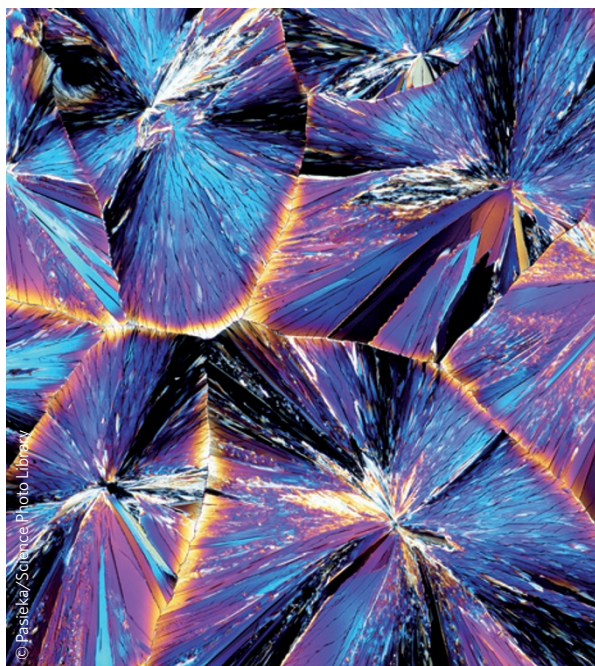


 MILESTONE 9

Spatial awareness

In the late 1800s, chemists started to develop ways to depict the spatial arrangements of atoms and groups in molecules possessing one or more stereogenic centres in two dimensions, and sought a means to distinguish between stereoisomers. At this time, however, only relative stereochemistry could be determined. More specifically, it was possible to recognize that two molecules with the same atom connectivity, but which rotate the plane of polarized light in opposite directions, are enantiomers (that is, mirror images of each other). The absolute configuration of the atoms and groups around a stereogenic centre, however, remained uncertain.

A light micrograph of tartaric acid crystals.



In 1951, Bijvoet *et al.* removed this uncertainty using X-ray crystallographic techniques.

About 50 years before this revelation, Emil Fischer suggested a way of representing stereoisomers by drawing a projection in two dimensions. These drawings, named Fischer projections, were used originally to depict carbohydrate stereochemistry but became steadily more widely used with amino acids and other organic molecules. In a completely arbitrary assignment, Fischer classified the D configuration of glucose to be the + isomer (more specifically, the isomer that rotates the plane of polarized light in a clockwise direction) and the L configuration to be the - isomer. This connection was further developed by Martin Rosanoff in the classification of other chiral molecules including the assignment of D-(+)-glyceraldehyde and L-(-)-glyceraldehyde.

Bijvoet and his colleagues confirmed that this arbitrary assignment of absolute configuration, as depicted in Fischer projections, in relation to the direction of optical rotation of polarized light, was correct after all. They arrived at this conclusion by X-ray diffraction analysis of the sodium-rubidium salt of the natural (+)-form of tartaric acid using a phenomenon called anomalous scattering, which relies on the ability of certain atoms to absorb X-rays strongly. The development of tunable X-ray sources would make anomalous scattering a useful technique for protein crystallography

(see Milestone 19), but at the time of Bijvoet's experiment, a heavy atom (the rubidium atom of the sodium-rubidium double salt) similar in atomic weight to the element used to generate the X-rays (here, zirconium) was needed. The ability to excite solely the rubidium ion, and not the rest of the atoms in the crystal, made it possible to determine the absolute configuration of all the atoms in the crystal rather than just the relative stereochemistry, which is typically obtained using X-ray crystallographic methods. Bijvoet *et al.* revealed that the natural (+)-form of tartaric acid indeed has the L-configuration as was assumed by Fischer.

The confirmation of the absolute configuration of atoms or groups around stereogenic centres using anomalous X-ray diffraction gave chemists the possibility to establish, with certainty, the absolute stereochemistry of a molecule they had isolated or synthesized. In addition, the chemical community could breathe a sigh of relief — the configurations of the many chiral molecules depicted in textbooks and in the chemical literature during more than half a century leading up to 1951 were correct, and there was no need to go back to the drawing board.

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Nature Materials

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