[CONTRIBUTION FROM THE VENEREAL DISEASE EXPERIMENTAL LABORATORY, U. S. PUBLIC HEALTH SERVICE, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF NORTH CAROLINA]

Application of the Hammett Equation to Fused Ring Systems

BY H. H. JAFFÉ

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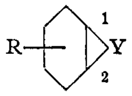
The Hammett equation is extended to compounds in which the reacting side chain is attached to a substituted benzene ring in two positions. This extension, represented by equation 2, permits the estimation of the relative importance of two alternate paths in transmission of electronic effects of substituents to the reaction site. The same equation may be applied to compounds in which two side chains react with each other. A special application of this equation to the treatment of substituent effects in naphthalene derivatives is proposed. It is shown that substituent effects in the alkaline hydrolysis of substituted phthalides are not transmitted through the methylene group.

The effect of substituents (R) on the reactivity of a side chain (Y) in disubstituted benzene derivatives, *m*- (or *p*-) RC_6H_4Y, can be expressed through the Hammett equation[1]

$$\log (k/k^0) = \sigma\rho \qquad (1)$$

Extensions of this equation to polysubstituted benzene derivatives recently have been proposed.[2] A special case arises when the reaction center (Y) is attached to the benzene ring in two places (*cf.* formula I), thus forming a fused ring system.



I

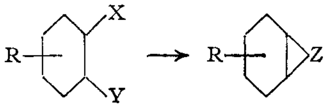
For such reactions we have suggested that the Hammett equation may be applicable in the form[2b]

$$\log (k/k^0) = \sigma_1\rho_1 + \sigma_2\rho_2 \qquad (2)$$

Here σ_1 and σ_2 refer to the substituent constants of R for the position (*meta* and *para*) relative to the points of attachments 1 and 2 of the side chain, respectively.

Equation 2 was originally proposed in connection with the alkaline hydrolysis of several series of substituted phthalides,[3] but not enough experimental data were available to permit an adequate test of the equation. Rates of hydrolysis of a long series of substituted phthalides in 15% methanol have recently been reported,[4] and now make possible an adequate test of equation 2. The relevant reaction constants are reported in Table I. The data indicate that the reaction rates are unaffected by electronic effects transmitted through the methylene group. This reaction has also been studied in different solvents with shorter series of compounds,[5] and the reaction constants reported in Table I lead to the same conclusion.

In compounds containing two side chains (X and Y) which react with each other (*cf.* formula II) we encounter a slightly different situation. However, since the reaction rate may be affected by the influence of substituents on both X and Y, equation 2 should again apply. The only such series which has been studied is the lactonization of 4- and 5-substituted 2-(hydroxymethyl)-benzoic acids.[6] The data in Table I show that the substituents affect the rate of the reaction primarily through their effect on the hydroxymethyl group. However, it should be noted that esterification reactions usually do not fit the Hammett equation well,[2b] and the apparent transmission through the hydroxymethyl group might be an artifact.



II

The success of equation 2 in the above two cases prompted us to look for other reaction series to which it might be applicable. Compounds in which the reacting group Y is hydrogen bonded to a vicinal substituent may be considered as belonging to type I. Accordingly, the reactions of all series of compounds in which such a hydrogen bond may exist have been fitted by equation 2. The results are shown in Table I and suggest an effect on the reaction site through the hydrogen bond and the *ortho* substituents of the *pK*'s of the *o*-(hydroxymethyl)-benzoic acids, the catechols, the *o*-chloro-(or bromo)-benzenephosphonic acids, and in the reaction of *o*-methylbenzoic acids with diphenyldiazomethane. In the first two of these reaction series strong hydrogen bonds can be expected and hence transmission of electronic effects through the *ortho* substituents appears reasonable. However, in the last two reaction series hydrogen bonds must be weak if they exist at all[7]; therefore, transmission of electronic effects through the *ortho* substituents would hardly have been anticipated particularly in view of the absence of such transmission in the *pK*'s of the *o*-nitro- and *o*-hydroxybenzoic acids, where hydrogen bonds probably exist. The data on the vibrational OH-frequencies in the catechols are inconclusive (*cf.* Table I).

In the light of these apparently inconsistent results we have applied equation 2 to several reaction series lacking an *ortho* substituent. In such cases non-vanishing values of ρ_2 are meaningless, since ρ_2 measures the transmission of electronic effects along a non-existent path. In a sample of 20 reaction series randomly chosen from our files, three series were found in which use of equation 2 represented the data *significantly*[8] better than equation 1. The

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(1) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chap. VII.

(2) (a) H. H. Jaffé, *Science*, **118**, 242 (1953); (b) *Chem. Revs.*, **53**, 191 (1953).

(3) A. Tasman, *Rec. trav. chim.*, **46**, 653 (1927).

(4) J. Tirouflet, Thesis, Paris, 1952; *Bull. soc. sci. Bretagne*, Spec. #26, 89 (1951); *C. A.*, **47**, 8694 (1953).

(5) J. Vène, J. Tirouflet and P. Carrié, *Compt. rend.*, **234**, 2074 (1952); J. Vène, J. Tirouflet and C. Pinel, *ibid.*, **236**, 1675 (1953).

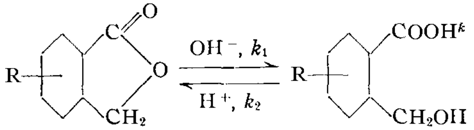
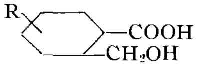
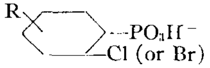
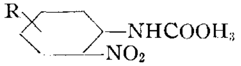
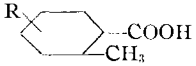
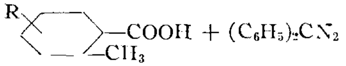
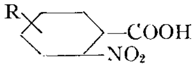
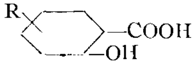
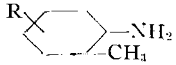
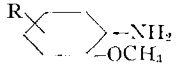
(6) J. Tirouflet, *ibid.*, **235**, 962 (1952).

(7) The existence of a hydrogen bond in the *o*-chloro-(or bromo-)-benzenephosphonic acids has been demonstrated; *cf.* H. H. Jaffé, L. D. Freedman and G. O. Doak, THIS JOURNAL, **76**, 1548 (1954).

(8) The 95% confidence level was taken as the limit of significance.

TABLE I

TEST OF EQUATION 2

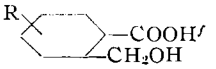
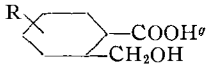
No.[a]	Reaction	T, °C.	Solvent[b]	ρ_1[c]	$s\rho_1$[d]	ρ_2[c]	$s\rho_2$[d]	n[e]	s[f]	R[g]	$-\log k°$[h]	F[i]	$r_{1,2}$[j]
57													
57		25	H_2O	0.859	0.434	0.290	0.629	7	0.144	0.972	[n]	0.21	0.957
[m]	k_1	25	15.1 wt. % C_2H_5OH	1.998	.104**	.009	.104	17	.108	.992	[n]	.00	.748
[m]		25	20 wt. % C_2H_5OH	1.951	.202**	− .053	.136	8	.105	.982	[n]	.15	.579
[m]		25	75.4 wt. % C_2H_5OH	2.696	.147**	.071	.155	8	.114	.995	[n]	.21	.594
[m]	k_2	60	H_2O	0.264	.202	− .910	.285*	8	.113	.860	3.735	.71	.778
[m]	pK's of 	20	H_2O	1.420	.053**	− .369	.074**	9	.029	.998	3.816	24.9**	.780
213	OH frequency in  free OH		C_2Cl_4	9.270	3.26*	6.021	5.32	9	1.92	.966	....	8.13*	.903
214	H-bonded OH		C_2Cl_4	14.831	8.996	0.049	14.7	9	5.31	.844	....	0.00	.903
24	pK's of 	25	40% Dioxane	1.534	0.173**	2.056	0.394**	8	0.158	.993	10.961	22.3**	.800
17a	pK's of 	25	H_2O	0.366	.056**	0.765	.072**	6	.028	.999	6.975	114**	.910
17b		25	50% C_2H_5OH	0.931	.194*	.245	.180	5	.029	.999	9.231	1.75	.981
125	Deacetylation of 		CH_3OH	1.862	.267**	− .204	.346	12	.176	.977	1.601	0.35	.880
3b	pK's of 	30	C_2H_5OH	1.718	.127**	− .059	.127	11	.111	.990	5.770	0.53	.761
45		25	50% C_2H_5OH	1.046	.031**	− .131	.031**	11	.027	.998	1.807	18.2**	.761
2	pK's of 	25	H_2O	1.020	.145**	− .121	.144	6	.039	.994	2.207	6.52	.946
4	pK's of 	25	H_2O	0.520	.222	.614	.222	6	.055	.994	3.979	0.70	.918
117	Benzoylation of 	25	C_6H_6	−2.448	.232**	− .358	.232	7	.182	.994	3.344	2.39	.779
118	Benzoylation of 	25	C_6H_6	−2.261	.281**	− .490	.263	5	.200	.994	3.010	3.46	.663

[a] The numbers in this column refer to reaction numbers from ref. 2b. [b] Where mixed solvents are indicated by a certain % of one component, the other component is water, and volume % are implied unless otherwise indicated. [c] ρ_1 refers to direct transmission to the reaction site, ρ_2 to transmission through a hydrogen bond and *ortho* substituent, unless

otherwise indicated. [d] The standard error of ρ; one asterisk indicates that the corresponding ρ is significantly different from zero at the 95% confidence level, two asterisks indicate significance at the 99% level. [e] The number of compounds involved in the series. [f] The standard error of the data from the regression plane. [g] The multiple correlation coefficients. [h] The intercept of the regression plane and the log (k/k^0)-axis. [i] The variance ratio, *cf.* reference 8, p. 219. Significance is indicated in the manner indicated in footnote *c*. [j] The correlation coefficient for correlation of σ_1 and σ_2. [k] σ's relative to the CO-group are taken as σ_1, those relative to the CH$_2$-group as σ_2. [m] Reaction constants from application of equation 1, which have not been reported previously, are given in Table II, where the appropriate references are given. [n] There appears to be a discrepancy in the units used in the various papers; hence no values are given. [o] The value of σ (σ_{meta} or σ_{para}) which is larger is taken as σ_1, that which is smaller as σ_2.

TABLE II

REACTION CONSTANT OBTAINED BY USE OF THE EQUATION 1[a]

Reaction	*T*, °C.	Solvent	ρ^b	$s\rho^b$	n^b	s^b	r^c	$-\log k^{\circ b}$	Ref.
Hydrolysis of phthalides[d]	25	15.1 wt. % C_2H_5OH	2.010	0.064**	18	0.101	0.992	[e]	4
	25	20 wt. % C_2H_5OH	1.905	.153**	8	.097	.981	[e]	5
	25	75.4 wt. % C_2H_5OH	2.736	.110**	8	.106	.995	[e]	5
Lactonization of  R —COOH[f] —CH$_2$OH	60	H_2O	−0.621	.189*	8	.119	.801	3.770	6
pK's of  R —COOH[g] —CH$_2$OH	20	H_2O	1.213	.013**	10	.058	.989	3.957	[h]

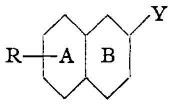
[a] Only constants not previously reported are given here. For all others, see ref. 2b. [b] *Cf.* the respective headings in Table I. [c] The correlation coefficient, which is closely related to the *R* of Table I. [d] Substituent constants for positions relative to the CO-group were used. [e] See footnote *n*, Table I. [f] Substituent constants for position relative to the CH$_2$OH group were used; the alternative use of substituent constants for position relative to the COOH-group gives a much poorer correlation. [g] Substituent constants for the position relative to the COOH-group were used. [h] J. Tirouflet, *Compt. rend.*, **236**, 1426 (1953).

reason for such spurious correlations is found in the fact that σ_{meta} and σ_{para} are not independent, but are highly correlated. Thus, in the three reaction series mentioned, σ_1 and σ_2 are correlated with a correlation coefficient $r_{12} > 0.9$. Hence it must be concluded that results obtained from use of equation 2 should be viewed with suspicion when the correlation between σ_1 and σ_2 is especially high. We suggest that $r_{12} > 0.9$ be arbitrarily taken as the limit of usefulness of equation 2. This limit eliminated most of the apparently inconsistent results of the preceding paragraph, since $r_{12} > 0.9$ for all the reaction series mentioned there, with the exception of the *pK*'s of *o*-(hydroxymethyl)-benzoic acids and the reactions of *o*-methylbenzoic acids with diphenyldiazomethane.

We may then conclude that equation 2 can be used to *demonstrate* which paths are involved in the transmission of electronic effects of substituents to a reaction site. Where the existence of two paths is *known*, use of equation 2 and of methods of multiple regression[9] permits evaluation of the best estimates of the relative importance of the two paths. Such an evaluation is equivalent to finding the best average of σ_{para} and σ_{meta} desired in the consideration of the *pK*'s and OH frequencies of substituted catechols.[10] The restriction that r_{12} should be small to permit the most efficient use of equation 2 permits the selection, among all the available substituents, of those which will give the most reliable information in an investigation aimed at the evaluation of the relative importance of alternate paths for the electronic effects of substituents.

Equation 2 should also apply to reactions of such fused ring systems as quinolines and isoquinolines substituted in the 6- and 7-position. Unfortunately, very few experimental data are available to test this prediction. The *pK*'s of a series of halogeno- and methylquinolines[11] are not well represented by equation 2. Whether or not this fact depends on the nature of the quinoline ring cannot be decided until more extensive series of measurements become available.

Another use of equation 2 suggests itself. 6- and 7-substituted naphthalenes with a reacting side chain in the 2-position are compounds of type I (*cf.* formula III). It should therefore be possible to



III

express the effect of the R on the reactivity of Y through equation 2, where R is the substituent and –CHCYCHCH– the side chain. However, it is equally possible to consider ring A (*i.e.*, –CHCRCHCH–) as the substituent and Y as the side chain, and to apply equation 1.[12] Consequently we have

$$\log(k/k^0) = \sigma_1(\mathrm{R})\rho_1(\mathrm{CHCYCHCH}) + \sigma_2(\mathrm{R})\rho_2(\mathrm{CHCYCHCH}) = \sigma(\mathrm{CHCRCHCH})\rho(\mathrm{Y}) \quad (3)$$

where the parentheses specify the radicals to which σ and ρ refer. Measurement of a single series of reactions sufficiently long to determine ρ_1 and ρ_2 accurately, coupled wtih a knowledge of ρ(Y) from a series of benzene derivatives, would permit determination of σ(CHCRCHCH) for any R for which σ_{meta} and σ_{para} are known.

The same line of reasoning also can be applied to naphthalene derivatives having the side chain in the 1-position. The only complication arising here

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(9) G. W. Snedecor, "Statistical Methods," 4th Ed., Iowa State College Press, Ames, Iowa, 1946, pp. 364–366.

(10) J. Corse and L. L. Ingraham, THIS JOURNAL, **73**, 5706 (1953); L. L. Ingraham, J. Corse, G. F. Bailey and F. Stitt, *ibid.*, **74**, 2297 (1952).

(11) W. K. Miller, S. B. Knight and A. Roe, *ibid.*, **72**, 4763 (1950); S. B. Knight and A. Roe, private communication.

(12) C. C. Price and R. H. Michel, *ibid.*, **74**, 3652 (1952).

is the evaluation of $\rho(Y)$. However, the fused ring A may be considered as a constant *ortho* substituent, and hence probably does not affect $\rho(Y)$.[2] An additional term X^{13} would have to be introduced into the second line of equation 3. Then application of equation 3 also permits evaluation of substituent constants for the 6- and 7-positions of naphthalene derivatives undergoing reaction at a side chain in the 1-position. Such substituent constants, however, would have to be used together with the X-terms, which must be evaluated separately for each reaction series. Similar arguments may also apply to quinoline and isoquinoline derivatives having reacting side chains. Unfortunately, sufficient experimental data to use the relations derived do not appear to be available at present.

A few comments concerning the calculations are necessary. Only reaction series for which data were available for more than 4 compounds were used. All data were fitted to equation 2 by the use of standard methods of multiple correlation.[8] The difference of a given value of ρ from zero was tested by use of Student's $t = \rho/s_\rho$.[14] Analysis of variance[15] was used to test whether or not equation 2 represented a given set of data *significantly*[9] better than the use of equation 1 alone.

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(13) See equation 7 of reference 2b.

(14) Reference 8, p. 62.

(15) Reference 8, Chapters X and XI.

CHAPEL HILL, NORTH CAROLINA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY, CALIFORNIA]

Thermal Decomposition of Nitryl Chloride. I. Second-order Unimolecular Rate Study

BY HERMAN F. CORDES[1] AND HAROLD S. JOHNSTON

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The thermal decomposition of nitryl chloride has been reinvestigated at low pressures in a 50-liter Pyrex flask from 180 to 250°. The mechanism of Schumacher and Sprenger has been confirmed, and although present conditions never coincide with those of the previous study, the results appear to be in essential agreement. The observed rate is twice that of the elementary unimolecular decomposition $NO_2Cl = NO_2 + Cl$. The results show quite clearly that the reaction is first order in reactant throughout a single run, and the first-order rate constants are themselves first order in initial concentration. Thus these results provide an illustration of the second-order region of a unimolecular reaction. The effect of argon was studied, and the results are that argon does not deactivate excited nitryl chloride upon every collision. The number of normal modes contributing to the reaction coördinate was computed by the Kassel-Slater method and found to be six, the number of normal modes of the molecule itself.

Introduction

Schumacher and Sprenger reported the thermal decomposition of nitryl chloride

$$NO_2Cl = NO_2 + {}^1/_2Cl_2 \qquad (1)$$

to be a first-order homogeneous gas phase reaction.[2] The data obtained by these workers were in the mid-range between the high and low concentration regions. The mechanism for this reaction was suggested as being

$$NO_2Cl \longrightarrow NO_2 + Cl \quad k_1 \qquad (2)$$

$$NO_2Cl + Cl \longrightarrow NO_2 + Cl_2 \quad k_2 \qquad (3)$$

From this mechanism and the assumption of a steady state for chlorine atom concentration, the empirical first-order rate constant can be identified with $2k_1$. It was felt that this reaction offered a good chance to obtain a clear-cut example of the region of second-order kinetics for a unimolecular reaction.[3]

Experimental

Materials.—Nitryl chloride was prepared by the method previously described.[4] Nitrogen dioxide was obtained from Matheson Co. and purified to oxidize the nitric oxide and to remove any nitric acid if present. Argon from the Matheson Co. was passed through a liquid nitrogen trap.

Apparatus.—The reaction vessel was a 50-liter Pyrex flask with quartz windows attached through a short graded seal. These windows were inset 7 cm. into the flask. The flask was placed in a double-walled steel furnace; the space between the walls was filled with 14 cm. of insulation, Monsanto Santo-Cel A. The top of the furnace was covered with 3 cm. of molded magnesia insulation and 3 cm. of fiber glass insulation. The flask rested on a sand-bath inside the furnace. Air inside the furnace was stirred strongly by a large blower which connected through the furnace wall to an external electric motor. A 20-ohm Chromel resistance heating wire was wound uniformly around the walls on the inside of the furnace, and by means of a stabilized power source (Superior Electric Co., Stabiline Electromechanical Voltage Regulator) and a variable transformer, the furnace was heated to within about 5° of the desired temperature. The final temperature control was obtained with two cone heaters mounted close to the blower in the bottom of the furnace and connected through a mercury switch to a thermometer control switch. Temperature, read by a mercury thermometer calibrated against a Pt-Rh thermocouple, was constant in time to 0.1° and was uniform over the bulb to 0.5°.

Reactant gas was stored in a 22-liter storage bulb blackened to prevent photochemical decomposition of nitryl chloride. Pipet bulbs, 0.01 the volume of the reaction flask, were filled with nitryl chloride, and the pressure was read on a glass bourdon gage used as a null instrument. The sensitivity of this gage was about 0.5 mm. and pressures were usually read in the range of 100 to 600 mm. Stopcocks were hollow specially ground high-vacuum type greased with polychloro-trifluoroethylene stopcock grease. This grease is not attacked by nitryl chloride, but it showed a vapor pressure of about 0.05 mm. on a thermocouple pressure gage.

Calibration.—The course of the reaction was recorded by following colorimetrically the nitrogen dioxide produced. The light source was a stabilized A-H4 mercury arc filtered

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[1] The material for this article was abstracted from a dissertation submitted in partial fulfillment of the requirements for the Ph.D. degree at Stanford University, 1954.

[2] H. J. Schumacher and G. Sprenger, *Z. Elektrochem.*, **35**, 653 (1929); *Naturwissenschaften*, **17**, 997 (1929); *Z. physik. Chem.*, **B12**, 115 (1931).

[3] Discussion with S. W. Benson at symposium on very fast reactions, Atlantic City, N. J., September, 1952; *J. Phys. Chem.*, **57**, 424 (1953).

[4] E. C. Freiling, H. S. Johnston and R. A. Ogg, Jr., *J. Chem. Phys.*, **20**, 327 (1952).