8 Cyclodextrin inclusion complexation

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8.1 Structure of cyclodextrin

The type of bonded phase for HPLC based on the class of oligosaccharides known as cyclodextrins employs inclusion complexing to achieve chiral selectivity. How inclusion complexing accomplishes this is best understood by examining the physical structure of cyclodextrins. Cyclodextrins are toroidally shaped molecules containing from six to twelve glucose units bonded through α-(1,4) linkages (Figure 8.1). The physical shape of the molecule is that of a

Figure 8.1 Cyclodextrin molecule.
truncated cone, the internal diameter of which is proportional to the number of glucose units. Due to the orientation of the glucose units, there are no hydroxyls on the interior cavity and it is therefore relatively hydrophobic. Each glucose unit contributes five chiral centres to the molecule, and the 2-hydroxyl groups at the entrance of the cavity are orientated in a clockwise direction. This can best be appreciated by studying Figure 8.2 which shows the geometry of β-cyclodextrin.

8.2 Mechanism of chiral separation

Chiral separations require the solute molecule to enter the hydrophobic cavity in such a way as to place the centre of asymmetry in association with the polar hydroxyl groups at the edge of the cavity. Where there is no association between these polar groups and the groups attached to or near the solute’s chiral centre, separation is minimal or nil. Generally it is not the degree or nature of the penetration into the cyclodextrin cavity that is the main criterion for resolution to occur, but the existence of interaction between the secondary hydroxyls and the guest molecule.

For a racemic molecule to be resolved into its enantiomers there must be a difference in stability of the inclusion complex formed for each isomer. This inclusion complex and the subsequent interaction is shown simply in Figure 8.3.