Some Applications of Valence-bond Theory to Aromatic Substitution.

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The electronic effects of substituents on aromatic substitution are described in terms of valence-bond theory. The influence of electron correlation on the transition-state energies for both electrophilic and nucleophilic aromatic substitution is discussed.

The electronic principles governing aromatic substitution, in particular the difference between *ortho-para*-directing and *meta*-directing substituents, have been known for many years, but there still remain several difficulties, among which predominates the problem of *ortho* : *para* ratios.

For dealing with aromatic substitution two general procedures have been employed. In the first of these, the reactivities of different positions are correlated with the charge distribution in the unperturbed molecule, while in the second an attempt is made to calculate the effect of substituents at different positions on the energy of the transition state for the substitution reaction. As Waters (*J.*, 1948, 727) and others have pointed out, the former method takes into account only the mesomeric effects of substituents and not the more important electromeric effects, and for this reason may prove to be unreliable in dealing with minor differences of reactivity.

Several attempts have been made to calculate accurately both charge distributions (Wheland and Pauling, *J. Amer. Chem. Soc.*, 1935, **57**, 2086) and transition-state energies (Wheland, *ibid.*, 1942, **64**, 900; Dewar, *J.*, 1949, 463) by means of the molecular orbital (MO) method. Unfortunately the results obtained depend on the importance attributed to the transmission of inductive effects along the σ carbon–carbon bonds. To obtain general agreement with experiment it is necessary to assume more extensive transmission than is normally regarded as likely (Brown, *Quart. Reviews*, 1952, **6**, 63). It may be that these high inductive effects have to be introduced in order to compensate for deficiencies in the MO technique, notably the neglect of electron correlation.

For this reason it seems worth while to try to apply the valence-bond (VB) theory to the same problem.

In VB theory the structure of any molecule is considered as a resonance hybrid of various simpler structures. The wave function Ψ of the molecule may be written as

$$\Psi = a\psi_1 + b\psi_2 + c\psi_3 + \ldots .$$

where ψ_1, ψ_2 . . . . are the wave functions of the contributing structures. The coefficients a, b, c . . . . (more exactly their squares) are regarded as measuring the importance of each contributing structure in the actual molecule. For numerical calculations the wave functions ψ_1, ψ_2 . . . . are determined by Slater's method (*Phys. Review*, 1931, **38**, 1109) and the total wave function Ψ and hence the coefficients a, b, c . . . . are determined by minimising the energy.

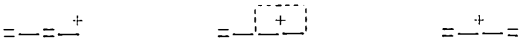
In qualitative resonance arguments it is usual to assume that the importance of any structure is directly related to its energy. This is true where there are two structures only; where there are more than two it is frequently in error (Sherman, *J. Chem. Phys.*, 1934, **2**, 488). The reason why the assumption is successful in practice is that the energy of any structure measures, not its actual importance in the total wave function, but the ease with which the molecule can be polarised into that particular form, and it is this which is usually determined by reactivity experiments. The actual coefficients needed in the calculation of the ground state electronic charge distribution depend, not only on the energy of each structure, but also on the effectiveness with which it interacts with other structures. It is only when these interacting powers are similar that the energies will give a fair measure of the relative importances.

The procedure for the introduction of ionic structures into the VB theory of conjugated systems has been discussed by Craig (*Proc. Roy. Soc.*, 1950, *A*, **200**, 391) and by Schomaker

and Simonetta (*J. Chem. Phys.*, 1951, **19**, 649). The main problem is the choice of numerical values for the large number of integrals which appear in the equations. The values given by Craig are derived from the spectrum of ethylene, but this procedure is subject to serious error if the spectrum is incorrectly interpreted and it seems preferable to deduce values for the integrals from their theoretical meanings provided this does not lead to absurdity in the final results.

The usual model for the transition state in aromatic substitution is that due to Wheland (*loc. cit.*). The carbon atom at which substitution occurs is considered to change its hybridisation from trigonal (sp^2) to tetrahedral (sp^3) and thus dissociate itself from the conjugated system. In benzene itself this process will leave a residual conjugated chain of 5 carbon atoms and 4, 5, or 6 electrons according to whether the reactant is electrophilic, homolytic, or nucleophilic.

The transition state for electrophilic substitution in benzene will be a pentadienate cation, which may be considered as a resonance hybrid of singly charged structures such as



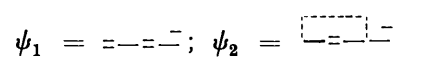
and multiply ionised structures such as

Provided the multiply ionised structures may be neglected the number of integrals required in the calculations is small. These are: Q = coulomb integral, an approximate measure of the electrostatic stability of the structure; α = exchange integral for the interchange of two electrons on adjacent atoms; η = resonance integral for a single-electron jump between adjacent atoms; and ρ = resonance integral for a single-electron jump between two atoms separated by a third atom.

The integral η represents a one-electron jump between two adjacent atoms and might be expected to be about $\frac{1}{2}\alpha$ (it is similar in form to the MO resonance integral β, which has an empirical value of just over $\frac{1}{2}\alpha$). The value of ρ is less easy to estimate. If it is considered to represent a single-electron jump to a non-adjacent atom then the value would be small, but interaction between two singly charged structures in which the charges are situated on alternate atoms can occur through a triply charged structure having like charges on these same atoms and an unlike charge on the intermediate atom. Since in this method singly charged structures alone are included explicitly, this interaction must be allowed for in the value given to ρ. Empirically the value $\frac{1}{4}\alpha$ leads to reasonable conclusions.

The matrix elements in the secular determinant ($H_{rs} = \int\psi_r H\psi_r d\tau$ and $S_{rs} = \int\psi_r\psi_s d\tau$) may be found by the following rules.

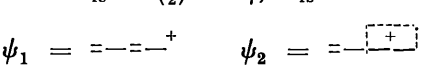
(I) Charges on the same atoms: The simple rules formulated by Pauling (*J. Chem. Phys.*, 1933, **1**, 280) may be used. The matrix term $H_{rs} - ES_{rs} = (\frac{1}{2})^{n-i}(Q - E + b\alpha)$ where n is the number of bonds and i the number of islands in the superposition pattern, and b = number of pairs of neighbour orbits in the same island + the number of unpaired neighbour orbits in the same island separated by an odd number of bonds − 2 (the number of unpaired neighbour orbits in the same island separared by an even number of bonds) − $\frac{1}{2}$ (number of pairs of neighbour orbits in different islands),

e.g., 

then $H_{12} - ES_{12} = \frac{1}{2}(Q - E + 2\alpha)$

(II) Charges on adjacent atoms:

$$H_{rs} = (\tfrac{1}{2})^{n-i} \cdot \eta; \quad S_{rs} = 0$$

e.g., 

then $H_{12} = \eta$

(III) Charges on atoms separated by a third atom :

$$H_{rs} = (\tfrac{1}{2})^{n-i} \cdot \rho; \quad S_{rs} = 0$$

e.g., ψ_1 = =—=—$^{+}$ ψ_2 = =$^{+}$—=—=

then $$H_{12} = \rho$$

Justification for these rules may be found in the theoretical papers referred to above.

Nine singly charged structures (ψ_1 to ψ_9 below) may be drawn for the pentadienate cation. The energy is written below each structure.

=—=—$^{+}$	$^{+}$—=—=	=—[+]——
ψ_1 $Q + \frac{3}{2}\alpha$	ψ_2 $Q + \frac{3}{2}\alpha$	ψ_3 $Q + \frac{1}{2}\alpha$
[+]——=—	——=—$^{+}$	$^{+}$—[——=—]
ψ_4 $Q + \frac{1}{2}\alpha$	ψ_5 $Q + 0\alpha$	ψ_6 $Q + 0\alpha$
[——=—$^{+}$]	[$^{+}$—=—]	=—$^{+}$—=
ψ_7 $Q + \frac{1}{2}\alpha$	ψ_8 $Q + \frac{1}{2}\alpha$	ψ_9 $Q + 2\alpha$

The wave function may be written as :

$$\Psi = a(\psi_1 + \psi_2) + b(\psi_5 + \psi_6) + c(\psi_3 + \psi_4) + d(\psi_7 + \psi_8) + e\psi_9$$

The four "*meta*" structures ψ_3, ψ_4, ψ_7, and ψ_8 have the same energy, so it is probably reasonable to equate coefficients c and d. The secular determinant then becomes

$$\begin{vmatrix} x + \frac{3}{2} & \frac{1}{2}(x+3) & \frac{3}{4} & \frac{1}{4} \\ \frac{1}{2}(x+3) & x & \frac{3}{4} & \frac{1}{8} \\ \frac{3}{4} & \frac{3}{4} & 3x + \frac{29}{8} & \frac{3}{4} \\ \frac{1}{2} & \frac{1}{4} & \frac{3}{2} & x + 2 \end{vmatrix} = 0$$

where $x = (Q - E)/\alpha$.

This equation may be solved to give an energy $E = Q + 2{\cdot}631\alpha$ and a positive charge distribution

0·114	0·090	0·592	0·090	0·114
$C_{(1)}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$

This distribution differs markedly from the normally accepted charge distribution as predicted by MO theory, *viz.* :

0·333	0	0·333	0	0·333

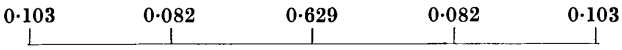
Of the two main reasons, the more important is the greater stability of structure 9 compared with structures 1 and 2, which results in an appreciable localisation of charge on the central atom. In this treatment, as is usual in VB theory, the interaction between the electrons in the C–H bonds and the π-electrons is neglected. When, as with homopolar molecules such as benzene, all the structures included have the same electron distribution this neglect will not affect the result, but when the electron distributions in the structures are different, as in the present case, such neglect will affect the calculated charge distribution. If these interactions were included in the calculation, the stabilities of structures 1 and 2 (*i.e.*, structures with a terminal charge) would be closer to that of structure 9 and the difference in charge would partly, though not entirely, disappear.

The second reason is the neglect of multiply charged structures. The importance of "*meta*-bonded" structures such as ψ_3 is largely due to their enabling the more stable

" Kekulé " structures such as ψ_1 and ψ_9 to interact. This interaction can also occur through multiply charged structures such as :

and although this interaction has been indirectly included in the energy E by the value given to ρ, explicit inclusion of these structures in the wave function would lead to a greater localisation of charge on carbon atoms 1, 3, and 5 as given by the MO theory. However, for such inclusion many new integrals of uncertain value would be required and the significance of the results would be doubtful.

The calculation may be considerably simplified if the " long-bonded " structures ψ_5, ψ_6, ψ_7, and ψ_8 are neglected. This approximation leads to an energy $E = Q + 2{\cdot}565\alpha$ and a charge distribution :



In view of the uncertainty in the values given to the various integrals, this approximation is sufficiently close for qualitative discussion.

To investigate the effect of inductive substituents (or heteroatoms) on the electrophilic substitution of benzene, it may be assumed that the energy of the benzene molecule itself is unaltered by the substituent, but that in the transition state the substituent will affect the coulomb integral for the ionic resonance form in which the positive charge is situated on the carbon atom to which the substituent is attached. The energy of the transition state is then calculated by replacement of the coulomb integral Q for this particular structure in the secular determinant by $Q + y\alpha$. For an electron-attracting $(+I)$ substituent, y will be negative, and for an electron-releasing $(-I)$ substituent y will be positive. The energy E may then be calculated for varying values of y for each of the three different positions in the ion.

For complete accuracy the calculation must be done in full for each value of y required and for each position, but the results may be obtained approximately by use of the theorem (proved in the Appendix) that the change of energy $\delta E = q_r\,\delta Q_r$, where q_r is the charge on atom r in the unsubstituted ion and δQ_r is the change in the coulomb integral (*i.e.*, $y\alpha$). The annexed Table gives the results for a substituent on $C_{(3)}$ in the ion (*i.e.*, *para*-substitution) calculated by the two methods for varying values of y :

y	$-\frac{1}{2}$	$-\frac{1}{5}$	$-\frac{1}{10}$	$\frac{1}{10}$	$\frac{1}{5}$	$\frac{1}{2}$
$\delta E(\alpha)$ (acc.)	−0·27	−0·121	−0·061	0·065	0·132	0·35
$\delta E(\alpha)$ (app.)	−0·31	−0·126	−0·063	0·063	0·126	0·31

The agreement is fair, even for quite large values of y.

These numerical results lead to the conclusion that, for electrophilic substitution in benzene derivatives, an electron-releasing inductive substituent would activate all three positions and give an order of reactivity *para* > *ortho* > *meta*. The $\frac{1}{2}o : p$ ratio should always be less than 1 and should decrease as the $-I$ effect increases. Electron-attracting substituents should deactivate all three positions and give an order of reactivity *meta* > *ortho* > *para*. The $\frac{1}{2}o : p$ ratio should always be greater than 1 and should increase as the $+I$ effect increases.

$(+I + E)$-Substituents such as the nitro- or cyano-group may be treated similarly. The electromeric effect of these substituents cannot operate to deactivate the reaction, so that the deactivation found with all such substituents must be largely due to their inductive effects together with some deactivation due to the loss of mesomeric conjugation energy, which will tend to strengthen and parallel the inductive effect as it will also be roughly proportional to the positive charge at the position of the substituent in the transition state. It would be predicted that all three positions would be deactivated and the order of reactivity would be *meta* > *ortho* > *para*, the ratios *meta* : *ortho* and *ortho* : *para* increasing with increasing electronegativity of the substituent.

Substituents possessing an activating electromeric effect $(-E)$ can no longer be treated

as simple inductive substituents since the resonance hybrid in the transition state will include triply bonded structures such as :

for *ortho*- and *para*-substitution. These structures are of approximately equal energy so that *ortho*- and *para*-substitution would be equally favoured if these structures were predominant in the transition state. The other main contributing structures for *ortho*- and *para*-substitution are :

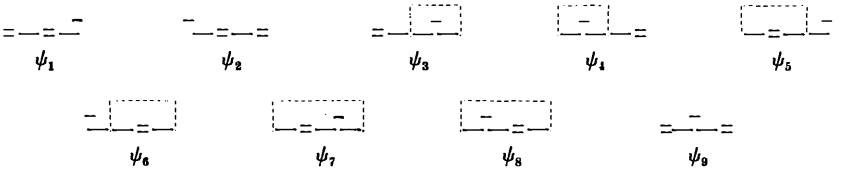
$E = Q + 1{\cdot}5\alpha$ $E = Q + 2{\cdot}0\alpha$

If these structures were predominant, then *para*-substitution would occur to a much greater extent than *ortho*-substitution. Structures ψ_c and ψ_d would be favoured relative to ψ_a and ψ_b by high electronegativity of the substituent X and by a low C–X exchange integral. For any $-E$ substituent it may be predicted that the $\frac{1}{2}o : p$ ratio would always be less than 1 and would decrease with increasing electronegativity of X and to a lesser extent with decreasing C–X exchange integral.

These predictions are generally in agreement with those derived by Dewar (*loc. cit.*) using MO theory and may be exemplified by the experimental evidence quoted there.

Diphenyl may be regarded as benzene with a $-E$ phenyl substituent, so that electrophilic substitution of diphenyl should give predominantly *para*- but together with considerable *ortho*, since the electronegativity of the phenyl group is low. According to MO theory in which electron correlation is ignored both electrophilic and homolytic substitution of diphenyl should occur preferentially at the same position, namely, the *ortho*-position. Experimentally it has been found that nitration (Bell, Kenyon, and Robinson, *J.*, 1926, 1242) gives much more *para*-substitution than phenylation (Cadogan, Hey, and Williams, *J.*, 1954, 794).

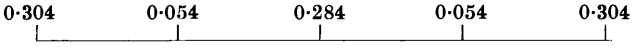
Nucleophilic substitution in benzene derivatives may be treated similarly to electrophilic substitution. The transition state for nucleophilic substitution in benzene itself will be a pentadienate anion which may be regarded as a resonance hybrid of the annexed nine structures.



It was shown that, for the corresponding cation, the structures ψ_5 to ψ_8 could be neglected without seriously affecting the result. If this approximation is made for the anion, the wave function becomes :

$$\Psi = a(\psi_1 + \psi_2) + b(\psi_3 + \psi_4) + c\psi_9$$

The secular determinant may be solved to give an energy $E = Q + 0{\cdot}953\alpha$, and a charge distribution :

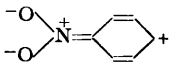
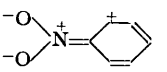


From this distribution it can be predicted that both $+I$ and $(+I + E)$ substituents such as a heteroatom (as in pyridine) or a nitro-group would activate nucleophilic substitution at all three positions and give an order of reactivity *ortho* $\geqslant$ *para* $>$ *meta*. The experimental evidence on this point is not decisive although *ortho*- and *para*-positions in molecules containing such substituents are invariably more active than the *meta*.

The chlorine atom in both *o*- and *p*-chloronitrobenzene is much more labile than in the *meta*-isomer or in chlorobenzene itself, but the relative reactivities of the *ortho*- and the *para*-isomer depend markedly on the reagent. For replacement by piperidine the chlorine atom is much more reactive in the *ortho*-position (Chapman, Parker, and Soanes, *Chem. and Ind.*, 1951, 148), whereas replacement by a methoxide ion occurs more readily in the *para*-position (Miller, *J.*, 1952, 3550). Nevertheless, although the actual rates of replacement depend on the reagent, the relative energies of activation are largely independent of the reagent and are approximately equal for *ortho*- and *para*-substitution, usually with slight favouring of the former. This agrees with the theoretical prediction.

A similar situation arises in nucleophilic substitution in pyridine and its derivatives. No accurate data are available on the activation energies for the replacement of halogen in the halogenopyridines themselves, but by measuring activation energies for the replacement of chlorine by piperidine in 2- and 4-chloroquinoline, Brower, Samuels, Way, and Amstutz (*J. Org. Chem.*, 1953, **18**, 1648) found that the 2-position is more reactive than the 4- and that both are more reactive than the 3-position in quinoline or the 1- and the 2-position in naphthalene.

To explain the high *ortho* : *para* ratio found in electrophilic substitution of nitrobenzene (see De La Mare, *J.*, 1949, 2871) it is usually assumed that in the unperturbed nitrobenzene molecule the " *para* " resonance structure (I) makes a more important contribution to the

(I)   (II)

molecule than the " *ortho* " structure (II), thus placing a larger positive charge on the *para*-position than on the *ortho*-position and deactivating the former more than the latter to electrophilic substitution. If this assumption were true, then in nucleophilic substitution the *para*- would be more reactive than the *ortho*-position, which is contrary to experiment. The assumption has no sound theoretical basis and it seems more probable that the unexpected behaviour of nitrobenzene and similar compounds in electrophilic substitution is due to the importance of electron correlation in determining the energy of the transition state or to the high transmission of inductive effects as discussed by Dewar (*loc. cit.*).

It has already been emphasised that little significance can be placed on the numerical results obtained in this paper because of the uncertainty in the integrals used and the limited number of ionic structures included, but the qualitative results suggest that electron correlation is of some importance in heterolytic substitution reactions. For homolytic substitution the agreement between the VB and MO theories is close, and accurate MO calculations for these reactions will probably give as much agreement with experiment as is possible by the use of molecular wave functions consisting solely of combinations of atomic orbitals.

Appendix

The wave function for any molecule may be written :

$$\Psi = c_1\psi_1 + c_2\psi_2 + c_3\psi_3 + \ldots\ldots$$

This may be substituted in the Schrödinger equation to give :

$$\Psi(H - E)\Psi = (c_1\psi_1 + c_2\psi_2 + \ldots)(H - E)(c_1\psi_1 + c_2\psi_2 + \ldots\ldots) = 0$$

Whence $$c_1^2(H_{11} - ES_{11}) + c_2^2(H_{22} - ES_{22}) + \ldots\ldots + 2c_1c_2(H_{12} - ES_{12}) + \ldots\ldots = 0$$

Now $$S_{11} = S_{22} = S_{rr} = 1 \quad \text{and} \quad S_{rs}\ (r \neq s) = 0$$

therefore $$E(c_1^2 + c_2^2 + \ldots.) = c_1^2H_{11} + c_2^2H_{22} + \ldots\ldots + 2c_1c_2H_{12} + 2c_1c_3H_{13} + \ldots \quad . \quad . \quad . \quad . \quad (1)$$

Since the wave function is normalised,

$$c_1^2 + c_2^2 + c_3^2 + \ldots\ldots = 1$$

and, if there is only one structure with the charge on any particular atom (or if all the structures with the charge on the same atom may be grouped with one coefficient), then $c_r^2 = q_r$, where q_r is the charge on atom r.

Equation (1) may now be written :

$$E = q_1H_{11} + q_2H_{22} + \ldots + 2c_1c_2H_{12} + 2c_1c_3H_{13} + \ldots\ldots$$

In an ion such as the pentadienate cation or anion, H_{rr} is of the form $Q_r + x_r\alpha$ and H_{rs} is of the form $z_{rs}\alpha$; thus

$$E = q_1(Q_1 + x_1\alpha) + q_2(Q_2 + x_2\alpha) + \ldots\ldots + 2c_1c_2z_{12}\alpha + 2c_1c_3z_{13}\alpha + \ldots\ldots$$

Therefore $dE/dQ_1 = q_1$, and hence $\delta E = q_1\delta Q_1$. This relation is true provided that c_1 is independent of Q_1. When δQ_1 is small this will be nearly true, but when δQ_1 is large the change in c_1 with Q_1 will be appreciable. Thus, if δQ_1 is positive, c_1 will increase and δE will be greater than $q_1\delta Q_1$; if δQ_1 is negative, δE will be less than $q_1\,\delta Q_1$.

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