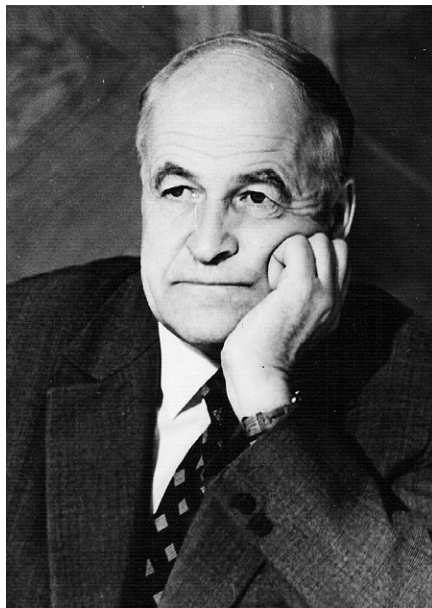


Obituary

Nikolay Konstantinovich Kochetkov 1915–2005



Nikolay K. Kochetkov was born on May 18, 1915, in Moscow. Following graduation from the M.V. Lomonosov Institute of Fine Chemical Technology (Moscow) in 1939, he joined the chair headed by Professor (later Academician) Alexander Nesmeyanov as a postgraduate fellow. However, after only two weeks he was called up for military service and served with the army during the Great Patriotic War of the USSR. The *Medal For Bravery* was his most precious award of many others he got that time and later.

Nikolay's scientific career re-started (under A. Nesmeyanov's supervision) at the end of 1945 in the Department of Chemistry of the M.V. Lomonosov Moscow State University as a lecture assistant. In 1948 he received a Ph.D. in Chemistry for his studies on the addition of mercuric chloride to alkynes. His next research topic that diverged substantially from organometallic chemistry (his tutor's favourite area) was studies on β -chlorovinyl ketones, and this proved to be extremely fruitful. N. K. Kochetkov explored the potential of these easily accessible compounds as sources of diverse carbo-

and heterocycles, and after only 5 years (in 1953) he was awarded D.Sc. (Chemistry) degree for these investigations. His students and associates successfully continued research in this field for a long term. In 1951 he became Assistant Professor and in 1955 full Professor of the Moscow State University.

Since 1954, Kochetkov headed the Chemistry Department at the Institute of Pharmacology and Chemotherapy of the Academy of Medical Sciences of the USSR. His achievements in the field of physiologically active compounds such as antibiotics, including antituberculosis drugs, antihistaminics, and anticonvulsants, were well acknowledged: in 1957 he was elected a Corresponding Member of the Academy of Medical Sciences.

Work at the Cambridge University with Sir Alexander Todd in 1956–1957 made a steep turn in Nikolay's fate. His great interest in chemistry of carbohydrates and nucleic acids acquired at that time emerged a couple years later when the Institute of Chemistry of Natural Compounds of the Academy of Sciences of the USSR was established in Moscow. Kochetkov was appointed its

Deputy Director and Head of the Laboratory of Carbohydrates and Nucleotides. It is since that time that the main studies conducted by him and his co-workers has been concentrated on these classes of compounds.

The first topics of investigation in the new field were structural studies of glycoproteins (V. Derevitskaya), plant glycosides (A. Khorlin) and animal glycolipids (I. Zhukova), synthesis in the monosaccharide series and radiation chemistry of carbohydrates (L. Kudryashov), chemical modification of nucleic acids and synthesis of analogues of nucleotide sugars (E. Budovsky, V. Shibaev). As time went by, glycoside synthesis (A. Bochkov), synthesis of halodeoxy-, deoxy- and amino-sugars (A. Usov), higher sugars (B. Dmitriev) and mass spectrometry of carbohydrates (O. Chizhov) became the subjects of research in the laboratory. The major achievement at that period was the structural elucidation of saponins from Far-Eastern medicinal plants, mainly of the Araliaceae family including ginseng (E. Budovsky, R. Shibaeva). For the first time, the structures of triterpene glycosides comprising up to 10 monosaccharide residues were established. A significant progress was made in the structural analysis of sphingoglycolipids of echinoderms. Gangliosides from starfishes and sea urchins were characterised in detail and found to differ significantly from mammalian gangliosides. In an effort to develop efficient methods for the structural analysis of nucleic acids, new reagents for their chemical modification were proposed, including cytosine-specific *O*-methylhydroxylamine (E. Budovsky, R. Shibaeva).

In 1966, Kochetkov was appointed a Director of N.D. Zelinsky Institute of Organic Chemistry of the Academy of Sciences and the major part of his Laboratory staff moved with him to the new institution. Some of the former topics turned into dominant lines of research. Considerable attention was paid to the development of new methodologies as applied to different aspects of both synthetic and structural carbohydrate chemistry.

Following in-depth investigations of the glycosylation reaction, a novel 'orthoester' method was elaborated for glycoside synthesis (A. Bochkov). It was successfully applied to the synthesis of various glycosides and oligosaccharides, and was accompanied later by mechanistic studies of the reaction (V. Betaneli). New types of glycosyl donors were introduced for stereospecific construction of both 1,2-trans and 1,2-cis glycosidic bonds. The discovery of trityl-cyanoethylidene condensation as a method for 1,2-trans glycosylation (A. Bochkov) paved the way to the synthesis of regular homo- and heteropolysaccharides, including those having the structures of naturally occurring polysaccharides (Ya. Wozney, L. Backinowsky, M. Ovchinnikov, Yu. Tsvetkov, N. Byramova, N. Nifantiev, S. Nepogodiev). Investigations into the kinetics and mechanism of this reaction (P. Kitov) resulted in novel synthetic implications. Tritylthiocyanate condensation was proposed as a valuable

method for 1,2-cis glycosylation (E. Klimov, N. Malysheva, A. Demchenko).

The synthesis of fragments of glycopolymers with phosphodiester linkages between the constituent monosaccharides was accomplished using a specially elaborated glycosyl H-phosphonate method (A. Nikolaev). A convenient method for the synthesis of glycosylamines for further conversion into neoglycoconjugates was developed (L. Likhoshervostov, O. Novikova) and acquired well-deserved popularity.

Yet another series of synthetic studies was connected with the use of simple monosaccharide derivatives (primarily, levoglucosan) as chiral precursors for the synthesis of aglycons of macrolide antibiotics (A. Sviridov). A number of gifted students (M. Ermolenko, D. Yashunsky, V. Borodkin) prepared their Ph.D. dissertations while executing this project, which culminated in the synthesis of erythronolides A and B and oleandomide.

Kochetkov and associates performed multilateral studies related to O-specific polysaccharides (O-antigens) of Gram-negative bacteria. These included synthesis of oligosaccharide fragments of the polysaccharides (E. Klimov, N. Malysheva, V. Torgov, N. Byramova, A. Chernyak, A. Nikolaev) and their transformation into neoglycoconjugates based on the copolymerisation of the corresponding allyl or acryloylaminoalkyl glycosides with acrylamide (A. Chernyak). The resultant polymeric artificial antigens were used for serodiagnostics of certain diseases.

Oligosaccharide fragments and their analogues in the form of glycosyl phosphates and glycosyl polyprenyl phosphates were synthesised (L. Danilov, S. Maltsev, V. Torgov) and employed in studies of biosynthetic pathways of bacterial polysaccharides (V. Shibaev, T. Druzhinina). Efficient procedures were developed to this end, which made these compounds readily accessible.

Structural elucidation of numerous O-specific polysaccharides, including those of *Shigella*, *Pseudomonas*, *Proteus*, *Francisella* and other medically important bacteria (B. Dmitriev, Yu. Knirel), have placed the laboratory to one of the leading positions in this field. Several classes of hitherto unknown monosaccharides, such as ethers with lactic acid, 2,3-diamino-2,3-dideoxyhexuronic acids and 5,7-diamino-3,5,7,9-tetraoxynon-2-ulonic acids, were identified as components of O-antigens and most of them were synthesised (V. Lvov, L. Backinowsky, Yu. Knirel, E. Vinogradov, N. Kocharova, Yu. Tsvetkov). Some unusual sugar constituents (O-methylated sialic acids, arabinofuranose) and unusual types of carbohydrate chains (internal sialic acid residues, including those linked through the hydroxy group of the *N*-glycolyl group) were found in the glycolipids of marine invertebrates (G. Smirnova).

Kochetkov and co-workers contributed significantly to the methodology of structural studies of complex car-

bohydrates. Considerable breakthrough in the polysaccharide analysis occurred when classical methods were implemented with novel chemical approaches, such as specific selective cleavage of glycuronans (A. Sviridov), hexosaminoglycans (B. Dmitriev, Yu. Knirel) and solvolytic cleavage of heteropolysaccharides with anhydrous hydrogen fluoride or trifluoromethanesulfonic acid (Yu. Knirel, E. Vinogradov, A. Perepelov). A mild procedure was elaborated for solvolytic desulfation of sulfated gel-forming polysaccharides of red seaweeds (A. Usov) and also applied to glycolipids containing O-sulfated sialic acid. New methods were devised for the selective cleavage of *N*- and *O*-glycosidic bonds in glycoproteins (L. Likhoshesterov, N. Arbatsky). Their application to blood-group substances and influenza virus haemagglutinin followed by isolation and identification of the resultant glycopeptides and oligosaccharides allowed a general concept of glycoproteins structures to be put forward.

After pioneering works in mass spectrometry of carbohydrates (O. Chizhov), modern NMR spectroscopy approaches were developed (A. Shashkov). Among them, computer-assisted ^{13}C NMR-based structural analysis of regular polysaccharides and oligosaccharides should be mentioned. It relied on the discovered dependence of ^{13}C NMR chemical shifts in disaccharides on the type of glycosidic bond and absolute configuration of the constituent monosaccharides, which was rationalised by conformational studies (G. Lipkind, A. Shashkov, E. Vinogradov).

Kochetkov was author of more than 1200 research papers, 50 review articles and book chapters. He wrote eight books, including *Chemistry of Natural Products* (with I. Torgov and M. Botvinik, 1961), which was the first of this kind in the USSR, and *Chemistry of Carbohydrates* (with A. Bochkov, B. Dmitriev, A. Usov, O. Chizhov and V. Shibaev, 1967). Two further books, *Organic Chemistry of Nucleic Acids* (with E. Budovsky), and *Radiation Chemistry of Carbohydrates* (with L. Kudryashov and M. Chlenov, 1978), were translated into English. The books *Carbohydrates in the Synthesis of Natural Products* (with A. Sviridov, M. Ermolenko and D. Yashunskii, 1984) and *Synthesis of Polysaccharides* (1994) reflected his latest objects of affection. The last book of Nikolay, *Selected Works* (2006), containing both scientific review articles and essays, appeared soon after his death.

It is also worth mentioning the activity of Kochetkov as a teacher. At the end of the 1950s, he lectured at the Moscow State University on the chemistry of carbo-

hydrates and nucleotides, the first course on this topic in the USSR. In the scientific school created by him, more than 100 Ph.D. and 30 D.Sc. dissertations were successfully defended. Many of his former pupils are world-renowned leaders in various fields of chemistry and biology, both in Russia and abroad; some became heads of their own scientific research teams (E. Nifantiev, M. Grachev, Yu. Ovodov, E. Sverdlov, V. Vaskovsky and others).

In 1960 Kochetkov was elected as a Corresponding Member and in 1979 as a full member (Academician) of the Academy of Sciences of the USSR. He won several State and Academy of Sciences awards, including the highest academic award in the USSR for scientific achievements – the Lomonosov Great Gold Medal. In 1986 Kochetkov received the Gold Medal of the Slovak Academy of Sciences and in 1989 the Haworth Memorial Medal from the Royal Society of Chemistry for achievements in carbohydrate chemistry. He was a member of the Chemical Society of France (since 1973) and a foreign member of the Polish Academy of Sciences (1988).

Kochetkov represented the USSR at the International and European Carbohydrate Organisations from the beginning of their founding until 1989. He organised and chaired a number of national and international scientific meetings. Being the Regional Editor of the journals of the *Tetrahedron* series for many years, Kochetkov encouraged Russian chemists to publish their results in these prestigious journals. He was a member of the Editorial Boards of many other scientific journals, including *Carbohydrate Research*.

For 60 years, Nikolay lived happily with his wife Vera Sergeevna Volodina. They raised daughter Maria and son Sergei, enjoyed three grandchildren and one great-granddaughter.

On December 21, 2005, soon after celebrating his 90th birthday, N. K. Kochetkov passed away. Those who had a privilege and a happiness working with him and learning from him, as well as the world scientific community, greatly appreciate his extraordinary contributions to the Carbohydrate Chemistry, to which he has devoted the major part of his life.

Leon Backinowsky
Yuriy Knirel
Andrei Nikolaev

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