# On the Theory of Structure–Reactivity Relationships

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By adding to it a factor to compensate for the neglect of the effects of the Pauli exclusion principle, the usual theory of the relationship between changes in reactivity and small changes in structure in organic systems is simplified in certain respects and is extended in its scope.

It is usual in organic chemistry to express variations in reactivity within a series of closely related reactions, in terms of variations in interactions between groups of atoms within the corresponding series of reacting molecular systems. In many cases variations in reactivity can be expressed quantitatively in terms of a small number of parameters, in what are commonly called 'linear free energy relationships.'[1] However, even the qualitative connection between the parameters of these relationships and specific intergroup interactions is far from clear.[2] In principle, the interactions between groups that are not bonded to one another may be transmitted through space, through intervening groups in the same molecular system, and through molecules of the medium that surrounds the molecular system. There is apparently conflicting evidence on the relative importance of these mechanisms of transmission when the groups are well separated in space. A possible source of this apparent conflict is that a major factor in the indirect transmission mechanism is not considered in the theories used in interpreting the evidence.

Types of intergroup interaction which are attributed to the effects of the Pauli exclusion principle, appear to be of major importance in the interpretation of electronic absorption spectra.[3] Here we consider the importance of such types of interaction in the indirect transmission mechanism of intergroup interactions through intervening hydrocarbons.

*The Method of Treating Intergroup Interactions.*[4]—Intermolecular interactions are formally divided into two classes according to whether or not they depend on the overlap between orbitals that are localised on different molecules (or molecular species). The overlap-independent interactions originate in the net coulombic fields of the atomic nuclei and electrons of each molecule. They give rise to the familiar electrostatic and inductive effects on the energies and the electron distributions of the interacting molecules. The overlap-dependent interactions are more difficult to treat. Overlap between occupied orbitals localised on one molecule and vacant orbitals localised on the other permits delocalisation of electronic charge. Overlap between occupied orbitals localised on one molecule and occupied orbitals localised on the other is subject to the constraints of the Pauli exclusion principle. The first, but not the second, of these factors is allowed for in many simple theories of intermolecular interactions. In the theory used in this study, the first factor is allowed for by taking into account electronic configurations of the interacting molecules in which an electron is transferred from an occupied orbital of one molecule to a vacant orbital of the other. The effects on the energies and the electron distributions of the interacting molecules are called 'charge-transfer' effects. The second factor is allowed for by introducing a hypothetical mutually repulsive field between the interacting molecules. This 'overlap' field differs in character from a coulombic field in that it is felt only at the atoms of the interacting molecules that are immediately adjacent to the region of overlap. The overlap field gives rise to analogues of the electrostatic and inductive effects of a coulombic field on the energies and the electron distributions of the interacting molecules, which we shall call exchange and exchange-polarisation effects. An important consequence of the difference in character between a coulombic field and an overlap field is that the patterns of electron redistribution produced by the inductive and the exchange-polarisation effects are different from one another.

In treating two interacting radicals the classification of interactions described above is modified so that the distinction is made between interactions according to whether or not they depend on overlap of the orbitals which contain zero or two electrons. Hence, the interactions that are independent of such orbital overlap include all those which involve the originally unpaired electrons. Interactions between two groups of atoms within a single molecule are treated in the same way as the interactions between two radicals.

Interactions between three or more groups within a single molecule are not pair-wise additive. For example, in the disubstituted hydrocarbon X–R–Y, the effects on the paired electrons in ·R· of interactions with ·Y are affected by the coulombic and overlap fields of X·, and *vice versa*. Also, the effects of charge-transfer within ·R–Y(·R·X) are affected by the coulombic and overlap

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[1] 'Advances in Linear Free Energy Relationships,' eds. N. B. Chapman and J. Shorter, Plenum Press, London, 1972.

[2] O. Exner, ref. 1, ch. 1.

[3] J. N. Murrell, 'The Theory of the Electronic Spectra of Organic Molecules,' Methuen, London, 1963.

[4] M. Godfrey, *J. Chem. Soc.* (*B*), 1971, 1534.

fields of X·(·Y). Therefore, in a sense, ·R· ' transmits ' interactions between X· and ·Y.

The energy of the interaction between X· and ·Y that is transmitted through ·R· should be related to measures of the coulombic fields and overlap fields for X· and for ·Y as in expression (1), since the inductive and exchange-polarisation effects on electron distribution should be directly proportional to the coulombic and overlap fields that are considered to produce them.

$$\begin{aligned}&\text{energy of interaction} \propto \\ &\quad(\text{coulombic field parameter for } \cdot\text{Y} + \\ &\qquad\text{overlap field parameter for } \cdot\text{Y}) \times \\ &\quad(\text{coulombic field parameter for X}\cdot + \\ &\qquad\text{overlap field parameter for X}\cdot) + \\ &\quad\text{terms involving charge-transfer effects} \qquad (1)\end{aligned}$$

*The Method of Relating Reaction Constants to Changes in Electronic Structure.*—It is assumed that for a small change in the nature of a reacting compound, the change in equilibrium constant or rate constant is determined by the change in the electronic energy of an isolated molecular system.[5] The details of the method are illustrated by the example of the variation with the nature of Y of the reaction constants for reaction (I).

$$\text{Z} + \text{X–R–Y} \rightleftharpoons \text{(ZX)–R–Y} \qquad \text{(I)}$$

For a fixed Y the change in energy in going from one side of the equilibrium to the other is labelled $\Delta E_X$. The effect on $\Delta E_X$ of varying the nature of Y is labelled $\delta\Delta E_{X,Y}$. The effect on the equilibrium constant of varying the nature of Y from Y′ to Y″ is given by expression (2), while the corresponding effect on the rate constant for the forward reaction is given by expression (3) in which $\Delta E_X{}^*$ represents the change in energy in going from the initial state to the transition state of the reaction.

$$\log (K_{Y''}/K_{Y'}) \propto (\Delta E_{X,Y''} - \Delta E_{X,Y'}) \qquad (2)$$

$$\log (k_{Y''}/k_{Y'}) \propto (\Delta E_{X,Y''}{}^* - \Delta E_{X,Y'}{}^*) \qquad (3)$$

The contribution to $\delta\Delta E_{X,Y}$ (or to $\delta\Delta E_{X,Y}{}^*$) that is of particular interest in this study, is the one that is transmitted through ·R·. Using the method of analysis described in the previous section, we obtained expression (4) for $\delta\Delta E_{X,Y}$, in which $\delta F_Y$ is the coulombic field parameter for the change in Y, $\delta S_Y$ is the overlap field parameter for a change in Y, $\Delta F_X$ is the coulombic field parameter for the change in ZX, and $\Delta S_X$ is the overlap field parameter for the change in ZX. We also obtained a corresponding expression [equation (5)] for $\delta\Delta E_{X,Y'}{}^*$.

$$\begin{aligned}\delta\Delta E_{X,Y} &\propto (\delta F_Y + \delta S_Y)(\Delta F_X + \Delta S_X) + \\ &\quad\text{terms involving charge-transfer effects} \qquad (4)\end{aligned}$$

$$\begin{aligned}\delta\Delta E_{X,Y}{}^* &\propto (\delta F_Y + \delta S_Y)(\Delta F_Y + \Delta S_Y) + \\ &\quad\text{terms involving charge-transfer effects} \qquad (5)\end{aligned}$$

*The Contribution to $\delta\Delta E_{X,Y}$ that is transmitted* via *the π-System in Benzene Derivatives.*—In benzene the π-electron population is evenly distributed over the six carbon atoms. The change in π-electron distribution on substituting one of the hydrogen atoms by a group Y has been determined by Hehre *et al.*[6] by means of *ab initio* MO calculations. We have analysed these redistributions in terms of inductive, exchange–polarisation, and charge-transfer contributions. Full details of the analysis are given in the Appendix. Figure 1 shows the unit redistributions for each contribution. The units are defined in the Appendix. Table 1 shows the values in these units, of the π-electron redistribution parameters for a number of common substituent groups.

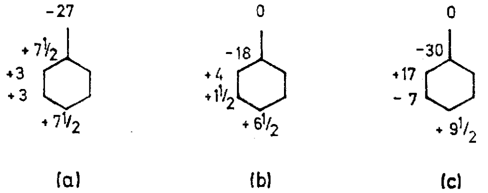

FIGURE 1 The π-electron redistributions for (a) unit charge-transfer, (b) unit coulombic field, and (c) unit overlap field, perturbations to the benzene ring, in units of $10^{-3}$ electrons

TABLE 1

Values of substituent parameters [a]

| Substituent | *F* | *S* | *T* |
|---|---|---|---|
| Me | (0) | (+1.0) | +0.3 |
| $NH_2$(planar) | −3.8 | +5.5 | +4.4 |
| $NH_2$(pyramidal) | −3.0 | +4.3 | +3.5 |
| OH | −4.5 | +4.6 | +3.8 |
| OMe | −4.2 | +4.2 | +3.9 |
| F | −4.3 | +3.2 | +3.0 |
| NC | −3.4 | +0.6 | +0.7 |
| $CH{=}CH_2$ | 0.0 | +0.1 | −0.2 |
| $C{\equiv}CH$ | −1.1 | −0.2 | −0.2 |
| $CF_3$ | −1.5 | −0.5 | −0.4 |
| CN | −2.3 | −0.7 | −0.8 |
| CHO | −0.2 | −0.9 | −1.2 |
| $CO_2H$ | −0.2 | −1.7 | −1.3 |
| $NO_2$(planar) | −2.9 | −1.6 | −1.2 |
| $NO_2$(orthogonal) | −4.5 | (0) | 0.0 |
| NO(planar) | −0.9 | −1.8 | −1.4 |
| NO(orthogonal) | −3.1 | +1.5 | +0.8 |

[a] The units are defined in the Appendix.

With most substituent groups the values of the exchange-polarisation and the charge-transfer parameters parallel one another fairly closely. However, this result is not a general one, and in particular it is not found when the substituent is a net charge-transfer accepting group. With the nitro- and nitroso-groups the value of the inductive parameter appears to depend markedly on the angle of twist about the C–N bond. A possible reason for this result is that there might well be a significant change in the exchange interactions among the original six benzene π-electrons because of their delocalisation over a π-electron-accepting substituent.

The information we obtained from the analysis of the *ab initio* π-electron population distributions enabled us to calculate for a *meta*- and a *para*-X,Y-disubstituted benzene, the nine individual contributions to $\delta\Delta E_{X,Y}$ that arise out of unit changes in the coulombic field,

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[5] M. J. S. Dewar, ' The Molecular Orbital Theory of Organic Chemistry,' McGraw-Hill, New York, 1969.

[6] W. J. Hehre, L. Radom, and J. A. Pople, *J. Amer. Chem. Soc.*, 1972, **94**, 1496.

overlap field, and charge-transfer parameters for changes in both ZX and Y. The results are set out in Table 2.

TABLE 2

Unit contributions to $\delta\Delta E$

| Z effect | *meta*-Y effect | | | *para*-Y effect | | |
|---|---|---|---|---|---|---|
| $F$ | $\delta F$ | $\delta S$ | $\delta T$ | $\delta F$ | $\delta S$ | $\delta T$ |
| $\Delta F$ | $+12\frac{1}{2}$ | $+6$ | $+7\frac{1}{2}$ | $+15\frac{1}{2}$ | $+10$ | $+10$ |
| $\Delta S$ | $+6$ | $-14$ | $+3$ | $+10$ | $+19$ | $+7\frac{1}{2}$ |
| $\Delta T$ | $+7\frac{1}{2}$ | $+3$ | 0 | $+10$ | $+7\frac{1}{2}$ | 0 |
| | $\delta F$ | $\delta S + \delta T$ | | $\delta F$ | $\delta S + \delta T$ | |
| $\Delta F$ | $+12\frac{1}{2}$ | $+13\frac{1}{2}$ | | $+15\frac{1}{2}$ | $+20$ | |
| $\Delta S + \Delta T$ | $+13\frac{1}{2}$ | $-8$ | | $+20$ | $+34$ | |
| | $\delta F/\delta F$ | $(\delta S + \delta T)/\delta F$ | | $\delta F/\delta F$ | $(\delta S + \delta T)/\delta F$ | |
| $\Delta F$ | $(+1)$ | $+1.10$ | | $(+1)$ | $+1.30$ | |
| $\Delta S + \Delta T$ | $(+1)$ | $-0.60$ | | $(+1)$ | $+1.70$ | |

By introducing the approximation that overlap field and charge-transfer parameters have parallel values, we were able to condense the nine individual contributions to $\delta\Delta E_{X,Y}$ to four independent individual contributions. The results for *non-unit* changes in the parameters can be written in the form of equation (6) by labelling the coefficients of $\delta F_Y$ and $\delta S_Y$, $f$ and $s$ respectively. The values of $f$ and $s$ depend on the site of the substituent group in the benzene ring, and on the values of $\Delta F_X$ and of $\Delta S_X + \Delta T_X$. The values of $s/f$ determine the *patterns* of substituent effects.

We have compared the values of $s_{meta}/f_{meta}$, $s_{para}/f_{para}$, and $f_{para}/f_{meta}$ for a hypothetical reaction in which there is no change in $\Delta S_X + \Delta T_X$, with the corresponding values of these quantities obtained by applying equation (6) to real reactions in aqueous solution in which the

$$\log (K_Y/K_H) = f_i F_Y + s_i S_Y \qquad (6)$$

change in the values of the overlap-dependent interactions between the functional group and the benzene ring must be small: the latter reactions are of the type for which log $(K_Y/K_H)$ is proportional to the substituent parameter $\sigma^0$. The results are contained in Table 3 together with data for similar analyses for other real reactions. They indicate that in order to interpret substituent effects on reactions of benzene derivatives that are proportional to $\sigma^0$, it is not *necessary* to consider as important any mechanism for the transmission of interactions between substituent groups and functional groups other than transmission, in the sense we have described, through the $\pi$-system of the benzene ring. Thus, the overall transmission mechanism can be taken to be more simple than it is usually considered to be. Some of the consequences of this conclusions are considered in the next section.

TABLE 3

Values of some reaction parameter ratios

| Reaction | $s_{meta}/f_{meta}$ | $s_{para}/f_{para}$ | $f_{para}/f_{meta}$ |
|---|---|---|---|
| Pure $\Delta F$ | 1.10 | 1.30 | 1.25 |
| $-\sigma^0$ | 0.85 | 1.15 | 1.15 |
| $-\sigma$ | 0.85 | 1.30 | 1.05 |
| $k$ for hydrolysis of $YC_6H_4(C{\equiv}C)_nMR_3$ | 0.85 | 1.30 | 1.05 |
| $K_A$ for anilinium ions in water | 0.85 | 1.30 | 1.05 |
| Aniline in acetic acid | | | |
| $K_i$ | 0.75 | 1.20 | 1.05 |
| $K_d$ | 1.10 | 1.05 | 0.65 |
| $k$ for esterification of benzoic acid | 1.15 | 0.85 | 0.80 |
| Phenol | | | |
| $K_A$ in water | 0.75 | 1.10 | 1.40 |
| $K_A$ in acetone | | 1.25 | |

*Some Consequences of the Interpretation of* $\sigma^0$.—(a) *The range of validity of equation* (6). It follows from the approximations on which it is based that equation (6) should be applicable only to reactions during which the perturbations of the electronic structures of the various groups within the reacting molecular system are small. It should not be applicable, for example, to reactions during which there is transfer of approximately a whole unit of electronic charge between the hydrocarbon group and the reacting group, because then there is no reason why the ratio of charge-transfer effects to overlap field effects should be even approximately independent of the nature of the substituent group. Among the reactions which might well involve the transfer of a substantial amount of electronic charge between the benzene ring and the reacting group, is the one that defines the $\sigma^+$ scale of substituent effects, *viz.*, the hydrolysis of αα-dimethylbenzyl chlorides in 90% aqueous acetone. We have confirmed that the rate constants for this process do not obey equation (6). On the other hand, reactions that are not expected to involve more than a small amount of electron migration from the benzene ring to the reacting group, for example, the equilibrium for complex formation between benzaldehyde and semicarbazide in ethanol at pH 8, *do* obey equation (6).

Equation (6) should also not be applied, in general, to reactions of compounds containing strong charge-transfer accepting groups even when the reactions do not involve appreciable charge-transfer between the benzene ring and the reacting group, because, if substituent groups of this type *do* perturb the electronic structure of the hydrocarbon group in the way that is described above, it is likely that the values of $F_Y$ and $S_Y$ should depend significantly on the electronic structure of the reacting group. (Note that we have not said that the values of $F_Y$ and $S_Y$ should depend on the change during the reaction in the electronic structure of the reacting group.) However, the values of log $(K_Y/K_H)$ for two reactions with similar $\Delta S_X : \Delta F_X$ ratios, should closely parallel one another for all substituent groups in the particular type of case in which the electronic structure of the functional group is very similar in the two reacting systems.

For reactions of series of compounds to which equation (6) is applicable, the values of $s/f$ must determine the pattern of substituent effects. The various patterns available for common substituent groups are displayed in Figure 2.

(b) *The interpretation of variations in the value of* s/f. The value of $s/f$ obtained through application of equation (6) should indicate the extent of the changes during a reaction (or during the rate-determining stage of a reaction) in the overlap-dependent interactions between ZX· and ·RY, relative to the extent of changes in the corresponding overlap-independent interactions. Hence, a knowledge of the value of *s*/*f* ought to be useful in elucidating the mechanism of a reaction. We illustrate this use in the following examples for which the values of *s*/*f* are given in Table **3**.

Reactions of series which follow the original Hammett scale of substituent effects have a slightly higher value of $s_{para}/f_{para}$ than reactions of series which follow the $\sigma^0$ scale, indicating a relatively small change in the overlap-dependent interactions between ZX· and ·RY. This set of reactions includes the base-catalysed hydrolysis of $YC_6H_4[C{\equiv}C]_nMR_3$ (M = Si or Ge) compounds (rate), and the dissociation of anilinium ions in aqueous solution (equilibrium), as well as the defining reaction, *viz.*, the dissociation of benzoic acids in aqueous solution (equilibrium). The fact that these reactions belong to the same set can be readily explained in terms of our theory, but it is difficult to explain in terms of theoretical treatments of substituent effects which involve separation into an effect which depends on the effectiveness of conjugation between the substituent and the reacting group, and an effect which depends only on the distance between these groups.[7]

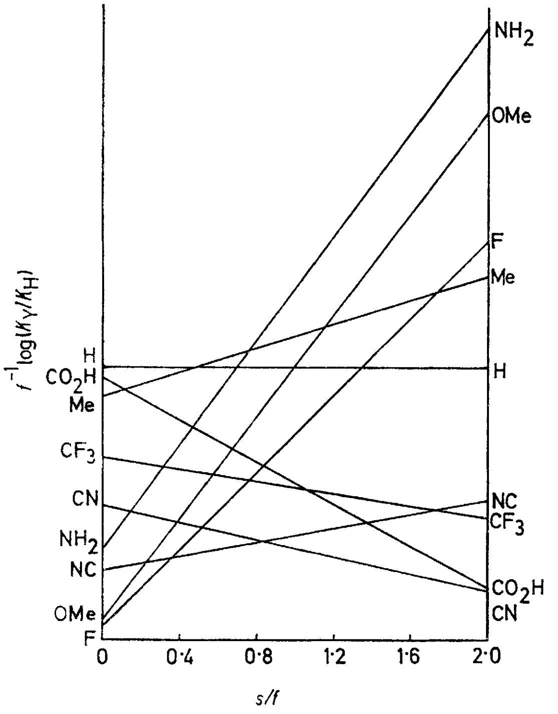

FIGURE 2 The variation with the value of *s*/*f* in the pattern of the effects of some common substituent groups. (The values of *F* have been adjusted where necessary to compensate for differences in value between *T* and *S*)

For anilines (A) in glacial acetic acid (HS), the equilibrium constants for processes (II) and (III) can be evaluated independently.[8] For (II) the value of *s*/*f* indicates that proton transfer causes a reduction in the overlap-dependent interactions between the amino-group and the benzene ring. For (III) the value of *s*/*f* indicates an increase in the overlap-dependent interactions between the amino-group and the benzene ring, which suggests to us that during the separation of an ion-pair one or more of the N–H bonds is loosened by interaction with the solvent. (A similar pattern of *s*/*f* values is observed for the acid-catalysed esterification of benzoic acids.)

$$A{\cdot}HS \rightleftharpoons AH^+{\cdot}S^- \qquad (II)$$

$$AH^+{\cdot}S^- \rightleftharpoons AH^+ + S^- \qquad (III)$$

The deduction that the dissociation of anilinium ions in water does not involve a major change in the overlap-dependent interactions between the amino-group and the benzene ring, can be reconciled with the deductions for the reactions of aniline in glacial acetic acid, only if there is no major change in the degree of N–H covalent bonding during the dissociation. The behaviour of nitroanilines indicates that it is the $NH_2$ group and not the $NH_3^+$ group that is present on both sides of the equilibrium.

Experimentally, the effects on the acidity or basicity of functional groups of replacing an α-hydrogen atom by a phenyl group appear to be very sensitive to the presence or absence of protic solvents. For example, aniline is a much stronger base than ammonia in the gas phase[9] although it is a much weaker base than ammonia in aqueous solution. In the gas-phase reaction a new N–H covalent bond is formed, which means that the overlap-dependent interactions between the amino and the phenyl groups must be reduced. The difference between the relative basicities of aniline and ammonia in the gas and solution phases would be accounted for, if the overlap-dependent interactions between the amino-group and the phenyl group in aniline were net destabilising, which is probable since the preferred conformation of aniline is not the one with maximum overlap between these groups.

The observed pattern of charge-transfer donating substituent effects on the acidity of phenol in hydroxylic solvents, but not in acetone, is very different from the corresponding pattern of substituent effects on the acidity of anilinium ions in hydroxylic solvents. The $s_{meta}/f_{meta}$ value indicates marked changes in the strength of the bond between the phenolate oxygen atom and the bridging hydrogen atom in going from one side of the equilibrium to the other, but the $s_{para}/f_{para}$ value obtained from consideration of the charge-transfer donating groups indicates no significant change in the strength of this bond. In a phenolate ion there is a balance between the destabilising (exchange) and the stabilising (exchange-polarisation and charge-transfer) overlap-dependent interactions. The addition of a proton

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[7] C. Eaborn, R. Eastmond, and D. R. M. Walton, *J. Chem. Soc.* (*B*), 1971, 127.

[8] G. W. Ceska and E. Grunwald, *J. Amer. Chem. Soc.*, 1967, **89**, 1371.

[9] I. Dzidic, *J. Amer. Chem. Soc.*, 1972, **94**, 8333.

should reduce both the destabilising and the stabilising interactions, and consequently, whether or not it is favoured depends on the position of the balance between these interactions. The stabilising interactions in substituted phenolate ions should theoretically be reduced, relative to the destabilising interactions, as the electron-repelling character of the substituent increases. Hence it becomes less likely that there will be a major change in the strength of the phenolic O–H bond in a substituted phenol the greater the electron-repelling character of the substituent. Groups with large electron-repelling character are usually strong charge-transfer donors.

The examples discussed in this section illustrate a way in which the inclusion of the overlap field factor can extend the scope of the theory of the relationship between structure and reactivity.

(c) *The transmission of substituent effects in derivatives of hydrocarbons other than benzene.* It is a common practice at the present time to interpret $\sigma^0$ in terms of linear combinations of two parameters, $\sigma_I$ and $\sigma_R{}^0$. The latter, but not the former, parameter is taken to be a measure of the ability of the $\pi$-system of benzene to transmit substituent effects to the reacting group. The former parameter is taken to be a measure of the ability of substituent effects to be transmitted by one or more of the other possible mechanisms. It is usually evaluated from substituent effects on the dissociation of the carboxy-group in 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids, compounds in which the separation in space of the substituent group and the reacting group is very similar to the corresponding separation in *para*-substituted benzoic acids. The assumption underlying this practice is that the transmission mechanism for the effects measured by $\sigma_I$ is similar in the bicyclo-octane and the benzene derivatives. If we accept the validity of this assumption and generalise it, the theory we have used to interpret $\sigma^0$ will lead us to the conclusion that substituent effects in derivatives of any hydrocarbon are transmitted principally by a mechanism which involves the polarisation of the more loosely bound electrons. There are two pieces of information which suggest that this conclusion might be a valid one. First, an analysis of $\sigma_I$ in terms of $F_Y$ and $S_Y$ (reported below) indicates that overlap-dependent interactions between the substituent group and the hydrocarbon group make an appreciable contribution. Secondly, the value of $f$ for the dissociation of the carboxy-group in 50% aqueous ethanol is not the same for derivatives of all hydrocarbons in which the separation in space of the substituent group and the carboxylic acid group is very similar (see Table 4).

The data listed in Table 4 also show that the value of $s/f$ is not independent of the nature of the transmitting hydrocarbon group. It follows that the pattern of substituent effects on the reactivity of the derivatives of any hydrocarbon should in general vary with the nature of the hydrocarbon and with the mechanism of the reaction.

(d) *A comparison of equation* (6) *with other dual substituent parameter equations.* We have compared equation (6) with an empirical equation, equation (7), proposed by Ehrenson *et al.*,[10] for analysing similar kinds of reaction. Equations (8) relate the parameters in the two equations. The approximate values of the constant $a$ and of the ratio of constants $B/A$ are 0.6 and 0.5 respectively. Ehrenson *et al.* have discussed the origins of variations in the values of $\rho_{R,i}/\rho_{I,i}$, and of deviations from their equation which they claim can be allowed for simply by modifying the $\sigma_R{}^0$ scale in one of three ways. Charton[11] has analysed data on derivatives of hydrocarbons other than benzene in terms of the parameters used by Ehrenson *et al.*

$$\log (K_{i-\mathrm{Y}}/K_{\mathrm{H}}) = \rho_{I,i}\sigma_{I,\mathrm{Y}} + \rho_{R,i}\sigma_{R,\mathrm{Y}}{}^0 \qquad (7)$$

$$\begin{aligned} \sigma_{I,\mathrm{Y}} &= A(F + aS) \\ \sigma_{R,\mathrm{Y}}{}^0 &= BS \\ f_i &= \rho_{I,i}A \\ s_i &= a\rho_{I,i}A + \rho_{R,i}B \\ s_i/f_i &= a + (B/A)(\rho_{R,i}/\rho_{I,i}) \qquad (8) \end{aligned}$$

TABLE 4

Values of the reaction parameters for the dissociation of some 4-substituted 1-carboxylic acids in 50% aqueous ethanol

| Hydrocarbon | $f$ | $s$ | $s/f$ |
|---|---|---|---|
| Bicyclo[2.2.2]oct-2-ene [a] | 0.30 | 0.10 | 0.30 |
| Dibenzobicyclo[2.2.2]octa-2,5-diene [a] | 0.22 | 0.16 | 0.70 |
| Bicyclo[2.2.2]octane [a] | 0.30 | 0.18 | 0.60 |
| Benzene [b] | 0.30 | 0.36 | 1.20 |

[a] F. W. Baker, R. C. Parish, and L. M. Stock, *J. Amer. Chem. Soc.*, 1967, **89**, 5677. [b] H. C. Brown, D. H. McDaniel, and O. Hafliger, 'Determination of Organic Structures by Physical Methods,' eds. E. A. Braude and F. C. Nachod, Academic Press, New York, 1955.

We predict that the treatment of Ehrenson *et al.* should fail to detect or interpret phenomena which rely critically on the dependence of the value of $\sigma_{I,\mathrm{Y}}$ on $S_{\mathrm{Y}}$, or on the dependence of the value of $\rho_I$ on $\Delta S_{\mathrm{X}}$.

(e) *Some predictions on the variation of reactivity with the nature of the reagent.* We have obtained equation (9) for the relative reactivities of a given substrate with two different reagents from the data in Table 2, after labelling the coefficients of the $\Delta F$ and the $\Delta S$ values for the changes in a ZX· group, $\phi$ and $\int$ respectively. For a given pair of reagents in a given medium at a given temperature, equation (9) reduces to the form of the Brønsted equation[1] (10), when the $\Delta S$ values are negligibly small for both reagents. Thus the Hammett

$$\frac{\log (K_{\mathrm{Y}})_2 - \log (K_{\mathrm{H}})_2}{\log (K_{\mathrm{Y}})_1 - \log (K_{\mathrm{H}})_1} = \frac{\phi\Delta F_2 + \int \Delta S_2}{\phi\Delta F_2 + \int \Delta S_1} \qquad (9)$$

$$\begin{aligned} \log (K_{\mathrm{Y}})_2 &= (\Delta F_2/\Delta F_1) \log (K_{\mathrm{Y}})_1 - \\ &\quad (\Delta F_2/\Delta F_1) \log (K_{\mathrm{H}})_1 + \log (K_{\mathrm{H}})_2 \\ &= m \log (K_{\mathrm{Y}})_1 + C \qquad (10) \end{aligned}$$

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[10] S. Ehrenson, R. T. C. Brownlee, and R. W. Taft, *Progr. Phys. Org. Chem.*, 1973, **10**, 1. Except where otherwise stated, all experimental data quoted in this paper are taken from this reference.

[11] M. Charton, *Progr. Phys. Org. Chem.*, 1973, **10**, 81.

and the Brønsted linear free energy relationships can be related to one another in terms of our theory.

The values of log $(K_H)_1$ and log $(K_H)_2$ should depend on interactions between the substituent and the reagent as described by Klopman.[12] When orbital overlap between the reagent and the substrate is unimportant in reactions with negligibly small changes in the overlap between the reacting group and the hydrocarbon group, our theory predicts that the values of $m$ and of $C$ should vary with the natures of: the non-functional substituent, the hydrocarbon, the functional substituent, and the reagent in the following ways. For a family of substrates in which only the nonfunctional substituent varies, $m$ and $C$ should be constants. For a set of such substrates in which only the parent hydrocarbon varies, $m$ should be a constant but the value of $C$ should in general depend on the nature of the hydrocarbon. The values of both $m$ and $C$ should in general depend on the natures of: the functional group, the reagents, and the reaction conditions. The variations in the values of $m$ and $C$ should parallel one another.

The introduction of significant orbital overlap between the reagents and the substrate should of itself affect the value of $C$ but not the value of $m$. However, if the introduction of such orbital overlap is accompanied by the development of marked overlap-dependent interactions between the functional group and the hydrocarbon group of the substrate, significant deviations from equation (10) should occur.

Although there are insufficient experimental data available to make a thorough test of the predictions made in this section, some recent experimental results [13] on the non-Brønsted variation of reactivity with the nature of the reagent are readily interpreted in terms of our theory.

## APPENDIX

*The Analysis of the Effects of a Substituent on the π-Electron Distribution within a Monosubstituted Benzene.*—The π-electron distributions were taken to be those calculated by Hehre *et al.*[6] using an *ab initio* MO method. The substituent effects were analysed into inductive, exchange-polarisation, and charge-transfer contributions by the method outlined below. The resulting patterns for each of the individual redistributions are shown in Figure 1.

The pattern for the charge-transfer contribution was determined by a method described by Murrell [3] with the further assumption that the energy of charge-transfer in a particular direction is independent of which benzene orbital is involved. The pattern for the inductive contribution was taken to be that for the total substituent effect in nitrobenzene in the conformation in which the nitro-group is orthogonal to the phenyl group. The pattern for the exchange-polarisation contribution was obtained from the total substituent effect in toluene after subtracting the charge-transfer contribution.

The implicit assumption of a zero inductive effect for the methyl group (relative to a hydrogen atom) is justified, at least as a good approximation, by the fact that our pattern for the exchange-polarisation effect can be reproduced in a calculation of the polarisation of the π-electrons of benzene due to a field perturbation at a single atom of the benzene ring, without having to use unreasonable values for the excitation energies of benzene. Our pattern for the inductive contribution can be reproduced in a corresponding calculation when the coulombic field has the same value at the carbon atoms of benzene which are *meta* and *para* to the substituent, and when the *additional* value of the coulombic field is two and a quarter times as great at the carbon atom which is adjacent to the substituent, as at the carbon atom which is *ortho* to the substituent.

The *unit* π-electron distribution for each type of contribution (Figure 1) was fixed so that (*a*) the exchange-polarisation parameter for the methyl group would be unity, and (*b*) unit *additional* coulombic field at the carbon atom of benzene which is adjacent to the substituent would be equal to unit overlap field at the same point.

[4/1121 *Received*, 10*th June*, 1974]

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