ASPECTS AND PROSPECTS OF THE CHEMISTRY OF ORGANIC HETEROCYCLES* (REVIEW).
PART I

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The systematics of heterocycles, their place in organic chemistry, and their significance for theory and practice are discussed. Problems of the chemistry of heterocycles are discussed on the examples of systems with various types of conjugation and ring sizes. The focus is on the principles of synthesis of heterocycles, in particular, those based on acetylene, various C₃ fragments, carbon disulfide, and maleic anhydride. Individual sections of the survey are devoted to the role of heterocycles in biosynthesis, as well as certain problems common to the chemistry of heterocycles, biochemistry, and macromolecular chemistry.

1. INTRODUCTION

1.1. Heterocycles and Heteroatoms

Compounds containing not only carbon atoms but also heteroatoms (i.e., any atoms other than carbon and hydrogen), have had an extremely important effect on the development and even the establishment of organic chemistry: the "artificial formation of urea" from ammonium cyanate discovered in 1828 by F. Wohler [3], is based essentially only on the heterofunctional transformation of C₄-compound. Carbon disulfide and carbon tetrachloride were intermediate stages in the multistep synthesis of acetic acid according to H. Kolbe (1845, [4]), representing the first genuine synthesis of a carbon framework from elementary components. Ultimately it was concluded that organic chemistry, which was first defined by C. Schorlemmer, can be considered as "the chemistry of hydrocarbons and the derivatives" (see [5, p. 9] and further [6, p. 122]), the chemistry of derivatives in which heteroatoms play the deciding role in giving variety to carbon compounds. Even in the case of a single carbon atom, bonded only to hetero-substituents, the possibility emerges for the construction of 75 main types of derivatives of carbonic acid with the aid of only four heteroatoms: oxygen (C=OH, C=O), nitrogen (C=NH, C=NH, C=N), sulfur (C=SH, C=S), and chlorine (C=Cl).

*The present survey represents a reworking of material on the major pressing problems of the chemistry of heterocyclic compounds, previously published by the author [1, 2].
†It should be mentioned that in this case a whole series of synthetic methods that are still important were used (chlorolysis, pyrolysis, photolysis, electrolysis, "relay" synthesis of intermediate products, and an auxiliary synthetic role of heteroatoms). Only here was the independence of the chemistry of carbon compounds from vie vitalis substantiated and accorded universal recognition (see the notes in [6, p. 199; 7, p. 156; 8, p. 7]). F. Wohler's student, H. Kolbe, also emphasized "that it is impossible to construct a boundary between organic and inorganic." Each approach associated with the "chemistry of the organism" should have received its logical development in the biochemistry and molecular biology of our time: "Sciences as a whole, in the course of their development, have moved away from light and are being rejoined only by roundabout routes" (I. W. Goethe, in: Maximen und Reflexionen. Freiburg/Br. (1950), p. 115; originally quoted in the book Wilhelm Meisters Wanderjahre (1829), i.e., only a year after Wohler's discovery — a curious coincidence). The use of the term synthesis instead of the term artificial formation, a unique sort of metamorphosis, was long overdue; this concept was already coined in 1845 by H. Kolbe [4] and A. Hofmann [9]; however, in the modern sense this term was introduced and first comprehensively defined in 1860 by M. Berthelot [10] (see also [8, p. 8]).
General aspects

Ring structure / Heterocycles
Stereochemistry
Unsaturation
Hetero-aryl compounds
Aromatization, etc.

Heteroatoms as reaction sites and sites of excitation
Charge distribution
Polarity
Syntheses, etc.

Fig. 1. Position of heterocycles in the system of organic chemistry.

Usually wide variety is exhibited in cases when heteroatoms, together with carbon atoms, form a circular framework of the molecule, i.e., an organic heterocyclic system (for general surveys see [11-18]; for the nomenclature of the heterocycles, see [16, 19]). In the broad meaning of the term, heterocycles include all compounds that have a ring-like molecular framework, consisting of at least two different types of atoms (a ring constructed from atoms of one type is a homocycle). In organic heterocycles, carbon is always present as an essential structural element (in the case of rings formed only by carbon atoms, it is a matter of carbocycles).

It is striking that at the early stages of development of organic chemistry, the autonomous classification of heterocycles caused obvious difficulties (cf. [5, 6, 11, 20, 21]). The classic definition of the "chemistry of hydrocarbons and their derivatives" essentially relegated heterocycles to a secondary role.* Heterocycles can be defined as products of "cyclizing H-substitution" of acyclic hydrocarbons, and thus can be considered as functional derivatives. For this reason the heuristic principle of H-substitution is rationally supplemented by a formal approach to the replacement of elements of the framework (see Sections 1.2 and 1.4).

The combination of carbon and heteroatoms into a cyclic molecule causes the appearance of a number of peculiarities. Compounds of this kind reflect the features of carbocyclic and functional structural classes to the same degree, and both these divisions, in turn, open up a broad spectrum of potentialities of organic chemistry, in which heterocycles thus occupy a central position (see Fig. 1). The possible variety of structures already known for carbon ring systems, obtained by variation of the size of the ring, the formation of polycyclic systems, and the nature of the bonds at the elements of the ring, is supplemented by possibilities of variation of the nature, number, and position of the heteroatoms in the cyclic system. The heteroatoms are most often nitrogen, oxygen, and sulfur atoms; however, many other elements are also used (for example, phosphorus [22, 23], arsenic [24, 25], and tin [26]), interest in which in the chemistry of heterocycles is constantly increasing. By 1963, 15,000 heterocyclic systems had already been recorded [16, 27], and their number continues to increase.

*Since C. Schorlemer ([6, p. 173]; cf. [7, p. 32]) characterized benzene as "marsh gases of the aromatic group, and since all other compounds are produced from it by replacement of hydrogen by elemental radicals," the definition of thiophene, pyrrole, pyridine, etc. as "marsh gases of heterocyclic groups" necessarily developed.