HAWORTH MEMORIAL LECTURE*

The Consequences of Some Projects Initiated by Sir Norman Haworth

By M. Stacey
DEPARTMENT OF CHEMISTRY, UNIVERSITY OF BIRMINGHAM, BIRMINGHAM B15 2TT

It is a very great honour indeed for me to receive the first Haworth Memorial Medal of the Chemical Society, and to be invited to deliver the Inaugural Lecture.

It is a matter of great personal regret that Lady Haworth cannot be with us but she now has joined her sons, Dr. James Haworth and Mr. David Haworth, and their families in Canada. Sir Norman always emphasized how much his successful career was due to Lady Haworth's support and to his happy family life. Lady Haworth and her family have been most generous in helping to endow the Memorial Lecture. I would on behalf of the Chemical Society express gratitude to them and to the many pupils and friends of Sir Norman who gave so generously to the Haworth Memorial Fund. The quite splendid Medal and the Lecture will inspire carbohydrate chemists in the international field in the years to come and I am delighted that its award will be associated with the enthusiastic and expanding Carbohydrate Group which I inaugurated five years ago. It is most appropriate that the first lecture should be given in this fine new Chemistry Department created by Professor E. J. Bourne, also a pupil and colleague of Sir Norman.

I was a student, research student and colleague of Sir Norman for over a quarter of a century and even in the periods when I was away from Birmingham, he expected and indeed got frequent reports of my work! Now after a further period of two decades his powerful presence is still with me and I have endeavoured to ensure that his name lives on in Birmingham in the Haworth Laboratories and Haworth Lecture Theatre. As with Sir Edmund Hirst before me, I came under the influence of his strong personality, and like Sir Edmund, I was able to work in full harmony with him. I probably came closer to him than did any of his other senior colleagues and I think I understood him better than anyone. He possessed a clear and brilliant mind; he was gifted with remarkable vision and had unusual administrative powers and ability to plan with military precision. He made decisions rapidly and nothing he ever did was left to chance, and although perhaps he was a little too autocratic to be liked by everyone, he was always admired and highly respected.

* Delivered on 5th April, 1971, at Royal Holloway College, University of London.

1 Introduction

In this lecture I intend to show how he created new areas for research in the carbohydrate field and to indicate the developments therein during the past quarter of a century—many of these developments being done by his own pupils.

The Chemistry Department, much of which was housed in Army Huts, which he inherited in Birmingham in 1925 from Sir Gilbert Morgan, was spacious and well equipped, so that there was no delay in his researches when he brought his team of pupils from Newcastle. There were very large classes of subsidiary students, mostly Medicals and Engineers—running into the hundreds even—but these could be handled by three or four lecturers and two teaching scholars (of which I became one in 1929). The Honours Chemists numbered 20 in each year and there were 20 or so members of the Research School, almost all engaged in carbohydrate studies.

Haworth later told me he had three immediate objectives when he first came to Birmingham: (i), to create a lectureship so that Dr. Edmund Hirst could join him; (ii), to create a chemical analytical system so that he could work on a much smaller scale than hitherto; and (iii), to develop physical techniques, especially the application of *X*-ray crystallography. As a result (i) Hirst was installed in Birmingham within two years, (ii) H. D. K. Drew was immediately sent to Professor Pregl in Gratz to learn microanalysis, and the first Kuhlman balance arrived for this work at the end of 1926, ('I beat my friend Heilbron to it' Haworth often boasted), and (iii) Haworth enlisted the help of Mr. James Young of the Physics Department to help in the *X*-ray crystallographic project, but later getting impatient, approached Braggs who sent in 1928 a quiet young man from Bristol frequently mistaken for a first-year student, by name of E. Gordon Cox. The consequences of the fulfilling of Haworth's first three projects were remarkable.

One of the first of the physical techniques which he encouraged was the study of Optical Rotatory Dispersion (o.r.d.), which although laborious, was usefully continued by Hirst and C. E. (Wee Georgie) Wood. Modern computer applications have made o.r.d. a most useful technique in the carbohydrate field.

Early in 1930 there was great excitement in the laboratory, for the Professor had thought up a project whereby he could demolish some of the views of the celebrated Dr. C. S. Hudson, a notable U.S. rival in the carbohydrate world, on the relationship of structure to the optical rotations of sugars. These referred particularly to the structure of a supposed new form of mannose having a 1,5-ring found in derivates of 4-glucosidomannose obtainable from cellobiose through cellobial. He organized a crash programme using a team of about six workers (to the team he gave the name 'a syndicate') and the work was completed within a few weeks. He neatly used the acceptance by Hudson that β-methyl-maltoside* gives rise by enzyme hydrolysis to β-methyl-glucoside without ring change. Consequently it was to be expected that 4-glucosido-α-methyl mannoside would yield by enzyme cleavage Hudson's 'hypothetical' α-methyl mannoside $[\alpha]_D$ +125° since this is the glycoside of the new form of mannose to which

* Using the nomenclature of the 1930's.

Hudson had given the 1,5-ring. The syndicate synthesized and investigated the chemical behaviour of 4-glucosido-α-methyl mannoside and 4-galactosido-α-methyl mannoside—compounds in which the 4-position in the mannose unit is bound in the disaccharide linkage with the result that the mannose unit cannot possess a 1,4-ring. Both substances were hydrolysed by emulsin to yield the ordinary known form of α-methyl mannoside with the pyranose ring. Haworth put these views to Hudson at a famous confrontation with Hudson in Liege in 1930 with the warning that Hudson's principle of optical super-position cannot be uniformly applied throughout the sugar group. It is to Hudson's great credit that he accepted these results and the two immediately became great friends. Haworth always had great admiration for Hudson and Isbell and colleagues at the Bureau of Standards in Washington.

Haworth's 'syndicate' system or team effort was one of the first to be used in Chemistry and it was shown to great advantage later in the Vitamin C work and in the wartime Atomic Energy project.

In considering all Haworth's ventures one must begin with *methylation*, which with acetylation dominated the Birmingham Carbohydrate School for years. Haworth's application of methylation followed that of Purdie, Irvine, and Hirst, but it was his use of sodium hydroxide and dimethyl sulphate which made so readily accessible a whole range of crystalline well-characterized methyl ethers and their oxidized derivates (see, *e.g.*, Figure 1).

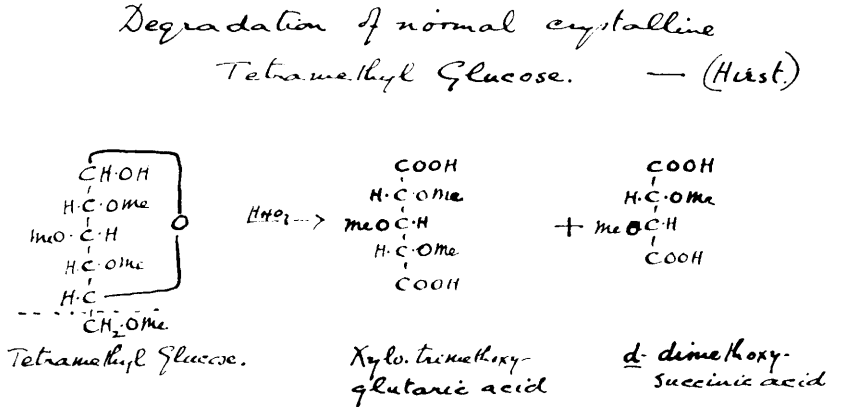


Figure 1 *Typical slide from 1926 in Haworth's handwriting*

This led to the determination of ring sizes of sugars and thus to the elucidation of the structures of the di-, tri-, oligo- and above all of the poly-saccharides. It led to the remarkable, and now classical story of gamma-(furano)-lactones and delta-(pyrano)-lactones and to the establishment of pyranose and furanose forms of sugars. One of the crowning triumphs of the methylation technique was the development of the polysaccharide end-group analysis technique—by estimating

the proportion of 'tetra' methyl sugar to trimethyl sugar in the hydrolysis products of a fully methylated polysaccharide. It is interesting to recall how this idea originated. The first heteropolysaccharide examined at Birmingham was varianose, a mould polysaccharide which was prepared by me in 1930 in Raistrick's laboratory. This was methylated readily and when in 1931 the methyl ether was hydrolysed and separated there was obtained a high proportion of tetramethyl-glucose, and no other glucose derivative was present. 'By Jove' said Sir Norman, 'this must come entirely from a chain end, now I've got a job for our German friend'—he being Hans Machemer whose quite epoch-making papers with Haworth on cellulose 'end groups' appeared in 1932. The quantitative fractional separation of the methyl ethers derived from polysaccharides using the useful Widmer column not only gave the measure of lengths of chains but also indicated where branch points occur.

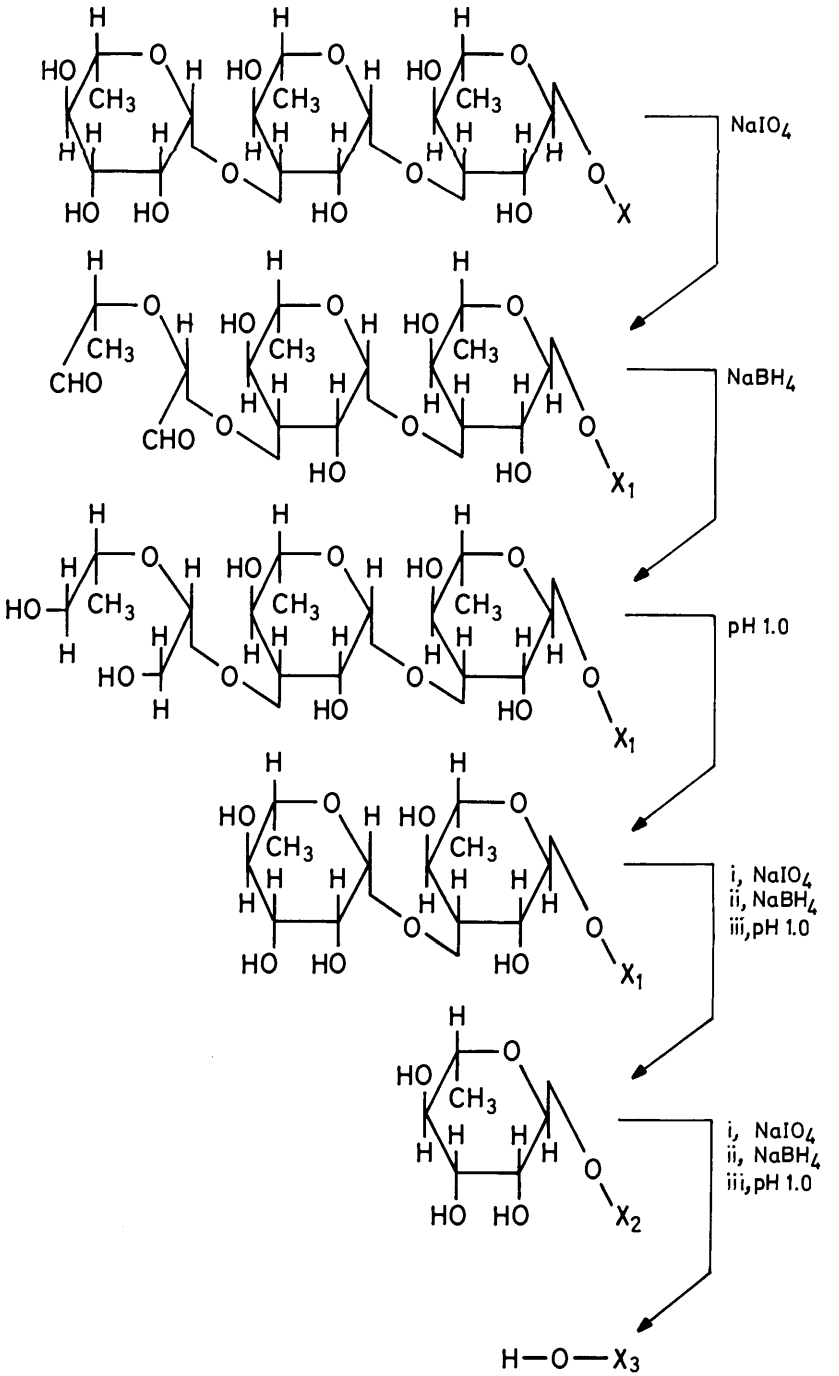
It should be appreciated that in the early days of the studies on methylated polysaccharides it was considered that the isolation of mono- and dimethyl-glucoses, for example from hydrolysates of methylated starch, was due to the failure of the methylation technique to methylate fully the polysaccharide. When it was shown by exhaustive treatment that methylation really was complete and that the partly methylated derivatives arose from single and multi-branched points, the concept of branched chain structures was born. Our conception of the structures of starch and glycogen was revolutionized, and the methylation methods have been applied as a standard technique right across the whole vast range of complex polysaccharides, especially with plant gums and sea-weed and bacterial poly-saccharides. Many other techniques, *e.g.* enzymic, oxidation, linkage analysis, *etc.* have since adequately backed up the methylation method (Scheme 1).

2 *X*-Ray Crystallography

Haworth's concepts of the pyranose and furanose forms and ring shapes of the sugars, glucose and cellobiose in particular, were seized on by Sponsler and Dore who attempted to fit the ideas into the spacings of the *X*-ray diagrams of cellulose.

They considered that cellulose could best be represented by cellobiose units joined by true ether linkages (eight glucose units in all). In 1928 however, H. Mark and K. H. Meyer adopted the Haworth formula for cellulose and fitted in their measurements of the cell dimensions of ramie cellulose to a 6-glucose unit system and their work (as outlined somewhat cautiously in Haworth's book) gave him great satisfaction and encouragement. Haworth mentions that he met Meyer at the Manchester Meeting of the Chemical Society and persuaded him to under-take these studies.

Cox's pioneer work on the *X*-ray crystallography of sugars was advanced most appropriately in 1932 in time to apply the single-crystal rotation method to Szent Gyorgy's hexuronic acid (Vitamin C or 'Godnose'). He wrote 'This suggests that the hexuronic acid has a ring structure with fewer groups projecting out of the ring than a normal carbohydrate and contains double bonds, possibly in carbonyl groups'. This whole remarkable collaborative work on the first vitamin



Scheme 1 *Sequential chemical degradation of pneumococcus type II polysaccharide*

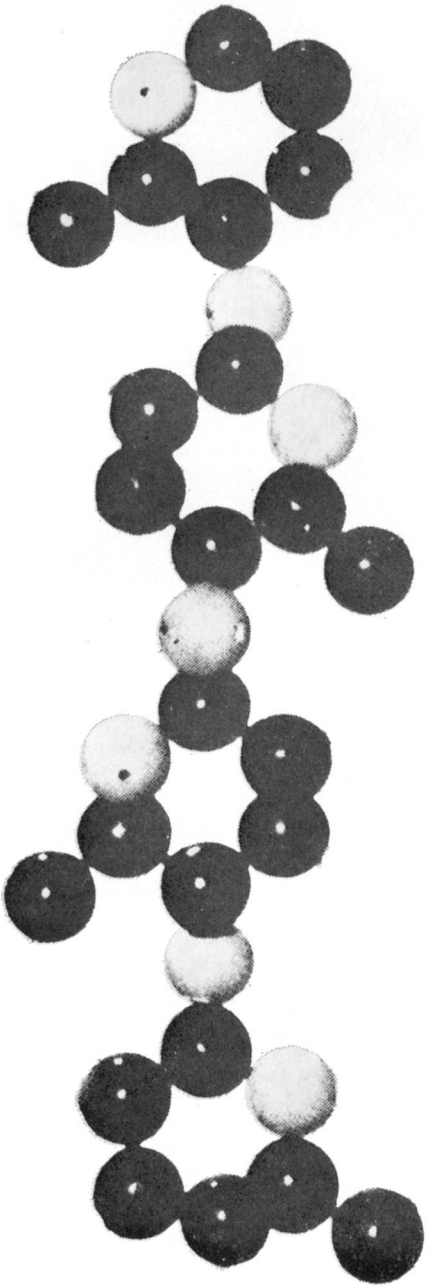


Figure 2 *Haworth model of cellulose*

to be identified and synthesized was a major triumph for the Haworth–Hirst Birmingham School. Dr. Beavers in Edinburgh and Professor Jeffreys in Pittsburg have considerably extended the application of *X*-ray crystallographic methods to the sugars. With Swiss improvements this work has led to the significant Vitamin C industry. Haworth certainly anticipated Linus Pauling in claiming that Vitamin C was a cure for all ills for he regularly consumed large quantities and proclaimed its virtues.

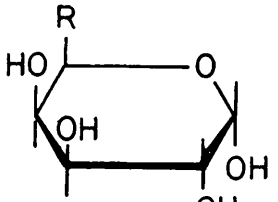
3 Conformation

As far as can be ascertained, Haworth was the first man to introduce the term 'conformation' into organic chemistry. Dr. R. S. Tipson has provided me with the following quotation from Edgar Allen Poe's *Beranice*, 'I held them in every light, I turned them in every attitude, I surveyed their characteristics, I dwelt upon their peculiarities, I pondered upon their conformation.' Although Haworth often quoted from the Poets, *e.g.* Milton, Robert Bridges, *etc.*, I doubt whether he got the word from this source, but certainly he was always pondering on the sizes of his now well-established ring systems and he was fascinated by the wide differences in the ring stabilities, and there is no doubt at all that he could think in three dimensions. He studied the work of Sachse very carefully. He was intrigued by the idea of strainless rings and appreciated the importance of measuring the 'angles between adjoining atoms'.

Very early he brought carefully constructed models to his aid—literally carrying a box of these around with him (see *e.g.*, Figure 2). He tended to speak of the 'conformation of models', but he was very much aware of the possibilities of the pyranose rings, for example, existing in 'puckered forms', planar and boat and chair forms. He was equally well aware of the fact that there would be differences in strain in these puckered ring systems. He appreciated that these forms would bring groups attached to the ring carbons more closely together and interactions would thereby be made more ready. His various papers on orthoesters showed this mode of thinking and he frequently spoke of 'bulky shielding groups', anticipating the idea of neighbouring-group reactions.

In considering the boat and chair forms he worked out the various ways of arranging the H and OH groups and he writes concerning the 'boat' form—'Such a choice can only be an arbitrary one but the selection of this model facilitates the closest possible packing for β-glucose units though not for α-glucose. A new aspect of stereoisomerism arises, however, if these assumptions be made in that there are evidently mirror forms of the ring and this produces an entio-morphism quite independently of the asymmetrical arrangement of the addenda of the ring.' Then in showing how the models relate to the Sachse principle, he predicted that there will be 16 possible arrangements for '*d*- and *l*-glucoses'.

Further developments in this way of thinking came from Hann, Merrill, and Hudson, who noted that groups of pyranose sugars have closely related chemical and physical properties. These were termed homomorphous since they have the same configurations of the atoms which form the ring, *e.g.* (1).



(1)

(1; R = H, CH_3, CH_2OH, or —CHOH—CH_2OH)

These compounds indeed have the same ring 'conformation'. Isbell advanced the conception of conformation and anticipated the idea of axial and equatorial attachments to the ring.

Crystallization of the conformational analysis ideas came from the famous paper of Hassel and Ottar and they suggested that their ideas obtained from work on cyclohexanes could be applied to the sugars. The really big step forward came from Reeves in 1949 and 1950, who noted the importance of cyclo-acetals, -ketals, -esters, borates, and carbonates, *etc.* He used cuprammonium complexes to study optical properties and conformation. He assigned conformation and provided the terminology. He wrote—here he could have been echoing Haworth —'Knowledge regarding shapes which sugar molecules take in solution is of importance to an understanding of many of their chemical reactions. Shape is probably the determining factor in all cases where a reactant makes even temporary contact with groups attached to more than a single carbon atom' (Figure 3). I must comment that Haworth always regarded Reeves as a genius.

These concepts of molecular shapes have been developed by Bentley, Whiffen, Lemieux, *etc.* and have been concisely described in the book on Conformational Analysis by Allinger, Morrison, and Angyal (Eliel).

Conformational analysis in the steroid field has been developed by Derek Barton and the significant consequence was the award jointly to him and to Hassel of the Nobel Prize for 1969!

Haworth was always fascinated by biological systems and indeed by all matters medical. As a member of the Faculty of Medicine he was always very friendly with its senior members, notably Sir Leonard Parsons. Although it was often rumoured that he and other leading organic chemists of his day were not sympathetic to Biochemistry this was quite untrue. He sent many of his students to seek their careers in the new departments of Biochemistry, *e.g.* J. A. B. Smith and J. V. Loach to Liverpool, C. G. Anderson and myself to Raistrick at the London School of Hygiene, and he called upon Sir Gowland Hopkins, PRS, to preside at the opening of his new Hills Laboratories in 1936. In the early and difficult days of the Second World War he quickly realized that many of the Biology and Brewing students would be called up to the Forces, so he had them

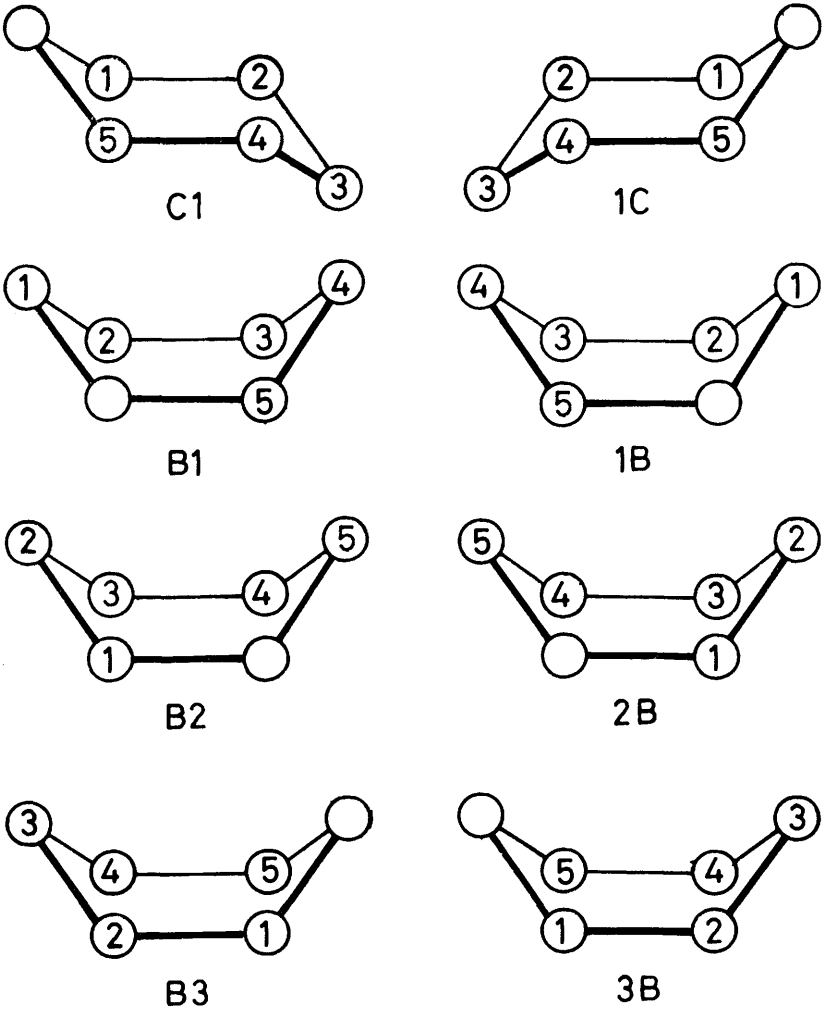


Figure 3 (*after Reeves*). *The eight pyranose strainless ring conformations and the corresponding symbols. By convention the heavy lines represent the sides of the three-dimensional figures nearer the observer. The numbered circles represent carbon atoms 1—5, the unnumbered circles the ring oxygen atoms.*

transferred and reserved as chemists remarking, 'we want no more Moseleys for the Trenches'. This action was misunderstood at the time but it was effective Haworthian technique and a number of able men benefited from his enterprise.

4 Enzymic Studies

Glycosidases.—From the beginning of his career Haworth had a profound interest in enzymes, though at a later stage he chose to interpret the results of enzyme action with some caution. He introduced in 1926 the use of Urease into the 2nd MB. classes. He made use of glycosidases in his studies on disaccharides and wrote in his book in 1928, 'Thus maltose has the α-configuration inasmuch as this sugar is completely hydrolysed by maltase which is the specific enzyme for the hydrolysis of α-methylglucoside. Cellulose is hydrolysed by emulsin which is specific for β-methyl glucoside while lactose undergoes scission with lactase which is specific for β-methyl galactoside'.

Always cautious, however, Haworth was quick to point out that these structural relationships had been confirmed by chemical and optical rotational methods.

Perhaps the most important consequence of these early disaccharide hydrolytic enzyme investigations is what we term the specific enzymic induction method for determining polysaccharide structure.

Synthesizing Enzymes.—In early studies on bacterial polysaccharides, especially dextran, we had noted that polysaccharides appeared to be formed when the amount of cellular material was scarcely detectable and Haworth had remarked that this could be the work of enzymes working outside the cells. He often commented that amylase action might be reversible so that when he learned of C. S. Hanes's synthesis in Cambridge of a so-called starch by phosphorylase he was tremendously excited, particularly when Hanes invited him to study the synthetic material. With Stanley Peat, he immediately put students, including E. J. Bourne, onto these investigations. Confirmation of Hanes's work was rapid and dramatic and it paralleled that of Coris' Nobel Prize-winning work on synthetic muscle glycogen. It was only just before this time that the separation of starch into the amylose straight-chain component, which stained blue with iodine, and the amylopectin branched chain component, which stained purple with iodine, had become evident. The synthetic material was shown to be an amylose and from thence Haworth's group searched for the enzyme which could synthesize amylopectin. Success in the hands of E. J. Bourne came quickly and the 'Q'-enzyme which was able to break the 1→4 linkages in amylose and make some 1→6 branch point links to form highly branched amylopectin, was obtained. This 'Q' enzyme was later obtained in crystalline form by Gilbert, an event which gave Haworth the greatest satisfaction. It should be noted that the Coris' work on their branching enzyme, which gave a glycogen type material, was a source of satisfaction to Haworth.

Further success were achieved in the use of enzymes to degrade amylopectin to form 'limit' dextrins and by the discovery that enzymic action is blocked at branch points in the structures. The consequence was the transferring of all the enzymic work by Peat to Bagnor and the discovery by Peat, Whelan, and their colleagues of a whole range of degrading enzymes, R and Z enzymes, which now continue to reveal the remarkable detail of starch and glycogen branched structures.

The major development of the polysaccharide synthesizing enzyme story has been the Nobel Prize-winning work of Professor Leloir and colleagues, who discovered the tissue enzyme system which builds up glycogen by transference of glucose from the nucleotide uridine diphosphate glucose, and such enzymes have been discovered for the synthesis of a wide range of polysaccharides. This work has tended to overshadow earlier work on amylosucrases, levansucrases, *etc.*; modern industrial applications of amylases would have delighted Haworth.

There is still much to be done on the chemistry, activity sites, *etc.*, of polysaccharide-synthesizing enzymes, especially those concerned with the build-up and break-down of cellulose, tissue polysaccharides, *etc.*, but the foundations have been well laid.

5 Studies on Anhydrosugars

Haworth was always fascinated by anhydrosugars and spent hours manipulating his models of these to show the possible effects of his chair and boat forms, as compared with flat-ring forms, on many reactions, known and predicted. It amused him to tell new research students to make 1→6 anhydroglucose by 'alchemical' means by heating glucose in an ancient retort. This he would call a 'proximity' condensation reaction, and would elaborate his views on the reactivity of 'building groups' and on the value of stable blocking groups such as methyl ethers.

His first venture into the anhydrosugar field was shown in the publication with Hirst and Bodycote on the conversion of '2-*p*-tosyl-β-methyl glucoside' into the methyl-epi-glucosamine of Fischer, Bergman, and Schott. Methanolic ammonia treatment of the tosyl compound gave an aminoglycoside and in the authors' words, 'the formation of the aminoglucoside from this material almost certainly involves the intermediate stage of an anhydro-compound which is possibly, in view of the following evidence, the 2:3-anhydromannoside', an idea previously suggested in both E. Fischer's and P. A. Levenes' laboratories. A 1:2-anhydroglucose (the Brigl compound) was known previously but this was unstable in water.

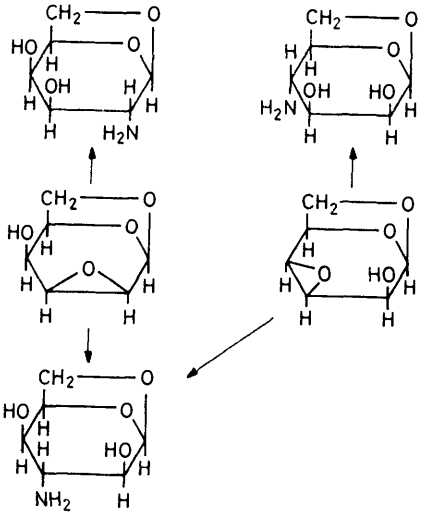
The epiglucosamine could have been a '3-aminoaltroside or a 3-aminoalloside'. The Birmingham workers next showed that treatment of a dimethyl 2:3-anhydro-β-methylmannopyranoside gave on treatment with sodium methoxide equal parts of 2:4:6-trimethyl-β-methyl-D-glucoside and 3:4:6-trimethyl-β-methyl-D-altroside. The epiglucosamine was shown to be the altrose derivative.

Haworth was now getting very interested in my own team's work with immunopolysaccharides and some of the bacterial polysaccharides which contained amino-sugars and he quickly turned to the opening of anhydro-rings with ammonia to solve problems of constitution of the only two known amino-sugars, 2-amino-glucose or glucosamine (2-amino-2-deoxyglucose) and '2-aminogalactose' or galactosamine (2-amino-2-deoxygalactose). He and Peat and colleagues settled the question by treating 2,3-anhydro-4,6-di-*O*-methyl-β-mannoside with ammonia to give a '2-aminoglucose' derivative and a '3-aminoaltrose' derivative. The latter had previously been synthesized and was of known structure. The former

was identical with the derivative of natural glucosamine, showing it to be a glucose and not a mannose derivative. Direct confirmation of this was shortly afterwards obtained by the *X*-ray crystallographic analysis of Cox and Llewellyn.

The structure of glucosamine as 2-amino-2-deoxy-D-glucose was confirmed by synthesis of suitable derivatives which allowed of 'no dubiety'.

One of the best examples of the application of the technique was the constitutional synthesis of chondrosamine. This work (Scheme 2) and related work to give deoxy-sugars has been of the greatest importance in the field of the



Scheme 2 *Synthesis of 2-amino-2-deoxygalactose*

nitrogen-containing immunopolysaccharides. Thus we have had more recently the identification and synthesis of two new amino-sugars in the Type V Pneumococcus polysaccharide.

Many of the commercially valuable antibiotics contain amino-deoxy-sugars and deoxy-sugars. Many papers on deoxy-sugars have been published from the Birmingham work.

Studies on the deoxy-sugars themselves have had a profound effect on structural studies of deoxyribonucleic acids.

6 Hexuronic Acids

Haworth became interested in the hexuronic acids in the early 1930's probably because he was friendly with Dr. John Pryde who with R. T. Williams was busy studying the structure of urinary glucuronides—so-called de-toxification products of various chemical substances such as menthol when taken by mouth. These workers' attempts to identify methylated derivatives of glucuronic acid gave 'glucuralones' which were difficult to characterize. In addition the specific

polysaccharides of the Pneumococcus were being shown by Heidelberger and Goebel to contain hexuronic acids. Haworth was also interested in a general way in the acidic substances present in pectic substances, gums, the microbial polysaccharides, hemi-celluloses, mucillages, and sea-weed polysaccharides.

The first substance chosen for examination was a so-called 'aldobionic acid' from gum arabic since complexes with this constituent in the molecule reacted immunologically with several of Heidelberger's Type specific polysaccharides from the Pneumococcus. Close structural and immunological relationships were quickly established and the consequences for all these studies have been tremendous. They were carried forward in many areas by Haworth's pupils, notably for the sea-weed polysaccharides. These with the pentosans have been extensively studied in Edinburgh by Sir Edmund Hirst and the Percivals. The immuno- and muco-polysaccharides, especially those from mould and from animal tissues, have been examined in Birmingham and elsewhere. Similarly plant gums and pectins have been extensively studied by the Schools of F. Smith in the U.S.A., Sir Edmund Hirst, and J. K. N. Jones in Canada.

It is noteworthy to recall that Haworth occasionally got very excited about what he called 'pioneer' discoveries. Notable among these were the discovery of 'anhydro-1-galactose' by W. G. M. Jones in agar, my own first chemical synthesis of glucuronic acid, F. Smith's unsaturated derivates of D-glucuronic acid, and the simultaneous discovery of L-fucose in gum Tragacanth by Fred Smith's group, and my discovery of this rare sugar in the blood-group polysaccharides.

This kind of event would call for yet another exhortation—'Well now, this is good but push on, push on, pioneer your way along' during the daily Haworth visitation. It is interesting, incidentally, to note that Haworth did predict the present commercial importance of the sea-weed polysaccharides (the alginates) and that of citrus and apple pectins.

The discovery of L-fucose residues in the blood group substances has had quite remarkable consequences in elucidating the specialist sub-groups and in stimulating research generally in this field.

7 Sucrochemistry

In the early 1940's Government advisers had become concerned with finding new industries for the bursting populations of our former Colonies and Dominions. The ill-fated peanuts project of Africa and the yeast protein factory in Frome, Jamaica, were efforts that went astray.

Following a visit to the West Indies by Sir Robert Robinson and Prof. (later Sir John) Simonsen, Haworth was called in to advise. He assisted in the setting up of the Colonial Products Research Council of which Simonsen became Director. Haworth agreed to undertake at Birmingham a major investigation into the chemical utilization of cane sugar, thereby hoping to create chemical industries based on sugar as the raw material. We already had a small group working on 'ropy' fermentation products of cane sugar—notably dextrans and levans originally designed to give new kinds of cheap plastics. L. F. Wiggins became the leader in Birmingham of the chemical project which aimed at producing a

number of basic materials in maximum yield, *e.g.* sorbitol, mannitol, lactic acid, laevulic acid, and ω-hydroxymethylfurfural. The dextran work which was financed by Mr. T. Usher of East Anglia Chemical Co. was successful in producing a blood plasma substitute while Wiggins's group produced many papers and patents on work capable of industrial development. Wiggins went out to Port of Spain, Trinidad, to set up the Sugar Technology Institute there while work continued at Birmingham—somewhat spasmodically and mainly under support from the Sugar Research Foundation of New York.

The latest publication from this Foundation shows the extent of the fundamental work which has since been done world wide, but there is comparatively little industrial use to show as yet. There are, however, signs of a revival of interest and sucrochemistry must be continued on the industrial scale.

Another venture with which Haworth was closely associated as founder and consultant with Sir Robert Robinson and Sir Eric Rideal, was the Natural Rubber Producers Research Institute at Welwyn. The most important thing he did to get this going was to extract Mr. John Wilson, C.B.E. from Triplex Glass Co. in Birmingham and to make him the director. This has undoubtedly been one of the most successful and important Research Institutes in this country. Sir Norman's remarkable capacity for selecting outstanding men for key positions was equalled only by that of Mr. Wilson in a later period.

8 Haworth's Industrial Contacts

Before going up to Manchester University, Haworth had been in business with his father and brother who were engaged in linoleum design and manufacture so that it was natural that he should always be keen on industrial matters. Almost from its foundation in 1926, he was a Consultant to I.C.I. Dyestuffs, Blackley, and remained so till his death. He received very generous research grants for joint work with the Division on cellulose and on oxy- and hydro-celluloses. His greatest industrial contribution at this time perhaps was his work on waterproofing agents for cellulose (with R. J. W. Reynolds) which led to the 'Velanising process'. So many of his research students found their career at Blackley that at times some sections looked like an extramural arm of Birmingham University. It is to I.C.I.'s eternal credit that when he retired (reluctantly may I say) from the Mason Chair at Birmingham, I.C.I. retained him as Consultant with a higher stipend. This gave him great joy.

In the mid 1930's Sir Harry Jephcott invited him along with Professor George Barger to form a consultancy team to advise Glaxo, and a few years later I was invited to join them in time to take part in the scientific beginnings in Glaxo, particularly of their vaccines and antibiotics work and of their innovations in the important industrial steroids projects. Birmingham's Chemistry Department and Glaxo have remained close ever since. Haworth became in 1948 a Director of Dextran Ltd. of Aycliffe, the firm developed from our Chemistry Department to exploit carbohydrate fermentation products including the blood plasma substitute, but he died before he could really make his influence felt. Later the Company became part of Glaxo.

He was also a consultant from 1942 onwards to the Birmingham Chemical Company of Lichfield, later taken over by Staveley Industries. This Company took over our wartime process for the direct production of glucose from potatoes —a useful venture in its day.

He was closely concerned with the affairs of Dobbies Ships Instrument Manufacturing Co. of Glasgow with which Lady Haworth's family had a connection. He had a considerable part in founding Nelsons Silk Co. of Lancaster.

In the 1920's Sir Amos Nelson, a wealthy cotton yarn and cloth manufacturer of Nelson in Lancashire, decided that the end of the cotton era was in sight and that he would invest money in making the new artificial silks. With this in mind he founded Lustrafil Ltd., in Nelson, to manufacture Viscose yarn and took advice on the manufacture of cellulose acetate yarn. For the latter he approached Professor N. V. Sidgwick of Oxford, who recommended the appointment of Professor W. N. Haworth to act as a consultant for the project. Haworth consented to this and recruited C. F. Allpress, a former pupil of P. F. Frankland of Birmingham, and Dr. W. G. Sedgwick, lately one of his research students at Durham, to commence work on building and running an experimental cellulose acetate plant. Later Haworth recruited Dr. G. C. Westgarth, a pupil of his at Durham, and Dr. C. W. Long, one of his research students at Birmingham. Between them a process was evolved which was carried out on a large scale by Nelsons Silk Ltd., in a works near the River Lune in Lancaster.

Haworth took a great interest in the preliminary work, on the design and erection of the buildings (his brother was the architect), and later on, when the process had become viable, in the large-scale manufacture of cellulose acetate. The process used on the large scale for the recovery of glacial from dilute acetic acid, obtained during the acetylation of cotton linters, was covered by a British Patent taken out by Haworth. Thirty per cent acetic acid was mixed with potassium acetate, the acid combining with the potassium acetate to form a double salt KOAcHOAc. The solution was heated and under high vacuum water was removed leaving the dry double salt. When this was heated further to 200 °C and a high vacuum applied, strong acetic acid was distilled off, leaving the original potassium acetate available to deal with more dilute acid. This process involved the use of the largest stainless steel stills made up to this time. Before the discovery of stainless steel, Haworth was a great advocate of the use of large copper vessels wherever possible.

Haworth remained as consultant until the beginning of the Second World War, but unfortunately he died before he could see the final result of the early efforts, when Nelsons Acetate Ltd. was founded on the same site in 1950. This Company was concerned only with the manufacture of cellulose acetate, but of various types, from the rayon grade (54% combined acetic acid) up to the fully acetylated triacetate used for *X*-ray film. The production of cellulose acetate ceased at the works of Nelsons Silk Ltd., which became solely concerned with the spinning and processing of the yarn, whilst cellulose acetate was produced on a much greater scale at Nelsons Acetate Ltd., whose products were (and still are) sent all over the world.

Nelsons Acetate Ltd. was developed and started up by two of Haworth's old pupils, Drs. Westgarth and Long, and a little later Nelsons Silk Ltd. became joint owners of Nelsons Acetate Ltd. with the Hercules Powder Co. Inc. of New Jersey, U.S.A., who provided 'know-how' and certain key personnel, and Erinoid Ltd. of Stroud, Glos. who became a big customer for acetate for moulding powders. Later, Nelsons Silk Ltd. and Hercules became the owners of Nelsons Acetate Ltd. on a 50:50 basis, but after the Nelson Group had been taken over by Courtaulds Ltd. the ownership passed into the hands of them and Hercules. Nelsons Silk Ltd. is now part of British Celanese Ltd., also owned by Courtaulds Ltd.

Two other important projects for carbohydrate chemistry which largely owed their initiation to Haworth were the Advances in Carbohydrate Chemistry series—(now about to produce Vol. 25) and the Anglo-American Committee for Carbohydrate Nomenclature. His colleagues and students on both sides of the Atlantic have played, and continue to play, a big part in these throughout.

Finally, this lecture would not be complete without a brief mention of Haworth's work on the Wartime Uranium Project, which had as consequence the origin and development of the British Atomic Energy Authority and nuclear power. Late in 1939 Professor Oliphant casually mentioned to Haworth and me that he had been talking to Peierls and Frisch, then in the Faculty of Science at Birmingham, who had said that they had calculated that if a solid block of 80 tons of uranium metal was kept in one place, there would be enough neutrons generated to set up a chain reaction and cause an atomic explosion. Oliphant said 'You chemistry chaps ought to make this metal and its salts, measure all their properties, and give the mathematicians more data; perhaps only 10 tons would be needed'. When Oliphant left that day Haworth with great excitement said to me, 'This is it, this is the important war project we need, get in the whole Staff tomorrow and we will assign tasks. Afterwards I will go to the Cabinet and get the necessary funds.' He came back with a blank cheque and immediately the whole Department was put on to the project.

Haworth became Chairman of the Chemistry Panel of the original M.A.U.D. Committee and its successor Tube Alloys. The total Birmingham effort in the Departments of Mathematical Physics, Chemistry, and Physics in collaboration later with others such as Professor Simons' Group at Oxford and the Billingham and Widnes Divisions of I.C.I. Ltd. rapidly led to the Diffusion Process for separating the isotopes of uranium and to the remarkable Oak Ridge Plant and its products. Sir Norman did a particularly fine job in finding Senior Personnel for Oak Ridge and later for the Canadian Chalk River projects. Our Department played a big part in the foundation of Harwell. I was particularly fortunate in being able to deputize for him in much of this pioneer work and later to act as Consultant for Harwell, Risley, *etc.* As a consequence of the work on uranium fluoride I was able later to go forward and found our now famous School of Organic Fluorine Chemistry and to back this and the rest of the Department with the establishment of the equally famous School of Analytical Chemistry.

All of Haworth's students, scattered as they are world wide, owe much to his

fine teaching, to his splendid character and example. I trust that I have said enough to show what a great man and what a great chemist he was and that the consequences of his pioneer work in chemistry, both academic and industrial, have been of great significance for mankind. His work in Education has been equally important and as Professor, Dean, Vice-Principal, and Acting Vice-Chancellor of the University of Birmingham he helped at a critical time to establish its greatness.

I conclude this lecture with a tribute to one man to whom Sir Norman owed so much as a colleague, namely my other carbohydrate teacher, Sir Edmund Hirst. They were ideally suited to be partners in research, the one continuously throwing out brilliant ideas left, right, and centre, often in a way disconcerting to the young student at the bench, the other adding equally brilliant ideas but with consolidating and constructive practical advice.

The decade of the Haworth and Hirst partnership in Birmingham will always rank as the golden age of Carbohydrate Chemistry.

I am indebted to Dr. C. Long for the information on Nelson's Silk Company.