Average local ionization energies on the molecular surfaces of aromatic systems as guides to chemical reactivity

PER SJOBERG

Nobel Chemicals, Nobel Industries Sweden, S-691 85 Karlskoga, Sweden

AND

JANE S. MURRAY, TORE BRINCK, AND PETER POLITZER[1]

Department of Chemistry, University of New Orleans, New Orleans, LA 70148, U.S.A.

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The average ionization energy, $\bar{I}(r)$, is introduced and is demonstrated to be useful as a guide to chemical reactivity in aromatic systems. $\bar{I}(r)$ is rigorously defined within the framework of self-consistent-field molecular orbital (SCF-MO) theory and can be interpreted as the average energy needed to ionize an electron at any point in the space of a molecule. An *ab initio* SCF-MO approach has been used to calculate $\bar{I}(r)$ at the 6-31G* level, using STO-3G optimized geometries. $\bar{I}(r)$ has been computed on molecular surfaces defined by the contour of constant electronic density equal to 0.002 electrons/bohr^3, for a series of aromatic systems. This surface $\bar{I}(r)$ provides site specific predictions for preferred positions of electrophilic aromatic substitution. Relative reactivity toward electrophiles increases as the magnitudes of the smallest $\bar{I}(r)$ values ($\bar{I}_{min}$) for these systems decrease. An excellent relationship, with a correlation coefficient of 0.99, has been found between the Hammett constants and $\bar{I}_{min}$; this allowed us to predict the values of these constants for the substituents NHF and NF$_2$, for which they were previously not known.

Key words: average local ionizations energy, chemical reactivity, electrophilic aromatic substitution, molecular surfaces, Hammett constants.

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On introduit le concept d'énergie moyenne d'ionisation locale, $\bar{I}(r)$, et on démontre qu'il est un guide utile pour prédire la réactivité chimique dans les systèmes aromatiques. On définit $\bar{I}(r)$ d'une façon rigoureuse dans le cadre de la théorie des orbitales moléculaires en champ auto-cohérent (OM-CAC) et on peut l'interpréter comme l'énergie moyenne nécessaire pour ioniser un électron dans un point quelconque de l'espace d'une molécule. On a utilisé une approche *ab initio* d'OM-CAC pour calculer $\bar{I}(r)$ au niveau 6-31G*, en utilisant des géométries optimisées au niveau STO-3G. Pour une série de systèmes aromatiques, on a aussi calculé $\bar{I}(r)$ sur les surfaces moléculaires définies par le contour d'une densité électronique constante de 0,002 électrons/bohr^3. Cette $\bar{I}(r)$ de surface fournit des prédictions spécifiques au site pour les positions préférées par les substitutions aromatiques électrophiles. La réactivité relative vis-à-vis des électrophiles augmente avec une diminution des amplitudes des valeurs $\bar{I}(r)$ les plus faibles $\bar{I}_{min}$ de ces systèmes. On a obtenu une excellente corrélation, avec un coefficient de corrélation de 0,99, entre les constantes de Hammett et les valeurs de $\bar{I}_{min}$; cette corrélation nous permet de prédire les valeurs de ces constantes pour les substituants NHF et NF$_2$ pour lesquels ils n'étaient pas encore connus.

Mots clés : énergie moyenne d'ionisation locale, réactivité chimique, substitution aromatique électrophile, surfaces moléculaires, constantes de Hammett.

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Introduction

The interpretation and prediction of molecular reactive behavior is a continuing focus of our computational studies (1–5). In this work we introduce the average local ionization energy, $\bar{I}(r)$, and show its applicability in predicting sites and relative reactivities for electrophilic attack in aromatic systems.

$\bar{I}(r)$ is rigorously defined within the framework of self- consistent-field molecular orbital (SCF-MO) theory, as given by eq. [1]:

$$[1] \quad \bar{I}(r) = \sum_i \frac{\rho_i(r)|\epsilon_i|}{\rho(r)}$$

$\rho_i(r)$ is the electronic density of the ith molecular orbital at the point r, ϵ_i is the orbital energy, and $\rho(r)$ is the total electronic density. Since Koopmans' theorem justifies regarding the orbital energies as good approximations to the ionization potentials of the respective electrons (6), $\bar{I}(r)$ can be interpreted as the average energy needed to ionize an electron at any particular point in the space of the molecule. Thus, the positions where $\bar{I}(r)$ has its lowest values are the points at which are found, on the average, the highest energy electrons.

In this study, we have computed $\bar{I}(r)$ for a series of benzene

derivatives, **I–IX**, on three-dimensional surfaces encompassing the molecules. These results will be discussed in relation to the experimentally observed reactive behavior of the repective molecules. Understanding and predicting the effects of substituents on electrophilic aromatic substitution reactions has long been an objective of both fundamental and practical interests (7, 8).

Methods and procedure

An *ab initio* SCF-MO approach (GAUSSIAN 82 (9)) has been used to compute 6-31G* wave functions for systems **I–IX**
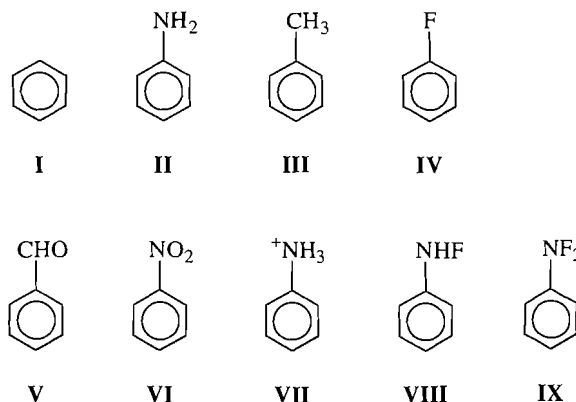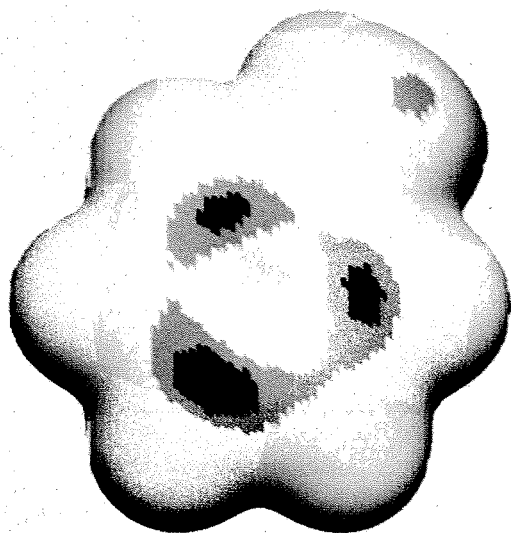
FIG. 1. Calculated $\bar{I}(r)$ on the molecular surface of aniline (**II**). Black is for $\bar{I}(r) < 11.84$ eV; gray is for 11.84 eV $< \bar{I}(r) < 12.11$ eV.
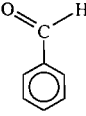
using STO-3G optimized geometries. These wave functions have then been used to calculate $\bar{I}(r)$ (eq. [1]) on the three-dimensional surfaces corresponding to the contour of constant electronic density equal to 0.002 electron/bohr^3. It has been shown, for a group of diatomic molecules and for methane, that this contour gives physically reasonable molecular dimensions, and encompasses at least 95% of the electronic charge (10–12). This surface is defined in terms of a molecular property, the electronic density function $\rho(r)$, and therefore reflects features such as bond formation, lone pairs, etc. that are unique to a molecule. This means of designating a molecular surface is in contrast to earlier methods in which it has been defined as the outer surface of a set of intersecting spheres centered on the nuclei of the molecule (12–22); such surfaces cannot take into account the very properties that are characteristic of a molecule. (This point has also been discussed by Bader *et al.* (23).) We have recently shown that the molecular electrostatic potential computed on the surface defined by the 0.002 contour is useful in studies of recognition interactions (24), and also permits predictions of sites for nucleophilic attack (25); the latter poses problems when two-dimensional plots are used.

Results

Figure 1 shows $\bar{I}(r)$ plotted on the molecular surface of aniline, **II**. The lowest average ionization energies are found above the *ortho* and *para* positions; slightly higher ones are associated with the amine lone pair.

In Table 1 are presented the locations and magnitudes of the smallest $\bar{I}(r)$ values, $\bar{I}_{min}$, for molecules **I–IX**. These are the points at which the least amount of energy is required to remove an electron from the surface; thus these sites are expected to be the most reactive toward electrophiles. (We have verified that there is no significant change in the magnitude of the surface $\bar{I}_{min}$ (less than 1% decrease) when the surface is defined by the 0.001 electrons/bohr^3 contour instead of the 0.002.) Also included in Table 1 is the energy of the highest occupied molecular orbital (HOMO) in each molecule. According to Koopmans' theorem (6), this should represent a good estimate of its ionization potential.

TABLE 1. Calculated 6-31G* $\bar{I}_{min}$ values, HOMO energies and Hammett constants[a] for **I–VIII**

Molecule	$\bar{I}_{min}$ (eV)	HOMO energy (eV)	Hammett constants[a] for substituent	
			σ_p	σ_m
II (NH$_2$)	11.51 (*para*) 11.69 (*ortho*) 11.71 (*ortho*) 12.08 (amine N)	−7.87	−0.57	−0.09
III (CH$_3$)	11.93 (*ortho*) 11.96 (*ortho*) 11.96 (*para*) 12.08 (*meta*) 12.10 (*meta*)	−8.68	−0.14	−0.06
I	12.12 (C)	−9.00	0.00	0.00
IV (F)	12.31 (*para*) 12.44 (*ortho*) 12.45 (*ortho*)	−9.11	0.06	0.34
V (CHO)	12.55 (*meta*) 12.59 (*meta*)	−9.44	0.47	0.41
VI (NO$_2$)	13.03 (*meta*) 13.04 (*meta*)	−9.97	0.81	0.71
VII ($^+$NH$_3$)	16.58 (*para*) 16.59 (*meta*)	−13.59	[b]	[b]
VIII (NHF)	12.22 (*para*) 12.24 (*ortho*) 12.38 (*ortho*)	−8.77	(0.06)[c]	[b]
IX (NF$_2$)	12.73 (*para*) 12.78 (*meta*) 12.81 (*ortho*)	−9.53	(0.49)[c]	(0.54)[c]

[a]Hammett constants are taken from Exner (28).
[b]Hammett constant for $^+$NH$_3$ not available.
[c]Estimated Hammett constants, using correlation shown in Fig. 2.

The minimum values of $\bar{I}(r)$ on the surface of unsubstituted benzene are located above the carbons and have magnitudes of 12.12 eV. The magnitude of the HOMO energy is considerably less, 9.00 eV, and is in good agreement with the experimentally-determined ionization potential of benzene, 9.24 eV (26). This difference between the magnitude of $\bar{I}_{min}$ and the HOMO energy brings out the interesting point that there is quite a significant likelihood of finding inner, more tightly-bound electrons on the molecular surface. Comparison of the magnitude of $\bar{I}_{min}$ and the HOMO energies in Table 1 shows that this is true as well for the other molecules that have been studied.

$\bar{I}_{min}$ values of **II–IV** are found over the *ortho* and *para* positions (Table 1), consistent with the observed *ortho-* and *para*-directing tendencies of NH_2, CH_3, and F (7, 8). In the case of toluene (**III**), there are also minima in $\bar{I}(r)$ above the *meta* positions. These are larger than the *ortho* and *para* values, suggesting a lesser tendency for *meta* substitution. The magnitudes of $\bar{I}_{min}$ relative to that of benzene indicate whether the respective substituents activate or deactivate the benzene ring toward electrophilic attack. Aniline and toluene have $\bar{I}_{min}$ values lower than that of benzene, while those of fluorobenzene are higher. These results are in agreement with the well-known activating effects of NH_2 and CH_3 and the deactivating tendency of F (7, 8).

The surface $\bar{I}_{min}$ of **V** and **VI** are greater than those of benzene, and are above the *meta* positions. These findings reflect the established deactivating and *meta*-directing tendencies of the CHO and NO_2 groups (7, 8).

The substituent NH_3^+ is known to have the interesting property of being a *meta–para* director and to strongly deactivate the benzene ring toward electrophilic substitution (7, 8). Our calculated $\bar{I}_{min}$ for **VII** are fully consistent with these observations, being the largest in Table 1 and located over the *meta* and *para* positions.

Experimental reactivity data are not available for the NHF and NF_2 derivatives of benzene; accordingly our findings for **VIII** and **IX** constitute predictions for the effects of these substituents. The $\bar{I}_{min}$ values of **VIII** are found over the *ortho* and *para* positions, while **IX** shows the feature of having an $\bar{I}_{min}$ over all three types of positions: *ortho*, *meta*, and *para*, as was found for toluene. Our results suggest that the NF_2 group is less specific than the substituents in **II** and **IV–VIII** in directing electrophilic aromatic substitution. The $\bar{I}_{min}$ values of **VIII** are only slightly larger than those of benzene, while those of **IX** are intermediate between those of benzaldehyde (**V**) and nitrobenzene (**VI**) (see Table 1.) These data indicate that NF_2 is a significantly stronger deactivator of the aromatic ring than NHF.

Discussion

Our $\bar{I}(r)$ computations provide position specific predictions for preferred sites of aromatic electrophilic substitution. In addition, the magnitudes of the $\bar{I}_{min}$ values for each molecule (Table 1) are indicative of the relative activating and deactivating tendencies of the various substituents (relative to benzene itself).

The ability of $\bar{I}(r)$ to order the reactivities of **I–VII** led us to investigate the possibility of $\bar{I}(r)$ correlating with the Hammett constants, σ_p and σ_m (27, 28). The latter are established measures of the electron-withdrawing and -donating tendencies of substituents on aromatic rings, with reference to the *para* and *meta* positions. σ_p and σ_m are listed in Table 1 for the substituents in **I–VI**.

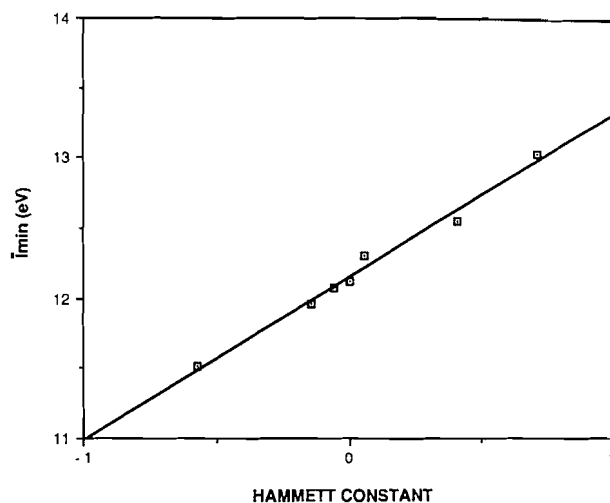We have found an excellent correlation between the Hammett

FIG. 2. Correlation between $\bar{I}_{min}$ and Hammett constants for six aromatic systems. Data are from Table 1. The least squares equation of the line is $y = 12.1547 + 1.1643x$, with a correlation coefficient of 0.99.

constant σ_p or σ_m and the corresponding $\bar{I}_{min}$. The relationship is shown in Fig. 2; the linear correlation coefficient is 0.99. This correlation strongly suggests tht our calculated $\bar{I}_{min}$ values are good indices of the relative electron-withdrawing and -donating effects of substituents on benzene rings.

The correlation shown in Fig. 2 allows us to predict Hammett constants that have not yet been determined. For example, we predict σ_p for NHF to be 0.06 and σ_p and σ_m for NF_2 to be 0.49 and 0.54, respectively. Thus, NF_2 is expected to be a relatively strongly electron-withdrawing substituent, intermediate between CHO and the more powerful electron-attracting CN and NO_2 groups, whereas NHF is apparently, overall, a very weak attracter of electronic charge. (In view of the fact that Hammett's treatment did not include charge substituents, we have not estimated values for NH_3^+.)

We have recently presented a procedure that allows the inductive constant σ_I of a substituent X to be estimated from the calculated molecular electrostatic potential of $X—NH_2$ (29). For X = NF_2, we find σ_I to be 0.53. Since $\sigma_p \approx \sigma_I + \sigma_R$ (28), where σ_R describes resonance effects, then we can also predict that $\sigma_R \approx -0.04$ for NF_2. Our estimated σ_I for NHF is 0.43; a corresponding σ_R value of -0.37 is predicted [σ_R(NHF) $\approx$ 0.06–0.43]. These σ_R predictions for NHF and NF_2 are indicative of NHF being a significantly stronger resonance donor of charge than NF_2; presumably the nitrogen lone pair can more readily be delocalized to the ring when this is opposed by only one fluorine rather than two.

We also investigated $\bar{I}(r)$ at the 3-21G level (using STO-3G geometries) and obtained results generally similar to the 6-31G*. However, the latter basis set provides smoother surface $\bar{I}(r)$ representations and yields a better correlation with the Hammett constants. (The correlation coefficient between $\bar{I}_{min}$ computed at the 3-21G level and the Hammett constants is 0.94, compared to 0.99 for the 6-31G*.) This improvement in our $\bar{I}(r)$ data at the 6-31G* level reflects the nature of the property; $\bar{I}(r)$ depends on the goodness of the densities $\rho_i(r)$ and $\rho(r)$ at any specific point r and therefore improves with a larger, more flexible basis set.

Summary

In this study, we have introduced a new molecular property, $\bar{I}(r)$, the average local ionization energy, and have demonstrated

its usefulness as a guide to chemical reactivity in aromatic systems. $\bar{I}(r)$ is rigorously defined within the framework of self-consistent-field molecular orbital theory and can be interpreted as the average energy needed to remove an electron at any point in space r. Thus those regions where $\bar{I}(r)$ has its smallest values can be viewed as having, on the average, the highest energy electrons, most reactive toward electrophiles.

For a series of aromatic systems, we have computed $\bar{I}(r)$ on molecular surfaces defined by the contour of constant electronic density equal to 0.002 electrons/bohr^3. This surface $\bar{I}(r)$ provides site specific predictions of preferred positions for electrophilic aromatic substitution. The relative reactivities of these systems toward electrophiles increase as the magnitudes of the smallest $\bar{I}(r)$ values ($\bar{I}_{min}$) decrease. An excellent relationship, with a correlation coefficient of 0.99, is found between the Hammett constant σ_p or σ_m and the corresponding $\bar{I}_{min}$. This has allowed us to predict the σ_p and/or σ_m values for the substituents NHF and NF_2.

Acknowledgement

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