Chemical reflections

The 2001 Nobel Prize for chemistry concerned work with chiral molecules. *Varinder Aggarwal*, Professor of Synthetic Chemistry, reflects on why this might be important to you and me.

Many important molecules required for life exist in two forms that are mirror images of each other. They are related like our left and right hands, but they are not the same. This property is called 'chirality', from the Greek word for hand, and the two forms are called 'enantiomers', from the Greek word for opposite.

Many drugs consist of chiral molecules. In the past a mixture of the two enantiomers was routinely employed since a mixture is much easier to produce than a single enantiomer. Unfortunately, in certain cases the other enantiomer may be harmful, as was the case in the thalidomide disaster in the 1960s. This drug was sold as a mixture of the two enantiomers to pregnant women suffering from severe nausea. Only later was it discovered that while one of the enantiomers of thalidomide helped prevent nausea, the other one caused severe foetal damage.

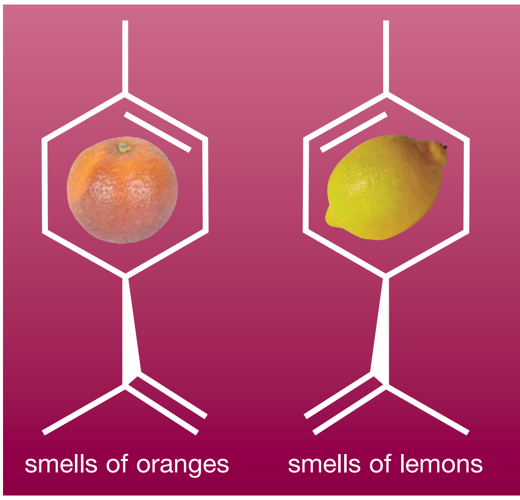
Subsequent regulations in the pharmaceutical industry demanded that the two enantiomers of a chiral compound be treated as different products that must be tested separately.

But chirality is important not only in medicinal chemistry, but also in taste, smell, and properties of materials. It has thus become big business. The prediction for chiral chemicals sold as single enantiomers is that the market will grow from its 2000 level of $6.63 billion to $16.0 billion by 2007. Consequently, there has been intensive research into developing methods for making one or other of the enantiomers – in other words, in being able to control chirality.

Since there is a requirement to test individual enantiomers, and because it is difficult to separate them from a mixture, it is important to be able to produce them separately, a process known as asymmetric synthesis. A key endeavour in asymmetric synthesis is to find a general method for making organic compounds, while controlling chirality. Organometallic compounds – compounds that contain a metal-carbon bond – are among the most important reagents in this process, since they readily react to make new bonds to carbon. However, chiral organometallic reagents are rare. If they could be readily synthesised, they would be extremely useful since they provide a direct means of making chiral molecules.

Preliminary investigations at Bristol have shown that by combining two well-established areas of chemistry – organoboranes and sulfur ylides – in a new and unconventional way, the resulting chiral organoborane was transformed into a range of chiral compounds with complete control of chirality. It represents a significant departure from the established work in these two areas and, Aggarwal believes, opens up a whole new field of research that could find wide application in the chemical industry, particularly in the synthesis of pharmaceuticals. Making the right enantiomer could be a matter of life or death. ■

Professor Aggarwal was awarded the Royal Society of Chemistry's 2004 prize for Green Chemistry.



The smells of oranges and lemons differ in being the left- and right-handed versions of the same molecule – limonene