A Survey of Progressive Science*

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AMONG the many aspects of progress in physics which tempt reference is that concerned with cosmic rays, so fascinating to most minds are speculations concerning their nature. Thinking of the more recent developments in this subject, one would like to express admiration of the enterprise which has enabled Prof. E. Regener to obtain records from many miles up in the atmosphere and deep below the surface of Lake Constance for measurements of their varying intensity ; admiration no less for the similar enterprises of Compton and Kolhörster. It is interesting to learn that Regener, as the result of the most recent researches by himself and colleagues, has formed the personal opinion that a part at least of cosmic radiation is electromagnetic.

It is difficult even in the briefest of references to the scientific progress of the year to ignore the claims of 'heavy hydrogen' and 'heavy water'. We knew that there was yet something to learn concerning the molecular species present at any moment in the liquid we daily handle under all sorts of varying conditions, but to learn that so familiar a friend as water should have kept hidden from us until now so deep a secret is almost disconcerting. The recognition of the hydrogen isotope H^2 and the realisation that we have been in constant contact with H^2_2O as well as H_2O shakes our scientific complacency, as did the proof forty years ago that the familiar atmosphere contained a gas until then unknown. Moreover, just as Lord Rayleigh's attention to a very small difference in the density of pure nitrogen and residual nitrogen from air led to the isolation of argon, so a small discrepancy between the chemical values for atomic weight of hydrogen and Aston's mass-spectrograph determinations (when in the latter allowance has been made for the existence of the oxygen isotopes) led Birge and Mengel to the suggestion that ordinary hydrogen might contain a heavier isotope. Once again an important discovery has followed from a firm faith in the great accuracy of modern physical measurements.

The brief history of our knowledge of heavy hydrogen assuredly illustrates the enterprise in research which is characteristic of to-day. The bare suggestion for its existence only arose in 1931, and it is scarcely more than a year since spectroscopic evidence provided by Urey and others made it sure. Yet already heavy hydrogen and heavy water have a big literature. Advances have been rapid ; Lewis and Macdonald, for example, have already prepared and studied nearly pure H^2_2O, and many of its properties have been studied by them and by others. We learn, for example, that its freezing point is $+ 3 \cdot 8°$ C., and its boiling point $101 \cdot 42°$, that ionic mobility in it is smaller than in H_2O, and many other of its constants have been determined.

Remembering that living cells and tissues contain 70–80 per cent or more of water, and recalling its all-important biological functions, it is not surprising that much curiosity has been awakened concerning the relations of H^2_2O to life. There seems to be evidence already that, when nearly pure, it is unable to maintain living organisms, though we do not know at what concentration it proves, if at all, to be actually toxic. We shall want to know to what degree living cells are permeable to it, and whether they have any selective power as between H_2O and H^2_2O. It is sure that many studies to determine such points will soon be made.

The suggestion that there may arise a new organic chemistry involving a synthesis of all known types of molecule with (if it prove possible) H^1 replaced by H^2 is intriguing, but, as others have remarked, somewhat alarming. There is at any rate much more yet to be done with compounds containing H^1.

All concerned with the chemistry of living things must feel satisfaction in the help that is now forthcoming in full measure from distinguished organic chemists towards the elucidation of the molecular constitution of such substances as vitamins and hormones, with their great biological importance. Professed biochemists are naturally making their own efforts in such directions, but they have their own problems to face in the study of events in the living plant and animal, and in that of biochemical reactions in general. The special experience and the developed intuitional skill of those whose minds are more continuously devoted to the art of synthesis cannot fail greatly to accelerate progress in this field.

I might illustrate this by several advances which have occurred during the year, but will be content with referring to the work upon vitamin C. No one acquainted with the dramatic history of scurvy in the past can fail to feel interest in the molecular constitution of a substance, the absence of which from the food involves the onset of that most serious malady. I think the history of recent dealings with this vitamin are of sufficient interest to bear recapitulation. Albert Szent-Györgyi, interested primarily in the oxido-reduction systems of animal tissues, was led, while working at Cambridge, to attempt the isolation of the substance responsible for the highly reducing properties of the adrenal cortex. He successfully obtained it from the gland in crystalline form, and afterwards separated it from orange juice. Its presence in the latter and certain of its properties made him suspect from the first that it might be related to vitamin C, but the amount available at the time was too small for successful biological tests.

Szent-Györgyi then went to the United States, where adrenal glands can be had in great abundance, and at the Mayo Clinic prepared the substance in relatively large amounts. On account of its acid character, strong reducing power, and colour reactions, recalling those of carbohydrate, he at first called it hexuronic acid, but later studies having shown that it did not belong to the uronic class, it now carries the name of ascorbic acid, based upon its biological properties.

Szent-Györgyi, returning to his chair at Szeged, in Hungary, soon became convinced that his substance possessed strong anti-scorbutic properties. His conviction that it was related to carbohydrate led him wisely to seek the help of Prof. W. N. Haworth at Birmingham, in the determination of its constitution. The amount of material available was at first very small, but Szent-Györgyi, seeking for fresh sources of the substance, had the remarkable good fortune to find that in *paprica*, a plant very common in Hungary, and used there as a condiment, ascorbic acid is present in relatively large amounts. Adequate material for study thus at once became available.

Much time has been devoted to constitutional studies in the Birmingham laboratory with conspicuous success. It is interesting to note that the methylation of hydroxyl groups, which has been of such value in carbohydrate research generally, has been also of service in this case. I must not, of course, stop to deal with the experimental steps, or the considerations which have led to the structural formula indicated by the work of Prof. Haworth and his colleagues. They have shown, in brief, that ascorbic acid is a derivative of the hexose sugar, 1-*gulose*; and that it is the lactone of a six-carbon acid with a five-membered ring. When in solution it is present as the enolic form of 3-keto-1-gulofuranolactone. It is right to say that certain Continental workers have come to somewhat different conclusions in detail, but the evidence for the above constitution as recently presented by a group of Prof. Haworth's colleagues is very convincing. The biological evidence for the normal activity of synthetic products is not yet complete, but it seems sure that the exact nature of vitamin C cannot fail to be known shortly. To the biochemist it is of much interest to learn that a substance with such specific activity in the animal body should be a relatively simple derivative of a sugar.

I will now direct attention to remarkable progress in another and quite different region of contact between organic chemistry and biology. The quest into the nature of the pigments of flowers is no new one, and most will know of the brilliant researches of Richard Willstätter which carried us so far into their secrets. Yet we owe to Prof. R. Robinson highly important recent additions to our knowledge. I have chosen this field partly because the successes reached in it demonstrate impressively enough how sure is the constructive skill of the modern organic chemist,

and also because it is a field in which chemistry, by joining hands with cytology and genetics, is giving its indispensable assistance to our understanding of the mechanisms of inheritance. Of much interest surely is the realisation that the infinite variety displayed in floral coloration is based essentially on variations within one fundamental chemical scheme. By contriving a variety of different substitutions in phenolic hydroxyl groups arranged round a common central aromatic structure, Nature has provided herself with a palette which provides all that is required for her gorgeous floral colour schemes. The central structure is that of a benzo-pyrane to which a phenolic ring is attached.

These pigments are collectively known as anthocyanins or, when sugar residues have been removed from their several molecules, as anthocyanidins. For in every case the central structure of the pigment molecule is associated with one or more sugar molecules; the nature of the sugar varying from case to case. Several different monoses and also bioses find a place in the molecule of one or other of these pigments. This peculiar association of carbohydrates with functional pigments is among the most striking facts of plant biochemistry. By determining the nature of the sugars and the exact position of each in the molecular architecture of individual anthocyans, as well as by many successful new syntheses in the group, the Oxford School has greatly advanced knowledge in this interesting field. Prof. Robinson has also developed a remarkable technique for the qualitative recognition of the nature of the anthocyans present in this or that flower, and with his method he has explored the factors of pigmentation in nearly two hundred species or varieties. This technique, apart from the preliminary guidance it gives to chemical research, will prove of the greatest value to the geneticist who studies the inheritance of floral colours.

Until modern physical methods lent him their aid, the chemist's thought-models were, as he well knew, incomplete. As an architect he built successfully in many styles without knowing precisely why the bricks he used held together. The bonds he so usefully pictured had no physical meaning. The development of the theory of electronic valency, however, has in the course of a few years carried thought surprisingly far towards an understanding of the forces which hold atoms together in organic molecules. It is only with brevity that I can refer to these advances, in which Prof. P. Debye has played so distinguished a part.

We have first to recognise the established distinction, clear if not absolute, between electrovalence and covalence. It is the form of atomic linkage denoted by the second of these terms which applies when electrons are shared by adjacent atoms, rather than transferred from one atom to the other, that is the special, though not the sole, concern of organic chemistry. With this conception of electron-sharing as a foundation,

a remarkable structure of fact and theory has arisen. The properties of the so-called covalent bond are indeed revealing themselves to ingenious experimentation with remarkable rapidity. The dimensions and strength of such bonds, and their heats of formation, have been measured by physical methods, and, moreover, by a variety of such methods, giving closely concordant results. One among the important conceptions which have emerged is that of the dipole moment. If at any locality in a molecule electrons are shared unequally by adjacent atoms, as, for various structural reasons, they often are, the molecule will be polar; the atom which has the larger share of the two binding electrons being the negative end of a bipole. The molecule as a result orientates itself in any electric field, and a measurable moment is involved. This dipole moment is one of the most fundamental characteristics of the covalent link.

I have ventured to say this much about polar factors in molecular structure because their recognition and their measurement have thrown much light on many constitutional problems both of structure and behaviour in the field of organic chemistry. In the elucidation of some aspects of isomerism, in determining the special configuration of the benzene ring and of condensed rings, and in aiding crucial decisions concerning the constitution of molecules like those of the oximes, azides, and other difficult cases, the recognition of polar properties has been of much service. In stereochemistry it has also greatly helped progress, and with the further all-important help of X-ray analysis this branch of structural chemistry has greatly advanced of late.

I have chosen the elucidation of the dipole moment as a single illustration of the value of modern applications of physical methods in chemistry. It is clear that studies of molecular structure will for the future be in the hands of the physicist no less than in those of the chemist, and that striking progress is thus assured. Aspects of the problems now arising, unlike those successfully faced at earlier stages, call for the aid of mathematical treatment. There is no suggestion, however, that pictorial thought about the organic molecule is failing in usefulness, or that modern investigators when using thought-models believe them to lack all relation with the actual.

The subject of biochemistry is likely to gain greatly from every advance that takes us further into the details of molecular structure: for in the crowded events in the living cell we may well believe that exact particularities of shape—the ability to fit with accuracy on this or that patterned surface—is prominent among the factors which determine the functions and fate of the biologically active molecules. X-ray studies and studies of surface orientations are already justifying this belief. In illustration let me remark on the interesting light which X-ray photography has thrown upon the structure of animal and vegetable fibres : silk, hairs, cellulose, and the like.

Observations made by several investigators, among whom I may mention Mr. W. T. Astbury, have shown that the basal structure of such fibres consists of bundles of long chain molecules which, as molecules, can undergo reversible or irreversible stretching. In general, they are formed by the polymerisation of relatively simple structural units and so in X-ray photographs display periodicity along their length due to the repetition of the unit in question. I will refer to silk and hairs alone. In the former the fibres are built of extended polypeptide chains consisting, for the most part, of united residues of glycine and alanine ; the unit of pattern repeating itself along the fibre axis at an interval of 2×3.5 A. The molecular chains in silk are, in the natural state, already fully extended ; there is no significant change in their X-ray photograph when the fibre is stretched. Hair, on the other hand, and also horn, nails, etc., are composed of the protein, α keratin. It would appear that the polypeptide chain of the keratin molecule in hair is not extended, but is, as it were, folded on itself. The molecules become fully extended, however, when the fibre is stretched. The photograph of stretched hair becomes then analogous to that of unstretched silk. This, however, is a reversible change.

The folding of the molecule protects elements in its structure from chemical attack. The unextended chain, for example, resists the action of steam, while the extended chain loses its power of recovery when steamed, being 'set' in the extended form. Hence the permanent wave produced by the modern hairdresser. A point of much interest is that though all have been wrongly looked upon as composed of the same keratin, the X-ray pattern which is common to feathers and tortoiseshell is quite different from that displayed by mammalian hair. "Thus the recognised affinity between reptiles and birds and their differentiation from mammals is confirmed by the methods of molecular physics."

I will refer to but one other illustration of progress in biochemistry from the application of physical measurements. Monomolecular films on air-water surfaces change the phase boundary potential. During the last few years Rideal and his co-workers have determined the alteration in the apparent molecular moment in a film when molecules with different polar 'heads' are compared, and when the film is compressed or expanded. Upon this basis they have developed investigations dealing with chemical reactions as they occur in these two-dimensional films ; obviously a study of great interest. It would seem, indeed, that film reactions differ in important respects from bulk reactions. In illustration of this I may mention a study recently published of the rate of oxidation of monolayers of unsaturated fatty acids, which may well contribute to an understanding of oxidations in the living cell. The authors are also studying enzyme catalysis in films.