

ON THE THEORY OF THE EFFECTS OF ORTHO SUBSTITUENTS ON THE SIDE-CHAIN  
REACTIVITY OF BENZENE DERIVATIVES

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We report some new linear free energy relationships involving ortho-substituted benzene derivatives, which we have obtained through application of the recently proposed<sup>1,2</sup> field and charge-transfer (FCT) treatment of substituent effects on side-chain reactivity.

Theory In a disubstituted benzene each of the substituents can interact directly with the benzene ring and with the other substituent. By FCT theory, the interactions are of two main types, namely,  $\pi$ -inductive and charge-transfer. The  $\pi$ -inductive interactions are the sum of electrostatic-field and exchange interactions. We define the disubstituted benzene to be free of steric effects when the interactions between any two of the molecular fragments can be expressed in terms of a set of parameters whose values are independent of the nature of the third fragment.

Suppose that one of the substituents is a complex of a functional group and a reactant species (hereafter called a functional complex and labelled Z). During a reaction within the functional complex, the values of the parameters which describe the interactions between Z and each of the other fragments will, in general, change. In the expression for the energy of interaction between fragments, the only terms which contribute to the effects of the non-functional substituent (hereafter labelled Y) on the reactivity constants, are those that simultaneously depend on the natures of both Y and Z. There are three sets of terms of that type in the expression for the interaction between the substituents and the benzene ring. We shall label them A, B and C. A represents the  $\pi$ -inductive effects of Y on the change in the charge-transfer interaction energy between Z and the benzene ring. B represents the change in the  $\pi$ -inductive effects of Z on the charge-transfer interaction energy between Y and the benzene ring. C represents the change in the non-additive part of the combined  $\pi$ -inductive interactions of Y and Z with the benzene ring.

Equation (1) gives the effect of Y, at position i relative to Z,<sup>3</sup> on an equilibrium constant, K.

$$RT\ln(K_{Y,i}/K_H) = A_i + B_i + C_i \quad (1)$$

At the transition state of a reaction only a fraction of the total change in any of the electronic effects will have occurred. The fraction,  $\gamma_1$ , of the change in the charge-transfer effect of Z is allowed to be different from the fraction,  $\gamma_2$ , of the change in the  $\pi$ -inductive effect of Z. Equation (2) gives the effect of Y on a rate constant, k.

$$RT\ln(k_{Y,i}/k_H) = \gamma_1 A_i + \gamma_2 (B_i + C_i) \quad (2)$$

For convenience we shall use equation (3) to represent either equation (1) or equation (2).

$$\log(K'_{Y,i}/K'_H) = A'_i + B'_i + C'_i \quad (3)$$

The  $\pi$ -inductive contributions to the energy of interaction between a substituent and the benzene ring can be expressed as a linear combination of only two parameters,  $\alpha_E$  and  $\alpha_S$ , whose values are characteristic of the substituent.<sup>1</sup> Hence, we can write equation (3) in the form:

$$\log(K'_{Y,i}/K'_H) = \lambda_A \alpha_{E,Y} + (\delta_{A,i} + \delta_{C,i}) \alpha_{S,Y} + B'_i.$$

The energies of the direct interactions between Y and Z must depend simultaneously on the natures of both substituents and, therefore, they must also contribute to  $\log(K'_{Y,i}/K'_H)$ . It does not seem likely that steric effects, as defined above, will be negligible when there is significant overlap between Y and Z. However, in many compounds, including some ortho ones, overlap will probably not be significant. Electrostatic interactions fall off with distance less rapidly than do overlap-dependent interactions. The interaction between the dipole in the C-Y bond and the charge distribution within Z does not necessarily affect the magnitudes of the substituent-hydrocarbon interactions, even in ortho compounds. We shall label this interaction, D. The energy of the D interaction can be taken to be proportional to  $\alpha_E$ , since the value of that parameter is determined by the magnitude of the dipole in the C-Y bond. Consequently, equation (3) can be modified to take into account the D effect by adding  $\lambda_{D,i} \alpha_E$  to the right-hand side. The effects on  $\log K'$  of all other direct interactions are taken to be steric. We shall label these effects, S'. The total effect of Y on  $\log K'$  is given by equation (4).

$$\log(K'_{Y,i}/K'_H) = (\lambda_A + \lambda_{D,i}) \alpha_{E,Y} + (\delta_{A,i} + \delta_{C,i}) \alpha_{S,Y} + B'_i + S'_i \quad (4)$$

The ratios  $\delta_{A,i}/\lambda_A$  have known values  $\epsilon_{A,i}$  which are independent of the nature of the reaction. The values of  $(\alpha_E + \epsilon_{A,i} \alpha_S)$  for many meta and para substituents are very nearly proportional to the Taft<sup>4</sup> substituent parameters  $\sigma^0$ . It is useful, therefore to define

theoretical  $\sigma_i^0$  scales by  $\kappa(\alpha_E + \epsilon_{A,i} \alpha_S)$ , where  $\kappa$  is the constant of proportionality. Then,  $\lambda_A/\kappa$  is a reaction constant which we shall label  $\rho_A^0$ . Equation (4) may be conveniently rewritten as:

$$\log(K'_{Y,i}/K'_H) = \rho_A^0 \sigma_i^0 + B'_i + \delta_{C,i} \alpha_{S,Y} + \lambda_{D,i} \alpha_{E,Y} + S'_i.$$

In the absence of steric effects the change in the charge-transfer power of Z during a reaction affects only the  $\rho\sigma$  terms, and the corresponding change in the  $\pi$ -inductive power of Z affects only the non- $\rho\sigma$  terms. The importance of the A, B and C electronic effects on the reactivity of meta and para compounds has been discussed in previous publications.<sup>1,2</sup>

Application to Ortho Compounds In the general case none of the four electronic contributions to  $\log(K'_{Y,o}/K'_H)$  can reasonably be neglected. However, only two of these effects contribute to  $\log(K'_{Y,o}/K'_{Y,m})$ . This is because, by theory,  $\rho_A^0 \sigma^0$  has the same value for an ortho compound and its meta isomer, and so does  $B'$ . Calculations show that  $\delta_{C,o}$  is very much bigger than  $\delta_{C,m}$ , and  $\lambda_{D,o}$  should, in general, have a very different value from  $\lambda_{D,m}$ . Therefore, the C and D electronic effects should not be negligible and in the absence of steric effects the following relationship should hold:

$$\log(K'_{Y,o}/K'_{Y,m}) = (\delta_{C,o} - \delta_{C,m}) \alpha_{S,Y} + (\lambda_{D,o} - \lambda_{D,m}) \alpha_{E,Y}.$$

We have found that such a relationship does indeed exist among the values<sup>5</sup> of  $\log(K_o/K_m)$  for the dissociations in water of phenols containing fluorine, chlorine, methyl, and methoxyl as substituents (the difference between the calculated and the observed value is less than 0.05 units in each case when  $(\delta_{C,o} - \delta_{C,m})$  is  $-0.11/\text{kiloKayser}$  and  $(\lambda_{D,o} - \lambda_{D,m})$  is  $-0.54/\text{kK}$ ). Our relationship does not correlate so well the data on  $\log(K_o/K_m)$  for the dissociations of the corresponding anilinium ions and benzoic acids. With each of the two smaller substituents, fluorine and methoxyl,  $\log(K_o/K_m)$  has almost the same value for the anilinium ion as for the phenol, but this is not so with either of the larger substituents. The data on fluoro- and methoxy-benzoic acids are in accord with the expected reduction in the  $\pi$ -inductive interactions of OH and  $O^-$  with the benzene ring in going from a phenol to a benzoic acid ( $(\delta_{C,o} - \delta_{C,m})$  is  $-0.08/\text{kK}$  and  $(\lambda_{D,o} - \lambda_{D,m})$  is  $-0.48/\text{kK}$ ).

None of the position-dependent parameters is theoretically required to have the same value for an ortho compound and its para isomer. Consequently we do not expect a simple relationship involving  $\log(K'_{Y,o}/K'_{Y,p})$  to exist.

A Comparison with Other Treatments of the Effects of Ortho Substituents. (a) Taft<sup>6</sup> divides the effects of ortho substituents into a sum of steric effects and two kinds of

electronic effect. The combination of the steric effects and one of the kinds of electronic effect is assumed to have the same magnitude,  $\delta E_S^0$ , in corresponding acid and base catalysed hydrolyses of esters and related compounds. In the FCT treatment there is no term which can reasonably be assumed to be insensitive to such a change in reaction mechanism.

The parameter  $E_S^0$  is directly proportional to  $(\alpha_{S,Y} - \alpha_{S,Me})$  when Y is fluorine, chlorine, or methoxyl. The constant of proportionality is  $0.11/kK$ , the same magnitude as  $(\delta_{C,o} - \delta_{C,m})$  for the dissociation of a phenol. We conclude that for the considered substituents,  $E_S^0$  is a measure mainly of the C electronic effect in the defining reaction. The Taft-Ingold equation,<sup>6</sup>  $\log(K'_{Y,o}/K'_{Me,o}) = \rho^* \sigma_o^* + \delta E_S^0$ , should appear to hold only when steric effects and B electronic effects are small both in the reaction under investigation and in the reactions that are used to define  $\sigma_o^*$  and  $E_S^0$ .

(b) Charton<sup>7</sup> has found that for many reactions  $\log(K'_{Y,o}/K'_H)$  can be quite well expressed in terms of a linear combination of the substituent constants  $\sigma_I$  and  $\sigma_R$ . Each of these substituent constants can be satisfactorily expressed as a linear combination of  $\alpha_S$  and  $\alpha_E$ .<sup>1</sup> Therefore, equation (4) may be written in the form:

$$\log(K'_{Y,o}/K'_H) = \lambda_o \sigma_I + \delta_o \sigma_R + B'_o + S'_o.$$

Obviously, the FCT treatment may be regarded as an extension of Charton's treatment.

#### REFERENCES AND FOOTNOTE

1. M. Godfrey, J. Chem. Soc. B, 1971, 1534, 1540.
2. M. Godfrey, Tetrahedron Letters, 1972, 753.
3. i becomes o in ortho compounds, m in meta compounds, and p in para compounds.
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7. M. Charton, Progress in Physical Organic Chemistry, 1970, 8, 235.