RELATIVE AND ABSOLUTE CONFIGURATION

Conventional X-ray structural analysis affords interatomic distances and angles, but does not provide any indication of which mirror image is present in a crystal of a chiral substance. Until the work of J.M. Bijvoet in 1951, there was no way of determining this. He showed that by choosing X-rays of a wavelength that excites an element in a crystal, a phase lag effect is produced that indicates which enantiomer is present. Since then, many such determinations have been done. For a particular substance, correlating the sign of rotation with the configurational designation of structure gives the absolute configuration. For example, in 1972 the cobalt (II) salt of (-)-malic acid was examined using CuKα X-rays to excite the Co atoms, and determined to have the structure below,

![Diagram](image)

which we label S by the Cahn-Ingold-Prelog system. Now that this is known, the absolute configurations of many other compounds immediately became known because they have been related by synthesis at an earlier time.

For example, in 1963 (+)-2-hydroxy-3-phenylpropionic acid was ozonolyzed to the (+)-enantiomer of malic acid. This now requires that the starting acid had the R configuration as shown below:

![Diagram](image)

In 1921 (+)-2,4-dihydroxybutyric acid was oxidized to (+)-malic acid, which now required this also be labeled R:

![Diagram](image)

Before the absolute determination, the relationship of these three compounds was known and useful, even though an enantiomeric picture could not be drawn with certainty. This relationship is called relative configuration. The early statement that (+)-2,4-dihydroxybutyric acid and (+)-malic acid and also (+)-2-hydroxy-3-phenylpropionic acid all have the "same" configuration is a statement of relative configuration. Since they do not have the identically same four groups around the stereogenic atom, the term "same" could be ambiguous,
especially if several groups were modified in reactions. Therefore, a statement of relative configuration should be accompanied by a description of the reactions to be sure of the meaning of "same".

It is interesting to note that the use of configurational information such as proof of inversion in $S_N2$ reactions was made with relative configurations before absolute ones were available. In fact, the absolute configurations are not useful in themselves, except as another means of obtaining more relative configurations.

Keep in mind that two compounds with the "same" configuration may have different configurational designations and/or they may have opposite signs of rotation, as shown below:

\[
\begin{align*}
\text{H}_2\text{C} &-\text{NH}_2 \\
\text{C}_6\text{H}_5 &+ \text{H}_2 & \text{catalyst} & \Rightarrow & \text{H}_3\text{C} &-\text{NH}_2 \\
(R)-(+)\text{-1-phenylethylamine} & & & & (R)-(\text{-})\text{-1-cyclohexylethylamine}
\end{align*}
\]

(This material is taken from Stowell's textbook "Intermediate Organic Chemistry")