CHAPTER V

CONCLUSIONS

A number of 1-phenylethanol derivatives were prepared with substituents of different type (e.g. F, Cl, Br, Me, OMe, NO_2, and CN) at various position (*ortho*, *meta*, and *para*) on an aromatic ring as well as with trifluoromethyl group, instead of methyl, at the chiral center of molecule. Chiral gas chromatographic separation of 1-phenylethanol and its derivatives were then examined on two chiral columns containing modified β-cyclodextrins dissolved in moderately polar polysiloxane solvent. The chiral selectors used are heptakis(2,3,6-tri-*O*-methyl)cyclomaltoheptaose (or BMe) and heptakis(2,3-di-*O*-methyl-6-*O*-*tert*-butyldimethylsilyl)cyclomalto heptaose (or BSiMe), both having identical number of glucose units and *O*-methyl substituent at chiral carbons of CD molecule but possessing substituent of different size at the C6 nonchiral carbons. The information acquired from the gas chromatographic experiments, e.g. retention factors and separation factors, were used to calculate thermodynamic parameters for the association between chiral analytes and CD derivatives in order to realize the effect of analyte and selector structures on retention and enantioselectivity.

Retention factors of all 1-phenylethanol derivatives on three columns (OV-1701, BSiMe and BMe) were greater than that of 1-phenylethanol and these values increased with increasing molecular weight and polarity of substituent. Furthermore, all chiral substances were more retained on modified CD columns than on nonchiral, OV-1701 column. However, retention factors and enantioselectivities do not exhibit the same trend. Often, compounds with high retention do not display large enantioselectivity.

Enthalpy and entropy values of chiral analytes revealed more detail involving the interaction between enantiomers and stationary phases. Enthalpy and entropy values calculated by method A correspond to the total interaction of chiral analyte with modified cyclodextrin and polysiloxane solvent. Comparing enthalpy and entropy values of the more retained enantiomers obtained from BSiMe and BMe

columns, it can be seen that $-\Delta H_2$ and $-\Delta S_2$ values of most analytes on both columns are very similar to those of 1-phenylethanol. This indicates that the main contribution rather occurs from primary functional group (aromatic alcohol) than the substituent.

On the other hand, thermodynamic parameters obtained by method B detailed only the interaction between enantiomers and chiral selector, modified CD. Enthalpy and entropy values of *ortho*-substituted derivatives were slightly higher than the remaining compounds. Moreover, values obtained for compounds analyzed on BSiMe column were greater than those on BMe column. This is possibly due to the additional interaction with the *tert*-butyldimethylsilyl group of BSiMe.

Enthalpy and entropy differences of enantiomeric pairs of all chiral analytes correlate to the degree of separation. It is evident that compounds with substituent at the *ortho*-position show highest enantioselectivities. These effects could be observed on both columns regardless the method of calculation. Nonetheless, the enthalpy and entropy differences of the *ortho*-substituted compounds are slightly higher on BSiMe column. This could be attributed to the *tert*-butyldimethylsilyl group at C6 carbons of BSiMe, which causes the cavity to narrow and obstructs the opening at the primary face of CD molecule. These changes in CD structure could result in a tighter fixation of analyte in the cavity and; consequently, a superior size and shape selectivity of BSiMe.

In general, it can be summarized that the position of substituent played a key role on enantioselectivity. Chiral analytes with *ortho*-substituent, regardless the type of substituent, appear to offer enhanced selectivity on both types of CD derivatives. The effect of substituent size could be clearly noticed only with the halogen, where larger substituent size yielded larger enantioselectivity. For better understanding of this size effect, a larger group of compounds of different type (e.g. electron donating, electron withdrawing) should be examined.

For the α-trifluoromethyl derivatives, it can be assumed that the methyl group at the α-position is essential for the resolution on BSiMe. Still, more compounds of this type should be investigated and compared with the α-methyl homologues. The

results from α-trifluoromethyl derivatives also indicated the importance of the modification on the nonchiral face of CD molecule, which may result in structural change and impact on enantioselectivity. Therefore, molecular modeling may be helpful to gain better understanding of the chiral recognition process of CDs.