

SUMMARY OF SCIENTIFIC ACHIEVEMENTS OF THE SYMPOSIUM

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It would be presumptuous for me, or anyone else for that matter, to pretend to be able to perform adequately the task which I must now attempt. For one thing, none of us has been able, as we might have wished, to be in three places at the same time. Furthermore, the preprinted abstracts are largely of the nature of appetizers, an invitation to the lunch; but with a masterly reticence in regard to the menu—to say nothing of the details of the cooking. Nevertheless, there is much more to be said than I can possibly cram into half-an-hour, and I can only plead for merciful consideration of the extenuating circumstances and recognition of the fact that my remarks will inevitably be coloured by personal scientific interests and by my own predilections and, perhaps, prejudices. It is in that light you should view my estimate of the Symposium as a whole. For me, it has been an entrancement throughout, a spectacular demonstration of rapid progress and vitality, and a pledge for future advances. I am not here to make dogmatic comparisons of merit or significance. The highlights which I shall mention may appear dazzling to me, because I am relatively near to them; more remote stars in the galaxy may, of course, be brighter for all I know.

Running right through the Symposium were lectures and other contributions dealing directly with the methods and principles, physical and physicochemical, applicable to the determination of molecular structure, or to various examples of the use of such techniques in the solution of particular problems. Dr Thompson gave a general survey in his Symposium Lecture, and, though himself a pioneer of infra-red spectrometry, gave pride of place to X-ray crystallography, chiefly, I think, because that method gives full structural information, including a solution of the stereochemical problems. In passing, I would remark that structure determinations by classical methods should be followed by X-ray studies wherever possible. A good example is afforded by strychnine: after the long chemical trail had ended at the correct two-dimensional structure, the work of Bijvoet was still needed to determine the configuration of the molecule in space.

Dr Mathieson contributed an authoritative paper on the direct determination of molecular structure by physical methods alone, especially, of course, his own methods of X-ray crystallography. Indeed, Dr Mathieson has given several convincing demonstrations of the validity of the implied claim: one was the alkaloid cryptopleurine, an Australian natural product, but here I would like to make a few comments.

Dr Mathieson and other enthusiastic physicists and physical chemists are entirely justified in the exclusion of the organic chemist in order to prove

a point, namely, their contention that it is possible to determine molecular structure by physical methods alone.

Although this is true, it must not be supposed that the molecular structure is the be-all and end-all of the matter. It has been the objective of the classical organic chemist, who has approached molecular structure by the methods of analysis and synthesis which are familiar to all of us. But the great value of this work has been the approach—the analysis and the synthesis—and the region of chemistry which has been explored in that way. It has not been, perhaps, so much the final result. Even if we know the structure, we shall still have to explore the surrounding chemical territory. I shall give just a few examples. Would it have been a good thing for organic chemistry as a whole if the structure of indigo had been determined by just looking at a few milligrams of the pigment, so that Baeyer did not carry out the wonderful work which led, *inter alia*, to the determination of the structure? I think not. Another example is that of camphor since, even after the structure was known, there was a tremendous effort directed to the preparation of derivatives and study of the manifold molecular transformations which that Proteus among chemical substances undergoes. Thebaine is another case. Even when we knew the structure, we still had many difficult problems to tackle in order to reveal the full beauty of the wonderful complex of migratory processes that occur. Similarly for strychnine and cholesterol. Other examples will occur to you very easily. Thus it is not to be imagined that the knowledge of molecular structure is the end of the chapter. It is rather the chemistry which we encounter, in arriving at the molecular structure and in carrying out the synthesis, which is of the greater importance.

Many other applications of physical methods were brought to our notice. I would wish to refer particularly to the relatively new method of optical rotatory dispersion which was described so well by Professor Djerassi, and of which he is a pioneer and enthusiastic advocate. Many examples of the use of infra-red spectroscopy and of nuclear magnetic resonance occurred during the course of the Symposium, and these methods are undoubtedly among the most powerful tools which have been placed in our hands. The older method of ultra-violet spectroscopy is still an essential resource, and was found extremely useful by Professor Jones in his study of the acetylenic derivatives formed as products of the life processes of moulds. Throughout this Symposium, we have heard not only arguments in favour of physical methods, but also very good applications and justifications of this propaganda by the special determinations of structure which have been possible in that way.

One result of this gathering will have been a clarification of our ideas as to what each of the newer methods can actually do. Thus, optical rotatory dispersion gives stereochemical information which cannot be obtained from the ultra-violet or infra-red absorption spectra. The ultra-violet absorption is highly constitutive and, with increasing knowledge, what were thought to be vices turn out to be virtues; the electronic spectra show up the conjugative displacements and their changes under various conditions. Similarly, the extensive study of infra-red absorption has led to a better understanding of the scope of the constitutive effects in this region. The newer method of

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nuclear magnetic resonance is chiefly used to classify the hydrogen atoms in the molecule. It has proved a searching instrument, even in the case of complex alkaloids and the like.

The Symposium showed very great, and still growing, interest in the alicyclic polycyclic series, including the poly-iso-pentanoids. The brilliant lectures of Professor Barton and Professor Sorm require detailed attention for their appreciation; they certainly deserve close attention. The same applies to many other lectures and contributions, for example, those of Professor Brockman, and Professor Sørensen, in all of which important new results and correlations were disclosed.

We were greatly privileged to hear the lecture of Professor Woodward, in which he described, I believe for the first time, the outstanding achievement of the total synthesis of chlorophyll. Professor Woodward is not only a most brilliant *synthetic* organic chemist, who gives us metaphorical left hooks and right jabs in bewilderingly quick succession, but also an expositor able to convey a sense of the drama of the development to his audience. His lecture was thoroughly enjoyable, even thrilling, as an experience. No doubt in places he admitted to a little good fortune, though he also made it clear that it was expected. I was reminded of Benjamin Franklin's wise saying—"Luck is the bonus that accrues to industry". Well, Woodward and his team were surely industrious. This achievement of the synthesis of chlorophyll is a very good example of the kind of comment that one often sees, "what good is it?" Presumably the "good thing", as Woodward has so admirably pointed out himself, is the new knowledge that is obtained; increased understanding of the chemistry of chlorophyll, and of how it is likely to behave in a variety of circumstances. We do not know where that new knowledge may lead us, but it is certainly a most important substance and, therefore, we must know everything we can about it.

The Section Lecture of Dr Lederer was quite outstanding in interest and importance, and in promise for future developments. I had no means at hand for measuring the decibels of the applause, or its duration, but it was clear that my assessment was widely shared. Dr Lederer described extensive studies of biologically-active lipids produced by bacteria, especially the tubercle bacteria. Using every applicable modern technique he explained how several classical problems in the field have been finally solved, and, even more useful, he indicated the stages reached in the solution of others, including some that may have great significance for the therapy of tuberculosis in the future. I do not think that my high estimate of Professor Lederer's contribution is coloured too much by the fact that he agreed with some conclusions reached in our laboratory in Oxford, but certainly that gave me the near angle of sight which I mentioned previously, and I was able to appreciate the rest of it very much. Professor Lederer's modesty and humorous style charmed us, whilst the scientific matters adumbrated were positively exciting. His contribution to the Symposium will certainly be long remembered.

Several lectures and papers dealing with surveys of natural products were given, and Dr Price's talk on Australian natural product research showed how well the opportunities have been exploited here, largely under

the guidance of Dr Price himself. Incidentally, may I say that the visits to laboratories, for example those to the John Curtin Laboratory and to the C.S.I.R.O. Laboratories, were all very much appreciated. The closer contact with the work which we obtained in that way was extremely valuable.

It is very difficult to summarize the chemo-taxonomic work, of which a remarkable example is Professor Erdtman's study of the constituents of conifers. His genial approach and obvious enthusiasm for his subject were quite infectious, and I think that Erdtman has made an almost unique contribution to the application of organic chemistry to taxonomy. It is a good example that should be followed by other similar researches in that kind of direction.

I have not yet mentioned the alkaloids. Of course, there were many papers dealing with alkaloid chemistry, and I would like to mention particularly the lecture of Professor Stoll, which described the applications which natural product research might have in industry. These repercussions may indeed be important, but Stoll's work is just as academic (whatever that word means) as anyone else's. He has made extraordinarily valuable and unique contributions to the chemistry, for example, of the digitalis and ergot series.

Another thread which has been running through the Congress was that of biogenesis, or relations of structures. Professor Birch, originally a Sydney student, and later a Professor here, gave many interesting further examples of the use of isotopic tracers in elaborating the hypothesis of the acetate condensations leading to natural products. But I think that the lecture of Dr Cornforth was another extremely important event in the Symposium—one of the real highlights.

The way in which Cornforth was able to describe the complete story of the synthesis of the iso-pentane skeleton, and then, for example, that of squalene, and through lanosterol to cholesterol and similar compounds, was quite remarkable. It was an extremely well prepared lecture, and of very great value to all of us. We admired the way in which the lecture was delivered, and found the matter, especially that which was contributed by Cornforth himself, quite fascinating. May I take this opportunity to say that Dr Cornforth was chiefly responsible for the successful termination of the first synthesis of the tetracyclic skeleton of the sterols which was effected in my laboratory at Oxford.

The scientific value of a symposium such as this is not wholly concentrated in the contributions. The opportunities it affords for personal contacts and discussions are also exceptionally valuable. That, I think, is part of the true *raison d'être* of a symposium such as this. It has been without question the most successful which I have ever followed. Never before has there been a symposium, concentrated on this section of organic chemistry, in which so many really significant papers have been delivered. Clear evidence of the enthusiasm of organic chemists in the last twenty years has been presented. The resurgence of interest has evidently been connected with the powers conferred by new techniques, which investigators have been as quick to adopt as the delays in delivery of apparatus permitted. We have had the great advantages conferred by new methods of separation including the ordinary methods of chromato-

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graphy on paper or column, partition chromatography, vapour phase chromatography, and Craig separators. Naturally, the micro-methods, of analysis and manipulation, and the new physical methods of examination of the products have taken much of the tedium from our bench work and freed us for the harder tasks. The availability of isotopes has enormously stimulated interest in biogenesis because this can now be studied experimentally, instead of from the conjectural point of view; all these things have come together to produce a flood of research, of which we have had the clearest evidence in this Symposium. It has, therefore, been a most significant occasion, and we hope that it will be repeated, as is promised, in Czechoslovakia in 1962.

Finally, as there may not be another opportunity, may I say something not directly concerned with an estimate of the value of the Symposium? I want to refer to our President, Sir Alexander Todd. It would be presumptuous, again, for me, and impertinent, to discuss his Presidential Address: that is not, for my present purpose, a part of the symposium which I have attempted to cover. It was an inspiring review, and we all thoroughly enjoyed it. However, I do want to thank Sir Alexander Todd for acting as President of this Symposium, and also for the way in which he has assisted everybody in their various tasks. There is no question but that the success of this Symposium has been in large measure ensured by his Presidency.