Electronic Perturbations of the Aromatic Nucleus: Hammett Constants and Electrostatic Potential Topography†

Shridhar R. Gadre* and C. H. Suresh

Department of Chemistry, University of Pune, Pune 411 007, India

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A substituent attached to a benzene nucleus is capable of perturbing the electronic distribution within that nucleus. Substituent constants, first introduced by Hammett,[1] give a measure of these electronic perturbations. The most widely used substituent constants are σ_m and σ_p which are obtained from the dissociation constant data of the *meta*- and *para*-substituted benzoic acids, respectively. The success of the Hammett parameters for the study and interpretation of thousands of organic reactions and mechanisms[2] underlines the consistency of a substituent to perturb the electronic environment of the benzene nucleus in different chemical systems. An organic chemist explains these perturbations classically in terms of inductive and resonance effects. These electronic perturbations were well-studied by correlating them with computed quantities such as total energy, atomic charges, electrostatic potentials, etc., derived from either *ab-initio* quantum chemical or semiempirical methods.[3] Very recently, Haeberlein and Brinck[4] have analyzed the substituent effects in *para*-substituted phenoxide ions and found a close, linear relation between the minima of the electrostatic potential, V_{min}, observed near the phenoxide oxygen and the gas phase acidities. However, they have not considered the electronic perturbations occurring *over the aromatic ring* due to a substituent. In the present work, we propose a method for directly assessing the effect of a substituent on the aromatic π-electron distribution based on the molecular electrostatic potential (MESP) topography of monosubstituted benzenes.

MESP is a well-established tool for exploring molecular reactivities, intermolecular interactions, and a variety of other chemical phenomena.[5] It has been extensively used by Politzer *et al.* for understanding the general electrophilic substitution reactions, in particular for substituted benzenes and many other chemical applications.[6−10] Average local ionization energy has also been employed[11] for this purpose. Recently, Gadre *et al.* have proposed that a detailed investigation of the topography of the MESP is capable of revealing subtle changes observed in the spatial electronic distribution due to changes in the molecular framework by locating and characterizing the critical points (CPs) of the MESP.[12−13] The MESP, $V(\mathbf{r})$, at a point $\mathbf{r}$ due to a molecular system with nuclear charges $\{Z_A\}$ located at $\{\mathbf{R}_A\}$ and electron density $\rho(\mathbf{r})$ is given by

$$V(\mathbf{r}) = \sum_A^N Z_A/|\mathbf{r} - \mathbf{R}_A| - \int \rho(\mathbf{r}')\mathrm{d}^3\mathbf{r}'/|\mathbf{r} - \mathbf{r}'|$$

Here N is the total number of nuclei in the molecule. The delicate balance between the two opposing terms in the above equation brings out the electron-rich regions or electron-deficient regions surrounding a molecule in terms of the corresponding MESP critical points (minima and saddle points).[12−15]

In this work, we report the results of a study of 13 typical neutral monosubstituted benzenes. These substituents cover a wide range of Hammett parameters and include halogens (F, Cl), electron-donating groups with unshared pair of electrons ($NHCH_3$, NHOH, NH_2, OH, OCH_3), alkyl groups (CH_3, CH_2CH_3), and electron-withdrawing groups (NO_2, CN, CHO, COOH). The molecular geometries were optimized at HF/6-31G** level using Gaussian 94 package,[16] and the minima were confirmed by the frequency calculations. The MESP topography of all these systems was obtained by employing the package INDPROP.[17]

The distribution of the MESP critical points over the benzene ring in four substituted bezenes (one each from the four classes of substituent described here) and benzene projected on to the carbon framework is shown in Figure 1. Out of all these CPs, we have considered the CPs which could be (3, +3) or (3, +1) in nature, labeled as "p" (close to the *para*-carbon) and "m" (close to the *meta*-carbon) for the correlation of σ_p and σ_m substituent constants,[18] respectively. In all the other systems, similar CPs are located and characterized.

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(1) Johnson, C. D. *The Hammett Equation*; Cambridge University Press: New York, 1973.

(2) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; John Wiley: New York, 1963. Chapman, N. B.; Shorter, J. *Correlation Analysis in Chemistry*; Plenum: New York, 1978.

(3) Bohm, S.; Kuthan, J. *Int. J. Quantum Chem.* **1984**, *26*, 21. Kim, K. H.; Martin, Y. C. *J. Org. Chem.* **1991**, *56*, 2723. Murray, J. S.; Brinck, T.; Politzer, P. *J. Mol. Struct. (THEOCHEM)* **1992**, *255*, 271. Karaman, R.; Huang, J. T. L.; Fry, J. L. *J. Comput. Chem.* **1990**, *11*, 1009. Krygowski, T. M.; Wozniak, K.; Bock, C. W.; George, P. *J. Chem. Res. Synop.* **1989**, 396.

(4) Haeberlein, M.; Brinck, T. *J. Phys. Chem.* **1996**, *100*, 10116.

(5) Scrocco, E.; Tomasi, J. in *Advances in Quantum Chemistry*; Löwdin, P.-O., Ed.; Academic: New York, 1978; Vol. 2. Politzer, P., Truhlar, D. G., Eds. *Chemical Applications of Atomic and Molecular Electrostatic Potentials*; Plenum: New York, 1981. Pullman, B. *Int. J. Quantum Chem. Quantum Biol. Symp.* **1990**, *17*, 81.

(6) Murray, J. S.; Politzer, P. *Chem. Phys. Lett.* **1988**, *152*, 364.

(7) Brinck, T.; Murray, J. S.; Politzer, P. *J. Org. Chem.* **1991**, *56*, 5012.

(8) Murray, J. S.; Brinck, T.; Politzer, P. *Int. J. Quantum Chem. Biol. Symp.* **1991**, *18*, 91.

(9) Haeberlein, M. Murray, J. S.; Brinck, T.; Politzer, P. *Can. J. Chem.* **1992**, *70*, 2209.

(10) Murray, J. S.; Paulsen, K.; Politzer, P. *Proc. Indian Acad. Sci. (Chem. Sci.)* **1994**, *106*, 267.

(11) Politzer, P.; Abrahmsen, L.; Söberg, P. *J. Am. Chem. Soc.* **1984**, 855.

(12) Gadre, S. R.; Kulkarni, S. A.; Shrivastava, I. H. *J. Chem. Phys.* **1992**, *96*, 5253. Shirsat, R. N.; Bapat, S. V.; Gadre, S. R. *Chem. Phys. Lett.* **1992**, *200*, 373.

(13) Mehta, G.; Gunasekaran, G.; Gadre, S. R.; Shirsat, R. N.; Ganguly, B.; Chandrasekhar, J. *J. Org. Chem.* **1994**, 59, 1953.; Mehta, G.; Khan, F. M.; Gadre, S. R.; Shirsat, R. N.; Ganguly, B.; Chandrasekhar, J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1390. Gadre, S. R.; Suresh, C. H. *Curr. Sci. (India)* **1996**, *71*, 130.

(14) Gadre, S. R.; Kulkarni, S. A.; Suresh, C. H.; Shrivastava, I. H. *Chem. Phys. Lett.* **1995**, *239*, 273.

(15) Kulkarni, S. A. *Chem. Phys. Lett.* **1996**, *254*, 268.

(16) *Gaussian 94.* Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Allaham, M. A.; Zatrezewski, V. G.; Ortiz, J. V.; Foresman, J. B. ; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian Inc., Pittsburgh, PA, 1995.

(17) The package *UNIPROP* developed by S. R. Gadre and coworkers, Department of Chemistry, University of Pune, Pune, 411007, India.

(18) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991,** *91*, 165.

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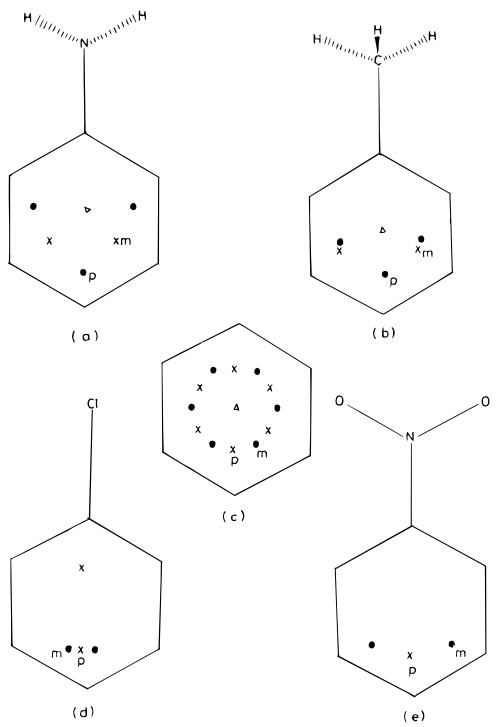

Figure 1. MESP critical points over the aromatic ring: (a) aniline, (b) toluene, (c) benzene, (d) chlorobenzene, (e) nitrobenzene. The "p" and "m" CP values in kJ/mol are (a) −102.56 and −97.31, (b) −90.76 and −89.18, (c) −84.72 and −84.72, (d) −51.41 and −51.41, and (e) −8.13 and −9.18, respectively. The symbols ●, ×, and △ denote (3, +3) , (3, +1), and (3, −1) CPs, respectively.

In benzene, the typical ("p" and "m" CP values are very close) CP value is −84.72 kJ/mol and is 1.73 Å away from the ring plane. Any substituent which changes these values to a higher value is considered as an *electron-withdrawing group*, and the one that produces more negative valued CPs than the "p" or "m" CPs of benzene is classfied as an *electron-donating group*. This classification is very straightforward and gives a combined result of resonance and field effects which are assumed to be responsible for these electronic perurbations. These are naturally included in the MESP topography, since the latter takes into account the overall charge distribution in the molecule. Notice that our classification is purely based on the MESP values observed over the *para*- and *meta*-carbons of the isolated gas-phase monosubstituted systems. Apart from the basis-set quality, these values can be considered as representatives of an ideal situation where intermolecular interactions, solvent effects, as well as effects due to other substituents are completely neglected. In fact, our earlier studies have revealed that HF/6-31G** MESP topography is normally adequate for a proper representation of the π-electron distributions in these systems.[14] Further, the effect of correlation does not change the overall topography of the MESP[15] at 6-31G** level.

The classical interpretation of the electron-donating or electron-accepting capacity of a substituent is based on the sign and magnitude of the σ-constants which are obtained from the doubly substituted benzenes under specific experimental conditions. The "p" and "m" CPs can be considered as the initial attractors for an incoming electrophile eventually leading to a π-complex for a *para*- or a *meta*-substitution, respectively.

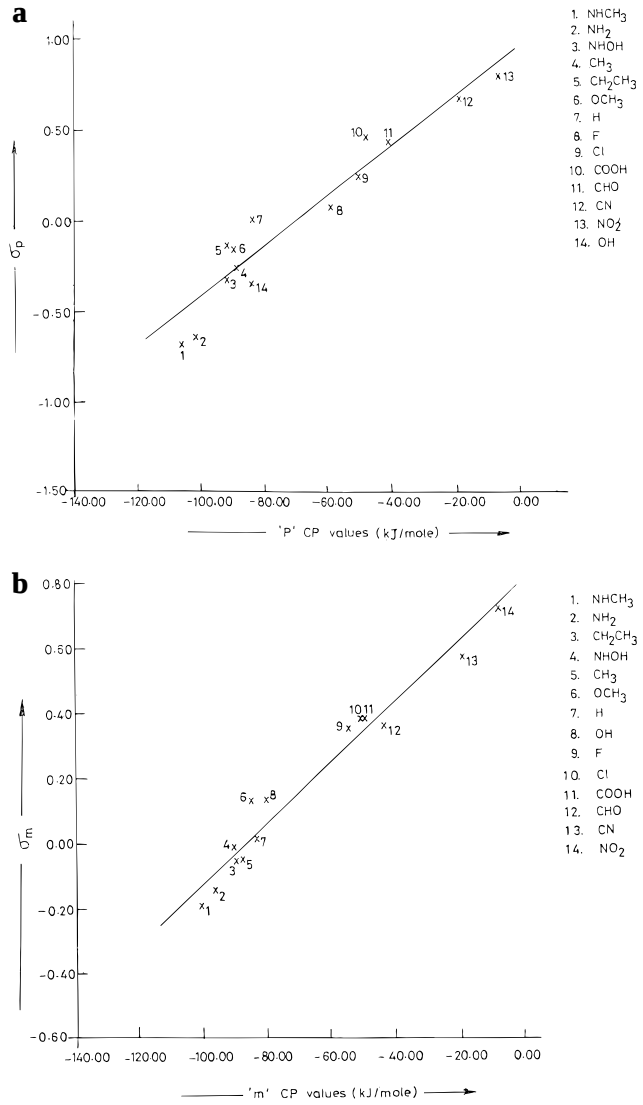

Figure 2. (a) Correlation between σ_p and "p" CP values. (b) Correlation between σ_m and "m" CP values.

Following this argument, we have tried a correlation of the "ideal" behavior and the experimental situation by plotting the "p" CP values against the σ_p values and "m" CP values against the σ_m values (Figure 2). Surprisingly, excellent correlations are obtained (correlation coefficients: 0.958 for the *para* and 0.980 for the *meta*). Though the experimental conditions are very much different from the ideal situation, correlations of these kinds clearly indicate, in general, the consistency of a substituent to perturb the electronic environment of the aromatic nucleus irrespective of its chemical environment. The small deviations from the linear plot can be attributed as due to the deviations from the "ideal" behavior, and it can be argued that these changes generally have little influence on σ values (cf. p 21 of ref 1). The OH group, a strong ortho−para-directing group shows the largest deviation from the "ideal" behavior. In MESP terms, it shows zero activation as (when compared with benzene) at the para-position probably due to the cancelation of the resonance and the inductive effects. The σ_p value of this group cannot be well correlated with the MESP since it reflects the intermediate electronic character between the OH and O^- in certain media (cf. p 23 of ref 1).

In addition to this, except the halogens (which are mostly *para*-directing), all the electron-withdrawing groups exhibit the most negative valued CPs in the vicinity of the *meta*-carbon, confirming the orientation effect of these groups (*meta*-directing). Similarly, in all the activated systems (*ortho*−*para*-directing) the most negative valued CP is observed near the *para*-carbons. They also show minima near the *ortho*-carbons. The distance of the CPs from the benzene ring plane changes depending on the nature of the substituent. The electron withdrawal from the aromatic ring leads to the formation of the CPs further away from the ring plane, and electron donation makes it closer to the ring plane as compared to benzene minima. For example, nitrobenzene shows the highest valued "p" MESP CP (−8.13 kJ/mol) at a distance 1.96 Å away from the ring plane, and aniline shows a minimum of value −102.56 kJ/mol, at a distance 1.68 Å close to the ring plane for the "p" CP. The substituents arranged in the increasing order of activation based on the "p" MESP CP values for *para*-substitution are NO_2 < CN < CHO < COOH < Cl < F < OH ≈ H < OCH_3 ≈ CH_3 < CH_2CH_3 ≈ NHOH < NH_2 < $NHCH_3$. The corresponding order for *meta*-substitution based on "m" CP values is NO_2 < CN < CHO < COOH ≈ Cl < F < OH < H < OCH_3 < CH_3 < CH_2CH_3 ≈ NHOH < NH_2 < $NHCH_3$. Further, it should be borne in mind that the MESP CP data are provided for the conformations indicated in Figure 1. However, for some molecules, a free rotation around a single bond is permitted, which will result in averaging of MESP values at CPs.

The electronic perturbations offered by different substituents over the benzene nucleus are thus directly explored by monitoring the electron localization patterns observed near the *meta*- and *para*-sites of monosubstituted benzenes. The good linear correlations between the "p" CP values and σ_p's and the "m" CP values and σ_m's show that a direct measure of the electronic effects of a substituent can be provided by the MESP topography. The present approach also eliminates the necessity of employing a standard compound or a standardized reaction for the measurement of the substituent effects. It is hoped that this work provides an impetus for the use of MESP topography toward a direct visualization of electronic perturbations offered by substituents to an aromatic ring.

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