OBITUARY NOTICES.

GEORGE WARD HEDLEY.

1871–1941.

GEORGE WARD HEDLEY, from 1894 until his retirement in 1931 an assistant master at Cheltenham College, died suddenly at his home in Cheltenham on March 13th, 1941. Hedley was born at Langho, Lancashire, in 1871 and was educated at Manchester Grammar School. He became an Exhibitioner of Merton College, Oxford, in 1890, and took first class honours in chemistry in 1894. After a short period of research with J. E. Marsh, Hedley joined the staff of Cheltenham College and soon became Head of the Science Department on the Military Side, and in that capacity taught almost all the boys who passed from Cheltenham into the Army during his long career.

His chief interest throughout his life was in the method rather than the content of science teaching : he was strongly convinced of the value of a limited amount of work done in the right way, and of the importance of good English teaching as the basis of general clarity of thought. He was completely opposed to any policy of cramming for examinations, although he served, himself, on almost all the Certificate Examining Boards in the country. He was one of three representatives of the Public Schools on the Executive Committee of the Government's enquiry into the position of science in education after the last war, and he was a member of the Board of Education's panel on the standardisation of Certificate Examinations. He was an active member of the Association of Public School Science Masters and of the Science Masters' Association; he became a Fellow of the Chemical Society in 1900. Wilson and Hedley's " Elementary Chemistry " was published in 1905, " School Chemistry " in 1911, and " School Chemistry for India " in 1921. One cannot leave any account of Hedley's work without paying a tribute to his keen interest in everything he did, his tremendous energy, and his intense belief in the value of science teaching. The simplest lessons, the choice of laboratory materials, his everyday affairs, became pieces of experimental investigation with Hedley, and hundreds of boys acquired something of his spirit.

He had always been a keen botanist, and after his retirement became largely responsible for the editing of the forthcoming " Flora of Gloucestershire ". He married Miss Winifred Cockshott, the daughter of Arthur Cockshott of Eton College, and he is survived by her and by a son and three daughters. H. R. STEVENS.

SIR JOCELYN FIELD THORPE.

1872—1940.

BY the death, on June 10th, 1940, of Sir Jocelyn Thorpe the profession of Chemistry loses one of its outstanding figures and the Chemical Society a devoted supporter who served it as Treasurer, Vice-President and President, and a large circle of friends will miss a remarkably kind, genial, and hospitable personality.

Jocelyn Field Thorpe was born on December 1st, 1872, and was the sixth son of the late William George Thorpe, F.S.A., a barrister-at-law of the Middle Temple. Thorpe's father had been educated at Cambridge in the classical tradition; but he was a man of liberal outlook and ready to encourage his son in the independent choice of a career.

After receiving his earliest education at a preparatory school near his home in Clapham, Thorpe went at the age of ten to Worthing College. He showed considerable aptitude for games in spite of having one leg shorter than the other, the result of infantile paralysis in his childhood, and was particularly good at cricket. He specialised in wicket keeping and retained his love of the game to the end. His holidays were spent on his father's estate in Devonshire, where he learnt to shoot and fish with his brothers.

After leaving school in 1888, he returned to London to study Engineering at King's

College. He derived much benefit in later life from this early training, particularly from the practical work in the machine shops of Alexander Wilson's works at Vauxhall, where he worked during the Long Vacation. However, Engineering was not his true vocation and at the end of two years he abandoned it for Chemistry. The change was made on the advice of his namesake, Sir Edward Thorpe, whom Thorpe's father consulted; this was a bold step at a time when the profession of Chemistry still lacked, in this country, the recognition it was to win in later years.

Thorpe entered the Royal College of Science at South Kensington in 1890 and took the first year's course in elementary Chemistry and Physics, and in the following year advanced Chemistry, mainly Organic. In 1892, following Sir Edward Thorpe's advice, he went to Heidelberg, where, at that time, the faculty of Science was second to none. Bunsen was still there, although he had retired; other famous men were Victor Meyer, Auwers, Jannasch, Gattermann, Brühl, Horstmann, Krafft and Knoevenagel, the physicist Quincke, and the equally celebrated mineralogist Rosenbusch. The number of English students at Heidelberg was considerable; amongst Thorpe's contemporaries were J. F. Bottomley, G. C. (now Sir Christopher) Clayton, J. C. Cain, J. N. Goldsmith, J. T. Hewitt, J. McRae, B. (now Sir Bernard) Pares, T. S. Patterson, and J. H. Wigner. There was a fair-sized English colony and Thorpe was welcome in many houses; he took part in theatricals and played cricket and lawn tennis. With so many distractions Thorpe did not work particularly hard until shortly before the examinations; then he would retire to the Black Forest, and come back to give a good account of himself. He took his degree in 1895; his Doctor's thesis, carried out under Auwers's guidance, dealt with the $\alpha\alpha'$-dimethylglutaric acids and was an excellent piece of work. Thorpe returned to Heidelberg for the summer of 1897, but devoted his whole time to the study of dyes and dyeing at the Badische Works at Ludwigshafen.

On obtaining his degree at Heidelberg, Thorpe returned to England and joined the great research school at Manchester University, where W. H. Perkin, jun., was then at the height of his fame. Here Thorpe found his true vocation; he worked hard and his enthusiasm was amply rewarded by results. He soon took the degree of D.Sc. and was appointed Lecturer in Organic Chemistry with special charge of a course, both theoretical and practical, on dyes and dyeing, which was particularly successful. The practical work was conducted in Thorpe's private laboratory, at that time a shed in the back quadrangle, a part of which he had fitted up for research; he generally had one research student working there. However, he kept in constant touch with Perkin in the main building and thus arose a productive collaboration extending over many years. Those who remember this period speak of Thorpe's excellence as a teacher, but especially of his great skill as a manipulator and of the delight he took in practical work. Although the work of Perkin's school was mainly concerned with the structure of natural products, Thorpe's own approach to these problems was almost entirely from the synthetic side and he took comparatively little interest in their analytical aspect. A fitting recognition of Thorpe's distinguished work at Manchester came with his election to the Royal Society in 1908.

During the early part of his stay in Manchester Thorpe shared rooms with the late Dr. J. C. Cain, and it was then that the project of their classical work on synthetic dyes first took shape.

In 1909 Thorpe was appointed Sorby Research Fellow of the Royal Society and moved to Sheffield, where he spent a fruitful period of his career. He had a pleasant and well-equipped laboratory and no teaching duties and could devote the whole of his time to research with the aid of an assistant. He did much of the practical work himself, keeping his assistant very busy carrying out analyses and preparing large amounts of starting materials, although he always discussed his plans and published his work in collaboration with the assistant. He liked working on a generous scale when tackling a synthetic problem, although his mastery of technique often enabled him to take a short cut to the required product. He worked hard, allowing himself, perhaps, a round of golf on Sunday by way of relaxation.

In 1913 came Thorpe's great opportunity : he applied for the Chair of Organic Chemistry at the Imperial College of Science and Technology in London and began his duties there early in 1914. He brought to his new task a contagious enthusiasm and this, combined with his great gifts as a lecturer, had an immediate vitalising effect on his Department. He attracted an eager band of pupils anxious to do research; but his first step was to try and improve the somewhat inadequate facilities then available, and this was in part achieved by the end of the summer.

The writer has vivid recollections of Thorpe during this period: he was full of ideas, which were always stimulating and greatly added to the interest of his lectures; in the laboratory he worked with gusto and delighted in such operations as the preparation of " molecular " sodium; he would often try a reaction on a small scale, always working in test-tubes (he even contrived to carry out extractions with ether in test-tubes) and leaving his students to repeat it on a larger scale if it turned out promising; he was seldom without a cigarette—sometimes a cigar—and generally in shirt sleeves and had a habit of propping up test-tubes in drawers or against gas taps. A characteristic attitude of Thorpe in the laboratory is portrayed in the accompanying photograph.

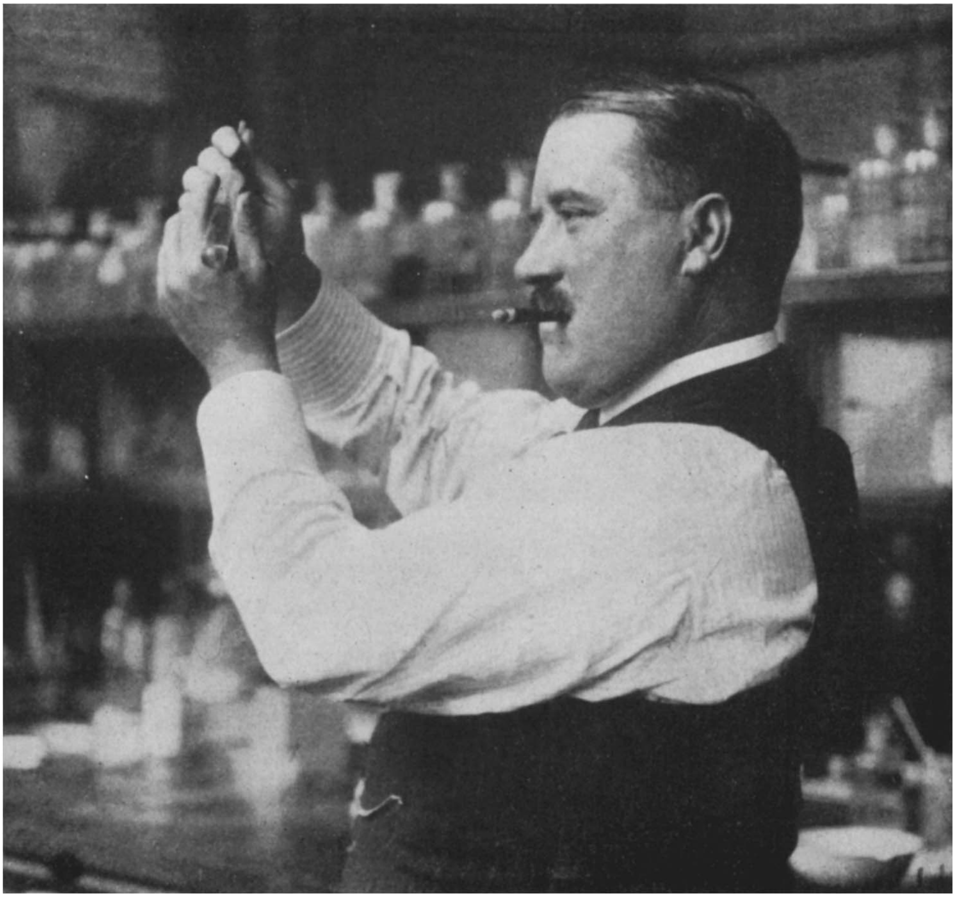
All plans of expansion were brought to an end by the outbreak of the World War. Thorpe immediately set about making the best possible use of the facilities and men available at South Kensington and started the manufacture of drugs—principally phenacetin, novocaine, and β-eucaine—which had until then been imported from abroad. War work, such as the investigation of war gases, explosives, etc., claimed more and more of his time. He became a member of the Trench Warfare Committee and carried out much experimental work, a good deal of it in collaboration with Dr. M. A. Whiteley, who was a member of his staff.

Teaching still went on; and in 1919 Thorpe was at last able to realise his ambition of founding a great research school. There was a large influx of research students in the years immediately following and a constant expansion of research accommodation; where two assistants had worked in 1914, some thirty research students and junior members of staff were housed by 1921. The number of members of staff was increased, notably by the creation of a post connected with the newly-founded Whiffen Laboratory. This laboratory had been built and equipped by the late William Whiffen and contained a representative selection of large and semi-large scale apparatus, where students could be taught the practical uses of plant; the first lecturer was C. K. Ingold, later followed by E. H. Farmer. Thorpe also had a private assistant, supported by a grant from the Department of Scientific and Industrial Research; the assistant's duties were, however, nominal and allowed him to devote his whole time to research.

By this time Thorpe had so much to do that he was no longer able to carry out experimental work himself, a circumstance he often regretted; but he was always ready to listen to anyone in difficulties and to give them advice; a favourite piece of advice was " try the unlikely " and he was never stereotyped in his suggestions. Characteristically, too, he seldom had his name included in the publications of his staff, although he took a great interest in them.

After 1919 Thorpe took an increasing share of public duties, as was inevitable for one of his ability and shrewd judgment. The first task of importance which fell to him was to preside over the Indian Chemical Services Committee; he spent some months in India in 1919 and did more than his share of the work of the Committee, being largely responsible for the report, which, however, hardly found the recognition it deserved; he himself regarded the time spent in India largely as wasted, except in so far as it served to bring him in contact with chemists there. He had a succession of Indian students from 1919 onwards as the result of his visit.

Thorpe remained a member of the Chemical Defence Committee until it was reconstituted in 1939, and received the C.B.E. in 1917. He gave much of his time and thought to the Advisory Council of the Department of Scientific and Industrial Research, on which he served from its formation in 1916 until 1922. He became scientific adviser to the Anglo-Persian (now Anglo-Iranian) Oil Co. and undertook a trip to Persia in 1929. He was also a member of the Advisory Board of the Dyestuffs Group of Imperial Chemical Industries from 1929 until his death, and of the Safety in Mines Research Board (1924—



[*To face p.* **446.**

1935), Chairman of the Explosives in Mines Committee, Department of Mines, a member of the Dyestuffs Development Committee of the Board of Trade (1925—1934), and served on the Royal Society's Council (1923—1925). He was president of the Institute of Chemistry from 1933 to 1936.

Thorpe's services to the Chemical Society, which he joined in 1893, deserve more than passing comment. From his arrival in London he took a prominent part in the work of the Society. He served on the Council from 1915 to 1918 and became a Vice-President in 1921; in the following year M. O. (now Sir Martin) Forster relinquished the post of Treasurer and Thorpe succeeded him, remaining in that capacity until he was elected President in 1928. During that time the Society was passing through a particularly difficult period: the receipts were barely sufficient to cover the cost of the Society's publications and Thorpe set himself the Herculean task of tapping fresh sources of income. He founded the Publications Fund with this end in view, having always maintained that the Society's primary function is the publication of new knowledge. He very early conceived the idea of co-ordinating the various chemical bodies in the country and so preventing the inevitable overlap of their functions and consequent waste. He took an active part in the Association of Scientific and Technical Societies, which had similar aims. After years of patient work the Scheme of Co-operation was ripe, only to be shelved owing to the financial depression of 1931. It was owing to his connection with this scheme that he was asked to serve as President for an additional year (1930—1931); it is satisfactory to note that, although the original scheme did not materialise, a variant of it is now in operation. He became the first Treasurer of the Chemical Council. During his Presidency Thorpe commissioned Herbert Budd to paint the fine portrait of the first President, Thomas Graham, which now hangs in the Society's rooms, and headed the subscription for it.

The Chemical Society honoured Thorpe by the presentation of the Longstaff medal in 1921 and the Royal Society presented him with the Davy medal in the following year; he received a Knighthood in 1939 for his valuable public services.

On his retirement from the Imperial College in 1938 Thorpe devoted himself to the task of editing, in collaboration with Dr. M. A. Whiteley, the "Dictionary of Chemistry" started by Sir Edward Thorpe.

Thorpe married in 1902 Lilian, the daughter of the late William Briggs, J.P., of Hale, Cheshire, who survives him. Lady Thorpe took a full share in her husband's career; she accompanied him on his trips abroad, helped him to entertain and so maintain his many contacts, and nursed him with devotion and firmness when his health began to give way. Many will remember the Thorpes' kindly hospitality at their house in Chelsea, amongst the fine collection of English porcelain of which Thorpe was a great connoisseur; Thorpe himself was a charming host and a discerning judge of wine and cigars.

Although he was always a good lecturer, it is said that he was not a particularly good public speaker until well on in his career. In the last 15 years he was certainly first-rate, spontaneous, interesting, and with a pleasantly light touch.

It is something of a paradox, in one so kindly and genial as Thorpe, that he was reticent and never talked about himself. His kindness was probably his outstanding feature; he always believed the best of everyone and this was, indeed, occasionally a source of embarrassment to his staff in their efforts to maintain discipline. He was cheerful and good-tempered, with a liking for the good things of life, and a lively sense of humour. He enjoyed telling a story against himself, emphasising the point with that characteristic "h'm?"—half-grunt and half-chuckle—that his friends knew so well.

Distinguished as were Thorpe's scientific achievements and great as were his services both to Chemistry and to the Chemical Society, it is perhaps his kindliness and humanity that will remain longest in the memory of those who knew him.

G. A. R. KON.

The Scientific Work of Jocelyn Field Thorpe.

THORPE'S chemical researches were carried out during the forty-year period from 1894 to 1934 in the Universities of Heidelberg, Manchester, Sheffield, and London. During this period he wrote 120 original memoirs, in addition to minor material. With two exceptions, his papers were published in the *Journal* of the Chemical Society.

His scientific life falls naturally into four periods. During roughly the first decade he was learning his chosen subject and acquiring " the tools of his trade," partly from K. Auwers and W. H. Perkin, jun., but mainly by prolonged and arduous work in the laboratory. In this way he acquired the mysterious " feeling " for compounds and reactions which characterises the more gifted organic chemists. Then he entered upon a great period of research from 1904 until 1914. There followed the Four Years' War, during which other duties stopped his academic work. With the end of the war Thorpe devoted himself to making the Imperial College a centre of research for organic chemistry. Students came to South Kensington from all over the world, and there ensued the second " flowering period " in Thorpe's life, which culminated in the vast activity of the years 1922 and 1923. Thereafter the call of administrative duties and his work for the Government, the Chemical Society, and the profession of Chemistry in general took up more and more of his time. He reconciled himself to exercising a general benevolent supervision over the research work of his department, although he remained actively interested in some of his favourite subjects until his retirement.

When Thorpe entered upon his career, organic chemistry was in the full tide of its extraordinary expansion in Germany, England, and France. It was, perhaps, inevitable for one of his character and abilities to become attracted to this branch of chemistry, and to it he remained faithful throughout his long career. At times he used the tools of physics to obtain results which interested him, but on the whole his attitude towards physical chemistry was one of genial tolerance. It is more remarkable that, with a few exceptions, his own experimental work had little direct contact with biology. This is probably due to the fact that, when once he had embarked upon his life work, he was caught up in a maelstrom of activity which took up his full attention and completely satisfied his scientific instincts.

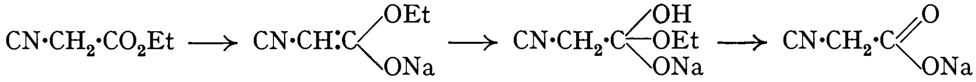
Thorpe's activities in organic chemistry were many-sided. At the outset of his career, his powerful and receptive mind was influenced by the varied activities of Perkin's laboratories at Manchester. In later life we find him picking up and developing lines of work suggested by his early experiences. Certain themes indeed run throughout his whole work : his interest in polybasic acids, dating back to his Heidelberg days, in tautomerism, arising from his first researches on cyanoacetic ester, and, perhaps above all, in the complexities of alicyclic rings, are three examples. The review which follows is not strictly historical, but illustrates the development of the various main themes.

1. *Synthesis and Properties of Saturated Polybasic Acids.*

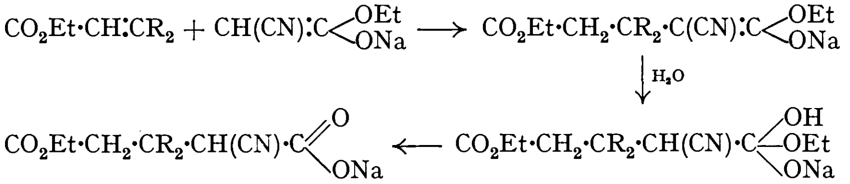
The problem assigned by Auwers to Thorpe for his doctorate research was the study of the trimethylsuccinic and dimethylglutaric acids. Zelinsky had reported the existence of two isomeric inactive trimethylsuccinic acids, whereas only one is required by stereochemical theory. Thorpe was able to show that Zelinsky's second acid was in fact a mixture of the two stereoisomeric αα'-dimethylglutaric acids (m. p. 140° and 127°). Moreover, the substance previously described as αα'-dimethylglutaric acid (m. p. 101°) was also a mixture of these two stereoisomerides. Zelinsky's acid had come from the hydrolysis of the condensation product of α-bromo*iso*butyric ester and sodio-α-cyanopropionic ester. The abnormal formation of the glutaric derivative was due to an elimination of hydrogen bromide, followed by an addition of the sodio-ester to the double bond so formed.

A similar condensation engaged Thorpe's attention after his arrival at Manchester. In his first paper with W. H. Perkin, he showed that α-bromo*iso*valeric ester condensed normally with sodiomethylmalonic ester in boiling xylene. Hydrolysis of the product yielded *cis*- and *trans*-methyl*iso*propylsuccinic acids. The same acids were obtained when α-bromo*iso*valeric ester was condensed with sodiomalonic ester, and the product methylated and hydrolysed (Bentley, Perkin, and Thorpe, J., 1896, **69**, 270). During these researches Thorpe became familiar with the technique of the Conrad–Guthzeit method and with the preparation of anhydrides from dibasic acids. These were later to affect his method of attack on the problems of glutaconic acid chemistry.

Thorpe became interested in the differences between the sodium derivatives of cyanoacetic and malonic esters. In 1900, he published a group of three papers (one with Young, one with Howles and Udall) on this point and on the use of cyanoacetic ester in synthesis. He observed that sodiocyanoacetic ester is considerably more stable than sodiomalonic ester and that its aqueous solution does not develop an alkaline reaction but, on evaporation, yields sodium cyanoacetate. He suggested that the reaction proceeded :



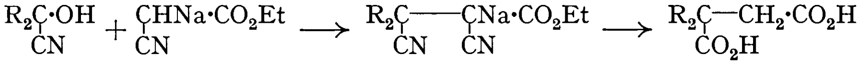
This was correlated with the formation of large quantities of acid esters during the addition of sodiocyanoacetic ester to unsaturated esters in alcohol, which was attributed to the process :



In the course of his paper with Howles and Udall (J., 1900, **77**, 942) Thorpe describes an important discovery, the value of which was not realised at the time. A quantity of ethyl α-methylacrylate was prepared from ethyl α-bromo*iso*butyrate and diethylaniline. Thorpe says of the product, " The clear mobile liquid passing over between 117° and 120° consists of pure ethyl α-methylacrylate ; it must at once be used, however, since on standing it slowly polymerises to a white, transparent substance resembling gelatine." It was not until more than thirty years later that this " white, transparent " polymeride of methacrylic ester was recognised as a valuable substitute for glass (" Leukon, Diakon ").

The separation of the " *cis* " and the " *trans* "-forms of these substituted glutaric acids was an important practical problem and Thorpe introduced a new method for this purpose in 1903 (J., **83**, 351).

Thorpe made two important general contributions to the methods available for the preparation of dibasic acids. One for the preparation of β-substituted glutaric acids will be more suitably considered later. The other was described in a paper with Miss Higson (J., 1906, **89**, 1455). It was observed that sodiocyanoacetic ester readily condensed with the cyanohydrins of aldehydes and ketones ; hydrolysis of the product yielded the corresponding succinic acid :



$$\underset{\mathrm{CN}}{\mathrm{R_2C{\cdot}OH}} + \underset{\mathrm{CN}}{\mathrm{CHNa{\cdot}CO_2Et}} \longrightarrow \underset{\mathrm{CN}}{\mathrm{R_2C}}\text{——}\underset{\mathrm{CN}}{\mathrm{CNa{\cdot}CO_2Et}} \longrightarrow \underset{\mathrm{CO_2H}}{\mathrm{R_2C}}\text{—}\mathrm{CH_2{\cdot}CO_2H}$$

(I.)

Moreover, the condensation product (I) could be alkylated and in this way a large range of substituted succinic acids became available. The yields by this process are very good (65—95%), and the method has passed into general use for preparative purposes.

2. *Investigations relating to Camphor and other Terpenes.*

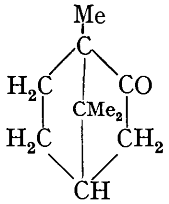
When Thorpe joined Perkin at Manchester, the problem of the structure of camphor was attracting the attention of organic chemists all over the world and was still far from solution. It was as if in this small enigmatic molecule Nature had thrown down a challenge to chemists. The structure of camphor seems to have had at that time a symbolic significance which transcended even the value of the actual scientific truth. At all events, there was a tremendous concentration of chemical talent on this single problem.

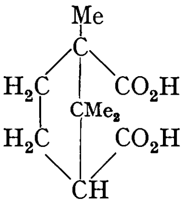
Perkin used entirely the synthetic approach, of which he was rapidly becoming a master. In 1896, some early experiments were directed, with Thorpe's assistance, towards the synthesis of camphoric acid. In the following year (J., 1897, **71**, 1169) Perkin and Thorpe announced the synthesis of inactive camphoronic acid. For a proper appreciation of this feat it will be convenient to review briefly some aspects of the state of camphor chemistry at the time.

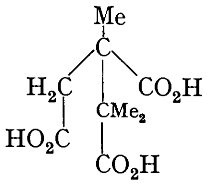
Camphor was known to be a monoketone, $C_{10}H_{16}O$. It was saturated and therefore dicyclic. Its oxidation with nitric acid was known to yield successively camphoric, camphanic, and camphoronic acid :

$$C_{10}H_{16}O \longrightarrow \underset{\substack{\text{Camphoric}\\ \text{acid}}}{C_{10}H_{16}O_4} \longrightarrow \underset{\substack{\text{Camphanic}\\ \text{acid}}}{C_{10}H_{16}O_5} \longrightarrow \underset{\substack{\text{Camphoronic}\\ \text{acid}}}{C_9H_{14}O_6}$$

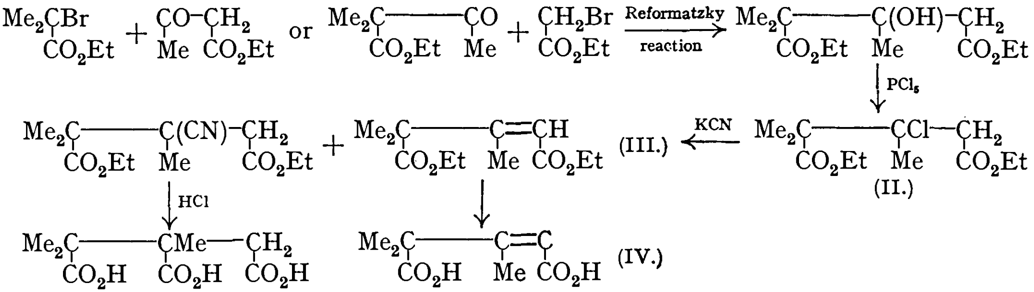
Bredt had shown that camphoronic acid was a tribasic acid and yielded trimethylsuccinic acid and *iso*butyric acid on destructive distillation. This led him to propose, in 1893, the following (now accepted) formulæ :


Camphor


Camphoric acid


Camphoronic acid

Tiemann (1895), however, rejected these and proposed alternatives, including the formula $CO_2H{\cdot}CHMe{\cdot}CMe_2{\cdot}CH(CO_2H)_2$ for camphoronic acid. This found little favour because of the fact that the acid can be distilled in a vacuum without decarboxylation. Nevertheless there was little positive evidence in favour of Bredt's formulæ, and it was to confirm this that the Perkin–Thorpe synthesis was undertaken. This classical series of reactions is so well known as to require no comment here. It is given in outline below :



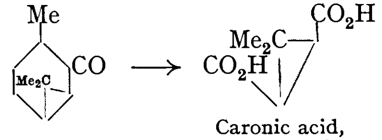
Camphoronic acid

The principal difficulty in the process lay in the tendency of the chloro-ester (II) to give trimethylglutaconic ester (III) on treatment with alkali cyanide, so that the final hydrolysis product contained far more of the unsaturated acid (IV) than of the desired camphoronic acid. However, the latter was isolated by means of its sparingly soluble barium salt. It was identical with the inactive acid which Aschan had made two years previously by mixing equal parts of *d*- and *l*-camphoronic acids, prepared from natural sources.

Occasion was taken to examine the trimethylglutaconic acid (IV), which was formed in large amounts as a by-product—an accidental circumstance which probably had a considerable effect on Thorpe's subsequent researches. The high resistance of the acid to bromine, permanganate, and reducing agents was noted. The corresponding *iso*- or *cis*-

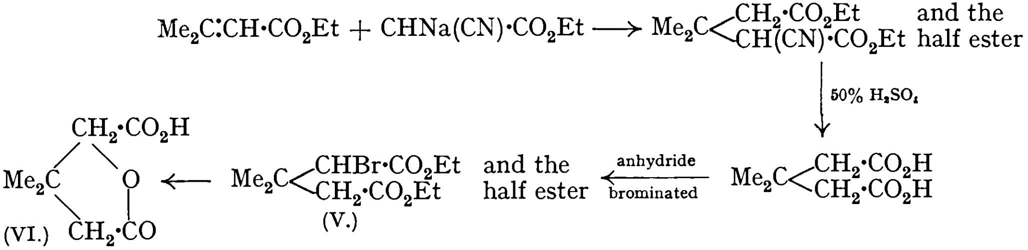
acid gave an anhydride with remarkable ease, even when the acid was dissolved in hot water and the solution allowed to cool.

Two years later Perkin and Thorpe synthesised the caronic acids (J., 1899, **75**, 48), which Baeyer and Ipatieff had prepared by oxidising carone with permanganate at 100°.



Caronic acid,
cis- and *trans*-forms.

The synthesis was as follows :

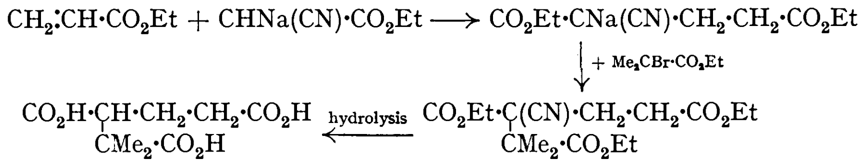


α-Bromo-ββ-dimethylglutaric ester (V) on treatment with hot alcoholic potash yielded caronic acid (mainly *trans*-) and the lactonic acid (VI). The half ester of the bromo-acid yielded *trans*-caronic acid alone.

In the same year Perkin and Thorpe were successful in synthesising αββ-trimethylglutaric acid and in proving its identity with the acid obtained by the complete reduction of Balbiano's acid, $C_8H_{12}O_5$. The latter had been obtained by the oxidation of camphoric acid with permanganate. It was to claim Thorpe's attention again in later years.

Encouraged by these successes, Perkin and Thorpe attempted the much more difficult task of synthesising camphoric acid. In 1903 (P., **19**, 61) they gave the preliminary, and in 1904 the complete account (J., **85**, 128) of their investigations. In the interval between the appearance of these reports Komppa sent the first description of his brilliant synthesis of camphoric and dehydrocamphoric acids to the *Berichte* (1903, **36**, 4332).

Perkin and Thorpe proceeded as follows :



$$CH_2{:}CH\cdot CO_2Et + CHNa(CN)\cdot CO_2Et \longrightarrow CO_2Et\cdot CNa(CN)\cdot CH_2\cdot CH_2\cdot CO_2Et$$

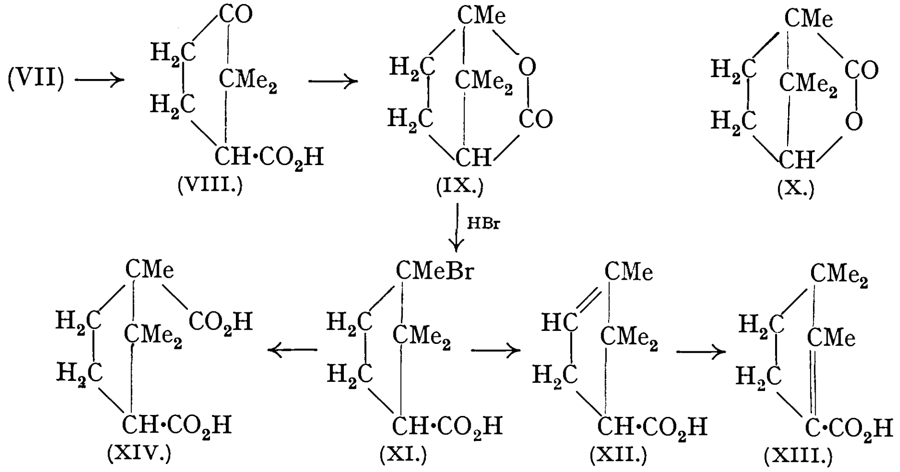
$$\downarrow + Me_2CBr\cdot CO_2Et$$

(VII.) $$\underset{CMe_2\cdot CO_2H}{CO_2H\cdot CH}\cdot CH_2\cdot CH_2\cdot CO_2H \xleftarrow{\text{hydrolysis}} \underset{CMe_2\cdot CO_2Et}{CO_2Et\cdot C(CN)}\cdot CH_2\cdot CH_2\cdot CO_2Et$$

The sodium salt of the acid (VII) was heated with acetic anhydride to yield the keto-acid (VIII). The corresponding ester on treatment with methylmagnesium iodide gave α-campholactone (IX), isomeric with the campholactone (X) which had already been obtained from natural sources.

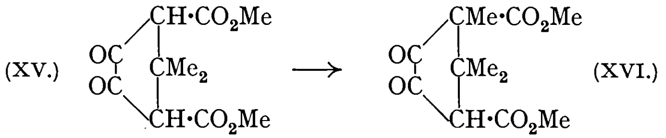
Treatment of the lactone (IX) with hydrogen bromide gave the bromo-acid (XI), which on successive treatment with sodium carbonate and dilute sulphuric acid gave (inactive) α-campholytic acid (XII) and *iso*lauronolic acid (XIII), the latter being identical with that prepared from " natural " camphoric acid.

Perkin and Thorpe also attempted the conversion of the bromo-acid (XI) into camphoric acid (XIV) by treatment with potassium cyanide, followed by hydrolysis. Again it was found that this method of introducing the carboxyl group was largely spoilt by the formation of a great deal of unsaturated material (in this case α-campholytic acid). Nevertheless they were able to isolate a small quantity of a crystalline substance having properties identical with those of inactive camphoric acid. The amount obtained was, however, insufficient for the comparatively exacting analyses of those times. With characteristic generosity they conclude, " The method of formation . . . and the properties leave scarcely room for doubt that it was *i*-camphoric acid. . . . In the meantime Komppa has published his brilliant synthesis of camphoric acid, which, once for all, establishes the correctness of Bredt's formula, and it is therefore quite unnecessary to investigate our much less satisfactory process any further."


(VII) (VIII.) (IX.) (X.)
(XIV.) (XI.) (XII.) (XIII.)

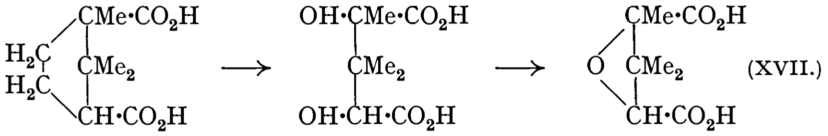
Nevertheless a few years later a sample of inactive camphoric acid, sent by Noyes, crossed the Atlantic, and Perkin and Thorpe were unable to resist the temptation of finding out whether their synthesis had been successful. The work was repeated and the product was fully identified with Noyes' material. There can therefore be no doubt that Perkin and Thorpe had achieved an independent synthesis of camphoric acid almost simultaneously with that of Komppa.

In 1909, Komppa published the full details of his work and a doubt arose as to its validity. The basis of the Komppa synthesis lay in the methylation of (XV) to (XVI), which was then reduced to camphoric acid :

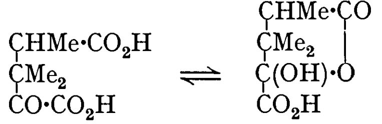

(XV.) (XVI.)

In a joint paper with Blanc, then at the Sorbonne, which was published simultaneously in England (J., 1910, **97**, 836) and in France, Komppa's synthesis was questioned on the ground that methylation of (XV) had yielded an *O*-methyl derivative. It was shown that treatment of the product with alkali led to elimination of the methyl group. Komppa, however, held his ground. He maintained that, whatever occurred during hydrolysis, the methyl group remained intact during the reduction and that the synthetic acid was undoubtedly camphoric and not apocamphoric acid. All doubt was removed when Blanc and Thorpe showed (J., 1911, **99**, 2010) that hydrolysis of (XVI) with very weak alkali yielded a C_8 diketone with the methyl group intact. Their earlier criticism was therefore invalid.

Many years later, Thorpe returned to the study of Balbiano's acid, $C_8H_{12}O_5$. To this the discoverer had assigned the formula (XVII), and had interpreted the formation from camphoric acid as follows :


(XVII.)

Thorpe (with Kon and Stevenson, J., 1922, **121**, 650; with Pandya, J., 1923, **123**, 2852; and with Rothstein and Stevenson, J., 1925, **127**, 1072) decided that Balbiano's formula was unacceptable and that the reactions of the acid could only be fully accounted for if it was represented as α-keto-α'ββ-trimethylglutaric acid (XVIII) in tautomeric equilibrium with the hydroxy-lactonic acid (XIX) :

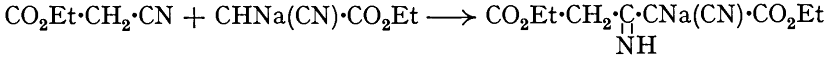
(XVIII.)  (XIX.)

$$\begin{array}{l}\text{CHMe}\cdot\text{CO}_2\text{H}\\ \text{CMe}_2\\ \text{CO}\cdot\text{CO}_2\text{H}\end{array} \rightleftharpoons \begin{array}{l}\text{CHMe}\cdot\text{CO}\\ \text{CMe}_2\\ \text{C(OH)}\cdot\text{O}\\ \text{CO}_2\text{H}\end{array}$$

Conclusive evidence in support of this view was provided subsequently by J. C. Bardhan, in Thorpe's laboratory. He was successful in synthesising the keto-acid (XVIII) by an unambiguous method (J., 1928, 2604). The synthetic acid was identical with Balbiano's acid.

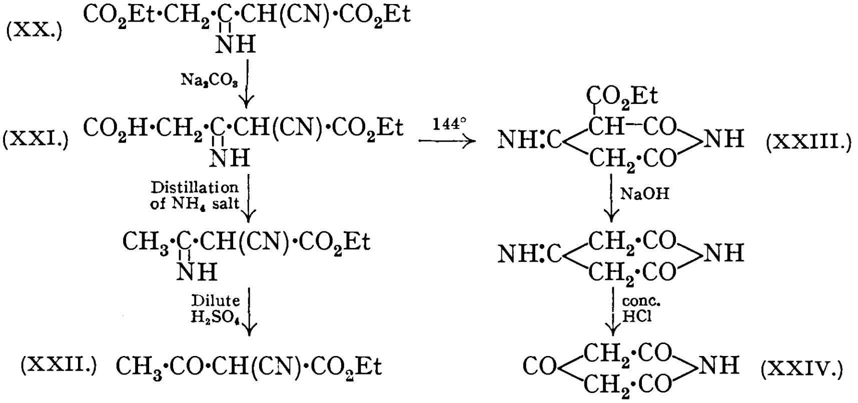
3. *The Formation and Reactions of Imino-compounds.*

Although Thorpe's work on tautomerism and on valency deflexion had a greater effect on contemporary chemical thought and aroused greater interest at the time of publication, his fundamental researches on the imino-compounds possibly represent his most permanently valuable contribution to chemical science. He was led to investigate this field in the first place through his interest in ethyl cyanoacetate, which might well rank as his favourite compound. In 1904, with Baron and Remfry (J., **85**, 1726), he discovered that this substance condensed with its own sodio-compound in the following way :



$$\text{CO}_2\text{Et}\cdot\text{CH}_2\cdot\text{CN} + \text{CHNa(CN)}\cdot\text{CO}_2\text{Et} \longrightarrow \text{CO}_2\text{Et}\cdot\text{CH}_2\cdot\underset{\text{NH}}{\underset{\|}{\text{C}}}\cdot\text{CNa(CN)}\cdot\text{CO}_2\text{Et}$$

(This scheme represents a slight later revision of that originally proposed.) From the product, acid liberated the free β-imino-α-cyanoglutaric ester (XX), the structure of which was shown by its degradation to the known α-cyanoacetoacetic ester (XXII) through the stages shown :



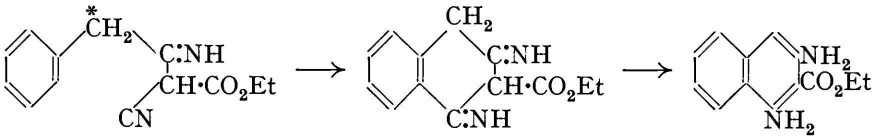
The intermediate acid (XXI) was decarboxylated at 160°, but at a few degrees above the melting point it was cyclised to ethyl glutazinecarboxylate (XXIII), which could be hydrolysed to 2 : 4 : 6-triketopiperidine (XXIV).

These results were of great interest both from the character and reactivity of the products formed, and from the novelty of the initial condensation. Thorpe promptly began to investigate the generality of the addition of sodiocyanoacetic ester to the cyano-group. In 1906, with Atkinson (J., **89**, 1906), he showed that the sodio-ester condensed with phenylacetonitrile to yield the additive compound (XXV). The structure of this was shown by its fission by means of alcoholic potash into phenylacetic and malonic acids. The sodium compound of (XXV) was methylated * at the starred carbon, for the methylated

---

* The methylation of β-imino-α-cyanoglutaric ester (XX) was fully studied some years later (with Campbell, J., 1910, **97**, 1299).

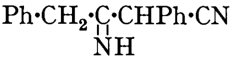
product was hydrolysed to α-phenylpropionic acid and malonic acid. Treatment of these substances with cold concentrated sulphuric acid produced a remarkable result; in the space of one minute, the following changes occurred :



(XXV.) (XXVI.) (XXVII.)

The ethyl 1 : 3-naphthylenediamine-2-carboxylate (XXVII) separated as a sulphate when the product was poured on ice. The free base was yellow and the salts were colourless, suggesting that they had the imino (XXVI) and the amino (XXVII)-structure, respectively. The diamino-ester on hydrolysis yielded the corresponding acid, which above the melting point yielded 1 : 3-naphthylenediamine, identical with that obtained from 1 : 3-dinitronaphthalene. It was found, moreover, that ethyl sodiocyanoacetate was not an essential component in the initial condensation, because phenylacetonitrile condensed with itself in the presence of sodium ethoxide to yield successively the compounds (XXVIII) and (XXIX) together with some cyanobenzyline (trimeride).

(XXVIII.)



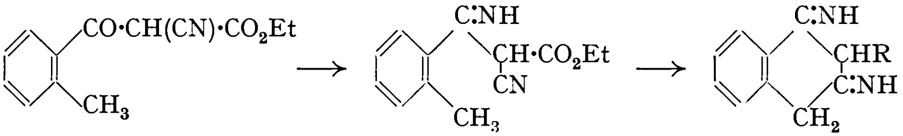
$Ph{\cdot}CH_2{\cdot}\underset{NH}{\underset{\|}{C}}{\cdot}CHPh{\cdot}CN$

$Ph{\cdot}CH_2{\cdot}CO{\cdot}CHPh{\cdot}CN$ (XXIX.)

The imino-nitrile (XXVIII) was cyclised by sulphuric acid to 2-phenyl-1 : 3-naphthylenediamine, a compound which was subsequently examined in detail (Lees and Thorpe, J., 1907, **91**, 1282).

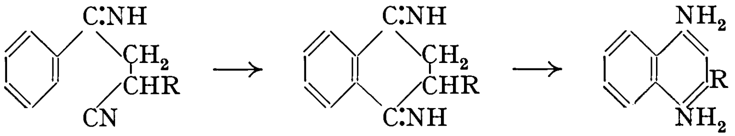
In 1907, with Atkinson and Ingham, Thorpe showed the reaction to be even more general, because benzonitrile condensed readily with ethyl sodiocyanoacetate. It was therefore clear that, of the two nitriles taking part in the Thorpe reaction (as it came to be called), only one needed to be able to form a sodium derivative.

o-Toluonitrile exhibited steric hindrance towards the reaction, the yield being low, but the product (XXXI) could be made by fusing the corresponding keto-ester (XXX) with ammonium acetate. It was found that the *o*-methyl group of (XXXI) was remarkably reactive, the compound being quantitatively cyclised by cold sulphuric acid to the corresponding naphthylenediamine derivative (XXXII, $R = CO_2Et$) :



(XXX.) (XXXI.) (XXXII.)

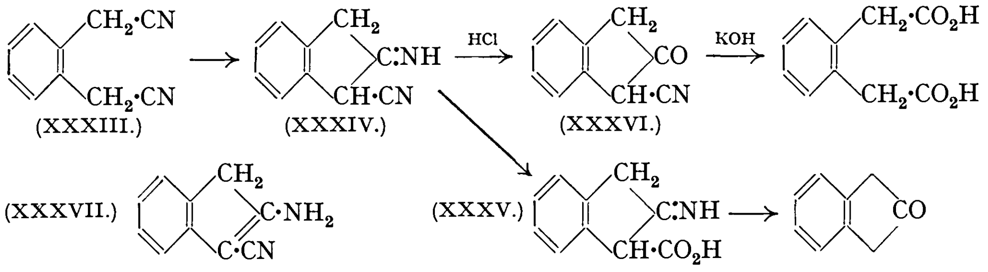
A similar series of reactions was performed by condensing *o*-toluonitrile with phenylacetonitrile, the final product having the structure (XXXII, R = Ph). It was found that there was no tendency for the formation of a di-iminohydrindene ring under the same conditions, but Thorpe (J., 1907, **91**, 1004) was able to prepare derivatives of 1 : 4-naphthylenediamine by a similar cyclisation :



Another paper with Atkinson (*ibid.*, p. 1687) describes similar condensations and cyclisations in which the starting materials were cyanoacetic ester and the three tolylacetonitriles.

Thorpe found, however, that ethyl α-cyano-γ-phenylacetoacetate, that is, the ketone corresponding to the imine (XXV), did not cyclise to the isomeric aminonaphthol derivative (J., 1907, **91**, 1899).

An important advance was made in the following year when the first intramolecular reaction involving two nitrile groups was discovered (Moore and Thorpe, J., 1908, **93**, 165). A trace of sodium ethoxide was found to convert the dinitrile (XXXIII) into β-imino-α-cyanohydrindene (XXXIV). The structure of the product was proved by the reactions shown below :

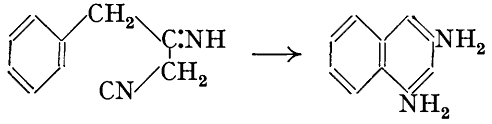


(XXXIII.) (XXXIV.) (XXXVI.) (XXXVII.) (XXXV.)

This work raised afresh the question of fine structure. Were the compounds better represented as imines or as amines? For example, was the original condensation product (XXXIV) or (XXXVII)? These questions could be answered with certainty in the case of most of the products. For instance, the original product was undoubtedly the imine (XXXIV) because of its ease of hydrolysis and lack of salt-forming properties. On the other hand, the acid (XXXV) and its derivatives behaved as amines (formulæ corresponding to XXXVII). The acid yielded a hydrochloride and lost carbon dioxide more readily than ammonia. α-Cyanohydrindone (XXXVI) also exhibited tautomeric properties, in this case of the keto-enol type. The substance yielded *O*-ethers from the enolic form and carbonyl derivatives from the keto-form.

Thorpe's next collaborator in this field was S. R. Best, and in 1909 the two published four important papers (J., **95**, 8, 261, 685, 1506). In the first it was shown that for the ring closure of β-imino-γ-phenylbutyronitrile (XXXVIII) to 1 : 3-naphthylenediamine (XXXIX) the α-substituents (phenyl, carbethoxyl) which had been present in previous

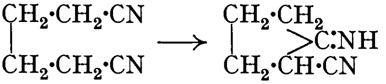
(XXXVIII.)



(XXIXX.)

compounds were unnecessary. The ring closure proceeded smoothly in cold concentrated sulphuric acid. Following this the auto-condensation of the three tolylacetonitriles was studied.

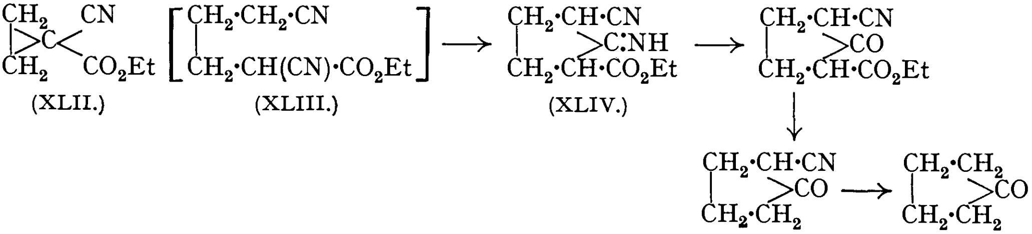
An important research on the extension of the reaction to the aliphatic field followed. Thorpe showed (J., 1909, **95**, 1901) that adiponitrile (XL) was cyclised to imino-2-cyano*cyclo*pentanone (XLI) when it was warmed with sodium ethoxide :



$$\begin{array}{l} CH_2\cdot CH_2\cdot CN \\ | \\ CH_2\cdot CH_2\cdot CN \end{array} \longrightarrow \begin{array}{l} CH_2\cdot CH_2 \\ |\qquad\quad >C:NH \\ CH_2\cdot CH\cdot CN \end{array}$$

(XLI.)

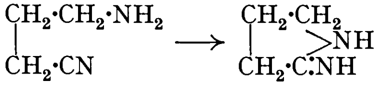
This represents the reaction stripped to its essentials. Best and Thorpe were able to show that the same process occurred in a slightly more complicated case. Carpenter and Perkin, by the action of ethyl sodiocyanoacetate on ethylene dibromide, had obtained *cyclo*propanecyanoacetic ester (XLII), together with a compound formed by reaction with a second molecule of the cyano-ester, and believed to be (XLIII). Best and Thorpe showed that this, too, was a *cyclo*pentane derivative (XLIV), and could be hydrolysed in the stages shown :



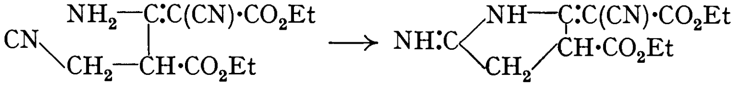
(XLII.) (XLIII.) (XLIV.)

An important distinction was noticed between the ketones, which were stable to acids but suffered ring-fission with alkalis, and the imino-compound, which was stable to alkali but lost ammonia on treatment with acids.

They next examined the possibility of forming heterocyclic compounds from amino-nitriles, *e.g.*,



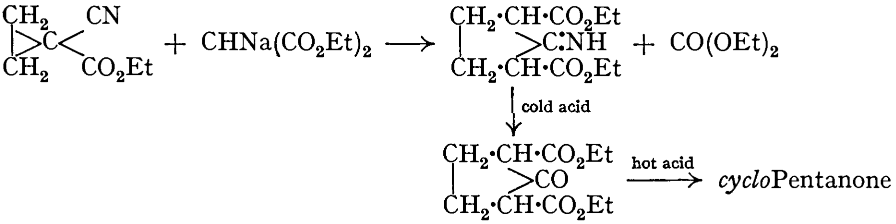
It was found that the amino-nitrile (XLV) could be cyclised to the pyrrolidine derivative (XLVI) :



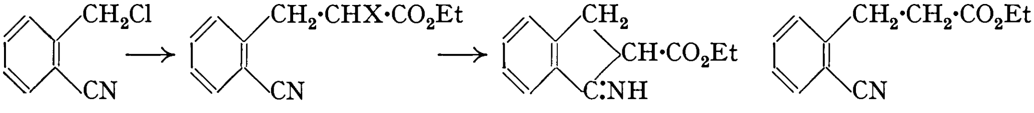
(XLV.) (XLVI.)

A remarkable series of transformations was observed when the product was treated by mild reagents. The chemistry of the substances in this group is much complicated by the ease of imino-amino tautomerism.

A. D. Mitchell and Thorpe (J., 1910, **97**, 997) next showed that for the intramolecular formation of a *cyclo*pentanone-imine only one cyano-group was essential, and the place of the second could be taken by some other activating group. Thus :

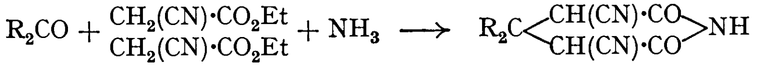


This established a close connection between the Thorpe and the Dieckmann condensation. It was shown (*ibid.*, p. 2261) that a similar cyclisation of a monocyano-compound, accompanied by loss of a carbethoxyl group as ethyl carbonate, also occurred in the condensations first studied by Gabriel and Hausmann. Thus the product of the interaction of *o*-cyanobenzyl chloride and a sodio-ester CHNa(X)·CO_2Et was proved to have the formula (XLVII) and not that (XLVIII) proposed by the discoverers.



(X = CO_2Et, CO·CH_3) (XLVII.) (XLVIII.)

Thorpe's interest in imino-compounds soon attracted him to the neglected reaction of Guareschi. In later years, with Kon (J., 1919, **115**, 686; 1922, **121**, 1765), he did much to improve and popularise this. It consists in the condensation of a ketone with cyanoacetic ester and ammonia and leads to the precipitation of the " Guareschi imide " (XLIX) as the ammonium salt :

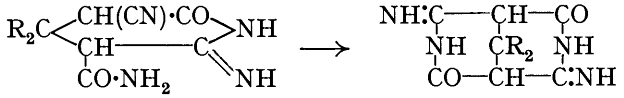


$$R_2CO + \begin{matrix} CH_2(CN)\cdot CO_2Et \\ CH_2(CN)\cdot CO_2Et \end{matrix} + NH_3 \longrightarrow R_2C{<}\begin{matrix} CH(CN)\cdot CO \\ CH(CN)\cdot CO \end{matrix}{>}NH$$

(XLIX.)

Hydrolysis of these imides with sulphuric acid gives excellent yields of ββ-dialkylglutaric acids, and the process constitutes perhaps the best existing preparative method for these substances. Thorpe's earliest experiences with the method were not very encouraging and he therefore (with Thole, J., 1911, **99**, 422) devised a modification. Cyanoacetamide in water containing a little piperidine or alkali was found to condense with ketones to yield crystalline precipitates. The main products, however, were not symmetrical like the Guareschi imides, but were of the structural type (L) :

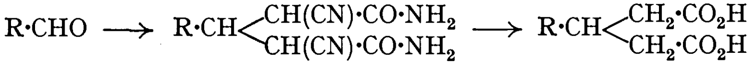
(L.)



(LI.)

Nevertheless a small amount of the corresponding Guareschi imide was formed as a by-product (Thorpe and Wood, J., 1913, **103**, 1569; Kon and Thorpe, J., 1919, **115**, 686). The unsymmetrical cyanoamides, such as (L), were able to cyclise further to the bridged di-imino-di-imides (LI).

The Guareschi reaction is not suitable for the preparation of β-monosubstituted glutaric acids from aldehydes, because the condensation products are stable pyridine compounds. The cyanoacetamide method, however, goes very well, to give the open-chain dicyano-glutaramides, which are smoothly hydrolysed to the corresponding acids (Day and Thorpe, J., 1920, **117**, 1465) :



$$R\cdot CHO \longrightarrow R\cdot CH{<}\begin{matrix} CH(CN)\cdot CO\cdot NH_2 \\ CH(CN)\cdot CO\cdot NH_2 \end{matrix} \longrightarrow R\cdot CH{<}\begin{matrix} CH_2\cdot CO_2H \\ CH_2\cdot CO_2H \end{matrix}$$

4. *Glutaconic Acids.*

Thorpe became interested in these substances at the time of his synthetic work with Perkin and remained actively concerned with their investigation for a quarter of a century. The chemistry of these substances is very complicated. There is an intricate interplay of stereochemical inversion and tautomeric change. We know today that the special hypothesis advanced by Thorpe to explain their behaviour is no longer valid. Nevertheless it is due to the stimulus given by his work in the field that the truth has finally come to light, mainly through the work of Kon and of Packer, both members of Thorpe's school.

Thorpe's cardinal point of view is well stated in a paper in 1923 (J., **123**, 3343). " All experiments on the glutaconic acids . . . combine to show that there is something in the constitution of these substances which conventional symbols do not explain, and that this ' something ' is connected with the mobile hydrogen atom of the system, because it disappears when that atom is absent; we assume, therefore, that this structural peculiarity is connected with the mode of attachment of the mobile hydrogen atom to the rest of the molecule."

It will be convenient at this point to summarise the abnormalities in glutaconic acid chemistry which led Thorpe to take up this position. They are :

(i) The apparent equivalence of the α- and the γ-position.
(ii) The absence of the full number of geometrical isomerides.
(iii) The apparent impossibility of obtaining optically active compounds.
(iv) The abnormal reactivity in additions.
(v) The peculiarities of anhydride formation.

It was the first two of these considerations which led to Thorpe's initial dissatisfaction with the conventional formula $CO_2H\cdot\underset{\alpha}{CH}{:}\underset{\beta}{CH}\cdot\underset{\gamma}{CH_2}\cdot CO_2H$. The system of graphic formulæ due to the genius of Frankland, Couper, and others has been the mainstay of organic chemistry. It nevertheless, like all systems, has its disadvantages, and one of these is its lack of ability to suggest abnormal reactivity. This shortcoming exercised the minds of many chemists at the beginning of the century. It was a time when the conception of valency lacked the comparative precision which it has acquired today and when men of bold minds were able to express themselves with freedom. The shadow of the physicist had yet to fall upon the landscape, and organic chemists were still living in a happy Arcadian simplicity. There arose the " centric " formula for benzene, the partial valencies of Thiele, and, in 1905, Thorpe's " normal " formula for glutaconic acid : $CO_2H\cdot\dot{C}H\cdot CH_2\cdot\dot{C}H\cdot CO_2H$. It was held that this best represented the structure of the ordinary crystalline acid. It indicated a resemblance to the aromatic type, a diminution of unsaturated reactivity, and explained the equivalence of the α- and the γ-position and the absence (at that time) of a second geometrical isomeride. As the facts stood in 1905, the " normal " formula was a better *reaction* formula than the conventional. It was, however, too adventurous to receive general acceptance, and was in particular the target for criticism by Feist. A long controversy ensued, singularly lacking in acrimony. It now appears that, although the " normal " form has outlived its usefulness, Feist tended to underestimate the possibilities of double-bond migration in glutaconic acids and to overemphasise the importance of a purely stereochemical inversion in explaining the various phenomena.

In 1911, with Thole, Thorpe returned to the study of the apparent equivalence of the α- and the γ-position, and examined the peculiar tendency of glutaconic acids to yield chloro- and hydroxy-anhydrides on treatment with acetyl chloride. This work was extended to other members of the glutaconic series and to the aconitic acids in 1912 (with Bland). It was emphasised that in unsymmetrically substituted molecules the tendency for the acid (or its derivatives) to exist in a conventionally double-bonded (labile) form was increased. Later, with Wood, the alkylation of glytaconic ester was studied. It was shown that the results obtained by alkylating the pure sodio-derivative in dry ether with methyl iodide differed from those obtained by the use of sodium ethoxide. The former led to successive α- and γ-methylations and the product was then capable of a final alkylation to an ααγ-trimethylglutaconic ester. In sodium ethoxide, however, both methyl groups entered the α-position, the system lost its mobile hydrogen atom, and was incapable of further alkylation. These results were correlated with the positions taken up by the double bond at the various stages.

In 1919, Thorpe (J., **115**, 679) extended some earlier observations on the additive reactions of glutaconic derivatives. He pointed out that, in general, the " normal " compounds do not form additive compounds readily, whereas the labile compounds exhibit the ordinary reactions of the double bond. He observed, however, that " normal " β-methylglutaconic ester reacted with sodiocyanoacetic ester to give, in low yield, a condensation product, which was hydrolysed to γ-methylbutane-αβδ-tricarboxylic acid The formation of this was attributed to 1 : 3-addition to the free valencies of the normal form. The possibility of such addition was elaborated in subsequent papers with Ingold (J., 1921, **119**, 492) and with Ingold and Oliver (J., 1924, **125**, 2128). The second of these papers illustrated the important point that, when additive reactions did occur to the " normal " form, the products very readily " reverted to type," *i.e.*, they tended to reacquire the stable " normal " glutaconic arrangement. In the present state of our knowledge it is preferable to attribute the anomalous 1 : 3-reactions to reversed 1 : 2-additions to αβ-double-bonded forms.

The main interest in the field then shifted to a cyclic acid of the glutaconic type, 3-methyl*cyclo*propene-1 : 2-dicarboxylic acid, which was investigated by Goss, Ingold, and Thorpe during the years 1923—1925, and subsequently by Kon in Thorpe's laboratories.

The rapid increase in the knowledge of three-carbon tautomerism during the nineteen-twenties led to the development of improved techniques and the time became ripe for a reinvestigation of the many puzzling features of glutaconic acid chemistry. This was carried out in Thorpe's laboratories during 1930—1933 and led to a general reinterpretation on the basis of three-carbon tautomerism and *cis–trans* isomerism. The death blow was simultaneously given to the " normal " form by Packer and Thorpe (see J., 1926, 1199;

1931, 547; 1934, 1653), who resolved " normal " $\alpha\gamma$-dimethylglutaconic acid into optically active forms by means of its acid strychnine salt. It was a fitting tribute to Thorpe's scientific integrity that he should at the end assist in the destruction of a theory which he had defended with so much skill and determination.

5. *Tautomerism and Bridged Rings.*

After Thorpe's translation from Sheffield to the Imperial College, his work becomes more varied and it is correspondingly more difficult to classify and review it.

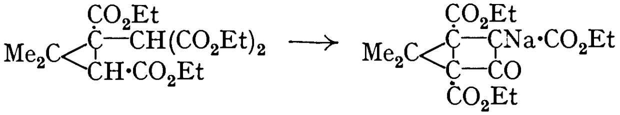
Ever since his earlier investigations on cyanoacetic ester, glutaconic acids and imino-compounds, Thorpe was keenly alive to the widespread occurrence of tautomeric change in organic compounds. He did as much as anyone in this country to propagate the idea of the shifting double bond and the mobile hydrogen atom, and he played an important part in laying the foundation on which our modern conceptions of tautomeric change are based. In 1922 (J., **121**, 650) he advanced what is perhaps the best and most logical definition of tautomerism which we have. " The word tautomerism is used to denote reversible isomeric change, such change being brought about in solution, or in the liquid state with or without the aid of catalysts, to form equilibrium mixtures of the individual showing tautomerism."

One of Thorpe's most important contributions to the subject was made in 1911. With Thole (J., **99**, 2182) he observed that, when the last mobile hydrogen atom in a tautomeric system was replaced by alkyl, then " . . . the tendency for the compound to acquire that hydrogen atom which is necessary to enable it to react in its tautomeric form is such that any group capable of replacement by hydrogen is at once eliminated in the presence of a suitable reagent." Thus an alkylated carbethoxyglutaconic ester would react with sodium ethoxide with the elimination of ethyl carbonate:

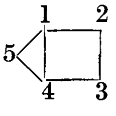
$$CO_2Et{\cdot}CR{:}CR'{\cdot}CR''(CO_2Et)_2 + NaOEt \longrightarrow CO_2Et{\cdot}CR{:}CR'{\cdot}CNaR''{\cdot}CO_2Et + CO(OEt)_2$$

It was shown that this was only a property of unsaturated and potentially mobile systems, saturated malonic esters being unaffected. The theme was further developed for indene derivatives with Ingold (J., 1919, **115**, 143). It was of the greatest importance in Thorpe's general work on imino-compounds and glutaconic acids.

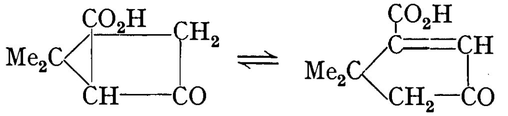
Some of Thorpe's most intricate work was on the tautomerism of bridged ring compounds. His interest in this field had been aroused during some early experiments with Perkin (J., 1901, **79**, 729). They had condensed $\alpha\alpha'$-dibromo-$\beta\beta$-dimethylglutaric ester and sodiomalonic ester to yield the *cyclo*propane derivative (I). This, when heated with sodium or sodium ethoxide, gave a yellow, stable sodium compound (II):

(I.)

(II.)

The investigations of the involved and often ambiguous degradation reactions of this bridged-ring compound occupied four years and left Perkin and Thorpe not entirely satisfied with the results. Thorpe returned to the study of these compounds in 1919 with Ingold (J., **115**, 320). They undertook a detailed comparison of the behaviour of substances of type (II) with that of the corresponding compounds with a *cyclo*hexane ring in place of the *gem*-dimethyl group. The research was centred around (i) a comparison of the ease of closure of the *cyclo*butane ring (3 : 4-bond formation), (ii) hydrolytic fission of the *cyclo*propane ring (4 : 5-bond fission), (iii) hydrolytic decomposition of the methylation products of the bridged compounds (stability of 4 : 5 and 2 : 3 bonds), and (iv) fission of the bridge (1 : 4) by reduction.

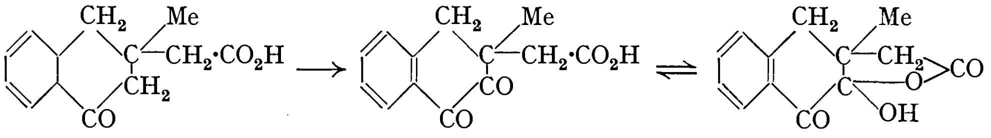


In 1922, a further investigation of compounds of this type was made (Farmer, Ingold, and Thorpe, J., **121**, 128), particularly of the keto-acid (III). The conclusion was reached that this substance was capable of reacting in a monocyclic unsaturated form (IV). For this phenomenon, the convenient term " intra-annular tautomerism " was coined.

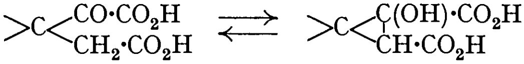
(III.)

(IV.)

To establish this fact, a thorough study was made of the oxidation with potassium ferricyanide and permanganate and of the reactions with chlorine, bromine, and nitrosyl chloride. A year later a study was made by Thorpe, Ingold, and their collaborators of the related intra-annular tautomeric system :

Contemporaneously, Thorpe was studying the keto-enol tautomerism which can occur between a ring compound and its open-chain isomeride. This is now recognised to be of widespread importance and Thorpe's term " ring-chain tautomerism " is in general use. The compound initially studied, with Kon and Stevenson, was the intermediate oxidation product of the acid (V). This was found to be capable of reacting either in the keto- (VI) or the hydroxy-lactone (VII) form :

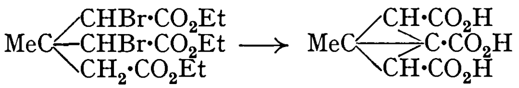

(V.) (VI.) (VII.)

The substance behaved as an α-diketone in yielding a quinoxaline derivative, and as a lactol in giving an acetyl compound. Moreover, it was observed that the solution in water or alcohol, initially colourless, became yellow when warmed, the colour change being reversible. This was interpreted as the reversible formation of the diketone (VI) from its tautomeride. Another example of ring-chain tautomerism was seen in Balbiano's acid, which has already been mentioned. Still another came from the related study of α-ketoglutaric acids containing various β-substituents.



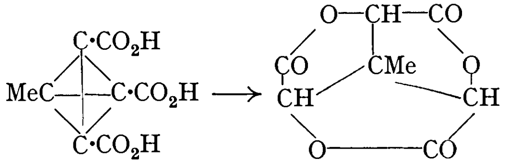
This will be more appropriately considered later, in connection with valency deflection. The conception of ring-chain tautomerism was used to interpret the colour reactions of the fluoresceins and rhodamines (Dutt and Thorpe, J., 1924, **125**, 2524). It was also the theoretical basis of an excursion made by Thorpe with Ingold and J. W. Baker into sugar chemistry. A study of the velocity of the mutarotation of tetra-acetyl *d*-glucose in dry and in moist ethyl acetate led to the view that the reaction was a pure example of ring-chain tautomerism and did not involve the intermediate formation of a hydrate (J., 1924, **125**, 268).

Thorpe was perennially interested in complex carbon ring structures. The most unusual with which he worked was described in a paper with Beesley (J., 1920, **117**, 598) after earlier preliminary work. It was found that the bromination of ββ-dimethylpropanetricarboxylic acid gave the dibromo-ester (VIII). When this was treated with aqueous potash at a high temperature (" as quickly as possible, consistent with safety," as Thorpe's phrase runs), it yielded the bridged *cyclo*butane acid (IX) :

(VIII.)

(IX.)

This acid was isolated in three forms, two of which gave anhydro-acids. The acids were stable to boiling acid and alkali, and did not react with bromine or permanganate. One of them, on treatment with bromine and phosphorus pentabromide, and subsequently with alcohol, gave a bromine-free product, which on hydrolysis yielded a tribasic acid, $C_8H_6O_6$. This remarkable substance appears to have the structure (X), the four cyclic carbon atoms being situated at the corners of a tetrahedron. In support of this the substance yields no anhydride, has no reaction with bromine, and does not reduce permanganate in the cold. It is oxidised by hot permanganate to methylsuccinic acid and converted by hydrochloric acid under pressure into the trilactone (XI).

(X.)



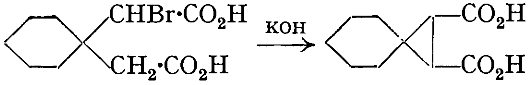
(XI.)

6. *Valency Deflection.*

The developments in this field are associated jointly with the names of Thorpe and Ingold. Their collaboration began in 1914 and lasted until 1928.

The point of departure in their work was the realisation that the regular tetrahedron was an inadequate general representation of the carbon atom. They were the first to give definite expression to the view that the angles between the valencies of a carbon atom could be modified by substitution. This fruitful idea marked a great advance. It at once permitted a correlation of a large number of observed facts in which highly substituted molecules behaved in a different manner from their unsubstituted analogues. This central conception has been abundantly verified by exact physical measurements of recent years. We may mention Debye's classical *X*-ray investigation of the chlorinated methanes, in which it was shown that the carbon–chlorine distance remained constant throughout the series, but the chlorine–chlorine distance altered owing to a change in the intervalency angle. The angle between the $C{<}^{Cl}_{Cl}$ valencies is calculated to rise from 116·4° in chloroform to 123·8° in methylene chloride.

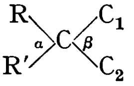
Thorpe and Ingold's first paper in this field (with Beesley, J., 1915, **108**, 1080) was concerned with the investigation of the effect produced by the alteration of the tetrahedral angle owing to ring formation on the formation of and stability of a second ring joined to the first by a common quaternary carbon atom. It was considered that a bending outwards of the valencies in the original ring would cause the other valencies to distribute themselves equally in the remaining space. They would come closer together than the usual 109° 28′ and hence there would be a greater facility for the formation of a second ring. The reaction chosen for investigation was the formation of the *spiro*-compound (XII) from a monobrominated derivative of *cyclo*hexane-1 : 1-diacetic acid (XIII). The formation of bromo-lactones from the corresponding dibromo-esters was also examined.



(XIII, as half ester.) (XII.)

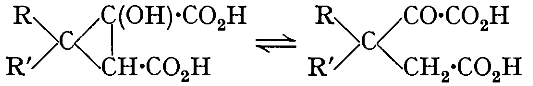
It was unfortunate that a *cyclo*hexane derivative was used in this early work. At the time it was almost universally believed that this ring was " strained " in the Baeyer sense, that it was uniplanar and had an internal angle of 120°. We now know that the *cyclo*hexane ring can adopt multiplanar forms, although these are not sufficiently permanent to lead to isolable isomerides unless stabilised by fusion with another ring. It is impossible as yet to draw any final conclusion as to the size of the internal angle in *cyclo*hexane, but most chemists now regard this as being approximately tetrahedral and the ring as being either largely or entirely free from strain.

In 1921, Ingold extended the original conception to acyclic compounds. For assessing the value of the angle α between two substituent groups R, a calculation based on the molecular volumes of the groups was used. As in the early work in which R,R′ were part of a ring, the value of the emergent angle β was calculated. This provided a theoretical basis for a study of the effect of substituents on the relative ease of ring formation involving the atoms C_1, C_2 and on the stability of the rings so formed.



On this basis a series of investigations was instituted over a period of years. The main reactions studied were (i) the ease of formation of *cyclo*propane compounds such as (XII); (ii) the stability of these acids (caronic acid type) towards fission by hydrochloric acid; (iii) the ring-chain tautomerism between the hydroxy- and keto-acids of types (XIV) and (XV) in concentrated aqueous alkali:

(XIV.)



(XV.)

One of the most interesting observations was the general agreement in behaviour between the *gem*-dimethyl compounds and their *cyclo*pentane analogues, as predicted by the theory. The results of the study of the ring-chain tautomerism (XIV $\rightleftharpoons$ XV) were perhaps the most striking, the following figures being obtained:

	% at equilibrium.			% at equilibrium.	
RR′.	Keto-acid.	Hydroxy-acid.	RR′.	Keto-acid.	Hydroxy-acid.
H, H	100	0	Et, Et	38	62
Me, Me	100	0	Pr^{α}, Pr^{α}	29	71
*cyclo*Pentane	100	0	*cyclo*Hexane	0	100
Me, Et	100	0			

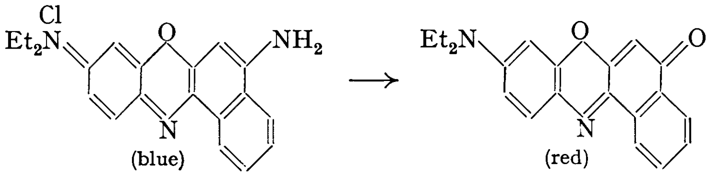
It was pointed out that these differences are those expected if the substituents produce successive contractions in the intervalency angle β.

Evidence from another point of view was advanced by Spiers and Thorpe (J., 1925, **127**, 538), who made a study of the dissociation constants of a large number of acids of the succinic and glutaric series. This work was based on the long-recognised conception that the primary and secondary dissociation constants of dicarboxylic acids are largely determined by the distance between the carboxyl groups. The greater the distance, the smaller the primary, and the larger the secondary, dissociation constant. Spiers and Thorpe's measurements of the primary dissociation yielded results in general agreement with the demands of the valency deflection hypothesis. A fuller investigation has since been made by Gane and Ingold. It remains, however, a matter of difficulty to obtain an entirely satisfactory method of calculating the distance between the carboxyl groups from the ratio of the first and the second dissociation constants, and to evaluate the relative importance of valency deflection and variation in the equilibrium configuration in determining this distance.

The hypothesis of valency deflexion was the target for a good deal of criticism, notably from W. Hückel, which led to a general restatement (Ingold and Thorpe, J., 1928, 1318). Thorpe's final summary of his work in the field was given in his Presidential Address in 1931 (J., p. 1020). We are not today in a position to say how important a rôle valency deflection plays in organic chemistry. We know without question that valency angles are deflected and we can be reasonably certain that in this way the ease of various reactions is affected. The task of disentangling this effect from the other influences at work is a task for the future. Thorpe's greatest achievement in this field was to release organic chemists from a habit of thought at once over-rigid and over-simplified.

5. *Miscellaneous.*

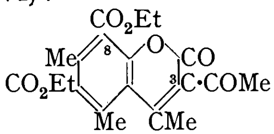
The wide range of Thorpe's chemical interests is reflected in the number of papers which he published from time to time on miscellaneous matters which caught his attention. The first of these, dealing with a subject quite foreign from anything he had previously investigated, was entitled " A reaction of certain colouring matters of the oxazine series " (J., 1907, **91**, 324). This research arose from a histological observation made by Professor Lorrain Smith and Dr. Powell White of Manchester. They had used certain oxazine colours for staining pathological specimens. They found that they not only stained the protein blue but the fat red. Thorpe revealed the underlying chemistry of the process. He showed that the red colour could be reproduced in hydrocarbon solvents and was due to a hydrolysis; for example, in the case of Nile Blue A :

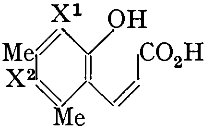


He published another paper with Lorrain Smith on Weigert's method of staining medullated nerve fibres in the following year (*J. Path. Bact.*, 1908, **13**, 14).

Two other interesting papers removed from Thorpe's usual lines of research appeared in 1915. One with Jordan (J., **107**, 387) was on the formation of coumarin derivatives and the preparation of stable coumarinic acids. It was shown that the neutral substance formed by the action of sodium ethoxide on ethyl *iso*dehydracetate was the coumarin derivative (XVI) :

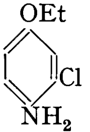
(XVI.)





(XVII.)

It was shown that the acetyl group in position **3** was remarkably stable. So also were the corresponding coumarinic acids (XVII) where $X^1 = CO_2H$ or CO_2Et and $X^2 = CO_2Et$ or H, which resisted cyclisation to the corresponding coumarins. The stability of these acids was due to the CO_2H (or CO_2Et) in position 8. When this was replaced by hydrogen, the lactone ring was easily formed.

The other research arose from the work done at South Kensington during the early months of the war of 1914—1918 on the preparation of phenacetin. Thorpe and Miss Hurst(J., 1915, **107**, 934) found that the reduction of *p*-nitrophenetole with tin and concentrated hydrochloric acid gave, not *p*-phenetidine, but the chloro-derivative : 

Later Thorpe investigated the formation of derivatives of tetrahydronaphthalene and of indene from γ-phenyl fatty acids (with Stevenson and others, J., 1922—1924). The titles given below will convey some idea of the variety of work in other fields :

" The Action of Bromine on β-Hydrindone " (with Creeth, 1908).

" The Replacement of Alkyl Groups in Tertiary Aromatic Bases " (with Wood, 1913).

" Asymmetric Replacement in the Meta-series " (with Gough, 1919).

" The Intermolecular Condensation of Methyl Ethyl Ketone in the Presence of Calcium Carbide " (with Becker, 1922).

" The Influence of Substituents on the Formation and Stability of Hydantoins " (with Ingold and Sako, 1922).

"The Formation of Bromine Derivatives of Carbon Compounds without the Production of Hydrogen Bromide " (with Gupta, 1922).

" The Formation of Stable β-Lactones " (with Bains, 1923).

" The Relative Stability of Open-chain Dibasic Acids containing Odd–Even Numbers of Carbon Atoms " (with Challenor, 1923).

" The Properties of Conjugated Compounds " (with Farmer and others, 1927—1928).

In addition to his original memoirs, Thorpe carried out a large amount of other writing. He undertook the gigantic task of editing, with Dr. M. A. Whiteley, the Supplementary and the New Editions of the " Dictionary of Applied Chemistry " founded by his namesake, Sir Edward Thorpe. He also wrote " The Synthetic Dyestuffs," in collaboration with J. C. Cain and later with R. P. Linstead; " The Vat Dyestuffs," in collaboration with C. K. Ingold; and " A Student's Manual of Organic Chemical Analysis," with M. A. Whiteley. He contributed to the " Annual Reports on the Progress of Chemistry " in 1914 and wrote a section of the Memorial to W. H. Perkin, jun. It is a volume of achievement which reflects on the wide knowledge of the chemist and the unquenchable vitality of the man.

R. P. LINSTEAD.

SIR WILLIAM FITZTHOMAS WYLEY.

1852—1940.

SIR WILLIAM WYLEY, Chairman of the well-known firm of manufacturing chemists and druggists bearing his name, died at his home, The Charterhouse, Coventry, on August 11th, 1940, in his 89th year.

He was born at Stoke House on June 12th, 1852, and received his early education at Rugby. After leaving there, he attended the College of the Pharmaceutical Society. Later, Wyley went abroad, studying manufacturing and industrial production with several important continental firms.

He entered the Firm of Wyleys, in which both his father and his uncle were members, eventually becoming chairman and managing director.

Wyley was one of the oldest Fellows of the Chemical Society, having been admitted as a life member in 1884. His association with the British Pharmaceutical Conference dates back to 1870.

The honour of knighthood was conferred on him in 1938 in recognition of his social and public services in Coventry and in the County of Warwick.

The life of Sir William was so intimately interwoven with the social and business fabric of Coventry's existence for some 60 years that he had become a living representative of the City's highest ideals in those matters intensely affecting her real welfare.

A man of culture and refinement, he brought an air of dignity and a natural charm of manner to the aid of the many public causes claiming his unfailing co-operation.

It was in 1872 that Sir William was appointed an Ensign in the second Volunteer Battalion of the Royal Warwicks, and he was for many years honorary Colonel Commandant. In the last war Sir William raised the third Battalion of the Coventry Regiment and for a year commanded the third Line Brigade.

Sir William Wyley was elected Mayor of the City of Coventry in 1911, and in 1924 the honorary freedom of Coventry was bestowed on him in recognition of his long and distinguished service to his native City.

In 1914 he was appointed Sheriff of Warwickshire and subsequently he became a Deputy Lieutenant of the County.

He had been a bank director for over half a century, first of the old Coventry Union Bank and then of the Midland Bank. He was a Governor of King Henry VIII School and of the Birmingham University.

In the world of Freemasonry Sir William was a distinguished figure. From 1916—1918 he was Deputy-Provincial Grand Master of Warwickshire, becoming Provincial Grand Master in the latter year, which position he held to the time of his death.

A keen churchman, Sir William had a life-long association with the Cathedral church of St. Michael. He had held many important offices, including those of churchwarden, treasurer, and lay-canon.

He was cremated on August 15th, 1940, and his ashes rest in the crypt-chapel of the Coventry Cathedral.

G. PINCHBECK.