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Mikhail M. Shemyakin

1908–1970

Mikhail Shemyakin, noted Soviet chemist, brilliant organizer of scientific endeavor, and member of the Editorial Board of this Journal died on June 26, 1970, in Riga, Latvia, in the prime of his creative powers. His untimely death occurred just before the final session of the VII International Symposium on the Chemistry of Natural Products, of which he was the honorary president.

Graduating in 1930 from the Moscow University where he majored in chemistry, his first studies were on hydrolytic and oxidative-hydrolytic rupture of the carbon-carbon bond. This work led to a theory, developed with A. E. Braunstein, of amino acid metabolism catalyzed by phosphopyridoxal enzymes.

The second series of studies carried out by Shemyakin concerned the structure, synthesis and mode of action of various antibiotics. Among these should be mentioned his work on the tetracyclines, which resulted in the establishment of their absolute configuration and in the first total synthesis of the parent substance tetracycline. He also developed methods for the synthesis of chloramphenicol and for its commercial preparation which formed the basis for its industrial production in the Soviet Union. In this area, his most recent studies were on the structure and configuration of a large group of anti-tumor antibiotics allied to aureolic acid (olivomycins, chromomycins, mithramycin, etc.).

This versatile chemist also made significant contributions to lipid chemistry. He studied the stereochemistry of the Witting reaction, found ways for its stereochemical control and, on this basis, achieved the synthesis of a large number of unsaturated acids.

Shemyakin's largest and most significant body of work, however, was concerned with protein-peptide compounds, particularly the depsipeptides. Shemyakin elucidated the structures of the enniatins, valinomycin and several other naturally occurring depsipeptides and confirmed these by synthesis. Concurrently a study was made of the intramolecular interaction of hydroxy- and amino-groups with activated amide groupings, leading to discovery of the hydroxyacyl and aminoacyl incorporation reactions of linear and cyclic peptides and depsipeptides. This series of investigations shed light on the causes, nature and scope of a number of rearrangements in peptide and protein systems earlier regarded as purely hypothetical. The hydroxyacyl and aminoacyl incorporation reactions have also found practical application, for instance in the synthesis of the antibiotic serratamolide.

Studies of the biological activity of a large number of naturally occurring peptides and depsipeptides (antibiotics, hormones and their synthetic analogs) made it possible for Shemyakin to arrive at the far-going conclusion of the possibility in principle of mutually substituting ester and amide groups without fundamental change in biological activity and also to determine the limits of such changes. He subsequently elaborated these studies into a new field – the topochemical approach to the structure-activity relations of peptides and depsipeptides.

Of considerable importance was Shemyakin's discovery of the rules governing the fragmentation of acyl peptide esters induced by electron impact. This made possible the development of a novel method for determining amino acid sequences in oligopeptides

and hence for primary structure determination of proteins. Proved to be especiall convenient was the recently developed procedure in which the mass-spectrometri method was combined with Edman cleavage (from the N terminus) or carboxypeptideas cleavage (from the C terminus) of part of the amino acids from the peptide, the mas spectrometric analysis being carried out on the shortened peptide. This method wa successfully used for studying the primary structure of such complex proteins as cytc plasmatic aspartate-aminotransferase and pepsin.

In the last years of his life, Shemyakin devoted particular attention to the study c the physicochemical basis of transport through membranes. He regarded this work, th logical outgrowth of his prior investigations into the chemistry of lipids, peptides depsipeptides and proteins, as the initial step toward a general theory of the structur and functioning of biological membranes. He was one of the first to elucidate the effec of depsipeptides and peptides on the cation permeability of artificial and natural mem branes. Using combinations of physical methods, Shemyakin showed that this effec is the result of the ability of the membrane-active compounds to bind alkali metal ions through ion-dipole interactions with the ester and amide carbonyls, into a lipophili complex in which the depsipeptides are in a quite rigid conformation, like a bracele in the case of valinomycin and like a disc in case of the enniatins. Valinomycin an enniatin analogs with unstable bracelet of disc conformations were found to be devoi of the ability either to form complexes or to induce ion transfer through artificial an natural membranes. These studies in turn provided an approach to the mode of th antibiotic action of these compounds. The latter was found to be intimately related t their ability of selectively effecting an increase in potassium ion transport across th cytoplasmic membrane of the bacterial cell.

It was suggested by Shemyakin that an analogous mechanism could underlie th functioning of the ion-exchange sites in transport ATPases and in other structura elements of biological membranes responsible for the transport of metal ions. As th result of conformational changes in the peptide chain of protein molecules, the carbony ligands can become ordered into an arrangement similar to that of the macrocyclic depsi peptides. In such a conformation, they may acquire the ability to bind selectively meta ions and thus provide the conditions for subsequent transport of the latter.

Shemyakin was the founder and director of the Institute for the Chemistry o Natural Compounds in Moscow and Academic Secretary of the Department of Bio chemistry, Biophysics and Chemistry of Physiologically Active Compounds of the Soviet Academy of Sciences. He was also Secretary of the Department of Chemical Science of the USSR Academy of Science, and had been decorated with an Order of Lenin and named a Hero of Socialist Labor.

He enjoyed an immense authority among scientists throughout the world and was a leading figure in the International Union of Pure and Applied Chemistry. He could not tolerate contentment in science; working, himself, with ardor and self oblivion, he required the same of all his pupils. All who knew Shemyakin closely could not but be fascinated by his charm. He won the love and respect of all around him who greatly mourn the loss of a demanding but solicitous teacher and a leader of uncommon wisdom.

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