

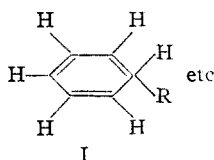
[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

A Quantum Mechanical Investigation of the Orientation of Substituents in Aromatic Molecules

BY G. W. WHELAND

In most of the previous discussions of orientation in aromatic molecules,¹ the more or less explicit assumption has been made that the ease of reaction at any given point is largely determined by the net electric charge at that point. Thus, in some reactions, including those of nitration, sulfonation, halogenation, diazo coupling, and so on, the substitutions are supposed to occur most readily at the most negative (or least positive) of the available positions; in certain other reactions, including those of hydrolysis, alcoholysis, and aminolysis of aromatic halides, and so on, the substitutions are supposed, on the contrary, to occur most readily at the least negative (or most positive) positions. In the former cases, the reagents, as well as the substitutions themselves, are said to be electrophilic; in the latter cases, they are said to be nucleophilic.²

A close connection exists between the above statement of the rules of orientation and the transition state theory of reaction rates. For any given substitution reaction, the activated complex that is formed between the aromatic molecule and the reagent is doubtless a resonance hybrid which receives contributions from a large number of different structures. Among these must be some of the type illustrated by I, in which



the reagent R is merely close to the carbon atom being attacked, but is not joined to it by a covalent bond. Such structures will be referred to hereafter as belonging to type I. It is to be noted that, in these, R need not correspond exactly to

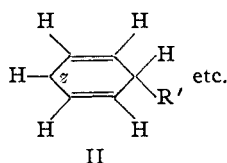
(1) (a) Robinson, "Outline of an Electrochemical (Electronic) Theory of the Course of Organic Reactions," Institute of Chemistry of Great Britain and Ireland, London, 1932; *Society of Dyers and Colourists, Jubilee Journal*, p. 65 (1934); (b) Ingold, *Ann. Rep.*, **23**, 129 (1926); *Rec. trav. chim.*, **48**, 797 (1929); (c) Hückel, *Z. Physik*, **72**, 310 (1931); (d) Wheland and Pauling, *THIS JOURNAL*, **57**, 2086 (1935); (e) Ri and Eyring, *J. Chem. Phys.*, **8**, 433 (1940); (f) Price, *Chem. Rev.*, **29**, 37 (1941).

(2) Ingold, *J. Chem. Soc.*, 1120 (1933); *Chem. Rev.*, **15**, 225 (1934). The terms "kationoid" and "anionoid" are used by some authors instead of "electrophilic" and "nucleophilic," respectively; for example, see Robinson, ref. 1a.

what one ordinarily thinks of as the reagent in the usual chemical sense. For example, in the reaction of chlorination, it may not be (and, in fact, almost certainly is not) a normal chlorine molecule, Cl-Cl; it may be instead a polarized chlorine molecule, $^+Cl\ Cl^-$, or a positive chloride ion, ^+Cl , or a complex formed with a catalyst molecule, such as Cl-Cl-AlCl₃, or something else of similar type. In view of the present lack of knowledge regarding the mechanism of the reaction and of the precise nature of the reagent that actually enters into the activated complex, it would be both pointless and dangerous to pursue this question any further here. It will be sufficient rather to state merely that, in an electrophilic substitution, the reagent R is supposed to be either a positive ion or else a neutral molecule with a dipole moment so oriented that its positive end is directed toward the point of attack; and that, in a nucleophilic substitution, R is supposed to be either a negative ion or else a neutral molecule with a dipole moment so oriented that its negative end is directed toward the point of attack. If, now, the further assumption is made that, in any activated complex, the various structures of type I are of so great importance that their stabilities determine that of the activated complex itself, the relationship postulated in the preceding paragraph between the charge distribution and the orientation of an entering substituent is suggested at once by elementary electrostatic considerations.

Although a self-consistent and generally satisfactory theory of orientation in electrophilic and nucleophilic substitutions can be built up in the above manner, a rather different, but closely related, approach seems to offer certain advantages. In an electrophilic substitution, the part of the reagent R which is closest to the aromatic molecule is considered not only to be positively charged, but also to have a gap (usually an open sextet) into which a pair of electrons can be put; while, in a nucleophilic substitution, that part of the reagent is considered not only to be negatively charged, but also to have an unshared pair of electrons which can be used to fill an open sextet.

This then suggests that an electrophilic substitution should occur most readily at the position at which an unshared pair of electrons, to fit into the open sextet in the reagent, can be provided most easily; and that a nucleophilic substitution should occur most readily at the position at which an open sextet, to accommodate the unshared pair in the reagent, can be provided most easily. This second statement of the rules of orientation can also be interpreted in terms of the transition state theory. The structures of type I are not the only ones which contribute to the activated complex, since others also can be written. An important further type of structure is illustrated by II, in which the reagent is linked by a covalent bond to the carbon atom attacked. Such structures will be referred to hereafter as belonging to type II. The symbol z represents here a positive



charge and an associated open sextet of electrons if the reagent is electrophilic, and it represents a negative charge and an associated unshared pair of electrons if the reagent is nucleophilic. The symbol R' represents the reagent R , modified by the formation of the bond and by the transference of a positive or negative charge, as the case may be, to the aromatic ring.

Relatively little attention has been paid in the past to these structures of type II, although Robinson^{1a} has considered them to be important, and Wheland and Pauling^{1d} have taken them into account to a limited extent by their consideration of the polarizabilities of the aromatic molecules. Ingold² also has emphasized the role of polarizability in orientation, and in a paper which appeared after the calculations reported below had been completed, Hughes and Ingold³ have suggested explicitly that the type II structures are of paramount importance in certain cases. In the present paper, the extreme point of view has been adopted that only the type II structures need be considered at all. This is certainly not correct, but it is probably no worse, and it may even be rather better, than the contrary view that has prevailed so widely heretofore. In any case, since no method is available at present for the

theoretical treatment of the interaction between the two different types of structure, it would seem desirable to examine *both* extremes separately.

As could have been anticipated from the close relationship between the two treatments, the qualitative conclusions reached on the basis of the structures of type II alone are found to be essentially the same as those reached on the basis of the structures of type I alone, in nearly all cases in which the substitution is either electrophilic or nucleophilic. There exists, however, still a third kind of substitution, the so-called radical substitution, which cannot be profitably treated on the basis of charge distribution. Thus, in the Gomberg and certain other reactions, the reagent R is apparently a free radical with an unpaired (odd) electron.⁴ In such cases, *all* substituent groups have been found to be ortho-para directing, regardless of their effects upon the charge distribution. It is evident, therefore, that a consideration of the structures of type I alone cannot account for the observed powerful orienting effects. This is hardly surprising, since there seems to be no reason to suppose that a structure in which a radical is close to a negative charge should be more stable than an analogous one in which it is close to a positive charge, or *vice versa*. There may be, however, a significant difference in the ease with which an odd electron, to be paired with the odd electron of the reagent, can be provided at the various positions. In other words, there may be a significant difference in the stabilities of the corresponding structures of type II (in which the symbol z now represents an unpaired electron upon an atom that has only seven electrons altogether in its valence shell). The calculations reported below show that this is indeed the case, and that the observed orientations can be accounted for in a simple and unambiguous manner. The present point of view, which has been foreshadowed by other authors,¹⁻⁴ has the advantage, therefore, not only of confirming and reinforcing the conclusions reached by the other method for electrophilic and nucleophilic substitutions, but also of making possible a single, unified treatment of all three classes of reaction.

Outline of the Method of Calculation

The calculations are based upon the molecular orbital treatment with the inclusion of the non-

(4) For discussions of the radical substitutions, see Hey and Waters, *Chem. Rev.*, **21**, 169 (1937); Hey, *Ann. Rep.*, **37**, 250 (1940).

(3) Hughes and Ingold, *J. Chem. Soc.*, 608 (1941).

orthogonality integral S^6 between adjacent atomic orbitals. As is usual, only the π electrons, of which there are six in benzene, eight in chlorobenzene, and so on, are considered. The effects of the ignored σ electrons are approximately constant in all the calculations, and so cancel out roughly when comparison is made between two different substances or between the various positions in a single substance. The procedure can be illustrated with the example of benzene. The problem is essentially to determine the amount of energy which must be supplied in order to provide at the point of attack an unshared pair of electrons, an open sextet, or an odd electron, depending upon whether the reagent is electrophilic, nucleophilic, or radical. This is equivalent to the problem of determining the difference in energy between, on the one hand, the normal benzene molecule and, on the other hand, a "polarized" benzene molecule in which 2, 0 or 1 electrons, respectively, are held fixed on the carbon atom attacked, and the remaining 4, 6 or 5 electrons, respectively, are distributed among the remaining 5 carbon atoms. The results of the calculations show that,⁶ with $S = S_0 = 0.25$, the energy of the normal benzene molecule (or, rather, the energy of its six π electrons) is $6\alpha + 5.8667\beta_0$, while the energies of the three different kinds of "polarized" benzene molecules are each $6\alpha + 4.0174\beta_0$. The difference, $\Delta W = -1.8493\beta_0$, is then a measure of the amount of energy that must be supplied in order to produce the postulated polarizations. The quantity β_0 has been found from thermochemical data⁷ to be equal approximately to -38 kcal. per mole, so that the calculated value of ΔW is of the order of 70 kcal. per mole. This is, of course, *not* the activation energy of the reaction, since, in its derivation, no account has been taken of the energies of the bonds that are broken or formed, and no allowance has been made for the effect of resonance with the structures of type I. The explicit assumption is made, however, that ΔW is a

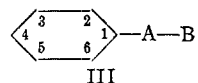
(5) The nomenclature used in this paper is essentially that employed by Mulliken and Rieke, *THIS JOURNAL*, **63**, 1770 (1941), and by Wheland, *ibid.*, **63**, 2025 (1941). In particular, the quantities S , α , β , and γ are defined as: $S = \int \varphi_i \varphi_j d\tau$, $\alpha = \int \varphi_i H \varphi_i d\tau$, $\beta = \gamma - S\alpha$, and $\gamma = \int \varphi_i H \varphi_j d\tau$, where φ_i is the π orbital upon the i th atom, φ_j is the π orbital upon an atom adjacent to the i th atom, H is the Hamiltonian operator corresponding to the self-consistent field, and $d\tau$ is the volume element in the configuration space of the electron. The energy of an electron in a given molecular orbital is represented as E . The remaining symbols, δ , ϵ , and ρ , which are introduced later, are defined at the time.

(6) The subscripts in the symbols S_0 and β_0 (and below in γ_0) signify throughout this paper that the values of the integrals appropriate to unsubstituted benzene are to be understood.

(7) Wheland, ref. 5.

part of the activation energy, and indeed that it is that particular part which is affected most strongly and in the most characteristic manner by any substituent that may be already present in the molecule. In other words, the assumption is made that the smaller the calculated value of ΔW is for reaction at a given position in a given molecule, the more rapidly the reaction will occur at that point.

In the extension of the treatment to more complex molecules, it is convenient to introduce the following system of nomenclature. In the generalized structure III, only those atoms, A and B,



of the substituent are to be taken into account which have electrons in π orbitals. In benzene and in pyridine, for example, neither A nor B exists; and in chlorobenzene and in phenol, only A exists. In toluene, when the treatment is based upon hyperconjugation,⁸ the "atom" B is actually a composite of the hydrogen atoms of the methyl group, and its π orbital is formed by hybridization of the hydrogen 1s orbitals; and in nitrobenzene, it consists of the *two* oxygen atoms of the nitro group, each with its own π orbital. Usually at least one of the atoms B, A, C₁, . . . must be assigned a different electron affinity from the others. In the mathematical treatment, this is done by setting the corresponding diagonal element of the secular equation equal not to $\alpha - E$ but to $\alpha + \delta\beta_0 - E = \alpha + \delta(\gamma_0 - S_0\alpha) - E$, where δ is a dimensionless parameter. The values of δ_b , δ_a , δ_1 , . . ., which correspond to the atoms B, A, C₁, . . ., respectively, are of uncertain magnitude, but their signs are determined by the relative electronegativities of the atoms concerned. In general, any atom that is more, or less, electronegative than a carbon atom in unsubstituted benzene is associated with a positive, or negative, value of δ , respectively; and the more the electronegativity of a given atom differs from that of a carbon atom of benzene, the larger is the magnitude of δ . Usually, also, at least one of the resonance integrals γ_{ba} , γ_{a1} , . . ., and at least one of the non-orthogonality integrals S_{ba} , S_{a1} , . . ., must be considered not to have the values γ_0 and S_0 , respectively, which are characteristic of unsubstituted benzene. In such a case, γ is *assumed* to be proportional to S . This means that, for each pair of

(8) Mulliken, Rieke and Brown, *THIS JOURNAL*, **63**, 41 (1941).

atoms, a single parameter ρ can be defined so that $\rho_{ba} = \gamma_{ba}/\gamma_0 = S_{ba}/S_0$, $\rho_{a1} = \gamma_{a1}/\gamma_0 = S_{a1}/S_0$, and so on. All of the various ρ 's are positive, but some may be greater, and some may be smaller, than 1. In all the calculations, S_0 is set equal to 0.25.

The fact that a number of adjustable parameters occur in the treatment in this way is unfortunate, especially since, for reasons of mathematical necessity, definite numerical values must be assigned in most cases to some or all of them. As a consequence, the results obtained appear to have more quantitative significance than they actually do. It must be realized that, since the assignment of values to the parameters must be made in a rather arbitrary manner, the magnitudes of the calculated quantities can be varied within wide limits. The *qualitative* conclusions reached in regard to orientation, on the other hand, are often dependent only on the sign of a single parameter, about which there is little or no uncertainty. In other cases, they are determined by merely the signs and approximate relative magnitudes of two or more parameters, about which again there is little or no uncertainty. It is evident, therefore, that the qualitative aspects of the treatment are upon a much firmer basis than the quantitative. This conclusion is reinforced by the further fact that the ignored structures of type I must actually be of considerable importance. Consequently, the purpose of the calculations described below will not be to obtain quantitative agreement with the experimental data. The most that can be expected is that the observed rules of orientation may be reproduced qualitatively, and that, with reasonable values of the parameters, the calculated effects may be of reasonable order of magnitude. The particular values assigned to the various parameters in the calculations were chosen by a trial-and-error method so as to give as good agreement as feasible with the rules of orientation and with the observed magnitudes and directions of the resonance moments. They are certainly not the only, and probably not the best, values that could have been chosen for this purpose, but they are good enough to serve as a basis for discussion.

A further example of the method of calculation is provided by chlorobenzene. Of all the substances considered in the present paper, this is the one for which the treatment is least satisfactory, and for which the conclusions reached are least

convincing. It forms, however, a particularly suitable example for discussion here, since it illustrates all of the remaining features of the calculation. The special difficulties which arise with this molecule (but which are of less importance, if they occur at all, in the other cases) are due to the fact that, for this substance, the correct orientation does not follow unambiguously from a consideration of merely the signs and approximate relative magnitudes of the various parameters, but can be obtained only with a rather careful choice of the exact values of the parameters. Since chlorine is a more electronegative element than carbon, the parameter δ_a must be positive in sign and fairly large in magnitude. Moreover, the carbon atom C_1 must have a somewhat greater electron-affinity than the other atoms of the ring, since it has lost electrons to the chlorine atom as a result of polarization of the σ bond. Consequently δ_1 must also be positive, but certainly smaller in magnitude than δ_a . Similarly, δ_2 and δ_6 , which are necessarily equal, may have still smaller positive values on account of the proximity of the atoms C_2 and C_6 to C_1 . In Table I are listed the results obtained when δ_a and ρ_{a1} are set equal to 1.6 and 0.85, respectively, and when δ_1 and δ_2 are treated by the first-order perturbation method.⁹ (As usual when no statement is made to the contrary, all remaining δ 's and ρ 's are assigned the values 0 and 1, respectively.) It is seen that, with this choice of parameters, and with $\delta_1 = 0.4$ and $\delta_2 = 0$, the calculation leads to the incorrect result that substitution by an electrophilic reagent should occur at the ortho and para positions in chlorobenzene more easily than at any of the six positions in unsubstituted benzene. If ϵ_1 is set equal to about 0.15 (so that δ_1 becomes equal to about 0.55) this difficulty is eliminated, but a new one arises in that then the orientation should be meta instead of ortho-para, as is observed. The logical next step is to assign some reasonable value to δ_2 .¹⁰ Clearly this must be positive, and smaller in magnitude than δ_1 . For substitution in the meta and para positions, the calculation can then still be carried through in a straightforward manner, and the results that are obtained with δ_2 equal to about 0.075 are satisfactory, as regards both electrophilic and radical

(9) Since it was desired to have the perturbation treatment as accurate as possible for fairly large values of δ_1 , a new constant, ϵ_1 , defined by the equation $\delta_1 = 0.4 + \epsilon_1$, was used as the perturbation parameter in place of δ_1 itself.

(10) It is to be understood here, and later, that any value assigned to δ_2 must be simultaneously assigned to δ_6 as well.

TABLE I

Compound	Values of parameters ^a	Point of attack	ΔW^b			Observed orientation ^c	Resonance moment	
			Electrophilic	Nucleophilic	Radical		Calcd.	Obsd. ^d
Benzene	1.849	1.849	1.849	0	0
Chlorobenzene	$\delta_a = 1.6$	ortho	$1.814 + 0.225 \epsilon_1$	$1.848 - 0.429 \epsilon_1$	$1.831 - 0.102 \epsilon_1$	Electrophilic: $B > o, p > m$ Radical: $o, p > m$	0.2D	0.6D
	$\delta_1 = 0.4 + \epsilon_1$	meta	$1.852 + 0.006 \epsilon_1$	$1.852 + 0.006 \epsilon_1$	$1.852 + 0.006 \epsilon_1$			
	$\rho_{a1} = 0.85$ $\epsilon_1 = 0.15$ $\delta_2 = 0.075$	para	$1.826 + 0.278 \epsilon_1$ $+ 0.018 \delta_2$	$1.860 - 0.377 \epsilon_1$ $+ 0.017 \delta_2$	$1.843 - 0.049 \epsilon_1$ $+ 0.017 \delta_2$			
Phenol (or aniline)	$\delta_a = 0.8$	ortho	1.619	1.950	1.785	Electrophilic: $o, p >> m$
	$\delta_1 = 0.2$	meta	1.854	1.854	1.854			
	$\rho_{a1} = 0.8$	para	1.647	1.986	1.816			
5-Hydroxyhydrindene	$\delta_a = 0.8$	4	1.592	1.945	1.768	Electrophilic: $4 > 6 > B$
	$\delta_5 = 0.2$ $\rho_{a5} = 0.8$ $\rho_{a8} = 0.9$	6	1.651	1.960	1.806			
Pyridine ^e	α	$1.849 + 0.239 \delta_1$ $+ (0.012 \delta_2)$	$1.849 - 0.427 \delta_1$ $+ (0.012 \delta_2)$	$1.849 - 0.084 \delta_1$ $+ (0.012 \delta_2)$	Electrophilic: $B > \beta > \alpha, \gamma$
	β	$1.849 + 0.007 \delta_1$ $+ 0.530 \delta_2$	$1.849 + 0.007 \delta_1$ $- 0.804 \delta_2$	$1.849 + 0.007 \delta_1$ $- 0.137 \delta_2$	Nucleophilic: $\alpha, \gamma >> B, \beta$		
	γ	$1.849 + 0.290 \delta_1$ $+ 0.013 \delta_2$	$1.849 - 0.376 \delta_1$ $+ 0.013 \delta_2$	$1.849 - 0.043 \delta_1$ $+ 0.013 \delta_2$	Radical: $\alpha, \gamma > B, \beta$		
Toluene ^f	$\delta_b = -0.2$	ortho	$1.816 + 0.004 \delta_a$	$1.832 + 0.004 \delta_a$	$1.824 + 0.004 \delta_a$	Electrophilic: $o, p > m > B$	0.15D ^g	0.4D ^h
	$\rho_{ba} = 2.0$	meta	$+ 0.234 \delta_1 + (0.014 \delta_2)$	$- 0.406 \delta_1 + (0.014 \delta_2)$	$- 0.086 \delta_1 + (0.014 \delta_2)$	Nucleophilic: $B > m > o, p$		
	$\rho_{a1} = 0.7$ $\delta_1 = -0.1$ $\delta_2 = -0.01$	para	$1.851 + 0.000 \delta_a$ $+ 0.006 \delta_1 + 0.528 \delta_2$	$1.851 + 0.000 \delta_a$ $+ 0.006 \delta_1 - 0.805 \delta_2$	$1.851 + 0.000 \delta_a$ $+ 0.006 \delta_1 - 0.138 \delta_2$	Radical: $o, p > m$		
Nitrobenzene	$\delta_b = 0.8$	ortho	1.886	1.783	1.834	Electrophilic: $B > m > o, p$	-1.1D ⁱ	-0.7D
	$\delta_a = 0.4$	meta	1.852	1.852	1.852	Nucleophilic: $o, p > m > B$		
	$\rho_{a1} = 0.6$	para	1.861	1.757	1.809	Radical: $o, p > m$		
Nitrosobenzene	$\delta_b = 0.8$	ortho	1.846	1.635	1.740	Electrophilic: ? ^j	-0.6D ^k	-0.8D
	$\delta_a = 0.4$	meta	1.854	1.854	1.854	Nucleophilic: $o, p >> B, m$		
	$\rho_{a1} = 0.6$	para	1.871	1.660	1.765			
Naphthalene	α	1.639	1.639	1.639	Electrophilic: $\alpha > B, \beta$	0	0
	β	1.794	1.794	1.794			
2-Naphthol	$\delta_a = 0.8$	1	1.397	1.755	1.576	Electrophilic: $1 >> 3, B$
	$\delta_2 = 0.2$ $\rho_{a2} = 0.8$	3	1.668	1.803	1.735			

^a In this column are listed not only the values assigned to the parameters introduced directly into the secular equation, but also the values suggested for the further parameters treated by the perturbation method. ^b Expressed in units of the positive quantity $-\beta_0 \cong 38$ kcal. per mole. The values given here have been rounded off by the omission of the last significant figure that was carried through the calculations. ^c In this column, the symbol $>$ may be read "is a more reactive position than." The letter B refers to unsubstituted benzene. Positions separated by a comma (as *o*, *p* or B, *m*) are not necessarily equally reactive. ^d Cf. ref. 13. ^e The calculations for pyridine can be applied also to toluene if hyperconjugation is neglected.¹⁷ ^f With hyperconjugation. ^g This value was obtained with the parameter values as listed in the second column, except that δ_1 and δ_2 were set equal to zero. The effect of putting $\delta_1 = -0.1$ and $\delta_2 = -0.01$ would be to increase the calculated resonance moment by a small amount, and so to improve the agreement. ^h On the assumption that the entire moment of toluene is due to resonance. ⁱ The calculated value of the moment of nitrobenzene due to the π electrons alone is $-4.4D$; that of an isolated nitro group is $-3.3D$. ^j Cf. Taylor and Baker, "Sidgwick's Organic Chemistry of Nitrogen," Oxford University Press, New York, N. Y., 1937, pp. 215-216. ^k The calculated value of the moment of nitrosobenzene due to the π electrons alone is $-2.1D$; that of an isolated nitroso group is $-1.5D$. ^l This value was obtained by interpolation between the values of $0.7D$ and $0.0D$, which were obtained by setting $\epsilon_1 = \delta_2 = 0$, on the one hand, and $\epsilon_1 = 0.2$ and $\epsilon_2 = 0.1$, on the other.

substitution. (Experimental data regarding nucleophilic substitution seem to be lacking in this case.) On the other hand, for substitution in the ortho position, the procedure is ambiguous and can only be carried through at all with the aid of arbitrary assumptions. In the "polarized" molecules for which the calculations are made, 2, 0 or 1 electrons (for electrophilic, nucleophilic or radical substitution, respectively) are considered to be held fixed upon the atom attacked, which in the present case is assigned a different electron-affinity from the other atoms of the ring. These electrons (together with 0, 2 or 1 additional ones, respectively, that are provided by the reagent R) are employed in the structures of type II in forming the covalent bond between the reagent and the aromatic molecule. The energy of this bond is, of course, affected by any change in the electron-affinity of the atom C_2 , and a suitable correction has to be made. The following completely arbitrary procedure has been adopted for this purpose: In the discussion up to this point, the energies of the 2, 0, or 1 electrons held fixed on the ortho carbon atom for substitution at the ortho position have been set equal to 2α , 0 and α , respectively; they will now be set equal instead to 2α

+ $0.75 \delta_2 \beta_0$, $0.75 \delta_2 \beta_0$ and $\alpha + 0.75 \delta_2 \beta_0$, respectively. The coefficient 0.75 is introduced here in order to make the calculated values of ΔW approximately equal for reaction at the ortho and para positions. A small amount of justification for this choice can be provided: if the electrons which form the bond between the reagent and the ring carbon atom were shared equally, the coefficient could be shown¹¹ to be somewhat smaller than 1; since, however, most such reagents are more electronegative than carbon, the sharing is not equal, and the coefficient should be somewhat smaller still. In view of the great uncertainty that attaches to this procedure, the numerical results obtained with its aid are enclosed in parentheses in Table I. Fortunately, this difficulty is serious only in the present case; with the remaining molecules for which calculations have been made, the values assigned to the parameter δ_2 are so small that the exact magnitude of its coefficient is immaterial. Since, however, the present uncertainty is always encountered in any calculation, the attempt has not been made to differentiate between the ortho and para positions, but only to distinguish these two from the meta.

Although, as has been discussed above, the present treatment cannot be expected to provide quantitatively accurate results, the magnitudes of the calculated quantities are nevertheless reasonable. For example, when δ_a , δ_1 , δ_2 and ρ_{a1} are equal to 1.6, 0.55, 0.075 and 0.85, respectively, the value of ΔW for electrophilic substitution is greater at the para position of chlorobenzene than at any of the positions of unsubstituted benzene by $-0.020 \beta_0$, or about 0.76 kcal. per mole. If this represented the difference in free energies of activation, the ratio of the rate constants for the corresponding reactions would be about $2/7$ at 25° . The experimental ratio for nitration with acetyl nitrate is about $1/7$ or $1/8$, depending upon the solvent used.¹² Moreover, the calculated value of the contribution of the π electrons alone to the dipole moment is about $0.2D$, with the chlorine positive; this is to be compared with the so-called resonance moment, which is equal to about $0.6D$ and is in the direction calculated.¹³

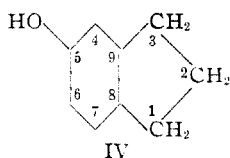
(11) This statement follows from first-order perturbation theory and might no longer be true if δ_2 were large. It should perhaps be mentioned also that, if the non-orthogonality integral between the atom C_2 and the reagent R were neglected, the coefficient would be just unity when the sharing is equal.

(12) Bird and Ingold, *J. Chem. Soc.*, 918 (1938).

(13) Sutton, *Trans. Faraday Soc.*, 30, 789 (1934); Smyth, *J. Org. Chem.*, 1, 17 (1936).

It is gratifying that such agreement, as regards order of magnitude, is possible in this particularly unfavorable case, with both the rates of reaction and the dipole moment. It is apparent, however, that the present treatment is of much less certain significance than the analogous treatments of the remaining molecules, in which corresponding difficulties arise to a more limited extent, if at all.

The remaining calculations reported in Table I require little further comment. It is to be noted that the calculations for phenol and for aniline are identical with the one for chlorobenzene, except for a different choice of values for the various parameters. The results of the similar calculation for 5-hydroxyhydrindene (IV) are of interest in that they provide a simple interpretation of the Mills-Nixon effect; the fact that the value of



ρ_{89} is apparently less than 1 may be due to a distortion of the bond angles as was postulated originally by Mills and Nixon¹⁴ and subsequently by other authors,¹⁵ or possibly to an elongation of the C₈-C₉ bond by a spring-like action of the five-membered ring. With pyridine, complete agreement with the observed rules of orientation is obtained if δ_1 is given any positive value.¹⁶ (In this molecule, the carbon atom C₁ is replaced by a nitrogen atom with, of course, a greater electron-affinity.) This agreement is not affected if δ_2 also is given a small positive value, less than that of δ_1 . In toluene, if the methyl group is considered

philic and nucleophilic, but not for radical substitutions.¹⁷ When hyperconjugation⁸ between the methyl and phenyl groups is considered, however, this difficulty is removed. The orienting effects of the nitro and nitroso groups are accounted for without complications. (In the latter case, recognition of the fact that δ_1 must actually have a small positive value may be required.)

The results of the calculations for naphthalene¹⁸ are in qualitative agreement with the observation that reaction with an electrophilic reagent takes place predominantly at the α position and occurs more easily than in benzene. The numerical magnitudes are out of line, however, with those obtained in the analogous treatments of simple benzene derivatives; in view of the wide difference in type of molecule, this is hardly surprising, since, for the reasons discussed above, quantitative agreement cannot in general be expected. Similarly, in 2-naphthol, the observed much greater ease of electrophilic substitution in the 1 than in the 3 position¹⁹ is accounted for by the calculation, but the comparison with the simple benzene derivatives is again not good. It is of interest that here, as in 5-hydroxyhydrindene, nothing corresponding to an appreciable fixation of the bonds in the unreacting molecule¹⁹ has had to be postulated.

Mathematical Appendix

The procedure for the carrying out of the numerical calculations can be explained most readily with reference to a specific example. The secular equation for the normal chlorobenzene molecule can be written down initially in the form

$$\begin{vmatrix} \alpha + \delta_a \beta_0 - E & \rho_a(\gamma_0 - S_0 E) & 0 & 0 & 0 & 0 & 0 & 0 \\ \rho_a(\gamma_0 - S_0 E) & \alpha + \delta_1 \beta_0 - E & \gamma_0 - S_0 E & 0 & 0 & 0 & \gamma_0 - S_0 E & 0 \\ 0 & \gamma_0 - S_0 E & \alpha - E & \gamma_0 - S_0 E & 0 & 0 & 0 & 0 \\ 0 & 0 & \gamma_0 - S_0 E & \alpha - E & \gamma_0 - S_0 E & 0 & 0 & 0 \\ 0 & 0 & 0 & \gamma_0 - S_0 E & \alpha - E & \gamma_0 - S_0 E & 0 & 0 \\ 0 & 0 & 0 & 0 & \gamma_0 - S_0 E & \alpha - E & \gamma_0 - S_0 E & 0 \\ 0 & \gamma_0 - S_0 E & 0 & 0 & 0 & \gamma_0 - S_0 E & \alpha - E & \gamma_0 - S_0 E \\ 0 & 0 & 0 & 0 & 0 & \gamma_0 - S_0 E & \alpha - E & \gamma_0 - S_0 E \end{vmatrix} = 0$$

merely to affect the electron-affinity of the carbon atom to which it is attached, complete agreement cannot be obtained. The observed direction of the dipole moment of this substance requires that δ_1 , and also presumably δ_2 , be negative. Then the correct orientations are predicted for electro-

All δ 's and ρ 's not explicitly mentioned here have been set equal to 0 and 1, respectively. The substitutions⁷

$$\frac{\alpha - E}{\gamma_0 - S_0 \alpha} = \frac{y}{1 - S_0 y}$$

(17) This can be seen from the figures for pyridine in Table I, if δ_1 and δ_2 are given small negative, instead of positive, values.

(18) For this substance, a consideration of charge distribution alone would lead to no prediction regarding orientation for any of the three types of substituting reagent; cf. Wheland and Pauling, ref. 1d.

(19) Fieser and Lothrop, *THIS JOURNAL*, **57**, 1459 (1935).

(14) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930).

(15) Sutton and Pauling, *Trans. Faraday Soc.*, **31**, 939 (1935).

(16) It is interesting that, with this substance, the orientation for a radical reagent could not have been predicted from the sort of qualitative reasoning employed by Hey and Waters,⁴ but follows only from the numerical calculation.

and

$$1 - S_0\delta = \zeta$$

bring this into the more easily managed form

$$\begin{vmatrix} \zeta_a y + \delta_a & \rho_{a1} & 0 & 0 & 0 & 0 & 0 \\ \rho_{a1} & \zeta_1 y + \delta_1 & 1 & 0 & 0 & 0 & 1 \\ 0 & 1 & y & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & y & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & y & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & y & 1 \\ 0 & 1 & 0 & 0 & 0 & 1 & y \end{vmatrix} = 0$$

The four lowest roots of the equation, when $\delta_a = 1.6$, $\delta_1 = 0.4$, $\rho_{a1} = 0.85$, and $S_0 = 0.25$, are found to be

$$y = -3.3034, -1.8934, -1.0000, -0.9338$$

or

$$E = \alpha + 1.8093 \beta_0, \alpha + 1.2851 \beta_0, \alpha + 0.8000 \beta_0, \alpha + 0.7571 \beta_0$$

The energy of the eight π electrons is accordingly

$$2(\alpha + 1.8093 \beta_0 + \alpha + 1.2851 \beta_0 + \alpha + 0.8000 \beta_0 + \alpha + 0.7571 \beta_0) = 8\alpha + 9.3036 \beta_0$$

In the "polarized" molecule, 6, 8 or 7 electrons (for electrophilic, nucleophilic, or radical substitution, respectively) are to be distributed among the six atoms other than the one at which reaction occurs. The secular equations, therefore, can be derived from the one given above for the normal molecule by striking out from it the third row and column for ortho substitution, or the fourth row and column for meta substitution,²⁰ or the fifth row and column for para substitution. In the case of para substitution, the four lowest roots are

$$y = -3.2997, -1.5764, -1.0000, 0.0168$$

or

$$E = \alpha + 1.8081 \beta_0, \alpha + 1.1308 \beta_0, \alpha + 0.8000 \beta_0, \alpha - 0.0169 \beta_0$$

when the parameters are assigned the same values as above. The energies of the "polarized" molecules are therefore

$$2(\alpha + 1.8081 \beta_0 + \alpha + 1.1308 \beta_0 + \alpha + 0.8000 \beta_0) + (0, 2, 1)(\alpha - 0.0169 \beta_0) + (2, 0, 1)\alpha = 8\alpha + 7.4778 \beta_0, 8\alpha + 7.4440 \beta_0, 8\alpha + 7.4609 \beta_0$$

for electrophilic, nucleophilic and radical substitution, respectively. The last term on the left side of the above equation represents the energy of the 2, 0 or 1 electrons, respectively, held fixed on the atom attacked (the para atom in the present case). The corresponding values of ΔW are $-1.8258 \beta_0$, $-1.8596 \beta_0$, and $-1.8427 \beta_0$, as given in Table I.

After the secular equations have been solved,

(20) Or, of course, the seventh row and column for ortho substitution, or the sixth row and column for meta substitution.

the normalized molecular orbitals can be found in the usual way. These have the general form

$$\psi_k = \kappa_{k0}\varphi_a + \kappa_{k1}\varphi_1 + \dots$$

where the φ 's have the same significance as before,⁵ and the κ 's are numerical coefficients. The summation in each case is extended over all the atomic orbitals involved—seven for the normal chlorobenzene molecule and six for each of the various "polarized" molecules. In the first-order perturbation treatment, the energy of each molecular orbital ψ_k is increased by an amount equal to $(\kappa_{kr})^2 \delta_r \beta_0$ for each δ_r ,²¹ which is considered to have a non-vanishing value (aside from those taken care of explicitly in the secular equation).

The calculation of the resonance moment requires that the charge distribution be determined. The assumption is made that this is given with sufficient accuracy by distributing the electrons among the atoms in the following manner: an electron occupying a molecular orbital ψ_k is divided up in such a way that a fraction of it, equal to $\sum_s \kappa_{kr} \kappa_{ks} S_{rs}$ of an electron, is assigned to each atom r . It is to be noted that in this summation, $S_{rr} = 1$, and $S_{rs} = 0$ if the atoms r and s are neither identical nor adjacent. The normalization of the orbital then makes it certain that the entire electron will be accounted for.

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Summary

A quantum mechanical discussion of orientation in aromatic molecules has been given. The present treatment, which is based upon the molecular orbital method, differs from the previous ones in that it centers attention not upon the charge distributions in the isolated molecules, but upon the energies of those structures contributing to the activated complex, in which a covalent bond is formed between the aromatic ring and the reagent. In this way, substitutions by electrophilic, nucleophilic, and radical reagents can be treated from a unified point of view. With the use of reasonable values for the various parameters that enter the calculations, complete qualitative agreement is obtained with the empirical rules of orientation. While quantitative agreement could not have been anticipated, the calcu-

(21) In the treatment of chlorobenzene from this point, the parameter δ_1 is to be replaced, of course, by ϵ_1 , since the latter is the actual perturbation parameter used.

lated effects are of correct order of magnitude, as regards both the rates of substitution and the values of the resonance moments. It is of particular interest that orientation in 5-hydroxyhy-

drindene and 2-naphthol is accounted for without the assumption of appreciable fixation of bonds in the unreacting molecules.

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Some Esters of Thiodiglycol

BY WEAVER R. CLAYTON¹ AND E. EMMET REID

Though thiodiglycol has been known for a long time^{1a} and has been manufactured on a large scale for making "mustard gas," it has not been extensively studied. It seemed worth while to prepare it and some of its esters in high purity so as to determine their properties. The formate, acetate, benzoate and phthalate are mentioned in a patent² but not fully characterized. The *p*-nitro and *p*-aminobenzoates have been made.³

Experimental

Thiodiglycol.—The crude thiodiglycol which had been made from chlorhydrin contained a considerable amount of dithiane and its polymers. Distillation at 153° (8 mm.) removed much of the impurities. The polymeric material is said to break down at 160°,⁴ The distillate was diluted with sufficient water to bring its boiling point down to 165° and superheated steam passed through it. After evaporating off the water the thiodiglycol was distilled at 147.5° (6 mm.).

Purified thiodiglycol melts at -10°, distills at 147.5° (6 mm.), 165° at 20 mm., 181.5° at 40 and has d_4^{20} , 1.1973, d_4^{25}

acid, it is stable at 180° for many hours. Heated at 100° for thirty minutes with 2.5 parts of 0.1 *N* sodium hydroxide an appreciable amount of sulfide ion is formed and much more with 1 *N*, though it is only half decomposed by solid sodium hydroxide at 140° in ten hours. Lead acetate and cupric nitrate decompose it at 100°, but barium hydroxide, calcium oxide and alumina have little effect even at 180° for ten hours. It was hoped that calcium oxide or alumina would dehydrate it to vinyl sulfide but they did not.

Esters.—The esters of Table I were made by heating thiodiglycol to 150–160° with the acid anhydrides for five hours or with the acids (caproic and *i*-valeric) for ten. At the end of the heating, suction was applied and the excess reagent, together with acid or water that had been formed, distilled out. To the residue of ester and unreacted glycol 1 volume of water and 1.5 of benzene were added. The benzene layer was twice washed with 0.5 volume of water and the benzene removed under vacuum. The esters were distilled twice at 8 mm. In making the formate, the glycol was refluxed with two parts of 85% formic acid, the acid and water distilled off and the refluxing repeated with one part of the acid. The yields of the esters were high, up to 95%. The saponification numbers were determined in the usual way.

TABLE I
ESTERS OF THIODIGLYCOL

Ester	M. p., °C.	B. p., °C.	Press., mm.	d_4^{20}	d_4^{25}	n_D^{20}	Saponification no.	
							Calcd.	Found
Formate	-15.5	134.5 ^b	8	1.2525	1.2275	1.4804	533.8	531.7
Acetate	..	139.5 ^b	8	1.1626	1.1382	1.4679	470.9	470.9
Propionate	-23	158	8	1.1112	1.0874	1.4648	421.2	419.9
Butyrate	-28	172	8	1.0716	1.0491	1.4627	375.6	374.1
Butyrate ^a	..	172-3	8	1.0721	1.0496	1.4630
<i>i</i> -Valerate	..	181-2	8	1.0384	1.0171	1.4598	348.1	247.4
<i>i</i> -Valerate ^a	..	182	8	1.0372	1.0158	1.4593
Caproate	7	207	7	1.0198	1.0024	1.4627	320.3	320.3

^a From the potassium salt and mustard gas. ^b Kränzlein and Corell² give 130–7° (7 mm.) for the formate and 142–50° (12 mm.) for the acetate.

1.1793 and n_D^{20} 1.5146. It is miscible with water, the lower alcohols, chloroform and ethyl acetate. At 25° 100 g. of benzene dissolves 1.07 g., 100 g. of absolute ether 7.09 g. and 100 g. of ligroin 0.06 g. Alone, or with an organic

Two of the esters were also made by refluxing mustard gas in 6 to 8 parts of absolute alcohol with the potassium salt of the acid for five hours. The most of the alcohol was taken off at reduced pressure and the salt filtered off and washed with alcohol. The crude ester was distilled at 8 mm., purified with the water-benzene treatment and again distilled. Acetyl chloride converts about two-thirds of thiodiglycol into the acetate and the rest to mustard gas.

(1) From Dissertation, June, 1928. Original manuscript received July 28, 1941.

(1a) Carius, *Ann.*, **124**, 263 (1862).

(2) Kränzlein and Corell, U. S. Patent 1,422,869 (1922).

(3) Major, *Bull. soc. chim.*, **41**, 634 (1927).

(4) Masson, *J. Chem. Soc.*, **49**, 236 (1886).