A Quantitative Study of Substituent Interactions in Aromatic Electrophilic Substitution. I. Bromination of Polysubstituted Benzenes

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Abstract: The slopes, ρ^+, of reactivity–structure correlation, log $k/k_0 = \rho^+\Sigma\sigma^+$, established for bromination in water of polymethylbenzenes ($\rho^+ = -10.7$), para-substituted anisoles ($\rho^+ = -5.6$), ortho-substituted anisoles ($\rho^+ = -6.5$), and para-substituted *N*,*N*-dimethylanilines ($\rho^+ = -2.2$), reveal a pseudoadditivity of substituent effects different from the strict additivity which should lead for the whole series of compounds to one single value of ρ^+ equal to that of monosubstituted compounds' bromination ($\rho^+ = -11.6$). Those multiple values cannot be used to discuss the transition state characteristics, although the HMO treatment constitutes a proof that the reaction mechanism is the same for all the subpopulations. To define the characteristics of the polysubstituted compound's transition state, we propose that the slope p of the equation log $k/k_0 = p\Sigma\sigma^+ + q\Sigma\sigma_X{}^+\sigma_Y{}^+$ should be considered as analogous to the ρ^+ parameter of monosubstituted compounds, and measures the charge developed in the transition state; q is related to the ability of substituents to delocalize the charge in the transition state. The application of this relation to the bromination reactivities of the 44 above mentioned compounds gives the equation log $k/k_0 = -11.3\Sigma\sigma^+ - 6.3\Sigma\sigma_X{}^+\sigma_Y{}^+$.

Nonadditivity of substituent effects is often observed when polysubstituted substrates having very electron-releasing or electron-attracting groups such as $N(Me)_2$, OMe, NO_2, etc., are used. This phenomenon has been observed for the solvolysis of polysubstituted benzhydryl chlorides,[1] electrophilic bromination of 1,1-diphenylethylenes,[2] infrared shifts of ketones,[3] acetamides,[4] and carbonyl groups, and nmr shifts of substituted olefins.[5] However, analysis of the various factors responsible for this nonadditivty has been complicated by the structure of the substrates used, for instance, when multiple aromatic nuclei each bear one or several substituents.[1-4] Actually, in such systems, it is very difficult to separate the interactions between substituents from other specific effects, such as noncoplanarity of the nuclei, steric inhibition factors, or exaltation of conjugation, and to isolate a parameter characterizing the charge distribution in the transition state. Therefore, in order to study quantitatively the nonadditivity of substituent effects and the charge in the transition state, it is important to choose simple polysubstituted substrates in which none of these previous effects interfere.

Accordingly, we have chosen a series of polysubstituted benzenes including alkyl or substituents containing heteroatoms and the bromination reaction which is known to be one of the most sensitive to substituent effects.[6a]

Results and Discussion

The SE2 process for the aromatic bromination, in aqueous solution, has a rate expression given by the equation

$$-\mathrm{d}[\mathrm{Br_2}]_\mathrm{a}/\mathrm{d}t = k_\mathrm{g}[\mathrm{Br_2}]_\mathrm{a}[\mathrm{ArH}]$$

in which $[Br_2]_a$ is the analytical bromine concentration ($[Br_2] + [Br_3{}^-]$). With an excess of bromide ions and using the steady-state treatment, the overall rate constant k_g is

$$k_\mathrm{g} = \frac{k_{\mathrm{Br_2}} + k_{\mathrm{Br_3}^-}K[\mathrm{Br}^-]}{1 + K[\mathrm{Br}^-]} \tag{1}$$

where K is the formation constant of $Br_3{}^-$ ion and k_{Br_2} and $k_{Br_3{}^-}$ are the elementary rate constants for Br_2 and $Br_3{}^-$ attack. We have shown in a previous paper[7] that the use of overall constants k_g in reactivity–structure linear free-energy relationships of the Hammett or Brown type is valid. In fact, the reaction constant $\rho_g{}^+$ established from the linear relation between log k_g and σ^+ is practically identical with the constant $\rho_{Br_2}{}^+$ established from the corresponding correlation in log k_{Br_2}.[8] This identity is valid if the ratio $k_{Br_2}/k_{Br_3{}^-}$ is between 1.6 and ∞ for the reaction in aqueous solution.[7] This condition is fulfilled for all substituted benzenes presently studied.[9-11]

The values of bromination rate constants for a single reaction center, *i.e.*, for polymethylbenzenes, methoxybenzenes, phenol, and substituted *N*,*N*-dimethylanilines, are listed in Table I. These rate constants extend over a wide reactivity range of 10^{15}. For the whole series, the correlation between reactivities and the sums of

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(1) S. Nishida, *J. Org. Chem.*, 32, 2697 (1967).

(2) E. D. Bergmann, J. E. Dubois, and A. F. Hegarty, *Chem. Commun.*, 1616 (1968).

(3) M. Liler, *ibid.*, 244 (1965).

(4) O. Exner, *Collect. Czech. Chem. Commun.*, 25, 1044 (1960).

(5) J. Niwa, *Bull. Chem. Soc. Jap.*, 40, 1512 (1967).

(6) (a) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, 1, 50 (1963); (b) *ibid.*, 1, 137 (1963); (c) *ibid.*, 1, 48 (1963).

(7) P. Alcais, R. Uzan, J. J. Aaron, F. Rothenberg, and J. E. Dubois, *Bull. Soc. Chim. Fr.*, 612 (1971).

(8) Actually the logarithmic form of eq 1 is

$$\log k_\mathrm{g} = \underset{\mathrm{I}}{\log k_{\mathrm{Br_2}}} + \underset{\mathrm{II}}{\log\left(1 + \frac{k_{\mathrm{Br_3}^-}K[\mathrm{Br}^-]}{k_{\mathrm{Br_2}}}\right)} + \underset{\mathrm{III}}{\log(1 + K[\mathrm{Br}^-])} \tag{2}$$

If the temperature and the solvent are kept constant, the term III is independent of the reaction studied. When the ratio $k_{Br_2}/k_{Br_3{}^-}$ is higher to certain values[7] (in water, 1.5), the variations in II are lower than 0.5 log unit and log k_g can be used in reactivity–structure correlations instead of log k_{Br_2}.

(9) F. Rothenberg, P. Alcais, and J. E. Dubois *Bull. Soc. Chim. Fr.*, 592 (1971).

(10) J. J. Aaron and J. E. Dubois, *ibid.*, 603 (1971).

(11) J. E. Dubois, R. Uzan, and P. Alcais, *ibid.*, 617 (1968).

Table I. Bromination Rate Constants of Benzene and Mono- and Polysubstituted Benzenes

No.	Nuclear substituents	Reactional center position	k, l. mol^{-1} sec^{-1}	log k	$\Sigma\sigma^+$	$L_\beta{}^+$	Ref
1	H	1	2.7×10^{-6}	−5.569	0	2.536	9
2	1-Me	2	1.8×10^{-3}	−2.745	−0.276	2.477	9
3	1-Me	3	4.7×10^{-5}	−4.328	−0.070	2.521	9
4	1-Me	4	1.1×10^{-2}	−1.959	−0.311	2.458	9
5	1,3-Me$_2$	4	8.0	0.903	−0.587	2.405	9
6	1,4-Me$_2$	2	3.4×10^{-2}	−1.469	−0.346	2.462	9
7	1,2,3-Me$_3$	4	1.52×10^{2}	2.182	−0.657	2.392	9
8	1,3,5-Me$_3$	2	9.0×10^{3}	3.954	−0.863	2.341	9
9	1,2,3,4-Me$_4$	5	4.6×10^{2}	2.663	−0.727	2.375	9
10	1,2,3,5-Me$_4$	4	2.75×10^{4}	4.439	−0.933	2.340	9
11	1,3,5-Me$_3$-2-Et[a]	4	1.94×10^{4}	4.288	−0.915		*a*
12	1,3,5-Me$_3$-2-Cl[a]	4	2.8	0.447	−0.453		*a*
13	1,3,5-Me$_3$-2-Br[a]	4	3.4	0.531	−0.464		*a*
14	1,2,3,4,5-Me$_5$	6	9.0×10^{4}	4.954	−1.003	2.330	9
15	1-MeO	4	9.54×10^{3}	3.980	−0.778	2.352	10
16	1-MeO	2	1.70×10^{2}	2.300	−0.678	2.389	10
17	1-MeO-2-Me[a]	4	4.84×10^{4}	4.685	−0.844	2.340	*a*
18	1-MeO-2-Me[a]	6	6.85×10^{2}	2.837	−0.748	2.376	*a*
19	1-MeO-3-Me[a]	4	5.70×10^{5}	5.757	−1.054	2.308	*a*
20	1-MeO-4-Me[a]	2	8.35×10^{2}	2.922	−0.748	2.372	*a*
21	1-MeO-2-F[a]	4	3.85×10^{1}	1.586	−0.426		*a*
22	1-MeO-3-F[a]	4	1.43×10^{3}	3.157	−0.491		*a*
23	1-MeO-3-F	6	6.28×10^{2}	2.799	−0.751		10
24	1-MeO-4-F	2	0.67	−0.173	−0.326		10
25	1-MeO-2-Cl[a]	4	2.5×10^{1}	1.399	−0.379		*a*
26	1-MeO-3-Cl	4	5.82×10^{2}	2.766	−0.515		10
27	1-MeO-3-Cl	6	3.71×10^{1}	1.570	−0.564		10
28	1-MeO-4-Cl[a]	2	0.36	−0.447	−0.279		*a*
29	1-MeO-2-Br[a]	4	4.3×10^{1}	1.635	−0.373		*a*
30	1-MeO-3-Br	6	1.45×10^{1}	1.162	−0.528		10
31	1-MeO-4-Br[a]	2	0.39	−0.404	−0.273		*a*
32	1-MeO-3-I	6	1.34×10^{1}	1.129	−0.543		10
33	1,4-MeO$_2$	2	2.06×10^{2}	2.315	−0.631	2.386	10
34	1-MeO-2,3-Me$_2$	4	1.02×10^{6}	6.010	−1.124	2.293	10
35	1-MeO-2,4-Me$_2$	6	6.54×10^{2}	2.816	−0.818	2.359	10
36	1-MeO-2,5-Me$_2$	4	1.55×10^{6}	6.190	−1.124	2.290	10
37	1-MeO-3,4-Me$_2$	6	1.49×10^{5}	5.174	−1.059	2.305	10
38	1-MeO-3,5-Me$_2$	4	1.30×10^{7}	7.140	−1.330	2.262	10
39	1-MeO-3,5-Me$_2$	6	7.12×10^{5}	5.854	−1.265	2.278	10
40	1-OH	4	4.05×10^{4}	4.608	−0.920		
41	1-N(Me)$_2$	4	2.17×10^{8}	8.336	−1.200	2.266	15
42	1-N(Me)$_2$-3-Me	4	9.83×10^{8}	8.992	−1.476	2.226	15
43	1-N(Me)$_2$-3-Br	4	5.91×10^{7}	7.772	−0.942		15
44	1-N(Me)$_2$-3,5-Me$_2$	4	3.40×10^{9}	9.531	−1.752	2.229	15

[a] Unpublished results.

Table II. Partial Reactivity-Structure Correlations for Monosubstituted Benzenes (log $k = f(\sigma^+)$) and Polysubstituted Benzenes (Log $k = f(\Sigma\sigma^+)$)

No.	Compounds	Reactional center[a]	$\rho^{+\,b}$	sd[c]	Corr coeff
1	Monosubstituted benzenes	Ortho, meta, para	−11.61	0.60	0.996
2	Benzene and mono- and polymethylbenzenes	Ortho, meta, para	−10.7	0.25	0.998
3	Anisoles	Ortho	−6.54	0.30	0.990
4		Para	−5.6	0.28	0.990
5	*N*,*N*-Dimethylanilines	Para	−2.2	0.10	0.998

[a] Position with respect to the GPA. [b] Reaction constant calculated by admitting an additivity of substituent effects on the reactivity. [c] Standard deviation of reaction constant.

Brown σ^+ is not linear, but characterized by quasi-linear segments having different slopes for each one of the subpopulations comprising polymethylbenzenes, anisoles, and *N*,*N*-dimethylanilines (Figure 1). Thus, partial linear correlations can be calculated for each one of the subpopulations and for each reaction center in an ortho or para position to the group of principal activation (GPA),[12] methoxy or dimethylamino. The ρ^+ values for these partial correlations (Table II, no. **2**–**5**) vary from −2.2 for *N*,*N*-dimethylanilines to −10.7 for polymethylbenzenes.

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(12) The GPA is the substituent having the more negative algebraic value for the σ^+ constant.

As we have shown in our previous studies dealing with the bromide ion effect[10,11] and the isotopic effect[10,13] the majority of substituted benzenes react by an SE2 mechanism in which the rate-determining step is the formation of the intermediate σ complex.[14] The differences of ρ^+ cannot then be attributed to a variation of the determining step for the different subpopulations.

In a first approach, we have noted ρ^+ variations for the three subpopulations to a different attenuation of the substituent effects by the methoxy GPA and the dimethylamino GPA.[9,10,15] Furthermore, similar ρ^+ variations have been observed for monosubstituted and tri- and tetramethyl-substituted compounds (-12.1 and -8.9, respectively) and attributed by Baciocchi and Illuminati[16] to steric effects. However, such an explanation is still open to question.[6b]

In order to study more precisely the origin of the attenuation of substituent effects by the GPA, we shall try to distinguish whether the ρ^+ variations are caused by electronic substituent–GPA interactions in the transition state or by a variation of the charge distribution in the transition state for each subpopulation or by a combination of these two effects. Preliminary information on the transition state charge is obtained by an examination of the correlations between reactivities and molecular orbital parameters.

HMO Treatment. In this study, we have used the localization energies L^+ (differences between the π electronic system energy in the ground state and in the Wheland σ complex are used as a model for the transition state[17,18]). The nuclear substituents are characterized by parameters previously used with success to give an interpretation of nmr spectra of arylalkenes[19] and to discuss physicochemical properties of anisoles and *N*,*N*-dimethylanilines.[20,21] A satisfactory linear correlation is obtained for the whole series of polymethylbenzene reactivities, where $r = 0.997$, 0.08 psi.

$$\log k = -49.9L^+ + 121 \qquad (3)$$

On the other hand, the reactivities of compounds having a GPA (OMe or NMe_2) are on two shifted straight lines. The straight line corresponding to the reactivities in an ortho position to the GPA agrees roughly with that of the polymethylbenzenes which, by the way, involve also reactivities measured ortho to a methyl group. This result indicates that the standard values of parameters used are not sufficient to give a precise analysis of substituent effects when the reaction center is in a para position to the GPA. Our basic aim being to distinguish eventual interactions between the substituents and the GPA, we tried to verify how parameters determined to explain the reactivities of monosubstituted compounds can be used in the case of polysubstituted derivatives, the calculation being performed with one single transition state model, the Wheland complex.

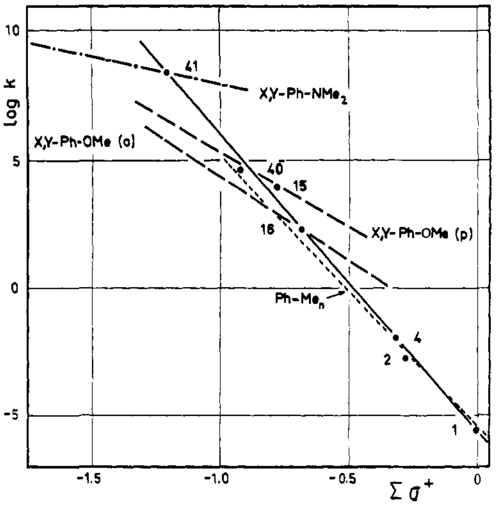

Figure 1. Correlation of reactivity and structure for the bromination of three subpopulations of substituted benzenes: polymethylbenzenes (Ph–Me$_n$), anisoles (with reactional centers ortho and para to the GPA), and *N*,*N*-dimethylanilines. The compounds indexed are taken from Table I. The solid line is representative of the monosubstituted compounds.

The parameters for substituent groups have been determined using the straight line (practically identical with that of the polymethylbenzenes) defined by compounds **1**, **2**, and **16**, for which the attack is ortho to the GPA. Corresponding points representing attack in the para and meta positions for compounds **3**, **4**, **15**, and **41** (Table I) have been adjusted to fall on this line[22] and the parameters have been used to calculate L^+ for polysubstituted derivatives.

The log k/L^+ correlation for monosubstituted compounds can be extended to the whole population of

$$\log k = -46.8L^+ + 117 \qquad (4)$$

polysubstituted structures, $r = 0.993$, 0.12 psi.

The correlation (Figure 2) looks very much like the one obtained with the first approach for reactivities ortho to the GPA, but the linearity of the diagram is much improved. These results agree with the conclusions obtained in a preceding study dealing with a limited number of structures.[18] The quality of the correlation obtained here can be favorably compared with the result obtained by crude quantic approaches for condensed rings hydrocarbon reactivity.[17,23–25]

It seems then that the postulated transition state model (Wheland complex) represents with a good approximation the substituent effects on the transition state obtained in the bromination. The existence of

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(13) J. E. Dubois and R. Uzan, *Bull. Soc. Chim. Fr.*, 3534 (1968).

(14) The other substituted benzenes for which the destruction of the intermediate σ complex is a totally or partially rate-determining step are not included in Table I.

(15) R. Uzan and J. E. Dubois, *Bull. Soc. Chim. Fr.*, 598 (1971).

(16) E. Baciocchi and G. Illuminati, *Progr. Phys. Org. Chem.*, **5**, 47 (1967).

(17) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemistry," Wiley, New York, N. Y., 1961.

(18) J. E. Dubois and J. P. Doucet, *Tetrahedron Lett.*, 3413 (1967).

(19) J. P. Doucet, *J. Chim. Phys.*, **65**, 1194 (1968).

(20) A. Zweig, W. G. Hodgson, and W. H. Jura, *J. Amer. Chem. Soc.*, **86**, 4124 (1964).

(21) A. Zweig, J. E. Lancaster, M. T. Neglia, and W. H. Jura, *ibid.*, **86**, 4130 (1964).

(22) Among the many possible types of correction that could be used we have arbitrarily chosen to perturb the exchange integral between the substituent and the aromatic carbon in the Wheland complex. This seems to be an empirical way to reach the differences of the interactions existing between the reaction center and the substituents, respectively, in ortho, meta, or para positions. The selected values (very near to those used in the first approach) are, respectively, for the Coulomb integral: Me = 2, OMe = 2, NMe_2 = 1; for the exchange integral in the σ complex: Me = 0.5 in ortho, 0.55 in meta, para, OMe = 0.8 in ortho, 0.87 in meta, para, NMe_2 = 0.83 in para.

(23) S. F. Mason, *J. Chem. Soc.*, 4329 (1958).

(24) M. J. S. Dewar and C. C. Thompson, Jr., *J. Amer. Chem. Soc.*, **87**, 4414 (1965).

(25) L. Altschuler and E. Berliner, *ibid.*, **88**, 5837 (1966).

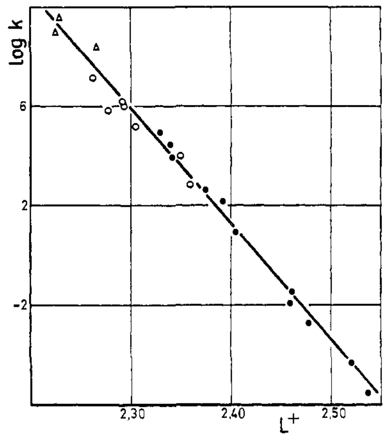


Figure 2. Correlation of reactivity and L^+ for the bromination of polysubstituted benzenes; resemblance degree between the σ complex and the transition state: ●, polymethylbenzenes; ○, anisoles; △, *N*,*N*-dimethylanilines.

log k/L^+ correlation indicates that all the terms which are not evaluated in our elementary quantic approach remain constant—or that their monotonous variations are hidden by those of L^+.[26]

It is therefore concluded that the transition state charge is roughly constant and its structure looks very much like that of a σ complex for all the studied polysubstituted benzenes. The ρ^+ variations observed for the subpopulations cannot then be attributed to notable variations of the transition state structures.

Quantitative Factorization Interaction Treatment. The linear regression between reactivity and structure for the bromination of monosubstituted benzenes is

$$\log k = -11.6\sigma^+ - 5.64 \quad (5)$$

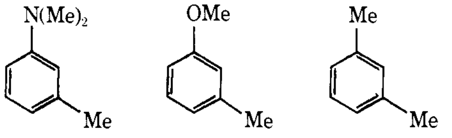
If there was strict additivity of substituent effects in aromatic bromination, the reactivities of polysubstituted benzenes ($\log k_{add}$) should fit a regression line of the same slope and origin (eq 6). Actually, as we

$$\log k_{add} = -11.6\Sigma\sigma^+ - 5.64 \quad (6)$$

mentioned above, the experimental reactivities do not fit a single regression line (Figure 1). The differences between experimental reactivities and those calculated using eq 6 give a measure of the deviation from strict additivity.

$$\Delta \log k = \log k_{exp} - \log k_{add} = \log k_{exp} + 11.6\Sigma\sigma^+ + 5.64 \quad (7)$$

The deviation from additivity, observed in Figure 1, is more important when the GPA is strongly electron releasing; for instance, position 4 of 3-methyl-*N*,*N*-dimethylaniline is roughly 400 times less reactive than what is expected assuming a strict additivity of multiple substituent effects; the same position in 3-methylanisole is 80 times less reactive than expected. Those differences are roughly parallel to the variations of the product σ values: $(\sigma_{NMe_2}{}^{+p})(\sigma_{Me}{}^{+o}) = 0.311$ and $(\sigma_{OMe}{}^{+p})\cdot(\sigma_{Me}{}^{+o}) = 0.215$. The dimethylamino and methoxy groups disturb in different ways the effect of a second or a third substituent on the reactivity. For the polymethylbenzenes, the methyl group electron-releasing effect being less important, the effect of the other methyl group will be less attenuated than for dimethylanilines and anisoles. Therefore, the para position of 3-methyltoluene is only 1.5 times less reactive than the predicted value; in this case, the σ product is $(\sigma_{Me}{}^{+p})(\sigma_{Me}{}^{+o}) = 0.086$.



k_{exp}/k_{add} 1/400 1/80 1/1.5

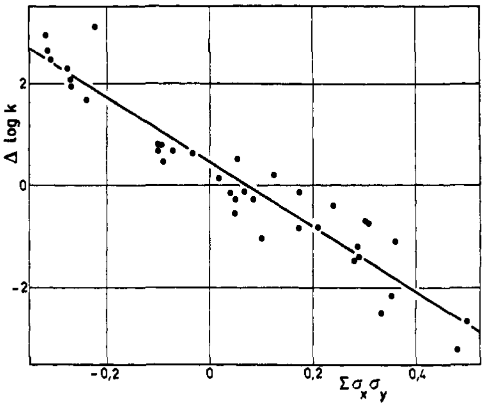


Figure 3. Bromination of polysubstituted benzenes; correlation between the deviation of the additivity effects on the reactivity and the product of substituent constants.

Among the different equation types linking such deviations to the effects of nuclear substituents, it has been found that a linear regression exists (Figure 3) between the deviations and the sums, for each compound, of products of individual substituent constant σ^+, taken two by two ($\Sigma\sigma_X{}^+\sigma_Y{}^+$) (eq 8) for 44 compounds,

$$\Delta \log k = -6.3\,\Sigma\sigma_X{}^+\sigma_Y{}^+ \quad (8)$$

$r = 0.988, 0.15$ psi.

Mathematically, the order of the factorized term must be n (n is the substituent number of the highest polysubstituted compound); practically, the introduction of the third-order term ($\sigma_X{}^+\sigma_Y{}^+\sigma_Z{}^+$) does not improve the quality of eq 8.

The above treatment attributes then the reactivity of polysubstituted benzenes to a sum of two terms which are the effects of substituents on the reactional center and the interactions between substituents. In

$$\log k_{exp}/k_0 = p\Sigma\sigma^+ + q\Sigma\sigma_X{}^+\sigma_Y{}^+ = -11.3\,\Sigma\sigma^+ - 6.3\,\Sigma\sigma_X{}^+\sigma_Y{}^+ \quad (9)$$

this equation, the parameter p[29] which is related to the

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[26] The correlation slope gives a β value near that obtained spectroscopically, 60 kcal/mol.[17] Although this value depends largely on the calculation techniques and on the adopted parameters, it is very near to that used by Ehrenson[27] for the evaluation of the basicity of polymethylbenzenes. On the other hand, the β values are generally less important for the condensed ring hydrocarbons. Thus, Berliner[28] finds 30 kcal/mol for bromination of such compounds. This difference cannot be attributed to the transition state being more or less near to the model arenonium ion, since in both cases the substituent effects are practically identical with respect to bromination rate constants and protonation equilibrium constants.

[27] S. Ehrenson, *J. Amer. Chem. Soc.*, **84**, 2681 (1962).

[28] L. Altschuler and E. Berliner, *ibid.*, **88**, 5837 (1966).

[29] The symbol p has been chosen in order to avoid a confusion between the polysubstituted compound reaction constants and the different reaction constants $\rho, \rho^+, \ldots$, rigorously characteristic of monosubstituted compounds.

substituent effects on the reactional center should be, like the ρ^+ parameter, a measure of the transition state charge. If an analogous equation has been used to correlate the benzolyation rates of anilines[30] and the basicity constants of substituted triphenylmethanol[31] the results are still inconclusive because of the lack of experimental data.

Significance of the *p* and *q* Parameters. By the HMO treatment, we have shown that for all the compounds the transition state charge is very near to that of a σ complex. This result is in contradiction with the fact that, for polysubstituted compounds, we observe very important ρ^+ variations (Table II). As a matter of fact, the p value calculated from eq 9, using the reactivities of polysubstituted benzenes ($p = -11.3$), is very near to the ρ^+ value obtained in the case of monosubstituted compounds ($\rho^+ = -11.6$). It can thus be assumed that the p parameter is a good measure of the transition state charge even comparable to the ρ^+ value of monosubstituted compounds. Moreover, this parameter can be considered as fundamental for all the comparisons of the sensitivities of reactions involving monosubstituted and polysubstituted compounds, comparisons for which many ambiguities have been observed.

The rough comparison between the reaction constant ρ^+ of the chlorination of monosubstituted benzenes and that of bromination of polysubstituted anisoles or *N*,*N*-dimethylanilines would indicate that the chlorine is less electrophilic than the bromine and that the bromine selectivity is lower than that of chlorine (Table III), which is contrary to the sequences commonly accepted.[6c] The comparison of the constant $\rho^+ = -10$ for chlorination of monosubstituted compounds and $p = -11.3$ for the bromination of polysubstituted compounds reestablishes the normal electrophilicity and selectivity sequences for bromine and chlorine. From similar considerations, it can be shown that $\rho^+ = -6.2$ for bromination of monosubstituted compounds by Br^+, and $\rho^+ = -2.2$, for bromination of polysubstituted *N*,*N*-dimethylanilines by molecular bromine, leads to the conclusion that Br_2 is more electrophilic than Br^+, which is contrary to all expectations.[6c] This contradiction is also removed when the p parameter is used.

Table III. Electrophilic Substitution Reactions of Polymethylbenzene. Comparison of Different Reaction Constants

Reaction	$\rho^{+\,a}$	Corr coeff	p^b	Corr coeff	$\rho^{+\,c}$
Bromination (Br_2)	−9.82	0.987	−10.5	0.989	−12.4
Chlorination (Cl_2)	−8.88	0.997	−10.3	0.998	−10
Deuteration	−8.25	0.999	−8.81	0.999	
Benzoylation	−5.86	0.970	−8.55	0.985	
Sulfonation	−4.19	0.950	−7.2	0.996	
Mercuration	−3.04	0.988	−3.49	0.990	−4.0

[a] ρ^+ calculated by admitting an additivity of substituent effects. [b] Calculated from eq 9. [c] Classical reaction constant for monosubstituted compounds.

The PMB approach for Baciocchi and Illuminati[16] applied to several electrophilic substitution reactions of polymethylbenzenes (Table III) has led them to attribute to steric effects the differences of ρ^+ constants found for mono- and polysubstituted compounds. We have applied eq 9 to these reactions and the p values found by this calculation are very much greater than the ρ^+ values and they approximate those of monosubstituted compounds. The results of Table III show that steric effects proposed by Baciocchi and Illuminati are not significant in aromatic substitution, but that electronic interactions between substituents seem to be important. Thus, the electron-donating effect of a methyl group, although relatively weak when compared to those of methoxy or dimethylamino groups, would be sufficient to delocalize the positive charge of activated complex and to attenuate the electronic effects of other methyl groups, which would explain the relative ρ^+ variation for polymethylbenzenes.

We shall now examine the significance of the interaction constant q.

The greatest number of reactivity–structure correlations established in the literature deal with monosubstituted compounds. For this reason, only a few values of interaction constants q are available and furthermore are subject to debate. Furthermore, we will discuss only the q value obtained in this present case.

The comparison of the reactivities of the disubstituted compound, the monosubstituted compound, and benzene (log k_X, log k_{X0}, and log k_{00}, respectively) gives

$$\log (k_{XY}/k_{00}) = \log \frac{k_{XY}k_{X0}}{k_{X0}k_{00}} = \rho_X^+\sigma_Y^+ + \rho_0^+\sigma_X^+ \qquad (10)$$

One can also write eq 9 as $\log (k_{XY}/k_{00}) = \rho_0^+(\sigma_X^+ + \sigma_Y^+) + q\sigma_X^+\sigma_Y^+$. The interaction constant q can be written

$$q = \frac{\rho_X^+ - \rho_0^+}{\sigma_X^+} \qquad (11)$$

Following eq 11, a linear relation can be drawn between the value of $\rho_X^+ - \rho_0^+$ and that of σ_X^+ of the GPA ($X = Me, OMe, NMe_2$). When the ρ_X^+ values are calculated for the disubstituted compounds belonging to the three subpopulations above defined, it is found that: for *N*,*N*-dimethylanilines, $\rho_X^+ = -2.28$, $r = 0.999$, 0.10 psi; anisoles (ortho position to OMe), $\rho_X^+ = -7.04$, $r = 0.996$, 0.12 psi; anisoles (para position to OMe), $\rho_X^+ = -6.14$, $r = 0.973$, 0.95 psi; xylenes, $\rho_X^+ = -10.7$, $r = 0.994$, 0.13 psi.

The slope of the correlation $\rho_X^+ = f(\sigma_X^+)$ which is a measure of q is -7.0 ($r = 0.990$, 0.4 psi). It can be seen that this q value is very near to that found by applying eq 9 to all the polysubstituted compounds including tri-, tetra-, and pentasubstituted ones. Such an observation is valid only when the compounds have a single GPA very electron active in comparison with the other substituents or when all the substituents are only weakly electron releasing. Moreover, this observation involves a total independence of q from a substituent effect.

By analogy with the physical interpretation of the reaction constant ρ^+ slope of linear free energy relationship the parameter q characterizes the sensitivity of the reaction to substituent interactions. This interaction constant q is then a function of the electronic

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structure of the reference substrate (for the compounds studied here, benzene), of the reagent, and so on. In order to estimate the relations between the interaction constant q and the reaction parameters such as the electrophilicity of the reactant, the charge of the transition state, etc., a large set of electrophilic substitution reactions should be used. For this reason, research is in progress to obtain new values for the electrophilic substitution reactions of polysubstituted compounds.

Rearrangement of the Benzene Molecular Ion on Electron-Impact Ionization

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Abstract: The scrambling processes which take place after electron-impact ionization of benzene have been studied using the isotopically labeled compound benzene-*1,2-*$^{13}C_2$*-3,4,5,6-*d_4. The abundances of the various isotopic neutral fragments of C_2H_2 and $C_3H_3\cdot$ which are lost from this molecular ion were measured. The experimental results were then compared to sets of several theoretical results derived from calculations which assumed the occurrence of various scrambling processes. This comparison, when taken with experimental data derived from processes occurring in the ionization chamber, showed predominantly that total randomization of carbons and hydrogens had occurred, although a moderate contribution of the process involving only hydrogen scrambling could not be ruled out. However, when metastable ions were studied, ions with much longer lifetimes were involved; the results in this case showed that total randomization had occurred.

Electron bombardment ionization of an organic molecule in a mass spectrometer may lead to an exchange or scrambling of atoms within an ion. Recent work with isotopically substituted[1,2] and unsubstituted[3] benzene, benzylic ions,[4,5] thiophenes,[6] and other aromatic and heteroaromatic compounds[7] shows that there is major scrambling of the carbon skeleton and of the hydrogens in the molecular ion of these compounds. Benzene is of particular interest in this regard because it is a symmetrical aromatic molecule and thus the scrambling process may be observed unhindered by the complicating effects of various groups substituted on the ring. In the mass spectrum of benzene, the molecular ion loses $H\cdot$, H_2, C_2H_2, $C_3H_3\cdot$, and $CH_3\cdot$, to yield, respectively, $C_6H_5^+$, $C_6H_4\cdot^+$, $C_4H_4\cdot^+$, $C_3H_3^+$, and $C_5H_3^+$. When these losses were studied in various deuterated benzenes, the data suggested that the hydrogens had become randomized as to position on the ring.[8,9] Of course, this phenomenon was not totally unexpected, since, in the loss of $CH_3\cdot$, a major rearrangement of the molecule must take place. Also, interconversion and rearomatization of Dewar benzenes, prismanes, and benzvalenes are known to occur thermally and photochemically, giving rise to scrambling of the carbon skeleton.

These considerations lead to the question: to just what extent do the individual atoms rearrange within this simple molecule? If the carbon atoms randomize to a large extent, do they carry their original hydrogen atoms along or are these hydrogens themselves also scrambling? Thus, for the molecular ion of benzene, one or more of the following mechanisms may operate: case 1, no randomization; case 2, randomization of carbon atoms only (each carbon carries along its original hydrogen); case 3, randomization of hydrogen only (carbon skeleton stable); case 4, total atomic randomization. It is possible to deduce the relative importance of these cases by the study of the isotopic composition of the neutral fragment lost from a particular isotopically substituted benzene molecular ion. The loss of fragments such as C_2H_2 and $C_3H_3\cdot$ does not necessitate *a priori* a rearrangement, as in the case of loss of $CH_3\cdot$, so that no studies on loss of the former fragments are possible without isotopic labeling. Such a study was done by measuring first the abundance of the various isotopic species in the mass spectrum for loss of "C_2H_2" and "$C_3H_3\cdot$" using high-resolution mass spectrometry. (The symbolism used throughout this paper is that quotation marks mean the inclusion of all isotopic species.) This gives a measure of the extent of the possible scrambling processes occurring within the ionization chamber.

The decompositions of metastable molecular ions of labeled benzene resulting in loss of "C_2H_2" and "$C_3H_3\cdot$" were also studied. Metastable ions decompose in a time of the order of 10^{-5} sec after ionization, while the stable ions normally seen in a mass spectrum arise

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