A REËXAMINATION OF THE HAMMETT EQUATION

H. H. JAFFÉ

Venereal Disease Experimental Laboratory, U. S. Public Health Service, School of Public Health, University of North Carolina, Chapel Hill, North Carolina

CONTENTS

I. INTRODUCTION

The correlation between the structure of compounds and their chemical reactivity is one of the most intriguing objectives of modern chemistry. Although certain qualitative theories have long existed, only in recent years have successful quantitative theories been developed. In particular, the effects of substituents (R) on the reactivity of a side chain (Y) in compounds of type I have received considerable attention.

I
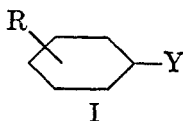
By the mid-1930's it had been repeatedly noted that the effects of substituents in many reaction series involving benzene derivatives could be correlated with the acid strengths of the corresponding benzoic acids (60, 91, 124, 176). These

observations led Hammett (125, 126) to propose a general quantitative relation between the nature of the substituent R and the reactivity of the side chain Y. This relation has become known as the Hammett equation, and is widely applied in the form

$$\log (k/k^0) = \sigma\rho \tag{1}$$

Here k and k^0 are rate or equilibrium constants for reactions of the substituted and the unsubstituted compounds, respectively, σ is the substituent constant, which depends solely on the nature and position of the substituent R, and ρ is the reaction constant, which depends on the reaction, the conditions under which it takes place, and the nature of the side chain Y. The validity of equation 1 is restricted to substituents in the meta- and para-positions of the benzene ring. This equation was tested by Hammett (127f) on fifty-two reaction series, and found to express a large body of experimental data with a mean deviation of about ±15 per cent.

Since the publication of Hammett's book, many additional reactions which permit the application of equation 1 have been investigated. One of the aims of this review is to gather together and thus render accessible all material pertinent to the Hammett equation. Some older work omitted by Hammett is also included. Further, Hammett has calculated reaction constants for only a single set of conditions in any one reaction series. To gain an understanding of the factors determining the reaction constants it was considered of interest to calculate and tabulate reaction constants for all sets of conditions for which data were available. Finally, additional or better measurements have been reported for many of the reaction series included by Hammett. For these reasons the original fifty-two reaction series are included in this review.

The accumulated information will be used as a basis for discussion of the factors determining reaction and substituent constants, and to evaluate new σ-values. Next, the precision of the Hammett equation will be examined in the light of the new information, and its range of application and usefulness will be considered. Finally, a number of extensions of the equation will be proposed and discussed.

Notation

Certain special notations will be used throughout this review. Compounds to which the Hammett equation is applied will be written in the form shown in formula I or as ArY. Y will always stand for the reacting side chain, and R for the substituent affecting the reactivity of Y. Ar will be used to denote the group RC_6H_4, with R in the meta- or para-position.

II. THEORETICAL

The Hammett equation was proposed (125) as an empirical relation suggested by the parallelism of the effects of substituents on the rate or equilibrium constants in many different side-chain reactions of benzene derivatives. In spite of several attempts to provide a good theoretical foundation or derivation of the equation (e.g., 109, 241), it has remained fundamentally an empirical relation.

The expression on the left-hand side of equation 1 is proportional to the difference in the free energies of reactions of substituted and unsubstituted compounds (if the k are equilibrium constants) or to the difference in energies of activation (if the k are rate constants). For this reason equation 1 is often referred to as a "linear free-energy relationship." It is not at all obvious that such a linear free-energy relation should hold. Hammett has discussed the relation between the structure of chemical compounds and free-energy changes of their reactions in general, and has suggested that the free-energy change can be considered as the sum of three terms: the entropy change, and changes in the kinetic and in the potential energies (127a,c). It follows that all three terms must be considered in any attempt to correlate structure with reactivity, but little is usually known about the first two. However, it has been demonstrated repeatedly that, in many side-chain reactions of benzene derivatives, the entropy term is not appreciably affected by substituents in the meta- or para-position (127d).

Hammett believes that the constancy of the entropy terms implies a similar constancy of the kinetic energy changes (127a,c), and hence that the free-energy differences are determined only by changes in the potential energy (127e). Therefore it has been assumed by some authors that constancy of entropy changes is a necessary condition for the validity of the Hammett equation. In many reaction series which obey equation 1, however, the entropy changes vary linearly with enthalpy changes, at constant temperature (e.g., 24, 77, 127b), and therefore can be incorporated into the latter (128).

In the light of this discussion it appears that the validity of the Hammett equation should be discussed in terms of the potential energy difference between the ground and transition states.[1] When the reaction site is insulated from the benzene ring, e.g., by one or more methylene groups, there will be no appreciable effect of substituents on the difference in resonance energy between ground and transition states. Substituents then affect the energy of activation primarily by the change they induce in the electron density at the reaction site. If the reaction site is not insulated from the benzene ring, however, the effect of substituents on the differences in resonance energy between ground and transition states must also be considered.[2]

A general discussion of the Hammett equation in terms of activation energies is rendered difficult by the paucity of information concerning the structures and energies of these states, and by the necessity of discussing almost every reaction series separately.

Fortunately, these difficulties can be avoided by the use of a rough approximation: the assumption that reactivity depends on the electron distribution in a molecule. Rates of nuclear substitution of benzene derivatives have been dis-

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[1] For reaction series involving the comparison of equilibrium constants, the discussion should be in terms of initial and final states. Since transition-state theory considers rate processes as governed by an equilibrium between ground and excited states, the discussion for equilibrium processes is quite analogous to the one given here and need not be dealt with separately.

[2] The author is indebted to Dr. J. F. Bunnett for help in clarifying the ideas presented in this paragraph and the related material in Section IV.

cussed in terms of the electron densities at the reaction site (252, 311). R. D. Brown has postulated a "chemical non-crossing rule," which suggests that the predictions of reactivities from electron densities will usually, although not necessarily, parallel predictions made from considerations of the structure, or calculations of the energy of the transition states (52). Since the "non-crossing rule" appears to hold widely for reactions of benzene derivatives, we shall assume its validity for the reactions discussed in this paper. This assumption will permit many inferences about reaction and substituent constants.

Hammett has discussed the factors determining σ and ρ (125). He suggested that reaction constants have the form:

$$\rho = (B_1/D + B_2)/RTd^2 \tag{2}$$

where R is the gas constant, T is the absolute temperature, D is the dielectric constant of the solvent, and d is the distance from the substituent to the reaction site. B_1 was assumed to depend on purely electrostatic interaction between the reacting benzene derivative and the medium, and B_2 was assumed to measure the susceptibility of the reaction to changes in the charge density at the reaction site. Little was said about σ, except that it must depend on the electrical effects of the substituent. On the basis of these assumptions Hammett concluded that the substituent effects must be almost exclusively electrostatic in nature. This view has been criticized by Schwarzenbach and Rudin (266), who demonstrated that resonance effects are not excluded by the arguments given.

Some attention has since been given to the interpretation of substituent constants. Westheimer (308) has calculated the effect of substituents on the acid strengths of various aromatic acids by the Kirkwood–Westheimer theory (177, 309), involving only direct electrostatic interaction between the substituent and the carboxy group. The results of these calculations correlate only roughly with substituent constants.

Price (241, 242) has postulated that the difference ($\Delta\sigma = \sigma_{para} - \sigma_{meta}$) of the substituent constants in the meta- and para-positions should correspond to the polarizing force of the substituent, which is an expression of its electrostatic effect on the benzene ring. The correlation between σ and polarizing force is good for electron-releasing but poor for electron-attracting substituents.[3]

Recently the present author has shown, by calculations based on molecular orbital theory, that substituent constants can be correlated with changes in electron density induced by the substituents (150–152). These calculations considered both inductive and resonance effects, and the inclusion of both effects was essential to permit interpretation of substituent constants in terms of changes in electron density.

Reaction constants have also been given some theoretical attention. Gallup, Gilkerson, and Jones (109) have calculated reaction constants for four reaction series based on an electrostatic model; they have obtained fair agreement for

[3] Price made the correlations using substituent constants valid only for reactions of anilines and phenols. The agreement is not improved by using the substituent constants for other reactions (table 7).

two series on the basis of ion–dipole interactions, but poorer agreement for two other series involving dipole–dipole interactions. This author has performed some calculations of relative values of reaction constants by molecular orbital theory, again involving both inductive and resonance effects, and fair agreement has been obtained (153). This work is further discussed in Section III,B.

III. REACTION CONSTANTS

A. Summary of existing data

Tables 1 to 3 list the reaction series which permit an application of the Hammett equation. Undoubtedly this list is not complete, since there seems to be no systematic means of searching the literature for such data. However, it is believed that the majority of pertinent information has been included, and it is hoped that no important reaction series have been omitted.[4]

The material included in the tables has been limited in several ways: (a) In calculation of reaction constants, only substituent constants listed in Hammett's tabulation (127f) were used, for reasons discussed in Section IV,B. Owing to doubt as to the accuracy of Hammett's value for the substituent constant for the p-dimethylamino group (see Section IV,D), compounds involving this group have been eliminated. (b) Only reaction series involving at least four substituents have been included, since reaction constants calculated from fewer data were considered too uncertain, and no reliable estimate of their precision could be obtained. (c) Substituent constants for certain groups of substituents do not appear to differ materially from each other (e.g., p-Cl, p-Br, and p-I; see Section IV,B). The author has not included reaction series involving less than two substituents aside from members of such a group. For a few reaction series which were omitted under the above restrictions, reaction constants were calculated on the basis of the substituent constants derived in Section IV,B and are indicated in *italics* in tables 1 to 3. These reaction series were not included in the compilation of the distribution of reaction constants and other parameters in later sections.

All reaction constants have been recomputed in this laboratory in order to make them strictly comparable. The standard deviation (s) from the best straight line and the correlation coefficient (r) have been calculated as measures of the precision with which the data fit the Hammett equation. Tables 1 to 3 also list the solvent[5] and temperature of the experiments, the number (n) of substituents involved in the calculation of reaction constants, and the literature references.[6] Finally, $(\log k^0)_{calcd}$, i.e., the value of the log k calculated for $\sigma = 0$, is given as a measure of the absolute magnitude of the rate or equilibrium constants.

[4] In order to have as complete a compilation as possible, the author would appreciate receiving information about any omissions.

[5] Where mixed solvents are indicated by a certain per cent of one component, the other component is water; volume per cent is implied unless otherwise indicated.

[6] Literature references in italics refer to data not utilized in the calculation of the reaction constant, but used with it in the computation of substituent constants in Section IV,B.

The information reported thus permits the estimation of the rate or equilibrium constants for any compound involving a substituent of known σ. In keeping with the procedure proposed by Hammett (127f), $(-\log k^0)_{calcd}$ is given in terms of reciprocal seconds wherever the units of the original measurements could be ascertained, and the few exceptions are indicated by appropriate footnotes. However, none of the other quantities depend on the units.

The arrangement of the reaction series in tables 1 to 3 requires some comment. All equilibria are collected in table 1. Section A lists the acid dissociation constants (basic dissociation constants have been converted into the acid dissociation constants of the conjugate acids), subdivided into carboxylic acids (part I), other oxygen acids (part II), and all other acids (part III). Section B contains all other equilibria.

Reaction constants based on rate measurements are collected in table 2. The reaction series were classified according to the relation of the reacting functional groups to the aromatic ring carrying substituents. Thus, amides ($ArCONH_2$) are considered as derivatives of acids, and anilides ($ArNHCOCH_3$) as derivatives of anilines. Some rather arbitrary decisions were required. Thus, $ArNO_2$, $ArN{=}CXY$, and $ArN{=}NX$ were considered as derivatives of amines, but $ArCH{=}NX$ as derivatives of aldehydes.

The details of the arrangement of table 2 are as follows:

    A. Side-chain reactions apparently of ionic type (heterolytic reactions)
        I. Acids and their derivatives
            a. Acids
            b. Esters
            c. Acyl halides
            d. Other derivatives of acids: amides, anhydrides, etc.
       II. Hydroxy compounds and derivatives
            a. Phenols and derivatives
            b. Alcohols and derivatives
      III. Alkyl halides
      IV. Amines and compounds considered derived from them
            a. Amines
            b. Amides
            c. Miscellaneous derivatives of amines
            d. Quaternary ammonium compounds
       V. Aldehydes, ketones, and derivatives
            a. Aldehydes and ketones
            b. Imines and related compounds
            c. Oximes, hydrazones, and related compounds
            d. Miscellaneous derivatives of aldehydes and ketones
      VI. Phosphines, silanes, arsonous acids, and diarylmercury compounds
     VII. Hydrocarbons
    B. Free-radical reactions
    C. Reactions involving nuclear substitution in the substituted ring

Several reaction constants included in table 2 and identified by footnotes are not based on true rate measurements, but on relative reactivities, reactivity ratios, and times required for a given per cent reaction. Provided the substituents do not affect the mechanisms of the reaction or the products, such data should be good relative measures of rate constants; hence their use for the evaluation of reaction constants seems reasonable.

Some attempts have recently been made to correlate various physical properties of benzene derivatives with substituent constants. "Reaction constants" for such correlations are collected in table 3. Section A contains the data, based on half-wave potentials, for several series of polarographic reductions. Although each such potential is a measure of some equilibrium constant, conversion to such constants involves large uncertainties and therefore was not attempted. In table 3A the reaction constants, the standard errors, and the values of $(-\log k^0)_{\text{calcd}}$ (in these cases $-E_{1/2}^0$) are not dimensionless, but are given in volts. Table 3B lists the data for a few studies of infrared frequencies in extensive series of benzene derivatives. These data were made dimensionless by correlating $(\nu - \nu^0)/\nu^0$ with substituent constants. In table 3C some other miscellaneous data are given, which are also made dimensionless by the same type of procedure used for the infrared frequencies.

The reaction series reported in table 3 do not constitute a careful literature survey for such data but are those series which have come to the attention of this author in the course of his collection of reaction series. Many more undoubtedly could be added, particularly if data from several laboratories were combined.

All reaction series are numbered consecutively through tables 1 to 3; the serial numbers will be used later in the text and in the tables to refer to these reactions. Only a single number is assigned to each reaction, and series determined under different conditions are indicated by small letters.

B. Factors determining reaction constants

The reaction constant (ρ) measures the susceptibility of the reaction to the influence of the substituents. We shall discuss the factors affecting this suceptibility under three headings: (1) the transmission of electrical effects to the reaction site; (2) the susceptibility of the reaction to changes of electron density at the reaction site; and (3) the effect of reaction conditions.

(1) Transmission of electrical effects to the reaction site

It has long been accepted that the validity of the Hammett equation depends on the fact that σ is an expression of the electrical effect of substituents (43c, 127f); hence, ρ must depend on the effectiveness with which the side chain can transmit the electrical effect of the substituent to the reaction site.

Hammett has attempted to treat this transmission term by including the factor $1/d^2$ in equation 2 (125), thus relating the magnitude of the reaction constant with the distance from the substituent to the reaction site. This treatment gave satisfactory results in the comparison of reaction constants of the series

TABLE 1

Reaction constants for equilibrium reactions

A(I). Acid dissociation constants of carboxylic acids

REACTION NO.	ACID	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k^{0(d)}$	REFERENCES[e]
			°C.						
1a	ArCOOH	H_2O	25	1.000	—	—		4.203	(13, 36a, 65, 87, 90, 93, 157, 172, 179, 186, 240, 262, 267, 275)
1b		H_2O	15	0.954	0.026	0.996	7	4.214	(49)
1c			20	0.958	0.025	0.996	7	4.209	(49)
1d			25	0.958	0.027	0.996	7	4.205	(49)
1e			30	0.961	0.026	0.996	7	4.207	(49)
1f			35	0.961	0.025	0.996	7	4.211	(49)
1g			40	0.968	0.029	0.995	7	4.215	(49)
1h			45	0.969	0.031	0.994	7	4.221	(49)
1i		50% CH_3OH	~20	1.085	0.062	0.928	10	5.239	(185, 180, 187)
1j		CH_3OH	25	1.537	0.091	0.988	5	6.514	(50)
1k		40% C_2H_5OH	25	1.668	0.219	0.970	8	4.871	(50)
1l		50% C_2H_5OH	25	1.423	0.075	0.992	9	5.681	(36, 157, 179, 258, 254, 255, 257)
1m		50% C_2H_5OH	25	1.601	0.120	0.989	9	5.516	(50)
1n		70% C_2H_5OH	25	1.738	0.127	0.989	9	6.174	(50)
1o		80% C_2H_5OH	25	1.791	0.132	0.990	8	6.522	(50)
1p		90% C_2H_5OH	25	1.869	0.148	0.990	8	6.864	(50)
1q		95% C_2H_5OH	25	1.890	0.152	0.990	7	7.045	(50)
1r		C_2H_5OH	25	1.957	0.155	0.989	9	7.206	(50)
1s[f]		C_2H_5OH	25	1.476	0.039	0.998	8	-0.029	(316)
1t		50% butyl Cellosolve	25	1.415	0.087	0.989	7	1.627	(26)
2	R—⬡—COOH (NO$_2$)	H_2O	25	0.905	0.037	0.992	6	2.206	(267)
3a	R—⬡—COOH (CH$_3$)	H_2O	25	1.430	0.064	0.955	4	3.875	(267)
3b		50% C_2H_5OH	25	1.673	0.106	0.990	11	5.772	(258)
4	R—⬡—COOH(g) (OH)	H_2O	25	1.103	0.089	0.978	6	3.997	(267)
5	R—⬡—COOH (Cl)	H_2O	25	0.855	0.135	0.970	4	3.693	(267)

No.	Compound	Solvent	Temp.				n		Refs.
6.........	$\begin{array}{c}CH_3\\R{-}⟨ring⟩{-}COOH\\CH_3\end{array}$	20% dioxane	26	1.116	0.030	0.999	4	3.974	(112)
7.........	$p\text{-}ArC_6H_4COOH$	50% butyl Cello-solve	25	0.482	0.046	0.981	9	5.636	(26)
8.........	$ArCH_2COOH$	H_2O	25	0.489	0.033	0.981	14	4.297	(92)
9.........	$ArCH_2CH_2COOH$	H_2O	25	0.212	0.016	0.979	8	4.551	(90)
10........	$ArCH{=}CHCOOH$	H_2O	25	0.466	0.040	0.977	9	4.447	(88, 89, 90)
11........	$\begin{array}{c}HC{-}\!\!-CH\\RC\;\;\;CCOOH^{(b)}\\\diagdown O\diagup\end{array}$	H_2O	24	1.396	0.079	0.988	6	2.819	(64)
12a.......	$ArCH{=}CHCOCOOH$	H_2O	25	−0.054	0.006	0.903	5	1.971	(271)
12b.......	$ArCH{=}CHCOCOOH$	50% CH_3OH	25	0.165	0.022	0.893	4	2.507	(271)

A(II). Acid dissociation constants of other oxygen acids

No.	Compound	Solvent	Temp.				n		Refs.
13........	$ArB(OH)_2$	25% C_2H_5OH	25	2.146	0.096	0.990	14	9.700	(28, 45, 70, 317)
14a.......	$ArPO(OH)_2$	H_2O	25	0.755	0.030	0.995	10	1.836	(157)
14b.......	$ArPO(OH)_2$	50% C_2H_5OH	25	0.986	0.059	0.986	12	3.132	(157)
15a.......	$ArPO_2OH^-$	H_2O	25	0.949	0.058	0.990	12	6.965	(157)
15b.......	$ArPO_2OH^-$	50% C_2H_5OH	25	0.885	0.091	0.972	13	8.197	(157)
16........	$R{-}⟨ring\;X⟩{-}PO(OH)_2$ (X = Cl or Br)	50% C_2H_5OH	25	0.995	0.031	0.998	4	2.942	(158)
17a.......	$R{-}⟨ring\;X⟩{-}PO_2OH^-$ (X = Cl or Br)	H_2O	25	0.908	0.152	0.964	6	6.901	(158)
17b.......	$ArAsO(OH)_2$	50% C_2H_5OH	25	1.191	0.033	0.998	5	8.249	(158)
18........	$ArAsO_2OH^-$	H_2O	18–25	1.050	0.117	0.975	9	3.540	(48, 237, 240)
19........	$ArSeOOH$	H_2O	22	0.874	0.102	0.965	11	8.491	(240)
20........	$\alpha\text{-}ArCH{=}NOH$	H_2O	25	0.905	0.125	0.906	16	4.740	(115, 201)
21........	$ArNOOH^+$	H_2O	25	0.857	0.047	0.994	6	10.695	(40, 41)
22........	$ArC(OH)CH_3^{(l)}$ (a)	H_2SO_4	81.4	3.270	0.195	0.970	8	−11.02	(46)
22A.......	$ArC(OH)OC_2H_5^{(l)}$ (n)	C_6H_6	81.4	0.968	0.055	0.991	9	−0.081 (n)	(154a, 238a)
22B.......	$ArOH$	C_6H_6	81.4	0.612	0.038	0.996	5	−0.375 (n)	(154a, 238a)
23a.......	$ArOH$	H_2O	25	2.113	0.119	0.990	17	9.847	(169, 179, 209, 262)
23b.......	$ArOH$	30% C_2H_5OH	25	3.197	0.148	0.954	9	10.614	(19)
23c.......	$ArOH$	48.9% C_2H_5OH	20–22	2.545	0.157	0.989	14	11.563	(264, 265, 266)
23d.......	$ArOH$	95% C_2H_5OH	20–22	2.364	0.203	0.980	14	12.572	(264, 265, 266)
23e.......	$ArOH$	8% dioxane	38	1.819	0.157	0.982	10	9.544	(110)
24........	$\begin{array}{c}R{-}⟨ring⟩{-}OH^{(i)}\\OH\end{array}$	40% dioxane	25	3.512	0.189	0.991	8	11.012	(74)

TABLE 1—Concluded

REACTION NO.	ACID	SOLVENT	T (°C.)	ρ	s[a]	r[b]	n[c]	—log k[d]	REFERENCES[e]
A(III). Acid dissociation constants of all other acids									
25a	ArSH	48.9% C2H5OH	20–22	2.236	0.110	0.975	12	7.666	(264, 265, 266)
25b		95% C2H5OH	20–22	2.847	0.150	0.971	12	9.211	(264, 265, 266)
26a	ArNH3+	H2O	25	2.767	0.105	0.995	14	4.557	(36, 70, 103, 122, 123, 129, 179, 240, 255, 257)
26aA [f][f]		CH3OH	25	3.016	0.343	0.973	9	−0.195	(171a)
26b		30% C2H5OH	25	3.435	0.076	0.989	9	4.320	(19)
26bA [f][f]		C2H5OH	25	3.535	0.302	0.985	9	−0.149	(171a)
26c		20% dioxane	25	3.250	0.038	1.000	4	4.397	(159)
26d		45% dioxane	25	3.558	0.063	0.999	4	3.950	(159)
26e		70% dioxane	25	3.567	0.048	0.999	4	3.547	(159)
26f		82% dioxane	25	3.430	0.077	0.999	4	3.425	(159)
26g		CH3COOH	25	2.009	0.277	0.962	9	2.507	(122)
27a	ArN(CH3)2H+	30% C2H5OH	20	2.507	0.202	0.974	10	3.285	(81, 82)
27b		50% C2H5OH	~25	3.426	0.073	0.946	5	2.065	(81, 82)
28	ArN=NC6H4N(CH3)2H+-p [i]	50% C2H5OH	~25	4.191	0.052	0.972	7	2.197	(260)
29	ArCH2NH3+	H2O	25	0.529	0.044	0.942	5	9.315	(63)
30	ArNH+=NC6H4N(CH3)2H+-p [i][k]	99% H2SO4	~25	3.652	0.493	0.948	7	−3.974	(260)
31	ArC(=NH)NH+(C2H5)2 [i]	50% CH3OH	25	1.412	0.105	0.966	6	11.139	(196)
31A	ArNH3+—C=N (ring: HN—N, N)	No conditions		0.857	0.083	0.956	10	2.153	(135)
B. Other equilibria									
32	ArNH2 + HCOOH ⇌ HCONHAr + H2O	67% C5H5N	100	−1.429	0.055	0.997	11	−0.630	(84)
32A	2ArNH2 + Ag+ ⇌ Ag(ArNH2)2+ [l]	59 wt% C2H5OH	25	−1.452	0.334	0.900	9	−3.18	(108b)
33	ArCHO + HCN ⇌ ArCHOHCN	95% C2H5OH	20	−1.492	0.211	0.832	16	2.138	(12, 14, 16)
34	2ArCONH2 ⇌ (ArCONH2)2	C6H6	30	−2.053	0.113	0.970	4	2.356	(143)
35	ArAr'Ar²CCl ⇌ ArAr'Ar²C+ + Cl− [m]	SO2	0	−3.974	0.291	0.955	4	4.128	(193, 194)
36	ArAr'SeI2 ⇌ ArAr'Se + I2 [m]	CCl4	25	0.782	0.061	0.979	4	1.344	(200)
37	ArAr'SeBr2 ⇌ ArAr'Se + Br2 [m]	CCl4	25	2.121	0.149	0.982	14	3.473	(198, 199)
38	ArAr'NNOCOC6H5 ⇌ 2ArAr'NNCOC6H5 [m]	C6H5CH3	−18	−1.302	0.074	0.985	5	3.189	(113, 263)
39	ArCOCH3 + H+ ⇌ ArCHOHCH3 [m]	H2O	25	1.630	0.120	0.966	7	−3.913	(1)
39A	H2NC=N (ring) ⇌ ArNHC=N [l] (ArN, N=N)	(CH3OH)2	197	0.978	0.080	0.990	10	−0.050	(135)

(a) The standard deviation of experimental measurements from the regression line.
(b) The correlation coefficient.
(c) The number of compounds involved in the calculation of ρ.
(d) The intercept of the regression line with the ordinate (σ = 0).
(e) Data from references in *italics* were not used in the calculation of reaction constants, but were used only in the derivation of new substituent constants (see Section IV,B).
(f) The calculation is based on relative values of K.
(g) The reaction constant is for the ionization of the carboxy group.
(h) σ$_{para}$ was used.
(i) The average value (σ$_p$ + σ$_m$)/2 was used for σ; cf. references 74 and 149.
(j) The assignment of the reaction constants in reactions 27 and 29 is the reverse of that made by the authors (260). The reasons for this reversal of assignments have been discussed in reference 153.
(k) The reaction constant is given for the ionization at the azo nitrogen atom; cf. footnote (j).
(l) These reactions were added after the work was essentially completed and were not included in the various tabulations and calculations of later sections of this paper.
(m) The Hammett equation was applied to these reactions in the form of equation 10 (see Section VII,D).
(n) σ was correlated with log [k/(k$_{blank}$ − k)]. This quantity is equivalent to the log of the dissociation constant (cf. 154a). The k's are rates of self-etherification of benzhydrol in the presence of the bases.

TABLE 2

Reaction constants from rate measurements

A. Heterolytic reactions. I. Acids and their derivatives

a. Acids

REACTION NO.	REACTION	SOLVENT	T (°C)	ρ	s[a]	r[b]	n[c]	−log k_0[d]	REFERENCES[e]
40a	ArCOOH + CH₃OH + H⁺ → ArCOOCH₃	CH₃OH	25	−0.229	0.141	0.457	16	3.841	(130, 131)
40b		Cyclohexanol	40	−0.216	0.138	0.444	16	3.352	(130, 131)
40c			50	−0.209	0.150	0.404	16	3.029	(130, 131)
40d			60	−0.213	0.148	0.427	15	2.738	(130, 131)
41a	ArCOOH + C₆H₁₁OH + H⁺ → ArCOOC₆H₁₁	Cyclohexanol	55	0.555	0.089	0.874	14	4.826	(132)
41b			65	0.518	0.091	0.855	14	4.432	(132)
41c			75	0.498	0.109	0.798	14	4.100	(132)
41d			85	0.479	0.089	0.842	10	3.772	(132)
42	ArCOOH + HN₃ → ArNH₂	CCl₂=CHCl	40	−1.415	0.150	0.940	7	5.280	(49a)
43	ArCOOH + (C₆H₅)₂CN₂ → ArCOOCH(C₆H₅)₂	C₂H₅OH	30	0.940	0.063	0.992		1.751	(253, 254, 255, 257)
44a	ArCOOH + (p-CH₃C₆H₄)₂CN₂ → ArCOOCH(C₆H₄CH₃-p)₂	C₆H₅CH₃	25	2.660	0.023	1.000	4	2.997	(216)
44b		CH₃COOC₂H₅	25	1.765	0.079	0.989	5	3.452	(216)
45	R–C₆H₁₀–COOH + (C₆H₅)₂CN₂ → R–C₆H₁₀–COOCH(C₆H₅)₂	C₂H₅OH	30	0.946	0.057	0.994	11	1.812	(258)

b. Esters

REACTION NO.	REACTION	SOLVENT	T (°C)	ρ	s[a]	r[b]	n[c]	−log k_0[d]	REFERENCES[e]
46a	ArCOOCH₃ + OH⁻ → ArCOO⁻	60% (CH₃)₂CO	0	2.460	0.097	0.995	9	3.083	
46b			15	2.299	0.122	0.991	10	2.449	(285, 286, 290, 291, 292)
46c			25	2.229	0.106	0.995	11	2.075	
46d			40	2.128	0.103	0.994	11	1.560	
46e			50	1.920	0.075	0.996	6	1.247	
46Aa		C₆H₅NO₂	80	0.518	0.085	0.906	9	2.453	(296a)
46Ab(n)	ArCOOCH₃ + C₆H₅NH₂ → ArCONHC₆H₅(p)		100	0.362	0.124	0.719	11	2.431	(296a)
46Ac(n)			115	0.336	0.102	0.834	7	2.346	(296a)
46Ad(n)			125	0.298	0.099	0.732	11	2.235	(296a)
46Ae(e)			145	0.235	0.099	0.512	7	2.086	(296a)
47a	ArCOOC₂H₅ + OH⁻ → ArCOO⁻	75% CH₃OH	25	2.193	0.053	0.998	7	3.239	(293)
47b			40	2.130	0.048	0.998	7	2.606	(293)
47c			50	2.116	0.054	0.998	7	2.227	(293)
47d		85% C₂H₅OH	25	2.537	0.061	0.998	12	3.217	(98, 147)
47e			35	2.464	0.075	0.997	6	2.748	(98, 147)
47f			50	2.322	0.067	0.996	10	2.210	(98, 147)
47g		87.83% C₂H₅OH	30	2.431	0.099	0.992	18	3.051	(136, 173, 174, 175, 176, 197, 210)

TABLE 2—Continued

REACTION NO.	REACTION	SOLVENT	T °C.	ρ	s[a]	r[b]	n[c]	−log k^0[d]	REFERENCES[e]
47h	$ArCOOC_2H_5 + H^+ \rightarrow ArCOOH$	60% $(CH_3)_2CO$	0	2.443	0.157	0.978	18	3.535	
47i			15	2.353	0.158	0.976	21	2.932	(178, 244, 245, 246, 285, 289, 290, 292, 294)
47j			25	2.265	0.141	0.984	25	2.557	
47k			40	2.181	0.131	0.985	25	2.046	
47l		70% dioxane	25	1.828	0.229	0.869	4	2.519	(247)
47m (j)		95% butyl Cellosolve	25	2.849	0.257	0.984	9	3.459	(244)
48a	$ArCOOC_2H_5 + OH^- \rightarrow ArCOO^-$	60% C_2H_5OH	100	0.144	0.050	0.789	7	4.111	(284)
48b		60% $(CH_3)_2CO$	100	0.106	0.075	0.535	7	4.086	(284)
49a	$ArCOOC_2H_5 + OH^- \rightarrow ArCOO^-$	60% $(CH_3)_2CO$	18	2.073	0.196	0.978	5	2.902	(288, 290, 291, 293)
49b			25	2.146	0.103	0.994	5	2.692	
49c			40	2.075	0.115	0.992	5	2.183	
49d			50	1.992	0.110	0.992	11	1.871	(280)
50a	$ArCOO(l\text{-menthyl}) + OH^- \rightarrow ArCOO^-$	CH_3OH	30	2.628	0.082	0.996	11	4.257	(280)
50b			40	2.552	0.080	0.996	11	3.859	(280)
50c			50	2.476	0.079	0.996	11	3.473	(280)
51	$R\!\!\begin{smallmatrix}CH_3\\ \\CH_3\end{smallmatrix}\!\!COOCH_3 + OH^- \rightarrow$	60% dioxane	125	1.176	0.237	0.949	5	—	(112)
52a	$p\text{-}ArC_6H_4COOC_2H_5 + OH^- \rightarrow p\text{-}ArC_6H_4COO^-$	88% C_2H_5OH	25	0.608	0.012	0.999	7	3.267	(23, 26a)
52b	$ArCH_2COOC_2H_5 + OH^- \rightarrow ArCH_2COO^-$	87.83% C_2H_5OH	40	0.583	0.009	0.999	8	2.636	(23, 26a)
53	$ArCH_2CH_2COOC_2H_5 + OH^- \rightarrow ArCH_2CH_2COO^-$	87.83% C_2H_5OH	30	0.824	0.105	0.974	6	1.813	(174)
54	$ArCH=CHCOOC_2H_5 + OH^- \rightarrow ArCH=CHCOO^-$	87.83% C_2H_5OH	30	0.489	0.038	0.960		2.198	(174, 175)
55	$ArCH=CHCOCOOCH_3 + H^+ \rightarrow ArCH=CHCOCOOH$	87.83% C_2H_5OH	30	1.329	0.046	0.996	15	2.752	(174, 176)
56		50% dioxane	25	0.049	0.014	0.669	4	5.783	(271)
57–60	$R\langle$ ring: CO, O, COO⁻, COHXY, CXY $\rangle + OH^- \rightarrow$								
57	X = Y = H (f)	H_2O	25	1.481	0.181	0.945	7	4.315	(281)
58	X = CH_3, Y = H (f)	H_2O	25	1.270	0.148	0.979	4	4.233	(281)
59	X = C_2H_5, Y = H (f)	H_2O	25	1.455	0.202	0.970	4	4.487	(281)
60	X = Y = CH_3 (f)	H_2O	25	1.129	0.050	0.997	4	4.691	(281)
60Aa	$ArSO_2OCH_3 + H_2O \rightarrow ArSO_3^-$ (u)	50% C_2H_5OH	50	1.248	0.031	0.999	4	4.159	(258a)
60Ab(m)		80% C_2H_5OH	50	1.338	0.057	0.997	4	4.447	(258a)
60Ac(n)		50 wt% dioxane	50	1.222	0.108	0.985	6	4.394	(258a)
60B	$ArSO_2OCH_3 + C_2H_5OH \rightarrow ArSO_3^-$ (u)	C_2H_5OH	70	1.324	0.060	0.996		4.134	(258a)

No.	Reaction	Solvent	t, °C	ρ	s	r	n	log k	Ref.
61	$ArSO_2OC_2H_5 + H_2O \rightarrow ArSO_3^-$	30% C_2H_5OH	25	1.168	0.053	0.997	4	5.254	(86)
61A	$ArSO_2OC_2H_5 + C_2H_5OH \rightarrow ArSO_3^-$ [n]	C_2H_5OH	70	1.305	0.083	0.992	6	4.519	(258a)
62a	$ArSO_2OC_2H_5 + C_2H_5O^- \rightarrow ArSO_3^-$	C_2H_5OH	35	1.372	0.023	0.999	5	2.881	(207)
62b	$ArSO_2OCH(CH_3)_2 + H_2O \rightarrow ArSO_3^-$ [n]	50% C_2H_5OH	45	1.467	0.014	0.999	4	2.392	(207)
62A	$ArSO_2OCH(CH_3)_2 + CH_3OH \rightarrow ArSO_3^-$ [n]	CH_3OH	25	1.565	0.044	0.998	5	4.563	(258a)
62B	$ArSO_2OCH(CH_3)_2 + C_2H_5OH \rightarrow$	C_2H_5OH	50	1.366	0.065	0.995	4	4.382	(258a)
62C	$ArSO_2OCH(CH_3)_2 + C_2H_5OH \rightarrow ArSO_3^-$ [n]	C_2H_5OH	70	1.468	0.058	0.997	5	3.979	(258a)

c. Acyl halides

No.	Reaction	Solvent	t, °C	ρ	s	r	n	log k	Ref.
63a	$ArCOCl + H_2O \rightarrow ArCOOH$	50% $(CH_3)_2CO$	0	0.797	0.383	0.654	9	3.269	(22)
63b		95% $(CH_3)_2CO$	25	1.782	0.109	0.992	5	4.200	(53)
64	$ArCOCl + CH_3OH \rightarrow ArCOOCH_3$	CH_3OH	0	1.469	0.097	0.982	10	3.362	(217)
65a	$ArCOCl + C_2H_5OH \rightarrow ArCOOC_2H_5$	C_2H_5OH	0	1.542	0.145	0.960	13	4.074	(214, 217)
65b		60% C_2H_5OH, 40% $(C_2H_5)_2O$	0	1.922	0.070	0.994	8	3.997	(44)
65	$ArCOCl + (CH_3)_2CHOH \rightarrow ArCOOCH(CH_3)_2$	$(CH_3)_2CHOH$	25	1.499	0.086	0.987	8	2.969	(44)
66			25	1.280	0.061	0.991	6	4.271	(215)
67a	$ArCOCl + C_6H_5NH_2 \rightarrow ArCONHC_6H_5$	C_6H_6	25	1.219	0.051	0.997	4	2.980	(314)
67b			40	1.114	0.048	0.996	4	2.723	(314)
68a	$ArSO_2Cl + H_2O \rightarrow ArSO_2OH$	H_2O	15	-0.300	0.158	0.748	4	2.945	(134)
68b			25	-0.281	0.149	0.746	4	2.491	(134)
68c		42.53% $(CH_3)_2CO$	15	0.843	0.134	0.966	4	3.827	(134)
68d			25	0.811	0.127	0.969	4	3.509	(134)
69	$ArSO_2Cl + C_6H_6 + AlCl_3 \rightarrow ArSO_2C_6H_5$	C_6H_6	30	-1.902	0.119	0.981	6	4.314	(221)

d. Other derivatives of acids: amides, anhydrides, etc.

No.	Reaction	Solvent	t, °C	ρ	s	r	n	log k	Ref.
70a	$ArCONH_2 + OH^- \rightarrow ArCOO^-$ [x]	H_2O	100	1.068	0.054	0.992	13	1.791	(249)
70b		60% C_2H_5OH	52.8	1.364	0.020	1.000	4	5.190	(205)
70c			64.5	1.273	0.060	0.996	4	4.661	(205)
70d			80.3	1.146	0.075	0.992	4	4.136	(205)
70e			100.1	1.100	0.035	0.998	12	3.523	(205)
71a	$ArCONH_2 + H^+ \rightarrow ArCOOH$ [x]	H_2O	100	0.119	0.058	0.597	4	3.513	(248, 249)
71b		60% C_2H_5OH	52.4	-0.483	0.020	0.998	4	5.606	(205)
71c			65	-0.310	0.039	0.985	4	5.072	(205)
71d			79.5	-0.298	0.095	0.847	4	4.428	(205)
71e			99.6	-0.222	0.084	0.883	8	3.906	(205)
72	$ArCONHC_6H_4NO\text{-}2\text{-}p + CH_3ONa \rightarrow ArCOOCH_3$	80% $(CH_3)_2CO$, 20% CH_3OH	—	0.264	0.074	0.802	5	3.981	(297)
73	$(ArCONOCOC_6H_5)^- + NH_3 \rightarrow ArNCO$	H_2O	30	-2.593	0.088	0.981	4	4.587	(251)
74	$(ArCOONOC_6H_5)^- + NH_3 \rightarrow ArCOO^-$	H_2O	30	0.867	0.003	1.000	4	4.634	(251)
75	$ArCN + H_2S + OH^- \rightarrow ArC(SH)=NH$	C_2H_5OH	60.6	2.147	0.078	0.991	7	3.698	(173)
76a	$(ArCO)_2O + H_2O \rightarrow ArCOOH$ [h]	75% dioxane	58.25	1.568	0.094	0.995	9	5.113	(24)
76b			79.65	1.246	0.088	0.969	7	4.470	(24)
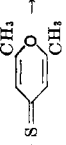
TABLE 2—Continued

A. Heterolytic reactions. II. Hydroxy compounds and derivatives

REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k^{(d)}$	REFERENCES[e]
			°C.						
a. Phenols and derivatives									
76A......	ArOH + C₆H₅COCl → ArOCOC₆H₅ [n]	None	20	0.564	0.214	0.525	6	3.738	(27a)
76B......	ArOH + CH₃COBr → ArOCOCH₃ [l][n]	CH₃COOC₂H₅	0	−1.446	0.214	0.953	11	3.939	(18a,b)
77........	ArO⁻ + CH₂CH₂O → ArOCH₂CH₂OH	98% C₂H₅OH	70.4	−0.947	0.063	0.992	9	4.254	(37)
78........	ArO⁻ + CH₂CHCH₂O → ArOCH(CH₃)CH₂OH	98% C₂H₅OH	70.4	−0.771	0.068	0.987	9	4.698	(37)
79........	ArO⁻ + C₂H₅I → ArOC₂H₅	C₂H₅OH	42.5	−0.994	0.024	0.996	5	3.955	(114)
80........	ArO⁻ + CH₃SO₂ → ArOCH₃	H₂O	100	−0.813	0.067	0.930	15	4.121	(117)
81........	ArOH + p-CH₃C₆H₄SO₂C₂H₅ → ArOC₂H₅ [i]	No conditions		−1.680	0.436	0.646	4	−0.013	(218)
82a.......	ArOCOC₆H₅ + OH⁻ → ArOH	60% (CH₃)₂CO	−20	1.051	0.268	0.950	6	1.801	(292)
82b.......			−10	1.034	0.248	0.955	6	1.408	(292)
82c.......			0	0.976	0.246	0.951	6	1.015	(292)
82d.......			15	0.930	0.234	0.951	6	0.490	(292)
83........	ArOPO(OC₂H₅)₂ + H₂O → ArOH	H₂O, pH = 7.6	37	1.903	0.351	0.966	4	8.379	(2)
84a.......	ArOCOCH₂Cl + H⁺ → ArOH	60% (CH₃)₂CO	25	−0.198	0.011	0.992	5	4.744	(292)
84b.......			40	−0.203	0.024	0.963	5	3.588	(292)
84c.......			60	−0.232	0.017	0.986	5	3.244	(292)
84d.......			80	−0.277	0.025	0.977	5	2.588	(292)
85a.......	ArOSO₂OH + H⁺ → ArOH	H₂O	48.7	0.596	0.050	0.987	14	3.937	(61, 62)
85b.......			78.7	0.466	0.057	0.969	11	2.519	(61, 62)
86........	ArOC₆H₃(NO₂)₂2,4 + CH₃OK → ArOCH₃	CH₃OH	20	1.450	0.006	0.999	6	2.319	(219)
86Aa.....	R☐OCH₃ + p-(CH₃)₂NC₆H₄OCH₃ → [p-(CH₃)₂NC₆H₄OCH₃]⁺	(CH₃)₂CO	35	2.220	0.150	0.996	4	6.519	(141)
86Ab.....	ArOPO(OC₂H₅)₂ + erythrocyte cholinesterase	H₂O, pH = 7.6	45	2.203	0.108	0.998	5	6.104	(141)
87........			37	4.058	0.178	0.998	4	1.727	(2)
b. Alcohols and derivatives									
88........	ArOCH₂OH + HBr → ArOCH₂Br	C₂H₅OH	97	−0.636	0.017	0.992	4	4.889	(21)
89a.......	ArCHOHCH=CHCH₂ →	40% dioxane	0	−6.086	0.580	0.909	7	4.053	(47)
89b.......	ArCH=CHCHOHCH₃		30	−4.672	0.348	0.941	7	2.743	(47)
89c.......			40	−4.435	0.355	0.932	7	2.323	(47)

REACTION	SOLVENT	T (°C)	ρ	s[a]	r[b]	n[c]	$-\log k_0$[d]	REFERENCES[e]
89d	60% dioxane	50	-4.379	0.341	0.936	7	1.944	(47)
89e		60	-4.351	0.275	0.957	7	1.515	(47)
89f		0	-5.995	0.574	0.903	7	4.775	(47)
89g		30	-4.765	0.362	0.939	7	3.313	(47)
89h		40	-4.710	0.338	0.948	7	2.845	(47)
89i		50	-4.515	0.317	0.952	7	2.397	(47)
89j		60		0.304	0.951	7	1.983	(47)
90a ArCH₂OCOCH₃ + OH⁻ → ArCH₂OH	60% (CH₃)₂CO	0	0.818	0.075	0.967	12	2.019	(287, 292)
90b		15	0.762	0.077	0.961	12	1.491	(287, 292)
90c		25	0.743	0.071	0.965	12	1.181	(287, 292)
90d		40	0.725	0.069	0.965	12	0.875	(287, 292)
91a ArCH₂OCOCH₃ + H⁺ → ArCH₂OH	60% (CH₃)₂CO	15	-0.021	0.015	0.612	4	4.888	(292)
91b		25	-0.054	0.017	0.856	5	4.377	(292)
91c		40	-0.053	0.035	0.622	5	3.938	(292)
91d		60	-0.046	0.031	0.615	5	3.265	(292)
91e		80	-0.065	0.027	0.782	5	2.667	(292)
92 ArCH₂OSO₂C₆H₄CH₃-p + H₂O → ArCH₂OH	55.6% CH₃OH	25.25	-2.2(i)					(181)
92A ArCH₂SC(=S)O cholesteryl → ArCH₂SH(n)	None	176	0.467	0.076	0.958	4	3.38	(217a)

A. Heterolytic reactions. III. Alkyl halides

REACTION NO.	REACTION	SOLVENT	T °C	ρ	s[a]	r[b]	n[c]	$-\log k_0$[d]	REFERENCES[e]
93a	ArCH₂Cl + OH⁻(0.0506 N) → ArCH₂OH	H₂O	30	-0.333	0.186	0.540	6	5.494	(228)
93b	(0.104 N)		30	-0.239	0.170	0.450	6	5.239	(228)
93c	(0.259 N)		30	-0.139	0.139	0.337	6	4.971	(228)
94a	ArCH₂Cl + H₂O → ArCH₂OH	47.7% C₂H₅OH	30	-2.178	0.216	0.948	12	5.608	(222, 223, 224, 225)
94b		50% (CH₃)₂CO	83	-1.937	0.214	0.937	12	5.399	(226, 227)
94c			30.4	-1.816	0.214	0.929	12	6.312	(226, 227)
94d			60	-1.688	0.217	0.921	13	4.987	(20)
94e			69.8	-1.840	0.197	0.935	12	4.495	(20)
94f			84.5	-1.435	0.106	0.958	11	4.120	(20)
95a	ArCH₂Cl + I⁻ → ArCHI	(CH₃)₂CO	0.1	0.809	0.118	0.863	11	4.383	(20)
95b		C₆H₆	20	0.786	0.116	0.860	11	3.389	(20)
96	ArCH₂Cl + (CH₃)₃N → ArCH₂N(CH₃)₃⁺ + Cl⁻		100	0.372	0.229	0.699	6	3.001	(273)
97	ArCH₂F + OH⁻ → ArCH₂OH	95% C₂H₅OH	76	0.452	0.097	0.733	12	4.548	(206)
98a	ArCH₂Br + C₅H₅N → ArCH₂NC₅H₅Br⁻	(CH₃)₂CO	20	-0.261	0.057	0.819	16	3.831	(10, 17, 18)
98b	Ar¹Ar²CHCl + CH₃OH → Ar¹Ar²CHOCH₃(k)	CH₃OH	40	-0.258	0.073	0.742	16	3.251	(10, 17, 18)
99			25	-4.072	0.527	0.932	5	2.792	(3)
100	Ar(C₆H₅)CHCl + C₂H₅OH → Ar(C₆H₅)CHOC₂H₅	C₂H₅OH	25	-5.090	0.330	0.957	10	2.062	(102, 145, 212, 213, 303)
101	Ar¹Ar²CHCl + (CH₃)₂CHOH → Ar¹Ar²CHOCH(CH₃)₂(b)	(CH₃)₂CHOH	25	-2.755	0.570	0.651	6	4.621	(3)
102a	Ar(C₆H₅)₂CCl + C₂H₅OH → Ar(C₆H₅)₂COC₂H₅	60% (C₂H₅)₂O, 40% C₂H₅OH	0	-2.923	0.256	0.960	8	2.608	(102, 145, 212, 213, 303)

TABLE 2—Continued

REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k_0^{(d)}$	REFERENCES[e]
			°C.						
102b...... 103...... 104......	$ArCH_2CH_2Cl + I^- \rightarrow ArCH_2CH_2I$ $ArCOCH_2Br + C_5H_5N \rightarrow$ $ArCOCH_2NC_5H_5^+Br^-$	$(CH_3)_2CO$ $(CH_3)_2CO$	25 75 20	-2.656 0.590 0.558	0.282 0.118 0.104	0.946 0.870 0.894	7 7 7	1.720 3.528 3.071	(211) (8) (11)
105a......	$ArCOCH_2Br + S$ (structure) $\rightarrow$	C_6H_6	14.8	0.868	0.080	0.970	10	3.006	(230)
105b...... 106......	$ArSCH_2CH_2Cl + H_2O \rightarrow$ $ArSCH_2CH_2OH$	50% $(CH_3)_2CO$	25.4 55	0.953 -1.671	0.088 0.062	0.969 0.996	10 6	2.766 0.618	(230) (8)
107a......	$ArSCH_2CH_2Cl + I^- \rightarrow$ $ArSCH_2CH_2I$	$(CH_3)_2CO$	55	0.626	0.097	0.918	6	4.570	(8)
107b...... 108......	$ArSO_2CH_2CH_2Cl + I^- \rightarrow$ $ArSO_2CH_2CH_2I$	$(CH_3)_2CO$	75 75	0.673 0.642	0.099 0.056	0.873 0.969	6 5	3.876 3.039	(8) (9)
109a......	$Ar^1Ar^2CClCCl_3 + NaOH \rightarrow$ $Ar^1Ar^2C=CCl_2^{(k)}$	92.5% C_2H_5OH	20.1	2.659	0.284	0.969	8	2.938	(76, 77)
109b(k)... 109c(h)... 110a......			30.4 40.2 20.1	2.604 2.459 2.456	0.270 0.212 0.192	0.970 0.966 0.972	8 6 6	2.441 1.984 3.432	(76, 77) (76, 77) (76, 77)
110b(h)... 110c(h)...	$ArCHClCHCl_2 + NaOH \rightarrow$ $ArC=CHCl^{(h)}$	92.5% C_2H_5OH	30.4 40.2	2.359 2.336	0.184 0.189	0.972 0.970	6 6	2.904 2.391	(76, 77) (76, 77)

A. Heterolytic reactions. IV. Amines and compounds considered derived from them
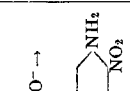
REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k_0^{(d)}$	REFERENCES[e]
			°C.						
						a. Amines			
111......	$ArNH_2 + HCOOH \rightarrow ArNHCHO$	67% C_5H_5N	100	-1.224	0.029	0.988	9	4.123	(85)
112a...... 112b......	$ArNH_2 + C_6H_5COCl \rightarrow ArNHCOC_6H_5$	C_6H_6	25 40	-2.781 -2.491	0.221 0.154	0.986 0.997	9 4	2.888 2.614	(272, 314) (314)
113a......	$ArNH_2 + FC_6H_3(NO_2)_2-2,4 \rightarrow$ $ArNHC_6H_3(NO_2)_2-2,4$	99.8% C_2H_5OH	20	-4.243	0.057	0.998	6	2.280	(67)
113b...... 113c......			30 40	-4.106 -4.006	0.052 0.051	0.998 0.998	6 6	2.109 1.949	(67) (67)
114a......	$ArNH_2 + ClC_6H_3(NO_2)_2-2,4 \rightarrow$ $ArNHC_6H_3(NO_2)_2-2,4$	C_2H_5OH	25	-3.976	0.140	0.967	5	3.952	(296)
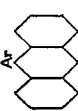
No.	Reaction	Solvent	Temp.	ρ	s	r	n	log	Ref.
114b			35	-3.204	0.098	0.992	10	3.930	(269)
114c			45	-3.055	0.080	0.993	10	3.670	(269)
114d			100	-2.415	0.209	0.979	10	2.324	(296)
115	ArNH₂ + Cl–⟨O₂N-naphthalene-NO₂⟩ → ArNH–⟨...NO₂⟩ / O₂N	C₂H₅OH	25	-3.728	0.127	0.987	6	1.644	(296)
116	ArNH₂ + 2-Cl-5-NO₂C₆H₃N → 2-ArNH-5-NO₂C₆H₃N	H₂O	65	-3.687	0.110	0.975	5	4.740	(32)
116Aa(i)	ArNH₂ + HONO → ArN₂⁺(i)	0.05 N HCl	0	2.310	0.193	0.987	7	3.394	(295)
116Ab(i)		0.5 N HCl	0	2.462	0.142	0.986	9	2.761	(295)
116Ac(i)		0.05 N HBr	0	2.679	0.029	0.999	4	1.706	(295)
117	R–⟨C₆H₄⟩NH₂ + C₆H₅COCl → R–⟨C₆H₄⟩NHCOC₆H₅ / CH₃	C₆H₆	25	-2.727	0.205	0.991	7	3.435	(272)
118	R–⟨C₆H₄⟩NH₂ + C₆H₅COCl → R–⟨C₆H₄⟩NHCOC₆H₅ / OCH₃	C₆H₆	25	-2.609	0.270	0.983	5	3.056	(272)
119a	ArN(CH₃)₂ + 1-CH₃O-2,4,6-(NO₂)₃C₆H₂ → ArN(CH₃)₃ 2,4,6-(NO₂)₃C₆H₂O⁻	(CH₃)₂CO	15	-2.857	0.057	0.997	4	5.352	(140, 141)
119b	ArN(CH₃)₂ + 1-CH₃O-3-CH₃C₆H → ArN(CH₃)₃ 2,4,6-(NO₂)₃-3-CH₃C₆HO⁻	(CH₃)₂CO	25	-2.334	0.209	0.933	4	4.994	(140, 141)
119c			35	-2.378	0.076	0.999	7	4.505	(140, 141)
120a			15	-3.137	0.071	0.996	4	5.755	(139)
120b	ArN(CH₃)₂ + CH₃I → ArN(CH₃)₃⁺ I⁻	CH₃OH	25	-2.917	0.056	0.997	4	5.329	(139)
120c		90% (CH₃)₂CO	35	-2.776	0.047	0.998	4	4.916	(139)
121a		C₆H₅NO₂	65	-2.142	0.034	0.996	7	1.940	(100)
121b			35	-3.303	0.162	0.991	8	3.366	(83)
121c			24.8	-3.069	0.058	0.997	5	6.802	(189)
121d			40.1	-2.961	0.066	0.996	5	6.365	(189)
121e			60	-2.710	0.066	0.996	5	5.812	(189)

TABLE 2—Continued

REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k^0{}^{(d)}$	REFERENCES[e]
			°C.						
	b. Amides								
122.........	$ArNHCHO + OH^- \rightarrow ArNH_2$	67% C_5H_5N	100	0.318	0.081	0.705	9	4.725	(84)
123.........	$ArNHCOCH_3 + CH_3O^- \rightarrow ArNH_2$	CH_3OH	—	2.151	0.400	0.945	6	6.536	(30, 182, 184)
124.........	$ArNHCOCH_3 + H^+ \rightarrow ArNH_2$	50% C_2H_5OH	70	0.293	0.048	0.963	6	2.770(m)	(170)
125.........	R—[ring with NH₂, NO₂, NO₂]—$NHCOCH_3 + CH_3O^- \rightarrow$	CH_3OH	—	1.723	0.170	0.976	12	1.627	(30, 306, 307)
126.........	$ArCH_2NHCOCH_3 + Cl_2 \rightarrow ArCH_2NClCOCH_3$	CH_3COOH	18	-1.051	0.033	0.997	6	-0.466	(313)
	c. Miscellaneous derivatives of amines								
127.........	$cis\text{-}ArN{=}NCN \rightarrow trans\text{-}ArN{=}NCN$	C_6H_6	25	-2.508	0.573	0.854	7	1.622	(107, 191)
127Au......	$cis\text{-}ArN{=}NC_6H_5 \rightarrow$ $trans\text{-}ArN{=}NC_6H_5{}^{(m)}$	C_6H_6	25	-0.610	0.179	0.820	6	5.481	(191a)
127Ab[n]...	$(trans)\text{-}ArN{=}NAr^2 + C_6H_5COOH \rightarrow$	C_6H_6	35	-0.638	0.162	0.856	6	4.405	(191a)
127Ba......	$(trans)\text{-}Ar^1N(O){=}NAr^2{}^{(k)}$ (m)	C_6H_6	15	-1.448	0.116	0.934	19	3.925	(9a)
127Bb(k)(m)	$ArN{=}CHC_6H_5 + H^+ \rightarrow ArNH_2$.	H_2O	25	-1.402	0.114	0.984	19	3.544	(9a)
127Bc(k)(m)			35	-1.370	0.112	0.984	19	3.371	(9a)
128a.......			-0.1	0.424	0.146	0.611	4	5.825	(312)
128b.......			10	0.280	0.143	0.461	4	5.652	(312)
128c.......			20	0.206	0.139	0.364	4	5.500	(312)
129a.......	$ArN{=}CHC_6H_5 + CH_3COOH \rightarrow ArNH_2$	H_2O	-0.1	0.384	0.250	0.377	4	0.992	(312)
129b.......			10	0.516	0.222	0.525	4	0.682	(312)
129c.......			20	0.679	0.208	0.655	4	0.333	(312)
129A.......	$ArN{=}CHC_6H_5 + H_2 + PtO_2 \rightarrow$ $ArNHCH_2C_6H_5{}^{(m)}$	C_2H_5OH	24–25	0.237	0.235	0.222	8	5.576	(259)
130........	$ArNCS + C_2H_5OH \rightarrow$ $ArN{=}C(SH)OC_2H_5$	C_2H_5OH	78	1.746	0.154	0.951	17	5.943	(54)
131........	$ArNCO + CH_3OH \rightarrow$ $ArN{=}C(OH)OCH_3$	$(C_2H_5)_2O$	20	2.460	0.155	0.994	4	2.259	(15)
131A.......	$ArN{=}C{=}NAr + OH \rightarrow$ $(ArNH)_2CO$ (b) (m)	75% tetrahydro-furan	20	1.780	0.276	0.937	10	3.229	(144a)
131B.......	$ArN{=}C{=}NAr + H_3O^+ \rightarrow$ $(ArNH)_2CO$ (b) (m)	75% tetrahydro-furan	20	-0.768	0.087	0.969	14	3.696	(144a)
132........	$ArNHNH_2 + SnCl_2 \rightarrow ArNH_2$	3 N HCl	100	-0.707	0.091	0.916	9	5.183	(105)
133........	$ArNO_2 + SnCl_2 \rightarrow ArNH_2$	H_2O	90	1.149	0.160	0.952	9	2.417(m)	(220)
134........	$ArNO_2 + TiCl_3 \rightarrow ArNH_2{}^{(l)}$	95% C_2H_5OH, HCl	25	2.064	0.201	0.963	13	2.721	(176)
135........	$ArNO_2 + H_2 + Rh \rightarrow ArNH_2$	75% C_2H_5OH	22	0.247	0.174	0.587	16	5.219	(137, 138)
	d. Quaternary ammonium compounds								
136........	$ArCH_2N^+(CH_3)_2CH_2COC_6H_5 + OCH_3^-$ $\rightarrow ArCH_2CH(COC_6H_5)N(CH_3)_2$	CH_3OH	37.7	0.887	0.155	0.793	9	4.073	(283)
137........	$ArCOCH_2N^+(CH_3)_2CH_2C_6H_5 + OCH_3^-$ $\rightarrow ArCOCH(CH_2C_6H_5)N(CH_3)_2$	CH_3OH	37.7	-0.211	0.063	0.725	8	4.210	(95)
138........	$ArCOCH_2NC_5H_5^+ Br^- + OH^- \rightarrow$ $ArCOO^-$	50% C_2H_5OH	20	1.276	0.071	0.984	9	2.137	(183)

A. Heterolytic reactions. V. Aldehydes, ketones, and derivatives

a. Aldehydes and ketones

REACTION NO.	REACTION	SOLVENT	T °C.	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k_0{}^{(d)}$	REFERENCES$^{(e)}$
139	ArCHO + HCN → ArCHOHCN	95% C₂H₅OH	20	2.329	0.074	0.991	13	7.703	(16, 50)
140	ArCHO + CH₂(COOC₂H₅)₂ → ArCH=C(COOC₂H₅)₂	C₆H₆	84	0.226	0.038	0.950	4	3.971	(239)
141a	2ArCHO → ArCH₂OH + ArCOOH	50% CH₃OH	40	3.633	0.229	0.988	9	5.058	(288)
141b			60	3.719	0.168	0.994	8	4.412	(288)
141c			80.2	3.860	0.090	0.993	8	3.874	(288)
141d			100	3.756	0.074	0.998	7	3.537	(288)
141e			30	3.973	0.395	0.971	6	4.584	(305)
142	ArCHO + C₆H₅N(CH₃)₂ → ArCHOHC₆H₄N(CH₃)₂-p	75% C₂H₅OH, C₆H₆	92.5	0.825	0.083	0.979	5	5.111	(238)
143	ArCOCH₃ + NH₂NHCONH₂ → Ar(CH₃)C=NNHCONH₂	83% C₂H₅OH	~25	0.91$^{(j)}$	—	—	5	—	(78)
144	ArCO₃r² + CH₃MgI → Ar¹C(OMgI)CH₃Ar²$^{(j)(k)}$	C₂H₅OC₂H₅	~25	0.363	0.057	0.923	7	−0.012	(192)
145	ArCOC₆H₄CH₂C₆H₅-o + H⁺ →	78% CH₃COOH	117.5	0.197	0.078	0.482	9	4.948	(39, 298)
146a	ArCOCH₃ + Br₂ → ArCOCH₂Br	H₂O	25	0.417	0.091	0.767	10	3.522	(208)
146b		50% CH₃COOH	25	−0.639	0.017	0.994	4	4.025	(210)
146c		idem + 1 M HCl	25	−0.494	0.017	0.990	4	2.235	(210)
146d		idem + 2 M HCl	25	−0.423	0.018	0.994	4	1.813	(210)
146e		75% CH₃COOH + 0.5 M HCl	15	−0.505	0.049	0.852	9	2.909	(99)
146f			25	−0.458	0.050	0.936	13	2.409	(99, 210)
146g			35	−0.441	0.042	0.942	12	1.917	(99)
146h		75% CH₃COOH + 1 M HCl	45	−6.379	0.041	0.916	11	1.474	(99)
146i			25	−0.341	0.074	0.885	5	1.863	(210)

b. Imines and related compounds

REACTION NO.	REACTION	SOLVENT	T °C.	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k_0{}^{(d)}$	REFERENCES$^{(e)}$
147	Ar(C₆H₅)C=NH + H₂O → ArCOC₆H₅	H₂O	0	1.704	0.150	0.942	7	2.125	(80)
148a	ArCH=NC₆H₅ + H⁺ → ArCHO	H₂O	−0.1	−0.216	0.142	0.637	4	5.840	(312)
148b			10	−0.209	0.111	0.716	4	5.660	(312)
148c			20	−0.206	0.085	0.797	4	5.502	(312)
149a	ArCH=NC₆H₅ + CH₃COOH → ArCHO	H₂O	−0.1	−0.725	0.264	0.831	4	1.091	(312)
149b	ArCH=NC₆H₅ + H₂ + PtO₂ → ArCH₂NHC₆H₅$^{(n)(o)}$	C₂H₅OH	10	−0.750	0.291	0.806	4	0.783	(312)
149c			20	−0.535	0.327	0.665	4	0.430	(312)
149A			24-25	−0.386	0.210	0.579	11	5.664	(259)

TABLE 2—Continued

REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k^{0(d)}$	REFERENCES[e]
			°C.						
c. Oximes, hydrazones, and related compounds									
150	$ArCH=NOCOCH_3 + H^+ \to ArCHO$	80% $(CH_3)_2CO$	25	-0.132	0.068	0.801	4	4.645	(42)
151	$ArCH=NOCOCH_3 \to ArCN$	Xylene	139	-0.434	0.055	0.983	4	3.737	(4)
152	$ArCH=NOCOC_6H_5 \to ArCN$	Xylene	120	-0.712	0.042	0.993	4	3.895	(4)
153	$ArCH=NOCOOC_2H_5 \to ArCN$	Xylene	118.6	-0.55	0.055	0.985	5	3.322	(4)
154	$Ar(CH_3)C=NOH + H^+ \to ArNHCOCH_3$	94.5% H_2SO_4	50.9	-2.110	0.280	0.957	6	4.623	(236)
155a (k)	$Ar \cdot Ar' \cdot C=NNH_2 \to Ar \cdot CH_2Ar'$(k)	Butyl carbitol	190.5	0.622	0.166	0.846	5	1.791	(276)
155b (k)			199.5	0.743	0.101	0.952	5	1.549	(276)
155c (k)			210.5	0.790	0.097	0.961	5	1.246	(276)
155d (k)			221.5	0.864	0.075	0.940	5	1.030	(276)
156a	$ArCOCHN_2 + CH_3COOH \to$ $ArCOCH_2OCOCH_3$	99.85% CH_3COOH	40.05	-0.914	0.027	0.997	5	4.275	(190)
156b			60.3	-0.911	0.023	0.998	5	3.480	(190)
157	$ArCH=NCl + OH^- \to ArCN$	92.5% C_2H_5OH	0	2.240	0.117	0.992	9	1.760	(133)
d. Miscellaneous derivatives of aldehydes and ketones									
158	$ArCH(OH)CN + H_2O \to ArCHO$	95% C_2H_5OH	20	1.233	0.126	0.921	13	9.704	(16, 50)
A. Heterolytic reactions. VI. Phosphines, silanes, arsonous acids, and diarylmercury compounds									
			°C.						
159	$ArP(C_6H_5)_2 + C_2H_5I \to ArP(C_2H_5)_3^+ I^-$	$(CH_3)_2CO$	35	-1.094	0.054	0.983	5	3.200	(83)
160	$Ar(C_6H_5)_2SiH + C_5H_{11}N \to$ $Ar(C_6H_5)_2SiOH$	Wet $C_5H_{11}N$	38.8	2.784	0.099	0.985	6	3.433	(111)
161	$ArAs(OH)_2 + cystine + OH^- \to$ $ArAsO(OH)_2$(°)	H_2O	20	-0.250	0.091	0.511	5	4.909	(71)
162a	$ArHg + H^+ \to ArH + ArHg^+$(p)	99.67% dioxane	30	2.282			7		(75, 171)
162b			40	2.189			7		(75, 171)
162c			50	2.104			7		(75, 171)
A. Heterolytic reactions. VII. Hydrocarbons									
			°C.						
163	$Ar_2(C_6H_5)C=CH_2 + NH_3 \to ArNH_2$(i)	$CHCl_3 + H_2SO_4$	25	-2.134	0.122	0.956	10	-0.261	(202)
164	Copolymerization of $ArCH=CH_2$ with $C_6H_5CH=CH_2$ in the presence of $SnCl_4$(q)	$CCl_4 + C_6H_5NO_2$	0	-1.932	0.129	0.979	5	-0.118	(229)

REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k_0^{(d)}$	REFERENCES$^{(e)}$
			°C.						
165.....	Copolymerization of ArCH=CH₂ with p-ClC₆H₄CH=CH₂ in the presence of SnCl₄⁽⁴⁾	C₆H₅NO₂	0	−1.627	0.116	0.940	5	−0.436	(229)
166.....	Copolymerization of ArCH=CH₂ with C₆H₅C(CH₃)=CH₂ in the presence of SnCl₄⁽⁹⁾	C₄H₅NO₂	0	−2.119	0.353	0.677	5	−0.571	(229)
167–182...	ArCH₂O⟨A B/D⟩C + Cl₂ → ArCH₂O⟨A B/C D⟩C(f) Cl								
167.....	A = COOH; B = C = D = H	99% CH₃COOH	20	−0.752	0.026	0.984	5	1.351	(160)
168.....	A = Cl; B = C = D = H	99% CH₃COOH	20	−0.923	0.210	0.826	8	1.266	(160)
169.....	A = F; B = C = D = H	99% CH₃COOH	20	−0.854	0.021	0.999	4	1.235	(162)
170.....	B = COOH; A = C = D = H	99% CH₃COOH	20	−0.851	0.020	0.987	6	1.736	(165)
171.....	C = F; A = B = D = H	99% CH₃COOH	20	−0.887	0.017	0.999	5	1.585	(162)
172.....	C = Br; A = B = D = H	99% CH₃COOH	20	−0.870	0.006	1.000	5	1.700	(160)
173.....	C = Cl; A = B = D = H	99% CH₃COOH	20	−0.884	0.021	0.998	13	1.868	(38, 100, 162)
174.....	A = COOH; A = B = D = H	99% CH₃COOH	20	−0.903	0.045	0.975	9	2.258	(160)
175.....	A = Br; C = C(CH₃)₃, B = D = H	99% CH₃COOH	20	−0.869	0.027	0.997	9	1.511	(164)
176.....	A = Br; C = C(CH₃)₂C₂H₅, B = D = H	99% CH₃COOH	20	−0.854	0.020	0.999	5	1.590	(164)
177.....	A = Br; C = CH₃, B = D = H	99% CH₃COOH	20	−0.872	0.024	0.997	8	1.204	(164)
178.....	A = Br; C = C₂H₅, B = D = H	99% CH₃COOH	20	−0.851	0.020	0.999	4	1.125	(163)
179.....	A = CH₃; C = Br, B = D = H	99% CH₃COOH	20	−0.850	0.029	0.995	9	1.426	(164)
180.....	A = D = Cl; B = C = H	99% CH₃COOH	20	−0.866	0.036	0.984	5	2.280	(163)
181a....	A = CH(CH₃)₂; C = Cl, D = CH₃, B = H	99% CH₃COOH	16	−0.853	0.007	0.999	4	−0.245	(165)
181b....	A = C = Cl; B = D = CH₃	99% CH₃COOH	20	−0.869	0.008	0.999	4	−0.454	(164)
182.....	ArCOC₆H₄OCH₃-p + Cl₂ →	99% CH₃COOH	20	−0.921	0.014	0.996	5	0.877	(163)
183.....	1-ArCO-3-Cl-4-CH₃OC₆H₃		20	−0.696	0.037	0.990	11	1.655	(161)

B. Free-radical reactions

REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k_0^{(d)}$	REFERENCES$^{(e)}$
			°C.						
184.....	4ArSbO → (ArSb)₂O + Sb₂O₃	Solid state	100	−2.554	0.260	0.963	6	5.363	(156)
185.....	(ArCOO)₂ decomposition induced by C₆H₅N(CH₃)₂	CHCl₃	20	−2.334	0.335	0.954	8	1.891	(144)
186a....	(ArCOO)₂ → ArCOO•⁽ᵇ⁾ ArCOOOCOAr² →	CH₃COC₆H₅	80	−0.201	0.172	0.687	10	4.232	(34)
186b....	ArCOO• + Ar²COO•. in the presence of 0.2 N 3,4-CH₃OC₆H₃CH=CH₂	Dioxane	80	−0.374	0.080	0.932	15	4.291	(274)

TABLE 2—*Concluded*

REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k_0^{(d)}$	REFERENCES[e]
			°C.						
187	Initiation by (ArCOO)₂ of polymerization of C₆H₅CH=CH₂	C₆H₅CH=CH₂	60	−0.550	0.139	0.884	21	5.099	[72]
188a	ArCOOC(CH₃)₃ decomposition	(C₆H₅)₂O	100.1	−0.903	0.022	0.996	4	5.192	[33]
188b			110.1	−0.678	0.035	0.994	5	4.597	[33]
188c			120.2	−0.568	0.014	0.999	5	4.056	[33]
188d			130.9	−0.525	0.036	0.990	5	3.532	[33]
189	ArCHO + C₄H₉COO· [i]	(CH₃CO)₂O	30	−0.488	0.071	0.922	4	−0.915	[301]
190	ArCHO + p-ClC₆H₄COO· [i]	(CH₃CO)₂O	30	−1.668	0.054	0.986	6	−1.071	[301]
190A	ArCH₃ + BrN(COCH₂)(COCH₂) →hv ArCH₂Br [i][m]	CCl₄	80	−1.806	0.161	0.977	9	−0.140	[181a]
190B	ArCH₃ + Br₂ → ArCH₂Br [i][n]	CCl₄	80	−1.369	0.193	0.964	6	−0.122	[181a]
191	Autoxidation of ArNHN=CHC₆H₅ [l]	C₆H₆	16–21	−1.714	0.117	0.964	7	2.909	[233]
192	Same, catalyzed by C₆H₅COOH [l]	C₆H₆	17–20	−2.253	0.151	0.965	7	2.789	[233]
193	Autoxidation of ArCH=NNHC₆H₅ [l]	C₆H₆	17–20	−0.347	0.184	0.544	8	3.111	[233]
194	Same, catalyzed by C₆H₅COOH [l]	C₆H₆	17–20	−0.663	0.215	0.744	9	3.034	[233]
195a	Autoxidation of ArCHOHCOAr [k]		10	1.429	0.117	0.963	7	2.792	[304]
195b[k]			20	1.335	0.099	0.975	7	2.536	[304]
196	Copolymerization of ArCH=CH₂ with C₆H₅CH=CH₂ [q]	No solvent	60	0.531	0.042	0.980	10	−0.045	[299, 300]
197	Copolymerization of ArCH=CH₂ with methyl methacrylate [q]	No solvent	60	0.038	0.147	0.091	11	−0.037	[300]
198	Copolymerization of ArCH=CH₂ with p-ClC₆H₄CH=CH₂ [q]	No solvent	60	0.103	0.062	0.767	5	−0.008	[300]
199	Copolymerization of ArC(CH₃)=CH₂ with maleic anhydride [q]	No solvent	60	−0.612	0.439	0.512	8	−0.248	[302]
199Aa	ArCOH(OHAr + (CH₃COO)₄Pb → 2ArCO(m)	CH₃COOH	18	−0.426	0.106	0.973	4	2.979	[73]
199Ab			25	−0.406	0.082	0.983	4	2.720	[73]
199Ac			35	−0.391	0.102	0.971	4	2.363	[73]
199B	ArI(OCOCH₃)₂ + iso-C₃H₇CHOHCHOHC₆H₅ → ArI [m]	CH₃COOH	34.7	1.438	0.050	0.996	6	2.609	[234]

C. Reactions involving nuclear substitution in the substituted ring

REACTION NO.	REACTION	SOLVENT	T	ρ	$s^{(a)}$	$r^{(b)}$	$n^{(c)}$	$-\log k_0^{(d)}$	REFERENCES[e]
			°C.						
200	ArH + NO₂⁺ → ArNO₂ [i]	(CH₃CO)₂O 20% CH₃COOH	18	−5.926	0.351	0.962	5	−0.103	[31, 146, 148]
201	ArB(OH)₂ + Br₂ → ArBr	C₆H₆	25	−4.504	0.136	0.966	7	3.206	[188]
202	ArBr + C₄H₉NH → ArNC₄H₉ [o]		99	4.871	0.163	0.987	4	11.463	[58]
203a	R–Br + C₅H₁₀NH → R–NC₅H₁₀ (NO₂)	C₅H₁₀NH	25	4.918	0.365	0.973	10	4.673	[27]

203b......	$R\langle\rangle Cl + CH_3ONa \rightarrow$ (with NO_2)		35	4.865	0.358	0.973	10	4.371	(27)
204......	$R\langle\rangle OCH_3$ (NO_2) [o]	CH_3OH	25	3.941	0.558	0.984	7	6.594	(57)
204A......	$R\langle\rangle F + C_2H_5O^- \rightarrow R\langle\rangle OC_2H_4$ (NO_2)	C_2H_5OH	49.6	4.071	0.280	0.994	7	1.780	(29)
204B......	$ArH + C_6H_5\bullet \rightarrow ArC_6H_4$ [n][q]	ArH	80	0.675	0.208	0.880	5	−0.137	(6, 7, 142)

(a) The standard deviation of experimental measurements from the regression line.
(b) The correlation coefficient.
(c) The number of compounds involved in the calculation of ρ.
(d) The intercept of the regression line with the ordinate ($\sigma = 0$).
(e) Data from references in italics were not used in the derivation of reaction constants, but were used only in the derivation of new substituent constants (see Section IV,B).
(f) σ_{meta} was used.
(g) It has been suggested that the rate constants in reactions 70a and 71a actually represent rates of solution rather than rates of reaction (205).
(h) The Hammett equation was applied to these reactions in the form of equation 8 (see Section VII,D).
(i) The calculations are based on relative rates.
(j) The reaction constant is the value given in the reference. The data reported are insufficient to permit recalculation.
(k) The Hammett equation was applied in the form of equation 10 (see Section VII,D).
(l) The calculations are based on time required for a certain per cent of the reaction to occur.
(m) No units of time are given by the authors.
(n) These reactions were added after the work was essentially completed, and were not included in the various tabulations and calculations of later sections of this paper.
(o) Data given in italics refer to reaction constants which were calculated with the substituent constants listed in table 7 (see Section IV,B). These data were not included in the tabulation of distribution of the various parameters (see Section V).
(p) This reaction series simultaneously involves a reaction of the side chain of one ring and a substitution in the other ring.
(q) The calculations are based on reactivity ratios.
(r) The number and relative importance of the positions chlorinated may vary between the different series depending on which of the groups A, B, C, and D are hydrogen, and may even vary slightly within any one series.
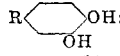(s) Based on partial rate factors obtained from competitive reactions.

TABLE 3

Miscellaneous physical data

A. Half-wave potentials from polarographic reductions

REACTION NO.	REACTION	SOLVENT	T	ρ	s[a]	r[b]	n[c]	$-E_{\frac{1}{2}}^{0}$[d]	REFERENCES
			°C.						
205.....	$ArNO_2 \rightarrow ArNHOH$	10% C_2H_5OH	25	0.165[d]	0.015	0.986	9	0.341[d]	(231, 235)
206.....	$Ar^1COAr^2 \rightarrow$ $(Ar^1Ar^2COH)_2$[f]	40% CH_3OH	25	0.235[d]	0.030	0.952	12	1.120[d]	(51)
207.....	$Ar^1CH{=}CHAr^2 \rightarrow$ $Ar^1CH_2CH_2Ar^2$[f]	75% dioxane	24	0.251[d]	0.022	0.960	5	2.158[d]	(116)

B. Infrared absorption frequencies[g]

REACTION NO.	REACTION	SOLVENT	ν^0[g]	ρ	s[a]	r[b]	n[c]	$-\log k^0$[e]	REFERENCES
			$cm.^{-1}$						
208a....	C=O frequency in ArCOCl 1	CCl_4	1778	0.00502	0.00125	0.987	5	0.0000	(104)
208b...	2		1744	0.0109	0.0033	0.846	5	−0.0002	(104)
209a....	C=O frequency in ArCOOH	CH_3OH	1705	0.0140	0.0013	0.982	9	0.0000	(104)
209b...		CCl_4	1743	0.00740	0.0007	0.973	6	0.0006	(104)
210.....	C=O frequency in $(ArCOOH)_2$	CCl_4	1696	0.00836	0.0003	0.996	6	0.0000	(104)
210A...	C=O frequency in Ar^1COAr^2[f]	CCl_4	1664	0.00849	0.0011	0.955	13	0.0005	(108a, 168)
210B..	C=O frequency in $ArCOCH_3$	Nujol Mull	(1659.3)	0.0195	0.0037	0.974	5	(0)	(270a)
211a....	NH_2 frequencies in ArNH₂ 1	CCl_4	3410	0.00604	0.0007	0.985	7	0.0006	(104)
211b...	2	CCl_4	3489	0.00977	0.0014	0.977	7	0.0003	(104)
212a....	OH frequency in ArOH	CCl_4	3551	−0.00296	0.0007	0.948	6	−0.0008	(104)
212b...		CCl_4	3610.1	−0.00346	0.0005	0.989	12	0.0001	(149)
212c....		C_2Cl_4	3610.1	−0.00397	0.0019	0.889	15	0.0001	(149)
213.....	OH frequency in R⟨⟩OH : OH								
	Free OH[h]	C_2Cl_4	3611.7	−0.00446	0.0005	0.965	9	−0.0004	(149)
214.....	Hydrogen-bonded OH[i]	C_2Cl_4	3568.2	−0.00416	0.0014	0.844	9	0.0006	(149)

C. Other measurements

REACTION NO.	REACTION	SOLVENT	T	ρ	s[a]	r[b]	n[c]	$-\log k^0$[e]	REFERENCES
			°K.						
215.....	CBr bond dissociation energy	$C_6H_5CH_3$		0.023	0.013	0.540	10	−0.007	(277)
216.....	Nuclear magnetic resonance absorption of F^{19} in ArF			1.446	0.302	0.872	20	0.378	(121)
217a....	Nuclear quadrupole coupling frequency of Cl^{35} in ArCl		196	0.0239	0.0070	0.865	7	−0.012	(204)
217b...			77	0.0245	0.0048	0.931	7	−0.003	(204)
217c....			0	0.0259	0.0057	0.916	7	0.001	(204)
218.....	Isotope effect in $ArC^{14}OOC_2H_5 +$ $OH^-(k_{C^{12}}/k_{C^{14}})$	Aqueous C_2H_5OH		0.0079	0.0023	0.812	6	0.337	(261)

[a] The standard deviation of experimental measurements from the regression line.

[b] The correlation coefficient.

[c] The number of compounds involved in the calculation of ρ.

[d] The reaction constants in table 3A are based on half-wave potentials; hence ρ, s, and $-E_{1/2}^0$ are in volts.

[e] The intercept of the regression line with the ordinate ($\sigma = 0$).

[f] The Hammett equation was applied in the form of equation 10 (see Section VII,D).

[g] The reaction constants in table 3B are based on frequency shifts in the form $(\nu - \nu^0)/\nu^0$, where ν and ν^0 are the frequencies of the substituted and unsubstituted compounds respectively; hence, ρ and s are dimensionless, and $(-\log k^0)_{calcd}$ also is dimensionless and reflects the deviation of the point for $R = $ H from the regression line.

[h] The average $(\sigma_p + \sigma_m)/2$ was used; cf. references 74 and 149.

[i] The more positive substituent constant (σ_m or σ_p) was used; cf. references 74 and 149.

[j] The data for reactions 209 to 211 are made dimensionless by dividing the change in values of the quantity measured by the absolute value for the unsubstituted compound; cf. footnote (g) of this table.

ArY and ArCH=CHY, but did not explain the small reaction constants for ArCH$_2$Y and ArCH$_2$CH$_2$Y (125). Consequently, Hammett concluded that the $1/d^2$ factor is applicable only if Y and Ar are conjugated. This conclusion is surprising, since the factor $1/d^2$ is introduced on the basis of electrostatic arguments, which should apply best when Ar and Y are not conjugated.

In a series of similar reactions it may be assumed that the reaction constants depend on the polarizability of the side chain. This hypothesis has been tested by correlating the reaction constants for the acid dissociations for several series of acids of the general form ArMO$_n$H$_m$ (M = boron, carbon, phosphorus, arsenic) with the polarizability of the ion derived from the element M and all the electrons it shares (157). Ionic refractivities extrapolated from Fajans' tables (101) were used for the polarizabilities. From the data, listed in table 4, it appears that the polarizability of M has a decisive influence on the magnitude of the reaction constant. Further work on similar acids, however, appears desirable.

TABLE 4

Comparison of reaction constants and polarizabilities

REACTION SERIES: IONIZATION OF	REACTION NO. [a]	ρ	ION	IONIC REFRACTIVITY [b]
ArB(OH)$_2$	13	2.53	B^{5-}	391
ArCOOH	1a	1.00	C^{4-}	88
ArAsO(OH)$_2$	18	0.95	As^{3-}	76
ArPO(OH)$_2$	14a	0.76	P^{3-}	67

[a] Reaction No. refers to the reaction series in table 1.
[b] Extrapolated from reference 101.

The data suggest that the reaction constants for the sulfonic and selenic acids should be quite small. Unfortunately, no experimental data appear to be available.

Pressman and Brown have attempted an interpretation of relative values of reaction constants for the acid dissociation of benzeneboronic, benzenearsonic, and benzoic acids on the basis of the resonance structures involved in the ground state of the compounds (240). Their interpretation does not take adequate account of the magnitude of the dissociation constants observed, and when extended to benzenephosphonic acids suggests reaction constants larger than those experimentally determined (reaction 14a) (157).

The transmission of the electrical effect of substituents through the side chain has also been treated from another viewpoint (153). Considering several types of reactions, A, B, $\cdots$ and several series of compounds, 1, 2, $\cdots$ which differ only in the group (Z) linking the reaction site Y with the substituted benzene ring Ar, it is reasonable to assume that

$$\rho_{A,1} : \rho_{B,1} : \cdots = \rho_{A,2} : \rho_{B,2} : \cdots = \cdots \tag{3}$$
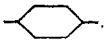
The scanty experimental data available to test the validity of equation 3 are summarized in table 5. Considering the large uncertainties in reaction constants, the agreement is encouraging.

In the same paper (153) it was shown that relative values of the reaction

constants can be calculated by molecular orbital theory from atom–atom polariz-
abilities. Thus, calculations were carried out on the effect of introducing a group
Z between the reacting side chain Y and the substituted ring Ar. Table 6 com-
pares the calculated and observed reaction constants. From general considera-
tion of the terms entering the calculation it was concluded that the reaction
constant should be greatly reduced, and probably change in sign, if the group Z

TABLE 5

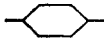*The effect of the introduction of groups Z between the substituted ring and reaction site Y*

Z	REACTION NO. [a]	REFERENCE REACTION NO. [a]	RELATIVE REACTION CONSTANT, ρ/ρ^0	MEAN ρ/ρ^0	DEVIATION
—CH$_2$—..	8 53	1a 47g	0.489 0.336	0.410	0.084
—CH$_2$CH$_2$—..	9 54	1a 47g	0.212 0.196	0.206	0.009
—CH=CH—......................................	10 55	1a 47g	0.466 0.542	0.508	0.038
⬡	7 52	1t 47g	0.341 0.262	0.303	0.040
—CH=CHCO......................................	21a 21b	1a (b)	—0.059 0.13	0.035	0.065

[a] The reaction numbers refer to the reaction series in tables 1 and 2.
[b] No reaction constant for the reference reaction is known, but it may be estimated as $\rho = 1.3$.

TABLE 6

Calculated and observed values of ρ/ρ^0

Z	ρ/ρ^0	
	Calculated	Observed
—CH=CH—.......................	0.683	0.508 [a]
⬡	0.177	0.303 [a]
—N=N—⬡	0.136	0.126 [b]
—CH=CHCO.......................	—0.010	+0.035 [a]
⬡	—0.013	

[a] From table 5.
[b] From reactions 28 and 27b.

is conjugated with Ar and Y and involves an odd number of atoms *between* Ar
and Y. The only examples of such systems for which data are available are the
acid dissociation constants of the benzylidenepyruvic acids and the acid hy-
drolysis of their methyl esters. The prediction is confirmed for the acid dissocia-
tion constants in water (reaction 12a). No exact comparison is possible for the
acid dissociation constants in 50 per cent methanol (reaction 12b) and the acid
hydrolysis of the esters (reaction 56). The reaction constants for both reaction
series are very small, but positive. Since reaction constants for acid hydrolyses

are generally small, the reaction constant of reaction 56 is of little value for the testing of the theory. However, the reaction constant for reaction 12b is very much smaller than the reaction constant for the acid dissociation constants of benzoic acids in water–alcohol mixtures.

Structural changes in the side chain may be expected to affect the reaction constants. In the alkaline hydrolysis of phthalides, for instance, introduction in the α-position of one or two methyl groups, or of one ethyl group, appreciably changes ρ (see reactions 57–60). In some reaction series the side chain contains a benzene ring. It is shown in Sections VII,C and VII,D that substituents in such a ring have no appreciable effect on the reaction constant. In reactions of a series of compounds of the type
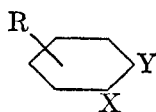
where X is the same for the whole series, reaction constants also are essentially independent of the nature of X (see Section VII,C).

(2) Susceptibility of the reaction to changes in electron density at the site of the reaction

The second factor on which reaction constants depend is the susceptibility of the reaction velocity or equilibrium constant to the electron density at the site of the reaction. It is apparent that a positive ρ indicates that the reaction is facilitated by low electron density at the reaction site, and a negative ρ implies a reaction favored by high electron density (250a).

The susceptibility of the reactions of the alkyl and acyl halides with nucleophilic reagents has been discussed in detail (273). The authors believe that these reactions occur as "concerted displacement reactions," and that the sign and magnitude of ρ are determined by the relative importance of the simultaneous electrophilic and nucleophilic reactions. The wide variation of the magnitude and sign of ρ for these reactions is considered as evidence for the concerted mechanism of these reactions. Regrettably, the transmission of electrical effects to the reaction site was not considered in this discussion (cf. preceding section), so that a direct comparison of the values of ρ is not warranted. Few measurements on a given series of compounds reacting with different reagents have been reported. However, the existing data appear to indicate that a wide variation of ρ-values can be observed, even for the same side chain.

(3) Effect of reaction conditions

Reaction constants for a given reaction depend on the conditions under which the reaction takes place. Hammett proposed that reaction constants can be expressed in the form of equation 2 (125). Little has been added to our knowledge of the dependence of ρ on the reaction conditions, and none of the implications of equation 2 have been tested adequately. The reaction constants collected in

tables 1 to 3 now permit such tests. In figure 1, ρ is plotted against $1/T$ for all the reaction series in which at least four reaction constants were evaluated under conditions differing only in the temperature of the experiments, and for which $\rho < 1.2$. With due allowance for the large uncertainties in reaction constants, the plots appear to be linear. A few reaction series would be somewhat better described by a curved line. Equation 2, however, not only implies that the plots of ρ against $1/T$ must be linear but also defines the slope of these lines. The slopes demanded by theory are indicated in figure 1 by dashed lines. The plots for six of the reaction series are seen to approximate these slopes closely; two appear to be appreciably too steep, and for two the slope has the wrong sign.
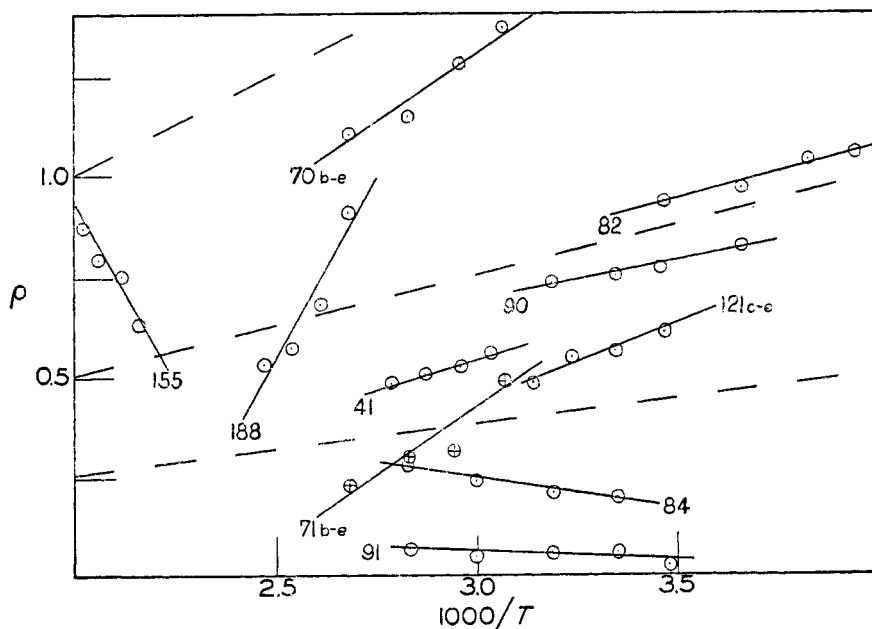
Fig. 1. The dependence of ρ on the temperature

Of the other reaction series ($\rho > 1.2$) for which more than three reaction constants are known, six approximate the theoretical slope, and one appears to have a negative slope. Tables 1 and 2 include thirty-five other reaction series in which two or three reaction constants were obtained under identical conditions except for differences in temperature. Considering the large uncertainties in ρ, it appears futile to attempt to test the magnitude of the slope of the plot of ρ against $1/T$ for these reaction series. However, in six of the series ρ appears to increase with the temperature, in violation of equation 2.

Thus, it can be concluded that in many cases equation 2 appears to express the temperature dependence of ρ satisfactorily, but that some cases are known in which the reaction constants increase with temperature. The extent to which deviations from linearity occur is difficult to determine because of the small range of temperature which is usually available.

Equation 2 also predicts the change of ρ with the dielectric constant of the solvent.[7] However, the data available to test this dependence are more difficult to interpret. The interpretation is simplest for the acid dissociation constants, since a large body of data is available, and it can be assumed that no changes in the mechanism of the reaction will interfere with the considerations. As a general rule, the reaction constants appear to increase with decreasing dielectric constant, as predicted by equation 2. Two exceptions may be noted: the reaction constants for the second pK's of the benzenephosphonic acids (reaction 15) appear to decrease slightly in going from water to 50 per cent ethanol; and in the acid dissociation constants of the anilinium ions (reaction 26) in aqueous dioxane, ρ appears to pass through a maximum between 45 per cent and 70 per cent dioxane.[8]

Reaction constants derived from rate constants show considerably more variation in their behavior on change of solvent. In at least one reaction series a change in mechanism with change in solvent has been postulated (53). However, it does not appear likely that changes in mechanism are responsible for the solvent dependence of reaction constants in many reaction series. Some reaction constants are found to increase and others to decrease with increasing polarity of the solvent, and several instances are observed where the reaction constants change sign with a change in solvent. In one case (reaction 89) the direction of the change of ρ with polarity appears to depend on the temperature. These facts can be understood in terms of equation 2 only if it is assumed that B_1 and B_2 may have opposite signs, and that either the first or the second term in the parentheses may predominate (see reference 125). Until the significance of B_1 and B_2 is better understood, these facts cannot be interpreted adequately.

Use of the "activity postulate" (120) leads to an alternate expression for the solvent dependence of reaction constants for the dissociation of acids. On the basis of the assumptions under which the postulate is valid, it was shown that the reaction constants for a given reaction series in various solvents can be expressed as a linear function of the "activity function" (Y), which depends on the nature of the ionizing group and the solvent involved (119, 120). A similar dependence of ρ on Y can be determined for solvolysis reactions (see 119a, 315).

IV. SUBSTITUENT CONSTANTS

A. Definition of substituent constants

Substituent constants were defined originally by the equation (127f)

$$\log (K/K^0) \equiv \sigma \tag{4}$$

where K^0 and K are the acid dissociation constants of benzoic acid and its monosubstituted derivatives, respectively. This definition was largely one of convenience. The acid dissociation constants of the benzoic acids were taken as

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[7] It may be preferable to replace the dielectric constant of the solvent with an effective dielectric constant of the molecule and its immediate surroundings (177).

[8] The existence of this maximum has been questioned (118). Using the differential potentiometric method, Grunwald was unable to duplicate the pK's in high concentrations of dioxane (118).

a reference reaction series because a large number of such constants were known accurately, and because many previous correlations had been made with these constants. Equation 4 implies the arbitrary definition of a reaction constant of unity for this reaction series, and a substituent constant of zero for the unsubstituted compound. In the calculation of further substituent constants from other reactions the definition of σ through equation 4 is retained, and the resulting values must then be considered as estimates of $\log (K/K^0)$. The substituent constants so derived, and hence the reaction constants, depend somewhat on the order in which the data were treated (125), particularly since the Hammett equation does not represent the data with high precision.

The definition through equation 4 is abandoned, although this has never been stated explicitly, when special substituent constants are derived for use with the reactions of phenols and anilines.[9] Since the usefulness of the Hammett equation depends on its application to a large number of reaction series, this author proposes to redefine the substituent constant, ideally, as the value of σ which best fits the entire body of experimental data. This definition has been implied by many workers, who have either derived substituent constants for groups not included in Hammett's tables (e.g., 36, 179, 253–255, 257) or reëvaluated existing ones (e.g., 136), and who have attempted to find the value which best fits the largest number of reaction series. Unfortunately all such determinations have been concerned with a single or a few substituents, and have always been based on a few reaction series which usually encompassed only the special interests of the authors. Such a procedure is natural, considering the tremendous amount of labor involved in a more thorough reëvaluation.

The new definition has several disadvantages. It makes substituent constants dependent on the body of knowledge available at the time of their evaluation, and implies that they should be revised at frequent intervals. Moreover, the evaluation of such substituent constants requires the formidable task of fitting the entire available data by some suitable statistical procedure. Such computation is not feasible without the use of electronic computing equipment.[10]

In spite of the shortcomings listed, the definition of substituent constants proposed here appears to be the only reasonable one. It further permits the definition of constants for special types of reactions wherever they should become necessary, without a redefinition of the substituent constant.

B. Evaluation of substituent constants

In the calculation of reaction constants summarized in tables 1 to 3 only substituents were considered for which Hammett had reported substituent

[9] The substituent constants for use with the reactions of phenols and anilines will be denoted by σ^* throughout this review and will be discussed in detail in Section IV,C and Section IV,D.

[10] Professor C. Gardner Swain has stated that he intends to undertake such a reëvaluation of substituent constants with the use of the electronic computing equipment available in Cambridge, Massachusetts. In connection with this work, Professor Swain would appreciate receiving any relevant data which have been omitted from this review.

constants. Although many workers have carefully evaluated and reported substituent constants for other groups (27, 36, 179, 253–255, 257), this restriction was imposed for several reasons: (*1*) The process of calculation of substituent constants from known reaction constants, and then using these substituent constants for the calculation of further reaction constants which in turn will be used for further calculation of substituent constants, leads to a set of constants which depends on the order in which the process is carried out. The inaccuracies introduced in this manner are the more serious the lower the precision of the equation on which they are based. Fortunately, only four reaction series are involved in Hammett's original evaluations (125), and three further reaction series in his later work (127f).

(*2*) If it had been decided to use substituent constants derived since the publication of Hammett's book, decisions would have been required concerning the best value known at the present time. In some cases, where different substituent constants had been derived by various authors, such decisions would have been difficult to make.

(*3*) Most of the computational labor in evaluating the reaction constants in tables 1 to 3 has been done over a period of several years. Use of newly derived substituent constants would have required extensive recomputations.

(*4*) The manner of computation adopted in this paper has permitted evaluation of as many as twenty-seven values for the substituent constant of a single group, and hence has led to various inferences about substituent constants which will be discussed in the following sections.

It might have been possible to recompute all reaction constants on the basis of the substituent constants adopted in this review. Since a systematic reëvaluation is anticipated, it was not felt advisable to make such laborious recomputation at this time.

Accordingly, substituent constants have been calculated by standard correlation methods (270a) for all substituents for which appropriate data were available. Since neither $\log k$ nor σ can be assumed to be without error, the computations, according to modern statistical theory, required modification of the commonly applied least-squares method. Since the method employed here is rarely used by chemists, the necessary calculations are outlined in an appendix.

Substituent constants derived from reactions which do not fit the Hammett equation reasonably well involve large uncertainties; hence, only reaction series with a correlation coefficient larger than 0.95 were used for the evaluation of substituent constants. This restriction simultaneously eliminates reactions which do not follow the Hammett equation and reactions for which the reaction constant is so small that the common random variations outweigh the systematic substituent effects. The necessity for such a restriction can be seen from the following example: Recently Roberts and Moreland (256a) have evaluated the substituent constant for the m-OH group. One of the reaction series used was reaction 46A. Although the standard deviation ($s = 0.124$) is not particularly large, the correlation coefficient ($r = 0.719$) is so small that this reaction series would not have been used in the evaluations in the present paper. Although the σ-value

TABLE 7

Substituent constants

R	σ_{meta}	$n^{(a)}$	REAC-TIONS[b]	σ_{para}	$n^{(a)}$	REAC-TIONS[b]	σ^*_{para}	$n^{(a)}$	REAC-TIONS[b]
a. Alkyl substituents									
CH₃	−0.069	*		−0.170	*				
C₂H₅	−0.043	1	212b	−0.151	*				
C₃H₇				−0.126	3	27b, 47g			
CH(CH₃)₂				−0.151	*				
C₄H₉				−0.161	2	27b, 47g			
CH₂CH(CH₃)₂				−0.115	2	27b, 47g			
CH(CH₃)C₂H₅				−0.123	1	47g			
C(CH₃)₃	−0.120	4	47j,k, 125, 35	−0.197	*				
(CH₂)₂CH(CH₃)₂				−0.225	1	47g			
C(CH₃)₂C₂H₅				−0.190	2	47g, 80			
CF₃	0.415	4	1a, 26a, 1l, 43	0.551	3	26a, 1l, 43			
CH₂Cl				0.184	1	133			
CH₂CN				0.007	1	134			
CH₂CH₂COOH	−0.027	*		−0.066	*				
b. Hydroxy and alkoxy groups									
OH	−0.002	16	*cf.* table 12	−0.357	27	*cf.* table 9			
OCH₃	0.115	*		−0.268	*				
OC₂H₅	0.150	*		−0.250	*				
OC₃H₇				−0.268	2	1a, 47g			
OCH(CH₃)₂				−0.286	1	47g			
OC₄H₉				−0.320	1	1a			
OC₅H₁₁				−0.340	1	1a			
O(CH₂)₃CH(CH₃)₂				−0.265	1	47g			
OCH₂C₆H₅				−0.415	1	212b			
OC₆H₅				−0.028	10	*cf.* table 8			
O⁻(d)	−0.708	1	70a	−0.519	1	31			
c. Amino and amido groups									
NH₂	−0.161	*		−0.660	*				
NHCH₃	−0.302	1	15a	−0.592	1	15a			
NHC₂H₅	−0.240	1	15a						
NHC₄H₉	−0.344	1	15a						
N(CH₃)₂	−0.211	*		−0.600	17[e]	*cf.* table 8			
NHCOCH₃				−0.015	4	14b, 15a,b, 18			
NHCOC₆H₅	0.217	1	13	0.078	1	13			
NHNH₂	−0.020	1	15b	−0.550	1	15a			
NHOH	−0.044	1	205	−0.339	1	205			
NH₃⁺	0.634	1	22						
NH₂CH₃⁺	0.958	1	14a						
NH₂C₂H₅⁺	0.958	1	14a						
N(CH₃)₃⁺	0.904	3	1l, 26a, 43	0.859	7	*cf.* table 10			
d. Carboxy, carbalkoxy, acyl groups and their derivatives									
COOH	0.355	*		0.265	7	*cf.* table 8	0.728	*	*cf.* table 8
COOCH₃[f]	0.315	6	*cf.* table 8				0.636	5	*cf.* table 8
COOC₂H₅	0.398	6	*cf.* table 8	0.522	7	*cf.* table 8	0.678	2	23a, 212b
COOC₄H₉							0.674	2	23a, 212b
COOCH₂C₆H₅							0.667	1	23a
CONH₂	0.280	1	134				0.627	1	134
CHO	0.355	*		0.216	3	47h,j,k, 11, 130, 184	1.126	*	
COCH₃[g]	0.306	*		0.516	3		0.874	*	
COC₆H₅				0.459	4	47h–k			
CN	0.678	*		0.628	16	*cf.* table 8	1.000	*	
COO⁻	0.104	11	*cf.* table 8	0.132	15	*cf.* table 8			
e. Miscellaneous groups									
NO₂[h]	0.710	*		0.778	*		1.270	*	
NO				0.123	1	27b			
F	0.337	*		0.062	*				
Cl	0.373	*		0.227	*				
Br	0.391	*		0.232	*				
I	0.352	*		0.276	*				
IO₂[i]	(0.70)	1	1a	(0.76)	1	1a			
SCH₃	0.144	5	*cf.* table 8	−0.047	*				
SOCH₃	0.551	1	47h	0.567	1	47h			
SO₂CH₃	0.647	7	*cf.* table 8	0.728	4	1a,l, 47h, 71	1.049	4	23a, 26a
SCN				0.699	1	28			
SeCN				0.664	1	28			
B(OH)₂	0.006	1	26a	0.454	1	26a			
Si(CH₃)₃	−0.121	2	1l, 43	−0.072	2	1l, 43			

TABLE 7—*Concluded*

R	σ_{meta}	n[a]	REAC-TIONS[b]	σ_{para}	n[a]	REAC-TIONS[b]	σ^*_{para}	n[a]	REAC-TIONS[b]
e. Miscellaneous groups—Concluded									
C₆H₅	0.218	*[j]		0.009	*[k]				
N=NC₆H₅				0.640	*				
C₆H₄N=NC₆H₅							1.088	1	26a
CH=CHC₆H₅	0.141	*					0.619	*	
AsO₂H⁻				−0.019	1	1a			
PO₃H⁻	0.228	2	1a,1	0.238	2	1a			
SO₃⁻				0.381	1	23a			
SO₂NH₂				0.621	4	14a,b, 15a, b			
f. Fused-ring systems									
3,4-(CH₂)₃				−0.259	1	125			
3,4-(CH₂)₄				−0.477	1	125			
3,4-(CH)₄ [l]				0.170	*				
3,4-CH₂O₂				−0.159	*				

[a] The number in this column indicates how many estimates were averaged to obtain the substituent constant listed. An asterisk indicates that the value is taken from Hammett (127f).

[b] The numbers in this column refer to the reaction numbers in tables 1 to 3.

[c] For the use with reactions of amines and phenols see Section IV,C.

[d] These values should be considered with reservation (see Section VI,A).

[e] Hammett's value for the dimethylamino group (127f) is apparently incorrect (*cf.* 111 and tables 8 and 9), and has not been used in the calculation of the reaction constants given in this paper.

[f] A separate constant for use with thiols is calculated from reaction 25: $\sigma_{para} = 0.608$, $n = 2$ (*cf.* Section IV,C).

[g] A separate constant for use with thiols is calculated from reaction 25: $\sigma_{para} = 0.697$, $n = 2$ (*cf.* Section IV,C).

[h] A separate constant for use with thiols is calculated from reaction 25: $\sigma_{para} = 1.04$, $n = 2$ (*cf.* Section IV,C).

[i] These values were calculated from a reaction at 50°C. rather than at 25°C. However, the reaction constant and the equilibrium constants vary only slightly with temperature, so that these constants are probably fair estimates (36a).

[j] This constant has been discussed by Lichtin and Leftin (195).

[k] This constant has been discussed by Berliner and Liu (26a).

[l] β-Naphthyl.

for *m*-OH found from this reaction series is well within the range of the other values found, this agreement is probably fortuitous. The standard error (s_σ) (270a) of the estimate of σ-*m*-OH obtained from this reaction series is 0.263, so that the probability is 67 per cent that the correct value lies between −0.22 and +0.30. Obviously, this information is neither precise nor very useful. A substituent constant for the *p*-OH group calculated from the same reaction series is +0.152 ± 0.259. This value of σ is not *significantly* different from the value ($\sigma = -0.357$) given in table 7, as can be shown by a "*t*"-test ($t = 1.97$) (270). Hence, this reaction series is worthless for the determination of new substituent constants. The above restriction of evaluation of substituent constants to only those reaction series for which $r = 0.95$ is necessary to avoid the use of reaction series such as 46A.

In some cases all the data for calculation of reaction and substituent constants did not come from the same investigation; in such cases care was taken that the reaction conditions were identical, or sufficiently similar to make the data comparable.

Table 7 lists all substituent constants so calculated and also includes those previously reported by Hammett (127f). Thus, all substituent constants available at the time of this writing are collected in a single place. The only exceptions are constants for substituents in fused rings, and for hetero atoms replacing the CH group of a ring; these constants are discussed in Sections VII,A and VII,B.

Further, no substituent constants were calculated for groups p-(C_6H_4Z) and p-($N=NC_6H_4Z$), although the necessary data are available from a combination of reaction series 7 and 1t (see 26a) and reaction series 28 and 27b, respectively. It is doubtful that such constants would be of much interest.

Each σ-value reported in table 7 is a mean if more than one value could be calculated, and the number of individual values entering the mean is indicated as n. The reaction series used in the computations are also indicated. Minor differences from values reported by other authors, sometimes even using the same reaction series, result from three factors: (a) the method of computation is somewhat different; (b) the reaction constants often disagree, since many authors have used substituent constants not in Hammett's table; (c) often the

TABLE 8

Precision of substituent constants

R	LIMITS		MEDIAN VALUE	MEAN VALUE [a]	n [b]	REACTION [c]
	Lower	Upper				
p-OH	−0.694	−0.209	−0.335	−0.357 ± 0.104	27	Cf. table 9
p-N(CH₃)₂	−1.049	−0.206	−0.653	−0.600 ± 0.213	17	Cf. table 10
m-OH	−0.134	0.192	−0.018	−0.002 ± 0.106	16	Cf. table 12
p-CN	0.232	0.756	0.660	0.628 ± 0.132	16	1a,l, 43, 47h-k, 50a-c, 90a-d, 130, 189
p-COO⁻	0.055	0.206	0.122	0.132 ± 0.050	15	13, 15a,b, 19, 23a, 47h-k, 203a,b, 82a-d
m-COO⁻	−0.023	0.197	0.099	0.104 ± 0.076	11	13, 15a,b, 47h-k, 82a-d
p-OC₆H₅	−0.109	0.118	−0.053	−0.023 ± 0.080	10	13, 37, 47h-k, 121a, 138, 155, 159
p-COOC₂H₅	0.402	0.554	0.538	0.522 ± 0.053	7	47h-k, 39, 200, 201
m-SO₂CH₃	0.560	0.683	0.666	0.649 ± 0.043	7	1a,l, 23a, 26a, 47h
p-N(CH₃)₃⁺	0.664	1.112	0.876	0.859 ± 0.149	7	1l, 23c,d, 25a,b, 26a, 43
p-COOH	0.210	0.434	0.257	0.265 ± 0.126	7	1a, 14a,b, 84a-d
m-COOC₂H₅	0.383	0.408	0.400	0.398 ± 0.008	6	47h-k, 200, 201
m-COOCH₃	0.258	0.360	0.320	0.315 ± 0.036	6	23c,d, 25a,b, 26a
m-SCH₃	0.109	0.178	0.135	0.144 ± 0.031	5	1l, 23a, 26a, 47j,k
p-COOCH₃ [d]	0.546	0.765	0.619	0.636 ± 0.080	5	23c,d, 26a, 205, 212b

[a] The mean ± its standard deviation is given.
[b] The number of determinations involved in the calculation of the median and mean.
[c] The numbers refer to reaction series in tables 1 to 3.
[d] Substituent constant for reactions of phenols and anilines (σ^*).

number of compounds involved in the calculation of ρ is different. However, considering the precision of the Hammett equation, the agreement is as good as could be anticipated.

For fifteen substituents from five to twenty-seven values of σ have been calculated. These include, in some cases, values from identical reaction series under different conditions, and even occasionally under identical conditions, but reported from different laboratories. For these groups table 8 lists not only mean values of substituent constants, but also their median values, their range, and the standard deviations of the mean values. This table thus illustrates the precision with which substituent constants are known. Median and mean values are seen to agree reasonably well in most cases. However, in many cases the range and the standard deviation of the mean are rather large, indicating the low precision of the Hammett equation. The factors affecting these constants are discussed in the next section.

Branch and Calvin have suggested that certain groups of substituents (e.g., Cl, Br, and I; OH, OCH₃, and OC₂H₅) have, for a given position, substituent

constants which are not significantly different from one another (43a,b). This suggestion is supported by the fact that the order of the effect of these substituents is not constant. A similar situation appears to hold for the p-alkyl groups (methyl, ethyl, isopropyl, and *tert*-butyl),[11] where reversals of order also have been observed (24, 25). The data in table 7 further suggest that, in a given position, substituent constants for amino and alkylamino groups, and for the carboxy, carbalkoxy, carbophenoxy, carbamido, and acetyl groups do not differ materially. Hence, a single substituent constant can probably be used for each of these groups of substituents, and possibly for other groups also. However, since no systematic reëvaluation of substituent constants is being undertaken at this time, and since the data for the evaluation of most of the substituent constants in table 7 are not very extensive, no combined constants for groups of substituents will be proposed.

C. Choice of substituent constants

The substituent constant for the p-nitro group, applicable to most reactions, does not give good results when used with reactions of phenols and anilines. Therefore, a special substituent constant has been defined for these reactions (127f), which we propose to denote by σ^*. Hammett suggested that similar special substituent constants would also be required for certain other electron-attracting substituents, such as CN, COOH, and CHO (127f). This prediction was confirmed for the p-cyano group (254), and a similar conclusion has been reached for the p-methylsulfonyl group (36). Table 7 shows further cases of dual substituent constants in the para-position for electron-attracting groups.

The range of application of the σ^* constants is of interest. The statement that this constant should be applied to the reactions of phenols and anilines leaves unanswered the question what structural changes in a phenol or aniline are permissible without removing the compound from this classification. In the calculations underlying the reaction constants of tables 1 to 3 there occasionally appeared some doubt as to whether σ or σ^* should be used with a given reaction. In such cases correlations with both sets of substituent constants were tried. Comparison of the results has led to the following conclusion: the σ^* constants provide the best fit with all the reactions of phenols, phenolic esters, anilines, and dimethylanilines. Two reaction series of phenolic ethers (ArOR') are included in this review (reactions 86 and 86A). In reaction 86, σ gives a much better fit with the experimental data than σ^*; this fact probably depends on the nature of the group R', which in this case bears two nitro groups, and hence strongly involves the polarizability of the oxygen atom. Reaction 86A, however, requires the σ^* constants.

The reactions of anilides in all of which the substituted aniline is the reaction product also require the use of σ^*, with the possible exception of the methanolysis of the 2-nitroacetanilides (reaction 125). It is doubtful that the applicability of the ordinary substituent constants to this reaction series can be explained by

[11] While little evidence is available for other p-alkyl groups, and for m-alkyl groups, the situation is likely to be quite similar.

the presence of the *o*-nitro group, since reaction 86A has two such groups and still requires the use of σ^*. None of the reactions of the azo, hydrazo, and imino-like compounds listed in section A,IV,d of table 2 require the use of σ^*,[11a] except the reduction of the arylhydrazines to anilines (reaction 132). Similarly, the reduction of substituted nitrobenzenes to anilines by catalytic hydrogenation (reaction 135), by chemical means (reactions 133 and 134), and by polarographic reduction (reaction 205) is best represented by the use of σ^*. Accordingly, it appears that the σ^* constants must be used not only for the reactions of phenols and their esters and ethers, and of anilines and alkylanilines, but also in reactions which lead to the formation of such compounds. Further, reactions in which the polarizability effects of electron-attracting substituents in the para-position are greatly reduced by the presence of other competing groups in the molecule apparently may not require the use of σ^*.

It is not known at this time whether σ^* should be used with reactions of anilides not leading to anilines (e.g., the pK's of anilides) and with reactions occurring in a group linked to the ring through an —O— or —NR— group, when the reaction site is actually beyond the linking group.

The σ^* constants do not appear to apply to reaction 28. Since the side chain in this series is —N=NC$_6$H$_4$N(CH$_3$)$_2$-*p*, so that the dimethylamino group is conjugated with the ring bearing the rate-affecting substituent, it might have been anticipated that σ^* should be used. This reaction series is the only example where a reacting amino or hydroxyl group is conjugated in this manner; hence no generalizations appear justified.

Examination of the data also shows that the free-radical polymerization reactions of substituted styrenes and related compounds appear to be somewhat better represented by the σ^* constants. This might be due to the importance of polarizability effects on the stabilization of the free-radical intermediates. However, the existing data are insufficient in number to permit a definite decision concerning the use of σ^* in this type of reaction. Moreover, substituent effects in most of these reactions are small, and the data are based on reactivity ratios, which do not permit great precision.

A further use of the σ^* constants has been proposed for nucleophilic substitution reactions on the benzene ring bearing the rate-affecting substituent (57), since polarizability effects can be expected to be specially important in such reactions. The available data are not numerous; only three reaction series are available to test this postulate (reactions 202, 204, 204A), and in all three cases σ^* gives very much better fit.

In a few reaction series there arises the problem of deciding whether a substituent is in the meta- or para-position to a side chain. Thus, in reactions of 4-substituted catechols either hydroxyl group may undergo reaction. In the acid dissociations of these compounds (reaction 24) the hydroxyl group in the position

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[11a] *Note added in proof:* The oxidation of the *trans*-azobenzenes (reaction 127B) also requires the σ^* constants. The explanation for this fact can probably be found in the great difference in resonance energy between azo- and azoxybenzene (or between azobenzene and the transition state of the oxidation).

for which the substituent has the larger (more acid-strengthening) substituent constant might be assumed to dissociate first (74). However, since the O^- and OH groups are hydrogen-bonded in the ion, there is very little difference between the ions formed by dissociation of either hydrogen. Hence, an average value of σ_m and σ_p may be expected to represent the data best; such is actually the case (74). Similar assumptions are made in correlating the infrared absorption frequencies of free and hydrogen-bonded hydroxyl groups in the same series of compounds (reactions 213 and 214) (149).

A somewhat similar situation is encountered in the alkaline hydrolyses of phthalide and its derivatives (reactions 57–60). In these compounds the reacting side chain is attached in two places to the ring bearing the rate-affecting substituent; hence the substituent effect may be transmitted to the reaction site by two paths, and separate reaction constants should apply. Since the substituent constants for the two points of attachment are different, the situation is complicated. As a first approximation we have neglected the transmission through the methylene group, and have correlated the hydrolysis rates with σ_m. If the effects through both parts of the side chain are to be included, we must write:

$$\log (k/k^0) = \sigma_m \rho_1 + \sigma_p \rho_2$$

Since only one of the reactions 57–60 involves more than four compounds, no test of this relation was made.

The acid dissociation constants of the 5-substituted 2-furoic acids (reaction 11) also require a choice between σ_m and σ_p. In this case there seems to be little reason to suggest either choice. We have followed Hammett (127f) in using σ_p, which gives a much better fit than σ_m in this series.

D. Factors determining the substituent constants

In Section II it was shown that the substituent constant is a measure of the effect of the substituent on the activation energy of the reaction of the unsubstituted compound.[1] This interpretation of substituent constants is of little practical use, since little is known about the estimation of such energies. Therefore, we shall discuss substituent constants from the viewpoint of electron densities introduced in Section II. This type of interpretation was first suggested by Hammett, who has stated that σ measures the effect of the substituent on the electron density at the reaction site (127f). This view is confirmed by a recent evaluation of the effects of substituents on the electron density in a side chain. The method consisted in measurements of the nuclear magnetic resonance absorption of F^{19} and Cl^{35} in substituted fluoro- and chlorobenzenes (121, 204).

On the basis of the assumption that substituent constants are proportional to changes in electron density induced by the substituents, σ-values can be correlated with electron densities calculated by molecular orbital theory (150–152). Although the theoretical work leaves much to be desired, particularly in terms of the parameters (Coulomb and resonance integrals, inductive parameter) involved in the wave-mechanical calculations, it appears to indicate in which direction theoretical interpretation of substituent constants can be found. Both

resonance and inductive effects are considered in the calculations, and neither effect alone leads to satisfactory results. Price (241, 243) and Westheimer (308) have made some calculations of the effect of substituents based on their electrostatic effects alone. However, their calculations do not appear to indicate that resonance effects can be neglected in the explanation of substituent constants. It seems reasonable to conclude that these constants depend on both inductive and resonance effects of the substituents.

The general applicability of the Hammett equation shows that substituent constants must be essentially independent of the nature of the reacting side chain. However, an important exception to this statement has been noted. Hammett found it necessary to assign two different substituent constants to the nitro group in the para-position (127f). As discussed in Section IV, C, this duality of substituent constants also applies to a number of other electron-attracting substituents in the para-position.

It is believed (36, 43b) that the duality of substituent constants for electron-attracting substituents is connected with the resonance of structures II and III.

Thus, different substituent constants describe the effect of R depending on whether or not structure III is important. Since the importance of structure III may vary widely in a series of side chains, it can be anticipated that there are side chains which require a substituent constant intermediate between the two extreme values. The only case for which such an intermediate value has been observed is Y = SH (reaction 25), and the special σ-values are listed in footnotes to table 7 (see also 35a). It might have been anticipated that special substituent constants would be required for Y = SH, since this group, although electronically closely related to OH, does not resonate as strongly with the benzene ring.

If resonance between structures II and III can lead to a dependence of substituent constant on the nature of the side chain for electron-withdrawing substituents, a similar dependence can be expected for strongly electron-releasing substituents in the para-position.[12] Data presented in this review concerning the substituent effects of the p-hydroxy and p-dimethylamino groups suggest such a dependence on the nature of the side chain. In tables 9 and 10 the various substituent constants obtained for these two groups have been arranged by classes of side chains, and there appears to be a definite variation in substituent constant. With the p-hydroxy group this dependence is further complicated by a solvent dependence, which is discussed below. It is likely that similar effects exist for other groups.

[12] Evidence for such an effect has recently been found by Bordwell (35). In a paper which appeared after this review was written, Hünig, Lehmann, and Grimmer (144a) have discussed the possibility of a multiplicity of substituent constants for electron-repelling substituents. These authors conclude that, for the p-dimethylamino group, there should be two distinct values of σ, rather than a continuous range, as found in this paper (see table 10).

The multiplicity of substituent constants may be interpreted qualitatively in terms of a difference in resonance stabilization between ground and transition states.[1] Any appreciable effect of a substituent on this difference in resonance stabilization can be expected to give rise to an increment in the substituent constant applicable to that particular reaction. This argument suggests that increments of all magnitudes should be observed. Graded series of substituent con-

TABLE 9

The dependence of the substituent constants for the p-OH group on solvent and side chain

SOLVENT	Y = —OH, —SH, —NR₂, —AsO₃H₂, —PO₃H₂			Y = —COOR			Y = —NO₂, —CH=CHC₆H₅, —C₆H₄COOH-p		
	n[a]	σ[b]	REAC-TIONS[c]	n[a]	σ[b]	REAC-TIONS[e]	n[a]	σ[b]	REAC-TIONS[c]
H₂O[d]	5	-0.268 ± 0.049	14a, 15a, 18 23e, 26a	3	-0.328 ± 0.008	1a	2	-0.475 ± 0.105	133, 205
40-80% C₂H₅OH	4	-0.279 ± 0.033	14b, 15b, 23c, 25a	4	-0.339 ± 0.041	1k-n			
90-100% C₂H₅OH Other	2 1	-0.300 ± 0.040 -0.403[e]	23d, 25b 185	4	-0.408 ± 0.043	1o-r	2	-0.628 ± 0.065[f]	7, 207
All	12	-0.288 ± 0.054		11	-0.361 ± 0.050		4	-0.552 ± 0.135	
All side chains and solvents				27	-0.357 ± 0.104				

[a] The number of separate estimates of σ.
[b] The error term is the standard error.
[c] The numbers refer to the reaction numbers in tables 1 to 3.
[d] Including up to 10 per cent of organic solvent.
[e] The solvent is chloroform.
[f] The solvents are 50 per cent butyl Cellosolve and 75 per cent dioxane.

TABLE 10

The dependence of the substituent constant for the p-N(CH₃)₂ group on the nature of the side chain

| Y	n[a]	σ[b]	REACTIONS[c]
NR₂, SiHR₂, Br	7	-0.425 ± 0.165	119a,b, 160, 203a,b, 211a,b
COOR	5	-0.642 ± 0.034	47g-k
CHO	2	-0.972 ± 0.077	141, 142
Others[d]	3	-0.622 ± 0.104	21, 125, 207
All	17	-0.600 ± 0.213	

[a] [b] [c] See table 9.
[d] Y = —CH=CHC₆H₅, —CH=NOH, —NHCOCH₃.

stants are actually encountered for electron-releasing groups (see tables 9 and 10) but have not been noted for electron-attracting groups. The data collected in this review have confirmed Hammett's conclusion (127f) that the substituent constants of the latter groups have either of two discrete values rather than a continuous range. Since our knowledge of the nature and particularly of the energy of transition states is at best sketchy, the argument presented permits little quantitative reasoning about the magnitude of the effects to be expected.[2]

A more quantitative understanding of the multiplicity of substituent constants

appears to be available through the interpretation of reaction rates in terms of electron densities at the reaction site (see Section II). In this approximation we consider only the electron distribution in the initial state. In compounds where resonance between structures II and III is important, the electron density at the reaction site is frequently greatly affected by this resonance. Where the side chain is electron-releasing and the substituent electron-withdrawing, only two sets of substituent constants (σ and σ^*) have been observed, with the exception of the special constants discussed above for Y = SH. However, electron-releasing side chains are few, and the available data refer to Y = NX_2 or OX, with X = H or a hydrocarbon or acyl radical. If the substituent is electron-releasing and the side chain electron-withdrawing (cf. structure IV), the range and variety of side

$$R^+ = \langle \underline{\quad} \rangle = Y^-$$

IV
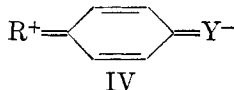
chains are much greater, and accordingly a much greater range of σ's is observed. The "normal" substituent constants for the electron-releasing substituents (e.g., OH and NH_2) should probably be evaluated from reaction series in which either the reaction site is insulated from the benzene ring (e.g., by a methylene group) or the side chain itself is electron-repelling, so that resonance II $\leftrightarrow$ IV is unimportant. Then the substituent constants for these substituents applicable for reactions of compounds involving electron-withdrawing side chains would be analogous to the σ^*. The substituent constants for these groups were actually derived by Hammett from reactions of compounds with moderately electron-withdrawing side chains (COOH or COOR) (127f); hence the values lie somewhere near the center of the possible range and represent roughly a median value. The wide validity of the Hammett equation is in some measure due to this rather fortuitous circumstance.

The above interpretation of the multiplicity of substituent constants leads to the conclusion that the "normal" σ-values must be numerically smaller (closer to zero) than the σ^* or their analogs for the electron-repelling groups. This conclusion is amply verified by the data in tables 7, 9, and 10.

The substituent constant for the p-dimethylamino group reported by Hammett (127f) was obtained from a reaction of N,N,N',N'-tetramethylphenylenediamine and therefore is a "normal" value. It is the lowest of the values given in table 10. This fact explains the difficulties encountered with this substituent constant (see, e.g., 111).

Experimental points for the p-methoxy group in plots of log (k/k^0) against σ frequently deviate greatly from the best straight line. This fact is probably due to a great variability of the substituent constant of this group (cf. 35), which can be expected to behave much like the p-hydroxy group.

Since a complete reëvaluation of substituent constants is anticipated, no separate "normal" values and σ^*-values for electron-releasing substituents are proposed in this paper.

The "English School" interprets the total effects of substituents in terms of

four separate effects (see 250c): inductive, mesomeric, inductomeric, and electromeric. The first two of these have been discussed at the beginning of this section. However, in considering substituent constants, the latter two, which may be combined into a single polarizability effect, have usually been neglected. If we consider these four effects as evaluated from nuclear substitution reactions in monosubstituted benzenes, it can easily be seen that the above explanation of the multiplicity of substituent constants is equivalent to an interpretation in terms of the polarizability of the *substituent groups*.

Polarizability effects may further play an important role. They are believed to operate only in one direction, and only if they can favor a reaction, and their importance varies greatly with the requirements of the reaction (250c). Hence, it is reasonable to assume that they are responsible for some of the deviations from the Hammett equation. In particular the existence of separate lines for the plots of the log (k/k^0) against σ for *m*- and for *p*-substituted compounds (273) may be explained in this manner, since electromeric effects can occur only with *p*-substituents. Hammett has suggested the possibility of including a term in equation 1 to take care of such effects (128):

$$\log (k/k^0) = [\sigma + \sigma'f(\rho)]\rho \tag{5}$$

Here σ' expresses the polarizability effects and vanishes when these effects are unimportant.

In one group of substituents the polarizability effects appear to be specially important. It has long been observed that the *m*- and *p*-phenyl and the β-naphthyl groups frequently lead to serious deviations from equation 1 (see, e.g., 115, 195, 247). The reason for this special position of these groups may be that resonance of the type V ↔ VI occurs in such a way that the substituent either attracts or

repels electrons. Although the *m*-phenyl group cannot be involved by an electromeric effect, its polarizability in terms of the inductomeric effect is large and may operate in either direction. Frequently, rate and equilibrium constants for unsubstituted compounds deviate seriously from the best straight line, possibly also owing to polarizability effects, since the phenyl group can enter in resonance VII ↔ VIII as either donor or acceptor. This effect may be responsible for the

occasional observation that *p*-fluoro and *m*-methoxy substituents appear to be electron-releasing, or that *m*-methyl substituents appear to be electron-attracting.

In considering the structure of substituents, one must recognize that many groups, particularly the more polar ones, can interact with solvent molecules.

Thus, many groups in dilute aqueous solution are almost certainly hydrogen-bonded to water molecules. If such solvent interaction were identical for all substituents, it would not affect substituent constants, but would be included in the solvent-dependent part of the reaction constant. However, solvent effects are probably neither identical nor similar for all types of substituents. Thus, hydrogen bonding of hydroxyl groups to solvent molecules must be important in water, ether, and dioxane, whereas a nitro group cannot be hydrogen-bonded to the latter two solvents, and for methyl groups hydrogen bonding must be much less important in all solvents. Consequently, substituent constants should not be independent of the solvent. Such a dependence for the p-methyl (but not for the m-methyl) group has recently been observed (cf. table 11), and has been

TABLE 11

The dependence of the substituent constant for the p-CH$_3$ group on the solvent (180)

SOLVENT	$n^{(a)}$	σ	SOLVENT	$n^{(a)}$	σ
H$_2$O	9	−0.17	C$_2$H$_5$OH	6	−0.14
25–50% C$_2$H$_5$OH	3	−0.17	CH$_3$OH	1	−0.11
87–98% C$_2$H$_5$OH	5	−0.15	C$_2$H$_5$OH/(C$_2$H$_5$)$_2$O	1	−0.105

(a) The number of values of σ calculated.

TABLE 12

The dependence of the substituent constant for the m-OH group on the solvent

SOLVENT	$n^{(a)}$	$\sigma^{(b)}$	REACTIONS$^{(c)}$
H$_2$O$^{(d)}$	6	0.102 ± 0.073	1a, 14a, 15a, 23e, 26a, 205
40–80% C$_2$H$_5$OH	6	−0.046 ± 0.056	1k, n–o, 14b, 15b
90–100% C$_2$H$_5$OH	3	−0.130 ± 0.004	1p–r
Others	1	0.021$^{(e)}$	212b
All	16	−0.002 ± 0.106	

(a)-(d) See table 9.
(e) The solvent was carbon tetrachloride.

interpreted in terms of the effect of hydrogen bonding on hyperconjugation of the methyl group (180). A solvent dependence of the substituent constant of the p-nitro group has been inferred indirectly by Gutbezahl and Grunwald (120). The evaluation of substituent constants in this review provides further evidence for this effect. When the substituent constants for the m- and p-hydroxy groups are arranged in groups of similar solvents, as in tables 9 and 12, it is seen that some systematic variations exist. The simultaneous variation with the nature of the side chain makes the evaluation of this effect for the p-hydroxy group somewhat uncertain. Similar dependence on solvent also appears to exist for the p-dimethylamino and the p-cyano groups, but in these cases the evidence is not clear-cut. Similar effects can probably be observed with other substituents. No attempt has been made to detect solvent effects on the substituents for which no new substituent constants were evaluated.

Considering the different precision of the reaction series from which the substituent constants have been evaluated, and the complications arising from the

effect of the nature of the side chain, the evidence presented for the solvent dependence of σ might not be completely convincing. Fortunately, a much stricter test of their dependence is available for the m- and p-hydroxy groups. Bright and Briscoe have measured the acid dissociation constants of several substituted benzoic acids in a series of mixtures of water and ethanol (reactions 1k, 1m–1r). These reactions permit evaluation of substituent constants for m- and p-hydroxy groups, in a long series of ethanol–water mixtures; not only is the same side chain involved in each solvent, but essentially the same set of substituents is used to calculate the reaction constants. From the data listed in table 13 it is seen that the substituent constants of both groups decrease uniformly with increasing alcohol concentration.

Hammett has shown that there is no theoretical reason to expect substituent constants to depend on the temperature (126), and no such dependence has ever been observed. If σ were a function of the temperature, the precision of reaction constants should also depend on the temperature, but no such effect can be ob-

TABLE 13

Solvent dependence of substituent constants in a single reaction series

ETHANOL	p-OH	m-OH	REACTION[a]	ETHANOL	p-OH	m-OH	REACTION[a]
per cent				*per cent*			
0	−0.328[b],[c]	+0.124[c]	1a	80	−0.384	−0.111	1o
40	−0.285	−0.014	1k	90	−0.414	−0.126	1p
50	−0.335	−0.055	1m	95	−0.429	−0.129	1q
70	−0.350	−0.102	1n	100	−0.442	−0.134	1r

[a] The numbers refer to the reaction numbers in table 1.
[b] The average of three values.
[c] The reaction constant is 1.000 by definition and the reaction is not strictly comparable to reactions 1k, 1m–1r.

served in tables 1 and 2. The precision with which the Hammett equation represents a given reaction is remarkably constant from temperature to temperature in practically all cases, especially if the reaction constants are based on the same set of substituents.

V. PRECISION OF THE HAMMETT EQUATION

A. General

When the Hammett equation is applied to a series of experimental data, the data are, of course, not exactly represented by the equation. The deviations observed are usually much larger than the experimental error in the determination of the rate or equilibrium constants (91, 125). Hence, it appears important to have reliable measures of the precision with which a given set of data is represented by equation 1.

Although the median deviation of experimental points from the best straight line (regression line) has been used as a measure of this precision (127f), we have chosen the standard deviation (s) from the regression line in order to simplify the computations. The standard and median deviations are equivalent, except that the former indicates the range of two-thirds of the deviations, whereas the latter involves half of them. The standard deviation is proportional to the

probable error ($s = 1.48 \times$ probable error), and the median deviation is usually considered as a measure of the probable error. According to modern statistical theory the standard deviation is the quantity of choice for the estimation of the precision with which data can be predicted by the use of a linear equation such as the Hammett equation. However, s is not independent of the magnitude of the reaction constant, but increases with it. This fact is illustrated in table 14,[13]

TABLE 14

The distribution of s and $| \rho |$[a]

s	$| \rho |$						TOTAL	MEDIAN
	0–0.2	0.2–0.5	0.5–1.0	1.0–2.0	2.0–4.0	>4.0		
0–0.05	11	19	45	13	7	3	95	.851
0.05–0.10	5	17	26	26	30	3	107	1.168
0.10–0.15	2	11	12	22	21	1	69	1.627
0.15–0.20		6	3	8	15	1	33	1.957
0.20–0.25		1	6	9	9	1	26	1.752
0.25–0.30		1	2	1	9	1	14	2.579
0.30–0.40			2	1	5	11	19	4.435
0.40–0.50			1	1	1		3	1.680
>0.50					2	3	5	4.072
Total..............	18	55	97	80	99	21	371	
Median..........	0.033	0.074	0.057	0.106	0.122	0.338	0.091	1.176

[a] The numbers in the table are the numbers of reactions for which the parameters lie between the limits given in the column and row headings. The medians at the right are the median values $| \rho |$ for the given range of r, and the medians at the bottom are the median values of r for the given range of $| \rho |$.

TABLE 15

The distribution of r and $| \rho |$[a]

r	$| \rho |$						TOTAL	MEDIAN
	0–0.2	0.2–0.5	0.5–1.0	1.0–2.0	2.0–4.0	>4.0		
>0.99	1	3	41	30	50	4	129	1.476
0.95–0.99	1	15	33	37	42	9	137	1.455
0.90–0.95	1	6	4	11	4	8	34	1.657
0.80–0.90	3	6	12	2	1		24	.557
0.50–0.80	9	17	7	1	2		36	.309
<0.50	3	8					11	.213
Total..............	18	55	97	80	99	21	371	
Median..........	0.718	0.842	0.984	0.985	0.990	0.957	0.977	1.176

[a] The numbers in the table are the numbers of reactions for which the parameters lie between the limits given in the column and row headings. The medians at the right are the median values of $| \rho |$ for the given range of r, and the medians at the bottom are the median values for r for the given range of $| \rho |$.

where the distribution of s and its dependence on the magnitude of ρ are given. Therefore s is not a good measure of the fit of data to equation 1 if one is interested in the use of the reaction series for the calculation of substituent constants or the prediction of relative values of substituent effects. Accordingly, we have also calculated the correlation coefficient (r) for all the reaction series treated. This latter quantity decreases with ρ (see table 15), and approaches zero when the reaction constant approaches zero, unless all rate or equilibrium constants in the series become identical.

[13] In the tabulations of this section, reactions from tables 1, 2, and 3A only have been considered. Reaction constants in tables 3B and 3C are based on data so different in character that direct comparison of the constants with those in tables 1, 2, and 3A does not appear justified.

Tables 14 and 15 also give the median values for s, r, and ρ for each of the ranges of the other parameters considered. Finally the median value of each of the parameters for the entire body of 371 reaction series[13] is given. The median value of s (0.091) agrees well with Hammett's value for the mean probable error (127f), if the relation between these two quantities mentioned above is recalled.

We have also computed the standard deviation (s_ρ) of the reaction constants in order to be able to apply statistical tests for the difference of such constants. However, owing to the large uncertainty in ρ, it was rarely possible to demonstrate significant differences where they might have been of interest; hence the s_ρ-values are not tabulated in this review. The precision with which reaction constants are known is indicated by the following figures: $s_\rho < 0.05 \times |\rho|$ in 25 per cent and $s_\rho > 0.10 \times |\rho|$ in 47 per cent of all reaction series. Thus, the median value of s_ρ is slightly smaller than 10 per cent of the absolute value of ρ. The large group of reaction constants having $s_\rho > 0.1 \times |\rho|$ includes the reactions which are not greatly affected by substituents, and which accordingly have small values of ρ.

Examination of tables 1 and 2A shows no major differences between the distributions of s and r in the various subsections of these tables; hence, no serious differences appear to exist between the precision with which reactions of different types of compounds are expressed by equation 1. A single exception to this generalization is found in the reactions of the alkyl halides (section A,III,b of table 2), which are discussed in detail below.

On the basis of the dependence of substituent constants on the solvent (*cf.* Section IV,D), the precision of the Hammett equation was expected to depend on the solvent used in the experimental measurements. Since the majority of the substituent constants were evaluated from reactions in aqueous solution, the precision was expected to be lowest in reactions in non-polar solvents. Accordingly, all the reactions in tables 1 and 2A[14] were arranged in groups according to the following solvent classifications: (*a*) water, (*b*) 30–70 per cent alcohol (all aliphatic alcohols), (*c*) alcohols above 80 per cent, (*d*) various mixed aqueous solvents, such as dioxane–water, acetone–water, etc. from 30 to 70 per cent, (*e*) the same solvents, above 80 per cent, (*f*) aromatic solvents (benzene, toluene), (*g*) acetic and sulfuric acids. For each of these groups the distribution of r and s was determined. No major differences in these distributions could be observed; some minor differences noted were probably fortuitous. Thus, the precision seems particularly good for group (*g*), but reactions 167 to 183 were a major portion of this group and are so similar that no normal distribution within such a closely similar group can be expected. Similarly, ten reaction constants from reaction 89 were included in group (*d*) and led to an apparently poor precision for this group. If such sets of similar reactions were not included separately, the differences observed would probably have disappeared.

[14] Tables 2B, 2C, and 3A were excluded from this consideration, since the precision in these tables may differ from that in tables 1 and 2A (see Section VI,A). The distribution of solvents is different in these two groups of tables; hence serious error could have been introduced by inclusion of tables 2B, 2C, and 3A.

On the preceding pages the two measures of the precision of the fit of data to the Hammett equation have been discussed. It seemed desirable to set up a scale of the significance of these parameters. While such a scale is entirely arbitrary, it has helped in the consideration of the data. This reviewer has considered $r >$ 0.99 to indicate excellent, $r > 0.95$ satisfactory, and $r > 0.9$ fair fit to the Hammett equation. If $r < 0.9$ but > 0.8 while $\rho > 1.0$, and if $r < 0.8$ while $\rho > 0.5$, the data are considered as not being adequately represented by equation 1. For small values of ρ the total range of rate or equilibrium constants is usually small, and the constants can therefore be predicted with reasonable precision from the Hammett equation, even when r is small. Such predictions are frequently little better than predictions based on the assumption that substituents have no effect on reactivity.

No scale will be proposed for the significance of the magnitude of the standard deviation from the regression line, since s depends too strongly on the magnitude of ρ. However, reactions are also considered to violate the Hammett equation if s exceeds certain values for certain ranges of ρ, as follows: $s > 0.4$ for all ρ, $s > 0.3$ for $\rho > 3$, $s > 0.25$ for $\rho > 2$, and $s > 0.2$ for $\rho > 1$.

Only 26 of the 371 reaction series listed in tables 1 through 3A are found to violate the Hammett equation according to the above criteria,[15] although many others are expressed only to a relatively rough approximation. In many reaction series reasons for the poor fit to equation 1 are apparent, and these will be discussed in the following paragraphs.

B. Causes of deviations

The reactions constants in tables 1–3 are based on measurements of widely varying precision. However, serious deviations from the Hammett equation probably do not depend on experimental error, except in rare cases (91, 125). Such exceptional cases may be reactions 129 and 149, where the rate constants were evaluated as differences between reactions catalyzed by H^+ and CH_3COOH $+ H^+$. Some reaction constants are based on relative measures of rate constants, such as reactivity ratios, migratory abilities, relative reactivities, and conversion times (see footnotes in table 2), which are subject to relatively large experimental uncertainties. Differences in kinetic order may also be involved in these cases.

Closely related to experimental error are deviations from equation 1 due to reactive or catalytic impurities in the compounds used (20, 155, 156), failure to isolate a single reaction, or complications arising from side reactions. In a few cases reaction constants are calculated from data which, owing to the experimental method employed, were necessarily obtained under slightly varying conditions (e.g., reaction 30).

Another cause for serious deviations from the Hammett equation is found in the approximation inherent in the equation. Thus, the assumptions of the independence of substituent constants of the nature of the side chain, the reaction,

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[15] These reaction series are reactions 30, 33, 47l, 63a, 81, 82c, 82d, 89a, 89f, 96, 99, 101, 123, 127, 129a, 129b, 129c, 136, 149a, 149b, 149c, 166, 168, 185, 193, and 199 of tables 1 and 2.

and the solvent have been shown above (see Section IV,D) to be only approximations. The necessary condition of constancy of entropy changes, or their linear dependence on free-energy changes (Section II), is occasionally violated (e.g., reaction 127). Since entropies of activation are rarely known accurately, the extent to which deviations from the Hammett equation occur for this reason is difficult to evaluate.

Some reaction series appear to violate equation 1, not because of many moderate deviations from the regression line but rather owing to the wide deviation of a single compound.[16] Reactions 33, 471, and 168 are examples of this situation. Thus, reaction 33 would fit the Hammett equation with a correlation coefficient $r = 0.968$ and a standard deviation $s = 0.069$, if the equilibrium constants for the p-methoxy and p-methylmercapto compounds (12) were not included. Similarly, the inclusion of the β-naphthyl derivative in reaction 471 and of the m-methyl derivative in reaction 168 has a great effect on the precision with which these series appear to be represented by the Hammett equation. The reasons for such single large deviations are not understood.

One of the underlying assumptions of the Hammett equation is that all the members of a given series undergo the reaction by the same mechanism. Changes in mechanism which occur within a series can frequently be detected by a change in the kinetic order of the reaction (e.g., 108). Since reaction rate constants derived from reactions of different order do not have the same dimensions, no comparison between such constants is possible. However, many reaction series are studied under conditions which lead to pseudo-first-order kinetics, and under such conditions changes in mechanism need not affect the kinetic order.

If a reaction occurs by two or more competing mechanisms, the susceptibility to the effect of substituents will in general differ between the different mechanisms. Accordingly, one may expect different reaction constants to apply. The situation is illustrated in figure 2. In the region where the rates due to the two mechanisms are comparable, the actual rate will correspond to the sum of the two. Hence, the actual dependence of log (k/k^0) on σ will be given by the curve shown, which must necessarily be concave upward.

Curves of the type of figure 2 have been observed (e.g., 273) and are most frequently encountered in the reactions of alkyl and acyl halides with nucleophilic reagents. A change in mechanism for such reactions is easily visualized (e.g., reaction 96). Brown and Hudson have postulated that transitions from S_N2 to S_N1 mechanisms are responsible for the partial reversal in the normal order of substituents observed in the hydrolysis of benzoyl chlorides in some solvents (53). Swain and Langsdorf doubt the existence of such duality of mechanism and propose that the reactions occur by a concerted process (273). According to their arguments, a delicate balance between bond-breaking and bond-forming steps exists in the transition states. They postulate that the reaction constant is not independent of the substituent constant and demonstrate that a concave

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[16] In such cases the median deviation may be a better measure of precision than the standard deviation, since the median deviation is not seriously affected by a single large deviation.

upward curve should be observed. This author prefers to consider the change in the balance between bond-forming and bond-breaking steps as a gradual change in mechanism. Accordingly, the curvilinear dependence of log (k/k^0) on σ is equally well explained if two distinct mechanisms are involved, or if a delicate balance of two concerted processes is slightly shifted.

If the reaction constants for the two mechanisms discussed above have opposite signs, the plot of log (k/k^0) against σ should have a minimum. Such plots with a minimum have occasionally been observed (e.g., 53).

Among the reactions which appear to fit the Hammett equation least satisfactorily we find, aside from the reactions of the alkyl and acyl halides just dis-
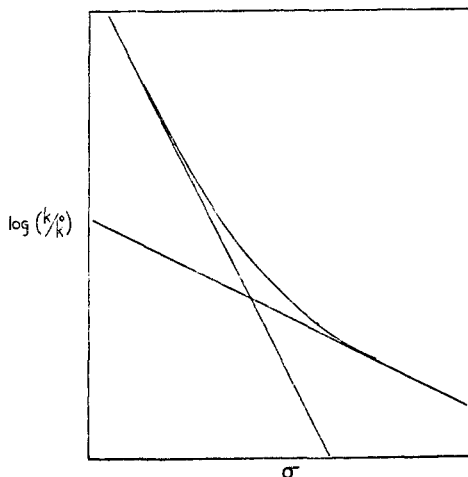
FIG. 2. A plot of log (k/k^0) vs. σ for a change in mechanism ($\rho_1 = 1/4\,\rho_2$ was assumed)

cussed, the esterifications (e.g., reaction 60), the acid hydrolyses of esters (e.g., reaction 84), and the allylic rearrangements of the phenylpropenylcarbinols (reaction 89). All of these reactions involve bond-breaking and bond-forming steps, and probably neither step alone is rate-determining. The balance between the importance of these steps, whether they are concerted or occur subsequent to each other, will depend on the nature of the substituent, and plots of the type of figure 2 can be expected. Such curves are frequently observed in the reactions named (273).

In connection with the above arguments it is interesting to note that a plot of the rates of decomposition of the aryldiazonium cations against σ for para-substituents only is concave downward (59, 79). Such a curve cannot result from a change in mechanism. The data have been interpreted as indicating a competition between a stabilization of the C—N bond by resonance, and an activation by electron-attracting (59) substituents. The rates for the meta-substituents show the normal order and, since no resonance stabilization of the C—N bond is possible, are in agreement with the argument (59).

VI. RANGE OF APPLICATION AND USES OF THE HAMMETT EQUATION

A. Range of application

When the Hammett equation was first proposed, no substituent constants were reported for any substituents carrying an integral charge (ionic substituents). Substituent constants for the $N(CH_3)_3^+$ group (253) and for the COO^- group (27) have since been evaluated. Table 7 lists substituent constants for some further ionic substituents. Since the available data indicate no greater uncertainty for substituent constants of ionic substituents than for those of neutral groups, the Hammett equation also appears to be applicable to substituents which carry an integral charge. Because ionic substituents should be especially subject to interaction with polar solvents, their substituent constants should be particularly solvent-dependent (253). Reactions of compounds with ionic substituents may further be expected to violate the requirement of constancy of entropy changes (or their linear relation to enthalpy changes), since they belong to a different class in terms of the classification according to the ionic or dipolar nature of the reactants (cf. 5). Such entropy effects for ionically substituted compounds have actually been observed in at least one reaction series (reaction 204).

The substituent constants for the O^- group reported in table 7 should be considered with special reservation, considering the difficulties encountered with the hydroxyl group.

Equation 1 was originally proposed to correlate the structure of benzene derivatives with the reactivity of a *side chain* (127f). Some authors have stated or implied that the range of application should be further restricted. Thus, Pearson, Baxter, and Martin (236) have proposed that the substituent constants tabulated by Hammett are valid only for reactions involving nucleophilic attack on the substituted benzene derivative, and must be modified if equation 1 is to be applied to reactions involving electrophilic attack. These authors cite four reactions as evidence for this point of view. One of these reactions involves nuclear substitution, which will be discussed below, and another involves relative migratory abilities, which are only a rough measure of rate constants. Owing to the obvious difficulties in classifying all the reactions listed in table 2A into nucleophilic or electrophilic reactions, no attempt at such a classification has been made. However, at least three groups of reactions undoubtedly involve electrophilic attack on the benzene derivative bearing the substituent. These groups are the reactions of the phenoxide ions in section IIa of table 2A, most of the reactions of the amines in section IVa of table 2A, and the chlorinations of the benzyl phenyl ethers (reactions 167–182). Examination of table 2A reveals that the Hammett equation represents these reaction series as well as the typically nucleophilic reactions, and some of these series are among those best represented. Furthermore, it may be inferred that the rate-determining step in every heterolytic reaction with a negative reaction constant is primarily electrophilic (see 273). Again, no difference in the precision with which the data are represented by equation 1 can be detected between reactions with positive and negative re-

action constants. Also, the substituent constants derived by Pearson, Baxter, and Martin do not differ from Hammett's values more than might have been expected from the variation of substituent constants in table 8. Hence, the Hammett equation applies equally to nucleophilic and electrophilic reactions.

No free-radical reactions were included in Hammett's tabulation (127f). Several authors have questioned whether equation 1 should be valid for such reactions (34, 263, 274). For this reason all free-radical reactions have been collected in table 2B. These reactions do not appear to fit the Hammett equation as well as the reactions in table 2A. However, the less satisfactory fit of the free-radical reactions may be due to the greater experimental difficulties encountered in the precise measurement of the rates of such reactions. Many of the reaction constants of table 2B are based on reactivity ratios and relative reactivities rather than true rate constants. In several reaction series reproducible rate constants could be obtained only by addition of catalysts (reactions 192 and 194) or inhibitors (reaction 186b), and some appeared to depend strongly on trace impurities (reaction 184) (see 155). In spite of these facts, some of the free-radical reactions appear to be represented very satisfactorily by the Hammett equation.

Equation 1 has recently been applied to several reaction series involving substitution in the benzene ring bearing the rate-affecting substituent. The reaction series involving such nuclear substitutions are collected in table 2C. Hammett (127g) recognized that the effect of substituents on the rate of electrophilic nuclear substitution followed σ, at least approximately. The median deviation of the reaction of 4-substituted 2-nitrobromobenzenes with piperidine is appreciably larger than the mean value given by Hammett (27). This fact has been interpreted as evidence that nucleophilic substitution reactions are not as well represented by the Hammett equation as are side-chain reactions (27). However, the reaction constants for nuclear substitution reactions are invariably large, since the reaction site is very close to the substituent; hence large deviations can be expected in view of the relation between the magnitudes of ρ and s. The values of s and r in table 2C are within the normal range for other reactions, if the magnitude of the reaction constants is considered.

The problem of the correlation of the structure of compounds and their biological activity has received considerable attention in recent years. The inhibition of erythrocyte cholinesterase by diethyl phenyl phosphates (reaction 87) is the only reaction involving a biological system included in table 2 and is seen to follow equation 1. However, the Hammett equation does not express, even qualitatively, such important biological properties as the toxicity or the antibacterial activity of arylarsenoxides (96), or the antibacterial (282) or anticholinesterase activity (106) of arylphosphonic and diarylphosphinic acids. Other examples of the failure of the Hammett equation to express such properties might be cited. No systematic search of the literature has been attempted, but the author has never seen any data on biological properties or reactions of biological systems, with the one exception cited above, which follow the Hammett equation even qualitatively. Information concerning the mechanism of such reactions, and particularly of biological activity, is usually extremely sketchy.

In many cases the reactions may not actually involve the side chain, but the molecule as a whole; or they may depend on a superposition of several individual reactions. However, in spite of these findings it seems reasonable that reactions of biological systems should follow the Hammett equation, provided the reaction system is sufficiently simple to permit the isolation of a single reaction of a side chain.

Although the Hammett equation was devised to correlate the structure of certain compounds with their chemical reactivity, certain physical properties of molecules have been correlated with substituent constants. It is not surprising to find that polarographic reduction potentials can be correlated with substituent constants, since these potentials are measures of equilibrium constants. The data in table 3A are listed separately only because of the uncertainties involved in their conversion into equilibrium constants, which arise largely out of the uncertainties of the reference potentials in the mixed solvents used. The data in table 3A fit equation 1 as well as other equilibrium data.

The application of the Hammett equation to infrared spectra is more surprising. The effects of substituents on the infrared frequencies associated with several side chains have recently been correlated with substituent constants (74, 104, 168, 270c). The relevant "reaction constants" are given in table 3B. In order to make these constants dimensionless, they have been calculated by correlating $(\nu - \nu^0)/\nu^0$ with σ. Although the relative effects of substituents are small, the correlation is satisfactory in almost all cases.

Table 3C lists several other "reaction constants" obtained by the correlation of physical properties with substituent constants. The carbon–bromine bond dissociation energies (reaction 215) in benzyl bromides do not appear to be even qualitatively expressed by the Hammett equation. Unfortunately, the kinetic details of the reactions have not been published, but it may be assumed that the free-radical dissociation of a series of benzyl bromides at high temperatures would not obey the Hammett equation. Two reaction series in table 3C involve measurements of the nuclear magnetic resonance phenomenon. This phenomenon is believed to depend on the electron density at the side-chain atom (F^{19} and Cl^{35}, respectively) (121, 204), and a correlation with substituent constants might have been anticipated. The correlation in the chlorine derivatives is reasonably satisfactory, but for the fluorine compounds the authors claim that the meta- and para-substituted compounds lie on separate curves with widely differing slopes (121). The range of meta-substituents studied is so small that this conclusion does not appear too certain. The correlation of the substituent constants with these physical properties appears to give further weight to the view that the reactivity is affected by substituents primarily through the changes they cause in the electron distribution.

Substituent constants have also been correlated with the ultraviolet absorption spectra of monosubstituted benzenes (94). The shift which a substituent causes in the wave length of the primary absorption band[17] of benzene is pro-

[17] The term "primary absorption band" is used as defined by Doub and Vandenbelt (94).

portional to the difference of the substituent constants in the meta- and para-positions ($\Delta\sigma$). Since the effect of substituents on the absorption spectrum of benzene is believed to depend largely on the resonance effect of the substituent (269), this proportionality suggests that $\Delta\sigma$ measures the resonance effect of the substituents and is at variance with Price's view that $\Delta\sigma$ depends primarily on electrostatic effects (241, 242).

It has been noted that the optical rotatory power of certain Schiff bases can be correlated with the pK's of the benzoic acids corresponding to the benzaldehydes used (27b). This fact suggests that there might be a correlation between optical rotatory power, not only in the compounds investigated by Betti but in aromatic compounds in general. This possibility is being examined and will be discussed elsewhere.

B. Uses of the Hammett equation

Equation 1 expresses the rate or equilibrium constants of a large series of reactions of side chains in benzene derivatives in a very simple form to a median accuracy of approximately ±15 per cent (127f). Thus, tables 1 and 2 together with table 7 and equation 1 represent rate and equilibrium constants for 3180 reactions which have been experimentally measured. The same equation furthermore permits the estimation of the rate or equilibrium constants of reactions which have not been determined experimentally, as long as a reaction constant is available for the series, and a substituent constant for the substituents involved. Since table 7 lists substituent constants for 111 different substituents[18] and tables 1 to 3A list 379 reaction constants, equation 1 potentially expresses a total of 42,000 rate or equilibrium constants at this time. This number is constantly growing, as more reaction constants and substituent constants become available. The figure given is somewhat of an overestimate, since it includes some compounds which are either incapable of existence or which cannot undergo a given reaction, owing to interference of the substituent with the reaction of the side chain. Use of equation 6 (see Section VII,A) further greatly extends the number of reaction rate and equilibrium constants which can be estimated.

Since progress is being made in the theoretical calculation of reaction and substituent constants, it is hoped that prediction of rate and equilibrium constants may become feasible without prior experimental determination of all the necessary reaction constants or substituent constants.

Workers interested in the mechanism of organic reactions have found other uses for the Hammett equation. Thus, a knowledge of the sign and magnitude of reaction constants permits certain inferences about the mechanism of a reaction (273) (see Section III,B).

The duality of substituent constants for some electron-attracting substituents (see Section IV, C and D) provides a test for the presence or absence of conjugation of such substituents with the benzene ring. Thus, the appreciable difference between σ and σ^* for the p-methylsulfonyl group has been interpreted as evi-

[18] Here the same group in the meta- and para-positions is counted as two substituents.

dence for strong resonance interaction of this group with the benzene ring (36, 179).[19] A similar use of the dependence of substituent constants of electron-repelling substituents on the nature of the side chain appears possible, although great care is indicated for all such arguments, owing to the relatively large uncertainty in substituent constants and their dependence on the solvents employed (see Section IV, C).[20]

VII. EXTENSIONS OF THE HAMMETT EQUATION

In the preceding sections of this paper the data to which the Hammett equation can be applied have been summarized, the reaction and substituent constants have been discussed, and the precision and range of application of the equation have been treated. In the present section we shall deal with a number of extensions of the equation which have been proposed.

A. Multiple substitution

In several reaction series the effect of substituents on activation energies in polysubstituted compounds can be expressed as the sum of the individual effects of the substituents in the corresponding monosubstituted compounds (166, 267, 272). Since entropies of activation (or entropy changes) are essentially constant in those reaction series, the effects of multiple substituents on rate (or equilibrium) constants must be the sum of the effects of the individual substituents. Hammett has listed a substituent constant for the 3,4-dimethyl substituent (−0.229) which appears to agree well with the sum of the values for m- and p-methyl groups (127f). It appeared desirable to test whether substituent constants are in general additive. Accordingly, substituent constants were calculated for all multiple substitutions for which data could be found, subject to the same restrictions as the calculation of substituent constants for groups not listed by Hammett (see Section IV, B). The relevant data are collected in table 16, where the mean value of the computed constants is compared with the sum of the value for the individual substituents. Considering the variability of substituent constants (see table 8) the agreement is satisfactory. The median deviation is 0.052. No systematic deviations or saturation effects are apparent, since both the mean value of the deviation and the mean value of $|\sigma_{\text{calcd}}| - |\Sigma\sigma|$ are small compared to the median deviation. The additive relation was not expected to hold if the two substituents were adjacent, particularly in cases where steric inhibition of resonance could occur, or where the substituents might be hydrogen-bonded to one another, or where some other strong interaction could be anticipated.

Deviations from additivity have been observed in the deacylation of acetanilides (reactions 123 and 125) and in these reaction series could be attributed to steric inhibition of resonance (307). However, such effects appear to be un-

[19] *Note added in proof:* Recently conjugation of the groups $p\text{-SO}_3^-$ (317a), $p\text{-(CH}_3)_2\text{S}^+$, $p\text{-CH}_3\text{SO}$ (35b), and $(\text{CH}_3)_3\text{Si}$ (18c) with the benzene ring has been demonstrated by similar methods.

[20] *Note added in proof:* Kloosterziel (178a) has recently used substituent constants to detect steric inhibition of resonance of functional groups by ortho-substituents.

important or absent in most reactions, since no systematic deviations are observed in table 16.

TABLE 16

Substituent constants for multiple substituents

R[1]	R[2]	$\Sigma\sigma$	σ_{found}	n[(a)]	REACTIONS[(b)]	Δ
a. 3,4-Disubstitution (3-R[1]-4-R[2]C[6]H[3]Y)						
Cl	Cl	0.600	0.525	4	11, 47j,k, 138	−0.075
Cl	OH	−0.016	−0.049	1	1a	−0.033
Cl	CH[3]	0.203	0.235	2	112, 120	0.032
Cl	OCH[3]	0.105	0.268	1	130	0.163
CH[3]	CH[3]	−0.239	−0.303	4	112, 125, 138, 173	−0.064
CH[3]	NO[2]	0.709	0.694	1	1a	−0.015
CH[3]	OCH[3]	−0.337	−0.265	1	1a	0.072
CH[3]	N(CH[3])[2]	−0.669	−0.302	3	47j,k, 125	0.367
CH[3]	Cl	0.158	0.174	1	130	0.016
CH[3]	NH[2]	−0.720	−0.716	1	125	0.013
OCH[3]	OCH[3]	−0.153	−0.117	5	1a, 8, 31, 47g, 130	0.036
OCH[3]	OH	−0.242	−0.329	1	1a	−0.087
OCH[3]	Cl	0.342	0.338	1	130	−0.004
NO[2]	NO[2]	1.488	1.379	1	1a	−0.109
NO[2]	Cl	0.937	0.901	4	1a, 22, 26g, 112	−0.036
NO[2]	Br	0.942	0.826	1	1a	−0.116
NO[2]	OCH[3]	0.442	0.414	2	1a, 157	−0.028
NO[2]	CH[3]	0.540	0.505	3	22, 125, 138	−0.035
NO[2]	NO[2](c)	1.980	2.036	1	23a	0.056
OH	OH	−0.359	−0.278	1	1a	0.081
NH[2]	CH[3]	−0.331	−0.209	2	47j,k	0.122
N(CH[3])[2]	CH[3]	−0.381	−0.176	2	47j,k	0.205
Br	CH[3]	0.221	0.150	1	138	−0.071
Br	OCH[3]	0.123	0.088	1	138	−0.045
b. 3,5-Disubstitution (3-R[1]-5-R[2]C[6]H[3]Y)						
NO[2]	NO[2]	1.420	1.395	2	1a, 47g	−0.025
NO[2]	Cl	1.083	1.073	1	1a	−0.010
OCH[3]	OCH[3]	0.230	0.050	3	1a, 80, 130	−0.180
OCH[3]	Cl	0.488	0.439	1	130	−0.049
CH[3]	CH[3]	−0.138	−0.173	7	47i–k, 112, 119c, 130, 212b	−0.035
CH[3]	Cl	0.304	0.347	1	130	0.043
Br	Br	0.782	0.720	3	47j,k, 112	−0.062
Cl	Cl	0.746	0.746	1	130	0.000
OH	OH	−0.004	0.162	1	1a	0.166

c. Trisubstituted compounds (3-R[1]-4-R[2]-5-R[3]C[6]H[2]Y)

R[1]	R[2]	R[3]	$\Sigma\sigma$	σ_{found}	n[(a)]	REACTIONS[(b)]	Δ
OCH[3]	OCH[3]	OCH[3]	−0.038	0.075	2	31, 47g	0.113
OCH[3]	OH	NO[2]	0.468	0.433	1	1a	−0.035
OH	OCH[3]	NO[2]	0.444	0.634	1	1a	0.190

[(a)] The number of estimates of σ_{found}.
[(b)] The numbers in this column refer to the reaction numbers in tables 1 to 3.
[(c)] The nitro group requires the σ^*-value.

The data presented demonstrate that the effect of multiple substitution on the reactivity of the side chain can be expressed by the Hammett equation in the form (154):
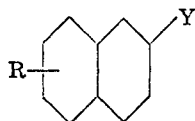
$$\log (k/k^n) = \rho\Sigma\sigma \qquad (6)$$

Another type of multiple substitution occurs where a benzene ring is fused to another ring. Hammett has given substituent constants for two such systems: namely, β-naphthyl and phenyl-3,4-methylenedioxy derivatives (127f). Two further constants for fused-ring systems are given in table 7: namely, for hydrindene [substituent 3,4-(CH[2])[3]] and tetralin [substituent 3,4-(CH[2])[4]] with

reacting side chains in the 5- and the 6-position, respectively. However, since each of these constants is based only on a single determination, no test of their constancy and usefulness is available.

Price (247) has initiated a program for the determination of substituent constants in naphthalene. Constants are reported for several substituents in the 5-, 6-, 7-, and 8-positions of naphthalene which have the reacting side chain in the 2-position. Unfortunately, these values are based on a reaction (the alkaline hydrolysis of ethyl benzoates in 70 per cent dioxane at 25°C., reaction 471) for which no reaction constant was available from prior work. Accordingly, the reaction constant was evaluated by inclusion in the reaction series of three compounds with substituents of known σ. The three rate constants on which the reaction constant was based fit the Hammett equation very well, but the rate for ethyl β-naphthoate did not. In spite of these shortcomings the substituent constants for the substitution in the naphthalene ring are probably not seriously

TABLE 17

Substituent constants in naphthalene derivatives

R	Y =			R	Y =		
	COOC₂H₅ (247)	NH₂ (55, 56)	OH (318)		COOC₂H₅ (247)	NH₂ (55, 56)	OH (318)
5-NO₂.......	0.407	0.501		8-NH₂.......	−0.206		
6-NO₂.......		0.594		8-N(CH₃)₂...	−0.071		
7-NO₂.......		0.512		5-SO₃⁻.......		0.215	
8-NO₂.......	0.322	0.608		6-SO₃⁻.......		0.293	0.349
6-OCH₃......	−0.164			7-SO₃⁻.......		0.218	
7-OCH₃......	−0.044			8-SO₃⁻.......		0.240	0.303
5-NH₂.......	−0.068						

in error. They are reproduced in table 17. The same table includes, for comparison, substituent constants calculated from the acid dissociation constants of substituted β-naphthylamines (55, 56) and β-naphthols (318). The few possible comparisons show reasonable agreement, with the exception of the 8-nitro group. Since the 8-position permits quinoid structures with the 2-position, this disagreement is not astonishing. Accordingly, dual substituent constants for the electron-attracting substituents will be necessary for the positions for which quinoid resonance structures can be written.

A similar program of evaluation of substituent constants for the substituents in the homonuclear ring of quinoline relative to side chains in the heteronuclear ring is being undertaken by McKee and Bailey (203).

B. Heterocyclic compounds

The acid dissociation constants of all the possible quinolinecarboxylic acids and the alkaline hydrolyses of their methyl esters have been investigated (97),

and the "substituent constants" for the side chains in the various positions in quinoline were thus derived. Jaffé has collected data from the literature for the reactivities of side chains in pyridine, quinoline, and isoquinoline, and has correlated these values with electron-density calculations (152). On the basis of such calculations substituent constants for all positions in isoquinoline, pyrimidine, acridine, phenanthridine, and phenazine were predicted. The experimentally determined substituent constants are reproduced in table 18.

Since the Hammett equation does not apply to substituents in the ortho-position, it appears questionable whether it can be applied to positions in heterocyclic compounds in which the side chain is vicinal to the hetero atom or the fused-ring system (152). Too few data are available at the present time to answer this question. The data available in the literature for other heterocyclic systems also are too scarce to be useful and are not collected in this review.

TABLE 18

"Substituent constants" for heterocyclic compounds

COMPOUND	POSITION[a]	SUBSTITUENT CONSTANT FROM		
		Reaction 47g	Reference 97[b]	Others [c]
Pyridine...	2	0.81		0.40 (196)
	3	0.62		
	4	0.93		
Quinoline.......................................	2	0.92	0.74	
	3	0.64	0.52	
	4	0.76	0.59	
	5		0.37	
	6		0.23	
	7		0.24	
	8		−0.06	−0.11 (23a)
Isoquinoline....................................	1	0.70		

[a] All positions are numbered in accordance with the *Ring Index* (232).
[b] These substituent constants were based on some reasonable assumptions of reaction constants by the authors (97).
[c] The number in parentheses is the reaction number from tables 1 and 2.

C. Constant ortho-substituents

The additivity of substituent constants for multiple substitution has an interesting corollary. Consider two series of compounds, IX and X:

IX   X

Since the effects of substituents R^1 and R^2 in X can be expressed through equation 6, it follows that

$$\log (k/k^0) = \sigma_1\rho + X \qquad (7)$$

where $X = \sigma_2\rho$, and σ_1 and σ_2 are the substituent constants of R^1 and R^2, respectively. It follows immediately that the series of reactions of compounds X in

which only R^1 is varied, while R^2 is the same for the whole series, can be expressed through equation 1,[21] and that the reaction constant for such a series is the same as for the same reaction of a series of compounds having structure IX. Hence, the substituent R^2 does not affect the reaction constant. The arguments presented are independent of the position of R^2. Furthermore, the additivity of substituent effects on activation energies referred to in Section VII,A also holds for substituents in the ortho-position (166, 267, 272). Hence, it can be assumed that the reaction constant for a series of reactions in compounds of structure XI is
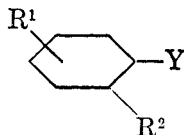
XI

independent of the nature of R^2, and therefore identical to the constants for the same reactions in compounds having the structure shown in IX. Experimental verification for this conclusion is available from the work of Roberts and Yancey (258) and from several other reaction series which are summarized in table 19. Accordingly, the effects of substituents R^1 in compounds having the structure shown in XI can be expressed by equation 7 (154), where X is a measure of log $k(o\text{-}R^2C_6H_4Y)$ — log $k(C_6H_5Y)$. Since the Hammett equation does not apply to ortho-substituents, the quantity X, however, cannot be evaluated in terms of substituent and reaction constants.

Two restrictions are necessary for the use of equation 7. (*a*) The reaction mechanism must not be affected by the ortho-substituent R^2. Thus, the relation does not hold for the alkaline hydrolysis of the para-substituted ethyl 2,6-dimethylbenzoates (reaction 51), since the mechanism is not the same as that for the alkaline hydrolysis of the ethyl benzoates (112). (*b*) Equation 7 does not usually hold for the substituent R^1 in the 3-position (when R^2 is in the 2-position), since the steric interaction of R^2 and Y is affected, and the resonance of R^2 may be inhibited by substituents in the 3-position.

D. Compounds involving several substituted benzene rings

The Hammett equation has occasionally been applied to compounds containing more than one benzene ring. The ethanolysis of benzhydryl chlorides (reaction 100), $Ar(C_6H_5)CHCl$, is an example of the simplest type of such applications. In this case only one ring is substituted, the side chain Y is C_6H_5CHCl, and the Hammett equation is strictly applicable. The situation is unchanged if the unsubstituted ring is replaced by a substituted ring (ZC_6H_4), provided the substituent Z is the same throughout a series of compounds.

A more complicated situation is encountered if both rings are equally sub-

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[21] It should be noted that for such a series k^0 refers to the compound $m\text{-}R^2C_6H_4Y$ and is given by

$$\log k(m\text{-}R^2C_6H_4Y) - \log k(C_6H_5Y) = \sigma_2\rho$$

TABLE 19

The effect of ortho-substituents on the reaction constant[a]

REACTION	SOLVENT	X = H	X = NO₂	X = OH	X = Cl	X = CH₃	X = OCH₃
R—⟨⟩(X)COOH, pK's	H₂O, 50% C₂H₅OH	1.000 (1a), (1.423) (1l), (1.601) (1m)	0.905 (2)	1.103 (4)	0.855 (5)	1.430 (3a), 1.673 (3b)	
R—⟨⟩(X)COOH, pK's	50% C₂H₅OH	1.000 (1a)[b]				1.116 (6)[i]	
R—⟨⟩(X)PO(OH)₂, pK's	50% C₂H₅OH	0.986 (14b)			0.995 (16b)[g]		
R—⟨⟩(X)PO₃OH⁻, pK's	H₂O, 50% C₂H₅OH	0.994 (15a), 0.885 (15b)			0.908 (17a)[g], 1.191 (17b)[g]		
R—⟨⟩(X)OH, pK's		3.197 (23b)[b]		3.512 (24)[c]			
R—⟨⟩(X)COOH + (C₆H₅)₂CN₂ → COOCH(C₆H₅)₂	C₂H₅OH	0.940 (43)				0.946 (45)	
R—⟨⟩(X)NH₂ + C₆H₅COCl → NHCOC₆H₅	C₆H₆	-2.781 (112)				-2.727 (117)	-2.609 (118)
R—⟨⟩(X)NHCOCH₃ + CH₃OH → NH₂	CH₃OH	2.151 (123)	1.723 (125)				
R—⟨⟩(X)Br + C₅H₁₀NH → NC₅H₁₀		4.871 (202)[d]	4.918 (203a)[e], 4.865 (203b)[f]				

(a) The numbers in the body of the table are the reaction constants taken from tables 1 to 3, and the numbers in parentheses are the reaction numbers from these tables.
(b) In 30 per cent ethanol.
(c) In 40 per cent dioxane.
(d) In benzene at 99°C.
(e) In piperidine at 25°C.
(f) In piperidine at 35°C.
(g) X = Cl or Br.
(h) In water.
(i) In 20 per cent dioxane.

stituted, as in the dehydrochlorination of the 1,1-diaryl-2,2-dichloroethanes (reaction 110). The validity of applying the Hammett equation to such systems (e.g., 24, 34) must be judged by the success in the treatment of experimental data. In the calculation of the reaction constants of tables 1 and 2 for symmetrically substituted compounds, the Hammett equation has been used in the form (24, 34)

$$\log (k/k^0) = n\sigma\rho \tag{8}$$

where n is the number of substituted rings. Equation 8 was used in order to make the magnitudes of substituent constants comparable. Had the factor n not been included, the reaction constants would express the simultaneous effect of two substituents. The reaction series belonging to this class are summarized in table 20; they obey equation 8 to a reasonable approximation.

TABLE 20

Reactions to which equation 8 is applicable

REACTION NO. [a]	ρ	s [b]	r [b]	n [b]	REACTION NO. [a]	ρ	s [b]	r [b]	n [b]
186a	−0.201	0.172	0.687	10	110a	2.456	0.192	0.972	8
109c	2.459	0.212	0.966	6	76a	1.568	0.094	0.995	9
110b	2.359	0.184	0.972	6	76b	1.246	0.088	0.969	7
110c	2.336	0.189	0.970	6	36	0.782	0.061	0.979	4

[a] Reaction numbers from tables 1 to 3.
[b] The column headings have the same meanings as in tables 1 to 3.

The validity of equation 8 shows that reaction constants are essentially independent of substituents in benzene rings forming part of the side chain. The correctness of this statement is verified by the following arguments. The left-hand side of equation 8 can be divided into the sum of two terms, as follows:

$$\log \frac{k(Ar_2 CHY)}{k((C_6 H_5)_2 CHY)} = \log \frac{k(Ar_2 CHY)}{k(Ar(C_6 H_5)CHY)} + \log \frac{k(Ar(C_6 H_5)CHY)}{k((C_6 H_5)CHY)} \tag{9}$$

The first term on the right-hand side corresponds to the variation of a substituent in one ring only, while the other ring remains constant, and the side chain is ArCHY. The second term in the right-hand side of equation 9 is similar, but it corresponds to the reaction series in which the second ring is unsubstituted (side chain is C_6H_5CHY). Since the side chains are not identical for these two terms, they should be expressed through equation 1 with different reaction constants, and the right-hand side of equation 9 becomes $\sigma(\rho_1 + \rho_2)$. The validity of equation 8 is possible only if ρ_2 is independent of the nature of the substituent and hence identical with ρ_1. In other words, the presence of a substituent in one ring has no effect on the reaction constant for a substituent in the other ring.

This argument leads immediately to a further extension of the Hammett equation (154) which has been used by some authors without a discussion of its implications (e.g., 198, 199, 274) and which has been justified only empirically.

In compounds which contain unequally substituted benzene rings symmetrically located with respect to the reaction site (e.g., $Ar^1Ar^2SeBr_2$, reaction 34), the Hammett equation has been applied in the form

$$\log (k/k^0) = \rho(\sigma_1 + \sigma_2) \tag{10}$$

where σ_1 and σ_2 are substituent constants of the substituents in groups Ar^1 and Ar^2, respectively. The reaction constants obtained by use of equation 10 are summarized in table 21. Wherever sufficient data were available, reaction constants have been calculated for the variation of the substituent in one ring only, and for the symmetrical variation of the substituents in both rings. These data permit comparison of the precision of reaction constants calculated by means of equation 10 and equation 1, and any decrease in the precision can be attributed directly to the use of equation 10. Therefore this comparison appears to be a

TABLE 21

Reaction series to which equation 10 is applicable

REACTION NO.[a]	Ar^1Ar^2Y				$(Ar)_2Y$				$Ar(C_6H_5)Y$			
	ρ	n	s	r	ρ	n	s	r	ρ	n	s	r
206	−0.235	12	0.030	0.952	−0.256	5	0.017	0.995	−0.248	7	0.035	0.976
37	2.121	14	0.149	0.982	2.098	8	0.133	0.982	2.244	6	0.106	0.985
35	−3.974	6	0.291	0.955	(b)				(b)			
155a	0.622	5	0.166	0.846	(b)				(b)			
155b	0.743	5	0.097	0.952	(b)				(b)			
155c	0.790	5	0.101	0.961	(b)				(b)			
155d	0.846	5	0.075	0.980	(b)				(b)			
207	0.251	5	0.022	0.960	(b)				(b)			
144	0.363	7	0.057	0.923	(b)				(b)			
186b	−0.374	15	0.080	0.932	−0.364	11	0.091	0.926	−0.431	4	0.075	0.942
109a	2.659	8	0.284	0.969	2.711	6	0.235	0.966	(b)			
109b	2.604	8	0.270	0.970	2.647	6	0.221	0.968	(b)			
210A	0.0085	13	0.0011	0.955	0.0078	5	0.0008	0.988	0.0093	8	0.0012	0.944
38	−1.302	5	0.074	0.985	(b)				(b)			
99	−4.072	5	0.527	0.932	(b)				−4.298	4	0.368	0.978
101	−2.755	6	0.570	0.651	(b)				0.184	4	0.640	0.034

[a] Reaction numbers from tables 1 to 3. The column headings have the same significance as in those tables.
[b] Insufficient data available for the calculation of a reaction constant.

better test of this equation than comparison of the standard deviations and correlation coefficients with median values derived from tables 1 and 2.

Table 21 shows that equation 10 expresses the data with approximately the same precision as equation 1 applied to the compounds involving only one substituted ring, or both rings substituted symmetrically.

Thus, the reaction constant for the variation of a substituent in one ring is not affected by a substituent in another ring in compounds where the rings are symetrically placed with respect to the reaction site. Hence, it is reasonable to assume that reaction constants for the variation of substituents in one ring will also be independent of substituents in the other ring in compounds where the rings are not symmetrically placed with respect to the reaction site. Accordingly, effects of substituents in these latter compounds should be represented by equation 11 (154):

$$\log (k/k^0) = \sigma_1\rho_1 + \sigma_2\rho_2 \tag{11}$$

Unfortunately, only a few reaction series to which equation 11 should apply have been investigated. In many of these series all compounds studied were substituted only in ring Ar^1 or Ar^2, but not in both. In that case the reaction series can be expressed in terms of equation 1, using different equations according to whether the substituent is in ring 1 or ring 2. The regression lines so obtained will generally not lead to identical values of $(\log k^0)_{calcd}$. Use of equation 11, on the other hand, permits only a single value of $(\log k^0)_{calcd}$, and hence will lead to slightly different values for the reaction constants and appear to give slightly lower precision. In accordance with these considerations it was felt of little interest to compute special reaction constants based on equation 11 for series which did not involve compounds in which both rings are substituted (reactions 128 and 148, 136 and 137, 129 and 149, 192 and 194, 193 and 195 are pairs of such reaction series).

Only five reaction series have been investigated which permit an actual test of the validity of equation 11. These series are summarized in table 22, where essentially the same information is given as in tables 1 to 3. However, the standard errors of the reaction constants (s_ρ) are included. The constants ρ_1 and ρ_2 refer to rings Ar^1 and Ar^2, respectively. R is the multiple correlation coefficient (270b) and is closely analogous to the correlation coefficient r. The calculations of the data in table 22 were made by standard least-square methods for multiple regressions (270b). Footnotes give the relevant data from table 2 for comparison. Since they do not appear in table 2, we have included two reaction series (the last two reaction series in table 22) which involve no compounds substituted in both rings.

The precision of the reactions in table 22 appears to be no poorer than the precision of the corresponding reactions involving variation of substituents in one ring only. Furthermore, equation 11 expresses many more reaction or equilibrium constants than are expressed by a single equation.

It might have been anticipated that rates and equilibrium constants of reaction series of the type:

$$Ar^1Y^1 + Ar^2Y^2 \rightarrow products$$
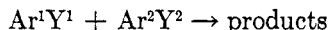
would also be represented by equation 11. Only three such reaction series have been found where rates were available for compounds substituted in both ring 1 and ring 2 (229, 272, 301, 314). In all cases serious deviations were observed. It thus seems that the reaction constant for the attack of Ar^1Y^1 on $R^2C_6H_4Y^2$ depends on the nature of R^2; hence equation 11 does not hold for such reactions.

E. Ortho-substituents and aliphatic compounds

Recently a linear free-energy relationship similar to the Hammett equation but applicable to aliphatic and ortho-substituted aromatic compounds has been proposed (278, 279). This relation, however, is applicable only to a restricted class of reaction series, and among the ortho-substituents fluorine, the amino group, and hydrogen (the unsubstituted compound) must be excepted. Since these substituents have the smallest Van der Waals radii, some of the steric inter-

TABLE 22

Test of the validity of equation 11(a)

REACTION	SOLVENT	T °C.	$\rho_1 \pm s_\rho$	$\rho_2 \pm s_\rho$	s	n	$R^{(b)}$	$-\log k^0$	REFERENCES
Ar¹CHOHCOAr² + O₂ → Ar¹COCOAr²(c)	(Not given)	10 / 20	1.553±0.379 / 1.362±0.297	1.437±0.379 / 1.442±0.297	0.142 / 0.112	12 / 12	0.966 / 0.976	2.746 / 2.323	(304) / (304)
H [Ar¹CONOCOAr²] + NH₃ → Ar¹NCO + Ar²COO⁻ (d)	1 N NH₃, H₂O	30	-2.751±0.102	0.851±0.036	0.069	11	0.993	4.009	(251)
Ar¹CAr² → Ar¹CONPicr(e) NOPicr Ar¹	CCl₄	80(f)	-4.113±0.574	-2.166±0.574	0.199	7	0.984	4.161	(66)
(trans)-Ar¹N=NAr² + C₆H₅CO₃H → (trans)-Ar¹N(O)=NAr²(i)	C₆H₆	15	-1.740±0.178	-1.351±0.082	0.110	19	0.987	3.984	(9a)
		25 / 30	-1.678±0.175 / -1.638±0.173	-1.309±0.081 / -1.281±0.080	0.108 / 0.107	19 / 19	0.986 / 0.986	3.566 / 3.393	(9a) / (9a)
Ar¹CH=NAr² + H₂ + PtO₂ → Ar¹CH₂NHAr²(h)	C₂H₅OH	24-25	-0.406±0.184	0.524±0.364	0.226	20	0.277	5.557	(259)
$Ar^1N=C(C_6H_5)NAr^1Ar^2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} Ar^1NC(C_6H_5)=NAr^2$(g) for k_1 for k_2	No solvent No solvent	330 / 330	1.521±0.068 / 1.978±0.127	-0.018±0.068 / -0.404±0.127	0.049 / 0.091	6 / 6	0.997 / 0.995	4.497 / 4.270	(68, 69) / (68, 69)

(a) The meaning of the column headings is the same as in table 1.

(b) The multiple correlation coefficient R closely corresponds to the correlation coefficient r used in tables 1 to 3.

(c) For comparison, from application of equation 1 to symmetrical compounds only, at 10°C.: $\rho_1 + \rho_2 = 2.858\pm0.357$, $r = 0.963$, $s = 0.166$, $n = 7$ and at 20°C. $\rho_1 + \rho_2 = 2.669 \pm 0.272$, $r = 0.975$, $s = 0.126$, $n = 7$ (reaction 195).

(d) For comparison, from application of equation 1 to compounds substituted in one ring only: $\rho_1 = -2.593\pm0.295$, $r = 0.982$, $s = 0.088$, $n = 5$, $-\log k^0 = 4.587$ (reaction 69); $\rho_2 = 0.867\pm0.005$, $r = 1.000$, $s = 0.003$, $n = 4$, $-\log k^0 = 4.634$ (reaction 70).

(e) Picr stands for the radical 2,4,6-(NO₂)₃C₆H₂.

(f) Many of the data were interpolated or extrapolated to 80°C.

(g) These reaction series involve 3,5-Cl₂C₆H₃— groups, for which $\sigma = 0.746$ ($= 2 \times 0.373$) was assumed (cf. Section VII,A). The series do not provide a test for equation 11, since Ar¹ and Ar² were not varied simultaneously. The series were included however, since they are not included in table 2.

(h) For comparison, from application of equation 1 to compounds substituted in one ring only: $\rho_1 = 0.386\pm0.181$, $r = 0.579$, $s = 0.210$, $n = 11$, $-\log k^0 = 5.664$ (reaction 149A); $\rho_2 = 0.237\pm0.424$, $s = 0.235$, $r = 0.222$, $n = 8$, $-\log k^0 = 5.576$ (reaction 129A).

(i) Based on $\sigma_1 < \sigma_2$, which assumes that reaction occurs only at the more active nitrogen atom. A better expression for the representation of this reaction series than equation 11 may be $k/k^0 = \frac{1}{2}[10^{(\sigma_1\rho_1 + \sigma_2\rho_2)} + 10^{(\sigma_2\rho_1 + \sigma_1\rho_2)}]$, which takes into account reaction at both nitrogen atoms. Badger and Lewis (9a) suggest the use of equation 10, which leads to: 15°C.: $\rho = -1.448 \pm 0.063$, $s = 0.116$, $r = 0.984$; 25°C.: $\rho = -1.402 \pm 0.062$, $s = 0.114$, $r = 0.984$; 30°C.: $\rho = -1.370 \pm 0.060$, $s = 0.112$, $r = 0.984$ (reaction 127B).

actions of the ortho-substituents with the side chain appear to be included in the Taft equation.

The constancy of the entropy terms, or their direct dependence on the enthalpy terms, is a necessary condition for the validity of the Hammett equation. These relations of entropy terms are believed to depend on the great rigidity of the benzene ring. This argument suggests that a linear free-energy relation similar to the Hammett equation should apply to aliphatic systems in which a similar rigidity of the grouping between rate-affecting "substituent" group and reacting "side chain" can be achieved. This hypothesis has recently been tested (256), and it was found that a linear free-energy relation holds if the benzene ring is replaced by a bicyclo[2.2.2]octane system. Substituent constants in this system, which must depend entirely on electrostatic effects, do not agree with those in the benzene derivatives. Hence, it may be concluded that substituent constants in aromatic systems must involve resonance effects.

VIII. APPENDIX: CALCULATIONS

In this appendix we shall outline the correlation methods used in the calculations reported in this review, since they include some features not commonly used in chemical applications. Only formulas will be given, and for their derivation and justification the reader is referred to standard texts on statistics (e.g., 270a).

We desire to correlate $\log k$ with σ, obtain the slope (ρ) of the regression line, the standard deviation (s) from this line, the correlation coefficient (r), etc. Let $\log k$ be denoted by Y. The computations then require the following quantities:

$$\Sigma(\sigma - \bar{\sigma})^2, \; \Sigma(Y - \bar{Y})(\sigma - \bar{\sigma}), \quad \text{and} \quad \Sigma(Y - \bar{Y})^2$$

which will be denoted by Σx^2, Σxy, and Σy^2, respectively; the barred quantities are the mean values of σ and Y. The above quantities are easily computed in terms of the sums of, and the sums of the squares of σ and Y:

$$\Sigma x^2 = \Sigma \sigma^2 - (\Sigma \sigma)^2/n$$
$$\Sigma xy = \Sigma(\sigma Y) - (\Sigma \sigma)(\Sigma Y)/n$$
$$\Sigma y^2 = \Sigma Y^2 - (\Sigma Y)^2/n$$

All quantities of interest can be directly computed in terms of these magnitudes:

$$\rho = \Sigma xy/\Sigma x^2$$
$$r = \sqrt{(\Sigma xy)^2/(\Sigma x^2)(\Sigma y^2)}$$
$$s = \sqrt{[\Sigma y^2 - (\Sigma xy)^2/\Sigma x^2]/(n - 2)}$$
$$s_\rho = s/\sqrt{\Sigma x^2}$$

$$(\log k^0)_{\text{calcd}} = \bar{Y} - \rho \bar{\sigma}$$

Hence, the best straight line for the prediction of rate or equilibrium constants is given by:

$$\log k = \bar{Y} - \bar{\sigma}\rho + \sigma\rho$$

However, since σ's are not known without uncertainty, this line should not be used for the calculation of new substituent constants (270a). For this purpose a different line is best suited; its slope b is given by

$$b = \Sigma xy / \Sigma y^2$$

If the correlation is perfect ($r = 1$), $b = 1/\rho$. Otherwise, b corresponds to minimizing the squares of the deviations along the σ-axis, whereas ρ corresponds to minimizing the squares of the deviations along the Y-axis. b can always be obtained from ρ by the relation $b = r^2/\rho$. New σ's are given by the expression:

$$\sigma = \bar{\sigma} - b\bar{Y} + bY$$

The correlations using equation 11 were performed using standard methods for multiple regression (270b) and require no further comment.

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