E- and C-Based Dual Parameter Substituent Constant Correlations

Russell S. Drago* and Andrew P. Dadmun

Contribution from the Department of Chemistry, University of Florida, Gainesville, Florida 32611

Received September 7, 1993. Revised Manuscript Received December 6, 1993[®]

Abstract: Previously reported ΔE^X and ΔC^X values for E- and C-based dual parameter substituent constant correlations are refined by extending the treatment to several new series of reactions that do not correlate well with Hammett or Taft substituent constants. The additivity of substituent constants for multiple substituents on a parent compound is tested. Saturation of the π contribution is proposed for conjugative substituents that are effective π bonding groups. A new series of two- or three-bond substituent constants, 2-X, are developed. The reactions of substituted acetic acids and esters are treated as 2-X, XCH_2 substituents in constrast to prior analyses which treated these systems with localized 3-X parameters. The consistency of the ΔE–ΔC approach with the E and C model is shown by testing the use of the ΔE^X and ΔC^X substituent parameters to calculate the E_A and C_A values of substituted phenols.

Introduction

In the first article in this series[1] it was shown that physicochemical measurements, $\Delta\chi$, which require different substituent constant scales for correlation could be fit to the E- and C-based dual parameter substituent constant equation:

$$\Delta\chi^X = d^E\Delta E^X + d^C\Delta C^X + \Delta\chi^H \tag{1}$$

The ΔE^X and ΔC^X parameters are the dual parameter analogues of the substituent constant, σ, in single parameter correlations (e.g., Hammett or Taft). The d^E and d^C parameters are the dual parameter analogues of ρ in single-parameter correlations. $\Delta\chi^X$ is the value of the measured property for the X substituent, and $\Delta\chi^H$ is the value of the same property for the parent hydrogen compound. Subscripts can be added to d to indicate if the donor, B, or acceptor, A, is held constant in the experiment. Two types of substituents were reported: (1) a localized set for electron density transmitted through the σ framework and (2) a delocalized set for electon density transmitted through π systems by a conjugative mechanism. Satisfactory fits of different data sets that previously required[2-5] either σ_H, σ_I, σ_R, $\sigma_R{}^\circ$, $\sigma_R{}^-$, or σ^+ substituent constants (collectively called σ constants) were obtained with the ΔE^X and ΔC^X parameters. Substituted phenols which previously required their own set of substituent constants[3] were also correlated with ΔE^X and ΔC^X substituent constants. Furthermore, the substituent constants correlated data that were previously employed to derive the E and C parameters,[6] and for this reason the ΔE^X and ΔC^X substituent constants are said to be E and C based. Several reports of dual parameter substituent constant correlations have appeared,[3,7] and the shortcomings of some[7] have been discussed.[3] However, the E and C basis for this model makes the ΔE^X–ΔC^X approach unique by providing a more firm, enthalpy based foundation for the parameters.

Like the ρ values of one-parameter correlations, the d values depend upon the demand made by the common reactant on the family and upon the sensitivity of the family to substituent change. The dual parameters d^E and d^C of eq 1 are related to the sensitivity and demand by eqs 2 and 3

$$d^E = s^E E^* \tag{2}$$

$$d^C = s^C C^* \tag{3}$$

where the demand is given by the E^* and C^* parameters of the E and C model[6] while s^E and s^C are the sensitivity of the parent hydrogen compound to substituent change. If the common reactant is an acceptor, the subscript A is used on d and E^* or C^* of eqs 2 and 3 while B is used on s. This emphasizes the contribution of both the acceptor and donor to d. The reader is referred to ref 1 for the derivation of these and ensuing equations.

The ΔE^X and ΔC^X values are consistent with the enthalpy-based E and C parameters.[6] If E and C are known for several donors or acceptors in a family of compounds, the E and C values can be calculated for any other member of the family whose ΔE^X and ΔC^X substituent constants are known by using the equations.

$$E_A \text{ or } E_B = E(\text{H}) + s^E\Delta E^X \tag{4}$$

$$C_A \text{ or } C_B = E(\text{H}) + s^C\Delta C^X \tag{5}$$

The $s_B{}^E$ and $s_B{}^C$ values are set at 1 for pyridine donors and can be determined for a new family if E_A or E_B and C_A or C_B are known for a few substituted derivatives. The known E and C values are substituted into eqs 4 and 5 along with the ΔE^X and ΔC^X values of the substituent to produce a series of simultaneous equations that are solved for s^E and s^C.

® Abstract published in *Advance ACS Abstracts*, February 1, 1994.

(1) Drago, R. S.; Dadmun, A. P. *J. Am. Chem. Soc.* **1993**, *115*, 8592.
(2) See: Exner, O. In *Correlation Analysis in Chemistry*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978.
(3) Ehrenson, S.; Brownlee, R. T. C.; Taft, R. W., Jr. *Prog. Phys. Org. Chem.* **1973**, *10*, 1.
(4) Charton, M. Electrical Effect of Substituent Constants for Correlation Analysis. *Prog. Phys. Org. Chem.* **1981**, *13*, 119.
(5) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1957**, *79*, 1913; **1958**, *80*, 4979.
(6) (a) Drago, R. S. *Coord. Chem. Rev.* **1980**, *33*, 251–277. (b) Drago, R. S.; Wong, N.; Bilgrien, C.; Vogel, G. C. *Inorg. Chem.* **1987**, *26*, 9–14. (c) Drago, R. S.; Vogel, G. C. *J. Am. Chem. Soc.* **1992**, *114*, 9527. (d) Drago, R. S.; Vogel, G. C.; Dadmun, A. P. *Inorg. Chem.* **1993**, *32*, 2473.
(7) (a) Swain, C. G.; Lupton, F. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328. (b) Yukawa, Y.; Tsuno, Y.; Sowada, M. *Bull. Chem. Soc. Jpn.* **1966**, *3*, 2274 and references therein.
(8) (a) Drago, R. S.; Zoltewicz, J. A. *J. Org. Chem.*, in press. (b) Drago, R. S. *Inorg. Chem.*, submitted.
(9) Libutti, B. L.; Wayland, B. B.; Garito, A. F. *Inorg. Chem.* **1969**, *8*, 1510.
(10) Burke, M. R.; Brown, T. L. *J. Am. Chem. Soc.* **1989**, *111*, 5185.
(11) (a) Bresciana-Pahor, N.; Forlolin, M.; Marzilli, L. G.; Randaccio, L.; Summers, M. F.; Toscano, P. J. *Coord. Chem. Rev.* **1985**, *63*, 1. (b) Marzilli, L. G., et al. *J. Am. Chem. Soc.* **1987**, *109*, 6045.
(12) Bodner, G. M.; May, M. P.; McKinney, L. E. *Inorg. Chem.* **1980**, *19*, 195.

0002-7863/94/1516-1792$04.50/0

Table 1. Parameters for *E*- and *C*-Based Dual Parameter Substituent Constant Correlations

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 (57)	0	0	0.2	3-$NCCH_2$ (12) [4.8][d]	–0.070	–0.333	0.3
3-$(CH_3)_2N$ (10) [23.9]	0.023	0.537	0.3	3-$HOCH_2$ (6)[d]	0.002	0.028	0.6
3-H_2N (12) [16]	0.017	0.269	0.3	3-$CH_3CO_2CH_2$ (6)[d]	–0.043	–0.211	0.6
3-$(CH_3)_3C$ (7) [6][d]	0.031	0.183	0.5	3-$(CH_3)_3SiCH_2$ (7)[d] [5]	0.058	0.262	0.6
3$(CH_3)_2CHCH_2$ (7)[b] [3.7][d]	0.035	0.129	0.5	3-F (19) [3.7]	–0.115	–0.429	0.2
3-$CH_3CH_2CH(CH_3)$ (8) [3.9][d]	0.054	0.213	0.4	3-Cl (32) [3.8]	–0.120	–0.461	0.2
3-$(CH_3)_2CH$ (17) [4][d]	0.050	0.198	0.3	3-Br (26) [3.9]	–0.118	–0.456	0.2
3-$CH_3CH_2CH_2$ (6)[b] [3.9][d]	0.040	0.151	0.6	3-I (18) [3.8]	–0.107	–0.405	0.2
3-$CH_3CH_2CH_2CH_2$ (4) [4][d]	0.041	0.160	0.8	3-$CH_3C(O)$ (9) [2.3]	–0.112	–0.260	0.3
3-CH_3CH_2 (17) [3.9]	0.039	0.153	0.2	3-$CH_3OC(O)$ (12) [3.7]	–0.083	–0.306	0.3
3-H_3C (41) [3.8]	0.034	0.128	0.2	3-HO (12)[b] [1.6]	–0.049	–0.079	0.4
3-C_6H_{11} (6) [4][d]	0.056	0.227	0.6	3-CH_3O (20) [±0.33]	–0.035	0.011	0.2
3-$(CH_3)_3Si$ (8)[b] [5][d]	0.035	0.174	0.4	3-C_2H_5O (4) [±7][d]	–0.020	0.147	0.9
3-C_6H_5 (16)[d]	0.001	–0.017	0.3	3-C_6H_5O (5) [1][d]	–0.064	–0.054	0.6
3-$ClCH_2$ (10)[b] [5.5][d]	–0.029	–0.160	0.4	3-C_6H_5CO (5) [4][d]	–0.065	–0.281	0.5
3-$C_6H_5CH_2$ (9)[b,d]	0.005	–0.015	0.4	3-CH_3S (8) [6][d]	–0.035	–0.216	–0.4
3-H_3C_2 (10)[b,d]	0.009	0.009	0.4	3-$CH_3C(O)NH$ (8) [2][d]	–0.050	–0.115	0.4
3-$BrCH_2$ (14) [5][d]	–0.038	–0.197	0.3	3-F_3C (14) [4.9]	–0.137	–0.670	0.2
3-CH_3OCH_2 (6)[d]	0.005	–0.043	0.5	3-NC (23) [4.6]	–0.192	–0.874	0.2
3-CF_3CH_2 (13) [5][d]	–0.052	–0.262	0.3	3-CH_3SO_2 (8)[b] [4.7][d]	–0.208	–0.982	0.4
3-ICH_2 (10) [5][d]	–0.043	–0.218	0.4	3-O_2N (25) [4.3]	–0.213	–0.968	0.3

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 (55)	0	0	0.2	4-$CH_3S(O)$ (5)[b] [1.4]	–0.201	–0.285	0.5
4-H_2N (16) [2.7]	0.180	0.480	0.2	4-$CH_3C(O)NH$ (6) [±62]	–0.004	0.260	0.5
4-$(CH_3)_2N$ (18) [6.3]	0.140	0.889	0.2	4-F_3C (14) [3.1]	–0.176	–0.545	0.2
4-$(CH_3)_3C$ (16) [2.6]	0.064	0.164	0.2	4-F (22) [4.7]	–0.036	–0.168	0.2
4-$(CH_3)_2CH$ (11) [4.1]	0.048	0.195	0.3	4-Cl (29) [3.6]	–0.090	–0.323	0.2
4-$CH_3CH_2CH_2$ (3)[b] [3.6]	0.051	0.186	1.2	4-Br (22) [5.1]	–0.074	–0.380	0.2
4-CH_3CH_2 (11) [7.6]	0.026	0.196	0.3	4-I (12) [2.7]	–0.082	–0.219	0.3
4-H_3C (49) [3.9]	0.050	0.192	0.2	4-$CH_3OC(O)$ (12) [0.71]	–0.191	–0.136	0.3
4-$C_6H_5CH_2$ (5)[b] [6.0]	0.017	0.101	1.2	4-$CH_3C(O)$ (13) [0.88]	–0.194	–0.170	0.2
4-C_6H_5 (11) [±5.2]	–0.024	0.123	0.3	4-C_6H_5CO (4) [0.06]	–0.243	–0.015	1.2
4$(CH_3)_3Si$[d] (7) [±26.6]	–0.008	0.205	0.5	4-NC (23) [2.4]	–0.252	–0.601	0.2
4-HO (7) [4.3]	0.099	0.426	0.5	4-CH_3SO_2 (10) [1.8]	–0.269	–0.487	0.3
4-CH_3O (29) [5.9]	0.048	0.285	0.2	4-O_2N (27) [2.5]	–0.254	–0.640	0.2
4-CH_3S (7) [±18.8]	–0.014	0.267	0.5				

[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 this value is less than 13 but more than 7, an n value of 0.3 is used; if this value is less than 8 but more than 4, a value of 0.5 is used; and if this value is four or less, a value of 0.8 is used. If the spectral probes used to establish the parameters do not span a d^C/d^E range of –0.1 to 1.0, the n value is increased by 50%. 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. [d] Refined by adding data subsequent to the master fit. See ref 8.

In the original article,[1] physicochemical measurements were fit to d^E, d^C, ΔE^X, and ΔC^X parameters. Most of the data came from established spectral probes or from data used for one-parameter σ-based substituent constant correlations. In applications of the original set of dual parameters, it was found that literature data that could not be correlated with the common substituent constant scales could be fit to the ΔE^X and ΔC^X parameters. Data that fit ΔE–ΔC and do not obey the one-parameter scales help to better define the minimum in the large data fit used to determine the ΔE^X and ΔC^X values. The substantial amount of this new type of data that could be correlated[8] with the ΔE–ΔC model encouraged the addition of these new systems to the large data base and a redetermination of the ΔE^X and ΔC^X parameters.

The essentially localized nature of the 3-substituents and delocalized nature of the 4-substituents led to a reconsideration of the analysis of the substituted acetic acids (XCH_2COOH) and the analogous esters. The CH_2 protons and the X substituent on carbon are not orthogonal to the carboxyl π system. Thus, it is incorrect to assume[3] that the substituent effect of X in substituted acetic acids is transmitted entirely through the σ bonds or through space. The $XCH_2C(O)OH$ systems were removed from the data fit for 3-substituents and the entire XCH_2 group was treated as a 2-substituent. The 2-substituents have a conjugative contribution like the 4-substituents but also have a nonconjugative contribution that is more efficient than that of a 4-substituent. Data for ortho substituents on a substituted benzene ring are combined with the data for the $XCH_2C(O)OR$ (R = H or alkyl) reactions to produce a set of 2-ΔE^X and 2-ΔC^X values. Several ortho substituents of phenyl compounds gave problems because groups in this position can interact directly in a steric or intermolecular associative manner[3,4] with the reactive group. These anomolies are detected and the substituent effect is understood with the ΔE–ΔC model.

This article reports the new set of dual parameter 2-substituent constants, the revised, better defined substituent constants for 3- and 4-substituents, and revised d^E and d^C values for the probes reported earlier. In addition, the scope of ΔE and ΔC analyses has been expanded by adding several new different types of inorganic families of measurements.

Results and Discussion

Redetermination of the 3- and 4-Substituent Constants. A total of 878 measurements were fit to eq 1, producing 3- and 4-ΔE^X and ΔC^X parameters as well as d^E, d^C, and $\Delta\chi^H$. The resulting ΔE^X and ΔC^X parameters are presented in Table 1. Some of the parameters had such a limited amount of data that high uncertainties exist. These are indicated by assigning large n values to them in Table 1. The weight that a substituent is given in a data fit is the reciprocal of n. By convention, the typical electron-releasing substituents, e.g., 3-CH_3, have positive ΔE^X and ΔC^X values while the typical electron-withdrawing substituents, e.g., 3-Cl, have negative ΔE^X and ΔC^X values. The d^E, d^C, and $\Delta\chi^H$ parameters from the data fit are reported in Table 2. Positive ΔE^X and ΔC^X values increase the magnitude of the measured quantity when d^E and d^C are positive. A donor or nucleophile in a family with positive $s_B{}^E$ and $s_B{}^C$ values becomes stronger when substituents with a positive ΔE^X and positive ΔC^X are employed. The donor strength is decreased when ΔE^X and ΔC^X are negative. When $s_A{}^E$ and $s_A{}^C$ are both negative for a family of acceptors or electrophiles, a substituent with a positive ΔE^X and ΔC^X decreases the electrophilicity or acceptor strength. The electrophilicity is increased for this family when ΔE^X and ΔC^X are negative. The 3-OCH_3 substituent is the only well-established system that has ΔE and ΔC values of opposite sign. For other substituents where opposite signs are reported, the parameters usually are not accurately determined.

In some cases, d^E and d^C have opposite signs. If d^E is positive and d^C negative, a substituent with a positive ΔE^X and positive ΔC^X will increase the electrostatic contribution to the measured property and decrease the covalent contribution. The significance of these reversals will be discussed later.

For the most part, the experimental data are fit very well by the parameters. The average deviations between the calculated and experimental values, $\bar{x}$, are given in the footnotes to Table 2. Also reported in Table 2 is a quantity called percent fit. This corresponds to $\bar{x}$ divided by the difference in the highest and lowest calculated values, expressed as a percentage. A satisfactory fit corresponds to a percent fit of 6 or less. In most cases where the percent fit is large, the range is small. This is considered to be a satisfactory fit if the average deviation is close to the experimental error in the measurement. The values of the d^E and d^C parameters are uncertain if the ratio of the $\Delta C/\Delta E$ values of the substituents used in the data fit does not vary much, vide infra.

For families of measurements where there is a large amount of data, substituents that do not fit the correlation can be spotted and more experimental work is in order to determine the cause of the deviation. For example, in the data fit of the BF_3 enthalpies of adduct formation with substituted benzophenones, the calculated enthalpy for the $N(CH_3)_2$ substituent deviates (dev) from the experimental value by 2.5 kcal mol^{-1}. The larger calculated value than that observed experimentally could result from coordination of BF_3 to the nitrogen of the substituent instead of the carbonyl. This deviation suggests unusual behavior, and measurement of the C=O stretching frequency of the adducts could confirm or eliminate the explanation offered for the deviation. This example illustrates the point that ΔE–ΔC analyses are more than just data fitting. The example also illustrates the merit of carrying out ΔE–ΔC analyses while performing experimental work. In the past, chemical reactions that do not correlate with a σ parameter often have led to new sets of substituent constants.

In families where there only is data for a limited number of the substituents, an improper system may be accommodated with incorrect parameters. As new data becomes available, these parameters should be refined, vide infra.

Very large deviations that clearly indicate a measurement should be eliminated from the fit and studied further are encountered in only a few instances in the data base used to derive the 3- and 4-substituent constants. The pK_a values of the 4-$N(CH_3)_2$ (dev −0.9) and 4-NH_2 (dev −1.33) substituted pyridines as well as the log K value of the 4-$N(CH_3)_2$ (dev 0.67) substituted benzoic acid in benzene solvent are among the few deviant systems found in this very extensive data set. The pK_a of 4-nitrophenol (dev 0.84) also deviates to an extent that indicates unusual behavior. All of these systems contain donor as well as acceptor groups in the same molecule, so complications could arise from association or interaction with the solvent.

Small deviations, that are larger than experimental error, are encountered in some systems. When the percent fit is small on such a system, the fit is considered satisfactory within the accuracy of the model. When a large percent fit arises from a data fit that spans a large range of measured values, enthalpic or entropic complications from solvation, aggregation, etc. may be contributing to the reactions of some of the compounds in the family. In general, water is a very reactive solvent and can hydrogen bond to many substituents. When the extent of this interaction cancels in the reactants and the transition state or the products, a solvation contribution will not be present. When the interactions differ in the reactants and products or transition state, a solvation contribution will result. Unusual entropy contributions from making and breaking the water structure can also contribute to a free energy type of measurement for a particular substituent. These effects are not considered to be valid reasons for defining new substituent constants. Instead, deviations of this type suggest that more work should be done to understand the system.

Trends in the Parameters. The 3-ΔE^X and 3-ΔC^X parameters show trends that are consistent with notions about substituent effects from one-parameter σ-type correlations. The essential difference is that the ΔE^X–ΔC^X model accommodates the fact that substituents can change the charge (electrostatic interaction) and polarizability (covalent interaction) to different extents. The electron-withdrawing nonconjugative substituents follow the order $NO_2 > CN > CF_3 > Cl > Br \sim F > I > CH_3C(O) > SCH_3 >$ OH. Since both the ΔE^X and ΔC^X values follow this trend, both the tendencies of a donor and a nucleophile to undergo covalent and electrostatic bonding will increase in this order when $s_B{}^E$ and $s_B{}^C$ are positive. The tendency of an acceptor or electrophile to undergo covalent or electrostatic bonding will decrease in this order when $s_A{}^E$ and $s_A{}^C$ are negative. Electron-releasing substituents follow the order $(CH_3)_2N > (H_2N > (CH_3)_2C(H)$–$CH_3CH_2 > C_2H_5 > H_3C$. The tendency of a nucleophile or donor to undergo covalent or electrostatic bonding will decrease in this order when d^E and d^C are positive. The tendency of an acceptor to undergo covalent or electrostatic bonding will increase in this order when s^E and s^C are negative. When the ΔE^X value of one substituent is larger and the ΔC^X value smaller than those of another substituent, the relative donor (acceptor) strengths will reverse depending on the magnitude of the covalent and electrostatic properties of the acceptor or donor. The 3- and 4-CH_3CO as well as the 3- and 4-$CH_3OC(O)$ derivatives or the 3-CH_3SO_2 and 3-NO_2 substituents can reverse orders of acceptor or donor strength. Reversals are not possible in one-parameter scales.

When the signs of ΔE^X and ΔC^X change, the substituent can increase the tendency to undergo either covalent or electrostatic bonding and decrease the tendency to undergo the other type of interaction. Depending on the covalent and electrostatic properties of the physicochemical property being studied, the substituent can behave as if it were electron withdrawing or electron releasing. It would be impossible to place these substituents into an order of electron-withdrawing or -releasing substituents.

Similar orders can be constructed for the conjugative substituents. In contrast to the 3-derivatives, the 4-CH_3 substituent is now seen to be more electron releasing than the 4-C_2H_5 substituent, as expected from conjugative interactions with the ring. Reversals in substituent orders from the relative magnitudes of ΔE and ΔC are much more common for the 4-X substituents. Reversals are also expected in several instances when 3-X and 4-X substituents are compared. The inability of a single-parameter σ type of substituent scale[6a] to accommodate these reversals leads to a proliferation of one-parameter scales.

The d^E and d^C parameters indicate the susceptibility of the measured property to the changes in the electrostatic or covalent

Table 2. Parameters (d^E, d^C) for Families of Compounds

family[a] (d^C/d^E) [n]	d^E	d^C	$\Delta\chi^H$
$\Delta\nu_{OH}CH_3OH/XC_5H_4N$[b] (0.65)* [0.95]	105	69.4	283
$\Delta\nu I_2/XC_5H_4N$[c] (1.0)* [7]	1081	1098	4557
pK_a $XC_5H_4NH^+$[d] (0.42) [0.2]	6.87	2.89	5.16
$-\Delta HI_2/XC_5H_4N$[e] (4)* [0.2]	0.50	2.00	8.16
$-\Delta HPhOH/XC_5H_4N$[f] (0.47)* [0.2]	2.27	1.07	7.94
$-\Delta GDMA/XPhOH$[g] (0.08) [0.4]	−5.17	−0.421	2.91
$-\Delta HBF_3/XC_5H_4N$[h] (0.68)* [0.5]	7.23	4.93	30.6
$\Delta\nu ICN/XC_5H_4N$[i] (3.3)* [1.5]	4.43	14.7	55.3
$-\Delta H$4F-PhOH/XC_5H_4N[j] (0.47)* [0.3]	2.27	1.07	7.89
$\Delta\nu_{OH}DMA/XPhOH$[k] (0.0) [1.5]	−351	0.99	343
$\Delta\nu_{OH}(CH_2)_4S/XPhOH$[l] (17) [1.5]	−3.7	−64.3	276
$-\Delta HC_5H_5N/XPhOH$[m] (0.47) [0.2]	−1.63	−0.79	7.8
$-\Delta H(CH_2)_4S/XPhOH$[n] (4) [0.2]	−0.3	−1.14	4.9
$\Delta\nu_{OH}CH_3OH/XPhC(O)NR_2$[o] (0.5) [1.5]	40.5	19.8	162
$-\Delta HBF_3/XPhC(O)N(CH_3)_2$[p] (0.4) [1]	2.93	1.27	24.3
$-\Delta HBF_3/XPhC(O)CH_3$[q] (1.1) [2]	(2.4)	(2.7)	18.2
σ_I parameters[r] (±0.1) [0.8]	−4.20	0.37	0.10
σ Hammett[s] (0.10) [0.4]	−2.10	−0.213	0.03
log k 4-NO_2PhOH/XPy[t] (2.0) [0.8]	0.59	1.18	2.47
pK_a $XPhCO_2H$[u] (0.06) [0.2]	2.55	0.156	4.21
pK_a $XBnzCO_2H$(10%)[v] (0.01) [0.6]	1.51	0.01	4.5
pK_a $XPhCO_2H$(44%)[w] (0.11) [0.6]	3.45	0.381	5.72
pK_a $XPhNH_3^+$[x] (∓0.05) [0.2]	12.32	−0.59	4.63
log k XPhOH/DMA[y] (0.10) [0.6]	−2.93	−0.29	2.12
log k_R OH^-/4XBnzOBz[z] (0.10) [0.6]	−2.32	−0.239	−2.16
log k_I $H^+/XPhSi(CH_3)_3$[aa] (0.64) [0.8]	4.35	2.81	−2.39
log k_R CH_3I/4XQuin[bb] (∓0.11) [0.4]	5.95	−0.645	−2.46
pK_a $XBnzCO_2H$ (75%)[cc] (∓0.0) [0.6]	2.21	−0.005	6.14
pK_a XPhSH (48%)[dd] (±0.02) [0.4]	−8.23	0.124	0.12
pK_a XPhOH (H_2O)[ee] (∓0.05) [0.2]	8.54	−0.42	9.79
pK_a $XPhCO_2H$ (CH_3NO_2)[ff] (0.38) [0.6]	3.01	1.15	13.4
log K_{BHA} $XPhCO_2H(C_6H_6)$[gg] (0.22) [0.4]	−3.34	−0.729	5.33
pK_a XNH_3^+ (H_2O)[hh] (±0.24) [0.8]	−976	230.5	14
pK_a $XPhCO_2H$ (13%)[ii] (0.04) [0.6]	3.48	0.150	5.85
pK_a $XC_7H_{12}NH^+$[jj] (∓0.13) [0.4]	30.03	−3.79	10.46
log K Ni TPP (0.21) [0.6][kk]	−3.39	−0.24	−0.43
$\delta^{19}FXC_6H_4F$[ll] (±0.11) [0.2]	34.55	−3.86	0.13
pK_a 3-XAdCOOH (50%)[mm] (∓0.14) [0.3]	11.09	−1.57	6.86
pK_a 4-$XPhC(OH)_2$[nn] (0.44) [0.6]	1.46	0.64	−4.70
pK_a 4-$XBznCO_2H(H_2O)$[oo] (∓0.05) [0.6]	2.05	−0.11	4.31
ln k_r C_2H_5I/XC_5H_5N[pp] (0.16) [0.6]	4.32	0.70	−3.49
log k_r $XC_6H_5CO_2Et$ aqac[qq] (0.07) [0.2]	−6.35	−0.42	−0.08
pK_a $XC_8H_6CO_2H$[rr] (∓0.11) [0.6]	8.54	−0.92	6.77
pK_a $XPhCO_2H$ (80% MC)[ss] (0.27) [0.2]	2.86	0.77	6.67
$\Delta\nu_{CO}DMA/XC_6H_4OH$[tt] (0.05) [1.5]	−18.6	−0.99	22.8
$E^{1/2}$ $XCo(DH)_2H_2O$[uu] (±0.22) [0.2]	0.0314	−0.385	0.812
Co–P dist[uu] (∓0.22) [0.2]	2.891	−0.612	2.396
$E^{1/2}$CpMn/XPy[vv] (1.0) [0.2]	−0.109	−0.110	0.0836
$E^{1/2}$ $Co(DH)_2XPy$[uu] (0.35) [0.2]	−0.231	−0.072	−0.647
ΔH XC_5H_5N-Cu[ww] (4.0) [0.3]	0.45	1.81	7.3
$E°$ $C_5H_5NCH_3^+$[xx] (∓0.02) [0.8]	1.93	−0.04	1.08
I.E. $XPhCr(CO)_3$[yy] (0.50) [0.6]	−0.591	−0.298	7.28
δ^{13}C–Co–P[uu] (±0.2) [0.6]	−72.24	14.17	52.98
log K 4-CNC_5H_4N–Co[uu] (∓0.23) [0.6]	29.88	−6.89	1.55
$\delta^{13}C$ $(XC_6H_5)_3PNi(CO)_3$[zz] (0.04) [0.8]	6.55	0.26	4.17
$\delta^{13}C$ $X_3PNi(CO)_3$[zz] (∓0.05) [0.4]	33.34	2.38	3.92
log k_I CpMn/XPy[zz] (∓12) [0.2]	0.0759	−0.892	2.15
I.E. XCp_2Ru[ab] (0.47) [0.3]	−20.27	−9.55	165.5

[a] The number in parentheses indicates the d^C/d^E ratio. The ± symbol indicates a positive d^C and a negative d^E. The ∓ symbol indicates a negative d^E and positive d^C. The number in brackets indicates the n value to be used in weighing fits to determine parameters for new substituents. 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. 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. calculated largest minus smallest $\Delta\chi$. [b] Changes in the OH stretching frequency (cm^{-1}) of methanol for a series of substituted pyridine adducts; see ref 1; $\bar{x}$ = 1.3. [c] Blue shifts, in cm^{-1}, of the visible transition of substituted pyridine adducts of iodine; see ref 1; $\bar{x}$ = 4.4. [d] Ionization of substituted pyridinium ions in H_2O at 25 °C; see ref 1; a σ+ system; $\bar{x}$ = 0.1; % fit = 1.8%. [e] Enthalpies of iodine adduct formation (kcal mol^{-1}) for a series of substituted pyridines in hexane; see ref 1; $\bar{x}$ = 0.21. [f] Enthalpies of phenol adduct formation (kcal mol^{-1}) for a series of substituted pyridines in cyclohexane; see ref 1; $\bar{x}$ = 0.04. [g] ΔG for adducts of $CH_3C(O)\ N(CH_3)_2$ with XC_6H_5OH in CCl_4 at 25 °C; see ref 1; $\bar{x}$ = 0.07; % fit = 3.6%. [h] Enthalpies of BF_3 adduct formation (kcal mol^{-1}) for a series of substituted pyridine donors in CH_2Cl_2; see ref 1; $\bar{x}$ = 0.12. [i] Change in the infrared C–I stretching frequencies for the ICN adducts of a series of substituted pyridines; see ref 1; $\bar{x}$ = 3.8. [j] Enthalpies (kcal mol^{-1}) of adduct formation for F–C_6H_4OH with a series of substituted pyridines in cyclohexane. 1 kcal mol^{-1} is added to enthalpies reported in CCl_4; see ref 1; $\bar{x}$ = 0.18. [k] Changes in the OH stretching frequency (cm^{-1}) of hydrogen-bonded adducts of *N,N*-dimethylacetamide with a series of phenols; see ref 1; $\bar{x}$ = 0.78; % fit = 0.71%. [l] Changes in the OH stretching frequency (cm^{-1}) of hydrogen-bonded adducts of tetrahydrothiophene with a series of substituted phenols; see ref 1; $\bar{x}$ = 0.84; % fit = 1.5%. [m] Enthalpies (kcal mol^{-1}) of adduct formation of pyridine with a series of substituted phenols; see ref 1; $\bar{x}$ = 0.15. [n] Enthalpies (kcal mol^{-1}) of adduct formation of tetrahydrothiophene with a series of substituted phenols; see ref 1; $\bar{x}$ = 0.07; % fit = 6.9%. [o] Change in the OH stretching frequency (cm^{-1}) of hydrogen-bonded adducts of methanol with a series of substituted *N,N*-dimethylbenzamides; see ref 1; $\bar{x}$ = 0.79; % fit = 1.7%. [p] Enthalpies (kcal mol^{-1}) of BF_3 adduct formation for a series of substituted *N,N*-dimethylbenzamides in CH_2Cl_2; see ref 1; $\bar{x}$ = 0.16; % fit = 5.2%. [q] Enthalpies (kcal mol^{-1}) of BF_3 adduct formation for a series of substituted benzophenones in CH_2Cl_2; see ref 1;

Table 2 (Continued)

see ref 1; $\bar{x}$ = 0.34; % fit = 11%. [r] Taft σ_I parameters; ref 4; $\bar{x}$ = 0.03; % fit = 4.6%. [s] Hammett substituent constants; ref 2; $\bar{x}$ = 0.05; % fit = 4.5%. [t] log K for the reaction of 4-$NO_2C_6H_5OH$ with XC_5H_4N; ref 17; $\bar{x}$ = 0.06; % fit = 2.7%. [u] Ionization of XC_6H_4COOH in water at 25 °C; see ref 1; a σ system; $\bar{x}$ = 0.05; % fit = 3.5%. [v] Ionization of $XCH_2C_6H_4COOH$ in 10% ethanol/water at 25 °C; see ref 1; a $\sigma_R{}^\circ$ system; $\bar{x}$ = 0.02; % fit = 4.4%. [w] pK_a of $XC_6H_4CO_2H$ 44.1% w/w in aqueous ethanol at 25 °C; see ref 1; a σ_R system; $\bar{x}$ = 0.04; % fit = 1.9%. [x] Ionization of $XC_6H_5NH_3{}^+$ in H_2O at 25 °C; see ref 1; a $\sigma_R{}^-$ system; $\bar{x}$ = 0.10; % fit = 2.6%. [y] log K for the adducts of XC_6H_5OH with DMA; ref 17; $\bar{x}$ = 0.09; % fit = 7.9%. [z] log k_R for the reaction of OH^- with a series of $XC_6H_4CH_2OBz$ in 70% v/v aqueous MeOAc at 25 °C; see ref 1; a $\sigma_R{}^\circ$ system; $\bar{x}$ = 0.02; % fit = 1.9%.[aa] log k_1 (min^{-1}) cleavage $C_6H_5Si(CH_3)_3$ in aqueous methanol/$HClO_4$ at 51.2 °C; see ref 1; a σ^+ system; $\bar{x}$ = 0.17; % fit = 7.9%. [bb] log k_R for the reaction of CH_3I with 4-substituted quinuclidines in CH_3OH at 10 °C; see ref 1; a σ_I system; $\bar{x}$ = 0.04; % fit = 5.2%. [cc] pK_a of $XC_6H_4CH_2COOH$ in 75% v/v aqueous C_2H_5OH at 25 °C; see ref 1; a $\sigma_R{}^\circ$ system; $\bar{x}$ = 0.05; % fit = 5.2%. [dd] Ionization of a series of substituted XC_6H_5SH compounds in 48% aqueous C_2H_5OH at 25 °C; see ref 1; a $\sigma_R{}^-$ system; $\bar{x}$ = 0.09; % fit = 2.9%. [ee] pK of substituted phenols in water at 25 °C; see ref 1; a $\sigma_R{}^-$(P) system; $\bar{x}$ = 0.08; % fit = 2.9%. [ff] pK_a of $XC_6H_4CO_2H$ in CH_3NO_2 at 25 °C; see ref 1; a σ_R system; $\bar{x}$ = 0.16; % fit = 5.0%. [gg] log K_{BHA} of $XC_6H_4CO_2H$ in C_6H_6 at 25 °C; see ref 1; a σ_R system; $\bar{x}$ = 0.06; % fit = 2.4%. [hh] pK_a $XNH_3{}^+$ in water at 25 °C; see ref 1; a σ_I system; $\bar{x}$ = 0.02; % fit = 0.34%. [ii] pK_a $XC_6H_4CO_2H$ in 12.7 mol % aqueous dioxane at 25 °C; see ref 1; a σ_R system; $\bar{x}$ = 0.05; % fit = 3.7%. [jj] pK_a of 4-substituted quinuclidinium ions in H_2O at 25 °C; see ref 1; a σ_I system; $\bar{x}$ = 0.11; % fit = 3.1%. [kk] log K for binding of piperidine to tetra-x-phenylporphine complexes in toluene; ref 19; $\bar{x}$ = 0.04; % fit = 3.2%. [ll] ^{19}F chemical shifts of XC_6H_4F; refs 20 and 21; $\bar{x}$ = 0.06; % fit = 4.7%. [mm] pK_a of 3-substituted adamantane-1-carboxylic acids in 50% v/v aqueous C_2H_5OH at 25 °C; see ref 1; a σ_I system; $\bar{x}$ = 0.02; % fit = 2.9%. [nn] –pK_a of $4XC_6H_4C^+$ (OH_2) in H_2SO_4; see ref 1; a σ^+ system; $\bar{x}$ = 0.02; % fit = 3.0%. [oo] pK_a of 4-$XC_6H_4CH_2CO_2H$ in H_2O at 25 °C; see ref 1; a $\sigma_R{}'$ system; $\bar{x}$ = 0.01; % fit = 2.3%. [pp] log k_r for the reaction of $4XC_5H_4N$ with C_2H_5I in nitrobenzene at 60 °C; see ref 1; a σ^* system; $\bar{x}$ = 0.04; % fit = 1.4%. [qq] Rate of hydrolysis of k_X/k_H of $XC_6H_5CO_2Et$ in aqueous acetone at 25 °C; see ref 1; $\bar{x}$ = 0.07; % fit = 2.1%. [rr] pK_a of 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids in 50% w/w EtOH/H_2O at 25 °C; see ref 1; σ_I system; $\bar{x}$ = 0.05; % fit = 4.8%. [ss] pK_a of substituted benzoic acids in 80% w/w methylcellusolve at 20 °C; see ref 1; a σ_R system; $\bar{x}$ = 0.05; % fit = 2.6%. [tt] Carbonyl frequency shift of XC_6H_4OH adducts with DMA; ref 17; $\bar{x}$ = 0.61; % fit = 9.4%. [uu] $\delta^{13}C$–Co is the ^{13}C chemical shift of $P(OCH_3)_3$ adducts of $XCo(DH)_2$ (DH is dimethyl glyoximate); log k_r $4CNC_5H_5N$–Co is the log of the rate constant for 4-CNC_5H_4N dissociation from $XCo(DH)_2$; log K $4CNC_5H_4N$–Co is the log of the equilibrium constant for displacement of d^6-DMSO by 4-CNC_5H_4N from $XCo(DH)_2$. $E^{1/2}$ $XCoDH_2$ is the peak potential for the oxidation of $XCo(DH)_2{\cdot}H_2O$, and $E^{1/2}$ $Co(DH)_2{\cdot}XPy$, the potential for a series of pyridine adducts of $N_3Co(DH)_2{\cdot}Xpy$. The CoP dist is the cobalt phosphorus distance in $(C_6H_5)_3P$ adducts of $XCo(OH)_2$; ref 22. [vv] log k_1 for the displacement of $XC_5H_4N(L)$ from n^5-$CH_3CpMn(CO)_2L^A$ by $(C_6H_5)_2POCH_3$; $E^{1/2}$ of $CH_3CpMn(CO)_2SC_5H_4N$; ref 23; $\bar{x}$ = 0.08; % fit = 6.3%. [ww] $-\Delta H$ in cyclohexanecopper(II) adducts of bis(*tert*-butylacetoacetate) with XC_5H_5N; ref 24; $\bar{x}$ = 0.13; % fit = 35%. [xx] E°, V vs Ag/AgCl for *N*-methylpyridinium; ref 26; $\bar{x}$ = 0.02; % fit = 7.5%. [yy] Ionization energies (eV) of a series of substituted benzene chromium tricarbonyls; see ref 1; $\bar{x}$ = 0.04; % fit = 7.3%. [zz] $\delta^{13}C$ $X^3P(CO)_3$ is the ^{13}C chemical shift for X_3P adducts of $Ni(CO)_3$; ref 25; $\bar{x}$ = 0.20; % fit = 2.7%. $\delta^{13}C$ $(XC_6H_5)_3PNiCO_3$ is the ^{13}C chemical shift for $(XC_6H_5)_3P$ adducts of $Ni(CO)_3$, ref 25; $\bar{x}$ = 0.05; % fit = 6.4%. [ab] Change in free energies of ionization of substituted ruthenocenes; ref 16; $\bar{x}$ = 0.18; % fit = 1.4%.

bond-forming properties induced by the substituent in the family. The Hammett σ_H parameters have a d^C/d^E ratio of 0.10. With this ratio, substituents that have a $\Delta C^X/\Delta E^X$ ratio of 4 will have an electrostatic contribution that is 2.5 times as important as the covalent one (4 × 0.1 = 0.4 for the covalent/electrostatic contribution). As reported[13] in the literature, a linear plot of experimental data with a wide range of donors or acceptors versus a one parameter scale requires that the scale have the same C/E ratio as the measured property. In a similar manner, a linear Hammett plot results when the measured property has a d^C/d^E ratio of about 0.10. The pK_a values of XC_6H_4COOH in water (d^C/d^E of 0.06) and 44% ethanol (d^C/d^E of 0.11) as well as the ΔG of XC_6H_4OH–DMA adducts (d^C/d^E of 0.08) are all similar to the Hammett parameters in their covalent and electrostatic demands and plot up well with the Hammett σ_H. The greater the deviation of the d^C/d^E ratio from 0.10, the better the anticipated data fit with ΔE^X and ΔC^X than with σ_H.

The failure of the Hammett scale and the need for a separate σ_I scale to handle the pK_a of 4-substituted bicyclo(2.2.2)octane-1-carboxylic acids and 4-substituted quinuclidinum ions are expected from the d^C/d^E ratios of ∓0.11 and ∓0.19, respectively, for these systems. The σ_I scale has a ratio of ±0.09. This indicates that increasing the covalent and electrostatic bond-forming tendencies (i.e., positive ΔE and ΔC) will lead to an increase in the measured property from one effect and a decrease in the other. Ratios of d^C/d^E with +/– or –/+ signs will plot up linearly with σ_I but with opposite slopes. All of the systems in Table 2 reported to correlate with σ_I have d^C/d^E ratios of about –0.1.

Most of the systems reported to correlate poorly with σ_H or σ_I have d^C/d^E ratios that differ appreciably from 0.1 or –0.1. In some cases, the substituents are divided into two classes and individual linear plots made for each class. This simply limits the $\Delta C^X/\Delta E^X$ ratios of the substituents for a given line, so a limited correlation with limited meaning results. Most of the organic systems used as the basis for substituent constant correlations have d^C/d^E ratios between +0.2 and –0.2. Any set of dual parameters based only on systems with this range of ratios will only vary over this range. The utility of the resulting parameters will be limited to reactions or physicochemical properties whose d^C/d^E ratios fall in this range.

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

Shortcoming exists in the tentative ΔE^X and ΔC^X parameters reported here that have been determined from systems whose d^C/d^E ratios are limited to this range. As new data become available on systems with larger d^C/d^E ratios, the tentative parameters should be refined, vide infra. The incorporation of systems outside this limited range is a very significant feature of the ΔE–ΔC approach.

Uses of the Parameters on New Systems. The ΔE^X and ΔC^X parameters in Table 1 are substituted into eq 1 to analyze new data sets to determine if d^E, d^C, and $\Delta\chi^H$ values can be found to correlate the measured property. This application is straightforward and similar to that employed to add new acceptors or donors to the ECW correlation.[6a] In the application of eq 1, it is necessary to employ a large number of substituents that vary in their $\Delta C^X/\Delta E^X$ ratio. If this is not done, limited data sets can be fit very accurately but meaningless d^E and d^C parameters result. Three basic types of applications exist: (1) to determine ΔE^X and ΔC^X for a new substituent; (2) to determine d^E, d^C, and $\Delta\chi^H$ for a new family of compounds; and (3) to carry out a substituent constant analysis on a set of data.

The data set used to establish the ΔE^X and ΔC^X values for a new substituent should contain physicochemical measurements with reactants (probes) that have different d^C/d^E ratios. This variation is required to produce independent simultaneous equations to solve for the unknowns. Ideally, the data set should include measurements made under solvation-minimized conditions, e.g., $-\Delta H(I_2)$, $\Delta\nu_{OH}$, etc. Each measurement is used to write an equation of the form of eq 1 containing two unknowns, ΔE^X and ΔC^X. The probes are assigned n values (n = 1/weight), given in Table 2, that depend upon the number and type of substituents used to establish the physicochemical parameters. The simultaneous equations are solved for the unknown ΔE^X and ΔC^X values. Tentative ΔE^X and ΔC^X values result when the probes used to determine the parameters are limited in number or have similar d^C/d^E ratios.

The applications of eq 1 to add a new physicochemical probe to the correlation and to determine if a data set can be fit to eq

Table 3. Physicochemical Correlations Resulting from Summing Substituent Constants

substituent	$\Sigma\Delta E$	$\Sigma\Delta C$	$\Delta\nu(CH_3OH)^b$	$\Delta\nu(I_2)^b$	I.E.^{c}
2,4-$(CH_3)_2C_5H_4N$	0.0537	0.05623	323/325	S	
2,6-$(CH_3)_2C_5H_4N$	0.0080	0.7400	326/321	S	
3,4-$(CH_3)_2C_5H_4N$	0.0834	0.3205	309/312	4970/5002	
3,5-$(CH_3)_2C_5H_4N$	0.0674	0.2566	307/306	4920/4915	
2,4,6-$(CH_3)_3C_5H_3N^a$	0.0577	0.9322	344/352	S	
3,5-$(Cl)_2C_5H_4N$	−0.2404	−0.9222	196/192	3380/3287	
1,3,5-$(CH_3)_3C_6H_3$	0.1171	0.4488			7.05/7.04
$(CH_3)_6C_6{}^d$	0.2502	0.9615			6.88/6.87

[a] The 2-substituent constants are taken from Table 7. S refers to anticipated steric problems. [b] Experimental values from ref 14. [c] Experimental values from ref 15. [d] Calculated by summing three 4-CH_3 and three 3-CH_3 substituents.

1 both use the same approach. A series of measurements on a family of compounds are substituted into eq 1 along with the reported ΔE^X and ΔC^X values for the substituent. The resulting series of equations weighted according to the reported n values are solved for d^E, d^C, and $\Delta\chi^H$. Even when $\Delta\chi^H$ is measured for the parent hydrogen compound, it is entered as $\Delta\chi^X$ with $\Delta E = \Delta C = 0$ to give one of the simultaneous equations that is solved for $\Delta\chi^H$ as an unknown. In this manner, undue weight is not given to the measurement on the hydrogen substituent in the data fit.

When a number of established ΔE^X and ΔC^X parameters are used to analyze a new data set along with a substituent that has tentative parameters, two scenarios can result. If a good fit results, the tentative parameters are appropriate, i.e., the parameters are accurate or probably were determined with systems that have similar d^C/d^E ratios to those of the new system. In the second scenario, the substituent deviates and there is no apparent reason for the deviation. When this result occurs, the new data set can be used to refine the tentative parameters. This is accomplished by using the entire set of probes including the new data set to refit the tentative substituent and obtain refined ΔE^X and ΔC^X values. The new ΔE^X and ΔC^X parameters are then used to redetermine new probe parameters for the new data set. The process is reiterated until the substituent and probe parameters do not change.

Additivity of Substituent Constants. In some families, compounds exist which contain several substituents. The question arises as to whether or not the substituent constants can be summed to predict the measured result. The data in Table 3 were calculated by adding the substituent constants (Table 1) and calculating $\Delta\chi$ with eq 1 using the d^E and d^C values in Table 2. The $\Sigma\Delta E$ for the hexamethylbenzene compound was obtained by summing three 3-ΔE and three 4-ΔE methyl values. The $\Sigma\Delta C$ were calculated with three 3-ΔC and three 4-ΔC methyl values. The 1,3,5 summation involved one 4-X and two 3-X substituent sets. In all instances, the experimental data are predicted well, suggesting that the perturbations made on the ring system by the substituents can be predicted by summing the substituent constants. This is a preliminary conclusion and remains to be tested when perturbations larger than those of six methyl groups or two chloro groups are made.

The next set of data to be examined is the free energy of ionization of substituted ruthenocenes. The data[16,17] are summarized in Table 4. The analysis indicates that the systems are fit very well except for the pentachloro and pentabromo derivatives. Assuming that s^E and s^C are positive for the metal–cyclopentadiene ring system, $E_B{}^*$ and $C_B{}^*$ (for the electron) are both negative, corresponding to decreased ionization energy from an increase in both the electrostatic and covalent bonding properties of the ring π system by electron-releasing substituents. Both the covalent and electrostatic bonding components make significant contributions to the ionization trend. For the pentamethyl substituents, 4.9 eV or 35% of the ionization energy decrease comes from the electrostatic term and 9.2 eV or 65% of the decrease comes from the covalent term. For the combined influence of five methyl and four trifluoromethyl substituents, 9.4 eV or 45% of the increase comes from the electrostatic term and 11.6 eV or 55% of the increase comes from the covalent term.

Table 4. Free Energies of Ionization of Substituted Ruthenocenes

substituents	$\Sigma\Delta E^a$	$\Sigma\Delta C^a$	n	ΔG_{exp}	$\Delta G_{calc}{}^c$
parent H	0	0	0.2	164.6 ± 2	165
$5CH_3(Cp^*Cp)$	0.2395	0.9610	0.2	152.3 ± 2	151
$4CF_35CH_3$	−0.4657	−1.216	0.6	192.0 ± 5	187
$5Cl5CH_3$	−0.2085	−0.656	90	165.4 ± 2	$(176)^d$
NO_25CH_3	−0.014	0.322	0.2	161.9 ± 2	163
$2(CH_3)_3Si^b$	−0.0154	0.409	0.3	158.4 ± 2	162
$(CH_3)_3Si5CH_3{}^b$	0.2318	1.1655	0.2	151.3 ± 2	150
$10CH_3$	0.4790	1.924	0.2	137.9 ± 2	137
$5F5CH_3{}^a$	−0.0969	−0.4019	0.3	170.8 ± 2	171
$5Br5CH_3$	−0.1305	−0.9375	90	165.1 ± 2	$(177)^d$

[a] The number of substituents on each Cp ring is indicated. Data fits employed the 4-substituents except that for $5F5CH_3$, which uses five 4-CH_3, three 4-F, and two 3-F. [b] Calculated with refined 4-$Si(CH_3)_3$ parameters of $\Delta E = -0.008$ and $\Delta C = 0.205$. Parameters from the initial fit were −0.014 and 0.048, respectively. [c] Calculated with $d_B{}^E = -20.27$, $d_B{}^C = -9.55$, and $\Delta\chi^H = 165.5$. [d] Omitted from the data fit and calculated with the resulting parameters.

In the inital data fit employing five 4-fluoro substituents, the pentamethyl/pentafluoro derivative deviated to a larger extent than the other systems. The miss is in the direction that indicates it is harder to ionize the complex than predicted. The 4-F substituent has a sizeable conjugative component, and three or four of these substituents on one cyclopentadienide ring may saturate the effectiveness of the ring to π bond with any more substituents. Each fluorine that back π bonds raises the energy of the ring π^* orbital. After a certain point, the energy match to π^* will become too large to effectively π bond to additional fluorines. If instead of using five 4-F plus five 4-CH_3 substituents, the ΔE and ΔC summations utilize five 4-CH_3, three 4-F, and two 3-F substituents, the ΔG value is predicted accurately. Other combinations of 3- and 4-CH_3 with 3- and 4-F substituents also give the correct ΔG.

Large deviations are encountered for the pentabromo- and pentachlorocyclopentadienide derivatives of Cp*Ru, indicating the electron is more easily removed than expected. The substituent effect may not be additive because the perturbation caused by adding two chlorines or bromines could be saturating the cyclopentadienide ring, i.e., the effect of adding the third, fourth, and fifth chlorines or bromines has the same effect as that calculated for adding one more. However, this explanation can be rejected because the sum of the substituent constants for four CF_3 groups makes a larger perturbation than the five chlorines and this compound fits the correlation. The deviation for the pentachloro or pentabromo compounds could result from ionization of a chlorine or bromine lone pair electron.

The ΔE and ΔC values obtained for 4-$Si(CH_3)_3$ from the original data fit are tentative. Hammett substituent constants

(14) Nicolet, P.; Laurence, C. *J. Chim. Phys. Phys.-Chim. Biol.* **1983**, *80*, 677.
(15) Levitt, L. S.; Levitt, B. W. *J. Inorg. Nucl. Chem.* **1976**, *20*, 1797.
(16) Ryan, M. F.; Siedle, A. R.; Burk, M. J.; Richardson, D. E. *Organometallics* **1992**, *11*, 4231.
(17) Abraham, M. H.; Duce, P. P.; Pror, D. V.; Barratt, D. G.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans. 2*, **1989**, 1355.

Table 5. Comparison of Reported[6d] and Substituent Constant E_B and C_B Values for Substituted Pyridines

substituent	E_B	$E_B(\Delta E)$	C_B	$C_B(\Delta E)$
H	1.78	1.78	3.54	3.54
3-CH_3	1.88[a]	1.81	3.60[a]	3.67
3-Cl	1.86	1.66	2.88	3.08
3-Br[a]	1.87[a]	1.66	2.87[a]	3.08
3-I	1.83[a]	1.67	2.98[a]	3.13
4-CH_3	1.79	1.83	3.78	3.73
4-C_2H_5	1.90[a]	1.81	3.64[a]	3.74
4-CH_3O	1.93[a]	1.83	3.73[a]	3.83
4-$N(CH_3)_2$	1.82[a]	1.92	4.53[a]	4.43
4-CN	1.66[a]	1.53	2.82[a]	2.94

[a] Tentative parameters based on limited data.

Table 6. E_A and C_A Parameters for Substituted Phenols Derived from ΔE^X and ΔC^X

substituent (n)[a]	E_A	$E_A(\Delta E)$[b]	C_A	$C_A(\Delta E)$[b]
H (0.05)	2.27	2.27	1.07	1.07
4-F (0.4)	2.27	2.30	1.07	1.11
3-F (0.2)	2.35	2.37	1.18	1.17
3-CF_3 (0.2)	2.40	2.38	1.21	1.22
4-Cl (0.4)	2.30	2.34	1.13	1.14
4-CH_3 (0.4)	2.24	2.23	0.98	1.03
4-$C(CH_3)$ (0.4)	2.16	2.22	0.95	1.03

[a] An n value of 0.2 is assigned to substituents that have 10 or more measured enthalpies, and 0.4 is assigned to systems with less than 10. [b] Calculated from eqs 4 and 5 with $s^E = -0.833$ and $s^C = -0.229$.

ranging from 0.06 to −0.07 have been reported. The $d_B{}^E$, $d_B{}^C$, and $\Delta\chi^H$ values from the data fit of the ruthenocene system were employed with the other reported probes to redetermine the ΔE^X and ΔC^X values for 4-$(CH_3)_3Si$. The new 4-$(CH_3)_3Si$ parameters are used to redetermine $d_B{}^E$, $d_B{}^C$ and $\Delta\chi^H$ for ruthenocene, which in turn are used to redetermine ΔE^X and ΔC^X for 4-$(CH_3)_3Si$. The process is repeated until only a small change in both sets of parameters occurs on successive fits. The iterated parameters are given in Table 1 and used in the fit reported in Table 4.

E_A and C_A Parameters for Phenols. The E_B and C_B values of any substituted pyridine whose substituent constants, ΔE^X and ΔC^X, are known can be determined by adding these values to the E_B and C_B values for pyridine; see eqs 4 and 5, respectively. Table 5 compares E_B and C_B values for substituted pyridines that are calculated from substituent constants to those reported in the E and C correlation.[6d]

The new ΔE^X and ΔC^X derived parameters reported in Table 5 are considered to be more accurate and should be used in future E and C analyses. The new parameters fit all of the experimental data that the earlier parameters were based on as well as the earlier parameters.

With the very extensive amount of data available on substituted phenols, we are now in a position to predict the E_A and C_A values of any phenol whose substituent constant is known. The reported phenol E_A and C_A parameters[6d] are given in Table 6.

The E_A values from Table 6 are substituted into eq 4, and the equation is solved for s^E. The C_A values of Table 6 are substituted into eq 5, and the equation is solved for s^C. Values of $s^E = -0.833$ and $s^C = -0.224$ are obtained. These values indicate that the electrostatic influence of the substituent is transmitted about 0.8 as effectively in phenol as in pyridine. The covalent influence is transmitted about 0.2 as effectively.

The s^E and s^C values for the phenol family can be substituted into eqs 4 and 5 to calculate the E_A and C_A values of any phenol whose substituent constant is known. These new E_A and C_A parameters calculate enthalpies and spectral shifts of data in the original E and C correlation as well as the reported paramters. The new parameters are considered to be more accurate and should be used in future E and C correlations.

The discussion of the substituted phenols and pyridines illustrates the direct connection that the ΔE–ΔC based substituent constants have to the ECW model.[6] This connection makes the dual parameter ΔE–ΔC substituent constants unique in providing a reactivity scale that is directly connected to and parametrized with solvation-minimized bond strengths.

2-Substituent Constants. The 4-substituent constants are dominated by the conjugative properties of the substituent with smaller contributions from transmission of the substituent effect through space and the σ bonds. The large falloff of inductive transmission through σ bonds is illustrated for example by the isotropic shift of alkyl amine complexes of nickel(II). A rapid decrease is observed[18] in the contact shift as one proceeds down an aliphatic chain of carbon atoms. This is not meant to imply that the localized contribution is zero for 4-substituents but that the dominant contribution is the conjugative effect. The ΔE and ΔC values for the 3-substituents are transmitted mainly through space and the σ bonds. When a second substituent is attached to a carbon at the meta position of a benzene ring, a node exists at this carbon in the π system. As a result, conjugative interactions do not occur and the meta substituents qualify for treatment as 3-substituents, i.e., a localized effect. The same parameters are used for meta substituents and aliphatic chains. There are systems in which the substituent change makes significant contributions to the reactive center via both localized and delocalized mechanisms. When both effects contribute, the 3- or 4-substituents will be inappropriate. A set of substituent constants is offered for systems in which the reactive group is two or three bonds removed from the carbon bearing the reactive group and has contributions from both localized and delocalized mechanisms. The ortho substituents on a phenyl ring would qualify for this data set. For the most part, only limited data is available and ortho-substituent variation is complicated by proximity effects. If one considers the electronic structure of substituted acetic acids, it is difficult to rationalize the traditional approach of treating this data with localized substituent constants. The methyl hydrogens and X substituents of CH_2X groups attached to the carbonyl carbon are not orthogonal to the carboxyl π system. The π bonding of a CH_2X group attached to the carboxyl group resembles a CH_2X group attached to the ortho position of a benzene ring. In both systems localized and delocalized mechanisms transmit the substituent effect. In the ΔE–ΔC approach, both rate and equilibrium data for $XCH_2C(O)OR$ (R = H or alkyl) groups are treated with 2-substituent constants for the 2-XCH_2 group. Any substituent that operates via localized and delocalized mechanisms and is attached to a carbon one to three bonds removed from the reactive group qualifies as a 2-substituent. The ΔE and ΔC values for the 2-substituents are summarized in Table 7. Data for the $\Delta\nu_{OH}$ shifts of methanol upon hydrogen bonding to 2-substituted pyridines are fit well ($\bar{x} = 0.6$ cm^{-1}). Monatomic substituents in the 2-position of pyridines give shifts in the electronic transition of iodine adducts which are free from steric effects, and these transitions are also fit well. The 2-$CH_3C_5H_4N$ transition deviates in the direction expected for a steric effect.

The ortho-substituted benzoic acids are poorly correlated with the 2-substituents. The 2-Cl, 2-Br, 2-I, and 2-CH_3 derivatives

(18) Fitzgerald, R. J.; Drago, R. S. *J. Am. Chem. Soc.* **1968**, *90*, 2523.
(19) Walker, F. A.; Hui, E.; Walker, J. M. *J. Am. Chem. Soc.* **1975**, *97*, 2340 and references therein.
(20) (a) Meyer, L. H.; Gutowsky, H. S. *J. Phys. Chem.* **1953**, *57*, 481. (b) Gutowsky, H. S.; McCall, D. W.; McGarvey, B. R.; Meyer, L. H. *J. Am. Chem. Soc.* **1953**, *74*, 4809.
(21) (a) Taft, R. W., Jr. *J. Am. Chem. Soc.* **1957**, *79*, 1045. (b) Hausch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165.
(22) (a) Bresciana-Pahor, N., et al. *Coord. Chem. Rev.* **1985**, *63*, 1. (b) Marzilli, L. G., et al. *J. Am. Chem. Soc.* **1987**, *109*, 6045.
(23) Zizelman, P. M.; Arnatore, C.; Kochi, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 3771.
(24) Libutti, B. L.; Wayland, B. B.; Garito, A. F. *Inorg. Chem.* **1969**, *8*, 1510.
(25) Bodner, G. M.; May, M. P.; McKinney, L. E. *Inorg. Chem.* **1980**, *19*, 195.
(26) Burke, M. R.; Brown, T. L. *J. Am. Chem. Soc.* **1989**, *111*, 5185.

Table 7. 2-Substituents for One- to Three-Bond Conjugative Interactions

substituent (n)	ΔE	ΔC
2-CH_3 (0.3)	0.004	0.370
2-C_2H_5 (0.8)	0.001	0.405
2-$CH_3CH_2CH_2$ (0.8)	0.007	0.404
2-$C_6H_5CH_2$ (0.8)	0.054	0.316
2-OCH_3 (1.2)	−0.012	−0.789
2-F (0.8)	−0.239	−1.26
2-Cl (0.8)	−0.227	−0.974
2-Br (1.2)	−0.221	−0.943
2-I (1.2)	−0.202	−0.686
2-Cl-CH_2 (0.8)	0.136	0.083
2-BrCH_2 (0.8)	0.127	0.075
2-ICH_2 (0.8)	0.120	0.138
2-CNCH_2 (0.8)	0.137	0.017
2-CH_3OCH_2 (0.8)	0.093	0.202
2-HOCH_2 (0.8)	0.071	0.221
2-$C_6H_5OCH_2$ (0.8)	0.131	0.135
2-HSCH_2 (0.8)	0.107	0.180

all have smaller pK_a values than predicted by the parameters. The proximity of the substituent to the carboxyl group probably gives rise to steric problems. If the carboxyl group or carboxylate anion is twisted out of the plane, the conjugative interaction would be diminished. Accordingly, an attempt was made to fit the ortho-substituted carboxylic acids of large substituents with the 3-substituent constants. An excellent fit resulted with $d^E = 5.36$, $d^C = 0.37$, and $\Delta\chi^H = 3.68$. The results of the fit are given in the order substituent/pK_a exp/pK_a calc 2-Cl/2.97/2.86; 2-CH_3/3.91/3.90; 2-Br/2.85/2.87; 2-I/2.86/2.95; 2-NO_2/2.17/2.17. The $\Delta\chi^H$ corresponds to the pK_a of benzoic acid with the carboxyl group distorted from planarity. This result suggests that for bulky groups the localized effect of the substituent dominates the substituent effect in ortho-substituted carboxylic acids.

Unfortunately, there are only a few substituents for which proximity effects do not exist that have been studied both on the ortho position of aromatic six-membered rings and on carboxyl groups. A large amount of data on different one-, two-, and three-bond delocalized systems is needed to test the validity of a set of delocalized 2-substituent parameters. The limited data available indicate that this approach is worth further effort.

In one- to three-bond systems involving substituents on different atoms than carbon, it is possible to have extensive variation in the relative importance of the localized and delocalized substituent contribution mechanisms. To accommodate all possible combinations of localized and delocalized effects, a large number of n-substituent constants would be required. The following alternative is offered as an extension of the arguments used to rationalize the need for a set of 2-substituents. The n-ΔE^X and n-ΔC^X substituent constants derived from measured properties on systems where the substituent effect is some combination of localized and delocalized mechanisms should fit the following equations

$$n\text{–}\Delta E^X = k^{3E}3\text{–}\Delta E^X + k^{4E}4\text{–}\Delta E^X \quad (6)$$

$$n\text{–}\Delta C^X = k^{3C}3\text{–}\Delta C^X + k^{4C}4\text{–}\Delta C^X \quad (7)$$

where k^{3E} and k^{4E} weight the *relative* importance of the localized and delocalized mechanisms in determining n-ΔE^X and k^{3C} and k^{4C} are similar weighting factors for the covalent contribution. When eqs 6 and 7 are applied to the 2-substituent constants whose 3- and 4-substituent constants are well-known (i.e., CH_3, C_2H_5, F, Cl, Br, I, and OCH_3), values of $k^{3E} = 1.72$, $k^{4E} = 0.14$, $k^{3C} = 3.57$, and $k^{4C} = -2.01$ result with average deviations, $\bar{x}$, in the calculated 2-ΔE and 2-ΔC substituent constants of 0.03 and 0.19, respectively. The localized mechanism makes the major contribution to the 2-ΔE substituent constants. The 2-ΔC constants are also dominated by the localized parameters with a contribution in the opposite direction from the delocalized mechanism. Considering the uncertainty in the values of the 2-substituent constants, this result is tentative but provides support for eqs 6 and 7.

Experimental Section

The least squares minimization program has been described previously.[6b] Several of the families of reactions treated correspond to enthalpies or spectral probes that have been established in reactions involving a wide range of donors. These quantities have been fixed in the data fit (i.e., $d^E = E_A{}^*$ or $E_B{}^*$ and $d^C = C_A{}^*$ or $C_B{}^*$).

In other systems, tentative E and C values are known. These are entered as a quantity called ddE, which is fit as one of the simultaneous equations with ΔE equal to 1, $\Delta C = 0$, $\Delta\chi^H = 0$, and one called ddC, which is fit as one of the simultaneous equations with $\Delta E = 0$, $\Delta C = 1$, and $\Delta\chi^H = 0$. The weight assigned to ddE or ddC represents the accuracy of the tentative E and C parameters.

The 2-ΔE^X and 2-ΔC^X substituents are only loosely connected by a few data sets in common with the 3-X and 4-X systems. Several of the measurements from the 2-X substituents are complicated by proximity effects. These measurements were given a small weight (large n) in the data fit.