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PROFESSOR NIKOLAY KONSTANTINOVICH KOCHETKOV

This issue of *Carbohydrate Research* is dedicated to Professor Nikolay Konstantinovich Kochetkov in celebration of his 70th birthday. We would like to honour him as a distinguished scientist, teacher, and administrator for his tremendous contributions to the development of carbohydrate chemistry.

N. K. Kochetkov was born in Moscow on May 18, 1915. Under the influence of his father, Konstantin Alexandrovich Kochetkov who was a chemical engineer, he became interested in chemistry at an early age. Between 1932 and 1934, he served as a technician at the Central Laboratory of the Dorogomilovo Chemical Plant in Moscow and in 1934 entered the M. V. Lomonosov Moscow Institute of Fine Chemical Technology. After graduation from the Institute in 1939, military service followed. Due to the outbreak of World War II, he was unable to continue his chemical career until 1945 when he joined the Chemical Faculty of the M. V. Lomonosov Moscow State University. He worked in the Laboratory of Elemento-Organic Chemistry headed by Professor A. N. Nesmeyanov. In 1948, N. K. Kochetkov obtained the degree of *Candidate of Chemical Sciences* (which roughly corresponds to a Ph.D.), and in 1953 he was granted the degree of *Doctor of Chemical Sciences* (equivalent to a D.Sc.). In 1955, he was appointed as a Professor of Organic Chemistry of Moscow University and stayed there until 1959.

In 1954, N. K. Kochetkov began his work in the Academy of Medical Sciences of the U.S.S.R. where he served until 1959 as head of the newly formed Department of Organic Synthesis in the Institute of Pharmacology and Chemotherapy. In 1956–1957, he spent six months in England working with Sir Alexander Todd at the University Chemical Laboratory, Cambridge, on the chemistry of nucleoside diphosphate sugars. In 1959, the Institute for Chemistry of Natural Products (now the M. M. Shemyakin Institute of Bioorganic Chemistry) was formed in the Academy of Sciences of the U.S.S.R. Professor Kochetkov became head of the Laboratory for Carbohydrates and Nucleotides, and served from 1959 to 1963 as a Deputy Director of the Institute. In 1966, he was appointed as Director of the N. D. Zelinsky Institute of Organic Chemistry, Academy of Sciences of the U.S.S.R. Most of his co-workers moved with him to the Zelinsky Institute, where the Laboratory of Carbohydrate Chemistry was established with Professor Kochetkov as its head. He remains very active and productive in both these positions.

Professor Kochetkov came to carbohydrate chemistry through organometallic chemistry, general organic chemistry, and heterocyclic chemistry. His first paper (1939) dealt with the synthesis of some imidazole derivatives. His first studies in Moscow University (published in 1949–1950) were connected with the interaction of mercury halides with acetylenes, and then (from 1950) the chemistry of β-chlorovinyl ketones became his main topic for almost ten years. These compounds, readily available through the addition of acyl chlorides to acetylenes, were

shown to be efficient reagents for ketovinylation (incorporation of the RCOCH=CH group) and the synthesis of cyclic structures especially in the heterocyclic field (pyrazoles, isoxazoles, triazoles, pyridines, benzopyrylium salts, *etc.*). From these studies of heterocyclic compounds, Professor Kochetkov moved to the synthesis of pharmacologically useful derivatives, including natural products. His team in the Institute of Pharmacology and Chemotherapy was successful in achieving the first syntheses of cycloserine (1956), dihydrosarcolysine (1957), and several pyrrolizidine alkaloids (1959–1964). A series of drugs with antihistamine, anticonvulsant, and antituberculosis activities was also synthesised.

N. K. Kochetkov's experience in heterocyclic chemistry was a starting point for his investigations in nucleotide chemistry. These studies, performed mainly during his stay at the Institute for Chemistry of Natural Products, were aimed at the development of specific and efficient methods for the modification of heterocyclic bases in mono- and poly-nucleotides. The interaction of nucleic acid components with hydroxylamine was studied in detail as well as the possibility of its use for the structural analysis of polynucleotides (1962–1968). Among new reagents suggested by Professor Kochetkov and his co-workers were *O*-methylhydroxylamine (1963), now widely used in the chemistry of polynucleotides, and chloroacetaldehyde (1971), employed for preparation of highly fluorescent analogs of adenine nucleotides.

In 1959, Professor Kochetkov began his studies of carbohydrates and became involved in many aspects of this field of research. From the beginning, both structural and synthetic investigations were developed side-by-side and closely interconnected.

Triterpene glycosides with long oligosaccharide chains, isolated from Far-East plants used in medicine, were the first subjects for structural studies (1960–1967). The wide distribution of such glycosides with carbohydrate chains containing up to 10 monosaccharide residues was demonstrated and several structures were elucidated. Unusual carbohydrate chains were identified in the gangliosides of several species of echinoderms (sea urchins and starfishes), the only representatives of marine invertebrates which are now known to possess these complex glycolipids.

Structural studies of blood-group-specific glycoproteins were started in 1963. A series of complex oligosaccharides was isolated and their structures were determined. The general pattern of the carbohydrate structures and their distribution along the core peptide chain emerged as a result of degradative studies of the biopolymer. Subsequently, studies of the carbohydrate chains of viral glycoproteins were started.

The structures of some sulfated polysaccharides from red marine algae were studied in the period 1967–1972, and in 1972 an investigation of the O-specific polysaccharides of Gram-negative bacteria was initiated. This thorough study of the structure and immunochemistry of the polysaccharides from various serogroups of *Shigella dysenteria, S. boydii,* and *Pseudomonas aeruginosa* has revealed many unusual structural features. Several new monosaccharide components have been

discovered in these polymers, including glycolactylic acids (lactyl ethers of hexoses, 1977), 2,3-diamino-2,3-dideoxyhexuronic acids (1982), and 5,7-diamino-3,5,7,9-tetradeoxynonulosonic acids (1984).

Several new approaches and techniques for structural analysis have been developed by Professor Kochetkov and his co-workers. Pioneer studies of the mass spectrometry of carbohydrate derivatives, including methyl glycosides of methylated monosaccharides (1963) and disaccharides (1964), formed the basis for subsequent development of this technique. Several types of derivative useful for the structural analysis of carbohydrates by mass spectrometry have been found, including alditol trifluoroacetates (1969), aldononitrile acetates (1971), and acetates of phenylosotriazoles or *N*-arylglycosylamines derived from oligosaccharides (1971). The potential of the ^{13}C-n.m.r. technique in the structural analysis of complex polysaccharides was realised early by N. K. Kochetkov, and many papers from his group demonstrated the effective application of this method. With the discovery of anomalous glycosylation effects dependent on particular spatial interactions of neighbouring protons (1984), the use of n.m.r. spectroscopy for determination of the absolute configuration of monosaccharide residues was suggested and the possibility of complete elucidation of polysaccharide structures using only ^{1}H- and ^{13}C-n.m.r. spectroscopy and polarimetry was demonstrated in favourable cases.

Several chemical methods for the selective degradation of polysaccharide chains were developed by Professor Kochetkov and his co-workers, including cleavage at uronic acid residues through the Hofmann rearrangement of their amides (1967). An efficient procedure was developed (1975) for *N*-deacetylation and the subsequent deaminative degradation of polysaccharides at amino sugar residues. Solvolysis with anhydrous hydrogen fluoride (1982) was found to be extremely useful for the degradation of *N*-acylated hexosaminoglycans. A mild solvolytic desulfation procedure was developed (1971) for the structural analysis of sulfated algal polysaccharides. A method for the reductive cleavage of the *N*-linked carbohydrate chains of glycoproteins by treatment with $LiBH_4$ in aqueous *tert*-butyl alcohol was recently suggested (1984).

In the synthetic chemistry of carbohydrates, the main topic of N. K. Kochetkov's investigations involved the development of efficient glycosylation methods for the chemical synthesis of polysaccharides. The value of sugar 1,2-orthoesters as stereoselective glycosylating agents was demonstrated in 1964 and a method for oligosaccharide synthesis was developed. The interactions of trityl ethers with 1,2-thioorthoesters (1977) and 1,2-*O*-cyanoethylidene derivatives (1975) of sugars were found to be even more efficient and highly stereoselective glycosylation procedures, and both methods were applied in the synthesis of oligosaccharides.

The first polysaccharide syntheses were performed in 1968–1969 from tricyclic or macrocyclic orthoesters; (1→5)-α-L-arabinofuranan and (1→3)-β-D-glucan were prepared. However, the 1,2-*O*-cyanoethylidene glycosylation procedure was the

more successful. After the first synthesis of (1→6)-β-D-glucan by this method (1967), many different polysaccharides were synthesised. These studies culminated in the first synthesis of a bacterial O-specific polysaccharide, the polymer from *Salmonella newington* composed of trisaccharide repeating-units (1981). More recently, the O-specific polysaccharide from *Shigella flexneri* was synthesised (1985). Several syntheses of oligosaccharide fragments of *Salmonella* O-specific polysaccharides were also accomplished (1974–1980) and a new method for preparation of synthetic oligosaccharide antigens based on the copolymerisation of oligosaccharide allyl glycosides with acrylamide was developed (1984).

Synthesis and biochemical studies of precursors of polysaccharide biosynthesis have been performed by Professor Kochetkov's group. These investigations included the first syntheses of nucleoside diphosphate sugars with modified nucleoside or hexose residues, an efficient method for preparation of polyprenyl pyrophosphate sugars (1981), and the development of a chemical–enzymic approach to polysaccharide synthesis (1983).

Professor Kochetkov was also active during the 1960's in monosaccharide chemistry. Methods were developed for the synthesis of deoxy sugars, using triphenyl phosphite methiodide (1963), and for the elongation of sugar chains through the Wittig reaction (1965). Syntheses of various aminoacyl derivatives of sugars were performed (1962). More recently, activity in this field has been renewed, and work on the synthesis of 12- and 14-membered macrolide antibiotics from monosaccharide synthons is in progress.

Significant contributions were made by N. K. Kochetkov and his co-workers to the radiation chemistry of carbohydrates (1964–1975). Many previously unreported radiolysis products were identified and mechanisms for their formation were suggested.

The researches of Professor Kochetkov are described in more than 900 scientific papers and reviews, and he is a co-author of five books on the chemistry of carbohydrates. His book "Chemistry of Natural Products", written in collaboration with Professors I. V. Torgov and M. M. Botvinnik and published in 1961, was the first textbook on the subject in Russian and influenced students very much at that time. Very significant for the development of carbohydrate and nucleotide chemistry in the U.S.S.R. were the following two books written by N. K. Kochetkov and his collaborators: "Chemistry of Carbohydrates" (1967, in Russian) and "Organic Chemistry of Nucleic Acids" (1970, in Russian; an English translation was published in 1972). More specific areas of carbohydrate chemistry were discussed in "Radiation Chemistry of Carbohydrates" (1978 in Russian; 1979 in English) and "Carbohydrates in the Synthesis of Natural Products" (1984 in Russian). More recent work of Professor Kochetkov and his group is reviewed in "Progress in Carbohydrate Chemistry" prepared by his co-workers (1985).

Professor Kochetkov was elected as a Corresponding Member of the Academy of Medical Sciences of the U.S.S.R. in 1957. Three years later, the Academy of Sciences of the U.S.S.R. granted him the same title and in 1979 he

became a full Member of the Academy. He serves as Chairman of the Scientific Council of the Academy of Sciences of the U.S.S.R. on organic synthesis as well as a member of many other committees dealing with the development of organic, bioorganic, and pharmaceutical chemistry in the U.S.S.R. He has been highly decorated by the Government for his service to science and education. He is a member of the Editorial Advisory Board of *Carbohydrate Research* and several other scientific journals, including *Tetrahedron, Organic Mass Spectrometry, Bioorganicheskaya Khimia,* and *Zhurnal Organicheskoi Khimii.*

Professor Kochetkov is well known to the international scientific community, not only through his publications but also through his active participation in many international meetings. He has been invited many times to deliver plenary lectures which have been characterised by good science brightly presented.

Professor Kochetkov lives in Moscow. He and his wife, Vera Sergeyevna Kochetkova, have a daughter, Marya, and a son, Sergei, both of whom are chemists. Two grandsons, Yuri and Nikolay, and a granddaughter Ekaterina are now in the Kochetkov family.

Nikolay Konstantinovich has had many pupils, some of whom have become prominent figures in various branches of organic and bioorganic chemistry or biochemistry. All of them were influenced very much by his deep devotion to science. His co-workers in the Zelinsky Institute constitute a closely linked team, and valued guidance and encouragement of the coach is greatly appreciated by all members of "Kochetkov United" who would like to have him in this position for many years to come.

As a former student of Professor Kochetkov and his co-worker for many years, I would like to offer him my cordial congratulations on the occasion of his seventieth birthday and to wish him and his family many more years of healthy and happy life.

VLADIMIR N. SHIBAEV