VITH SYMPOSIUM ON THE CHEMISTRY OF HETEROCYCLIC COMPOUNDS

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The VIth symposium on the chemistry of heterocyclic compounds, which was organized by the Czechoslovakian chemical society and natural science department of J. E. Purkine Brno University, was held July 4-7, 1978. As in the previous symposiums, which are organized in Czechoslovakia every three years, this symposium was conducted with the participation of a considerable number of foreign guests and was clearly international in character: of the 127 papers (plenary, sectional, and display papers) included in the program, only three were by Czechoslovakian authors. Representatives of 18 countries — Austria, Bulgaria, Hungary, the German Democratic Republic (GDR), Holland, Egypt, Iran, Canada, Poland, the USA, the USSR, France, the Federal Republic of Germany (FRG), Czechoslovakia, Switerzerland, Sweden, Yugoslavia, and Japan — participated in the work of the symposium. Fifteen individuals, who represented the scientific-research institutes and colleges of Moscow, Riga, Saratov, and Ufa, were present from the USSR; they presented two plenary, four sectional, and ten display papers.

The papers included in the program of the symposium dealt with an extremely wide range of problems associated with the chemistry of heterocycles (the organizers of the symposium imposed no limitations whatsoever on the topics of the papers). Nevertheless, a number of papers were of general interest. In addition, several problems were discussed in some papers, and this made it possible to get a sufficiently clear idea of their state. This is above all true with respect to the chemistry of furan, which is undergoing successful development in Czechoslovakia. Various aspects of the chemistry of furan were reflected in a plenary paper by J. Kovač (Bratislava), as well as in other papers presented by both the organizers of the symposium and by the guests, particularly those from the USSR and Sweden.

The greatest number of papers were devoted to the development of methods for the synthesis and study of the reactivities of nitrogen-containing heterocycles. I. Ban (Japan) proposed a new method for the synthesis of benzolactams in the presence of palladium catalysts. It was shown that the reaction of carbon monoxide with o-bromoalkylbenzenes proceeds readily at 100°C in the presence of palladium acetate and triphenylphosphine to give five-, six-, or seven-membered benzolactams in good yields. The method was used for the synthesis of the alkaloid sendaverine.

Many alkaloids (isoboldine, corituberine, palladine, etc.) were obtained by oxidation of hyroxyphenyl derivatives of isoquinoline with oxygen and copper salts in pyridine. The ability of 3,4-dihydro-1-methylisoquinolines to react like enamines was also used for the synthesis of isoquinoline alkaloids. Thus, for example, the stereoselective synthesis of emetine was accomplished (T. Kametani, Japan).

The results of many years of research on the synthesis of the alkaloids vinblastine and vincristine, which have antitumorigenic activity, were presented in a paper by J. Kutney (Canada).

The use of lactones as synthetic "blocks" for the construction of heterocycles similar to alkaloids was illuminated in a paper by Zimalkovskii and Maize (FRG).

Of the other methods for the formation of six-membered nitrogen-containing heterocycles, one should mention the condensation of cyclopentan-2-one-1-carboxylic acid anilide with malononitrile K. Bogdanowicz-Swed, Poland), the synthesis of quinazoline from formamidinoyl isothiocyanates (S. Stanikovski, Czechoslovakian SSR), and the preparation of thio-5-azauracil from thiobiuret (A. Piskal, Czechoslovakian SSR).

H. Vamgoff (FRG) used a number of examples to show the new possibilities in the use of the photochemical method of synthesis of five-membered nitrogen-containing heterocycles. The irradiation of dibromomaleinimide in benzene led to a new 2 + 2 adduct. In addition to this, photocyclization to give phenanthra[9, 10-c]pyrrole derivatives was also observed.

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In a study of the synthesis of condensed four-membered nitrogen-containing heterocycles it was shown that for the cis isomers the rates of formation of azetidines from 2-bromomethyl cycloalkylamines as a function of the size of the cycloalkane increase in the order $7 < 5 < 6$, as compared with $7 < 6$ for the trans isomers, whereas trans-2-(bromomethyl)cyclopentylamine did not form the corresponding azetidine derivative (G. Gendes, Hungary).

In a study of the oxidation of pyridine, 3-picoline, 3,5-lutidine, quinoline, isoquinoline, and acridine with copper sulfate it was established that the reaction products are the corresponding pyridones (P. Tomasik, Poland). The homologs of pyridine with methyl groups in the α and γ positions are demethylated under these conditions. In the case of 2- and 4-ethylpyridines the unusual oxidation of not only the α- but also the β-carbon atom, which leads to the formation of 2- and 4-picolines, was observed.

A catalytic method for the oxidation of methyl and dimethyl derivatives of pyridine, pyrazine, and pyrimidine to the corresponding aldehydes was developed (M. Shimanskaya, Riga, USSR).

In a study of the transformation of heterocycles it was shown that the photochemical transformations of diazo ketones to carboxylic acids proceed with retention of the ring (B. Stanovnik, Yugoslavia).

A plenary paper by H. van der Plas (Holland) devoted to the transformations of N-methyl- and N-aminopyrimidinium salts, as well as pyrimidine N-oxides, under the influence of nucleophilic reagents to give substituted pyrimidines and pyrazole and isoxazole derivatives generated a great deal of interest. It was shown by application of ^{15}N-labeled compounds that most of the transformations of pyrimidines proceed with ring opening and subsequent new cyclization. Ring opening also occurs in the amination of 3-methylthio-1,2,4-triazine with potassium amide in liquid ammonia at $-75°$C, which, after cyclization, leads to the formation of a 3-amino derivative (A. Rikowski, Poland).

A plenary paper by K. Gewald (GDR) in which the syntheses of heteroaromatic amines by cyclization of nitriles were examined was of considerable interest. The speaker is well known as the author of original methods for the synthesis of aminothiophenes, and in his paper he also illuminated new possibilities for the synthesis of amines of the furan, pyrrole, and pyrazole series, as well as condensed systems that include these rings.

The problems involved in the transmission of electronic effects in silyl-substituted heterocyclic amines were examined in a plenary paper by É. Ya. Lukevits (USSR). A paper by H. Elguero (France) was devoted to some application of ^{13}C NMR spectroscopy to heterocycles. Although the paper was restricted to compounds studied by the author that in a number of cases can be considered to be extremely specific, the material presented was of general interest, since the principal methods for the assignment of the signals in the spectra and the effect of various substituents on the ^{13}C spectra were described, and a comparison of the latter with the ^{1}H and ^{15}N spectra was made.

A review of the properties of several related classes of compounds that make it possible to reveal the general features and specific differences is an extremely appropriate type of plenary lecture for a symposium with such a broad scope. A paper by S. D. Sokolov (USSR), devoted to the modern state of the chemistry of 1,2-azoles and a paper by A.-B. Hornfeldt (Sweden), in which the spectral and chemical properties of compounds of the furan, thiophene, and selenophene series were compared, were papers with precisely this characteristic.

A paper by A. Shafi (Iran) was devoted to the synthesis of two new condensed systems — pyrrole[3,2-d]thiazole and pyrrolo[3,2-d]selenazole. A convenient synthesis of thieno[2,3-b]pyridines was described in a paper by L. Lalezari (Iran). Three papers involving the synthesis of condensed systems that include seven-membered heterorings, many of which have psychotropic activity, were presented by M. Protiva and co-workers (Czechoslovakian SSR). The formation of polycyclic systems that include seven-membered rings were also described in papers by H. Bischof (GDR) and K. Gall-Istok (Hungary).

A number of sectional papers were devoted to alkaloids and related systems. In particular, J. Trojanek and J. Hajcek (Czechoslovakian SSR) investigated the products of degradation of the indole alkaloid Vincamine; a group of Bulgarian chemists headed by M. Khaimova worked out the synthesis of 1(2H)-isoquinolines and 8-oxoberbines. The structural modification of ergoline derivatives, which leads to compounds with prolactin-inhibiting activity, was examined in a paper by J. Krzepelki and M. Semonski (Czechoslovakian SSR).

The Soviet participants in the symposium presented four sectional papers: A. V. Varlamov on the synthesis and properties of dihydrosilaazaanthracenes, V. G. Kharchenko on some transformations of thiopyrans, S. S. Zlot-skii on the radical reactions of acetals and their heteroanalogs, and L. I. Belen'kii on some peculiarities of the structures and properties of complexes of carbonyl compounds of the furan, thiophene, and benzene series with aluminium halides.

Extensive research on furan compounds is being carried out in the Slovakian Technical University in Bratislava under the supervision of Professor J. Kovač: New methods for the synthesis of 5-nitrofurylethylene and its derivatives have been developed, reactions involving cycloaddition of nitrones to the furan ring on the basis of 2-amino-3-cyanofuran have been studied, and new condensed furan-containing heterocyclic systems have been obtained.

Methods for the synthesis of furylhydrosilanes were developed in the Institute of Organic Synthesis of the Academy of Sciences of the Latvian SSR, and the properties of these compounds were studied (É. Ya. Lukevits and N. P. Erchak). It is shown that they readily add to the double bond of 1-vinyl-2,8,9-trioxa-5-aza-1-silatricyclo$[3.3.3.0^{1,5}]$undecane to give β isomers. The dehydrocondensation of furylhydrosilanes with amino alcohols proceeds without a catalyst. The rate of the reaction increases as the number of furyl groups increases and decreases as a function of the substituent attached to the silicon atom in the order 2-furyl > 2-thienyl > phenyl (M. Dzintara).

K. Meyers (USA) showed that the reactions of sulfones with $KOH-CCl_4$ in tert-butyl alcohol proceed through the intermediate formation of thiirane 1,1-dioxides, which readily undergo decomposition to olefins or unsaturated sulfinic acids, the structures of which depend on the character of the substituents in the starting sulfone.

P. Kristian (Czechoslovakian SSR) established that the reaction of phenylcyclopropane with selenium tetrahalides gives 1,1,4-trihalo derivatives of 1-selenochroman and 1,1-dihalo derivatives of 1-selenochromene, which are converted to 1-selenochromene on treatment with sodium sulfide.

The display papers of the Soviet participants dealt with various problems in the chemistry of heterocycles. In particular, the reactions of aryloxyfurans (A. F. Oleinik, K. Yu. Novitskii, and co-workers), the polarography of isoxazoles and their aza analogs (I. G. Markova, M. K. Polievktov, and S. D. Sokolov), the chromatographic behavior of some oxygen- and nitrogen-containing heterocycles (A. A. Anderson and M. V. Shimanskaya), and the synthesis and transformations of some condensed nitrogen-containing systems (A. S. Elina, I. S. Musatova and co-workers, and O. S. Kuptsova, N. E. Britikova, and K. Yu. Novitskii) were examined.

Data on the physiological activity of the investigated compounds were presented in a number of papers. In particular, the considerable antibacterial activity of some mercapto and amino derivatives of benzothiazole, polycyclic azines (azaphenanthrene and azafluorene derivatives), and sulfonyl-substituted pyrimidines was noted; the latter also had inhibiting activity with respect to dihydrofolatereductase and p-aminobenzyl glutamate. Upon the whole, the program of the symposium was extremely diversified and included papers devoted to various aspects of the chemistry of heterocycles, particularly the synthesis, reactivities, and physiological activity of these compounds.

The next symposium will be held in 1981 in Bratislava.