

Electrophile Affinity: A Reactivity Measure for Aromatic Substitution

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Abstract: The reactivity and regioselectivity of the electrophilic chlorination, nitration, and alkylation of benzene derivatives were rationalized by comparing literature data for the partial rate factors ($\ln f$) for these S_EAr processes with theoretical reactivity parameters. The *Electrophile Affinity* ($E\alpha$), a new quantity, is introduced to characterize reactivity and positional selectivity. $E\alpha$ is evaluated theoretically by the energy change associated with formation of an arenium ion by attachment of a model electrophile to the aromatic ring. The dependence between $E\alpha$ and $\ln f$ values for chlorination for 11 substitutions of benzene and methyl benzenes had a high correlation coefficient ($r = 0.992$). Quite satisfactory correlations between $E\alpha$ values and partial rate factors also were obtained for the nitration of substituted benzenes ($r = 0.971$ for 12 processes) and benzylation of benzene and halobenzenes ($r = 0.973$ for 13 processes). These results provide clear evidence for the usefulness of the electrophile affinity in quantifying reactivity and regiochemistry. Satisfactory relationships ($r > 0.97$) also were found between EPN (electrostatic potential at nuclei) values, which reflect the variations of electron density at the different arene ring positions, and the experimental partial rate factors ($\ln f$) for the chlorination and nitration reactions, but not for the benzylation. This discord is attributed to strong steric influences on the reaction rates for substitutions involving the bulky benzyl moiety.

Introduction

Despite numerous experimental and theoretical attempts to elucidate the principal factors governing the rates and regioselectivity of the electrophilic substitutions of arenes (S_EAr), a consistent reactivity treatment has not been achieved.^{1–30}

Experimental data show that the rates of S_EAr processes can be associated with the stability of the intermediate σ complexes,^{1–13} the formation of which, in most cases, has been established to be the rate-controlling step.^{1–13} Hence, the σ complex is the crucial intermediate governing reactivity and regioselectivity.^{1–3} Key organic chemical concepts have been based on the reactivities and positional selectivities in S_EAr reactions. These include inductive through-bond and through-space field effects, the resonance (or mesomeric) effect, and the ortho effect and other intramolecular influences. Hammett's^{31,32} equations quan-

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tifying the relationships between structure and site reactivity in aromatic systems, based on linear free energy relationships and substituent constants, have influenced chemistry profoundly.

Electronic structure theory provides effective tools for studying chemical interactions and for describing the properties of reacting species. Electrophilic aromatic substitutions have been used as model reactions to test frontier orbital characterizations of chemical reactivity.^{14,15} Many theoretical approaches, applied to analyze the factors determining reactivity and regioselectivity of various S_EAr processes,^{14–30} have contributed to a deeper understanding of their mechanisms. Nevertheless, no definitive theory of electrophilic aromatic substitution reactivity has emerged. Hirao and Ohwada's²⁹ recent analysis of arene mercuration, nitration, chlorination, and protodetrifiation reactivity emphasized that a single frontier orbital (HOMO) cannot account for the regioselectivities. They showed that a new RHO (Reactive Hybrid Orbital) index accounts for the reactivity more accurately. The RHO index reflects the interaction between a model electrophile (H⁺) and the frontier orbitals of the arenes.

A detailed understanding of S_EAr processes requires elucidation of the relationship between the electronic structure of an arene and its reactivity at the various possible positions. Epiotis and Shaik's¹⁶ investigation of the qualitative potential energy surfaces of arene substitution reactions concluded that the regiochemistry of S_EAr processes is related to the electron density distributions of the highest occupied arene MO. Bader and Chang²⁵ employed the atoms-in-molecule theoretical approach to seek links between the electronic structure of arenes and their S_EAr reactivity and regioselectivity. The results suggested that the ability of polar substituents to activate or deactivate the phenyl ring cannot be associated with the total charge on the ring or the partial charges at the constituent atoms. Much more complex relationships between reactivity and the π -electronic populations as well as the quadrupole moment of the ring carbon atoms were established. Politzer et al.^{21,22} showed that the molecular electrostatic potential of substituted arenes can be employed in characterizing the activation or deactivation of aromatic rings toward electrophilic attack.

Reactivity indices based on density functional theory (DFT)^{33,34} offer alternative descriptions of chemical reactions. Zhou and Parr²⁶ employed their "activation hardness" concept to predict regioselectivity in electrophilic aromatic substitutions. The "activation hardness," defined as the difference in hardness between the aromatic reactant and the Wheland-like transition state, correlated qualitatively with Hammett σ^+ constants. Geerlings and co-workers^{19,20} applied their "local hardness index" (based on properties of the initial arene reactants), to quantify reactivity in S_NAr processes. The "local hardness" could be approximated by the partial charge at each ring carbon atom. Fuster et al.²⁸ used a topological analysis of the electron localization function to partition the molecular space of arenes. Domains of increased electron density are more effective in attracting electrophiles in S_NAr reactions. However, correlations of the orientation effects of polar substituents with the σ^+ constants were only qualitative.

McKelvey et al.²⁴ found that theoretically evaluated proton affinities of arenes link linearly to σ^+ substituent constants.

Wang and Streitwieser¹⁸ extended the analysis to the reaction of protodetrifiation of condensed aromatic hydrocarbons and established analogous relationships between proton affinities and the positional selectivity of the arenes. Olah¹⁰ and Ridd¹¹ emphasized that the reaction rates of S_NAr processes can be related to the stabilities of the intermediate complexes. All of these studies emphasize that properties of the reaction intermediates, rather than those of the initial aromatic substrates, are of key importance in determining reactivity.

Many questions concerning the factors governing S_NAr reactivities still arise. Can reactivity and regioselectivity be associated with the static charge distribution in the initial arenes? Do the frontier MOs really play a role? Is reactivity dominated by the energetic stability of the intermediate π and σ complexes? The present research assesses these alternative possibilities employing results from electronic structure computations to examine reactivities in a classical S_EAr reaction: the chlorination of benzene and a series of its methyl derivatives. Based on the results, the reactivity and regioselectivity in two more S_EAr processes—the nitration of variously substituted benzenes and the benzylation of benzene and halobenzenes—were characterized theoretically.

Our recent studies of charge-controlled chemical interactions^{36–42} involving hydrogen bonding,^{36–38} solvolytic reactions of amides and esters,^{39,40} and S_N2 reactions of benzyl halides⁴¹ established that the electrostatic potential at nuclei (EPN) (which reflect the electron density at different arene ring positions) can function as an excellent local reactivity index. EPN also was employed in an efficient computational procedure for evaluating substituent constants.⁴² The EPN approach also might provide a method for determining sigma constants for particular ring positions in polysubstituted and polycondensed arenes. Hence, we applied EPN as a probe of electron densities at different ring positions in arenes, specifically analyzing their reactivities in the S_EAr processes. The reactions studied were characterized further by the energies required to form the intermediate complexes as well as by additional electronic parameters.

Theoretical Methods

All geometries were optimized at the B3LYP^{43–45}/6-311+G-(2d,2p) level,^{46,47} as implemented in Gaussian 03⁴⁸ (fully optimized Cartesian coordinates and energies are included in the Supporting Information). Harmonic vibrational frequencies characterized the nature of all optimized structures. Chlorination S_EAr reactions

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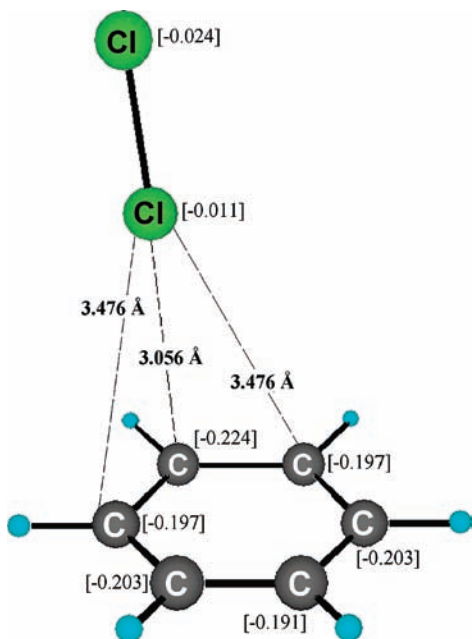


Figure 1. Optimized structure and NBO atomic charges of the benzene–Cl₂ π complex (C_5 symmetry) at B3LYP/6-311+G(2d,2p).

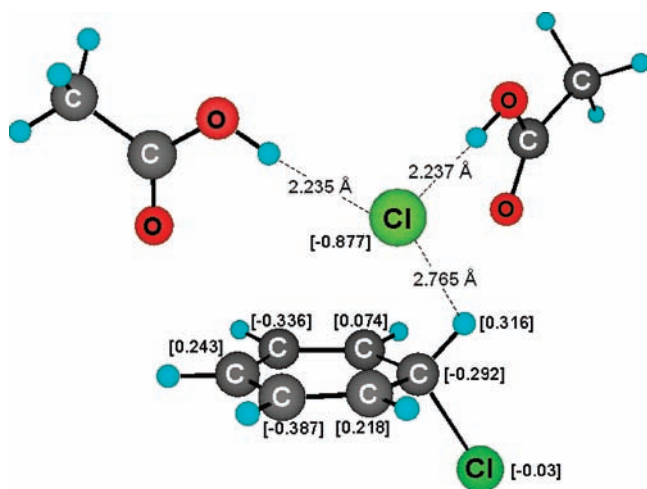
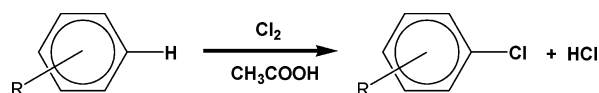


Figure 2. Optimized structure and NBO atomic charges of the benzene–chlorine σ complex with two acetic acid molecules (computed at HF/6-311+G(d,p)).

precede first through intermediate π complexes (see Figure 1) and then σ complexes (Figure 2 shows the latter solvated by two acetic acid molecules). The benzene–Cl₂ π complex (Figure 1) was optimized with a C_5 symmetry constraint starting with the chlorine molecule situated perpendicular over the arene ring center. Other arene–Cl₂ π complexes were optimized without symmetry constraint starting from similar initial geometries. The benzene–Cl₂ σ complex, with two acetic acid molecules, was optimized at the HF/6-311+G(d,p) level (Figure 2).

Electrostatic potentials (V_C)^{49,50} and natural bond orbital (NBO) charges^{51,52} of the S_EAr reaction centers also were computed at the B3LYP/6-311+G(2d,2p) level. Unlike charges, which depend strongly on their definition and additional approximations, V_C values reflect the variations of electron densities at particular nuclear sites rigorously. More negative V_C values indicate greater electron densities. Politzer⁵⁰ has employed eq 1 to define the electrostatic potential at a particular nucleus (Y) positioned at \mathbf{R}_Y by eq 1 (in

Scheme 1. Chlorination S_EAr Reactions for Benzene, Toluene, 1,2-Dimethylbenzene, 1,3-Dimethylbenzene, 1,4-Dimethylbenzene, 1,3,5-Trimethylbenzene, 1,2,4,5-Tetramethylbenzene, and Pentamethylbenzene



atomic units; bold font denotes vector quantities), in which the singular term $\mathbf{R}_A = \mathbf{R}_Y$ has been excluded:

$$V_Y \equiv V(\mathbf{R}_Y) = \sum_{A(\neq Y)} \frac{Z_A}{|\mathbf{R}_A - \mathbf{R}_Y|} - \int \frac{\rho(\mathbf{r})}{|\mathbf{r} - \mathbf{R}_Y|} d\mathbf{r} \quad (1)$$

In this relationship, Z_A is the charge on nucleus A with radius vector \mathbf{R}_A , and $\rho(\mathbf{r})$ is the electron density function.

Results and Discussion

The performance of various reactivity/regioselectivity index candidates—electrophile affinities ($E\alpha$), electrostatic potentials at the reaction nucleus (EPN), and NBO charges of the initial arene reactants—was examined, based on correlations with experimentally derived partial rate factors (\mathbf{f})^{1,35,56} of representative S_EAr arene chlorination, nitration, and benzylation reactions. All partial rate factors for particular ring positions were scaled to fit the overall relative rates.^{1,54} The electrophile affinity ($E\alpha$), first introduced here, is the energy change (eq 2) associated with formation of an arenium ion σ -complex from the initial arene and electrophile at the reacting carbon center.

$$E\alpha = [E_{\text{Arene}} + E_{\text{Electrophile}}] - E_{\text{Arenium ion}} \quad (2)$$

We considered data for 11 chlorinations involving eight methyl benzene derivatives (Scheme 1). In addition, 12 nitrations and 13 benzylation were evaluated for benzene and other monosubstituted benzenes.

Electrophile Affinity ($E\alpha$). The electrophile affinities ($E\alpha$) of the arenes at various distinguishable positions correlate remarkably well with the experimental partial rate factors $\ln \mathbf{f}$ for chlorination ($r = 0.992$; see also Table 1, Figure 3). Note that $E\alpha$ values are “regiospecific” and, thus, are different for the ortho, para, and meta positions of toluene and the distinguishable positions of *o*-, *p*-, and *m*-xylene (Table 1). The very good correlation between $E\alpha$ and $\ln \mathbf{f}$ is understandable, as the energies of the sigma complexes dominate the variations of both $E\alpha$ and $\ln \mathbf{f}$ values. While the energies of the arenes and electrophiles also are employed in computing $E\alpha$'s, their influence is far less important. The arene ground states are identical for the regiospecific cases above. If the same idealized electrophile is used (e.g., the singlet Cl⁺ cation, the nitronium ion NO₂⁺, and the benzyl cation employed in the present study), its energy is constant in each of the $E\alpha$ evaluations for chlorination, nitration, and benzylation, respectively. Although experimental $\ln \mathbf{f}$ values are influenced strongly by the nature of the electrophiles, the choice of the electrophile model

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Table 1. Proton Affinities (PAs) and Electrophile Affinities ($E\alpha$) (Singlet Cl^+ Ion) of Methyl Arenes, And Their Experimental Partial Rate Factors ($\ln f$) for Chlorination (All Computations Performed at the B3LYP/6-311+G(2d,2p) Level)

reactants	position of Cl^+ attachment	PA [kcal mol ⁻¹]	$E\alpha$ [kcal mol ⁻¹]	$\ln f^a$
benzene	1	182.4	183.7	0
toluene	2	189.7	192.0	6.4
	4	191.2	193.6	6.7
1,2-dimethylbenzene	3	192.6	194.6	7.9
	4	193.9	196.7	8.2
1,3-dimethylbenzene	2	196.3	199.0	12.6
	4	197.8	200.9	12.9
1,4-dimethylbenzene	2	193.0	195.8	8.0
1,3,5-trimethylbenzene	2	203.7	206.9	17.9
1,2,4,5-tetramethylbenzene	3	201.0	203.5	15.4
pentamethylbenzene	6	207.6	210.9	20.5
correlation coefficient (r)		0.999^b	0.992^c	

^a Partial rate factors were evaluated from the experimental rate constants of ref 35 using the procedure described in refs 1 and 54.

^b Correlation coefficient for the relationship between $E\alpha$ and PA.

^c Correlation coefficient for the relationship between $E\alpha$ and $\ln f$.

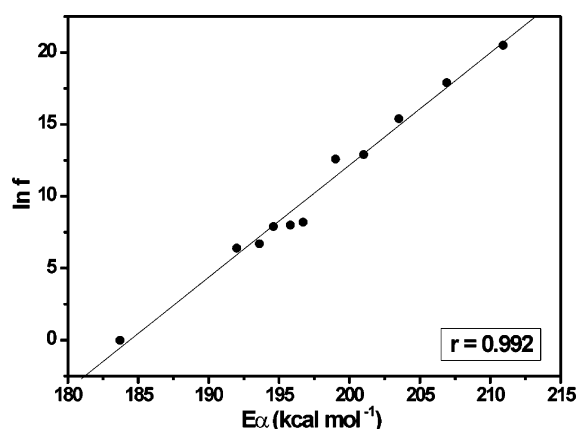


Figure 3. Partial rate factor ($\ln f$) vs electrophile affinity ($E\alpha$) plot for the chlorination of benzene and methyl benzenes.

Table 2. Electrophile Affinities ($E\alpha$), Electrostatic Potentials at the Reacting Carbon Atoms (V_C), NBO Charges q_C (NBO) of Benzene and Various Substituted Benzenes, and Their Experimental Partial Rate Factors ($\ln f$) for Nitration (All Computations Performed at the B3LYP/6-311+G(2d,2p) Level)

reactants	position of NO_2^+ attachment	$E\alpha$ [kcal mol ⁻¹]	V_C (reactant)+401 (volts)	q_C (NBO) (electrons)	$\ln f^a$
benzene	1	30.89	-1.069	-0.204	0.0
nitrobenzene	3	13.84	-0.229	-0.196	-15.6
	4	13.03	-0.170	-0.170	-18.7
toluene	3	35.17	-1.158	-0.196	0.7
	4	40.92	-1.210	-0.213	3.9
<i>tert</i> -butylbenzene	3	39.28	-1.202	-0.195	1.3
	4	44.27	-1.238	-0.212	4.1
chlorobenzene	3	24.26	-0.672	-0.187	-7.1
	4	32.61	-0.768	-0.208	-2.0
bromobenzene	3	25.02	-0.699	-0.186	-6.9
	4	33.34	-0.817	-0.206	-2.3
fluorobenzene	4	31.49	-0.869	-0.221	-0.3
correlation coefficient (r)^b		0.971	0.971	0.749	

^a From refs 6 and 58. ^b Correlation coefficients for relationships with $\ln f$.

employed computationally is immaterial since comparisons are based on computed relative $E\alpha$'s. Thus, $E\alpha$'s and proton affinities (PAs) track each other well ($r = 0.999$, see Table 1). This is the limiting case, since there are no strong interactions (steric or electronic) between the attached electrophile and the

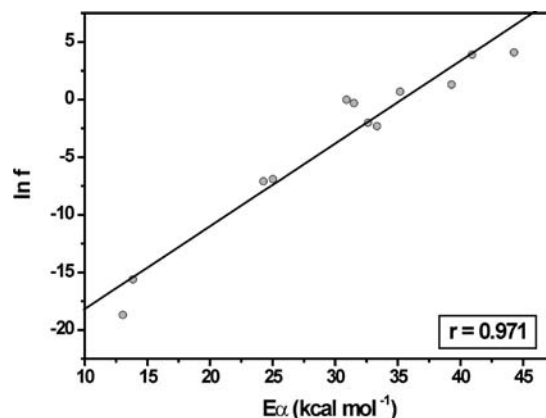


Figure 4. Partial rate factor ($\ln f$) vs electrophile affinity ($E\alpha$) plot for the nitration of benzene and substituted benzenes.

Table 3. Electrophile Affinities ($E\alpha$), Electrostatic Potentials at the Reacting Carbon Atoms (V_C) and NBO Charges q_C (NBO) of Benzene and Halobenzenes, And Their Experimental Partial Rate Factors ($\ln f$) for Benzylation (All Computations Performed at the B3LYP/6-311+G(2d,2p) Level)

reactants	position of $C_6H_5CH_2^+$ attachment	$E\alpha$ [kcal mol ⁻¹]	V_C (reactant)+401 (volts)	q_C (NBO) (electrons)	$\ln f^a$
benzene	1	6.1	-1.069	-0.204	0.0
fluorobenzene	2	5.9	-0.767	-0.268	-1.6
	3	0.1	-0.694	-0.185	-5.9
	4	6.9	-0.869	-0.221	0.9
chlorobenzene	2	5.7	-0.653	-0.227	-1.4
	3	0.7	-0.672	-0.187	-5.4
	4	6.8	-0.768	-0.208	0.0
bromobenzene	2	5.8	-0.554	-0.230	-1.7
	3	1.1	-0.699	-0.186	-5.6
	4	7.0	-0.817	-0.206	-0.3
iodobenzene ^b	2	6.3	-0.611	-0.232	-1.4
	3	1.9	-0.666	-0.187	-5.1
	4	7.8	-0.729	-0.203	0.1
correlation coefficient (r)^c		0.973	0.463	0.531	

^a The partial rate factors were evaluated from the experimental data of refs 60 and 61 using the procedure described in ref 1. ^b For iodobenzene, separate basis sets were used for the carbon and hydrogen atoms (6-311+G(2d,2p)) and for the iodine atoms (DGDZVP for iodine). ^c Correlation coefficient for relationships with $\ln f$.

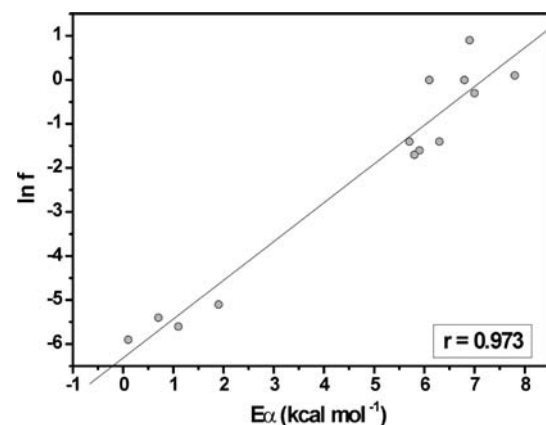


Figure 5. Partial rate factor ($\ln f$) vs electrophile affinity ($E\alpha$) plot for the benzylation of benzene and halobenzenes.

arenes. But in other cases where strong intramolecular steric or electronic interactions involving the attached electrophile in the σ -complex exist, computed $E\alpha$'s are not expected to correlate

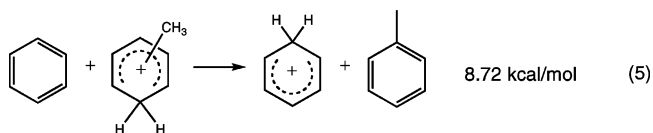
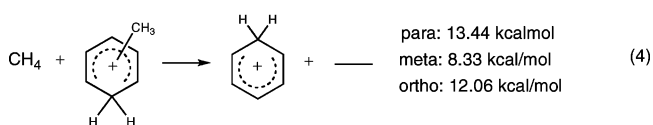
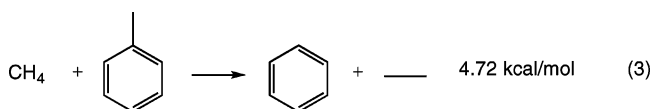
Table 4. Electrostatic Potentials at the Reacting Carbon Atoms (V_C) and NBO Charges q_C (NBO) of Methyl Arenes, And Their Experimental $\ln f$ Values for Chlorination (All Computations Performed at the B3LYP/6-311+G(2d,2p) Level)

reactants	position of chlorination	V_C (reactant)+401 (volts)	q_C (NBO) (electrons)	$\ln f^a$
benzene		-1.069	-0.204	0.0
toluene	2	-1.225	-0.206	6.4
	4	-1.210	-0.213	6.7
1,2-dimethylbenzene	3	-1.310	-0.199	7.9
	4	-1.298	-0.205	8.2
1,3-dimethylbenzene	2	-1.372	-0.209	12.6
	4	-1.359	-0.215	12.9
1,4-dimethylbenzene	2	-1.307	-0.197	8.0
1,3,5-trimethylbenzene	2	-1.500	-0.218	17.9
1,2,4,5-tetramethylbenzene	3	-1.521	-0.194	15.4
pentamethylbenzene	6	-1.686	-0.201	20.5
correlation coefficient (r)^b		0.972	0.101	

^a $\ln f$ values were evaluated from the experimental rate constants of ref 35 using the procedure described in refs 1 and 54. ^b Correlation coefficients for relationships with $\ln f$.

with PAs. Thus, $E\alpha$'s offer a more general treatment of electrophilic reactivity and the possibility of analyzing reactivity trends for S_EAr reactions involving different electrophiles.

When $E\alpha$ and $\ln f$ of different arenes are compared, the energetic and reactivity effects of methyl substitution are far greater on the charged sigma complex than on the parent arenes. For example, the methyl hyperconjugation stabilization is much less for benzene (4.7 kcal/mol, see eq 3) than for protonated benzene (13.4 kcal/mol, see eq 4). Equation 5 assesses the PA difference between benzene and toluene (8.8 kcal/mol; based on the most favorable para position). As the sigma complexes are generally good models for the reaction transition states, the same analysis applies to reactivity; $\ln f$ is larger when more methyl groups are present since these stabilize the charged transition state more than the neutral arene ground state.



The correlation coefficients of $E\alpha$ values with the respective $\ln f$ value, for nitration^{6,57,58} ($r = 0.971$, see Table 2, Figure 4)

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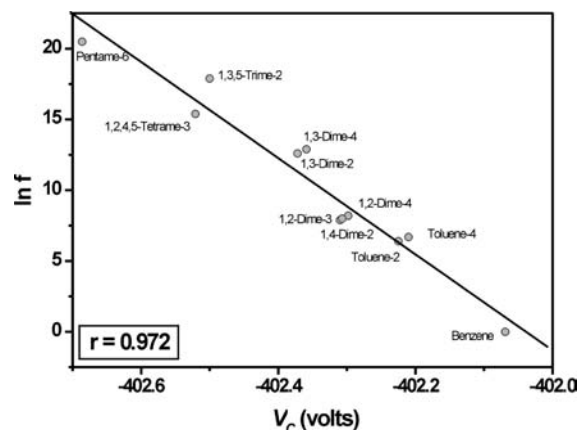


Figure 6. Partial rate factor ($\ln f$) vs electrostatic potential at the reaction carbon center (V_C) plot for the chlorination of benzene and methyl benzenes. Abbreviations of the methyl derivatives and the position of substitution are given at each point.

Table 5. Methyl Arene- Cl_2 π Complex Formation Energies and Relative Rates (RR) (Compared to Benzene) Computed at B3LYP/6-311+G(2d,2p)

reactant	$E_{\pi \text{ complex}}$ [kcal mol ⁻¹]	relative rate (RR) ^a	$\ln \text{RR}$
benzene	-1.2	1	0
toluene	-1.5	340	5.8
1,2-dimethylbenzene	-1.8	2030	7.6
1,3-dimethylbenzene	-2.1	180 000	12.1
1,4-dimethylbenzene	-1.8	2000	7.6
1,3,5-trimethylbenzene	-2.5	30 000 000	17.2
1,2,4,5-tetramethylbenzene	-2.6	1 580 000	14.3
pentamethylbenzene	-2.6	134 000 000	18.7
correlation coefficient (r)^b	0.972		

^a From ref 35. ^b Correlation coefficient for the relationship between $E_{\pi \text{ complex}}$ and $\ln \text{RR}$.

and for benzylation^{60,61} ($r = 0.973$, see Table 3, Figure 5), also are quite satisfactory.

Electrostatic Potentials at Nucleus (EPN). Electron densities at individual ground state ring positions could anticipate the increase in electron density during bond formations of the electrophilic reactions; these are reflected rigorously by computed electrostatic potentials at the nucleus (EPN) of the reaction carbon centers (V_C). Unlike charges, V_C values do not depend on additional approximations. The V_C 's for the methyl benzenes correlate quite satisfactorily with their $\ln f$ values for chlorination ($r = 0.972$, Table 4, Figure 6). Only small exceptions are noted when the data in Table 4 are examined in detail. The ortho position of toluene has the higher V_C , but the reactivity ($\ln f$ value) for the para position is greater. The same discrepancies exist for the 3- and 4-positions of 1,2-dimethylbenzene and the 2- and 4-positions of 1,3-dimethylbenzene (Table 4). These disagreements are logically rationalized by ortho steric effects, which are not accounted for by electron densities. Hence, the V_C values at the reaction centers of the various arenes correlate satisfactorily with the experimental $\ln f$ values for nitration ($r = 0.971$; Table 2) but not for benzylation ($r = 0.463$, Table 3). However, V_C values differentiate correctly the reactivities of meta and para positions for all examples in Table 2 and

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Table 6. HOMO and LUMO Orbital Energies, HOMO–LUMO Gaps and the Relative Chlorination Rates for Methyl Arenes (All Computations Performed at B3LYP/6-311+G(2d,2p))

reactant	HOMO [eV]	LUMO [eV]	HOMO–LUMO gap [eV]	relative rate (RR) ^a	ln RR
benzene	−7.076	−0.472	−6.604	1	0
toluene	−6.741	−0.429	−6.311	340	5.8
1,2-dimethylbenzene	−6.558	−0.283	−6.275	2030	7.6
1,3-dimethylbenzene	−6.554	−0.354	−6.200	180 000	12.1
1,4-dimethylbenzene	−6.445	−0.395	−6.050	2000	7.6
1,3,5-trimethylbenzene	−6.482	−0.260	−6.221	30 000 000	17.2
1,2,4,5-tetramethylbenzene	−6.133	−0.146	−5.987	1 580 000	14.3
pentamethylbenzene	−6.087	−0.072	−6.015	134 000 000	18.7
correlation coefficient (<i>r</i>)^b	0.857	0.858	0.758		

^a Taken from ref 35. All reaction rates given are relative to that of benzene. ^b Correlation coefficients for relationships with ln RR values.

reproduce the general polymethylbenzene order (Table 4, Figure 6). The substituent perturbations (range of V_C values) are larger in these cases.

In addition to possible steric effects, the deviant V_C vs ln **f** benzylation behavior (Table 3) may be influenced by the delocalized electronic character of the electrophile, which, to some extent, resembles an exo methylene-substituted cyclohexadienyl cation. For such cases, the ground state electron density of the electrophile may be influential. However, the exocyclic CH_2 carbon of the benzyl cation, which has the lowest V_C value (lowest electron density) (see Figure S1 in the Supporting Information), is involved in the “attacking” and is the favored position of attachment, also because no loss in the benzyl aromaticity results.

NBO Charges and π Complexes. Despite earlier attempts to establish a connection between reactivity and arene ring atom charges,⁵⁸ no clear relationship exists. The NBO charges at reacting carbon atoms of the methyl benzene derivatives have a rather small range (−0.194 to −0.218) and correlate poorly with the ln **f** values ($r = 0.101$, see Table 4). This is not surprising in view of the low polarity of the methyl substituents. However, the π complex formation, which proceeds through a reversible and almost barrierless exothermic reaction (ranging from 1.2 to 2.6 kcal/mol; see Table 5), does lead to some charge redistribution, e.g. due to the unsymmetrical positioning of Cl_2 over the benzene plane (Figure 1). The exothermicity due to π complex formation is not substantial but increases with the number of methyl groups present and also correlates well with the relative chlorination rates (Table 5). Thus, methyl groups do increase the basicity (through hyperconjugation) of the more substituted arenes somewhat.

The NBO charges for the different ring positions also correlate poorly with the ln **f** values for both nitration ($r = 0.749$, Table 2) and benzylation ($r = 0.531$, Table 3).

HOMO and LUMO Orbitals. Are properties of frontier orbitals important in $\text{S}_{\text{E}}\text{Ar}$ reactions, as has been suggested?^{14,15,29} The HOMO and LUMO orbital energies correlate poorly with the experimental relative rates for the chlorination reactions (Table 6); the HOMO–LUMO gaps ($r = 0.758$, Table 6) offer no significant improvement. Such global ground state properties are not useful for predicting site reactivity and regioselectivity

for $\text{S}_{\text{E}}\text{Ar}$ reactions. Hirao and Ohwada’s reactive hybrid orbital (RHO) index revealed satisfactory correlations for several $\text{S}_{\text{E}}\text{Ar}$ reactions, but this index reflects the possible orbital interactions of arenes with a model electrophile, rather than properties of the initial reactants.

Conclusions

Although ground state properties of initial reactants and intermediates are not expected to correlate with the reaction rates and reflect positional selectivities of $\text{S}_{\text{E}}\text{Ar}$ reactions, there are reasons why certain ground state properties might correlate. Both E_{α} and V_C values depend on the ground state properties of the intermediate σ -complexes/initial arenes but can be useful in characterizing the reactivities and regioselectivities of $\text{S}_{\text{E}}\text{Ar}$ reactions and are very easy to compute. E_{α} are good candidates for predicting reactive sites for $\text{S}_{\text{E}}\text{Ar}$ reactions, as the thermodynamic stabilities of the sigma complexes dominate the variations of both E_{α} and ln **f** values for given idealized electrophilic reactions. Electron densities at individual ground state ring positions (as given by V_C) anticipate the electron density increase at the same positions during electrophile attachment with bond formation; electrophiles prefer to attack positions (or various substrates) having the highest electron density. For this reason, the V_C index functions better than carbon charges or HOMO/LUMO energies.

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Supporting Information Available: Complete Gaussian reference, electrostatic potential for benzyl cation, total energies and Cartesian coordinates of all optimized geometric structures. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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