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 ($CDCl_3$) 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 Varian CP-3800 gas chromatograph instrument equipped with flame ionization detector with N_2 as a carrier gas. The column used for gas chromatograph was CP-Wax 30 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 nickel complexes and all epoxides were purchased from Fluka and Aldrich chemical companies and were used without further purification.

2.3 Synthesis and characterization of nickel reagents

2.3.1 Synthesis of nickel salen and carboxylate complexes

Ni(II) salen, Ni(II) stearate, Ni(II) palmitate and Ni(II) 2-naphthenate were kindly obtained from Mr. Jirasak Imurai and Mr. Adisak Chaitanee [51,52].

2.4 Synthesis of authentic samples

2.4.1 Synthesis of 2-halo-2-phenylethanol (3) and 1-iodododecan-2-ol (11)

LiX (X= Cl, Br) 10 mmol was dissolved in THF 15 mL, followed by the addition of epoxide 5 mmol and $Ni(NO_3)_2 \cdot 6H_2O$ 0.73 g (2.5 mmol). The reaction was refluxed for 6 h. The mixture was extracted with Et_2O 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:EtOAc (8:1) as an eluent.

*2-Chloro-2-phenylethanol (**3a**)*: yellow liquid (77%); ^{1}H-NMR (Fig. A1) ($CDCl_3$) δ (ppm): 7.38 (5H, m), 4.98 (1H, t, *J*= 6.6 Hz), 3.95 (2H, m) and 2.29 (1H, s); ^{13}C-NMR (Fig A2) ($CDCl_3$) δ (ppm): 137.9, 129.9 (2C), 128.8, 127.5 (2C), 67.8 and 64.7.

*2-Bromo-2-phenylethanol (**3b**)*: yellow liquid (89%); ^{1}H-NMR (Fig. A3) ($CDCl_3$) δ (ppm): 7.36 (5H, m), 5.04 (1H, dd, *J*= 6.5, 7.2 Hz), 4.04 (1H, dd, *J*= 7.2, 12.5 Hz), 3.93 (1H, dd, *J*= 6.5, 12.5 Hz) and 2.22 (1H, s); ^{13}C-NMR (Fig A4) ($CDCl_3$) δ (ppm): 138.2, 128.8 (2C), 128.5, 127.9 (2C), 67.6 and 56.9.

*1-Iodododecan-2-ol (**41**)*: brown liquid (97%); ^{1}H-NMR (Fig A5) ($CDCl_3$) δ (ppm): 3.72 (1H, m), 3.51 (1H, s), 3.40 (1H, m), 3.24 (1H, m), 1.55 (2H, q, *J*= 6.8 Hz), 1.26 (16H, s) and 0.88 (3H, t, *J*= 6.8 Hz).

2.4.2 Synthesis of diphenylacetaldehyde [53]

In a separatory funnel was placed a solution of *trans*-stilbene oxide 1.96 g (10 mmol) in 22.5 mL of benzene. To the solution was added $BF_3 \cdot Et_2O$ 0.66 mL (5 mmol). The solution was swirled, allowed to stand for 1 min, and then washed with two 15 mL portions of water. The organic layer was separated, and the residual crude diphenylacetaldehyde was purified by silica gel column chromatography.

*Diphenylacetaldehyde (**12**)*: colorless liquid (82%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 9.91 (1H, d, *J*= 1.7 Hz), 7.33 (10H, m) and 4.89 (1H, d, *J*= 1.7 Hz).

2.4.3 Synthesis of 1-chlorododecan-2-ol (26) [54]

To a stirred solution of 1-dodecene oxide 1 mmol and PPh_3 2 mmol in dry CH_2Cl_2 2 mL was added Cl_3CCONH_2 2 mmol at RT (30 °C) under N_2 atmosphere. After 15 min, H_2O 4 mL was added and the reaction was continuously stirred for 6 h.

The corresponding product was isolated by purification through silica gel column chromatography.

1-Chlorododecan-2-ol (39): colorless liquid (58%); ^{1}H-NMR (Fig. A6) ($CDCl_3$) δ (ppm): 3.80 (1H, s), 3.64 (1H, dd, *J*= 3.1, 11.0 Hz), 3.49 (1H, m), 2.18 (1H, s), 1.52 (2H, m), 1.26 (16H, s) and 0.88 (3H, t, *J*= 6.1 Hz); ^{13}C-NMR (Fig. A7) ($CDCl_3$), δ (ppm): 71.5, 50.6, 34.2, 31.9, 29.6, 29.5, 29.4 (2C), 29.3, 25.5, 22.7 and 14.1.

2.4.4 Synthesis of cyclopentanecarboxaldehyde (31) [55]

In a three-necked flask fitted with reflux condenser, mechanical stirrer, thermometer, and nitrogen gas inlet was placed a solution of H_2SO_4 0.80 g (8.2 mmol) in 30 mL of water. The solution is stirred under nitrogen, and Hg_2SO_4 7.49 g (24.9 mmol) was added to form a suspension of deep-yellow, basic mercuric sulfate. The mixture was stirred and heated to 55°C under nitrogen, and cyclohexene 0.82 g (10 mmol) was added at once. A temperature of 55–65°C was maintained for 1 h. The crude product was removed in a separatory funnel from the aqueous layer, which was extracted with three 0.5 mL portions of Et_2O, dried over anhydrous Na_2SO_4. The cyclopentanecarboxaldehyde was purified by silica gel column chromatography.

Cyclopentanecarboxaldehyde (23): yellow liquid (52%), ^{1}H-NMR ($CDCl_3$) δ (ppm): 9.60 (1H, d, *J*= 2.6 Hz), 2.75 (1H, m) and 1.80 (8H, m).

2.5 Synthesis of starting materials

2.5.1 Synthesis of styrene oxide derivatives and alkyl-epoxides [56].

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. The residue was characterized their identities by ^{1}H-NMR and ^{13}C-NMR spectra that were shown on appendices.

4-Chlorostyrene oxide (5): yellow liquid (64%); ^{1}H-NMR (Fig. A8) ($CDCl_3$), δ (ppm): 7.26 (4H, m), 3.83 (1H, m), 3.14 (1H, m) and 2.75 (1H, m); ^{13}C-NMR (Fig. A9) ($CDCl_3$), δ (ppm): 136.1, 133.9, 128.7 (2C), 126.8 (2C), 51.8 and 51.3.

α-Methylstyrene oxide (7): colorless liquid (quantitative yield); ^{1}H-NMR (Fig. A10) ($CDCl_3$), δ (ppm): 7.33 (5H, m), 2.98 (1H, d, *J*= 5.4 Hz), 2.81 (1H, d, *J*= 5.4 Hz) and 1.72 (3H, s); ^{13}C-NMR (Fig. A11) ($CDCl_3$), δ (ppm): 141.2, 128.3 (2C), 127.5, 125.3 (2C), 57.0 and 21.8.

4-Chloro-α-methylstyrene oxide (9): colorless liquid (90%); ^{1}H-NMR (Fig. A12) ($CDCl_3$), δ (ppm): 7.27 (4H, m), 2.95 (1H, d, *J*= 5.3 Hz), 2.73 (1H, d, *J*= 5.3 Hz) and 1.67 (3H, s); ^{13}C-NMR (Fig. A13) ($CDCl_3$), δ (ppm): 139.8, 133.2, 128.4 (2C), 126.8 (2C), 57.0, 56.3 and 21.6.

1,1-Diphenylethylene oxide (11): yellow oil (87%); ^{1}H-NMR (Fig. A14) ($CDCl_3$), δ (ppm): 7.36 (10H, m) and 3.31 (2H, s).

Anethole oxide (14): yellow liquid (77%); ^{1}H-NMR (Fig. A15) ($CDCl_3$), δ (ppm): 6.99 (4H, m), 3.74 (3H,s), 3.48 (1H, s), 2.99 (1H, m) and 1.39 (3H, d, *J*= 5.2 Hz); ^{13}C-NMR (Fig. A16) ($CDCl_3$), δ (ppm): 159.6, 129.6, 126.9 (2C), 113.8 (2C), 59.3, 58.7, 55.2 and 17.8.

Methyl-cyclohexene oxide (25): colorless liquid (89%); ^{1}H-NMR (Fig. A17) ($CDCl_3$), δ (ppm): 2.89 (1H, s), 1.81 (3H, m), 1.60 (2H, m), 1.36 (3H, m) and 1.23 (3H, s); ^{13}C-NMR (Fig. A18) ($CDCl_3$), δ (ppm): 59.5, 57.5, 29.8, 24.7, 23.9, 19.9 and 19.6.

4-(3,3-Dimethyloxiran-2-yl)butan-2-one (37): colorless liquid (74%); ^{1}H-NMR (Fig. A19) ($CDCl_3$), δ (ppm): 2.62 (1H, m), 2.51 (2H, m), 2.06 (3H,s), 1.79 (1H, m), 1.54 (1H, m) and 1.18 (6H, d, *J*= 9.6 Hz).

2.6 The general procedure for the rearrangement of epoxides

The solution of epoxide 1 mmol in THF (5 mL) containing a nickel reagent (0.5 mmol) in a round bottom flask was stirred at reflux temperature for 2 h. After the specific time or the reaction was completed (followed by TLC), 1 mL of the reaction mixture was taken and extracted with Et_2O. Finally, it 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 styrene oxide rearrangement

2.7.1 Effect of types of nickel reagents

The rearrangement of styrene oxide was carried out employing $NiCl_2$ (anhydrous), $NiCl_2 \cdot 6H_2O$, $NiBr_2 \cdot 3H_2O$, NiI_2 (anhydrous), $NiCl_2(PPh_3)_2$, $NiBr_2(PPh_3)_2$, Ni(stearate)$_2$, Ni(palmitate)$_2$, Ni(naphthenate)$_2$, Ni(acac)$_2$, Ni(salen), $NiSO_4 \cdot 6H_2O$ or $Ni(NO_3)_2 \cdot 6H_2O$ as a reagent.

2.7.2 Effect of solvent

The rearrangement of styrene oxide by $NiBr_2 \cdot 3H_2O$ was carried out in the same manner as previously described but changing the reaction medium from toluene to various solvents, namely hexane, CH_2Cl_2, 1,2-DCE, THF, EtOAc, 1,4-dioxane and CH_3CN.

2.7.3 Effect of time and temperature

The rearrangement of styrene oxide was performed according to the general procedure mentioned earlier using $NiBr_2 \cdot 3H_2O$ as a reagent, but different reaction temperatures (50°C, reflux temperature) and reaction times (5 min, 15 min, 30 min, 1 h, 2 h, 4 h, 6 h, 24 h) were varied.

2.7.4 Effect of the amount of $NiBr_2 \cdot 3H_2O$

The rearrangement of styrene oxide was carried out by different amount of $NiBr_2 \cdot 3H_2O$ (0.1, 0.25, 0.5 and 1 mmol).

2.8 Rearrangement of various selected epoxides

Selected epoxides including 4-chlorostyrene oxide, α-methylstyrene oxide, 4-chloro-α-methylstyrene oxide, 1,1-diphenylethylene oxide, *trans*-stilbene oxide, anethole oxide, methyl*trans*-3-(4-methoxyphenyl)-glycidate, 1-dodecene oxide, cyclohexene oxide, methyl-cyclohexene oxide, butyl glycidyl ether, *tert*-butyl glycidyl ether, phenyl glycidyl ether, epichlorohydrin and 4-(3,3-dimethyloxiran-2-yl)butan-2-one were subjected to this developed rearrangement system by nickel reagents. Other procedures were carried out as previously described.

2.9 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. The residue was characterized their identities by ^{1}H-NMR and ^{13}C-NMR spectra that were reported on appendices.

Phenylacetaldehyde (2): colorless oil; ^{1}H-NMR (Fig. 3.1) ($CDCl_3$), δ (ppm): 9.75 (1H, s), 7.31 (5H, m) and 3.68 (2H, s); ^{13}C-NMR (Fig. 3.2) ($CDCl_3$), δ (ppm): 199.8, 133.5, 129.6 (2C), 129.0 (2C), 127.4 and 50.5.

4-Chloro phenylacetaldehyde (6): yellow oil; ^{1}H-NMR (Fig. A20) ($CDCl_3$), δ (ppm): 9.74 (1H, s), 7.25 (4H, m) and 3.69 (2H, d, *J*= 1.8 Hz); ^{13}C-NMR (Fig. A21) ($CDCl_3$), δ (ppm): 198.7, 130.9 (2C), 129.7, 129.1 (2C), 128.8 and 49.8.

Hydratropaldehyde (8): colorless liquid; ^{1}H-NMR (Fig. A22) ($CDCl_3$), δ (ppm): 9.70 (1H, s), 7.37 (5H, m), 3.66 (1H, q, *J*= 7.0 Hz) and 1.49 (3H, d, *J*= 7.0 Hz); ^{13}C-NMR (Fig. A23) ($CDCl_3$), δ (ppm): 201.2, 137.8, 129.1 (2C), 128.4 (2C), 127.6, 53.0, and 14.7.

4-Chlro-α-hydratropaldehyde (10): colorless liquid; ^{1}H-NMR (Fig. A24) ($CDCl_3$), δ (ppm): 9.66 (1H, d, *J*= 1.3 Hz), 7.25 (4H, m), 3.62 (1H, q, *J*= 7.1 Hz) and 1.43 (3H, d, *J*= 7.1 Hz).

(ρ-Methoxyphenyl)acetone (15): deep yellow oil; ^{1}H-NMR (Fig. A25) ($CDCl_3$), δ (ppm): 6.98 (4H, m), 3.78 (3H, s), 3.61 (2H, s) and 2.12 (3H, s); ^{13}C-NMR (Fig. A26) ($CDCl_3$), δ (ppm): 207.0, 158.6, 130.4 (2C), 126.3, 114.2 (2C), 55.2, 50.1 and 29.1.

Methyl-3-hydroxy-2-(4-methoxyphenyl)acrylate (17): deep yellow oil; ^{1}H-NMR (Fig. A27) ($CDCl_3$), δ (ppm): 7.30 (4H, m), 6.49 (1H, s), 3.87 (3H, s) and 3.80 (3H, s).

Laurinaldehyde (19): colorless liquid; ^{1}H-NMR (Fig. A28) ($CDCl_3$), δ (ppm): 9.75 (1H, s), 2.41 (2H, dt, *J* = 1.7, 7.4 Hz), 1.61 (2H, m), 1.24 (16H, s) and 0.87 (3H, t, *J* = 6.8 Hz); ^{13}C-NMR (Fig. A29) ($CDCl_3$), δ (ppm): 202.5, 43.8, 39.9, 29.6 (2C), 29.4, 29.3 (2C), 29.1, 22.6, 22.0 and 13.4.

1-Bromododecan-2-ol (20): colorless liquid; ^{1}H-NMR (Fig. A30) ($CDCl_3$), δ (ppm): 3.76 (1H, m), 3.53 (1H, dd, *J*= 3.1, 10.2 Hz), 3.37 (1H, dd, *J*= 7.1, 10.2 Hz),

2.24 (1H, s), 1.53 (2H, m), 1.25 (16H, s) and 0.87 (3H, t, *J*= 6.5 Hz); ^{13}C-NMR (Fig. A31) ($CDCl_3$), δ (ppm): 71.1, 40.5, 35.1, 31.9, 29.6, 29.49 (3C), 29.3, 25.6, 22.7 and 14.1.

*2-Bromocyclohexanol (**24**)*: yellow liquid; ^{1}H-NMR (Fig. A32) ($CDCl_3$), δ (ppm): 3.88 (1H, m), 3.58 (1H, m), 2.66 (1H, s), 2.32 (1H, m), 2.11 (1H, m), 1.76 (3H, m) and 1.31 (3H, m); ^{13}C-NMR (Fig. A33) ($CDCl_3$), δ (ppm): 75.3, 61.7, 36.2, 33.5, 26.6 and 24.1.

*2-Methyl-1-cyclohexanone (**26**)*: colorless liquid; ^{1}H-NMR (Fig. A34) ($CDCl_3$), δ (ppm): 2.37 (2H, m), 2.29 (1H, m), 2.06 (2H, m), 1.82 (1H, m), 1.68 (1H, m), 1.66 (1H, m), 1.38 (1H, m) and 1.01 (3H, d, *J*= 6.6 Hz); ^{13}C-NMR (Fig. A35) ($CDCl_3$), δ (ppm): 213.8, 45.4, 41.8, 36.2, 27.9, 25.2 and 14.7.

*2-Bromo-1-methylcyclohexanol (**27**)*: colorless liquid; ^{1}H-NMR (Fig. A36) ($CDCl_3$), δ (ppm): 4.14 (1H, dd, *J*= 4.2, 11.6 Hz) , 2.24 (1H, m), 1.98 (1H, m), 1.85 (1H, m), 1.70 (2H, m), 1.51 (1H, m), 1.43 (1H, m), 1.38 (1H, m) and 1.34 (3H, s); ^{13}C-NMR (Fig. A37) ($CDCl_3$), δ (ppm): 72.6, 66.2, 39.3, 37.2, 34.8, 26.3 and 22.9.

*1-Bromo-3-butoxypropan-2-ol (**30**)*: yellow liquid; ^{1}H-NMR (Fig. A38) ($CDCl_3$), δ (ppm): 3.94 (1H, m), 3.49 (6H, m), 2.67 (1H, d, *J*= 5.7 Hz), 1.55 (2H, m), 1.36 (2H, m) and 0.91 (3H, t, *J*= 7.3 Hz); ^{13}C-NMR (Fig. A39) ($CDCl_3$), δ (ppm): 71.8, 71.4, 69.9, 35.1, 31.6, 19.2 and 13.9.

*1-Bromo-3-tert-butoxypropan-2-ol (**32**)*: yellow liquid; ^{1}H-NMR (Fig. A40) ($CDCl_3$), δ (ppm): 3.89 (1H, m), 3.48 (4H, m), 2.68 (1H, d, *J*= 6.0 Hz) and 1.19 (9H, s); ^{13}C-NMR (Fig. A41) ($CDCl_3$), δ (ppm): 73.5, 70.2, 62.8, 35.0 and 27.5 (3C).

*1-Bromo-3-phenoxypropan-2-ol (**34**)*: yellow liquid; ^{1}H-NMR (Fig. A42) ($CDCl_3$), δ (ppm): 7.32 (2H, m), 6.98 (3H, m), 4.19 (1H, m), 4.09 (2H, m), 3.63 (2H, m) and 3.22 (1H, s); ^{13}C-NMR (Fig. A43) ($CDCl_3$), δ (ppm): 158.2, 129.6 (2C) , 121.5, 114.6 (2C) , 69.6, 69.2 and 35.0.

*1-Bromo-3-chloropropanol (**36**)*: colorless liquid; ^{1}H-NMR (Fig. A44) ($CDCl_3$), δ (ppm): 4.02 (1H, m), 3.68 (2H, m), 3.55 (2H, m) and 2.93 (1H, s); ^{13}C-NMR (Fig. A45) ($CDCl_3$), δ (ppm): 70.5, 46.5 and 34.8.

*6-methylheptane-2,5-dione (**38**)*: yellow liquid; ^{1}H-NMR (Fig. A46) ($CDCl_3$), δ (ppm): 2.73 (4H, m), 2.66 (1H, m), 2.20 (3H, s) and 1.12 (6H, d, *J*= 6.9 Hz).