PAUL HAAS

Obituary Notice

PAUL HAAS

(1877–1960)

Paul Haas was born in London in 1877 and died at Cheam, Surrey, on 6 April 1960. His father was Professor of Sanskrit at University College and his mother was an accomplished pianist who had a European reputation as a specially gifted interpreter of Bach. Her son inherited her musical appreciation.

Paul attended University College School in its Gower Street days before entering the parent College as an undergraduate. Then, as always, University College was one of the most stimulating academic centres in the world. He was there in the days of Ramsay, Bayliss, Starling, Oliver and Flinders Petrie. After obtaining the B.Sc. degree Haas went to Geneva, where he worked with Carl Graebe, who is well known for his synthesis of alizarin, carried out with Liebermann. Haas prepared the methyl and the phenyl ketones of acenaphthene and studied their oxidation to carboxyacenaphthenes. By the Beckmann transformation of the oximes he finally obtained 4-aminoacenaphthene, thus establishing that Friedel-Crafts substitution occurs at position 4. This was checked by conversion of the phenyl ketone into benzoynaphthalic acid. This, on loss of carbon dioxide, gave α -naphthyl phenyl ketone and finally α -naphthylamine. His results were presented in July 1901 at the University of Freiburg im Breisgau as a thesis for the degree of Ph.D., the senior examiner being L. Gattermann. Haas did not, however, publish any research work from Freiburg. It does not appear that his time in Geneva influenced his choice of a theme for future work, and fourteen years were to elapse before he began his researches on marine algae. During that time he enlarged his experience in organic chemistry and acquired that skill in following up unusual or unexplained results which characterized so much of his later work.

His first post was with A. W. Crossley in the Chemistry Department of St Thomas's Hospital Medical School. Crossley had worked with Emil Fischer at Würzburg on the oxidation of saccharic acid and mucic acid, but on returning to England he began a long series of researches on 1:1-dimethylcyclohexane-3:5-dione (dimedone). Haas associated himself with this work and described the reaction of dimedone and of the corresponding 5-chloro compound (obtained by the action of phosphorus trichloride) on ammonia and primary amines. With dimedone one or two molecules of water can be eliminated. The chloro derivative reacts with $2R \cdot NH_2$. When one amine residue is introduced

the remaining oxygen is enolic, but is ketonic when the amine residue is acetylated. Another paper appeared a few months later, and from the super-scription (degrees were appended to authors' names in those days) it appears that Haas had obtained his D.Sc. in the interval. One molecule of *m*- or *p*-phenylenediamine reacts with either (a) one molecule or (b) two molecules of dimedone. The relations of the two products (A) and (B) to each other were studied. Acetylation of (A) occurs on the $-NHR$ group and not on the hydroxyl group. The chloro derivative reacts with two molecules of diamine, giving a compound (C) containing no oxygen.

On analysis of many compounds of these types Haas obtained low figures for carbon and hydrogen and a high nitrogen value when a copper oxide tube and a copper spiral were used. The hydrochlorides of the bases, however, gave normal values. Dunstan and Carr in 1896 had made an exactly similar observation with aconitine and its hydrochloride, which they attributed to formation of methane. Admixture of the aconitine with cuprous chloride gave correct figures. Somewhat analogous results are described in *J. chem. Soc.* (1923, 123, 1050). Analyses by Haas of the evolved 'nitrogen' confirmed the formation of methane. By mixing his compounds with cuprous, cupric or lead chloride, and by using a tube containing lead chromate with a silver spiral, correct results were obtained. Traces of chlorine appeared to suffice in some cases. Several compounds gave normal results for nitrogen because the copper oxide tube had been used for the combustion of a hydrochloride. Haas showed that, on passage of methane with carbon dioxide through a copper oxide tube, up to 43% was unburned; when he used the oxide and cuprous chloride combustion was complete. Methane formation was attributed by Haas to the presence of the hydroaromatic ring; with compounds of type B containing two such rings, the abnormal results were more pronounced. He considered that the *gem*-dimethyl group might be concerned, as the compound from 1-methylcyclohexane-3:5-dione and *m*-phenylenediamine gave a correct result for nitrogen in a tube containing only copper oxide. Other monomethyl compounds of this type were not tested.

In 1912 Haas published some work on reactions of hippuric acid. This compound has always had an attraction for students of science and medicine as it represents the first established case of detoxication by glycine. R. T. Williams in *Detoxication Mechanisms* (Chapman and Hall, 1959, pp. 13–14),

states that it was Keller in 1842 who, in Wöhler's laboratory in Göttingen, definitely established that benzoic acid and glycine were concerned in the biological formation of hippuric acid. It is therefore not surprising that Haas, familiar with this acid through the instruction of students in the laboratory, should examine critically any published work on its derivatives. Drechsel had obtained, on benzoylation of the products from the acid hydrolysis of casein, a substance believed to be α -aminohippuric acid (2-amino-2-benzamidoacetic acid) and which he stated to yield diaminoacetic acid on hydrolysis. Other workers found difficulty in preparing this second acid. From hippuric acid, bromine and red phosphorus Haas obtained, on treatment of the product with (a) water and (b) ammonia, α -hydroxyhippuric acid and either benzamide or the amide of α -hydroxyhippuric acid respectively. No α -aminohippuric acid was isolated. α -Hydroxyhippuric acid,

with acids or alkalis readily gives benzamide and glyoxylic acid, a reaction which is analogous to the fission of 'aldehyde-ammonias' by acid:

This formation of glyoxylic acid on bromination and hydrolysis is a delicate test for hippuric acid. The reaction mixture when treated with sulphuric acid and a trace of protein gives the well-known purple colour.

Another paper again illustrates Haas's scientific curiosity and careful observation. α -Hydroxyhippuric acid exhibits a peculiar behaviour on heating. It melts and froths at about 150°, resolidifies and finally melts and decomposes about 210°. Haas identified the products of this reaction, in which dibenzamidoacetic acid is formed. This, on acid hydrolysis, gave as primary products glyoxylic acid and benzamide. Drechsel's diaminoacetic acid was not obtained.

In 1913 he joined the Department of Botany at University College, where he was associated for many years in teaching, authorship and research with T. G. Hill, then Reader in Vegetable Physiology and later Professor of Plant Physiology. Hill had also been on the staff at St Thomas's. Haas's introduction to marine algae arose from the shortage of gelatin in 1915, and Professor Oliver suggested that Haas and Hill should study carrageen or Irish moss (*Chondrus crispus*) with a view to its use as a substitute. The ready gelatinization of aqueous extracts of the alga was well known and had already found some technical applications. In 1921 Haas announced in *The Biochemical Journal* that carrageen contained 'etheral sulphates' in the form of salts, chiefly of calcium, and that the $-\text{O} \cdot \text{SO}_3 \cdot \text{O}-$ group was linked to carbohydrate. Compounds of this type were already known in

animals, but Haas remarked: 'the present instance would appear to be the first recorded case of the existence of carbohydrate esters of sulphuric acid among plant products'.

It was already known that the ash of carrageen is mainly calcium sulphate and that dialysis of aqueous extracts of the alga does not remove the calcium. Haas showed, however, that the sulphate ion is absent from such extracts but appears on hydrolysis with hydrochloric acid. The amount of sulphate then present in solution is twice as great as that contained in the ash, and he showed that carrageen on heating loses sulphuric acid. Later Haas and Miss Russell-Wells found that polysaccharide sulphates from certain other algae lost less sulphuric acid on heating owing to the simultaneous formation of a very basic ash. The occurrence of carbohydrate esters of sulphuric acid in plants is now so well recognized that this fundamental work of Haas tends to be overlooked. A few months later Neuberg and Ohle, in the *Biochemische Zeitschrift*, reported the presence of conjugated sulphuric acid, possibly linked to carbohydrate, in agar. They cited Haas's results and some early work of Tamman in 1882 on the occurrence of 'ätherschwefelsäuren' in green peas.

In 1925 Haas and Hill showed that on anaerobic extraction of *Mercurialis perennis* (dog's mercury) or *M. annua* with water the colourless solution rapidly turned blue in air and finally yellow. The unknown compounds involved were named hermidin, cyanohermidin and chrysohermidin. The volumes of oxygen used in these two stages are equal. The redox potential of the system was measured by R. K. Cannan. This was the first study of a plant redox system to be made in Great Britain by botanists. In 1936 Haas, Hill and Miss B. Russell-Wells briefly reported in a letter to *Nature* on the stable blue substance formed on drying young shoots of *M. perennis* in air. It is different from cyanohermidin, and on keeping or boiling with water forms a red product. From this, by chemical and physical methods, they separated a series of red glycosides containing nitrogen and sulphur. No further information has been published on these pigments.

This work was followed by a study of the hexahydric alcohols in marine algae. Mannitol had been isolated by Stenhouse in 1844 from brown seaweeds, but Haas and Hill established its presence in *Pelvetia* species along with a mannitan. This was isolated as a dibenzal derivative under conditions which appeared to exclude the possibility of its formation as an artifact from mannitol. They also obtained dulcitol from alcoholic extracts of the dried red alga *Bostrychia scorpioides* and oxidized it to mucic acid. The syrup from the separation of the dulcitol was treated with benzaldehyde and hydrochloric acid in the hope of obtaining a benzal-

dulcitol, but the crystalline product was found to be a mixture of the di- and tri-benzal compounds of sorbitol and to yield this hexitol on acid hydrolysis. The hexa-acetate of sorbitol was also obtained on acetylation of the original syrup. No dulcitol or sorbitol could be found in eight other members of the Rhodophyceae.

During an examination of the carbohydrate metabolism of brown seaweeds Haas found on testing concentrated extracts with Fehling's solution that a mauve tint developed. This recalled the biuret reaction and was shown to be due to an octapeptide which yielded glutamic acid hydrochloride on hydrolysis. Then followed in 1933-35 two papers on algal metabolism in the *Annals of Botany*. These display the intimate knowledge acquired during twenty years, they draw analogies with fungi and with land plants and afford much stimulus to further work. The authors made the tentative suggestion that the peptides of brown algae are intermediate products, arising from a disturbance of metabolism due either to desiccation on exposure to air, or to low illumination and consequent interference with photosynthesis and protein metabolism. Ten red algae which grow under conditions of minimum exposure to air were found to contain no peptides. Two red 'calcareous' algae, which are incrustated with calcium carbonate containing some magnesium carbonate and consequently suffer from lack of illumination, contained peptides. A third red alga growing under shaded conditions also contained a peptide. The amino acids produced on hydrolysis were identified. These experiments, while not conclusive, certainly afford a *prima facie* case for the authors' hypothesis.

Chemists in the textile industry will recall the interest aroused by alginic acid in 1942. In 1931 Miss G. M. Bird and Haas made a useful contribution to the early chemistry of this compound by showing that it gave mannuronic acid on hydrolysis and confirming the formation of mannosaccharic acid on oxidation. They also proved that fucoidin, which accompanies alginic acid in the cell wall of *Laminaria* species, is a polysaccharide sulphate. The ash of seaweeds had long been known to contain phosphates, but in 1935 Haas and Hill showed that in *Chondrus crispus*, *Polysiphonia fastigiata* and *Dilsea edulis* the whole of the phosphorus in dialysed aqueous extracts is present as organic phosphate and is liberated as orthophosphoric acid on hydrolysis.

In 1935 Haas studied the volatile, odorous compound evolved by the red seaweed *Polysiphonia fastigiata* on removal from its habitat. The alga is frequently found growing on *Ascophyllum nodosum* in rock pools at low-water mark. Early in 1935, after a meeting of the Council of the Chemical Society, Paul Haas, William Wardlaw and I met under the Piccadilly archway. Haas showed us a

small bottle containing a colourless liquid. 'I wish', said he, undoing the stopper, 'that you would tell me what you think this smell is. It reminds me of a phosphorus compound or of butadiene'. We asked what the liquid was. 'Water', he said, 'through which air has been drawn after passing over a wet red seaweed'. Wardlaw and I recognized the odour as that of a dialkyl sulphide, probably dimethyl sulphide, because he and E. G. Cox had made X-ray examinations of its co-ordination compounds with platinum salts and I had encountered methylated alkyl sulphides during work on mould metabolism. Shortly afterwards, in a paper read before The Biochemical Society in Oxford, Haas announced its identification as dimethyl sulphide and its characterization as the dibromide, the mercurichloride and the platinochloride. With Haas's permission and lively interest Miss Margaret Simpson in Leeds was able to show in 1947 that the precursor of the dimethyl sulphide in *P. fastigiata* was *S*-dimethyl- β -propiothetin,

to isolate the thetin as its hydrochloride, to characterize it amply and to show that its fission to the sulphide was almost certainly enzymic. Later Cantoni furnished complete proof of this and studied the enzyme. In July 1947 du Vigneaud, at a lecture in London, recalled his earlier demonstration that *S*-dimethylacetotheitin,

was a methyl donor and supported the growth of young white rats on a diet containing homocystine but not methionine. He remarked that one would expect so excellent a methyl donor to occur in Nature. When a preliminary account of Miss Simpson's work appeared, G. A. Maw in du Vigneaud's laboratory tested the seaweed thetin and found that it also was a powerful methyl donor in white rats under the same dietary conditions. Dubnoff and Borsook then showed that the two thetin hydrochlorides could methylate homocysteine to methionine in liver or kidney preparations from rats. Neither thetin has been found in animals, nor has dimethylacetotheitin been detected in Nature. The transmethylation observed by the American workers may possibly be due to the action of betaine transmethylese, which, Maw has suggested, may be identical with the thetin transmethylese of Dubnoff and Borsook. These results, followed by Cantoni's striking discovery of active methionine—the *S*-adenosylmethioninesulphonium ion, also a thetin—greatly stimulated interest in natural sulphonium compounds.

In 1910 Haas published *Laboratory Notes on Organic Chemistry for Medical Students*, most of which could be used to-day. Three years later the first volume of Haas and Hill's *The Chemistry of*

Plant Products appeared, followed by Volume II in 1922. In an obituary notice of Hill in *Nature* (1956) we read: 'Volume II on Metabolic Processes can still be read by students with profit for its dynamic method of approach and presentation'. These three volumes were almost unique at the time they appeared and only considerations of space preclude further comment.

Haas had a flair for languages which was probably inherited from his father, and a particular affection for France, its language and its people. His German was fluent, and he also had a working knowledge of other European languages and taught himself Russian. It is not surprising that he was very interested in foreign students, who must have found him particularly sympathetic and a clear teacher. He never lost his tremendous desire to learn what people did, how things were done and how they worked. These things were an endless source of interest to him. The sea greatly attracted him and he made many trips on cargo boats, serving as one of the crew. He was an expert swimmer and a keen walker.

At the age of 61 he married Miss Beryl Grace Wood, a biologist whom he met while inspecting schools for the University of London. Their son, in a most happy continuity, is a student at St Thomas's Hospital Medical School, for which his father had a great affection that was also shared by Hill. Haas had a tall and dignified presence; his kindly courtesy recalled the manners of earlier and more spacious days. He was perhaps a little shy in the best sense of the term, and had that intangible, but true, humility which Dr C. H. Newman once so happily associated with the late R. H. A. Plimmer. The devotion with which he pursued, steadily and quietly, his chosen research, and his generous appreciation of the work of others, endeared him to his friends. He believed in personal work at the laboratory bench and, throughout his life, apart from T. G. Hill and Dr Barbara Russell-Wells, who were concerned in nearly all his biochemical work, he had only three or four collaborators.

Haas was a Fellow of University College, an Original Member of The Biochemical Society and a Fellow of the Chemical Society.

A colleague has sent me an appreciation of Haas's work from a somewhat unusual angle.

'Throughout the war of 1939-1945 he worked for the Inter-Services Research Bureau. This necessitated a very considerable change in his way of life but he adapted himself to it extraordinarily well; his natural charm of manner and his kindly benevolence towards his juniors secured for him a warm regard in the very mixed group of serving officers, scientists and engineers, young and old, among whom he worked. Although the problems with which he was concerned, nearly always unusual and often very urgently requiring a solution, were remote from normal

University research, Haas always maintained the highest academic standard. He worked steadily, with constant attention to detail, and he never considered a problem as solved until he had applied to the solution the most exacting tests. On several occasions he showed great courage in experimenting with dangerous material which he felt he could not recommend for use until he had himself tested it. His colleagues will remember him for his absolute integrity and his stubbornness when he felt he was right: once he refused, point-blank, to give, to the high-ranking administrator who controlled his laboratory, information about the composition of an important material on the grounds that it was a scientific and technical matter and that security required that as few people as possible should know about it. On the other hand, he never made unreasonable demands on the administration; moreover, when his scientific colleagues were in need, his extensive knowledge of the by-ways of science was put freely at their disposal and he could nearly always make a suggestion which helped towards the solution of their problems. He was a fine scientist—conscientious, individual and dedicated.'

Dr Barbara Russell-Wells, who was associated with Haas in teaching and research in the Department of Botany at University College London for nearly 20 years, writes:

'it would be impossible to find a pleasanter or more loyal colleague than he was. I think that as both teacher and research worker his outstanding qualities were enthusiasm and patience. As a teacher he took a personal interest in each of his pupils and was always eminently approachable. He encouraged them to discuss their difficulties with him and was never too busy to listen to them. He took endless trouble in preparing demonstrations for practical classes and never set an experiment which we had not tried out first. I think all his students regarded him as a friend as well as a teacher.'

Each year he gave a course of elementary lectures on economic botany including such subjects as tobacco, tea, sugar, paper, rubber and so on. For each one he obtained an enormous number of specimens for each stage from the raw material to the finished product and, where possible, showed experiments illustrating the various processes of manufacture. He took great pains to make his lectures interesting and living.

His enthusiasm for research amounted to a passion. He could become very depressed when things went wrong and correspondingly excited when they went right. I clearly remember his delight when final proof was obtained of the existence of polysaccharide sulphates in the seaweeds.

He was extremely modest and most generous in sharing the credit for his own achievements with his colleagues. He hated injustice and would be most indignant if he thought that any of his colleagues or students had been unfairly treated in any way. In fact, he was a most lovable man, with many friends, who always seemed to bring out the best in the people with whom he came in contact.'

To extend and impart knowledge has been one of the greatest privileges of disciplined minds throughout the ages. It may truly be said of Haas:

'—and gladly wolde he lerne, and gladly teche.'

FREDERICK CHALLENGER