ROBERT BURNS WOODWARD (ON HIS 60TH BIRTHDAY)

A. N. Kost and L. N. Yakhontov

Professor Robert Burns Woodward, the Nobel prize laureate who was recently elected to the Academy of Sciences of the Soviet Union (as a foreign member), celebrated his 60th birthday on April 10, 1977. The importance of his research for the development of organic chemistry and, in particular, the chemistry of natural (including complex heterocyclic) compounds is difficult to overestimate. The talented youth, who graduated from Harvard University at the age of 16, rapidly displayed his brilliant capabilities, discipline, and purposefulness in scientific-research. After a series of primary scientific studies published at the end of the thirties and at the start of the forties, which were characterized by a search for his own scientific direction and rapid mastery of one field of organic synthesis after another, he turned to the directed synthesis of the most complex natural compounds, simultaneously solving problems of general methodical character. During this preliminary stage, Woodward investigated the role of acidic agents in the diene synthesis, proposed a new reagent (methyl carbazinate) for the separation of carbonyl compounds into their optical antipodes, developed an original method for the cis-hydroxylation of double bonds by means of iodine and silver acetate in acetic acid ("Woodward cis hydroxylation"), and discovered a method for the cleavage of 1,2-dihydroxycyclanes to formyl alcohols. By this time organic chemistry had sufficiently accurate and reliable devices for the study of electronic spectra at its disposal. Woodward undertook a study of the informativeness of the method, logically analyzed hundreds of spectra, and in 1941 formulated the empirical "Woodward rule," which links the position of the maximum in the spectrum of a compound having a conjugated system of π bonds with the number and position of substituents attached to this conjugated system. We note that later, when optical rotatory dispersion began to be widely used in organic chemistry and experimental data began to accumulate rapidly, Woodward (together with K. Djerassi, V. Moffit, et al.) proposed the "octant rule" which determines the sign of the Cotton effect in the spectra of optically active carbonyl compounds and their analogs.

Of course, one should enumerate the studies on the directed synthesis of complex and most complex natural compounds carried out by Woodward and co-workers, starting with the total synthesis of quinine, published in 1944. This research, on which Woodward and W. E. Doering spent 14 months of intensive work, solved the problem with which many outstanding chemists had unsuccessfully struggled. The characteristic traits of Woodward's scientific approach — nontrivial approach to a solution and his special interest in stereochemical problems — were displayed here. The achievement of the necessary configuration of substituents attached to chiral centers through the stereospecific synthesis of cyclic structures, which, if necessary, were subsequently opened, i.e., the use of specific characteristics of ring formation (in both the carbocyclic and heterocyclic series) for the creation of regiospecific and stereospecific synthetic methods, including the synthesis of acyclic fragments, was typical of his research.

After the synthesis of quinine he published brilliant papers in which a number of alkaloids and antibiotics (sempervirine, patuline, santoninic acid) were synthesized and their structures were established, and, together with S. Sondheimer and a number of other coworkers, he synthesized steroids — cholesterol, lanosterol, and cortisone — and almost simultaneously completed the synthesis of strychnine and lysergic acid (the principal ring of ergot alkaloids). In the course of these latter studies he created a series of new synthetic methods that are in use today for the synthesis of indole and quinoline derivatives, discovered a new type of cleavage of organic molecules, and made a substantial contribution to the understanding of the pathways of biogenesis of alkaloids. The complex problem of the

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synthesis of reserpine, the molecules of which have six asymmetric contenters, was solved elegantly. The principles lying at the formation of these studies made it possible to subsequently develop a method for the preparation of this important substance on an industrial scale.

In the large group of studies dealing with the synthesis and establishment of the structures of alkaloids, one must single out the synthesis of colchicine, in which Woodward thoroughly demonstrated the strength of his scientific intuition, since the most important six steps (which include two ring openings with subsequent ring closing and rearrangement) were accomplished only on the basis of the UV spectra of the intermediates without isolation of them from the reaction mixture. However, the greatest significance in Woodward's research was achieved in his investigations of macrocyclic systems. In 1960 he reported the total synthesis of chlorophyll, after which he extensively developed research on chlorins and corrins; in 1972 (together with Eschenmoser and a large group of co-workers) he completed some research of extreme complexity — the total synthesis of vitamin B_{12} — which required 10 years.

Woodward's successes in the synthesis and establishment of the structures of the most complex natural compounds are intimately associated with the development in his research on new synthetic methods, primarily in the area of dynamic stereochemistry, and of new basis concepts that are of general character for organic chemistry and, in part, for biochemistry. He was the first to understand the nature of sandwich organometallic compounds and demonstrated that the five-membered rings of ferrocene have aromatic character. His intuitive ideas regarding the regiospecificity and stereospecificity of ring formation, which are the result of a knowledge and comprehension of an enormous amount of data in organic chemistry, were gradually formulated in the form of the broad concept of retention of orbital symmetry. The well-known "Woodward—Hoffman rules" created on its basis have become one of the fundamental tenets of modern organic chemistry. His research on the synthesis of cholesterol have made it possible to establish a direct stereochemical correlation between sesquiterpenes and steroids, and this provided a strong impetus for an understanding of the mechanism of their biogenesis.

The words "art," "artistry," and "aestheticism" are frequently called upon to characterize the creative features of R. B. Woodward. They are extremely valid, since Woodward works beautifully indeed, choosing worthy ends and arriving at them by the most reasonable and frequently unexpectedly exquisite route. In 1965 on receiving the Nobel prize Woodward said: "I scarcely have any doubts that something with the characteristic signs of life may be created under laboratory conditions, but I would not like to predict how much time will be required for this." However, Woodward's path is directed to the solution of increasingly complex problems on the road to the creation of this Something. In the process he rejects tasks that do not require great creative forces for their solution ("I like to undertake the synthesis of substances the preparation of which everyone believes to be impossible," says Woodward). This principle of research requires colossal labor, and Woodward works systematically 12-15 h a day. Each morning this stooped, sturdily built professor, attired in an austere suit with an invariably blue tie, having traveled the 50 miles that separate his home from Harvard University in a half hour of rapid travel, arrives at work at eight o'clock. "I do not believe," he says, "that good ideas can come at the peak of a mountain or on the sea coast; good ideas come only during work." In an interview with Soviet correspondents Woodward said: "Only rare experiments are successful; many more of them are unsuccessful. But even the experiment that failed is just as valuable as the successful one... Of course there are special moments when things really do work well. But this does not last for long, only a few hours. And the next day you have to press on. One cannot live with a single success. It is important to obtain pleasure from the work constantly, from the work itself, since defeats and victories in science are parts of a single whole." To Woodward's credit, it should be stated that he knows how to overcome failures, to inspire his co-workers, and to draw them to the solution of extremely complex problems.

Woodward is currently working on the total synthesis of erythromycin — macrocyclic antibiotic with 18 asymmetric centers.