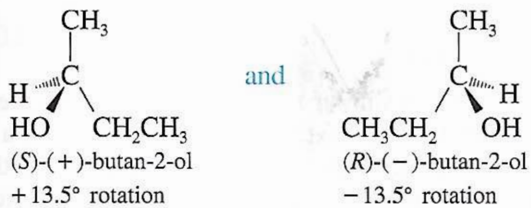
5-6 Racemic Mixtures

Suppose we had a mixture of equal amounts of (+)-butan-2-ol and (−)-butan-2-ol. The (+) isomer would rotate polarized light clockwise with a specific rotation of +13.5°, and the (−) isomer would rotate the polarized light counterclockwise by exactly the same amount. We would observe a rotation of zero, just as though butan-2-ol were achiral. A solution of equal amounts of two enantiomers, so that the mixture is optically inactive, is called a **racemic mixture.** Sometimes a racemic mixture is called a **racemate,** a **(±) pair,** or a ***(d,l)* pair.** A racemic mixture is symbolized by placing (±) or (*d,l*) in front of the name of the compound. For example, racemic butan-2-ol would be symbolized by "(±)-butan-2-ol" or "(*d,l*)-butan-2-ol."

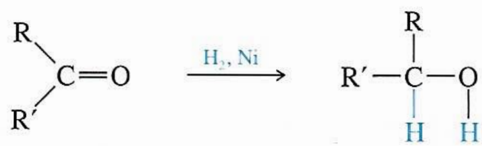


A racemic mixture contains equal amounts of the two enantiomers.

You might think that a racemic mixture would be unusual, since it requires exactly equal amounts of the two enantiomers. This is not the case, however. Many reactions lead to racemic products, especially when an achiral molecule is converted to a chiral molecule.

> A reaction that uses optically inactive reactants and catalysts cannot produce a product that is optically active. Any chiral product must be formed as a racemic mixture.

For example, hydrogen adds across the C=O double bond of a ketone to produce an alcohol.

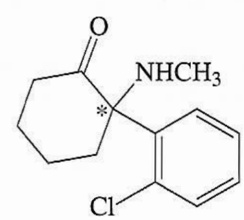


Because the carbonyl group is flat, a simple ketone such as butan-2-one is achiral. Hydrogenation of butan-2-one gives butan-2-ol, a chiral molecule (Figure 5-16). This reaction involves adding hydrogen atoms to the C=O carbon atom and oxygen atom. If the hydrogen atoms are added to one face of the double bond, the (*S*) enantiomer results. Addition of hydrogen to the other face forms the (*R*) enantiomer. It is equally probable for hydrogen to add to either face of the double bond, and equal amounts of the (*R*) and (*S*) enantiomers are formed.

Logically, it makes sense that optically inactive reagents and catalysts cannot form optically active products. If the starting materials and reagents are optically inactive, there

Application: Drugs

Many drugs currently on the market are racemic mixtures. Ketamine, for example, is a potent anesthetic agent, but its use is limited because it is hallucinogenic (making it a drug of abuse widely known as "K"). The (*S*) isomer is responsible for the anesthetic effects, and the (*R*) isomer causes the hallucinogenic effects.



ketamine

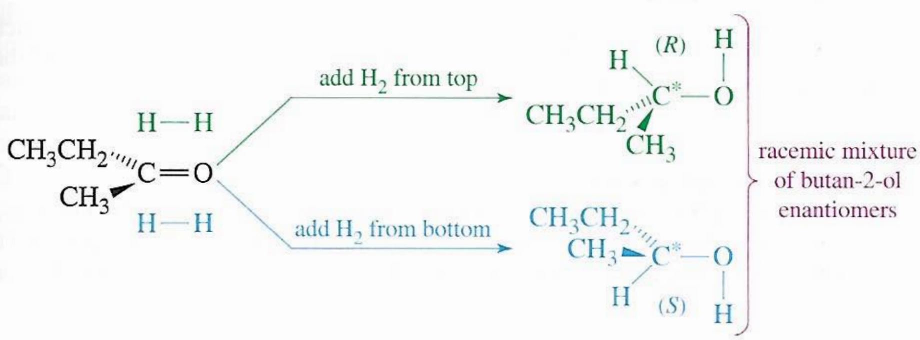


FIGURE 5-16 Hydrogenation of butan-2-one forms racemic butan-2-ol. Hydrogen adds to either face of the double bond. Addition of H_2 to one face gives the (*R*) product, while addition to the other face gives the (*S*) product.

is no reason for the dextrorotatory product to be favored over a levorotatory one or vice versa. The (+) product and the (−) product are favored equally, and they are formed in equal amounts: a racemic mixture.

5-7 Enantiomeric Excess and Optical Purity

Sometimes we deal with mixtures that are neither optically pure (all one enantiomer) nor racemic (equal amounts of two enantiomers). In these cases, we specify the **optical purity (o.p.)** of the mixture. The optical purity of a mixture is defined as the ratio of its rotation to the rotation of a pure enantiomer. For example, if we have some [mostly (+)] butan-2-ol with a specific rotation of +9.72°, we compare this rotation with the +13.5° rotation of the pure (+) enantiomer.

$$\text{o.p.} = \frac{\text{observed rotation}}{\text{rotation of pure enantiomer}} \times 100\% = \frac{9.72^\circ}{13.5^\circ} \times 100\% = 72.0\%$$

The **enantiomeric excess (e.e.)** is a similar method for expressing the relative amounts of enantiomers in a mixture. To compute the enantiomeric excess of a mixture, we calculate the *excess* of the predominant enantiomer as a percentage of the entire mixture. For a chemically pure compound, the calculation of enantiomeric excess generally gives the same result as the calculation of optical purity, and we often use the two terms interchangeably. Algebraically, we use the following formula:

$$\text{o.p.} = \text{e.e.} = \frac{|d - l|}{d + l} \times 100\% = \frac{\text{(excess of one over the other)}}{\text{(entire mixture)}} \times 100\%$$

The units cancel out in the calculation of either e.e. or o.p., so these formulas can be used whether the amounts of the enantiomers are expressed in concentrations, grams, or percentages. For the butan-2-ol mixture just described, the optical purity of 72% (+) implies that $d - l = 72\%$, and we know that $d + l = 100\%$. Adding the equations gives $2d = 172\%$. We conclude that the mixture contains 86% of the d or (+) enantiomer and 14% of the l or (−) enantiomer.

Application: Drugs

Several racemic drugs have recently become available as pure active enantiomers. For example, the drug Nexium® (for controlling acid reflux) contains just the active enantiomer of the racemic mixture in Prilosec®.

SOLVED PROBLEM 5-5

Calculate the e.e. and the specific rotation of a mixture containing 6.0 g of (+)-butan-2-ol and 4.0 g of (−)-butan-2-ol.

SOLUTION

In this mixture, there is a 2.0 g excess of the (+) isomer and a total of 10.0 g, for an e.e. of 20%. We can envision this mixture as 80% racemic [4.0 g(+) and 4.0 g(−)] and 20% pure (+).

$$\text{o.p.} = \text{e.e.} = \frac{|6.0 - 4.0|}{6.0 + 4.0} = \frac{2.0}{10.0} = 20\%$$

The specific rotation of enantiomerically pure (+)-butan-2-ol is +13.5°. The rotation of this mixture is

$$\text{observed rotation} = \text{(rotation of pure enantiomer)} \times \text{(o.p.)}$$
$$= (+13.5^\circ) \times (20\%) = +2.7^\circ$$

PROBLEM 5-12

When optically pure (*R*)-2-bromobutane is heated with water, butan-2-ol is the product. The reaction forms twice as much (*S*)-butan-2-ol as (*R*)-butan-2-ol. Calculate the e.e. and the specific rotation expected for the product.

PROBLEM 5-13

A chemist finds that the addition of (+)-epinephrine to the catalytic reduction of butan-2-one (Figure 5-16) gives a product that is slightly optically active, with a specific rotation of +0.45°. Calculate the percentages of (+)-butan-2-ol and (−)-butan-2-ol formed in this reaction.

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