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Global and Local Electrophilicity Patterns of Diazonium Ions and Their Reactivity toward π-Nucleophiles

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The global and local electrophilicity patterns of a series of 15 diazonium ions have been evaluated using the absolute scale of electrophilicity proposed by Parr et al. (_J. Am. Chem. Soc._ **1999**, _121_, 1922). The predicted global electrophilicity pattern of the whole series of diazonium ions correctly compares with the experimental electrophilicity recently determined for these charged electrophiles. The global electrophilicity is then projected into the different potential active sites of the molecular ions using the electrophilic Fukui function. The highest regional electrophilicity power is found at the terminal nitrogen atom of the arenediazonium ions, yet the highest positive charge is located on the nitrogen atom directly attached to the aromatic ring. This result is consistent with the observed reactivity displayed by diazonium ions toward substituted alkenes, thereby suggesting that the formation of the azocarbocation intermediate is mostly orbital rather than charge controlled.

1. Introduction

The prediction of the global electrophilicity pattern of positively charged reagents provides useful clues about their reactivity toward neutral or charged nucleophiles. The formation of a covalent bond between a Lewis acid and a Lewis base has been the object of increasing attention from the seminal Ritchie review.[1] Useful classifications in terms of the concepts of softness and hardness introduced by Pearson[2] have been consolidated in the form of empirical reactivity rules such as the HSAB principle.[3] At present, the theoretical models of reactivity based on the density functional theory of Parr and Yang[4] have provided a more precise classification of charged and neutral electrophiles, in terms of electronic reactivity indexes, including the electronic chemical potential μ, the chemical hardness η, and the global softness S.[5] While the electronic chemical potential (the negative of electronegativity[4]) describes the direction and amount of charge transfer during a chemical interaction, the chemical hardness describes the resistance of the system to exchange electronic charge with the environment.[2,4] The electronic chemical potential and the chemical hardness have been given an operational expression in terms of the vertical ionization potential and electron affinity, I and A, respectively, as follows:[4]

$$\mu = -\frac{(I+A)}{2} \tag{1a}$$

and

$$\eta = I - A \tag{1b}$$

It has been recently proposed that the electrophilicity power of atoms and molecules may be conveniently described by a single number, namely, the electrophilicity index defined as[6]

$$\omega = \mu^2/2\eta \tag{2}$$

The concept of electrophilicity proposed by Parr et al. contains two meaningful contributions. On one hand, there is the effect of the square of electronegativity measuring the tendency of the system to acquire an additional amount of electronic charge from the environment, and the contribution from the chemical hardness acting as a resistance to the electronic exchange. In this sense, a good electrophile will be characterized by a high value of the electronic chemical potential and a low value in chemical hardness. Physically, the ω quantity describes the stabilization in total energy when the system acquires a maximum amount of electronic charge given by[6]

$$\Delta N_{max} = -(\mu/\eta) \tag{3}$$

Parr's definition of electrophilicity has been tested for the case of molecular systems coupled to an external field induced by a polarizable continuum environment that mimics solvent effects.[7] For the neutral and charged

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systems it was found that while the global electrophilicity of neutral electrophiles is mostly unaffected by solvation, the effect of the solvent on the electrophilicity power of charged electrophiles is in general lower than the intrinsic gas-phase electrophilicity. This means that the intrinsic (gas-phase) scale would suffice to establish an absolute scale of electrophilicity. This intrinsic absolute scale has been tested against experimental data for small molecules,[8] as well as for the case of larger systems such as benzhydryl cations.[9] An excellent source for experimental values of global electrophilicity is the kinetic scale proposed by Mayr et al.[10−15]

Once the theoretical scale of electrophilicity has been validated against the experimental scales, additional useful information concerning the local electrophilicity patterns may be obtained by extending Parr et al.'s definition.[8,9,16,17] This is readily obtained by using the inverse relationship between hardness and the global softness $S = 1/\eta$. Using the additive rule of global softness, the following definition of local electrophilicity may be obtained:[8,9,16,17]

$$\omega_k^+ = \frac{\mu^2}{2} s_k^+ \qquad (4)$$

where $s_k^+ = f_k^+ S$ is the local electrophilic softness condensed to site k in the molecule and f_k^+ is the electrophilic Fukui function (i.e., the Fukui function for a nucleophilic attack[4]). Using the relationship between local softness and the Fukui function together with the definition in eq 2, one may further write

$$\omega_k^+ = f_k^+ \omega \qquad (5)$$

While eq 4 predicts that the site with highest electrophilicity power will be the softest site in the electrophile, eq 5 predicts that the global electrophilicity will be distributed following the electrophilic Fukui function. Equation 5 also predicts that the maximum value in electrophilic Fukui function corresponds with the most favorable electrophilic site (i.e., the active site of the electrophile).

2. Results and Discussion

To test the theoretical scale of electrophilicity, we selected a series of diazonium ions whose global electrophilicity pattern has been recently evaluated by Mayr et al.[18] The series includes the benzenediazonium ion (**12**)
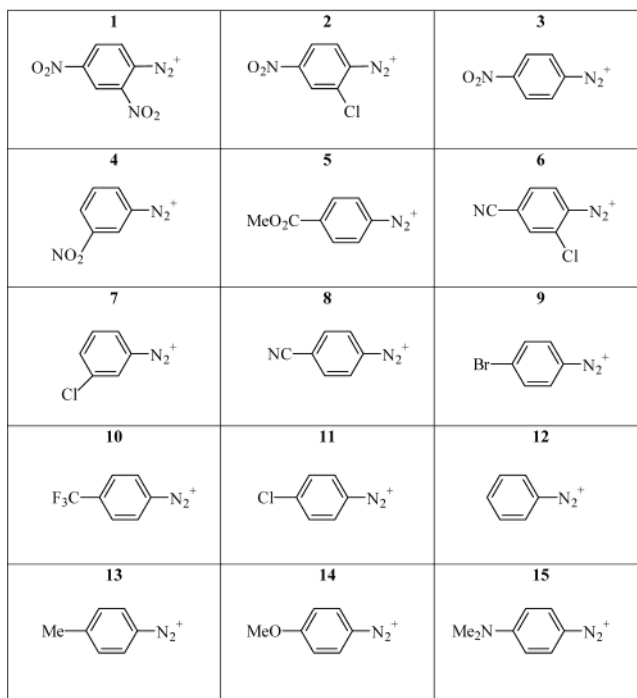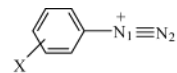

FIGURE 1. Structures of diazonium ions and nitrogen atom numbering.

and a series of substituted derivatives containing a wide variety of electron-withdrawing (**1**−**11**) and electron-releasing (**13**−**15**) groups in the *ortho*- and *para*-positions. Their structures and atom numbering are depicted in Figure 1. All the calculations were performed for the optimized structures at the B3LYP/6-31G(d) level of theory using the GAUSSIAN98 suite of programs.[19] The global electrophilicity values were obtained at the same level of theory using eq 2, with the electronic chemical potential and chemical hardness values obtained from eqs 1a and 1b. The vertical ionization potential and electron affinity, I and A, were approached by Koopmans' theorem, in terms of the one-electron energy levels of the frontier molecular orbitals HOMO and LUMO, respectively. The results of the calculations are reported in Table 1.

It is worth stressing that both scales have an inverse relationship.[9] While within the experimental scale the electrophilicity numbers E are negative, the theoretical quantity ω is definitely positive (see eq 2). In both scales,

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TABLE 1. Electronic Chemical Potential μ, Chemical Hardness η, Electrophilicity Index ω, Experimental Electrophilicity E, Relative Electrophilicity $\Delta\omega$, and Relative Charge Capacity Measured by $\delta\Delta N_{max}$ for the Whole Series of Diazonium Ions

diazonium ion	μ (eV)	η (eV)	ω (eV)	E^a	$\Delta\omega^b$ (eV)	$\delta\Delta N_{max}$
1	−10.82	3.36	17.42	−2.5	5.49	0.900
2	−10.50	3.50	15.77	−3.2	3.84	0.682
3	−10.44	3.46	15.77	−5.1	3.84	0.700
4	−10.40	3.68	14.70	−5.2	2.77	0.508
5	−9.74	3.28	14.47	−6.1	2.54	0.649
6	−10.53	3.88	14.31		2.38	0.396
7	−10.02	3.59	13.98	−6.0	2.05	0.470
8	−10.53	3.98	13.94	−5.5	2.01	0.328
9	−9.81	3.64	13.22	−6.7	1.29	0.377
10	−10.56	4.40	12.67	−5.7	0.74	0.079
11	−10.05	3.99	12.64	−6.6	0.71	0.197
12	−10.26	4.42	11.93	−7.2	0.00	0.000
13	−9.95	4.40	11.27	−7.7	−0.66	−0.055
14	−9.34	4.00	10.91	−8.4	−1.02	0.016
15	−8.46	3.55	10.08	−10.4	−1.85	0.062

[a] Experimental electrophilicity values from ref 18. [b] Relative electrophilicity is measured by $\Delta\omega = \omega$(diazonium ion) $- \omega$(compound 12).
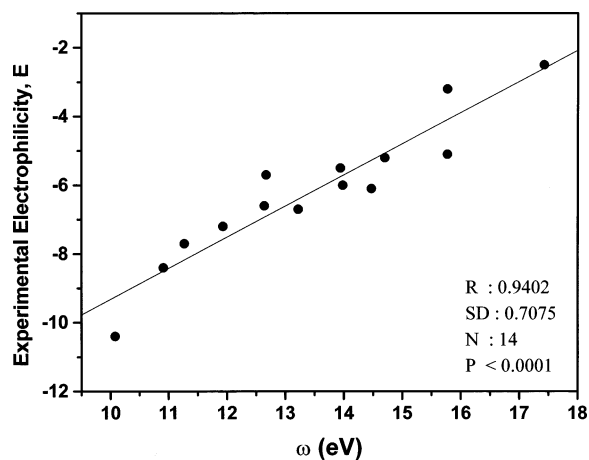

FIGURE 2. Linear correlation between experimental electrophilicity (E) and theoretical global electrophilicity (ω) at the B3LYP/6-31G(d) level of theory. R is the regression coefficient, SD is the standard deviation, N is the number of points, and P is the probability that the observed relationship between the variables was randomly obtained.

however, a big relative value means a higher electrophilicity pattern of the molecule. Figure 2 summarizes a qualitative comparison between the theoretical and experimental scales of global electrophilicity. Both scales qualitatively compare fairly well. The resulting regression equation is $E = -18.38 + 0.906\omega$. This empirical equation may be used for predictive purposes. For instance, the electrophilicity power for compound 6, not evaluated in the experimental database of Mayr et al.,[18] is predicted to be about −5.4 eV. These results give some confidence about the representation of electrophilicity using Parr et al.'s index, and also reinforce the reliability of this reactivity index that was already demonstrated for the case of benzhydryl cations.[9]

On the basis of the theoretical scale, we may discuss the global electrophilicity pattern of molecules in terms of electronic information, including inductive effects promoted by chemical substitution. For instance, the

reference compound 12 in Table 1 displays a global electrophilicity of 11.93 eV. It is predicted to be the hardest species within the series. Compounds 13−15 appear as electrophilically deactivated with respect to the reference compound 12 ($\Delta\omega < 0$; see Table 1, sixth column). This result may be traced to the electron-releasing effect of Me, MeO, and Me₂N groups at the *para*-position in the phenyl ring. Compounds 1−11 exhibit, on the other hand, electrophilic activation ($\Delta\omega > 0$) promoted by the electron-withdrawing inductive effect of the NO₂, MeO₂C, CN, Cl, CF₃, and Br groups at the 2,4-positions in the aromatic ring. Note that chemical substitution by NO₂ at the 2,4-positions of the aromatic ring in compound 1 dramatically increases the electrophilicity pattern with respect to the reference compound 12. These results are in agreement with the experimental scale of Mayr et al.[18] Replacement of a Cl atom by a NO₂ group in compound 1 decreases the electrophilicity power with reference to compound 1. Replacement of a Cl atom in the *ortho*-position, on the other hand, predicts the electrophilicity to be almost invariant, independent of the substituent at the *para*-position (compare for instance compounds 2 and 3 and 6 and 8). Note also that a NO₂ group in the *para*-position is predicted to have a more significant electrophilic activation than a CN group at the same position (compare for instance compounds 2 and 6 and 3 and 8).

On the other hand, it is possible to quantitatively establish the inductive effect of the substituents at the aromatic ring of the diazonium ions. We analyze this effect within a simplified model of electrostatic inductive effects. It is based on eq 3 describing the responses in the maximum electronic charge that the ion may accept from the environment. If we define

$$\delta\Delta N_{max} = \Delta N_{max}\text{(diazonium ion)} - \Delta N_{max}\text{(compound 12)} \quad (6)$$

then eq 6 describes the change in the maximum charge capacity of the cation. The results are shown in the last column of Table 1. It may be observed that electron-withdrawing groups in compounds 1−11 induce an increase of the charge capacity of the cation, whereas the presence of electron-releasing groups (compounds 13−15) induces a marginal variation of the charge capacity of the electrophile.

As stated before, the availability of absolute reactivity scales, based on descriptors of the electronic structure, opens the possibility of characterizing the semilocal or regional reactivity patterns within a molecule. This is the case for the local electrophilicity index defined in eqs 4 and 5. Using an approximate method to evaluate the electrophilic Fukui function described elsewhere,[20,21] we obtained the electrophilic Fukui functions f_k^+ condensed to atom k and the corresponding projected local electrophilicity ω_k^+ via eq 5. For instance, the active sites (i.e., the sites with the largest values in local electrophilic Fukui function) for nucleophilic additions are the N1 and N2 sites of the diazonium ions. The results are sum-

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TABLE 2. Electrophilic f_k^+ and Nucleophilic f_k^- Fukui Functions, Electronic Population Q at N1 and N2 Sites of Diazonium Ions, and the Local Electrophilicity ω_{N1}^+ and ω_{N2}^+ [a]

diazonium ion	$f_{N_1}^+$	$f_{N_2}^+$	$Q(N_1)$	$Q(N_2)$	ω_{N1}^+ (eV)	ω_{N2}^+ (eV)
1	0.1609	0.2927	0.1230	0.0238	2.80	5.10
2	0.1917	0.3147	0.1133	0.0041	3.02	4.96
3	0.2046	0.3284	0.1315	−0.0012	3.23	5.18
4	0.2260	0.3539	0.1320	−0.0043	3.32	5.20
5	0.2130	0.3346	0.1240	−0.0213	3.08	4.84
6	0.1896	0.3118	0.1072	−0.0045	2.71	4.46
7	0.2298	0.3557	0.1304	−0.0124	3.21	4.97
8	0.2017	0.3243	0.1228	−0.0114	2.81	4.52
9	0.2125	0.3318	0.1132	−0.0295	2.81	4.39
10	0.2233	0.3494	0.1286	−0.0110	2.83	4.43
11	0.2139	0.3343	0.1167	−0.0239	2.70	4.23
12	0.2301	0.3541	0.1283	−0.0185	2.74	4.22
13	0.2232	0.3427	0.1163	−0.0324	2.52	3.86
14	0.2131	0.3243	0.0958	−0.0513	2.32	3.54
15	0.1983	0.2991	0.0715	−0.0807	2.00	3.01

[a] See the text for details.

TABLE 3. Electronic Chemical Potential μ, Chemical Hardness η, Electrophilicity Index ω, and the Nucleophilic Fukui Function f_k^- at the C1 and C2 Sites of Some Substituted Alkenes

substituted alkene C1(R1R2)=C2(R3R4)	μ (eV)	η (eV)	ω (eV)	f_{C1}^-	f_{C2}^-
1. $CH_2=CHCH_3$	−3.01	7.57	0.60	0.5063	0.4034
2. $CH_2=CH(CH_2)_3CH_3$	−3.00	7.48	0.60	0.4924	0.3772
3. cis-$CH_3CH=CHCH_3$	−2.77	7.17	0.53	0.4288	0.4197
4. $trans$-$CH_3CH=CHCH_3$	−2.70	7.38	0.49	0.4166	0.4166
5. $CH_2=C(CH_3)_2$	−2.84	7.37	0.55	0.5186	0.3452
6. $CH_2=C(CH_3)(CH_2CH_3)$	−2.85	7.32	0.56	0.5153	0.3399
7. $CH_2=C(CH_3)(CH(CH_3)_2)$	−2.83	7.34	0.55	0.5143	0.3360
8. $CH_2=C(CH_3)(C(CH_3)_3)$	−2.83	7.36	0.55	0.5146	0.3373
9. $CH_2=C(CH_3)(CH_2CH_2CH_3)$	−2.84	7.30	0.55	0.5112	0.3331
10. $CH_2=C(CH_3)(CH_2C(CH_3)_3)$	−2.89	7.13	0.59	0.4962	0.3208
11. $CH_3CH=C(CH_3)_2$	−2.55	7.17	0.45	0.4343	0.3635
12. $(CH_3)_2C=C(CH_3)_2$	−2.46	6.94	0.43	0.3818	0.3818

marized in Table 2, together with the Mulliken population analysis at the same N1 and N2 sites. It may be seen that while the positive atomic charge appears to be condensed on the N1 site, the largest values in the electrophilic Fukui function are preferentially located on the terminal N2 center. This makes the N2 site significantly more electrophilic than the N1 site.

To test the usefulness of the local electrophilicity index, we examined the nucleophilic addition reactions of diazonium ions to a series of substituted alkenes (π-nucleophiles) shown in Table 3. In this case, the most favorable interaction will be that of the terminal N2 site of the diazonium ion with the more nucleophilic site of the alkene. Therefore, if the electrophile−nucleophile interaction is hard, then the active sites for the C−N bond making process will be the N1 site of the diazonium ion and the hardest site of the alkene. The nucleophilicity pattern of alkenes is in general lower than that presented by charged nucleophiles, and these molecules are expected to behave as soft nucleophiles. This means that the more favorable local interaction will be between the more nucleophilic center of the alkene and the most electrophilic and softest site of the diazonium ion, namely, the N2 site. This prediction is in agreement with the local reactivity pattern exhibited by the diazonium ions toward the electrophilic addition to substituted alkenes to form

SCHEME 1. Mayr et al. Proposal for the Formation of the Azocarbocation in the Addition Reaction of Diazonium Ions to Alkenes[18]
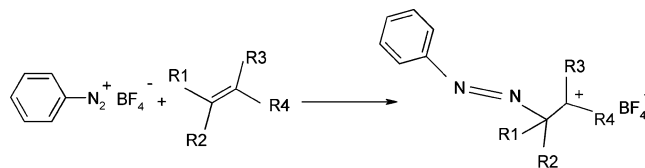
the azocarbocation intermediates proposed by Mayr et al.,[15] which is shown in Scheme 1. The formation of the azocarbocation intermediate is therefore predicted to be more orbital controlled rather than charge controlled. In the absence of a precise definition of local nucleophilicity, we will assume that the most nucleophilic site at the nucleophile moiety will be the one presenting the highest value of the Fukui function for an electrophilic attack, f_k^-. For instance, the best site for the formation of the azocarbocation will be the one which is consistent with the Markovnikov regioselectivity rule,[22] i.e., the less substituted site. Table 3 contains the local nucleophilicity patterns for this series of alkenes as described by the f_k^- index. Note that the Markovnikov sites (C1 center) present the largest values of local nucleophilicity described by the nucleophilic Fukui function f_k^-. This reactivity pattern is in agreement with the intermediate azocarbocation proposed by Mayr et al.[18]

3. Concluding Remarks

The global electrophilicity pattern of a series of diazonium ions as described by the global electrophilicity index introduced by Parr et al. compares fairly well with the kinetic scale of electrophilicity proposed by Mayr et al. The electrophilicity hierarchy in both scales seems to be in agreement with the expected inductive effects promoted by the functional groups attached to the aromatic ring. The availability of an absolute theoretical scale of electrophilicity permits the identification of the more electrophilic sites in the molecule. This is easily achieved by using the condensed Fukui function to project the electrophilic potential of the different atoms in the molecule. Both the global and local information may then be used to explain (and hopefully) to predict the most probable kinetic products in an electrophile−nucleophile interaction. This has been illustrated for the nucleophilic addition of a series of diazonium ions (electrophiles) to a series of substituted alkenes (π-nucleophiles). These reactions are predicted to be mostly orbital rather than charge controlled.

Supporting Information Available: Optimized geometries of the whole series of diazonium ions and substituted alkenes in the **Z** matrix format. This material is available free of charge via the Internet at http://pubs.acs.org.

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