Progress in

PHYSICAL ORGANIC CHEMISTRY

VOLUME 16

Editor

ROBERT W. TAFT, *Department of Chemistry*
University of California, Irvine, California

An Interscience® Publication

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Introduction to the Series

Physical organic chemistry is a relatively modern field with deep roots in chemistry. The subject is concerned with investigations of organic chemistry by quantitative and mathematical methods. The wedding of physical and organic chemistry has provided a remarkable source of inspiration for both of these classical areas of chemical endeavor. Further, the potential for new developments resulting from this union appears to be still greater. A closing of ties with all aspects of molecular structure and spectroscopy is clearly anticipated. The field provides the proving ground for the development of basic tools for investigations in the areas of molecular biology and biophysics. The subject has an inherent association with phenomena in the condensed phase and thereby with the theories of this state of matter.

The chief directions of the field are: (a) the effects of structure and environment on reaction rates and equilibria; (b) mechanisms of reactions; and (c) applications of statistical and quantum mechanics to organic compounds and reactions. Taken broadly, of course, much of chemistry lies within these confines. The dominant theme that characterizes this field is the emphasis on interpretation and understanding which permits the effective practice of organic chemistry. The field gains its momentum from the application of basic theories and methods of physical chemistry to the broad areas of knowledge of organic reactions and organic structural theory. The nearly inexhaustible diversity of organic structures permits detailed and systematic investigations which have no peer. The reactions of complex natural products have contributed to the development of theories of physical organic chemistry, and, in turn, these theories have ultimately provided great aid in the elucidation of structures of natural products.

Fundamental advances are offered by the knowledge of energy states and their electronic distributions in organic compounds and the relationship of these to reaction mechanisms. The development, for example, of even an empirical and approximate general scheme for the estimation of activation energies would indeed be most notable.

The complexity of even the simplest organic compounds in terms of physical theory well endows the field of physical organic chemistry with the frustrations of approximations. The quantitative correlations employed in this field vary from purely empirical operational formulations to the approach of applying physical principles to a workable model. The most common procedures have involved the application of approximate theories to approximate models. Critical assessment of the scope and limitations of these approximate applications of theory leads to further development and understanding.

Although he may wish to be a disclaimer, the physical organic chemist attempts to compensate his lack of physical rigor by the vigor of his efforts. There has indeed been recently a great outpouring of work in this field. We believe that a forum for exchange of views and for critical and authoritative reviews of topics is an essential need of this field. It is our hope that the projected periodical series of volumes under this title will help serve this need. The general organization and character of the scholarly presentations of our series will correspond to that of the several prototypes, e.g., *Advances in Enzymology*, *Advances in Chemical Physics*, and *Progress in Inorganic Chemistry*.

We have encouraged the authors to review topics in a style that is not only somewhat more speculative in character but which is also more detailed than presentations normally found in textbooks. Appropriate to this quantitative aspect of organic chemistry, authors have also been encouraged in the citation of numerical data. It is intended that these volumes will find wide use among graduate students as well as practicing organic chemists who are not necessarily expert in the field of these special topics. Aside from these rather obvious considerations, the emphasis in each chapter is the personal ideas of the author. We wish to express our gratitude to the authors for the excellence of their individual presentations.

We greatly welcome comments and suggestions on any aspect of these volumes.

Robert W. Taft

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I. INTRODUCTION

Some 10 years ago one of us (RDT) wrote a chapter of the same title (1) for this series. Since that time, interest in understanding and predicting the effects of substituents on various physical properties, equilibria, and reactivities of organic molecules has continued unabated. Substantial progress has been made in the field by using new experimental and theoretical approaches. The study of organic equilibria, notably proton transfers in the gas phase, has provided much information on inherent substituent effects (those in the absence of the perturbing influences of a solvent or counter ion). In particular, the substituent polarizability effect (2–4) (whose importance has special dependencies on structure and reaction conditions) is now properly appreciated. Theoretical calculations have been shown to be capable of reproducing to useful approximation the experimental ΔG^0 data for proton transfer reactions of many series of organic molecules. Using theoretical calculations (4–5) with model systems has allowed analysis of these ΔG^0 values which has improved the understanding of the nature of substituent electronic effects (6).

In 1983 RWT wrote a chapter in this series reviewing substituent effect data for gas-phase proton transfer equilibria which were then available (4). Comparisons were made between the observed ΔG^0 values and corresponding calculated ΔE^0_{el} (Section II). Emphasis was placed upon all of the available evidence for the three kinds of electronic substituent effects that generally contribute (singly or in any combination) to the effects of molecular structure on proton transfer acidity or basicity: (a) field/inductive, (b) resonance, and (c) polarizability. Also included was evidence which showed that there are also extremely large effects on acidity or basicity of the atomic protonation center. The structural effects on acid/base behavior which are due only to variation of the reaction center have been considered elsewhere (7) and will not be included in this chapter.

More recent ab initio calculational results have strongly suggested that the field/inductive substituent effect should probably be considered as two separate primary effects, the field and electronegativity (or sigma-electron acceptor) substituent effects (8). A summary of this position is presented in this chapter together with evidence for and methods of analysis of this generalized substituent effect theory. Parameterized scales (σ values) for the four primary substituent effects are presented. These are used (with restrictions) to approximately quantitatively analyze typical observed data. This treatment also provides a background that is used in the following chapters of this volume. A key requirement in the procedures used is that for valid multiple linear regression analysis of substituent effect data a selected set of substituents must be used for which each of the four kinds of σ-parameters are mutually noncolinear with one another, i.e., the parameters act statistically in accord with the theory that all four parameters are nearly independent variables (Section IV).

The next two sections review the background necessary for treatment of electronic substituent effects.

II. TREATMENT OF ELECTRONIC SUBSTITUENT EFFECTS

In principle, we could use theoretical calculations with a pseudosubstituent to cause a gradual change in charge and examine the consequences with respect to the effects on various properties. In practice, substituents lead to changes in properties via several principal interaction mechanisms with numerous subcategories. As mentioned earlier (1), it is a human desire to want to put chemical and physical relationships into concepts that can be mentally pictured and readily used and communicated to others. For large complex organic molecules in particular the application of concepts is still the most effective means for interpretation of experimental data. The total observed or theoretically calculated electronic substituent effect on equilibria, reaction rates, and spectroscopic properties can be broadly represented by the formalism of Equation 1:

$$\mathrm{XGY} + \mathrm{HGY}' \rightleftarrows \mathrm{XGY}' + \mathrm{HGY} \tag{1}$$

$$\delta_x \Delta E^0 = \Delta E^0_{\mathrm{el}} = \left(E^0_{\mathrm{XGY}'} - E^0_{\mathrm{XGY}}\right) - \left(E^0_{\mathrm{HGY}'} - E^0_{\mathrm{HGY}}\right)$$

$$= \left(E^0_{\mathrm{XGY}'} - E^0_{\mathrm{HGY}'}\right) - \left(E^0_{\mathrm{XGY}} - E^0_{\mathrm{HGY}}\right)$$

E^0_{el} is the ground-state electronic energy for the indicated molecule or ion. For reactions, the standard free energy, $G^0_{(T)}$, or the standard enthalpy, $H^0_{(T)}$, can replace E^0_{el} to give corresponding expressions for the standard free-energy change, $\Delta G^0_{(T)}$, and the standard enthalpy change, $\Delta H^0_{(T)}$, respectively, at the temperature T^0K.

In Equation 1, the molecules are arbitrarily (and somewhat idealistically) considered to be of three distinct parts. A geometrically fixed molecular framework is represented by G. It is generally one of many widely available in various carbon–carbon bonded structures. In the lower limit, it appears that the formalism of Equation 1 is adequate only if G is at least one or two fixed atoms. X represents a general substituent replacing hydrogen; that is, this grouping may be either a single atom (e.g., F or Cl) or structurally well-defined composites of atoms (e.g., NH_2, OH, NO_2, etc.).

As indicated by Equation 1, a hydrogen atom is generally taken as the substituent of reference. Equation 1 can be readily modified, of course, if it is necessary or desirable to use another substituent of reference. The choice of hydrogen as the substituent of reference is based upon its simplicity, since all bonding interactions are restricted to the use of its 1*s* orbital.

The Y and Y′ parts of Equation 1 designate two different reaction centers or two different spectroscopic "probe sites," or "chromophores." For example, for the proton transfer equilibria of a series of substituted methanols, Equation 2, Y is OH_2^+, Y′ is OH, and G is CH_2. Equation 2 is written to give the effects of various substituents, X, on the acidities of the conjugate acids of the methanols as expressed by $-\delta_x \Delta G^0 = -\Delta G^0_{(2)}$

$$XCH_2OH_2^+ + CH_3OH \rightleftarrows XCH_2OH + CH_3OH_2^+ \qquad (2)$$

In the measurement of an absorption frequency of a series of molecules represented by XGY, Y is the ground electronic state for a well-defined probe or chromophore site, Y′ is the corresponding excited state, and $\delta_x \Delta E^0 = h\,\Delta\nu$. In all cases, the term "series" is used in the sense that all measurements of a given kind of property are for particular G, Y, and Y′ group structures with only the substituent X changing. As implied by the title, we restrict ourselves in this review to measurements where there are constant or quite minor changes in nonbonded interactions in the process of Equation 1. That is, our concern is with substituent-induced changes in net "electronic" bonding energies as distinguished from changes in repulsive nonbonded energies.

In using the formalism of Equation 1, care must be exercised to avoid certain properties for series of molecules in which the substituent may become an intimate part of the "chromophore," rather than only causing an electronic perturbation on a distinctly separate "chromophore." A good example (8) of where this restriction applies is for $\pi \rightarrow \pi^*$ electronic transitions of monosubstituted benzenes. Other spectroscopic properties such as infrared and ultraviolet intensities which are not simply fitted within the formalism of Equation 1 are considered in a later chapter in this volume.

Great care must also be exercised for both physical and chemical properties measured in solution. First, the measurements must be conducted at sufficiently high dilution to avoid concentration effects of the various solutes. Second, one must recognize that the experimental measurements will generally be significantly modified (even reversed) by the nonspecific and specific interactions (4) of solvent molecules. That is, while the formal reactions of Equation 1 can be applied in solution, the $-\delta_x \Delta G^0$ values observed are likely to differ very significantly from gas-phase results and from solvent to solvent. This can only be known with certainty by haivng available the data for gas phase to compare with those in a given solvent. Since the measure of solution $-\delta_x \Delta G^0$ values for a given series must be the sum of inherent substituent effects and corresponding differential solvent effects, special cases in which plots of $-\delta \Delta G^0_{(g)}$ versus $-\delta \Delta G^0_{(soln)}$ are approximately linear will occur. This happens when the differential solvent effects are approximately inversely proportional to the inherent substituent effects. That is, the solution measurements then show a pattern corresponding to inherent behavior. This appears to be reasonably common *only* when the substituents, X, and the solvent do not form specific interaction complexes. Several examples of this kind are illustrated in the results section (IV.D.4).

A final point of importance is that the process of Equation 1 need not be series of directly determined values. Thus, for example, in proton transfer equilibria, it is usual in solution to directly measure reactions, for example, such as Equation 3:

$$XCH_2OH_2^+ + H_2O \rightleftarrows H_3O^+ + XCH_2OH$$

and (3)

$$CH_3OH_2^+ + H_2O \rightleftarrows H_3O^+ + CH_3OH$$

where H_2O is both a standard base and the solvent. The data for a series of XCH_2OH are then combined to obtain the $-\delta_x \Delta G^0$ values for Equation 2—a specific example of the general reaction (Equation 1). Another alternative is to directly measure the proton transfer equilibria for a whole series of standard bases of known basicity (10) and combine these results in the form of Equation 1. Indeed, the proper combination of thermodynamic data to obtain results in the form of Equation 1 with substituents, molecular frameworks, and/or reaction or probe centers that are particularly discerning of specific kinds of structural effects offers a powerful means of studying those effects.

Spectroscopic data are most frequently measured as quantized frequency (or energy) difference between XGY and XGY′, including results for HGY and HGY′. It should be recognized that these results can equally well be combined to give the values corresponding to the process of Equation 1.

III. PRIMARY KINDS OF SUBSTITUENT EFFECTS

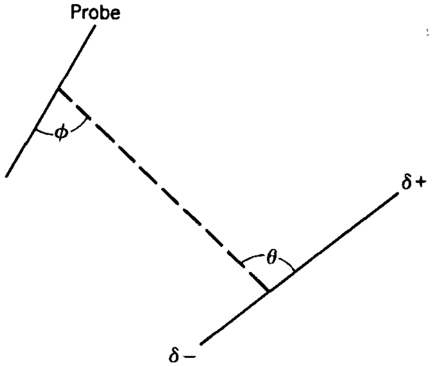
Any substituent X for hydrogen may alter the bonding electronic energy differences $E^0_{\mathrm{XGY}} - E^0_{\mathrm{HGY}}$ compared to $E^0_{\mathrm{XGY'}} - E^0_{\mathrm{HGY'}}$. Substituent interactions through G (or space) with Y or Y′, which cause such energy changes are of four principal kinds. They differ in their origin and in their mode of transmission. The four kinds of primary substituent effects, their symbol and parameter symbol, whether or not significant substituent charge transfer occurs, and the relative range of the effect are indicated below:

Effect	Symbol	Substituent Parameter	Substituent Transfer of Charge	Range
Electronegativity	χ	σ_χ	Yes	Short
Field	F	σ_F	No	Long
Resonance (π-electron transfer)	R	σ_R	Yes	Long (in an extended pi system)
Polarizability	P	σ_α	No	Short

Various secondary effects can occur, and the most important of these are considered either under the primary effect or in Section IV.

A. Field Effects

When the reference H atom substituent is replaced by any substituent, X, there will in general be a change in the local dipole (or dipoles) interacting with the groups Y and Y′. This follows from the fact that the bonds between most atoms are not completely covalent, but possess partial ionic characters which impose electrical assymetry either in the bonds to H— or X— or in the bonds within X. The through space dipolar interactions with Y and Y′ are of several possible kinds. All of these are regarded as electrostatic effects transmitted through space which either raise or lower the energy differences $E^0_{\mathrm{XGY}} - E^0_{\mathrm{HGY}}$ and $E^0_{\mathrm{XGY'}} - E^0_{\mathrm{HGY'}}$, (depending upon charge sign and dipole orientation).



1

If the detailed charge distribution is known, the field effect can be calculated by simple electrostatics. In the point charge approximation, for a dipolar substituent and a charged probe site (11), Equation 4 is applicable.

$$\Delta E = \frac{q_1 \mu \cos\theta}{Dr^2} \tag{4}$$

where q_1 is the charge on the probe site, μ is the local dipole, θ is the angle the dipole subtends to the probe site as shown in **1**, D is the effective dielectric constant, and r is the distance from the dipole centre to the probe site. When the measurements refer to the polarization of a bond, the appropriate equation is 5,

$$\Delta E_{\text{bond}} = \frac{\mu(2\cos\theta\cos\phi - \sin\theta\sin\phi)}{Dr^3} \tag{5}$$

If the substituent has a charge q_2, then the correspoding equations are 6 and 7. Equation 7 is the simplified form referring to a substituent lying on the axis of the polarized bond probe.

$$\Delta E = \frac{q_1 q_2}{Dr} \tag{6}$$

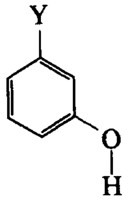
$$\Delta E_{\text{bond}} = \frac{2q_2\cos\phi}{Dr^2} \tag{7}$$

Equations 4–7 are based on the assumption of point charges and dipoles. In organic molecules with complex charge distributions the equation cannot be applied quantitatively unless the charge distribution is known. A further difficulty with direct calculations using these equations is the uncertainty associated with the effective dielectric consant. Even in a vacuum where $D = 1$, the transmission usually involves lines of force going through the molecule where the dielectric constant is likely to be significantly greater than one. In solvents of relatively high dielectric constant, it is also likely that the electrostatic lines of force will pass in part through the solvent which will significantly increase the effective dielectric constant.

Field effects of distant dipolar substituents are currently considered to be the most important mechanism of electronic substituent effect in molecules where the substituent is not able to conjugate with a π-electron system. This is discussed further in Section III.B. Since the field effect originates in dipoles caused by the attachment of the substituent, the field effect is roughly correlated by the corresponding dipole moments of series of molecules such as CH_3X. This relationship is of conceptual value, but it is not quantitatively of use for estimating field effects (cf. discussion of Chapter 3 of this volume).

In summary, the general order of increasing magnitude of substituent field effects for common substituents is: metal (M) or MH_x, MMe_x < H, alkyl group (R), < C_6H_5 < OR, SR, COR < halogen, CF_3 < CN < NO_2 < SO_2CF_3. The effect diminishes with distance as the above Equations 4–7 show. For a substituent that has the positive end of its dipole oriented toward a negative reaction center, there is a loweing of energy (stabilization), whereas if the reaction center is positive, destabilization occurs.

It is important to realize (12) that field effects may have certain dependences on molecular geometry. For example, a change in the conformation of the substituent, such as between **2** and **3**, can alter the field effect experienced at a given site.



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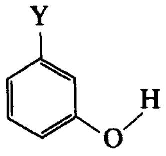
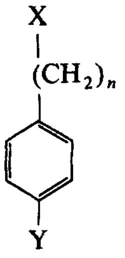


3

When the framework G of Equation 1 is a π-electron system (such as a benzene ring), the polarization of the π-electrons by the dipolar substituent becomes an important part of the substituents' field effect (13). Thus, in molecules such as **3**, the effect felt at the probe site Y is made up not only of a primary field effect transmitted directly from the substituent (X), but also the indirect effect of the polarization of the π-system of a benzene ring. This later field effect on a π-system is given the symbol F_π, although it has earlier been referred to as the π-inductive effect.



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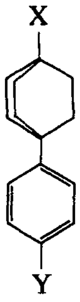
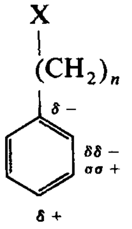


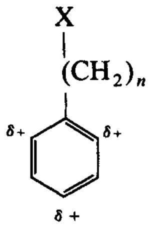
5

Evidence such as the carbon-13 chemical shifts at various positions in the benzene ring in molecules such as **4** and **5** (Y=H) show this to be an important effect (13).

In molecules of type **4** and **5**, the relative effect on the various carbon atoms of the benzene ring will differ according as to whether the ring is polarized as a unit, as in **4A**, or a primary polarization occurs at the ring carbon atom nearest to the substituent and the effect is then relayed to the other aromatic carbon, as in **4B**. (The δ values show general trends, not specific amounts of charge.)



4A



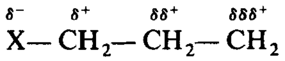
4B

Theoretical calculations suggest that both processes contribute to the overall F_π effect (14).

Secondary field effects on sigma systems, F_σ, such as the CH bonds in the carbon framework G, may also modify the interaction of a substituent with a probe or reaction center.

B. Electronegativity Effects

The origin of these effects is the difference in electronegativity between a substituent X and the carbon atom to which it is attached. The magnitue of the effect should thus follow the group electronegativity of the substituent X. The effect has been thought historically to be transmitted by a progressive, but diminishing, relay of charge through a chain of σ-bonds between atoms as depicted in **6**.



$$\overset{\delta^-}{X}-\overset{\delta^+}{CH_2}-\overset{\delta\delta^+}{CH_2}-\overset{\delta\delta\delta^+}{CH_2}$$

6

The effect is now given the symbol χ (for electronegativity) although it was earlier referred to as a sigma-inductive effect. While the matter cannot yet be regarded as finalized, nearly all current experimental and theoretical evidence indicates that the substituent electronegativity effect acts importantly only at the atom to which the substituent is attached and that any effect beyond the second atom is probably in general negligible. A further point continually brought out in theoretical calculations is that the relay of significant charges in σ-bonds has essentially no effect on the π-electrons of a conjugated framework. That is, the π-electrons are polarized by substituent field but not by substituent electronegativity effects.

Earlier studies on the relative importance of electronegativity (χ) and field (F) effects concentrated on model compounds having different numbers of paths, or atoms between the substituent and the probe, and on effects of reversed substituent dipoles. The results generally suggested that at a distance electronegativity effects are of little significance compared to the corresponding field effects. It has been recently appreciated (8) that the χ and F substituent effects have different scales because of their different origins. Thus, χ substituent effects for common substituents follow the order: metal (M) or MH_x, MMe_x < SR < H, alkyl, COR, CF_3, Cl < CN < NR_2, NO_2 < OR < F. Analysis of results in nonconjugated systems indicate that when the probe is more than one atom removed from the substituent, the observed substituent effects follow the order expected from a dipolar rather than an electronegativity parameter. Indeed it is hard to find properties that are well correlated only by χ effects (8c). The best established examples of this kind are carbon-13 chemical shifts in CH_3X compounds and the J^1_{CC} coupling constant values for vinyl or phenyl (*ipso–ortho*) compounds. We emphasize then that it is not direct electron withdrawal by electronegative atoms through saturated molecular frameworks, but instead it is the dipoles created by electronegativity differences between bonded atoms which cause most observed heteroatom substituent effects.

C. Polarizability Effects

In the two effects above, the substituent can be visualized as affecting the probe. Within the overall occurrence of a substituent-probe interaction, the probe may also cause an effect at the substituent which leads to a change in the energy. Specifically, a substituent may interact with a probe by virtue of its polarizability.

Thus, in particular, a charged probe (either positive or negative) may polarize the substituent leading to charge-induced dipole stabilization. The appropriate electrostaic equation (Equation 8) for a substituent interacting with a point charge q is

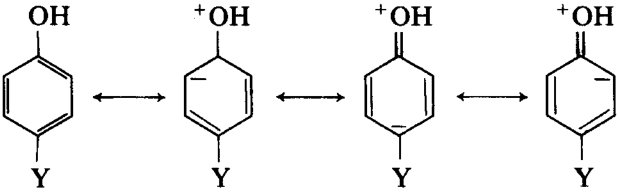
$$E = \frac{-\alpha q^2}{2Dr^4} \tag{8}$$

where α is the polarizability of the substituent and r the distance of the charge to the center of substituent polarizability. The substituent polarizability α is determined by the total number of electrons and by the effective nuclear charges that act on these electrons. For a point dipole rather than a charge center, the stabilizing energy, E, follows $1/r^6$. In either case, the polarizability effect obviously is very small if r and D are relatively large. Substituent polarizability effects are of particular significance for the general reaction, Equation 1, when gas-phase ions and very polarizable alkyl substituents are involved. Further, the polarizability effect, P, may also be more important than previously appreciated for other substituents both in the gas phase and in solutions containing relatively poorly solvated ions, or in solvents of low dielectric constant containing highly dipolar molecules.

D. Resonance (π-Electron Transfer) Effects

A substituent may be either a π-electron acceptor or donor in its partial (or full) π-bonding interaction with the molecular framework, G. Depending upon the nature of G, Y, and Y′, the consequence may be significant contribution to ΔE^0 for Equation 1. The largest substituent resonance (R) effects, of course, involve optimal conjugation between a strong pi-electron donor substituent and a strong pi-electron reaction or probe center in either Y or Y′ (but not both), or the converse of this. Any contribution to ΔE^0 for the general reaction, Equation 1, which is caused by the X substituent donating or accepting π-charge in its interaction with GY or GY′ (compared to none by the reference H substituent) is called a resonance effect.

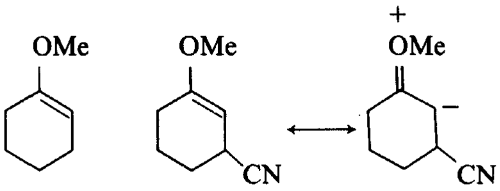
Thus in substituted benzenes, for example, the interaction of substituent orbitals of suitable symmetry with the π-orbitals of the ring can lead to charge transfer either to or from the substituent. In molecules such as substituted phenols, both experiment and theoretical calculation are in agreement that there occurs a charge transfer of the type represented by the canonical forms **7**.



7

Transmission to Y is thus via the resulting changes in electron distribution in the π-system. Secondary effects can also result, for example, from a field effect transmission through space of pi charges localized in the molecular framework by the primary resonance interaction. Formally saturated substituents such as CH_3 and CF_3 groups have orbitals of suitable symmetry to interact by electron donation or acceptance with a π-system and can thus produce changes in ΔE^0_{el}. These effects are called hyperconjugative substituent resonance effects.

Resonance effects can be altered by the field effect of a second group. Thus, the interaction between the methoxy substituent and the pi system in **8** may be increased (15) by the action of a group such as cyano (**9**), which stabilizes the contribution of the canonical form (**9A**).



8 **9** **9A**

However, such field-induced resonance effects, $F_{\pi\pi}$, are not usually of major significance compared to the primary substituent effects (16).

It is also possible for the electrons in orbitals of substituents such as methyl or halogen to repel the electrons in orbitals on the attached π-system without any actual transfer of charge. Such orbital repulsion effects, O_{π}, have been proposed, and some evidence for this effect is available from theoretical calculations. Nevertheless, the explanation of most experimental results in terms of pi-charge transfers seems adequate without the need to invoke the O_{π} effect.

E. Summary

We summarize below the features of each of the four primary kinds of substituent effects and the idealized interactions that cause them.

Field effects F: substituent parameter, σ_F: origin, charge–charge, charge–dipole, or dipole–dipole interactions between substituent, the polarized bonds of framework G, and (in particular) the reaction or probe center Y (Y′); transmission mode, through space or polarizable bonds in G; interaction range, long; transfer of charge from substituent, none; interaction energy, either stabilizing or destabilizing (depending upon sign of charge and dipole orientation).

Resonance effect, R: substituent parameter, σ_R (the value appropriate to pi-electron rich or poor systems); origin, pi-electron bonding and delocalization between substituent and framework, G; transmission mode, through pi bonds of G and Y (Y′); interaction range, long in an extended π-electron system; transfer of charge from substituent, either positive or negative pi charge; interaction energy, pi-electron delocalization energy which only stabilizes molecules.

Polarizability effect, P: substituent parameter, σ_α; origin, charge-induced dipole or dipole-induced dipole interactions between substituent and the reaction or probe center, Y (Y′); transmission mode, through space (effective dielectric constant, D); interaction range, short; transfer of charge from substituent, none; interaction energy, molecular stabilization (only).

Electronegativity effect, χ: substituent parameter, σ_χ; origin, partial ionic character of sigma bond between substituent and its bonded atom of the molecular framework, G; transmission mode, the above and perhaps other σ-bonds of G; interaction range, short (mostly a single atom); transfer of charge from substituent, either positive or negative sigma-electronic charge; interaction energy, either stabilizing or destabilizing. The χ effect is negligible in most observed effects of distant substituents.

IV. ANALYSIS OF OBSERVED SUBSTITUENT EFFECTS

A. General Principles

A useful approximately quantitative treatment of experimental values of ΔE^0, ΔG^0, ΔH^0, and other observed substituent effects is made possible by the assignment of substituent parameter values (σ). These sigma values characterize a given substituent's potential (relative to the hydrogen substituent as zero) to exert each of the four kinds of substituent effects on any series of processes that may be properly represented by the formalism of Equation 1. The signs and magnitudes of each of the individual substituent effects depend not only upon the substituent parameter sign and magnitude, but also on the specific molecular cavity G, the specific change (in orbitals and charge) involved between Y and Y′, and experimental conditions. For example, if the Y → Y′ change is for the carbon-13 nuclear spin states ($\pm 1/2$) of the *para* carbon of a series of monosubstituted benzenes, the nuclear spin "probe" apparently does not alter the ground-state electronic distributions. The nature of the *para*-carbon substituent chemical shifts and their general correlation and prediction by substituent parameters are then relatively simple from the standpoint of the influence of the probe site. On the other hand, the observed substituent effects will depend strongly on the probe if the Y → Y′ change involves a strongly interactive charged functional group being converted to a weakly interactive neutral function, as for example, a proton transfer equilibria such as for a series of *para*-substituted *tert*-cumyl cations forming the corresponding α-methyl styrenes, or benzyl anions forming the corresponding toluenes.

We have noted that field and polarizability effects occur without significant transfer of electrons into or out of the substituent, whereas electronegativity and resonance effects involve this kind of charge transfer. Nevertheless, a general treatment of substituent effects is preserved to the extent that the measured effects can be represented and reproduced with reasonable precision by the sum of $\sigma\rho$ contributions for each kind of substituent effect. Here, the empirically measured ρ values give the susceptibilities of the particular process to the substituent's potential (the σ values) to exert each type of effect. By definition, the ρ values are then dependent upon the nature of G, Y, and Y′, and the conditions (solvent and temperature), but are independent of the substituent σ values.

This empirical treatment of a data series corresponds to Equation 1, taking the form of Equation 9:

$$-\delta_x \Delta E^0 = \sigma_F \rho_F + \sigma_\chi \rho_\chi + \alpha_\alpha \rho_\alpha + \sigma_R \rho_R \qquad (9)$$

Similar expressions may be applied for $-\int_x \Delta G^0_{(T)}$ and $-\int_x \Delta H^0_{(T)}$ where ρ_F, ρ_χ, ρ_α, and ρ_R are the indicated susceptibility (or reaction) constants for the given data set. The sign convention for the ρ_F, ρ_R, and ρ_χ values is the same as that employed originally by Hammett. That is, these values are positive for processes in which Y′ is electron rich compared to Y of Equation 1 and negative for processes of the reverse kind. For ρ_α the sign is taken to be positive for processes in which a cation center Y is changed to a neutral Y′ center or is negative for a neutral Y changing to an anionic center Y′. In order for the energy changes of Equation 9 to involve ρ values of the same signs as for $\log(K/K_0)$ values (which are used in the Hammett treatment), $-\delta_x \Delta E^0$, $-\delta_x \Delta G^0$, or $-\delta_x \Delta H^0$ values must be employed in Equation 9. With this usage, it should be remembered that the ρ values of Equation 9 are $2.303RT$ times greater than those (such as Hammett ρ values) that are based upon $\log(K/K_0)$ values.

Since it is not expected that the four kinds of substituent effects are completely independent of one another, or that all other effects are negligible, Equation 9 represents a simplified idealization that has limitations to be further explored. Indeed, it will be shown that the $\sigma\rho$ relationships for the R and P effects do require further modifications for adequate applications of Equation 9. It will also be shown (as expected) that when certain specific structural considerations are involved in a given data set, one, two, or even three of the ρ_F, ρ_χ, ρ_R, or ρ_α values become essentially zero, so that Equation 9 is applicable in simplified forms.

Table 1 gives values of σ_χ, σ_α, σ_F, and σ_r parameters for many common and important substituents. The sign convention is for positive values given to substituents which, relative to H, are electron withdrawing or which destabilize positive charge. Negative values are given substituents which are electron donating relative to H or which stabilize positive charge. Consequently, the general process of Equation 1 is shifted to the right by each kind of substituent effect for which both σ and ρ values are of the same sign, but it is shifted to the left for each kind of substituent effect for which the σ and ρ values are of opposite sign.

Most of the substituent parameter values of Table 1 came from sources that are completely independent of the gas-phase proton transfer equilibria that are used in this chapter to provide definite evidence for the validity of Equation 9, or simplifications of it. The σ_α and σ_χ values have been derived from ab initio theoretical calculations which are more fully described in Chapter 3 of this volume. The polarizability effect parameters, σ_α, are based upon calculations of substituent polarization potentials of CH_3X compounds which result from polarization of the X substituents by a full positive charge placed at 3 Å from the carbon atom (3). Several of the

TABLE 1
Substituent Parameters[a]

− R (D) Substituent	σ_X	σ_α	σ_F	σ_R	σ_R^-	+ R (A) Substituent	σ_X	σ_α	σ_F	σ_R	σ_R^+
1. $N(CH_3)_2$	.34	−.44	.10	−.64	−.26	H	.00	.00	.00	.00	.00
2. $NH(CH_3)$	.34	(−.30)	.12	−.58	−.27	1. $Si(CH_3)_3$	—	−.72	−.02	.02	.00
3. NH_2	.33	−.16	.14	−.52	−.28	2. CCl_3	(.02)	−.70	.44	.02	.00
4. OC_2H_5	.55	(−.23)	.25	−.45	(−.27)	3. SF_5	—	−.48	.59	.05	.00
5. OCH_3	.55	−.17	.25	−.42	−.27	4. CF_3	.02	−.25	.44	.07	.00
6. OH	.54	−.03	.30	−.38	(−.28)	5. $SOCH_3$	—	(−.65)	.40	.08	.00
7. SCH_3	−.15	−.68	.25	(−.27)	—	6. SCF_3	—	(−.64)	.48	.10	.00
8. SH	−.11	−.55	(.28)	(−.25)	—	7. CN	.30	−.46	.60	.10	(.00)
9. F	.70	.13	.44	−.25		8. SO_2CH_3	—	−.62	.59	.12	.00
10. Cl	.16	−.43	.45	−.17		9. CO_2CH_3	.04	(−.49)	.24	.16	.00
11. t-C_4H_9	−.02	−.75	.00	−.07		10. $COCH_3$	−.04	−.55	.26	.17	(.00)
12. i-C_3H_7	−.02	−.62	.00	−.07		11. NO_2	.46	−.26	.65	.18	.00
13. n-C_3H_7	−.01	−.54	.00	−.07		12. CHO	−.05	−.46	.31	.19	(.00)
14. C_2H_5	−.01	−.49	.00	−.07		13. SO_2CF_3	—	(−.58)	.84	.21	.00
15. CH_3	.00	−.35	.00	−.08		14. NO	.39	(−.25)	.41	.26	.00
16. CH_2F	−.02	−.30	.22	−.06		15. $COCF_3$	(.03)	(−.51)	.50	.26	.00
17. $CH_2{=}CH$	.00	−.50	.06	—	—	16. COCN	—	(.60)	.66	.28	.00
18. $HC{\equiv}CH$	.12	−.60	.23	—	—						

[a] Values in parenthesis have been estimated but appear to give satisfactory results.

values of σ_α in Table 1 are given in parentheses, denoting that the value is estimated from the regular behavior shown by related substituents. The σ_X values are based upon the H atom charge in H—X compounds. The ab initio calculations give the charge transferred through the H—X sigma bond compared to that (zero) for H—H (8c).

The substituent field effect parameters, σ_F, are based upon measured dipolar substituent effects on physical properties in either the gas phase or in hydrocarbon or similar solvents (17). The values for some of the substituents have been previously confirmed to satisfactorily apply to gas-phase proton transfer equilibria of *m*- and *p*-substituted aromatic bases (5c, 18). The method of Taft and Lewis (19) was used to approximately eliminate from $-\delta\,\Delta G^0_{(g)}$ values the substituent resonances and polarizability effects. More stringent experimental tests of the σ_F values are given in the next section of this chapter, and a critical theoretical examination is made in Chapter 3 of this volume.

With respect to obtaining a scale of parameters, substituent resonance effects (R) provide the greatest challenge among the four kinds of substituent effects. Hammett noted the necessity with derivatives of phenols and anilines for a second set of sigma values (σ^-) for *para* pi-electron