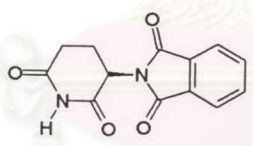
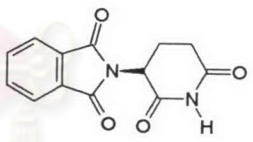
CHAPTER I

INTRODUCTION

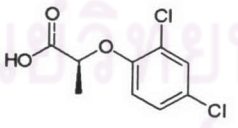
Nowadays, enantiomeric separation interested many scientists since most of natural organic and chemical products that are closely related to human health, particularly pharmaceuticals, are asymmetric molecules. Enantiomers are molecules with nonsuperimposable mirror image structures and are often viewed as a single entity because they posses identical physical and chemical properties, except for the direction of rotation polarized light. Enantiomers, however, can exhibit distinct chemical behaviors when they are subjected to a chiral environment. Scientific studies have demonstrated that stereochemistry is very important for the biological activities of chiral drugs, agrochemicals, food additives, fragrances, amino acids, and more [1-2]. For example, (*R*)-thalidomide could be used as a sedative drug whereas its (*S*)-enantiomer causes fetal abnormality [3]. (*R*)-Dichlorprop exhibits herbicidal property, but (*S*)-dichlorprop is inactive [4]. Another example is limonene; (*R*)-enantiomer smells likes orange, while the other enantiomer gives a lemon-like smell [5].



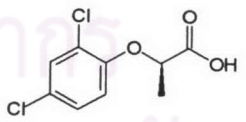
(*R*)-(+)-thalidomide



(*S*)-(-)-thalidomide



(*R*)-(+)-dichlorprop



(*S*)-(-)-dichlorprop

(*R*)-(+)-limonene

(*S*)-(-)-limonene

Figure 1.1 Chemical structures of thalidomide, dichlorprop, and limonene

The great importance of chirality was also reflected in the pharmaceutical market as the use of racemic drugs has been reduced from 32% to 8% in the last two decades. Concurrently, the use of single enantiomer drugs has been increased from 25% to 58% [6]. Thus, the investigation of the activity, toxicity, and metabolic pathways of both enantiomers is necessary. The development of asymmetric synthesis is important for the derivation of desired pure enantiomer. Appropriate techniques such as polarimetry, nuclear magnetic resonance spectroscopy, chromatography or capillary electrophoresis are employed to investigate enantiomeric purity. Among these, gas chromatography (GC) is a preferred technique to analyze enantiomeric composition of small, volatile, and thermostable organic compounds because of its high efficiency, sensitivity, and short analysis time [2, 7-9]. Furthermore, this technique can reduce the consumption of many organic solvents, which help reducing the analysis cost and protecting the environment. Generally, a number of cyclodextrin (CD) derivatives have been widely and successfully utilized as chiral stationary phases [7, 9]. However, most chiral separations have been performed through trial and error, and extensive experience is generally required. Since the enantioseparation mechanisms of cyclodextrins are extremely complicated and are not well understood, the relationship between the structure of each cyclodextrin derivative and analytes still need more investigation.

The parameters affecting enantiomeric separation are the types and concentration of CD derivatives, the polarity of polysiloxane, and the nature of analyte structures. The study of enantiomeric separation by varying analyte structure instead of chiral stationary phase seems to be the easiest way to vary in chiral separation system. In the past, there are only a few studies into the relationships between enantioselectivity of CD derivatives and chiral analytes [10-14]. Therefore, this research aims to systematically examine the influence of analyte structure on the enantiomeric separation.

Alcohols were selected as the analytes of interest owing to their significance as building block in many synthetic reactions. Furthermore, chiral alcohols are important component of pheromone systems of various insect species [2, 15]. Alcohol derivatives based on the structure of 1-phenylethanol, i.e. with different type and number of substituents on aromatic ring, different type and number of side chain substituents, as well as different base structure, are separated by gas chromatography using heptakis (2,3-

di-*O*-methyl-6-*O*-*tert*-butyldimethylsilyl)cyclomaltoheptaose (or BSiMe) and octakis(2,3-di-*O*-methyl-6-*O*-*tert*-butyldimethylsilyl)cyclomaltooctaose (or GSiMe) as chiral selectors. BSiMe has proved to be among successful chiral selectors for GC, while GSiMe, having similar derivatization as BSiMe, has not been extensively explored. Both of them are mixed separately in polysiloxane OV-1701 and used as chiral stationary phases. Thermodynamic parameters attained through van't Hoff approach are used to evaluate the interaction between analytes and stationary phase as well as the enantiodifferentiation. Hopefully, the information derived from this work will be valuable for selecting suitable chiral stationary phase and separation condition for chiral recognition of these alcohol derivatives, including other alcohols having similar structure.