

## SECTION I: POLYSACCHARIDES

### INTRODUCTORY REMARKS BY THE HONORARY PRESIDENT OF THE SECTION

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The Scientific Programme Committee has asked me, as honorary section president, to present my views on polysaccharide chemistry, past and future. This I do with pleasure. The past I can vouch for—the future I can only guess at. Just 30 years ago E. L. Hirst accepted the Chair of Chemistry at Bristol University, U.K. I had just obtained the Ph.D. degree and was fortunate in that he invited me to come with him. At that time polysaccharide chemistry was in its infancy. The following figures show how this branch of chemistry has grown. In the American *Chemical Abstracts* Decennial Index (1937–1946), references to polysaccharide chemistry covered 2 pages, *i.e.*, about 480 references. References to starch covered five pages (1200 references), and those to cellulose and its derivatives, 20 pages (4800 references). A total of 6480 references, including patents, in a ten year period. During 1947–1956 references to polysaccharides covered  $6\frac{1}{2}$  pages, *i.e.* 1360 references, and the total number of references to cellulose and its derivatives, starch and polysaccharides was 10 640. During the period 1957–1961 (5 years) the references have doubled to about 9360 including 1680 on polysaccharides (many on muco-polysaccharides). This is an average of 2000 references per year, nearly six a day. The increase was due, in part, to the growing interest of biologists and biochemists in polysaccharide chemistry and to the growth of science in the U.S.S.R. and Japan. Who can hope to read all of these publications, even if only in abstract, and still get some bench work done? It will be noted that I have not included the nucleic acids, although they could also be considered as polysaccharide derivatives.

One of E. L. Hirst's interests was in the biological origin of the sugars. A hypothesis advanced was that pentoses resulted from hexuronic acids by decarboxylation. To test this hypothesis he decided to examine the structures of complex polymers which were built up of pentose, uronic acid and hexose residues. This was the beginning of a systematic chemical analysis of gums, mucilages and pectins. It soon became clear that the available methods, for a quantitative analysis of the methylated sugars resulting from hydrolysis of a methylated polymer, were inadequate.

When I first became interested in research I remember asking a graduate student what sort of research work was done in polysaccharide chemistry. The disgruntled reply was "All you do is methylate and hydrolyse". However, as is usually the case in times of depression and frustration, a new technique—paper chromatography—was developed and applied to the separation of carbohydrates, by Partridge. This put colour and glamour into carbohydrate chemistry and, more important, the purity of fractions of sugars and their derivatives could be assessed very quickly and on very small quantities. These are the advances I wish to emphasize—speed and the use of micro techniques; ever quicker and ever smaller. In 1936 a student might take 2–3 years to determine the chain length of starch using 50 g of polysaccharide. Now the operation can be carried out with greater accuracy in 3 days using 50 mg or less. Moreover, the present-day carbohydrate chemist knows that starch is a mixture, whereas this was a matter for dispute in 1936.

About 1939 we investigated the structure of certain plant gums by the methylation–fractional distillation procedure. A few years ago I had the opportunity of examining these fractions using paper chromatography and I was horrified to see how impure some of them were. I fear that some of the earlier work should be repeated, from a quantitative angle at least, and I am happy to see that this is now being done.

The next techniques used by polysaccharide chemists were periodate and lead tetraacetate oxidations, from which was developed the elegant Smith degradation procedure. These methods gave much new evidence, ambiguous in some cases and unsatisfactory in others. Nevertheless its use gave further information and enabled ideas on polysaccharide structure to be checked on a micro scale.

Enzymes were also employed to break down polymers and to isolate smaller fragments which were not obtainable by other methods. This procedure is open to some criticism, because of possible resynthesis, but it is perhaps superior to acetolysis techniques and partial hydrolysis by acids. The use of synthetic "enzymes" of the type used by T. J. Painter has now been developed.

It soon became clear that many polysaccharide preparations were mixtures and physical procedures were developed to facilitate the fractionation of these polymers. Paper electrophoresis, Tiselius type electrophoresis, ultra centrifugation, immuno-electrophoresis and other techniques were developed in order to test the homogeneity or, more usually, the lack of chemical and physical homogeneity of polysaccharide preparations.

Now gel electrophoresis, using both aqueous and non-aqueous solutions, gas liquid chromatography and mass spectrometry are used as means of separating and analysing polymers and their fragmentation products on an ever smaller scale. In 1948 W. H. Wadman built the first fraction collector to be used in conjunction with a cellulose column. This apparatus was made, in part, from a bomb release mechanism bought, *by weight*, from war surplus suppliers. Carbohydrate chemistry had become automated. Despite all these advances, with the possible exception of cellulose, it is doubtful whether the complete structure is yet known of any polysaccharide.

What of the future? The time is rapidly approaching when polysaccharide

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analysis will be fully automated. Some 27 years ago Professor E. L. Hirst and I tried, unsuccessfully, to follow the fractional distillation of methylated sugars using an automatic collecting apparatus in which the refractive index could be followed without releasing the vacuum. It seems to me that it should now be possible to devise, *at a cost*, an automated apparatus which would check the purity of a polysaccharide and fractionate it if necessary. It would also analyse its sugar composition, periodate oxidize a portion of it, acetylate and/or methylate it and refractionate the methylated derivative. The determination of the physical constants of the fractions, such as the n.m.r. spectrum, viscosity, etc., and hydrolysis of each fraction could also be automated. The identities and quantities of the sugar derivatives, determined in each fraction by a finger print technique or by mass spectrometry, could all be recorded automatically at the end of the sequence. Dr. S. A. Barker and his colleagues have worked out other procedures in which one sugar at a time can be removed and identified and you will hear more about this later.

The finger print technique involves the preparation of every one of the possible methyl ethers of all the known common sugars. These are examined under standard conditions, by paper chromatography, as their reducing sugars, or by thin layer chromatography and by gas-liquid chromatography as their methyl glycoside acetates, as the glycitol acetate derivatives and as the lactone acetate or tri- or dimethyl silyl derivatives. Each compound is expected to have a characteristic pattern of colour and rates of movement and the results would be scanned, stored and analyzed in the computer. So far D-glucose, L-arabinose, and D-xylose derivatives have been prepared and could be utilized in this fashion. To build such an apparatus and to pay for technical assistance would be very expensive but I believe that the knowledge is now available to make it. Technologies which allow the landing of television transmitters on the moon should have no difficulty in solving this problem.

Great progress has been made in the determination of the structure of polysaccharides. The biological origin and function of these polymers, however, has only attracted attention, mainly from biologists, within the last few years. Little is known of the biosynthesis of complex polymers such as gums and mucilages and it is likely that big advances will be made in this field and in the chemical synthesis of polysaccharides within the next few years.

Our speaker this afternoon, Dr. G. O. Aspinall knows as much about the structure and chemistry of gums and mucilages as anyone. He started as an aromatic chemist but since 1948 has been engaged in studying the chemistry of carbohydrates. He has done a lot of work on the use of the gas-liquid chromatographic apparatus in the analysis of methylated sugars obtained from gums and mucilages. He is known internationally for his work on polysaccharides and has given lectures, by invitation, in East and West Europe and at centres in North America. Today he will indicate the advances that have been made, mainly by his colleagues and himself, in this branch of polysaccharide chemistry, at the University of Edinburgh, and he will show that some order can be developed from apparent chaos.