# Ringing the changes 'opens the road to new medicines'

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Inspired by the classic 'ball-in-a-cup' children's toy, researchers at the University of York have discovered an innovative method to make medicinally important molecules.

The molecules contain atoms arranged in large rings, known as macrocycles, whose importance in medicine has been known for decades.

But translating this knowledge into the development of new medical treatments is a major challenge because macrocycles are notoriously difficult to make.

Lead researcher, Dr Will Unsworth of the Department of Chemistry at York, explained: "The ball-in-a-cup is a simple, but surprisingly accurate analogy for a ring forming reaction. To produce a molecule containing a ring, the two ends of a molecule must collide with the right energy and trajectory to form a new chemical bond, just as the flight of the 'ball' must be judged perfectly if it is to land in the 'cup' without bouncing out, or missing entirely! "Making macrocycles is like tackling the ball-in-a-cup with an extra-long string, which unsurprisingly raises its difficulty significantly.'"

Existing methods for making macrocycles seek to minimise the impact of this difficult process, but they are generally inadequate for their production on a commercially viable scale. The new approach developed by Dr Unsworth and his team allows macrocycles to be 'grown' from

existing rings using ring enlargement reactions, while the difficult ring closing reaction that blights current methods is avoided entirely.

Dr Unsworth added: "Macrocycles have long been known to display unique medicinal properties, but a lack of effective and scalable methods to make them, means that they have historically been under-investigated. We hope that by simplifying their production through the techniques we have discovered will pave the way for the development of new classes of life-saving medicines."

**More information:** Christiana Kitsiou et al. The Synthesis of Structurally Diverse Macrocycles By Successive Ring Expansion, *Angewandte Chemie International Edition* (2015). DOI: 10.1002/anie.201509153

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