Organic Chemists: Fighting Blindness

Introduction for teachers

This story is one of a number of case studies that show how chemistry studied at A-level is used by organic research chemists and how and why their work is important.

In this case study the catalytic addition of hydrogen to convert a carbon – carbon double bond to a single bond alters the 3D shape of a molecule and converts a natural product into a highly effective drug to combat river blindness.

More detail for students about the disease and how the drug is produced is provided below. This document is accompanied by a number of PowerPoint slides than can be used as a 'starter' to lessons to provide a context when teaching about the hydrogenation of alkenes to form alkanes.

Background – What was the problem?

Onchocerciasis, also known as river blindness, causes debilitating skin disease and is the second-leading infectious cause of blindness. Today, 140 million people in Africa are at risk of infection.

This Neglected Tropical Disease (NTD) is caused by wolbachial bacteria that live within the nematode worm, *Onchocerca volvulus*. When the worms that have infected a person die, they release the bacteria, leading to severe itching and the destruction of the tissue in the human eye resulting in blindness.

Globally, over 37 million people are infected, often living in poor, rural African communities.

Figure 1 Picture showing child holding Mectizan

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What did the organic chemists do?

Modern synthetic organic chemistry played a crucial role in the discovery and manufacture of the highly effective drug Ivermectin. Ivermectin (Mectizan^{TM}) is a broad spectrum anti-parasitic medicine that kills the larvae and prevents them from causing damage. It is an effective drug that only needs to be taken twice a year.

Specifically, organic chemistry helped to convert a natural product, avermectin, which was less effective into Ivermectin.

A reaction called catalytic hydrogenation is used to change one of the five carbon-carbon double bonds in the chemical structure of avermectin into a single bond.

Changing this one bond alters the 3D shape of the molecule hence improving its safety and efficacy making it a more effective drug against the spread of the disease.

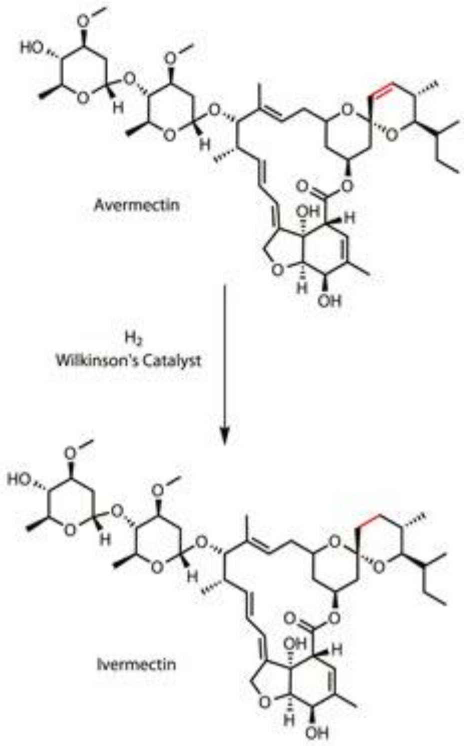

Figure 2 Catalytic Hydrogenation of avermectin

The transformation of the double carbon-carbon bond into a single bond is tricky, because the other double bonds in the avermectin molecule must be left unchanged for the drug to work. By using a specific catalyst called Wilkinson's catalyst, the reaction can take place. Wilkinson's catalyst is one of the prototype organometallic catalysts, $(Ph_3P)_3RhCl$, which is named after the British chemist and 1973 Nobel Laureate, Sir Geoffrey Wilkinson.

What was the impact?

In collaboration with the World Health Organisation, Ivermectin has been used in over 200 million people worldwide.

Catalysis was recognized with the 2001 Nobel Prize in Chemistry (Knowles, Noyori and Sharpless) and it is still an important area of new chemistry research today. It has been used in the manufacture of many other medicines but scientists are still restricted in the types of new molecules that can be made in the laboratory.

Fortunately, new research into organic synthesis is underway in many UK universities which allows medicinal chemists to design new drugs for cancer, heart disease, diabetes and infections.