

## 3.1: Prelude to Conformations and Stereochemistry

### Molecular models are your friend!

*Because this chapter deals extensively with concepts that are inherently three-dimensional in nature, it will be very important for you to use a molecular modeling kit that is specifically intended for organic chemistry. Many of the ideas we will be exploring can be extremely confusing if you are limited to the two dimensions of this page. Be prepared to follow along with these discussions in **three** dimensions, with a molecular model in your hands!*

### Introduction: Louis Pasteur and the discovery of molecular chirality

In 1848, a 25 year old chemist named Louis Pasteur made a startling - and some thought brash - claim to the scientific community. Pasteur was inexperienced, to say the least: he had only earned his doctorate the previous year, and had just started his first job as an assistant to a professor at the *Ecole normale superieure*, a university in Paris. Jean-Baptiste Biot, a highly respected physicist who had already made major contributions to scientific fields as diverse as meteorites, magnetism, and optics, was intrigued but unconvinced by Pasteur's claim. He invited the young man to come to his laboratory and reproduce his experiments.



(Photo credit: <https://www.flickr.com/photos/nate/>)

Decades earlier, Biot had discovered that aqueous solutions of some biologically-derived substances, such as [tartaric acid](#), [quinine](#), [morphine](#), and various sugars, were optically active: that is, the plane of polarized light would rotate in either a positive (clockwise, or right-handed) or negative (counter-clockwise, or left-handed) direction when passed through the solutions. Nobody understood the source of this optical property. One of the biological substances known to be optically active was a salt of [tartaric acid](#), a compound found in abundance in grapes and a major by-product of the wine-making industry.

The compound was dextrorotatory in solution – in other words, it rotated plane-polarized light in the positive (right-handed, or clockwise) direction. Curiously, though, chemists had also found that another form of processed tartaric acid was optically *inactive*, despite that fact that it appeared to be identical to the optically active acid in every other respect. The optically inactive compound was called '*acide racémique*', from the Latin *racemus*, meaning 'bunch of grapes'.

Louis Pasteur's claims had to do with experiments he said he had done with the 'racemic' acid. Jean-Baptiste Biot summoned Pasteur to his laboratory, and presented him with a sample of racemic acid which he himself had already confirmed was optically inactive. With Biot watching over his shoulder, and using Biot's reagents, Pasteur prepared the salt form of the acid, dissolved it in water, and left the aqueous solution in an uncovered flask to allow crystals to slowly form as the water evaporated.

Biot again summoned Pasteur to the lab a few days later when the crystallization was complete. Pasteur placed the crystals under a microscope, and began to painstakingly examine their shape, just as he had done in his original experiments. He had recognized that the crystals, which had a regular shape, were asymmetric: in other words, they could not be superimposed on their mirror image. Scientists referred to asymmetric crystals and other asymmetric objects as being 'chiral', from the Greek word for 'hand'.

Your hands are chiral objects, because although your right hand and your left hand are mirror images of one another, they cannot be superimposed. That is why you cannot fit your right hand in a left-handed glove.

More importantly, Pasteur had claimed that the chiral crystals he was seeing under the lens of his microscope were of two different types, and the two types were mirror images of each other: about half were what he termed 'right handed' and half were 'left-handed'. He carefully separated the right and left-handed crystals from each other, and presented the two samples to Biot. The eminent scientist then took what Pasteur told him were the left-handed crystals, dissolved them in water, and put the aqueous solution in a polarimeter, an instrument that measures optical rotation. Biot knew that the processed tartaric acid he had provided Pasteur had been optically inactive. He also knew that unprocessed tartaric acid from grapes had right-handed optical activity, whereas left-handed tartaric acid was unheard of. Before his eyes, however, he now saw that the solution was rotating light to the left. He turned to his young colleague and exclaimed, "*Mon cher enfant, j'ai tant aimé les sciences dans ma vie que cela me fait battre le coeur!*" (My dear child, I have loved science so much during my life that this makes my heart pound!)

Biot had good reason to be so profoundly excited. Pasteur had just conclusively demonstrated, for the first time, the concept of **molecular chirality**: molecules themselves - not just macroscopic objects like crystals - could exhibit chirality, and could be separated into distinct right-handed and left-handed 'stereoisomers'. Tying together ideas from physics, chemistry, and biology, he had shown that nature could be chiral *at the molecular level*, and in doing so he had introduced to the world a new subfield which came to be known as 'stereochemistry'.

About ten years after his demonstration of molecular chirality, Pasteur went on to make another observation with profound implications for biological chemistry. It was already well known that 'natural' tartaric acid (the right-handed kind from grapes) could be fermented by bacteria. Pasteur discovered that the bacteria were selective with regard to the chirality of tartaric acid: no fermentation occurred when the bacteria were provided with pure left-handed acid, and when provided with racemic acid they specifically fermented the right-handed component, leaving the left-handed acid behind.

Pasteur was not aware, at the time of the discoveries described here, the details of the structural features of tartaric acid at the molecular level that made the acid chiral, although he made some predictions concerning the bonding patterns of carbon which turned out to be remarkably accurate. In the more than 150 years since Pasteur's initial tartaric acid work, we have greatly expanded our understanding of molecular chirality, and it is this knowledge that makes up the core of this chapter. Put simply, stereochemistry is the study of how bonds are oriented in three-dimensional space. It is difficult to overstate the importance of stereochemistry in nature, and in the fields of biology and medicine in particular. As Pasteur so convincingly demonstrated, life itself is chiral: living things recognize different stereoisomers of organic compounds and process them accordingly.

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