

mmol, 35%), mp 75° dec. In ether the same compound was obtained in a poor yield with ethyl acrylate and ethyl propionate. This compound can be dissolved in cold benzene without appreciable deterioration for some minutes, but the solution slowly decomposed at room temperature as indicated by conspicuous color change to yellow; the yellow compound was isolated from the solution and identified as $[\text{PdBr}(t\text{-BuNC})_2]_2$.²³ The optical rotation measured at 22° immediately after dissolution in benzene was found to be nil. Ir (Nujol): 2240 cm^{-1} (ν_{CN}), 1700 (ν_{CO}).

Anal. Calcd for $\text{C}_{15}\text{H}_{27}\text{N}_2\text{O}_2\text{BrPd}$: C, 39.71; H, 6.00; N, 6.17. Found: C, 40.19; H, 6.04; N, 6.16.

(m) (S)-(+)-Ethyl Bromophenylacetate to " $\text{Pd}(t\text{-BuNC})_2$." (S)-(+)-Ethyl bromophenylacetate (0.34 g, 1.4 mmol, $[\alpha]_D^{25} +56.4^\circ$, c 1.65, ethanol) was added to a suspension of " $\text{Pd}(t\text{-BuNC})_2$ " (0.38 g, 1.4 mmol) at -78° . Under stirring the temperature was allowed to reach to room temperature during a few hours. Similar treatment as above produced $\text{PdBr}(\text{PhCHCO}_2\text{C}_2\text{H}_5)(t\text{-BuNC})_2$ (0.22 g, 0.4 mmol, 30%) as yellow crystals showing no optical activity in CH_2Cl_2 at 24°, mp 95–97.5° dec. Ir (Nujol): 2200 cm^{-1} (ν_{CN}), 1695 (ν_{CO}).

Anal. Calcd for $\text{C}_{20}\text{H}_{29}\text{N}_2\text{O}_2\text{BrPd}$: C, 46.58; H, 5.67; N, 5.43; Br, 15.49. Found: C, 46.45; H, 5.77; N, 5.34; Br, 15.33.

(n) Methyl Bromoacetate to " $\text{Pd}(t\text{-BuNC})_2$." To a stirring suspension of " $\text{Pd}(t\text{-BuNC})_2$ " (0.20 g, 0.75 mmol) in 20 ml of *n*-hexane was added $\text{BrCH}_2\text{CO}_2\text{CH}_3$ (0.1 ml, excess) at -78° . The temperature was allowed to reach room temperature. After 3 hr of stirring at ambient temperature, the yellow crystalline precipitate was isolated and recrystallized from toluene–*n*-hexane to give $[\text{PdBr}(t\text{-BuNC})_2]_2$ ²³ (0.025 g, 10%) and *trans*- $\text{PdBr}(\text{CH}_2\text{CO}_2\text{CH}_3)(t\text{-BuNC})_2$ (0.25 g, 78%) as colorless crystals, mp 101–104° dec (in air). The latter was identified from elemental analysis and the spectral data. Nmr (C_6D_6): τ 6.53 (s, 3H, CH_3), 7.45 (s, 2H, CH_2), and 9.15 (s, 18, *t*-Bu). Ir (Nujol): 2205 cm^{-1} (ν_{CN}) and 1695 (ν_{CO}).

Anal. Calcd for $\text{C}_{13}\text{H}_{23}\text{N}_2\text{O}_2\text{BrPd}$: C, 40.96; H, 6.08; N, 7.35. Found: C, 40.76; H, 5.98; N, 7.10.

Thermal Reactions of Alkyl or Aryl-Nickel and Palladium Complexes. The following alkyl complexes were prepared *in situ* by mixing the alkyl halides and zerovalent nickel or palladium complexes in solution and subjecting the solution to thermal decomposition: $\text{NiCl}[\text{CH}(\text{Ph})\text{CH}_3](\text{PPh}_3)_2$, $\text{NiBr}(n\text{-C}_6\text{H}_{13})(\text{PPh}_3)_2$, $\text{NiBr}(\text{CH}_2\text{Ph})(\text{PPh}_3)_2$, $\text{NiBr}(\text{CH}_2\text{CO}_2\text{H}_3)(\text{PPh}_3)_2$, $\text{NiBr}(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5)(t\text{-BuNC})_2$, $\text{PdCl}[\text{CH}(\text{Ph})\text{CH}_3](\text{PPh}_3)_2$, and $\text{PdBr}(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5)(t\text{-BuNC})_2$.

The following aryl-nickel complexes were isolated in a pure state and subjected to thermal reactions: $\text{NiBr}(\text{Ph})(\text{PPh}_3)_2$ and $\text{NiBr}(\alpha\text{-Naph})(\text{PPh}_3)_2$.⁴³ Solvent, temperature, reaction time, and organic products are listed in Table VII.

Olefin Insertion Reactions. The following alkyl or aryl-nickel and palladium complexes were treated with olefins in the presence of PPh_3 : $\text{NiBr}(\text{Ph})(\text{PPh}_3)_2$, $\text{PdBr}(\text{Ph})(\text{PPh}_3)_2$, and $\text{PdCl}(\text{CO}_2\text{CH}_3)(\text{PPh}_3)_2$. For the reaction of unstable alkyl complexes, e.g., $\text{NiBr}(\text{CH}_2\text{CO}_2\text{C}_2\text{H}_5)(\text{PPh}_3)_2$, the organometal compounds were prepared in the presence of olefins. Main organic products and their yield were determined by glpc method (Table VII). Some typical examples are shown below.

(a) **Reaction of Styrene with $\text{MBr}(\text{Ph})(\text{PPh}_3)_2$ (M = Pd, Ni).** A mixture of $\text{PdBr}(\text{Ph})(\text{PPh}_3)_2$ (0.20 g, 1.17 mmol) and PPh_3 (0.04 g, 0.17 mmol) in 3 ml of styrene was heated at 110° for 0.5 hr. After usual work-up with ether, the ether extract was analyzed by glpc on Apiezon-Grease-L (0.7 m, 180°, 1.3 atm) showing the presence of *trans*-stilbene (28%) and 1,2-diphenylethane (4%) at 11.3 and 3.8 min, respectively. A similar reaction of $\text{NiBr}(\text{Ph})(\text{PPh}_3)_2$ under the same condition as above produced styrene oligomers, *trans*-stilbene and 1,2-diphenylethane in ratio of 192:21:1, respectively.

(b) **Reaction of Styrene with $\text{PdCl}(\text{CO}_2\text{CH}_3)(\text{PPh}_3)_2$.** A mixture of $\text{PdCl}(\text{CO}_2\text{CH}_3)(\text{PPh}_3)_2$ (0.23 g, 0.2 mmol) and PPh_3 (0.11 g, 0.4 mmol) in 3 ml of styrene was heated at 145° for 1.5 hr. The glpc analysis on PEG-6000 (0.7 m 180°, 1.5 atm) showed the formation of methyl cinnamate and four unidentified products in ratio of 12:2.5:5:1:5 at 5.2, 10.6, 14.0, 19.0, and 21.0 min, respectively.

(c) **Reaction of $\text{BrCH}_2\text{CO}_2\text{C}_2\text{H}_5$ with $\text{Ni}(\text{PPh}_3)_3$ in the Presence of Styrene.** To a suspension of $\text{Ni}(\text{PPh}_3)_3$ (1.83 g, 2.1 mmol) in 4 ml of benzene–styrene (1:1) was added $\text{BrCH}_2\text{CO}_2\text{C}_2\text{H}_5$ (0.24 ml, 2.1 mmol) and the mixture was stirred for 1 hr at room temperature. After filtration of yellow precipitate, $\text{NiBr}(\text{PPh}_3)_3$ (1.3 g, 68%), the organic product was analyzed by glpc (Apiezon-Grease-L) with only one major peak being detected. This was assigned as ethyl 4-phenyl-3-butenolate (21%) by comparing the retention time and ir and nmr spectra with those of an authentic sample.

(43) J. Chatt and B. L. Shaw, *J. Chem. Soc.*, 1718 (1960).

A Simple Correlation of Hyperfine Splitting Constants of Radical Ions and Orientation in Aromatic Substitution Reactions

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Abstract: The hyperfine splitting constants of radical ions can be used in order to make predictions about the preferred orientation of aromatic substitution reactions. A simple model on the basis of which such a correlation becomes possible is presented and actual experimental cases are discussed. The advantage of this approach lies in the fact that it allows predictions to be made in the case of reactions of mono- and polysubstituted aromatics where chemical intuition is insufficient for making correct predictions.

Electron spin resonance has been primarily used in connection with the study of the properties of radical ions.^{1,2} The determination of spin densities has been a major research target³ and the concomitant

testing of molecular orbital theory has been of great importance.⁴ On the other hand, interest in the direction of relating esr data to reactivity parameters in organic chemistry has only recently surfaced. For example, Bowers has discussed the Hammett equation in terms of esr data.⁵ Perturbation theory⁶ provides

(1) E. T. Kaiser and L. Kevan, Ed., "Radical Ions," Interscience, New York, N. Y., 1968.

(2) K. W. Bowers, *Advan. Magn. Resonance*, 1, 317 (1965).

(3) B. H. J. Bielski and J. M. Gebicki, "Atlas of Electron Spin Resonance Spectra," Academic Press, New York, N. Y., 1967; see also ref 2.

(4) J. R. Bolton and G. K. Fraenkel, *J. Chem. Phys.*, 40, 3307 (1964); G. Vincow, in ref 1.

(5) K. W. Bowers, in ref 1.

a simple theoretical framework for interpreting organic reactivity by reference to esr data. In this paper we examine how one can use such an approach to study the relative reactivity of various positions of substituted aromatic molecules toward nucleophilic, radical, and electrophilic substitution.

According to perturbation theory, the interaction of a doubly occupied orbital, ϕ_m , with an empty orbital, ψ_n , results in stabilizing the occupied orbital and destabilizing the unoccupied orbital and this leads to net lowering of the energy of the two-orbital system. The stabilization energy can be written as follows

$$SE = 2\langle\phi_m|H|\psi_n\rangle^2/(E_m - E_n) \quad (1)$$

In actual chemical systems, one seeks to find the stabilization attending the interaction of two molecules. A complete treatment would involve the calculation of all orbital interactions and the energy changes for which they are responsible. This procedure is often laborious and does not lend itself to simple qualitative analysis of organic problems of interest. In the frontier orbital approximation,⁷ one considers only the most important orbital interactions between two molecules, and these involve the HOMO or NBMO of one molecule and the LUMO of the other molecule and *vice versa*.⁸ It is this theoretical approach that we follow in the rest of the discussion.

Nucleophilic Aromatic Substitution. The dominant orbital interactions at the transition state of nucleophilic aromatic substitution involve the NBMO of the charged or uncharged nucleophile which is occupied by the lone pair and the LUMO of the aromatic system. This is illustrated in Figure 1a. Of course, this analysis is appropriate only when the rate-determining step of the reaction is formation of the σ complex. The factors which determine whether the rate-determining step of a nucleophilic aromatic substitution reaction entails formation or destruction of the σ complex have been elegantly discussed by Miller.^{9,10} Application of eq 1 to the case of interest along with LCAO expansion of the LUMO of the aromatic leads to the following equation

$$SE_k = 2(c_N^2 c_k^2 \gamma_{Nk}^2)/(E_N - E_{LUMO}) \quad (2)$$

In this equation, c_k is the coefficient of the k th p atomic orbital of the LUMO of the aromatic molecule, c_N is the coefficient of an atomic orbital of the NBMO of the attacking nucleophile, γ_{Nk} is the resonance integral between the interacting orbitals, and E_N and E_{LUMO} are the appropriate orbital energies. Obviously, the squares of the coefficients c_k and c_N are the corresponding electron densities of the LUMO of the aromatic and the NBMO of the nucleophile, respectively. Now, the factor c_k^2 is related to the hyperfine split-

(6) M. J. S. Dewar, "The Molecular Orbital Theory of Organic Chemistry," McGraw-Hill, New York, N. Y., 1969.

(7) K. Fukui, T. Yonezawa, and C. Nagata, *J. Chem. Phys.*, **27**, 1247 (1957); *J. Chem. Phys.*, **31**, 550 (1959); R. D. Brown, *J. Chem. Soc.*, 2232 (1959); S. Nagakura and J. Tanaka, *Bull. Chem. Soc. Jap.*, **32**, 734 (1959).

(8) This is true for thermal reactions, in general.

(9) J. Miller, *J. Amer. Chem. Soc.*, **85**, 1628 (1963); J. Miller and K. W. Wong, *J. Chem. Soc.*, 5454 (1965); J. Miller and K. W. Wong, *Aust. J. Chem.*, **18**, 117 (1965); D. L. Hill, K. C. Ho, and J. Miller, *J. Chem. Soc. B*, 299 (1966); K. C. Ho, J. Miller, and K. W. Wong, *J. Chem. Soc. B*, 310 (1966).

(10) E. Buncl, A. R. Norris, and K. E. Russell, *Quart. Rev., Chem. Soc.*, **22**, 123 (1968).

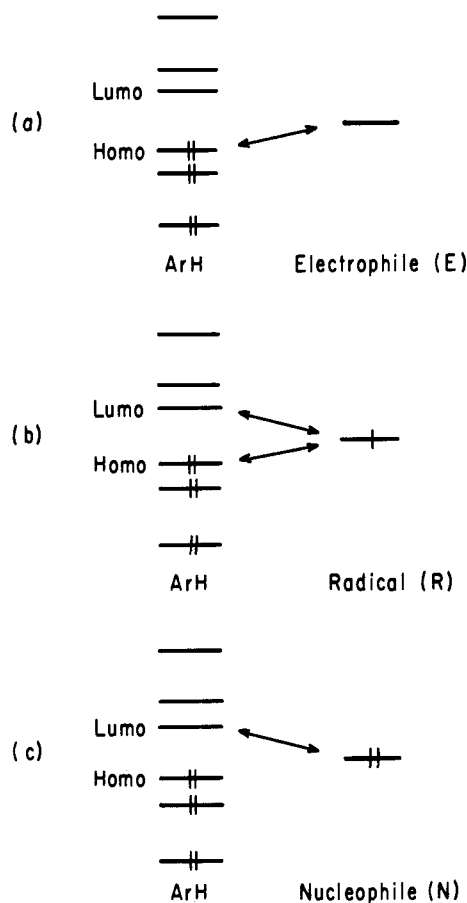


Figure 1. Principal orbital interactions at the transition state of (a) electrophilic, (b) radical, and (c) nucleophilic aromatic substitution. ArH is a typical monosubstituted benzene and for simplicity only the benzenoid orbitals of ArH are depicted. Diagrams are schematic.

ting constant, a_k^H , by the McConnell equation

$$a_k^H = Q\rho_k \quad (3)$$

where

$$\rho_k = c_k^2 \quad (4)$$

Now, in most nucleophiles of interest the nucleophilic lone pair occupies a single nonbonding atomic orbital; hence, we can set $c_N^2 = 1$. Also, γ_{Nk} can be assumed to have constant value for attack of a nucleophile at the different positions of the same aromatic molecule. Of course, this assumption might fail if a substituent on the aromatic molecule is very bulky. In such a case adjacent and nonadjacent positions with respect to the bulky group will involve different degrees of bond making at the transition state, and, hence, different γ_{Nk} 's. Another way of saying the same thing is that, unless there is a bulky substituent, γ_{Nk} will be constant for all k . With the above simplifications, we can rewrite eq 2 as

$$SE_k \propto \frac{a_k^H}{E_N - E_{LUMO}} \quad (5)$$

Before we apply this model to actual chemical reactions, it is appropriate to clarify a fine point. Our theoretical approach is a simple frontier orbital one-electron approach. According to eq 4, there are only positive values of ρ_k and, consequently, only negative

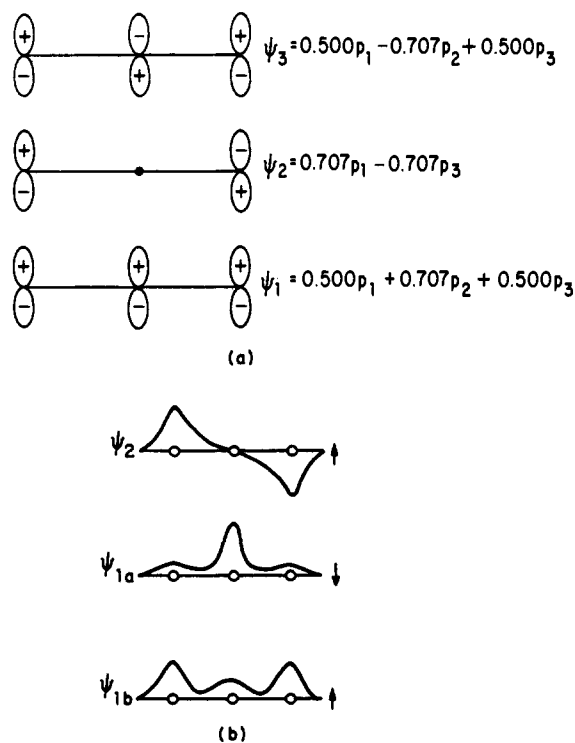


Figure 2. (a) The π MO's of allyl. (b) The occupied spin orbitals of the allyl radical.

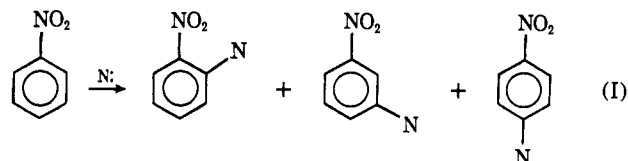
values for a_k^H since the constant Q is a negative number. This means that the stabilization energy can vary from large values to zero, at most. Now, if two-electron effects are taken into consideration, this simple picture is slightly modified and one can have negative spin densities instead of zero spin densities due to exchange correlation. This well-known effect has been discussed by many authors¹¹ and we just include here a brief qualitative description.

The Hückel MO's of the allyl radical are shown in Figure 2. The unpaired electron in allyl will occupy ψ_2 and, accordingly, the π -electron spin density will be $1/2$ on the end atoms and zero in the middle carbon. This is a prediction made on the basis of eq 4. Now, if two-electron effects are considered, the Coulomb repulsion between two electrons of the same spin is lowered by virtue of their exchange interaction. The odd electron in ψ_2 spends most of its time on the two outer carbons and attracts the electron of the same spin in ψ_1 toward the same two outer carbons. This exchange effect gives rise to a net concentration of $\psi_{1\alpha}$ electrons on the outer carbons and a net concentration of $\psi_{1\beta}$ electrons on the middle carbon. Hence, there is finite negative spin density on the middle carbon. In other words, we can state that within the one-electron framework eq 4 is satisfactory, but when two-electron effects are considered the hyperfine splitting constants can become positive rather than zero. We are now ready to apply eq 5 toward making qualitative reactivity predictions. Equation 5 tells us that large stabilization and, hence, high reactivity of an aromatic position toward nucleophilic substitution are associated with a large and negative hyperfine splitting constant, e.g., large positive spin density, of the corresponding aromatic anion

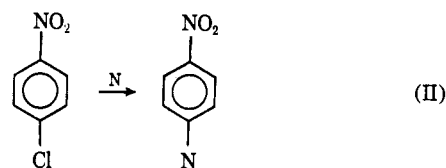
(11) For example, see A. Carrington and A. D. McLachlan, "Introduction to Magnetic Resonance," Harper and Row, New York, N. Y., 1967.

radical. On the other hand, small stabilization and, hence, low reactivity of an aromatic position toward nucleophilic substitution is associated with a small and negative hyperfine splitting constant, e.g., small positive spin density, of the corresponding aromatic anion radical. Now, if the exchange or spin polarization effect is taken into account, it becomes apparent that small stabilization and, hence, low reactivity of an aromatic position toward nucleophilic substitution can be associated with a small hyperfine splitting constant which is either negative or positive, e.g., small positive or negative spin density. Rieger and Fraenkel,¹² in an important work, have examined the relationship between hyperfine splittings and spin densities calculated by the McLachlan procedure in aromatic anion radicals. It was found that there is a nice linear relationship between these two quantities and that small hyperfine splittings ranging from -1 to $+1$ G correspond to small spin densities ranging from 0.05 to -0.05 . On the basis of these esr results, it is clear that while our model predicts that positions of small hyperfine splittings will have low reactivity, it does not allow comparisons to be made between aromatic positions which have small but opposite in sign hyperfine splitting constants. Such comparisons between unreactive positions are of little practical interest.

Equation I describes a model nucleophilic substitu-



tion reaction. The relative reactivity of the ortho, meta, and para positions of nitrobenzene can be predicted if one knows the hyperfine splitting constants of the radical anion of nitrobenzene. In actual cases, nucleophilic aromatic substitution occurs when a good leaving group is present. Equation II describes a



typical nucleophilic substitution reaction.

The relative reactivity of the isomeric nitrochlorobenzenes can be predicted simply from esr data on the nitrobenzene radical anion if one makes two assumptions.

(a) The effect of chlorine on the energy of the LUMO of nitrobenzene is small so that the LUMO's of the three isomeric nitrochlorobenzenes and the LUMO of nitrobenzene have similar energies. We have carried out CNDO/2 calculations¹³ on these molecules and the results shown in Table I indicate that this assumption is a reasonable one.¹⁴

(12) P. H. Rieger and G. K. Fraenkel, *J. Chem. Phys.*, **39**, 609 (1963).

(13) We have used the CNDO/2 computer program described by Pople and Dobosh adapted to a CDC-6400 computer: J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory," McGraw-Hill, New York, N. Y., 1970.

(14) The LUMO's of the three isomeric nitrochlorobenzenes are within 0.27 eV, certainly a small variation considering the inherent accuracy of the calculations.

Table I. Energies of the Lowest Unoccupied Orbitals of Nitrobenzene and the Isomeric Nitrochlorobenzenes

Molecule	E (LUMO), au
Nitrobenzene	0.0578
<i>o</i> -Nitrochlorobenzene	0.0407
<i>m</i> -Nitrochlorobenzene	0.0430
<i>p</i> -Nitrochlorobenzene	0.0328

(b) The effect of chlorine on the electron density of the LUMO of nitrobenzene is small so that the LUMO's of the three isomeric nitrochlorobenzenes and the LUMO of nitrobenzene have qualitatively similar electron distributions. CNDO/2 calculations of the electron densities of the LUMO of the neutral molecules support our assumption. In all four

C_1^2 0.154	C_1^2 0.172	C_1^2 0.156	C_1^2 0.241
C_2^2 0.095	C_2^1 0.138	C_2^2 0.052	C_2^2 0.082
C_3^2 0.023	C_3^2 0.001	C_3^2 0.045	C_3^2 0.042
C_4^2 0.177	C_4^2 0.161	C_4^2 0.203	C_4^2 0.184
	C_5^2 0.056	C_5^2 0.012	
	C_6^2 0.051	C_6^2 0.136	

molecules shown the LUMO charge density varies in the order $C_4^2 > C_2^2 > C_3^2$. ESR data on the radical anions of nitrobenzene and the three isomeric nitrochlorobenzenes¹⁵ shown below further indicate that this assumption is a reasonable one. On the basis of

$a_2^H = 3.30$ G	$a_4^H = 3.92$ G	$a_4^H = 4.07$ G	$a_2^H = 3.42$ G
$a_3^H = 1.03$ G	$a_5^H = 1.13$ G	$a_6^H = 0.93$ G	$a_3^H = 1.12$ G
$a_4^H = 3.82$ G	$a_6^H = 3.30$ G	$a_6^H = 3.20$ G	

this approximation, the relative rate of nucleophilic attack at the ortho, meta, and para positions of nitrobenzene will parallel the relative rate of nucleophilic attack on *o*-nitrochlorobenzene, *m*-nitrochlorobenzene, and *p*-nitrochlorobenzene. Hence, it becomes apparent that the relative reactivity of the three isomeric nitrochlorobenzenes can be predicted from knowledge of the hyperfine splitting constants of the nitrobenzene radical anion. We shall illustrate this approach with actual experimental cases.

We first consider the relative rates of nucleophilic substitution of *o*-, *m*-, and *p*-chloronitrobenzene. Their relative rates will depend on the relative magnitude of the hyperfine splitting constants of the radical anion of the parent molecule nitrobenzene. As we have already seen, the hyperfine splitting constants of nitrobenzene vary in the order $a_p^H > a_o^H > a_m^H$.¹⁶ Hence, the rates of nucleophilic aromatic substitution

(15) T. Fujinaga, Y. Deguchi, and K. Umemoto, *Bull. Chem. Soc. Jap.*, **37**, 822 (1964); J. F. Freed and G. K. Fraenkel, *J. Chem. Phys.*, **41**, 699 (1964).

(16) The meta position of the nitrobenzene anion radical, characterized by a small splitting constant, is actually a position of negative spin density according to McLachlan calculations reported in ref 12.

Table II. Rate Data on Nucleophilic Aromatic Substitution

Molecule	Conditions	E_A^a	Log A	Ref
<i>o</i> -Nitrochlorobenzene	EtO ⁻ -EtOH	22.2	10.0	<i>b</i>
<i>p</i> -Nitrochlorobenzene	EtO ⁻ -EtOH	20.1	9.0	<i>b</i>
<i>o</i> -Nitrochlorobenzene	Piperidine-EtOH	18.1	6.4	<i>b</i>
<i>p</i> -Nitrochlorobenzene	Piperidine-EtOH	17.1	5.3	<i>b</i>
4-Chloro-1,3-dinitrobenzene	Piperidine-EtOH	10.7	6.2	<i>c</i>
2-Chloro-1,3-dinitrobenzene	Piperidine-EtOH	12.2	5.9	<i>d</i>

^a In kcal/mol. ^b N. B. Chapman, R. E. Parker, and P. W. Soames, *J. Chem. Soc.*, 2109 (1954). ^c B. Capon and N. B. Chapman, *J. Chem. Soc.*, 600 (1957). ^d N. B. Chapman and C. W. Rees, *J. Chem. Soc.*, 1190 (1954).

in the case of the three isomeric nitrochlorobenzenes should vary in the same order. This has been found to be so and typical results are given in Table II.

The relative reactivity of the isomeric dinitrochlorobenzenes toward nucleophilic aromatic substitution can be similarly analyzed. One can predict relative reactivities by referring to the hyperfine splitting constants of the dinitrobenzene radical anion.¹⁷

	$a_2^H = 2.77$ G
	$a_4^H = a_6^H = 4.49$ G
	$a_5^H = 1.08$ G

It is predicted that the 4-Cl isomer will undergo nucleophilic aromatic substitution faster than the 2-Cl isomer. Experimental results which are in agreement with these predictions are shown in Table II.

An interesting situation arises when one considers the nucleophilic substitution of chlorine at various positions of the 3-nitroanisole. The anion radical of 3-nitroanisole has been studied by esr, and the hyperfine splitting constants are shown below.⁵ Accord-

	$a_2^H = 3.85$ G
	$a_4^H = 3.29$ G
	$a_5^H = 1.01$ G
	$a_6^H = 3.29$ G

ing to the esr data, one predicts that chlorine located at the 2 position will be substituted faster than chlorine located at the 4 or 6 position. This is borne out experimentally for the case of nucleophilic attack by piperidine in benzene.¹⁸

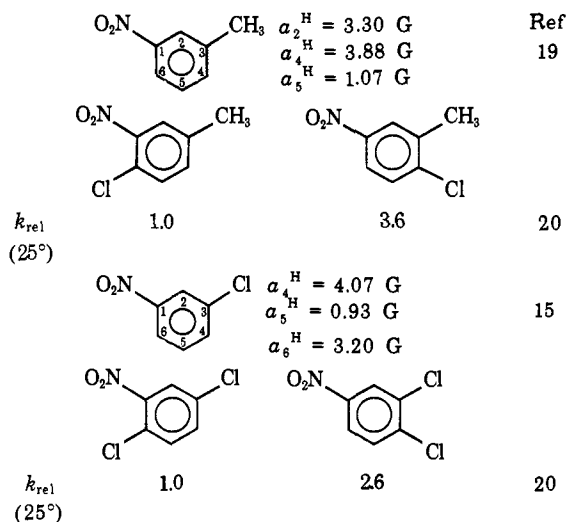
	1	k_{rel}
	4.2	

Some additional correlations of nucleophilic reactivity with esr data for the type of molecules considered in this section are given in Chart I. In these cases, the esr data on the parent radical anion are given along with relative rates toward nucleophilic displacement of Cl by methoxide in methanol.

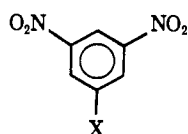
(17) The 2 and 5 positions, characterized by small splitting constants, are actually positions of negative spin density according to McLachlan calculations reported in ref 12.

(18) J. A. Brioux and V. Deulofeu, *J. Chem. Soc.*, 2579 (1954).

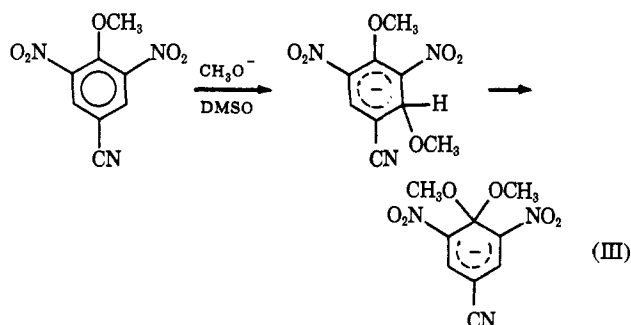
Chart I



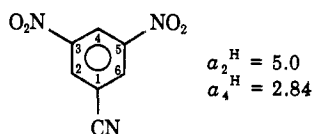
An interesting problem arises when one is asked to predict the site of preferred nucleophilic attack on molecules of the type shown below. For example,



the transformations in eq III have been recently docu-



mented.²¹ If we disregard the influence of the leaving group on orbital energies and charge distributions, we can refer to esr data on the appropriate radical anion and predict the site of the initial nucleophilic attack. The esr data shown below would have led us to the correct prediction.^{22, 23}



Homolytic Aromatic Substitution. In this case there are two important orbital interactions, namely, that between the singly occupied orbital of the radical and the LUMO of the aromatic and that between the singly

(19) D. H. Geske, J. L. Ragle, M. A. Bambenek, and A. L. Balch, *J. Amer. Chem. Soc.*, **86**, 987 (1964).

(20) J. Miller, "Aromatic Nucleophilic Substitution," Elsevier, New York, N. Y., 1968.

(21) E. J. Fendler, C. E. Griffin, and J. H. Fendler, *Tetrahedron Lett.*, 5631 (1968).

(22) P. H. Rieger, I. Bernal, W. H. Reinmuth, and G. K. Fraenkel, *J. Amer. Chem. Soc.*, **85**, 683 (1963).

(23) Position 4 is actually a position of negative spin density according to McLachlan calculations reported in ref 12.

occupied orbital of the radical and the HOMO of the aromatic. These interactions are illustrated in Figure 1b. The stabilization energy which results from the interaction of these orbital interactions is given by eq 6.

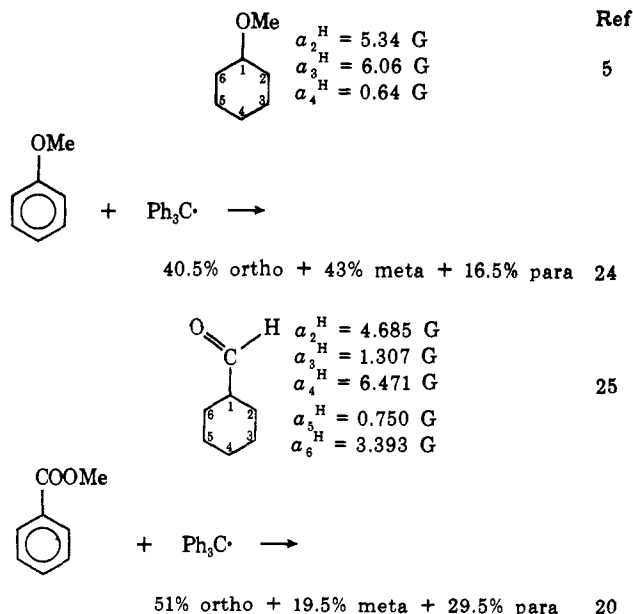
$$SE_k = \frac{c_R^2 c_k^2 \gamma^2 R_k}{E_R - E_{LUMO}} + \frac{c_R^2 d_k^2 \gamma^2 R_k}{E_{HOMO} - E_R} \quad (6)$$

In this equation c_R is the coefficient of the singly occupied orbital of the radical, c_k and d_k are the coefficients of the k th p atomic orbital of the LUMO and HOMO, respectively, of the aromatic molecule, and the rest of the symbols have their usual meaning. By using the same reasoning as before, one can rewrite the equation as follows

$$SE_k \propto \frac{a_k^-}{E_R - E_{LUMO}} + \frac{a_k^+}{E_{HOMO} - E_R} \quad (7)$$

Here, a_k^+ and a_k^- are the hyperfine splitting constants of the k th atom of the aromatic cation radical and anion radical, respectively. It is apparent that when the attacking radical has a low ionization potential (nucleophilic radical) the first term of eq 7 is the dominant one and the orientation of radical attack is controlled by the hyperfine splitting constants of the related aromatic anion radical. On the other hand, when the attacking radical has a high ionization potential (electrophilic radical) the second term of the equation becomes dominant and the orientation of radical attack is controlled by the hyperfine splitting constants of the related aromatic cation radical. Typical results for nucleophilic radical are shown in Chart II.

Chart II



In homolytic aromatic substitution one does not have to worry about approximations since the leaving group is hydrogen atom. Thus, in the case of nucleophilic radicals the relative reactivity of the various positions

(24) G. H. Williams, "Homolytic Aromatic Substitution," Pergamon Press, New York, N. Y., 1960.

(25) N. Steinberger and G. K. Fraenkel, *J. Chem. Phys.*, **40**, 723 (1964). Positions 3 and 5, characterized by small splitting constants, are actually positions of negative spin density according to McLachlan calculations.

of the aromatic molecule toward homolytic substitution can be derived from the hyperfine splitting constants of the aromatic radical anion without any assumptions. In the examples given above, the triphenylmethyl radical has a high nucleophilic character on account of its low ionization potential.²⁶ The predictions based on esr data are in agreement with experiment after statistical correction of the isomer yields, e.g., division of the ortho and meta percentages by 2. In the case of methyl benzoate, we assumed benzaldehyde as a suitable model for obtaining the esr data. Actually, all monosubstituted benzenes where the substituent is conjugatively electron withdrawing in character exhibit splitting constants in the order $a_p^H > a_o^H > a_m^H$ simply because in such cases the substituent stabilizes the symmetric π_4 benzenoid orbital relative to the antisymmetric π_5 benzenoid orbital.^{2,3} Unfortunately, there are no available esr data on radical cations of monosubstituted benzenes which would allow for additional test of our model.

Electrophilic Aromatic Substitution. In this case, the dominant orbital interactions involve the HOMO of the aromatic molecule and the LUMO of the electrophile. These interactions are illustrated in Figure 1c. The stabilization energy which results from the interactions of these orbitals can be written as follows

$$SE = 2(c_E^2 c_k^2 \gamma_{Ek}^2) / (E_{\text{HOMO}} - E_E)$$

Unfortunately, there are no available esr data on radical cations of monosubstituted benzenes which would allow correlation with the very extensive experimental data on the orientation of electrophilic aromatic substitution reactions.

Discussion

The MO treatments of aromatic substitution can be grouped into the static and dynamic methods.²⁷ The static method deals with electron properties of the reacting molecule at the initial or nonreacting stage, i.e., at the earliest stage of reaction when the molecule is slightly perturbed by the approach of the reagent. The dynamic method is based on the postulated structure of the reacting molecule at the transition state. Free valence, π -electron densities and MO polarizabilities are indices of the static method, while localization energies are indices of the dynamic method. Prior to the advent of approximate SCF computational schemes, these indices could be arrived at by some type of empirical or semiempirical π -electron calculation. The results of such calculations were not reliable enough to be used

(26) The ionization potential of the triphenylmethyl radical has been calculated to be 7.26 eV as compared with 9.82 eV being the experimentally determined ionization potential of the methyl radical: A. Streitwieser, *J. Amer. Chem. Soc.*, **82**, 4123 (1960); E. A. Elder, C. Giese, B. Steiner, and M. Ingraham, *J. Chem. Phys.*, **36**, 3292 (1962).

(27) A. Streitwieser, "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N. Y., 1961.

for *a priori* predictions, especially when the reactant was a conjugated system containing heteroatoms. Indeed, it was found that very frequently indices like π -electron densities, etc., depended on the method of calculation not only quantitatively but also qualitatively. For example, Shepherd and Fedrick²⁸ have reviewed nucleophilic aromatic substitution of heteroaromatic molecules and have concluded that theoretical calculations have not been reliable guides to relative nucleophilic reactivity at different positions in the same molecule or at comparable positions in different molecules. The SCF approximate calculation schemes introduced by Pople and others treat both π and σ electrons and provide hope that reactivity indices could be accurately computed. For example, we have seen previously that the relative magnitude of the hyperfine splitting constants of the radical anions of nitrobenzene and the isomeric nitrochlorobenzenes can be predicted from CNDO/2 calculations on the neutral molecules. Unfortunately, there is also a limit to the applicability of these approximate SCF computation schemes. This limit is reached when the molecule is large and contains several heteroatoms including second row elements. In view of these considerations, it appears that the model discussed in this paper can be useful for making predictions regarding large molecules on the basis of available esr data rather than quantum mechanical calculations.

Finally, some cautionary remarks are in order. Firstly, the model presented here is an approximate one since the connection between esr and reactivity is made *via* perturbation theory within the frontier orbital approximation. Secondly, it is important to emphasize that there are other factors such as solvation, hydrogen bonding, steric interactions, etc., which in some instances can become dominant and influence the course of a reaction. These factors are not taken under consideration by this approach and one should be aware of their possible importance. Despite that, the general approach described here seems to give rise to interesting correlations.²⁹ Indeed, some of the cases examined in this paper have been regarded as reactivity puzzles.^{18, 21, 24} The massive esr data currently available will hopefully provide the basis for additional reactivity correlations.

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(28) R. G. Shepherd and J. L. Fedrick, *Advan. Heterocycl. Chem.*, **4**, 146 (1965).

(29) Some of the experimental relative rate factors cited in this paper are admittedly small. However, the corresponding relative stabilization energies are also small because the relative magnitude of the LUMO coefficients varies only to a small extent.