

## Using Simpler Synthesis and Greener Chemistry to Improve Medicines



An estimated 170 million people worldwide are infected with hepatitis C, which kills more than 350,000 every year from related illnesses like liver cancer. There is no vaccine for it, and treatments are costly thanks to the complicated chemistry used to make the drugs. However, if a way was found to simplify and speed up the manufacture of hepatitis C drugs, it could slash the costs of treatment and at a stroke promise to wipe out the insidious killer disease.

And that is what a European Union research project has been doing: improving the chemical processes used in making pharmaceuticals and plastics. EUMET, a four-year project backed by a €3.6 million EU grant, has made the process of synthesising compounds simpler, more efficient and greener.

EUMET is working on the same principles pioneered by the three scientists who won the 2005 Nobel Prize for Chemistry: a reaction process called olefin metathesis.

Metathesis, which means to change places, allows groups of atoms to be moved efficiently from one molecule to another. "Metathesis is very simple and appealing: it is a beautiful way of assembling molecules," says EUMET's project coordinator, Steven Nolan, the Chair in Inorganic Chemistry at the University of St Andrews, Scotland. It allows double bonds to be broken and made between carbon atoms, he says. "The chemical reaction is like a dance in which one couple exchanges partners with another. We make the exchange go faster by using novel catalysts."

EUMET, which ran until November 2012, gathered nine European leaders in metathesis from various areas: led by Nolan at St Andrews, it includes the University of Salerno, Italy; University of Warsaw, Poland; Leibniz University of Hannover, Germany; Technical University of Graz, Austria; Ecole Nationale Supérieure de Chimie de Rennes, France; Umicore, Germany; Janssen Pharmaceutica, Belgium; and IFP Energies Nouvelles (IFPEN), France.

It was at Janssen that the hepatitis C breakthrough occurred. Thanks to EUMET research, the company is now on the verge of validating an affordable oral pill treatment, which is due to market in 2013. "This is a life changer that could affect millions," says Nolan. Using metathesis, Janssen catalysed what would otherwise have been a convoluted, expensive and resource heavy process. "Without metathesis, it would need a completely different synthetic approach with at least 10 supplementary synthetic steps, a huge increase in cost and time," Nolan adds.

Since the molecules involved in metathesis are the basis of industries as diverse as petrochemicals and drugs, this methodology has a potentially huge practical impact. Within EUMET, IFPEN has used metathesis to develop a process to manufacture molecules that can be used to synthesise detergents; Umicore is selling the catalysts; and most recently the technology has been used to develop new battery technologies. Other potential benefits include advanced herbicides, additives for polymers and fuels, and research into new treatments for bacterial infection, cancer, Alzheimer's disease, arthritis, migraine and HIV.

Furthermore, as Nolan notes, metathesis is a step towards green and sustainable chemistry, reducing waste through smarter production. "We hope industry and science will take a close look at metathesis because Europe could really benefit from this technology," he says.

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