Progress in

PHYSICAL ORGANIC CHEMISTRY

VOLUME 17

Editor

ROBERT W. TAFT, *Department of Chemistry*
University of California, Irvine, California

A WILEY-INTERSCIENCE PUBLICATION
John Wiley & Sons, Inc.
NEW YORK / CHICHESTER / BRISBANE / TORONTO / SINGAPORE

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An Interscience® Publication

Library of Congress Cataloging in Publication Data:

Library of Congress Catalog Card Number:

ISBN 0-471-50912-4

Printed in the United States of America

10 9 8 7 6 5 4 3 2

Dedicated to the memory of
Louis P. Hammett

Contributors to Volume 17

T. William Bentley
Department of Chemistry
University College of Swansea
Swansea, Wales, United Kingdom

Jean François Gal
Laboratoire de Chimie Physique Organique
Université de Nice–Sophia Antipolis
Nice, France

Ernest Grunwald
Department of Chemistry
Brandeis University
Waltham, Massachusetts

Tadeusz Marek Krygowski
Department of Chemistry
University of Warsaw
Warsaw, Polland

Gareth Llewellyn
Department of Chemistry
University College of Swansea
Swansea, Wales, United Kingdom

Pierre Charles Maria
Laboratoire de Chimie Physique Organique
University de Nice–Sophia Antipolis
Nice, France

John Shorter
Department of Chemistry
The University
Hull, England

R. D. Topsom
Department of Chemistry
La Trobe University
Melbourne, Australia

Introduction to the Series

Physical organic chemistry is a relatively modern field with deep roots in chemistry. The subject is concerned with investigations of organic chemistry by quantitative and mathematical methods. The wedding of physical and organic chemistry has provided a remarkable source of inspiration for both of these classical areas of chemical endeavor. Further, the potential for new developments resulting from this union appears to be still greater. A closing of ties with all aspects of molecular structure and spectroscopy is clearly anticipated. The field provides the proving ground for the development of basic tools for investigations in the areas of molecular biology and biophysics. The subject has an inherent association with phenomena in the condensed phase and thereby with the theories of this state of matter.

The chief directions of the field are: (a) the effects of structure and environment on reaction rates and equilibria; (b) mechanisms of reactions; and (c) application of statistical and quantum mechanics to organic compounds and reactions. Taken broadly, of course, much of chemistry lies within these confines. The dominant theme that characterizes this field is the emphasis on interpretation and understanding that permits the effective practice of organic chemistry. The field gains its momentum from the application of basic theories and methods of physical chemistry to the broad areas of knowledge of organic reactions and organic structural theory. The nearly inexhaustible diversity of organic structures permits detailed and systematic investigations that have no peer. The reactions of complex natural products have contributed to the development of theories of physical organic chemistry, and, in turn, these theories have ultimately provided great aid in the elucidation of structures of natural products.

Fundamental advances are offered by the knowledge of energy states and their electronic distributions in organic compounds and the relationship of these to reaction mechanisms. The development, for example, of even an empirical and approximate general scheme for the estimation of activation energies would indeed be most notable.

The complexity of even the simplest organic compounds in terms of physical theory well endows the field of physical organic chemistry with the frustrations of approximations. The quantitative correlations employed in this field vary from purely empirical operational formulations to the approach of applying physical principles to a workable model. The most common

procedures have involved the application of approximate theories to approximate models. Critical assessment of the scope and limitations of these approximate applications of theory leads to further development and understanding.

Although he may wish to be a disclaimer, the physical organic chemist attempts to compensate his lack of physical rigor by the vigor of his efforts. There has indeed been recently a great outpouring of work in this field. We believe that a forum for exchange of views and for critical and authoritative reviews of topics is an essential need of this field. It is our hope that the projected periodical series of volumes under this title will help serve this need. The general organization and character of the scholarly presentations of our series will correspond to that of the several prototypes, e.g., *Advances in Enzymology*, *Advances in Chemical Physics*, and *Progress in Inorganic Chemistry*.

We have encouraged the authors to review topics in a style that is not only somewhat more speculative in character but which is also more detailed than presentations normally found in textbooks. Appropriate to this quantitative aspect of organic chemistry, authors have also been encouraged in the citation of numerical data. It is intended that these volumes will find wide use among graduate students as well as practicing organic chemists who are not necessarily expert in the field of these special topics. Aside from these rather obvious considerations, the emphasis in each chapter is the personal ideas of the author. We wish to express our gratitude to the authors for the excellence of their individual presentations.

We greatly welcome comments and suggestions on any aspect of these volumes.

Robert W. Taft

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Hammett Memorial Lecture

BY JOHN SHORTER
Department of Chemistry
The University
Hull, England

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I. INTRODUCTION

Louis Plack Hammett was born in Wilmington, Delaware, on 7th April 1894 and died in his ninety-third year at Medford, New Jersey, on 23rd February 1987. Hammett was awarded his bachelor's degree from Harvard University in 1916 and his doctorate from Columbia University, New York City in 1923. He served on the chemistry faculty of Columbia University from 1920 to 1961 (having risen to the status of full professor in 1935) and thereafter he had the title of Mitchill Professor Emeritus of Chemistry at Columbia (1).

Hammett is commonly regarded as one of the founding fathers of physical organic chemistry, particularly in relation to the subject's development in the United States, whose chemical community has contributed so much to the advancement of the subject (2,3). Actually the term "physical organic chemistry" only began to be widely used after Hammett had employed it for the title of the book he published in 1940 (4). By that year the foundations of his own main original contributions to the subject had been well and truly laid. These were, of course, the equation for summarizing the effects of *meta*

Figure 1 Professor Louis P. Hammett. (This portrait was taken about 1960. The present author was lent the negative by Professor Hammett for use in connection with reference 75f.)

and *para* substituents on the rate or equilibrium constants for side-chain reactions of benzene derivatives (5) and the study and applications of concentrated solutions of acids, and in particular strong acids, through the acidity function (6). Hammett's preeminent connection with these is indicated by the commonly used terms: the Hammett equation and the Hammett

acidity function, a usage that Hammett himself did not encourage (7). The second edition of his book *Physical Organic Chemistry* was published in 1970 and it contains much evidence of the way in which the first edition and his own original contributions had influenced the development of the subject in the intervening 30 years (8). Hammett retained his interest in physical organic chemistry throughout his quarter century of retirement; indeed, he was 76 years of age when the second edition of *Physical Organic Chemistry* was published.

II. HAMMETT AS A PHYSICAL CHEMIST

In the last edition of *American Men and Women of Science* (1) to include an entry for him, Hammett described his research area as "Physical organic chemistry; reaction rates and mechanisms," and it is in some such terms that most chemists would expect Hammett to describe his research interests. This description, however, rather obscures the fact that in background, experience, and outlook Hammett was very different from most physical organic chemists, particularly those of the United States. These tend to regard themselves as primarily organic chemists, who use physicochemical techniques to attack problems of structure, mechanism, and reactivity. Hammett regarded himself as a *physical* chemist, who found his research outlet in studying organic compounds and their reactions. In 1961 he was presented with the highest award of the American Chemical Society, the Priestley Medal, and in his acceptance address he stated his position in this way (9): "I have always considered myself a physical chemist, but I find large areas in what is called organic chemistry which interest me very much, and contrariwise large areas in physical chemistry on which I have not thought I could afford to spend time and energy." We can only really begin to understand Hammett as a chemist if we look carefully at the early stages of his career.

III. HAMMETT'S ORIGINS AS A CHEMIST

The examination of the early stages of Hammett's career is made easier by the fortunate circumstance that when he received the James Flack Norris Award in Physical Organic Chemistry in 1966, he was in a reflective mood and gave an address entitled "Physical Organic Chemistry in Retrospect," which was subsequently published in the *Journal of Chemical Education* (10).

Hammett began this address by pointing out that when he started chemical research half a century earlier, physical organic chemistry as such, let alone the title, scarcely existed. Organic chemistry and physical chemistry

were largely in separate compartments. Organic chemistry was dominated by the drive to synthesize new compounds and to investigate natural products. According to Hammett, physical chemistry appeared mainly to be concerned with such problems as the existence (or otherwise) of unimolecular gas reactions and the behavior of electrolyte solutions which were so dilute that they could be described aptly as slightly polluted water!! In terms of this dichotomy, Hammett characterized as "anomalous" the way in which his own research experience developed from 1916 and through the 1920s. He claimed that what happened was due to a series of accidents.

At Harvard Hammett was greatly impressed by the lectures of E. P. Kohler (1865–1938), who had interests both in synthetic organic chemistry and theoretical organic chemistry, such as it was at that time. Hammett's slightly senior contemporary at Harvard, J. B. Conant (1893–1978), who was later President of Harvard, was similarly impressed and went on to do a substantial part of his Ph.D. under Kohler's supervision (3). Hammett, however, followed in the footsteps of many young American chemists of that era and went to Europe, in fact, to Switzerland, then a haven of relative calm in the midst of the Great War that was raging over much of the Continent. He spent 1916–1917 with H. Staudinger (1881–1965) in the Chemisches Institut of the Eidgenössische Technische Hochschule (E.T.H.) at Zürich, participating in Staudinger's massive work on the preparations and properties of aliphatic diazo compounds and thereby contributing to Parts 21 and 22 of *Über aliphatische Diazoverbindungen* as his first published work (11).

By the time Hammett returned home the United States had entered the war, and he became involved in analytical control work on organic materials and in research on cellulose acetate solutions in connection with aircraft fabric. For about a year and a half after the war he was engaged in development research on dyes and pharmaceuticals for a chemical company in New Jersey, but he then heard through a friend of an opening as instructor in the Chemistry Department of Columbia University, for which he applied successfully. Thus a chance meeting with a friend resulted in employment for the next 40 years!!

In his early years at Columbia, Hammett was particularly influenced by several senior colleagues. There was J. M. Nelson (1876–1965), who had participated in the attempts to work out an electronic theory of valency that had preceded the work of G. N. Lewis (1875–1946) and W. Kossel (1888–1956). Nelson was interested in making various physicochemical measurements on organic systems. There was also James Kendall (1889–1978), a physical chemist who pursued studies of a wide variety of condensed systems, including both electrolyte and nonelectrolyte systems. Hammett, however, chose to pursue his doctoral studies under the analytical chemist Hal T. Beans (1883–1960) in examining the factors that affect the reliability of the hydrogen

electrode (12). The discharge of hydrogen ions at platinum and other metals (13,14), and related matters such as catalytic properties (15) and overvoltage (16), continued to interest Hammett for a number of years; the publication of several papers with various collaborators extended well into the 1930s (17,18).

IV. HAMMETT'S FIRST BOOK

As an instructor working in analytical chemistry, Hammett became involved in teaching qualitative inorganic analysis and apparently did this for many years (19,20). This work generated his first book, published in 1929 and entitled *Solutions of Electrolytes*, with the subtitle *With Particular Application to Qualitative Analysis* (21). The book was a slim octavo volume in the McGraw-Hill International Chemical Series and appears to have had some success, for it went through a second edition in 1936. The copy I have examined is of the third impression of the second edition. In his preface to the first edition Hammett wrote:

> This book is based upon the belief that a course in qualitative analysis is an ideal method of presenting and of illustrating by copious examples the general principles relating to the behavior of solutions of electrolytes; and that this part of physical chemistry is an indispensable part of the preparation for advanced work in chemistry and for the study of medicine and engineering. It is an attempt to make the fullest use of qualitative analysis as a means of teaching chemistry. The book is not an attempt to teach an immediately useful practical art.

And so Part I, entitled "Principles," and amounting to about three-quarters of the book, expounds the fundamentals of valency, electrolysis, ionization in solution, acids and bases, chemical equilibrium, solubility products, weak electrolytes, the ionization of water, salt hydrolysis, formation of complexes in solution, oxidation–reduction reactions, and oxidation potentials. The rest of the book, Part II, "Experiments," details the course of laboratory instruction to accompany the lectures, including a list of reagents and apparatus required and suggested demonstrations to be carried out by the lecturer during the lectures. Any student pursuing the course conscientiously would certainly have learned a great deal of fundamental inorganic and physical chemistry.

It should also be mentioned that Hammett's participation in analytical chemistry included a research collaboration with his colleague George H. Walden (1894–1973) in the early 1930s. This led to the introduction of the *ortho*-phenanthroline–ferrous ion complex as a high potential indicator for oxidimetric titrations (22–27), particularly with dichromate and ceric ion

solutions, which had previously required the somewhat inconvenient use of an external indicator (28).

V. THE ACIDITY FUNCTION

In his Norris Award Address (10) Hammett mentions that in the early 1920s he was profoundly influenced by reading the papers of A. R. Hantzsch (1857–1935), A. Werner (1866–1919), G. N. Lewis, and J. N. Brønsted (1869–1947). The influence of Werner, Lewis, and Brønsted is clearly shown in Hammett's general interest in electrochemistry and particularly in his presentation of the subject matter in his *Solutions of Electrolytes* (21). The influence of Hantzsch was also in connection with electrochemistry. This led to Hammett carrying out a great deal of research and to one of his major contributions to physical organic chemistry: the acidity function.

Hantzsch was one of the most distinguished German organic chemists of the late nineteenth and early twentieth centuries (29). He and his assistants worked on an extraordinary variety of topics, and he was often involved in controversies. Much of his work had a distinctly physical organic flavor, which was unusual at the time it was done, and the results often led Hantzsch to challenge the cherished beliefs of physical chemists. The part of Hantzsch's work that appealed to Hammett was his investigations of acids and bases in nonaqueous solutions, particularly solutions in anhydrous sulfuric acid (30). These studies led Hantzsch to recognize the chemical as opposed to physical role of the solvent in acid–base equilibria in solution. In the light of the then recent advances in the theory of acids and bases through the work of Brønsted (31), Hammett saw the examination of the behavior of organic compounds in solution in highly acidic media as a promising field of research. Maybe it appealed especially to Hammett as an attempt to make sense of the physical chemistry of solutions that were rather different from the usual "slightly polluted water"!

At all events, Hammett's first contribution in this area was published in 1928 (32). In this he proposed a generalized theory of acidity, which was given mathematical expression, and considered both the effect of the basicity and of the dielectric constant of the solvent. He showed that the predictions of the treatment were in agreement with the available evidence on acidity in nonaqueous solutions, including the work of Hantzsch. In his Norris Award address (10) Hammett recalled that he received an appreciative letter from Hantzsch, who was greatly pleased with the quantitative treatment his ideas had been given. Hantzsch asked for a supply of reprints to send to some of the physical chemists who had tended to pay little attention to his own work in this area!! This paper (32) was really Hammett's first paper in physical organic chemistry, and at about the time it appeared he started two graduate students,

Dietz and Deyrup, on experimental work on acid–base systems, which led to the publication of several further papers in physical organic chemistry in the early 1930s.

Dietz's work was on acid–base titrations in the very strongly acid solvent, formic acid (33). There were various interesting findings, but the work of the other student Deyrup has proved to be of more lasting significance, for it was in the first paper of Hammett and Deyrup, published in 1932, that the term "acidity function" was introduced (6). Hammett had recognized that the tendency of a solution to transfer hydrogen ion to a neutral organic molecule would be a particularly valuable, albeit empirical, measure of the acidity of the solution. And so he came to define the acidity function H_0 in terms of the equilibrium between a suitable indicator B and its protonated form BH^+ in a given solution. Thus:

$$B + H^+ \rightleftharpoons BH^+$$

$$H_0 = pK_{BH^+} - \log\left(\frac{C_{BH^+}}{C_B}\right)$$

where C_{BH^+}/C_B is the directly observable concentration ratio of the indicator in its two differently colored forms and K_{BH^+} is the thermodynamic ionization constant of BH^+ in terms of molar concentrations, referred to *ideal dilute solution in water*. Hammett and Deyrup (6) developed a series of indicators whereby H_0 could be measured for any solution in the range from dilute aqueous sulfuric acid to 100% sulfuric acid by the so-called step method. They also studied mixtures of perchloric acid and water from 0 to 70% acid. At that time the only instrumentation available was a simple visual colorimeter, and this greatly restricted the choice of indicators, which were mainly nitroanilines. Actually this turned out to be a fortunate circumstance in that it led to a fairly simple pattern of results (10). A wider choice of indicators might well have led to such bewildering results that serious doubts might have been cast on the validity of this approach to acidity and on the worthwhileness of the entire enterprise.

The first paper of Hammett and Deyrup (6) envisages two possible types of application of the indicator method: "One is the determination of the strengths of bases and of acids too weak and too strong, respectively, to permit measurements in aqueous solutions.... The other is in the interpretation of reaction velocity data." The authors then gave a survey for the latter topic, based on available data for acid-catalyzed reactions in sulfuric acid–water mixtures. It was suggested that

> An exact parallelism between the reaction velocity and the acidity can only be expected if the velocity is proportional to the concentration of the ion formed by

the addition of one hydrogen ion to one molecule of the neutral substrate, if the ratio of the concentration of this ion to the total concentration of substrate is small, and if there is no further ionization by addition of another hydrogen ion. If these conditions are fulfilled the equation

$$H_0 + \log k = \text{constant}$$

where k is the velocity constant, should hold.

They found just three cases in which the equation held: the decomposition of malic acid, the cyclization of *ortho*-benzoylbenzoic acid to anthraquinone by loss of H_2O, and the Beckmann transformation of acetophenone oxime. Several other reactions (all decompositions of carboxylic acids) did not conform to the equation.

The second paper of Hammett and Deyrup, also published in 1932, addresses the question of studying very weak bases and very strong acids in solution in formic acid (34). In such solutions sulfuric acid was found to be a strong monobasic acid; benzenesulfonic acid, a nearly but not quite strong acid; and sodium formate and aniline, strong bases. The behavior of acetanilide and propionitrile as weak bases was also studied. A third paper of Hammett and Deyrup (35), published in 1933, was devoted to freezing-point measurements of electrolytes in sulfuric acid, a type of study that had been pioneered by Hantzsch (29,30). The results of such measurements were expressed as the van't Hoff i factor. Even at moderately large ionic strengths the values of i for some inorganic salts were very close to whole numbers, corresponding to 100% dissociation, for example, for

$$KHSO_4 \rightleftharpoons K^+ + HSO_4^-$$

$i \approx 2$. Various organic compounds tested gave no evidence of any behavior as electrolytes in sulfuric acid (e.g, 1,3,5-trinitrobenzene and picric acid), while organic bases, including many of the indicators used in Deyrup's work, gave results corresponding to the equilibrium:

$$B + H_2SO_4 \rightleftharpoons BH^+ + HSO_4^-$$

lying well over to the right-hand side, that is, $i \approx 2$. Triphenylcarbinol, previously studied by Hantzsch (29,30), gave $i \approx 4$, corresponding to

$$Ph_3COH + 2H_2SO_4 \rightleftharpoons Ph_3C^+ + H_3O^+ + 2HSO_4^-$$

lying well over to the right-hand side (36).

Hammett pursued research in this general field throughout the 1930s with some seven further collaborators, leading to 17 further papers (37–53). At an early stage he sought to publicize the merits of studies involving strongly acidic solutions through talks given in American Chemical Society (ACS) symposia, whose proceedings were subsequently published in *Chemical Reviews*. At a Symposium on Electrolytes given in the Division of Physical and Inorganic Chemistry at the 85th ACS National Meeting in Washington, D.C. in March 1933, Hammett talked on "The Quantitative Study of Very Weak Bases" (39). At a Symposium on Indicators given in the same division at the 88th ACS National Meeting in Cleveland, Ohio, in September 1934, Hammett talked on "Reaction Rates and Indicator Acidities" (45). The titles of these two talks of course refer to the two main areas of applications of indicator-based acidity functions as envisaged in the first paper of Hammett and Deyrup (6). The study

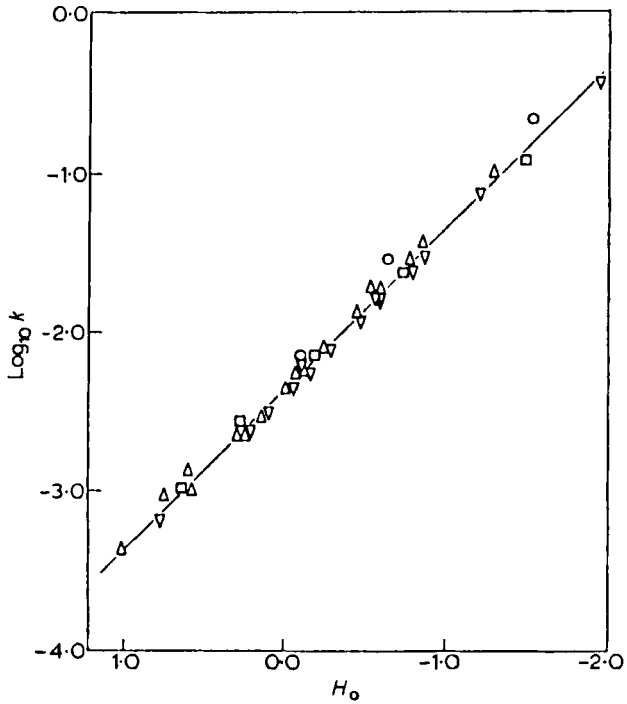

Figure 2 Correlation between rate constant and H_0 for the hydrolysis of sucrose, 25°C. The catalysing acids were as follows: ○ $HClO_4$; □ H_2SO_4; ▽ HNO_3; △ HCl. The line drawn is of unit slope. [Diagram as redrawn for C. H. Rochester, *Acidity Functions*, Academic Press, London, 1970; from L. P. Hammett and M. A. Paul, *J. Am. Chem. Soc.*, *56*, 830 (1934) and L. P. Hammett, *Chem. Rev.*, *16*, 67 (1935). Reproduced by kind permission of Academic Press Inc. (London) Ltd.]

of very weak bases was pursued in work with R. P. Chapman on the solubilities of some organic oxygen compounds in sulfuric acid–water mixtures (37,38), and in particular in work with Dingwall and Flexser on the measurement of the strengths of very weak bases (43,44,48,49). This latter work, published from 1934 onward, saw the extension of colorimetry to the ultraviolet with a crude form of spectrophotometer, thereby increasing very greatly the range of compounds that could be studied. At around the same time, with his collaborator M. A. Paul, Hammett was refining the acidity function scale (40) and pursuing the relationship between the rates of some acid-catalyzed reactions and the acidity function H_0 (41). As we shall see shortly in connection with the Hammett equation, Hammett himself was now embarking on kinetic studies, and some of these involved strongly acidic media. Thus Hammett and Paul measured the rate of bromination of *meta*-nitroacetophenone in mixtures of sulfuric acid and acetic acid (46). Perhaps

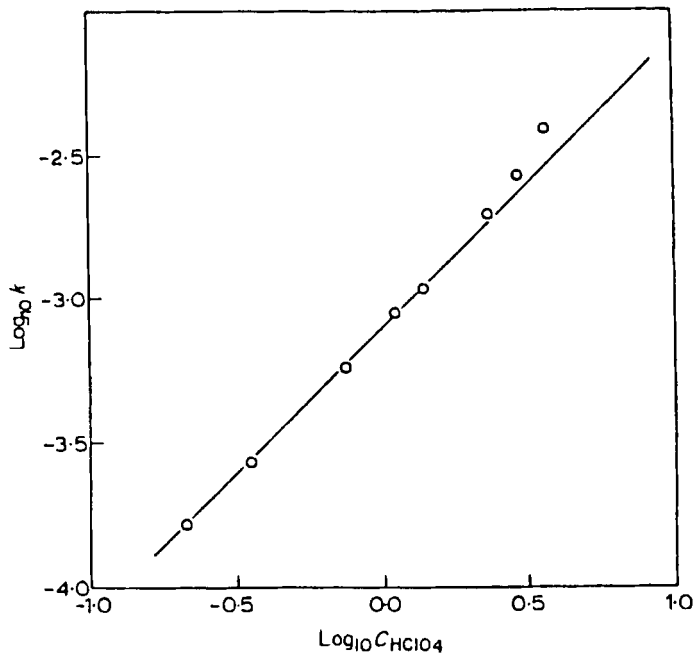

Figure 3 Correlation between rate constant and acid concentration for the iodination of acetophenone in aqueous $HClO_4$ at 25°C. The line drawn is of unit slope. [Diagram as redrawn for C. H. Rochester, *Acidity Functions*, Academic Press, London, 1970; from L. Zucker and L. P. Hammett, *J. Am. Chem. Soc.*, *61*, 2791 (1939). Reproduced by kind permission of Academic Press Inc. (London) Ltd.]

best known, however, is the series of papers on various aspects of the acid-catalyzed halogenation of acetophenone and a number of its derivatives, published by Zucker and Hammett in 1939 (50–52). These papers led to the ideas that have become known as the "Zucker–Hammett hypothesis." Briefly, it was found that the rates of some acid-catalyzed reactions, such as the hydrolysis of sucrose, conformed to the acidity function (see Fig. 2), while others, such as the iodination of acetophenone, conformed to the *concentration* of strong acid in the medium (see Fig. 3). It was suggested that this indicated a distinction in mechanism. In the modern terminology due to Ingold this would be the difference between the $A_{AC}1$ and the $A_{AC}2$ mechanisms for the hydrolysis of an organic substrate in acidic solution (54,55).

$A_{AC}1$ Mechanism

$$S + H^+ \rightleftharpoons SH^+ \quad \text{(fast, preequilibrium)}$$
$$SH^+ \rightarrow A^+ \quad \text{(slow)}$$
$$A^+ + H_2O \rightarrow \text{products} \quad \text{(fast)}$$

$A_{AC}2$ Mechanism

$$S + H^+ \rightleftharpoons SH^+ \quad \text{(fast, preequilibrium)}$$
$$SH^+ + H_2O \rightarrow \text{products} \quad \text{(slow)}$$

Like many good initial simple generalizations, the Zucker–Hammett criteria were fairly soon recognized to have their limitations, but the development of alternatives continued for many years. Only in the 1960s was there much success, notably in the work of Bunnett and Olsen (56).

Hammett's original contributions to acidity functions and similar ended largely with the work of Zucker and Hammett, apart from a brief excursion into the acidity of solutions of sulfuric acid in nitromethane, in work with L. C. Smith published in 1945 (57) and with H. van Looy published in 1959 (58); the latter paper was Hammett's last publication of experimental work. Hammett himself took no part in the proliferation of acidity functions, which has resulted in the definition of over 400 different types (59)!! It had probably been Hammett's hope that H_0 would be applicable to the behavior of a wide range of substrates in highly acidic media. However, in the first edition of *Physical Organic Chemistry* in 1940 (4), he did define the function H_- for the tendency to transfer a proton to a base with a single negative charge and he recognized that, for a given acidic medium, H_0 and H_- might have very different values (60).

VI. STRUCTURE–REACTIVITY RELATIONSHIPS

It has already been mentioned that Hammett was much influenced by reading the papers of Brønsted. These included the paper of Brønsted and Pedersen (61) in 1924 on the decomposition of nitramide catalyzed by general bases, in which it was shown that for a series of bases the values of the logarithm of the rate constant plotted against the values of the logarithm of the ionization constant of the conjugate acid of the catalyst gave a straight line of negative slope. This was the first example of the type of relationship that was generalized by Brønsted to include acid catalysis in 1926 (62). Hammett thus became familiar with the Brønsted equation, and we may remind ourselves of the forms this equation takes by means of Hammett's presentation of it in a *Chemical Reviews* article, which I shall mention again shortly (63).

Hammett represented a general acid-catalyzed reaction as

$$HA + S \rightarrow \text{products} + HA$$

where HA is the catalyst and S is the substrate. The Brønsted equation may then be written as

$$k = GK^x \qquad \text{or} \qquad \log k = x \log K + \log G$$

where k is the rate constant of the reaction when catalyzed by an acid whose ionization constant is K, and G and x are constants characteristic of the reaction.

Hammett became interested in the possibility of finding analogous relationships for other types of reaction. The initial stage of this interest was his starting of experimental studies on rates of reaction in solution early in the 1930s. By that time Hammett was well aware of what he described in his Norris Award address (10) as the "renaissance of solution kinetics" as a means of studying organic reaction mechanisms and of investigating the relationship between the structure and the reactivity of organic compounds. Studies of reaction mechanisms by kinetic techniques had begun around the turn of the century with the work of G. Bredig (1868–1944), J. F. Norris (1871–1940), A. Lapworth (1872–1941), K. J. P. Orton (1872–1930), and others, but this had not had any great impact on the majority of chemists or on the general nature of organic chemistry. In the late 1920s and early 1930s the field of kinetics and mechanism suddenly began to flourish through the work of C. K. Ingold (1893–1970), E. D. Hughes (1906–1963), C. N. Hinshelwood (1897–1967), R. P. Bell (b. 1907), E. A. Moelwyn-Hughes (1905–1978), J. B. Conant (1893–1978), P. D. Bartlett (b. 1907), and others (64).

Hammett's first kinetics paper, with H. L. Pfluger and published in 1933,

was a study of the reactions of methyl esters with trimethylamine in methanol as solvent (65):

$$RCO_2CH_3 + N(CH_3)_3 \rightarrow RCO_2^- + N(CH_3)_4^+$$

For a variety of groups R they found a logarithmic relation between the rate constants and the ionization constants of the corresponding carboxylic acids in water (see Fig. 4). There was no analogous relationship for the rate constants of the alkaline hydrolysis of the same esters. Hammett and Pfluger attributed this difference to the absence of steric hindrance by R in the amine reaction, involving attack of the trimethylamine on the ester methyl carbon, compared with the ester hydrolysis, which is subject to steric hindrance from R because the OH^- reagent attacks the carbon of the ester carbonyl group.

As the 1930s advanced, Hammett became increasingly aware that there was already a great deal of data scattered throughout the literature that conformed to logarithmic relationships analogous to the Brønsted equation. He drew attention to this situation in a talk given in the Symposium on Kinetics of Reaction held in the Division of Physical and Inorganic Chemistry

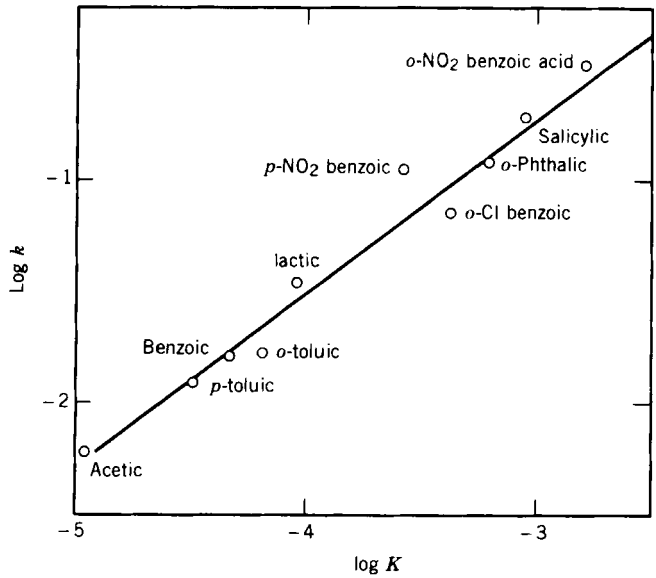

Figure 4 Correlation between values of log k for the reactions of trimethylamine with methyl esters of carboxylic acids in methanol at 100°C and values of log K for the ionization of the carboxylic acids in water, extrapolated to 100°C. (Reproduced from reference 63 by kind permission of the American Chemical Society.)

at the 89th National Meeting of the ACS in New York City in April 1935 and later published in *Chemical Reviews* (63). The morning session, arranged by H. S. Taylor (1890–1974) of Princeton, was devoted to gas-phase reactions and to the then very new activated complex theory of reaction rates, while the afternoon session, arranged by Hammett, emphasized reactions in solution. Hammett's paper contains plots of log k for a variety of reactions against log K for the ionization of carboxylic acids corresponding to the substrates, with an emphasis on the side-chain reactions of *meta*- and *para*-substituted benzene derivatives. He also pointed out some analogous relationships for oxidation–reduction reactions, in which the oxidation–reduction potential played the role corresponding to log K.

The opening sentences of Hammett's article in *Chemical Reviews* (63) are worth quoting, for they indicate the rather ambiguous environment in which linear free-energy relationships, as they soon came to be called, were born.

> The idea that there is some sort of relationship between the rate of a reaction and the equilibrium constant is one of the most persistently held and at the same time most emphatically denied concepts in chemical theory. Many organic chemists accept the idea without question and use it, frequently with considerable success, but practically every treatise on physical chemistry points out that such a relationship has no theoretical basis and that it is in fact contradicted in many familiar cases. The contradiction is, however, more apparent than real. It is true that there is no universal and unique relation between the rate and equilibrium of a reaction; it is equally true that there frequently is a relation between the rates and the equilibrium constants of a group of closely related reactions. It is the purpose of this paper to review the known examples of this kind of relationship, to point out the quantitative form which it assumes, and to state certain limitations to its application.

Subsequent to Hammett's talk at the ACS meeting and to his finalization of the paper for submission to *Chemical Reviews*, Hammett became aware of the work of G. N. Burkhardt (b. 1900) at the University of Manchester in England (3). Burkhardt had been a pupil of Arthur Lapworth, and in the mid-1930s he was actively pursuing structure–reactivity relationships through kinetic studies. Burkhardt and his collaborators had found, independently of Hammett, the widespread occurrence of logarithmic relationships involving rate or equilibrium constants for the side-chain reactions of *meta*- and *para*-substituted benzene derivatives (66). One of their papers contains about ten examples of plots based on their own work and on other people's work in which values of log k (or log K) for a certain side-chain reaction of a series of benzene derivatives are plotted against values of log K for the ionization of the corresponding substituted benzoic acids as a convenient standard of comparison (67). Burkhardt's contribution has been rather overlaid by Hammett's,