

Prof. Stephen Geoffrey Pyne

RESEARCH DETAILS

Prof. Pyne's research has made significant contributions to Research in Organic Chemistry in Australia and Internationally in the following research areas:

1. Chiral Sulfur Chemistry and Asymmetric the Synthesis of Alkaloids (1985-2002)

He has developed novel synthetic methodology for the asymmetric synthesis of several bioactive alkaloids ((+) and (-)-sedamine, (+)-carnegine and (+)-canadine) and chiral allylic amines, amino acids and cyclopropanes using chiral sulfoxides and sulfoximines under anionic conditions or under the influence of Pd(0) catalysts. He has done pioneering research on the mechanisms and the stereochemical outcomes of these reactions. Much of this work has been heavily cited in the chemical literature. For example, his *J. Org. Chem.* 1989, and his 2 *J. Org. Chem.* 1990 articles have been cited, 46, 59 and 59 times, respectively (ISI 22/3/2005), while his relatively more recent chiral sulfur chemistry paper (*J. Org. Chem.* 1997) has been cited 29 times.

He has worked in collaboration with G. Boche (Marburg, Germany), and G. Solladie (Strasbourg, France) on fundamental structural, stereochemical, mechanistic and synthetic aspects of chiral sulfur chemistry. From this work he received the following prizes, Von Humboldt Fellowship, 1992; Young Researcher of the Year Award for 1992 (offered by the Australian Research Council & the von Humboldt Foundation), a Rhone Poulenc Fellowship in 1994 under the Bede Morris Fellowship Scheme and an ARC Senior Fellowship 1994-1998. In 1998 he received a DIST grant to work in collaboration with A. Pfaltz (then at Mulheim, Germany) on palladium(0) catalysed reactions of chiral sulfoximines.

He was an invited lecturer of the 17th International Symposium on the Organic Chemistry of Sulfur, in Tsukuba, Japan, in July, 1996 and was invited Keynote Speaker at the 11th Royal Australian Chemical Institute Convention, Canberra, 6-11th February 2000.

He was a Member of the Editorial Advisory Board of *Sulfur Letters* and of *Sulfur Reports* 1997-99 and then Managing Editor of these journals in 1999-2002. He has written chapters based upon his expertise in chiral sulfur chemistry for the following books, 'Studies In Natural Products Chemistry', 1992, 'Stereoselective Synthesis,

Houben-Weyl Methods for Organic Chemistry', 1995 and 'Advances in Sulfur Chemistry', 2000.

2. *Asymmetric Synthesis of Bioactive Alkaloids (2000-2005)*

More recently he has developed novel and elegant methods for the asymmetric synthesis of bioactive polyhydroxylated indolizidine and pyrrolizidine alkaloids using the aminolysis of chiral vinyl epoxides and the ring-closing metathesis reaction. A significant innovation was the use of pyrrolo[1,2-*c*]oxazol-3-ones as substrates to diastereoselectively introduce the *syn*-1,2-diol functionality into his target alkaloids through diastereoselective *syn*-dihydroxylation reactions. These substrates provided products with opposite facial selectivities to that of the more traditional 2-substituted-2,5-dihydropyrrole substrates. This work has been very productive over the past 5 years and has resulted in two total syntheses of the alkaloid, swainsonine and the total syntheses of epi-australines and the synthesis of the putative structure of uniflorine A. More recently this research has focussed on the synthesis of the structurally challenging *Stemona* alkaloids. He has written an Invited Account on this work for the journal *Synlett* (2004). He was an Invited Lecturer at the 10th Asian Symposium on Medicinal Plants, Spices and other Natural Products, in 2000, Dhaka, Bangladesh, an Invited Plenary Lecturer at the Heterocyclic Chemistry Symposium, Pacificchem 2000, Hawaii, 2000, an Invited Lecturer, at the 1st Japan Australia Symposium on Organic Chemistry, Monash University, Melbourne, 2001 and an Invited Lecture at the 20th Royal Australian Chemical Institute Organic Chemistry Conference, Cairns, Australia in 2004. In addition he is an Invited Plenary Lecturer to the Gordon Conference on Natural Products Chemistry in 2006.

3. *Drug Design and Synthesis (1995-2005)*

He has been very successful in obtaining research funding from Johnson and Johnson Research Pty. Limited for drug design, synthesis and development. This collaboration has resulted in the building of a new laboratory in 2005 for drug discovery in the Department of Chemistry at the University of Wollongong. While much of this work is confidential and subject to patenting, a number of papers have been published from studies on novel chiral immunosuppressive agents and more recently on novel chiral glutamate analogues, that required the development of new synthetic and diastereoselective methods.

Through ongoing support from Avexa (initially AMRAD), and in collaboration with J. Bremner and P. Keller, he has developed new peptoid antibacterial agents that are potent on drug resistant strains. Two patents have arisen from this ongoing project. Some of this work has been also supported by the ARC (Linkage grants) and by the NHMRC (Development Grant in 2004).

4. Fullerene Chemistry (2000-2005)

Fundamental work is being developed with P. Keller on the regioselective functionalization of the fullerene surface to make higher-order fullerenes. Novel amino acid derivatives, including fullerenylglycines have been realized. This innovative work on fullerenes is now supported by the new ARC Centre for Nanostructured Electromaterials at the University of Wollongong. The team has been invited to give lectures at the 201st (Philadelphia), 205th (San Antonio) and 207th (Quebec City) Electrochemical Society Meetings. In collaboration with Dr. G. Ball (UNSW), they are developing new NMR methods for the unequivocal structural analysis of highly functionalized fullerenes.

5. Natural Products Chemistry (2003-2005)

In a new collaboration with A. Prof. A. Jatisatienr at Chiang Mai University, Thailand he has an ongoing project concerned with the discovery of new alkaloids from the many different species of *Stemona* plants growing in Thailand. The extracts of these plants are important in traditional medicines. To date (2003-5) he has published 4 papers on the structure and biological activities of 5 new *Stemona* alkaloids. In 2003 he reported the structure of stemocurtisine, the first example of a *Stemona* alkaloid with a pyrido[1,2-*a*]azepine A,B-ring system (that is, a 6,7-bicyclic A,B-ring system), and not the more common pyrrolo[1,2-*a*]azepine (5,7-bicyclic A,B-ring system) nucleus. These discoveries disclosed a new and 6th structural class of *Stemona* alkaloids. He has been an Invited Lecturer at the 11th Asian Symposium on Medicinal Plants, Spices and other Natural Products, 2003, Kunming, China and the 3rd International Conference on Natural Products, 2004, Nanjing, China. In addition, he is an Invited Plenary Lecturer to the 10th International Symposium on Natural Product Chemistry (Pakistan) in 2006.

6. Cycloaddition Chemistry and the Synthesis of Non-proteinogenic Amino Acids and Novel Spiro-Heterocycles

He has developed (2*S*)-*N*-benzoyl-2-*tert*-butyl-4-methylene-1,3-oxazolidin-5-one and related exo-cyclic methylene compounds as substrates to prepare non-proteinogenic chiral amino acids through cycloaddition (Diels-Alder, 1,3-dipolar reactions and phosphine-catalysed [3+2] cycloadditions) and free radical reactions. This chemistry has also been used to synthesise novel conformationally restricted glutamate analogues and novel spirocyclic heterocycles, including carbocyclic hydantocidins (papers submitted to *J. Org. Chem.* and *Tetrahedron*).