ORGANIC SYNTHESIS, METHODOLOGY AND HOST-GUEST CHEMISTRY

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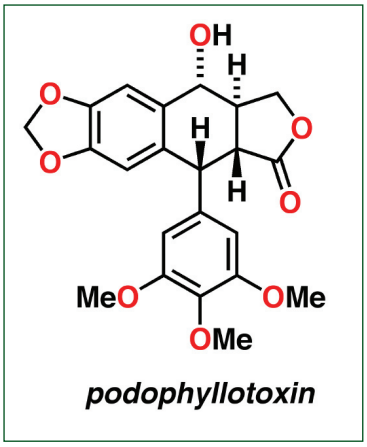
Domino reactions are spectacular events in which many bonds are made and broken in a single step. These reactions hold much promise for achieving more efficient syntheses: a pressing need in times of increasing production costs and given the importance of protecting the environment by reducing waste. Our research program involves the design and implementation of sequences of cycloaddition reactions, free radical reactions and transition metal-mediated reactions to prepare polycyclic molecules with important biological properties. This program also targets new ways to achieve molecular recognition, complexation and catalysis. Overall, the primary goal is to synthesise such complex molecules in a practical manner.

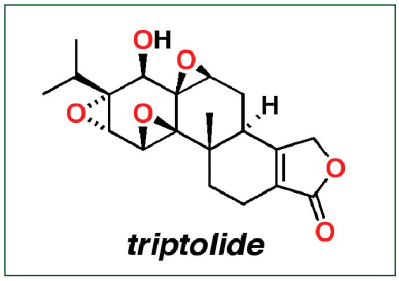
Efficient Total Synthesis: Anti-tumour and Anti-Alzheimer's Natural Products

Lignans like podophyllotoxin have cancer-fighting properties and are used in chemotherapy. An efficient and highly modular approach for the synthesis of lignan natural products has been developed, culminating in several total syntheses, including that of podophyllotoxin. This strategy has several advantages over previous syntheses, the most significant being that it allows a high level of convergency at the end of the synthetic route.

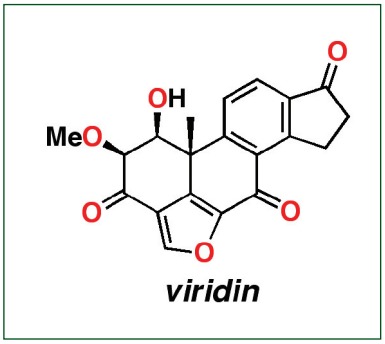


podophyllotoxin

We have developed a novel, efficient and very general way to produce complex polycyclic molecules with useful biological properties from simple, unsaturated, acyclic precursors using sequences of Diels–Alder reactions. Major advances this year in this area include the first practical synthesis of [4]dendralene and a demonstration of its use in the rapid formation of different polycyclic frameworks. This work was featured as a news item in the influential magazine *Chemical and Engineering News [Chem. Eng. News* (2005), 83(34), 38]. These methods are being applied in the total synthesis of the biologically important compounds triptolide and viridin. Significant progress has been made this year on these projects. *(With G Bojase-Moleta, T A Bradford, L Carpinelli, S K Goodwin, L C H Kwan, N A Miller, A D Payne, D Robinson)*



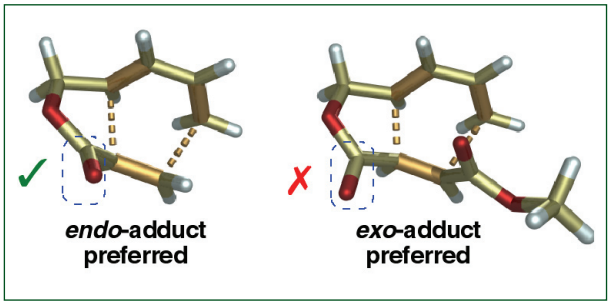
triptolide



viridin

A Deeper Understanding of the Most Important Organic Reaction

The Diels–Alder reaction is one of the most powerful and most commonly used reactions in synthetic organic chemistry. Predicting, controlling and explaining the stereochemical outcome of this reaction continues to be a major activity within the group. The location of transition structures at high levels of theory is providing stimulating new insights into the reaction. Our better understanding of the Diels–Alder reaction is driving the development of new methodology. *(With T N Cayzer, W Lording, E L Pearson, R J-P Tripoli, C I Turner, and M N Paddon-Row [UNSW])*



Host-guest Chemistry

Research in this area is concerned with the design and synthesis of host molecules for molecular recognition, complexation and catalysis. Investigations into uses of these intriguing hosts as molecule-sized devices are underway. A major achievement includes the synthesis of the superbowl container molecules, a new class of synthetic hosts with non-collapsible interiors which encapsulate molecules of the size of medicinal agents (Figure 1). This paper was the subject of press releases by the ANU and the American Chemical Society (ACS) in February 2005 and was featured in *The Sydney Morning Herald/The Age*, *The Canberra Times*, ABC radio, Channels 9 and 7, newspapers around the world and on TV in the USA. The superbowl molecule was named "molecule of the week" on the ACS website, featured as a highlight article in the journal *Angewandte Chemie* [*Angew. Chem. Int. Ed.* (2005), 44(24), 3652–3654], and in a news item in the journal *Drug Discovery Today* [*DDT (*2005), 10(7), 454]. A Google search using the terms "superbowl" with "molecule" or "sherburn" will provide the interested reader with a large number of relevant documents. We have also demonstrated for the first time that molecules imprisoned in separate cells of a "cell-block" host molecule "communicate" with each other (Figure 2). *(With E S Barrett, M W Carland, A J Edwards, N Kanizaj, D J Sinclair)*

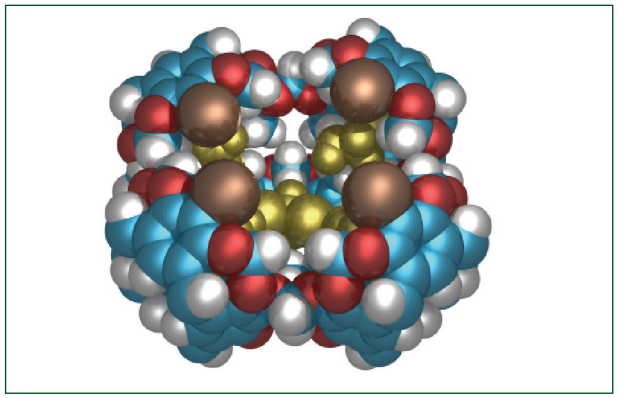


Figure 1: Crystal structure of a "superbowl" host molecule binding one chloroform and four ethanol molecules (bronzed). This new type of host can encapsulate molecules up to 100 atoms, *i.e.* the size of small medicinal agents.

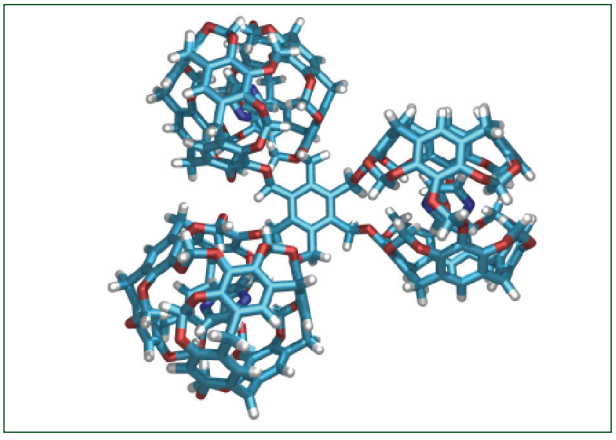


Figure 2: Energy minimised structure of a triple cage, single molecule host molecule. One pyrazine molecule is encapsulated within each cage. These encapsulated molecules "sense" one another.

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