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ANNIVERSARIES AND DATES

ALEKSEI VSEVOLODOVICH BOGATSKY

(75th Anniversary of his Birth)

Seventy five years have elapsed since the birth of one of the leading organic chemists, prominent scientist in the field of fine organic synthesis, structure, and stereochemistry of organic compounds and the chemistry of physiologically active substances, able teacher, and scientific administrator A. V. Bogatsky (August 26, 1929 to December 19, 1983).

After graduating from the Chemical Faculty of I. I. Mechnikov Odessa State University in 1951 and successful completion of postgraduate studies under the guidance of Prof. A. K. Plisov, A. V. Bogatsky was appointed assistant in the Department of organic chemistry. In 1958 he was elected associate professor and in 1962 head of the Department of Organic Chemistry and dean of the Chemical faculty. In 1968 Bogatsky was appointed prorector of academic work and in 1970 rector of Odessa University.

He organized in 1971 The Problem Scientific-Research Laboratory of the Synthesis of Psychotropic Products and the Department of the Chemistry of Nitrogen Heterocycles, Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR in 1972 in Odessa. In 1974 the department became part of the Odessa Laboratories of the Institute of General and Inorganic Chemistry, Academy of Sciences of the Ukrainian SSR.

Bogatsky fulfilled one of the principles of the training of highly qualified young specialists – the students' instruction included participation in the scientific research of the department and the problem laboratory. In 1974 Bogatsky was appointed scientific leader of the Odessa laboratories of the Institute of

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General and Inorganic Chemistry, Academy of Sciences of the Ukrainian SSR, and in 1975 he moved to a permanent job in the system of the Academy of Sciences of the Ukrainian SSR. This period was possibly the most important of his life, for there appeared the real possibility of organizing the first academic institute in Odessa, of which he was a true patriot. He accomplished a great organizational project, culminating in 1977 in the creation of the Physical Chemistry Institute, Academy of Sciences of the Ukrainian SSR, on the basis of the above-mentioned laboratories and the pilot plant belonging to them.

In 1972 Bogatsky was elected Corresponding Member and in 1976 Full Member of the Academy of Sciences of the Ukrainian SSR. An important position in his life was taken up by work in the post of President of the Youth Scientific Center, Academy of Sciences of the Ukrainian SSR; under his leadership and direct involvement a series of development programs of the region were developed.

In the first stage of Bogatsky's scientific activity the main subject of research was alkoxy-substituted malonic and acetoacetic esters and acetylacetones. As a result of study of the formation of these compounds, their structure, and reactivity it was shown that the reaction of the sodiomalonic esters obeys the relationships of an S_N1 mechanism with α-halo esters and an S_N2 mechanism with β-halo esters. It was established that the yield of the desired products depends on the nucleophilicity of the respective enolate anions and on the steric strain of the α-alkoxy derivatives.

It was shown for the first time that mineral acids, sulfo cation exchangers, and aluminum oxide are effective catalysts for the dealcoholization of alkoxy acids and their esters. On the basis of the obtained data a catalytic method was proposed for the synthesis of α,β-unsaturated acids, their esters, and their γ-lactones.

By the reduction of alkyl α-alkoxyalkylmalonates and acetoacetates and acetylacetones with lithium aluminum hydride a series of previously undescribed 2-alkoxyalkylpropane-1,3-diols and 2-alkoxyalkylbutane-1,3-diols were obtained. Reaction of the latter with aldehydes, ketones, phosphorus trichloride and dichlorophosphite, and boric acid led to the synthesis of alkoxyalkyl-substituted 1,3-dioxanes, 1,3,2-dioxaphosphorinanes, and 1,3,2-dioxaborinanes. Extensive investigations into the preferred conformations and conformational mobilities of the obtained six- and seven-membered 1,3-heterocycles were carried out.

Bogatsky demonstrated the preference for the 5-C-axial position of the alkyl group in 1,3-dioxane compared with the analogous position of the substituent in 1,4-substituted cyclohexane. The axial positions at the 2-C and 4,6-C atoms in 1,3-dioxane are less favorable than the corresponding positions in cyclohexane. In the series of 1,3-dithianes the axial positions of the substituents at these atoms are more favorable than in the 1,3-dioxanes on account of the greater length of the C–S bonds.

The *chair* of the *cis* isomers of 2,5-substituted 1,3-dioxanes is less "flattened" in the $C_{(4)}$–$C_{(5)}$–$C_{(6)}$ region than in 2,5-substituted 1,3-dithianes, while the *trans* isomers of the former are more "flattened" than the *trans* isomers of 1,3-dithianes. Realization of the flexible form of the ring is most likely in the series of 4,4,6-substituted 1,3-dioxanes and 1,3-oxathianes. The 2,4- and 2,5-disubstituted 1,3-dioxepanes are characterized by a dipseudoequatorial arrangement of the substituents both in the *cis* and in the *trans* isomers. For the molecules of monoalkyl-substituted 1,3-dioxepane the *pseudochair* (*twist-chair*) is the energetically most favorable conformation.

A linear relation was found between the difference in the boiling points of the stereoisomers of substituted 1,3-dioxanes and the number of carbon atoms in the molecule.

From 1967 in the Department of Organic Chemistry and the Problem Scientific-Research Laboratory for the Synthesis of Psychotropic Products at the I. I. Mechnikov Odessa State University and later in the Physico-Chemical Institute, Academy of Sciences of the Ukrainian SSR, extensive investigations were carried out under the leadership of A. V. Bogatsky into the chemistry the derivatives of pyrimidine, quinazoline, 1,4-benzodiazepine, 1,5-benzodiazocine, 1,6-benzodiazonine, nitrogen and other macroheterocycles, and polynuclear heterocyclic and aromatic systems. The principal aim of the investigations was to develop methods of synthesis and to study the relation between the structure, conformation, and physicochemical and pharmacological characteristics of the obtained substances and on this basis to create specific methods for the production of new medicinal products. Methods were proposed for the synthesis of 1,4-benzodiazepinones, their

six- and seven-membered cyclic homologs, and other related heterosystems. Framework derivatives of 1,4-benzodiazepines – 1,2-dihydro-3H-1,4-benzodiazepin-2-onespiro-2'-adamantanes and 3,4-dihydro-5H- and 1,2,3,4-tetrahydro-5H-1,6-benzodiazonines – were obtained for the first time.

It was shown that the hetero ring of 1,4-benzodiazepines, 1,5-diazocines, and 1,4,5-benzotriazocines has a *pseudoboat* form. The kinetics of the inversion of the compounds and the basic relationships between the structure and kinetic and thermodynamic parameters of the process were studied. The structure of the associates of the molecules of 1,4-benzodiazepines was established, and the correlation of the spectral characteristics, polarity, basicity, and lipophilicity with the physicochemical constants characterizing the electronic nature and steric features of the substituents was studied. The applicability limits of the Hantsch approach to quantitative assessment of the relation between the structure, physicochemical, and pharmacological parameters of the compounds were determined.

The analgesic, anxiolytic, and antitumor properties of quinazolinones were discovered. For quinazolinones and 1,4-benzodiazepinones the most important property in their pharmacological spectra is the anxiolytic effect, while in their eight- and nine-membered cyclic homologs the hypnosedative effects prevail.

Derivatives of fluorene, anthracene, and acridine promising in medical biological respects and having high interferon-inducing and antiviral activity and also highly effective antioxidants and autoprotectors in the series of 2-aminoalkylmercaptodihydropyrimidines were found.

The use of modern methods of isolation, identification, and quantitative analysis of the substances (chromatography, gel filtration, spectral methods, etc.) made it possible to thoroughly scrutinize the special features of the metabolism and pharmacokinetics of the obtained substances. The main relationships and the specific characteristics of biotransformation, distribution in organs and tissues,and the excretion of 1,4-benzodiazepine derivatives were studied. It was established that in a number of cases (medazepam, sulazepam, etc.) the pharmacological effect is due to a significant degree to the action not of the product but of its metabolites on the central nervous system. An important result of this series of investigations was the creation of the first tranquillizer in the USSR fenazepam.

The exceptionally fruitful collaboration of Bogatsky with Profs. Yu. Yu. Samitov and Yu. I. Vikhlyaev, Academician Yu. A. Ovchinnikov, and many other scientists had a profound effect both on the results of the joint investigations and on the development of the institute as a whole.

From the middle of the seventies the scientific interests of A. V. Bogatsky have been concentrated to an ever greater degree on problems in the chemistry of macroheterocycles. Here too, as previously, he paid most attention to the development of methods of synthesis, the study of structure, properties, and complex-forming ability of crown compounds containing ester, amide, thiocarbamide, and carbamide groups. The idea of using the polyesters of dicarboxylic acids as intermediate compounds in the synthesis of macrocyclic lactones and lactone lactams proved very fruitful. On this basis a general approach was developed for the synthesis of both symmetrical and unsymmetrical tri-, tetra-, and octalactones and lactone lactams. The principle of matrix synthesis was brilliantly applied to the production of azacrown ethers with excellent yields under phase-transfer conditions. Methods were developed for the synthesis of novel types of porphyrins, including "hidden" porphyrins.

An important aspect of his researches on the chemistry of macroheterocycles concerned the development of synthetic methods using crown ethers as catalysts and modifiers of organic reactions. Convenient methods were proposed for the production of stable crown etherates of alkyl(aryl)calcium(magnesium) halides. It was found that with simultaneous participation in the reaction of metallic magnesium or calcium, alkyl (aryl) halide, and a carbonyl compound in the presence of catalytic amounts of crown ethers in any inert solvent crown etherates of alkyl(aryl)calcium(magnesium) halides are formed, and they enter immediately into reaction with the carbonyl component.

It was established that the synthesized polyfunctional macroheterocycles in most cases exhibit complexing and ion-selective characteristics not characteristic of normal crown ethers and depending on the nature of their functional groups, the substituents, and the size and symmetry of the macrocycle. Compounds

having high cationic selectivity were found. Compositions were proposed for the liquid membranes in lithium-, copper(II)-, chromium(III)-. cesium-, and rubidium-selective electrodes. It was found that macrocyclic octalactones and thioureas form complexes with *d*-transition metals. It was established for the first time that certain macroheterocycles and their complexes have mesomorphous characteristics and are in fact a new type of current-conducting mesomorphogen.

Bogatsky led a program of fundamental investigations at the Academy of Sciences of the USSR on "Macrocyclic complexones and their analogs," during the realization of which significant advances were made in the region of supramolecular chemistry, and the industrial release of a series of macroheterocyclic compounds was organized.

The results of the researches carried out by Bogatsky in collaboration with his coworkers have been published in more that 600 scientific papers. He was scientific consultant in five doctoral dissertations and scientific leader of 30 candidate's theses. Aleksei Vsevolodovich was awarded three orders of the Labor Red Banner, an S. I. Vavilov medal, the I. V. Pisarzhevskii prize of the Academy of Sciences of the Ukrainian SSR, and state prizes of the USSR and Ukraine. His name has been conferred upon the Physicochemical Institute of the National Academy of Sciences of Ukraine.

S. A. Andronati, A. I. Gren

THE MOST IMPORTANT PUBLICATIONS OF ACADEMICIAN A. V. BOGATSKY

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