Professor Laurence M. Harwood: Organic Synthetic Methodology and Natural and Unnatural Product Total Synthesis.

Work in the group revolves around the development of new synthetic methods and their application to the synthesis. Currently there is a range of projects underway, with the aims of developing synthetic approaches towards terpenoids, heterocycles and amino acids with an increasing emphasis on chemistry at the biological interface at one end of the synthetic spectrum and materials chemistry at the other.

Much of the work of the group is concerned with selective carbon – carbon bond formation using pericyclic reactions, such as the Claisen rearrangement and the Diels – Alder, ene and dipolar cycloadditions,[1] under very mild and controlled conditions. This has led to a particular interest in the application of ultra-high pressure chemistry to promote reactions which involve a decrease in volume in going from starting materials to the transition state.[2] A further novel application of ultra-high pressure chemistry is in the area of generation of bridged bisimidazolium ionic liquids. This technology has much potential generally in the area of green chemistry.

A great deal of effort has been put into the development of a "chiral memory" system for efficient diastereocontrolled chirality transfer allowing several distinct synthetic approaches to enantiopure amino acids in either optical series.[3] This has led to the development of “general chemical ligation”, a methodology permitting convergent peptide synthesis that is being commercialized by TechnoPep (http://www.technopep.com/).[4]

In the materials area, we are the pre-eminent group internationally for the synthesis of actinide-selective ligating heterocycles for application in nuclear reprocessing and the group currently holds a grant worth €225K within the framework of the SACSESS programme.[5] We are now heavily involved in developing the next generation of ligands capable of distinguishing between minor actinides and separating americium from curium.[6]

1. L. M. Harwood and F. W. Lewis, “Recent Applications of the Intramolecular Diels-Alder Reaction of Furan (IMDAF) Reaction in Natural Product Synthesis”, Targets in Heterocyclic Synthesis, Editors O. A. Attanasi and D. Spinelli, Italian Society of Chemistry, 2013, 16, 1

2. L. M. Harwood and R. J. Vickers “Ultra-High Pressure as a Mild Synthetic Tool”, New Perspectives in the Frontiers of Chemical Research, Editor S. S. Chakravorti, Golden Jubilee Commemorative Scientific Monograph, R.S.C. (E. I. S.), 2005, pp 118-141.
3. Y. Gan, L. M. Harwood, S. C. Richards, I. E. D. Smith and V. Vinader, “Cycloadditions of chiral carbonyl ylides with imine dipolarophiles as a route to enantiomerically pure α-amino-β-hydroxy acids”. Tetrahedron Asymmetry, 2009, 20, 723.
4. L. M. Harwood, D. A. Wellings and D. J. Moody, “Chemical Ligation by Ring Opening of Oxo-Thiomorpholines”, February 2012, International PCT application number WO2012/020231 A1.
5. F. W. Lewis, M. J. Hudson, L. M. Harwood, “Development of Highly Selective Ligands for Separations of Actinides from Lanthanides in the Nuclear Fuel Cycle”, Synlett, 2011, 2609.
6. A. Afsar, D. M. Laventine, L. M. Harwood, M. J. Hudson and A. Geist, “Utilizing Electronic Effects in the Modulation of BTPhen Ligands with Respect to the Partitioning of Minor Actinides from Lanthanides”, Chem. Comm., 2013, 8534