13. *Nitrosation, Diazotisation, and Deamination. Part I. Principles, Background, and Method for the Kinetic Study of Diazotisation.*

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Diazotisation will be shown to depend kinetically on a process ending in *N*-nitrosation to form a nitrosammonium ion, all subsequent steps being fast; and the process leading to nitrosation may consist of several steps, and take a number of alternative courses, depending on the nitrosation carrier. Nitrosation carriers are considered in relation to the kinetics to which they should give rise, and it is seen that there is not a one-to-one correlation. The result is that we have to demonstrate a variety of kinetic forms, and trace transitions between them, before any certainty can be attained as to the carriers.

The earlier history of diazotisation kinetics contains many apparent disagreements which require reconciliation.

The conditions to be satisfied in an experimental kinetic investigation are considered. It is emphasised that, in a reaction between members of Brönsted acid–base systems, a clear distinction must be kept between stoicheiometric and molecular rate-constants.

The general study indicated in the serial title is here begun with a group of papers on the kinetics of the diazotisation of aromatic amines. This paper deals with the approach, the next four record experimental results, whilst in the last of the set a collective discussion is given.

The approach has three aspects, that of general theoretical principles, that of known results and conclusions, and that of the basically known, but now refined, experimental method, and the computational procedure.

(1) The Conditions governing Deduction of Mechanism from Observed Kinetics of Diazotisation

(a) *Outline Mechanism.*—It will shorten discussion partly to anticipate conclusions by stating at once that results will be interpreted on the basis that diazotisation is rate-controlled by the formation of a primary nitrosamine, and that, accordingly, the investigation is one of *N*-nitrosation of primary aromatic amines, and so is valid as a contribution to the kinetics of nitrosation generally:

$$\mathrm{Ar{\cdot}NH_2} \xrightarrow{\text{Slow}} \mathrm{Ar{\cdot}NH{\cdot}NO} \xrightarrow{\text{Fast}} \mathrm{Ar{\cdot}N{:}N{\cdot}OH} \xrightarrow{\text{Fast}} \mathrm{Ar{\cdot}N{:}N^+} + \mathrm{OH^-} \quad . \quad . \quad (1)$$

Evidence that the reaction goes through the nitrosamine comes first from the behaviour of secondary amines: here, a prototropic change cannot occur, and hence the reaction stops at the nitrosamine stage. According to Hantzsch,[1] primary aromatic nitrosamines pass into diazonium ions in aqueous acid. The assumed high rate of prototropic change is consistent with all that is known of the speed of protolysis from nitrogen and oxygen. Further, the consistency of the kinetic picture now to be described itself shows that transformations of the primary nitrosation product do not affect the kinetics of diazotisation.

Nitrosation is an electrophilic substitution, and hence must consist in the binding, by externally disposed electrons, usually atomic $2p$- or molecular 2π-electrons, of the entity NO^+, furnished either in the free form, or in a carrier NOX from which the binding p- or π-electrons can extract the NO portion. This implies that, supposing the nitrosating agent to have been supplied, the first step of diazotisation is attack of the latter on the lone-pair electrons of the primary amine. That is to say, the formation of the nitrosamine must itself involve two steps, of which the second, as a protolysis from nitrogen, is assumed to be rapid:

$$\mathrm{Ar{\cdot}NH_2} \xrightarrow{\text{Slow}} \mathrm{Ar{\cdot}NH_2{\cdot}NO^+} \xrightarrow{\text{Fast}} \mathrm{Ar{\cdot}NH{\cdot}NO} \quad . \; . \; . \; . \; . \; . \quad (2)$$

(b) *The Reactants.*—It is implied in section (1a) that the aromatic amine is attacked in its molecular, basic form, not as its ammonium ion. This was suggested by Bamberger[2] and again, with reasoned support, by Hammett,[3] though expressions of the opposite idea, notwithstanding that it is contrary to the long-established classification of polar reagents, were much more frequently seen up to 1950. Although specific proof that the free base is attacked is supererogatory in the light of modern theory, such proof is contained in the kinetic pattern to be disclosed, the consistency of which requires this conclusion.

As to carriers, nitrosation is expected to resemble other electrophilic substitutions, such as nitration and chlorination, in having a family of them: quite generally in electrophilic substitution a carrier is the introduced group, electron-depleted, and thereafter combined either with nothing or with a molecular or anionic base of any basicity up to that of the lyate ion. We shall refer to the following actual or possible carriers in nitrosation.

$$\mathrm{NO^+,\ NO{\cdot}OH_2^+,\ NO{\cdot}Hal,\ NO{\cdot}NO_3,\ NO{\cdot}NO_2,\ NO{\cdot}OAc,\ NO{\cdot}OH} \quad . \; . \; . \; . \; . \quad (3)$$

They are here arranged in order of increasing basic strength of the combined base, that is, decreasing the electrophilic reactivity of the carrier. But the relative practical value of different carriers in given conditions depends, not only on their specific activities, but also on concentration limits governed by their thermodynamic stabilities. The generally opposed variation of these two factors from case to case leads to a certain spread of nitrosating value among the different carriers. It is thus a task in experimental kinetics to identify them in operation. The distinction required is not an elementary one, as if each carrier produced a distinct form of kinetics. To identify a carrier it is usually necessary to establish at least two kinetic forms, and particularly to demonstrate a transition between them, as in the recognition of the nitronium ion NO_2^+, and the chlorinium ion Cl^+, in nitration and chlorination, respectively. Our anticipation of this situation governs the kinetic approach to the mechanism of diazotisation.

We start with a maximally simplified nitrosating system, one from which all carrier-forming anions, such as halide, nitrate, carboxylate ions, etc., that can be excluded, have been. Since nitrosonium perchlorate does not exist in molecular form, a dilute aqueous solution of sodium nitrite and perchloric acid satisfies the required conditions. Our list of possible carriers is now reduced to the following:

$$\mathrm{NO^+,\ NO{\cdot}OH_2^+,\ NO{\cdot}NO_2,\ NO{\cdot}OH} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (4)$$

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[1] Cf. Saunders, " The Aromatic Diazo-compounds," Edward Arnold and Co., London, 1949, p. 134.

[2] Bamberger, *Ber.*, 1894, **27**, 1948.

[3] Hammett, " Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 294.

(c) *Reactants and Kinetic Form.*—We may use the abridged list (4) in order to provide a concise illustration of the type of correlation that exists between the active carrier and the kinetic form of reaction. With a general carrier, two limiting kinetic forms can be found (and one of these may have alternatives), according as the attack or formation of the carrier is rate-controlling. In the former case, the carrier remains in equilibrium with other nitrous species, and the concentration of carrier thus determined has to be multiplied by the concentration of the attacked amine in the rate-equation. In the latter case, the carrier is consumed by the amine as fast as the carrier is produced, and so the concentration of amine does not appear in the rate-equation: what is measured now is the rate of a purely inorganic process, and we have to consider the required kinetics of this, or, if there is more than one conceivable process for producing the carrier, of all of them.

The resulting kinetic equations are listed below. With molecular nitrous acid as carrier (to take the simplest of the four examples first), one kinetic case disappears, since there can be no question here of carrier-supply being rate-controlling. Only the attack of this carrier could be rate-controlling, and then the kinetic equation is (5). Similarly, the supply of nitrous acidium ion, as the first conjugate acid of nitrous acid, formed in pre-equilibrium, could not be rate-controlling. Its attack might be, and since its equilibrium concentration is determined by nitrous acid and hydrogen ion, the kinetic equation is (6). Here it may be noted that the expressions " amine " and " HNO_2 " in our kinetic equations are to be taken literally: the represented concentrations are of non-ionised molecules, not including ionic forms, which would be included in expressions of stoicheiometric concentration. Solvation is not expressed, and hence the hydrogen ion is written H^+.

Dinitrogen trioxide is a carrier of which either the attack or the formation could conceivably be rate-controlling. In the former case, an equilibrium concentration of carrier, controlled by the thermodynamics of the process, $2HNO_2 \rightleftharpoons N_2O_3 + H_2O$, will be maintained; and this concentration will be available for the attack of the amine: hence the kinetic equation is (7). In the latter case, the amine concentration drops out from the rate equation, which now represents the rate of self-dehydration of nitrous acid: this is equation (8). The nitrosonium ion also presents alternatives. If an equilibrium concentration is maintained by the thermodynamic situation, $H^+ + HNO_2 \rightleftharpoons NO^+ + H_2O$, the attack of the nitrosonium ion being rate-controlling, the kinetic equation will be (9). If the formation of nitrosonium ion is rate-controlling, and it is formed by loss of water from the nitrous acidium ion, the equation will be (10). But if formation is rate-controlling, and is by loss of nitrite ion from nitrous anhydride, the equation will be (11):

HNO_2	slow attack	Rate $\propto$ [amine][HNO_2] . . .	(5)
$H_2NO_2^+$	,, attack	,, $\propto$ [amine][HNO_2][H^+] . .	(6)
N_2O_3	,, attack	,, $\propto$ [amine][HNO_2]^2 . . .	(7)
	,, supply	,, $\propto$ [HNO_2]^2	(8)
NO^+	,, attack	,, $\propto$ [amine][HNO_2][H^+] . .	(9)
	,, supply *via* $H_2NO_2^+$	,, $\propto$ [HNO_2][H^+]	(10)
	,, supply *via* N_2O_3	,, $\propto$ [HNO_2]^2	(11)

The duplication of equations here seen is sufficient to show that one cannot expect to " locate " oneself in the total pattern without experimentally disclosing a larger part of it than would appear through the observation of just one kinetic form. Indeed, at the outset, before one has convinced oneself that none but the first steps of schemes (1) and (2) affects the kinetics, a number of additional equations, some the same as, and some different from, those here written down, have to be thought of, which allow for slow proton-transfers in the succeeding steps, *i.e.*, for general acid and general base catalysis by various nitrous species, not excluding nitrite ion as a general base. For this reason also, a kinetic investigation is not expected to lead to proved conclusions unless it demonstrates, and elucidates, a certain kinetic variety.

The scheme represented by equations (5)—(11) is more limited than the total scheme of theoretical considerations required, and actually applied, in this work, in the following additional respect. The given set of equations applies to the abridged list of carriers (4); and our original object was to discriminate among the carriers of this list. However, we found that, in order thoroughly to confirm one of these carriers, and to complete the identification of another, we had to admit competing carriers, outside those of the abridged list: we had to study the kinetic changes which occur when the original nitrosating system is deliberately thus complicated.

However, these elaborations will be discussed when we come to them. The object of this section has been, not to set out fully all the theoretical details which have to be envisaged for the purpose of shaping the kinetic approach, but to make clear, by illustration for a limited but central area of the total field, the general nature of the approach, and the power and limitations of the kinetic method.

(2) PREVIOUS RESULTS AND CONCLUSIONS ON *N*-NITROSATION, DIAZOTISATION, AND DEAMINATION

The pioneer work was that of Hantzsch and Schumann, who, in 1899, first studied the kinetics of diazotisation.[4] They used aqueous solutions made weakly acid (0·002M) with hydrochloric acid; and they followed the reaction by an iodometric method, using equivalent amounts of reactants. They established approximate second-order kinetics, and wrote the rate-equation thus:

$$\text{Rate} = k[\text{ArNH}_3^+][\text{HNO}_2] \quad \text{. . . . .} \quad (12')$$

The quantities in these brackets were representing stoicheiometric concentrations of amine and of nitrous acid, to which, at constant acidity, the concentrations of molecular amine and nitrous acid are respectively proportional. Hence the equation may be re-expressed as follows with the conventions used for the rate-equations of section 1:

$$\text{Rate} \propto [\text{amine}][\text{HNO}_2] \quad \text{. . . . .} \quad (12)$$

Hantzsch and Schumann also concluded, though it may be doubted if anyone believed them (then or subsequently up to 1950), that to within their experimental error all aromatic primary amines diazotise at the same rate.

Tassilly [5] introduced the colorimetric method, based on coupling, for following diazotisation, and was the first to do experiments with unequal concentrations of reactants. However, he also found that the reaction, in dilute mineral acid, was approximately of second order.

Boeseken, Brandsma, and Schoutissen [6] considered all previous work in the field to be inaccurate. They developed Tassilly's principle into a more exact procedure. They used reactants in equivalence. Their results for the diazotisation of a number of amines in dilute hydrochloric acid (0·01M) confirmed that the reaction is approximately of second order. But they failed to confirm Hantzsch and Schumann's finding that the rates for different amines are equal.

However, we are reminded of the earlier finding by Reilly and Drumm's report [7] that the three anilines, $p\text{-NH}_2\cdot\text{C}_6\text{H}_4\cdot[\text{CH}_2]_n\cdot\text{NMe}_3^+$ with $n = 0, 1, 2$, which must have very different basic strengths, diazotise at the same second-order rate in dilute hydrochloric acid (0·002M), the reagents again being in equivalence. Disbelief in these results was at once expressed by Boeseken and Schoutissen.[8]

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[4] Hantzsch and Schumann, *Ber.*, 1899, **32**, 1691.

[5] Tassilly, *Compt. rend.*, 1913, **157**, 1148; 1914, **158**, 335, 489; *Bull. Soc. chim. France*, 1920, **27**, 19.

[6] Boeseken, Brandsma, and Schoutissen, *Proc. Acad. Sci. Amsterdam*, 1920, **23**, 249.

[7] Reilly and Drumm, *J.*, 1935, 871.

[8] Boeseken and Schoutissen, *Rec. Trav. chim.*, 1935, **54**, 956.

It will not be overlooked that equation (12) is not fully proved, since, excepting for a few somewhat uncritical experiments by Tassilly on sulphanilic acid, the reagents were always taken in equivalence. But all workers from 1899 to 1935 agree that the overall kinetic order is second. They differ as to whether different amines diazotise at the same rate or at different rates, the former opinion arising from experiments in the lower range of acidity (near 0·002M), and the latter from experiments at a somewhat higher acidity (0·01M).

In 1936, Schmid observed kinetics of a different kind.[9] He worked in a markedly higher acidity range (of the order of 0·2M). With acidities set by added sulphuric acid, the reaction was now of third order overall, as represented by the rate-equation (13):

$$\text{Rate} \propto [\text{amine}][\text{HNO}_2]^2 \qquad (13)$$

The use of hydrochloric or hydrobromic acid in place of sulphuric acid introduced additionally a catalysed reaction, into the details of which we need not enter now. As to the basic reaction of equation (13), Schmid made no attempt to reconcile his third-order kinetics with the second-order kinetics found by all previous workers on diazotisation: he makes no reference to the previous work.

Equation (13) was not new. It had been discovered in 1928, by T. W. J. Taylor in application to the deamination of primary aliphatic amines.[10, 11, 12] In 1929, Taylor observed it again in the simplest, and kinetically most basic, of the whole family of reactions between amines and nitrous acid, the formation of a nitrosamine from a secondary amine.[12] In his first work,[10] Taylor confirmed an early suggestion by Arndt that the same equation governed the reactions of ammonia with nitrous acid; and in this he was in turn confirmed by Abel *et al.*[13]

In the many theoretical discussions of equation (13), the simplest line taken was that of Earl and Hills, who " preferred to consider " the third kinetic order as spurious.[14] They made it clear that they preferred equation (12), which they explained by supposing that the amine adds to nitrous acid, somewhat as it might add to a carbonyl compound.

Kenner, and also Hammett, on the other hand, accepted equation (13); and they offered interpretations of it. Adamson and Kenner explained it[15] by assuming that the second step, not the first, of process (2) is slow, that the first step involves specific hydrogen-ion catalysis (the reagent therefore being the nitrous acidium ion), and that the second step involves general base catalysis (with nitrite ion as the effective base), the two catalyses between them bringing into the transition state the equivalent of the second molecule of nitrous acid. Apart from the improbability that the second step of process (2) could be slow, it has been shown by Austin[16] that deamination is not subject to general base catalysis. Finally, Hammett[3] made the suggestion, which we show to be correct, that equation (13) represents a rate-controlling attack by dinitrogen trioxide, whilst in catalyses by hydrogen halide the attack is by nitrosyl halide.

We have set down this history for two reasons. The first is that, despite its recurrent disagreements, we can show that all previously recorded work can be understood, and could be accepted as essentially correct, apart from one purely logical slip, which entered at the outset and remained undetected until we noticed it. The second is that, whilst all previous authors have turned a blind eye on one " half " or the other of the recorded facts, with the consequence that their interpretations can only have the status of patently questionable suggestions, we shall show that an interpretation is available which accommodates all known facts, and is, indeed, proved by them.

[9] Schmid, *Z. Elektrochem.*, 1936, **42**, 579; 1937, **43**, 626; Schmid and Muhr, *Ber.*, 1937, **70**, 421.
[10] T. W. J. Taylor, *J.*, 1928, 1099.
[11] *Idem, J.*, 1928, 1897.
[12] T. W. J. Taylor and Price, *J.*, 1929, 2052.
[13] Abel, Schmid, and Schrafranik, *Z. phys. Chem.*, *Bodenstein Festschrift*, 1931, 510.
[14] Earl and Hills, *J.*, 1939, 1089.
[15] Adamson and Kenner, *J.*, 1934, 838; Kenner, *Chem. and Ind.*, 1941, **60**, 443, 899.
[16] Austin, Thesis, London, 1950; cf. ref. 17.

We break off the history at 1950, because it was then that we first published [17] in preliminary form the main findings of which the details are now presented. Subsequent related work will be considered in the comparative discussion of Part VI.

(3) THE MEASUREMENT OF DIAZOTISATION

(a) *Side-reactions in Diazotisation.*—Diazotisation has been followed by extracting samples, and determining the diazonium-ion concentrations colorimetrically. The obtained values were subtracted from the initial (stoicheiometric) concentrations of amine and nitrous acid, in order to give the reagent concentrations at the time of sampling. This method is valid only if the side-reactions of the nitrous acid and diazonium ion can be ignored. Consideration was therefore given to these side-reactions.

Several previous kinetic studies have been made of the decomposition of solutions of nitrous acid. The reaction almost certainly involves the formation and hydrolysis of dinitrogen tetroxide, but the rate-determining stage appears to depend on the experimental conditions,[18] with the result that previous work cannot be used to estimate the extent of the decomposition under the conditions of our experiments.

Therefore a brief experimental study was undertaken of this decomposition. We started with the Griess–Ilosva method for the colorimetric determination of nitrous acid; but it has the grave disadvantage that several hours are required for the colour development. However, in some joint work with Dr. E. A. Halevi, it was possible to modify the Griess–Ilsova method, so that the colour production became almost instantaneous.[19]

It was shown that, at 0°, a 0·0001M-solution of nitrous acid decomposed at a rate of 0·5—1·0% per hour, that in a 0·001M-solution the rate was 1—2% per hour, and that in a 0·005M-solution decomposition became non-uniform, the rate falling with time. These results were obtained in 0·002M-perchloric acid, but as there is no evidence for acid catalysis, other than that arising from the conversion of nitrite ions into nitrous acid, they should hold at other acidities. When these rates are compared with diazotisation rates, it becomes clear that the decomposition of nitrous acid should not greatly affect the kinetics of diazotisation.

The two conceivably significant side-reactions of diazonium ions are their hydrolysis, and their *N*-coupling with unchanged amine to give diazoamino-compounds. The hydrolysis is a simple S_N1-reaction, kinetically of the first order, and its rate has been measured.[20] From rates at higher temperatures it can be estimated that at 0° the diazonium ion from aniline will undergo hydrolysis at a rate of about 0·3% per hour. The diazonium ions from the toluidines are expected to be of the same order of stability, and those having electronegative nuclear substituents to be more stable. This reaction, then, is not an important source of error.

The *N*-coupling reaction could introduce large errors; but it can be seen, because it leads to colour. In our conditions it makes little trouble in the diazotisation of aniline and the toluidines but, in that of amines with electronegative nuclear substituents, the solutions may become coloured, and the diazonium-ion concentration may fail to reach its theoretical value and, at late times, begin to decrease. Whenever this has been observed, the amine concentration has been reduced, or the acidity has been increased, until the diazotisation goes to completion.

(b) *Kinetic Methods.*—The aromatic amines, purchased or pure, were further purified by conventional methods. The perchloric acid and sodium nitrite were " AnalaR ". The latter was of better than 99% purity, as determined by the Fischer–Steinbach

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[17] Hughes, Ingold, and Ridd, *Nature*, 1950, **166**, 642.

[18] Bray, *Chem. Rev.*, 1932, **10**, 161.

[19] Bunton, Halevi, and Llewellyn, *J.*, 1952, 4916.

[20] Moelwyn-Hughes and Johnson, *Trans. Faraday Soc.*, 1940, **36**, 948.

method,[21] and no correction was made for the difference from 100%. The R-salt had to be purified by repeated crystallisation from a hot solution of sodium chloride.

The temperature of the measurements was 0·00° ± 0·05°. Solutions of the amine in an equivalent of aqueous perchloric acid, and of perchloric acid in water, were mixed to such volume that, when, after temperature adjustment, the run was started by the addition of temperature-adjusted aqueous sodium nitrite, the volume was 100 ml. Samples of 2 or 5 ml. were withdrawn at timed intervals, and run each into 27 ml. of the coupling solution, which contained R-salt (0·01M) and borax (0·025 or 0·05M).

Colour densities were measured in well-screened cells, 0·25—4·00 cm. thick, in a Hilger Spekker photo-electric absorptiometer, with a narrow-transmission-band filter, so that Beer's law was obeyed, and a sensitive galvanometer. Calibration was obtained with a colour standard, prepared in various ways for purposes of checking, but usually, and most conveniently, by diazotising the amine in known amount, with excess of nitrous acid and a slight excess of perchloric acid, conditions under which the reaction is rapid and complete. The calibration curve, obtained by dilution of the standard, was linear.

In recording the initial conditions of runs done in excess of perchloric acid, allowance was always made for the fact that the total acid is partly neutralised, not only by the amine, but also by the sodium nitrite. It is the excess, beyond these allowances, that is cited as the acidity.

Runs in buffers, or with added catalysis, were done by obvious adaptations of the methods described.

(c) *Types of Rate-constant.*—Each of our reactants is a Brönsted acid–base system. We can therefore calculate various types of rate-constant, of which two have had their uses in this work. One, which we call a stoicheiometric rate-constant, is the proportionality constant of a rate-equation containing only stoicheiometric concentrations of the reactants, *i.e.*, for each reactant a total of the concentrations of its acidic and basic forms. The other, which we call a molecular rate-constant, is the constant of a rate-equation involving the concentrations in which the reagents are present in their uncharged molecular forms. In a constant excess of acid, or, more generally, at constant hydrogen-ion concentration, the ratio of the molecular to the stoicheiometric concentration for each reactant remains constant throughout a run. Therefore, it makes no difference to the kinetic form of the run, which type of constant we calculate; but it does make a difference to the value of the constant.

The stoicheiometric rate-constants are easily computed, inasmuch as they depend only on quantities which we ourselves measure. However, the computation of molecular rate-constants requires a knowledge also of the acidity constants of the arylammonium ion and of nitrous acid. These equilibrium constants have been measured accurately only at low ionic strengths, and they have not been well measured at the moderate ionic strengths of some of our experiments. This makes no great difficulty as regards the arylammonium ion, the dissociation of which does not create or destroy charges, with the consequence that its acidity constant is insensitive to ionic strength, except at high ionic strengths. However, the acidity constant of nitrous acid must be appreciably greater at moderate than at low ionic strengths.

Our policy has therefore been to calculate stoicheiometric rate-constants whenever nothing of importance depended on what type of constant was chosen, and to calculate molecular rate-constants only when they were needed, giving the employed acidity constants, so that the data could easily be corrected should more accurate acidity constants become available. The first procedure is fully satisfactory, except when we are comparing experiments at different acidities for the purpose of determining the effect of acidity; for an acidity change could in general have two kinds of effect, which it would be necessary to distinguish. First, added acid could replace amine by ammonium ion, and nitrite ion by

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[21] Fischer and Steinbach, *Z. anorg. Chem.*, 1912, **78**, 134.

nitrous acid; and if the kinetics corresponded to equation (5), (7), (8), or (11) of section (1c), that would be all that it could do. But if the kinetics corresponded to equation (6), (9), or (10), or to one of the equations, not given in section (1c), which express catalysis by hydrogen halides, then an acidity change would have a further effect, inasmuch as, in these kinetic forms, hydrogen-ion becomes a reactant. For the purpose of sorting out this mechanistically significant, second effect of acid, we have to calculate molecular rate-constants.

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