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SUGARS IN THE SERVICE OF CHEMISTRY[1]

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SUGARS are the most popular topic of chemical literature to-day. There must be a reason for it, and the question arises—What is it? The importance of carbohydrates in our daily life, the numerous uses made of them in our foodstuffs, in textiles, in building materials, in the many substitutes for the more costly natural products may sound like a logical answer to the question. Indeed, it may be claimed that the progress of civilization can be measured by the extent of the uses made of carbohydrates for constructive and destructive purposes. Yet the answer would be only partially correct. It would be hard to believe that men of the type of Scheele, Baeyer, Fischer and van't Hoff devoted themselves to the problems of sugar chemistry for reasons purely practical.

Admitting even for the sake of argument that to many workers the incentive was the applied phase of sugar chemistry, the great activity in this special field of work could not pass without leaving a deep impression on chemical philosophy. Indeed, it should be an easy matter to defend the thesis that every important industrial research extended over a long period of time must furnish a contribution to chemical philosophy which by generations to come will be adjudged to be of greater moment than the practical end which by its very nature can be of temporary value only. The history of chemistry furnishes many instances supporting this thesis, but it suffices to mention the trivial practical task which suggested to Dumas the theory of substitution.

With this thought in mind it may be proper to review briefly the contributions made by sugar chemistry to chemical theory.

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[1] Delivered before the Chemical Society of Washington on the occasion of the award of the Hillebrand Prize to C. S. Hudson, March 26, 1931.

The evolution of every science begins with the selection and assembly of material, the description and the analysis of which will constitute that special branch of science. It begins with a purely empirical phase which may be referred to as the period of discovery. To discover and to describe individual substances, separated from a mass of other substances, was the aim of the early chemists. It was then a purely intellectual pursuit. At this period the sugars were a great help and comfort to the chemist for the reason that many natural sugars possess great crystallizing powers. Indeed, cane sugar had been known for a long time in the Orient and was introduced to Europe by Alexander the Great. Milk sugar was crystallized in 1615 by an Italian chemist, Bartaletti, and in 1660 grape sugar was crystallized by Glauber. The important achievement of this period of chemical history was the announcement by the Russian chemist Lowitz in 1793 of the principle of crystallization as a method of purification. Another important achievement of the same period was the introduction of the microscope as a chemical instrument. The occasion for this was the analysis of beets for cane sugar. The incident led to the beet-sugar industry.

The period of discovery of natural substances was followed in the evolution of our science by the one that may be termed the period of discovery of derived substances. In this period the source of discovery was not a complex mixture of natural substances but a mixture derived artificially from a single natural substance. Again the chemist found in sugars suitable medium for these exploits for among the many decomposition products of sugars, some crystallized readily. Such substances were oxalic acid discovered by Bergmann and by Scheele, saccharic and mucic acids discovered by Scheele and many others. This purely intellectual pursuit then led to the discovery of substances which played an important part later when problems of structure came to the front.

As a rational and truly scientific discipline organic chemistry was recognized with the formulation of the ideas of chemical structure or of molecular architecture. To-day it is impossible to conceive of the term "chemical structure" without including in it that of "isomerism." Yet the idea that substances of the same composition might possess different properties was unacceptable even to Berzelius. But gradually the idea gained ground, being sponsored by the authority of Gay-Lussac, who called attention to the fact that sugar, gum and starch had similar compositions and different properties which, he maintained, were attributable to differences in the arrangements of the atoms in the individual components. True, the evidence of Gay-Lussac was not as good as his idea, but one must bear in mind that the concept "polymerism" was not yet known and that the analytical methods of Gay-Lussac were the best available. However, if it be permitted to classify tartaric acids among the sugar derivatives, then to sugar derivatives will belong the credit first for having suggested the idea of isomerism and second, for having brought about its general recognition. Indeed, it was after the discovery of mesotartaric acid by Gmelin that Berzelius withdrew his opposition to the idea that substances of identical composition might possess different properties, and indeed it was Berzelius who introduced the term "isomerism."

The term "polymerization" had a still longer struggle for recognition. But no sooner was it recognized than it was realized that simple sugars may be regarded as polymers of formaldehyde, and the Russian chemist Butlerow proceeded to demonstrate the truth of the assumption by condensing formaldehyde to a sugar. It must be added that the term "polymerization" even to-day embraces many diverse phenomena of which only some justly belong under that heading while others may be separated under the heading "condensation." The classification of these concepts and the unraveling of the nature of the forces which are responsible for the process of polymerization are some of the outstanding problems of chemical theory of to-day, particularly the phase bearing on the structure of the natural products of high molecular weight. The nature of these forces, which in a general way may be termed molecular in distinction to the primary-valence atomic forces, as yet is unknown. Their existence, however, nobody familiar with substances related to sugar, namely, α-hydroxy aldehydes, will ever doubt. For these substances remain in monomolecular state only for a brief space of time and pass spontaneously with the evolution of heat into a dimolecular, as if by this means liberating energy which subsequently may be utilized for the condensation of the simple substances into those more complex. Whether or not the complex substances such as starches, cellulose, gums, proteins, lignins, etc., are the products of molecular or of atomic forces is as yet not certain but the work on sugars now in progress in many laboratories is bound eventually to furnish the answer.

The most monumental contributions of sugar chemistry belong to the chapter on stereoisomerism. At the time Fischer began his researches on sugars, stereochemistry was a novelty looked upon with scepticism by many and was not tested experimentally from the view-point of predictions which the theory permitted. Fischer set out to test these predictions on sugars and verified the theory completely. Thus, sugar chemistry, more than any other branch of our science, helped to gain recognition for the views of van't Hoff and Le Bel. In the hands of Hudson the sugars attained another triumph by furnishing evidence to the optical superposition theory of van't Hoff. This triumph is of special significance for the reason that it was based not on a qualitative but on a quantitative method, and a science enters the category of an exact science only when it is based on quantitative arguments.

The contributions of sugar chemistry to stereochemistry go beyond these points. The more intimate knowledge of the relationship between structure and optical activity will depend upon establishing configurational relationships between simple substances containing one asymmetric carbon atom. The early work in this direction was based upon the knowledge of the configurations of simple sugars and of the acids derived from them.

One of the very disturbing observations in the field of stereochemistry was made by P. Walden in 1893 when he found that the reaction of substitutes on an asymmetric carbon atom may be accompanied by a stereochemical inversion. The observation, since then known as the Walden Inversion, has intrigued many chemists, and again the sugars offered a valuable medium for the study of the phenomenon.

From all that has been said, an impression may be gained that for the evolution of chemical theory sugars played rather a modest rôle to test theories which came to the front through observations in other fields of chemistry. At least one case may be mentioned where the observations on sugars suggested a new thought, the one of the possibility of an asymmetry produced by a carbon atom combined with three other groups only. It was the observations on the ethyl ester of the diazogluconic acid which suggested the possibility of the existence of optically active aliphatic diazoesters.

Finally, it would be no exaggeration to state that the most recent phase of sugar chemistry holds out more promise of general significance than any of the preceding phases. It deals with the migration of groups in the partially substituted sugars and with the dynamic isomerization of ring structures.

Passing now from organic to bio-chemistry, we find that there also sugars contributed much to theory. The difficult and exhaustive work done by Nef on the dissociation of sugars had for its objective the explanation of the process of fermentation. The work of Evans aims at the same end. The problem of fermentation is one of the most important problems of general biology, not because of the commercial or medicinal value of alcohol, but because the process of utilization of sugars by higher and lower living forms in many respects resembles that of fermentation and because what is learned about one of these processes may help towards understanding the other. The mechanism of biological dissociation of sugar as it is seen to-day could not have been conceived without the preceding work on the chemistry of sugars. It is enough to mention the discovery of phosphoric esters of the sugars as an essential step in fermentation as well as in animal combustion of sugar.

Above all, sugars have contributed to our understanding of the most important biological agents, the enzymes, the agents which occupy the intermediate place between non-living and living matter. For it was sugar chemistry which removed much of the mystery of the nature of these agents and placed them in the category of simple chemical substances acting in solution. How else can one explain the stereospecificity of the enzymes? The deduction formulated by E. Fischer in regard to relationship between enzyme and substrate, when the substrate was a sugar, is now accepted in relation to practically all enzymes.

All the contributions of sugar chemistry to general chemical theory, however, were the result of the progress in the knowledge of the details in the structure of simple and complex sugars. It is therefore appropriate to enumerate briefly the landmarks in the history of sugar chemistry. I should like to begin the modern history of sugar chemistry with the name of Butlerow, who was the first to prepare a sugar from the simplest components—from formaldehyde. No really great progress was made after the days of this Russian chemist until Kiliani's synthesis of sugars. On the foundation of Kiliani's work and on the basis of van't Hoff's theory, Fischer erected the wonderful structure of the stereochemistry of sugars. Mention also should be made of Tollens' suggestion of the cyclic structure of glucosides. After Fischer's work was completed, it seemed as if human ingenuity had exhausted all the accessible knowledge in the field of sugar chemistry. But then two new methods came to the front, the result of which is the recent work in the field of sugar chemistry.

One of the methods is that of methylation first introduced by Purdie and made popular by Irvine and the second is the application to sugars of van't Hoff's optical superposition theory by Dr. Hudson. About his latest work on the ring structure of sugars you have heard from him personally, and the gathering here to-night is evidence of your appreciation of this work; but may I remind you of Dr. Hudson's earlier pioneer contributions—which are as serviceable to-day as they were on the dates of their discovery. They are:

The rational classification of alpha and beta forms of sugars and of glucosides. All sugar chemists still remember the arbitrary manner of the older classification and the chaotic state of nomenclature of the various forms of glucose and of other monosaccharides. Hudson's rule then permitted him to elucidate the alpha and beta structure of di- and trisaccharides, a problem which previously could be solved only with much difficulty.

Then came the rule correlating the structure of lactones with their optical properties. This rule subsequently played an important part in determining the ring structure of glucosides.

Then came the amide rule of rotation which permitted the correlation of the structure of hydroxy-acids and sugar acids, and as by-products of his theoretical work are many discoveries of new forms of isomerisms and of rearrangements.

It is a rare occurrence that a single principle has led to so many discoveries. All sugar chemists of to-day have been assisted in their work on more than one occasion by the rules which are known as Hudson's rules.

MICHAEL FARADAY. II[1]

By Dr. W. F. G. SWANN

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IN the fall of 1831 Faraday began the first section of his great work, "Experimental Researches in Electricity," the work which he continued for some twenty-three years. These researches appear from time to time as papers transmitted to the Royal Society and they were subsequently put together in a single set of three volumes. They give a most detailed description of his thoughts and work. Experiments are described in the minutest detail. Every paragraph is numbered consecutively from beginning to end, and cross references are added to serve as connecting links between the various researches. His first experiments are on the induction of electric currents. Following the general notions evolving from the known facts that charged bodies induce electrical charges in others in their vicinity, he inquires whether any such phenomena can occur in the case of electric currents. Such problems as these present themselves to him. Suppose we have a wire in which a current is flowing, do we alter in any way the magnitude of that current by bringing into its vicinity another wire carrying a current? The kind of effect he is looking for is one where there will be some permanent alteration or at least an alteration which will persist for the whole of the time that current No. 2 is brought into the vicinity of current No. 1. He makes tests in all sorts of different ways and is finally led to the now well-known result that the induced current occurs only at the moment of change of the other current or during the periods of motion of the circuit carrying that current. Nevertheless, the nature of these phenomena is such as to cause his mind to lay hold of the idea that the various circuits which are involved are not actually ignorant of each other's presence. He thinks of them as being conscious of that presence in sort of a silent way. He thinks of them as being in what he calls an electrotonic state. His mind lays hold of the thought that it is in the change of that state that the current manifests itself. In order to appreciate the whole significance of his attitude in this matter, we must transport ourselves to a state of mind where we do not have the pictures of lines of force which we enjoy to-day. All that came later as an extension by Faraday himself of the ideas which he formulated in the early history of the subject. We have before us simply a set of wires all apparently unconscious of each other's presence. Yet any one of them has the power to know if any change is made in the other. It is one of the characteristic features of Faraday's way of thinking that he seemed to have the faculty of arriving at the essential elements which matter in a qualitative form long before he was able to place that exact significance to them which is associated with quantitative relationships. The quantity which was associated with the electrotonic state appeared in the hands of Clerk Maxwell as the electromagnetic momentum associated with the circuit. Or in terms of more intuitive concepts it refers to the product of the current and the total flux of magnetic induction through the circuit. It is this quantity, a purely mathematical quantity having no physical significance in the ordinary sense of the word, which Faraday succeeded in ferreting out of his experiments as the quantity essential for the coordination of his results. Speaking of this electrotonic state, as visualized by Faraday, the great Clerk Maxwell writes:

> By a course of experiment, guided by intense application of thought, but without the aid of mathematical calculations, he (Faraday) was led to recognize the existence of something which we now know to be a mathematical quantity, and which may even be called the fundamental quantity in the theory of electromagnetism. But as he was led up to this conception by a purely experimental path, he ascribed to it a physical existence, and supposed it to be a peculiar condition of matter, though he was ready to abandon this theory as soon as he could explain the phenomena by any more familiar forms of thought. Other investigators were

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[1] An address given on February 14, 1931, at the Massachusetts Institute of Technology, under the auspices of the Department of English and History.