58. *The Localization Theory of Organic Reactions. Part III.* Radical Substitution in Pyridine.*

By R. D. Brown.

Kooyman and Farenhorst's data (*Trans. Faraday Soc.*, 1953, **49**, 58) for the rates of attack of polycyclic aromatic hydrocarbons by radicals have been used to determine the quantitative relation between rates of attack and the corresponding molecular-orbital localization energies, A_r. This relation has been used in conjunction with Hey and Williams's results (*Discuss. Faraday Soc.*, 1953, **14**, 216) for the partial rate factors for phenylation of pyridine to yield a unique set of molecular-orbital parameters for nitrogen, *viz.*: $\alpha_N = \alpha_C + 0{\cdot}5\beta$, $\beta_{CN} = \beta_{CC} = \beta$.

Rates of attack at the pyridine positions relative to a benzene position calculated from atom-localization energies, A_r, by using these parameters, agree within 10% with experimental rates.

The molecular-orbital theory of chemical reactivity in conjugated compounds has been used successfully to interpret and predict chemical properties of hydrocarbons. For heterocyclic compounds the theory has been somewhat limited because the numerical values of the

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parameters applying to heteroatoms are not at all well known. Thus in the molecular-orbital treatment of nitrogen heterocycles it is customary to use two parameters, h and k, defined by:

$$\alpha_N = \alpha_C + h\beta; \quad \beta_{CN} = k\beta$$

in which α_C is the coulomb integral of carbon and β the standard resonance integral of a carbon–carbon bond. Recent work on homolytic substitution in aromatic compounds has provided valuable evidence for evaluating the theoretical parameters. Thus if Hey and Williams's results (*Discuss. Faraday Soc.*, 1953, **14**, 216) on the relative yields of isomers in the phenylation of pyridine are assumed to be a measure of the relative rates of radical substitution at positions 2, 3, and 4 the values of the parameters h and k which yield localization energies in best agreement with experiment can be determined, as shown below.

It is not satisfactory to discuss the reactivities of heterocycles (or, for that matter, benzene derivatives) towards radicals in terms of free valencies because the theoretical justification in terms of approximate activation energies cannot then be made (Brown, *J. Chim. phys.*, 1953, **50**, 109; further results to be published; cf. Burkitt, Coulson, and Longuet-Higgins, *Trans. Faraday Soc.*, 1951, **47**, 553). One must therefore use the localization theory, interpreting the reactivities in terms of the appropriate atom-localization energies, A_r (Brown, *Quart. Rev.*, 1952, **6**, 63).

The localization energies represent the part of the activation energy arising from π-electron redistributions. In the localization theory we assume that it is only this contribution to the activation energy which varies from one aromatic position to another; this assumption has been shown to be extraordinarily good for another type of homolytic reaction (Brown, *J.*, 1951, 1955; *Quart. Rev.*, 1952, **6**, 90) and is justified in the present instance by the correlation exhibited in Fig. 1. The relation of partial rate factors is therefore:

$$\boldsymbol{R}T \log k_1/k_2 = a(A_2 - A_1) \quad \ldots \ldots \ldots (1)$$

where the constant a might vary with the nature of the attacking radical. Kooyman and Farenhorst's results for radical reactivities of hydrocarbons towards trichloromethyl radicals at 91° (*Nature*, 1952, **169**, 153; *Trans. Faraday Soc.*, 1953, **49**, 58) may be used to determine a. In Fig. 1 their data for logarithmic partial rate factors are plotted against A_r for the relevant positions in the hydrocarbons. Some corrections to the partial rate factors have been made in view of more recent work on diphenyl (Cadogan, Hey, and Williams, *J.*, 1954, 794) and the fact that, if localization energies are considered, positions 9 and 10 of phenanthrene are the most reactive so that the reaction rate for position 9 is one-half of the total molecular rate, and not one-quarter as assumed by Kooyman and Farenhorst. The slope of the line in Fig. 1 is 7·5 kcal./β. This value for a means that quite small differences in localization energies correspond to appreciable differences in rates of chemical attack; *e.g.*, if two positions differ in localization energy by 0·03β, one will be attacked twice as fast as the other at 91°.

The above value of a is appropriate for attack by trichloromethyl radicals. Experiments by Dunn, Waters, and Roitt (*J.*, 1954, 580) showed that approximately the same value is suitable for benzoyl radicals. Therefore it is reasonable to assume, in the absence of more definite evidence, that a similar value may be employed when the attack is by phenyl radicals.

From this value of a the experimental partial rate factors (relative to a benzene position) for positions 2, 3, and 4 in pyridine may be converted into localization-energy differences (from the value for a benzene position, $-2·5359\beta$). These are listed in the accompanying Table.

Reactivities of pyridine positions at 80°.

Position	Partial rate relative to a benzene position	$\boldsymbol{R}T \log k$	" Experimental " atom-localization energy
2	1·91	0·197	2·510 ($-\beta$)
3	0·86	−0·046	2·542
4	1·01	0·003	2·536

It seems reasonable to attribute an experimental uncertainty of about 10% to the measured partial rate factors, which corresponds to an uncertainty in the "experimental" localization energies of $\pm 0{\cdot}004\beta$.

A contour plot of the value of h and k which produce theoretical localization energies for each of the positions covering the "experimental" range of values is given in Fig. 2. This was obtained by preparing a series of graphs of localization energies as a function of k^2 for various constant values of h and reading from the graphs the values of k which corresponded to the two extremes of "experimental" localization energies.

From Fig. 2 it is seen that the three "experimental" localization energies of the Table are obtained only when values of h and k falling in two very small regions of the (h,k) plane are used in the theoretical calculations. These two regions are around the points (i) $h = 0{\cdot}5$, $k = 1$ and (ii) $h = -0{\cdot}5$, $k = 1$. The second of these regions must be rejected because negative values of h correspond to a nitrogen atom's being less electronegative than carbon, which is physically unacceptable. Therefore the calculated atom-localization energies can be brought into agreement with the observed radical reactivities of the pyridine positions only if numerical values of the parameters close to $h = +0{\cdot}5$, $k = 1$, are used.

FIG. 1. *Relation between localization energies and rates of attack by trichloromethyl radicals.*

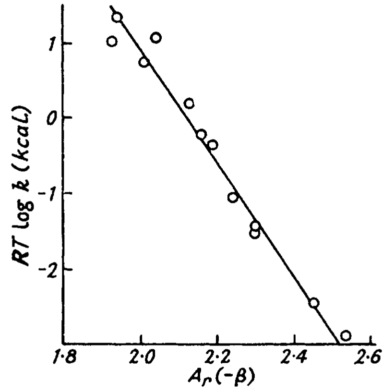
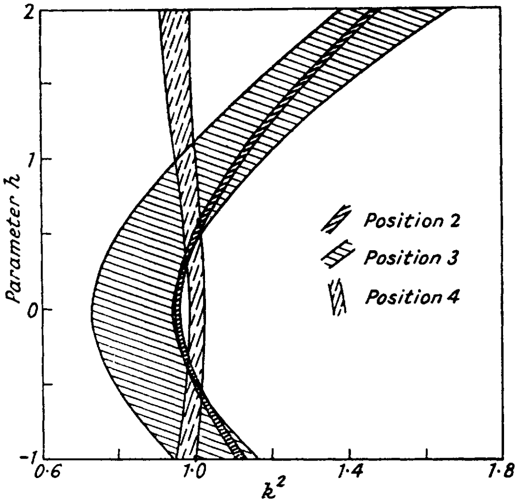


FIG. 2. *Values of the molecular-orbital parameters h and k giving agreement with experiment.*



It is interesting that these values are in reasonable agreement with those derived by other considerations. For example, calculations of dipole moments have been used to derive a value of 0·6 for h (Lowdin, *J. Chem. Phys.*, 1951, **19**, 1323; cf. Odiot and Roux, *J. Chim. phys.*, 1953, **50**, 141) while thermochemical considerations have been used to deduce a value of 1·2 for k (Orgel, Cottrell, Dick, and Sutton, *Trans. Faraday Soc.*, 1951, **47**, 113). However the present values are to be preferred for calculations pertaining to chemical reactivities. Certain defects in the simple molecular-orbital method are ameliorated by adjustment of the parameters to optimum values and there is no reason why the best values for dipole-moment calculations, for example, should also be the best values for calculations of chemical reactivity.

It is also of interest that the simple molecular-orbital approximation is capable of reproducing theoretical rates of attack of pyridine in excellent agreement with experiment when the major hetero-parameters are suitably chosen. The disagreement between theory and experiment, discussed by Hey and Williams (*loc. cit.*) and by Maccoll (*Discuss. Faraday Soc.*, 1953, **14**, 251), is to be ascribed to poor selection of the parameters for pyridine. It is likely that similar agreement between theory and experiment could be obtained for the benzene derivatives studied by Hey, Williams, and their co-workers by a suitable choice of parameters, at least so far as the sterically unhindered *meta*- and *para*-positions are concerned.

Levy and Szwarc (*J. Amer. Chem. Soc.*, 1955, **77**, 1949) have shown that the parameter *a* of equation (1) has a value for attack by methyl radicals appreciably different from that for attack by trichloromethyl radicals. It is possible therefore that the value of *a* used above for phenyl radicals is not the most appropriate. If so, the values derived above for the hetero-atom parameters may need revision. For this reason an experimental study of reactivities of phenyl radicals towards polycyclic aromatic hydrocarbons would be important for the development of the theory of radical reactivities.

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