $J = 1.7$  Hz), 6.88 (1H,  $\text{ArH}$ , t,  $J = 1.7$  Hz)

**$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):**  $\delta$  29 ( $\text{C}(\text{CH}_3)_3$ ), 35 ( $\text{C}(\text{CH}_3)_3$ ), 59 ( $\text{OCH}_3$ ), 68 ( $\text{ArOCH}_2\text{CH}_2\text{O}$ ), 71 ( $\text{ArOCH}_2\text{CH}_2\text{O}$ ), 111, 115, 117, 138, 149, 152 (Ar)

### 2.2.1.3 Preparation of 3-*t*-butyl-5-(2-methoxyethoxy)salicylaldehyde (3)

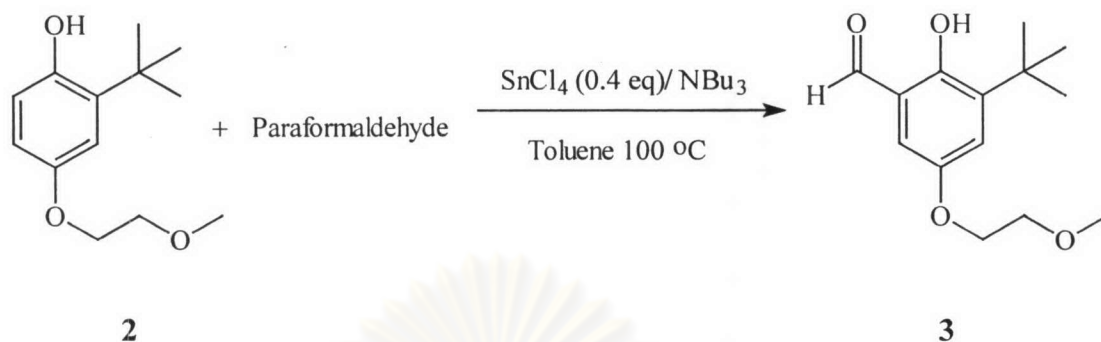
#### Method I



In a 100 mL round-bottomed flask equipped with a magnetic bar and a reflux condenser, 2-*t*-butyl-4-(2-methoxyethoxy)phenol, **2** (0.80 g, 3.5 mmol) and hexamethylenetetramine (HMT) (1.02 g, 7.2 mmol) were mixed in glacial acetic acid (10 mL). The mixture was heated at 110 °C for 2 hours. The mixture was cooled to 70-80 °C and aqueous H<sub>2</sub>SO<sub>4</sub> (6 M, 10 mL) was added. The stirred mixture was heated at reflux (105-110 °C) for 1 hour. The mixture was allowed to cool to room temperature and extracted with diethyl ether (20 mL). The extract was washed with water (2 x 20 mL) then brine (20 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was removed by rotary evaporator. The residue was eluted through a silica gel column by hexane/ethyl acetate (100:0 to 90:10). The product was collected and the solvent was removed to give a viscous orange liquid (0.14 g, 16 %).

**<sup>1</sup>H-NMR (CDCl<sub>3</sub>):** δ 1.36 (9H, C(CH<sub>3</sub>)<sub>3</sub>, s), 3.41 (3H, OCH<sub>3</sub>, s), 3.72 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.5 Hz), 4.06 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.5 Hz), 6.80 (1H, ArH, d, *J* = 3.0 Hz), 7.20 (1H, ArH, d, *J* = 3.0 Hz), 9.77 (1H, ArCHO, s), 11.48 (1H, ArOH, s)

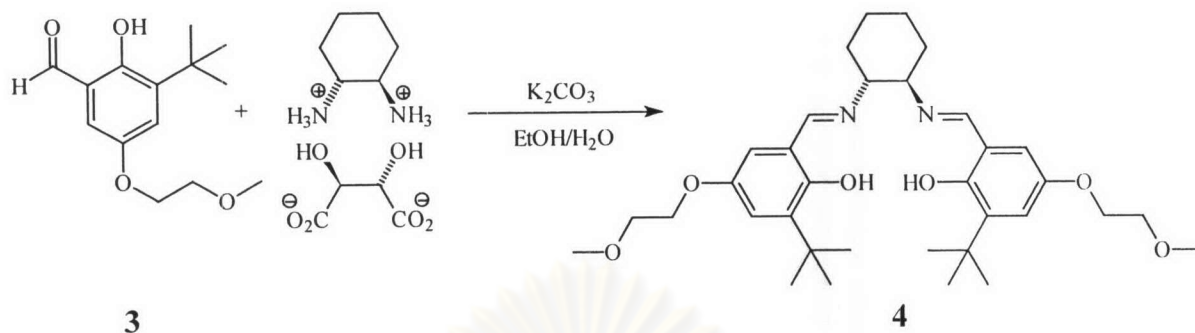
**<sup>13</sup>C-NMR (CDCl<sub>3</sub>):** δ 29 (C(CH<sub>3</sub>)<sub>3</sub>), 35 (C(CH<sub>3</sub>)<sub>3</sub>), 59 (OCH<sub>3</sub>), 68 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 71 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 113, 120, 125, 140, 151, 156 (Ar), 197 (CHO)

**Method II**

In a 100 mL two-necked flask equipped with a magnetic bar and a reflux condenser, 2-*t*-butyl-4-(2-methoxyethoxy)phenol, **2** (1.99 g, 8.3 mmol) and tributylamine (2.64 g, 14.3 mmol) were mixed in anhydrous toluene (12 mL). The reaction mixture was cooled to  $0\text{ }^\circ\text{C}$  for 15 minutes and  $\text{SnCl}_4$  (0.45 mL, 3.8 mmol) was added dropwise by a syringe. The reaction was allowed to warm to room temperature and stirred 20 minutes at which time paraformaldehyde (1.77 g, 58.8 mmol) was added. The mixture was heated at  $100\text{ }^\circ\text{C}$  for 8 hours. The thick and yellow oily layer was cooled to room temperature, poured into water (50 mL) and acidified to approximately pH 2 with HCl (2 M). The mixture was extracted with diethyl ether (30 mL). The extract was washed with brine (20 mL) and dried over anhydrous  $\text{Na}_2\text{SO}_4$  and filtered. The solvent was removed by rotary evaporator. The residue was eluted through a silica gel column by hexane/ethyl acetate (100:0 to 90:10). The product was collected and the solvent was removed to give a viscous orange liquid (1.34 g, 60%).

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### 2.2.1.4 Preparation of (*R,R*)-*N,N'*-bis(3-*t*-butyl-5-(2-methoxyethoxy)salicylidine)-1,2-cyclohexanediamine (**4**)



In a 100 mL two-necked round-bottomed flask equipped with a magnetic bar, a reflux condenser and an addition funnel, (*R,R*)-1,2-diammoniumcyclohexane mono-(+)-tartrate (1.06 g, 4.0 mmol) and potassium carbonate (0.58 g, 4.2 mmol) were mixed in water (10 mL) until dissolution was achieved and then ethanol (30 mL) was added. The resulting cloudy mixture was heated to 75-80 °C and a solution of 3-*t*-butyl-5-(2-methoxyethoxy)salicylaldehyde, **3** (2.00 g, 7.9 mmol) in ethanol (10 mL) was added dropwise. The funnel was rinsed with ethanol (5 mL). The mixture was refluxed for 2 hours and was allowed to cool to room temperature. The reaction mixture was extracted with dichloromethane (2 x 25 mL). The combined organic layer was washed with brine (25 mL). After drying over anhydrous Na<sub>2</sub>SO<sub>4</sub>, the solvent was removed by rotary evaporator. The residue was eluted through a silica gel column by hexane/ethyl acetate 80:20. The product was collected and the solvent was removed to give the desired product as a viscous yellow liquid (1.93 g, 83 %).

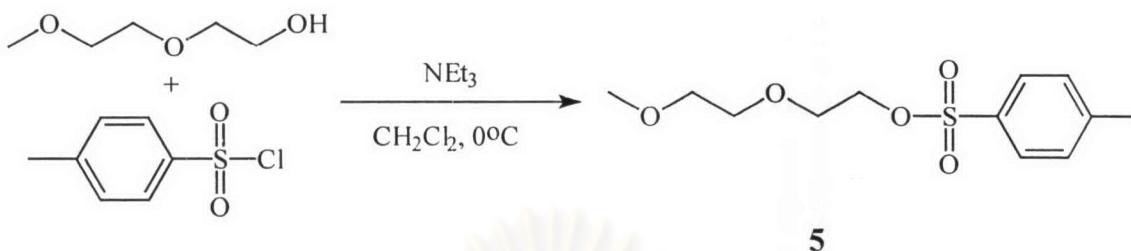
**<sup>1</sup>H-NMR (CDCl<sub>3</sub>):** δ 1.36 (18H, C(CH<sub>3</sub>)<sub>3</sub>, s), 1.67-2.02 (8H, cyclic CH<sub>2</sub>, br), 3.31 (2H, cyclic CH, m), 3.42 (6H, OCH<sub>3</sub>, s), 3.68 (4H, ArOCH<sub>2</sub>CH<sub>2</sub>O, m), 3.93 (4H, ArOCH<sub>2</sub>CH<sub>2</sub>O, m), 6.46 (2H, ArH, d, *J* = 3.0 Hz), 6.93 (2H, ArH, d, *J* = 3.0 Hz), 8.19 (2H, ArCH=N, s), 13.50 (2H, ArOH, br)

**<sup>13</sup>C-NMR (CDCl<sub>3</sub>):** δ 24 (cyclic), 29 (C(CH<sub>3</sub>)<sub>3</sub>), 33 (cyclic), 34 (C(CH<sub>3</sub>)<sub>3</sub>), 59 (OCH<sub>3</sub>), 68 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 71 (C=N-CH), 72 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 112, 118, 119, 139, 150, 155 (Ar), 165 (C=N)

**IR (neat):** ν 1141, 1600, 1637, 2871, 2931

## 2.2.2 Preparation of (*R,R*)-*N,N'*-bis(3-*t*-butyl-5-((2-(2-methoxy)ethoxy)ethoxy)salicyli dine)-1,2-cyclohexanediamine (8)

### 2.2.2.1 Preparation of diethylene glycol monomethyl tosylate (5)

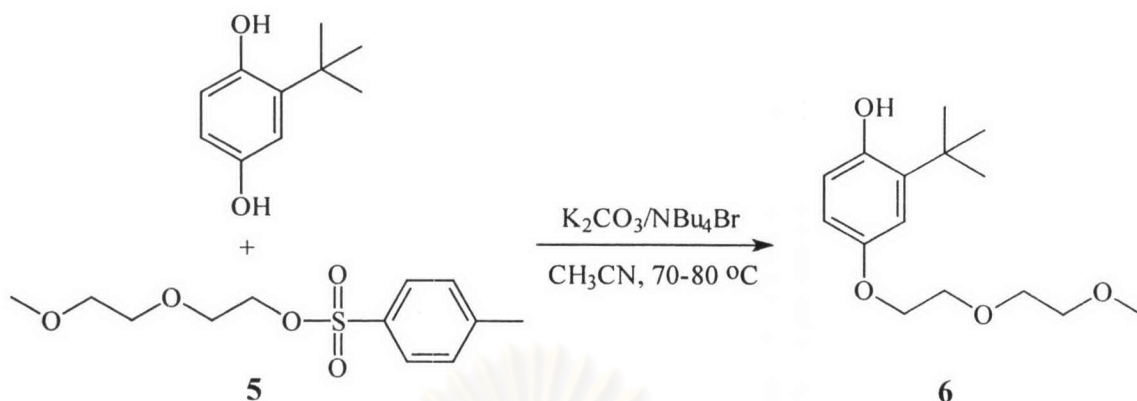


In a 250 mL round-bottomed flask equipped with a magnetic bar and an addition funnel, diethylene glycol monomethyl ether (8.04 g, 66.9 mmol) and triethylamine (16 mL) were dissolved in dichloromethane (20 mL). The solution was stirred and cool to 0°C for 15 minutes. A solution of 4-toluenesulfonyl chloride (12.72 g, 66.7 mmol) in dichloromethane (25 mL) was added dropwise into this solution. The funnel was rinsed with dichloromethane (5 mL). The mixture was allowed to warm to room temperature and stirred for 15 hours. The mixture was filtered and the salt was washed with dichloromethane. The combined filtrate was extracted with HCl (2 M, 30 mL) and water (2 x 25 mL). The organic layer was separated, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and filtered. The filtrate was evaporated to give the desired product as a viscous pale yellow liquid (15.61 g, 85 %). This product was pure enough for the next synthesis without further purification.

**<sup>1</sup>H-NMR (CDCl<sub>3</sub>)** : δ 2.40 (3H, ArCH<sub>3</sub>, s), 3.31 (3H, OCH<sub>3</sub>, s), 3.43 (2H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, m), 3.53 (2H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, m), 3.68 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.7 Hz), 4.13 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.7 Hz), 7.30 (2H, ArH, d, *J* = 8.3 Hz), 7.75 (2H, ArH, d, *J* = 8.3 Hz)

**<sup>13</sup>C-NMR (CDCl<sub>3</sub>)** : δ 21 (ArCH<sub>3</sub>), 58 (OCH<sub>3</sub>), 68 (OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>), 69 (OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>), 70 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 71 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 128, 130, 133, 145 (Ar)

### 2.2.2.2 Preparation of 2-*t*-butyl-4-((2-(2-methoxy)ethoxy)ethoxy)phenol (6)



In a 100 mL round-bottomed flask equipped with a magnetic bar and a reflux condenser, *t*-butylhydroquinone (3.56 g, 21.4 mmol), diethylene glycol monomethyl ether tosylate, **5** (5.81 g, 21.2 mmol), potassium carbonate (3.11 g, 22.5 mmol) and tetrabutylammonium bromide (0.70 g, 2.1 mmol) were mixed in acetonitrile (40 mL). The mixture was refluxed for 2 days and then allowed to cool to room temperature. HCl (2 M, 30 mL) was added into the mixture and the resulting mixture was poured into a separatory funnel. The brown organic layer was separated. The aqueous layer was extracted with dichloromethane (2 x 25 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was removed by a rotary evaporator. The residue was eluted through a silica gel column by hexane/ethyl acetate (100:0 to 80:20). The product was collected and the solvent was removed to give a viscous brown liquid (2.21 g, 39 %).

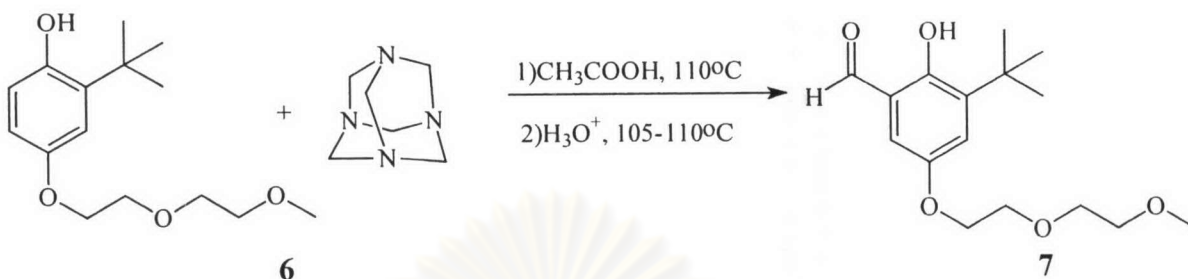
**<sup>1</sup>H-NMR (CDCl<sub>3</sub>):** δ 1.35 (9H, C(CH<sub>3</sub>)<sub>3</sub>, s), 3.38 (3H, OCH<sub>3</sub>, s), 3.60 (2H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, m), 3.70 (2H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, m), 3.81 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.5 Hz), 4.02 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.5 Hz), 5.17 (1H, ArOH, br), 6.55 (2H, ArH, dd, *J* = 8.5, 2.6 Hz), 6.85 (1H, ArH, d, *J* = 2.6 Hz)

**<sup>13</sup>C-NMR (CDCl<sub>3</sub>):** δ 30 (C(CH<sub>3</sub>)<sub>3</sub>), 34 (C(CH<sub>3</sub>)<sub>3</sub>), 59 (OCH<sub>3</sub>), 68 (OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>), 70 (OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>), 71 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 72 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 112, 115, 117, 137, 149, 152 (Ar)



### 2.2.2.3 Preparation of 3-*t*-butyl-5-((2-(2-methoxy)ethoxy)ethoxy)salicylaldehyde (7)

#### Method I

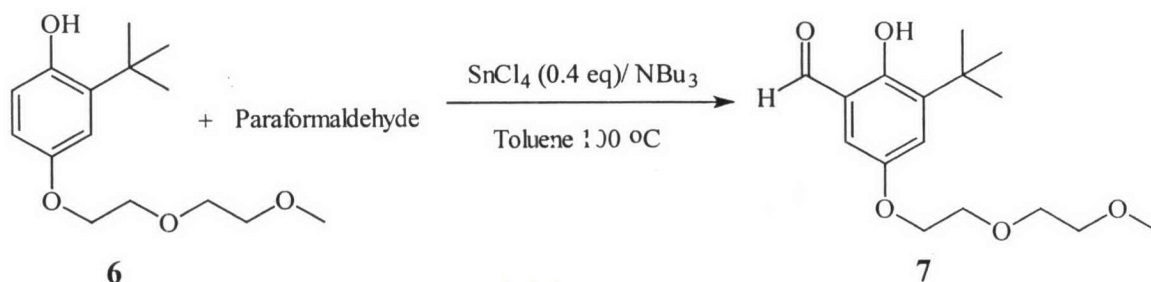


In a 100 mL round-bottomed flask equipped with a magnetic bar and a reflux condenser, 2-*t*-butyl-4-((2-(2-methoxy)ethoxy)ethoxy)phenol, **6** (2.49 g, 9.3 mmol) and hexamethylenetetramine (HMT) (2.65 g, 18.9 mmol) were mixed in glacial acetic acid (25 mL). The mixture was heated at 110 °C for 2 hours. The mixture was cooled to 70-80 °C and aqueous H<sub>2</sub>SO<sub>4</sub> (6 M, 25 mL) was added. The stirred mixture was heated at reflux (105-110 °C) for 1 hour. The mixture was allowed to cool to room temperature and extracted with diethyl ether (25 mL). The extract was washed with water (2 x 25 mL) and then brine (25 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and filtered. The solvent was removed by a rotary evaporator. The residue was eluted through a silica gel column by hexane/ethyl acetate (90:10 to 60:40). The product was collected and the solvent was removed to give a viscous orange liquid (0.37 g, 14 %).

**<sup>1</sup>H-NMR (CDCl<sub>3</sub>):** δ 1.39 (9H, C(CH<sub>3</sub>)<sub>3</sub>, s), 3.40 (3H, OCH<sub>3</sub>, s), 3.58 (2H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, m), 3.70 (2H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, m), 3.84 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, m), 4.10 (2H, ArOCH<sub>2</sub>CH<sub>2</sub>O, t, *J* = 4.4 Hz), 6.81 (1H, ArH, d, *J* = 3.0 Hz), 7.19 (1H, ArH, d, *J* = 3.0 Hz), 9.79 (1H, ArCHO, s), 11.48 (1H, ArOH, s)

**<sup>13</sup>C-NMR (CDCl<sub>3</sub>):** δ 29 (C(CH<sub>3</sub>)<sub>3</sub>), 35 (C(CH<sub>3</sub>)<sub>3</sub>), 59 (OCH<sub>3</sub>), 68 (OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>), 70 (OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>), 71 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 72 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 113, 120, 125, 140, 151, 156 (Ar), 197 (CHO)

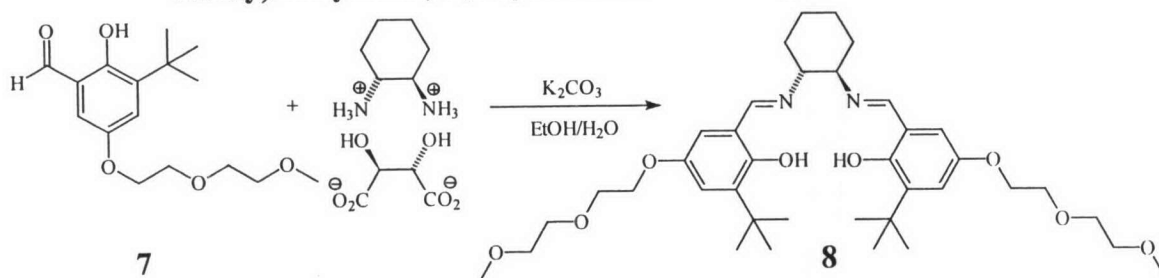
### Method II



In a 100 mL two-necked flask equipped with a magnetic bar and a reflux condenser, 2-*t*-butyl-4-((2-(2-methoxy)ethoxy)ethoxy)phenol, **6** (2.86 g, 10.6 mmol) and tributylamine (3.26 g, 17.6 mmol) were mixed in anhydrous toluene (12 mL). The reaction mixture was cooled to 0 °C for 15 minutes and SnCl<sub>4</sub> (0.50 mL, 4.3 mmol) was added dropwise by a syringe. The reaction was allowed to warm to room temperature and stirred 20 minutes at which time paraformaldehyde (2.12 g, 70.6 mmol) was added. The mixture was heated at 100 °C for 8 hours. The thick and yellow oily layer was cooled to room temperature, poured into water (50 mL) and acidified to approximately pH 2 with HCl (2 M). The mixture was extracted with diethyl ether (30 mL). The extract was washed with brine (20 mL) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After filtration, the solvent was removed by a rotary evaporator. The residue was eluted through a silica gel column by hexane/ethyl acetate (100:0 to 70:30). The product was collected and the solvent was removed to give a viscous orange liquid (2.03 g, 64 %).

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#### 2.2.2.4 Preparation of (*R,R*)-*N,N'*-bis(3-*t*-butyl-5-((2-(2-methoxy)ethoxy)ethoxy)salicylidine)-1,2-cyclohexanediamine (**8**)



In a 100 mL two-necked round-bottomed flask equipped with a magnetic bar, a reflux condenser and an addition funnel, (*R,R*)-1,2-diammoniumcyclohexane mono-(+)-tartrate (1.13 g, 4.3 mmol) and potassium carbonate (0.61 g, 4.4 mmol) were mixed in water (10 mL) until dissolution was achieved and then ethanol (30 mL) was added. The resulting cloudy mixture was heated to 75-80 °C, and a solution of 3-*t*-butyl-5-((2-(2-methoxy)ethoxy)ethoxy)salicylaldehyde, **7** (2.51 g, 8.5 mmol) in ethanol (10 mL) was added dropwise. The funnel was rinsed with ethanol (5 mL). The mixture was refluxed for 2 hours and was allowed to cool to room temperature. The reaction mixture was extracted with dichloromethane (2 x 25 mL). The combined organic layer was washed with brine (25 mL). After drying over anhydrous  $Na_2SO_4$ , the solvent was removed by rotary evaporator. The residue was eluted through a silica gel column by hexane/ethyl acetate 80:20. The product was collected and the solvent was removed to give a viscous yellow liquid (2.78 g, 98 %).

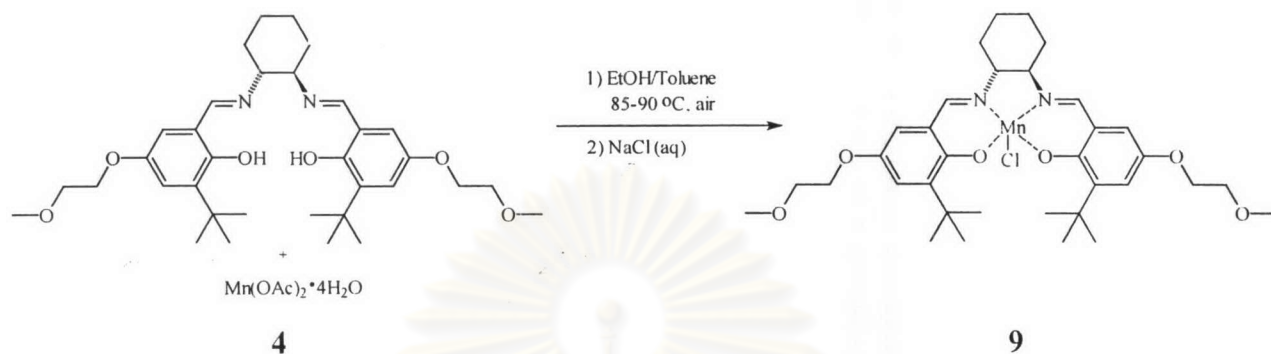
**<sup>1</sup>H-NMR (CDCl<sub>3</sub>):** δ 1.35 (18H, C(CH<sub>3</sub>)<sub>3</sub>, s), 1.72-2.02 (8H, cyclic CH<sub>2</sub>, br), 3.31 (2H, cyclic CH, m), 3.36 (6H, OCH<sub>3</sub>, s), 3.54 (4H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, m), 3.65 (4H, OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>, m), 3.76 (4H, ArOCH<sub>2</sub>CH<sub>2</sub>O, m), 3.97 (4H, ArOCH<sub>2</sub>CH<sub>2</sub>O, m), 6.46 (2H, ArH, d, *J* = 3.0 Hz), 6.90 (2H, ArH, d, *J* = 3.0 Hz), 8.18 (2H, ArCH=N, s), 13.50 (2H, ArOH, br)

**<sup>13</sup>C-NMR (CDCl<sub>3</sub>):** δ 24 (cyclic), 29 (C(CH<sub>3</sub>)<sub>3</sub>), 33 (cyclic), 35 (C(CH<sub>3</sub>)<sub>3</sub>), 59 (OCH<sub>3</sub>), 68 (OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>), 70 (OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>3</sub>), 71 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 72 (ArOCH<sub>2</sub>CH<sub>2</sub>O), 113, 118, 119, 139, 150, 155 (Ar), 165 (C=N)

**IR (neat) :** ν 1135, 1597, 1631, 2867, 2934

## 2.3 Synthesis of chiral salens manganese(III) complexes containing ethylene glycol chains

### 2.3.1 Preparation of [(*R,R*)-*N,N'*-bis(3-*t*-butyl-5-(2-methoxyethoxy)salicylidine)-1,2-cyclohexanediaminato(2-)] manganese(III) chloride (9)



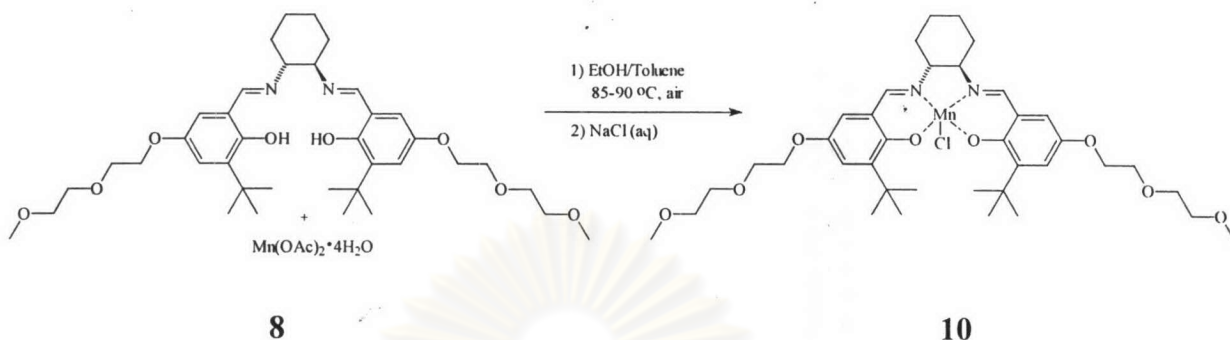
In a 100 mL two-necked flask equipped with a magnetic bar, a reflux condenser and an addition funnel,  $\text{Mn(OAc)}_2 \cdot 4\text{H}_2\text{O}$  (2.46 g, 10.0 mmol) was stirred in ethanol (20 mL). The solution was heated to 80-85 °C, and a solution of (*R,R*)-*N,N'*-bis(3-*t*-butyl-5-(2-methoxyethoxy)salicylidine)-1,2-cyclohexanediamine, 4 (1.93 g, 3.3 mmol) in toluene (15 mL) was added dropwise. The funnel was rinsed with toluene (5 mL), and the mixture was stirred at 80-85 °C for 2 hours. The addition funnel was replaced with a gas dispersion tube and air was bubbled through the reaction mixture for 45 minutes. After the heating and air addition were discontinued, the mixture was allowed to cool to room temperature, and brine (20 mL) was added. The organic layer was extracted with brine (25 mL) and then dried over  $\text{Na}_2\text{SO}_4$ . The solvent was removed by a rotary evaporator. The residue was redissolved completely in  $\text{CH}_2\text{Cl}_2$  (15 mL). To this solution was added heptane (15 mL) and it was concentrated by rotary evaporator until the precipitation was observed. The mixture was cooled in an ice bath for 1 hour. The brown precipitate was collected by vacuum filtration to give the desired product (1.11 g, 50 %).

**Elem. Anal.:** Calcd for  $\text{C}_{34}\text{H}_{48}\text{ClMnN}_2\text{O}_6$ ; C, 60.85%; H, 7.21%; N, 4.17%  
 Found : C, 60.75%; H, 7.20%; N, 4.19%

**MS (ESI) :**  $m/z$  635.7 [calculated  $(\text{M}-\text{Cl})^+ = 635.69$ ]

**IR (KBr) :**  $\nu$  1128, 1613, 2869, 2928

**2.3.2 Preparation of [(*R,R*)-*N,N'*-bis(3-*t*-butyl-5-((2-(2-methoxy)ethoxy)ethoxy)salicylidine)-1,2-cyclohexanediaminato(2-)] manganese(III) chloride (10)**



In a 100 mL two-necked flask equipped with a magnetic bar, a reflux condenser and an addition funnel,  $\text{Mn(OAc)}_2 \cdot 4\text{H}_2\text{O}$  (3.66 g, 15.0 mmol) was stirred in ethanol (20 mL). The solution was heated to 80-85 °C, and a solution of (*R,R*)-*N,N'*-bis(3-*t*-butyl-5-((2-(2-methoxy)ethoxy)ethoxy)ethoxy)salicylidine)-1,2-cyclohexanediamine, **8** (2.84 g, 4.2 mmol) in toluene (15 mL) was added dropwise. The funnel was rinsed with toluene (5 mL), and the mixture was stirred at 80-85 °C for 2 hours. The addition funnel was replaced with a gas dispersion tube and air was bubbled through the reaction mixture for 45 minutes. After the heating and air addition were discontinued, the mixture was allowed to cool to room temperature and brine (20 mL) was added. The organic layer was extracted with brine (25 mL) and then dried over  $\text{Na}_2\text{SO}_4$ . The solvent was removed by rotary evaporator. The residue was redissolved completely in  $\text{CH}_2\text{Cl}_2$  (15 mL). To this solution was added heptane (15 mL) and it was concentrated by a rotary evaporator until the precipitation was observed. The mixture was cooled in an ice bath for 1 hour. The brown precipitate was collected by vacuum filtration to give the desired product (1.23 g, 38%).

**Elem. Anal.:** Calcd for  $\text{C}_{38}\text{H}_{56}\text{ClMnN}_2\text{O}_8$ ; C, 60.11%; H, 7.43%; N, 3.69%  
 Found: C, 60.18%; H, 7.41%; N, 3.70%

**MS (ESI):**  $m/z$  723.7 [calculated  $(\text{M}-\text{Cl})^+ = 723.79$ ]

**IR (KBr):**  $\nu$  1101, 1613, 2865, 2931

## 2.4 Catalytic property studies of the chiral manganese(III)-salen complexes

### 2.4.1 Enantioselective epoxidation of alkenes by *m*-CPBA/NMO system

#### General procedure for enantioselective epoxidation by *m*-CPBA/NMO system

A solution of styrene (50 mg, 0.48 mmol), *N*-methylnmorpholine *N*-oxide (NMO) and catalyst in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was cooled to -10-0 °C. Solid *m*-chloroperbenzoic acid (*m*-CPBA) (237 mg, 0.96 mmol) was added as a solid in four roughly equal portions over a 2 minutes period. The reaction mixture was stirred for 20 minutes at -10-0 °C, and then 1 M NaOH (10 mL) was added. The organic layer was separated and extracted with saturated NaCl solution (15 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The residual catalyst was removed by filtration through a short plug of silica gel. The resulting filtrate provided a crude of remained styrene and styrene oxide product that was analyzed by GC for % conversion and % yield with cyclohexanone as an internal standard. The % ee of styrene oxide was determined by <sup>1</sup>H-NMR spectrometry with europium (III) tris[3-heptafluoro propylhydroxymethylene)-*d*-camphorate] (Eu(hfc)<sub>3</sub>) as a chiral shift reagent.

#### Condition studied in the enantioselective epoxidation by *m*-CPBA/NMO system

##### a) Solvents

The epoxidation reaction was carried out according to the general procedure described above with varied solvents: acetone, ether, methanol, acetonitrile and dichloromethane.

##### b) The amounts of NMO

The epoxidation reaction was carried out according to the general procedure described above using varied amount of NMO: 0, 1, 2.5, 5 and 7.5 equivalent to the substrate.

##### c) Effect of reaction time

The epoxidation reaction was carried out according to the general procedure described above for two reaction periods: 20 and 60 minutes.

**d) The amounts of catalysts**

The epoxidation reaction was carried out according to the general procedure described above with varied amounts of catalysts: 2, 3, 4, 10 mol% of substrate for catalyst **9** and 4, 10 mol% of substrate for catalyst **10**.

**e) Effect of substrate**

The enantioselective epoxidation was carried out according to the general procedure described above on two substrates: styrene and indene.

**2.4.2 Enantioselective epoxidation of alkenes by NaOCl/4-PPNO system**

**General procedure for enantioselective epoxidation by NaOCl/4-PPNO system**

A solution of styrene (50 mg, 0.48 mmol), 4-phenylpyridine *N*-oxide (4-PPNO) and catalyst in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was cooled to 0-10 °C. Precooled buffered bleach solution (0.6 M, 1.6 mL, 0.98 mmol, buffered to pH ~ 11 with 0.05 M Na<sub>2</sub>HPO<sub>4</sub> and 1 M NaOH) was added. The reaction mixture was stirred for 6 hours at 0-10 °C, and then the organic layer was separated and extracted with 1 M NaOH (10 mL) and saturated NaCl solution (15 mL). The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The residual catalyst was removed by filtration through a short plug of silica gel. The resulting filtrate provided a crude of remaining styrene and styrene oxide that was analyzed by GC for % conversion and % yield with cyclohexanone as an internal standard. The % ee of styrene oxide was determined by <sup>1</sup>H-NMR spectrometry with Eu(hfc)<sub>3</sub> as a chiral shift reagent.

**Condition studied in the enantioselective epoxidation by NaOCl/4-PPNO system**

**a) The amounts of 4-PPNO**

The epoxidation reaction was carried out according to the general procedure described above using to different amounts of 4-PPNO: 0 and 0.15 equivalent to substrate.

**b) Effect of the amount of catalyst**

The epoxidation reaction was carried out according to the general procedure described above with two different amount of the catalysts: 4 and 10 mol% of the substrates for both catalysts **9** and **10**.

### c) Effect of substrate

The enantioselective epoxidation was carried out according to the general procedure described above on two substrates: styrene and indene.

#### 2.4.3 The determination of the enantiomeric excess of epoxide by $^1\text{H-NMR}$

The ee (enantiomeric excess) of the epoxide product was determined by analysis of  $^1\text{H-NMR}$  spectrum of the sample in the presence of the NMR chiral shift reagent ( $\text{Eu}(\text{hfc})_3$ ). It is a paramagnetic complex that will shift the  $^1\text{H-NMR}$  signals of chiral molecules that coordinate to it. Since ( $\text{Eu}(\text{hfc})_3$ ) is chiral, the signals of two enantiomers of epoxide will shift to a different degree.

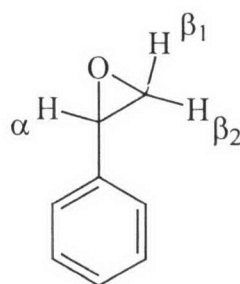
$^1\text{H-NMR}$  spectrum of a crude styrene in  $\text{CDCl}_3$  was collected. A solution of  $\text{Eu}(\text{hfc})_3$  (15 mg in  $\text{CDCl}_3$  1 mL) was added a few drops into the sample and the spectrum was rerun. Notice how some of the signals have been resolved into 2 sets. The solution of  $\text{Eu}(\text{hfc})_3$  was added until the peak around 3.1 ppm was resolved. Expand the scale of  $^1\text{H-NMR}$  spectrum and carefully integrate the signals of the two enantiomers. Using this integrals to calculate the % ee obtained in the epoxidation reaction according to the following equation.

$$\% \text{ enantiomeric excess} = \frac{(I_{R \text{ isomer}} - I_{S \text{ isomer}})100}{(I_{R \text{ isomer}} + I_{S \text{ isomer}})}$$

where  $I_{R \text{ isomer}}$  = integral of  $\beta_1$ -proton of  $R$  isomer

$I_{S \text{ isomer}}$  = integral of  $\beta_2$ -proton of  $S$  isomer

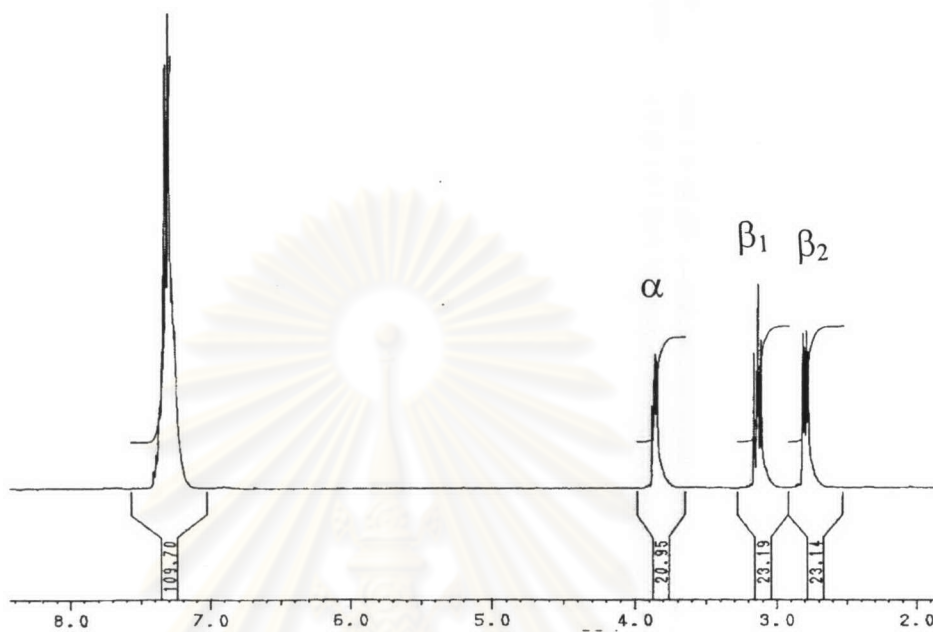
$I_{R \text{ isomer}} > I_{S \text{ isomer}}$



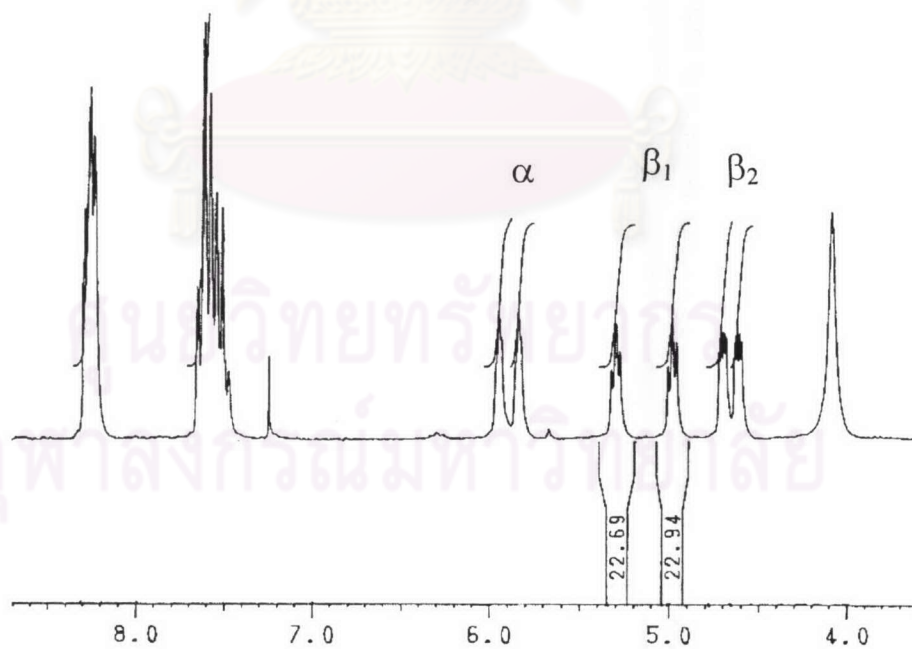
Styrene oxide



a)



b)



**Figure 2.1** The  $^1\text{H-NMR}$  spectra of racemic styrene oxide a) before adding  $\text{Eu}(\text{hfc})_3$  b) after adding  $\text{Eu}(\text{hfc})_3$ .

In the case of indene oxide,  $^1\text{H-NMR}$  spectrum of a crude indene in  $\text{CDCl}_3$  was collected. A solution of  $\text{Eu}(\text{hfc})_3$  (15 mg in  $\text{CDCl}_3$  1 mL) was added a few drops into the sample and the spectrum was rerun. Notice how some of the signals have been resolved. The solution of  $\text{Eu}(\text{hfc})_3$  was added until the peak around 4.6 ppm was resolved from overlapped peaks around 4.8 ppm. Expand the scale of  $^1\text{H-NMR}$  spectrum and carefully integrate the signals. Using these integrals to calculate the % ee obtained in the epoxidation reaction according to the following equations.

$$\% \text{ minor enantiomer (1S,2R isomer)} = \frac{I_{\beta\text{-H (1S,2R)}} \times 2 \times 100}{I_{\alpha\text{-H(1R,2S)}} + I_{\alpha\text{-H(1S,2R)}} + I_{\beta\text{-H(1R,2S)}} + I_{\beta\text{-H(1S,2R)}}$$

Where  $I_{\alpha\text{-H(1R,2S)}}$  = integral of  $\alpha\text{-H}$  (1R,2S isomer)

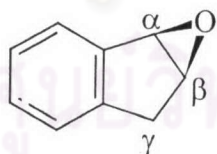
$I_{\alpha\text{-H(1S,2R)}}$  = integral of  $\alpha\text{-H}$  (1S,2R isomer)

$I_{\beta\text{-H(1R,2S)}}$  = integral of  $\beta\text{-H}$  (1R,2S isomer)

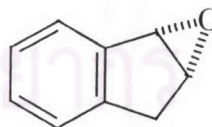
$I_{\beta\text{-H(1S,2R)}}$  = integral of  $\beta\text{-H}$  (1S,2R isomer)

$$\% \text{ major enantiomer (1R,2S isomer)} = 100 - \% \text{ minor enantiomer (1S,2R isomer)}$$

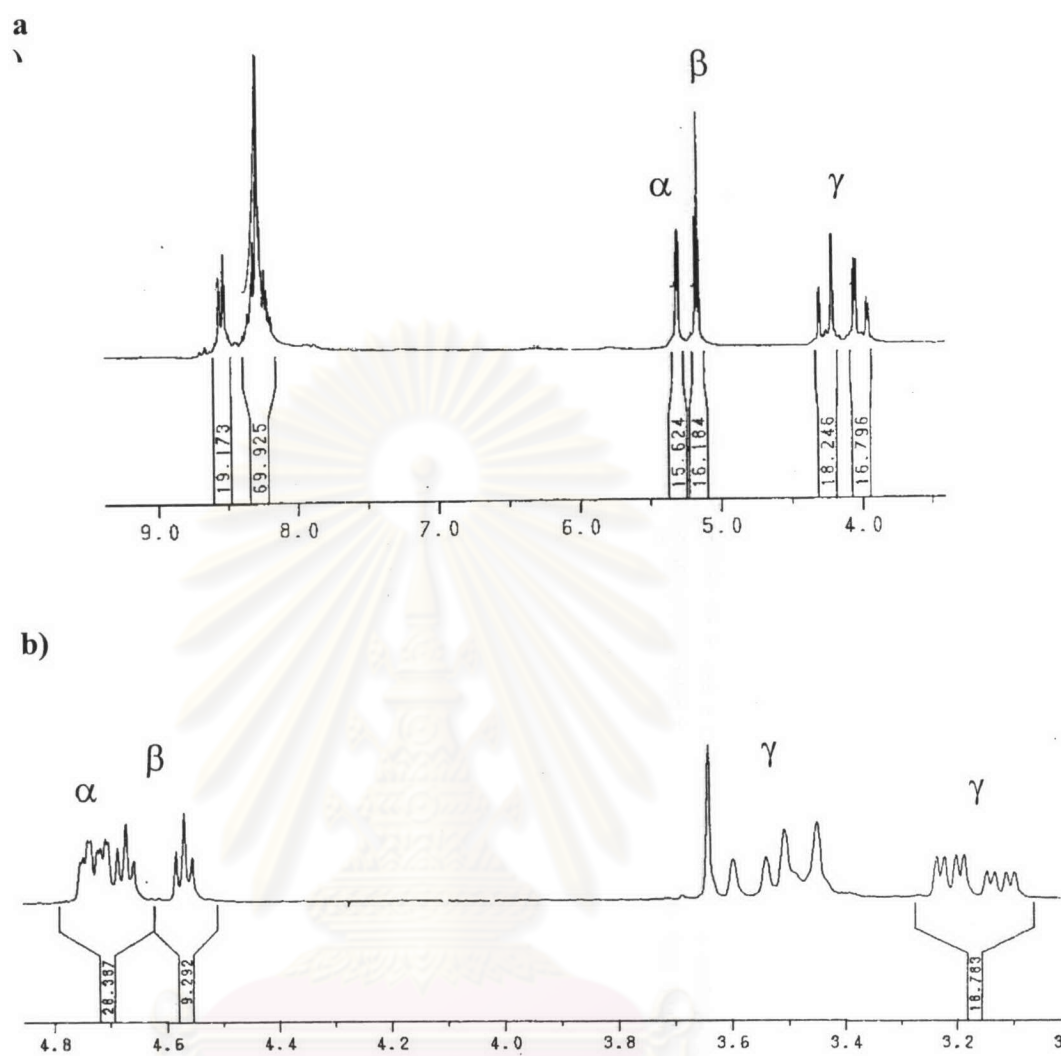
$$\% \text{ ee} = \% \text{ major enantiomer (1R,2S isomer)} - \% \text{ minor enantiomer (1S,2R isomer)}$$



(1R,2S)-Indene oxide



(1S,2R)-Indene oxide



**Figure 2.2** The  $^1\text{H}$ -NMR spectra of racemic indene oxide a) before adding  $\text{Eu}(\text{hfc})_3$  b) after adding  $\text{Eu}(\text{hfc})_3$ .

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#### 2.4.4 The determination of % conversion of alkenes and % yield of epoxide

The gas chromatograph was equipped with a carbowax column. The temperature program was as follows: isothermal at 60 °C for 4 min → 10 °C/min ramp to 160°C → isothermal at 160 °C for 5 min. This GC condition gave satisfactory baseline separation between the alkenes, epoxides and cyclohexanone internal standard (See Appendix). The determination of % conversion and % yield by GC technique was carried out. The % conversion and % yield was calculated by comparing to the integral of known quantity of cyclohexanone internal standard with a correction factor.



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