

## PERTURBATION THEORY OF SUBSTITUENT EFFECT

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Received February 4th, 1974

A quantum chemical analogue of the Hammett equation was derived on the basis of second order perturbation theory to HMO wave functions. The equation was used to interpret several selected reactions. The suitability of quantum chemical reactivity indices and their relation to LFER parameters are discussed.

The Hammett equation proved extraordinarily useful in mechanistic studies, owing to conclusions which can be reached from the sign of the reaction constant  $\rho$ . Also its absolute value is important, since it bears upon the nature of transition state and selectivity of the reagent, as shown *e.g.* for electrophilic substitutions in benzene series<sup>1</sup>. Constants  $\rho$  for reactions of different substrates with a common reagent, *i.e.*  $\rho$  constants as "transmission constants" for various structural skeletons, could, however, be compared only rarely<sup>2</sup>. It is evident that the solution of this difficulty based on determining  $\sigma$  constants for skeletons other than benzene ring<sup>3</sup> is not fruitful way. From this viewpoint Dewar's FM method<sup>4</sup> is valuable contribution, since it enables to calculate  $\sigma$  constants theoretically, presuming the knowledge of geometry and of pertinent quantum chemical data.

An approach suggested in the present work, which is based on perturbation theory, renders it possible to interpret  $\rho$  constants of analogous reactions on different, but structurally similar skeletons, to ascertain some differences in mechanism of these reactions, and finally to discuss, at least to a certain extent, the suitability of quantum chemical reactivity indices.

### THEORETICAL

Let us consider the following model where  $G$  is a general conjugated unit,  $i$  is the site of attachment of a substituent, and  $j$  is the reaction center. According to the theory of absolute reaction rates, the reactivity is determined by the energy difference between the ground and transition state (Eq. (1)). Providing that changes in the ground state

$$\log k = E_z - E_t \quad (1)$$

energy are due solely to substitution ( $\Delta\alpha_i$ ) and in the transition state energy also due to the change of  $\alpha_j$  by polarisation effect of approaching reagent, *i.e.*  $E_z = f(\alpha_i)$  and  $E_t = f(\alpha_i; \alpha_j)$ , then from Taylor expansion it follows:

$$\log k_i = -(q_j \Delta\alpha_j + \frac{1}{2} \pi_{jj} \Delta\alpha_j^2) + (\pi_{ij} \Delta\alpha_j) \Delta\alpha_i, \quad (2)$$

since  $\partial E/\partial\alpha_j = q_j$ ,  $\partial^2 E/\partial\alpha_i \partial\alpha_j = \pi_{ij}$  and  $\partial^2 E/\partial\alpha_j^2 = \pi_{jj}$ .

This equation is formally identical with the Hammett equation, if

$$\log k_0 = -(q_j \Delta\alpha_j + \frac{1}{2} \pi_{jj} \Delta\alpha_j^2), \quad (3)$$

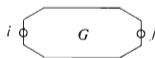
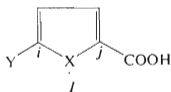
$$\rho = \pi_{ij} \Delta\alpha_j, \quad (4)$$

$$\sigma_i = \Delta\alpha_i. \quad (5)$$

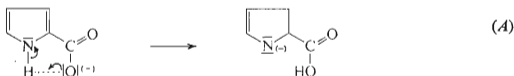
In this approximation substituent effect is modelled only by the change of Coulombic integral  $\alpha_i$ , which is equivalent to the requirement of proportionality of the resonance and  $\pi$  inductive effects. Furthermore, in this approximation substituent effects are additive. Equations of similar type were already reported<sup>5</sup>.

## RESULTS AND DISCUSSION

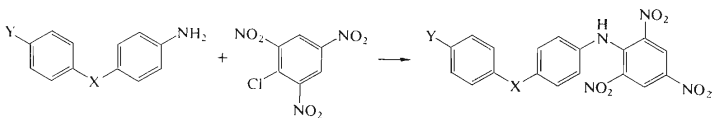
Eq. (4) can be used to interpret dissociation constants of carboxylic acids of general formula I (ref.<sup>6</sup>) (X = O, S, Se, Te, NH, CH=CH; Y = substituent). Let us take



unsubstituted hetero ring as a pertinent model. The effect of dissociation in this model would result in change of Coulombic integral  $\alpha_j$  of the carbon bearing the carboxylic group. As the above compounds constitute structurally very similar set, it is reasonable to expect that  $\Delta\alpha_j$  is constant. Therefore,  $\rho$  constants should correlate with polarisabilities  $\pi_{ij}$ . This correlation is shown in Fig. 1. Table I presents the values of corresponding  $\rho$  constants, along with polarisabilities calculated by HMO method. On using generally accepted value of Coulombic integral of the pyrrole nitrogen,  $\alpha_N = -1.5\beta$ , the point for pyrrole does not lie on the regression line. If  $\alpha_N$  is changed to  $-3.0\beta$ , which corresponds to an increase of electronegativity of the nitrogen, the value of  $\pi_{ij}$  so obtained fits the regression line. This change of  $\alpha$  can be easily substantiated by assuming intramolecular hydrogen bonding (Equation (A)). A similar



change of  $\alpha$  integral of nitrogen atom is needed also in another example of such a reaction<sup>7</sup> (equation (B)). In this case respective unsubstituted amines were taken as a pertinent quantum chemical model, the value of  $\alpha_j$  represents the change of  $\alpha$  integral



(B)

of the amino group in transition state of the reaction. As these compounds constitute again structurally very similar set,  $\alpha_j$  can be considered constant, and then  $\rho$  constants could be expected to correlate with  $\pi_{ij}$ . Despite of nonplanarity of these compounds, the HMO model can be employed, as far as the compounds structurally alike are considered. On the other hand, it is evident that such correlations cannot be extended, for instance, to series of substituted anilines, aminodiphenyls, or aminostilbenes, since steric effects in these compounds would not be similarly important. The corresponding correlation is shown in Fig. 2. Contrary to the previous case, the corrected value of coulombic integral  $\alpha_N$  is here  $-0.8 \beta$ , which corresponds to a decrease of electro-

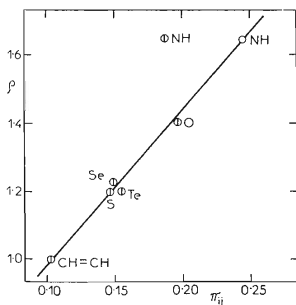


FIG. 1

Dependence of  $\rho$  Constants of Dissociation of Carboxylic Acids  $I$  on  $\pi_{ij}$

$$\rho = (4.67 \pm 0.33) \pi_{ij} + (0.51 \pm 0.05);$$

$$r = 0.990, \textcircled{\circ} \alpha_N = -1.5 \beta \text{ and } \circ \alpha_N = -3.0 \beta.$$

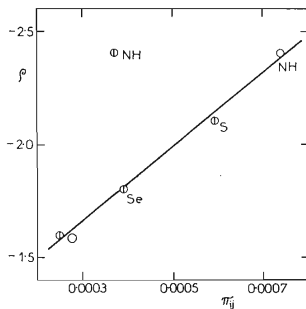


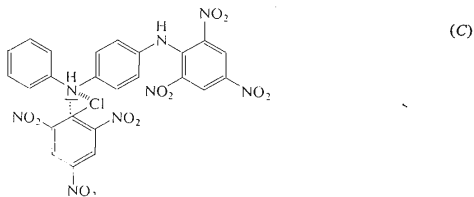
FIG. 2

Dependence of  $\rho$  Constants of the Reaction of Amines with Picryl Chloride (equation (B)) on  $\pi_{ij}$

$$\pi_{ij} \cdot 10^4 = (6.2 \pm 0.3) \rho - (7.2 \pm 0.7);$$

$$r = 0.997, \textcircled{\circ} \alpha_N = -1.5 \beta, \circ \alpha_N = -0.8 \beta.$$

negativity of the bridging nitrogen atom, as visualized by *e.g.* structure C ("solvation by the reagent"). This might explain the so called positive bridging effect<sup>7</sup> which is strongest in the series of nitrogen-containing compounds.



From Eq. (4) conclusions can also be made concerning the nature of transition state of the reactions of structurally similar substrates with different reagents. Thus, for example, comparison of  $\rho$  values for various electrophilic substitutions in benzene series<sup>1</sup> shows that the  $\Delta\alpha_j$  value increases with increasing absolute value of  $\rho$ , which corresponds to the greater breaking of the conjugation of atom  $j$ . This is consistent with the current interpretation according to which the greater absolute value of  $\rho$  means that transition state is rather  $\sigma$  complex. A somewhat more complicated situation arises on comparing  $\rho$  constants of the reactions of structurally different substrates<sup>2</sup>.

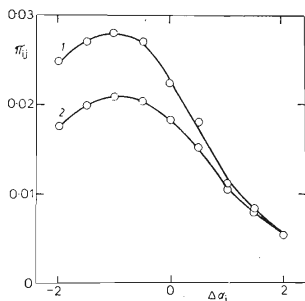


FIG. 3

Model of Substituent Effect. Dependence of  $\pi_{ij}$  on  $\Delta\alpha_i$  for 4-Substituted Diphenylsulfides (1) and 2-Substituted Benzothio-phenes (2)

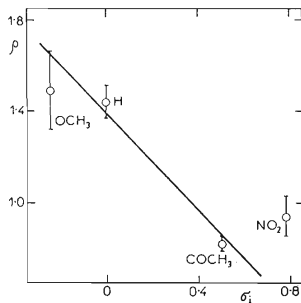


FIG. 4

Dependence of  $\rho$  Constants of Oxidation of Substituted Diphenylsulfides 3, 5-7 (Table II) on  $\sigma_i$

Apart from possible differences in  $\Delta\alpha_j$ , the differing sensitivity of different skeletons to substituent effects is also due to the differences in  $\pi_{ij}$ . The ratio of  $\rho$  constants of reactions of two substrates is given by Eq. (6), where  $k = (\Delta\alpha_j)_1/(\Delta\alpha_j)_2$ . Eq. (6) renders it possible to find relative values of  $\Delta\alpha_j$  and to discuss therefore differences in

$$\frac{\rho_1}{\rho_2} = \frac{(\pi_{ij})_1 (\Delta\alpha_j)_1}{(\pi_{ij})_2 (\Delta\alpha_j)_2} = \frac{(\pi_{ij})_1}{(\pi_{ij})_2} k, \quad (6)$$

the nature of transition states. As an example, this equation was used to interpret  $\rho$  constants of oxidation of aromatic sulphides by perbenzoic acid in dichloromethane<sup>8</sup>. Table II presents the values of  $\rho$  constants and polarisabilities  $\pi_{ij}$  of corresponding compounds. According to Eq. (6)  $\Delta\alpha_j$  values equal to

$$(\Delta\alpha_s)_{\text{TN}} = (1.01 \pm 0.1) (\Delta\alpha_s)_{\text{DBT}} \approx (\Delta\alpha_s)_{\text{DBT}},$$

and

$$(\Delta\alpha_s)_{\text{DPS}} = (1.49 \pm 0.1) (\Delta\alpha_s)_{\text{DBT}} \approx 1.5 (\Delta\alpha_s)_{\text{DBT}},$$

where DBT denotes dibenzothiophene, DPS diphenylsulphide, and TN thianaphthene. The greater  $\Delta\alpha_s$  for diphenylsulphide corresponds to the more extensive breaking of the conjugation of the sulphur atom in a given transition state. The value of  $\Delta\alpha_j$  does not need to be therefore constant for different skeletons and depends, besides on the type of reagent, also on the mode of bonding of the reaction center in a given molecule.

In connection with Eq. (4) it is worthwhile to note that Forsyth<sup>11</sup> reported correlation of  $\rho$  constants of solvolysis of 1-aryl-1-methylalkyl chlorides with  $\Delta q_i$  (the difference of electron densities on atom  $i$  bearing a substituent between  $\text{R}-\text{CH}_3$  and  $\text{R}-\text{CH}_2^+$

TABLE I  
 $\rho$  Constants of Dissociation of Substituted Carboxylic Acids  $I$  and Polarisabilities  $\pi_{ij}$

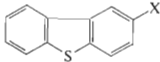
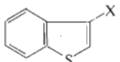
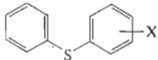
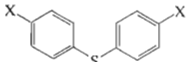
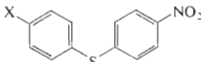
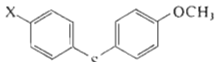
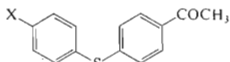
X	$\rho^a$	$\pi_{ij}$	X	$\rho^a$	$\pi_{ij}$
O	1.40	0.1932	$\setminus\text{CH}=\text{CH}/$	1.0	0.1018
S <sup>b</sup>	1.20	0.1436	NH	1.65	0.1727
Se	1.23	0.1466	NH <sup>c</sup>	1.65	0.2383
Te	1.20	0.1579			

<sup>a</sup> Taken from ref. 6. <sup>b</sup>  $p$ -Model used for sulphur. <sup>c</sup> Polarisability  $\pi_{ij}$  calculated with the use of corrected values of integral  $\alpha_N = -3.0\beta$ .

(R = aryl) which were taken as a model of the initial and transition states of the reaction). However, an explanation of this correlation has not been suggested. Based on Eq. (4), this correlation is to be expected, since  $(\pi_{ij} \Delta\alpha_j) = \Delta q_i$ . As  $\Delta q_i$  is calculated as a difference between R—CH<sub>3</sub> and R—CH<sub>2</sub><sup>+</sup>, the authors<sup>11</sup> assume that transition state is in all cases fully developed carbonium ion. If  $\rho$  constants are analysed by means of Eq. (6), the values of relative changes of  $\Delta\alpha_j$ , presented in Table III, indicate that transition states of these reactions are different. However,

TABLE II

Reaction Constants  $\rho$  of Oxidation of Aromatic Sulphides to Sulphoxides by Perbenzoic Acid in Dichloromethane and Corresponding Polarisabilities  $\pi_{ij}$

No	Compound	$\rho^a$	$\pi_{ij}$	$r^b$	$s^c$	$n^d$
1		$-0.78 \pm 0.03$	0.0185	0.997	0.03	5
2		$-2.52 \pm 0.24^e$	0.0591	0.977	0.31	7
3		$-1.44 \pm 0.07$	0.0232	0.991	0.06	8
4		$-2.50 \pm 0.30$	0.0232	0.985	0.19	5
5		$-0.94 \pm 0.09^f$	—	0.989	0.11	4
6		$-1.49 \pm 0.17^f$	—	0.993	0.09	3
7		$-0.82 \pm 0.03^f$	—	0.999	0.02	3

<sup>a</sup> Taken from ref.<sup>8</sup>. <sup>b</sup> Correlation coefficient. <sup>c</sup> Standard deviation. <sup>d</sup> Number of derivatives measured. <sup>e</sup> Calculated from reported data. <sup>f</sup> Taken from ref.<sup>10</sup>.

TABLE III  
Reaction Constants  $\rho$  of Solvolysis of 1-Aryl-1-methylalkyl Chlorides and Corresponding Quantum Chemical Quantities

No	Compound	$q^a$	$\pi_{ij}$	$k$	$q_j^b$	$\delta q_j^c$	$\pi_{jj}$	$\Delta q_i^d$
1		-5.82	0.0013	1.0	0.0035	-0.0043	-0.0043	0.141
2		-6.05	0.0012	1.12	0.0029	-0.0040	-0.0036	0.145
3		-7.42	0.0046	0.36	0.0062	-0.0038	-0.0106	0.301
4		-7.06	0.0041	0.38	0.0063	-0.0040	-0.0106	0.259
5		-6.68	0.0030	0.49	0.0049	-0.0038	-0.0078	0.249
6		-3.94	0.0011	0.80	0.0051	-0.0066	-0.0083	0.084
7		-4.41	0.0012	0.82	0.0054	-0.0073	-0.0090	0.091

<sup>a</sup> Taken from ref.<sup>11</sup>. <sup>b</sup> Electron density on atom  $j$  in  $R-CH_3$  ( $R = \text{aryl}$ ). <sup>c</sup>  $\delta q_j = \pi_{jj} \Delta \alpha_j \approx \pi_{jj} \cdot k$ . <sup>d</sup>  $\Delta q_i = q_i(R-CH_3) - q_i(\Delta rCH_2^{\ddagger})$  (HMO quantities).

the values of  $\delta q_j$  ( $\pi_{jj} \Delta\alpha_j \sim \pi_{jj} k$ ) differ much less from one another, which shows that charge changes on atom  $j$  on going from the ground to transition state are nearly the same in all cases. This fact could provide explanation of the successful  $\log k$  vs  $\Delta q_i$  correlation obtained. The absolute magnitude of the charge on atom  $j$  in transition state has not to be however identical ( $q_j^{\ddagger} = q_j + \delta q_j$ ). Non-constant  $\Delta\alpha_j$  may explain the grouping of experimental reactivities of aromatic hydrocarbons according to positions<sup>12</sup>, frequently observed in their correlations with HMO data.

In the cases where  $\Delta\alpha_j$  can be expected to be constant a  $\rho - \pi_{ij}$  correlation should exist. This situation arises, e.g. in oxidation of substituted diphenylsulphides 3, 5, 6, and 7 (Table II). These compounds have similar structure and differ only by substituents in the 4' position. Fig. 3 shows dependence of polarisability  $\pi_{ij}$  on  $\Delta\alpha_i$  for 4-substituted diphenyl sulphides and 2-substituted dibenzothiophenes. Despite of the lack of the knowledge of the actual values of  $\Delta\alpha_i$  corresponding to substituents  $\text{CH}_3\text{O}$ ,  $\text{COCH}_3$ , and  $\text{NO}_2$ , and despite of the fact that, as already shown<sup>8</sup>, the approximation of substituent effect only by change of  $\alpha_i$  is not sufficient for the nitro group, it undoubtedly holds that

$$(\Delta\alpha_i)_{\text{CH}_3\text{O}} > 0; (\Delta\alpha_i)_{\text{COCH}_3} < 0; (\Delta\alpha_i)_{\text{NO}_2} < 0$$

and

$$|\Delta\alpha_i|_{\text{NO}_2} > |\Delta\alpha_i|_{\text{COCH}_3}.$$

It is evident that pertinent  $\alpha$  constants follow the trend in  $\pi_{ij}$  values. As the function  $\pi_{ij} = f(\alpha_i)$  in the vicinity of the point  $\Delta\alpha_i = 0$  can be considered linear over a broad region,  $\rho$  constants may be expected to correlate with  $\sigma_1$ . Deviations from this dependence should occur only with strong acceptors. This correlation is shown in Fig. 4.

TABLE IV

Values of Empirical Parameters Used in HMO Calculations<sup>a</sup>

X	$h_X$	$k_{CX}$	X	$h_X$	$k_{CX}$
O	-2.0	-0.8	NH <sup>c</sup>	-3.0	-0.8
S <sup>b</sup>	-1.0	-0.8	NH <sup>d</sup>	-0.8	-0.8
Se	-0.8	-0.7	<del>N</del>	-0.5	-1.0
Te	-0.7	-0.6	CH <sub>3</sub>	+0.5	-0.1
NH	-1.5	-0.8			

<sup>a</sup> Parameters from ref.<sup>14</sup>. <sup>b</sup>  $p$ -Model used for sulphur. <sup>c</sup> Corrected values of  $\alpha_N$  for correlation of dissociation constants of carboxylic acids. <sup>d</sup> Corrected value of  $\alpha_N$  for the reaction of amines (equation (B)).



From comparison of the  $\pi_{ij} = f(\Delta\alpha_i)$  dependences for substituted dibenzothiophenes and diphenylsulphides it becomes further clear that dibenzothiophene skeleton is less sensitive to changes caused by further substitution than diphenylsulphide skeleton.

Eq. (3) cannot be used, however, for correlating reactivities of unsubstituted compounds, since only relative, and not absolute, values of  $\Delta\alpha_j$  are known. Equations formally identical with Eq. (3) have however been reported<sup>13</sup>  $\log k = \varphi\phi + \pi\phi^2$  where  $\varphi$  is the measure of polarity of substrate and  $\pi$  is the measure of its polarisability. Eq. (3) shows also the limitation of using the electron density as a reactivity index. Only the product  $q_j \Delta\alpha_j$  as an energetic quantity can be used as a reactivity index providing that first approximation of perturbation theory is sufficient. The quantity  $q_j$  can be taken as a reactivity index only when  $\Delta\alpha_j$  is constant. Parameters adopted for HMO calculations are presented in Table IV.

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Translated by J. Hetflejš.