1960s, Thalidomide was widely prescribed as a sleeping pill and as a treatment for morning sickness, with claims that it was completely safe. We all know of the terrible birth defects suffered by children born to mothers who took the drug during pregnancy. The drug was taken as the racemate, and it has been shown that the R-enantiomer is responsible for the drug's anti-inflammatory activity, whereas the S-enantiomer causes the teratogenicity. Separation of the racemic mixture to give the patient only the R-enantiomer is not a simple answer to the problem. The liver contains an enzyme that converts the R- into the *S*-enatiomer, thus negating the benefit of giving the single enantiomer (4).

As described in this chapter, there are many reactions that can be performed by chemists to create new chiral centers. When these reactions are performed in such a way as to create one enantiomer in greater amounts than the other the process is called asymmetric or stereoselective synthesis. The term enantioselectivity refers to the efficiency with which the reaction produces one enantiomer. This efficiency is quantitatively described as the enantiomeric excess (ee) of the product, which is the percentage by which one enantiomer is produced in excess of the other. Thus a 45:8 mixture of two enantiomers will have an enantiomeric excess of $[(45 - 8)/(45 + 8)] \times 100$, which equals 70%. It should be noted that if neither the starting material or reaction system is chiral and non-racemic, then the product will be formed as an equal mixture of the enantiomers (i.e., a racemate).

Glucose is perhaps the most widely available chiral compound. It is a monosaccharide and part of the sugar group (carbohydrates) that occur naturally. Sugars, along with amino acids, constitute a special example and are commonly classified with a D- or L-configuration. In the case of sugars, the D-configuration is given when the hydroxyl group on the highest numbered chiral carbon atom is on the righthand side (with the structure drawn in the Fischer convention as shown in Fig. 18.3). Likewise for L-configured sugars, the hydroxyl group is on the lefthand side. In the case of the tetrose sugars there are two enantiomer pairs as illustrated in Fig. 18.3. Here, the enantiomer pairs of erythrose (4, 5), namely D-(−)-erythrose (4), and L-(+)-erythrose (5), and threose (6, 7), and L-(−)-threose (6) and D-(+)-threose (7), are shown, with each pair of enantiomers being diasteromeric with the other pair. Diastereomers can be simply defined as stereoisomers that are not enantiomers. The prefixes *erythro*- and *threo*- are applied to such systems that contain two asymmetric carbons where two of the groups are identical and the third is different. The *erythro* pair has the identical groups on the same side, whereas the *threo* pair has them on opposite sides.

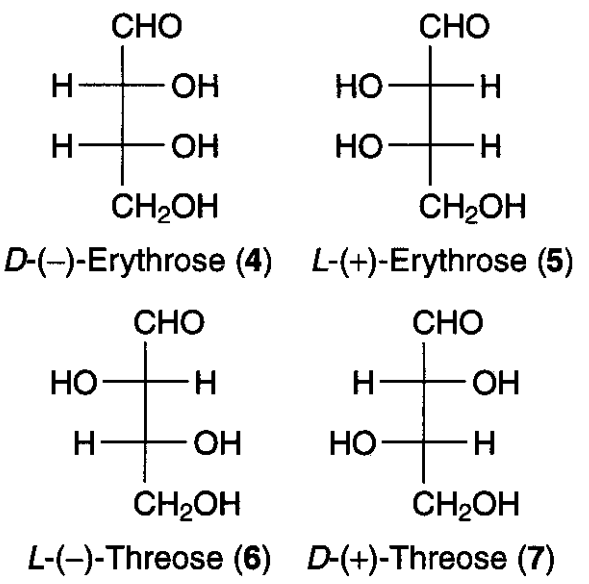

Figure 18.3.

Finally, as further elucidation of this relationship where the molecule contains more than one chiral center the number of stereoisomers increases. In the case of the drug glycopyrrolate which contains two chiral centers, there are four possible stereoisomers as shown in Fig. 18.4. In general, the number of possible isomers can be calculated from the formula 2^n where n is the number of chiral centers.

The four stereoisomers can be divided as shown into two pairs of enantiomers, where the (*R*,*R*)-(8) and (*S*,*S*)-(9) stereoisomers are enantiomers of one another, and the (*S*,*R*)-(10) and (*R*,*S*)-(11) stereoisomers are also an enantiomeric pair. The stereoisomers that do not have an enantiomeric relationship to one another, such as (*R*,*R*)-(8) and (*R*,*S*)-(11) are known as diastereomers. Like enantiomers, these molecules are not superimposable on one another, but unlike enantiomers, they do not exhibit the same physical, chemical, and spectral characteristics. Thus, they have different melting/boiling points, lipid solubility,