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Tribute

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Professor Dr. Teodoro S. Kaufman

A tribute

This special issue of Arkivoc is dedicated to Professor Teodoro S. Kaufman, in recognition of his outstanding contribution to synthetic organic chemistry in Argentina

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Dr. Teodoro S. Kaufman (Teo) was born in Sunchales (Santa Fe, Argentina) and received his primary and secondary education in the towns of Las Palmeras and Moisés Ville, where he also accomplished the degree of teacher of Hebrew. The latter two are small villages founded at the end of the nineteenth century by immigrants from central-eastern Europe, Moisés Ville being the first Jewish agricultural colony in Argentina and a living symbol of the community's memory and identity in the country. After finishing secondary school, during which his passion for chemistry and biochemistry was born, his move to Rosario was driven by the youthful ambition of someone seeking to understand and transform the world through science.

He therefore decided to pursue his university studies at the Faculty of Biochemical and Pharmaceutical Sciences (FBioyF) of the National University of Rosario (UNR). It was there that he obtained his degrees in Biochemistry and Pharmacy, graduating with the highest distinctions and marks. From that moment, Teodoro demonstrated his ability to integrate diverse bodies of knowledge, traits that have accompanied him at every stage of his career.

Once graduated, in 1982 he began his doctoral training with a CONICET scholarship under the supervision of Dr. Humberto Riccomi at the Institute of Immunobiology (INIBI), a unit dependent of the UNR, on a topic related to his biochemical background, studying the molecular bases and immunochemical applications of the human complement system. After a promising start, the vicissitudes of politics were felt, causing the unexpected closure of that institution. This prompted Teodoro to seek new horizons overnight in order to complete his doctorate. Fortune led him to synthetic organic chemistry, an entirely different and emerging area in our city. At that time, under the guidance of Dr. Edmundo A. Rúveda, recently arrived from Campinas (São Paulo, Brazil), the Institute of Organic and Synthetic Chemistry (IQUIOS) was created, and it was there that he considered continuing his scientific training. Indeed, in 1985 and after an extensive conversation, Dr. Rúveda agreed to supervise his doctoral thesis, although on a somewhat different subject: the synthesis of polycyclic terpenoids present in petroleum sands, also known as molecular fossils. This move undoubtedly implied a Copernican shift in his academic training. However, far from feeling out of place in this new field, he gladly accepted the arduous challenge, which would not only be a technical exercise but a quest to understand the complex chemistry of these substances and to provide tools that would impact practical areas such as hydrocarbon prospecting and the interpretation of geological processes. That dual dimension — curiosity for knowledge and the will to translate it into useful applications — defines much of his career. It is worth noting that his thesis was completed in a record two years, since much of his scholarship had been used in the initial project at INIBI.

Having completed that stage in 1987, the logical next step was to continue his studies with a postdoctoral fellowship, for which he moved to the Department of Medicinal Chemistry at the University of Mississippi under the advice of Dr. Robert Sindelar. There, he deepened his knowledge in the synthesis and evaluation of terpenoid analogues based on K-76, a fungal natural product with notable inhibitory activity on the complement system, a subject that was familiar territory. Given the marked biological activity of the compounds synthesised, this period not only produced publications and patents, but also sharpened his ability to design ambitious projects and achieve new concrete goals.

Slightly over two years later, he returned to Argentina and re-entered the national scientific system at IQUIOS, nowadays evolved into the Institute of Chemistry of Rosario (IQUIR), which bears the name of its founder "Dr. Edmundo A. Rúveda". This place saw the beginning of an independent career that, over time, led him to occupy the highest ranks of CONICET, such as Superior Researcher, and to become Head of IQUIR. In parallel, his passion for university teaching led him to hold various positions, eventually becoming a Full Professor of the Organic Chemistry Department of the FBioyl.

Shortly after his return, Teodoro married Miriam and, over time, their three children joined the family: first Gabriela, then Uriel and finally Cintia, now graduates as a lawyer, an engineer and a biotechnologist

respectively; the latter, following in his footsteps, is about to complete her Ph.D. in Medical Sciences. On more than one occasion Teodoro has expressed his deep gratitude to his family, who, understanding his passion for chemistry and his vocation for teaching and training new scientists, agreed to share that commitment with the scientific community and to firmly support his career.

By 1990, already established in his laboratory, he began to shape his working strategy using the modern "Drug Development Process" paradigm as a template. This working approach is part of a complex, long-term path that demands substantial material and human resources. He sought to be active in key parts of it such as organic synthesis, analytical chemistry, pharmaceutical development, and quality control. The latter three combined in the form of "Pharmaceutical Analysis", an academic area of the FBioyF in which Teodoro obtained a professorial position at an early age. These action points do not arise as isolated parcels, but as links in the same chain aimed at improving public health and the quality of medicines. Since then, his research group has been dedicated to developing various facets of that process, from structural verification via total synthesis, exploration of bioactivity, discovery, identification and optimisation of lead molecules, to the study of formulations, analytical quality control and post-marketing surveillance. In each of these stages, his contribution was two-fold: on the one hand, the development and adaptation of synthetic methodologies that allowed access to complex structures and the study of pharmaceutically relevant solids; on the other hand, the development of analytical techniques and strategies capable of guaranteeing the quality, efficacy and safety of active pharmaceutical ingredients.

That combination of synthetic creativity and analytical rigour is, in essence, the hallmark of his scientific contribution which, over the past 35 years, has resulted in a massive body of work, making him a reference not only among the synthetic organic chemistry community of our country, but also in drug analysis; his participation in drafting the latest edition of the Argentine Pharmacopoeia being particularly noteworthy.

As a highlight of his contribution to organic chemistry, a plethora of natural products synthesised to date is revealed, among the earliest of which are arizonine (**1**), (*S*)-salsolidine (**2**), (*S*)-calycotomine (**3**) and the complex MY336-a (**4**), a tetrahydroisoquinoline alkaloid whose structure can be seen as a formative unit of ecteinascidin ET-743. These works, which included the first and longest complex total synthesis carried out at IQUIOS to date and the institute's first asymmetric syntheses, were achievements born out of perseverance and inventiveness.

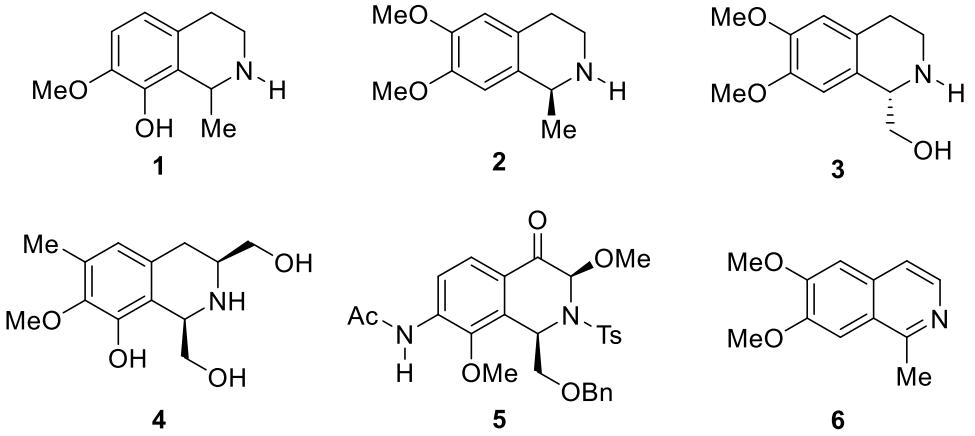

Figure 1.

In addition to focusing efforts on natural products, he also synthesised a set of partial fragments and analogues of MY336-a and other natural products such as the related tetrazomine (**5**). Other synthetic targets were reached over time: isobackebergine, isonortehuanine and nigellimine (**6**). These three isoquinoline alkaloids were achieved during my undergraduate thesis project in Chemistry in 1996, when I joined his research group.

New projects involving *N*-heterocyclic substances such as β-carbolines, stephaoxocanes and aaptaminoids emerged over the years, successfully employing the Jackson modification, a variation of the classic Pomeranz-Fritsch synthesis of isoquinolines. Other complex *N*-heterocyclic systems such as 2-methyltricyclisine (**7**), optically active azetidines, schefferine and 3-methylpterine (**8**) were the logical consequence of a growing synthetic repertoire that expanded over time. In addition, new reactions on tosyliminium ions, carbonyl transpositions on α-hydroxyamides, together with sophisticated asymmetric chemistry using both, lithiomethyl ethers and chiral reductants, were reflected in numerous bibliographic citations.

Other singular natural products such as the proposed structure of aspergillitine (**9**), along with total syntheses of cassiarin-C, *O*-methylcassiarin-A, aqabamycin-G (**10**), quindoline (**11**), 6-*O*-methyl anciscochine, neocryptolepine, DMDMI, and ampullosine were among the natural product targets conquered by his group, now employing new high atom-economy constructive strategies such as 6-π azaelectrocyclization and C–H activation, without neglecting metal catalysis and photocatalytic processes. His collaborations with colleagues in Brazil led him to explore organochalcogen chemistry, both methodologically and in the synthetic application of these substances, incorporating them into several of his total syntheses. He has also ventured into the chemistry of oxygenated heterocycles, both natural and synthetic, with isochromane, benzofuran and chromone cores as those preferred, among others; remarkable examples include chromanone A (**12**), pterophyllins 2 and 4 (**13**, **14**), and 2-isopropylidene-2*H*-benzofuran-3-one (**15**) and methyl dihydromarmesinate.

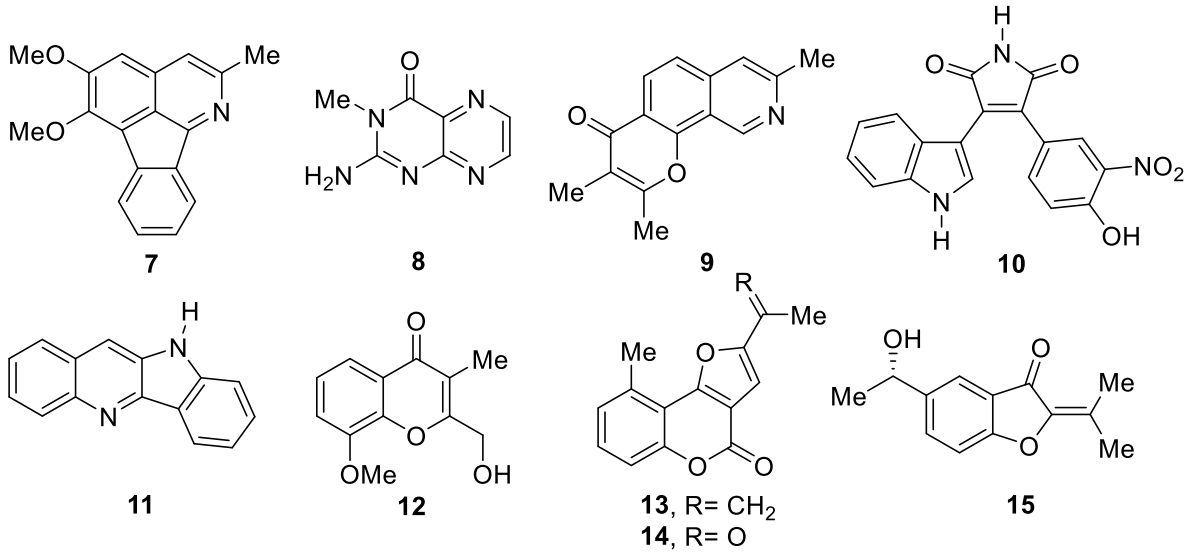

Figure 2.

One of the distinguishing features of the syntheses designed by Teodoro has been to minimise the use of protecting groups, to seek starting materials that are readily accessible and economical, and whenever possible to undertake the most chemically ingenious, eco-friendly and elegant route. As a corollary of each of his synthetic endeavours, or arising logically from his constant curiosity, are the numerous review articles published in the highest-impact journals in the discipline. Thanks to an assertive, brilliant and distinctive conceptual

structuring, enhanced by privileged writing, these reviews have not only achieved high citation counts in record time, but have also catalysed the emergence of new knowledge into the laboratory.

A particular hallmark of his intellectual output is the contribution to mechanistic questions, supported by experimentation, spectroscopic interpretation and computational calculation, especially in those aspects of research that present peculiar biases and require deeper inquiry. Countless of these natural products, their synthetic intermediates, derivatives and analogues were explored across various branches of biology (antimicrobials, complement system inhibitors, plant growth regulators, antiproliferatives, chemical probes, etc.), increasing knowledge about functional bioactivity. This research fructified as a result of numerous productive interdisciplinary collaborations with colleagues at home and abroad.

From the pharmaceutical analysis perspective, Teodoro and his group made contributions in areas as varied as the development of chemometric methods to ensure pharmaceutical quality, the study of pharmaceutical impurities, drug dissolution, and the development and characterisation of new solid phases of pharmaceutical interest, including polymorphs, salts, cocrystals and eutectics.

In view of the compact summary above and to put his personal achievements into perspective, it is worth mentioning that, at the time of writing this Tribute, Teodoro has reached *ca.* 200 scientific papers published in prestigious journals of the discipline, more than 300 communications to local and international congresses and symposia, and has been repeatedly invited to give plenary lectures. He has also edited three books and five book chapters, and is co-author of 10 patent applications, two of them national.

The training of human resources has also been a central point throughout his career. He supervised or co-supervised 5 CONICET researchers, 22 doctoral theses and postdoctoral fellows, 2 master's theses, numerous undergraduate theses, and many research interns. Most of his disciples currently hold teaching and/or research positions at the UNR; in addition, some of his former students are in Germany, Belgium, Bulgaria, France, Switzerland and Colombia, among other countries. Those of us who got to know him and have worked alongside with him, as well as those who have shared scientific and academic spaces with him, are aware of his personal and professional qualities. He has never spared his time when it comes to discussing chemistry, whether a reaction, a mechanism, a spectroscopic interpretation, or a strategic approach, and also manuscript writing, even on formative matters beyond the discipline.

Several of the theses conceived in his laboratory have received national awards and seven of his publications were included in the TOP25 list published by Elsevier some 15 years ago. His research has received economic support from various provincial, national (Antorchas, ANPCyT, CONICET, etc.) and international science organisations, such as CAPES, TWAS and IFS, among others, and was properly used to develop high quality science, as reflected by his presence in the list of the top 2% of the most cited scientists in the world during his career, according to a metric from Stanford University (2022-) and being "Top Scholar" in the ScholarGPS ranking "Overall (All Fields)" category in 2023, 2024 and 2025. In addition, he has taken part in editorial committees of reputed scientific journals and has served as editor (Organic Chemistry chapter) of the Journal of the Brazilian Chemical Society, one of the most influential chemistry publications in the Latin American region.

For his research work, he received several awards and distinctions, including the IFS-King Baudouin Prize for research of exceptional merit, the Elsevier Prize for the most cited work in the period 2004–2007 and the Diploma of Merit in Science and Technology, Organic Chemistry Area, awarded in 2013 by the Konex Foundation. As an amplification of this prize, he has been honoured as a "Distinguished Researcher" of the city of Rosario, and subsequently by the Honourable Argentine Senate. In addition, he has recently become a member of the National Academy of Sciences (ANC) of Argentina, received a similar honor from the Academy of Medical

Sciences of Santa Fe (Acacimesfe), and was also appointed as a Member of the Academy of Sciences of Latin America (ACAL), among other prestigious institutions of which he is a member.

Among Teodoro's recreational activities, he likes gardening at his weekend house, where he does not forget his rural roots, and also performing genealogical research, where the application of search skills developed during his scientific life has allowed him to trace parts of his family as far back as to the late sixteenth century, understand various historical processes, find distant relatives and even reunite families for other people.

To close these lines, written with deep pride, I wished not only to recount the milestones of a career but to show the coherence between life and vocation. Following Woodward's teachings, Teodoro reminds us constantly that synthesis is an intellectual expression, where the elegance of the path and the imagination to overcome obstacles are as relevant as selectivity or yield, and that this turn the synthetic endeavour into an art. His career demonstrates that perseverance, creativity, intelligence, responsibility, resilience and human quality can converge in scientific contributions that transcend the laboratory. This Tribute is, therefore, a homage to a life dedicated to chemistry, teaching and the training of many outstanding professionals, whose legacy will inspire those who embark on their own journey to Ithaca.

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