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Nobel Prize in Chemistry 1957

Lord (Alexander R.) Todd

The Nobel Prize in Chemistry 1957 was awarded to Lord Todd *"for his work on nucleotides and nucleotide co-enzymes"*.

RESEARCH INFORMATION:

Nucleotides and nucleotide coenzymes are words that may seem strange and abstruse, but these compounds are of great importance to all of us. We have such substances everywhere in our bodies and they regulate many of the processes of life. The term is derived from nucleus, which here refers to cell-kernels or nuclei. The Nobel Prize of this year has nothing to do with atomic nuclei, nuclear fission or hydrogen bombs. Nucleotides are regularly found in the chromosomes of the cell-kernels, where they are connected with the units of heredity, but also in the cell plasma. In combination with proteins they constitute the virus molecules and many coenzymes are nucleotides of low molecular weight but with a special structure. Thus they are a group of substances of very great biological importance, perhaps the most important of all.

The nucleotides have been known for nearly 90 years and they have been frequently studied by both chemists and biologists, but for a long time they were, from the chemist's point of view, an underdeveloped field of research. The difficulties were too great.

Gradually it was established that they are built up of three different kinds of "building-stones" of quite different chemical character: phosphoric acid, a sugar, and a heterocyclic base containing nitrogen. I cannot express it more popularly, except to mention that these bases are compounds related to caffeine. Two different sugars are found, ribose and desoxy-ribose, and about half a dozen different bases. The simple building-stones may then be combined in hundreds or thousands to form macromolecules, the nucleic acids.

It is, however, not enough to know the building-stones; we must also know how they are connected to each other. The building-plan, the pattern or whatever you prefer to call it, must be very essential for the behaviour of the macromolecule in chemical and biological processes. The sugars and the heterocyclic bases are both somewhat complicated molecules, which may be connected to each other in several different ways, and finally it must be established how the phosphoric acid is bound. The task is very difficult; the combination of three quite different kinds of building-stones in one macromolecule gives it a very special character and neither the traditional methods of organic chemistry, nor those of inorganic chemistry are directly applicable. It is, however, pre-eminently a task for an organic chemist, and for more than ten years Sir Alexander Todd has held a leading position in this field.

Some idea of the building-plan may be obtained by examining the products formed by partial degradation of the macromolecule into small fragments containing a limited number of building-stones. Conclusive evidence can, however, only be obtained by synthetic methods, by building up possible combinations of sugars and bases - with or without phosphoric acid and comparing them with the degradation products. It is of course imperative to use such methods that the structure of the synthetic products is irrefutable.

The work has been very comprehensive, and many special methods have been evolved, but it is hardly possible to give a non-chemist a clear idea of the brilliant experimental work accomplished. Perhaps I should specially mention the methods for introducing phosphoric acid, the phosphorylation. In recent years, the fundamental role of phosphoric acid in the biochemical processes has become more and more evident, and the

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new phosphorylation methods - now approximating to those used in the biosynthetic procedures - are also of interest outside the special domain of nucleotide chemistry.

The building-plan of the nucleic acids is now established, at least in its outlines. We have a long chain, where the links are alternately sugar and phosphoric acid, and to each sugar molecule is attached a heterocyclic base as a small pendant. Thus there is an equal number of acid and basic groups. The different building-stones are always connected according to the same pattern and the difference between various nucleic acids must therefore be due to the kinds of bases and their relative arrangement. The number of different types is small - in a certain chain usually only four different bases occur - but in a macromolecule with thousands of appendant base molecules the number of possible combinations must be very great. We are familiar with the coding potentialities of the Morse alphabet, which has only two symbols, dots and dashes.

Through Sir Alexander's work a solid foundation is laid for the future development in this field. Starting from this work, other scientists have advanced very fascinating theories as to the arrangement of the chains; it seems that they may be coiled up as a helix with the bases inside. This model can perhaps explain how a nucleic acid chain can bring about the formation of another similar chain or even of a protein. We are here approaching very fundamental biological questions.

The synthetic methods have also been successfully applied to the preparation of low-molecular nucleotide coenzymes, for instance the cozymase, which plays a part in alcoholic fermentation and other biochemical processes. The ways are now open for synthetic preparation of the different types occurring in nature. It is also possible to synthesize coenzymes with slightly modified structure and study the effect of these modifications on the activity, and hence gain better insight into the mode of action of the enzymes.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1957/press.html