often an enzyme. Either the unreacted enantiomer of the starting material can be isolated or the single enantiomer of the product can be obtained. For example, Louis Pasteur found that fermentation of \((\pm\)-tartaric acid with *penicillium glaucum* resulted in the metabolism of the \((\pm\)-enantiomer. The unreacted \((\pm\)-tartaric acid could be recovered from the fermentation mixture.

Another method that is becoming very important is chromatography using a chiral phase. Often, a chiral stationary phase, prepared by covalently bonding a chiral compound to the surface of silica beads, is used.

### 7.8 Fischer Projections

Representing these chiral molecules, especially those with more than one chirality center, using only the two dimensions of a piece of paper, requires some special conventions. We have become accustomed to using wedged and dashed bonds for this purpose. Another method was developed by one of the pioneers in the area of organic stereochemistry, Emil Fischer. To construct a Fischer projection, the molecule is first arranged with the horizontal bonds to its chirality center projecting above the plane of the page and the vertical bonds projecting behind the page. In the Fischer projection the bonds are “projected” into the plane of the page, resulting in a cross.

---

**Figure 7.5**

**Resolution of a Racemic Carboxylic Acid.**

\[
\begin{align*}
(R)\text{-RCO}_2\text{H} \\
(S)\text{-RCO}_2\text{H} \\
(S)\text{-RNH}_2 \\
(R)\text{-RCO}_2^- \quad (S)\text{-RNH}_3^+ \\
(S)\text{-RCO}_2^- \quad (S)\text{-RNH}_3^+ \\
(S)\text{-RNH}_2 \\
(R)\text{-RCO}_2\text{H}
\end{align*}
\]
with the chirality center at its center, as shown in the following Fischer projection of 
(R)-glyceraldehyde:

![Fischer projection of (R)-glyceraldehyde]

Focus On

The Historical Development of Understanding Stereochemistry

An understanding of the three-dimensional structures of molecules has played an
important part in the development of organic chemistry. The first experiments of importance to
this area were reported in 1815 by the French physicist J. B. Biot, who discovered that cer-
tain organic compounds, such as turpentine, sugar, camphor, and tartaric acid, were opti-
cally active: that is, solutions of these compounds rotated the plane of polarization of
plane-polarized light. Of course, the chemists of this period had no idea of what caused a
compound to be optically active because atomic theory was just being developed and the
concepts of valence and stereochemistry would not be discovered until far in the future.

The next major contribution was made in 1848 by the great scientist Louis Pasteur.
During the fermentation of wine, large quantities of (+)-tartaric acid precipitate in the
barrels. Pasteur was studying a salt of this acid when he discovered that it had a very
interesting property. The crystals of this salt had a chiral shape—that is, an individual
crystal had a shape that was not superimposable on its mirror image—and all of the
crystals had the same handedness. Another tartaric acid, which today is known as
racemic tartaric acid, is also produced during the production of wine. It was known that
this acid had the same formula as (+)-tartaric acid but was optically inactive, that is,
it did not rotate plane-polarized light. Upon careful observation of the salt of this acid,
Pasteur found that the individual crystals were chiral, as was the case for (+)-tartaric
acid, but in this case the left-handed and the right-handed versions of the crystals were
present in equal amounts. Using a tweezers and a magnifying glass (and considerable
patience), Pasteur was able to separate these crystals. He found one to be completely
identical to the salt of (+)-tartaric acid that he had studied previously. The other had
identical physical and chemical properties except that it rotated plane-polarized light
in the opposite direction. Pasteur had accomplished the first resolution of a racemic or-
ganic compound! Because the salts that gave mirror-image crystals also gave opposite
rotations, Pasteur associated optical rotation with chirality. And because solutions of
these salts were optically active, he proposed that chirality was not just a macroscopic
property of the crystals, but the arrangement of the atoms in a molecule of tartaric acid
must also be chiral. He was postulating a chiral shape for the arrangement of these
atoms at about the same time that Kekulé was proposing the concept of valence!
PROBLEM 7.12
Draw Fischer projections for these compounds:

a) \( H\overset{\uparrow}{\text{C}}\overset{\downarrow}{\text{Cl}} \quad \text{b) } H\overset{\downarrow}{\text{C}}\overset{\uparrow}{\text{OH}} \quad \text{c) } H\overset{\downarrow}{\text{C}}\overset{\uparrow}{\text{CH}}\overset{\downarrow}{\text{CH}}\overset{\uparrow}{\text{CH}}\overset{\downarrow}{\text{CH}}\)

It took about another 20 years for the explanation of chirality to be completed. In 1874, two young chemists, Jacobus van’t Hoff from Holland and Joseph Le Bel from France, independently proposed that the four bonds to a carbon were arranged in a tetrahedral manner. Their arguments were based on the number of isomers that exist for various formulas. Although we will not go into all of the details here, the following discussion presents some of the reasoning they used. At the time, it was well accepted that all four of the bonds to a carbon were identical. This was based on the fact that, for a multitude of compounds with the formula \( \text{CH}_3\text{X} \), only one isomer had ever been found. There is only one \( \text{CH}_3\text{Cl} \), one \( \text{CH}_3\text{OH} \), one \( \text{CH}_3\text{CH}_3 \), and so on. Many geometries with low symmetries can be eliminated on the basis of this observation. Two arrangements of the four bonds around a carbon that meet the criterion of having all of the bonds identical are the one with a square planar geometry and the one with a tetrahedral geometry. The square planar geometry can be eliminated on the basis of the observation that, for a multitude of compounds with the formula \( \text{CH}_2\text{X}_2 \), only one isomer has ever been found. There is only one \( \text{CH}_2\text{Cl}_2 \). If carbon had a square planar geometry, then two isomeric compounds with the formula \( \text{CH}_2\text{Cl}_2 \) would be expected, as shown here. However, a tetrahedral geometry predicts only one \( \text{CH}_2\text{Cl}_2 \).

Two isomers with square planar geometry

One isomer with tetrahedral geometry

At the time of van’t Hoff’s and Le Bel’s work, there were only a few optically active compounds whose structures had been determined. All of these compounds had a carbon bonded to four different groups, a carbon that we today call a chirality center. van’t Hoff and Le Bel pointed out that a tetrahedral arrangement of four different groups around a carbon produced a structure that is not superimposable on its mirror image, a chiral structure. Thus, their postulate of a tetrahedral carbon explained the existence of enantiomeric compounds.
Because they are two-dimensional representations of three-dimensional objects, extreme care must be used in manipulating Fischer projections to avoid changing the configuration. Structures may not be “lifted” out of the plane of the paper. A 180° rotation in the plane is permitted, but 90° and 270° rotations are not allowed. As illustrated next for (S)-alanine, a 180° rotation of the drawing in the plane of the paper does not change the configuration. A 90° or 270° rotation in the plane or a 180° rotation out of the plane all result in a representation of the enantiomer of the original structure. If you are in doubt, it is always advisable to draw the three-dimensional representation for the structure before manipulating it. Remember that horizontal bonds project above the paper and vertical bonds project behind the paper.

**MODEL BUILDING PROBLEM 7.4**
Build models of the compounds represented by these Fischer projections. Determine whether the models superimpose. (Note that these Fischer projections are related by a 90° rotation in the plane of the page.)

Fischer projections are especially useful in the case of compounds with more than one chirality center. For example, it is easy to see the plane of symmetry in meso-tartaric acid. As was the case with regular structures, interchanging any two groups in a Fischer projection results in inversion of configuration at the chirality center. Thus, interchanging the H and OH on the lower chirality center of meso-tartaric acid inverts the configuration at that chirality center, resulting in the (2R,3R)-stereoisomer, (+)-tartaric acid. It is also easy to see that this stereoisomer does not have a plane of symmetry.
PRACTICE PROBLEM 7.3

Assign the configuration of this compound as $R$ or $S$:

\[
\begin{align*}
\text{CH}_2\text{OH} \\
\text{H}_3\text{C} \quad \text{Cl} \\
\text{H}
\end{align*}
\]

Solution

One way to work this type of problem is to draw the structure, showing its stereochemistry, and then proceed as in previous examples.

The configuration can also be assigned directly from the Fischer projection. First assign priorities to the groups:

If group 4 is attached to a vertical bond, as in this case, it is already pointed away from you. Therefore, the direction of rotation given by proceeding from group 1 to 2 to 3 gives the configuration directly. In this case the rotation is counterclockwise, so the configuration is $S$.

If group 4 is attached to a horizontal bond, it is pointed toward you and you are viewing the molecule from the wrong side.
This simply means that the configuration is opposite that given by the direction of rotation proceeding from group 1 to 2 to 3. In this example the direction of rotation is counterclockwise but the H is pointed toward you, so the configuration is $R$. (Try drawing the stereochemistry to confirm this.)

**PROBLEM 7.13**

Assign the configurations of the compounds represented by these Fischer projections as $R$ or $S$.

7.9 **Reactions That Produce Enantiomers**

A reaction of an achiral molecule may introduce a chirality center, producing a chiral product. For example, reaction of the following ketone with hydrogen in the presence of a catalyst results in addition of the hydrogen to the carbon–oxygen double bond, producing 2-butanol:

The starting ketone is not chiral, but the product alcohol is chiral. Approach of the hydrogen from above the plane of the ketone (as drawn) produces ($R$)-2-butanol, whereas approach from behind the plane produces ($S$)-2-butanol. There is no apparent reason why the hydrogen should prefer one approach over the other; in fact, the two enantiomers are produced in exactly equal amounts—the product is racemic. As long as there is nothing else that is chiral in the reaction, the enantiomeric products (and the enantiomeric reaction pathways leading to them) have identical energies and must be produced in equal amounts. If all the reagents in a reaction are achiral (or racemic), then the product must be racemic. If the initial reaction mixture does not rotate plane-polarized light, the product mixture cannot rotate plane-polarized light. On the other hand, if one of the components of the initial reaction mixture (a reagent, a catalyst, even the solvent) is chiral and only one enantiomer of it is present, enantiomers of the product may be produced in unequal amounts. Devising methods that produce only one enantiomer of a chiral product, called asymmetric synthesis, is one of the most challenging areas of research facing organic chemists today.