# Some pioneers of the kinetics and mechanism of organic reactions

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**Sir Christopher Ingold played a key role during the late 1920s and through the 1930s and 1940s in getting the study of the kinetics and mechanism of organic reactions established as an integral part of organic chemistry. Such studies, however, had already been considerably pursued by many chemists, whose work has now largely been overlaid by later developments. The article highlights the contributions made between about 1895 and 1930 by James Walker, Arthur Lapworth, N. V. Sidgwick, J. J. Sudborough, K. J. P. Orton, and H. M. Dawson, with brief mention of others who helped to found this area of physical organic chemistry.**

## 1 Introduction

A few years ago the centenary of the birth of Sir Christopher Ingold (1893–1970) was commemorated.[1] No-one would dispute that Ingold played a key role during the late 1920s and through the 1930s and 1940s in getting the study of the kinetics and mechanism of organic reactions established as an integral part of organic chemistry. Because Ingold's contribution was so substantial and important, many chemists today doubtless believe that there was almost no study of the kinetics and mechanism of organic reactions before his time. Louis Hammett (1894–1987) described the first quarter of the 20th century as the 'Dark Ages' before the 'Renaissance' of organic solution kinetics,[2] although he distinguished a few exceptions to this generalization. An examination of the literature citations in the first edition (1940) of Hammett's own book reveals that this description was rather an over-simplification. In fact a considerable amount of good work was done in the first quarter of the 20th century, but such studies tended to be regarded as contributions to physical chemistry rather than organic chemistry. Most organic chemists considered that their proper business was the synthesis of new compounds or determining the structures of natural products, and they regarded studies of kinetics and mechanism as irrelevant to the progress of organic chemistry.

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One may have some sympathy with those who took this view at that time, because it must be admitted that many studies of the kinetics of organic reactions carried out before 1920 were 'before their time', in that, for various reasons, the results could not be satisfactorily explained. The most general problem arose from inadequate understanding of molecular structure and the nature of the chemical bond. Also, the underlying theory of chemical kinetics was still very primitive: collision theory and transition state theory had yet to be developed. The theory of solutions was floundering with the 'anomaly of strong electrolytes' and was unable to deal satisfactorily with the physical or chemical interactions of such electrolytes with organic compounds.

However, there were some organic chemists even at that time who recognized that the investigation of kinetics and mechanism was important. Julius Berend Cohen (1859–1935)[3] was professor of organic chemistry at the University of Leeds from 1904 to 1923, when he was succeeded by Ingold. Cohen had previously studied with Schorlemmer at Manchester and under von Pechmann in Baeyer's laboratory at Munich. He wrote several textbooks of organic chemistry, including *Organic Chemistry for Advanced Students*, which first appeared in 1907. By the 4th edition (1923) the work was being published in three Parts, and Part I (entitled *Reactions*) had many features which we would classify as belonging to physical organic chemistry. In particular there was a chapter on the 'Dynamics of Organic Reactions', and it would be appropriate to quote its opening paragraph:

> Of the various methods which have been resorted to in seeking information relative to the mechanism of organic reactions, one of the most important is that afforded by a study of the velocity of change, and of the way in which this velocity is modified by variations in conditions under which a given reaction occurs. In the early study of chemical dynamics, chief interest centred in the discovery of simple reactions, which by reason of their freedom from any disturbing complications, might be made use of in testing the applicability of the law of mass action to account for the observed course of the change. Now, however, that the factors which control the velocity of chemical change have been established, the main object of a dynamical investigation lies in the information which it affords in regard to the mechanism by which the final products of a reaction are produced from the original substances.

The inclusion of material of this sort in a textbook of organic chemistry at that time was very unusual.

The present article is based on lectures which the author has given on various occasions, drawing examples from the work of British chemists. Through studies of the kinetics and mechanism of organic reactions between about 1895 and 1925, they provided the immediate background to Ingold's own work and he had definite links with some of them. This pattern will be followed in the present article, with six chemists being selected for particular attention; there will be incidental mention of various others. However, to avoid giving any impression of chauvinism, contributions by chemists of other nationalities will be mentioned *passim* where appropriate and some special (but necessarily brief) attention will be paid to these in a final section.

## 2 James Walker (1863–1935)

Walker[4] was born in Dundee, Scotland, the only child of James Walker, a flax merchant, and his wife Sarah. He was educated at Dundee High School, where the teaching was apparently very good, especially in English, French and Science. At the age of 16 Walker was apprenticed to David Low, a flax and jute spinner, and during the next three years gained some experience of business methods. He also attended evening classes in science, conducted by Frank W. Young, who had taught him at high school. In later life Walker attributed his interest in science to Young's enthusiasm and inspiration. At the end of his apprenticeship he decided to study science seriously and in 1882 he entered the University of Edinburgh. In the practice of Scottish university degrees he attended classes in several subjects, and was particularly impressed by Crum Brown's lectures in organic chemistry. After graduating with a BSc in 1885, Walker returned home to Dundee, where a University College had been founded in 1882. He started research with Thomas Carnelley, the professor of chemistry at the new college, and after one year was able to submit a thesis on 'The Dehydration of Metallic Hydroxides by Heat' for the DSc degree of the University of Edinburgh.

Walker acted as a demonstrator in the Edinburgh laboratory during 1886–1887, but realised that if he was to pursue an academic career in chemistry, experience in a German university was highly desirable. He felt drawn towards physical chemistry and to working with Ostwald, who was then in Riga. However, friends who knew the Baltic countries advised against this, so he went in 1887 to Baeyer's laboratory in Munich, where he worked under Ludwig Claisen. In the meantime, Ostwald had moved to Leipzig and so Walker transferred there for the summer session of 1888. His work with Ostwald was on the measurement of affinity constants (*i.e.* dissociation constants) of bases and he graduated with a PhD in July 1889. Walker returned to Edinburgh and became research assistant to Crum Brown, a position he held for three years. During this time Walker, as Ostwald's first pupil from Britain, played an important part in introducing the theories of osmotic pressure and electrolytic dissociation into the country. These initially encountered much opposition, although they were supported strongly by William Ramsay. There was a historic discussion of the theories in a meeting of the British Association at Leeds in 1890, in which van't Hoff, Ostwald and Ramsay participated and Walker read a paper on behalf of Arrhenius. A further meeting of the B.A. at Edinburgh in 1892 was attended by Arrhenius, Ostwald, and Ramsay. On the conclusion of his post with Crum Brown, Walker joined Ramsay's staff at University College, London, and might well have spent the rest of his career there. However, in 1894 the Chair of Chemistry at Dundee fell vacant and Walker was appointed to it.

During his fourteen years at Dundee (Fig. 1), the Chemistry Department grew both in size and facilities. In 1908 Walker succeeded Crum Brown in the Chair at Edinburgh and held it for twenty years, a period which covered the difficult times of World War I (when members of the Department ran an explosives factory) and the expansion of the Department post-war, which involved the construction of a new building on another site. Walker resigned in 1928, but remained scientifically active until his death in 1935. Among various honours he received were F.R.S. in 1900, the Davy medal of the Royal Society in 1926 (for his work on the theory of ionization), the presidency of the Chemical Society in 1921–1923, and a knighthood in 1921.

In 1895 James Walker and Fred J. Hambly published in the *Journal of the Chemical Society* a twenty page paper entitled 'Transformation of Ammonium Cyanate into Urea.[5] The paper describes a study of the kinetics of the reaction and a mechanism was proposed. The work was presumably undertaken during the first few months after Walker took up his post in Dundee. There is no clear indication as to why Walker selected this particular topic for research. He does not appear to have had any special interest in chemical kinetics, although he returned from time to time to the study of this particular reaction over the next forty years. The opening paragraph reads as follows:

> Since Wöhler's memorable observation that ammonium cyanate spontaneously undergoes transformation into urea, the subject, probably from the very magnitude of the result achieved, has been entirely neglected. One or two points of interest, however, occur in connection with this transformation, and it is the object of the present paper to draw attention to them.

Almost certainly it was essentially the electrochemistry of the system which interested Walker, disciple of Ostwald as he was.

Walker and Hambly followed the course of the reaction in aqueous solution by argentometric determination of cyanate and showed that there were two complications: the reaction was slightly reversible and a side-reaction, namely hydrolysis of cyanate to ammonium carbonate, occurred to the extent of a few percent. Both these disturbances were considered to be allowed

**Fig. 1** James Walker, probably *ca*. 1900. The photograph was taken in Dundee. (Reproduced courtesy of the Library and Information Centre, Royal Society of Chemistry.)

for by formulating the kinetic equations in terms of $x$, the concentration of ammonium cyanate that has reacted by time $t$ and $A$, the 'practical end-point', the limiting value of $x$ as $t$ tends to $\infty$. Since the chemical equation involves only one molecule of ammonium cyanate, *i.e.* $NH_4CNO = CO(NH_2)_2$, they expected the 'unimolecular' rate equation to be applicable. (Walker apparently preferred van't Hoff's use of 'molecularity' to Ostwald's use of 'order' in kinetics.) To their surprise the calculated unimolecular velocity constants diminished steadily over the course of the reaction. They commented:

> We are thus forced to conclude that the production of urea from ammonium cyanate does not proceed in so simple a way as we might be disposed to imagine.

They now applied the bimolecular rate equation in the form:

$$C = x/tA(A - x) \qquad (1)$$

The quantity $C$ remained essentially constant over the course of the reaction, although it increased slightly with decreasing initial concentration of ammonium cyanate.

In starting to discuss the reaction mechanism, the authors wrote:

> We have now to consider the reason why the transformation of ammonium cyanate into urea is a bimolecular reaction, and not a unimolecular reaction as might *a priori* be expected. The two reacting substances must be present in the ammonium cyanate solution in equivalent proportions, otherwise the expression $x/t(A - x)$, would not remain constant. The assumptions which might account for this are, 1st, that two molecules of ammonium cyanate meet to form urea; 2nd, that the ammonium cyanate is dissociated by the water wholly or largely into ammonia and cyanic acid, and 3rd, that the ammonium cyanate is electrolytically dissociated into ammonium ions and cyanic (*sic*) ions. A means of ascertaining which of these assumptions is correct is to be found in the influence exercised by various substances on the constant.

The substances referred to are ammonium sulfate and potassium cyanate (both producing considerable acceleration), potassium sulfate (slight inhibition) and ammonia (almost no effect). These results led Walker and Hambly to conclude that their 3rd assumption above was correct, *i.e.* that the mechanism involved ammonium ions and cyanate ions. they wrote:

> We find, then, that the consistent application of the theory of electrolytic dissociation accounts for the bimolecular nature of the transformation of amonium cyanate into urea, the quantitative influence on it of dilution, and of the presence of potassium sulphate, potassium cyanate, ammonium sulphate, and ammonia. On no other theory, as it appears to us, can even a qualitative explanation of our results be given.

In their 2nd and 3rd assumptions Walker and Hambly correctly identify the two main possibilities for the reacting species, but they were wrong in supposing that these can be distinguished in the way suggested. This matter will be best explained by a brief discussion in a modern style, which summarises the more detailed exposition given in the article written by the present author in 1978.[6]

Since ammonium cyanate is highly ionized, the observed second order kinetics may be expressed by eqn. (2):

$$\text{Rate} = k[NH_4^+]\,[CNO^-] \qquad (2)$$

The straightforward interpretation of this expression, which has been accepted by numerous authors, is that the reaction proceeds by the *ionic mechanism* (3):

$$NH_4^+ + CNO^- \rightarrow CO(NH_2)_2 \qquad (3)$$

This is, however, not the only possibility. Ammonium cyanate, as the salt of a weak base and a weak acid, participates in the mobile equilibrium (4):

$$NH_4^+ + CNO^- \rightleftharpoons NH_3 + HNCO \qquad (4)$$

This is essentially what Walker and Hambly suggested in their 2nd assumption, but they were wrong in believing that the process goes 'wholly or largely' to completion. The equilibrium constant is *ca.* $2.5 \times 10^{-6}$ at 25 °C. The equilibrium concentrations of ammonia and isocyanic acid (unless added in excess) are thus small, but the existence of (4) means that the second-order kinetics may also be expressed as in (5):

$$\text{Rate} = k'\,[NH_3]\,[HNCO] \qquad (5)$$

and interpreted in terms of the *molecular mechanism* (6):

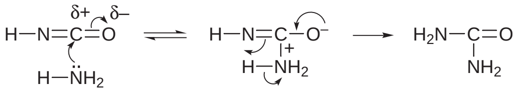
$$NH_3 + HNCO \rightarrow CO(NH_2)_2 \qquad (6)$$

It can easily be shown that the effects of ammonium sulfate, potassium cyanate, ammonia, and potassium sulfate on the rate, which were believed by Walker and Hambly to support their 3rd assumption unequivocally, may be interpreted equally well as direct effects on (3) or as indirect effects on (6) *via* the equilibrium (4).

To return to Walker and Hambly: their pioneering work in 1895 began what the present author has described as a 'Saga in Reaction Mechanisms', which continued to the 1970s, and was examined in detail in the earlier article.[6] Further papers by Walker and his colleagues appeared in the period 1896–1900. These were mainly concerned with the reaction in aqueous organic solvents and the results were interpreted in terms of the ionic mechanism. Other authors soon became interested in the reaction mechanism. The kinetic ambiguity was widely recognized, even by Walker himself, but some authors produced evidence of other kinds or devised subtle arguments which, it was claimed, supported either the ionic or the molecular mechanism. Those who participated in various ways in the saga between 1900 and 1914 included F. D. Chattaway, D. L. Chapman, Arthur Michael, A. Lapworth, N. V. Sidgwick, T. M. Lowry, H. E. Armstrong and E. A. Werner, some of whom will be mentioned again in later sections.

During World War I and the 1920s there was little work done on the mechanism of the urea synthesis and not until the 1930s does it again feature significantly in the chemical literature. Various studies of kinetic salt and solvent effects utilised the reaction, the interpretation of the results nearly always being given in terms of the ionic mechanism. After World War II the kinetic ambiguity was again emphasized in various studies, but arguments in favour of the molecular mechanism were increasingly put forward. In this connection the kinetic study of reaction series closely related to the classical urea synthesis and the application of linear free energy relationships were particularly important. By the 1970s the molecular mechanism was widely accepted. For accounts of these developments the earlier article should be consulted.[6]

One of the most convincing arguments in favour of the molecular mechanism, however, is that it is inherently more plausible than the ionic mechanism. It is easy to envisage the nucleophile ammonia attacking the positively polarized carbon of HNCO to form a zwitterionic intermediate. A simple proton shift is then all that is necessary to form urea, as in (7).



(7)

Such a mechanism must operate in the related reaction of an alkyl isocyanate RNCO with ammonia to give a substituted urea. The direct reaction of an ammonium ion with a cyanate ion to give urea is difficult to envisage, because the formation of C–N bond is blocked by the four-co-ordination of the N. The ions could conceivably form (reversibly) a hydrogen-bonded complex, as in (8):

$$H_3NH^+ + NCO^- \rightleftharpoons H_3N\cdots H\cdots NCO \qquad (8)$$

but subsequent rearrangement of this to urea seems improbable.

The mechanism of the urea synthesis was further clarified by Williams and Jencks in 1974 through a study of the kinetics of the reactions of isocyanic acid with a wide variety of amines.[7] The molecular mechanism along the lines of (7) was assumed to operate. In the case of weakly basic amines the reactions were found to be subject to general acid-base catalysis, but this feature was absent when strongly basic amines were involved. The conclusion was that for the latter the formation of the zwitterionic intermediate was rate-determining, while for the former the decomposition of the intermediate to products was rate-limiting. It seems probable, however, that for the strongly basic amines, including ammonia itself, the transfer of the proton is not by internal shift as represented in (7), but is by relay through the aqueous solvent.

Walker and Hambly's work in 1895 is particularly interesting because it is one of the earliest examples of a kinetic study in which something really unexpected was found, *i.e.* the course of the reaction, which, from the chemical equation of the urea synthesis, should 'obviously' be unimolecular was found not to be so, but bimolecular. Further, the work provided the first example of kinetic ambiguity, the inability of kinetic studies to distinguish between mechanisms whose respective reactant species are interconverted through a mobile equilibrium.

## 3 Arthur Lapworth (1872–1941)

Lapworth[8] was born in Galashiels, Scotland. His father was Charles Lapworth F.R.S., an eminent geologist, who became professor at Mason College, Birmingham (the predecessor of the University of Birmingham). After early education in St. Andrews and at King Edward's School, Birmingham, he studied science at Mason College and then (1893–1895) at the Central Technical College of the City and Guilds of London in South Kensington (which later became one of the constituents of Imperial College). At the Central he worked with the redoubtable Professor H. E. Armstrong on the sulfonation of ethers of β-naphthol and with F. S. Kipping on derivatives of camphor and camphene. He received a DSc (London) for a thesis on the naphthalene topic.

Lapworth was demonstrator in the School of Pharmacy in Bloomsbury from 1895 to 1900 and then became Head of the Chemistry Department at the Goldsmiths' Company's Institute at New Cross (known as Goldsmiths' College from 1906). He moved in 1909 to the University of Manchester as Senior Lecturer in Inorganic and Physical Chemistry and four years later he succeeded W. H. Perkin Jr. in the Chair of Organic Chemistry (Fig. 2). In 1922 he became Sir Samuel Hall Professor, primarily responsible for physical and inorganic chemistry, and Director of the Laboratories. He retired in 1935 and died in 1941. Among various honours, he was elected F.R.S. in 1910, and was awarded the Davy Medal of the Royal Society in 1931. He served periods as a Vice-President of the Chemical Society and on its Council. The titles of his successive appointments indicate Lapworth's remarkable versatility and the breadth of his interests.

Lapworth's interest in the mechanisms of organic reactions was certainly stimulated by his early experiences of aromatic substitution and of the complexities of camphor chemistry. [It is interesting that Thomas Martin Lowry (1874–1936), who likewise played an important part in the development of physical organic chemistry in Great Britain, was also a pupil of Armstrong at the Central and worked extensively in camphor chemistry.] Lapworth continued to work in camphor chemistry during his time at the School of Pharmacy and at Goldsmiths', and this led to his interest in tautomerism and in particular to his work on the kinetics and mechanisms of the reactions of ketones, which is discussed in some detail below. Connected with all this was his development of a theory of organic reactivity, which became known as the theory of alternate polarities; it was essentially electrical in nature, but pre-electronic. Among Lapworth's colleagues at Manchester between 1909 and 1912 was the young Robert Robinson (1886–1975), then a junior demonstrator working in natural product chemistry in association with W. H. Perkin Jr. The contact between Lapworth and Robinson was fruitful in encouraging the latter to develop his own theory of organic reactivity, which incorporated Thiele's notion of partial valencies, and was later (early 1920s) translated into electronic terms. Lapworth's change of Chairs in 1922 was at least partly to enable Robinson to return to Manchester as Professor. From about 1923 to 1927 Lapworth, Robinson, Flürscheim, Ingold and others were involved in the controversies surrounding the development of electronic theories of organic reactions. Ultimately the theories took on a form which was largely determined by Ingold, but owed a great deal to the earlier input by Lapworth and Robinson. These matters have been much discussed in recent years (see the bibliography of the history of physical organic chemistry prepared by the present author[9]) and will not be pursued here. We shall examine some of the contributions of Lapworth to kinetics and mechanism in the period 1900–1914. For a much more detailed account, see Schofield's article.[10]


**Fig. 2** Arthur Lapworth, *ca*. 1913. (Reproduction courtesy of the late Dr G. N. Burkhardt. © Royal Society of Chemistry.)

Lapworth[11] made a tentative start in the application of rate measurements to elucidate reaction mechanisms in 1903. It was a study of cyanohydrin formation and in the first paragraph of his paper he indicates why he had decided to investigate this:

> It is probably a general experience that in preparing cyanohydrins by the addition of the elements of hydrogen cyanide to ketones and aldehydes, the speed of the reaction and the yield of cyanohydrin obtained may vary in an extraordinary manner, even when the experimental conditions are apparently constant. Hitherto, no systematic attempts seem to have been made to discover the cause of the variation. . .

Lapworth appears to have considered the possibility of doing a formal kinetic study, but to have concluded that it would be difficult or impossible to devise a suitable analytical method.

> It was therefore decided to resort to a method of investigation in which the speed of reaction could be roughly gauged by means of a colour change, and for this purpose, advantage was taken of the fact that camphorquinone has a bright yellow colour, which is perceptible even in very dilute solutions, whilst its cyanohydrin is almost, if not quite, colourless.

The quinone was used in dilute alcoholic or aqueous solution. Lapworth showed quite simply that the yellow colour disappeared only over several hours when the quinone was treated with HCN, but the addition of small quantities of base to such a mixture led to decolourization within a few seconds. Conversely the addition of a small amount of mineral acid so retarded reaction that no noticeable change in colour occurred over several weeks. The results of such experiments and related studies were presented in a carefully argued ten page paper. The conclusion was that in the formation of cyanohydrins the attacking agent was not the HCN molecule but the cyanide ion. Thus the mechanism was represented as in (9) and (10).

$$R_2C{=}O + CN^- \rightleftharpoons R_2C(CN){-}O^- \qquad (9)$$

$$R_2C(CN){-}O^- + H^+ \rightleftharpoons R_2C(CN)OH \qquad (10)$$

> . . . if the second stage is very rapid in comparison with the first, it may readily be seen that the velocity will be proportional to the concentration of the cyanogen (*sic*) ions present.

Lapworth's paper ended with some suggestions concerning the mechanism of the benzoin reaction, in which two molecules of benzaldehyde are converted into one molecule of benzoin, PhCOCHOHPh, under the catalytic influence of cyanide ion. It was suggested that mandelonitrile is formed first and this then condenses with another molecule of benzaldehyde to form the unstable cyanohydrin of benzoin, which breaks up reversibly into benzoin and hydrogen cyanide. In the following year, 1904, Bredig and Stern[12] published a kinetic study of the benzoin reaction, finding it to be of the second order in benzaldehyde, with the rate proportional to the concentration of cyanide ions. This essentially confirmed the mechanism proposed by Lapworth, and indicated that both steps in which a molecule of benzaldehyde is involved govern the observed rate. Lapworth made further contributions to the study of the cyanohydrin reaction, one of them almost thirty years later, at the end of his research career.

Lapworth's most celebrated work in kinetics and mechanism was his study of the bromination of acetone, published in 1904.[13] We begin by indicating in Lapworth's own words why he carried out such work. (The whole of the first page of the paper makes interesting reading, but considerations of space require some excision.)

> The question of the nature of the mechanism of substitution in carbon compounds has attracted much attention during recent years, more especially in certain cases where the compounds are benzenoid in character . . . Considerably less is known of the mode in which substitution occurs in fatty compounds . . . The case of substitution in the group of compounds containing the complex CH–CO . . . is one of considerable interest . . . for there is here a possibility that the characteristic replaceability of the α-hydrogen atom may not be a direct process, but one due to the initial formation of the enolic form C=COH . . . the work described in the present paper was commenced in the hope that, after all, the bromination of simple ketones might prove to be mainly the result of 'direct' substitution. The results obtained, however, can only be interpreted on the opposite assumption . . .

Lapworth found that the action of bromine on acetone in dilute aqueous solution was exceedingly slow, but was strongly accelerated by mineral acids, such as HCl, with the reaction velocity being nearly proportional to the concentration of the acid. The velocity was also nearly proportional to the concentration of acetone, but was practically independent of the concentration of the bromine. The last-mentioned was the most striking finding and showed:

> . . . first, that the reaction proceeds in at least two stages, in one or more of which the bromine is not involved, and, secondly, that in the stage or stages in which the bromine takes part, the velocity of the reaction is so great that the time occupied is not measurable. The approximate proportionality of the velocity to the concentration of acetone indicates that in the reaction representing that stage, the velocity of which is measured, only one molecule of acetone takes part, whilst the observations as to the influence of acids of different concentration are best explained on the supposition that in this reaction one hydrogen ion is involved . . . It seems probable, then, that the bromination of acetone under the conditions maintained is best regarded as the result of a slow, reversible change effected in the acetone by the hydrogen ions, followed by an almost instantaneous bromination of the product, a change which is not appreciably reversible. This intermediate product is perhaps the enolic form of the ketone, as it has already been shown that in many cases the rapid attainment of equilibrium between the tautomeric forms of carbonyl compounds is brought about by acids, whilst there is ample reason for believing that the enolic forms are the more rapidly attacked by substituting agents.

Like the urea synthesis, the bromination of acetone is of particular interest because one of the findings, the zero order with respect to bromine, was completely unexpected. Lapworth also studied the acid-catalysed chlorination of acetone, finding that, at the lowest concentrations of chlorine used, the rates of chlorination and bromination were approximately the same, but at higher concentrations the rate of chlorination was greater. He also carried out a few experiments on the halogenation of other carbonyl compounds and on the bromination of acetone in solvents other than water. Rather oddly he did not apparently try the acid-catalysed iodination of acetone; it fell to Dawson to examine this (Section 7).

Carbonyl addition reactions involving other well known reagents were also investigated kinetically during the first decade or so of the century. Lapworth began the study of oxime formation around 1907, following slightly earlier work by A. W. Stewart (1880–1947), then at University College, London. The kinetics of acetoxime formation proved to be somewhat complicated, the reaction being accelerated both by bases and by low concentrations of acid, but the use of higher concentrations of acid led to progressive inhibition of oxime formation. Lapworth discussed his results in terms of the possible presence in solution of various species including $NH_2OH$, $NHOH^-$, $NH_3OH^+$, MeCOMe and $MeC(OH)^+Me$.[14] However, he abandoned this investigation to S. F. Acree, who had independently begun work on the kinetics of oxime formation.

In 1912 Ferns and Lapworth[15] contributed an important mechanistic detail for the acid-catalysed hydrolysis of esters. They contrasted the reactions of alkyl esters of sulfuric or sulfonic acids with those of alkyl esters of carboxylic acids and concluded that in the former it is the bond between the alkyl group and oxygen which is broken, while in the latter the bond between the acyl group and oxygen is broken. This mechanistic feature was confirmed much later through various experiments, mainly in the 1930s. (See also the mention of Emmet Reid in Section 8.)

## 4 Nevil Vincent Sidgwick (1873–1952)

Sidgwick[16,17] was born in Oxford, the son of William Carr Sidgwick and Sarah Isabella née Thompson. The families on both sides were highly gifted and many members achieved considerable distinction in various fields. He was educated at Rugby School, which was then in the forefront of the movement for the teaching of science in schools, without neglecting the classics. Sidgwick in fact sat for an entrance scholarship in classics at Oxford in 1891, but was not successful. He then resolved to devote himself to science and in 1892 won a scholarship in natural science at Christ Church. He thus became a pupil of Augustus George Vernon Harcourt (1834–1919), the pioneer in the study of chemical kinetics, who was Dr Lee's Reader in Chemistry in the college. Sidgwick graduated with a first class degree in the Honour School of Natural Science in 1895, and then decided to make use of his classical background by studying in the Honour School of Literae Humaniores, in which he obtained a first class degree in 1897.

After acting as a demonstrator in the Christ Church laboratory for a year, he went to Ostwald's laboratory in Leipzig, where he studied under Bredig. Unfortunately he fell ill and had to spend the next academic year in Oxford. He returned to Germany in the autumn of 1899 to work under von Pechmann in Tübingen. His research was on derivatives of acetone dicarboxylic acid, for which he was awarded a doctorate in July 1901. Before he left Tübingen Sidgwick was elected to a Fellowship at Lincoln College, Oxford, where he went into residence in October 1901. This was his home for the rest of his life. He was an unsuccessful candidate for the Dr Lee's Readership in 1902 and was considered for the newly established Dr Lee's Chair in 1920, but otherwise he seems to have made no attempt to leave his appointment at Lincoln College. From 1903 to 1907 he also acted as lecturer in chemistry at Magdalen College (Fig. 3). In 1924 he was given the title of University Reader in Chemistry and in 1935 that of Professor. He was elected F.R.S. in 1922 and was appointed C.B.E. in 1935. Sidgwick was President of the Chemical Society in 1935–1937, and served several periods as a member of Council, as a Vice-President, and as Chairman of Publications Committee. He was also prominent in the Faraday Society, serving as President in 1932–1934. Sidgwick retired from his Fellowship of Lincoln College in 1948, but continued to live in the College until a few weeks before his death in 1952.

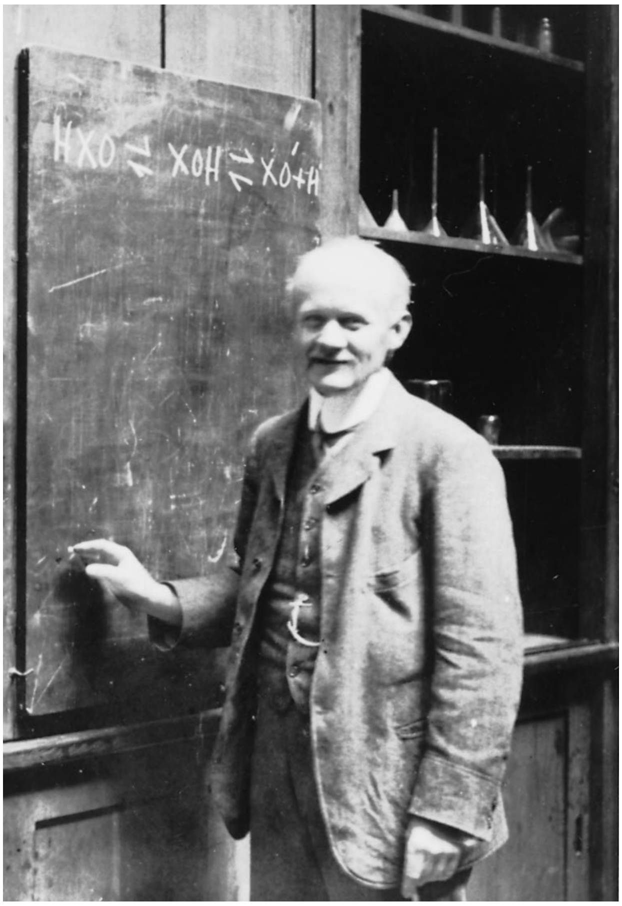


**Fig. 3** Nevil Vincent Sidgwick, *ca.* 1910, in the Balliol-Trinity Laboratory, Oxford. (Reproduced by permission of the Museum of the History of Science, Oxford.)

In the middle of the 20th century Sidgwick's considerable reputation rested largely on his book *The Electronic Theory of Valency*, which had appeared in 1927. His interest in atomic and molecular structure was stimulated initially by contacts with Ernest Rutherford (1871–1937), starting on the voyage out to Australia for the British Association meeting in 1914. It was given further stimulus by the writings of Niels Bohr (whose book *Theory of Spectra and Atomic Constitution* appeared in 1922) and by the influence of G. N. Lewis, who stayed with Sidgwick in June 1923 and whose book *Valence and the Structure of Atoms and Molecules* appeared in the same year. In the previous few years Sidgwick and his pupils had already carried out experimental work on certain topics relating to molecular constitution, notably the hydrogen bond, then a new and controversial concept. From 1923 onwards Sidgwick set out to broaden the application of the electronic theory of valency in various directions, particularly to give an electronic interpretation of the concept of coordination number as developed by Werner for complexes. The resulting book made him famous.

But what of Sidgwick's work before the 1920s and particularly pre-1914? According to L. E. Sutton,[16] his motive in going to Germany in 1898 to 1901 was

> . . . to gain wider experience in methods both of physical and of organic chemistry, for the fulfilment of the aim which he had already formed, namely the application of physicochemical principles to the study of organic chemistry.

(Sutton was a pupil of Sidgwick in the late 1920s, and was closely associated with him for the rest of Sidgwick's life.) Progress in this matter proved, however, to be very slow. Probably the organization and general atmosphere of the Oxford chemistry school at that time were not conducive to rapid progress in research programmes. With a few co-workers over a dozen years Sidgwick studied rates of reaction of triphenylmethane dyes with acids and alkalis, rates of hydration of carboxylic anhydrides, phase equilibria and solubility, and the colour of copper salts in relation to ionization. According to Sutton,[16] by 1915:

> . . . he had published only sixteen original papers and it must be said that although most of them were interesting, and all described careful, well-planned work, none of them was of high importance.

The study of rates of hydration of carboxylic anhydrides was certainly interesting and will be outlined below.

Probably his main contribution to encouraging the development of physical organic chemistry in this period was his first book, *The Organic Chemistry of Nitrogen* (a topic on which he had lectured to undergraduates), published in 1910. In the preface Sidgwick wrote:

> It is becoming generally recognized that organic chemistry cannot be treated satisfactorily without reference to those questions of physical chemistry which it involves. To attempt a separation of the two is to refuse all the assistance which can be derived from what is the quantitative side of chemistry.

The book contained much reference to kinetic studies by, for example, Menshutkin, Wedekind, Blanksma and Goldschmidt. The edition of 1250 copies was soon sold out. Planning for a second edition began in 1922, but work on it was delayed by Sidgwick's absorption in his study of valency. (In addition to the 1927 book, Sidgwick also published his George Fisher Baker Lectures, given at Cornell University in 1932, as *Some Physical Properties of the Covalent Link in Chemistry*.) It ultimately appeared in 1937, in a completely revised form edited by Sidgwick's colleagues T. W. J. Taylor and Wilson Baker. A 3rd edition, edited by I. T. Millar and H. D.<⩾ √τ τηε τιμε *The Electronic Theory of Valency* was published in 1927, Sidgwick envisaged producing a further volume in which the theory would be applied widely in great detail to the elements and their compounds. This work was subject to much delay and was ultimately brought to completion during and in the years immediately following World War II. It appeared in 1950 in two volumes, *The Chemical Elements and their Compounds*, totalling over 1700 pages and incorporating almost ten thousand references.

The reactions of acid anhydrides with alcohols were subjected to kinetic study as early as 1887, when N. A. Menshutkin measured the rates of esterification of various alcohols by acetic anhydride in benzene solution. Somewhat later (the work was published in 1910–1915[18]) Sidgwick and his co-workers made very careful measurements by a conductimetric technique of the rates of hydration, in water as solvent, of several anhydrides of the lower fatty acids and benzoic acid, and of several (intramolecular) anhydrides of dicarboxylic acids. Contrary to expectation, these reactions did not show any sign of being catalysed by hydrogen ions. Selected results are presented in Table 1.

**Table 1** Relative rate constants at 25 °C for the hydration of carboxylic anhydrides

| Anhydride | Relative *k* |
|---|---|
| Acetic | 1.00 |
| Propionic | 0.49 |
| Butyric | 0.27 |
| Benzoic | 0.13 |
| Chloroacetic | *ca.*200 |
| Succinic | 1.01 |
| Methylsuccinic | 1.40 |
| Methylenesuccinic | 1.13 |
| Maleic | 10.06 |
| Methylmaleic | 6.69 |
| Phthalic | 4.03 |
| Camphoric | 0.0023 |

No explanation was offered for the retarding effect of introducing $CH_2$ groups into acetic anhydride, for the rather stronger retarding effect of Ph, or the very strongly accelerating effect of Cl, although some parallel effects on the strengths of the corresponding acids were pointed out. More of an attempt was made to rationalize the results for the cyclic anhydrides along the following lines, taking acetic anhydride as an open-chain reference standard. The reactivity of succinic anhydride is very similar to that of acetic anhydride because the five-membered ring of the former is almost strainless and thus this compound resembles an open-chain compound in behaviour. Sidgwick noted that the introduction of unsaturation into the ring increased reactivity in the order succinic < phthalic < maleic, and he suggested that the ring strain might increase in this order. He pointed out that the effect of the extracyclic C=C in methylenesuccinic anhydride was very small. He was rather puzzled by the opposite effects of introducing a methyl group into succinic and maleic acids, but pointed out that methyl had similar opposite effects on the strengths of the corresponding acids. The enormous retarding effect of the camphor skeleton elicited no comment.

The reactions of acid anhydrides continued to attract kinetic study for many years, at least until the 1950s.

## 5 John Joseph Sudborough (1869–1963)

Sudborough[9] was born in Birmingham and educated at secondary schools in that city. In 1886 he entered Mason College, where he studied under Professors W. A. Tilden (chemistry) and Charles Lapworth (geology). He obtained a London External BSc in 1889, with double First Class Honours. Sudborough remained at the college for a further two years, working under Tilden on the reaction between nitrosyl chloride and terpenes. In 1891 he was awarded a scholarship by the Commissioners of the 1851 Exhibition and proceeded to Heidelberg to work under the direction of Victor Meyer (1848–1897). A thesis on 'Isomeric Change in the Stilbene Series' secured for him the PhD degree in 1893. Sudborough was then invited to act as Professor Meyer's private assistant for a year, during which he worked on steric hindrance in reactions of di-*ortho*-substituted benzoic acids. A stay of six months in the laboratories of Owens' College, Manchester (later the University of Manchester) enabled him to obtain the London External DSc.

From 1895 to 1901 he was lecturer in organic chemistry at University College, Nottingham (later the University of Nottingham) under Professor F. S. Kipping. With the assistance of some senior students he continued his research on steric hindrance and began work on the addition compounds of trinitrobenzene. In March 1901 he succeeded Dr Lloyd Snape as Professor of Chemistry at the University College of Wales, Aberystwyth. It was a time of great educational activity in Wales, several colleges having recently become linked together to form the federal University of Wales. The Aberystwyth college was small, but expanding, and this applied particularly to the Chemistry Department. During Sudborough's first few years there, the accommodation for chemistry was somewhat makeshift, but he was able to pursue fruitfully various lines of research. In 1907 the accommodation was greatly improved with the opening of the Edward Davies Chemical Laboratories. At Aberystwyth Sudborough's research interests turned very definitely towards physical aspects of organic chemistry, with extensive studies of the kinetics of esterification of organic acids and of the hydrolysis of the esters. Examples of this work will be discussed below.

In 1911, after the death of his wife, he accepted appointment as Professor of Organic Chemistry at the Indian Institute of Science, Bangalore (Fig. 4). This had recently been founded by the generosity of the Tata family, the first Director being Professor M. W. Travers. In Bangalore Sudborough developed a sound and thorough system of training in organic chemistry, particularly directed towards the role of organic chemists in

**Fig. 4** John Joseph Sudborough. (Reproduction courtesy of the Department of Organic Chemistry, Indian Institute of Science, Bangalore.)

India. Thus his research interests shifted largely, but not entirely, away from physical organic chemistry to matters of technical importance. Over the years Sudborough and his assistants published many papers on Indian natural products, for example, malabar sardine oil, the extraction of tartaric acid from tamarinds, mohua oil, and tar from coconut shells. He also studied the perishing of paper in libraries under the rigours of the Indian climate.

Sudborough retired on reaching the age limit of 55 years in 1925, having remarried in India. He is not known to have made any attempt to continue being active scientifically, but he enjoyed about thirty-eight years of retirement in South Devon, firstly in Ermington and later in Torquay. He occupied himself in local affairs, serving for many years as a member of Plympton Rural District Council and later for some years as an office-holder in Torquay Natural History Society. He died in Torquay in 1963.

Sudborough's work on the rates of esterification of organic acids and of acidic and alkaline hydrolysis of esters yielded much information on structure–reactivity relationships, most of which could not then be properly explained. It was very much 'work before its time'.[20] About 1950 R. W. Taft used many of Sudborough's data in his analysis of ester/carboxylic acid reactivity.[21]

He studied the effects of carbon chain length and branching on the reactions of aliphatic esters/acids, and the effects on reactivity of introducing polar substituents into various positions in alkyl chains or the benzene ring, particularly in the *ortho* position to the carboxylic function. He obtained many hundreds of interesting results, but was always reluctant to offer explanations, even to invoke steric effects, which, as we can recognize, would have been particularly appropriate for the acid-catalysed reactions. This seems odd, considering the work he had done with Victor Meyer (see above).

Sudborough was particularly interested in the effect of C=C on the rate of esterification of aliphatic carboxylic acids in methanol, catalysed by HCl, a topic which was dealt with in several papers from 1905 onwards.[22] Selected results are shown in Table 2. He commented on the strongly retarding effect of α,β-unsaturation, and the mildly rate-enhancing or rate-diminishing effect of a more remote C=C, but no explanation was attempted. Many similar examples were studied.

**Table 2** Rate constants ($h^{-1}$ for 1.00 M HCl) at 15 °C for esterification of carboxylic acids in methanol

| Structural type | Acid | Rate constant |
|---|---|---|
| ∝,β-unsaturated | $CH_2{=}CHCOOH$ | 3.09 |
| | $CH_3CH_2COOH$ | 91.9 |
| | *trans*–$CH_3CH{=}CHCOOH$ | 1.26 |
| | $CH_3(CH_2)_2COOH$ | 50.0 |
| β,γ-unsaturated | *trans*–$CH_3CH{=}CHCH_2COOH$ | 74.0 |
| | $CH_3(CH_2)_3COOH$ | 53.5 |
| γ,δ-unsaturated | $CH_2{=}CH(CH_2)_2COOH$ | 45.5 |
| | $CH_3(CH_2)_3COOH$ | 53.5 |

## 6 Kennedy Joseph Previté Orton (1872–1930)

Orton[23] was born in St. Leonards-on-Sea, the eldest son of W. P. Orton, an Anglican clergyman. He was educated at Kibworth Grammar School (1882–1885) and then Wyggeston School, Leicester (1885–1888), before entering St. Thomas's Hospital, London to study medicine. After a year, however, he moved to St. John's College, Cambridge, where he took a first class in Part I of the Natural Science Tripos in 1893. He then abandoned medicine for chemistry, obtaining a second class in Part II of the Tripos in 1895. He was somewhat disappointed at this result, but he was nevertheless awarded a research scholarship, which he used to go to Heidelberg to study under Karl von Auwers. In 1896 he was awarded his doctorate *summa cum laude*; it was the first occasion on which such a distinction had been been conferred at Heidelberg on an Englishman.

After a year in Ramsay's laboratory at University College, London, he became in 1897 Senior Demonstrator in Chemistry at St. Bartholomew's Hospital Medical College in London, where the Head of Department was F. D. Chattaway (1860–1944). Six years later, in 1903 at the age of 31, Orton became Professor of Chemistry at the University College of North Wales, Bangor—a position he occupied until his death from pneumonia in 1930 (Fig. 5). During his twenty-seven years at Bangor, Orton participated fully in the life of the College and of the University of Wales. He was elected F.R.S. in 1921 and served various periods on the Councils of the Chemical Society and Institute of Chemistry. In addition to his work as an organic chemist (discussed below) Orton conducted important studies of the geology and bird-life of North Wales and was an enthusiastic mountaineer.

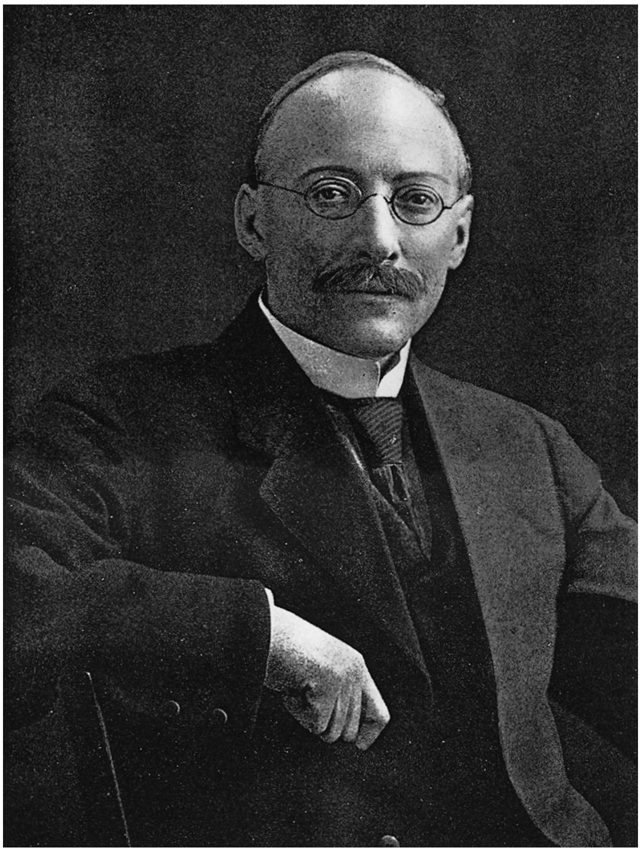


**Fig. 5** Kennedy Joseph Previté Orton. (Reproduction courtesy of the Royal Society.)

The six years Orton spent with Chattaway determined the main area of organic chemistry in which he worked for the rest of his life. Chattaway and Orton collaborated extensively in studies of the preparation and properties of *N*-halogeno compounds, and after he went to Bangor Orton pursued further studies of such systems independently. The main difference between his later work and that of Chattaway, however, was that Orton was gradually drawn into studies of reaction mechanisms, through measurements of reaction rates and equilibria. This was probably under the influence of his friend Arthur Lapworth and led to an extraordinary quarrel and breakdown of relations with Chattaway. (The present author has discussed this matter in some detail in another article.[24]) Particularly after World War I Orton's small department at Bangor became one of the main centres of physical organic chemistry in the UK, and exerted an important influence on the development of the subject. Among his pupils and junior colleagues in the 1920s were:[25]

Herbert Ben Watson (1894–1975), from 1930–1955 Head of the Chemistry Department of Cardiff Technical College, South Wales. He was author of *Modern Theories of Organic Chemistry* (1937) and of many papers on kinetics and mechanism of organic reactions.

Alan Edwin Bradfield (1897–1953), lecturer at Bangor until 1939. He then worked for the Indian Tea Association (London) and finally in the biochemical section of East Malling Research Station, Kent, his main interest having moved from physical organic chemistry to natural products.

Edward David Hughes (1906–1963), the longtime collaborator of Ingold at University College, London. He returned to Bangor as Professor in 1943–1948 and then held a Chair at U.C.L. until his death.

Brynmor Jones (1903–1989), Professor of Chemistry (1946–1956) and finally Vice-Chancellor (1956–1972) at the University of Hull. He and his students carried out many kinetic studies of halogenation.

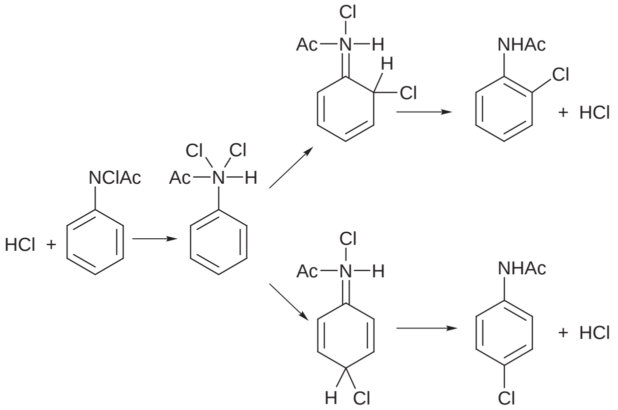
Gwyn Williams (1904–1955), Professor of Chemistry at Royal Holloway College, London from 1946 until his death. He did much work on the mechanism of nitration.

Frederick George Soper (1898–1982), Professor of Chemistry at Otago, New Zealand (1936–1953) and then Vice-Chancellor of Otago University (1953-1963).

In September 1941, under wartime conditions, the Faraday Society organized a one-day discussion in London on 'Mechanism and Kinetics of Organic Reactions in Liquid Systems'.[26] It proved to be a Bangor reunion, because Watson, Bradfield, Gwyn Williams, Hughes, and Brynmor Jones were all present; not Soper, who was on the other side of the world. Ingold concluded some introductory remarks as follows:

> 'Finally, you will not fail to observe that more than half of the reading matter we are to consider has come from the pens of five distinguished pupils of the late Professor Kennedy Orton. Those who remember him must well appreciate the enthusiasm with which he would have participated in a discussion, whose motive was his own, and whose official title might appropriately have been applied to his own life's work. A great leader and a pioneer of the movement we are here to further, it is appropriate to notice the large part which, through the first generation of his successors, he has taken in our proceedings.'

The migration of a halogen atom from side chain to ring, as in the conversion of *N*-chloroacetanilide into *p*- and *o*-chloroacetanilide, is sometimes called the Orton rearrangement. This was not, however, discovered by Orton; its association with him arises from his extensive investigations of the reaction, spanning over three decades. Neither was this reaction discovered by Chattaway (see above) but by Georg Bender of Munich, whose paper on substituted nitrogen chlorides (as he called them) appeared in the *Berichte* in 1886. The article on Chattaway and Orton by the present author outlined the early history of these compounds.[24] We will therefore jump to 1897, when Chattaway and Orton began their joint work, which lasted for six years and led to over 20 papers. In 1900 H. E. Armstrong criticised Chattaway and Orton for not recognising what was already apparent in Bender's work 14 years earlier—that HCl was the catalyst for the rearrangement. He viewed the reaction as involving an initial combination of the *N*-chloro-compound with HCl, followed by intramolecular migration of a chlorine atom. This idea was taken up by Orton, who suggested that the HCl and *N*-chloro compound formed a complex in which the nitrogen was pentavalent. This, and its subsequent fate, are shown in Scheme 1.[27]

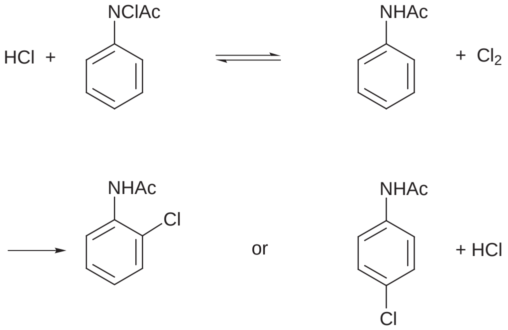


**Scheme 1** The proposed intramolecular mechanism of the Orton rearrangement (1902)

Shortly after Orton went to Bangor, the British Association for the Advancement of Science set up a committee to encourage chemists to investigate 'The transformation of aromatic nitroamines and allied substances and its relation to substitution in benzene derivatives'. Orton was secretary (Lapworth was one of the members) and it was apparently envisaged that the experimental work would be done at Bangor. The early reports of the committee (1905 onwards)[28] and papers in the *Journal of the Chemical Society*, indicate that the initial emphasis was on nitroamines, but within a few years Orton worked round to *N*-halogeno compounds again, and these featured prominently from 1909 onwards. His first collaborator in this work was W. J. Jones, later professor of chemistry at University College, Cardiff. Increasingly Orton and Jones turned their attention to the physicochemical aspects of the reactions of aromatic *N*-chloro compounds. They found that the general effect of adding HCl to an *N*-chloroacylanilide was to liberate chlorine, and if an anilide was chosen that reacted in the ring only very slowly with chlorine or not at all, the setting up of an equilibrium could be observed, as in eqn. (11).[29]

$$\text{ArNCl (COR)} + \text{HCl} \rightleftharpoons \text{ArNH (COR)} + \text{Cl}_2 \qquad (11)$$

In several cases they were able to measure the equilibrium constant and show that this varied with the ring substituents and composition of aqueous acetic acid used as solvent. For *N*-chloroacetanilide itself the equilibrium could not be observed because acetanilide reacted rapidly with chlorine to give *p*- and *o*-chloroacetanilide. These observations led naturally to the suggestion that the rearrangement was intermolecular, involving the liberation of molecular chlorine, which then attacked acetanilide in the ring, as in Scheme 2. The results of kinetic studies carried out by Orton and Jones could be interpreted satisfactorily in terms of this Scheme, although Orton did not rule out the possibility of some reaction occurring intramolecularly. The mechanism of the rearrangement intrigued Orton for the rest of his life, although work on it was interrupted by World War I. He later worked on the kinetics of chlorination of other aromatic compounds, for which reaction (11) involving 2,4-dichloro-*N*-chloroacetanilide was used as a convenient way of obtaining a standard solution of chlorine; the equilibrium lies very much to the right and 2,4-dichloroacetanilide is *C*-chlorinated only very slowly.



**Scheme 2** The proposed intermolecular mechanism of the Orton rearrangement (1909)

## 7 Harry Medforth Dawson (1876–1939)

Dawson[30] was born in Bramley, Leeds and throughout his career was closely associated with his home city. His early education was at Leeds Modern School, but in 1891 he won a scholarship to the Yorkshire College (which later became the University of Leeds) and began life as a student at the age of fifteen. He was attracted to specialise in chemistry through the teaching of Professor Arthur Smithells. Dawson obtained a London External BSc in 1896 and won a 1851 Exhibition studentship, which enabled him to proceed to Germany for further study. He worked mainly with van't Hoff in Berlin, but also at Giessen with Elbs, in Ostwald's laboratory at Leipzig, and with Abegg at Breslau. Dawson presented a thesis for his doctorate at Giessen.

Returning to England in 1899, he was appointed to the chemistry staff of the Yorkshire College as demonstrator in physical chemistry. In 1905 he was promoted to lecturer and in 1920, a Chair of Physical Chemistry was established and Dawson was appointed to it. He was a very energetic and loyal servant of the University of Leeds for forty years, until illness ended his life before he reached normal retiring age (Fig. 6). He was elected F.R.S. in 1933.

**Fig. 6** Harry Medforth Dawson. (Reproduction courtesy of the Royal Society.)

Dawson's earliest research work was in studies involving phase equilibria or chemical equilibria and complex ion formation in solutions, not only in water but also in organic solvents. It was not until about 1909 that he turned his attention to the kinetics of reactions in solution and this happened more or less accidentally. Dawson and Leslie were interested in the physical properties of solutions of iodine in various solvents and they found that a solution of iodine in acetone was not stable. This observation led them to measure the rate of disappearance of iodine in aqueous mixtures of acetone, iodine, potassium iodide, and mineral acid. The kinetics were similar to those which had been found by Lapworth for bromination (Section 3). The authors concluded:

> . . . Lapworth's view that the reaction between between halogen and acetone takes place in two stages appears to afford a simple explanation of the observed facts. Since the rate at which the iodine disappears is independent of its concentration, the particular reaction which determines the observed velocity of change is one in which iodine is not directly involved. This reaction, according to Lapworth, is the transformation of the ketonic form of acetone into the enolic form, and this is accelerated by acids. In the second stage, the iodine reacts with the enolic acetone, and the velocity with which this takes place is relatively so large that this stage in the complete reaction is practically without influence on the rate at which the iodine disappears.

Dawson and Leslie demonstrated that under the same conditions the rates of iodination and bromination were the same to within a few percent and that the amount of KI present (necessary to secure a suitable concentration of iodine as $KI_3$) did not affect the rate, both these observations being in accord with the enolization hypothesis. They also carried out some rate measurements on solutions of acetone and iodine in various non-aqueous solvents, the results being rather complicated.

Dawson and Leslie's work was the start of studies by Dawson on the iodination of ketones which continued for more than twenty years. Dawson and Wheatley (1910) compared the reactivities of various ketones under the same conditions. However, the focus of interest soon became the application of the reaction to studying the nature of acid catalysis. Following Ostwald it had generally been assumed that the catalysing power of acids was due to hydrogen ions, but around 1910 evidence began to accumulate from the work of Goldschmidt and others that undissociated acid could also contribute to the catalysis, in certain reactions at least. For the iodination of acetone, Dawson and Powis (1913) were able to distinguish the catalytic activities of the hydrogen ion and of the undissociated forms of several organic acids. (They also included what they believed to be the catalytic activity of undissociated HCl.) They realised:

> . . . that the catalysing power of the undissociated acid diminishes rapidly as the ionisation tendency decreases, a relation which has already been pointed out by Snethlage. As yet, however, it has not been possible to find any quantitative relationship between the activity of the undissociated acid and the specific affinity coefficient . . .

(Specific affinity coefficient means dissociation constant.) In fact, as shown in Fig. 7, a log $k$ *vs.* p$K$ plot of the values they give for four acids is an excellent straight line. They were close to discovering the relationship established by Brönsted some ten years later! By 1915 Dawson and Reiman were using the phrase 'the dual theory of catalysis' and investigating the catalytic activity of monochloroacetic acid in the presence of its salts. In the 1920s the dual theory became incorporated in the theory of general acid–base catalysis. The work of Dawson and his colleagues up to about 1931 contributed greatly to the development of this area of kinetics and mechanism. See especially the series of 25 papers on 'Acid and Salt Effects in Catalysed Reactions', published in the *Journal of the Chemical Society* between 1925 and 1931.[30] Dawson's work is examined in detail in R. P. Bell's book *Acid–Base Catalysis*, published in 1941. Bell (1907–1996), having worked with Brönsted, began to study acid–base catalysis intensively at about the same time that Dawson retired from the field.

Dawson was Professor of Physical Chemistry at Leeds during Ingold's time there as Professor of Organic Chemistry, 1924-30. Recalling his Leeds days, Ingold wrote:[31]

> It was in Leeds that I began systematic work on the mechanism of organic reactions . . . Dawson taught me a lot of physical chemistry in a quiet way, and I became very

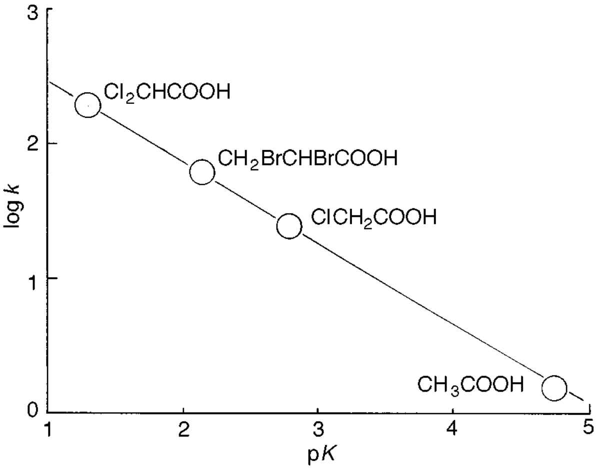


**Fig. 7** Catalysis of the iodination of acetone by undissociated molecules of carboxylic acids in water at 25 °C. Relationship between the catalytic activity $k$ and the dissociation constant of the acid $K$. (The values of $k$ were based on measurement of initial rate under standard conditions, and the position of the scale of ordinates is arbitrary.)

interested in his attempts to sort out the kinetic effects of the constituents of electrolytic solutions.

## 8 Some other pioneers

In Section 1 the intention in this article to concentrate on six British chemists was justified in so far as these provided immediate background to Ingold's own work and he had definite links with some of them. A study of the bibliography of the history of physical organic chemistry recently prepared by the present author will reveal that chemists of many nationalities contributed to the early history of physical organic chemistry and particularly to the study of kinetics and mechanism.[9] Some of these pioneers have already been mentioned in passing and they and a few more will be treated briefly below. Considerations of space prevent a more extended account.

Bredig's work in 1904 on the benzoin condensation was mentioned in Section 3. Georg Bredig (1868–1944)[32] was at that time a Professor in Heidelberg. From 1911 he was Professor in Karlsruhe until 1933, after the Nazi party came to power. He left Germany for the USA in 1939. He was essentially a physical chemist, but in addition to his work on benzoin condensation, his studies of the catalysed decomposition of diazoacetic ester and of reactions in concentrated sulfuric acid are of interest for physical organic chemistry.

Hans Meerwein (1879–1965)[33] was a prominent German organic chemist who worked on many different topics. His name is still familiar to present-day organic chemists for the Meerwein–Ponndorf reduction and the Wagner–Meerwein rearrangements in camphor chemistry. As in Lapworth's case (Section 3), the complexities of camphor chemistry stimulated an interest in reaction mechanisms. In 1922 Meerwein carried out kinetic studies of the reversible interconversion of the isomers: bornyl chloride, isobornyl chloride and camphene hydrochloride in various solvents and concluded that carbocations were involved. At that time this was considered to be an outrageous idea and, to get the work published, he had to disguise the reaction intermediates as 'cryptoions'. He was professor in succession at Bonn, Königsberg, and finally Marburg (1928–1952).

In Section 3 S. F. Acree (1875–1957)[34] was mentioned in connection with studies of the kinetics of oxime formation. He carried out kinetic studies of many organic reactions before World War I. He was a professor at Johns Hopkins University. Also associated with Johns Hopkins University was Emmet Reid (1872–1973), who in 1898 studied the kinetics of the acidic and the alkaline hydrolysis of substituted benzamides and later (1910) correctly identified the normal mechanism of ester hydrolysis as involving acyl-oxygen fission by analogy with his findings of the behaviour of certain thioesters and thiols. (See also Lapworth's contribution in Section 3.) A personal account of this work may be found in his fascinating autobiography, published in his 100th year.[35]

A pre-eminent pioneer was N. A. Menshutkin (1842–1907).[36] Most of his life was spent in St. Petersburg. The association of his name with the reaction between tertiary amines and alkyl halides to form quaternary ammonium salts is a tribute to the enormous amount of work he did on the kinetics of this reaction. Perhaps his most famous study was of the reaction between triethylamine and ethyl iodide in a series of solvents; he found that the rates varied by a factor of about 760 between the 'fastest' and 'slowest' solvents. Much of Menshutkin's work (mainly carried out between 1876 and 1907) was very much 'work before its time'; he could give little interpretation of his findings.

In a way the kinetics and mechanism aspect of physical organic chemistry was born in the Netherlands. The connection between kinetics and mechanism was first made by J. H. van't Hoff (1852–1911),[37] through his formulation of kinetics in terms of *molecularity*. The 2nd edition of van't Hoff's book[38] contains accounts of several kinetic studies which we would regard as belonging to physical organic chemistry. For instance, rate coefficients are tabulated for the acidic and the alkaline hydrolysis of several series of esters, and the effect of various structural features of the reactants is pointed out, but no explanation is attempted. Another Dutch chemist A. F. Holleman (1859–1953) was the first to realise the importance of measuring rates of aromatic substitution and the proportions of isomers formed.[39] He was professor at Amsterdam from 1905 to 1924.

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