# 278. *The Influence of Nuclear Substituents upon Side-chain Reactions. Part IV. A Reconsideration of the Quantitative Relationship between Energies of Activation and Dipole Moments.*

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The recently-acquired knowledge of the values of dipole moments, and the recognition of these as a numerical expression of the relative electron-attractive or electron-repulsive characters of groups, have led to the consideration of polar influences on quantitative lines. The values of the dissociation constants of monocarboxylic acids provide a series of figures upon which such quantitative considerations can be based, and Waters (*Phil. Mag.*, 1929, **8**, 438) sought to correlate the dissociation constants of a number of benzoic acids, $X\cdot C_6H_4\cdot CO_2H$, with the dipole moments of the corresponding substituted benzenes, $X\cdot C_6H_5$. He suggested a linear connection of log $K$ with $\mu$ in cases where the issue was not obscured by electromeric or steric effects, but this simple relationship was far from accurate. Later, Nathan and Watson (J., 1933, 890) obtained a smooth curve on plotting the values of log $K$ for a series of substituted acetic acids against the dipole moments of the corresponding methane derivatives $X\cdot CH_3$, and they deduced the formula $\log K = \log K_0 - C(\mu + a\mu^2)$, $K_0$ being the value of $K$ for the unsubstituted acid, $C$ and $a$ constants for the series, and $\mu$ having its conventional sign. The expression held with a considerable degree of accuracy. A recent examination (Dippy and Watson, *Chem. and Ind.*, in the press) of the applicability of the expression to the dissociation constants of substituted benzoic and phenylacetic acids has led to the conclusion that in these series also it holds when the inductive effect of the substituent is alone operative, divergences being found for resonating groups and halogens in the *p*-position, and possibly for halogens in the *m*-position. Some progress has thus been made in the quantitative correlation of dissociation constants of acids with the dipole moments of the appropriate substituted methanes or benzenes.

The possibility of a similar relationship between dipole moments and an appropriate function of reaction velocity is suggested by Hammett and Pfluger's observation (*J. Amer. Chem. Soc.*, 1933, **55**, 4079) that an approximately straight line is obtained when values of log $k$ for the reaction of trimethylamine with certain esters are plotted against those of log $K$ for the corresponding acids. Such a relationship was, indeed, found to exist * (Nathan and Watson, *loc. cit.*) for the acid-catalysed prototropy of a series of nuclear-substituted acetophenones; it was based, however, on the postulate that the observed velocities were a measure of the speeds of reaction of the ketones with the catalyst, and the fuller investigation described in Part II of this series (this vol., p. 1167) has indicated that this is probably not the case. Nathan and Watson (Part I, J., 1933, 1248; *Nature*, 1934, **133**, 379) also examined the velocities of 13 other side-chain reactions (the only ones for which suitable data were available), and suggested that the following expressions were widely applicable :

for reactions of Type A, $E = E_0 - C(\mu - a\mu^2)$,
for reactions of Type B, $E = E_0 + C(\mu + a\mu^2)$,

$E$ and $E_0$ being the energies of activation relating to the substituted and unsubstituted compounds respectively. The assumption was made throughout that no factor other than $E$ is changed by the introduction of substituents, and divergences were found in cases where the operation of electromeric effects was to be anticipated. Waters (J., 1933, 1551; *Nature*, 1934, **134**, 178) has suggested that the terms in $\mu$ and $\mu^2$ represent the field and inductively-transmitted effects respectively.

The sign of the $\mu^2$ term presented difficulty, and the object of this communication is to show that, with certain reservations concerning reactions and groups of special characters, the expression $E = E_0 \pm C(\mu + a\mu^2)$ is probably applicable to all side-chain reactions for which suitable data are available, the alternative positive and negative signs referring to reactions of Types B and A respectively.

The demonstration by Williams and Hinshelwood (J., 1934, 1079) that, in the benzoylation of anilines, substituents either in the amine or in the acid chloride influence almost exclusively the energy of activation, and the further proof by Hinshelwood and Legard (this vol., p. 587) of the predominating importance of $E$ in esterification processes, make it clear that the energy of activation is the correct quantity for consideration in any attempt to relate reaction velocities with dipole moments. Since the benzoylation of aromatic amines is the only case where it has been shown definitely that, for a whole series of nuclear substituents, changes in factors other than $E$ are inconsiderable, and since accurate values

* A logarithmic connection between reaction velocities and dipole moments ($\log k/k_0 \propto \mu$) was previously sought by Waters (*loc. cit.*) on the basis of Olivier's results for the hydrolysis of substituted benzyl chlorides, and by Drs. Shoppee and Goss (private communication) for the prototropy of the *αγ*-diphenylmethyleneazomethine system.

of $E$ are here available, Williams and Hinshelwood's results clearly form a convenient starting point. The reaction is facilitated (*a*) by electron-repulsive substituents in the amine and (*b*) by electron-attractive substituents in the acid chloride, and hence the two sets of data provide one example of each type of side-chain process. The halogen-substituted compounds being omitted, the energies of activation are given by the following expressions:

substituent in amine, $E = E_0 - 1352(\mu + 0{\cdot}043\mu^2)$,
substituent in acid chloride, $E = E_0 + 1055(\mu + 0{\cdot}165\mu^2)$.

It should be emphasised (since the expressions refer to substituents in the *p*-position) that the existence of the $\mu^2$ term is not to be ascribed to the electromeric or mesomeric effects of nitroxyl, which are of the same sign as the inductive effect, since a linear relationship between $E$ and $\mu$ would demand, in both cases, a *larger* and not a *smaller* effect for *p*-$NO_2$.

FIG. 1.

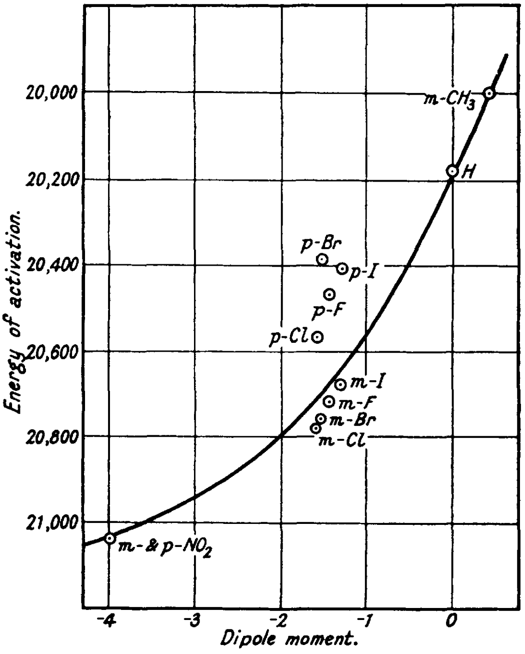
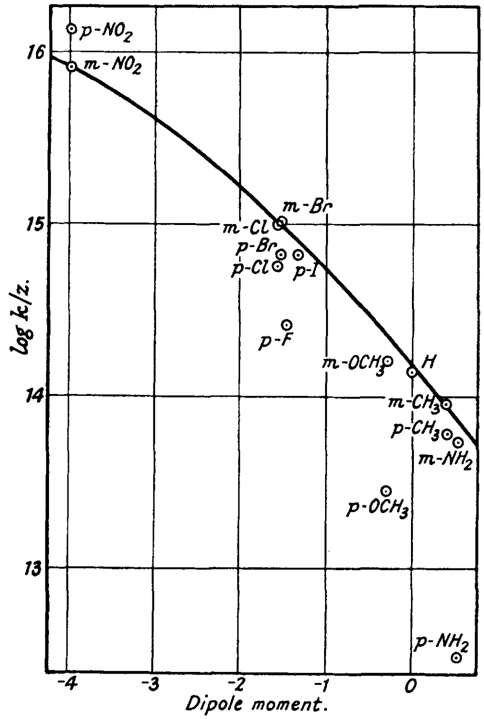


FIG. 2.



Williams and Hinshelwood's results therefore indicate that, for one reaction of Type A and one of Type B, where values of $E$ are known accurately, and where changes in other factors are negligible, the expression $E = E_0 \pm C(\mu + a\mu^2)$ is applicable for $CH_3$, H, and $NO_2$.

The values of $E$ for the reaction of an acid catalyst with a series of substituted acetophenones have been recorded in Part II (*loc. cit.*), and the plot of these against the dipole moments of the appropriate substituted benzenes is shown in Fig. 1. The curve connecting the points for $CH_3$, H, and $NO_2$ is given by the expression, $E = E_0 - 429(\mu + 0{\cdot}125\mu^2)$. The deviations of the *m*-halogeno-compounds from this curve are within the limits of experimental error, but halogen in the *p*-position leads to a larger divergence, always in the same direction, the value of $E$ being less by 200—300 cals. than that calculated (see table below).

| Substituent. | $E_{calc.}$. | $E_{obs.}$. | Substituent. | $E_{calc.}$. | $E_{obs.}$. |
|---|---|---|---|---|---|
| $CH_3$ ......... | 20,000 | (*m*) 20,000 | Cl ............ | 20,720 | (*m*) 20,780; (*p*) 20,570 |
| H ............ | | 20,180 | Br ............ | 20,710 | (*m*) 20,760; (*p*) 20,390 |
| $NO_2$ ......... | 21,040 | (*m* and *p*) 21,040 | I ............ | 20,650 | (*m*) 20,680; (*p*) 20,410 |
| F ............... | 20,690 | (*m*) 20,720; (*p*) 20,470 | | | |

The more detailed investigation of this reaction has thus confirmed Nathan and Watson's observation of a quantitative relationship involving terms in $\mu$ and $\mu^2$, but has led to a modification of their original formula, the $\mu^2$ term retaining the positive sign found in the expressions referring to the dissociation constants of carboxylic acids and the benzoylation of amines (above). *p*-Halogen is also found to show irregularity.

When an attempt is made to extend the survey to other side-chain reactions, the difficulty arising from lack of data is at once encountered. It is, moreover, difficult to estimate the relative accuracy of the data available, and in the majority of cases measurements are restricted to one temperature. The thirteen reactions selected for consideration in Part I included the (acid) hydrolysis of benzyl chlorides (Olivier, *Rec. trav. chim.*, 1922, **41**, 301, 646; 1923, **42**, 516, 775), and recent work (Olivier and Weber, *ibid.*, 1934, **53**, 869) has shown that the mechanism of this reaction is doubtless of a composite character, a unimolecular hydrolysis being superimposed upon the bimolecular change (Hughes and Ingold, this vol., p. 244). This probably accounts for the unexpectedly high velocity of hydrolysis induced by *p*-methyl, which will favour the unimolecular change $Ph{\cdot}CH_2Cl \longrightarrow Ph{\cdot}CH_2^{\oplus} + Cl^{\ominus}$ (compare the hydrolysis of alkyl halides, Hughes and Ingold, *loc. cit.*). An unusually powerful effect of *p*-alkyl is also found in the alcoholysis of benzhydryl chloride (Norris, Banta, and Blake, *J. Amer. Chem. Soc.*, 1928, **50**, 1804) and in the *N*-chlorination of acetanilide (Williams, J., 1930, 37), and it is obvious that complications render these reactions unsuitable for consideration. It may be pointed out, however, that unusual features do not appear to be present in the *N*-chlorination of acetobenzylamides (Williams, *loc. cit.*) and in the acid hydrolysis of β-chloro-sulphides (Baddeley and Bennett, J., 1933, 261), where the carbon atom at which substitution occurs is not attached directly to the nucleus. Reference may also be made to Cain and Nicoll's observation (J., 1902, **81**, 1412) that the decomposition of diazo-compounds is accelerated by *m*- but retarded by *p*-methyl.

We have made a careful re-examination of the data for the remaining 11 reactions which were dealt with in Part I (where full references and figures are given), and we find that, if certain postulates are accepted, there is no reason to doubt the applicability throughout of the expression $E = E_0 \pm C(\mu + a\mu^2)$. The necessary postulates are as follows :

(1) That changes in factors other than $E$ are not sufficiently great to have an important influence upon the velocities. This assumption was made by Nathan and Watson prior to the appearance of Williams and Hinshelwood's demonstration of its correctness for one reaction, and they pointed out (Part I) that it leads to the expression

$$E = E_0 - 2{\cdot}303\, RT\, (\log k/z - \log k_0/z_0)$$

which, when combined with the formula $E = E_0 \pm C(\mu + a\mu^2)$, gives the equation $\log k/z = \log k_0/z_0 \mp x(\mu + a\mu^2)$. We have followed the procedure adopted in Part I of examining the relationship of $\log k/z$ to $\mu$.

(2) That the "effective polarity" of an "inclined" group is measured by $\mu \cos \theta$, where $\mu$ is the experimentally determined dipole moment of the appropriate benzene derivative, and $\theta$ is the angle of inclination of the group to the plane of the nucleus. This assumption was also made by Nathan and Watson (*Nature*, 1934, **133**, 379). The valency angles of oxygen and nitrogen being taken as 105° and the tetrahedral angle respectively (Mecke, *Z. Physik*, 1933, **81**, 313; Dennison and Uhlenbeck, *Physical Rev.*, 1932, **41**, 313), the values of the "effective moments" in anisole, aniline, and dimethylaniline become − 0·31, 0·51, and 0·53 respectively.

(3) That the relationship between $E$ and $\mu$ is not applicable for resonating groups and halogens in the *p*-position, and is doubtful for *m*-halogens. If *p*-substituted compounds alone are considered, the resonance effect of nitroxyl may lead to a lower value of $a$ (less curvature) than would be found if data for $m$-$NO_2$ were available.

Our survey of the available data in the light of the above postulates has led us to conclude that, their correctness being granted, the equation $E = E_0 \pm C(\mu + a\mu^2)$ applies fairly accurately to all these reactions, and it is not unreasonable to suggest that the agreement found may be regarded as some justification for the suggestion that the constancy of factors other than $E$ throughout a series of substituted compounds, although actually proved for one reaction only, may be found to hold for a considerable number of side-chain processes. Throughout the reactions examined, *p*-alkoxyl and *p*-halogens show marked divergences, but *m*-halogens, where data are available, diverge but little, if at all, from the expected relationship. The influence of *p*-methyl is almost invariably greater than that of *m*-methyl, and this may be ascribed to electromeric displacements set up by the group in accordance with the scheme usually accepted to explain the *op*-directive influence of alkyl substituents (Allan, Oxford, Robinson, and Smith, J., 1926, 409; Ingold and Ingold, *ibid.*, p. 1312); the effect of *p*- but not of *m*-methyl would thereby be enhanced.

Fig. 2 shows the plot of log $k/z$ against $\mu$ for a typical reaction (alkaline hydrolysis of benzoic esters; Kindler, *Annalen*, 1926, **450**, 1; 1927, **452**, 90; 1928, **464**, 278), where data for both *m*- and *p*-substituents are available. No attempt is made in this paper to deal with *o*-substituted compounds, which present special problems.

## SUMMARY.

1. In three cases where energies of activation have been determined for a given reaction of a series of *m*- or *p*-substituted aromatic compounds, their relationship with the dipole moments of the corresponding substituted benzenes is given by the expression $E = E_0 \pm C(\mu + a\mu^2)$, although divergences are found for substituents, such as the halogens, where the complete polar effect is not measured by the dipole.

2. This expression is comparable with the relationship previously found for the dissociation constants of carboxylic acids. It represents a slight modification, in the light of new experimental data, of Nathan and Watson's original formula.

3. The same relationship is found in eleven other reactions which have been measured at one temperature only, on the assumption that, throughout a series of nuclear-substituted compounds, all factors other than the energy of activation are constant.

4. It is suggested that both the constancy of factors other than $E$ and the relationship between $E$ and $\mu$ may persist throughout a large number of side-chain processes, reservations being made with regard to reactions and groups of a special character.

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