Dual-Parameter Substituent Constants, ΔE^x and ΔC^x, for the Correlation of Physicochemical Measurements

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Abstract: Since chemical bonds have independent covalent (soft or frontier controlled) and electrostatic (charged or charge controlled) contributions, fundamental problems arise when substituent-constant correlations are made with a single-parameter, Hammett-type reactivity scale. A method is offered and parameters are reported to carry out dual-parameter electrostatic ΔE^x and covalent ΔC^x substituent-constant analyses. The equation $\Delta\chi^X - \Delta\chi^H = d_A{}^E\Delta E^x + d_A{}^C\Delta C^x$ is offered as a substitute for current approaches to substituent-constant correlations for reactions of a family of donors or nucleophiles. For a family of electrophiles, the equation becomes $\Delta\chi^X - \Delta\chi^H = d_B{}^E\Delta E^x + d_B{}^C\Delta C^x$. The ΔE^x and ΔC^x parameters are the dual-scale electrostatic and covalent substituent constants. These parameters are the counterparts of the single-scale Hammett σ-parameters, while d^E and d^C are the electrostatic and covalent counterparts of ρ. The A subscript on d^E indicates that the reactions involve the same acceptor (electrophile) reacting with a family of donors. The B subscript indicates reactions of a donor with a family of acceptors. Values of ΔE^x and ΔC^x for a series of substituents are given, and a procedure is reported for estimating these quantities for other substituents. Data requiring different single-parameter scales (σ^+, σ_I, σ_R, and σ_R^-, etc.) are correlated by the same set of ΔE^x and ΔC^x parameters with the two-term equation. The different scales of σ-parameters are shown to correspond to reactions with different ratios of d^C/d^E, i.e., different covalent and electrostatic contributions. The multitude of different one-parameter substituent-constant scales in the literature can be replaced by the single set of ΔE^x and ΔC^x parameters reported here, and more meaningful correlations and interpretations of data result. When a substituent-constant analysis is carried out using a probe molecule whose E and C values are known, the components of d^E can be separated. This leads to a determination of the efficiency with which intervening atoms transmit the substituent effect to the reactive center. The ΔE^x and ΔC^x values can also be used to calculate E and C values for an entire family of donors and acceptors if the E and C values for four or more members of the family are known accurately.

Introduction

It is now generally accepted[1–5] that there is no inherent order of donor strength that can be used to describe the reaction of a series of donors (bases or nucleophiles) toward any acceptor (acid or electrophile). Likewise, there is no inherent order of acceptor strength that can be used to correlate or predict the reactions of a series of acceptors with any base. According to the electrostatic–covalent models of Pauling[6a] and Mulliken,[6b] two independent factors contribute to bond strengths and thus to the bond-strength component of chemical reactivity and spectroscopy. The E and C model[1]

$$-\Delta H = E_A E_B + C_A C_B + W \quad (1)$$

provides an empirical scale of electrostatic E_A and covalent C_A acceptor tendencies as well as donor tendencies E_B and C_B. With separate covalent and electrostatic terms in eq 1, varying contributions to $-\Delta H$ by these terms, as the acceptor is changed, produces a very large number of different donor orders.[1b,4] Different acceptor orders arise in the same way when the donor is changed. The term W of eq 1 is usually zero. This quantity includes any constant contribution to a measurement that is present in all the enthalpy values of that acceptor (or donor). For example, the enthalpy of dissociation of a dimeric acceptor upon 1:1 adduct formation gives rise to a constant W contribution for this acceptor in all of its reactions with donors.

The E and C parameters have utility not only for the prediction of bond strengths but also as a scale for the analysis of spectroscopic and reactivity measurements.[1b] When applied to properties other than enthalpies, the equation takes the form

$$\Delta\chi = E_A E_B + C_A C_B + W \quad (2)$$

where $\Delta\chi$ is a general symbol for the physicochemical measurement. Asterisks are used on the terms in eq 2 to indicate parameters that correlate measurements other than solvation-minimized enthalpies. For general derivations that include both $\Delta\chi$ and $-\Delta H$, the asterisk will be dropped. When the acceptor is held constant in a series of measurements, reported[1c] E_B and C_B values are substituted into eq 2 along with their corresponding measured $\Delta\chi$ value to produce a series of simultaneous equations (one equation for each donor). These equations are solved[8] for the values of E_A* and C_A* that best fit the experimental $\Delta\chi$ values.

The ECW approach described above is to be contrasted with analyses that plot some measured property versus a single-parameter basicity or acidity scale, e.g., pK_B, pK_A, H–X bond

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(6) (a) Pauling, L. *The Nature of the Chemical Bond*, 3rd ed.; Cornell University Press: Ithaca, NY, 1960. (b) Mulliken, R. S. *J. Am. Chem. Soc.* **1950**, *72*, 600, 4493; **1952**; *74*, 811.
(7) Drago, R. S.; Meek, D. W.; Longhi, R.; Joesten, M. D. *Inorg. Chem.* **1963**, *2*, 1056.
(8) A least-squares minimization program is used to find the best-fit parameters. See reference 1c.

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energies, electronegativities, donor numbers,[9] and Hammett σ[10] and other substituent constants. Single-parameter scales assume an inherent order of donor or acceptor strength.[11] This assumption imposes a severe limitation on the applicability of these scales that is often not appreciated. The limitation that is imposed on eq 2 to convert it to a single-parameter donor scale can be shown by dividing both sides of eq 2 by E_A and rearranging:

$$\frac{\Delta\chi - W}{E_A} = E_B + \frac{C_A}{E_A}C_B \quad (3)$$

When the C_A/E_A ratio is fixed, the right-hand side of eq 3 gives a parameter, B_i, where

$$B_i = E_B + \frac{C_A C_B}{E_A} \quad (4)$$

For each base, B_i indicates its relative strength of interaction with any acceptor with this fixed C_A/E_A ratio. The i subscript on B indicates the fixed C_A/E_A ratio to which the B_i scale applies. The single-scale counterpart of eq 2 becomes

$$\Delta\chi = B_i E_A + W \quad (5)$$

Thus, any single-parameter scale corresponds to a fixed ratio of the covalent to electrostatic contribution in the interaction and only applies to reactions or to spectral changes of other acceptors with the same C_A/E_A ratio.[11]

Whenever the donor parameters of any single-parameter reference scale (e.g., pK_B) are plotted versus the corresponding measured physicochemical properties ($\Delta\chi$), the correlation is of the form of eq 5, and an implicit assumption is being made that the C_A/E_A ratio of $\Delta\chi$ is the same as that of the reference scale employed. The C_A/E_A ratio of the various one-parameter scales in common use is generally unknown and ignored in their application. In a recent article,[12] the errors that can arise by using the wrong one-parameter scale in the analysis of data are discussed. Seemingly good, straight line plots may not be valid, and poor plots can result when the parameters selected and the measured physicochemical properties differ in the relative importance of the covalency in the bond.

The Hammett equation and other single-parameter substituent-constant equations suffer the same shortcomings as the one-parameter equations discussed above. The Hammett equation:

$$\log \frac{K_x}{K_H} = -\sigma\rho \quad (6)$$

is a one-parameter equation used to predict how substituents in a family of compounds will change the donor or acceptor strength of the parent hydrogen derivative. The equation:

$$-\Delta H^x + \Delta H^H = \Delta\Delta H = -\sigma\rho \quad (7)$$

is similar in form[13] to eq 6. When Hammett parameters are used to analyze a physicochemical property, $-\Delta H$ is replaced by $\Delta\chi$ and $-\Delta\Delta H$ by $\Delta\Delta\chi$. The equivalence of eq 5 to the Hammett equation is shown by first casting eq 5 into a form to analyze $\Delta\Delta\chi$ by subtracting $\Delta\chi^H$ from $\Delta\chi^X$.

$$\Delta\Delta\chi = B_i^x E_A - B_i^H E_A = (B_i^x - B_i^H)E_A = \Delta B_i E_A \quad (8)$$

Note the constant W in eq 5 disappears in the subtraction. When the C/E ratio for the B_i scale is the same as that implied for the one-parameter σ-scale in eq 7, we can write

$$\Delta\Delta\chi = \Delta B_i E_A = -\sigma\rho \quad (9)$$

Thus, $\Delta B_i E_A$ is equal to $-\sigma\rho$, and either ΔB_i or σ can be used to correlate[14] the substituent-constant changes of $\Delta\Delta\chi$ with eq 7 or 8. Since the B_i- and σ-scales utilize different reference points, the values of ΔB_i and σ or E_A and ρ are not equal but are directly proportional to one another. Equation 9 can be extended to a family of acceptors studied with a single donor by interchanging the acceptor and donor symbols in the equation.[11]

When the Hammett substituent constants fail to correlate data, other types of substituent constants are used. For example, H. C. Brown, in his derivation of σ^+ values, states,[15] "It has long been recognized that Hammett substituent constants are not satisfactory for treating electrophilic substituent reactions." These different scales would be needed if the C/E ratio implied in the Hammett parameters is no longer appropriate for the new types of reactions or the measurements correlated by the new scales. With different values for C_A/E_A in eq 4, new scales of B_i values result which differ from the Hammett scale in the relative importance of covalent and electrostatic contributions. We shall show that many of the different substituent-constant scales correspond to single-parameter scales with different C_A/E_A ratios. We will also show that eq 2 can be cast in a form that enables one to correlate most of the data fit by these various scales with a dual-parameter E- and C-based scale. With a dual-parameter approach, the appropriate C_A/E_A ratio for the correlation is determined from the data fit.

Results and Discussion

General Approach. We begin this discussion by considering the donor strengths of substituted pyridines. This family has been thoroughly studied, and the changes in the C_B/E_B ratios[16] of the compounds are larger than for most families. Equation 2 is to be applied to the changes that occur in a measured property, $\Delta\Delta\chi$ ($\Delta\chi^X - \Delta\chi^H$), for a family of pyridine molecules. Equation 10 results by subtracting eq 2 written for $\Delta\chi^H$ from eq 2 written for $\Delta\chi^X$ of the substituted pyridine

$$\Delta\Delta\chi = \Delta\chi^X - \Delta\chi^H + E_A{*}\Delta E_B{}^x + C_A{*}\Delta C_B{}^x \quad (10)$$

where $\Delta E_B{}^x = E_B{}^x - E_B{}^H$ and $\Delta C_B{}^x = C_B{}^x - C_B{}^H$. Now consider a second family of donors reacting with the same acceptor A. The equation is

$$\Delta\chi^X - \Delta\chi^H = E_A{*}\Delta E_{B'}{}^x + C_A{*}\Delta C_{B'}{}^x \quad (11)$$

Substituent-constant analyses assume that in proceeding from one substituent to another, proportional changes are made in the acidity or basicity of any family of compounds. Thus, eqs 10 and 11 are related to each other by $\Delta E_B{}^x = s^E \Delta E_{B'}{}^x$ and $\Delta C_B{}^x = s^C \Delta C_{B'}{}^x$, where s^E and s^C are the proportionality constants. Since the proportional substituent changes made in the E and C values for any family of compounds apply to donors or acceptors, the subscript B is dropped and the substituent constants are labeled

(9) Mayer, V.; Gutmann, V.; Gerger, W. *Z. Chem.* **1975**, *106*, 1235.

(10) See: Exner, O. In *Correlation Analysis in Chemistry*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978.

(11) When the donor is held constant and a series of acceptors is studied, the relevant single-parameter equation is obtained by dividing both sides of eq 2 by E_B, giving eq (i) where $A_i = E_A + (C_B C_A)/E_B$. The A_i values give the order of acceptor strength for any measurement whose C_B/E_B ratio is that specified by i of A_i. This entire discussion and derivation is presented in terms of substituent changes made on a series of donors (nucleophiles) with the acceptor held constant. It applies as well to a series of acceptors by interchanging the words donor and acceptor as well as the symbols B_i, C_B, E_B and A_i, C_A, E_A throughout the discussion.

$$-\Delta\chi = A_i E_B + W \quad (i)$$

(12) Drago, R. S. *Inorg. Chem.* **1990**, *29*, 1379.

(13) Recall log k_x/k_H equals log k_x − log k_H which equals $-\Delta G_x/RT + \Delta G_H/RT$. The linear free energy enthalpy assumption of the Hammett model is not required when enthalpies are used. The constants for converting ΔG to ΔH are picked up by the ρ-values.

(14) An additional complexity in interpreting Hammett ρ-values can also be appreciated from this analysis. When there are small variations in the C/E ratio of data sets, this variation can be, in part, compensated for in a Hammett correlation by the ρ-value. Thus, σ-scales can fit data with slightly varying C/E ratios at the expense of meaning for the ρ-values.

(15) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1957**, *79*, 1913; **1958**, *80*, 4979.

(16) (a) Drago, R. S.; Vogel, G. C. *J. Am. Chem. Soc.* **1992**, *114*, 9527. (b) Drago, R. S.; Dadmun, A.; Vogel, G. C. *Inorg. Chem.* **1993**, *32*, 2473.

ΔE^x and ΔC^x. The proportional substituent-constant changes of a family are related to the $\Delta E_B{}^x$ and $\Delta C_B{}^x$ values of pyridine by the equations

$$\Delta E_B{}^x = s_B{}^E \Delta E^x \qquad (12)$$

$$\Delta C_B{}^x = s_B{}^C \Delta C^x \qquad (13)$$

The values of $s_B{}^E$ and $s_B{}^C$ are defined as 1 for pyridine derivatives. For other families of compounds, s^E and s^C indicate the sensitivity of the families to substituent change relative to pyridine. Substituting $s_B{}^E\Delta E^x$ and $s_B{}^C\Delta C^x$ for $\Delta E_B{}^x$ and $\Delta C_B{}^x$ of eq 10 leads to:

$$\Delta\chi_X - \Delta\chi_H = E_A{}^* s_B{}^E \Delta E^x + C_A{}^* s_B{}^C \Delta C^x \qquad (14)$$

For substituent-constant analyses on the usual systems, where $E_A{}^*$ and $C_A{}^*$ are not known, we set

$$d_A{}^E = s_B{}^E E_A{}^* \qquad (15)$$

and

$$d_A{}^C = s_B{}^C C_A{}^* \qquad (16)$$

Substituting eq 15 and 16 into eq 14 leads to eq 17 for the general case of substituent-constant analyses for families of donors reacting with an acceptor or an electrophile.

$$\Delta\Delta\chi = \Delta\chi^X - \Delta\chi^H = d_A{}^E \Delta E^x + d_A{}^C \Delta C^x \qquad (17)$$

Comparing eq 17 and 7, ΔE^x and ΔC^x are seen to be the two-parameter analogues of σ, while $d_A{}^E$ and $d_A{}^C$ are the two-parameter analogues of ρ. In eq 17, $d_A{}^E$ is the product of the acceptor's electrostatic strength $E_A{}^*$ and the family's susceptibility to substituent changes in its electrostatic bond-forming property $s_B{}^E$ relative to a value of 1 arbitrarily assigned to pyridine (eq 12). The symbol $d_A{}^C$ represents similar changes in the covalent property with the $s_B{}^C$ component again relative to a value of 1 arbitrarily assigned to pyridine (eq 13).

When a family of acceptors (electrophiles) undergoes reaction with the same donor, a similar derivation leads to

$$\Delta X^x - \Delta X^H = d_B{}^E \Delta E^x + d_B{}^C \Delta C^x \qquad (18)$$

The subscript on d^E indicates if an acceptor or donor is held constant in the experiment. The quantities ΔE^x and ΔC^x indicate the proportional changes made by the substituent in the E and C values of any family of compounds involved in the experiment. When a methyl substituent group (a positive ΔE) increases the electrostatic contribution to a physicochemical measurement of a family of compounds, d^E will be positive. When a methyl group (a positive ΔE) decreases the electrostatic contribution to a physicochemical measurement of a family of acceptors, the sign of d^E will be negative.

The problem is to find ΔE^x and ΔC^x parameters. These parameters could then be used for dual-scale substituent-constant analyses of physicochemical measurements by determining if d^E and d^C values can be found that correlate the data set. The E- and C-based, dual scale could eliminate the need for the many different sets of substituent constants in the literature and the need to guess about which scale to use in data correlation. In the next section, the procedure for determining ΔE^x and ΔC^x values will be presented.

Calculation of ΔE^x and ΔC^x. Consider first the measured properties $\Delta\chi^X$ accompanying reaction of the same acceptor (electrophile) with a family of donor (nucleophilic) compounds X–R–Y where Y is the donor group. The measured data $\Delta\chi^X$ are substituted into eq 17, giving one equation for each measured substituent X. The ΔE^x and ΔC^x parameters are characteristic of the X-substituent, and the $d_A{}^E$ and $d_A{}^C$ parameters are characteristic of the physicochemical property studied. The series of equations that results, one for each measured data point, has two unknowns $d_A{}^E$ and $d_A{}^C$ for each reaction and two unknowns for each substituent studied. The reactions of this same family of donors with a new acceptor give rise to a new series of equations with the same ΔE^x and ΔC^x values and a new set of unknown d^E and d^C values. New $d_A{}^E$ and $d_A{}^C$ values arise for this new set of reactions even though the s^E and s^C values of the family are the same because $E_A{}^*$ and $C_A{}^*$ are different for the new acceptor. A new family of donors, with the same X-substituents, reacting with a third acceptor will give rise to a new series of equations with the same ΔE^x and ΔC^x values for the substituents but different $d_A{}^E$ and $d_A{}^C$ values. Though s^E, s^C, $E_A{}^*$, and $C_A{}^*$ all change for this new family reacting with a third acceptor, we need only to solve for the new $d_A{}^E$ and $d_A{}^C$ values to determine if a correlation exists.

The ΔE^x and ΔC^x parameters also apply to acceptors. When $\Delta\chi$ values are measured for a given donor reacting with a family of acceptors, a new series of equations arises with the same ΔE^x and ΔC^x values for the substituents but different $d_B{}^E$ and $d_B{}^C$ values. In this article, 50 families of reactions involving 65 substituents give rise to over 700 simultaneous equations (one for each $\Delta\chi$ measured) which are solved for 228 unknown $\Delta\chi^H$, ΔE^x, ΔC^x, d^E, and d^C parameters. When the $\Delta\chi^H$ value for the hydrogen compound is known, this value is entered as $\Delta\chi^X$ in eq 17 or 18 to give one of the simultaneous equations with ΔE^x and ΔC^x set as zero. Entering the hydrogen value as one of the simultaneous equations recognizes that error may exist in the measured value of $\Delta\chi^H$ and allows its best-fit value to be calculated in the least-squares minimization.

Data for the substituted pyridines play an important role in the least-squares fit. The values of s^E and s^C (eqs 12 and 13) are fixed at 1 for this family. Therefore, if measurements for substituted pyridines are available with acceptors or spectral acceptors whose E_A and C_A or $E_A{}^*$ and $C_A{}^*$ are known,[16] then $d_A{}^E$ and $d_A{}^C$ are fixed at these values in the data fit. Fixing the d^E values with E_A and C_A parameters for known acceptors and the $E_A{}^*$ and $C_A{}^*$ for known spectral acceptors connects the ΔE^x and ΔC^x substituent constants reported here to the E and C model.

There are two main mechanisms whereby substituent effects can be transmitted through the molecule to change the reactivity of another group in the molecule. One involves transmission of the substituent's properties through the σ-bonding system of the molecule and the other involves transmission through both σ- and π-systems. The former mechanism will be referred to as a nonconjugative interaction and the latter a conjugative interaction. The nonconjugative interaction is operative for substituents in the 3-position of a phenyl ring. The conjugative interaction dominates the mechanism for transmission by 4-substituents.[17] π-Delocalization gives rise to large π-contributions from substituents like 4-OCH_3, 4-$N(CH_3)_2$, 4-NH_2, 4-F, and 4-Cl that are not present when these groups are attached to the 3-position. This conjugative interaction adds electron density to the reactive group in the position para to the substituent and affects both the E value and the C value.[18] Even the CH_3 group, via hyperconjugative effects, can enhance the electron density at a reactive group para to the methyl by a conjugative mechanism. Some substituents (e.g., NO_2) can undergo conjugative interactions that decrease the electron density in the para position.[17] As a result of the direct π-interactions of the substituent with the reactive center, a different set of fundamental substituent constants is needed to describe a substituent for conjugative systems. The two sets of constants can be distinguished by labeling the nonconjugatice parameters ΔE^x and ΔC^x and the conjugative parameters $\Delta E_C{}^x$ and $\Delta C_C{}^x$. The substituents will be labeled

(17) The perturbation made on the ring carbon by the σ-bonding of a 3-X-substituent is transmitted to the reactive center by changes in both the σ- and π-system of a benzene ring. This is referred to as the σ-effect of the substituent. The 4-substituent has a contribution from this C–X σ-bonding effect and an additional contribution from delocalization of filled or empty orbitals of the X-substituent with the π-system.

(18) When the functional group is separated from the conjugated system by a $(CH_2)_n$ chain, the nonconjugative substituents should be employed.

Table I. Parameters for *E*- and *C*-Based Dual-Parameter Substituent-Constant Correlations

A. Nonconjugative Substituents[a]

X(a)[$\Delta C/\Delta E$][c]	ΔE^x	ΔC^x	*n*	X(a)[$\Delta C/\Delta E$][c]	ΔE^x	ΔC^x	*n*
H (50)	0	0	0.2	3-Br (21) [3.5]	–0.126	–0.445	0.2
3-$(CH_3)_2N$ (8) [6.0]	0.080	0.482	0.4	3I (16) [3.5]	–0.113	–0.397	0.2
3-H_2N (8) [6.3]	0.031	0.193	0.4	3-$CH_3C(O)$ (8) [2.8]	–0.099	–0.273	0.4
3-$(CH_3)_3C$ (5) [18]	–0.002	–0.029	0.6	3-$CH_3OC(O)$ (10) [3.6]	–0.085	–0.303	0.4
3-$(CH_3)_2CHCH_2$ (4)[b]	0.048	0.093	1	3-HO (9)[b]	0.049	–0.145	0.4
3-$CH_3(CH_2)_2CH_2$ (4)[b]	0.030	0.104	1	3-CH_3O (18) [1.5]	–0.030	–0.046	0.2
3-$(CH_3)_2CH$ (6)	–0.003	–0.049	0.6	3-HS (2)[b]	–0.088	–0.347	1
3-$CH_3CH_2CH_2$ (4)[b]	0.026	0.109	1	3-CH_3S (6) [3.0]	–0.055	–0.165	0.6
3-CH_3CH_2 (12) [4.1]	0.038	0.155	0.4	3-$CH_3S(O)$ (3)[b]	–0.185	–0.692	1
3-H_3C (27) [3.5]	0.037	0.128	0.2	3-CF_3S (4)[b]	–0.133	–0.458	1
3-$(CH_3)_3Si$ (5)[b]	0.000	0.014	0.6	3-$CH_3C(O)NH$ (8) [2.9]	–0.045	–0.130	0.4
3-C_6H_5 (11) [3.7]	–0.035	–0.130	0.4	3-F_3C (13) [4.0]	–0.159	–0.643	0.2
3-$ClCH_2$ (4)[b]	–0.038	–0.138	1	3-NC (17) [3.9]	–0.217	–0.844	0.2
3-$C_6H_5CH_2$ (3)[b]	0.001	–0.076	1	3-CH_3SO_2 (7)[b]	–0.216	–0.764	0.4
3-H_3C_2 (4)[b]	–0.035	–0.154	1	3-O_2N (19) [3.7]	–0.234	–0.868	0.2
3-F (15) [3.3]	–0.120	–0.401	0.2	3-F_5S (4)[b]	–0.201	–0.738	1
3-Cl (22) [3.5]	–0.127	–0.451	0.2				

B. Conjugative Substituents

X_c(a)[$\Delta C_c/\Delta E_c$][c]	ΔE_c^x	ΔC_c^x	*n*	X_c(a)[$\Delta C_c/\Delta E_c$][c]	ΔE_c^x	ΔC_c^x	*n*
H (50)	0	0	0.2	4-$CH_3S(O)$ (4)[b]	–0.165	–0.384	1
4-$(CH_3)(CH_3CH_2)CH$ (4)[b]	0.057	0.151	1	4-F_3CS (3)[b]	–0.184	–0.641	1
4-$(CH_3)_2CHCH_2$ (2)[b]	0.050	0.161	1	4-H_2N (12) [4.2]	0.129	0.538	0.4
4-$(CH_3)_3C$ (17) [2.8]	0.063	0.177	0.2	4-$(CH_3)_2N$ (16) [5.3]	0.164	0.866	0.2
4-$CH_3(CH_2)_2CH_2$ (2)[b]	0.019	–0.082	1	4-$CH_3C(O)NH$ (5) [16]	0.012	0.184	0.6
4-$(CH_3)_2CH$ (11) [3.2]	0.054	0.173	0.4	4-F_3C (11) [3.0]	–0.181	–0.537	0.4
4-$CH_3CH_2CH_2$ (3)[b]	0.050	0.170	1	4-F (20) [3.6]	–0.040	–0.143	0.2
4-CH_3CH_2 (11) [4.3]	0.042	0.181	0.4	4-Cl (26) [3.3]	–0.095	–0.315	0.2
4-H_3C (42) [3.7]	0.052	0.191	0.2	4-Br (21) [4.1]	–0.086	–0.355	0.2
4-$C_6H_5CH_2$ (3)[b]	0.022	0.108	1	4-I (13) [3.0]	–0.074	–0.223	0.2
4-C_6H_5 (12)	0.000	0.081	0.4	4-$CH_3OC(O)$ (9) [1.5]	–0.138	–0.202	0.6
4-$(CH_3)_3Si$ (6) [0.9]	–0.014	–0.013	0.6	4-$CH_3C(O)$ (9) [1.5]	–0.147	–0.218	0.6
4-$ClCH_2$ (2)[b]	–0.041	–0.158	1	4-NC (18) [2.2]	–0.234	–0.618	0.2
4-HO (6) [3.3]	0.060	0.195	0.6	4-CH_3SO_2 (8) [2.4]	–0.226	–0.550	0.4
4-C_6H_5O (4)[b]	–0.606	–9.64	1	4-O_2N (20) [2.8]	–0.242	–0.685	0.2
4-CH_3O (22) [4.7]	0.059	0.275	0.2	4-F_5S (3)[b]	–0.256	–0.952	1
4-CH_3S (6) [25]	0.007	0.175	0.6				

[a] The number of systems studied with a substituent is indicated in parentheses after the substituent. If this value is more than 12, an *n* value of 0.2 should be used in data fits, if less than 13 but more than 7, an *n* value of 0.4 is used, if less than 8 but more than 4, a value of 0.6 is used, and if 4 or less, a value of 1 is used. The weight given a substituent in a data fit is given by $1/n$. [b] The parameters are determined from reactions with a limited range of d^C/d^E values. [c] The ratio of the $\Delta C/\Delta E$ value.

3-X for nonconjugative and 4-X for conjugative. The Hammett equation also has different substituent constants for the 3- and 4-substituents. In our correlation, though 3- and 4-labels are employed, the use of these substituents is not restricted to phenyl rings. The 3-substituent parameters are employed on any nonconjugative system, and the 4-substituent parameters are employed on systems[18] where the conjugative mechanism dominates.

The least-squares minimization of the data fit of over 700 equations of the form of eqs 17 and 18 gives rise to the ΔE^x, ΔC^x, ΔE_C^x, and ΔC_C^x parameters in Table I. The total data fit is available as supplementary material. The d^E, d^C, and $\Delta\chi^H$ parameters for the various families of reactions are given in Table II. Selected systems will be discussed in subsequent sections to illustrate the generality of the data fit and the insights about chemical reactivity gained from the model.

General Applicability of ΔE and ΔC Substituent Constants. The data used in the derivation of the parameters come from a variety of measurements that have been previously interpreted with *E* and *C*, Hammett σ-, Taft σ_I-, σ°-, σ_R-, and σ^--, and Brown σ^+-parameters. In this section, the various sets of data will be discussed to illustrate the quality of the data fits and the insights gained from the dual-parameter analysis. The values calculated for the measured property result by substituting the ΔE^x and ΔC^x values for the substituents (Table I) and the d^E, d^C, and $\Delta\chi^H$ values for the families of reactions (Table II) into eq 17 or 18.

1. Substituted Pyridines. The substituted pyridines are the reference data set for which both s_B^E and s_B^C (eqs 12 and 13) are equal to 1. Accordingly, if E_A^* and C_A^* are known from the fit of other donors,[16] these values are assigned to d^E and d^C and held fixed in the data fit. Fixing the d^E and d^C parameters of eq 17 for these data, with the E_A^* and C_A^* values from the fit of a wide range of donors in the *E* and *C* correlation, provides the connection between the ΔE and ΔC substituent-constant correlation and the *E* and *C* correlation.[1] An asterisk on the systems in Table II indicates those systems for which E_A^* and C_A^* are known.[15]

The ΔE and ΔC values in Table I that have resulted from the fit of the entire substituent-constant data set are used in eq 17 to produce the calculated values in Table III. The calculated and experimental data are in excellent agreement for systems whose E_A^* and C_A^* values are known. The quality of the fit is gauged by the average absolute deviation $\bar{x}$ between the calculated and measured $\Delta\chi$ as well as the percent fit.[16] The percent fit (% *F*) is given by 100 times the ratio of $\bar{x}$ to the range of $\Delta\chi$, with the range defined as the largest calculated value minus the smallest one. A percent fit of 2 is excellent and 5–6 is good. Values of $\bar{x}$ and % *F* are given in the footnotes to the tables.

With s_B^E and s_B^C equal to 1, the E_A^* and C_A^* values for a new acceptor can be obtained directly from the d_A^E and d_A^C values obtained from measurements of a new acceptor reacting with a series of substituted pyridines. However, with the $\Delta C_B/\Delta E_B$ ratio of many substituents equal to 3.3 ± 0.3, care must be exercised in substituent selection. The ratios for established substituent constants for the pyridine family vary from 1.5 to 6.0. As wide a range as possible must be employed to divide the interaction into the E_A^* and C_A^* components when measurements involving

Table II. Parameters (d^E and d^C) for Families of Compounds

family[a]	d^E	d^C	$\Delta\chi^H$	family[a]	d^E	d^C	$\Delta\chi^H$
$\Delta\nu_{OH}$ CH_3OH/XC_5H_4N[b] (22*)	105.4	69.4	282.5	pK_a XCO_2H[x] (10, I)	(5.76)	(4.36)	3.8
$\Delta\nu$ I_2/XC_5H_4N[c] (22*)	1081	1098	4557	pK_a XC_6H_4COOH[y] (37, H)	4.09	−0.29	4.24
pK_a $XC_5H_4NH^+$[d] (31, +)	6.09	3.36	5.20	pK_a $XPhCH_2COOH$ (10%)[z] (17, R°)	2.36	−0.22	4.51
$-\Delta H$ I_2/XC_5H_4N[e] (3*)	0.50	2.00	8.17	pK_a XC_6H_4COOH (44%)[aa] (16, R)	6.16	−0.36	5.80
$-\Delta H$ C_6H_5OH/XC_5H_4N[f] (7*)	2.27	1.07	7.94	pK_a $XC_6H_4NH_3^+$[bb] (39, R⁻)	20.3	−2.97	4.65
$-\Delta G$ DMA/XPhOH[g] (17)	−7.8	0.41	2.91	log k/k_H $XPhC(CH_3)_2Cl$[cc] (25, +)	15.0	0.07	0.33
$-\Delta H$ BF_3/XC_5H_4N[h] (4*)	7.23	4.93	30.61	log k_R OH^-/rXPhCH_2OBz[dd] (12, R°)	−3.3	0.08	−2.15
$\Delta\nu$ ICN/XC_5H_4N[i] (7*)	4.43	14.65	55.2	log k_1 $H^+/XPhSi(CH_3)_3$[ee] (11, +)	(3.0)	(3.2)	−2.4
$-\Delta H$ 4F-PhOH/XC_5H_4N[j] (4*)	2.27	1.07	7.89	log k_R CH_3I/4XQuin[ff] (17, I)	13.2	−2.7	−2.4
$\Delta\nu_{OH}$ DMA/XPhOH[k] (16)	−523	55.4	343	pK_a $XPhCH_2CO_2H$ (75%)[gg] (15, R)	3.0	−0.2	6.2
$\Delta\nu_{OH}$ $(CH_2)_4S$/XPhOH[l] (7)	(−5.8)	(−66.1)	276	pK_a XC_6H_4SH (48%)[hh] (19, R⁻)	−15.1	2.0	0.07
$-\Delta H$ C_5H_5N/XC_6H_4OH[m] (7)	−1.94	−0.69	7.8	pK_a XC_6H_4OH (H_2O)[ii] (40, N)	15.56	−2.52	9.80
$-\Delta H$ $(CH_2)_4S/XC_6H_4OH$[n] (7)	−0.02	−1.43	4.84	pK_a $XPhCO_2H$ (CH_3NO_2)[jj] (14, R)	0.60	1.79	13.36
$\Delta\nu_{OH}$ $CH_3OH/XPhC(O)NR_2$[o] (8)	38.8	19.7	162	log K_{BHA} $XPhCO_2H(C_6H_6)$[kk] (20, R)	−3.9	−0.62	5.30
$-\Delta H$ $BF_3/XPhC(O)N(CH_3)_2$[p] (8)	1.66	1.57	24.3	pK_a XNH_3^+ (H_2O)[ll] (7, I)	(−2.5)	(0.45)	10.67
$-\Delta H$ $BF_3/XPhC(O)CH_3$[q] (8)	(−18.0)	(9.59)	18.0	pK_a $XPhCO_2H$ (13%)[mm] (11, R)	5.39	−0.44	5.86
σ_I-parameters[r] (32, I)	−7.7	1.41	0.08	pK_a XCH_2NH_2[nn] (9, I)	(0.16)	(4.4)	10.2
σ Hammett[s] (66, H)	−3.66	0.23	0.007	pK_R Mal[oo] (10, +)	−3.23	2.95	7.34
IE $XC_6H_5Cr(CO)_3$[t] (13, N)	−0.862	−0.231	7.26	pK_a 3-XAdCOOH (50%)[pp] (9, I)	26.5	−6.1	6.90
pK_a XC_8H_6COOH[u] (10, I)	16.5	−3.30	6.77	pK_a 4-$XPhC(OH)_2$[qq] (9, +)	(2.00)	(0.47)	−4.70
pK_a XCH_2COOH[v] (11, I)	51.9	−10.9	4.57	pK_a 4-$XPhCH_2CO_2H$ (H_2O)[rr] (11, R°)	3.28	−0.51	4.31
pK_a $XC_7H_{12}NH^+$[w] (16, I)	67.1	−14.3	10.7	ln k_r C_2H_5I/XC_5H_4N[ss] (8, +)	0.25	2.17	−3.59

[a] The number of substituents studied is indicated in parentheses under the column headed family. When followed by a letter, it indicates the subscript on the σ-constants used to correlate the data. If no letter is given, the system is part of the *E* and *C* data base. The letter N indicates no set works well. An asterisk on the number of systems studied indicates a pyridine family for which d^E and d^C were held fixed at known E_A^* and C_A^* values. Parentheses around a d^E or d^C value indicates a tentative number. The average deviation between the calculated and experimental measurement is given by $\bar{x}$ and reported in the footnote for each reaction. The percent fit is 100 times the ratio of $\bar{x}$ to the range of $\Delta\chi$, i.e., largst minus smallest $\Delta\chi$. [b] Changes in OH stretching frequncy (cm^{-1}) of methanol for a series of substituted pyridine adducts; ref 20. [c] Blue shifts (cm^{-1}) of the visible transition of substituted pyridine adducts of iodine; ref 20. [d] Ionization of substituted pyridinium ions in H_2O at 25 °C; refs 25 and 26; a σ^+-system. [e] Enthalpies of iodine adduct formation (kcal mol^{-1}) for a series of substituted pyridines in hexane; ref 3. [f] Enthalpies of phenol adduct formation (kcal mol^{-1}) for a series of substituted pyridines in cyclohexane; ref 24. [g] ΔG for adducts of $CH_3C(O)N(CH_3)_2$ with XC_6H_5OH in CCl_4 at 25 °C; ref 23. [h] Enthalpies of BF_3 adduct formation (kcal mol^{-1}) for a series of donors in CH_2Cl_2; ref 21. [i] Change in the infrared C–I stretching frequencies for the ICN adducts of a series of substituted pyridines; ref 3. [j] Enthalpies (kcal mol^{-1}) of adduct formation for FC_6H_4OH with a series of substituted pyridines in cyclohexane; 1 kcal mol^{-1} is added to enthalpies reported in CCl_4; ref 5b. [k] Changes in the OH stretching frequency (cm^{-1}) of hydrogen-bonded adducts of *N*,*N*-dimethylacetamide with a series of phenols; ref 23. [l] Changes in the OH stretching frequency (cm^{-1}) of hydrogen-bonded adducts of tetrahydrothiophene with a series of substituted phenols; ref 24b. [m] Enthalpies (kcal mol^{-1}) of adduct formation of pyridine with a series of substituted phenols; ref 24a. [n] Enthalpies (kcal mol^{-1}) of adduct formation of tetrahydrothiophene with a series of substituted phenols; ref 24b. [o] Change in the OH stretching frequency (cm^{-1}) of hydrogen-bonded adducts of methanol with a series of substituted *N*,*N*-dimethylbenzamides; ref 22. [p] Enthalpies (kcal mol^{-1}) of BF_3 adduct formation for a series of substituted *NN*-dimethylbenzamides in CH_2Cl_2; ref 22. [q] Enthalpies (kcal mol^{-1}) of BF_3 adduct formation for a series of substituted benzophenones in CH_2Cl_2; ref 22. [r] Taft σ_I-parameters; ref 26. [s] Hammett substituent constants; ref 10. [t] Ionization energies (eV) of a series of substituted benzenechromium tricarbonyls; ref 27. [u] pK_a of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids in 50% w/w EtOH–H_2O at 25 °C; ref 26; a σ_I-system. [v] pK_a of substituted acetic acids in water at 20 °C; ref 26; a σ_I-system. [w] pK_a of 4-substituted quinuclidinium ions in H_2O at 25 °C; ref 26; a σ_I-system. [x] Ionization of RCO_2H in H_2O at 25 °C; ref 26; a σ_I-system. [y] Ionization of XC_6H_4COOH in water at 25 °C; ref 25; a σ-system. [z] Ionization of XCH_2H_4COOH in 10% EtOH–H_2O at 25 °C; ref 28; a $\sigma_R°$-system. [aa] pK_a of $XC_6H_4CO_2H$ in 44.1% w/w aqueous ethanol at 25 °C; ref 26; a σ_R-system. [bb] Ionization of $XC_6H_6CNH_3^+$ in H_2O at 25 °C; refs 25 and 26; a σ_R^--system. [cc] log $k/k°$ for the solvolysis of cumyl chloride at 25 °C in 90% acetone; refs 14 and 25; a σ^+-system. [dd] log of k_R for the reaction of OH^- with a series of $XC_6H_4CH_2OBz$ in 70% v/v aqueous MeOAc at 25 °C; ref 26; a $\sigma_R°$-system. [ee] log of k_1 (min^{-1}) cleavage $C_6H_5Si(CH_3)_3$ in aqueous methanol/$HClO_4$ at 51.2 °C; ref 28; a σ^+-system. [ff] log of k_R for the reaction of CH_3I with 4-substituted quinuclidines in CH_3OH at 10 °C; ref 26; a σ_I-system. [gg] pK_a of $XC_6H_4CH_2COOH$ in 75% w/w aqueous C_2H_5OH at 25 °C; ref 26; a $\sigma_R°$-system. [hh] Ionization of a sries of subsituted XC_6H_5SH compounds in 48% aqueous C_2H_5OH at 25 °C; ref 25; a σ_R^--system. [ii] pK_a of substituted phenols in water at 25 °C; ref 25; a σ_R^-(P)-system. [jj] pK_a of $XC_6H_4CO_2H$ in CH_3NO_2 at 25 °C; ref 26; a σ_R-system. [kk] log K_{BHA} of $XC_6H_4CO_2H$ in C_6H_6 at 25 °Cl ref 26; a σ_R-system. [ll] pK_a of XNH_3^+ in water at 25 °C; ref 26; a σ_I-system. [mm] pK_a of XC_6H_4 CO_2H in 12.7 mol % aqueous dioxane at 25 °C; ref 26; a σ_R-system. [nn] pK_a of XCH_2NH_2 in H_2O at 25 °C; ref 26; a σ_I-system. [oo] pK_R of 4-substituted malachite green; ref 26; a σ^+-system. [pp] pK_a of 3-substituted adamantane-1-carboxylic acid in 50% v/v aqueous C_2H_5OH at 25 °C; ref 26; a σ_I-system. [qq] pK_a of 4-$XC_6H_4^+$ (OH_2) in H_2SO_4; ref 26; a σ^+-system. [rr] pK_a of 4-$XC_6H_4CH_2CO_2H$ in H_2O at 25 °C; ref 26; a $\sigma_R°$-system. [ss] log k_r for the reaction of 4-XC_5H_4N with C_2H_5I in nitrobenzene at 60 °C; ref 26; a σ^*-system.

only substituted pyridines[19] are employed. The resulting E_A^* and C_A^* values are expected to predict with good accuracy properties of donors with a C_B/E_B ratio whose range corresponds to that employed in the data fit and to provide rough estimates of interactions with other donors.

With s_B^E and s_B^C equal to 1, the C_B and E_B values of any substituted pyridine can be obtained by adding ΔE^x to the *E* value of pyridine and ΔC^x to the *C* value of pyridine. In general, the values of ΔE^x and ΔC^x from this correlation are much more accurately known than the E^* and C^* values.

2. Families of Donors Other Than Pyridine Reacting with Acceptors Whose E_A^* and C_A^* Values Are Known. When donors other than pyridine are considered, the s^E and s^C values are unknown. If d^E and d^C are determined from a data fit with a probe whose E_A^* and C_A^* values are reported,[15] s_B^E and s_B^C can be calculated as the only unknowns in eqs 15 and 16. The O–H infrared frequency shift of CH_3OH upon coordination to the carbonyl oxygen of a series of substituted *N*,*N*-dimethylbenzamides[20] is fit as shown in the first two columns of Table IV with $d_A^E = 38.8$ and $d_A^C = 19.7$. Since E_A^* and C_A^* are known[15] for methanol shifts with a wide range of donors ($E_A^* = 104$ and $C_A^* = 69.4$), eqs 15 and 16 lead to values of $s_B^E = 0.4$ and $s_B^C = 0.3$. This value for s^E indicates that the substituent influence on the E_B value is transmitted about 0.4 times as effectively in this system as it is transmitted in pyridine. The value of 0.3 for s_B^C indicates that the covalent effect of the substituent is transmitted about

(19) If a new acceptor is studied with the series of pyridines, then solving for d^E and d^C produces the E_A^* and C_A^* values. However, since the C_B/C_B ratios of pyridines and most families of compounds are similar, the resulting E_A^* and C_A^* values are considered tentative and should be used only with donors that have a C_B/E_B ratio in the range employed to determine E_A^* and C_A^*. For such studies, the 4-$N(CH_3)_2$, 4-NO_2, and 4-CN derivatives should be studied to provide a $\Delta C_B/\Delta E_B$ range of 5.3–2.2 for the family. In the case of pyridine derivatives, this $\Delta E_B/\Delta E_B$ only provides a C_B/E_B range of 1.9–2.3.

(20) Nicolet, P.; Laurence, C. *J. Chim. Phys. Phys.-Chim. Biol.* **1983**, *80*, 677.

Table III. Sample Data Fits of Substituted Pyridines with Reactants Whose E_A^* and C_A^* Values are Known (d^E and d^C are fixed)

	reactant									
	$\Delta\nu_{OH}$ CH_3OH		$\Delta\nu$ I_2		pK_a		$-\Delta H$		$\Delta\nu_{Cl}$ ICN	
subst	exp	calc[a]	exp	calc[b]	exp[c]	calc[d]	exp[e]	calc	exp	calc[f]
4-$C(CH_3)_3$	298	301	4870	4819						
4-$CH(CH_3)_2$					6.04	6.11				
4-C_2H_5	299	299	4800	4800	6.03	6.06			62.0	58.1
3-C_2H_5	300	297	4760	4769						
4-CH_3	301	301	4830	4823	6.03	6.16	8.3[g]	8.3	61.5	58.3
							8.3[h]	8.2		
							8.9[i]	8.6		
							32.0[j]	31.9		
3-CH_3	297	295	4730	4737	5.67	5.85	8.3[i]	8.4	61.5	57.3
							31.3[j]	31.5		
4-$N(CH_3)_2$	361	360	5680	5685	9.59	9.11	8.8[h]	9.2		
							36.2[j]	36.1		
3-$N(CH_3)_2$	325	324	5170	5172						
4-NH_2	335	333	5280	5287	9.12	(7.79)				
4-OCH_3	308	308	4920	4922	6.58	6.48				
H	281	282	4560	4557	5.21	5.20	7.9[g]	7.9	57.5	55.2
							8.1[h]	7.9		
							8.0[i]	8.2		
							30.6[j]	30.6		
4-$COCH_3$	254	252	4150	4158	3.51	3.57				
3-$COCH_3$	251	253	4160	4150	3.22	3.68				
4-CO_2CH_3	251	254	4210	4186	3.49	3.68				
3-CO_2CH_3	251	253	4140	4132	3.09	3.66				
4-Cl	250	251	4110	4109	3.83	3.57				
3-Cl	239	238	3920	3923	2.81	2.91	7.2[h]	7.1	45.5	48.1
3-Br	239	238	3930	3932	2.85	2.94			42.0	48.2
3-I	243	243	4000	3999	3.29	3.18			44.0	48.9
4-CF_3	224	226	3780	3771						
3-CF_3	223	221	3670	3678						
4-CN	216	215	3620	3624	1.86	1.70				
3-CN	202	201	3390	3396	1.35	1.04				

[a] The shift in the O–H stretching vibration of methanol upon adduct formation; ref 16. For substituted pyridines, $\bar{\nu} = 1.4$ cm^{-1} and % $F = 1$. [b] The blue shift of iodine adducts; ref 16. For substituted pyridines, $\bar{x} = 8$ cm^{-1} and % $F = 0.3$. [c] Reference 27; pK_a of substituted $C_5H_4NH^+$ in water at 25 °C. [d] Calculated with d^E and d^C from Table II and $\Delta\chi^H = 5.21$; $\bar{x} = 0.13$ and the % F is 2. In addition to the systems shown, the following experimental and calculated results were obtained: found exp/calc, 3-NO_2 1.18/0.86; 3-F 2.97/3.12; 4-Br 3.75/3.48; 4-NO_2 1.39/1.43; 4-C_6H_5 5.35/5.47; 3-OCH_3 4.81/4.86; 4-I 4.01/4.00; 3-SCH_3 4.31/4.31; 4-SCH_3 5.83/5.84; 3-C_6H_4 4.80/4.55; 3-NH_2 6.04/6.03; 3-$CH_3C(O)NH$ 4.46/4.49; abnd 4-$CH_3C(O)NH$– 5.89/5.89. The value of $\bar{x}$ is 0.15, and % F is 1.8. [e] These are enthalpies measured in cyclohexane or for BF_3 in CH_2Cl_2. The superscript g refers to the acceptor phenol, h to fluorophenol, i to I_2, and j to $BF_3(CH_2Cl_2)$. In addition to these acceptors, six additional enthalpies with other acceptors were entered for the H and 4CH_3 systems. [f] The change in the I–C stretching vibration upon adduct formation; see ref 16 for $\bar{x}$ and % F.

0.3 times as effectively by this family as it is transmitted in pyridine. Fitting the BF_3 enthalpies[22] for this same family of amides produces $d^E = 1.66$ and $d^C = 1.57$. Equations 15 and 16, with $E_A^* = 7.23$ and $C_A = 4.93$, lead to an s_B^E value of 0.2 (1.66/7.23) and an s_B^C value of 0.3 (1.57/4.93). The same values of s_B^E and s_B^C should have resulted from the BF_3 and methanol analyses. However, experimental error leads to the slight differences in the s_B^E and s_B^C values from those of the two acceptors with the more accurate transfer values for the benzamides resulting from the methanol shifts.

When the probe E^* and C^* values are known, d^E and d^C can be solved for s^E and s^C which provide the added information about the effectiveness with which substituent effects are transmitted through the framework to the reactive center. Furthermore, knowing s_B^E and s_B^C for a family and the E and C values for the parent hydrogen compound enables one to determine E and C values for any member of the family whose substituent constant is known. The E_B^x value is calculated from eq 19.

$$E_B^x = E_B^H + s_B^E \Delta E_B^x \qquad (19)$$

In a similar fashion, eq 20 leads to the C_B value.

$$C_B^x = C_B^H + s_B^C \Delta C_B^x \qquad (20)$$

With 65 substituent constants in Table I, the enthalpies of interaction of these 65 donors with the 65 acceptors in the E and C correlation can be predicted. This corresponds to the prediction of 4225 enthalpies and physicochemical quantities.

Accurate solution of a series of equations like (17) or (18) for the d^E values requires that substituents be employed whose ΔC^x to ΔE^x ratio varies. When only substituents with similar ratios are used, large errors can result in the d^E and d^C values for a property, $\Delta\chi$. Tentative values of d^E and d^C should not be used to make comparisons of the covalency in the interaction and sensitivity of the family to substituent changes. The $\Delta C^x/\Delta E^x$ ratio of the various substituents are indicated in brackets in Table I. Several of the ratios are large, but the ΔE^x and ΔC^x values are very small.

Electron-withdrawing substituents in general have negative signs for ΔE^x and ΔC^x, while electron-releasing substituents generally have positive signs. In certain families, e.g., the aliphatic amines, substitution of a hydrogen for CH_3 increases the polarizability and the C_B value. The methyl substituent on a nitrogen decreases the lone-pair dipole moment and decreases the E_B value. This substituent effect would be manifested in a negative value of s_B^E and a positive value of s_B^C for the family. In other instances, the covalent contribution can increase the size of the physicochemical property and the electrostatic contribution can decrease the size of the physicochemical property, i.e., E_A^* and C_A^* have different signs. The combination of a negative s_B^E and a negative E_A^* could lead to a positive d^E. Thus, either E_A^* and C_A^* or s_B^E and s_B^C have to be known in order to interpret the sign of d_A.

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Table IV. Fits of Spectral Shifts and Enthalpies for Families of Compounds with Eq 19[a]

subst	$-\Delta\nu$ exp[b]	$-\Delta\nu$ calc[c]	$-\Delta H(BF_3)R'CONR_2$, $R'COCH_3$ exp[d]	$-\Delta H(BF_3)R'CONR_2$, $R'COCH_3$ calc[e]	$\Delta\nu_{OH}$ DMA exp[f]	$\Delta\nu_{OH}$ DMA calc[h]	$\Delta\nu_{OH}$ DMA calc σ[i]	$\Delta\nu_{OH}$ THTP exp[j]	$\Delta\nu_{OH}$ THTP calc[k]	$-\Delta H$ Py, THTP exp[l]	$-\Delta H$ Py, THTP calc[m]
3-CH_3			(18.2)	(18.5)	330	331	334				
4-CH_3	168	168	24.5	24.7	327	327	323	264	263	7.8	7.6
			(18.6)	(18.9)						(4.6)	(4.6)
H	159	162	24.3	24.3	345[g]	343	341	274	276	7.9	7.8
			(17.8)	(17.9)						(4.9)	(4.8)
4-OCH_3	171	170	24.7	24.8	328[g]	328	324				
			(19.8)	(19.5)							
3-NO_2					418	417	422				
3-F					384[g]	384	380	303	303	8.4[e]	8.3
										(5.5)	(5.4)
4-F	158	157	24.1	24.0	357[g]	357	355	286	286	8.1	8.0
										(5.0)	(5.1)
3-Cl					385[g]	385	384				
4-Cl			(17.4)	(16.6)	376[g]	376	369	298	297	8.1	8.2
										(5.3)	(5.3)
3-Br					384	385	384				
4-$N(CH_3)_2$	185	185	26	25.9							
			(23.9)	(23.3)							
4-Br	152	151	23.6	23.6	369	369	371	301	300		
3-CF_3					391[g]	391	394	319	319	8.5	8.6
										(5.7)	(5.8)
3-CN					410	410	412				
4-CN					432	432	422				
			(16.0)	(16.3)							
4-NO_2	139	139	22.5	22.8	431	432	434				
4-CF_3	144	144	23.5	23.3							
4-*t*-Bu					320[g]	321	322			7.2	7.6
										[4.5]	[4.6]

[a] This table combines data in which families of donors and families of acceptors are studied. For families of acceptors, the subscript on the d^E and d^C parameters of eq 17 is changed to B. [b] Reference 21. R′ refers to a series of substituted phenyl groups. The OH shift of CH_3OH upon hydrogen bonding to the carbonyl is measured. [c] Calculated with parameters from Table II and eq 17. The value of $\bar{x}$ is 0.8 cm^{-1},k and the % *F* is 1.7%. [d] Reference 21. The enthalpy of adduct formation of $XC_6H_4CON(CH_3)_2$ and $XC_6H_4COCH_3$ with BF_3 in CH_2Cl_2. [e] Calculated with parameters from Table II and eq 17. The $\bar{x}$ values are 0.2 and 0.4 kcal mol^{-1}, and the % *F* values are 4 and 5, respectively, for $XC_6H_4CON(CH_3)_2$ and $XC_6H_4COCH_3$. [f] Data from ref 22 unless labeled with *g*. The OH shift of substituted phenols hydrogen bonding to *N*,*N*-dimethylacetamide is measured. [g] Data from ref 24a. [h] Calculated using the parameters from Table II and eq 18. [i] Calculated by fitting the shifts to the Hammett σp equation. [j] Reference 24b. [k] Calculated with parameters from Table II and eq 18. The value of $\bar{x}$ is 0.8, and the % *F* is 1.5. [l] The enthalpy of adduct formation between the substituted phenol and the donor is indicated; refs 24a (C_5H_5N) and 24b ($(CH_2)_4S$). [m] Calculated with parameters from Table II and eq 18. For pyridine, the $\bar{x}$ value is 0.16 kcal mol^{-1} compared to an experimental error of 0.2. The % *F* is large because the range of ΔH values is small. For $(CH_2)_4S$, the value of $\bar{x}$ is 0.06.

3. Analysis of Families of Acceptors Reacting with a Given Donor. The next set of data to be considered involves the application of the ΔE^x and ΔC^x substituent constants to a family of acceptors. The change in the OH stretching frequency of a series of substituted phenols upon hydrogen bonding to *N*,*N*-dimethylacetamide, DMA, is analyzed.[23] For a series of acceptors (electrophiles) which is studied with the same donor (nucleophile), eq 18 is employed. An excellent fit of the data results. The average absolute difference of the calculated and experimental values, $\bar{x}$, is less than 0.5 cm^{-1} for a system in which the experimental error is 3 cm^{-1}. The overall fit $\Delta E/\Delta C$ is better than that obtained by fitting the data to the Hammett equation (i.e., eq 6), as shown in the column $\Delta\nu_{OH}$(calc σ) in Table IV, where the average deviation is 3 cm^{-1}. The signs of the d^E and d^C parameters change if the electrostatic and covalent changes from a methyl substituent, for example, were to make a donor more basic and an acceptor more acidic. The data fit gives $d_B{}^E = -523$, $d_B{}^C = 55.4$, and $\Delta\chi^H = 343$. This suggests that the electrostatic property of DMA dominates the shift induced by a substituent change on the phenol with a small covalent contribution of opposite sign. The signs of the $d_B{}^E$ and $d_B{}^C$ parameters are a function of $E_B{}^*$ and $C_B{}^*$ of DMA, vide infra.

Additional tests of the extension of the ΔE^x and ΔC^x parameters to other probes that have been shown[15] to fit the E and C model are also reported in Table IV. The $\Delta\nu_{OH}$(THTP),[24] ΔH(PY),[24] and ΔH(THTP)[24] columns involve systems in which the donor is held constant and a family of acceptors is studied. (THTP refers to tetrahydrothiophene.) Excellent fits of this wide range of spectral and thermodynamic measurements result. The value of $\bar{x}$ is generally small compared to the error in the measurement. The d^E and d^C parameters for all three systems are both negative. The frequency shift and enthalpy for the THTP adducts are dominated by changes made in the tendency of the acceptor to undergo covalent interactions. Both C_B for THTP enthalpies and $C_B{}^*$ for the shifts are larger than the corrresponding *E* parameter. With E_B and C_B known for pyridine and THTP, the $s_A{}^E$ and $s_A{}^C$ values for phenols can be calculated. Using the d^E and E_B values for pyridine leads to an $s_A{}^E$ value of 1.1. The average $s_A{}^C$ value calculated from d^C is 0.27 ± 0.07. Errors in the d^E values are reflected in $s_A{}^E$ and $s_A{}^C$ because the $\Delta C/\Delta E$ ratio of the substituents studied only varies from 1 (for H) to 4.0 (for 3-CF_3), with all but one substituent falling in the range of 2.8 to 4.0.

4. ΔE and ΔC Analysis of Systems Correlated by Hammett and Localized σ_I-Substituent Constants. The data fits reported above show that the ΔE^x and ΔC^x parameters can be used on either donors or acceptors and when $E_A{}^*$ and $C_A{}^*$ or $E_B{}^*$ and $C_B{}^*$ are known, the d^E values can provide a measure of the transfer of the substituent effect in a system. The next tests of the two-parameter analysis involve systems correlated with the Hammett σ-parameters and Taft σ_I.[25,26] The fit of the pK_a values of substituted benzoic acid derivatives is excellent. Sixteen of the

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Table V. Dual Parameter Fit of σ- and σ_I-Systems

subst	pK_a XC_6H_4COOH exp[a]	calc[b]	σ_I exp[c]	calc[d]	log k_r CH_3I/XQuin exp[e]	calc[f]	pK_a XC_8H_6COOH exp[g]	calc[h]	pK_a $XC_7H_{12}NH^+$ exp[i]	calc[j]
3-$C(CH_3)_3$			–0.01	0.05	–2.38	–2.37				
3-$CH(CH_3)_2$			0.01	0.04	–2.39	–2.33			11.20	11.19
3-C_2H_5			–0.01	0.00	–2.40	–2.34	6.89	6.89	11.09	11.04
3-CH_3	4.27	4.35	–0.01	–0.02	–2.41	–2.29	6.89	6.98	11.01	11.31
3-H	4.20	4.24	0.0	0.08	–2.35	–2.43	6.87	6.77	11.12	10.69
3-$N(CH_3)_2$			0.17	0.15	–2.65	–2.68				
3-CH_2Cl			0.17	0.18	–2.57	–2.55			10.15	10.15
3-OCH_3	4.08	4.13	0.30	0.25	–2.77	–2.69	6.40	6.43	9.31	9.35
3-CO_2CH_3	3.83	3.98	0.32	0.31			6.40	6.37	9.42	9.33
3-F			0.54	0.44						
3-Cl	3.83	3.85	0.47	0.43	–2.91	–2.88	6.13	6.17	8.61	8.62
3-Br	3.81	3.85	0.47	0.42	–2.89	–2.88	6.14	6.17	8.47	8.64
3-I	3.85	3.89	0.40	0.40	–2.83	–2.85			8.78	8.78
3-CF_3	3.77	3.77	0.40	0.40			6.25	6.27		
3-NO_2	3.48	3.54	0.67	0.66	–3.18	–3.16	5.82	5.79	7.64	7.47
3-CN	3.64	3.59	0.57	0.57	–3.00	–3.01			8.08	8.21

[a] The pK_a of substituted benzoic acids in water at 25 °C; a Hammett σ-system. [b] Calculated with the paramters in Table II. Sixteen of the 37 systems studied are listed in this table. For the total fit $\bar{x}$ = 0.04 and % F = 3.6. [c] Taft σ_I-parameters from ref 26. [d] Calculated with d^E, d^C, and $\Delta\chi^H$ from Table II. Sixteen of the 32 substituents studied are shown. For the total fit, $\bar{x}$ = 0.04 and % F = 5.2. [e] log k_r for the reaction of CH_3I with 4-substituted quinuclidines in CH_3OH at 10 °C; ref 26. [f] Calculated with the parameters in Table II. Thirteen of the 17 substituents fit are shown. For the total fit $\bar{x}$ = 0.04 and % F = 4.7. [g] pK_a of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids in 50% w/w EtOH–H_2O at 25 °C. Holtz, H. D.; Stock. *J. Am. Chem. Soc.* **1964**, *86*, 5188; **1967**, *89*, 5677. [h] Calculated with the parameters in Table II. Nine of the 10 substituents fit are shown. For the total fit, $\bar{x}$ = 0.04 and % F = 3.7. [i] pK_a of 4-substituted quinuclidinium ions in water at 25 °C. Grob, C. A.; Schlageter, M. G. *Helv. Chim. Acta* **1976**, *59*, 264. [j] Calculated with the parameters in Table II. Twelve of the 16 substituents fit are shown. For the total fit, $\bar{x}$ = 0.09 and % F = 2.6.

37 substituents fit are shown in Table V. The average deviation of this fit is 0.04, and the percent fit is 3.6. The d_B values cannot be analyzed in terms of the $s_A{}^E$, $s_A{}^C$, $E_B{}^*$, and $C_B{}^*$ components. Even the sign of the parameters cannot be attributed to the $s_A{}^E$ or $E_B{}^*$ or to the $s_A{}^C$ or $C_B{}^*$ components. The combined influence suggests domination by the electrostatic properties of the substituent.

The Hammett substituent constants can be entered into eq 19 as a $\Delta\chi$. The resulting set of simulations equations is solved to give $d^E = -3.65$, $d^C = 0.227$, and $\Delta\chi^H = 0.01$. The average deviation is 0.03, and the percent fit is 3. The d^E and d^C values are opposite those found for the pK_a of benzoic acid because of the sign convention used by Hammett. The ratios of d^C/d^E afford comparisons of the net importance of covalent and electrostatic contributions for the combined effects of the reactant demand and the substituent transfer. The combined properties d^E are referred to as the *system demand*. The ratios of d^C/d^E are –0.07 for the pK_as and –0.06 for the Hammett parameters. Data correlated with the Hammett parameters are dominated by the E term with a small covalent contribution of opposite sign.

The localized substituent constants σ_I have been used on aliphatic families where the substituent is bonded to an sp^3 carbon. The σ-constants do not correlate this data, therefore a separate scale is needed. The very large amount of work in this area is summarized in comprehensive reviews by Ehrenson, Brownlee, and Taft[25] and by Charton.[26] Nine different reactions that are correlated with these parameters[18] are included in the ΔE^x–ΔC^x fit (Table II). The consistency of the ΔE^x–ΔC^x approach with this voluminous set of experimental data is illustrated in Table V by presenting the fit of representative systems. The ideal reference set[25] for definition of σ_I is the 4-substituted bicyclo[2.2.2]octane-1-carboxylic acid series. The pK_as in 50% w/w aqueous ethanol at 25 °C are fit, and 9 of the 10 substituents reported are presented in Table V under the column labeled XC_8H_6COOH. An excellent correlation results for the 10 substituents with an average deviation of 0.04 and a percent fit of 3.7. Table V also contains correlations of the pK_as of 12 of the 16 reported 4-substituted quinuclidinium ions ($XC_7H_{12}NH^+$, average deviation of 0.09 and percent fit of 2.6 for the 16 substituents). The correlation of kinetic data is illustrated with data for the fit of the log of the rate constant for the reaction of CH_3I with 13 of 17 reported 4-substituted quinuclidines (CH_3I/XQuin, $\bar{x}$ = 0.04 and % F = 5). These three systems are reported to correlate with σ_I and are fit very well to ΔE^x and ΔC^x. The d^C/d^E ratios of all the well-established parameters for σ_I-systems are –0.20 ± 0.02.

The constancy of the d^C/d^E ratio for all systems correlated by σ and a different constant ratio for σ_I-systems supports the earlier conclusion (eq 4) concerning the requirement of a one-parameter data fit. The different ratios for the σ- and σ_I-data sets also explain why different one-parameter scales are needed for σ- and σ_I-systems. The dual-substituent approach provides a set of substituent constants that eliminates the need for a separate Hammett and σ_I-scale.

It is also interesting to note that the ΔE^x and ΔC^x parameters fit data in both nonprotonic (Tables III and IV) and protonic solvents (Table V). This fact indicates that the trends in these aqueous systems are dominated by bond-strength considerations. Caution should be employed in treating substituents that are basic enough to interact with protonic solvents, e.g., 3-OCH_3 and 3-$N(CH_3)_2$ substituents. If compounds with these substituents hydrogen bond or are protonated, then one must consider whether or not this interaction will be different in the free base and the reaction product. If the interaction is the same, then the hydrogen bonding will cancel out and not influence the measured property. If the interaction is different, then the correlation with ΔE and ΔC will fail.

5. ΔE and ΔC Analysis of Data Correlated with σ^+-, σ_R-, $\sigma_R{}^\circ$-, and σ^--Substituent Constants. Electrophilic reactions are correlated[14] with σ^+. Six reactions correlated with these parameters are included in the ΔE^x–ΔC^x fit. The scale is based, to a large extent, on the hydrolysis of meta- and para-substituted α-cumyl chlorides. The fit of log k/k_H for this reaction with the ΔE^x and ΔC^x values for the substituents from Table I is shown in column 1 of Table VI for 12 of the 25 reported substituents. The solution of the resulting 25 simultaneous equations produces $d_A{}^E = 15.0$, $d_A{}^C = 0.070$, and $\Delta\chi^H = 0.33$. The average deviation is 0.3, and the percent fit is 6. The d^C/d^E ratio of this data set is ~0. This system has a slight covalent contribution which is in the same direction as the dominant electrostatic term.

Data fits for the rates of acid-catalyzed cleavage of 11 substituted phenyltrimethylsilane[27] derivatives (Table VI) and the pK_as of 31 substituted pyridinium ions[25,26] (Table III) are also shown as examples of systems correlated with σ^+. Values

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Table VI. $\Delta E - \Delta C$ Fit of σ_R-, $\sigma_R{}^\circ$-, σ^--, and σ^+-Systems

	log k/k_H σ^+		log k $XC_6H_4Si(CH_3)_3$ σ^+		pK_a $XC_6H_4NH_3{}^+$ $\sigma_R{}^-$		pK_a $XC_6H_4CO_2H(C_6H_6)$ σ_R		pK_a $XC_6H_4CH_2COOH$ $\sigma_R{}^\circ$	
subst	exp[a]	calc[b]	exp[d]	calc[e]	$\sigma_R{}^-$ exp[f]	calc[g]	exp[h]	calc[i]	exp[j]	calc[k]
3-CH_3	0.30	0.89	−2.4	−1.8	4.73	5.01	5.13	5.07	4.56	4.56
3-F	−1.6	−1.5			3.59	3.41	5.94	6.02	4.34	4.32
3-Cl	−1.8	−1.6			3.50	3.41	6.06	6.08	4.33	4.31
3-Br	−1.8	−1.6			3.58	3.42	6.06	6.07	4.33	4.31
3-I	−1.6	−1.4			3.61	3.53	6.05	5.99		
3-$C(CH_3)_3$	0.27	0.31								
H	0.00	0.33	−2.7	−2.4	4.60	4.65	5.26	5.30	4.50	4.51
4-C_6H_5	0.81	0.33	−2.2	−2.1	4.24	4.40				
4-NH_2					5.89	5.66	4.45	4.45		
4-$N(CH_3)_2$							4.89	(4.11)		
4-CH_3	1.4	1.1	−1.4	−1.6	5.08	5.14	5.03	4.97	4.57	4.59
4-$CH(CH_3)_2$	1.3	1.2	−1.5	−1.7						
4-OCH_3	3.5	(1)[c]			5.34	5.03	4.92	4.89	4.55	4.58
4-F	0.3	−0.28	−2.9	−3.0	4.65	4.26	5.61	5.54	4.43	4.45
4-Cl	−0.52	−1.1	−3.6	−3.7	3.98	3.66	5.82	5.87	4.37	4.36
4-Br	−0.7	−1.0	−3.7	−3.8	3.86	3.95	5.86	5.86	4.36	4.39
4-CO_2CH_3					2.46	2.45				
4-NO_2	−3.6	−3.3			1.00	(1.79)	6.80	6.68	4.05	4.10
4-CN	−3.0	−3.2			1.71	1.74	6.53	6.61	4.11	4.10
4-$C(CH_3)_3$	1.2	1.3	−1.5	−1.6	4.95	5.40				
4-C_2H_5	1.3	1.0	−1.5	−1.7						
4CF_3	−2.8	−2.4			2.75	2.58				

[a] Reference 14. [b] Calculated from d^E and d^C from Table II and $\Delta\chi^H = 0.33$. For the total fit, $\bar{x}$ is 0.29 and the % F is 6. [c] Omitted from fit and calculated with the resulting parameters. [d] Reference 26. log k (min^{-1}) of acid-catalyzed cleavage of substituted phenyltrimethylsilanes. [e] Calculated with d and d′ from Table II and $\Delta\chi^H = -2.4$. For the total fit, $\bar{x}$ is 0.17 and % F is 7. [f] References 25 and 26. Ionization of substituted anilinium ions in water; a $\sigma_R{}^-$-system. [g] Calculated with d^E and d^C from Table II and $\Delta\chi^H = 4.65$. For the total fit, $\bar{x} = 0.14$ and the % F is 3.6. [h] Reference 26. [i] Calculated with d^E and d^C from Table II and $\Delta\chi^H = 5.30$. For the total fit, $\bar{x} = 0.06$ and the % F is 2.2. [j] Reference 26. Ionization in 10% C_2H_5OH. [k] Calculated with d^E and d^C from Table II and $\Delta\chi^H = 4.51$. For the total fit, $\bar{x} = 0.022$ and the % F is 4.7.

of $\bar{x} = 0.17$, % $F = 7$ and $\bar{x} = 0.15$, % $F = 1.8$ result, respectively. The average deviation of the silane is acceptable, but the percent fit indicates that this system is poorly fit because the range of rates is small. This makes the d^C/d^E ratio tentative with a value of 1.1. The average deviation in the pK_a values of substituted pyridines is comparable to that for the hydrolysis of phenyl-substituted trimethylsilanes. However, the percent fit is excellent because of the wide range of the measured values. The d^C/d^E ratio for this system is 0.55. Covalency in the interaction is in the same direction as the electrostatic term for this data in contrast to that in data correlated with either σ or σ_I.

A significant feature of the ΔE–ΔC analysis is its ability to recognize a deviant system. Something unusual is going on in the pyridinium system with the 4-NH_2 substituent. This data point was omitted from the fit. The calculated value is given in parentheses (Table III). Since the dimethylamino substituent is well behaved, hydrogen bonding of the amino hydrogen with the pyridine nitrogen may be the source of the problem.

Most importantly, we have shown that by simply changing the mix of the fundamental ΔE^x and ΔC^x substituent constants with d^E and d^C, data that correlate with σ^+ can be accommodated with the dual ΔE^x and ΔC^x parameters in Table I. The need for a separate σ^+-scale is also eliminated. Furthermore, in contrast to trying to fit everything to accommodating parameters, the dual-parameter approach indicates when there are unusual effects (errors and solvation, etc.) with a particular substituent.

The data fit to determine ΔE^x and ΔC^x also included three $\sigma_R{}^\circ$-, five σ_R-, and two $\sigma_R{}^-$-systems. The pK_a values of 4-substituted anilinium ions[25,26,28] in water at 20 °C are correlated with $\sigma_R{}^-$-substituent constants. Representative values for 11 of the substituents are given in Table VI. The 39 substituents for this system are fit with $d_A{}^E = 20.3$ and $d_A{}^C = -2.97$ with $\bar{x} = 0.14$ and % $F = 3.6$. The d^C/d^E ratio is −0.15 which is in between σ and σ_I.

The log K(BHA) data[26] is a σ_R-system that is fit for 20 substituents with $d_A{}^E = -3.94$ and $d_A{}^C = -0.62$ with $\bar{x} = 0.06$ and % $F = 2.2$. The d^C/d^E ratio is 0.15 with both the electrostatic and covalent properties of the substituent making contributions in the same direction. The 4-$N(CH_3)_3$ substituent was eliminated from the fit. Hydrogen bonding of the carboxyl group to this basic substituent may lead to aggregation of this derivative in benzene.

The final entry in Table VI is the ionization of $XC_6H_4CH_2$-COOH in 10% ethanol at 25 °C. The 17 substituents are fit very well to $d_B{}^E = 2.35$ and $d_B{}^C = -0.23$ with $\bar{x} = 0.022$ and % F = 4.7. Though the range of measured values is small, the excellent average deviation leads to an acceptable percent fit. The d^C/d^E ratio is −0.10.

6. Data Not Fit by σ, σ_I, σ^+, σ_R, $\sigma_R{}^\circ$, or $\sigma_R{}^-$. The ionization of phenols in water has been regarded by some authors as the prototype of $\sigma_R{}^-$-reactions. Ehrenson, Brownlee, and Taft[25] state, "The data set for this reaction series is not fitted with acceptable precision by $\sigma_R{}^-$. The data for this set appear truly exceptional." Twenty of the 40 substituents studied are listed in Table VII. An excellent fit to ΔE^x and ΔC^x is obtained. Out of 40 substituents, only 2 miss the calculated value by more than 0.3 and only 10 miss it by more than 0.1. The value of $\bar{x}$ is 0.087, and % F is 3.1. The d^C/d^E ratio for this reaction is −0.16 with the dominant contribution coming from the electrostatic term.

The final set of data to be discussed involves ionization energies, IE, for a series of monosubstituted benzenechromium tricarbonyl molecules. When IE is plotted against the σ_I-substituent constants,[29] two familes of straight lines result, one for carbon substituents and one for substituents with lone pairs. This type of family-dependent behavior is typical of plots that use parameters with an improper amount of covalency in the interaction.[11] When the data are fit to ΔE^x and ΔC^x, an excellent correlation results for all the substituents except the fluoro group. The d^E value of −0.86 and d^C value of −0.23 lead to a d^C/d^E ratio of 0.27. The covalent and electrostatic terms go in the same direction, and both effects contribute significantly to the change in IE.

Correlating the Results of Reactivity or Physicochemical Studies with ΔE^x and ΔC^x. The substituent constants in Table I and eq 17 or 18 form the basis for analysis of reactivity or physicochemical measurements. The $\Delta\chi$ values for the measured properties of a family of compounds are substituted into eq 17 along with the

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Table VII. Data Fit of Systems Not Correlated with Any Set of Substituent Constants

subst	$XOCr^{a,b}$ exp	$XOCr^{a,b}$ calc	$pK\ X_6H_4OH$ exp	$pK\ X_6H_4OH$ calc
$3\text{-}CH_3$			9.99	10.05
3-F			9.11	8.95
3-Cl			9.00	8.96
3-Br			8.93	8.96
3-I			8.97	9.04
$3\text{-}C(CH_3)_3$				
H	7.30	7.26	9.90	9.80
$4\text{-}C_6H_4$	7.27	7.25	9.52	9.59
$4\text{-}NH_2$	7.05	7.03	10.22	10.45
$4\text{-}N(CH_3)_2$	6.92	6.92	10.17	10.18
$4\text{-}CH_3$	7.19	7.17	10.16	10.13
$4\text{-}CH(CH_3)_2$			10.14	10.21
$4\text{-}OCH_3$	7.11	7.15	10.11	10.03
4-F	7.47	7.33	9.81	9.54
4-Cl	7.40	7.42	9.32	9.12
4-Br	7.37	7.42	9.26	9.35
$4\text{-}CO_2CH_3$	7.41	7.43	8.43	8.16
$4\text{-}NO_2$			7.06	7.77
4-CN			7.87	7.71
$4\text{-}C(CH_3)_3$	7.08	7.17	10.25	10.33
$4\text{-}C_2H_5$			9.93	10.00

[a] Ionization energy (eV) of $XC_6H_5Cr(CO)_3$. [b] $\bar{x}$ is 0.04, and the % F is 6.7.

ΔE^x and ΔC^x values for the substituents from Table I. If the parent hydrogen compound has been measured, it is entered as a $\Delta\chi$ with ΔE^x and ΔC^x values of zero for hydrogen. The substituents are weighted as indicated by n in Table I. In designing an experiment, it is important to use substituents whose $\Delta E/\Delta C$ ratio varies. Three categories exist, and substituents should be selected from each group to best define d^E and d^C for new systems. One group consists of the majority of the substituents with $\Delta E/\Delta C$ values between 3.2 and 3.7. The second group consists of values below 3.2. The third group consists of values above 3.7. A selection of several substituents from each group is desirable. The resulting simultaneous equations are solved for the three unkowns $d_A{}^E$, $d_A{}^C$, and $\Delta\chi^H$. A good data fit indicates that the changes in the measured property with the substituent are dominated by the same covalent and electrostatic factors that influence bond strength. A rationalization of the d^E values can be proposed. If a poor data fit results, then one or two of the substituents can be omitted and the data refit. If a pattern can be discerned in the omitted substituents, then experiments can be undertaken to determine the cause of the deviation. If no pattern is recognized or if the data cannot be fit properly by omitting one type of the substituents, then it would be concluded that other factors besides those related to bond strength make significant contributions to the measured property.

An occasion may arise in which parameters for a new substituent are needed. Values of $\Delta\chi$ for this new substituent interacting with the probes in Table II are substituted into eq 17 along with the d^E and d^C values for the probes. The probes are assigned the n values given in Table II. The simultaneous equations are solved for ΔE^x and ΔC^x.

We have avoided intentionally the use of NMR chemical shifts and electronic transitions in the derivation of the ΔE^x and ΔC^x parameters. In reactivity studies, the specific interaction of the solvent with a substituent will cancel if the interaction is of comparable magnitude in the reactants and in the products or transition state. This is not true for an NMR chemical shift. The interpretation of NMR data with ΔE^x and ΔC^x is not precluded on this basis but is encouraged. Deviations in the data fit of such systems by specific solvation would be reflected by a poor fit. The existence of π–π-interactions also has been shown to influence both NMR shifts and electronic transitions.[30]

(30) Drago, R. S. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1827.

Interpretation of the Parameters. The interpretation of the ΔE^x and ΔC^x parameters parallels the interpretation of the σ-values in the Hammett correlation. When combined with positive d^E values, positive ΔE^x and ΔC^x indicate an increase in donor strength or nucleophilicity of the substituent in its tendency to undergo both electrostatic and covalent interaction. Negative ΔE^x and ΔC^x indicate a decrease in both the electrostatic and covalent contributions of the substituent to the nucleophilicity. When combined with negative d^E values, positive ΔE^x and ΔC^x indicate decreased acceptor strength or electrophilicity relative to the hydrogen derivative, while negative ΔE^x and ΔC^x indicate an increase in these properties. Different orders for the influence of the substituent on reactivity can result by taking different ratios of ΔE^x and ΔC^x.

The interpretation of the d^E and d^C values parallels the interpretation of Hammett ρ-values. Both the acceptor or donor strength of the common reactant and the sensitivity of the family to substituent change are involved as seen in eqs 15 and 16. When the E^* and C^* values of the reaction are known, the sensitivity of the family to substituent change s relative to that of pyridine can be determined. When these quantities are not known, it becomes difficult to even interpret the sign of d^E. For example, it is known that substituting a hydrogen of ammonia with CH_3 decreases E_B and increases C_B. This is accommodated in eqs 15 and 16 by a minus s^E and a positive s^C. It is also possible that a physicochemical change, $\Delta\chi$, could be increased by electrostatic bonding E^* and decreased by covalent bonding C^*, leading to a positive value for E^* and a negative value for C^*. Different combinations of the signs of E^* and s^E determine the sign of d^E, while different combinations of the signs of C and s^C determine the sign of d^C. In the absence of information about the signs of the components, the combined effect of *substituent sensitivity* and *reactant demand* is incorporated into the interpretation of the d^E value description of the electrostatic or covalent *demands of the system*.

Finally, when a good fit of a data set for a reaction results, we conclude that the reaction is dominated by the same factors that influence bond strength. This does not mean that the reaction has minimal solvation contributions or is dominated by the enthalpy contribution. Conditions that lead to good data fits when large solvation energies exist have been described.[16b] In earlier work from this laboratory,[31] it was shown that entropies for reactions could be fit to E and C. Mechanisms whereby bond-strength arguments influence entropies of reactions are presented.[31] It was also shown[31] that in order to get a linear plot of ΔH vs ΔS for a wide range of reactants, the C/E ratio of the enthalpy and entropy components must be the same. However, ΔG can fit the E and C model even when ΔH and ΔS do not plot-up linearly, if ΔH and ΔS each fit the E and C model with different C/E ratios. Thus, a detailed interpretation of d^E and d^C for a complex reaction is difficult. An interpretation based on system demand that parallels that of a ρ-value interpretation is possible. More information is available from d^E and d^C than from ρ because the net covalent and electrostatic components of the system demand can be obtained.

Procedure

Data for families of compounds undergoing reactions are fit with a least-squares minimization routine to the equation

$$\Delta\chi^x - \Delta\chi^H = d^E\Delta E^x + d^C\Delta C^x$$

Value of ΔE^x and ΔC^x are found for each substituent that best fits the over 700 physicochemical measurements. Each reaction or physicochemical measurement is characterized by a d^E and a d^C. The values of d^E and d^C are related to $s^EE_B{}^*$ and $s^CC_B{}^*$ (eqs 15 and 16) with values of s^E and s^C equal to 1 for the family of substituted pyridines. When $E_A{}^*$ and $C_A{}^*$ are known for a particular reactant (ref 16) and when a family of substituted pyridines is studied, the values of d^E and d^C are fixed at

(31) Doan, P. E.; Drago, R. S. *J. Am. Chem. Soc.* **1984**, *106*, 2772.

the values of E_A* and C_A*. All known enthalpy data for pyridine derivatives were also entered into the data fit with d^E and d^C fixed at the reported values for E_A and C_A.

E_A and C_A values are known for a series of substituted phenols. After the initial data fit, the ΔE parameters were found to be about 1.2 times the $E_A{}^x - E_A{}^H$ parametr for pyridine. This defines the s^E value for phenols as 1.2. For those donors whose E_B or E_B* values are known, this leads to a d^E value of 1.2E_B*. In order to put additional pressure on the data fit to conform to the EC model, the quantity 1.2E_B* was entered as a $\Delta\chi$ called d^E sub. The $\Delta\chi$ (d^E sub) is fit to a substituent constant, E sub, defined as having $\Delta E = 1$, $\Delta C = 0$, $\Delta\chi_H = 0$, and a value of $\Delta\chi^X$ equal to the d^E value calculated from 1.2E_B*. This quantity is entered with an n value equal to 0.5 for the measured enthalpy values of substituted phenols reacting with pyridine and THTP. This procedure enables the fit to come close to the reported[16] $E_A{}^x - E_A{}^H$ parameters for phenol without introducing substantial error into the fit of the $\Delta\chi$ values for other reactions with these substituents. Two systems, pK_a of XCH_2-$NH_3{}^+$ (H_2O at 25 °C) and pK_a of $XNH_3{}^+$ (H_2O at 25 °C), were studied with a limited number of substituents. The least-squares fit of these reactions gave large values for d^E and large values of the opposite sign for d^C while fitting the experimental $\Delta\chi$ values to 0.01. In order to gain some information concerning ΔE^x and ΔC^x from these reactions, a $\Delta\chi$ (d^E sub) was entered with a small value and $n = 4$. The value of n weights the data point according to $n = 1/\text{weight}$.

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