COVER FEATURE

Professor Anthony G. M. Barrett*

Recipient of the 1997 RSC Award in Synthetic Organic Chemistry sponsored by CIBA Specialty Chemicals

Career

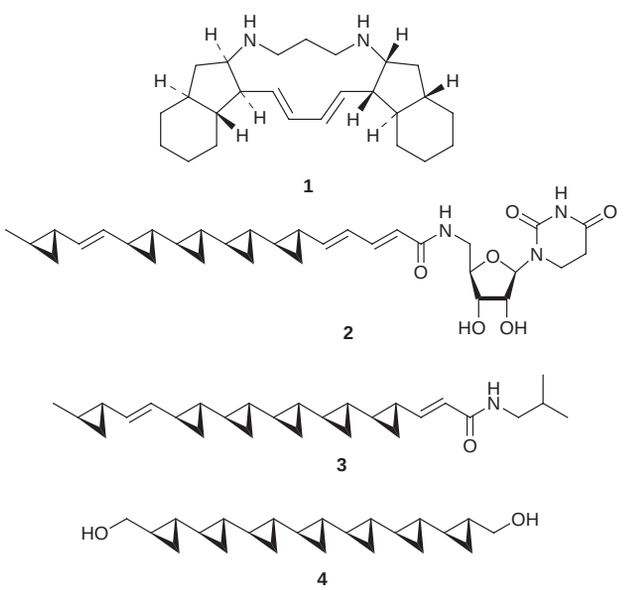
Tony Barrett obtained his BSc First Class Honours in Chemistry (1973) and PhD (1975) at Imperial College and then joined the faculty as a lecturer (1975–1982) and senior lecturer (1982–1983). He subsequently held the position of Professor of Organic Chemistry at Northwestern University (1983–1990) and Colorado State University (1990–1993) after which he returned to Imperial College as Glaxo Professor of Chemistry, Director of the Wolfson Centre for Organic Chemistry in Medical Science and Head of the Organic Section. Following the restructuring of the Chemistry Department in 1998, he is now Head of the Synthesis Section.

He has received numerous awards including the Meldola Medal (1980), Harrison Medal (1982), Corday–Morgan Medal (1986), Tilden Lectureship (1994) and the Award in Synthetic Organic Chemistry sponsored by CIBA Specialty Chemicals (1997) from the Royal Society of Chemistry; an American Chemical Society Arthur C. Cope Scholar Award (1986); a Camille and Henry Dreyfus Foundation Teacher-Scholar Award (1987); a Japan Society for the Promotion of Science Fellowship (1989); the University of Gröningen, Netherlands Backer Lectureship (1996); the East Carolina University, USA GlaxoWellcome Lectureship (1998) and the Royal Australian Chemical Institute Organic Divisional Interim Lectureship (1999).

Research

Tony Barrett has carried out extensive original studies on the preparation of heterocyclic compounds, organometallic intermediates, macrocyclic ethers and lactones and bio-active natural products. He has widely applied organometallic reagents for the concise synthesis of complex organic target molecules. He has made many pioneering contributions to the synthesis of structurally complex natural products of relevance to the pharmaceutical industry. For example he has carried out research on the milbemycins, a group of potent anthelminic agents, showdomycin, a C-glycoside antibiotic, the β-lactam antibacterial agents, several members of the polyoxin/nikkomycin group of chitin synthase inhibitors and bulgecin, the penicillin synergist. He has introduced a new strategy for the synthesis of glycosides, redox glycosidation. Finally, he has published extensively on novel organic methodology particularly directed towards asymmetric synthesis.

The Barrett research is, in part, currently directed towards the identification of effective fungicidal agents. There is considerable alarm amongst the medical profession regarding fungal disease. Pathogens such as *Candida albicans*, *Cryptococcus neoformans*, *Pneumocystis carinii* and *Aspergillus fumigatus* are the cause of considerable morbidity and mortality in immuno-compromised patients. Thus very considerable efforts are being directed to the discovery of new antifungal drugs. Targets of interest include restricticin, the palmarumycins, the marine antifungal agent papuamine (**1**), the multiple cyclopropane nucleoside FR-900848 (**2**) and the structurally related CETP inhibitor U-106305 (**3**). Research on the first total syntheses of **2** and **3** has led to extensive studies on the asymmetric assembly and characterisation of multiple cyclopropane arrays as represented by the helical heptacyclopropanedimethanol **4** whose X-ray crystallographic structure is depicted in Fig. 1.



The Barrett group is additionally studying other aspects of natural product synthetic chemistry including research on oxazole natural products, β-lactam antibiotics, and various oligosaccharides including ceramide derivatives. New asymmetric organoboron reagents for the synthesis of vicinal diols, β-amino alcohols, and functionalised allylic ethers have been designed. New catalysts for important chemical transformations have been designed including lanthanide salts for electrophilic aromatic substitution reactions. The group has also carried out research on combinatorial chemistry for the

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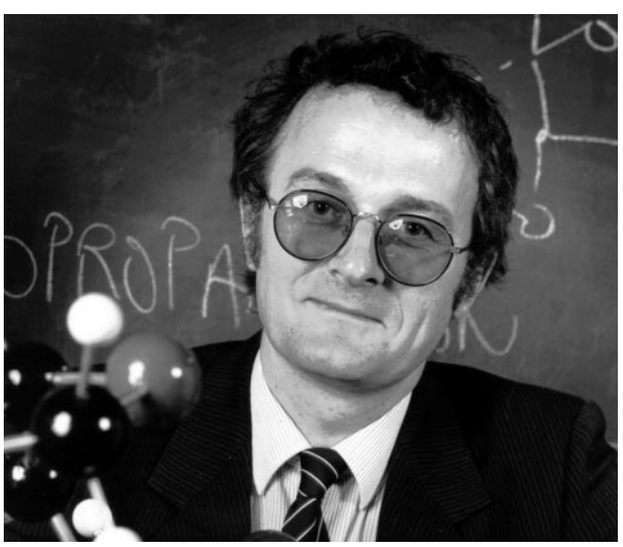


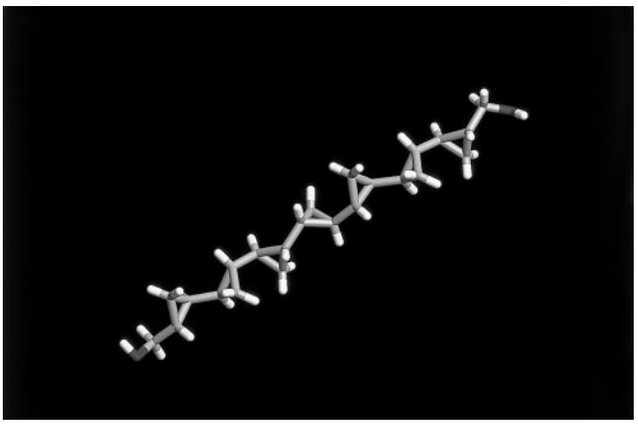
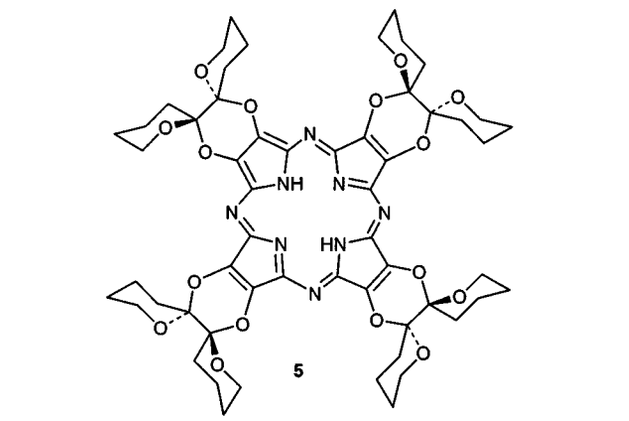


Fig. 1



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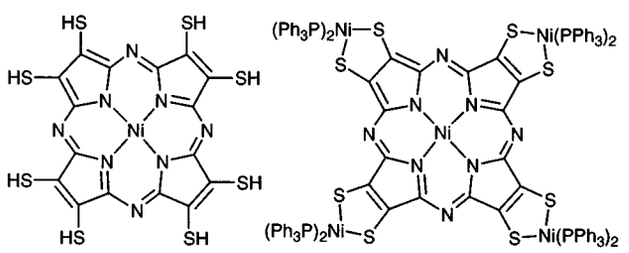

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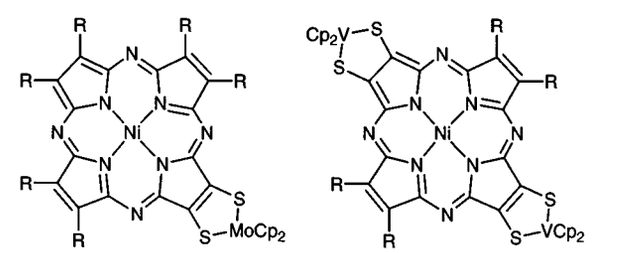
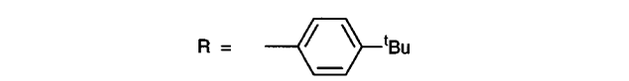
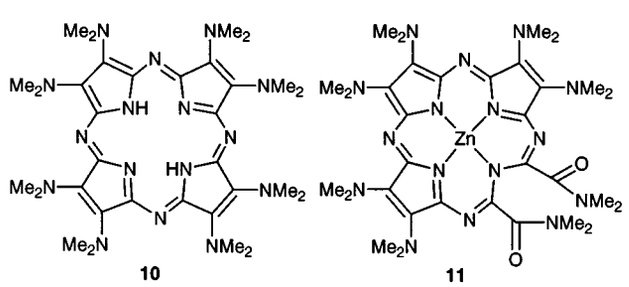


8 **9**





10 **11**

rapid and automated synthesis of bio-active compounds and has introduced both impurity annihilation and chameleon catches for parallel synthesis.

Finally, the Barrett group, in collaboration with Brian Hoffman's group in Northwestern University, has started to address problems in the materials and polymer arenas. A new class of multimetallic macrocyclic molecules, the star porphyrazines, has been designed. Representative porphyrazines prepared include the porphyrazine octaphenol protected as the Ley dispoke derivative **5**, the X-ray crystallographic structure of which is shown on the cover, the air sensitive octathiol **6** which has been converted into diverse star porphyrazines including **7**, the structurally related solitaire and gemini porphyrazines as exemplified by the macrocyclic coordination complexes **8** and **9**, and porphyrazinoctaamines such as **10** which has been converted into charge transfer complexes and into novel secoporphyrazines such as the zinc complex **11**. These macrocycles and their derived coordination complexes should be of considerable use as novel magnetic, optical and imaging materials and as therapeutic agents.

Representative publications from 1998

Facile and regioselective synthesis of *trans*-heterofunctionalized porphyrazine derivatives, T. P. Forsyth, D. B G. Williams, A. G. Montalban, C. L. Stern, A. G. M. Barrett and B. M. Hoffman, *J. Org. Chem.*, 1998, **63**, 331.

Total syntheses of palmarumycins CP_1 and CP_2 and CJ-12,371: novel spiroketal fungal metabolites, A. G. M. Barrett, D. Hamprecht and T. Meyer, *Chem. Commun.*, 1998, 809.

Molybdocene porphyrazines: a peripheral dithiolene metallocycle fused to a porphyrinic core, D. P. Goldberg, S. L. J. Michael, A. J. P. White, D. J. Williams, A. G. M. Barrett and B. M. Hoffman, *Inorg. Chem.*, 1998, **37**, 2100.

Porphyrazines and norphthalocyanines bearing nitrogen donor pockets: metal sensor properties, L. S. Beall, N. S. Mani, A. J. P. White, D. J. Williams, A. G. M. Barrett and B. M. Hoffman, *J. Org. Chem.*, 1998, **63**, 5806.

Nucleophilic substitution of (alkoxymethylene)dimethylammonium chlorides, A. G. M. Barrett, D. C. Braddock, R. A. James, N. Koike and P. A. Procopiou, *J. Org. Chem.*, 1998, **63**, 6273.

Chemeleon catches in combinatorial chemistry: Tebbe olefination of polymer supported esters and the synthesis of amines, cyclohexanones, enones, methyl ketones and thiazoles, C. P. Ball, A. G. M. Barrett, A. Commerçon, D. Compère, C. Kuhn, R. S. Roberts, M. L. Smith and O. Venier, *Chem. Commun.*, 1998, 2019.

A well-defined metallocene catalyst supported on polystyrene beads, A. G. M. Barrett and Y. R. de Miguel, *Chem. Commun.*, 1998, 2079.

Novel recyclable catalysts for atom economic aromatic electrophilic nitration, F. J. Waller, D. Ramprasad, A. G. M. Barrett and D. C. Braddock, in *Catalysis of Organic Reactions*, ed. F. E. Herkes, Marcel Dekker, Inc., New York, 1998, p. 289.

Rapid entry into mono-, bi-, and tricyclic β-lactam arrays *via* alkene metathesis, A. G. M. Barrett, S. P. D. Baugh, D. C. Braddock, K. Flack, V. C. Gibson, M. R. Giles, E. L. Marshall, P. A. Procopiou, A. J. P. White and D. J. Williams, *J. Org. Chem.*, 1998, **63**, 7893.

Impurity annihilation: a strategy for solution phase combinatorial chemistry with minimal purification, A. G. M. Barrett, M. L. Smith and F. J. Zecri, *Chem. Commun.*, 1998, 2317.

Polymer backbone disassembly: vanishing supports and high loading in parallel synthesis, C. P. Ball, A. G. M. Barrett, L. F. Poitout, M. L. Smith and Z. E. Thorn, *Chem. Commun.*, 1998, 2453.