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Kinetics of Reactions in Moderately Concentrated Aqueous Acids. II. An Empirical Criterion of Mechanism^{1,2}

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Consideration of w - and w^* -values for reactions of defined mechanism reveals that certain magnitudes of these parameters are associated with characteristic modes of involvement of water in rate-determining steps. The correlations thus deduced constitute an empirical criterion of mechanism which is advocated as successor to the Zucker-Hammett hypothesis. A distinction is drawn between substrates which, in the reaction pathway, are protonated on oxygen or nitrogen and those which are hydrocarbon-like bases. For the former class, w of -2.5 to zero indicates that water does not participate in transformation of SH^+ to transition state, w of $+1.2$ to $+3.3$ that water acts as a nucleophile, and $w > +3.3$ (or better, $w^* > -2$) that water acts as a proton transfer agent. For substrates which are hydrocarbon-like bases, w of about zero is associated with mechanisms of rate-determining proton transfer. Certain limitations of this empirical criterion are cited.

In the preceding paper,³ a new system for the classification of reactions in moderately concentrated mineral acids is presented. Reactions are classified according to their w -values, and secondarily by their w^* -values.

Hitherto, reactions have generally been classified in one or another of two categories defined by Zucker and Hammett.^{4,5} Reactions which gave linear plots of $\log k_\psi$ versus $-H_0$ formed the one category, and those which gave linear plots of $\log k_\psi$ versus $\log [\text{HX}]$ constituted the other.

Zucker and Hammett suggested that the two categories comprised, respectively, reactions in which water was not and was involved in transformation of protonated substrate (SH^+) to transition state. This suggestion was generally accepted, and the Zucker-Hammett hypothesis gained the status of a standard criterion of mechanism.⁶ However, doubts about its theoretical justification lingered⁶⁻⁹ and gained strength from the demonstration of inconsistencies, both internally and with respect to other criteria of mechanism.¹⁰⁻¹⁵ Several investigators have questioned its basic worth.

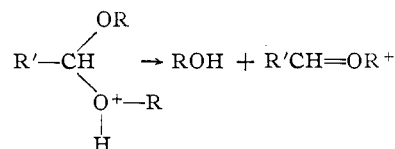
Although it was given some theoretical justification, the Zucker-Hammett hypothesis was basically empirical. Fundamentally, it was a generalization of Hammett's judgment that sucrose hydrolysis (correlated with h_0) does not utilize water in forming the transition state from SH^+ whereas acetophenone enolization (correlated with

oxonium ion concentration) requires water in the critical step. The most cogent criticism of the hypothesis is also empirical: demonstration that conclusions from it are at variance with conclusions from other criteria of mechanism.

In these circumstances, a re-examination of the situation from an empirical point of view is warranted. Let us approach the matter with the classification of reactions by w - and w^* -values in mind. Considering reactions of well defined mechanism, we shall seek to correlate w - or w^* -values with mechanism type, with special attention to the manner of participation by water in the rate-determining step.

Three modes of participation by water were recognized by Zucker and Hammett.⁴ In their words, "There are three possibilities: (a) the rate determining step is a proton transfer as it is in the enolization; (b) it involves a water molecule in some other way than as a base. . . ; (c) it involves a spontaneous cleavage or other change of the conjugate acid of the substrate. . ." I prefer to state the same idea as follows: Water may participate in the rate-determining step: (a) as a proton transfer agent, either accepting a proton from an acid or (as the oxonium ion) furnishing a proton to a base,¹⁶ (b) as a nucleophile or (c) not at all.

Reactions in Which Water Does Not Participate in the Rate-determining Step.—Representatives of this class include hydrolyses of acetals, *t*-butyl acetate and methyl mesitoate. The acid-catalyzed hydrolysis of acetals has been quite thoroughly studied. Several items of evidence⁶ indicate that the rate-determining step is unimolecular heterolysis of the protonated acetal



The zero or small positive volume change of activation¹⁷ also attests to this mechanism; w for acetal hydrolyses is typically about zero to -2 in sulfuric or perchloric acid, but a negative number of

(16) Proton donation in this sense is the reverse of proton acceptance by water, which forms oxonium ion. Proton donation by water itself (leaving a hydroxide ion residue) apparently plays no part in the rate-determining steps of measurably slow reactions in strongly acidic media.

(17) J. Koskikallio and E. Whalley, *Trans. Faraday Soc.*, **55**, 809 (1959).

(1) Financial support by the Office of Ordnance Research, U. S. Army, and by the National Science Foundation (Grant No. G-6210) is gratefully acknowledged. Presented in part to the Eighth Conference on Reaction Mechanisms, Princeton, N. J., Sept., 1960.

(2) Described tersely in a preliminary communication: J. F. Bunnett, *J. Am. Chem. Soc.*, **82**, 499 (1960).

(3) J. F. Bunnett, *ibid.*, **83**, 4956 (1961).

(4) L. Zucker and L. P. Hammett, *ibid.*, **61**, 2791 (1939).

(5) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 273-277.

(6) F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 935 (1957).

(7) E. Grunwald, A. Heller and F. S. Klein, *J. Chem. Soc.*, 2604 (1957).

(8) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt & Co., New York, N. Y., 1959, pp. 190-192.

(9) L. Melander and P. C. Myhre, *Arkiv. Kemi*, **13**, 507 (1959).

(10) R. W. Taft, Jr., N. C. Deno and P. S. Skell, *Ann. Rev. Phys. Chem.*, **9**, 306 (1958).

(11) J. Koskikallio and E. Whalley, *Can. J. Chem.*, **37**, 788 (1959).

(12) J. Koskikallio and E. Whalley, *Trans. Faraday Soc.*, **55**, 815 (1959).

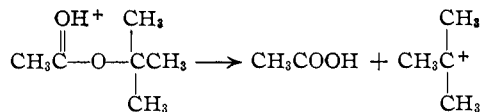
(13) H. Kwart and A. L. Goodman, *J. Am. Chem. Soc.*, **82**, 1947 (1960).

(14) A. J. Kresge and Y. Chiang, *ibid.*, **81**, 5509 (1959).

(15) R. H. Boyd, R. W. Taft, Jr., A. P. Wolf and D. R. Christman, *ibid.*, **82**, 4729 (1960).

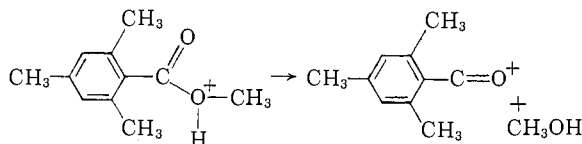
greater magnitude in hydrochloric acid (1, 2, 3, 5, 6).¹⁸

The acid-catalyzed hydrolysis of *t*-butyl acetate appears also to involve rate-determining unimolecular heterolysis of its conjugate acid



Evidence has been discussed by Ingold¹⁹; also pertinent is the nearly quantitative scission of the alkyl-oxygen bond, as shown by hydrolysis in oxygen-18 enriched water,²⁰ and the high positive entropy of activation²¹; *w* for hydrolysis of *t*-butyl acetate in hydrochloric acid (64) is -1.2 .

Hydrolysis of methyl mesitoate (67) in moderately concentrated acids involves, according to the best information,^{22,23} a slow step in which the protonated ester breaks into a methanol molecule and an acylium ion



The *w*-values are -1.1 and -2.5 in sulfuric and perchloric acids, respectively.

Evidence is thus excellent that hydrolyses of simple acetals, of *t*-butyl acetate and of methyl mesitoate involve rate-determining unimolecular heterolysis of the substrate conjugate acid. Excluding acetal hydrolyses in hydrochloric acid, because their *w*-values are so different from the rest,²⁴ these reactions have *w* of 0.0 to -2.5 . Thus, empirically, reactions in which transformation of SH^+ to transition state requires no water are associated with *w*-values of 0.0 to -2.5 .

Reactions which, in the Zucker-Hammett treatment, give linear plots of $\log k_{\psi}$ versus $-H_0$ with slope *unity* have *w* of zero, while slopes slightly greater than unity correspond to small negative *w*-values. Thus the foregoing deduction resembles

(18) Numbers in parentheses refer to the location of reactions in Table I, ref. 3.

(19) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 779.

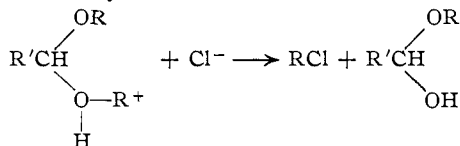
(20) C. A. Bunton and J. L. Wood, *J. Chem. Soc.*, 1522 (1955).

(21) P. Salomaa, *Suomen Kemi*, **32B**, 145 (1959).

(22) C. T. Chmiel and F. A. Long, *J. Am. Chem. Soc.*, **78**, 3326 (1956).

(23) M. L. Bender, H. Ladenheim and M. C. Chen, *ibid.*, **83**, 123 (1961).

(24) The exceptionally high *w*-values for acetal hydrolyses in hydrochloric acid signify that hydrolysis in this medium accelerates unusually rapidly as the acid concentration is increased. Possibly the reason is a side reaction in which chloride ions effect bimolecular nucleophilic displacement on alkyl carbon

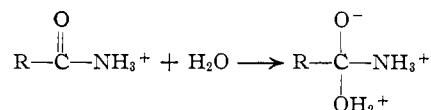


A similar exaltation of rate stemming from nucleophilic participation by chloride ions has been noted in hydrolyses of dialkyl sulfites in hydrochloric acid.²⁵

(25) C. A. Bunton, P. B. D. de la Mare and J. G. Tillett, *J. Chem. Soc.*, 4754 (1958); 1766 (1959).

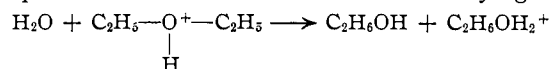
that of Zucker and Hammett. An important difference is that small positive *w*-values, corresponding to slopes somewhat less than unity in plots of $\log k_{\psi}$ versus $-H_0$, are not in the present treatment associated with rate-determining unimolecular heterolysis of SH^+ .

Reactions in Which Water Acts as a Nucleophile in the Rate-determining Step.—In the acid-catalyzed hydrolysis of carboxylic amides, the critical step is attack of water on the carbonyl carbon of the protonated amide^{26,27}



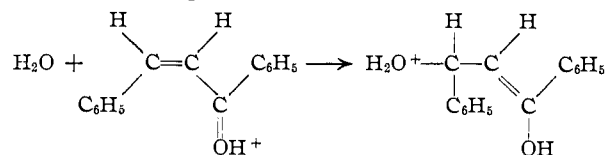
Evidence includes the non-occurrence of oxygen exchange between the carbonyl oxygen and water of the medium³¹ during hydrolysis and the direction and magnitude of substituent effects at high acid concentrations.³² For hydrolysis of amides of type RCONH_2 , where R is an alkyl or aryl group (32-37),¹⁸ *w* ranges from $+1.2$ to $+2.6$.

The hydrolysis of diethyl ether in perchloric acid solutions involves bimolecular reaction of the protonated substrate with water. Evidence is the negative entropy (-9 e.u.) and volume change (-8 cc./mole) of activation.¹¹ The only reasonable bimolecular substitution mechanism is $\text{S}_{\text{N}}2$ displacement on the α -carbon of an ethyl group



w for diethyl ether hydrolysis in perchloric acid (56) is $+2.7$.

The isomerization of *cis*- to *trans*-benzalacetophenone involves, according to Noyce, Pryor and King,³³ rate-determining nucleophilic attack of water on the protonated ketone



This is followed by rapid rotation about the erstwhile $\text{C}=\text{C}$ bond and then rapid detachment of a water molecule to form the conjugate acid of the product. Part of their argument was based on

(26) This step is probably an addition to form a tetrahedral adduct, as shown, but synchronous displacement of ammonia is not altogether excluded. In either case water acts as a *nucleophile*.

(27) The oxygen-protonated form, RCNH_2^+ , is the dominant conjugate acid of amides.²⁸⁻³⁰ However, attack of water on the nitrogen-protonated form is believed to account for most of the hydrolysis products.²⁸ Acyltrialkylammonium ions, $\text{R}'\text{CONR}_3^+$, are very rapidly attacked by nucleophiles.²⁹

(28) R. Huisgen and H. Brade, *Ber.*, **90**, 1432 (1957).

(29) F. Klages and E. Zange, *Ann.*, **607**, 35 (1957).

(30) A. Berger, A. Loewenstein and S. Meiboom, *J. Am. Chem. Soc.*, **81**, 62 (1959); G. Fraenkel and C. Franconi, *ibid.*, **82**, 4478 (1960).

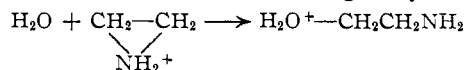
(31) M. L. Bender, R. D. Ginger and K. C. Kemp, *ibid.*, **76**, 3350 (1954); C. A. Bunton, T. A. Lewis and D. R. Llewellyn, *Chemistry & Industry*, 1154 (1954); M. L. Bender and R. D. Ginger, *J. Am. Chem. Soc.*, **77**, 348 (1955).

(32) J. A. Leiston, *J. Chem. Soc.*, 765 (1959).

(33) D. S. Noyce, W. A. Pryor and P. A. King, *J. Am. Chem. Soc.*, **81**, 5423 (1959).

the Zucker-Hammett hypothesis; that part must be set aside in the current discussion. But there is other cogent support for the mechanism proposed. The low entropy of activation (-22 e.u.) and the fact that deuterons from the medium do not become bonded to carbon³⁴ are notably important; w for isomerization of *cis*- to *trans*-benzalacetophenone (81) varies from $+2.8$ to $+3.3$, depending somewhat on the mineral acid and temperature employed.

The hydrolysis of ethyleneimine is catalyzed by acid in low concentrations but retarded by increase of perchloric acid concentration above $1 M$. Evidence that the rate-determining step is S_N2 displacement of the iminium nitrogen by a water

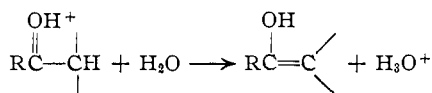


molecule has been marshalled by Buist and Lucas³⁵ and by Earley, O'Rourke, Clapp, Edwards and Lawes³⁶; w for ethyleneimine hydrolysis is $+2.5$.³⁷

Evidence is thus good that hydrolyses of ethyleneimine, of diethyl ether and of ordinary carboxylic amides, and isomerization of *cis*- to *trans*-benzalacetophenone involve nucleophilic attack by water in the rate-determining step. In the former two cases water effects S_N2 displacement; in the latter two it adds to an unsaturated carbon. These reactions have w -values of $+1.2$ to $+3.3$. Empirically, reactions in which the rate-determining step is nucleophilic attack of water on SH^+ are associated with w -values in this range.

Reactions in Which Water Participates as a Proton Transfer Agent in the Slow Step.—These are, as has been pointed out,^{6,38} in the category of general acid-catalyzed reactions. In catalysis by oxonium ion, this species acts as a general acid or water acts as a general base.

The acid-catalyzed enolization of ketones has been extensively studied. Insofar as catalysis by oxonium ion is concerned, there is general agreement that the slow step is removal of a proton from the α -carbon of the protonated ketone by water acting as a base



Much of the evidence has been presented by Bell³⁹; additional contributions have been made by Swain and co-workers.⁴⁰ Enolization rates are frequently measured by determining the rates of acid-catalyzed iodination or bromination, reactions in which formation of the enol is rate determining. w -Values for the iodination or bromination of aceto-

phenone (77) and acetone (76) range from $+3.6$ to 6.7 , depending on the mineral acid and concentration range used; w^* -values are in the narrower range of -1.4 to -1.7 .

Hydrogen isotope exchange between NH_3D^+ , $\text{CH}_3\text{NH}_2\text{D}^+$ or $(\text{CH}_3)_3\text{ND}^+$ and the medium (reactions 99-101) is quite slow in moderately concentrated sulfuric acid solutions.⁴¹ Whatever the details of the mechanism, proton transfer (or deuteron transfer; the equivalent for our purposes) occurs in the slow step. The w -values lie between $+3.1$ and $+6.8$; the incidence of curvature in the w -plots makes the w^* ($+0.7$ to $+2.8$) better index parameters.

According to evidence obtained and presented by Kreevoy,⁴² the cleavage of methylmercuric iodide by mineral acids (89) is a bimolecular electrophilic displacement on carbon, the mercuri group being displaced by a proton furnished by the oxonium ion or other acid species. The rate-determining step is proton transfer concerted with breaking of the C-Hg bond; w is $+3.4$ in perchloric acid and $+6.6$ in sulfuric acid; w^* is, respectively, -1.3 and $+1.3$.⁴³

Thus three types of reactions which involve proton transfer in the rate-determining step have high w -values (over $+3.1$). The situation is more precisely described by the w^* -values which range from -1.7 to $+2.8$. Provisionally, let us take w or w^* parameters of these magnitudes as indicative of proton transfer in the rate-determining step.

This identification can be made firm if two important questions can be answered satisfactorily. First, does it imply that the many substitution reactions of high w (e.g., hydrolyses of piperazine-2,5-dione (42), of γ -butyrolactone (74), of thioacetamide (85), of methyl benzimidate (86))¹⁸ are limited in rate by slow proton transfer steps? The possibility cannot be altogether excluded, since NH_3D^+ exchange with sulfuric acid is slow.⁴¹ However, in general, proton transfers between oxygen and/or nitrogen atoms appear to be much faster than formation or rupture of bonds to carbon.

There is another possibility. Proton transfer may be concerted with the making or breaking of a C-O or C-N bond. Because of their non-synchronous character,⁴⁴ substitutions at unsaturated carbon are easily formulated with a rate-determining step of this type. Indeed, several types of mechanism with proton transfer in the slow step are conceivable:

(a) There may be general acid catalysis of leaving group departure from a tetrahedral intermediate, as in the probable mechanism for hydrolysis of piperazine-2,5-dione (42)¹⁵ shown.

Analogies are found in the general acid-catalyzed hydrolyses of *ortho* esters⁴⁶ and in mechanisms

(34) D. S. Noyce, G. L. Woo and M. L. Jorgenson, *J. Am. Chem. Soc.*, **83**, 1180 (1961).

(35) G. J. Buist and H. J. Lucas, *ibid.*, **79**, 6157 (1957).

(36) J. E. Earley, C. E. O'Rourke, L. B. Clapp, J. O. Edwards and B. C. Lawes, *ibid.*, **80**, 3458 (1958).

(37) F. Olsen and J. F. Bunnett, *Abstr. Am. Chem. Soc. Meeting*, Cleveland, Ohio, April, 1960, p. 77-O.

(38) V. Gold, *Ann. Reports for 1959*, **56**, 46 (1960).

(39) R. P. Bell, "Advances in Catalysis," Vol. IV, Academic Press, Inc., New York, N. Y., 1952, pp. 165-182; R. P. Bell and P. Jones, *J. Chem. Soc.*, **88** (1953).

(40) C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *J. Am. Chem. Soc.*, **80**, 5885 (1958); C. G. Swain, A. J. Di Milo and J. P. Cardner, *ibid.*, **80**, 5983 (1958).

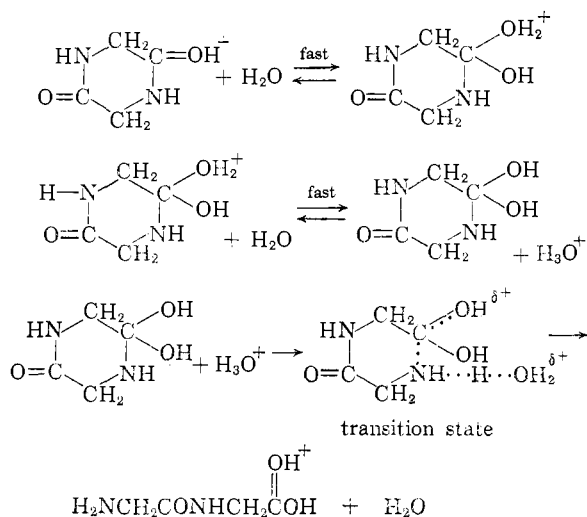
(41) M. T. Emerson, E. Grunwald, M. Kaplan and R. A. Kromhout, *ibid.*, **82**, 6307 (1960).

(42) M. M. Kreevoy, *ibid.*, **79**, 5927 (1957).

(43) This w^* in sulfuric acid is w_a less 1.6.²

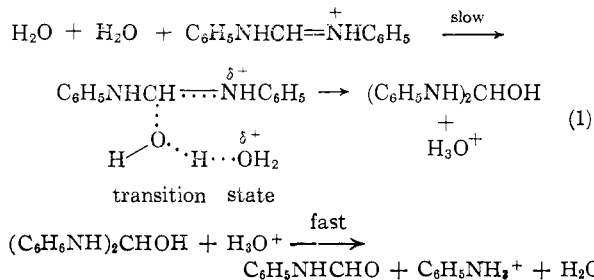
(44) J. F. Bunnett, "Theoretical Organic Chemistry: Proceedings of the Kekule Symposium," Butterworths, London, 1959, p. 144.

(45) The conjugate acids of reactant and product are understood to be in rapid equilibrium with the uncharged reactant and product. Reasons for favoring the mechanism given are presented in paper IV: J. F. Bunnett, *J. Am. Chem. Soc.*, **83**, 4978 (1961).



proposed for the general base-catalyzed reactions of *n*-butylamine with ethyl formate and of *N*-methylaniline with 2,4-dinitrofluorobenzene.⁴⁷

(b) There may be general base-catalyzed nucleophilic attack of water on the protonated substrate, as in the following possible mechanism for hydrolysis of *N,N'*-diphenylformamidine (84)⁴⁸



The fact of general acid catalysis⁴⁸ affirms that proton transfer occurs in the slow step of this reaction. Mechanism b is, in a sense, the same as a but in the opposite direction. Nucleophilic attack and proton transfer are combined in the slow step, but the aspect of higher *w* determines the over-all *w*-values.

(c) A proton may be transferred to a carbonyl oxygen in concert with nucleophilic attack of water on carbon, or (d) the departure of a protonated leaving group may be facilitated by concerted removal of a proton from a resident hydroxy group. (c) and (d) are in essence the same, though opposite in direction, and are illustrated by the generally accepted mechanism for hydration of acetaldehyde or dehydration of the hydrate^{49,50}

For substitutions at *saturated* carbon, two mechanisms with concerted proton transfer are

(46) J. N. Brønsted and W. F. K. Wynne-Jones, *Trans. Faraday Soc.*, **25**, 59 (1929); H. Kwart and M. B. Price, *J. Am. Chem. Soc.*, **82**, 5123 (1960).

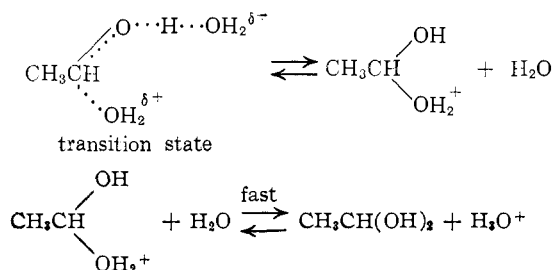
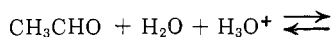
(47) J. F. Bunnett and G. T. Davis, *ibid.*, **82**, 665 (1960); J. F. Bunnett and J. J. Randall, *ibid.*, **80**, 6020 (1958).

(48) R. H. DeWolfe, *ibid.*, **82**, 1585 (1960); R. H. DeWolfe and R. M. Roberts, *ibid.*, **75**, 2942 (1953).

(49) R. P. Bell, M. H. Rand and K. M. A. Wynne-Jones, *Trans. Faraday Soc.*, **52**, 1093 (1956); Y. Pocker, *Proc. Chem. Soc.*, 17 (1960).

(50) These hydration and dehydration reactions are not substitutions in the formal sense, but they involve the same two processes of addition of a nucleophile to an unsaturated center, and the reverse, as do the substitutions in question.

conceivable: (e) nucleophilic attack of water concerted with general acid catalysis of leaving group departure, and (f) general base-catalyzed nucleophilic attack of water with synchronous departure of the protonated leaving group. These are, in a sense, the opposite of one another. The fact that bimolecular hydrolyses at saturated carbon (the ring opening of ethyleneimine⁴⁷ and of epoxides^{6,12,51} and reactions 18, 19, 56 and 88),¹⁸ with the exception of methyl dihydrogen phosphate (53) and dimethyl hydrogen phosphate (54) hydrolyses, have relatively low *w*-values (*ca.* +2 to +3) suggests that mechanisms e and f are infrequent of occurrence. Their termolecular character is doubtless a handicap.



The second important question concerns reactions of hydrogen isotope exchange at aromatic carbon (24-31); *w*-values are near zero, much lower than deduced above for reactions of slow proton transfer. Originally, Gold and Satchell,⁵² with reference to the Zucker-Hammett hypothesis, proposed rapidly reversible protonation of the aromatic substrate to form a π -complex, followed by slow rearrangement to a σ -complex, and finally these same processes in reverse order for expulsion of the hydrogen atom displaced. However, Kresge and Chiang⁵³ have shown that protodetritiation of 1,3,5-trimethoxybenzene-2-*t* is general acid catalyzed in acetate buffers, and recently Kresge⁵⁴ has obtained data showing *w* to be -0.8 (31) for the same reaction. General acid catalysis is evidence, in the present instance, for rate-determining proton transfer. Presumably the other aromatic protonation reactions (24-30), which have similar *w* values, have the same mechanism.⁵⁵

Closely related is the hydration of olefins, which also has *w*-values near zero. One of two mechanisms consistent with the extensive evidence involves rate-limiting initial protonation of the alkene.¹⁵

These facts are accommodated by recognizing a second classification of proton transfer reactions. *Proton transfer to hydrocarbon-like bases, or from their conjugate acids, is empirically associated with w-values near zero.*

(51) J. G. Pritchard and F. A. Long, *J. Am. Chem. Soc.*, **78**, 2667 (1956).

(52) V. Gold and D. P. N. Satchell, *J. Chem. Soc.*, 3609 (1955).

(53) A. J. Kresge and Y. Chiang, *J. Am. Chem. Soc.*, **81**, 5509 (1959); **83**, 2877 (1961).

(54) A. J. Kresge, personal communication.

(55) General acid catalysis of hydrogen isotope exchange with azulene has been demonstrated by J. Colapietro and F. A. Long, *Chemistry & Industry*, 1056 (1960). However, data from which to reckon *w*-values are not available.

It should not surprise us that two categories of proton transfer reactions, one for bases that accept the proton on oxygen or nitrogen, another for hydrocarbon-like bases, have greatly differing w -values. For *equilibrium* protonation, two categories of bases are recognized: those whose protonation is represented by H_0 , and those whose protonation is correlated with $(H_R - \log a_{H_2O})$.⁵⁶ If two categories of bases differ in their behavior in *thermodynamic* protonation, why should not the same two categories differ in w -values which refer to kinetic protonation?⁵⁹

An interesting question arises. Are there also two categories in which (in the slow step) SH^+ is transformed into transition state without participation by water, and again two where water acts as a nucleophile, corresponding to the substrate being a hydrocarbon-like base or one which accepts the proton on oxygen or nitrogen? Looking back at our landmarks for those two modes of participation by water, we see that all of them concern substrates of the latter type. Confirmed examples of rate-determining unimolecular transformation within, or nucleophilic attack of water upon, the conjugate acids of hydrocarbon-like bases are not available at present. One guesses that when they do come to light they will be characterized by w -values of perhaps -6 and -3 , respectively.

The New Empirical Criterion of Mechanism.—The foregoing conclusions concerning correlation of w - or w^* -values with reaction mechanism are assembled in Chart I. Collectively, they constitute

CHART I
MECHANISTIC INTERPRETATION OF w - AND w^* -VALUES

w -Values	w^* -Values	Function of water in the rate-determining step
For substrates protonated on oxygen or nitrogen		
-2.5 to 0.0		Is not involved
$+1.2$ to $+3.3$	$< -2^a$	Acts as a nucleophile
$> +3.3^b$	$> -2^a$	Acts as a proton transfer agent
For substrates which are hydrocarbon-like bases		
About zero		Acts as a proton transfer agent

^a This boundary is not precisely defined. ^b For fine distinctions, w^* should be heeded.

a new criterion of reaction mechanism for reactions in moderately concentrated mineral acids. This criterion is advocated as successor to the Zucker-Hammett hypothesis.

The one zone of overlap, concerning w -values about zero, is not apt to cause much difficulty in application of this criterion. The atoms which receive protons can usually be deduced from general principles, and sometimes are experimentally determinable.

Because reactions of high w often give distinctly curved plots of $(\log k_p + H_0)$ versus $\log a_{H_2O}$, their w -values are often dependent on the range

(56) Bases which require $(H_R - \log a_{H_2O})$ include diarylolefins^{57a} and 1,3,5-trimethoxybenzene.^{57b} Closely related are the triarylcarbinol \rightleftharpoons triarylcarbonium ion equilibria correlated with H_R .⁵⁸

(57) (a) N. C. Deno, P. T. Groves and G. Saines, *J. Am. Chem. Soc.*, **81**, 5790 (1959); (b) A. J. Kresge and Y. Chiang, *Proc. Chem. Soc.*, **81** (1961).

(58) N. C. Deno, H. E. Berkheimer, W. L. Evans and H. J. Peterson, *J. Am. Chem. Soc.*, **81**, 2344 (1959).

(59) Stimulating conversations with Dr. A. J. Kresge had an important influence on development of these ideas.

of acid concentrations covered by the experiments.³ For such reactions, w^* are reasonably independent of concentration range. Therefore, fine distinctions between water acting as a nucleophile or as a proton transfer agent (nitrogen or oxygen bases) are better made with reference to w^* -values.

But even here the boundary is not sharply defined. w^* -Values as low as -1.7 are associated with good examples of proton transfer activity in the critical step (e.g., 76a)¹⁸; and good examples of water acting as a nucleophile (e.g., 56, 81c) have w^* around -3.2 . However, w^* (actually $w_a - 1.6$) for reaction 81b is -1.9 ; it should be noted that the data comprise only three points. The boundary is somewhere around -2 , but needs better definition.

Application of this criterion to data from the literature is deferred to paper IV.

Comparison with the Zucker-Hammett Hypothesis.—With respect to substrates protonated on oxygen or nitrogen, the new criterion recognize three classifications corresponding to three ranges of w -values, and associates each with a characteristic mode of participation by water in the rate-determining step. The Zucker-Hammett hypothesis recognized only two classifications and, accordingly, two interpretations.

With regard to *classification*, the Zucker-Hammett hypothesis placed the first two categories of Chart I within the group of reactions correlated with h_0 , and the third in the group correlated with oxonium ion concentration. In *interpretation*, it assigned a mechanism to the first two of the present categories which is now reserved for the first, and to the third the two mechanisms now associated with the second and the third. Thus the Zucker-Hammett treatment confused the first two of the present categories in classification and the second two in interpretation. Small wonder that it led to some inconsistent conclusions!⁶⁰

The special behavior of proton transfers to hydrocarbon-like bases was a further reason why the Zucker-Hammett hypothesis gave confusing answers. This category corresponds in classification to the first but in interpretation to the second of their categories.

Difficulties with the New Criterion.—The new criterion has its problems too. For example, it offers no way around the γ -hydroxybutyric acid \rightleftharpoons γ -butyrolactone enigma.¹⁰ It is not logical that one of these reactions, lactonization with $w + 2.2$ (83), should involve water acting as a nucleophile in the transition state and the other, hydrolysis with $w + 6.1$ or $+ 8.5$ (74), water acting as a proton transfer agent. Since they must have the same transition state, if water is transferring a proton in hydrolysis it must be doing the same, in the opposite direction, in lactonization.

Another poser is the hydrolysis of methyl dihydrogen phosphate (53) whose w^* of -0.3 sug-

(60) While exposing the Zucker-Hammett hypothesis to objective criticism, let us not lose sight of what a remarkable creative achievement it was. Considering the comparative imperfection of knowledge of mechanisms in 1939 and the paucity of data available (only about four good sets), one can appreciate the keen insight required for formulation of a hypothesis which struck as close to the mark as it did.

gests proton transfer in the critical step but which, on good testimony,⁶¹ is probably an S_N2 displacement on methyl carbon. If so, w^* should be about -3 .

Yet another is presented by hydrolyses of three pyridine-carboxamides (38-40) which have w -values (about $+4.9$) indicating a mechanism different from hydrolyses of benzamide or acetamide. It is difficult to see why changing from a

(61) C. A. Bunton, D. R. Llewellyn, K. G. Oldham and C. A. Vernon, *J. Chem. Soc.*, 3574 (1958).

benzene to a pyridine ring should cause a change in mechanism.

Some understanding of these difficulties is provided by a theory of w -values developed in the following paper.

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[CONTRIBUTION FROM THE METCALF CHEMICAL LABORATORY, BROWN UNIVERSITY, PROVIDENCE, R. I.]

Kinetics of Reactions in Moderately Concentrated Aqueous Acids. III. Theory of w - and w^* -Values¹

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An extreme interpretation of w^* -values would be that they represent the number of water molecules of change of hydration between reactants and transition states, and that w represents the same quantity on an adjusted scale. The extent to which this extreme view may be valid is examined. Expressions are developed showing how w , w^* and the divergence of $-H_0$ from $\log[HX]$ are related to the extent of hydration change and to the activity coefficients for hydrated species. These expressions are shown to be consistent with the more conventional treatment of these problems. Evidence is presented that this extreme interpretation cannot be wholly correct. However, correlation of w with ΔS^\ddagger values indicates that hydration change is a major influence. Advantages of interpretation in terms of hydration change are discussed and demonstrated.

In paper I,² it was shown that plots of $(\log k_\psi + H_0)$ and of $(\log k_\psi - \log [HX])$, or appropriate other functions for more basic substrates, against $\log a_{H_2O}$ are often linear or approximately so, and that their slopes define parameters (w and w^* , respectively) useful for the classification of reactions. In paper II,³ an empirical criterion of mechanism was developed by associating w - or w^* -values for reactions of established mechanism with the manner of involvement of water in rate-determining steps.

All of this was empirical in the sense that the activity of water entered the treatment only in a mechanical way. No theoretical significance was attached to the fact that the quantities mentioned are more or less linear with $\log a_{H_2O}$.

These linear relationships suggest that the activity of water may be a fundamental variable in these systems. The objective of this paper is to examine this question.

The straight line plots do not prove that the activity of water is a fundamental variable. It is possible that, for example, both $(\log k_\psi + H_0)$ and $\log a_{H_2O}$ depend on some more fundamental factor, and that the correlations noted merely reflect mutual dependence on that factor. Or the linear plots may be wholly fortuitous. Indeed, leading authors⁴⁻⁶ have dismissed the activity of water as

a significant variable in these systems. Only a few publications⁷⁻⁹ have regarded the activity of water as an important influence.

When the activity of water is taken as a fundamental variable, it is admitted into the rate or equilibrium law to a power greater than the minimum number of water molecules called for by the ordinary chemical equation for the reaction concerned. This admission may be partial or total. In the extreme, w becomes virtually the kinetic order in water of the transformation of protonated substrate, SH^+ , to transition state.

The conventional treatment^{4,5,10} of these phenomena does not admit the activity of water to be a major influence. For reactions not requiring water for transformation of SH^+ to transition state, eq. 1 was developed.^{4,11}

$$k_\psi = \frac{k}{K_{SH^+}} \cdot h_0 \cdot \frac{f_{BH^+} f_S}{f_B f_{\ddagger^+}} \quad (1)$$

(7) V. K. Kriehle and K. A. Holst, *ibid.*, **60**, 2976 (1938); M. Duboux and A. de Sousa, *Helv. Chim. Acta*, **23**, 1381 (1940); J. A. Leisten, *Chemistry & Industry*, 397 (1959); C. A. Bunton and S. G. Perry, *J. Chem. Soc.*, 3070 (1960).

(8) K. N. Bascombe and R. P. Bell, *Faraday Soc. Disc.*, **24**, 158 (1957).

(9) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **82**, 2965 (1960).

(10) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 267-277.

(11) Definition of symbols:

k_ψ measured pseudo-first order rate coefficient
 K equilibrium constant for protonation of substrate, S
 k rate coefficient for conversion of protonated substrate to products
 a no. of waters of hydration of indicator conjugate acid, BH^+
 b no. of waters of hydration of indicator base, B
 f activity coefficient
 n no. of waters of hydration of proton, H^+
 p no. of waters of hydration of protonated substrate, SH^+
 s no. of waters of hydration of substrate, S
 t no. of waters of hydration of transition state, \ddagger
 $[S]_{st} = [S] + [SH^+]$

(1) Described tersely in a preliminary Communication: J. F. Bunnett, *J. Am. Chem. Soc.*, **82**, 499 (1960). Presented in part to the Eighth Conference on Reaction Mechanisms, Princeton, N. J., Sept., 1960.

(2) J. F. Bunnett, *J. Am. Chem. Soc.*, **83**, 4956 (1961).

(3) J. F. Bunnett, *ibid.*, **83**, 4968 (1961).

(4) F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 935 (1957).

(5) R. W. Taft, Jr., N. C. Deno and P. S. Skell, *Ann. Rev. Phys. Chem.*, **9**, 303 (1958).

(6) C. G. Swain and A. S. Rosenberg, *J. Am. Chem. Soc.*, **83**, 2154 (1961).