

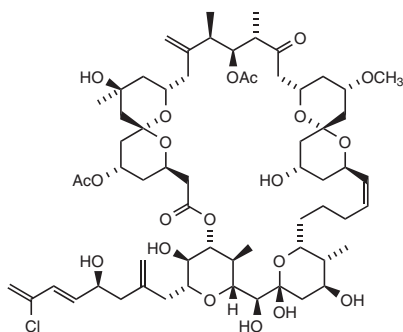
# SYNTHESIS



Steven Ley

Dear Reader,

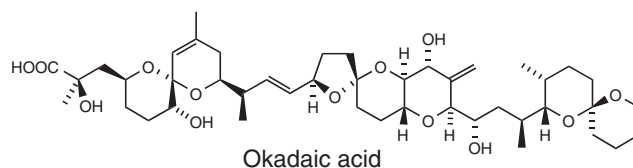
It is a very pleasant task indeed to provide a few words of introduction to this Special Issue of SYNTHESIS which celebrates the 60<sup>th</sup> birthday of Professor Steven Ley, the current incumbent of the prestigious BP 1702 Chair of Chemistry in Cambridge.



Spongistatin 1

As every synthetic organic chemist knows, his list of achievements is indeed formidable. First and foremost, as a master of the Art of Organic Synthesis, the total synthesis of over one hundred natural products has now fallen to the Ley group. Over the

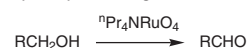
years, I have been especially impressed by strategic masterpieces such as the Milbemycins, Avermectins, Okadaic acid, Tetrinasin and Routiennocin, and earlier this year, I was fortunate to be present on the day when hitherto unrecognised symmetry elements led to completion of the shortest synthetic route thus far to Spongistatin. It is also characteristic of Steve's forays in total synthesis that the final route should bear his own hallmark in terms of the incorporation of new reactions, reagents and methods discovered and invented within the group, and this element leads automatically to the second interwoven theme of chemistry in which he has made a considerable impact on the community.



Okadaic acid

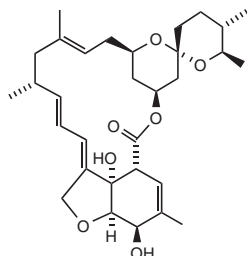
His many and varied contributions to methodology include the catalytic oxidant tetrapropylammonium perruthenate (TPAP) which is used by chemists worldwide, the useful diequatorial selective diol protecting groups for carbohydrates and the ensuing differentiation of enantiotopic 1,2-diols, and a beautiful series of papers on the use of  $\pi$ -allyl irontricarboxyl complexes for natural product synthesis. His visionary insight is also evident in that he was one of the first organic chemists to recognise the importance of using the microbial oxidant from *Pseudomonas putida* for elaboration of inositols from arenes *via* cyclohexadiene diols. Parenthetically and perversely, this inspired A. N. Other to invent a purely chemical variant! His very recent work on cyclopropanation *via* ammonium ylides and double conjugate addition of dithiols to electron deficient alkynes for polyketide synthons, emphasises that this flow of original ideas for fundamental carbon-carbon bond-forming reactions continues unabated.

**Tetra-*N*-propylammonium Perruthenate (TPAP) as an Organic Oxidant**



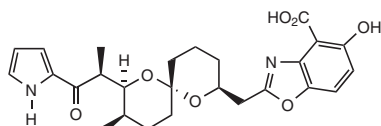
*Synthesis*, 1994, 639.

A further facet of his research which has become more dominant in recent times stems from his conviction that Organic Synthesis in the 21<sup>st</sup> Century must be clean, highly efficient and take advantage of modern technology. His use of microwaves, microreactors, solid-supported or encapsulated reagents, and scavenging agents in designed multi-step flow systems are all clearly paving the way for others to follow in this area.

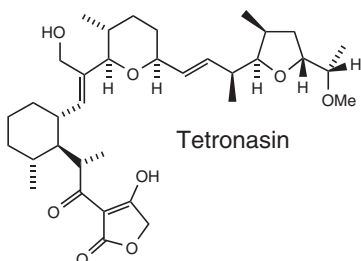
Milbemycin  $\alpha$ 1

In a much more personal vein, it is now over thirty years since we first met, the exact date and location in fact being April 1<sup>st</sup> 1975 in the NMR room at Imperial College. On that day, I had arrived to work with Professor Sir Derek Barton as a postdoctoral fellow, whilst Steve, having returned from his postdoctoral work with Leo Paquette in the previous year, had, together with Tony Barrett,

just been newly appointed to a lectureship. Having hoped to convince the great man that I might have been the one worthy of hire, I bemoaned my fate to the “student” with the blond page-boy hair style, who then turned to me and simply said, “I’m Ley.” To be in such an environment fully convinced me that the date of my arrival must have been preordained.



Routiennocin



Tetroneasin

Over the ensuing years, and especially during our time as faculty members together at Imperial, it has been a wonderfully illuminating experience for me to observe the way in which Steve’s restless creativity has continued

to grow. In those days, we shared adjoining labs in “the old building” and worked together in truly Victorian surroundings. My own office was in the corner of Steve’s Whiffen lab, and so I was emotionally exposed, on a daily basis, to all of the heartaches, frustrations and the triumphs of total synthesis whilst the sagas of molecules such as the Milbemycins (and azadirachtin!) evolved. Many Bartonian traits were clearly in evidence including the work ethic of early morning arrival, superb organisational skills, and a tireless determination to set himself objectives and then achieve them. There is however, at least one perceptible difference. Unlike Barton, Steve has always tended to be more pragmatic in practising the lessons of Sir Peter Medawar concerning “The Art of the Soluble”. A simple graph of his annual number of publications as a function of time clearly proves the point, revealing that his least productive period ever was the year spent with Sir Derek in attempting to solve the question of the existence of thiooximes.

Finally, on a much more human note, and outwith chemistry, is Steve’s love of cars, skiing, art, opera, and fine food, wine and cheeses. His gourmet (and occasionally gourmand) tastes in the latter area are legendary. With the exception of skiing, we share all of these interests, but with differing tastes and to varying degrees. I am always amused by the fact that Steve’s preference in sleek sports cars is for the latest technological miracle Porsche whilst my own resides in the classic era, albeit that the journey time has been proven to be the same, or even, on one memorable occasion, less, in the latter.

Some measure of the esteem and affection in which Steve is held can be gleaned from the fact that this Special Issue of SYNTHEsis is one of the largest on record and contains many contributions from his friends and colleagues worldwide. All of us wish him well, and know, without any doubt, that as an initiate sexagenarian, his chemistry will continue to enthrall us. I therefore wish to thank all of the authors in this issue, and also Dr Andrew Thomas, Professor Erick Carreira and the Editorial office of SYNTHEsis for making this Special Issue possible.

William B Motherwell,  
Christopher Ingold Laboratories,  
University College London,  
London, August, 2005

### Curriculum Vitae

Steve was born in on the 10<sup>th</sup> December 1945 in Stamford, Lincolnshire, England. His extensive and varied research is published in 600 papers spanning 35 years. A full list of his publications can be obtained from the Ley Group website at <http://leygroup.ch.cam.ac.uk>.

### Academic Career

Fellow of Trinity College, Cambridge (since 1993). Head of Organic Chemistry, University of Cambridge (since 1992). BP (1702) Professor of Organic Chemistry, Cambridge (since 1992). Head of Department, Imperial College (1989–1992). Professor of Organic Chemistry, Imperial College (1983–1992). Lecturer, Imperial College (1976–1983). Probationary Lecturer, Imperial College (1975–1976). Post Doctoral Fellowship with Professor Sir Derek H. R. Barton at Imperial College (1974–1975). Post Doctoral Fellowship with Prof. Leo A. Paquette at Ohio State University (1972–1974). Ph.D. Loughborough University with Prof. H. Heaney (1969–1972).

### Qualifications and Appointments

F.Med.Sci Fellow of the Academy of Medical Sciences (2005). Honorary Fellowship from Cardiff University (2004). C.Sci. Science Council, Chartered Scientist (2004). C Biol. Fellowship of the Institute of Biology (2003). D.Sc. (Hon) University of Huddersfield (2003). Commander of the British Empire CBE (2002). Honorary Fellowship from the Chemical Research Society of India (2001). Fellow of Imperial College FIC from Imperial College of Science, Technology and Medicine (2001). DSc Honoris Causa from the University of Salamanca, Spain (2000). ScD from the University of Cambridge (1999). MA from the University of Cambridge (1997).

DSc Honoris Causa from Loughborough University (1994). Fellow of the Royal Society FRS from The Royal Society (1990).

### Education

DSc from London University (1983). C Chem, FRSC from the Royal Society of Chemistry (1980). PhD from Loughborough University (1972). Diploma in Industrial Studies DIS from Loughborough University (1969). BSc (First Class Honours) from Loughborough University (1969).

### Prizes and Awards

**Royal Society of Chemistry Awards** • Robert Roberston Lectureship, Medal and Prize (2006) • Teamwork in Innovation Award (2004) • Industrially Sponsored Award in Carbohydrate Chemistry (2003) • Haworth Memorial Lectureship, Medal & Prize (2001) • Rhône-Poulenc Lectureship, Medal & Prize (1998) • Flintoff Medal (1996) • Natural Product Chemistry Award (1994) • Simonsen Lectureship & Medal (1993) • Pedler Lectureship, Medal & Prize (1992) • Organic Synthesis Award (1990–1989) • Tilden Lectureship & Medal (1988) • Corday Morgan Medal & Prize (1982) • Hickinbottom Research Fellowship - first recipient (1981–1983). **Royal Society Awards** • Wolfson Merit Award (2003) • Davy Medal (2000) • Bakerian Lecturer (1997). **Gesellschaft Deutscher Chemiker Awards** • August-Wilhelm-von Hofmann Medal (2001) • Adolf Windaus Medal Georg-August University, Göttingen (1994). **American Chemical Society Awards** • Ernest Guenther Award (2003). **Other Awarding Bodies** • The Yamada-Koga Prize (Japan) (2005) • Alexander-von-Humboldt Award (Germany) (2004) • iChemE Award for Innovation in Applied Catalysis (2004) • Innovation of the Year Award (2004) (jointly with AstraZeneca, Avecia and Syngenta) Chemical Industries Association • The Messel Medal Lecture - The Society of Chemical Industry (2004) • Novartis Research Fellowship (1995–2007) • Medal for Innovative Science - Pfizer Global R & D (2001) • Glaxo-Wellcome Award for Outstanding Achievement in Organic Chemistry - first recipient (1999) • George Kenner Prize & Lectureship - University of Liverpool (1996) • Paul Janssen Prize For Creativity in Organic Synthesis - Janssen Research Foundation (1996) • Pfizer Academic Award - first recipient (1983).

### Major Lectureships

2006: The Merck Lectures (University of Wisconsin, Madison, USA). 2005: Behringer-Simon Lecture (ETH, Zurich, Switzerland) • The 13th Bhatnagar Lecture (Hyderabad, India). 2004: The Class of 1960 Lecturer, Williams College, USA • The 6th Rothamsted Lecture, Rothamsted Research, Harpenden • Messel Medal and Lecture, Society of Chemical Industry, London • The Eli Lilly Lecture, University of Pittsburg, USA • The Daniell Lecture, University College, London. 2003: The Irvine Review Lecture (St Andrews) • The Thomas Graham Lecture (University College, London) • Chambers Distinguished Lecturer (University of Rochester, USA) • The Boehringer Lecturer (Yale, USA) • The Derek Barton Lecture (Texas A&M University, USA). 2002: Amgen Lecturer (UCLA, USA) • Chemical Record Lecturer (Tokyo, Japan) • Andrews Lectures (University of New South

Wales, Australia) • Malcolm Campbell Memorial Lecture (Dublin, Ireland) • Pfizer Lecture (Scripps Research Institute, La Jolla, USA). 2001: AstraZeneca Pharmaceuticals Group Lecturer (Ohio State University, USA) • Carl Shipp Marvel Lectures (University of Illinois, Urbana USA) • Boehringer Lecture (University of Montreal, Canada) • Gordon L. Hogson Jr. Memorial Lecture (Glaxo Smith Kline, USA) • August-Wilhelm-Von-Hofmann Medal Lecture (Würzburg, Germany) • Visiting Distinguished Lecture for the Michigan Chemsitry Tour (Michigan, USA). 2000: Hofmann Distinguished Lecture (Imperial College of Science, Technology and Medicine, London) • Bristol Myers Squibb Lecturer in Organic Synthesis (Stanford University, USA). 1999: Sandin Lectures (University of Alberta, Edmonton, Canada) • Robert Robinson Memorial Lecturer (University of Oxford) • Vista Chemical Company Regents Endowed Memorial Lectureship (University of Texas at Austin) • Paul Gassman Lecture (University of Minnesota, Minneapolis, USA) • Herbert C. Brown Lecturer (Purdue University, West Lafayette, USA). 1998: Organic Synthesis Lecturer (University of California Irvine) • Montana University Distinguished Organic Chemistry Lecturer (Bozeman, USA) • Sir Robert Price Lecture (CSIRO Clayton, Victoria, Australia). 1997: Schering Lecture in Organic Chemistry (Berlin, Germany) • Marker Lecturer (University of Maryland, USA) • Smith and Nephew Lecture (University of York). 1996: Kenner Lecture (University of Liverpool) • 35th Annual W. E. Bachmann Memorial Lecture (University of Michigan, Ann Arbor, USA) • Andersonian Chemical Society 4th Centenary Lecturer (University of Strathclyde) • 4th W. G. Dauben Lecture (University of California, Berkeley) • Brian Fitzsimmons Memorial Lecture (University of Waterloo, Ontario, Canada) • Fred Pattison Senior Lecturer for 1996 (University of Western Ontario, Canada) • 1996 Burton Memorial Lecture (Kings College, London). 1995: Ian Johnson Memorial Lecture (University of Sussex) • Merck Frosst Lecture (University of Toronto, Canada). 1994: Merck Frosst Lecture (University of Alberta, Canada) • Wyeth Ayerst Lectureship (University of Pennsylvania, USA) • Wilson Baker Lecture (University of Bristol) • S. Saddiqui Lecture (19th IUPAC Symposium on Chemistry of Natural Products, Karachi, Pakistan) • John Phillips Memorial Lectureship (Loughborough University). 1993: Kabi-Pharmacia Lecture (University of Uppsala, Sweden) • Glaxo Lecturer (Duke University, USA). 1992: Syntex Distinguished Lecturer (Boulder, Colorado, USA) • Lilly Lecturer (Ohio State University, USA) • Bristol-Myers Squibb Distinguished Lecturer (Syracuse, USA). 1984–1989: Merck Lecturer (University of Cambridge, 1989) • Syntex Pacific Coast Lecturer (USA, 1988) • Bio-Mega Lecturer (McGill University, Canada, 1988) • B.D. Steele Lecture (Queensland, Australia, 1985) Andrews Club Lecturer (Belfast, 1984).