Chemists crack the chirality code

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Chemists at Trinity College Dublin have cracked the chirality code. The chirality (or left/right-handed asymmetry) of amino acids presented a long-standing challenge that complicated efforts to create certain types of proteins, which have applications in drug development.

Proteins are the building blocks of life, but amino acids are the cement. This is because different amino acids join up in chains to build different proteins, which in turn perform different functions – from speeding up biomolecular reactions to replicating DNA and transporting molecules from cell to cell.

'Peptide-based' drugs tend to have a high specificity and low toxicity, which is the 'magic bullet' drug designers are continually looking for; highly specific, non-toxic drugs should be very effective in getting to where they are supposed to go in a patient, and then doing what they are supposed to do with minimal side effects.

However, these drugs must be built from amino acids and, because of their defined structure, you can't just 'glue' these together as you would like.

Amino acids (save one) are typically asymmetric in form. This means that they are usually 'left-handed' or 'right-handed.' This is crucial, because it means that the peptides that are made from these amino acids are also 'handed'. Both of these 'hands' function similarly as individuals, but they can behave differently in the presence of other handed molecules, much in the same way that shaking someone's left hand with your right feels normal but doing so with your left results in a very different interaction.

But now, the chemists from Trinity have found a way around this problem that will allow them – or others using the same technique – to create a suite of highly useful artificial amino acids and proteins.

Professor of Synthetic Chemistry in the School of Chemistry, Stephen Connon, said: "We were able to devise a method for making one 'hand' of an amino acid almost exclusively from a molecule derived from a 50:50 ratio of left:right amino acid 'hands'. For the first time these products are formed ready for linking to other amino acids, which makes them far more useful to the chemist than ever before."

He added: "We think this technology could be used to create a very wide range of coupling-ready artificial amino acids for use in pharmaceutical and materials applications."

The research has just been published in the prestigious peer-reviewed journal *Angewandte Chemie International Edition*.

More information: "A Practical Aryl Unit for Azlactone Dynamic Kinetic Resolution: Orthogonally Protected Products and A Ligation-Inspired Coupling Process" *Angewandte Chemie International Edition* DOI: 10.1002/anie.201406857

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