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CONGRATULATIONS TO PROFESSOR ALBERT ESCHENMOSER ON HIS 85TH BIRTHDAY

It is my great privilege to write the foreword too the Special Issue of HETEROCYCLES on the occasion of the 85th birthday of PROFESSOR ALBERT ESCHENMOSER. Mine is, indeed, a humbling task, as few chemists enjoy fame, as world-wide, as Professor Eschenmoser, who is renowned as a most profound master of organic chemistry. As many of his major scientific contributions are associated with complex heterocyclic natural products, such as vitamin B_{12}, and nucleotides related to DNA and RNA, it is unquestionably most fitting to dedicate this issue of HETEROCYCLES to Professor Eschenmoser.

When we celebrate Professor Eschenmoser's 85th birthday we are reminded of his birth in the year 1925 in Uri, a 'Canton' in the central mountainous region of Switzerland, as well as of his life-long association, in his career as a scientist and teacher, with the Laboratory of Organic Chemistry at the Eidgenössische Technische Hochschule (ETH) in Zürich, Switzerland. There the young Eschenmoser first embarked on the study of natural sciences, expanded his scientific mind rather freely as an exceptionally talented organic chemist in the laboratory of Leopold Ruzicka, who was a pioneer in natural products chemistry and recipient of the Nobel Prize of Chemistry in 1939. Albert Eschenmoser rose through the ranks quickly, to become Professor of General Organic Chemistry at the age of 40. Except for a recently terminated fourteen year long and very fruitful tenure as Professor at the 'Skaggs Institute for Chemical Biology' at the Scripps Research Institutes in La Jolla, California, he has spent most of his very prolific life as a scientist and teacher at the ETH, in Zürich.

Professor Albert Eschenmoser's scientific work is documented in over 270 outstanding scientific publications, as well as in numerous prestigious lectures. He is a founding member of the Academia Europaea, London (UK) and has become member, or honorary member, of several other renowned scientific academies and societies, including, e.g. the National Academy of Sciences, USA, the Royal Society, London (UK), the Pontifical Academy, Vatican (Rome), and, last but not least, the Pharmaceutical Society of Japan. He has been awarded a great number of very prestigious prizes, such as e.g. the Marcel Benoist Prize (Switzerland), the R.A.Welch Award (Houston, Texas), the (first) Tetrahedron Prize for Creativity in Organic Chemistry (London, UK), the Wolf Prize in Chemistry (Israel), the Nakanishi Prize (Tokyo, Japan), and the Roger Adams Award (Washington, USA). He has been given an Honorary Doctoral degree by nine universities from seven countries, one of them Harvard University (Cambridge, USA).

Within the framework of this foreword, it is hardly possible to appraise, at an adequate level, Albert Eschenmoser's scientific contributions to modern organic chemistry. His early scientific interest concerned the area of acid catalyzed polyene cyclizations. He contributed to providing mechanistic guidelines for the elucidation of the structures of terpenes and for the critical evaluation of structural proposals in this area. This work led to the development of the 'biogenetic isoprene rule' (its 50th birthday was celebrated not long ago[1]) and paved the way for pioneering synthetic achievements of other groups in the steroid field.

I will now take the liberty of quoting from a superb text from a eulogy given by Duilio Arigoni on the occasion of Professor Eschenmoser's 60th birthday[2]: '*Over and over Eschenmoser has proved his uncanny ability to shed new light on fundamental problems in organic chemistry. Examples of his many-faceted interests are his study of the geometry of the transition state in the* SN_2 *reaction at carbon centers, his clarification of important stereomechanistic aspects of the oxidation of alicyclic alcohols with chromium trioxide, his preparation of organic molecules with a slowly inverting pyramidal nitrogen atom, and his manifold preparative use of fragmentation reactions* ('Eschenmoser Fragmentations')*, the nature and importance of which he had recognized ahead of others already at the start of his research career, and which appear throughout his work as a Leitmotiv, always in a subtle new form.*

Eschenmoser is probably best known for his accomplishments in natural products synthesis. His singular command of strategy and tactics already apparent in the total synthesis of the alkaloid colchicine, became more and more manifest in the course of his long and difficult investigations on the corrins, in part carried out in a competitive collaboration with the late R.B. Woodward, crowned with two quite distinct total syntheses of vitamin B_{12}*. Their completion clearly confirmed the power of modern organic synthesis to achieve extraordinarily complex goals. In the course of this work Eschenmoser developed a multipronged set of synthetic routes to corrinoid and porphinoid compounds, enabling the first systematic investigation of the chemical properties of the corrinoids. He uncovered reaction paths entirely unsuspected before, which are central to an understanding of the biogenetic relationships within this biologically crucial class of pigments*'.

Professor Eschenmoser's synthetic efforts towards corrins and vitamin B_{12} provided truly outstanding contributions to the field of heterocyclic compounds. Among others, a crystalline formiminium reagent, called 'Eschenmoser Salt', and the imino ester/enamine condensation were developed. The sulfide contraction (in alkylative and oxidative variants), provided reliable paths for the construction of vinylogous amidines, e.g. as part of the corrin hetero-macrocycle. The great synthetic and intellectual efforts on both sides of the Atlantic towards the total synthesis of vitamin B_{12} also laid the foundations for stereo-electronic considerations that gave birth to the Woodward-Hoffmann 'Orbital Symmetry Rules'.

Albert Eschenmoser's groundbreaking research on B_{12}-synthesis and biosynthesis, eventually, led to the idea that the two unique major moieties of the complete vitamin B_{12} might 'find' the natural site of their connection without any external instructions. Indeed, he and his group could lay bare an amazing potential of Nature's most complex cofactor for the non-enzymatic self-assembly of its essential structural units.[3] In the course of this work towards the 'demystification' of the outwardly complex structure of vitamin B_{12}, Albert Eschenmoser's research interests underwent a transition from dealing with questions on the chemistry of life, as we know it, to the even more breath-taking and demanding search of the 'chemistry of life's origin'.[4]

One of the fundamental questions (among others) that Albert Eschenmoser thus asked was the following: 'What allowed the nucleic acids, as we know them, the conquest of their central place in Life?' In addressing the hypothesis that Nature's choice of RNA and DNA was possibly made in an evolutionary process on the basis of functional criteria, Eschenmoser and his coworkers created a number of concise structural alternatives, which were constitutionally related to the natural nucleic acids. Professor Eschenmoser's exquisite design, his synthetic and structural work on selected nucleic acid alternatives, was accompanied by critical investigations of chemical properties that are considered fundamental to the biological function of the natural nucleic acids. By comparing the chemical and structural properties of the 'analogues' with those of the natural nucleic acids, important criteria were established, by which Nature (might have) selected ribo- and deoxyribonucleic acids as the genetic system. Albert Eschenmoser was also fascinated by the problem of the homochirality of essential biological 'molecules', such as those constituting informational systems, as provided by oligonucleotide sequences. It became evident to him, that *'breaking molecular mirror symmetry by de-racemization is an intrinsic property of such a system whenever the constitutional complexity of the products of co-oligomerization exceeds a critical level'*,[5] a profound contribution to the question on the 'origin' of bio-molecular homochirality.

Few have contributed to organic chemistry as fundamentally as Albert Eschenmoser has. The legendary depth of the questions that he addressed, the foresight for scientific developments and tasks in his field,[6] and the bold experimental explorations of new domains of organic chemistry made his group a world-famed training ground. Over 140 doctoral students and even more post doctoral coworkers from Switzerland and abroad were his students. Most of them have had, or are still occupying, leading positions in important academic or industrial research institutions. This has clearly become an outstandingly fruitful seed in the field of organic chemistry.

The current issue of HETEROCYCLES is dedicated to Professor Albert Eschenmoser on the occasion of his 85th birthday. It is with deepest respect and admiration that I contribute these remarks about his life and his unique impact on Organic Chemistry. We are wishing him and his wife Elisabeth, many more fruitful and enjoyable years, and a life in fulfillment and happiness.

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Bernhard Kräutler was born in Dornbirn, Austria in 1946. He studied chemistry at the ETH in Zürich (Switzerland) and obtained his Ph.D. there, under the guidance of Professor Albert Eschenmoser. He then spent a year each in the groups of Professor Allen J. Bard in Austin (Texas, USA) and of Professor Nicholas J. Turro at Columbia University (New York, USA). He returned to the ETH (Zürich) in 1979 for independent research in the porphyrin field and to obtain his 'Habilitation' in 1985. In 1991 he accepted the chair of Organic Chemistry and the position of Full Professor of Organic Chemistry at the University of Innsbruck. Currently, he is the Head of the Institute of Organic Chemistry of the University of Innsbruck.

His research on the (bio)chemistry of chlorophyll breakdown, on (semi)natural corrinoids and B_{12}-cofactors, on synthetic porphyrinoids useful in solar energy conversion, on C_{60} and fullerene derivatives, explores design, and uses natural products isolation, synthesis, structure analysis, electro- and photochemistry for experimental realization. He is author and co-author of over 200 scientific publications and of several patents. Recent awards include the Josef Loschmidt Medal of the Austrian Chemical Society (2005) and the Erwin Schrödinger Prize of the Austrian Academy of Sciences (2001), whose full member he became in 2009. In 2006 he was elected member of the German Academy of Sciences Leopoldina.