CHAPTER III

EXPERIMENT

3.1 Preparation of Alcohol Derivatives

All chemicals and solvents were purchased from Aldrich and Fluka and were used without further purification. Some chiral alcohols were obtained commercially. However, most of alcohol racemates were prepared from reduction of ketones with sodium borohydride in ethanol. Acetophenones with substitutents at *o*-, *m*- and *p*-position of the phenyl group were used as substrate. Different types of substitutents include fluoro, chloro, bromo, methyl, methoxy, hydroxy, nitro, and cyano. The progress of the synthesis was followed by thin layer chromatography (TLC aluminum sheet, silica gel 60 F_{254}, Merck) under UV light at 254 nm. The alcohol products were confirmed by IR spectroscopy (Perkin Elmer 1600 series) and NMR spectroscopy (Bruker ACF200 and Varian 360A). The chiral alcohols and ketones used in this study are:

3-acetylbenzonitrile, 97% (Aldrich)

4-acetylbenzonitrile, 98% (Fluka)

2′-bromoacetophenone, 99% (Aldrich)

3′-bromoacetophenone, 99% (Aldrich)

4-bromo-α-methylbenzyl alcohol, 97% (Aldrich)

4′-bromo-2,2,2-trifluoroacetophenone, 98% (Fluka)

2′-chloroacetophenone, 97% (Aldrich)

3-chloroacetophenone, 97% (Fluka)

1-(4-chlorophenyl)ethanol, 98% (Aldrich)

4′-chloro-2,2,2-trifluoroacetophenone, 98% (Fluka)

2-fluoroacetophenone, 97% (Fluka)

3′-fluoroacetophenone, 99% (Aldrich)

4-fluoro-α-methylbenzyl alcohol, 99% (Aldrich)

2′-hydroxyacetophenone, 99% (Aldrich)

3′-hydroxyacetophenone, 97% (Aldrich)

4-hydroxyacetophenone, 98% (Fluka)

2-methoxyacetophenone, 99% (Fluka)

3-methoxyacetophenone, 97% (Fluka)

4-methoxyacetophenone, 99% (Fluka)

2-methylacetophenone, 98% (Fluka)

3-methylacetophenone, 97% (Fluka)

4-methylacetophenone, 95% (Fluka)

2-nitroacetophenone, 95% (Fluka)

3-nitroacetophenone, 98% (Fluka)

4-nitroacetophenone, 97% (Fluka)

1-phenylethanol, 98% (Fluka)

2,2,2,4′-tetrafluoroacetophenone, 98% (Fluka)

3.1.1 2-fluoro-α-methylbenzyl alcohol

2-Fluoroacetophenone 2.008 g (0.01 mol) and sodium borohydride ($NaBH_4$) 0.4 g (0.02 mol) were dissolved in 20 mL ethanol. The mixture was refluxed for 3 hours. The reaction mixture was then cooled and the solvent was removed by rotary evaporator. The white precipitate was dissolved in 2 M hydrochloric acid. Then the aqueous phase was extracted with chloroform. All organic layers were combined, dried with anhydrous sodium sulfate and evaporated to dryness, yielding a colorless liquid of 2-fluoro-α-methylbenzyl alcohol (1.828 g, 89.7%).

All other 1-phenylethanol derivatives were prepared using the above-described method, except hydroxy-substituted 1-phenylethanol.

3.1.2 2-hydroxyl-α-methylbenzyl alcohol

A solution of 2′-hydroxyacetophenone 0.500 g (3.67 mmol) in 10 mL ethanol was added dropwise into a mixture of $NaBH_4$ 0.55 g (14.7 mmol) and 20 mL ethanol chilled in an ice bath. The reaction mixture was stirred at room temperature for 2 hours and then refluxed for 1 hour. The solvent was removed by rotary evaporator. The white precipitate was dissolved in 2 M hydrochloric acid and worked up using the same procedure described in 3.1.1. A pale yellow solution was obtained and purified by column chromatography with EtOAc-CH_2Cl_2 1:9 → 1:1 → 10:0 as eluent.

3.2 Capillary Column Coating

Cyclodextrin derivatives were diluted in polysiloxane matrix before using as stationary phases. Two types of cyclodextrin derivatives employed for chiral separations are:

- heptakis(2,3-di-*O*-methyl-6-*O*-*tert*-butyldimethylsilyl)cyclomaltoheptaose (BSiMe): received from Professor Gyula Vigh
- heptakis(2,3,6-tri-*O*-methyl)cyclomaltoheptaose (BMe): in-house synthesis

Capillary gas chromatographic columns were prepared by statically coating [36] fused silica tubing (deactivated, 33 m long, 0.25 mm i.d., J&W Scientific) with a solution of stationary phase (0.4% w/v) to obtain a film thickness of 0.25 μm. Two chiral columns contained identical cyclodextrin concentration of 0.12 M in polysiloxane OV-1701 (14%cyanopropylphenyl 86%dimethylpolysiloxane, Supelco). All columns were conditioned at 200 °C until a stable baseline was observed. Column characteristics were evaluated by Grob test [37] and by determining the column efficiency at different temperatures with *n*-alkanes. Three capillary GC columns used in this study are:

- achiral reference column: OV-1701
- chiral BSiMe column: 25.5% (w/w) of BSiMe in OV-1701
- chiral BMe column: 17% (w/w) of BMe in OV-1701

3.3 Gas Chromatographic Analyses

All chromatographic separations were performed on a gas chromatograph (Agilent 6890) equipped with a split/splitless injector and a flame ionization detector (FID). Hydrogen was used as carrier gas at an average linear velocity of 52 cm/sec (measured by injecting methane as unretained compound). Injector (split ratio of 100:1) and detector were maintained at 250 °C. All analyses were performed isothermally in the temperature range of 130-200 °C at 10 °C interval (at least in duplicate).

Thermodynamic data were calculated by both method A and B. In method A, thermodynamic parameters were calculated from retention factors and separation factors obtained from each cyclodextrin derivative-containing column. Relative retentions, which obtained from chiral columns and a reference column using *n*-alkanes (decane, undecane, and dodecane) as reference compounds, were used to calculate the retention increment and the thermodynamic parameters in method B.