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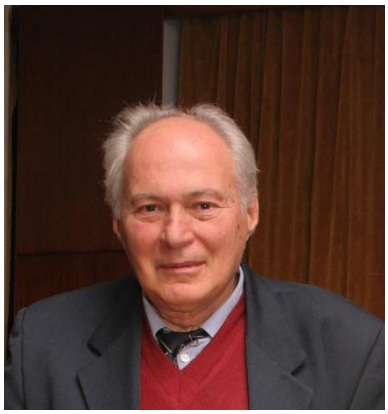
In memoriam Prof. DSc Ivan Pojarlieff (Johnny)



(03.11.1935 – 03.05.2024)

On May 3, 2024, we lost our teacher, colleague and friend, the corresponding member of the Bulgarian Academy of Sciences Professor DSc Ivan Georgiev Pojarlieff. Tribute to his bright memory!

Prof. Pojarlieff is among the pioneers in the field of mechanistic organic chemistry in Bulgaria. His achievements in stereochemistry, conformational analysis and kinetics and mechanism of organic and bioorganic reactions raised the organic chemistry in the country to a qualitatively new level.

After graduating from the Faculty of Chemistry of the Sofia University in 1958, Ivan Pojarlieff became a full-time graduate student of Acad. Bogdan Kurtev at the Institute of Organic Chemistry at the Bulgarian Academy of Sciences (BAS) and defended his PhD dissertation entitled "Synthesis, stereochemistry and mechanism of cyclization of 3-ureido acids" in 1964. In 1987 he obtained the scientific degree Doctor of Sciences with a dissertation on the „Quantitative dependences of steric effects of substituents in the closing and opening of ring compounds". In 1971 he became Associate Professor, in 1987 Professor, and in 2004 he was elected Corresponding Member of the BAS. Prof. Pojarlieff published more than 125 publications, which have found a wide response in the world literature, one rationalization, 3 patents and 23 author's certificates.

He specialized in nuclear magnetic resonance and chemical kinetics with Prof. Alan Katritzky at the University of East Anglia and had a long-term collaboration with Cambridge University on enzyme reaction models. During this specialization, he applied modern NMR techniques to clarify problems on Bulgarian topics. With the help of a significant set of dihydrouracils, including model ones, he established the relationship between the proton NMR-parameters and the stereochemistry of the flattened ring. The publication became a primary source in determining configurations and conformations of dihydrouracil systems.

The main achievements of Prof. Pojarlieff in the field of reaction mechanisms are related to his conviction that establishing the mechanism of biochemical reactions is practically possible only if the mechanism of the corresponding non-enzymatic reactions and the ways in which they can be accelerated are known. For this purpose, he organizes and conducts research on the mechanism of acyl group transfer in urea systems; a reaction of special biological interest related to the metabolism of pyrimidine bases and the action of the coenzyme biotin. Kinetic principles and rate-determining stages have been established in relation to the conditions and structure of the substrates: formation or decay of the tetrahedral intermediates, the type of acid-base catalysis, the participation of slow proton transfers and to which atoms they refer. These questions are particularly important for elucidating the catalytic action of the respective enzymes. Crucial is the development of "sterically strained" substrates, in which the accelerations induced by the gem-dimethyl effect are used to study reactions under physiological conditions. Thus, the locations and nature of proton transfers during the interaction of a ureido group with a carboxylate anion, a model of the interaction of biotin with a bicarbonate anion, were established.

For the first time, it was found that steric hindrance of proton transfers between heteroatoms can make them rate-controlling, due to strong retardation contrary to the general case of diffusion control. This explains a number of anomalies in the

gem-dimethyl effect and changes in the rate-determining step in strained substrates. For these scientific results published in a series of articles, J. R. Knowles commented: “To select a single model reaction from a field that has received so much more than its share of attention from the bioorganic community may seem gratuitous, yet Blagoeva, Pojarlieff and Kirby have reported a model reaction of particular appropriateness and simplicity”.

The detailed studies of the gem-dimethyl effect, the subject of Prof. Pojarlieff's dissertation for the scientific degree of Doctor of Sciences, prove the enthalpic nature of the effect, contrary to the widespread notions of “stereo population control”. The established linear correlations of the free energies, rates - equilibria (Leffler relationship) of the gem-dimethyl effect open up new possibilities for its prediction and understanding. These studies also have a practical application, since based on the gem-dimethyl effect, synthesis can be performed by simply replacing with alkyl groups (most often methyl) substrates of bioorganic reactions, reacting up to 10^6 times faster than the unsubstituted example. Thus, the rate of the cyclization reaction can be controlled by the structure of the substrate. Due to the steric nature of the effect, this is a possibly mild perturbation of the molecule, making the conclusions drawn from its study transferable. His top article in the area has been included in the list of excellent publications of the Royal Society of Chemistry.

Prof. Pojarlieff made significant achievements in the field of stereochemistry and conformational analysis. A dramatic example of the demonstration of stereoelectronic effects, a long-time highly debated area, has been found using conformationally constrained systems. Studying compounds with triphenylpropane skeleton, complete inversion of the ratio of migration rates of the acyl transfer upon *N*-methylation is observed, which can be explained only by a “stereoelectronically controlled intermediate cleavage” requirement for two lone Krisztián Buzathe cleaving C-N or C-O bond, i.e. equatorial orientation of the nitrogen lone pair in the tetrahedral intermediates. The main article on the matter is quoted in great details both in the book "Stereoelectronic Effects in Organic Chemistry" by the creator of the theory P. Deslongchamps, and by its main critic M. Sinnott.

For the first time, the role of allylic strain in heterocycles with an endocyclic amide group is shown. Allylic strain has been found to account for the unexpected axial conformation of substituents adjacent to a substituted trigonal nitrogen atom in several saturated heterocycles. It was established that the preference of gauche conformations in compounds with adjacent phenyl groups is due to a complex of reasons, and not only to favourable non-valent interactions.

Prof. Pojarlieff managed a number of contracts of the Institute with several Bulgarian factories in connection with the development and implementation of the production of additives to galvanic baths, for printed circuit boards, for galvanization, etc. Together with Prof. I. Juchnovski and Prof. S. Rashkov, he was a leader of a significant industrial development, the additives for acid bright copper plating. The Bulgarian team reached a complete replacement of the imported additives in the automobile factories of the former USSR, Czechoslovakia and DDR in 1975. Three additives have been regularly produced for more than 15 years.

Prof. Pojarlieff led the seminars of Academician B. Kurtev's course "Structure and Reactivity of Organic Compounds" in the Faculty of Chemistry of the Sofia University. He took over the regular reading of the course from 1977, which continued until 2003. In the 1980s, the course was significantly modernized and changed to "Physical Organic Chemistry". In 1992 and 1993 he taught the course in the University of Toronto.

Prof. Pojarlieff was the teacher of generations of Bulgarian chemists, from whom they have learned what physical organic chemistry is and how it can be applied in organic and bioorganic chemistry. His textbooks "Physical Organic Chemistry” and "Physical Organic Chemistry and Dynamic Stereochemistry" were the desk books not only of undergraduate organic and bioorganic chemists, but also of established researchers.

Prof. Pojarlieff wrote in a memoir article in 2016: “It was a honour for me to work 47 years at the Institute of Organic Chemistry mostly because of the amazingly large concentration of decent and very talented colleagues”. We, in turn, can confidently say that it was a great honour and privilege for us to have a teacher, leader and friend like Johnny.

Farewell, Teacher!

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