VOL XVII NO 7 24 JUNE 1966

Journal of the Society of Cosmetic Chemists

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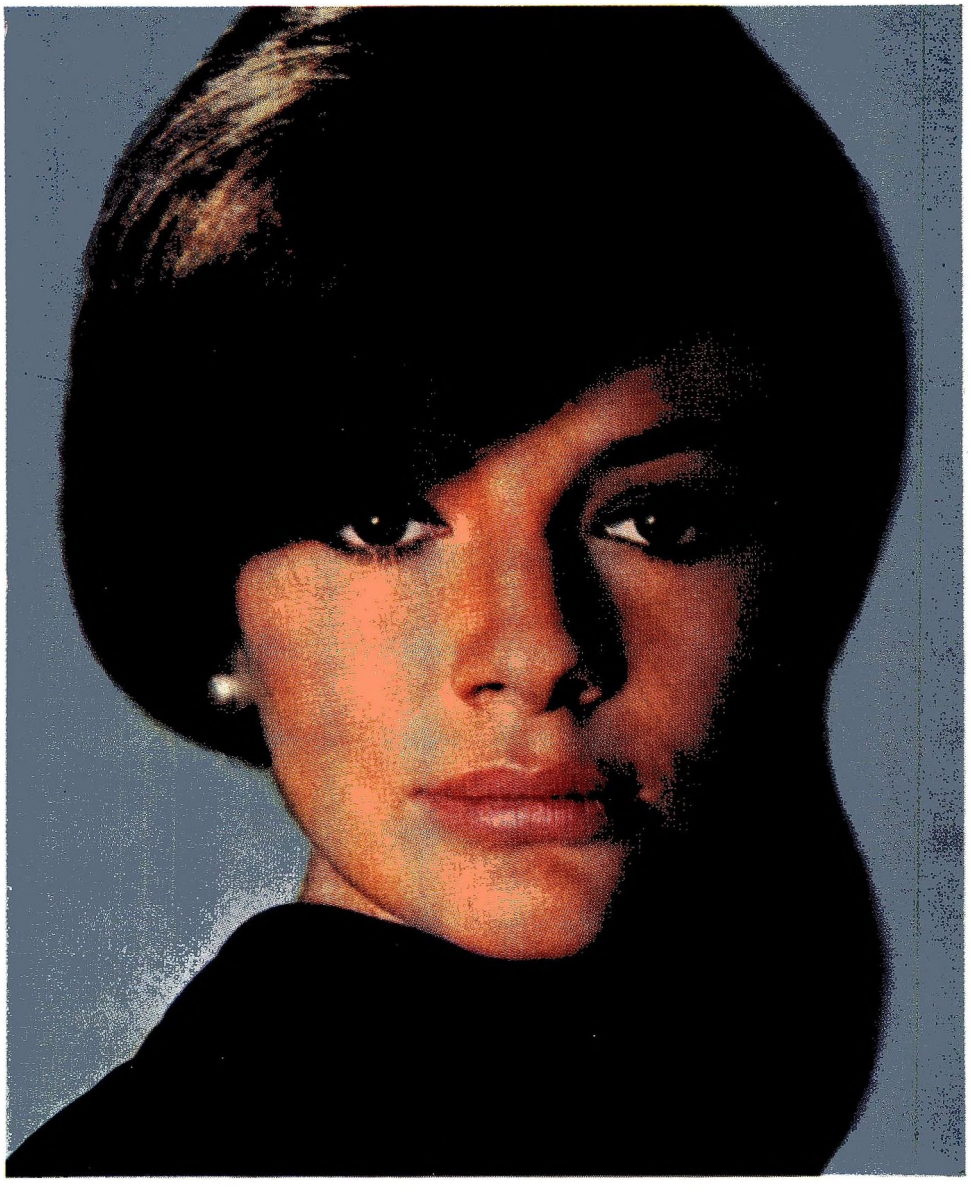

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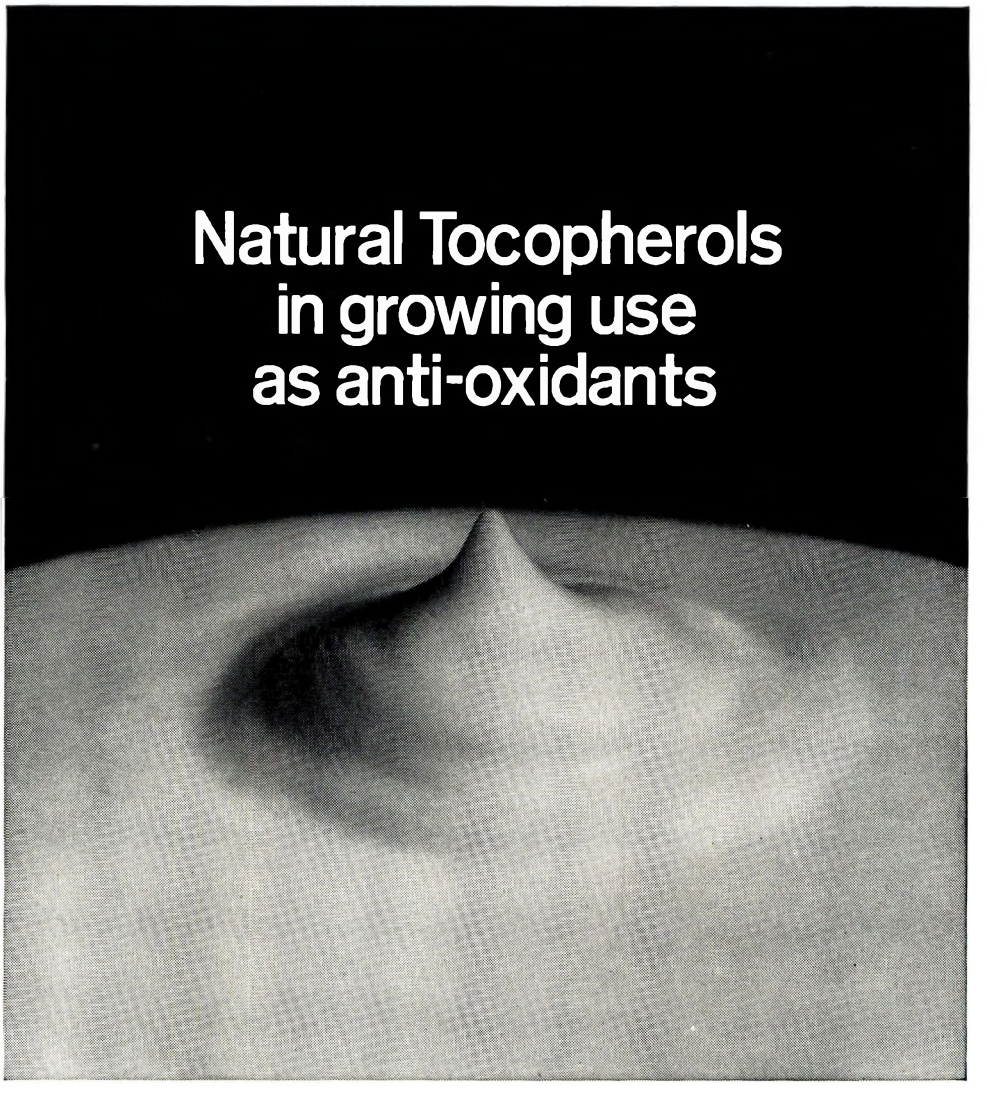

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SYNOPSES FOR CARD INDEXES

The following synopses can be cut out and mounted on 5″ × 3″ index cards for reference without mutilating the pages of the Journal.

The changing face of organic chemistry: TODD.
Journal of the Society of Cosmetic Chemists **17** 377-390 (1966)

Synopsis—The development of organic chemistry from its early days as a science is reviewed and the changes in direction leading to the present new phase in the subject are discussed. The problems now facing organic chemistry in its drive towards biology are considered and possible future developments outlined.

IR spectroscopy of aqueous detergent solutions: N. A. PUTTNAM and B. H. BAXTER. *Journal of the Society of Cosmetic Chemists* **17** 391-400 (1966)

Synopsis—The literature relating to the application of IR spectroscopy to the qualitative and quantitative analysis of aqueous detergent systems has been briefly summarized. The information that can be obtained directly by IR spectroscopy, using either transmission or the Attenuated Total Reflection technique, concerning the nature of components in such systems has been described and a comparison of the two techniques made. The direct approach could only be applied to relatively concentrated systems ; concentrations greater than 0.5% for transmission and greater than 4-5% for ATR. It was concluded that the ATR approach was more suitable to the analysis of raw materials, intermediates and finished detergent products and examples are quoted of the determination of sodium xylene sulphonate, in commercial solutions of this sulphonate, and sodium dodecylbenzene sulphonate in a light duty detergent product, with a relative accuracy of ± 2%.

Analysis of aerosol propellants: R. J. BROOK and B. D. JOYNER.
Journal of the Society of Cosmetic Chemists **17** 401-414 (1966).

Synopsis—Methods are described for the analysis of aerosol propellants of the chlorofluorocarbon type, including the analysis of aerosol packs. The methods include those used for the estimation of boiling range and of inert gases, and of deleterious impurities such as water and chloride ion, and the analysis of mixed propellants by gas chromatographic methods.

The relation between structure and properties in plastics used in packaging: A. SHARPLES. *Journal of the Society of Cosmetic Chemists* **17** 415-427 (1966)

Synopsis—The recent developments which have taken place in our understanding of the crystalline structure of polymers are considered in relation to the effects which they are likely to have on dependent physical properties. The properties considered are those likely to be of greatest relevance to film and blow-moulded products used in the packaging industry; namely, thermal stability, optical properties, permeability, and mechanical behaviour.

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J. Soc. Cosmetic Chemists **17** 377-390 (1966)

The changing face of organic chemistry

The 1966 Medal Lecture by PROFESSOR LORD TODD OF TRUMPINGTON, F.R.S., University of Cambridge, delivered before the Society of Cosmetic Chemists of Great Britain on 3rd March 1966, with Ronald Clark, President of the Society, in the Chair.

THE CHAIRMAN: I would like to welcome you all to this, the Society's 2nd Medal Lecture, and in particular give an especially warm welcome to our very distinguished lecturer tonight – Lord Todd of Trumpington. We are indeed most honoured to have with us, in this context, a man whose contribution to science has been marked by a Nobel Prize in 1957 and whose contribution to public as well as academic life was acknowledged by a Life Peerage in 1962. Tonight, amongst the audience I know there are several people who were fortunate enough to have had Professor Todd as their mentor of organic chemistry at Cambridge. Many others, like myself, have not had the privilege of enjoying such an experience. However, I know that we all eagerly await to hear Lord Todd.

Synopsis—The development of organic chemistry from its early days as a science is reviewed and the changes in direction leading to the present new phase in the subject are discussed. The problems now facing organic chemistry in its drive towards biology are considered and possible future developments outlined.

I am indeed greatly honoured to be the recipient of the Society's Silver Medal this year and to be privileged to give this lecture. But when I began some time ago to consider what I should talk about I found myself in some difficulty. I fear I have made no direct contribution to cosmetic chemistry – if indeed I have made any contribution at all it must be an indirect one. The possibility of such an indirect contribution I cannot wholly rule out since, although my interests have lain primarily in the general area of structure and function of natural substances of physiological importance, this area does have points of contact with some aspects of cosmetic chemistry, and, of course, organic chemistry is our common discipline. To speak on a topic directly in the field of your professional interest would be for me – a non-specialist – highly dangerous if not actually

impertinent; to discuss in fine chemical detail a topic wholly unrelated might well bore you. And so I came finally to a much broader topic – the changing face of organic chemistry. For science, like everything in this world, never stands still and it is no bad thing to stand back from time to time and have a look at it to see if we can discern from what has already occurred a possible pattern for the future.

Organic chemistry is one of the most remarkable of all the sciences, and is usually regarded by the layman as one of the most abstruse and remote from everyday life and thought. This view is, perhaps, based on its content of jargon and its use of abbreviated molecular formulae as a kind of hieroglyphic script. It is difficult to believe, however, that a science can properly be described as abstruse which permeates almost every material aspect of modern civilization, which stands as the bridge which links the physical with the biological sciences, and which is possibly the biggest of the sciences in its factual content and in the number of its adherents. Organic chemistry is, perhaps, the most logical of the sciences, and in its history of about 150 years it has suffered fewer theoretical upsets than other sciences. It is a remarkable fact that the whole towering edifice of the subject rests essentially on three basic concepts propounded in the third quarter of the nineteenth century, namely Frankland's concept of fixed combining power or valence, the Kekulé-Couper theory of the tetravalency of carbon, and the capacity of carbon atoms to join together into chains and rings, and van't Hoff and Le Bel's theory of the tetrahedral carbon atom, which gave us stereochemistry. All these concepts were purely empirical, but they have stood the test of time, and on them the whole of modern organic chemistry rests; advances in theory have occurred since they were first enunciated, but these have been essentially refinements giving more precise meaning to them, and have in no way upset or destroyed their validity. I doubt whether the same claim could be made of any other science.

There have been two definitions of organic chemistry. The first, that of Berzelius, was that it was "the chemistry of substances found in living matter." The second, commonly ascribed to Gmelin, appeared about fifty years later when more was known about the peculiarities of the substances found in living matter, and described it simply as "the chemistry of the carbon compounds." Each of these definitions is valid; but neither is wholly satisfactory, since the first is too restricted and the second is in certain respects too general. A very large number of known carbon compounds are of purely synthetic origin and do not, so far as we are aware,

occur in living matter; but it is undoubtedly true that the study of substances which are found in living organisms has provided most of the major stimuli to the advance of organic chemistry throughout its history, and there is little reason to believe that this will not continue to be the case. After all, it was Pasteur's work on the tartaric acids from wine that led to the van't Hoff-Le Bel theory, the anthraquinone dyestuffs stem from Graebe and Liebermann's work on alizarin from madder root, and work on polymerization and plastics goes back to the studies of Harries on natural rubber. Many other examples could be quoted, but I shall mention only one other because it is probably not very well known. It was the work of Windaus on the isomeric sterols that influenced Hückel to develop his theoretical studies on stereoisomerism in fused ring systems and through this developed in the fullness of time a realization of the deep significance of conformational analysis in reduced ring systems – beginning with Hassel and developed by Barton and others – and with it the concept of a new dynamic aspect of stereochemistry which has in recent years exerted a profound influence over a very large area of organic chemistry.

The original impetus to natural product chemistry – and, indeed, the move to divide chemistry into inorganic and organic sections – undoubtedly came from medicine and the use of natural drugs in its practice, and was partly scientific and partly commercial in character. Already in the eighteenth century what we may describe as scientific medicine was under way, and drugs such as extracts of *Digitalis* and *Cinchona* were being used rationally; again in connexion with medical work, the animal product cholesterol was isolated and described by Poulletier in 1780. First the pharmacists and then the chemists, actuated by curiosity or by the prospect of financial reward, began to busy themselves with the extraction and purification of natural drugs known to be of value, and to study their chemistry. But this turned out to be far from easy, and indeed the decision to put all such things into a separate section of the science to be called organic chemistry was little more than a confession that the natural products were different from, and much more complicated than, the inorganic substances of the mineral world. One thing soon became clear – the natural products were all compounds of carbon and contained few other elements beyond hydrogen, oxygen and nitrogen: and until a lot more was known about carbon chemistry, both theoretically and practically, little progress was likely to be made. So it was that the nineteenth century saw relatively little progress in the natural product field, such progress as there was being largely confined to the last two decades of the century. First

the general theory of organic chemistry was developed, and then the experimental methods necessary for structural elucidation and synthesis of organic compounds, these latter stemming in part from the development of the organic chemical industry, notably in Germany, towards the end of the nineteenth century. But let us not forget that it was from work aimed at natural products in the shape of colouring matters that the dyestuffs industry developed. Nor should one forget the continuous and often unrewarding effort of the workers in the field of physiological chemistry in the second half of the nineteenth century – work which has provided a base-line for much more recent organic chemical studies, and which also gave birth to the now flourishing science of biochemistry. And here let me note in passing that organic chemistry and biochemistry are complementary, and indeed merge into one another in the natural products field, so that distinction between them is at times rather artificial.

One cannot, of course, put precise dates to changes in scientific patterns, but round about the beginning of the twentieth century natural product chemistry suddenly started to come into the forefront of organic chemistry. One reason for this was, no doubt, the appearance of some scientific giants in the field – Perkin, Willstätter and Fischer, to mention but three. But there was, I think, more to it than that. Organic chemistry had, by that time, progressed to a point where it had the experimental techniques and the background knowledge necessary to ensure real progress in the study of complex natural materials. Furthermore, the rise of the organic chemical industry and the growing outlets for new materials encouraged work on natural materials with the aim of producing synthetic analogues which might at once have their virtues and be free of their defects, just as the synthetic dyes had in many cases proved better than their natural counterparts. Finally, the steady development of scientific medicine and the opening up of tropical colonial territories by the major powers had provided a further stimulus to the search for new natural drugs and their synthetic analogues as well as to the study of bodily components, both normal and pathological. Be that as it may, the fact of the development of natural product chemistry is not in doubt, and it became an increasingly prominent feature of organic chemistry during the first twentyfive or thirty years of this century.

Not only science as a whole, but also individual sciences, tend to advance irregularly on a broad front, and during any one phase of development there are always individual investigators who stand apart and who break new ground or who see new vistas or horizons not apparent to others at the

time. For this reason it is difficult – especially with recent events – to put precise dates to changes in scientific patterns. But in broad terms it seems to me that during the first thirty years or so of the present century most organic chemists dealing with natural products were preoccupied almost entirely with the structure of compounds, while the biochemists were interested essentially in their function. During this period the organic chemists developed their methods of degradation and synthesis to a high degree of perfection and, aided by the introduction of new physical methods of analysis, they have since taken them to the point at which the synthesis of molecules as complex as cholesterol, strychnine, chlorophyll, and a number of the coenzymes, has been realized. However, since the mid-thirties, slowly at first, but later with increasing rapidity, interest has been moving to a study of structure in relation to function among natural products. It is this which has taken organic chemistry much closer to biology than it has ever been before. Equally, of course, it is the increasing realization that function must be considered in relation to structure that is bringing the biochemists closer to their organic chemical colleagues, to the advantage of both. What brought about this change? In a sense, I believe it originated in the movement of biology, spurred on by biochemical work, away from purely taxonomic and descriptive studies. A major influence was exerted by the work on accessory food factors or vitamins. The study of nutritional problems by Eijkmann, Hopkins, McCollum, and others had reached, by the nineteen-twenties, a point at which it was realized that these mysterious vitamins could actually be isolated as chemical individuals capable of structural investigation and eventual synthesis. The opportunity was seized upon by the chemists, and with it the very similar opportunity presented by the sex hormones. Structures were worked out, and soon synthetic vitamins and, later, hormones became available. But it was inevitable that the chemists who entered this field should find themselves fascinated by the further problem which turned up – why and how do the vitamins and hormones act, and what is the secret of their specificity? And so the advancing front of the subject began to take a definite orientation towards the solution of biological problems.

When one looks back over the past thirty or forty years the most spectacular results in organic chemical research appear to have been in or associated with research on natural products. But it would be wrong to think of natural product studies as the only advancing front in the subject. Major advances have also occurred on the side of theory, and particularly

in our understanding of the intimate mechanism of organic chemical reactions. Through them it has been possible to rationalize many experimental observations and, by this provision of a firmer basis for prediction of reactivity, to add to the power and precision of synthetic methods. And not least, perhaps, it has lessened somewhat the task of the student in assimilating the essentials of the subject. Theoretical advances must, of course, keep pace with the experimental side of any science if overall progress is to be satisfactory. We may recall that lack of adequate theory in the mid-nineteenth century got organic chemistry into acute difficulties which were only resolved by the advent of Frankland, Couper, Kekulé and others, and also, I believe, it is reasonable to attribute the relative decline of German organic chemistry from its pre-eminent position at the opening of the twentieth century to lack of attention to theoretical aspects of the subject. At that time the German organic chemists, backed by a powerful industry reared on their experimental work, were all too ready to ignore the young science of physical chemistry through which were, indeed, to come many of the theoretical ideas which in due course illumined their own field.

Great strides have been made, too, in what might be called the chemistry of synthetic carbon compounds – the area on whose development industrial organic chemistry largely depends. True, a substantial part of the stimulus in this vast area came initially from work on natural products, but in its development it has moved in many cases far from them. Thus, for example, the oldest organic chemical industry – the dyestuffs industry – began by seeking to make natural materials, but it has long since progressed to a stage where it operates in areas chemically remote from the natural colouring matters used in the past. On the other hand several of the more recent industries, such as the petrochemical industry, have had little or no contact with the natural product field in the ordinary sense of that term, either in outlook or in method. It is, of course, developments in industrial chemistry that have made the greatest impact on our everyday life and have virtually revolutionized the material aspects of our civilization. From it have come a bewildering array of products – dyes, drugs and detergents, fibres and fungicides, plastics and pesticides, and many another. The future seems to hold promise of almost unlimited advance and we are likely, in due course, to find ourselves using entirely new materials in all aspects of our daily life, each fashioned to meet some specific need and each representing a further triumph of synthesis by the organic chemist.

But let me return to the field of natural product chemistry for not only

is it my own field of work but I believe that it will remain one of the main spearheads of advance in the future as it has been in the past. When one looks back over its development during this century one is struck by the fact that in many cases the appearance of new techniques have determined its advance. It does exemplify very clearly the German saying, "Jeder Fortschritt der Wissenschaft ist ein Fortschritt der Technik." Early examples are to be found in the development of microanalysis by Pregl and others, which enabled the chemist to work with substances obtainable only in amounts which would have been useless if the older analytical methods had to be used; again refined distillation procedures greatly promoted certain aspects of your own field of natural cosmetic substances. Later techniques have included chromatography in all its aspects – column, paper, thin-layer, vapour phase, and ion-exchange – electrophoresis, countercurrent distribution and perhaps above all the immensely powerful analytical tools of ultraviolet, infrared, nuclear magnetic resonance and mass spectroscopy, and X-ray crystallographic analysis, to mention only those physical methods of particular value in organic structural work. Without these much of the more widely acclaimed work of the past twenty years would have been literally impossible. These techniques have enormously simplified the problems of structural elucidation of organic compounds and there are many examples where the structure of a new compound has been worked out using them alone without resorting to the classical degradative methods of organic chemistry. There are, indeed, some who say that these methods have rendered the organic chemist and even his subject obsolete or at least obsolescent. To my mind anyone who holds that view has a totally wrong idea of the position. Certainly, if a chemist approaches the study of natural products as a pure exercise in degradative chemistry – that is in the spirit of a man solving a crossword puzzle – then it is true that these new methods will remove much of his fun. But the determination of the structure of a natural product has never been an end in itself. It has only been of value in relation to function, to its origin in nature or as a preliminary to synthetic work aimed at some practical goal. Organic chemists have always avidly accepted any methods which will remove drudgery from structural studies and they gladly accept these new physical methods which, especially with complex molecules, enable them to concentrate more readily on the issues in the chemistry of living matter from whose study they have hitherto been barred by the sheer complexity of the materials with which they would have to deal. To me these new methods give a hope of getting to grips

with the problem of chemical specificity in biological systems; this problem of specificity or, if you like, the relation between chemical structure and physiological activity if we could solve it, would open up enormous new vistas, many of practical significance.

This problem of specificity is one which has long interested me – indeed it has been in many respects the main driving force behind my own work and that of my many colleagues ever since I went to Edinburgh in 1934 at the invitation of George Barger to try my hand at the structure and synthesis of vitamin B_1, or thiamine, as it is now generally called. The study of vitamin B_1 was in a sense decisive, for it led me in the first instance to search for and to study other vitamins – vitamins E and B_{12} for example – and then to interest myself in the reasons for their importance. This interest led me to the coenzymes and from these naturally to the nucleotides and the nucleic acids. All this work kept me in contact with its offshoots, and particularly with the attempts to link the increasingly detailed structural knowledge which emerged with chemotherapy. Chemotherapy in the original sense of the treatment of disease due to living organisms with synthetic chemical agents is, of course, only a part of the general field of treatment of diseases of all types with synthetic (or natural) drugs. From the practical standpoint there have been great advances in the development of drugs for the treatment of disease during the present century – advances which have improved the general health of human beings enormously and have greatly improved man's expectation of life. I need not enlarge upon this here: the revolution wrought in the practice of medicine by chemistry in recent times is universally known and recognized. And yet it must be admitted that these advances have been achieved by largely empirical methods and that there has been little in the way of a sound theoretical basis for the production of new synthetic drugs. The most widely used approach in recent years has been based upon the idea of competitive antagonism which has owed much to studies on vitamins and anti-vitamins. The idea behind this approach can be readily understood by quoting the original work of Woods and Fildes in 1940 on the mode of action of sulphanilamide. It is known that *p*-aminobenzoic acid is required by micro-organisms (and also animals) for growth and that it is indeed one of the B group vitamins. Now it is possible to offset the action of sulphanilamide on micro-organisms by giving large amounts of *p*-aminobenzoic acid, and it is equally possible to negative the effect of *p*-aminobenzoic acid by administering sulphanilamide. The inference drawn is that *p*-aminobenzoic acid is essential to the proper functioning of some enzyme system in the micro-

bial organism and that sulphanilamide competes with it for its place on the enzyme protein or, alternatively, displaces it from the protein. It was suggested that this successful competition was bound up with the geometrical, and possibly the physicochemical, similarity between sulphanilamide and *p*-aminobenzoic acid. Since the work of Woods and Fildes this concept of antagonism, of interfering with the functioning of substances or of enzyme systems, has formed the basis of what has been described as the first rational approach to chemotherapy. In this approach the synthesis and testing of *iso*steres and analogues of vitamins and coenzymes has played a large part, but it must be admitted that, although many indications have been obtained that the idea is sound, few successful drugs have emerged from its application. The reason for this is clear anough – we know far too little about the way in which enzyme systems function, and about the factors which govern specificity, to enable us to fashion antagonists on any rational basis with any certainty of success. Until we have much more knowledge about the intimate mechanisms of the cell the discovery of commercially successful drugs or pest control chemicals will continue to have about it a considerable element of luck.

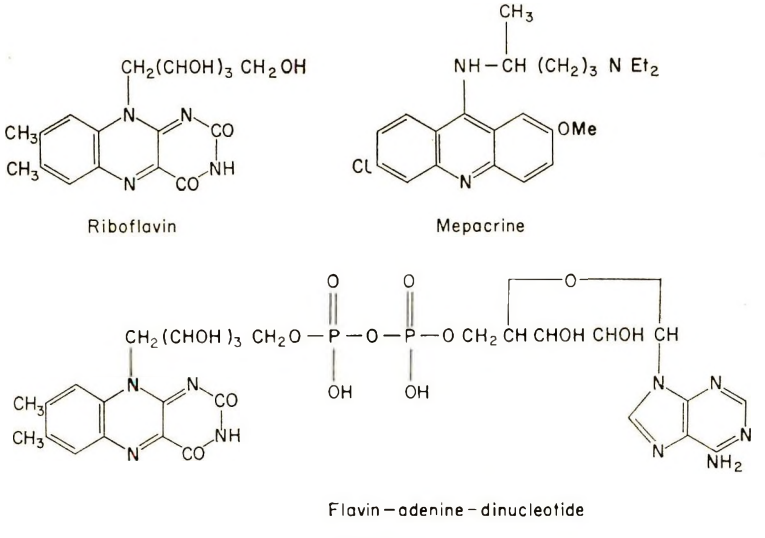


Figure 1

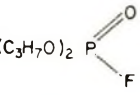
Let us take one or two simple examples to illustrate my point. It can be shown in laboratory experiments with micro-organisms that the well-known antimalarial drug mepacrine can act as an antagonist to the vitamin

riboflavin, and one might argue that this is because of a superficial geometrical resemblance in the formulae of the two compounds (*Fig. 1*). But riboflavin functions in enzyme systems mainly as the coenzyme flavin-adenine-dinucleotide. If, then, we are to proceed from mepacrine we are certainly hampered by the fact that we do not know whether the antagonist acts at the stage of the synthesis of riboflavin, the conversion of riboflavin to the active dinucleotide, or in the carrying out of reactions by the coenzyme.

Examples of this type could be multiplied. And yet there is clearly something in the idea. 5-Fluorouracil, and its deoxyriboside, have been used in the treatment of certain forms of cancer, and they appear to act by interfering with thymidine synthesis and incorporation, and 5-bromouracil has been shown to be incorporated into phage nucleic acid within bacteria, thereby greatly lowering the infectivity of the new phage produced. But with 5-fluorouracil one is using an inefficient blunderbuss method for it does not discriminate between one type of rapidly dividing cell and another – between, say, cancer cells and bone-marrow cells – and so it is too generally toxic to be a really effective therapeutic agent.

If we are to get any further along these lines it is obvious that we must get to know much more about enzymes themselves – not just what reactions they catalyse (which has hitherto been the major interest of enzymologists) but how they carry out these reactions and what structural features are responsible for their substrate specificity. This is a subject which is now attracting the attention of chemists, biochemists and molecular biologists, and some quite remarkable progress has already been made.

Enzymes are essentially large proteins, and in general it must be assumed that each enzyme has an "active site" (or sites) to which the substrate gets attached in some way (together, presumably, with the coenzyme in those cases where one is necessary) in order that reaction may occur. One approach to enzyme studies is therefore to search for active sites. It is now a number of years since Sanger, through his brilliant studies on amino-acid sequences in polypeptide chains, was able to establish by chemical means the structure of the relatively small protein insulin. Since then he, and his colleagues, have refined their methods so that quite large proteins can be dealt with – for example, Hartley has defined the residue sequence in the proteolytic enzyme chymotrypsin which contains some 259 amino acid residues in its molecule. Very interesting work has been done by the same group on determining the active site in chymotrypsin. A very useful inhibitor of this enzyme is the substance di*iso*propyl phosphorofluoridate

(DFP)  which reacts stoichiometrically with it to give an inactive monophosphorylated chymotrypsin. By using DFP, containing radioactive phosphorus as a marker, it is possible to degrade the inactivated product and to show that the phosphorylation occurs on one particular serine residue and to locate that residue in the chymotrypsin chain. One can conclude that this serine residue is part of, or very close to, the active site of the enzyme. This is not the place to go into detail on the various reagents used, but it will be enough to say that by using other reagents, and especially carefully designed synthetic bifunctional compounds, as inhibitors to locate other residues involved in the active site a picture is now building up of the part of chymotrypsin which is actually involved in carrying out the reactions it catalyses. (I should point out, of course, that one cannot simply say on the basis of the DFP reaction that only the residues immediately adjacent to the reactive serine in the polypeptide sequences are involved; the enzyme has a complex secondary structure in which the chain is looped up in a rather complicated fashion so that some amino acid residues far removed from one another in the sequence are in fact in close spatial proximity at the active site.)

Perhaps the most remarkable recent finding in the field of active sites is that of Phillips who by X-ray analysis has worked out the structure of one of the group of enzymes known as lysozymes. In this enzyme the polypeptide chain is looped up into a large three-dimensional lump with a kind of cleft or gully in it at one side. He has further treated it with an inhibitor, again examined the inactivated material by X-ray methods, and shown that the inhibitor molecule is sitting snugly in the cleft of the original lysozyme. It certainly looks as if this is direct location of the active side, and everyone is waiting for a further refinement of the present X-ray diagrams to the point where Phillips may be able to show exactly what the active site is chemically, and how substrates and inhibitors get attached to it. I think I need hardly elaborate on the importance of such studies and their implications for future developments in the drug field and elsewhere.

It is certain, of course, that in determining substrate specificity and in bringing about reaction, the secondary structure of the macromolecular protein must be important. There is plenty of evidence to support the view that conditions can be quite different on the surface of the macromolecule from what they are in the main bulk of the solution in which an enzyme reaction is carried out *in vitro*. The function of the enzyme is in

part to remove the substrate from the macro-medium of the solution to a micro-medium in the immediate vicinity of the protein, where conditions can be quite different from those which might be judged to exist on the basis of pH measurements made in the bulk of the solution. The secondary structure of a protein presumably depends primarily on its size and amino acid sequence, and it is certainly remarkable how specific this is in an enzyme from a given species in all cases that have been studied. When one thinks of it, it is astonishing that there should be such precision in making these very large protein molecules all with a rigidly defined sequence which is adhered to even through successive generations of living cells. How is it done?

Here again we have no complete answer but we are, I believe, on the way to getting it and already we know a good deal. The picture as we now see it is in general terms something like this. It involves the nucleic acids, the chemistry of which has long been a subject of research in my own laboratories. Since the establishment of their general structure nearly fifteen years ago geneticists and molecular biologists have established that the primary genetic material – the genes which are responsible for the transmission of hereditary characteristics – are deoxyribonucleic acids (DNA), long chain polyneucleotides made up of several thousand simple nucleotides (normally four in number) linked together through their phosphate groups. We know two major functions for the genic DNA. First, it replicates itself by a synthetic process in the cell nucleus in which the existing molecule acts as a kind of template for building up the new one. Secondly, it acts again as a template for producing smaller but still macromolecular ribonucleic acids (RNA) – the "messenger RNA's" in which the sequence of nucleotide residues provides a code which controls the synthesis of a specific protein, i.e. determines the precise sequence in which amino acids are joined together. What is more we now know what this code is – it is one in which a triplet of nucleotides in the messenger RNA corresponds to one particular amino acid. Since the amino acids are brought to the site of synthesis themselves attached to small polynucleotides (each specific for one of the twenty or so amino acids) it is clear that we are here dealing also with a template method of synthesis. It is by means of this mechanism that organisms ensure, or seek to ensure, absolute constancy in the composition of all the vitally important enzymes and other proteins which they synthesize and on which their existence depends. It is of some interest to speculate a little here on the possibility of cells making occasional mistakes in these replication syntheses. One would imagine

that in a process such as that used by cells for protein synthesis there would be a small but finite chance of error in the selection of amino acids. Where the enzyme protein being produced is only concerned with some process of intermediary metabolism, an error will have no serious consequence since it will be confined to very few molecules of only transient importance. But if the error occurs in making an enzyme protein concerned in the series of reactions leading ultimately to the production of fresh genetic material, the situation is very different; for the error may be passed on and, especially in animals which are long-lived and contain a vast number of individual cells acting in concert, the cell will change gradually and ultimately its capacity to grow and divide may cease. It is conceivable that some such process is responsible for the process of ageing in animals, although I would emphasize that, however attractive such a hypothesis may be, it is wholly speculating. But perhaps it warrants experimental study.

We have still far to go before we really understand the chemistry of genetic control and mechanisms such as those I have mentioned for protein synthesis. Only now are people trying to develop techniques for determining the residue sequence in nucleic acids – a fantastically difficult problem but one whose solution is essential to further progress. I think you will agree that the progress already made gives grounds for believing that we are perhaps not too far away from an understanding of what goes on in living organisms which will revolutionize our approach to many diseases and may well permit us also deliberately to alter the characteristics of living creatures by chemical methods – with all which that implies in the way of dangers as well as benefits for mankind.

These developments to be expected from the researches I have discussed are primarily biological. But there are features of them which are potentially of purely chemical importance, and which perhaps foreshadow developments of considerable practical moment. One possibility lies in the field of catalysis. Enzymes are remarkably efficient catalysts as well as being highly specific. One of their drawbacks, when considered for use in many chemical reactions, is that they are soluble, and thus operate only in aqueous solution. In recent years there have been some studies by Kachalsky in which by various means he was able to attach non-hydrophilic residues to enzyme proteins, thereby rendering them soluble in non-aqueous solvents without destroying their activity. Such a development has possibilities, but perhaps more promising would be the synthesis of synthetic enzymes by incorporating active sites into large polymeric

molecules. This might be done by synthesizing an "active site" as a small molecule and then building up a polymer around it.

It is interesting that nature uses a template mechanism for the synthesis of nucleic acids and proteins. This type of procedure has not in the past been applied in organic chemistry, but the chance discovery of stereospecific polymerization in the polyolefine series indicates that it can be a practical possibility. I believe that one of the new ways in which the plastic-polymer field will develop is along such lines, and that template mechanisms will not only yield new and exciting materials with novel properties, but that their use may lead to a kind of mechanization of synthetic processes in which molecules of any desired composition may be produced by a fully automatic process. The possibility of ready synthesis of specific macromolecules which might also lead to the development of artificial repair mechanisms for damaged tissues in animals might very well have repercussions also in cosmetic chemistry.

One could speculate further about things that may happen in the future but perhaps I have said enough. One thing is certain; the new knowledge that waits to be gathered by applying our growing arsenal of modern research tools in fields such as I have mentioned will open up wholly new vistas for the future – vistas which make me believe that organic chemistry will remain as I have always known it – a vigorous and exciting science whose further progress will add materially to the welfare and happiness of mankind.

(*Received: 3rd March 1966*)

The Chairman then presented the lecturer with the Society's silver medal, amidst applause from the audience.

MR. A. HERZKA: In the unavoidable absence of our Vice-President it is my pleasant duty to propose a formal vote of thanks. I feel certain that I am expressing the sentiments of all when I say what a privilege it has been to listen to such an authority on organic chemistry. Thank you once again.

Lord Todd being presented with the Society's silver medal by the President

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J. Soc. Cosmetic Chemists **17** 391-400 (1966)

IR Spectroscopy of aqueous detergent solutions

N. A. PUTTNAM and B. H. BAXTER*

Presented at the Symposium on "Physical Methods," organised by the Society of Cosmetic Chemists of Great Britain, in Bristol on 16th November 1965.

Synopsis—The literature relating to the application of IR spectroscopy to the qualitative and quantitative analysis of aqueous detergent systems has been briefly summarized. The information that can be obtained directly by IR spectroscopy, using either transmission or the Attenuated Total Reflection technique, concerning the nature of components in such systems has been described and a comparison of the two techniques made. The direct approach could only be applied to relatively concentrated systems; concentrations greater than 0.5% for transmission and greater than 4-5% for ATR. It was concluded that the ATR approach was more suitable to the analysis of raw materials, intermediates and finished detergent products and examples are quoted of the determination of sodium xylene sulphonate, in commercial solutions of this sulphonate, and sodium dodecylbenzene sulphonate in a light duty detergent product, with a relative accuracy of ± 2%.

Introduction

A considerable number of reports have been published on the application of IR spectroscopy to the qualitative and quantitative analysis of aqueous detergent systems. In most instances, these reports have described methods which involved isolation of the detergent from the aqueous media. Jenkins and Ellis (1) carried out this isolation by evaporation of a solution on to KBr and recording the spectrum as a KBr disc; by this method they were able to identify sodium dodecylbenzene sulphonate at the 10 ppm level. An alternative procedure for the identification of alkylbenzene sulphonates, and alkyl sulphates, was described by Jenkins and Kellenbach (2) in which the anionic was precipitated as the barium salt and the spectrum recorded in a KBr disc.

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For the determination of very low levels of alkylbenzene sulphonate in water, especially waste waters, the isolation and purification was carried out by adsorption on to carbon followed by desorption with alkaline benzene-methanol and extraction of the 1-methylheptyl ammonium salt of the sulphonate with chloroform. To determine the amount of sulphonate present, the chloroform was removed by evaporation and the intensities of the IR absorptions at 9.6 μ (1040 cm^{-1}) and 9.9 μ (1010 cm^{-1}) then measured in carbon tetrachloride or carbon disulphide solution (3). Ogden *et al* (4) modified this procedure for the determination of biologically "soft" and "hard" alkylbenzene sulphonates in sewage. In their procedure the total sulphonate was determined at 9.9 μ (1010 cm^{-1}) and the "hard" alkylbenzene sulphonate content determined from the intensity of the absorption at 7.31μ (1365 cm^{-1}); the "soft" sulphonate content being obtained by difference. They found that the sensitivity of the method could be increased by using the *n*heptyl ammonium salt instead of the 1-methylheptyl ammonium salt. This method was also employed by these workers to determine the "hard" and "soft" sulphonate contents of powdered detergent products. An alternative method for the determination of the relative amounts of "hard" and "soft" alkylbenzene sulphonates in sewage, based on the ratio of the intensities of the absorptions at 1367 and 1410 cm^{-1}, has been described by Frazee and Crisler (5). In this case the sulphonate was isolated as the 1-methylheptyl ammonium salt and then converted to the *n*octyl ammonium salt, prior to the IR determination, in order to avoid an additional methyl branch absorption in the analytical region. The application of IR spectroscopy to the determination of residual alkylphenol polyethoxylates in the river die-away test has also been described (6). The polyethoxylates were examined in carbon tetrachloride or carbon disulphide solution after isolation by adsorption chromatography, solvent extraction or foam stripping.

Recently two groups of workers have applied IR spectroscopy directly to aqueous detergent systems. This is now possible with the development of new cell materials, which, while still reasonably transparent to IR radiation, are unaffected by such systems. Kullbom and Smith (7) determined the sulphonate content of ca. 40% aqueous solutions of sodium or ammonium toluene and xylene sulphonates. The determination, carried out by transmission through a 0.024 mm Irtran II cell, was based on the intensity of the sulphonate absorption at 1175 cm^{-1}, which was found to be insensitive to isomeric variations. These workers extended this method to the analysis of detergent sulphonate slurries (8). The total sulphur

content of the slurry was determined by an X-ray fluorescence procedure and the alkylbenzene sulphonate content determined from the intensity of the IR absorption at 1172 cm^{-1}, the sodium sulphate content being calculated from the difference in the sulphur content. The other group of workers employed the Attenuated Total Reflectance technique, which produces spectra from bulk samples equivalent to those obtained by transmission through thin films, for the identification of the routine ingredients of light duty liquid detergents and shampoos (9). This work was extended to the quantitative determination of sulphated alcohols in shampoos and alkyl benzene sulphonates in all purpose cleaners (10).

The purpose of this communication is to show the type of information that can be obtained from aqueous detergent systems by the direct application of IR spectroscopy, without any prior isolation, using either transmission or the ATR technique and to compare the two approaches.

Experimental

The transmission and ATR spectra were recorded on *Unicam* SP100 and SP200 IR spectrometers with increased slit width and gain.

The transmission spectra were recorded in fixed path-length cells (0.025 mm) which were fitted with KRS-5 or Irtran II windows, and the reference beam was attenuated to give an absorbance reading of ca. 0.1 at a wavelength where the sample showed no absorption.

A TR-3 ATR unit, manufactured by *Research* and *Industrial Instruments Co.*, was used for the determination of the ATR spectra. A KRS-5, or Irtran II prism was employed as the analysing crystal and the spectra were recorded at an angle between 33 and 40° with the reference beam attenuated to give approximately 0.1 absorbance units at a wavelength where the sample showed no absorption. The sample was introduced with a syringe through the filler ports, into the cell formed by fitting the backing plate to the prism mount. In the case of a viscous liquid this was poured on to the back face of the prism, held in a horizontal position, and the backing plate clamped in position.

Quantitative analyses were carried out by comparison with calibration curves. These curves were prepared by recording the spectra of a series of standard samples, of known concentrations, and measuring the absorbance of the characteristic peak in each spectrum, using a tangent baseline.

Results and discussion

It was necessary to employ KRS-5 or Irtran II as cell and prism

materials for two reasons. Firstly, to avoid precipitation of insoluble salts by reaction of the detergent system with the optical material; such an effect occurred with barium fluoride, which is commonly used for IR studies of aqueous systems. Secondly, the principle of the ATR technique (11) demanded that the prism material be of high refractive index. Either material could be used for the detergent systems studied except for highly alkaline solutions where Irtran II was necessary, due to the formation of a bright yellow film on KRS-5.

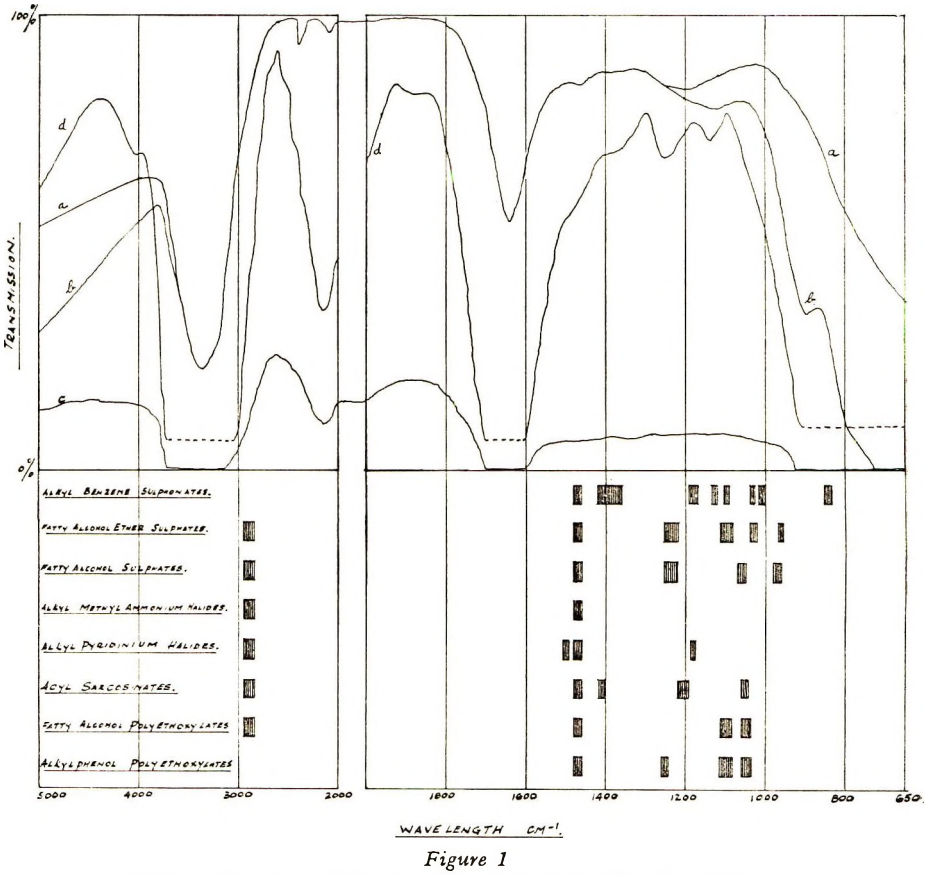

Figure 1

Spectra of water and frequencies of characteristic absorptions
(a) ATR with KRS-5 prism
(b) ATR with Irtran II prism
(c) Transmission in 0.025 mm KRS-5 cell
(d) As in (c) but with the reference beam attenuated

In *Fig. 1* are shown the ATR spectra obtained for water with a KRS-5 prism (a) and an Irtran II prism (b). Also shown is the transmission

spectrum of water in a 0.025 mm KRS-5 cell (c) together with the same spectrum after the reference beam had been attenuated; the dotted lines are regions where there was no response on the recorder pen. It can be seen immediately that virtually no information can be obtained from the transmission spectrum unless the reference beam is attenuated. An alternative procedure would be to place a variable cell, filled with water, in the reference beam and to adjust the thickness of it until the water absorptions are compensated out. Such a procedure is tedious due to the almost complete lack of signal on the detector in the regions of very strong absorption. However, in the ATR spectrum there is no wavelength at which the water absorption is complete; the complete absorption at 650 to 750 cm^{-1} in spectrum (b) is due to the decreased transmission of the prism. This difference between the transmission and ATR spectra is due to the fact that in ATR the attenuation of the reflected radiation only occurs in the first few microns of the sample and hence the resulting spectrum is equivalent to that which would be obtained by transmission through an equivalent thickness. As it is a surface effect the actual thickness of the sample is not important with the result that bulk samples can be used. This immediately eliminates the need to obtain reproducible thin films and removes the experimental difficulties of filling very short path-length cells with viscous liquids and the troublesome interference patterns associated with such cells. Goulden and Manning (12) have pointed out that the intensity of the 1640 cm^{-1} water absorption in an ATR spectrum is equivalent to that obtained by transmission through a 5 μ film. However, since the depth of penetration is dependent upon the closeness of the angle of incidence to the critical angle, which is itself dependent upon the refractive index of the sample and for an absorbing medium this varies within the absorption bands, it is probable that the actual depth of penetration varies throughout the whole spectrum, being least where the sample shows strongest absorptions and greatest at those wavelengths where the sample shows no absorption. It follows directly from the above, therefore, that the ATR spectrum of a solution will be considerably weaker than the corresponding transmission spectrum.

Also shown schematically in *Fig. 1* are the frequencies of the characteristic absorptions of components commonly encountered in aqueous detergent systems. The C-H stretching vibrations at 2850 to 2950 cm^{-1} could only be clearly detected for those components which possessed a relatively large fatty alkyl group and were not usually detected for alkylbenzene sulphonates and alkylphenol polyethoxylates. The relative intensities

of the four absorptions shown by alkylbenzene sulphonates in the wavelength range 1000 to 1145 cm^{-1} varied with the hydrocarbon fraction of the molecule and these differences could be used to distinguish between dodecylbenzene, xylene and toluene sulphonates. The weak absorption at 840 cm^{-1}, which is due to a 1:4-disubstituted aromatic system, was only shown by dodecylbenzene sulphonates. Straight and branched chain dodecylbenzene sulphonates, at the concentrations encountered in finished liquid products, showed differences in the wavelength range 1360 to 1420 cm^{-1} which could be used to distinguish between them. In the case of fatty alcohol ether sulphates, the relative intensities of the sulphate absorption at 1220 to 1250 cm^{-1} and the ether absorption at 1080 to 1110 cm^{-1} gave an indication of the number of moles of ethylene oxide in the component. Similar information could be obtained for alkylphenol polyethoxylates by comparison of the intensities of the absorptions at 1080 to 1110 cm^{-1} and 1240 to 1260 cm^{-1}. It was found for a fatty alcohol sulphate that the exact frequency of the absorption in the wavelength range 1050 to 1070 cm^{-1} depended upon whether it was present as the sodium, monoethanolamine or triethanolamine salt. A much higher concentration was needed to obtain absorptions which could be correlated with the presence of a cationic; for transmission work the concentration had to be at least 5% while for ATR it needed to be considerably greater.

From the quantitative aspect, an ATR procedure has been developed, based on the transmission method described by Kullbom and Smith (7), for the analysis of commercial sodium xylene sulphonate solutions, utilizing the sulphonate absorption at 1175 cm^{-1}. The method, the relative accuracy of which was $\pm$ 2%, was applicable to solutions containing more than 5% w/w sodium xylene sulphonate and did not require knowledge of the isomer distribution, which is necessary for any UV spectrophotometric procedure. This accuracy was of the same order as had been found earlier for the ATR determination of lauryl ether sulphate or sulphated fatty alcohols, in shampoos (10). Another example of a quantitative application is the determination of sodium dodecylbenzene sulphonate in a light duty detergent product. The analysis was based on the intensity of the sulphonate absorption in a ATR spectrum, using a tangent base-line drawn between 990 and 1310 cm^{-1}. The standard deviation of the method was found to be $\pm$ 0.4% at the 25% level of active ingredient.

Conclusion

It must be emphasized that the direct application of IR spectroscopy,

either transmission or ATR, to aqueous detergent systems can only be made for relatively concentrated systems. In general terms, for concentrations less than 0.5% some form of concentration and/or isolation must be carried out prior to any IR spectroscopic studies. Further, the ATR technique, which eliminates the practical difficulties associated with the determination of transmission spectra of aqueous solutions, required concentrations of at least 4-5% and is more suitable to the qualitative and quantitative examination of raw materials, intermediates and finished detergent products.

(Received: 1st September 1965)

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Introduction by Dr. Puttnam

First of all I would draw your attention to our conclusion, namely that if the concentration of the component is less than 0.5% it is necessary to carry out an initial concentration or isolation. Above this concentration, ir spectroscopy can be applied directly to aqueous detergent systems. For concentrations in the range 0.5-4.0%, the sample must be examined by transmission. For concentrations above 4%, which is usually the case in raw materials, intermediates and finished products, the sample can be examined by ATR, which eliminates difficulties associated with the transmission technique.

Secondly, since most are probably familiar with ir spectroscopy but not with the ATR technique, I would like to describe the procedure for recording such spectra and show you its simplicity. *Fig. 2* is an optical drawing of the TR-3 ATR unit. The three mirrors are necessary to divert the beam, normally travelling through the sample compartment of the spectrometer, so that it makes an angle at the prism/sample interface. The first step is to fit the backing plate to the prism mount (*Fig. 3*), so forming a cell approximately 2 mm thick on the back face of the prism. The sample is then introduced into this cell through the filler port (*Fig. 4*) with the aid of a syringe. In the case of viscous liquids these are poured, as shown in *Fig. 5*, on to

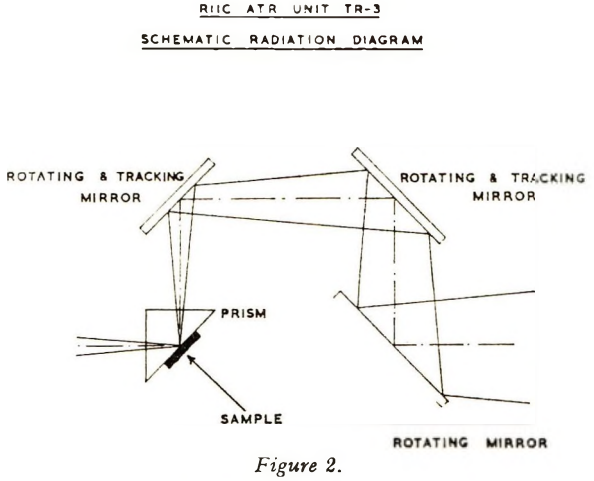

Figure 2.

the back face of the prism, held in a horizontal plane, and the backing plate is then clamped in position.

The prism mount is then placed in the ATR unit as shown in *Fig. 6*, and the angle of incidence set (*Fig. 7*). After the ATR unit has been placed (*Fig. 8*) in the sample beam of the spectrometer, the reference beam must be attenuated (*Fig. 9*), since the transmission of the ATR unit is only approximately 60%. The manual gain of the instrument is checked and the spectrum then recorded.

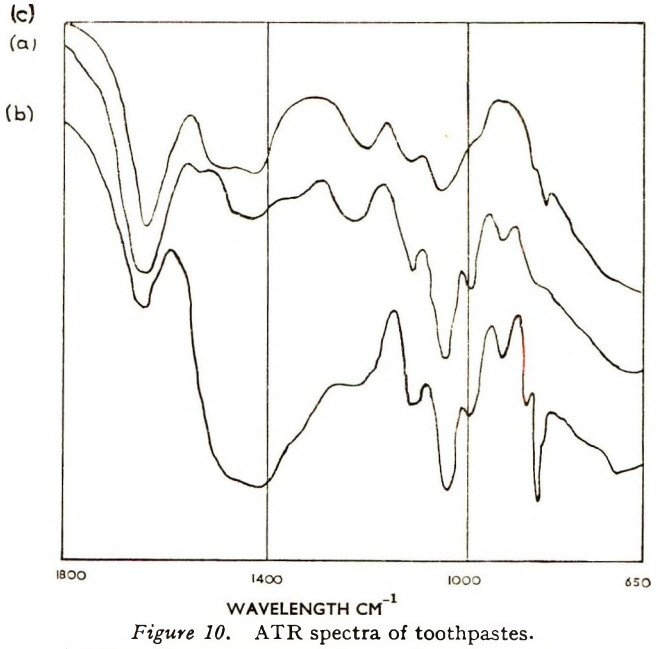

Figure 10. ATR spectra of toothpastes.
(a) Glycerine humectant and phosphate abrasive.
(b) Glycerine humectant and carbonate abrasive.
(c) Sorbitol humectant and phosphate abrasive.

Figure 3

Figure 4

Figure 5

Figure 6

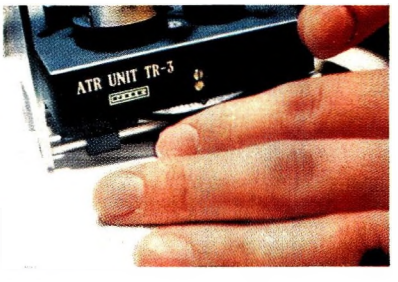

Figure 7

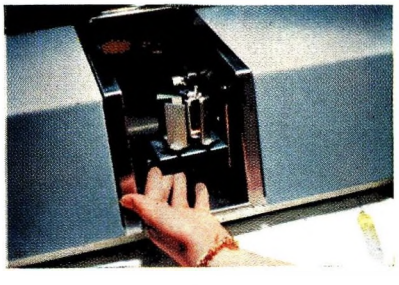

Figure 8

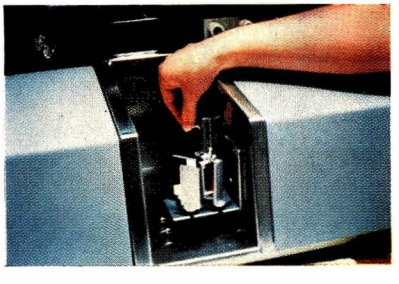

Figure 9

Fig. 10, of various dental creams, indicates that it is possible to distinguish between a cream which contains a carbonate as the abrasive and one containing a phosphate. Examination of the absorptions close to 1000 cm^{-1} indicates whether the humectant is glycerine or sorbitol.

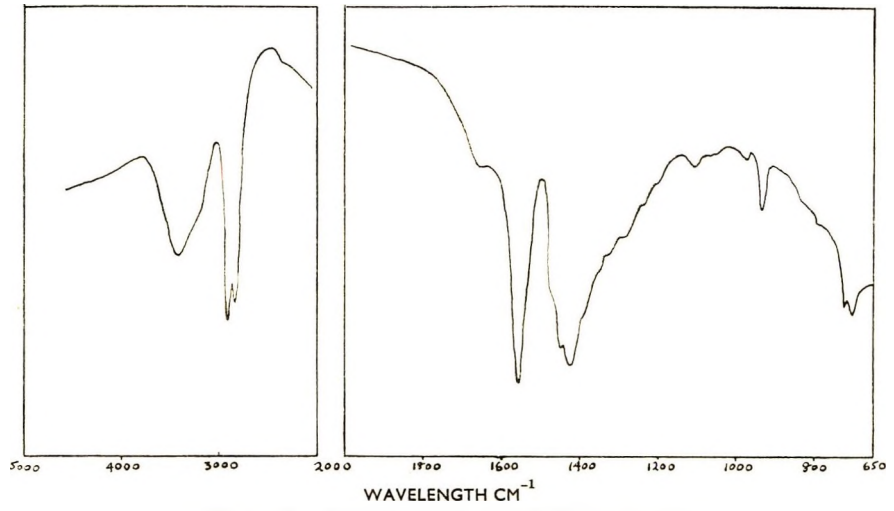

Figure 11. ATR spectrum of grated soap sample.

Fig. 11 shows the ATR spectrum of a grated soap sample pressed on to the back face of the prism. Since there are no absorptions due to glycerine, we can assume that the hydroxyl absorption at ca. 3400 cm^{-1} is due solely to moisture. Since it is not possible to obtain reproducible contact between the sample and the prism in the determination of moisture in soap, it is necessary to measure the ratio of intensity of this absorption compared to that at 2800 cm^{-1}, which is due to the soap hydrocarbon chain.

From the quantitative aspect, the accuracy of the method depends first of all on the spectrophotometric accuracy of the spectrometer. Other factors which will influence the accuracy of the analysis are the area of the prism in contact with the sample; for liquids this is obtained by ensuring that the cell is completely filled, and the reproducibility of the setting angle. We have found that the reproducibility of an absorbance peak of 0.3 units is $\pm$ 0.004, i.e. the reproducibility is the same as that obtained by transmission.

In the analysis of liquid products it should also be borne in mind that the calibration curve is prepared by dissolving known weights of the component being determined, e.g. the active material, in known weights of water. In the sample this is usually not strictly true, since a given weight of sample will contain other dissolved components, so that the water content of the sample is not 100 minus the weight of active material being determined, and hence a correction factor must be employed.

DISCUSSION

DR. A. R. ROGERS: Would I be correct in concluding that experimentally the ATR technique is no more difficult for handling liquid samples than conventional ir methods, and that it is easy to learn?

DR. PUTTNAM: Basically the ATR technique is much simpler. For aqueous solutions the ATR spectrum is equivalent to that which would be obtained by transmission through a cell thickness of about 5 μ. *Figs. 1a* and *1b* show that there are no wavelengths at which absorption is complete. The ATR technique eliminates the need to attempt to introduce, for example, a light duty detergent or a shampoo into a cell of 25 μ thickness. ATR also eliminates the troublesome interference patterns which arise from thin cells, and the difficulties of filling these cells with very viscous liquids. For such liquids the method of filling is that shown in *Fig. 5*.

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Analysis of aerosol propellants

R. J. BROOK and B. D. JOYNER*

Presented at the Symposium on "Physical Methods," organised by the Society of Cosmetic Chemists of Great Britain, in Bristol on 17th November 1965.

Synopsis—Methods are described for the analysis of aerosol propellants of the chlorofluorocarbon type, including the analysis of aerosol packs. The methods include those used for the estimation of boiling range and of inert gases, and of deleterious impurities such as water and chloride ion, and the analysis of mixed propellants by gas chromatographic methods.

Introduction

The aerosol industry has continued to expand rapidly during the last decade. Excluding food products marketed in aerosol form, production has risen from 6 million in 1955 to 110 million in 1964. By common usage, the term "aerosol" in this context has deviated from its strictly scientific meaning, and in the packaging field is applied to any product—solid, liquid or foam—which is expelled from its container by a liquefied or compressed gas.

A wide range of propellants is used, including inert gases such as nitrogen, hydrocarbons such as butane and propane and a number of chlorofluorocarbons. This paper is concerned with the analysis of the latter compounds, both alone and when part of an aerosol formulation.

The chlorofluorocarbons are distinguished by a numbering system, used throughout the world, which is related to their chemical formulae (*Table I*). They are marketed in this country as *Isceon* and *Arcton*

*Imperial Smelting Corporation Ltd., Avonmouth, Bristol.

Table I
Properties of propellants

Propellant no.	Chemical formula	B.Pt. (°C)	Vapour pressure (Atm. at 21°C)
11	$CFCl_3$	23.8	0.91
12	CF_2Cl_2	–29.8	5.78
13	CF_3Cl	–81.4	32.2
21	$CHFCl_2$	8.9	1.57
22	CHF_2Cl	–40.8	9.34
114	$CF_2Cl.CF_2Cl$	3.6	1.88

and are the compounds which come nearest to possessing the ideal chemical and physical properties required of an aerosol propellant, which are:

(i) Suitable vapour pressure,
(ii) nonflammable, non-toxic and odourless,
(iii) high chemical stability over long periods of time in the presence of both the formulation and the materials of construction of the container and valve, and
(iv) satisfactory solubility characteristics.

The most commonly used chlorofluorocarbon propellants are 12 (CCl_2F_2), mixtures of 11 (CCl_3F) and 12, and 114 ($CClF_2.CClF_2$), either alone or mixed with 12.

Propellants 11 and 12 are produced by reacting hydrogen fluoride with carbon tetrachloride in the presence of a catalyst in either a liquid or vapour phase process and propellant 114 in a similar way but using hexachlorethane instead of carbon tetrachloride. Hydrogen chloride is a by-product of the reaction and in addition chlorofluorocarbons are obtained containing more or less fluorine than the specified propellants.

Table II
Propellant specifications

	Propellant 11	Propellant 12	Propellant 114
Maximum water content (p.p.m. by wt.)	10	10	10
Maximum boiling range (°C, 5%–85%)	0.25	0.25	0.25
Maximum high boiling residue (vol. %)	0.01	0.01	0.01
Maximum non-absorbable gas content (vol. %)	–	2.0	1.5
Chlorides (ppm by wt.)	0.5	0.5	0.5

Thus the likely impurities in the chlorofluorocarbon propellants are hydrogen chloride and hydrogen fluoride, inert gases such as air and other chlorofluorocarbons of higher or lower boiling point. The specifications detailed in *Table II* are designed to ensure the virtual absence of these impurities. It can be justly claimed, because of the very rigid specifications for these compounds, that they are among the purest organic chemicals produced on a tonnage scale.

Analysis of propellants

The methods used for the analysis of propellants vary from simple tests in inexpensive equipment to gas chromatographic analysis requiring sophisticated apparatus and a considerable amount of experience. The following section describes the methods employed.

Water content

Many aerosol formulations are liable to deteriorate in the presence of any appreciable quantity of water. The amount of water in chlorofluorocarbon propellants, however, is far too low to cause any trouble of this description. The water content is often determined with an electrolytic water analyser. This instrument employs a phosphoric acid film to absorb water from vaporized propellant and the water absorbed is simultaneously electrolysed from the film. The current consumed is a direct measure of the water content. This electrolytic method is used wherever possible for routine analysis since it is rapid and convenient. However, it is not applicable to all chlorofluorocarbons, and then the Karl Fischer method is used. This method is also used to standardize the electrolytic analyser.

Boiling range

This is determined in a "Goetz" flask, in which a 100 ml sample is evaporated to 15 ml and the temperature range recorded. Compliance with this test ensures that the high-boiling and low-boiling chlorofluorocarbon impurities do not amount to more than about 0.1% by weight. Any high-boiling residue is then determined by raising the remaining 15 ml to a temperature 30°C above the boiling point of the sample.

Non-absorbable gas content

Gases such as air or nitrogen would, if present in substantial quantities, lead to excessive and unreliable pressures in aerosol packs. To determine these a test is carried out on the vapour phase of a cylinder by bubbling the vapour through tetrachloroethylene and measuring the volume of gas

not absorbed. The vapour phase, as would be expected, contains a much higher proportion of such gases then the liquid phase, so that this is a very sensitive test.

Chloride

The original method required that chloride should not be detected on the addition of a solution of silver nitrate in methanol to a solution of the propellant in methanol. However, the lowest level of chloride detectable by this method is only about 5 ppm and an alternative method was devised, in which a vaporized sample is bubbled through water which had been first acidified, then neutralized with $\frac{N}{100}$ sodium hydroxide to a pH of 4.5. The chloride content is calculated from the quantity of alkali required to return the pH to 4.5 after passage of the sample. The level of detection is 0.1 ppm and normally the chloride content of chlorofluorocarbon propellants is below this level, although an on-grade specification of 0.5 ppm is applied.

ANALYSIS OF PROPELLANTS IN AEROSOL PACKS

A more rapid and convenient method than those previously described (1–3) has been established. An accuracy of about $\pm 1\%$ has been achieved which is considered adequate, since it is greater than the accuracy of filling the aerosol packs.

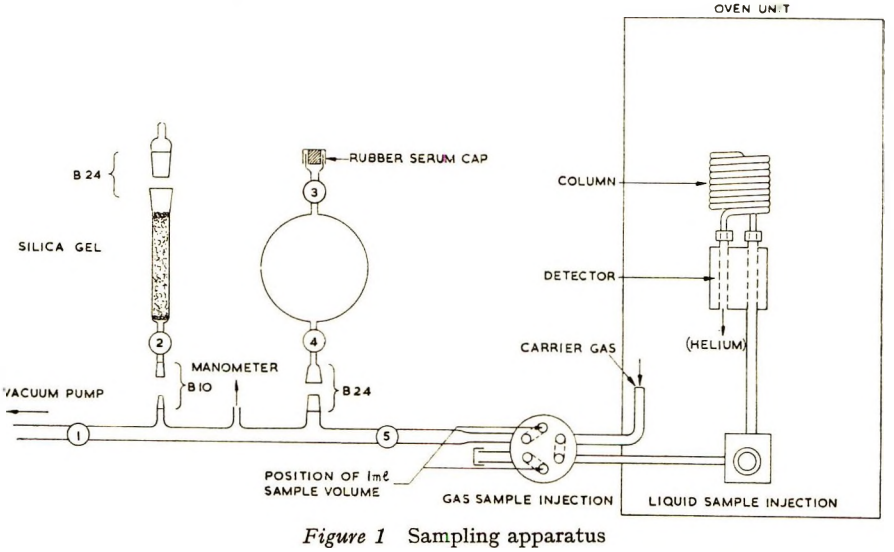

Figure 1 Sampling apparatus

The analysis is carried out by gas chromatography, using a *Perkin-Elmer* 451 Vapor Fractometer fitted with a gas sampling valve. A thermal

conductivity detector is employed, and the higher sensitivity of thermistors at low temperatures makes them preferable to the hot wire type. The gas sampling valve is fitted with a 1 ml sample volume and connected to a glass manifold (*Fig. 1*).

The basis of the method is the injection of a sample directly from an aerosol container into an evacuated glass flask by means of a suitable adaptor, a hypodermic needle and a rubber serum cap. The low-boiling components of the sample vaporize almost instantaneously. The adaptors required for two of the common aerosol can valves are illustrated in *Fig. 2*. The needle is a No. 1 "Hypo," 2" long, to pass through the tap into the flask.

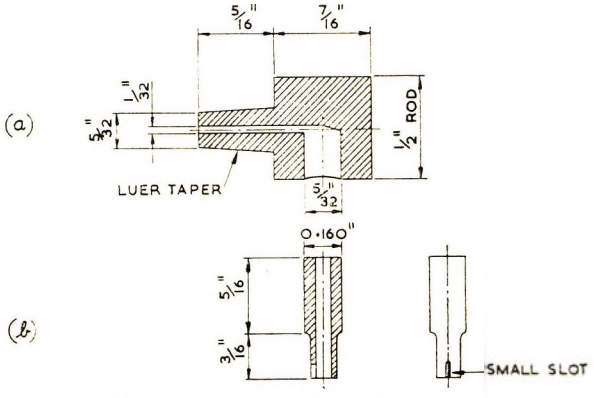

Figure 2 (a) Adaptor for Precision valves
(b) Additional adaptor for Newman-Green valves

There are a variety of methods available for calibration, the choice of method often being governed by the type of sample, and, in some cases, by the type of sample valve fitted to the gas chromatographic apparatus. For our present purpose calibrations were obtained from binary mixtures of propellants 11/12 and 12/114 of known composition prepared in cans from cans of the pure components. Adaptors to connect the cans can be made from either two Newman-Green type control buttons, or from a piece of ptfe rod drilled with a $\frac{5}{32}$" hole, depending on which type of aerosol valve is being used. An empty or evacuated can is weighed and a suitable weight of the propellant with the lower vapour pressure introduced. The second propellant is then injected until a mixture of the required composition is obtained.

The calibration procedure from this stage is as follows (*Fig. 1*):

1. Evacuate the flask and manifold with taps 1, 3 and 4 open and taps 2 and 5 closed.
2. Shake the aerosol pack if the formulation requires it. Connect the adaptor and needle in place of the control button and discharge sufficient of the contents to ensure that the dip tube contains a representative sample.
3. Push the needle through the serum cap and into the flask. Pump away any residual volatile material.
4. Close tap 1 and inject the aerosol slowly until a pressure slightly in excess of 10 cm is obtained in the system (see note).
5. Close tap 4, open taps 1 and 5 and pump out the manifold and sample volume.
6. Close tap 1 and open tap 4 slowly to give a pressure of 10 $\pm$ 0.1 cm in the system. Close tap 4.
7. Turn the sample valve to inject the sample into the gas stream passing to the column. After 5 sec return the sample valve to its former position to allow maximum pumping time for the manifold and sample volume.

Note: By using a 1 l flask a reasonable sized sample may be taken with a final pressure in the flask low enough to ensure that a negligible quantity of propellant remains dissolved in any non-volatile component of the aerosol formulation.

Table III gives the conditions employed for the gas chromatographic analysis and the retention times of the components sought. The recorder

Table III

Conditions for gas chromatographic analysis

Column: 15 ft., $\frac{3}{16}$" i.d., 25% silicone oil on 70–80 mesh *Celite*.
Temperature: 40°C.
Inlet Pressure: 10 p.s.i.
Helium Flow Rate: 43 ml/min.

Component	Formula	Retention time
Air		2′ 22″
P–13	CF_3Cl	2′ 40″
P–22	CHF_2Cl	3′ 30″
P–12	CF_2Cl_2	3′ 46″
P–114	$CF_2Cl.CF_2Cl$	4′ 46″
P–21	$CHFCl_2$	8′ 00″
P–11	$CFCl_3$	10′ 42″

is run at a fairly high chart speed (24″/hr), and when the required settings for the peak attenuator have been determined, this control is preset for each individual peak. The peak width at half peak height is then measured with a travelling microscope and the values obtained plotted against the true peak height (*Fig. 3*), i.e. observed peak height multiplied by the attenuation factor for each component. This is repeated with mixtures

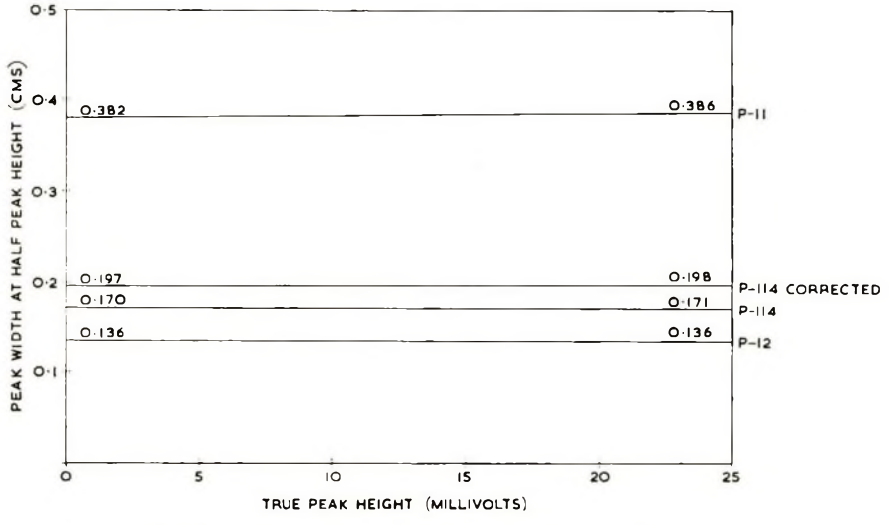

Figure 3 Calibration graphs for propellants 11, 12 and 114

over a wide range of composition of the propellants concerned. With a high sensitivity detector, which permits the use of small samples, the lines obtained will be almost horizontal and with the thermistor detector the variation found was so small that a constant figure for the peak width may be taken for the range of peak heights obtained. The areas of the component peaks may then be obtained directly from the peak heights. The weight percentage of each component is given approximately by the area of the peak for that component expressed as a percentage of the total area of all the peaks. Using helium as the carrier gas this method gives accurate results for mixtures of propellants 11 and 12 but not for mixtures containing propellant 114, due to differences in thermal conductivity. A correction factor for this effect may be calculated from the results obtained on the standards, and the calibration re-plotted, for propellant 114. It is normally found that this line is parallel to the original line as shown in *Fig. 3*.

Calibration lines having been obtained by this method for the three most common propellants, some further binary mixtures of propellants were made up and typical aerosol packs were prepared and analysed by the above method. The results obtained are given in *Tables IV* and *V* and typical values for reproducibility, both for the same and for repeated injections, are given in *Table VI*.

Table IV
The results of the analysis of synthetic binary mixtures

Propellants	% Propellant 12			Number of analyses
	Actual	Found (mean)	Range	
11/12	29.9	29.6	29.5–29.8	3
11/12	50.9	51.5	50.9–51.9	4
11/12	70.1	70.3	69.7–70.8	5
12/114	10.0	9.8	9.7– 9.9	9
12/114	29.9	29.7	29.5–29.9	3
12/114	50.2	51.0	50.9–51.3	3
12/114	70.1	70.6	70.3–71.1	6
12/114	90.1	90.1	89.9–90.3	9

Note: % Propellant 11 or 114 = 100% propellant 12

Table V
The results of the analysis of synthetic aerosol packs

Type of Pack	Propellant mixture	Propellant content of pack approx. %	% Propellant 12 in propellant mixture			Number of analyses
			Actual	Found	Range	
Hair lacquer	11/12	60	50.9	50.4	50.2–51.6	4
Air freshener	11/12	85	50.2	50.6	50.4–50.8	2
Insecticide	11/12	75	52.7	52.7	50.7–54.1	11
Perfume A	12/114	50	49.9	51.0	50.4–51.6	3
Perfume B	12/114	50	70.7	71.9	71.4–72.3	6
Perfume C	12/114	50	30.3	29.9	29.8–29.9	3

Note: % Propellant 11 or 114 = 100% propellant 12

Table VI
Reproducibility of samples

	% Propellant 12		
	Found	Mean	Actual
Replicates from flask	70.0, 70.6, 70.6, 70.3, 70.2, 69.5	70.2	70.0
Replicate injections (Mean of three analyses)	50.6, 50.3, 49.6, 49.9, 50.0, 49.9	50.1	51.0

Two points must be stressed. Firstly, all glassware must be thoroughly cleaned as any high boiling materials which do not pump away rapidly may interfere with succeeding analyses. Kerosene from insecticides and *iso*propyl alcohol from some air fresheners are examples of this problem. In the former case it was found necessary to take smaller samples (5 cc or less) to obtain good results in series analysis.

Secondly, a stopcock grease must be used which does not absorb propellants. The most satisfactory one found (4) uses the formulation, dextrin, mannite and glycerol in a weight ratio of 7:3.5:18. These ingredients are gently heated together until a clear solution is obtained, then brought just to the boil and allowed to cool. This grease tends to absorb water and alcohols, therefore it must be stored in an air-tight container or a desiccator, and taps must be regreased frequently. Hot water easily removes it from glassware.

Ratio of propellant to fill in aerosol packs

The approximate ratio (to within a few per cent) of propellant to fill is often required. The work described has been limited to hair sprays but could be extended to certain other formulations. The principle of the method is to pass the aerosol can contents through an aqueous calcium chloride solution in which all but the propellant is retained. Water alone was used initially but erratic results were obtained (*Table VII*). Suitable

Table VII
Comparison of water and calcium chloride solution as separation media

Replicate analyses % propellant found		
	Separation Medium	
	Water	Calcium chloride solution
Mixture (a)	46.5	49.8
	48.4	50.9
	51.9	49.0
	48.4	48.4
	47.7	49.5
Mixture (b)	46.5	48.6
	48.3	50.3
	51.9	50.0
	42.7	49.5
	40.9	49.0

(a) 50% w/w methylated spirit
25% w/w propellant 11
25% w/w propellant 12

(b) 47.5% w/w methylated spirit
25% w/w propellant 11
25% w/w propellant 12
2.5% w/w shellac

weighings of the can and solution container enable calculation of the propellant content to be made. The procedure has not been finalized but results accurate to $\pm 1\%$ have been obtained.

The spray head of an aerosol can is modified by cutting a small notch from the outlet orifice to the top and then inserted into a 3″ length of PVC tubing. The other end of this tubing is connected to the inlet end of a Drechsel bottle of 300 ml capacity. The inlet tube of the Drechsel bottle is vertical, i.e. no right angle bend, and the end of the dip tube is drawn out to a jet. The head of the Drechsel bottle is secured with a spring.

Procedure

1. Place 150 ml of a 10% $^{w}/_{w}$ calcium chloride solution in the Drechsel bottle.
2. Pass about 3 g of propellant 12 through the bottle to purge the air from the headspace. Weigh immediately.
3. Weigh the aerosol pack to be analysed and connect to the Drechsel bottle making sure the aerosol valve is not actuated, keeping the can upright.
4. Depress the can valve carefully, allowing sample to pass into the bottle with a minimum of spray.
5. Allow 10–15 g of sample to pass, measuring the volume of gas leaving the system as an indication of the weight taken.
6. Invert the aerosol pack and allow the liquid remaining in the PVC tube to drain into the Drechsel bottle.
7. Detach the can leaving the spray head within the PVC tubing then insert a plug of known weight in the inlet orifice of the spray head. Weigh the can.
8. Warm the Drechsel bottle in a water bath at 30°C for 30 min to remove higher boiling propellants. Cool to room temperature.
9. Pass about 3 g propellant 12 through Drechsel bottle. Reweigh immediately. Calculate propellant ratio from the weight changes recorded.

Blank determination

As a check on possible loss during either the heating stage or during the passage of propellant 12 in stage 9, the following test was carried

out. 6 g of the product of a PVP-based hair lacquer were placed with 150 ml of the calcium chloride solution in the Drechsel bottle and passed through stages 2, 8 and 9. The weight losses in five experiments ranged from 0.01 to 0.03 g which is negligible compared with the normal gain in weight of 5–10 g.

Results obtained

Table VII gives the results obtained with two mixtures of methylated spirits with propellants 11 and 12, one of which contained shellac. Early results obtained with water as the separation medium are included, demonstrating the better reproducibility obtained with the calcium chloride solution.

When an attempt was made to analyse a commercial hair lacquer using water as separation medium, it was noted that addition of calcium chloride to the resultant solution caused effervescence, indicating that some propellant had been retained.

Table VIII
Analysis of hair lacquers

		% Propellant found	
Control	61.8% propellant	61.9 61.2 61.3 62.4 62.8	
Unknown	Can 1	61.0	59.8
	2	59.6	58.3
	3	61.6	61.8
	4	58.7	60.2
	5	61.6	60.6
	6	63.0	63.1

The procedure was checked with a commercial hair lacquer formulation known to contain 61.8% of propellant and used to analyse six packs of a product of unknown composition. The results obtained are in *Table VIII*. Work on this method is continuing.

(*Received: 13th September 1965*)

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(2) Thonet, T. A. *Aerosol Age* **4** 20 (August 1959).
(3) Percival, W. C. *Anal. Chem.* **29** 20 (January 1957).
(4) Federal Specification BB-F-671a (July 1952).

Introduction by Mr. Brook

With regard to the G.L.C. apparatus I ought to mention that the needle should go right through the tap into the flask. A length of 2″ is convenient for our flask, but it is difficult to get the glass blown in a 2″ length. We now use 6″ needles.

At the time of preparing this paper we were using a May and Baker silicone oil, 15′ analytical column, of ordinary ¼″ O.D. soft annealed copper tubing. At that time we were analysing the hydrocarbon propellants separately on this column, but had not mixed them with chlorofluorocarbons. Unfortunately we found that *iso*butane only separated by 5 sec from propellant 114, so we had to find some other columns quickly. The one we use now is apiezon grease on chromosorb; it was obtained from Perkin Elmer Ltd [DE 101]. This will separate them fairly satisfactorily.

Some manufacturers use vapour phase tap valves. This improves atomization of the spray, and is rather common for deodorants and similar preparations; it also reduces body cooling on contact. This will introduce errors in both the G.L.C. and the propellant-to-fill ratio techniques.

DISCUSSION

MR. A. HERZKA: In your determination of boiling ranges have you ever come across azeotropes of alcohols in propellants, and if so, which alcohols and which propellants?

MR. R. J. BROOK: The determination of boiling range as described in this paper is used as a means of establishing the purity of propellants during production. Consequently, the question of the presence of alcohol has not arisen.

MR. A. HERZKA: What sort of errors occur in gas chromatography and what is their magnitude?

MR. R. J. BROOK: The errors referred to arise from the presence of high-boiling constituents in aerosol formulations. Because of their low volatility, these compounds tend to accumulate in the glassware, causing absorption of propellants. For example, when analysing insecticides, we find that traces of kerosene remain and cause an increasing error with each successive sample. We have found it advisable to reduce the sample vapour pressure to 5 cm of mercury and recommend cleaning out the glassware after three or four analyses.

MR. A. HERZKA: What sort of errors do you get with the vapour phase tap?

MR. R. J. BROOK: We have very little experience of vapour phase tap valves as yet, but the few samples handled have shown us that these valves give rise to additional errors, arising from the fact that this type of valve discharges material from both the liquid and vapour phases simultaneously.

The presence of such a valve can be ascertained by inverting the can and operating the valve. If any liquid continues to be expelled after a few seconds, then the presence of a vapour phase tap valve can be assumed. In this case it should be possible to take a representative sample from an inverted can, as the dip tube will contain liquid and the vapour phase tap hole will be submerged. A small sample will not deplete the dip tube, and if a larger sample is required, this can be obtained by taking a series of small samples. The dip tube will be replenished each time via the vapour phase tap because of the hydrostatic head outside the dip tube.

This procedure would probably not be satisfactory with a capillary dip tube. In such doubtful cases it would be best to sample the liquid directly by using one of the proprietary can-piercing devices.

MR. A. HERZKA: For your information, such a container–piercing device is supplied by Builders Sheet Metal Works, Wooster Street, New York.

MR. B. H. BAXTER: I would like to comment on the vapour phase tap problem. In our experience with ir techniques these variations can be considerable and it is our practice to calibrate with known mixtures in cans fitted with various valve types. Furthermore, possible variations in the valve orifice diameter can alter the ratios of propellants when injected into the sampling apparatus.

MR. R. J. BROOK: The samples having this type of valve, which we have handled, have required only a qualitative assessment of propellants. It seems possible that the inverted can method just described could give quantitative results and eliminate the need for further calibration.

MR. B. H. BAXTER: From *Fig. 1* it would appear that the rubber serum cap was at the top of the input tube. This arrangement would necessitate the use of the aerosol can in the inverted position. Could you please amplify this point.

MR. R. J. BROOK: If a simple dip tube is present the can is vertical. You must take off liquid phase and we use a bent needle.

MR. A. HERZKA: Mr. Baxter mentioned that the vapour phase tap varies from manufacturer to manufacturer. One can obtain various proprietary valves each with at least three different sizes of vapour phase tap, which presumably is not known in advance. I therefore presume that in order to carry out your analysis you would require two samples–one to get the valve out, so that you would know which calibration chart to use.

MR. B. H. BAXTER: You mentioned the difficulty of resolving butane from halocarbons by GLC. Without introducing arguments on the respective merits of the two techniques, ir spectroscopy has been found ideal for the analysis of tertiary mixtures of propellants containing butane.

MR. R. J. BROOK: One or our customers uses a 12′ dibutyl maleate column which gives satisfactory separation of hydrocarbons from halocarbons at room temperature.

MR. J. D. CHESHIRE: Has the technique for ratio of propellant-to-fill been modified for samples containing methylene chloride?

MR. R. J. BROOK: We have not tried it, but we would think that methylene chloride would be determined by the GLC technique using the bulb as before, and a somewhat shorter column. It would be necessary first of all to ascertain which propellants were present. We get quite a satisfactory trace for propellants and methylene chloride using a Ucon oil LB–550 X, a polypropylene glycol column. This would again depend upon methylene chloride not absorbing into any high boiling materials in the flask.

MR. A. HERZKA: Could you give us details of the exact procedure for determing the nonabsorbed gas content, i.e. nitrogen added as a booster. Such a method would be of interest either in routine analysis, or in the spot analysis of an unknown product.

MR. R. J. BROOK: We have not tried this with products. The procedure consists of taking a known volume of the propellant in a gas burette and bubbling it through

tetrachlorethylene which absorbed the propellants. The inert gases are collected in another gas burette which is adjusted to atmospheric pressure, and measured. I doubt whether this could be used without drastic modification for the purpose you mention.

We could probably develop a method, with modifications to the existing inerts apparatus. By gas chromatography, using helium as carrier gas it should be possible to determine the nitrogen content in the gas phase if it is present in small amounts.

DR. N. A. PUTTNAM: It must be mentioned that in the GLC analysis for halocarbons it has been found that the much more sensitive flame ionization detector now being fitted to instruments is not as suitable as a thermal conductivity detector.

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The relation between structure and properties in plastics used in packaging

A. SHARPLES*

Presented at the Symposium on "Physical Methods," organised by the Society of Cosmetic Chemists of Great Britain, in Bristol on 17th November 1965.

Synopsis—The recent developments which have taken place in our understanding of the crystalline structure of polymers are considered in relation to the effects which they are likely to have on dependent physical properties. The properties considered are those likely to be of greatest relevance to film and blow-moulded products used in the packaging industry; namely, thermal stability, optical properties, permeability, and mechanical behaviour.

Introduction

Ideas on the solid state structure of polymers, which had remained almost unchanged for the previous 20 years, underwent a revolution about seven or eight years ago, stemming from the discovery of polymer single crystals (1). The consequences of these new concepts are now beginning to be better understood, and it is the purpose of this article to review the present state of knowledge of polymer structure, with reference to the effect it is likely to have on product properties; in particular, on those properties which are of importance in the packaging industry.

Flexibility and the rubber-like state

Polymeric materials can be conveniently classified as follows:

(a) Structures with ordered covalent bonding in two or three dimensions, e.g. graphite and diamond.

(b) Structures with disordered, but extensive, covalent bonding in three dimensions, e.g. phenol-formaldehyde and urea-formaldehyde resins.

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(c) Linear polymers, e.g. polyethylene, polyvinyl chloride, polystyrene, with covalent bonding in one dimension.

In the first two classes, because the covalent bonding extends in more than one dimension, the structures cannot be made more fluid, either by melting or by dissolving and, as a consequence, predetermined shapes can only be obtained during the actual chemical synthesis of these materials, by a thermosetting process. With linear polymers, however, the forces between the molecules in two dimensions are only secondary in nature, and so can be broken down, reversibly, by heat or by solvents, to enable thermoplastic processes, such as film extrusion or blow-moulding, to be carried out. In addition to being thermoplastic, polymers of this type possess a property which is unique in the field of materials and which stems from the linear configuration of the polymer molecules. This property, which can be summed up loosely by the word "flexibility," involves the ability to undergo extension without rupture to the extent of at least 5%, and in some cases to as much as 500%; and subsequently to recover, so that the original dimensions are almost completely regained. It is this property which distinguishes polymers such as polyethylene and nylon from other classes of materials, such as metals, molecular crystals, and ionic crystals. It arises because individual chain molecules, or segments of them, can take up a variety of configurations, which in the unstressed state can be typified by the structure shown in *Fig. 1(a)*. The application of a stress causes the chain to *tend* towards the configuration shown in *Fig. 1(b)*. As this can occur simply by rotation about the intermonomeric linkages, without any deformation of bond singles or distances, the free-energy

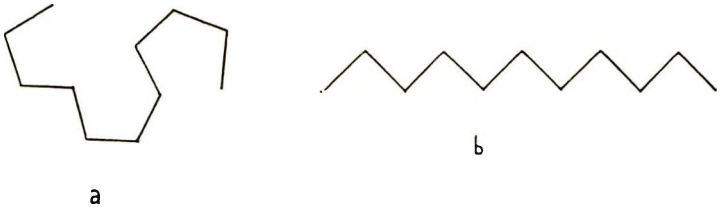

Figure 1
(a) Unstretched and (b) stretched states of flexible polymer chain.

change involves only an entropy component; in an ideal system, the heat or enthalpy component is zero. This is similar to the situation where an ideal gas is subjected to a stress which compresses it to a smaller volume,

and, in both cases, the removal of the stress enables the original, and *more probable*, state to be regained.

In order to observe this long-range elasticity in a polymeric system, it is necessary to choose a polymer where the forces between the chains are small, so that the enthalpy of deformation is correspondingly negligible, and then to link the molecules together with *occasional* cross-links, in order to enable the deformation to be maintained for a reasonable time. This is the case of a lightly cross-linked natural rubber at room temperature, where reversible extensions of several hundred per cent can be observed. In polyethylene the interchain forces are too strong to enable such large elastic effects to be observed at room temperature, but if a cross-linked sample is raised to more than 150°C elastic properties similar to those in rubber can be observed.

The property of long-range elasticity is a highly desirable one, and constitutes one of the main reasons for the extensive use of plastics, particularly in packaging applications. In the examples described so far, however, it is necessarily associated with the disadvantageous characteristic of low modulus. Compared with a typical film-forming plastic such as polyethylene, a lightly-cross-linked natural rubber has a modulus at room temperature which is three orders too low, and consequently the material is far too easily deformed.

The effect of crystallization

The process of crystallization increases the modulus of an initially rubbery material by reinforcing the structure with what are essentially cross-links, composed of crystalline regions. A similar increase in modulus could be obtained by increasing the extent of *chemical* cross-linking, but in this case an irreversible chemically-formed structure is involved, which is no longer thermoplastic, as is a semi-crystalline polymer. Crystallization in a polymer can be obtained by the appropriate choice of polymer molecule – polyesters, for example, which involve strong interchain forces, yield highly crystalline products, with only a small residue of rubber-like amorphous material; or a material which is rubber-like at room temperature – for example, natural rubber itself – can be cooled, until the increase in secondary-bonding between the chains becomes sufficient to induce the formation of stable crystalline regions. Raw rubber at 0°C increases in crystallinity to such an extent that its modulus is raised by more than 100x (2).

The increase in modulus caused by the presence of crystalline regions in a polymer, is unfortunately accompanied by a corresponding decrease in

the extent to which long-range elasticity can occur. The figure of several hundred per cent typical of natural rubber is reduced to not much more than 5% in semi-crystalline products, but nevertheless this is sufficient to result in behaviour which is acceptable for most practical purposes; it is also very much greater than the figure of 0.1% for the yield point extension of typical low molecular weight materials.

The glassy state

The tough, but flexible behaviour of polymers which is so necessary for the production of film and moulded articles, is thus a consequence of the co-existence of rigid crystalline regions, and rubbery amorphous ones, linked together to form a coherent network. Before passing to a consideration of the nature of this structure, however, it is worthwhile pointing out that the rubber-like state is not the only one possible for a wholly amorphous polymer. Some products, usually vinyl polymers whose sequences of monomer units are not ordered – the so-called atactic polymers formed by free-radical polymerization – are incapable of being crystallized no matter how much the temperature is lowered. Such materials eventually pass over into a glassy state, usually at a fairly well-defined temperature – the glass or second-order transition point – where the mobility of the chains has been lost due to the "freezing-in" of interchain forces. The relatively sudden increase in these forces with decreasing temperature is similar to the process occurring on crystallization. One big difference, however, is that no rearrangement of the molecules is involved during vitrification, so that the volume change characteristic of a first order (crystallization) transition, is absent. A typical sequence of events on heating and cooling is shown in *Fig. 2* for an amorphous, and a semi-crystalline polymer.

Typical of the polymers which cannot crystallize are atactic polymethylmethacrylate and polystyrene; polyvinyl chloride, also, has a negligible crystalline component. The glass point for all these materials is in the region of 80°C, so that at room temperature they are all in the glassy state. As a result, rubber-like behaviour is almost completely absent, and the modulus is even higher than for a semi-crystalline product. A stiff (non-flexible), near-brittle behaviour is thus observed. The strong secondary inter-chain forces characteristic of this state can, of course, be reduced by raising the temperature, but a more practical approach to inducing flexibility is to incorporate a non-volatile solvent, or plasticizer. Products prepared in this way from polyvinyl chloride can have properties which simulate those of a semi-crystalline material. They suffer from the

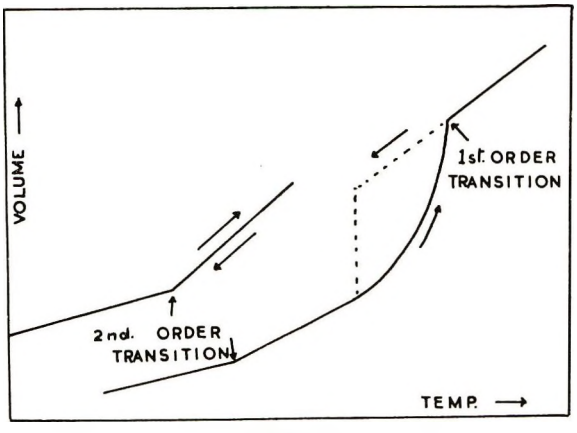

Figure 2

First and second order transitions (melting and glass points) observed during the heating and cooling of glassy (upper curve) and semi-crystalline (lower curve) polymers.

disadvantage, however, that the plasticizer can be leached out during use because of its relatively low molecular weight.

Current concepts of crystalline structure

The crystalline regions in a semicrystalline polymer are normally too small to be detected by light microscopy, although as will be seen later, these are often organised into polycrystalline aggregrates – spherulites – which can themselves be observed. In 1957, however, (1) it was discovered that distinct single crystals of polymers could be isolated after slow crystallization from very dilute solution. The conditions for preparing these structures are completely different from those involved in any commercial crystallization process, where the material is cooled from the melt, and in fact much of the recent developments have been concerned with trying to establish the relevance of single crystals to melt-crystallized structures.

The picture which has emerged is roughly as follows. When a molten polymer is super-cooled to below its melting point (supercoolings of 10–20°C are usually necessary to result in appreciable crystallization rates), the two component processes which constitute crystallization, namely nucleation and growth, commence. Nucleation is generally considered to initiate at heterogeneities, and the subsequent growth is initially in the form of single crystals, or a multilayer stacks of single crystals. Single crystals in polymers grown from dilute solution take the form of pyramidal, flat lozenges, with

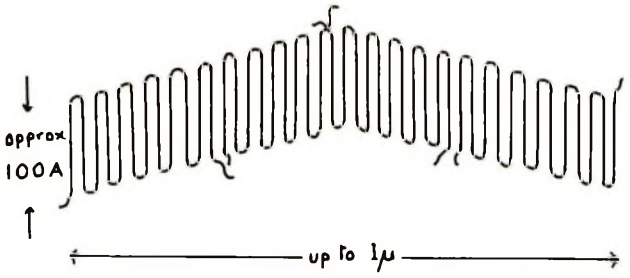

Figure 3
Cross-section of a solution-grown, polymer single crystal.

lengths and breadths up to a few microns, and widths in the region of 100Å. The chains lie perpendicularly to the narrow dimension, and as they are usually much greater than 100Å in length, they can only be accommodated by folding (*Fig. 3*). During growth from the melt, owing to the exceptionally high viscosity of the medium, the crystal faces tend to become unstable and cellulate, ultimately to form branched fibrillar structures which are in effect single crystals which have developed by the dominant growth of one axis (3). This situation is represented schematically in *Fig. 4*, where it can be seen that the nucleus becomes a point from which a radiating fibrillar structure develops, which, through branching of the fibrils, results in a spherically symmetrical growth unit, known as a spherulite. The spherulite, which is a polycrystalline aggregate, is the dominant form of growth in polymers, and the single-crystal-like fibrils develop within its outline. A microphotograph of spherulites developing in a polyethylene oxide sample is shown in *Fig. 5*, and in this particular case it can be seen that the growing bodies are quite large in size – up to 0.1 mm in diameter. In polymers used commercially, however, such as polyethylene and polyethylene terephthalate, the size is much smaller, and often the spherulotes are not resolveable microscopically. Diameters of less than 1μ may be involved, and at such levels of development, the growth unit may not have had the opportunity to progress much beyond the single crystal stage.

During the later development of the spherulites, the constituent fibrils may develop defects (*Fig. 4*) which will constitute part of the amorphous component of the fully-solidified product. Most of the amorphous component, however, arises from the fact that less readily crystallizable species such as branched molecules and low-molecular weight fractions are rejected during growth, to become trapped between the fibrils, or ultimately

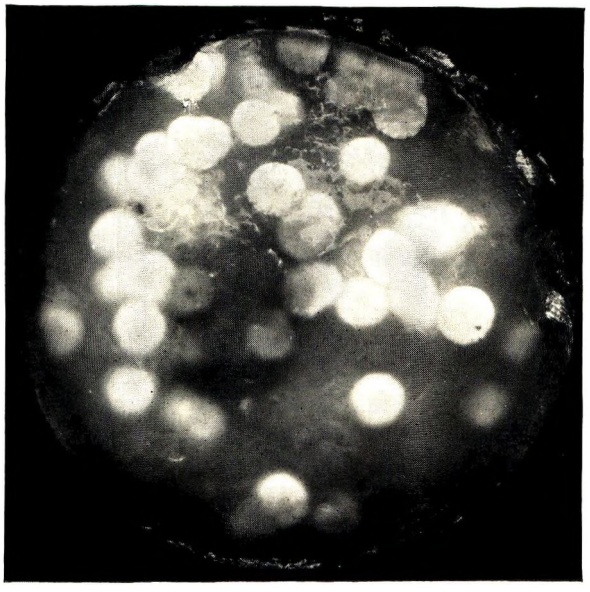

Figure 5

Spherulites growing in a super-cooled sample of molten poly-ethylene oxide. The spherulites are approx. 0.1 mm in diameter, and can be seen growing at various depths in the sample.

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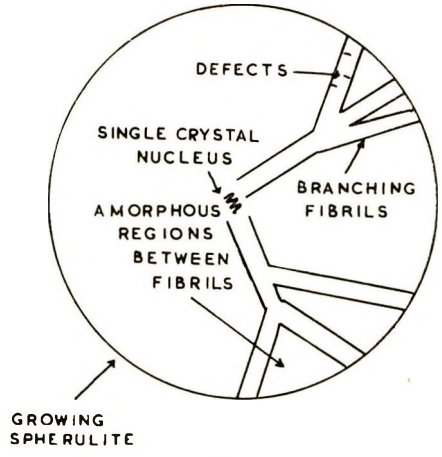

Figure 4
Schematic representation of spherulite growth-units in a semi-crystalline polymer.

between the spherulites (3). It is important to recognize that this amorphous phase is continuous, and that as a result its rubber-like properties are conferred to some extent on the solidified structure as a whole. In contrast to other structural materials such as metals, this phase plays not only an important but also a beneficial part in determining properties; in addition it may constitute the major component, by weight.

Control of properties

In order to obtain control over final product properties, two factors are of importance: Chemical structure and physical structure.

Chemical structure is of relevance, in that it is the chemical nature of the polymer chain which determines whether it will crystallize strongly, weakly, or not at all. Molecules with polar side-groups, capable of yielding strong interchain forces, allow the greatest probability of forming stable crystalline regions, and this is particularly true if the groups are relatively compact. An example of this type of polymer is polythene terephthalate which forms solid structures the crystalline content of which is high, and the crystallites of which have a high melting point (ca. 270°C). In polyethylene, the interchain forces are individually very much lower, but because the molecules can pack compactly, cooperative bonding is high, and high crystallinities are again produced (>80% in some cases). In natural rubber, the presence of a methyl side group, and the restriction to rotation resulting from the presence of double bonds in the chain prevents

the material from crystallizing at all above 20°C, although at reduced temperatures, crystallinity does develop at a slow rate. One of the biggest factors, which applies particularly to vinyl polymers, is the stereoregularity of the sequence of monomer units in the $-(CH_2-CHX)_n-$ chain. Irregular or atactic arrangements, as found in the products of most free-radical polymerizations, are not capable of yielding significant amounts of crystalline regions; this is the case with atactic polymethylmethacrylate, polystyrene, and polyvinyl chloride. The stereoregular products, however, formed from Ziegler and similar type catalysts, can crystallize, although, for example, in the case of polystyrene, the rate is slow, owing to the presence of the bulky side-group, and practical use cannot be made of the effect.

Apart from the gross chemical composition of the material, relatively minor differences, for example in the form of branches to the main chain, can also modify the ease of crystallization considerably. Cross-linking can be similarly effective in reducing the crystalline content in a given polymer while copolymerization with a small amount of a different monomer is also frequently used commercially.

Physical structure can be characterized quantitively in relation to the picture given in *Fig. 4*, in terms of such parameters as percentage crystalline content, the size of the crystalline fibrils, and also the final average spherulite size. All of these quantities depend to some extent on the conditions of crystallization – for example, lower temperatures, and hence higher rates of crystallization tend to yield smaller spherulites – and in addition small amounts of additives capable of acting as nucleating agents can influence spherulite size. Molecular weight is also an important factor. Apart from these readily-definable structural parameters, however, there are less precise features, such as the extent to which both fibrils and spherulites are tied together by common polymer chains, which are of considerable relevance.

All of these structural factors are of importance in determining properties, and it is because control over product behaviour can be obtained that the subject of polymer crystallization is of such practical importance.

Dependent properties

Thermal stability

The thermal stability that we are concerned with here is that of the physical rather than of the chemical structure. If a low molecular weight crystalline solid is raised in temperature, its eventual transition to the liquid state at the melting point is quite sharp. In a polymer, however, the

crystallites are quite small (*Fig. 4*), and because of the associated high value of the surface to volume ratio, their melting points are depressed. As, in addition, the crystallites are distributed in size, there is a corresponding variation in melting point, leading to a melting *range*, in the overall sample (*Fig. 2*), which may extend over as much as 100°C. In fact, melting tends to begin once the temperature is raised above the original temperature of crystallization.

Two important consequences arise from this fact. First, if deliberate attempts are made to control properties (e.g. transparency), by encouraging crystallization to occur at low temperatures (by "quenching"), some of the crystalline regions may not be stable at ambient temperature during the subsequent use of the product and in consequence its structure and dependent properties may change with time. Secondly, although the ultimate melting point of one polymer may be greater than that of another, its thermal stability may be less, if its crystallization temperature has been lower. Polyethylene, in spite of its relatively low melting point (110°C for the linear product), shows surprisingly good thermal stability because it crystallizes so rapidly, quite close to the melting point, and certainly at lower *supercoolings* than do some of the high polyolefins.

Optical properties

Practical optical behaviour is usually broken down into gloss (a fine structure surface effect), see-through (a coarser-textured surface effect), and haze (a combination of surface and bulk effects). In the broadest sense, all are scattering phenomena, and scattering arises when, in any given direction, there are variations in refractive index on a scale within an order of the dimensions of the wave-length of light (say 0.1 to 1 μ). These variations can occur either from variations in orientation or in density.

In the glassy state, provided that there are no cracks or voids, scattering should be at a minimum. This is the case with atactic polystyrene, polymethylmethacrylate, polyvinyl chloride, and of course in glass itself (which is also a polymer). As soon as crystallization sets in, however, the conditions for enhanced scatter are present, owing to the attendant local variations in orientation, and degree of packing. High crystallinity in itself does not necessarily result in a hazy product, as can be seen from the case of cellulose (in *Cellophane* film). Here, the crystalline regions are small (approx. 100Å) compared with the wavelength of light, and are not organised into well-developed spherulites; as a result the clarity can be little worse than in a glassy product, such as polyvinyl chloride. In poly-

mer films generally, haze and poor see-through arise predominantly from surface irregularities, which themselves are associated with the spherulitic structure of the material. As the thickness of the product increases, until we are dealing, for example, with blow-moulded bottles, the scattering contribution from the bulk increases, but in all cases clarity can be improved if spherulite size can be reduced, or if the crystallinity within the spherulites can be minimized. The former can be achieved through the use of nucleating agents, which have proved to be so successful in the case of polypropylene; while crystallinity can be controlled, for example, through the introduction of branch-points, cross-links, or copolymerization units capable of disrupting crystal structure. Copolymers of vinyl acetate can yield extremely clear products, and the new poly-4-methyl pentene 1 probably makes use of this effect. The transparent "ionomers," recently announced by Du Pont, are also copolymers based on ethylene, but here the comonomer is actually ionisable and can, in the presence of suitable cations, introduce an ionic bond component, which is an additional factor likely to reduce crystallinity.

Finally, initial crystalline structure in a film, and its associated scattering, can be modified considerably by the orientation process which occurs during stretching, and successful biaxially-oriented products have been produced.

Permeability

Permeability in polymer films usually involves a solution/diffusion process, and so is largely dependent on chemical structure. It should be mentioned, however, that the presence of a few defect pores can completely alter the permeability characteristics of a film. Similarity in chemical nature between polymer film and the gas or vapour under consideration is thus a rough guide to likely permeation rate, and, for example, with polyethylene, nonpolar vapours or liquids diffuse readily, whereas water shows an extremely low permeation rate. Physical structure for a given polymer affects the permeation rate slightly, but significantly, and as the path for the adsorbed vapour is through the amorphous regions, more crystalline products are less permeable.

Surface modification might appear to be a possible approach to altering permeation behaviour, but grafting on of polar molecules to non-polar substrates does not achieve the hoped for effect to any appreciable extent. This may be because in the thin layers involved, a suitably consolidated physical structure is not laid down. Multilayer sandwiches of polymers

with paper, metal, or other polymers, however, do constitute a very satisfactory way of obtaining the best behaviour from each component.

Mechanical properties

The relation between structure and mechanical behaviour in any type of material is usually the field about which least is known, and polymers are no exception in this respect. The effect of crystallinity on modulus has already been discussed, but it is in the field of ultimate strength that the greatest uncertainties exist. In general, products formed under conditions of slow crystallization are able to form the most perfect, and the largest, fibrils within the spherulite outlines (3), and in consequence their breaking behaviour resembles more that of a brittle polycrystalline mass, with weak forces between the component growth-units. During rapid crystallization, however, it is far more difficult for the chain molecules of the melt to arrange themselves ideally in the solidified phase, and as a result, "tie-molecules" tend to link the component spherulite together, and so to minimize brittle failure. This is particularly the case when the chains are long, as in a high molecular weight product.

A further important factor is the concentration of low molecular weight and other less readily crystallizable species, which are rejected during growth to become concentrated between the fibrils and the spherulites. These can constitute a source of weakness, and this is no doubt the explanation for the deleterious effect of such constituents on environmental stress-cracking resistance, in blow-moulded articles. That this is not the entire story, however, is obvious from the fact that some polymers which contain quite high concentrations of such species, e.g. polypropylene, show no evidence at all of environmental stress-cracking.

Conclusion

Our present understanding of polymer crystal structure, and the effect which chemical structure has on it, is now sufficiently advanced to enable many dependent physical properties to be satisfactorily interpreted. As a result, new polymers can be assessed more readily with respect to their potential uses, while the continuing ideal of being able to design polymers with suitable combinations of desirable properties, becomes a more readily-obtainable objective.

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DISCUSSION

MR. A. MOËS: One generally considers that selective permeability of plastics to water and or non-porous vapours depends upon the hydropholic or lipophilic properties of the polymers. Are there other properties of plastics which influence their permeation behaviour?

THE LECTURER: I have tried to stress that physical structure is often more important than chemical structure. In the *particular* case of permeability, however, chemical structure, as you imply, is more important. Secondary changes can nevertheless be effected by altering physical structure, and one should not overlook that pores are extremely important in determining whether one gets an enchanced rate of solvent or vapour permeability, although most polymers used in practice are free from pores. Crystallinity is important; the crystalline regions are very much less mobile and so permit the diffusion of solvents much less readily, products with higher amorphous contents will therefore have higher permeabilities. This has been established for polyethylene.

The organisation of the crystallites and amorphous regions at a higher level to give spherulites leaves part of the amorphous component contained between the spherulites. Permeation takes place preferentially through this route rather than through the spherulites themselves. This is apparent, for example, if you carry out oxidative degradation of spherulitic material, when the reaction takes place preferentially between the spherulites so that you can isolate them from the originally coherent mass.

MR. A. MOËS: What are the physical, or chemical, properties of plastics which determine the suitability of two polymer films to adhere to each other. How can one make two polymer films adhere if their hydrophilic or lipophilic properties are quite different?

THE LECTURER: No material has ideal behaviour – particularly resistance to both polar and non-polar vapours – so it is very good if two films with complementary properties can be combined. The trouble is adhesion.

This problem has been tackled for many years, in the sense that a material like *Cellophane*, which does not have much resistance to water permeation, can be made waterproof by putting on it a very thin layer of the more waterproof nitrocellulose, and this has been a standard way of waterproofing *Cellophane* for some time. One approach which came very much into favour, at least research-wise, some 10 years ago, was that of chemically attaching the different layer to the one underneath, by carrying out grafting reactions. In recent times this has fallen into disfavour, because it often transpires that to begin with you need a very thick layer of grafted polymer, far thicker than you would have hoped for; the other difficulty is that for the reaction to be effective it should be confined to the surface; in fact it occurs to an unexpected extent in the interior of the substrate.

Nowadays it seems to be much easier, through purely empirical approaches, to devise formulations of such materials as polyvinylidene chloride and polyacrylonitrile in emulsion form, which can be used successfully as coatings for less polar substrates.

DR. J. J. MAUSNER: How far can physical changes in a polymer alter its chemical characteristics and to what extent? If polystyrene is attacked by a solvent, is it possible to alter its resistance to this particular solvent by altering its physical characteristics?

THE LECTURER: One achieves this by incorporating more crystalline regions which are, generally speaking, less prone to attack. A fair amount of work has been done on the relation between physical structure and ease of chemical attack, but strangely enough it has usually been looked at from the point of using chemical reactions to tell us something about physical structure, rather than controlling physical structure to get control over chemical resistance. There seems no doubt that crystalline regions are more resistant to chemical attack, whatever the nature of the chemical reaction. Experiments with polypropylene have shown that oxidation is confined almost exclusively to the regions between the spherulitic growth units, and that very much less oxidation takes place within the spherulites. Similarly, in cellulosic materials there is no doubt that in acidic hydrolysis the degradation takes place almost exclusively in the amorphous regions.

MR. A. HERZKA: How practical is it to alter these structures and how easy and cheap is it for the manufacturer to effect these changes if the user finds them necessary?

THE LECTURER: Not much has been done to try and effect chemical resistance. Physical structure is controlled all the time on a large scale, for example, in the case of polyethylene. The introduction of branch points produces a far more amorphous material which has completely different characteristics from that produced by the low pressure process. The recent Dupont ionomer, with a small number of ionic linkages between the chains, has a very different structure, and hence dependent properties.

MR. A. HERZKA: This can presumably lead to difficulties, because if you alter the structure in order to alter chemical resistance, you also affect the processing properties.

THE LECTURER: Yes. To take a recent example – the introduction of nucleating agents into polypropylene yields a better product in terms of impact resistance, and transparency, but the manufacturer does not like this because there seems to be an optimum in the number of nuclei required, which is different from that required to produce the maximum enhancement of properties.

DR. A. W. MIDDLETON: How far do manufacturing conditions such as blow-moulding or injection moulding alter the degree of crystallization?

THE LECTURER: Very much, and perhaps more important than the degree of crystallization is the stability of the crystallites. There is always a tendency, whatever the crystallization temperature, for the polymer to melt as soon as one subsequently raises the temperature above the original crystallization temperature. Polyethylene, for example, melts at 140° and starts to crystallize at 120°, if cooled slowly. But it can be cooled very much more rapidly so that most of the crystallization takes place at a very much lower temperature, let us say approx. 80°. If this is taken down to room temperature you have a product which will retain its properties until you reach approx. 80°C, the original crystallization temperature; above 80°C the crystals will start to melt. If you crystallize more slowly you would have a product which would be stable to a correspondingly higher temperature.

Book reviews

APPLICATIONS OF MASS SPECTROMETRY TO ORGANIC CHEMISTRY. R. I. Reed. Pp. ix + 256 + Ill. (1966). *Academic Press, London and New York.* 63s.

For many years mass spectroscopy has been a Cinderella among her sister techniques of organic chemistry; the results of implicit cost effectiveness surveys had tended to direct elsewhere the necessarily large appropriations required. It is only within the last few years that a wider acceptance of utility justifying the expense of instrumentation, together with improvements in design and sufficient publicity to dispel doubts regarding the excessively complex re-arrangements of initial ion fragments, have all tended to convert organic chemists to this physical technique. Today, simple relatively cheap single focussing mass spectrometers are rapidly becoming a normal appurtenance of organic research laboratories – and even analytical chemists have their expectations! Whilst the high resolution double focussing instruments are still extremely costly, reference to results of their use are becoming increasingly common. It is into this relatively favourable climate that Dr. Reed has introduced his monograph. He deliberately takes an ambient position, somewhere between the diagnosticians plumbing the mysterious recesses of complex natural products and those anxious to explain the energetics of the fragmentation – and perhaps derive the stereochemistry – of known structures. It is clear that the latter experience, with believedly related compounds, must validly assist the former type of enquiry.

In reviewing instrumentation, distinction is made between sector (90°) and Dempster (180°) single focussing systems and their limitation is contrasted with Nier geometry high resolution instruments. Detectors, amplification methods and sample admission techniques are briefly described and examples are given of differences in the ranking or relative abundances between various types of instruments. The general mechanism of production of mass spectra is introduced – both for primary fragmentation and that following re-arangement of initial products. Some indication is given of the rather limited value of determining the ionization potential. General methods for deriving the molecular formula are discussed; examination of the isotopic satellites relative to the parent molecular ion is described in detail. With double focussing spectrometers the very high resolution permits unique identification of the composition of ions of molecular weight up to about 400 using published tables of exact mass for all likely combinations of elements. Some preliminary indication is given of the examination of fragments where the parent molecular ion is absent. Attention also is given to ion-molecule collisions and to the rejection of known structures by comparison with established cracking patterns.

In chapters 3 and 4 detailed examination is first made of the fragmentation of a great variety of hydrocarbons and then structures containing O, S or N hetero functions, for which polarization and conjugation modify the cracking mechanisms. Typical aliphatic and aromatic bond fissions are tabulated, and a comprehensive

series of individual functions examined. The application of mass spectroscopy to natural products is a relatively new development and it is assumed that Dr. Reed's interest in terpenes and steroids largely stems from his collaboration with the Barton school in the mid 1950's. In this volume, he selects from a wide field of natural products typical substances that show significant cracking patterns. It is not so much a criticism of the book, as of the limitations of our present knowledge of fragmentation mechanisms, that he is forced to dwell on the correlation of mass fragments with known structures or achieving a distinction between competing possible structures, rather than at this stage draw detailed empirical conclusions that might be a guide in deciphering unknown naturally occurring molecules. However, in the most widely studied – but highly complex – indole alkaloid field, the author has attempted to pick out some generalized mechanisms for which the argument is "consistent rather then compelling."

In later chapters, the necessary criteria for reproducible analysis are set out and the experimental conditions examined in detail. Appropriate mathematical treatment of the analysis of mixtures is indicated and related to the fractionation of components of differing volatility. Having regard to the cautionary notes elsewhere, Dr. Reed collects together in 32 pages empirical guidance for analysis of mass spectra – here is the distillation of the practising spectroscopist's experience. Of less practical interest is a short chapter setting out the logical inductive approach in deciphering the mass spectrum of the related hydrocarbon. Suitable reductive processes and various useful parameters are listed in Appendices.

Curiously, this monograph appears to complement, rather than supplement, sections on mass spectroscopy that Dr. Reed has contributed to other works; in fact it has a somewhat more academic mien but is none the less valuable for that.

G. F. PHILLIPS.

THE STRUCTURE OF LIPIDS. D. Chapman. Pp. xii + 323 + Ill. (1965). *Methuen & Co. Ltd., London.* 63s. U.K. only.

This volume covers not only the structure of lipid molecules but also the arrangements of these molecules in solid and liquid phases and even in biological systems.

The book is divided into chapters on the various instrumental techniques applicable to the study of lipid structure. The chapters all take a similar form: A brief assessment of the status of the technique in its application to lipid studies; a short theoretical treatment; a short description of experimental techniques; a main section on applications; a list of references. Each main section on applications starts with simple lipids such as fatty acids and alcohols, and is developed to cover glycerides, steroids, phospholipids and the complex lipoproteins. The presentation demonstrates the scope of the method and shows how experimental data is interpreted. It also summarizes much present-day knowledge as well as exposing the gaps.

The three major chapters deal with ir spectroscopy (including Raman), nuclear magnetic resonance spectroscopy and X-ray diffraction. There are three similar but shorter chapters on uv spectroscopy, mass spectroscopy and electron spin resonance spectroscopy. An introductory chapter summarizes the classes of compounds in the lipid field and a final chapter looks to the future and mentions other methods such as electron microscopy, surface studies and thermal techniques.

There is also a chapter on separation techniques. Although this is not part of the main theme of the book nor perhaps written with quite the same authority, it does bring together a useful summary of the methods that must precede most structural studies.

The tables, diagrams and references are numerous and valuable. The index is short but adequate. A number of minor errors were noted in text and figures, e.g. *Fig. 42* does not correspond to its textual description, *Figs. 104* and *106* are apparently transposed and the description of *Fig. 119* in the text is muddled.

The chemist and biologist engaged upon the more basic aspects of cosmetic science should find this a valuable book. R. N. BEVITT

ADVANCES IN DRUG RESEARCH, Vol. 2. Editors: N. J. Harper and A. B. Simmonds. Pp. ix + 205 + Ill. (1965). *Academic Press, London and New York.*

The editors of this series have encouraged authors to write in a manner that is understood by scientists in disciplines apart from their own. In this volume the articles are mainly concerned with the action of drugs at the molecular level.

"The inhibition of noradrenaline uptake by drugs" (L. L. Iverson) deals with those drugs which inhibit the physiological mechanism of inactivation of catecholamines. This mechanism is currently thought to be, not by metabolic degradation of the amine, but by uptake into a tissue where a system of intracellular storage exists. The major pharmacological effect of inhibition of this mechanism is potentiation of the effects of adrenaline and noradrenaline.

"Substrates and inhibitors of dopamine-β-hydroxylase (DBH)" (J. B. van der Schoot and C. R. Creveling) discusses properties of one of the enzymes concerned in synthesis of noradrenaline, and assesses significance of its inhibition *in vivo*.

"Conformational perturbation in relation to the regulation of enzyme and receptor behaviour" (B. Belleau) gives a theoretical background to the concept of drugs exerting their effect by directing the conformation of the protein receptor.

"Structure and activity at adrenergic receptors of catecholamines and certain related compounds" (P. Pratesi and E. Grana) discusses drugs affecting the adrenergic receptors. The different effects of different drugs result from their different relative degrees of reaction with the α– and β– receptor sites.

"Muscarinic receptors in the peripheral and central nervous systems" (A. Bebbington and R. W. Brimblecombe) discusses a topic, the main clinical importance of which lies in the use of muscarinic inhibitors or, to use the name by which they are better known, of anticholinergics. Structural requirements for activity are discussed at some length.

"2-Halogenoethylamines and receptor analysis" (D. J. Triggle) describes the use of these compounds in locating the noradrenaline receptor sites at the molecular level. This makes use of the fact that their adrenergic blocking activity cannot be overcome even by very high concentrations of noradrenaline, indicating that irreversible alkylation of the receptor site may occur.

The book carries author and subject indexes, and is produced to a high standard. B. G. OVERELL.

INTERPRETATION OF NMR SPECTRA. R. H. Bible. Pp. ix + 150 + Ill. (1965). *Plenum Press, New York.* $12.50.

The practical application of nuclear magnetic resonance owes much to predictions from theoretical physics, but an adequate knowledge of electromagnetic theory and familiarity with, for example, nuclear quadrupole moments and magnetic susceptibility, should not be required of the busy organic chemist concerned only with the optimum use of a diagnostic tool, any more than he should be expected to understand every electronic or vibration transition in an uv or ir absorption spectrum. To meet his basic need, here is an empirical textbook designed as a crash course specifically to teach the interpretation of pmr spectra. Whilst no prior knowledge of the subject is assumed, a purely theoretical treatment has been avoided. It is considered that the author has been largely successful in his intention to set out the relevant fundamentals, review complications, limitations and potential pitfalls, and then indicate methods of their solution. In particular, the section citing a sequence of 1,2-disubstituted ethanes showing increasing spin pattern multiplicity constitutes an excellent introduction to complex coupling. A notable feature of the presentation is a series of useful summary tables interspersed through the text: these are neatly boxed for rapid consultation and the author claims – with some justification – that the entire book can be recapitulated by reading only these summaries.

The monograph is replete with useful charts and tables, particularly in connection with complex or unequal coupling and prediction of spin multiplicity. Especially helpful are charts showing respectively the absorption observed with the commonly used solvents and a comprehensive presentation of the characteristic positions of a wide variety of proton signals at 60 Mc/s referred to tetramethylsilane (TMS). The latter chart incorporates much of L. M. Jackson's published compilation (1); a convenient enlargement, 50 × 30 cm, is supplied with the book. All spectra illustrated are related to TMS as internal reference and are run on the Varian A-60 spectrometer: the standard charts therefore show all three commonly used systems of notation, although the delta (ppm) and tau (10-delta) dimensionless scales cannot be directly interpolated where multiples of a 500 c/s scan have been employed. For discussion purposes the text consistently used the c/s nomenclature although chemical shifts are parenthetically reiterated in ppm. Relatively few typographical errors were observed and these caused little more than momentary confusion. The index is generally adequate, although one might like to find in addition more cross references or explanations in the main text. Thus as an example – there are a number of references early in chapter 2 to the existence of negative coupling constants, without any explanation of the significance or reality of this concept; later (p. 40) the reader is generally referred to chapter 4 in this connection but, having found the correct page from the index, the explanation there is not satisfactory in the context of chapter 2. In addition to a short bibliography and some practical notes for operating the Varian A-60 spectrometer, there is a glossary comprising over 50 terms that are not explained elsewhere in the text but which may well be encountered in the more sophisticated nmr literature. G. F. PHILLIPS.

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(1) *Applications of nmr spectroscopy in organic chemistry* (1959), Pergamon Press, New York.

SURFACE ACTIVE AGENTS. M. Bell. Pp. 24 (1965). *Glovers (Chemicals) Ltd., Leeds.* 5s.

This monograph gives a very concise account of methods for the isolation, separation, characterization and determination of surface active agents found in a variety of materials as diverse as oil paints and plastics or duplicating inks and deodorants. It also contains notes on physical and chemical methods of control of surface active agent concentration in a particular process. Domestic soap and detergent powders and washing-up liquids have been deliberately excluded, although references for analytical schemes of this type of material are given.

The monograph is a series of schemes. Materials in which surface active agents are present are divided into four groups and each group has a scheme for the extraction of the active ingredient. Isolation of the surfactants from the material is followed by a separation of the two, or possibly more, active agents before characterization is begun. The characterization scheme is based on determining the ionogenic type and then, by using about a dozen chemical tests, classifying it into one of the major groups of surfactants. This scheme, although less sophisticated than the classification by elements present, or the use of their techniques, is quite adequate for the chemist who merely requires a knowledge of the ionogenic type of the surface active ingredients.

Quantitative methods are indicated but literature references are quoted more liberally than precise directions: a source of irritation to the analyst using the monograph in preference to a standard work.

The monograph should appeal to the chemist of limited experience with surface active agents for its practical approach to the subject, and also for its collection of references to the literature of surfactant analysis. T. J. BOWDITCH.

STATIONARY PHASE IN PAPER AND THIN-LAYER CHROMATOGRAPHY. Editors: K. Macek and I. M. Hais. Pp. 358 + Ill. (1965). *Elsevier Publishing Co., Amsterdam–London–New York.* 85s.

Today the cosmetic chemist has recourse to a wide variety of techniques and must be prepared to weigh their respective merits for a particular analytical problem. Guidance for his choice frequently is provided by review symposia or the collections of papers that they produce. This volume constitutes such a collection. The Chromatography Group of the Czechoslovak Chemical Society organised an International Symposium in 1961 which dealt with structural correlation and systematic treatment in paper partition chromatography. The second symposium (June 1964) was made deliberately narrow, to limit the discussion of stationary phase to the two related paper and tlc techniques; the exclusion of glc stationary phases was considered desirable so as to restrict the field and enhance the prospect of useful discussion. The papers are printed in the language of their presentation, i.e. English or German, without any corresponding summary in the other tongue; the transliteration of Cyrillic Terms follows the C.A. standard principles.

The papers are sub-divided according to the five sections of the symposium, each section comprising introductory papers, with complementary and experimental

reports, and a consolidating discussion. The first section, simply entitled "Chromatography Papers" is of a more general character and occupies about one sixth of the total length. It deals with paper supports, based on cellulose (with or without chemical modification), glass-fibre and ion-exchange matrices. A necessarily wider selection of materials for tlc is discussed in the longer second section, whilst sections 3 and 4 deal with stationary liquids and absorbents/impregnants for paper and thin-layers respectively. General problems and particular theoretical aspects of the stationary phase are the province of the last group of papers. The book is well produced, appears comprehensive within its stated field and has an impressive number of contributors to both papers and discussions, although the U.K. does not seem to have been overtly well represented. G. F. PHILLIPS.

INTERPRETED INFRARED SPECTRA, Vol. 1. H. A. Szymanski. Pp. vii + 293 + Ill. (1964). *Plenum Press, New York.* $10.75.

Dr. Szymanski has set out to present a text which does more than either of the traditional approaches, i.e. tabulations of empirical correlation tables with general guidance on diagnostic pitfalls, or more or less comprehensive catalogues of spectra observed by a variety of spectroscopists in a given field. It is his aim to assist chemists to learn to interpret their own ir spectra and make their own identifications. It is an advantage of this approach that for the numerous examples given, not only are the diagnostic group frequencies seen but interfering and all confirmatory bands can be checked at the same time.

Ultimately in this series all common groups of substances will be examined: in the first volume acyclic, benzenoid and alicyclic hydrocarbons are analysed. The author begins from the assumption that each isolated structural group exhibits a characteristic frequency of vibration. Where molecules are small and relatively symmetrical, their spectra are submitted to complete vibrational analysis, in which every individual observed frequency is assigned to a specific mode of vibration. From this basis are deduced the characteristic group frequencies, and detailed correlation tables are constructed for all the bands recorded which may then be employed predictively for the presence of similar isolated groups. The author goes further – he feels that vibrational analysis may reveal bands that are not normally considered reliable yet may be useful in limited correlation within a restricted series of closely related molecules. A variety of spectra of specific members of the class of substances exhibiting the particular group frequency are then presented, and features of especial interest discussed and interpreted.

Compounds are divided into classes of increasing complexity: each class in turn is considered in the manner described above. No spectrum is illustrated unless every group frequency in that molecule has already been discussed. The first class dealt with, naturally, is the alkanes: the vibration modes for CH_3, CH_2 and CH groups are analysed and only saturated hydrocarbon spectra included. Successive classes, with in parenthesis the number of specific spectra discussed, comprise the alkenes (38 examples), substituted monocyclic aromatics (41), and the alicyclic propanes (10), butanes (6), pentanes (37) and hexanes (50). The great majority of the spectra are taken from the API collection. Both the spectra and the discussion refer to frequencies in reciprocal cm units, but for the convenience of wavelength (micron) users, the front and end papers carry a table of the function 1000/n for the integers 1 to 999.

Dr. Szymanski has written, or contributed to, a wide variety of books on ir spectroscopy, ranging from basic theoretical principles to massive compendia of spectra. In this series he offers a paedogogic text that will reap its reward in the long term education of the worker who will learn to make his own diagnosis. However at the price for the first (hydrocarbon) volume, this clearly is not a reference book for the busier analyst who has neither time nor inclination to qualify as a competent physical organic chemist. G. F. PHILLIPS.

Society of Cosmetic Chemists of Great Britain

ELECTION OF HONORARY MEMBER

A SPECIAL MEETING was held at the Royal Society of Arts, John Adam Street, London, W.C.2, on Wednesday, 13th April 1966. 20 Members and Associates were present.

The Chair was taken by the President, Mr. R. Clark, who called on Mr. G. A. C. Pitt to propose the motion that

> *F. ATKINS, B.Sc., F.R.I.C., be elected an Honorary Member of the Society of Cosmetic Chemists of Great Britain.*

Mr. A. Foster seconded the motion, which was put to the vote and carried unanimously.

SYMPOSIUM ON COLOUR

A Symposium on Colour, organised by the Society, took place on 26th and 27th April 1966, at the Grand Hotel, Eastbourne. It was attended by 93 participants, including visitors from Germany, Holland, Norway and the U.S.A.

On the afternoon of the 26th April, the participants visited the laboratories of the School of Pharmacy, Brighton College of Technology, Moulsecoomb, by kind invitation of Dr. E. A. Rawlins.

Participants also attended a Civic Reception at the Congress Theatre given by the Mayor of Eastbourne, Councillor Mrs. K. J. Underhay, J.P.

1966-67 PROGRAMME

Lectures will be delivered on the following Thursdays:

6th October 1966	2nd February 1967
1st December 1966	4th May 1967
5th January 1967	

MEDAL LECTURE: Wednesday, 22nd March 1967.

1967 DINNER AND DANCE: Saturday, 4th February 1967, at the Europa Hotel, Grosvenor Square, London, W.1.

SYMPOSIUM ON PRODUCT TESTING

The Symposium on Product Testing will take place in Eastbourne, Sussex, and not in Leamington Spa as previously announced, on 14th and 15th November 1966. Full details will be available at the beginning of August.

MANAGEMENT SEMINAR

A working seminar on THE MANAGEMENT OF LABORATORIES IN CONSUMER SUPPLY INDUSTRIES, with particular reference to the needs of the cosmetic, toiletry, and allied industries, is to be held in Buxton, Derbys. from 6.00 p.m. Monday, 10th April 1967—6.00 p.m. Thursday, 13th April.

Basic Programme: Eight sessions of lecture with discussion,

Four sessions of discussion by groups of eight members dealing with specific set subjects,

Two sessions of discussions by groups of half the members dealing with subjects chosen by the group.

Language: All lectures in English. Simultaneous translation into French/German if sufficient number of participants require it.

Membership: Limited to 64.

Members will be supplied with a reading bibliography before the seminar and given a synopsis of the lectures on arrival at the venue. Lectures and discussion will be published and will be supplied to each member free of charge.

Fees: Including accommodation and all meals, but not wines and spirits . . . Members of Societies of Cosmetic Chemists affiliated to the I.F.S.C.C. . . . 35 guineas; non-members 45 guineas.

Participants should have some experience in the management of a laboratory, and are expected to take an active part in the discussions in order to get the maximum benefit from the seminar.

Further information from Hon. Organiser, 33 Devereux Drive, Watford, Herts., England.

SYMPOSIUM ON PROCESSING AND MANUFACTURING

A Symposium on Processing and Manufacturing will take place in Royal Leamington Spa, Warwicks., on 13th and 14th November 1967. *Programme Secretary:* Dr. J. J. Mausner, Helena Rubinstein Laboratories, Ltd., Central Avenue, West Molesey, Surrey.

DIPLOMA COURSE

The course leading to the Diploma of the Society of Cosmetic Chemists of Great Britain has been held at Brunel College since its foundation in 1957. In view of the revised charter of the college, the next course, which is due to commence on the 16th September 1966, will be held at

BOROUGH POLYTECHNIC,
BOROUGH ROAD,
LONDON, S.E.1.

It is a one-year, part-time day-release course. There are three 3-hour sessions per week, on Monday and Wednesday evenings and Wednesday afternoons, for a total of 32 weeks in the year. The examination, consisting of two 3-hour papers, will be held in June 1967.

The course is the only one of its kind and is designed to give a comprehensive training in all aspects of cosmetic science to persons employed in research or development work in the cosmetic and allied industries. The minimum entry qualification is GCE "A" level, preferably in chemistry, but young graduates will also find it a valuable introduction to industry.

Some of the lectures are from the college and some are from industry. The following topics are covered :

SURFACE CHEMISTRY
SPECTROSCOPY, CHROMATOGRAPHY
PHYSICAL CHEMISTRY (PRACTICAL)
EMULSION THEORY
CHEMISTRY OF OILS, FATS AND WAXES
MICROBIOLOGY
HAIR ; HAIR PRODUCTS
SKIN ; SKIN CREAMS
TEETH ; DENTAL PRODUCTS
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PERFUMERY
LIPSTICKS AND POWDERS

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