BIOCHEMICAL REACTIONS AND MOLECULAR RECOGNITION

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One aspect of our research involves the manipulation of biochemical reactions. Our objectives in this area are: i) to develop methods to regulate biochemical processes associated with disease states, ii) to produce physiologically active compounds with potential as pharmaceuticals, iii) to develop biomimetic synthetic methods, and iv) to produce enzymes with novel functions and mechanisms of action, to efficiently catalyse classes of chemical processes outside the normal biological range. The other main field of research is in the area of supramolecular chemistry and molecular recognition, and involves the design, synthesis and evaluation of molecular hosts. Applications of this chemistry in the development of catalysts, molecular reactors and devices, and photochemical and thermal switches are being pursued.

Highlights of our recent results include the development of:

(i) enzyme inhibitors to down-regulate, and prohormones to up-regulate, the biosynthesis of peptide hormones;

(ii) models to predict the susceptibility of amino acids and peptides towards free radical processes associated with disorders such as Alzheimer's and cardiovascular disease;

(iii) molecular ratchets, sensors, shuttles, tweezers and switches;

(iv) molecular reactors to catalyse and control the regioselectivity of carbon–carbon bond forming reactions;

(v) novel spectroscopic techniques to analyse melamine–urea–formaldehyde and related resins, and improve the manufacture thereof, and

(vi) compounds to inhibit and stimulate ion-flux through calcium ion channels.

Personnel highlights included the completions of PhD students B Barratt, A Philbrook and M Cieslinski, MPhil student L Chow and BSc(Hons) student R Coulston. I Li presented an invited lecture at the Gordon Conference on Free Radicals, in New Hampshire, and A Philbrook presented an invited lecture at Wood Composites 2005, in San Diego. Professor Gary Weisman of the University of New Hampshire was a welcome visitor for several months.

We were pleased to be part of successful bids for an ARC Centre of Excellence in Free Radical Chemistry and Biotechnology and for a CSIRO Emerging Science Initiative in Synthetic Enzymes for Synthetic Chemistries. Our work on hormone regulation also gained support through the award of a new ARC Discovery Grant, while our research with Orica (Australia) Pty Ltd with wood adhesives attracted an ARC Linkage Grant.

Free Radical Reactions of Amino Acids, Peptides and Proteins

Free radical reactions of amino acids and their derivatives are associated with a wide variety of disease states, including inflammation, and Alzheimer's and cardiovascular disease. They are also involved in the biosyntheses of many of the hormones that regulate biological activity, and are therefore intimately linked to the associated physiological and pathological conditions. This has prompted us to study aspects of the fundamental free radical reactions that are involved. Through this work we have developed models to predict the susceptibility of amino acids and peptides towards free radical processes associated with physiological disorders, and radical-resistant amino acids and peptides have been designed and

synthesised. We have produced enzyme inhibitors to down-regulate, and prohormones to up-regulate, the biosynthesis of peptide hormones. We are currently evaluating the potential of these compounds as pharmaceutical agents for treating human and animal disease states associated with hormone imbalances. *(With D Brittain, L Y F Chow, M L Coote, A J Herlt, I Li, A J Mortimer, G M Statham, Y-C Tsai, Z I Watts, A Wright, and L Radom [U Sydney], R O'Hair [U Melbourne])*

Supramolecular Chemistry and Molecular Recognition

This work exploits cyclodextrins as molecular hosts. Our early work in this area resulted in pharmaceutical formulations that are in everyday clinical use worldwide. In more recent studies modified cyclodextrins are being developed and exploited as molecular scaffolds for the construction of catalysts, molecular ratchets, shuttles, tweezers and switches, and photochemical devices. Another application of cyclodextrins involves their use to control the assembly of the components of chemical reactions, to facilitate the reactions and alter the outcomes. The cyclodextrins thereby act as reaction vessels, but at the molecular level. In this regard, we have developed demonstration systems to change the regio- and stereo-selectivity of reactions, and increase their rates by up to 100,000 times. We have also been exploring the synthesis of cyclodextrin rotaxanes, catenanes, knots and daisy chains of various topologies. These form the basis of molecular devices such as ratchets and motors, temperature and light sensors, photochemical frequency switches and molecular tweezers. Solid state and solution studies of cyclodextrin host-guest complexes and rotaxanes show that these assemblies may be designed to exploit the cyclodextrins as insulators of molecular filaments formed by the guests. This has potential, for example, in the development of microelectronic systems. *(With L Barr, S Bowen, M M Cieslinski, R J Coulston, R Dawson, A J Herlt, S Maniam, and M A Buntine, J Gerber, S F Lincoln, B L May, J Patrick [U Adelaide])*

Other Collaborative Research

Other research involves studies of the structure of melamine–urea–formaldehyde resins, and the search for alternative reagents and improved manufacturing processes. Biochemical molecular recognition processes are also being studied, including the design and development of compounds to inhibit and stimulate ion-flux through calcium ion channels, and the development of novel enzymes. *(With A Buchan, J Khurana, A Philbrook, J K Robinson, M G Teese, and M Casarotto, A Dulhunty, [JCSMR, ANU], N Dunlop, S Earnshaw, N Walker [Orica (Australia) Pty Ltd and the UnIChe program], A Ferrante, A Poulos [Adelaide Medical Centre for Women and Children], S Brown, J Oakeshott, R Russell [CSIRO Entomology], G P Savage, G W Simpson [CSIRO Molecular and Health Technologies])*

http://rsc.anu.edu.au/research/easton.php