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An Efficient Computational Approach for the Evaluation of Substituent Constants

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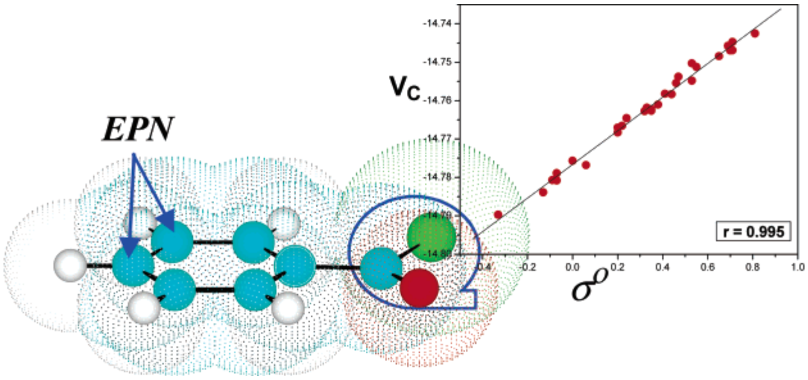

Density functional theory computations at the B3LYP/6-311+G(2d,2p) and BPW91/6-311G(d,p) levels were carried out for a series of 15 monosubstituted benzene derivatives to study dependencies between electronic structure parameters and experimental reactivity constants. An efficient and accurate computational approach for the evaluation of σ^0 substituent constants for substituted benzene systems is outlined. It is based on the excellent linear correlation between the experimental reactivity constants and the theoretical electrostatic potential values (EPN) at the carbon atoms in the para and meta positions. The results underline the usefulness of the EPN as a local reactivity descriptor. Theoretical computations to assess the influence of water solvent using the SCIPCM method showed that the solvent enhances the overall effect of polar substituents by about 30%. The results obtained indicate also that the relative values of the σ^0 constants are predominantly determined by intramolecular influences.

Introduction

For many years the Hammett equation was a significant driving force behind the development of organic chemistry as a quantitative science.[1−13] The characterization of the influence of structural variations, or substituent effects, on the thermodynamics and kinetics of numerous organic reactions provided by the Hammett approach has also played a significant role in elucidating the mechanisms of the reactions studied. The determination of different types of substituent constants from experimental kinetic or thermodynamic studies has also contributed to the clear definition of important phenomena such as inductive/field effects, resonance effects, and other intramolecular influences.[4−13]

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The progress of computational quantum chemistry has offered alternative possibilities for rationalizing the reactivity of organic molecules. Theoretically evaluated charge density parameters, frontier orbital energies, and other electronic structure parameters have found wide application in interpreting the effects of structural variations on the kinetics and thermodynamics of chemical reactions.[14−19] Significant progress has also been achieved via the electronic reactivity indexes defined in the framework of density functional theory.[16−18] Despite these new opportunities, there is a continuing interest in applying the different types of substituent constants in analyzing chemical reactivity because of the simplicity of the approach and the prevailing trust of many chemists in experimentally derived parameters such as the Hammett σ constants. The current importance of the substituent constants is further underlined by their key application in the field of structure−property and structure−activity studies.[20−23] Despite the accumulation of reactivity constants for a considerable variety of substituents,[13,24] the number of available parameters is restricted by the necessity to carry out a series of kinetic or chemical equilibrium studies in their experimental determination. Spectroscopic data such as NMR chemical shifts, vibrational frequencies, and IR intensities have also been utilized in deriving correlation equations for the evaluation of reactivity constants of new substituents.[25−27]

Relationships between substituent constants and electronic structure parameters have been found in numerous cases.[28] Gross and Seybold[28b−e] considered correlations between electronic structure parameters and the experimental $\mathrm{p}K_a$ values of substituted phenols, anilines, and benzoic acids in a comparative context with the performance of the empirical σ constants. In the case of substituted benzoic acids,[28d] Hollingsworth, Seybold, and Hadad considered several types of atomic charges, as well as the Wiberg bond index. The correlation coefficients for the relationship between the experimental $\mathrm{p}K_a$ values and the theoretically estimated parameters ranged from 0.956 to 0.989. The total Löwdin charge on the carboxylic group appeared to be the best parameter describing the variations of the benzoic acid $\mathrm{p}K_a$ values. A similar study on the $\mathrm{p}K_a$ values of substituted anilines[28e] considered, in addition to atomic charges, several other types of theoretical quantities: the relative proton-transfer enthalpies, the minima in the molecular surface local ionization energies, as well as the molecular electrostatic potential (MESP) total and surface minima. The correlation coefficients (r) relating these quantities and the $\mathrm{p}K_a$ values were 0.957 for the natural charges, 0.960 for the relative proton-transfer enthalpies, 0.974 for the minima in the molecular surface local ionization energies, 0.972 for the MESP minima, and 0.965 for the MESP surface minima. Morao and Hillier[28h] found linear correlations between the σ^+ constants and NBO bond orders and charges, the nuclear-independent chemical shifts, and the LUMO energies in the case of para-substituted benzyl cations. The correlation coefficients (r) for these dependencies were somewhat low, ranging from 0.89 to 0.94. Barbour and Karty[28i] discussed the acidities of para-substituted phenols and *para*-alkylphenols in terms of inductive/field and resonance parameters. In a recent study, Elango et al.[28j] discussed the relationships among the Parr electrophilicity index,[29] Hammett constants, and nuclear-independent chemical shifts.[30] Domingo et al.[28k] studied the relationship between σ_p constants and the electrophilicity index for a series of substituted ethylenes.

A direct theoretical approach in deriving substituent constants was also proposed by Topsom and co-workers.[31] The method employs theoretically estimated atomic charges as well as other theoretically derived quantities in evaluating substituent constants. A quantum chemical approach was recently applied by Wiberg in rationalizing the nature of intramolecular effects induced by the substituents.[32] The Hammett equation was also interpreted by Liu and co-workers in terms of the Paulings electronegativity equation.[33]

In the present study, we outline a computational approach for the evaluation of reactivity constants based on relationships between the experimental constants and theoretically estimated values for the electrostatic potential at nuclei (EPN) for a series of 15 monosubstituted benzenes. Two types of atomic charges were also considered for similar relationships. Recent studies showed that the electrostatic potentials at nuclei can be employed as an excellent local reactivity descriptor.[34−38] Minima and

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maxima of MESP have been shown to describe satisfactorily chemical reactivity in general.[39−43]

Computational Methods

Theoretical Methods Employed. Full geometry optimization of the 15 monosubstituted benzene derivatives studied was carried out via density functional theory computations using the Gaussian 94 program package.[44] The theoretical calculations were performed employing the B3LYP hybrid functional[45] with the 6-311+G(2d,2p) basis set[46] and using the BPW91 gradient-corrected functional[47] combined with the 6-31+G(d) basis set.[48] Harmonic vibrational frequency computations were also carried out to verify that all optimized structures were true minima on the respective potential energy surfaces and also to evaluate the dipole moment derivative matrixes.

Atomic Charges. Atomic charges from two different partitioning methods were obtained. Natural bond orbital (NBO) charges[49] for the carbon atoms situated in the meta and para positions with respect to the substituents were determined. The NBO charges have been extensively used in describing charge distributions in molecules. Atomic charges derived from dipole moment derivatives (atomic polar tensors) were also evaluated. The mean dipole derivatives[50] or generalized atomic polar tensor (GAPT) charges[51] represent the trace of the matrix of the dipole derivatives associated with a particular atom α in the molecule:

$$P_X^{(\alpha)} = \begin{pmatrix} \partial p_x/\partial x_\alpha & \partial p_x/\partial y_\alpha & \partial p_x/\partial z_\alpha \\ \partial p_y/\partial x_\alpha & \partial p_y/\partial y_\alpha & \partial p_y/\partial z_\alpha \\ \partial p_z/\partial x_\alpha & \partial p_z/\partial y_\alpha & \partial p_z/\partial z_\alpha \end{pmatrix} \qquad (1)$$

In eq 1, p_x, p_y, and p_z are the Cartesian components of the molecular dipole moment, whereas x_α, y_α, and z_α are the coordinates of atom α. In a series of studies, Bruns et al.[52] showed that the mean dipole derivatives (or GAPT atomic charges) can be successfully employed in characterizing electric charge properties in a number of molecules.

Electrostatic Potentials at Nuclei. The electrostatic potential at a nucleus (EPN) was also evaluated. The electrostatic potential at a particular nucleus (A) is defined by eq 2 at $r = R_Y$ (radius vector of the respective nucleus) as the term at $R_Y = R_A$ is dropped out.[41,53]

$$V_Y \equiv V(R_Y) = \sum_{A \neq Y} \frac{Z_A}{|R_Y - R_A|} - \int \frac{\rho(r')}{|R_Y - r'|}\, \mathrm{d}r' \qquad (2)$$

In this equation, Z_A is the charge on nucleus A with radius vector R_A, $\rho(r)$ is the electronic density of the molecule, and r' is a dummy integration variable. Equation 2 is written in atomic units and contains a summation over all atomic nuclei, treated as positive point charges, as well as integration over the continuous distribution of the electronic charge. It should be emphasized that, within the level of electronic structure theory employed, the EPN values reflect perfectly accurately the changes in the electronic density at the atomic sites induced by structural variations. From a theoretical point of view the EPN should, therefore, be considered superior as a local reactivity index in describing the Coulombic attraction between the reactants compared to the differently defined atomic charges that are always evaluated via approximate partitioning schemes.

Results and Discussion

The effect of substituents on electronic parameters characterizing the para and meta positions in the aromatic ring was assessed by computations at two levels of density functional theory, as discussed in the preceding section. A series of 15 monosubstituted benzenes were studied. The molecules treated are given in Table 1. The results from the B3LYP/6-311+G-(2d,2p) computations involving the C−H bond in the para position to the substituents are presented in Table 1. The electronic parameters evaluated are as follows: the electrostatic potential values for the carbon and hydrogen atoms, the NBO charges at the same atoms, and the mean dipole moment derivatives or GAPT atomic charge for the hydrogen atom of the para C−H bonds. The theoretical values are compared to two types of substituent constants. The standard Hammett σ constants are given in the penultimate column of Table 1. The last column contains the σ^0 constants introduced by Van Bekkum et al.[54] and Taft.[5] The σ^0 constants are defined to reflect the isolated effect of individual substituents unperturbed by possible resonance interactions with a second substituent.

It follows from this definition that the σ^0 constants are expected to represent in a more plausible way the effect of the polar groups in the monosubstituted benzenes. The standard Hammett constants were taken from the review of Hansch et al.[13] The σ^0 constants for the para and meta substituents were taken from the compilation of Exner.[24] The two rows at the bottom of the table contain the correlation coefficients (r) between the theoretical parameters and the two sets of σ

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TABLE 1. Experimental Reactivity Constants and Theoretical Parameters for the para C−H Bond in Monosubstituted Benzenes from B3LYP/6-311+G(2d,2p) Computations

	V_C[a] [au]	V_H[a] [au]	V_C sol[b] [au]	V_H sol[b] [au]	q_C (NBO) [e]	q_H (NBO) [e]	q_H (GAPT)	σ_p[c]	σ_p^0[d]
−H	−14.77568	−1.11031	−14.77912	−1.10875	−0.20356	0.20355	0.03175	0	0
$-CH_3$	−14.78082	−1.11381	−14.78544	−1.11376	−0.20983	0.20250	0.03074	−0.17	−0.12
$-OCH_3$	−14.78389	−1.11533	−14.78832	−1.11494	−0.23644	0.20466	0.03398	−0.27	−0.13
$-NH_2$	−14.78970	−1.12017	−14.79790	−1.12398	−0.24596	0.20356	0.03180	−0.66	−0.33
−F	−14.76831	−1.10237	−14.76788	−1.09690	−0.22005	0.20775	0.03981	0.06	0.20
−Cl	−14.76459	−1.09929	−14.76354	−1.09310	−0.20709	0.20806	0.03920	0.23	0.24
−CN	−14.74692	−1.08484	−14.74050	−1.07388	−0.17764	0.21012	0.04388	0.66	0.71
−CHO	−14.75382	−1.09184	−14.74958	−1.08266	−0.17035	0.20756	0.03989	0.42	0.47
$-NO_2$[e]	−14.74255	−1.08122			−0.16875	0.21106	0.04689	0.78	0.81
−COOH	−14.75834	−1.09562	−14.75776	−1.08927	−0.17417	0.20669	0.03842	0.45	0.44
−COF	−14.74695	−1.08553	−14.74042	−1.07407	−0.16534	0.20916	0.04318	0.70	0.70
−COCl	−14.74579	−1.08432	−14.73840	−1.07210	−0.16212	0.20952	0.04313	0.61	0.69
−CCH	−14.76657	−1.10214	−14.76694	−1.09703	−0.19381	0.20589	0.03590	0.23	0.22
$-CHF_2$	−14.76266	−1.09829	−14.76352	−1.09315	−0.19185	0.20704	0.03745	0.32	0.35
$-CF_3$	−14.75484	−1.09158	−14.75196	−1.08450	−0.18302	0.20856	0.04090	0.54	0.53
r (σ_p)	0.980	0.975	0.973	0.970	0.940	0.872	0.883		
r (σ_p^0)	0.996	0.996	0.994	0.994	0.921	0.920	0.937		

[a] Electrostatic potential at nuclei. [b] Obtained using the SCIPCM method for water solution ($\epsilon = 78.39$) and full geometry optimization. [c] From Hansch et al.[13] [d] From Exner.[24] [e] The SCIPCM computations for nitrobenzene did not converge.

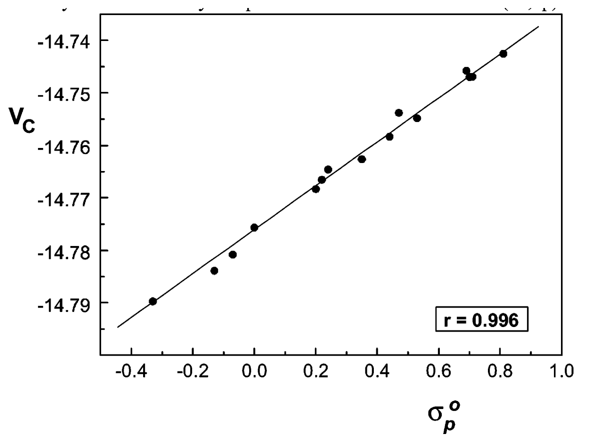

FIGURE 1. Relationship between the theoretical electrostatic potential at the *para*-carbon atom in monosubstituted benzenes and the σ_p^0 constants.

constants. The best correlations are found for the relationships between the theoretically estimated electrostatic potential at the carbon and hydrogen atoms and the respective σ^0 constants. The linear plot with the standard σ constants is less satisfactory. The correlations between substituent constants, the natural charges at the carbon and hydrogen atoms, and the GAPT charges at the hydrogen atoms of the para C−H bond reveal that overall linearity between the theoretical and experimental quantities exists, though the respective correlation coefficients are low.

The excellent linear plot between the carbon EPN values (V_C) and the σ_p^0 constants is illustrated in Figure 1. In view of the usual experimental errors in determining the reactivity constants as well as the approximations inherent in the theoretical methods employed it is not reasonable to expect a better linear correlation between these two quantities.

Analogous results from theoretical computations for the meta C−H bonds in monosubstituted benzenes and the respective experimental reactivity constants are presented in Table 2. Again, the best correlation between theoretical parameters and experimental reactivity constants is found for the linear plot between the electrostatic potential at the carbon atom (V_C) and the σ_m^0 constants ($r = 0.994$). The V_C/σ_m^0 plot is shown in Figure 2. The dependence between V_H and σ_m^0 has a slightly lower correlation coefficient ($r = 0.987$). It can be seen that the NBO charges for the hydrogens of the meta C−H bond follow closely the variations of the σ_m^0 constants ($r = 0.991$). Somewhat unexpectedly, the NBO charges at the *meta*-carbon atom do not correlate linearly with the respective σ_m^0 constants ($r = 0.367$). The reason can be sought in the participation of the carbon atoms in the conjugated system and the resulting inaccuracies in the partitioning of the electron charge density between the atoms in such systems. The *meta*-hydrogen atoms, on the other hand, are isolated from these effects and experience the distant influence of the polar substituents.

The correlation between GAPT charges and substituent constants is less satisfactory.

It is certainly of interest to plot simultaneously the electrostatic potential values for both para and meta C−H bonds. The following linear regression was obtained:

$$V_C = 0.044\sigma^0 - 14.777 \qquad (3)$$

and $n = 29$, $r = 0.995$, and $s = 0.001$.

This relationship is illustrated in Figure 3. The quality of the linear dependence between the σ^0 substituent constants and the theoretically estimated EPN values for the carbon atom in the para and meta positions of the aromatic ring indicates that the relationship found offers a useful computational approach for the evaluation of reactivity constants. The results from the present study emphasize also the accuracy of the electrostatic potential at nuclei as a local reactivity descriptor.[34−38]

It should be emphasized that the σ^0 constants are determined from solution kinetic and chemical equilibrium studies.[5,54] It is, therefore, quite surprising to find such a nearly perfect linear correlation between these experimental quantities and the theoretical EPN values obtained without consideration of the solvent effect. To analyze the influence of solvent, computations employing the SCIPCM method[55] were carried out. Full geometry optimization for the molecules studied at the B3LYP/

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TABLE 2. Experimental Reactivity Constants and Theoretical Parameters for the meta C−H Bond in Monosubstituted Benzenes from B3LYP/6-311+G(2d,2p) Computations

	$V_C{}^a$ [au]	$V_H{}^a$ [au]	V_C sol^b [au]	V_H sol^b [au]	q_C (NBO) [e]	q_H (NBO) [e]	q_H (GAPT)	$\sigma_m{}^c$	$\sigma_m{}^{0d}$
−H	−14.77568	−1.11031	−14.77912	−1.10874	−0.20356	0.20355	0.03175	0	0
$-CH_3$	−14.77890	−1.11321	−14.78312	−1.11264	−0.19341	0.20187	0.02650	−0.07	−0.07
$-OCH_3$	−14.77681	−1.11253	−14.78019	−1.11059	−0.18538	0.20415	0.03063	0.12	0.06
$-NH_2$	−14.78071	−1.11596	−14.78761	−1.11796	−0.18129	0.20194	0.02918	−0.16	−0.09
−F	−14.76184	−1.09893	−14.76209	−1.09351	−0.18425	0.20762	0.03967	0.06	0.33
−Cl	−14.76104	−1.09930	−14.76076	−1.09134	−0.18562	0.20891	0.03386	0.37	0.38
−CN	−14.74846	−1.08502	−14.74407	−1.07546	−0.19691	0.21288	0.04235	0.56	0.65
−CHO	−14.75821	−1.09508	−14.75514	−1.08538	−0.20131	0.20907	0.03586	0.35	0.41
$-NO_2{}^e$	−14.74474	−1.08249			−0.19586	0.21398	0.04396	0.71	0.71
−COOH	−14.76230	−1.09829	−14.76296	−1.09330	−0.20485	0.20899	0.03672	0.37	0.35
−COF	−14.75127	−1.08788	−14.74700	−1.07846	−0.20359	0.21196	0.04240	0.55	0.55
−COCl	−14.75031	−1.08674	−14.74538	−1.07680	−0.20258	0.21244	0.03908	0.53	0.53
−CCH	−14.76706	−1.10226	−14.76844	−1.09794	−0.19958	0.20747	0.03213	0.21	0.20
$-CHF_2$	−14.76276	−1.09868	−14.76352	−1.09450	−0.19570	0.20770	0.03578	0.29	0.32
$-CF_3$	−14.75545	−1.09187	−14.75402	−1.08515	−0.19556	0.21011	0.03985	0.43	0.46
r (σ_m)	0.947	0.946	0.939	0.941	0.481	0.967	0.850		
r ($\sigma_m{}^0$)	0.994	0.987	0.989	0.987	0.371	0.991	0.941		

[a] Electrostatic potential at nuclei. [b] Obtained using the SCIPCM method for water solution ($\epsilon = 78.39$) and full geometry optimization. [c] From Hansch et al.[13] [d] From Exner.[24] [e] The SCIPCM computations for nitrobenzene did not converged.

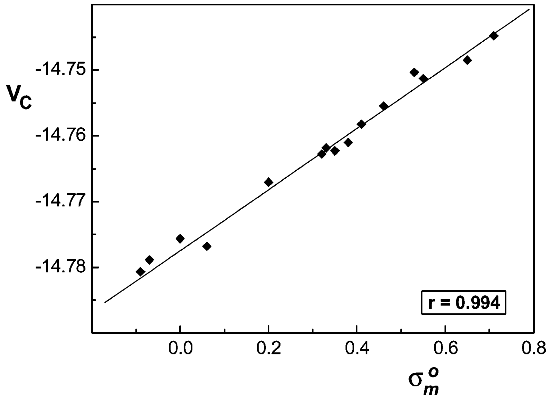

FIGURE 2. Relationship between the theoretical electrostatic potential at the *meta*-carbon atom in monosubstituted benzenes and the $\sigma_m{}^0$ constants.

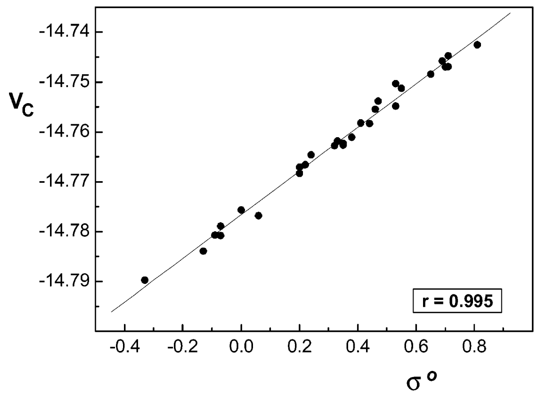

FIGURE 3. Dependence between the theoretical electrostatic potential at the *meta*- and *para*-carbon atoms in monosubstituted benzenes and the σ^0 constants.

6-311+G(2d,2p) level of theory was performed. The results obtained for the theoretical EPN values of the *meta* and *para* carbon and hydrogen atoms in the case of water solvent are given in Tables 1 and 2. It is seen from the correlation coefficients obtained that the excellent linear dependence between V_C and V_H and the respective σ^0 constants is retained. The regression equation obtained is as follows:

$$V_C = 0.057\sigma^0 - 14.780 \qquad (4)$$

and $n = 27$, $r = 0.993$, and $s = 0.002$.

Comparison between eqs 3 and 4 reveals that the water solvent enhances the overall effect of the substituents by about 30%. It is important to point out, however, that the theoretical results show that the relative influence of the substituents does not change with the transition from isolated molecules to solutions. The data obtained illustrate the influence of the overall polarity of the water solvent on the electronic parameter evaluated. As is known, the different SCRF methods incorporated in the electronic structure software packages do not reflect the specific interactions between substituents and polar solvents, such as hydrogen bonding or other types of local interactions. Such effects are expected to influence the experimental reactivity constants. The high correlation coefficients for the linear dependencies between electronic parameters obtained without consideration of the possible specific interactions between solvent and aromatic substituents indicate that the role of these intermolecular effects on the relative values of the σ^0 reactivity constants for the treated series of benzene derivatives may not be too significant. Pearson[56] pointed out that the electronic chemical potential and the global hardness do not change substantially upon solvation. It is certainly well-known from both experiment and theory that solvents may induce considerable changes in the energy profiles of chemical reactions. The detailed analysis of the solvent influence on the relative effects of substituents on reactivity deserves, therefore, special attention. The problem is beyond the scope of the present study.

To verify the reliability of the results obtained, analogous computations on the monosubstituted benzenes were performed using an alternative DFT method as well as a smaller basis set. The results from BPW91/6-311G(d,p) computations on monosubstituted benzenes are presented in Table 3.

The correlation coefficients given in the two bottom rows show that the established linear relationship between the σ^0 constants and the respective carbon EPN values is confirmed

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(56) Pearson, R. G. *J. Am. Chem. Soc.* **1986**, *108*, 6109.

TABLE 3. Experimental Reactivity Constants and Theoretical Parameters for the para and meta C−H Bond in Monosubstituted Benzenes from BPW91/6-311G(d,p) Computations

	$V_C{}^a$ [au]	$V_H{}^a$ [au]	q_H (GAPT)
H	−14.7842	−1.1089	0.02724
p-CH_3	−14.7890	−1.1120	0.02496
p-OCH_3	−14.7932	−1.1143	0.02854
p-NH_2	−14.8008	−1.1058	0.02628
p-F	−14.7780	−1.1018	0.03587
p-Cl	−14.7726	−1.0972	0.03563
p-CN	−14.7561	−1.0840	0.04058
p-CHO	−14.7629	−1.0910	0.03601
p-NO_2	−14.7531	−1.0816	0.04381
p-COOH	−14.7686	−1.0957	0.03420
p-COF	−14.7568	−1.0853	0.03973
p-COCl	−14.7527	−1.0815	0.04090
p-CCH	−14.7751	−1.1006	0.03166
p-CHF_2	−14.7724	−1.0980	0.03339
p-CF_3	−14.7649	−1.0915	0.03700
m-CH_3	−14.7876	−1.1117	0.02103
m-OCH_3	−14.7866	−1.1121	0.02566
m-NH_2	−14.7923	−1.1169	0.02313
m-F	−14.7719	−1.0989	0.03633
m-Cl	−14.7690	−1.0951	0.03093
m-CN	−14.7573	−1.0840	0.03937
m-CHO	−14.7669	−1.0939	0.03152
m-NO_2	−14.7544	−1.0825	0.04011
m-COOH	−14.7719	−1.0979	0.03218
m-COF	−14.7604	−1.0872	0.03881
m-COCl	−14.7566	−1.0833	0.03649
m-CCH	−14.7755	−1.1008	0.02848
m-CHF_2	−14.7725	−1.0983	0.03086
m-CF_3	−14.7654	−1.0917	0.03575
$r(\sigma)^a$	0.962	0.949	0.819
$r(\sigma^0)^a$	0.988	0.982	0.908

[a] Correlation coefficients for the dependencies between the electronic parameters and the σ and σ^0 constants as given in Tables 1 and 2.

TABLE 4. Predicted σ^0 Constants Using Eq 3

substituent	*para* V_C [au]	*meta* V_C [au]	$\sigma_p{}^0$	$\sigma_m{}^0$
$-CH_2Cl$	−14.766347	−14.766594	0.24	0.23
$-CH_2OH$	−14.775841	−14.776238	0.02	0.01
$-CONH_2$	−14.762773	−14.765865	0.32	0.25
−NCS	−14.760351	−14.757927	0.37	0.43
−NHOH	−14.783846	−14.775668	−0.16	0.02
$-OCF_3$	−14.758756	−14.755801	0.41	0.48
−OCN	−14.753583	−14.747275	0.53	0.67
$-OCOCH_3$	−14.771655	−14.768148	0.11	0.19
$-ONO_2$	−14.754753	−14.753540	0.50	0.53

at this level of theory as well. The use of lower levels of electronic structure theory is very often desirable if substituents of larger size or large numbers of substituents need to be quantitatively characterized by the respective σ constants in view of possible application in QSAR and QSPR studies. By using eq 3 a number of σ^0 constants were predicted for substituents, for which no such data are available. These values are reported in Table 4.

It is certainly of interest to discuss the physicochemical grounds for the established linear dependence between the theoretically evaluated electrostatic potential at nuclei and the reactivity constants. As stressed earlier, the EPN values reflect accurately the variation of the electron densities at the atomic sites in the respective reaction centers. The relationship between charge densities and chemical reactivity is quite clear. It is, therefore, not surprising that EPN values offer more accurate theoretical predictions of reactivity than electronic parameters evaluated following approximate procedures. This is confirmed by the results of the present study.

In view of the importance of the Hammett type of constants for organic chemistry and their wide QSAR and QSPR application, a similar study on di- and poly-substituted benzene derivatives would be important.

Conclusions

An efficient and meaningful computational approach for the evaluation of σ^0 substituent constants for substituted benzene systems is outlined. It is based on the linear relationship between experimental constants and the theoretical EPN at the carbon atoms in the para and meta positions for a series of monosubstituted benzenes. The results emphasize the reliability of EPN as a local reactivity descriptor. Theoretical computations to assess the influence of water solvent using the SCIPCM method showed that the solvent enhances the overall effect of polar substituents by about 30%. The results obtained indicate also that the relative values of the σ^0 constants are predominantly determined by intramolecular influences.

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Supporting Information Available: Cartesian coordinates for B3LYP/6-311+G(2d,2p) and BPW91/6-311G(d,p) optimized geometries of the monosubstituted benzenes. Cartesian coordinates for B3LYP/6-311+G(2d,2p) optimized structures in water solvent using the SCIPCM method. This material is available free of charge via the Internet at http://pubs.acs.org.

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