The Scope of Organic Chemistry.[1]

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THE chemistry of the compounds of carbon covers a wide field, wider than that covered by any other element. Its scope embraces all living matter, as well as the vast number of non-living substances which are produced through the agency of life. Moreover, it includes a very great number of compounds unrelated to life or to living processes which have been built up by the chemist in the laboratory by methods he has devised.

Already some 200,000 definite compounds have been tabulated in Richter's Lexicon and in the supplements thereto, and this number is increased yearly by several thousands through the agency of a band of zealous workers scattered over the globe. It may well be asked what is the good of continuing to increase this already astonishing number ; and is the expenditure of time, labour, and energy justified which lead to the discovery of some new fact having, apparently, no useful application to any department of human activity ?

The answers to these questions are quite clear and definite. We must acquire a knowledge of the simple before we can attack the complex with any hope of *success.* The element carbon has been used by Nature as the basis of organised life because the capacity of carbon to combine with itself is shared by no other element, and it is upon this capacity that Nature has relied in order to build up the tissues and reserve materials which form the living world around us. Moreover, since the compounds of carbon containing a moderate number of atoms of the element are usually crystalline or capable of becoming crystalline, and there are obvious disadvantages attaching to the use of potentially crystalline substances as the basis of living matter, it has been found necessary to employ the more complex carbon derivatives containing many hundreds of elemental atoms, which by reason of their high molecular complexities no longer possess, or seem capable of acquiring, a crystalline structure, but belong to the class of jelly-like or colloidal substances.

Until we can determine how a small number of carbon atoms combine one with the other, we cannot hope to obtain any insight into the manner in which the more complex natural substances are built up, or any information regarding the way in which they are utilised to bring about the changes occurring during animal and vegetable metabolism.

STRUCTURE.

The science of structural organic chemistry is only just fifty years old. It was born when the genius of van 't Hof gave to the world the clue upon which the three-dimensional formula we now use is based. It is therefore no inconsiderable achievement to have gained in so short a time a knowledge of many of the reactions and properties of the more simple complexes of carbon in combination with oxygen, nitrogen, and other elements. But much yet remains to be done before we can attack with any real hope of success the problems which the chemistry of Nature presents.

[1] From the presidential address to Section B (Chemistry) of the British Association, delivered at Oxford on August 5.

It is true that the knowledge already gained has led to the synthetic preparation of quite a number of natural products, many of which are of service in relation to human needs. Many of the alkaloids, colouring matters like indigo and alizarine, camphor, and a large number of natural products, have yielded the secrets of their structures and have been produced by laboratory methods and, where necessary, on the factory scale. But the synthesis of such compounds has not provided much insight into the mechanism leading to their production in Nature, and indeed the reason for their occurrence in the plant is not understood. They are, moreover, crystalline substances which either occur in the plant as such or are formed by·the hydrolytic fission of some more complex plant materials. Their homogeneity is therefore not open to doubt, and their degradation into known fragments and the rebuilding of these fragments into the original substances, although by no means easy, is nevertheless comparatively simple when the difficulties attending the investigation of more complex natural products are taken into account. Even so, some of the simpler type, for example, strychnine, still resist the attack of the chemist.

BIOCHEMISTRY.

In its earliest days the science of organic chemistry dealt only with those compounds which were derived from natural sources, and it was regarded as certain that such substances could be produced only through the agency of life and by no other means. Since then this theory has been shown to be wrong by the preparation in the laboratory of many substances identical with those formed during the operation of life processes. Nevertheless, the more complex substances which Nature utilises in building up her animal and vegetable structures still show no signs of yielding the secrets of their constitutions, or the mechanism by which they are produced. Indeed, although we can imitate in the laboratory certain natural operations such as the hydrolysis of starch to glucose, we are still quite ignorant of the means by which glucose is converted, by the appropriate enzyme, into alcohol and carbon dioxide, neither can we imitate this process in the laboratory.

When once the chemist has passed beyond the crystalline and the distillable he enters a region full of difficulties, because he has few means either of purifying the materials with which he has to deal, or of determining their homogeneity when they have been purified. These are the real difficulties which confront the biochemist when he approaches his subject from the structural side of organic chemistry.

It is far from my object to disparage the wonderful work which has been done and is being done by physiologists and pathologists in their attack on the mechanism of normal and abnormal life processes. Their record speaks for itself. But too little is being done to approach the problems from the purely organic chemical side, and too few of the people engaged in biochemical research have an adequate knowledge of organic chemistry or the methods of the organic

chemist. The number of organic chemists who are co-operating with biologists in their attack on natural processes is too few. Indeed, the very difficult question arises here as to how best to organise methods for dealing with problems which are essential borderland problems between two great sciences.

It seems that the best method to attack problems in borderland subjects is by co-operation between two types of trained investigators. In the case of bio-chemistry, for example, by the provision of trained students of two kinds, one trained in physiology but with a sufficient knowledge of organic chemistry to promote sympathy with and knowledge of the chemist's point of view, and the other trained as an organic chemist with a similar knowledge of the methods and requirements of the physiologist. The former would be a trained physiologist who would devote his final year to organic chemistry, the latter an organic chemist who would devote his final year to a study of physiology. This is, of course, no new idea, but is one which is being carried out in at least one institution in Great Britain in connexion with other borderland subjects.

It is the absence of any real attempt to approach biochemical problems from the chemical side that renders it particularly desirable that the need for some such scheme should be emphasised. It is true that the fault is largely on the side of the organic chemists who, for the most part, seem appalled by the difficulties attaching to the study of natural processes. The difficulties are indeed great, but not insurmountable. We are far from gaining any insight into the meaning of life, but it is not unlikely that we shall, in the near future, obtain some information regarding the mechanism of the action of the enzyme, the important agent in the non-living transformation of living matter into chemical products. It may be that organic chemists are waiting to see how Willstätter, who has already made great progress in enzyme chemistry, will surmount the difficulties confronting him, and it may well be that this great organic chemist will introduce new methods of attack which will open up fresh fields for investigation.

PETROLEUM.

The complex hydrocarbons which form the main constituents of crude petroleum belong to a section of organic chemistry at present too little explored. Although many millions have been made through the production and sale of petroleum products, it is safe to say that the percentage of profit devoted to research in oil products has been infinitesimal. It is true that in the United States large sums are given by the oil interests towards research in other subjects, but until quite recently none of these was, curiously enough, given for the purpose of improving our knowledge of the science on which the utilisation and isolation of petroleum products depends. The reason is not far to seek. The apparently inexhaustible supplies of petroleum render it unnecessary to devise means for economical working. The crudest and most wasteful methods were employed, because economy and the conservation of the natural product were not paying propositions.

This applies not only to the methods used in fractionisation, but also to those employed for the purpose of 'cracking' the higher boiling fractions into liquids of lower boiling point. For at the present moment it is the fraction up to 200° C. which is the important product, because it is the 'petrol' of the internal combustion engine. Time was, before the introduction of this particular machine, when the light fraction from crude petroleum was a drug on the market, and in many cases was actually set on fire at the refinery because no use could be found for it. In those days the chief product was the kerosene fraction which was used as lamp oil. At the present time the rapid increase in the use of the motor-car for personal and commercial transport indicates that at no distant period, if progress continues to be made in the same direction, the amount of the 'petrol' fraction will be insufficient for the world's needs. This point has already been reached in America, where approximately 70 per cent. of the world's consumption of petrol (gasoline) is effected. During 1925 the consumption of petrol in the U.S.A. approached 800,000,000 gallons a month, which is about twelve times the amount consumed in Great Britain.

The 'cracking' operation is now carried out on an enormous scale by numerous processes, all subject to patents, but differing from one another only slightly on the question of principle. All depend on the well-established fact that hydrocarbons of high molecular weight will break down into those of lower molecular weight if they are subjected to the requisite degree of temperature. Pressure appears to play an important part in the character of the product, as does also the surface action of the container or material used in the container to promote surface action. All are wasteful, because little or no research has been carried out on the true chemical nature of the cracking operation. Much permanent gas is always produced, consisting for the most part of ethylene and propylene. In the States the ethylene is allowed to go free, because its obvious utilisation in the form of ethyl alcohol is attended with difficulties, but the propylene is usually absorbed in sulphuric acid, and thus converted into *iso*propyl alcohol, useful as a solvent.

The production of these two unsaturated hydro-carbons provides a clue to the mechanism of the cracking process which is of some significance. If you break a long-chain saturated hydrocarbon, one of your products must be an unsaturated hydrocarbon, and it is evident that cracked spirit contains a considerable proportion of such unsaturated bodies. Moreover, the cracking processes at present in use do not produce aromatic hydrocarbons, and it is on the presence of a proportion of these aromatic hydrocarbons that certain special properties of petrol depend. For example, the tendency at the present time is to produce for motor-cars internal combustion engines of increased compression ratio, in order mainly to diminish the petrol consumption and thus increase mileage per gallon consumed. For some reason, which research has not yet ascertained, the use of petrol which does not contain the right quantity of aromatic hydrocarbons of the benzene type leads to 'detonation,' 'knocking,' or 'pinking' when ignited in cylinders giving more than a small compression ratio. This detriment diminishes the value of cracked spirit as such for any but low-compression engines, and many have been

the devices suggested in order to overcome this difficulty.

A vast number of substances, selected more or less at random, have been tried as ' anti-knock ' materials, and as an outcome it has been found that one, namely, lead tetraethyl, possesses the property, when present in exceedingly small quantities, of preventing the ' detonation ' of the explosion mixture in the cylinder. For a time lead tetraethyl (ethyl gas) fell under a ban in the States owing to a fatal accident which attended the spilling of a certain amount in one of the American factories, but it is understood that further investigation has led to a revision of the view first formed, and that considerable quantities of ' ethyl gas ' are now being used. I remember visiting Wilmington in 1924, when some 500 gallons of lead tetraethyl were being made daily. Although there was naturally a strong smell of the material in the factory building, and I remained for some hours there, no ill-effects were noticed.

It is obvious that the conditions which produce ' knocking,' and the reason why certain substances are ' anti-knock ' compounds, and why the presence of aromatic hydrocarbons prevents the phenomenon, must be made the subject of systematic research.

The question is also one of national importance, because in the case of high-compression engines, such as those used in aeroplanes, it is essential that a petrol should be used containing a high percentage of aromatic hydrocarbons. In war-time these aromatic compounds will be required for the manufacture of explosives, and it is quite certain that there will not be enough for both purposes.

Nevertheless, it must be remembered that it is only at the moment that the low boiling fraction of petroleum is the chief marketable product. It is probable that progress in the future will tend more and more to produce a motor-car engine of the Diesel type, or one having a carburettor capable of effectively vapourising the higher fractions of petroleum. In these circumstances it may well be that the low fraction will become the less important part of crude petroleum, and that, instead of having to resort to ' cracking,' a process of synthesis, by which the lower hydrocarbons can be converted into higher ones, will have to be adopted. As a matter of fact there are methods known by which this can be effected. Pure *iso*amylene can, for example, be converted into diamylene by interaction with stannic or aluminium chloride, and the process can be carried further, so that perfectly good lubricating oils can now be made by the polymerisation of the lower unsaturated hydrocarbons.

Polymerisation and depolymerisation are therefore the two operations which the petroleum industry must investigate and establish on a firm scientific basis by research, so that it may be in a position to supply the public need for any particular form of engine which the engineer may evolve. Especially is it desirable to ascertain under what conditions polymerisation leads to the formation of aromatic and naphthenic hydrocarbons. Considerable attention has been directed within recent times to what may be termed in general the Bergius processes for depolymerising organic substances. The operation, which consists in heating the material under high pressure in the presence of hydrogen, was introduced in the first instance for the treatment

of coal. There can be no question that great and fundamental changes are brought about in organic substances by the treatment whether a catalyst is present or not, and that a wide field for research is opened up thereby, but it is doubtful if, at the moment, general operations of this type can be regarded as commercial propositions. The plant is exceeding costly and the conditions subject to wide variations which are difficult to control. Actually, it has been ascertained that in the ' cracking ' of the kerosene fraction of petroleum, hydrogen is unnecessary and can be replaced by nitrogen without affecting the character of the final product.

Little is known of the constituents of crude petroleum, or indeed of the fractions into which it can be separated after purification and distillation. Some of the simpler hydrocarbons of the pentane and hexane type have been isolated and the presence of cyclic compounds has been established. Many of them are classed under the head of ' naphthenes,' but these are of uncertain structure. No doubt many are present in the crude oil, but it is certain that others are formed during the distillation process. It is clear that much opportunity for research work offers itself here, and it is probable that small alterations in the method of distillation may cause deep-seated changes in the character of the distillate, causing it to be of greater service for particular purposes. The occurrence of hydrocarbons of the naphthalene series in petroleum products has also been clearly established. The higher fractions which constitute the valuable lubricating oils also need attention, for it is now certain that viscosity bears no relation to oiliness, that is, the capacity for acting as an efficient lubricator. The addition of small quantities of ' polar ' substances of the type of fatty oils or acids confers increased oiliness on these compounds, and although we are now gradually reaching a stage when we know more about the effects of such ingredients, the field for research is still a large and important one.

The formation of free carbon occurs during both the distillation and ' cracking ' process, in some cases to a very considerable extent. The utilisation of this carbon for the purposes of making electrodes is an important part of the industry, and the formation of carbon in a condition in which it can be used by the rubber tyre manufacturers is also likely to become practicable as an outcome of the thermal decomposition of hydrocarbons.

At present we know nothing about the structure of the hydrocarbons present in the lubricating oils. Indeed, it seems possible that these may not be long-chain hydrocarbons with which the organic chemist is familiar, but rather polymerised products formed from unsaturated components liable to be formed or destroyed under comparatively mild conditions. The relative ease with which the oil in the engine sump of a motor-car loses its oiliness through continued use is not characteristic of the stability usually associated with an organic hydrocarbon.

It is clear, therefore, that the need for systematic research into the character of petroleum products is urgent, and it is gratifying to note that the Anglo-Persian Oil Company has established a research laboratory at Sunbury-on-Thames, in which the

important principles underlying the industry have been and will be studied.

DYESTUFFS AND INTERMEDIATES.

Prior to the War, Germany manufactured three-fourths of the dyestuffs required for the world's markets. Of the remaining one-fourth, one-half was made from German intermediates and was therefore dependent on Germany. Switzerland, although without a domestic source of raw materials, ranked second with about 7 per cent. of the world's production. Great Britain produced about one-tenth of her requirements, and France produced in French-owned and operated plants from 10 to 15 per cent. of her consumption. In order to meet the patent requirements of France and Great Britain, German manufacturers operated plants in those countries where the final assembling operations were completed. The small dye industry of the United States was almost entirely dependent upon German intermediates. At the present time Great Britain produces 80 per cent. of the dyestuffs required for its own use, and we are therefore in a position to review the conditions which have led to this remarkable change and to consider the procedure necessary to strengthen it.

It cannot be said that any fundamental advance in the chemistry of the dyestuffs has been made since Bohn discovered indanthrene in 1901, although great advances have been made since then in the preparation of new colours belonging to this and other known series. Consequently, the research work necessary in order to establish our position as a dye-making country has been mainly along known lines, involving the extension of reactions which had already been established rather than the discovery of new ones. Nevertheless, it is no inconsiderable achievement for our research chemists to have established a position such as that indicated above in so short a space of time, for many of the preparations, the details of which could only be found in the patent literature, had to be worked out *de novo* and the correct conditions found for their adaptation to the technical scale.

It is probably along the lines of decreased cost of production that research work in the immediate future will be mostly engaged, and especially is this the case with the intermediate products from which the dyestuffs are derived. Moreover, the intermediate products are of the greatest importance for other industries, for example, the fine chemical industry, the perfumery, and the explosives industries, and any improvement in the processes for their manufacture or the production of new compounds having enhanced value from the commercial point of view is of the greatest importance to all these industries alike. The parent substances of the intermediate products are the hydrocarbons of coal-tar or the coke-oven by-products. The operations required to convert these hydrocarbons into the finished intermediates often involve many stages, any one of which depends for its cost on the purity and yield of the product. There is thus a wide field for research into the improvement of technical methods which may well occupy the attention of our dyestuffs chemists for some time to come.

On the other hand, the question of fundamental research into new processes, both for the preparation of new intermediates and new dyestuffs, must not be lost sight of. The intermediate determines the character of the dyestuff, and it is always possible that a new intermediate may be discovered which will yield a dyestuff with just that difference of shade as to catch the public fancy, and will lead to the replacement of the older dyestuff on the market. The sulphonic acids of naphthol, naphthylamines, and amino-naphthols are cases in point. These substances are used extensively for the preparation of azo dyes. There is a great number of these compounds theoretically possible, but only a few have found technical application, owing mainly to the high cost of producing the others. The high cost is nearly always caused by poverty of yield, an objection which may be at any time removed by the discovery of an improved process. The same argument holds good for the dyestuffs themselves.

It is futile to say that the vast field of organic chemistry has been thoroughly explored for the production of new types. At any moment one or other of the men or women engaged in fundamental research may repeat Bohn's discovery of 1901, and obtain a new compound which will be the forerunner of a new series of dyestuffs. It is perhaps too much to ask an industry which is struggling to hold its own to expend large sums on the prosecution of abstract research, most of which will be of no use to it, but it is not too much to expect that the industry will take every means to foster and encourage abstract research in our university institutions, and even to give some lead as to the direction in which its experience leads it to think that advances may be made. There is at present no organisation which can bring the manufacturers of dyestuffs and intermediates into touch with the work being carried on in our university laboratories, and it is possible that if at the present time a valuable discovery were to be made it would be unrecognised as such, and, following the usual course of academic research, would be published and thus lost to the country. What is required is a lead from manufacturers which will indicate the matters which they regard of importance, but which they do not consider as likely to yield results sufficiently quickly to justify them in employing their own research staff for investigating them.

This aspect is of all the more importance at the present time, when organic chemistry is entering on a new phase which will undoubtedly revolutionise many of the existing processes of manufacture. It is now recognised that the presence of a small quantity of a catalyst may either alter the course of a reaction or may lead it to proceed to completion where otherwise a totally inadequate yield would be obtained. The catalyst may either be added or the containing walls of the reaction vessel may act in this capacity. The well-known example of the oxidation of naphthalene to phthalic anhydride by vanadium pentoxide is an example of this, but similar cases are continually recurring, and it has only recently been found that the classical method for preparing ketones by the distillation of the calcium salt of the appropriate acid can be utilised in the most unexpected directions if the thorium salt instead of the calcium salt is employed.