
Professor Gerald Pattenden*

Recipient of the 1997 RSC Industrially-sponsored award for Natural Product Chemistry (Roche Products)

Career

Professor 'Gerry' Pattenden is the Sir Jesse Boot Professor of Organic Chemistry and also Pro Vice-Chancellor for Research at the University of Nottingham.

He studied for his doctorate at Queen Mary College, London and moved to University College, Cardiff as Lecturer in Organic Chemistry in 1966. Thereafter he held a similar appointment at Nottingham University, before becoming Reader (1975), Professor of Chemistry (1980), and Sir Jesse Boot Professor in 1988.

Pattenden researches in the broad area of design and development of new and novel organic synthesis methods, addressing the total synthesis of natural products and problems at the biology/chemistry interface. He has published over 400 papers and written several review articles. His contributions have been recognised by numerous Awards including the Corday–Morgan, Simonsen, Tilden and Pedler Medals of the Royal Society of Chemistry and the Society's special awards for Synthetic Organic Chemistry and for Heterocyclic Chemistry. In addition, he has received many named Distinguished Lecturer Awards, both in academe and in Industry. Pattenden was elected Fellow of the Royal Society in 1991.

Research

Although the main impact of Pattenden's researches has been in the area of synthesis of target natural products, these studies

* School of Chemistry, Nottingham University, University Park, Nottingham, UK NG7 2RD.



have been interwoven with structural, biosynthetic and biomimetic research work associated with a variety of biologically important natural substances. Thus, his early research uncovered the structures and biogenetic relationships of the striking poly-*cis* carotenoids found in Tangella tomatoes¹ and other mutant lines of tomato fruits,² and he was the first to study the biosynthesis of the novel cyclopropane terpene chrysanthemic acid found in pyrethrin insecticides³ using tissue culture techniques⁴—research which was complemented by extensive structural and synthetic studies. These latter studies blossomed into extensive structural and synthetic investigations of the squalene precursor presqualene,⁵ its prenylogue prephytoene, and casbene,⁶ the cyclopropane diterpene precursor of such important natural products as taxane, phorbol, ingenol, *etc.*, which has been an enduring program in Pattenden's research laboratories.

Pattenden's synthetic work uncovered the stereostructures of the novel ylidenebutenolide and ylidenetetrone acid families of pulvinones, pulvinic acids, aspulvinone, and multicolic acids,⁷ together with the related aspertetrone, gregatins,⁸ grevillins and calythrone.⁹ The biogenetic relationships between these families of natural products were investigated, and the studies were extended to natural tetramic acids and pyridones.

Over the period 1978–1983, Pattenden developed the use of the intramolecular de Mayo–Groβ fragmentation process and other photocycloadditions in the synthesis of a wide range of important sesquiterpenoid compounds including zizaane, capnellane, hirsutane, taylorone and pentalenene.¹⁰ From these early fundamental studies, other significant target terpene natural products were later synthesised including cedrene, alliacolide,¹¹ isoamijiol,¹² allamcin,¹³ capnellenediol¹⁴ and forskolin.¹⁵

Another enduring area of natural product research Pattenden has pursued, largely *via* synthesis, is the biogenetic interrelationships between the ether–polyene–pyrone natural products citreoviridinoids, aurovertins and asteltoxins.¹⁶ Total synthesis work based on biogenetic lines from poly-epoxide precursors made a significant contribution to unravelling the intricacies of the origins of these important mycotoxins.¹⁷

In 1986 Pattenden began studies of the free radical chemistry of the cobalt-based vitamin coenzyme B₁₂ which culminated in several publications,¹⁸ demonstrating the scope for the carbon–cobalt bond in synthesis, including important targets such as the β-lactam antibiotic thienamycin.¹⁹ Recent work has extended these studies into enantioselective synthesis involving “cobalt π-cation” intermediates,²⁰ mimicking still further the novel biological role of this important co-enzyme.

Pattenden's recent and extensive studies of the scope for free radical intermediates in the synthesis of complex terpenoid ring systems and steroids, based on cascade macrocyclisation–transannulation reactions and consecutive 6-*endo-trig* processes²¹ have their origins in his underlying interests in biomimetic synthesis. Many polycyclic ring syntheses have been achieved during these studies including a route to the taxanes,²² to the full steroid system, and to several important natural products, *e.g.* spongianone, modhephene, zearalenone, mukulol,

pentalenene.²³ A cascade of seven consecutive 6-*endo-trig* radical cyclisations from a polyene precursor, leading to a unique all-*trans,anti* heptacycle, demonstrates the power of this chemistry in contemporary synthesis.²⁴

Over recent years, Pattenden and his group have widened and extended their interests into the areas of polythiazoline, polyoxazole macrolide, and heterocyclic-based cyclopeptide natural products, many of marine origin. These studies underlie the group's interest in metal recognition and transport in the marine milieu and the importance of these phenomena in natural product assembly and their *modus operandi*. A definitive review was published in 1993,²⁵ and extensive synthetic studies of the mirabazoles/tantazoles and thiangazole²⁶ families of natural polythiazolines, together with the cyclopeptides lissoclinamide, cyclodidemnamide and mollamide,²⁷ the tris-oxazole macrolide-based ulapualide,²⁸ phorboxazole,²⁹ curacin A and pateamine³⁰ have been published.

References

- 1 'Stereochemical Assignment of Prolycopene and other Poly-Z-Isomeric Carotenoids in Fruits of the Tangerine Tomato *Lycopersicon esculentum* var. "Tangella"', *J. Chem. Soc., Perkin Trans. 1*, 1983, 3011–3018 (with J. M. Clough).
- 2 'Carotenoid Differences in Isogenic Lines of Tomato Fruit Colour Mutants', *Phytochemistry*, 1984, **23**, 1707–1710 (with E. A. Frecknall).
- 3 'Investigation of the Role of Chrysanthemyl, Lavandulyl and Artemisyl Alcohols in the Biosynthesis of Chrysanthemic Acid', *J. Chem. Soc., Chem. Commun.*, 1975, 290–291 (with C. R. Popplestone and R. Storer).
- 4 'Production of Chrysanthemic Acid and Pyrethrins by Tissue Cultures of *Chrysanthemum cinerariaefolium*', *Plant Cell Rep.*, 1985, **4**, 118–119 (with J. S. H. Kuey and I. A. MacKenzie).
- 5 'Synthesis of (±)-Presqualene Alcohol, (±)-Prephytoene Alcohol and Structurally Related Compounds', *J. Chem. Soc., Perkin Trans. 1*, 1975, 896–912 (with R. V. Campbell, L. Crombie, D. A. R. Findley, R. W. King and D. A. Whiting).
- 6 'Total Synthesis of the Macrocyclic Diterpene (–)-Casbene, the Putative Biogenetic Precursor of Lathyrane, Tigliane, Ingenane and Related Terpenoid Structures', *J. Chem. Soc., Perkin Trans. 1*, 1980, 1711–1777 (with L. Crombie, G. Kneen and D. Whybrow).
- 7 'Total Synthesis of Pulvinones, 4-Benzylidene-2-Phenyltetronic Acid Pigments of Fungi', *J. Chem. Soc., Perkin Trans. 1*, 1979, 70–76 (with D. W. Knight). 'Aspulvinones, a New Class of Natural Products from *Aspergillus terreus*. Re-Investigation of Structures by X-Ray Crystallographic and Spectroscopic Analysis', *J. Chem. Soc., Perkin Trans. 1*, 1979, 77–83 (with M. J. Begley, D. R. Gedge and D. W. Knight). 'Structure and Stereochemistry of Multicolanic, Multicolic and Multicolosic Acids, 4-Ylidenetetronic Acid Metabolites from *Penicillium multicolor*. Synthesis of Methyl-*E-O*-Methylmulticolanate', *J. Chem. Soc., Perkin Trans. 1*, 1979, 89–91 (with D. R. Gedge).
- 8 'Synthesis of Isoaspartetrone, Isogregatin and Related *O*-Methyltetronic Acids. Re-assignment of 5-Methoxy-3(2*H*)-furanone Structures to the Aspartetrone Group of Natural Products', *J. Chem. Soc., Perkin Trans. 1*, 1985, 2407–2411 (with N. G. Clemo).
- 9 'Synthesis of Grevillins and their Biogenetic Interrelationship with Terphenylquinones, Xylerythrins and Pulvinic Acids', *Tetrahedron Lett.*, 1987, **28**, 4749–4752 (with N. A. Pegg and R. A. Kenyon).
- 10 'Synthetic Photochemistry. A New Synthesis of (±)-Zizaene via an Intramolecular Variant of the de Mayo Reaction', *J. Chem. Soc., Perkin Trans. 1*, 1983, 1901–1904 (with A. J. Barker). 'Capnellene Sesquiterpenes. Total Synthesis of Epi-Precapnelladiene and Δ⁸⁽⁹⁾-Capnellene', *J. Chem. Soc., Perkin Trans. 1*, 1983, 1913–1918 (with A. M. Birch). 'Transannular Cyclisation as a Stratagem in Synthesis. A Total Synthesis of (±)-Pentalenene', *Tetrahedron*, 1987, **43**, 5637–5652 (with S. J. Teague).
- 11 'Radical Additions onto Enols and Enol Ethers as a Stratagem in Synthesis. Total Synthesis of the Unique Epoxy-lactone (±)-Alliacolide found in *Marasmius alliaceus*', *J. Chem. Soc., Perkin Trans. 1*, 1988, 1107–1118 (with M. Ladlow).
- 12 'Synthetic Radical Chemistry. Total Synthesis of (±)-Isoamijiol', *J. Chem. Soc., Perkin Trans. 1*, 1988, 1085–1094 (with M. J. Begley and G. M. Robertson).
- 13 'A Total Synthesis of Allamcin. An Approach to Antileukaemic Iridoid Lactones and Formal Syntheses of Plumericin and Allamandin', *J. Chem. Soc., Perkin Trans. 1*, 1988, 1119–1134 (with K. E. B. Parkes).
- 14 'Total Synthesis of (+)-Δ⁹(12)-Capnellene-8b,10a-diol', *J. Chem. Soc., Perkin Trans. 1*, 1988, 1077–1083 (with S. J. Teague).
- 15 'A New Synthetic Route to Forskolin', *Tetrahedron*, 1989, **45**, 5215–5246 (with M. J. Begley, D. R. Cheshire, T. Harrison, J. H. Hutchinson and P. L. Myers).
- 16 'A Total Synthesis of (±)-Citroviral, Based on a Biogenetic Model, and Formal Synthesis of (±)-Citroviridin', *J. Chem. Soc., Perkin Trans. 1*, 1991, 1947–1950 (with M. C. Bowden and P. Patel). 'A New Stereoselective Approach to Hydroxy-Substituted Tetrahydrofurans. Total Synthesis of (±)-Citroviral', *J. Chem. Soc., Perkin Trans. 1*, 1991, 1951–1958 (with M. J. Begley and M. C. Bowden). 'Epoxides in Synthesis. Synthesis of the Novel 2,6-Dioxabicyclo[3.2.1]octane Units in the Citroviridinols and Aurovertins', *J. Chem. Soc., Perkin Trans. 1*, 1991, 1967–1973 (with M. C. Bowden and J. E. Forbes).
- 17 'Total Synthesis of Preaurovertin, Putative Biogenetic Precursor of Aurovertin. Biosynthetic Interrelationships between the Aurovertins, Citroviridinoids and Asteltoxin', *J. Chem. Soc., Perkin Trans. 1*, 1991, 1959–1966 (with J. E. Forbes).
- 18 'Cobalt-mediated Intermolecular Radical Additions to Carbon-to-Carbon Double Bonds Leading to New Functionalised Alkenes', *J. Chem. Soc., Perkin Trans. 1*, 1990, 2709–2714 (with H. Bhandal, A. R. Howell and V. F. Patel). 'Acylcobalt Salophen Reagents. Precursors to Acyl Radical Intermediates for use in Carbon-to-Carbon Bond Forming Reactions to Alkenes', *J. Chem. Soc., Perkin Trans. 1*, 1990, 2721–2728 (with D. J. Coveney, V. F. Patel and D. M. Thompson).
- 19 'Synthesis of (±)-Theinamycin based on a New Approach to β-Lactams via 4-*exo-trig* Cyclisation of Carbamoylcobalt Salophens', *J. Chem. Soc., Perkin Trans. 1*, 1994, 379–385 (with S. J. Reynolds).
- 20 'Cobalt π-Cations in Carbocyclic Ring Constructions', *Tetrahedron Lett.*, 1996, **37**, 9369–9372 (with G. B. Gill and G. A. Roan).
- 21 'A Cascade Radical Macrocyclisation–Transannulation Approach towards the Construction of Ring-Fused Tricycles and Polycycles', *J. Chem. Soc., Perkin Trans. 1*, 1996, 21–29 (with M. J. Begley, A. J. Smithies, D. Tapolczay and D. S. Walter). 'Acyl Radical-Mediated Polyene Cyclisations Directed Towards Steroid Ring Synthesis', *J. Chem. Soc., Perkin Trans. 1*, 1996, 45–54 (with A. Batsanov, L. Chen and G. B. Gill).
- 22 'Studies Towards the Taxane Ring System via a Cascade Macrocyclisation–Transannulation Strategy', *J. Chem. Soc., Perkin Trans. 1*, 1997, 1091–1093 (with S. J. Houldsworth, D. C. Pryde and N. M. Thomson).
- 23 'Total Synthesis of (±)-Spongian-16-one. Cascade Radical Cyclisations Leading to Polycyclic Diterpenes', *J. Chem. Soc., Perkin Trans. 1*, 1998, 863–868 (with L. Roberts and A. J. Blake). 'α-Kentenyl Radical Intermediates in the Synthesis of Propellanes. A Formal Synthesis of Modhephene', *Tetrahedron Lett.*, 1998, **39**, 6975–6978 (with B. De Boeck). 'A New Synthesis of Pentalenene using a Novel Tandem Cyclisation Involving Ketene Radical Intermediates', *Tetrahedron Lett.*, 2000, **41**, 403–405 (with N. M. Harrington-Frost).
- 24 'Novel Cascade of Seven 6-*endo-trig* Radical-Mediated Cyclisations leading to a Unique all-*trans,anti* Heptacycle', *J. Chem. Soc., Perkin Trans. 1*, 1999, 843–845 (with S. Handa).
- 25 'Marine Metabolites and Metal Ion Chelation: The Facts and the Fantasies', *Angew. Chem., Int. Ed. Engl.*, 1993, **105**, 1–24 (with J. P. Michael).
- 26 'A Total Synthesis of Thiangazole, a Novel Naturally Occurring HIV-1 Inhibitor from *Polyangium* sp.', *Tetrahedron*, 1995, **51**, 7321–7330 (with R. J. Boyce and G. C. Mulqueen).
- 27 'The Total Synthesis of Mollamide, A Cytotoxic Cyclic Peptide from *Didemnum molle*', *Tetrahedron Lett.*, 1999, **40**, 9317 (with B. McKeever).
- 28 'Total Synthesis of Ulapualide A, a Novel tris-Oxazole Containing Macrolide from the Marine Nudibranch *Hexabranchnus sanguineus*', *Tetrahedron Lett.*, 1998, **39**, 6095–6098 (with S. K. Chattopadhyay).
- 29 'Synthetic Studies Towards Phorboxazole A. Stereoselective Synthesis of the C3–C19 bis-Oxane Portion of the Phorboxazole Macrolide', *Tetrahedron Lett.*, 2000, **41**, 983–986 (with A. Plowright).
- 30 'Synthetic Studies towards Pateamine, a Novel Thiazole-based 19-Membered Bis-lactone from *Mycale* sp.', *Tetrahedron Lett.*, 1996, **37**, 9107–9110 (with D. J. Critcher). 'A Concise Total Synthesis of (+)-Curacin A, a Novel Cyclopropyl-substituted Thiazoline from the Cyanobacterium *Lyngbya majuscula*', *Tetrahedron Lett.*, 1998, 2861–2864 (with J. Muir and T. Ye).