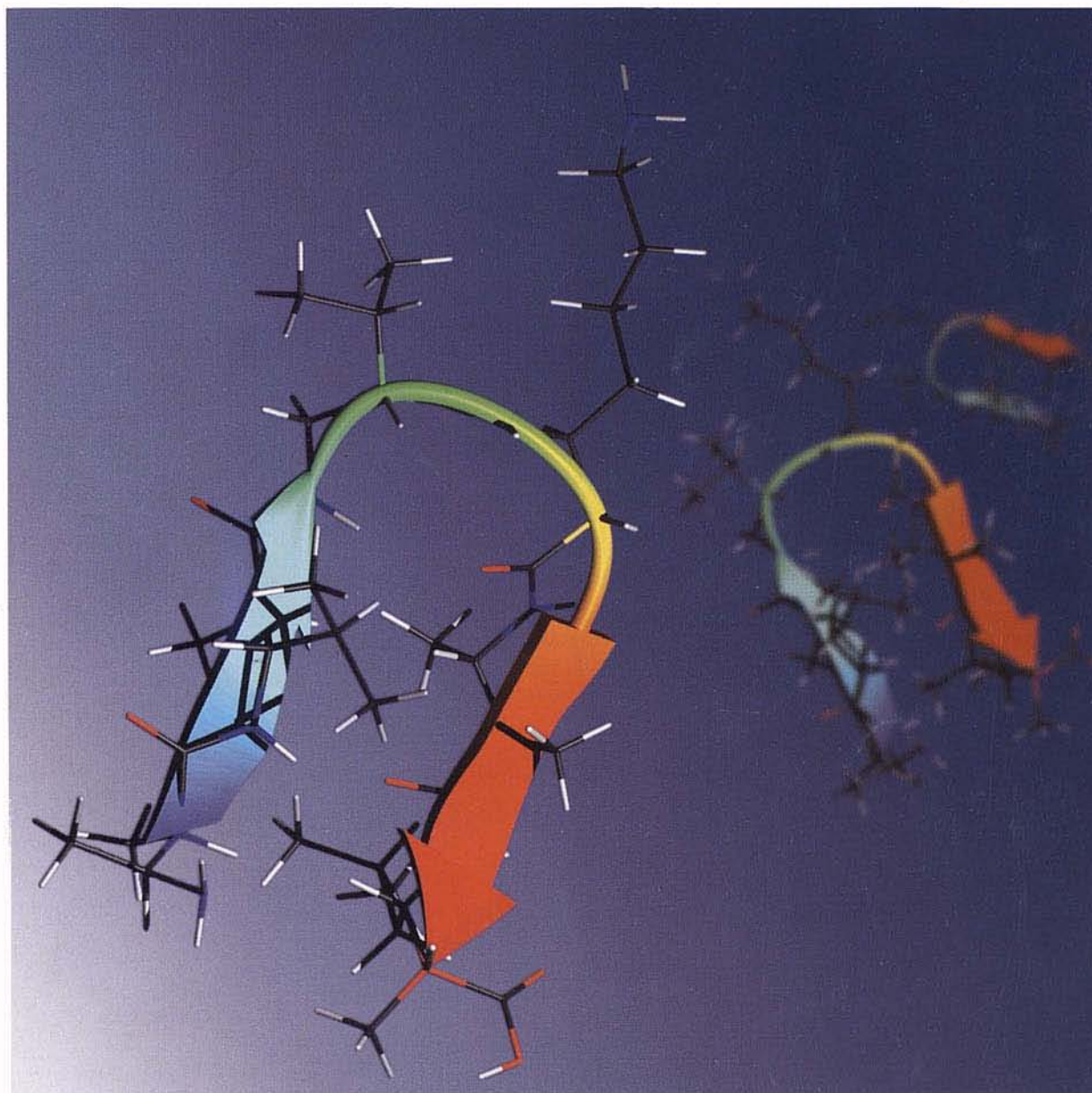

THE EUROPEAN PEPTIDE SOCIETY NEWSLETTER



Issue Number 23, 1 July 2000



Pleated Sheets and Turns of Beta-Peptides with Proteinogenic Side Chains

Determined by Dieter Seebach, Stefan Abele, Karl Gademann, Bernhard Jaun
Angew. Chem. 1999, *111*, 1700-1703; *Angew. Chem. Int. Ed. Engl.* 1999, *38*, 1595-1597

Illustrating the Fluka Peptide Synthesis Catalogue (Cover)

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New!

Synthesis of Peptides and Peptidomimetics

Houben-Weyl Vol. E22

Editor-in-Chief:

Murray Goodman

La Jolla, USA

Editors:

Arthur Felix

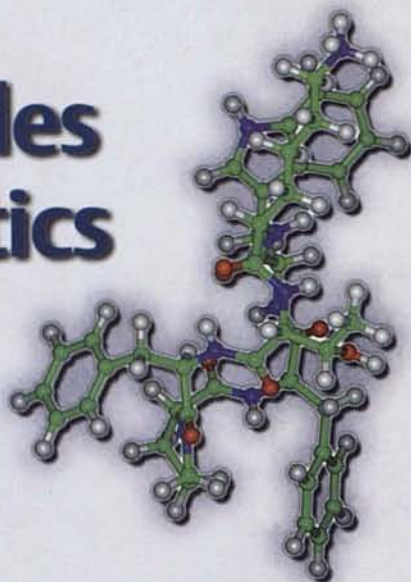
Mahwah, USA

Luis Moroder

Martinsried, Germany

Claudio Toniolo

Padova, Italy



The publication of **Synthesis of Peptides and Peptidomimetics** is to celebrate the 100th anniversary of the first report of peptide synthesis by Emil Fischer in 1899. This new English language volume will reflect the current challenges of a discipline which is at the center of modern chemistry and biology.

The three-volume set, edited by internationally renowned peptide chemists *Professors Murray Goodman, Arthur Felix, Luis Moroder, and Claudio Toniolo* will comprise a critical selection of synthetic methods in a consistent style.

Synthesis of Peptides includes protecting groups, peptide bond formation, the synthesis of peptides and proteins detailing general and specific methods, and analytical techniques used to determine the structure and composition of peptides.

Synthesis of Peptidomimetics features side and/or main chain modified peptides, peptides with secondary structure mimetics and inducers, de novo peptide structures, macropeptide structures and reactive peptides.

Author Index and Compound Index

Synthesis of Peptides and Peptidomimetics will be an indispensable work for every synthetic chemist.

E22a: 800 pages (approx.)/ISBN 3 13 219604 5

E22b: 800 pages (approx.)/ISBN 3 13 114424 6

E22c: 800 pages (approx.)/ISBN 3 13 125514 5

Publication starting autumn 2000.



Murray Goodman
La Jolla, USA



Arthur Felix
Mahwah, USA



Luis Moroder
Martinsried, Germany



Claudio Toniolo
Padova, Italy

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Author Index and Compound Index

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 **Thieme**

15th POLISH PEPTIDE SYMPOSIUM



Delegates, 15th Polish Peptide Symposium

The 15th Polish Peptide Symposium was held 2-4 September 1999 at a beautiful location by a lake amidst forest - Waplewo near Olsztyn. It was organised by Elżbieta Kostyra of the Olsztyn High Pedagogical School. More than 150 peptide scientists, from most of the Polish academic centres, took part in the Symposium. Six plenary lectures were presented. The first, concerning the combinatorial chemistry of peptides, was delivered by K Rolka; this was followed by a lecture on the application of mass spectroscopy in the analysis of peptides and proteins by Z Szewczuk. On the second day of the Symposium H Kostyra outlined the evolution of the peptide chain, and G Kupryszewski gave a presentation on polypeptide inhibitors of serine proteinases. On the last day, J Przała spoke on the role of opioids in the local regulation of the ovary. The three-day programme also included 15-minute oral presentations and posters covering a wide range of fields: isolation and analysis of endogenous peptides, structure-activity relationships, conformational analysis, and the synthesis of peptidomimetics.

The participants enjoyed a social programme including a bonfire and the closing dinner. During both events participants were entertained by the students' folk music ensemble. It was decided that the next (16th) Polish Peptide Symposium will be organised in Cracow 1-4 September 2001 by J Silberring (e-mail: SILBER@chemia.uj.edu.pl).

Contributed by Krzysztof Rolka

PROTEINASE INHIBITORS AND ACTIVATORS



John Deadman

The new Garden Quadrangle lecture theatre of St John's College in Oxford is the envy of at least one nearby much older but correspondingly more Spartan establishment. A better venue for a small (ca. 100 delegates) conference could hardly be imagined, and it was there that the mini-Epton symposium on Proteinase Inhibitors and Activators took place 17-20 April 2000. It was organised under the auspices of the UK BS/RSC Protein and Peptide Science Group and the EPS, with Drs John Deadman (Thrombosis Research Institute, London) and Robin Leatherbarrow (Imperial College, London) as co-chairmen. There was a full programme of lectures and posters covering a wide range of proteinase science with special reference to therapeutic intervention. No Proceedings will be published as such, but I am very glad to announce that Dr Deadman is to co-ordinate a Special Issue of *J Peptide Science* as Guest Editor, drawing on the principal contributions to the Symposium.

Contributed by the Editor

VII IBERIAN PEPTIDE SYMPOSIUM



Delegates, VII Iberian Peptide Symposium

The VII Iberian Peptide Symposium (EPI) was held 10-13 February 2000, at the University of Valencia. The Symposium attracted 130 participants, mainly from academic institutions, but with a sprinkling from the pharmaceutical companies located in Spain, reflecting the increasing interest in the development of peptide science by these companies. At this EPI we had the participation of our Portuguese colleagues from the Universidade do Minho (Braga). A very encouraging aspect was the presence of many young scientists at the meeting, which was arranged under four headings, namely Synthetic Methodology, Bioactive Peptides, From Peptides to Proteins (including combinatorial aspects) and Structural and Computational Methodologies. The keynote lectures were delivered by Professors Fernando Albericio, Concepción Abad, Rosario Herranz and Luis Serrano. In addition, there were some 40 short lectures, mainly by graduate and postdoctoral students: the scientific level was an indicator of the consolidation peptide research is undergoing in Spain. Furthermore, there were excellent spontaneous discussions. The two poster sessions were complemented with an open discussion.

Drs Miriam Royo, Isabel Haro and Ernesto Nicolas (University of Barcelona and the Spanish Research Council), have volunteered to organise the 2002 Symposium, in Barcelona.

Contributed by Enrique Perez Paya

MISCELLANEOUS NEWS IN BRIEF

- The four leading Internet sites devoted to combinatorial chemistry have formed the "Combi-Web Consortium" to centralise the vast array of information relating to this rapidly growing field. For more information contact kbrowne@combi-web.com
- A delegation from the Amphibian Peptide Society (Chairman Professor Litoria Splendida) will attend future peptide symposia: see *Nature*, 1999, **401**, 444-445 and *Eur.J.Biochem*, 2000, **267**, 1-8.

2nd HELLENIC FORUM ON BIOACTIVE PEPTIDES

The 2nd Hellenic Forum on Bioactive Peptides was held on April 14 and 15 at the Conference and Cultural Center of the University of Patras. The Forum was organised under the auspices of the Leonidas Zervas Foundation and the University of Patras. It was chaired by the Chairman of the Department of Pharmacy, Professor Paul Cordopatis. There were some 240 participants. The programme comprised 18 plenary lectures, 6 oral communications and 48 posters. The excellent translation service allowed also the non-Greek speaking participants to follow the presentations given in Greek. The Proceedings will be published, in English, by Typorama Press. It is hoped that the Forum will become a regular event based on Patras.

The opening lecture "On the synthesis of *N*- β -glycosylated, α,β -diaminoacid containing peptides" was presented by Raniero Rocchi, the Chairman of the Society. The other plenary lectures were: "From amino acids and peptides to medicinally interesting dideoxynucleosides and polyamine conjugates" by Dionyssios Papaioannou; "New approaches to the synthesis of bioactive non-natural alfa-amino acids and their derivatives" by George Kokotos; "Convergent synthesis of peptides and proteins" by Kleomenis Barlos; "Peptide conformation and the design of mimetics" by John Matsoukas; "NMR Study of protein-bound ligands. Application to antibody-antigen and enzyme-cofactor systems" by Michel Marraud; "The triad: NMR-biomolecular structure-thermodynamics" by Ioannis Gerotheranassis; "Synthetic peptide based specific tumor immunotherapy: present and future" by Kostas Kosmatopoulos; "Residue-based conformational control of secondary structure in peptides containing β -amino acid residues" by Ettore Benedetti; "Synthesis of substance P C-terminal analogs and studies on their antiproliferative activity *in vitro*" by George Korakakis; "Interaction of cysteine-substituted neurokinin A analogs with human neurokinin-2 receptor" by Nikolaos E Labrou; "Mapping of the integrin GPIIb-IIIa regions participating in platelets aggregation" by Eftichia Tenente; "A novel series of potent B1 and B2 receptor bradykinin analogs" by Jean Martinez; "Analysis of peptides by capillary electrophoresis" by Nikos Karamanos; "The employment of random phage-displayed peptide libraries for the identification of antigens associated with autoimmune diseases" by Dimitris S Monos; "Peptides and molecular recognition" by Ernest Giral; "Sequential oligopeptide carriers (SOCs): new developments and applications" by Constantinos Sakarellos; "Radioactive peptides for receptor-mediated targeting of tumours" by Alex Eberle; "Synthetic peptides and recombinant polypeptides in the study of the nicotinic acetylcholine receptor and myasthenia gravis" by Socrates J Tzartos; "Production of recombinant human cytokines from genetically modified *E. coli* cells via PCR technology and formulation as biopharmaceuticals" by Asterios S Tsiftoglou; "RXP 407: a phosphinic inhibitor able to differentiate the two active sites of ACE" by Athanasios Yiotakis; "Relation of interleukin 2 (IL-2) and P-glycoprotein (Pgp) expression in cancer cell lines" by Evangelia Pateraki; "Elucidation of the role of somatostatin receptors in the retina; a biochemical and immunohistochemical study" by Anna Vasilaki; "Epitope mapping approaches for developing oligoclonal antibodies against thymosins" by Leondios Leondiadis.



**Professors Cordopatis, Rocchi
and Benedetti**

The Forum Chairman and the Organising Committee (E Manessi-Zoupa, G Pairas, V Magafa, A Galanis, E Bissyris and S Papazaharias) gave the welcome reception for all participants on Thursday 13th at the Tzaki Hotel, and the Forum banquet was held on Friday 14th at the Danniilida Cellar of the Achaia Clauss Winery.

Compiled from notes provided by the Chairman of the Forum and the Chairman of the Society, to which the latter adds:

The Forum was certainly a great success, and it is encouraging for the future that a large number of enthusiastic young researchers attended the meeting, in witness of the continuation of the well established Greek tradition in peptide chemistry. Sincere thanks go to Paul Cordopatis and all his colleagues involved in the organisation for their excellent work.

BRIEF BOOK REVIEWS

GC Barrett (Ed.). *Amino Acid Derivatives. A Practical Approach*.
Oxford University Press. 1999. ISBN 0-19-855853-8.

The Practical Approach Series has been well established in biochemistry and molecular biology for over a decade, with many titles and a considerable following. A parallel venture has now been launched for the service of chemistry, *The Practical Approach in Chemistry Series*. One has some doubts as to whether it will be as popular as the trail-blazer series, because working from set protocols is so much less part of the culture in chemistry than it is in bioscience. But this title edited by Graham Barrett is very much on chemistry for bioscience. It deals with a pretty wide range of α -amino-acid derivatisation including α -acylation, α -alkoxycarbonylation, α -thioacylation, α -amino-alkylation and dialkylation, α -esterification, α -carboxyl reduction and modification, side-chain modification, and reactions at the α -carbon. Of course there are small gaps. I was sorry not to find anything about histidine, a long time love, and ring-substituted tryptophans seem to have been left out. And I could not find anything on diazoketones derived from α -aminoacids or on homologations leading to β -aminoacids. But lines had to be drawn somewhere, and these are trifling reservations. The procedures set out are detailed, and all read as if they really are tried and tested. Safety comments are helpfully given, which should simplify the solemn risk-assessment which must now precede every experiment in all severely regulated laboratories. It will be of considerable interest and practical value to anyone making peptides and peptide analogues.

WC Chan and PD White (Eds.). *Fmoc Solid Phase Peptide Synthesis*.
Oxford University Press. 2000. ISBN 0-19-963724-5.

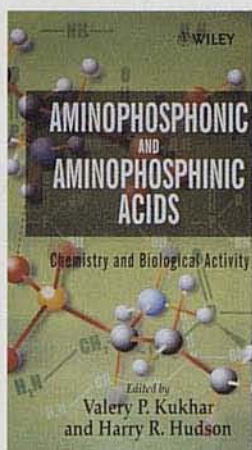
This book is the successor to Atherton and Sheppard in the Practical Approach series, but it is not a second edition. It is a completely fresh book. It comprises a total of 14 chapters, most of them team efforts, but there is a magisterial introductory chapter by RC Sheppard himself. Accounts of "Basic Principles" and "Basic Procedures" by the editors lead in to chapters on Met and Cys peptides; difficult peptides; modified peptides; phosphopeptides; glycopeptides; convergent peptide synthesis; peptide-carrier conjugates; ligation; purification using chemoselective tags; instrumentation; and manual multiple synthesis. It concludes with two useful appendices on sources of hardware and consumables, a table of residue and group weights and an index. It bears the publication date 2000, but that is misleading as the book has clearly been a long time in assembly (an almost invariable fate of works depending on large numbers of contributors) and does not contain many 1999 or 1998 references. The emphasis throughout is on practical detail and best procedures. It is a goldmine. Every lab using the Fmoc approach should have several copies, but junior inexperienced staff should not be allowed to work from it unsupervised, as there is only limited safety guidance.

JP Tam and PTP Kaumaya (Eds.). *Peptides. Frontiers of Peptide Science* [Proc. 15th APS].
Kluwer Academic Publishers. 1999. ISBN 0-7923-5160-6.

The proceedings of APS-15 (Nashville, 1997) arrived just too late for review in the last Newsletter. Probably many EPS Members have already seen it - if not, hurry, as by the time you see this review the contributions will have matured by a full three years. It is still worth getting, however. The usual very wide range of peptide science is covered in the 350 or so short papers which are published, and it is full of interesting material. It appears from the data about the Symposium given in the preface and back cover blurb that over 650 oral and poster presentations were made, so those who have the abstracts book had better hang on to it. But any who have only the abstracts book will miss out on some gems - most especially Ralph Hirschmann's reflections on milestones in peptide science under the title taken from *Through the Looking Glass* "The time has come, the Walrus said, To talk of many things...". A fuller reading of what the Walrus had to say does not clarify what was in our sage's mind when he chose his text to preach from, but that is entirely in the spirit of Lewis Carroll, and we get the gist. After a captivating and elegantly written personal overview of the last century's main discoveries, trends and successes in peptide science, he looks forward with confidence to continued growth in the field which feeds and entertains us all so well, but hedges his bets by quoting Niels Bohr (who must have been a relative of the Walrus): "Prediction is a very difficult art, especially when it involves the future".

N Fujii (Ed.). *Peptide Science 1999*. [Proc. 36th JPS]. JPS. 2000. ISBN 4-931541-00-3 (ISSN 1344-7661).

The Proceedings of JPS-36, which was held in Kyoto towards the end of October 1999 arrived in Oxford before the end of March 2000: this is only consistent with the Japanese track record (which greatly enhances the value of their Proceedings), but remarkable all the same. Although uniform with recent volumes in familiar gold-lettered olive green, there is a subtle change in the bibliographic minutiae: the publisher is no longer the Protein Research Foundation but the Japanese Peptide Society, reflecting the growth in the persona of that organisation.



VP Kukhar and HR Hudson (Eds.). *Aminophosphonic and Aminophosphinic Acids*. Wiley. 2000. ISBN 0-471-89149-5.

It is strange to reflect that only a few years ago, before the explosive proliferation of peptidomimetic studies, it would have seemed absurd overkill to produce a vast tome such as this on such a narrow area. But as it is this is a valuable contribution, comprising eighteen authoritative chapters - mostly on the synthesis and chemistry of aminophosphonic and aminophosphinic acids and their derivatives, but extending to peptide analogues. Such analogues are of particular interest because of the tetrahedral geometry at phosphorus, making them peptide bond hydrolysis transition-state analogues and thus potential protease inhibitors. All groups working on peptidomimetics, and especially those developing therapies based on protease inhibition, should have access to a copy of this book.

RE Reid (Ed.). *Peptide and Protein Drug Analysis* [Drugs and the Pharmaceutical Sciences Vol. 101]. Marcel Dekker, Inc. 2000. ISBN 0-8247-7859-6.

This book has a most remarkably misleading title, to the detriment of its own market, because the coverage is in fact much wider than it implies. *The New Shorter Oxford English Dictionary* defines "analysis" in the chemical context as "The qualitative or quantitative determination by chemical or instrumental means of the constituents of a substance, or of particular components (e.g. contaminants)", and goes on to contrast it with its antonym "synthesis". But here we find substantial chapters on the synthesis of peptides and proteins, as well as quite a lot of other material (on design, modeling, protein engineering etc) which can only be accepted as "analysis" after very adroit lexicographic gymnastics. It is not only Ralph Hirschmann (see above) who has been studying *Through the Looking Glass*. There we find that Humpty Dumpty said to Alice ("in a rather scornful tone") "When I use a word, it means what I choose it to mean - neither more nor less". So do not be put off by what might seem a restrictive title. The 27 chapters span a wide spectrum of techniques and topics in peptide and protein science, mostly on the molecular/chemical side, but with some coverage of more biological aspects such as pharmacogenomics. The actual chapter headings are Practical Principles of Protein Design; Peptidomimetic and Nonpeptide Drug Discovery: Concepts, Strategies, and Technologies; Structure Prediction and Molecular Modeling; Chemical Synthesis of Peptides; Chemical Synthesis of Proteins; Introduction of Unnatural Amino Acids into Proteins; Combinatorial Chemistry and the Structure-Function /Analysis of Proteins; Folding Polypeptides for Drug Production and Discovery; Protein and Peptide Chemical and Physical Stability; Bioinformatics and Computational Chemistry in Molecular Design: Recent Advances and their Applications; High Pressure Liquid Chromatography of Peptides and Proteins; Practical Aspects of Peptide and Protein Analysis by Capillary Electrophoresis; Gel Electrophoresis of Peptides and Proteins; Carbohydrate Analysis of Glycoproteins and Glycopeptides; Protein Sequence Analysis; Mass Spectrometry; Protein and Peptide Immunoassays; Pharmacogenomics; Analysis of Polypeptide Bioactivity; Pharmacokinetics and Pharmacodynamics of Protein Therapeutics; Approaches to Validating the Identity of Peptides and Proteins; Solution Structure Determination of Proteins by NMR Spectroscopy; NMR Studies of Protein-Peptide Complexes: Examples from the Calmodulin System; Circular Dichroism and FT-IR Analysis of Polypeptide Conformation; EPR of Peptides and Proteins; UV-Visible and Fluorescence Spectroscopy of Polypeptides and Proteins; Ultracentrifugation, Light-, X-ray-, and Neutron Scattering of Peptides, Proteins, and Nucleic Acids in Solution. With 3400 literature citations up to 1997, it is a useful resource.

Contributed by the Editor

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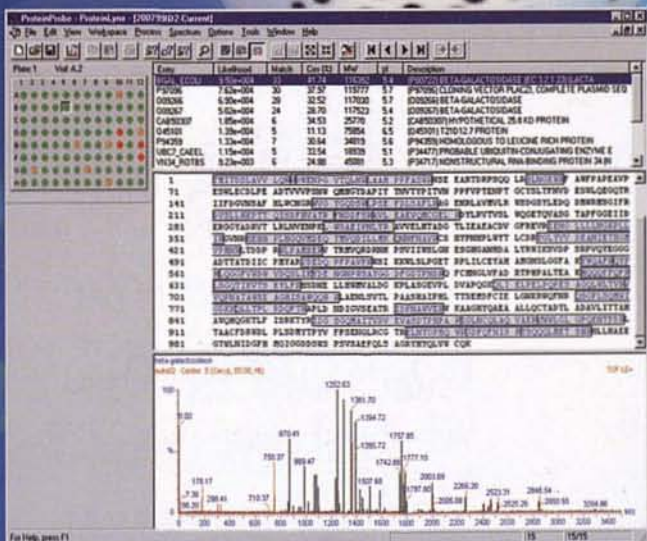
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Bert Schram

In Memoriam BERT SCHRAM

Members will be very sad to hear of the untimely death on 25 October 1999 of Dr Bert L Schram, who had become a familiar genial figure at EPS Symposia.

Bert was born in Amsterdam on 9 June 1934, and attended both school and university there. His PhD research was carried out at AMOLF/The FOM Institute for Atomic and Molecular Physics from 1961-1966. The title of his dissertation was *Ionization of noble and molecular gases by high energy electrons (0.1-20 keV)*: the absolute cross sectional measurements made by Bert are still used as reference material in the Database of the International Atomic energy Agency in Vienna. On completion of his PhD, Bert joined Unilever - first at Duiven (near

Arnhem) and later at Vlaardingem (close to Rotterdam). His early work was on isolating and identifying compounds responsible for meat flavours using MS (Bert was Chairman of the Dutch MS Society 1971-1973). In 1974, Unilever sent him to the USA (this was when he met Elizabeth, in New Orleans at the Institute of Food Technologists' Annual Meeting) to prepare for a move from Analytical Chemistry to Process Engineering. In the Chemical Engineering Group, Bert worked on various aspects of food processing at the pilot plant level and, in the eighties, was closely involved in simulation of manufacturing systems for Unilever companies in the UK, Scandinavia, Belgium and France. In 1990/1991 Bert took early retirement from Unilever to work full-time for ESCOM Science Publishers BV, which he had founded jointly with Elizabeth in 1987. The rest is history which Members know well, with ESCOM Science Publishers making an important contribution to peptide-related publishing (which is being continued by Kluwer), and more recently generous support from the ESCOM Science Foundation (ESF). The ESF Directors have decided that the ESF Poster Award for which arrangements had been made will be renamed The Dr Bert L Schram Award. The first Award, for the young researcher from academia judged by the Selection Committee to have presented the best drug discovery poster, will be made at EPS-26.

We shall miss his good-humoured presence, and extend our condolences to Elizabeth.

NEW PUBLICATION NOTICES

Information has been received on the following new books, journals, conference proceedings etc. which may be of interest to Members. Notices will be repeated in a future issue if it is necessary to correct them or desirable to provide fuller information. Suggestions for future entries in this section should be sent to the Editor, who will welcome them: full data should be provided, including the ISBN or ISSN. Listing here does not preclude a subsequent review in the Newsletter or the *Journal of Peptide Science*.

AMINO ACID DERIVATIVES. A PRACTICAL APPROACH
Ed. GC Barrett.
For bibliographic details and a review, see above.

AMINOPHOSPHONIC AND AMINOPHOSPHINIC ACIDS
Eds. VP Kukhar and HR Hudson.
For bibliographic details, see above.

COMBINATORIAL CHEMISTRY - A PRACTICAL APPROACH
Eds. W Bannwarth and E Felder.
NB: not part of the multi-title similarly entitled series published by Oxford University Press.
420pp approx, 2000. Wiley-VCH.
ISBN 3527-30186-0.

Fmoc SOLID PHASE PEPTIDE SYNTHESIS
Eds. WC Chan and PD White.
For bibliographic details and a review, see above.

PEPTIDE AND PROTEIN DRUG ANALYSIS
Ed. RE Reid.
For bibliographic details and a review, see above.

PEPTIDE SCIENCE 1999
Ed. N Fujii.
For bibliographic details and a comment, see above.

PEPTIDES. FRONTIERS OF PEPTIDE SCIENCE
Eds. TP Tam and PTP Kaumaya.
For bibliographic details and a review, see above.

CALENDAR OF SOCIETY MEETINGS

An exhaustive list of meetings relevant to the interests of members used to be given under this heading, but as from January 1999 this list, updated every month, has been printed in the *Journal of Peptide Science*.

It was felt that this would be much more useful to the Peptide Community because of the greater frequency of publication. Organisers of Meetings are asked to continue feeding the Editor with information, however. The Newsletter Calendar now only lists Society Symposia and Small Meetings being arranged under its auspices.

7th NAPLES WORKSHOP ON BIOACTIVE PEPTIDES and 2nd PEPTIDE ENGINEERING MEETING

5-8 September, 2000, Capri, Italy.

Arranged as a Satellite Meeting associated with EPS-26.

Co-Chairmen: Professor E Benedetti [e-mail benedetti@chemna.dichi.unina.it], Dr S Yoshikawa [e-mail yoshikawa@onri.go.jp] and Professor C Toniolo.

26th EUROPEAN PEPTIDE SYMPOSIUM

10-15 September 2000, Montpellier, France.

Professor Jean Martinez [e-mail martinez@pharma.univ-montpl.fr].

http://ww2.pharma.univ-montpl.fr/26_EPS

2nd INTERNATIONAL PEPTIDE SYMPOSIUM (17th AMERICAN PEPTIDE SYMPOSIUM)

9-14 June 2001, San Diego, California
For more information contact Eileen Weiler, e-mail: weiler@tpims.org

7th INTERNATIONAL SYMPOSIUM, SOLID PHASE SYNTHESIS

18-22 September 2001, Southampton, UK
Professor Roger Epton
[e-mail r.epton@mayflower.demon.co.uk]

27th EUROPEAN PEPTIDE SYMPOSIUM

31 August - 6 September 2002, Sorrento, Italy.

Professor E Benedetti
[e-mail benedetti@chemna.dichi.unina.it].

28th EUROPEAN PEPTIDE SYMPOSIUM

Early September 2004, Jerusalem.

Professor M Fridkin.

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SOCIETY NOTICES

YEAR 2000 AWARDS EPS-26, Montpellier September 2000

JOSEF RUDINGER MEMORIAL LECTURE **Sponsored by PolyPeptide Laboratories**

This award is presented "in commemoration of Josef Rudinger's role in the foundation of the European Peptide Symposia and of the diverse contributions he made to peptide chemistry." There is no restriction as to the nationality, age or position of those nominated, but they must be distinguished.

The Josef Rudinger Memorial Lecturer for 2000 is Bernard Roques.

LEONIDES ZERVAS AWARD **Sponsored by Bachem AG Switzerland**

This award is presented "to the scientist who has in the opinion of the Council of the Society made the most outstanding contribution to the chemistry, biochemistry, or biology of peptides in the five years preceding the date of selection." There is no restriction as to the nationality or position of the candidate, but the regulations give preference to younger candidates.

The Leonides Zervas Awardee for 2000 is Antonello Pessi.



Antonello Pessi



Bernard Roques

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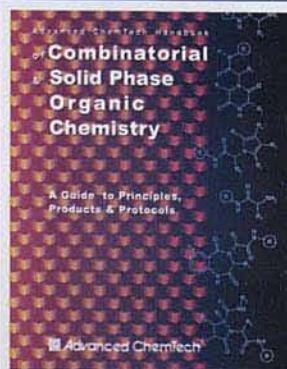
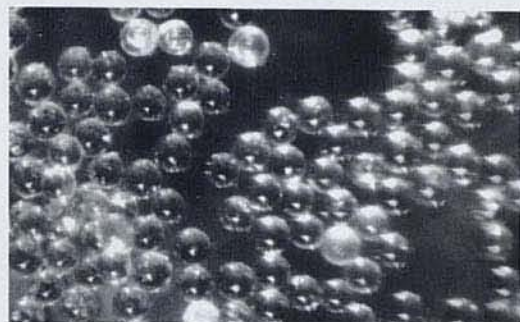
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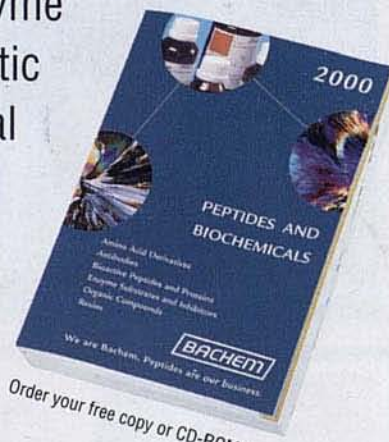
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