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Nobel Prize in Chemistry 1964

Dorothy Crowfoot Hodgkin

The Nobel Prize in Chemistry 1964 was awarded to Dorothy Crowfoot Hodgkin *"for her determinations by X-ray techniques of the structures of important biochemical substances"*.

RESEARCH INFORMATION:

Exactly 50 years ago, a Nobel Prize was awarded which we have much reason to be reminded of today. Max von Laue was awarded the 1914 Nobel Prize for physics for, according to the citation, "his discovery of the diffraction of X-rays by crystals". It is this phenomenon which has formed the basis of the work for which Mrs. Dorothy Crowfoot Hodgkin has been awarded the Nobel Prize for chemistry this year.

Very soon after von Laue's discovery, the two English scientists Bragg, father and son, began to apply X-ray diffraction in order to determine how the atoms of a compound are situated in relation to each other in a crystal. In other words, they tried to find out what is usually known as the "structure" of the compound. Their successes in this field resulted in their being jointly awarded the 1915 Nobel Prize for physics.

Knowledge of a compound's structure is absolutely essential in order to interpret its properties and reactions and to decide how it might be synthetized from simpler compounds. To begin with, only very simple structural problems could be solved by X-ray

diffraction, and these problems were taken almost entirely from the field of inorganic chemistry. Organic compounds, compounds containing carbon, usually have more complicated structures, and these presented too many difficulties at this stage. However, even then considerable possibilities existed for determining how the atoms of an organic compound are bonded to each other, by purely chemical methods. These methods were based largely upon the knowledge obtained from the latter half of the nineteenth century concerning the geometry of the bonds directed from a carbon atom. Large molecules were broken down into components whose structures were already known, and when some idea had been obtained of how these components were joined together in the large molecule this could often be confirmed by synthetizing the molecule.

Gradually, however, such large and complicated molecules were reached that these "classical" methods no longer yielded a result. This was particularly so in the case of the structures of many of the molecules which form part of living organisms and participate in the vital processes. In these instances it was necessary to obtain help from the field of physics, and in the first place use was made of X-ray diffraction by crystals of the compound concerned. During the period following the discovery of X-ray diffraction, this method of structure determination had been developed to such a degree that by the 1940's it began to be possible to use it for solving the structures of organic compounds which were insoluble by classical methods.

However, even today structure determination by X-ray methods does not yield a direct route from the experimental data to the structure. In complicated cases the scientist only obtains a result after considerable mental effort, in which chemical knowledge, imagination and intuition play a significant part. In addition, the experimental data often have to be processed using different mathematical treatments, which must be varied according to the circumstances. Add to this the fact that the more complicated the structure, the greater becomes the volume of experimental data which must be amassed and processed. For relatively simply built compounds it was possible to carry out the calculations with pencil and paper. Nowadays it is nearly always necessary to use

electronic computers, and their arrival has made an enormous difference to the possibility of carrying out structure determinations. However, it is not usually possible to just feed in the experimental data, and get out the figures which give the final structure; the scientist's ability to handle the data is still of vital importance. It is in this respect that Mrs. Hodgkin has shown such exceptional skill.

Mrs. Hodgkin has carried out a large number of structure determinations, primarily of substances which are of importance biochemically and medically, but two of these substances deserve especial mention. These are penicillin and vitamin B_{12}, whose structures have become completely and definitely known through her efforts.

The use of penicillin in medicine began to be tested about the beginning of the second world war, and its exceptional antibiotic properties meant that the demand increased enormously. It was therefore obviously desirable to find out whether penicillin itself or other related compounds having a similar effect could be prepared by chemical methods. For this purpose it was essential to determine the composition and structure of penicillin, and a large number of chemists and X-ray crystallographers in both England and the U.S.A. were put on to this problem. Mrs. Hodgkin was to play a leading part in the X-ray crystallographic work, and it was chiefly her efforts which brought it to a satisfactory conclusion. The work was begun in 1942 and the structure was elucidated after four years' intensive work. This was marked by close cooperation between organic chemists, X-ray crystallographers and scientists in other branches of physical chemistry and physics. A number of X-ray crystallographic methods were also used here for the first time.

Mrs. Hodgkin's determination of the structure of penicillin bears evidence of exceptional skill and great perseverance. The difficulties were considerable, but this was not because the molecule was particularly large. However, it possessed some unknown features, which meant that the chemical properties did not give sufficient guidance.

In 1948 Mrs. Hodgkin began her attempts to determine the structure of vitamin B_{12}, which had been isolated in the same year. This vitamin can be synthetized by certain bacteria and fungi, of which some play an active part in the digestive processes of animals.

The production of B_{12} is most pronounced in the ruminants, who seem to require this vitamin in particularly large amounts. In most of the other higher animals, for example in man, the production of B_{12} is small, and their food must therefore contain sufficient quantities of ready-made B_{12}. Lack of B_{12} in the diet, or a reduced ability to absorb this vitamin *via* the walls of the alimentary canal, leads in man to the fatal blood condition of pernicious anaemia. The illness can always be arrested by injections of B_{12} which is only needed in very small quantities. It is still not clear how B_{12} functions in the metabolic processes, but in order to begin to come to grips with this problem it is essential to know the structure in detail.

In 1956, after eight years' work, Mrs. Hodgkin and her collaborators had clarified the B_{12} structure. Never before had it been possible to determine the exact structure of so large a molecule, and the result has been seen as a triumph for X-ray crystallographic techniques. It was also, however, a triumph for Mrs. Hodgkin. It is certain that the goal would never have been reached at this stage without her skill and exceptional intuition.

There is reason to hope that the detailed knowledge of the B_{12} structure, revealed as a result of this work, will make it possible both to understand how this vitamin assists in the body's metabolism and to synthetize it. For the time being it has to be produced via bacterial fermentation

Professor Hodgkin. You have for many years directed your efforts towards the determination of crystal structures by means of X-ray diffraction techniques. You have solved a large number of structural problems, the majority of great importance in biochemistry and medicine, but there are two landmarks which stand out. The first is the determination of the structure of penicillin, which has been described as a magnificent start to a new era of crystallography. The second, the determination of the structure of vitamin B_{12}, has been considered the crowning triumph of X-ray crystallographic analysis, both in respect of the chemical and biological importance of the results and the vast complexity of the structure.

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Scientists working in many different fields, in X-ray crystallography, in chemistry, and in medicine admire the great determination and skill, involving what can only be described as gifted intuition, which has always been the mark of your work.

In recognition of your services to science the Royal Swedish Academy of Sciences decided to award you this year's Nobel Prize for Chemistry. To me has been granted the privilege of conveying to you the most hearty congratulations of the Academy and of requesting you to receive your prize from the hands of his Majesty the King.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/chemistry/laureates/1964/press.html