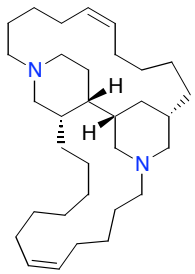
Professor Martin Banwell

The group's activities continue to be focused on the development of new synthetic strategies and methodologies. The application of these in the total synthesis of biologically active natural products and various analogues represents another ongoing theme as does the exploitation of novel starting materials for the same purposes. Of particular note is the preparation, in collaboration with Dr Gregg Whited of Genencor International Inc (Palo Alto, CA), of new, genetically engineered forms of the bacteria *E. coli* that are capable of effecting novel whole-cell biotransformations of various poly-substituted aromatics. The metabolites resulting from such processes are not only enantiomerically pure but also sufficiently rich in functionality that they can serve as important new starting materials in our synthesis program. Aspects of our work are funded by Australian companies. For example, an APA(I)-funded PhD scholar has recently completed his collaborative studies with Biota Holdings and another has just started and will continue work in the same area. Progen Industries, a Brisbane-based biotech company, is continuing to fund two post-Doctorals who have been working on a very enjoyable collaborative project focused on novel carbohydrate chemistries. Collaborations with the Melbourne-based company Cytopia have also commenced. The Alexander von Humboldt Foundation is providing Feodor Lynen Fellowships to two German postdoctorals working in the group. Ecological and other evaluations of analogues of the marine natural product haliclonacyclamine A have been undertaken in collaboration with A/Professor Mary Garson of the University of Queensland while related assessments of the two enantiomeric forms of natural product aiphanol are being undertaken in a joint venture involving Professor Chris Parish of the JCSMR (ANU), Dr Paul Savage of CSIRO Molecular Science and Professor Gerd Dannhardt of the University of Mainz in Germany. A PhD student from Professor Armin de Meijere's group at the University of Göttingen has spent six months in our labs working on a collaborative project directed towards the synthesis of steroids, whilst two students from Professor Hans Reissig's group at the Free University in Berlin each stayed in our labs for one month working on the exploitation of pyrroles as scaffolds in natural products synthesis.




Haliclonacyclamine A, a marine alkaloid derived from a sponge found on the Great Barrier Reef

Research highlights in 2003 include:

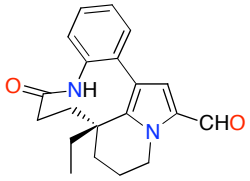
(i) completion of a total synthesis of the *C*-riboside (+)-showdomycin and two unusual analogues,

(ii) development of simple methods for the preparation of the (+)- and (–)-forms of the complex sialic acid KDN from a common and readily available chiron,

(iii) completion of enantioselective total syntheses of the potent antimitotic agents rhazinal and rhazinilam as well as the related alkaloid tashiromine,

(iv) efficient construction of seco-analogues of the alkaloid cryptopleurine and,

(v) total synthesis of the nonenolide (+)-microcarpalide, the (–)-form of which displays potent microfilament disruption activity whilst being only weakly cytotoxic.




Rhazinal, a terrestrially-derived alkaloid exhibiting potent anti-mitotic properties

In the methodological area, development of palladium[0]-catalysed Ullmann cross-coupling methods for the regiocontrolled synthesis of indoles and other heterocycles has been another important activity. Patents relating to this work

have or are being filed.

## Exploitation of *cis*- and *trans*-1,2-Dihydrocatechols as Starting Materials for Chemical Synthesis

The title compounds, which can be obtained by enantioselective microbial oxidation of the corresponding arene or through manipulation of the shikimic acid biosynthetic pathway, continue to serve as important starting materials for the preparation of a structurally diverse array of poly-oxygenated natural products and their analogues. Methods for the enantiodivergent elaboration of *cis*-1,2-dihydrocatechols through Diels–Alder chemistry has been a major area of activity and the adducts derived from such processes have been converted, using photochemical processes, into the polycyclic skeleta associated with a diverse range of terpenoid natural products. Other natural products being targeted include the alkaloids galanthamine (a useful agent for the treatment of Alzhiemer's disease), brunsvigine and vindoline (a clinically important anti-cancer agent) as well as the macrolide tricholomenyn B (and potent anti-mitotic agent), the fungal metabolite diversonol and the plant-growth regulating substance cladospolide B. The preparation of various rare sugars together with certain sugar mimetics has been another activity in this area and one that has been carried out with commercial partners. *(with K. Austin, M. Bonnet, C. Chun, M. Essers, M. Friend, P. Guan, G.J. Harfoot, N.L. Hungerford, J. Jury, O.P. Karunaratne, D.T.J. Loong, D.W. Lupton, X.H. Ma, J. Renner, and R.H. Don. V. Ferro [Progen Industries Ltd, Brisbane], J.N. Lambert [Biota Pty Ltd, Melbourne], G.M. Whited [Genencor International Inc, Palo Alto])*

## New Synthetic Strategies and Methodologies

The exploitation of pyrroles as nucleophilic scaffolds for the construction various heterocyclic compounds continues to be a major activity within the group. Novel modes of reactivity involving this ring system have been developed recently and these have been or are currently being exploited in the construction of various biologically active systems including showdomycin analogues. The electrocyclic ring-opening of ring-fused *gem*-dibromo- and *gem*-dichlorocyclopropanes continues to be employed in various contexts, with one especially notable activity being focused on the construction of seco-analogues of the cytotoxic Australian alkaloid cryptopleurine. Other work has focused on the development of chemoenzymatic routes to the spinosyin class of insecticides and the carbotricyclic core of these natural products has now been obtained but more efficient routes to this important substructure will need to be developed before total syntheses can be completed. *endo*-Selective Diels–Alder cycloaddition reactions are being developed with this objective in mind. Novel aldol chemistries have been exploited as a means for construction of the *bis*-piperidinyl core associated with the Australian marine natural product haliclonacyclamine A. Significantly, ecological and other evaluations of this core molecule, as carried out by our collaborators including A/Professor Mary Garson, reveal that the compound retains much of the potency of the structurally much more complex parent (natural) compound. *(with D.A.S. Beck, S. Chand, M.J. Coster, J. Crossman, O. Floegel, S. Gross, M.J. Harvey, N.L. Hungerford, B.D. Kelly, O.J. Kokas, M. Plath, J. Renner, P. Stanislawski, M.O. Sydnes, R. Taylor, and C. Burns [Cytopia, Melbourne], G. Dannhardt [U. Mainz], R.H. Don, V. Ferro [Progen Industries Ltd, Brisbane], A. de Mijere [U. Göttingen], M.J. Garson [U. Queensland], C.R. Parish [JCSMR, ANU], H. Reissig [Free U. Berlin], G.P. Savage [CSIRO Molecular Science, Melbourne], J.A. Smith [U. Tasmania])*

**http://rsc.anu.edu.au/research/banwell.php**