The Application of the Hammett Equation to Polycyclic Aromatic Sets. I. Quinolines and Isoquinolines

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We have studied the application of the Hammett equation to 17 sets of quinolines and isoquinolines substituted in the benzenoid ring. Values of pK_a taken from the literature were correlated with the σ_I, σ_m, and σ_p constants and with substituent constants calculated by the method of Dewar and Grisdale. We find that the more readily available σ_m and σ_p constants generally afford better correlations than do the Dewar–Grisdale constants. The Dewar–Grisdale treatment assumes that the value of ρ is constant and is therefore unaffected by the nature of the group to which substituent and reaction site are attached. We find that this is not the case; ρ values obtained from correlations with the Dewar–Grisdale substituent constants differ by a significant amount in the majority of the cases examined. We have re-examined the question of tautomerism in the 7-hydroxyquinolines, and the 4-, 6-, and 8-hydroxyisoquinolines. In contradiction to an earlier report, we find that the phenol tautomer predominates for 4-hydroxyisoquinoline in water. Electrical effects in quinolines and isoquinolines are discussed.

We have recently had occasion to examine the application of the Hammett equation[1] (eq. 1) to quinolines and isoquinolines substituted in the heterocyclic ring.[2] It seemed of interest to extend this work to the benzenoid ring of these systems. Although no previous studies on this problem have appeared, several authors have examined the related problem of substituent effects in naphthalene sets.[3-6] Three approaches to the treatment of substituted naphthalene sets have been reported. In the first of these, new substituent constants are calculated for each possible combination of reaction site and substituent location from the ρ value for the corresponding benzene sets (*e.g.*, the set of substituted benzene undergoing the same reaction under the same conditions). There are 14 such possible combinations. This method was originally proposed by Price and Michel[3]; it has since been studied by several other groups.[4] The second approach is that of Bryson[5] who applied the extended form of the Hammett equation (2) first suggested by Taft.[7]

$$Q_X = \rho\sigma_X + Q_H \qquad (1)$$

$$Q_X = \alpha\sigma_I + \beta\sigma_R + Q_H \qquad (2)$$

The third method, that of Dewar and Grisdale,[6] is like the first to the extent that new substituent constants are required for each possible combination of reaction site and substituent constant locations. In this case, however, an attempt was made to calculate the necessary substituent constants from localized and delocalized electrical effects. These effects have been calculated from the σ_m and σ_p constants.

Of the three methods cited, the second has the disadvantage of requiring the more cumbersome four-parameter eq. 2. The first and third methods necessitate the determination or calculation of a large number of new substituent constants.

We have considered, as an alternative to these methods, the possibility of correlating data for substituted naphthalene sets with eq. 1 by means of the σ_m or σ_p constants. This approach would require a separate value of ρ for each combination of substituent and reaction site locations. It would however, have the great advantage of requiring no new substituent constants.

To determine the applicability of our proposal, we have correlated data taken from the literature for substituted quinoline and isoquinoline sets with the σ_m and σ_p constants. For comparison purposes we have also correlated the data with σ_I constants, and with the σ_{DG} constants of Dewar and Grisdale. The sets studied are listed in Table I. The data used in the correlations are given in Table II. The σ_m and σ_p constants were generally taken from the compilation of McDaniel and Brown[8]; the σ_I constants are from our recent collection.[9] The σ_{DG} values are from Dewar and Grisdale when possible, otherwise they were calculated as described by these authors. The calculated values are given in Table III, together with σ_I, σ_m, and σ_p constants taken from sources other than those noted above. The results of the correlations are presented in Table IV; the correlations are made as described by Jaffé.[1]

The inclusion of the pK_a values for aminoquinolines and aminoisoquinolines in the correlations is based on the reported predominance of the amino over the imino tautomers.[10] The pK_a values for hydroxyquinolines and hydroxyisoquinolines have been included in the correlations for those cases in which the hydroxy tautomer predominates.[10] The pK_a values for X = NH_2 and OH were excluded from set A18 as it has been reported that intramolecular bonding occurs in these cases.[10]

To provide a check on our method, we have correlated several sets with eq. 2. The results obtained are given

(1) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953); R. W. Taft, Jr., "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 565; V. Palm, *Russ. Chem. Rev.*, **31**, 471 (1961); P. R. Wells, *Chem. Rev.*, **63**, 171 (1963); in particular, see the recent excellent review by H. H. Jaffé and H. L. James, *Advan. Heterocyclic Chem.*, **3**, 209 (1964).

(2) M. Charton, *J. Am. Chem. Soc.*, **86**, 2033 (1964).

(3) C. C. Price and R. H. Michel, *ibid.*, **74**, 3652 (1952); R. C. Elderfield and M. Siegal, *ibid.*, **73**, 5622 (1951).

(4) P. R. Wells and E. R. Ward, *Chem. Ind.* (London), 528 (1958); A. Fischer, H. M. Fountain, and J. Vaughan, *J. Chem. Soc.*, 1310 (1957); A. Fischer, W. J. Mitchell, G. S. Ogilvie, J. Packer, and J. Vaughan, *J. Chem. Soc.*, 1426 (1958); A. Fischer, J. D. Murdoch, J. Packer, R. D. Tompsom, and J. Vaughan, *ibid.*, 4358 (1957).

(5) A. Bryson, *J. Am. Chem. Soc.*, **82**, 4862 (1960).

(6) M. J. S. Dewar and P. J. Grisdale, *ibid.*, **84**, 3539, 3546, 3548 (1962).

(7) R. W. Taft, Jr., and I. C. Lewis, *ibid.*, **80**, 2436 (1958); *J. Phys. Chem.*, **64**, 1805 (1960).

(8) D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).

(9) M. Charton, *ibid.*, **29**, 1222 (1964).

(10) S. F. Mason, *J. Chem. Soc.*, 674 (1958); A. R. Katritzky and J. M. Lagowski, *Advan. Heterocyclic Chem.*, **1**, 339 (1963).

TABLE I

SETS STUDIED

Set		Q	Solvent	Temp., °C.	Ref.
A15	5-Substituted quinolines	pK_a	H_2O	20	a
B15	5-Substituted quinolines	$10^{12}K_B$	10% EtOH-H_2O	25	b
C15	5-Substituted quinolines	pK_a	50% dioxane-H_2O	25	c
D15	5-Substituted quinolines	pK_a	75% dioxane-H_2O	25	c
A16	6-Substituted quinolines	pK_a	H_2O	20	a
B16	6-Substituted quinolines	$10^{12}K_B$	10% EtOH-H_2O	25	b
E16	6-Substituted quinolines	pK_a	7.7% EtOH-H_2O	25	d
A17	7-Substituted quinolines	pK_a	H_2O	20	a
B17	7-Substituted quinolines	$10^{12}K_B$	10% EtOH-H_2O	25	b
E17	7-Substituted quinolines	pK_a	7.7% EtOH-H_2O	25	d
A18	8-Substituted quinolines	pK_a	H_2O	20	a
B18	8-Substituted quinolines	$10^{12}K_B$	10% EtOH-H_2O	25	b
A24	4-Substituted isoquinolines	pK_a	H_2O	25	a
A25	5-Substituted isoquinolines	pK_a	H_2O	25	a
A26	6-Substituted isoquinolines	pK_a	H_2O	25	a
A27	7-Substituted isoquinolines	pK_a	H_2O	25	a
A28	8-Substituted isoquinolines	pK_a	H_2O	25	a

[a] A. Albert, "Physical Methods in Heterocyclic Chemistry," Vol. 1, Academic Press Inc., New York, N. Y., 1963, p. 1. [b] W. K. Miller, S. B. Knight, and A. Roe, J. Am. Chem. Soc., **72**, 4263 (1950); S. B. Knight, R. H. Wallick, and J. Bowen, ibid., **76**, 3780 (1954); S. B. Knight, R. H. Wallick, and C. Balch, ibid., **77**, 2577 (1955). [c] J. C. Tomkinson and R. J. Williams, J. Chem. Soc., 2010 (1958). [d] E. Baciocchi, G. Illuminati, and G. Marino, J. Am. Chem. Soc., **80**, 2270 (1958).

TABLE II

DATA USED IN CORRELATIONS

X	A15	B15	C15	D15	A16	B16	E16	A17	B17	E17	A18	B18	A24	A25	A26	A27	A28
H	4.957	493	4.08	3.14	4.957	493	3.72	4.957	493	3.72	4.957	493	5.40	5.40	5.40	5.40	5.40
Me	5.200		4.24		5.219	773	3.96	5.344	1075		5.047	440					
MeS	4.50				4.75						3.50						
NO$_2$	2.73				2.76			2.44			2.59		1.35	3.53	3.47	3.61	3.59
NH$_2$	5.46				5.63			6.65					6.28	5.59	7.17	6.20	6.06
CF$_3$	3.10[a]							3.16[a]									
F		48	2.76	2.20		103	2.95		110	3.04		12					
Cl		23				54	2.81		39	2.80		7.2					
Br		25	1.93			45	2.83		41	2.83		7.4	3.31[a]				
I				1.64													
EtO$_2$C			2.88	2.00													
MeO$_2$C					3.80												
CHO			2.51														
CN			2.02														
HCNOH			3.52														
MeO					5.06		3.93										
EtO							3.82										
OH	5.20				5.17									5.40	5.70		

[a] At 25°.

TABLE III

SUBSTITUENT CONSTANTS FROM SOURCES OTHER THAN REF. 8 AND 9[a]

X	σ_m[b]	σ_p	$\sigma_{16(25)}$[c]	$\sigma_{16(25)}$[d]	σ_{17}	σ_{26}	σ_{27}	σ_I
Me			−0.08	−0.04	−0.09	−0.08	−0.03	
MeS			0.05	0.09	0.04			
NO$_2$			0.52	0.41	0.53	0.41	0.36	
NH$_2$			−0.29	−0.09	−0.32	−0.29	−0.08	
CF$_3$			0.34		0.35			
F			0.14	0.19	0.12			
Cl			0.21	0.22	0.20			
Br			0.22	0.23	0.21			
I			0.19					
EtO$_2$C			0.29	0.21				
MeO$_2$C		0.43[e]		0.18				
CHO		0.42[f]	0.28					0.36[f]
CN	0.615[f]		0.43					
HCNOH	0.216[f]	0.103[f]	0.11					0.27[f]
MeO			−0.05	0.07	−0.08			
EtO				0.06				
OH			−0.09	0.07	−0.12	−0.14	0.06	

[a] All Dewar-Grisdale constants calculated from eq. 3. [b] $\sigma_m = \sigma_{18} = \sigma_{24}$. [c] $\sigma_{15} = \sigma_{28}$. [d] $\sigma_{16} = \sigma_{26}$. [e] M. Charton and H. Meislich, J. Am. Chem. Soc., **80**, 5940 (1958). [f] M. Charton, J. Org. Chem., **30**, 557 (1965).

TABLE IV.

RESULTS OF CORRELATIONS

Set		ρ	r^a	s^b	t^c	Q_H	n^d
A15	I	−4.02	0.880	0.568	4.152	5.37	7
	m	−3.44	0.958	0.344	7.464	5.03	
	p	−2.10	0.957	0.347	7.397	4.48	
	DG	−3.87	0.976	0.260	10.05	4.70	
B15	I	−2.42	0.939	0.263	3.848	2.65	4
	m	−3.35	0.993	0.0884	12.12	2.70	
	p	−4.64	0.874	0.371	2.542	2.39	
	DG	−6.08	0.990	0.107	9.938	2.65	
C15	I	−3.26	0.945	0.296	6.473	4.09	7
	m	−3.43	0.983	0.164	12.15	4.05	
	p	−2.47	0.885	0.422	4.241	3.68	
	DG	−4.41	0.949	0.285	6.749	3.88	
D15	I	−2.32	0.818	0.379	2.463	2.97	5
	m	−3.28	0.938	0.229	4.689	3.13	
	p	−2.24	0.699	0.472	1.695	2.64	
	DG	−4.43	0.841	0.358	2.690	2.93	
A16	I	−3.69	0.845	0.539	3.981	5.49	8
	m	−3.34	0.964	0.268	8.900	5.16	
	p	−1.97	0.964	0.268	8.896	4.61	
	DG	−5.80	0.962	0.275	8.664	5.17	
B16	I	−1.91	0.944	0.215	−4.946	2.73	5
	m	−2.51	0.988	0.0996	−11.18	2.71	
	p	−3.17	0.949	0.205	−5.221	2.42	
	DG	−4.32	0.992	0.0822	−13.60	2.71	
E16	I	−1.96	0.829	0.330	3.318	3.97	7
	m	−2.69	0.938	0.204	6.072	3.91	
	p	−2.38	0.925	0.224	5.438	3.38	
	DG	−4.62	0.934	0.210	5.863	3.91	
A17	I	−4.94	0.851	1.03	2.812	5.60	5
	m	−4.43	0.968	0.494	6.666	5.32	
	p	−2.96	0.998	0.118	28.71	4.80	
	DG	−4.96	0.999	0.0984	34.54	4.98	
B17	I	−2.15	0.925	0.285	4.201	2.79	5
	m	−2.84	0.976	0.162	7.815	2.78	
	p	−3.73	0.972	0.177	7.104	2.46	
	DG	−4.95	0.997	0.542	23.82	2.63	
E17	I	−2.15	0.699	0.545	1.695	4.07	5
	m	−3.18	0.845	0.408	2.734	4.12	
	p	−3.11	0.964	0.202	6.302	3.50	
	DG	−5.13	0.985	0.131	9.948	3.80	
A18	I	−3.75	0.978	0.302	6.668	4.80	5
	m	−3.11	0.925	0.555	3.434	4.64	
	p	−2.38	0.850	0.768	2.281	4.39	
B18	I	−3.36	0.980	0.218	8.563	2.56	5
	m	−4.25	0.991	0.146	12.95	2.51	
	p	−4.92	0.868	0.545	3.034	1.97	
A24	I	−7.09	0.947	0.865	4.188	6.18	4
	m	−5.63	0.999	0.0873	43.78	5.41	
A25	I	−3.26	0.928	0.442	3.532	5.78	4
	m	−2.49	0.974	0.269	6.091	5.40	
	p	−1.45	0.930	0.436	3.586	4.89	
	DG	−4.33	0.975	0.265	6.180	5.40	
A26	I	−4.36	0.798	1.58	1.324	6.41	3
	m	−3.79	0.748	0.836	2.968	6.04	
	p	−2.57	0.9997	0.0586	44.67	5.45	
	DG	−5.25	0.997	0.193	13.55	5.56	
A27	I	−3.50	0.859	0.707	2.375	6.09	4
	m	−2.89	0.971	0.328	5.793	5.71	
	p	−1.79	0.986	0.234	8.242	5.11	
	DG	−5.71	0.972	0.324	5.863	5.71	
A28	I	−3.47	0.917	0.720	2.306	5.86	3
	m	−2.75	0.996	0.158	11.42	5.52	
	p	−1.74	0.977	0.386	4.574	5.08	
	DG	−3.10	0.995	0.181	9.956	5.25	

[a] Correction coefficient. [b] Standard deviation. [c] Student's t test. [d] Number of points in the set.

in Table V. The σ_R constants required were obtained from eq. 3.[7]

$$\sigma_R = \sigma_p - \sigma_I \tag{3}$$

Results

Quinolines.—The results obtained for the four sets of 5-substituted quinolines show that correlation with σ_m is best for three of the sets studied, A-, B-, and C15, and adequate for the fourth, D15. Good results for sets A-, B-, and C15 were also obtained with the appropriate Dewar–Grisdale constants (σ_{15}); set D15 gave poor results. For the three sets of 6-substituted quinolines studied, A-, B-, and E16, the σ_m and the Dewar–Grisdale (σ_{16}) constants both gave good correlation. There is no significant difference in the results obtained with these constants. In the three sets of 7-substituted quinolines studied, A-, B-, and E17, the Dewar–Grisdale constants consistently gave the best results although the results with σ_p were good. The Dewar–Grisdale constants for 8-substituted quinolines are identical with the σ_m constants. Correlations were therefore made with σ_I, σ_m, and σ_p. On the basis of the two sets studied, A- and B18, the σ_I constants are to be preferred as they gave good correlation in both sets whereas the σ_m constants gave only fair results for A18 but excellent results for B18. The results obtained from correlation with eq. 2 are in accord with the above conclusions.

Isoquinolines.—The data available for substituted isoquinolines are limited to one very short set for each of the 4-, 5-, 6-, 7-, and 8-substituted isoquinolines. No certain conclusions can be arrived at on the basis of these data. With regard to the 4-substituted isoquinolines, σ_m and the Dewar–Grisdale constants are identical as was the case for the 8-substituted quinolines. Correlations were therefore made only with σ_I and σ_m; the results obtained with σ_m were excellent. For the 5-substituted isoquinolines, σ_m and the Dewar–Grisdale constants (σ_{25}) both gave good results. The case of the 6-substituted isoquinolines shows best results with σ_p, but the Dewar–Grisdale constants (σ_{26}) also gave good results. No decision can be made among the σ_m, σ_p, and Dewar–Grisdale (σ_{27}) constants in the case of the 7-substituted isoquinolines; all gave good results. The 8-substituted isoquinolines gave good correlation with σ_m and Dewar–Grisdale (σ_{28}) constants.

Discussion

Dewar–Grisdale Method.—It is of interest to examine the Dewar–Grisdale method[6] in some detail. It is in many respects similar to that of Taft, since it assumes a separation of the over-all electrical effect of a substituent into localized and delocalized components. Consider a set of substances XGY in which X is the substituent, Y the reaction site, and G the group to which they are attached. Then the effect of the substituent upon the observed quantity Q is determined by the substituent constant σ_X which is given by eq. 4 or, alternatively, eq. 5. F and F' are factors representing the localized effect, M and M' represent the delocalized effect. The quantity r_{ij}

$$\sigma_{X,DG} = \frac{F_X}{r_{ij}} + M_{q_{ij}} \tag{4}$$

$$\sigma_{X,DG} = \frac{F'_X}{r_{ij}} - M'\tau_{ij} \tag{5}$$

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TABLE V

RESULTS OF CORRELATION

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Set	$-\alpha$	$-\beta$	Q_H	$S_{\sigma I}{}^a$	$S_{\sigma R}{}^a$	$S_{QH}{}^a$	$S_{QX}{}^a$	r^b	R^c	F^d	n^e
A15	3.17	1.49	4.86	0.384	0.258	0.149	1.09	0.381	0.988	80.80	7
C15	3.36	1.14	4.03	0.307	0.366	0.112	0.827	0.102	0.984	61.89	7
D15	3.37	1.51	3.12	0.960	0.885	0.297	0.572	0.641	0.930	6.410	5
A16	2.96	1.49	4.95	0.224	0.139	0.0812	0.0935	0.306	0.994	206.6	8
E16	2.74	1.62	3.76	0.515	0.646	0.164	0.539	0.601	0.938	14.56	7
A17	3.28	2.73	4.90	0.115	0.0903	0.0415	1.70	0.479	0.997	1660	5

^{a} Standard deviation. ^{b} Partial correlation coefficient of σ_I on σ_R. ^{c} Multiple correlation coefficient. ^{d} F test for significance of regression. ^{e} Number of points in set.

represents the distance between the atom i of G to which X is attached and the atom j to which Y is attached, expressed in units of the bond lengths in benzene (e.g., 1 length unit = 1.39 Å.). The quantity q_{ij} is the charge at the atom bearing Y in the carbanion $H_2\bar{C}-GY$. The quantity π_{ij} represents the atom-atom polarizability of atoms i and j. The constants calculated from eq. 3 and 4 are in good agreement with each other. It must be noted that, in the Dewar-Grisdale approach, the localized effect is presumed to be a function of r, while the delocalized effect is a function solely of q or π. The required values of F and M (or for F' and M') can now be calculated from the σ_m and σ_p constants as r, q, and π are all known.

According to Taft, the over-all electrical effect can be separated into an "inductive" (localized) and a resonance (delocalized) effect. For $\sigma_{p,X}$ $\lambda = \delta = 1$; for

$$\sigma_X = \Delta\sigma_I + \delta\sigma_R \quad (6)$$

$\sigma_{m,X}$ $\lambda = 1, \delta = 0.3$–$0.6$. Let us assume a reasonable value of δ_m of 0.4. Now for the meta position in benzene, $q = 0$ and $r = 1.73$. Then from eq. 3 and 5, for σ_m

$$\frac{F_X}{1.73} = \sigma_{I,X} + 0.4\sigma_{R,X} \quad (7)$$

or

$$F_X = 1.73\sigma_{I,X} + 0.69\sigma_{R,X} \quad (8)$$

while for σ_p

$$\frac{F_X}{2} + \frac{M_X}{7} = \sigma_{I,X} + \sigma_{R,X} \quad (9)$$

From eq. 7 and 8

$$M_X = 0.94\sigma_{I,X} + 4.58\sigma_{R,X} \quad (10$$

The results are not affected significantly by choosing values of σ_m in the range 0.2–0.8.

If we accept the separation of Taft, then that of Dewar and Grisdale is unsuccessful, as both F and M are functions of σ_I and σ_R. The converse is of course also true. We believe that the Taft separation[7] is valid however, as the σ_I constants give excellent correlations of substituent effect in sets such as the pK_a values of XCH_2NH_2, which are free of delocalized substituent effects.

Further evidence for the superiority of the Taft separation over that of Dewar and Grisdale may be found in the work of Holtz and Stock.[11] These authors have studied the ionization of 4-substituted tricyclo[2.2.2]octane-1-carboxylic acids. This set must be free of delocalized electrical effects. They find that, although the appropriate Dewar-Grisdale constants give a satisfactory correlation with the pK_a values of

(11) H. D. Holtz and L. M. Stock, J. Am. Chem. Soc., **86**, 5188 (1964).

these acids, some serious deviations are apparent. These are attributed to the resonance effects inherent in the σ_m constants from which the Dewar-Grisdale constants were derived. They have observed, however, that the pK_a values of these acids gave an excellent correlation with the σ_I constants.

Another interesting observation may be made concerning the Dewar-Grisdale treatment. It is implicit in their method that ρ for a reaction should be the same for all G, as the σ constants have been adjusted to account for the change in localized and delocalized effects with change in G. In Table VI, we have listed values of ρ_{DG} for almost all of the pyridines and quinolines free of "ortho effects." ρ_{DG} for 3- or 4-substituted pyridines is the same as ρ for correlation with the appropriate σ_m and σ_p constants, as for benzene (and therefore pyridine) $\sigma_{4DG} \equiv \sigma_p$. The values of the standard deviation of ρ are also given in Table VI.

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TABLE VI

VALUES OF ρ_{DG} AND S_ρ FOR pK_a VALUES IN WATER AT 20°

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G	ρ_{DG}	S_ρ	G	ρ_{DG}	S_ρ
3- or 4-Pyridyl	-5.70^a	0.242^a	4-Isoquinolyl	-5.63	0.129
5-Quinolyl	-3.87	0.385	5-Isoquinolyl	-4.33	0.701
6-Quinolyl	-5.80	0.669	6-Isoquinolyl	-5.25	0.387
7-Quinolyl	-4.96	0.144	7-Isoquinolyl	-5.71	0.973
8-Quinolyl	-3.11	0.906	8-Isoquinolyl	-3.10	0.311

^{a} From ref. 2.

The results set forth in Table VI show that for five of the nine groups G the value of ρ differs from that for the pyridine set by considerably more than the standard deviation. This clearly shows that ρ is a function of G, and therefore that the Dewar-Grisdale separation is theoretically unsuccessful. That this approach often results in successful correlation shows that substituent effects are not extremely sensitive to the composition of the substituent constant. Thus, the σ_m constants will give a good correlation for a range of substituent constant composition. This is one of the reasons for the success of the simple form of the Hammett equation (eq. 1).

Tautomerism.—Mason has calculated the pK_a values of the phenol tautomers for several hydroxyquinolines and isoquinolines for which he finds that the keto tautomer predominates.[10] It is of interest to compare his values with values calculated from our correlations. Our results are compared with his in Table VII. The observed pK_a values for the equilibrium mixture of tautomers are also included in the table.

There is good agreement between our value and that of Mason for 6-hydroxyisoquinoline. Our value for 4-hydroxyisoquinoline is close to the observed value and suggests that the phenol tautomer predominates in this compound.

Table VII
Calculated and Observed pK_a Values

| | | pK$_a$ | |
| | | Calcd. | |
Compound	Obsd.	Mason	Present work[a]
7-Hydroxyquinoline	5.48	5.64	5.90 (5.98)
4-Hydroxyisoquinoline	4.80	5.48	4.73
6-Hydroxyisoquinoline	5.85	6.32	6.40 (6.30)
8-Hydroxyisoquinoline	5.66	5.93	5.19 (5.53)
8-Hydroxyquinoline	5.13	5.14	3.86
8-Aminoquinoline	3.99	...	4.42

[a] Values in parentheses are calculated from the correlations with the Dewar–Grisdale constants. The other values are calculated from the correlations with the σ_m or σ_p constants as recommended in Table VIII.

Hydrogen Bonding.—We have calculated the pK_a values for 8-hydroxy- and 8-aminoquinoline from our correlation; the values are given in Table VII. These values represent the pK_a values to be expected in the absence of hydrogen bonding. The effect of hydrogen bonding on the pK_a of the amino compound is comparatively small, 0.5 pK_a unit, corresponding to a threefold difference in K_a; the hydroxy compound shows a larger effect, 1.3 pK_a units. This corresponds to a 12-fold increase in K_a.

Correlation of Data for Quinolines and Isoquinolines.—Our results show that useful correlations of substituted quinolines and isoquinolines can be made with either the Hammett σ_m and σ_p constants, as shown in Table VIII, or the appropriate Dewar–Grisdale constants.

Table VIII
σ Values Preferred for Correlation

5-Substituted quinolines	σ_m	5-Substituted isoquinolines	σ_m
6-Substituted quinolines	σ_m	6-Substituted isoquinolines	σ_p
7-Substituted quinolines	σ_p	7-Substituted isoquinolines	σ_m
8-Substituted quinolines	σ_I	8-Substituted isoquinolines	σ_m

There is no reason to prefer the Dewar–Grisdale constants over the σ_m and σ_p constants, except perhaps in the 7-substituted quinolines. Ritter and Miller have recently studied the application of the Dewar–Grisdale treatment to substituted phenylpropiolic, cinnamic, phenylacetic, 3-phenylpropanoic, 2,5-furanoic, and 2,5-thienoic acids.[12] They found good results for the 2,5-furanoic and 2,5-thienoic acids, fair results for cinnamic and phenylacetic, and poor results for phenylpropiolic and 3-phenylpropanoic acids. We therefore suggest that it is more convenient to use the widely available σ_m and σ_p constants in the study of substituent effects.

Electrical Effects.—We have previously had occasion to define

(12) J. D. S. Ritter and S. I. Miller, *J. Am. Chem. Soc.*, **86**, 1507 (1964).

$$\epsilon = \frac{\delta}{\lambda} = \frac{\beta}{\alpha} \tag{11}$$

as a parameter which characterizes the composition of the electrical effect of a substituent. The quantities λ and δ were defined in eq. 6. They represent the coefficients of the localized and delocalized effects, respectively. Values of ϵ for various substituent constants are given in Table IX. From Tables VIII and IX, the composition of the electrical effect in 5-, 6-, 7-, and 8-substituted quinolines and isoquinolines can be ascertained. From those sets which have been correlated with eq. 2 we can obtain average values of ϵ of 0.42 and 0.55 for 5- and 6-substituted quinolines, respectively.

Table IX
Values of ϵ[a]

Substituent constant	ϵ	Substituent constant	ϵ
σ_I	0	σ_p^0	0.67[b]
σ_m	0.33	σ_p^+	1.60[b]
σ_p	1	σ_p^-	1.47[b]

[a] M. Charton, *J. Org. Chem.*, **30**, 969 (1965). [b] M. Charton, unpublished results.

If we accept the proposal of Dewar and Grisdale that the delocalized effect is proportional to q, then the delocalized effect must be the same for 8-substituted isoquinolines as it is for 6-substituted isoquinolines. If the localized effect is a function of the distance between substitutent and reaction site, then the effect must be much greater for the 8-substituted isoquinolines than for the 6-substituted isoquinolines. Then, if the 6-substituted isoquinolines are best correlated by σ_p ($\epsilon = 1$), the 8-substituted isoquinolines ought to be better correlated by a substitutent constant with ϵ less than 1, such as σ_m. The same argument can be presented for the 5- and 7-substituted quinolines. The somewhat better correlation of 8-substituted quinoline with σ_I can be explained in the same manner. The results given in Table VIII are in accord with this discussion.

It would be possible to calculate α and β. We may calculate ρ and therefore α as a function of G from the Kirkwood–Westheimer equation.[13] We have shown[14] that β may be calculated from eq. 12 in accord with the

$$\beta = mq + c \tag{12}$$

concept of Dewar and Grisdale. Thus, it should be possible *a priori* to calculate ϵ, and so choose the appropriate substituent constant for a given set.

(13) M. Charton, Abstracts, 137th National Meeting of the American Chemical Society, Cleveland, Ohio, April 1960, p. 92-O; Abstracts, 140th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1961, p. 57-T.

(14) M. Charton, Abstracts, 149th National Meeting of the American Chemical Society, Detroit, Mich., April 1965, p. 13S.