CHAPTER V

CONCLUSION AND SUGGESTION FOR FUTURE WORK

Fourty-six racemic phenoxy acid methyl esters with different type, position, and number of substituent were synthesized. The separation of enantiomers of the synthesized esters was studied by gas chromatography using two chiral stationary phases containing modified β-cyclodextrins: heptakis(2,3-di-*O*-methyl-6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (or BSiMe) and heptakis(2,3-di-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (or BSiAc). Both derivatized cyclodextrins possess identical ring size and 6-*O*-*tert*-butyldimethylsilyl substituents, but have different substituents at C2 and C3 chiral carbons. Approximately 93% of chiral analytes could be successfully enantioseparated with either BSiMe or BSiAc, or both columns. Most analytes could be completely enantioresolved by BSiMe derivative with higher degree of separation than by BSiAc derivative. The higher enantioresolution of BSiMe is probably ascribed to the appropriate orientation of cyclodextrin derivative and analyte structure to form a diastereomeric intermediate during enantiorecognition process.

The gas chromatographic results were used to calculate thermodynamic parameters for the association between chiral analytes and cyclodextrin derivatives to realize the influence of analyte and selector structures on enantiorecognition. The $-\Delta H_2$ and $-\Delta S_2$ values acquired from each chiral column exhibited similar trend, with a few exceptions. Besides, these values of all analytes on the same column are relatively comparable demonstrating that the main analyte contributions to the interaction arise from ester and phenyl groups. From thermodynamic data obtained by van't Hoff approach, the $-\Delta H$ and $-\Delta S$ values of analytes on two chiral columns are greater than those on a nonchiral polysiloxane column, indicating stronger interaction and more interaction sites between analytes and cyclodextrin derivatives. Nonetheless, the interaction strength does not necessarily correlate with the discrimination of enantiomers, since some analytes showing strong interaction with stationary phase do not exhibit high enantioseparation.

On BSiMe phase, the type of substituent played a major role in enantiomeric separations. The small and highly electronegative substituents, such as fluoro and trifluoromethyl, on an aromatic ring of analytes tend to promote enantioresolution, while the highly polar and bulky substituents are likely to decrease enantioresolution. These were obviously observed in halogen-substituted analytes. The substitution at *ortho*- or *para*-position of the aromatic ring seems to enhance the enantiorecognition, while substitution at *meta*-position tends to diminish the enantiorecognition of most analytes. Among all tested analytes, methyl 2-(4′-trifluoromethyl)propanoate (**4CF$_3$**) show the highest degree of enantioseparation (largest -Δ(ΔH) and -Δ(ΔS) values).

On BSiAc column, the enantioseparations were quite opposite from those observed on BSiMe column. The enantioseparations of most *meta*-substituted analytes on BSiAc column were improved and the -Δ(ΔH) values were higher than on BSiMe. Many poorly separated analytes on BSiMe could be efficiently resolved on BSiAc column. Of all analytes, the methyl substituted analytes tended to exhibit higher -Δ(ΔH) values than others, suggesting that methyl group probably promoted the enantiorecognition of esters on this stationary phase.

Furthermore, the differences in enantioseparation of phenoxy acid methyl esters on BSiMe and BSiAc columns came from the difference in substitution at C2 and C3 chiral carbons of cyclodextrin molecule, which results in different shape and position favorable for interaction with particular analytes. In addition, a preliminary study of the number of aromatic substituent towards enantioseparation on both chiral columns was carried out as well. Due to the unavailability of many poly-substituted analytes, the complete effect of number of substituent on the enantioseparation could not be achieved.

All the above results demonstrated that the differences in retention and degree of separation of all of phenoxy acid methyl ester enantiomers on BSiMe and BSiAc columns depended on several factors, such as type, position and number of substituent on the aromatic ring as well as type of substituent on cyclodextrin ring.

Hopefully, further study with larger number of phenoxy acid methyl ester analytes with various substitution patterns as well as molecular modeling experiments will lead to precise assumption about analyte-stationary phase interaction and better understanding of enantiorecognition mechanism.