265. *The Effect of Nuclear Halogen Substituents on Triad Prototropic Systems in Relation to Aromatic Side-chain Reactions.*

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INVESTIGATION of the effect of nuclear substitution on mobility (= velocity of interconversion, $k_1 + k_2$) in simple triad prototropic systems of the type

$$\text{(I.)} \qquad \mathrm{R{\cdot}C_6H_4{\cdot}X{:}Y{\cdot}Z[H]Ph} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{R{\cdot}C_6H_4{\cdot}X[H]{\cdot}Y{:}ZPh} \qquad \text{(II.)}$$

has shown (Shoppee, J., 1930, 968; 1931, 1225; 1932, 696) that the variants R, in either the *m*- or the *p*-position, fall into the serial order $\mathrm{NMe_2 < Me < OMe < I < Br < Cl < NO_2}$, which is also the order of the dipole moments of the compounds $\mathrm{R{\cdot}C_6H_5}$. In such comparisons (*i.e.*, for cases in which the only variable is a substituent placed at a relatively large distance from the seat of reaction), it is assumed that effects of environment differ sufficiently little from case to case to justify this (cf. Williams, J., 1930, **35**; *per contra*, Conant, *J. Amer. Chem. Soc.*, 1925, **47**, 480; Lapworth, J., 1931, 1964).

The special feature of the foregoing sequence to which it is desired to direct attention is the appearance of the methoxyl group and the halogens in the *normal* theoretical order (compare Baddeley and Bennett, this vol., p. 261; Bennett, this vol., p. 1112).

The experimental sequence shows that the processes

$$\text{(i)} \quad \mathrm{R{\cdot}C_6H_4{\cdot}X{:}Y{\cdot}Z[H]\!-} \xrightarrow{k_1} \mathrm{R{\cdot}C_6H_4{\cdot}X{:}Y{\cdot}\overset{\ominus}{Z}\!-}$$

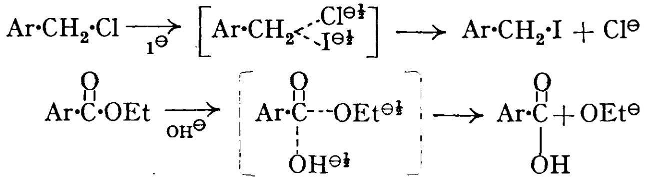
$$\text{(ii)} \quad \mathrm{R{\cdot}C_6H_4{\cdot}X[H]\!-} \xrightarrow{k_2} \mathrm{R{\cdot}C_6H_4{\cdot}\overset{\ominus}{X}\!-}$$

are unequivocally facilitated by electron recession from the seat of ionisation, and may therefore be regarded as aromatic side-chain reactions of Ingold and Rothstein's " type B " (J., 1928, 1217). Hence it is legitimate to compare the above results with those relating to the variation in reaction velocity produced by the same nuclear substituents in other side-chain reactions of " type B."

A comprehensive examination of the literature relating to such side-chain reactivity shows that, apart from triad prototropic systems, in no case do the effects of *m*- or *p*-substituents on reaction velocity conform to the dipolar order. The anomalies invariably involve groups of dual polar capacity, and relate (*a*) to the position of the methoxyl group in the experimental velocity sequence, and (*b*) to the inversion of the halogens amongst themselves. The case of (*a*) has already been discussed (Shoppee, J., 1931, 1225) in relation to the experimental sequences afforded by *m*-substituents in which the anomaly disappears. Anomaly (*b*) remains.

The position, then, is broadly: side-chain reactivity—inversion of the halogens; triad prototropic systems—no inversion.

It is suggested that the underlying reason for the strictly dipolar sequence given by systems of the form (I $\rightleftharpoons$ II) is that these represent a specially simple and possibly unique aromatic side-chain reaction of " type B." In the processes (i) and (ii), electron recession from X (or Z), giving $\mathrm{R{\cdot}C_6H_4} \longleftarrow \overset{\delta+}{\mathrm{X}}\mathrm{[H]}$, *i.e.*, tending to produce an electron deficit at X, facilitates the approach of negative (catalytic) ions; but the same electron recession also facilitates the separation of hydrogen as the *positive* ion. In all other side-chain reactions of " type B " familiar to the writer, the ultimate phase * concerns the separation of a *negative* ion, a process which will be retarded by the electron recession which facilitated attack by a negative ion. The following examples are symbolic.



$$\mathrm{Ar{\cdot}CH_2{\cdot}Cl} \xrightarrow[\mathrm{I}^{\ominus}]{} \left[\mathrm{Ar{\cdot}CH_2}\begin{smallmatrix}\cdots\mathrm{Cl}^{\ominus\frac{1}{2}}\\ \cdots\mathrm{I}^{\ominus\frac{1}{2}}\end{smallmatrix}\right] \longrightarrow \mathrm{Ar{\cdot}CH_2{\cdot}I} + \mathrm{Cl}^{\ominus}$$

$$\mathrm{Ar{\cdot}\overset{\overset{\displaystyle O}{\|}}{C}{\cdot}OEt} \xrightarrow[\mathrm{OH}^{\ominus}]{} \left[\mathrm{Ar{\cdot}\underset{\underset{\displaystyle OH^{\ominus\frac{1}{2}}}{\vdots}}{\overset{\overset{\displaystyle O}{\|}}{C}}\cdots OEt^{\ominus\frac{1}{2}}}\right] \longrightarrow \mathrm{Ar{\cdot}\underset{\underset{\displaystyle OH}{|}}{\overset{\overset{\displaystyle O}{\|}}{C}}} + \mathrm{OEt}^{\ominus}$$

The experimental results for very many side-chain reactions of " type B " (and also of " type A ") may be summarised in the statement that interpenetrating a series of uniquely electron-repelling or electron-attracting ($\pm I$) groups, a series of ambipolar ($-I+T$) groups occurs in which the expected order is inverted.

	$+I.$	$-I+T.$	$-I.$
Theoretical sequence	Me	I Br Cl F	$\mathrm{NO_2}$
" Type B " Reaction	Retardation	Order inverted	Acceleration
" Type A " Reaction	Acceleration	,, ,,	Retardation

Inversion might also be anticipated for ambipolar groups of the type $+I-T$, but, since the only available example is the substituted vinyl group, $\mathrm{CR_1R_2{:}CH{\cdot}}$, no comparisons are possible.

The behaviour described above for side-chain *reaction velocities* is closely analogous to that found experimentally for the influence of substitution on the *equilibrium constant, K,* in tautomeric triad systems such as (I $\rightleftharpoons$ II) :

	$+I.$	$-I+T.$	$-I.$
Theoretical sequence	Me	I Br Cl	$\mathrm{NO_2}$
K	Large	Order inverted	Small

On the assumption that tautomeric equilibrium is attained through a single mechanism, it has been shown (Shoppee, *loc. cit.*, pp. 1227, 1228) that K involves two rate-affecting phases of opposite polar character, and that the values of K should theoretically therefore, and do, pass through a maximum (compare Ingold and Patel, *J. Indian Chem. Soc.*, 1930, **7**, 95).

It is proposed to carry over from tautomeric equilibria to side-chain reaction velocities the hypothesis of control by co-existing oppositely polar phases. The suggestion is put forward that the mechanism(s) of aromatic side-chain reactions may involve two rate-affecting phases, one phase being of each polar type; the condition becoming marked and experimentally observable in the velocity coefficients for ambipolar substituents. If this hypothesis contains some part of the truth, then for reactions proceeding by a single reaction route, the velocity coefficients for ambipolar substituents should pass through a maximum.

The simplest way of illustrating the matter is to plot the experimentally observed velocity coefficients against an appropriate polar sequence. Now, it so happens that the same sequence OMe,† I, Br, Cl, F represents, not only increasing electron attraction ($-I$; facilitating one polar phase), but also decreasing electron release ($+T$; facilitating the oppositely polar phase); this progression is therefore uniquely suitable for use in constructing the following curves. (It is, of course, true that no numerical values can be assigned to the intervals separating the ambipolar groups on the horizontal axis, but

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* In speaking of reactions and formulating them as occurring in separate phases, it is not implied that the phases are necessarily separate in time, *i.e.*, stages in the sense of consecutive reactions.

† The methoxyl group, although capable of inclusion in the illustrations given in the sequel, is not further considered; see, however, Baker (this vol., p. 1128).

there is little doubt as to the *order* in which they should be placed (compare, however, Baddeley and Bennett, *loc. cit.*) Fig. 1 exemplifies the "type B" reaction of *p*-aryl β-chloroethyl sulphides with iodine ions (Baddeley and Bennett, *loc. cit.*); there is no inversion of the velocity coefficients.

According to the way in which molecular circumstances weight the opposing polar phases and their facilitation, so the position of the maximum on the horizontal axis will vary from case to case. The effect of this consideration is most readily visualised by imagining the curve in Fig. 1 to move as a whole from right to left along the horizontal axis: Fig. 2 is then obtained, representing the complete inversion of the halogens found, *e.g.*, by Kindler (*Annalen*, 1926, **450**, 1; 1927, **462**, 90), for the velocity coefficients relating to the alkaline hydrolysis of ethyl *m*- or *p*-halogenobenzoates (for other examples, see Baddeley and Bennett, *loc. cit.*).

Fig. 1.

I<Br<Cl(<F).

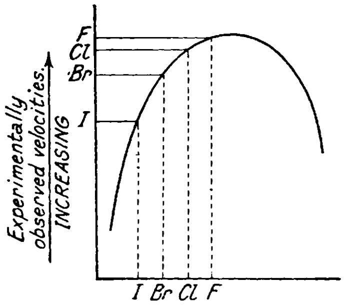
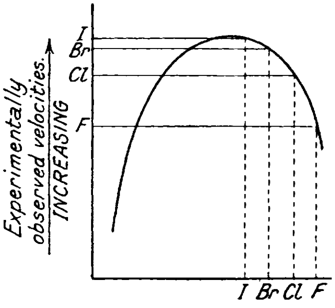


Fig. 2.

I>Br>Cl>F.



Between the extremes represented by Figs. 1 and 2, there will be an infinite number of positions on the horizontal axis which the maximum may occupy. The hypothesis here suggested consequently accommodates the possible existence of certain "mixed series," which may involve equalities such as I<Cl<Br, I<Cl = Br, or Br = F<Cl.

Fig. 3*a*.

I<Cl = Br.

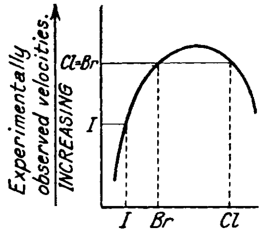


Fig. 3*b*.

I<Cl<Br.

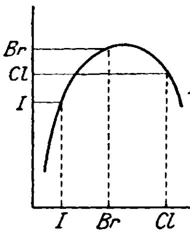


Fig. 3*c*.

I = Cl<Br.

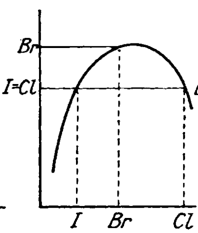


Fig. 3*d*.

Br = F<Cl.

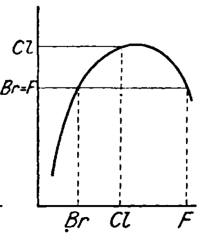


Fig. 3*a*.—*Alkaline hydrolysis of p*-$Ar{\cdot}CO{\cdot}NH_2$ (*Reid*, Amer. Chem. J., 1900, **24**, 403).
Fig. 3*b*.—p-$Ar{\cdot}COCl$ *and* $Pr^{\beta}OH$ (*Norris*, J. Amer. Chem. Soc., 1928, **50**, 1813). *Alkaline hydrolysis of* m- *and* p-N-*arylsuccinimides* (*Sanna*, Gazzetta, 1927, **57**, 761).
Fig. 3*d*.—*Reduction of* m- *and* p-$Ar{\cdot}CH_2Br$ (*Shoesmith and Slater*, J., 1926, 214).

Such mixed series occur in the literature with some frequency; Figs. 3*a*, 3*b*, and 3*c* show the gradual movement of the maximum through a series of intermediate positions, corresponding with the results obtained by the workers named. The writer is not aware of work involving the substituents I, Br, Cl, and corresponding with Fig. 3*c*, but Fig. 3*d* shows the precisely analogous case for the substituents Br, Cl, F.

When the experimentally observed values for the effect of ambipolar groups on side-chain reactions of "type A" are plotted against the polar sequence previously used, *minima* are obtained, although the characteristics of non-inversion (Fig. 4), complete inversion (Fig. 5), and of the occurrence of certain "mixed series" (Figs. 6, 7) are reproduced.

Such minima should arise when a reaction, influenced by unipolar substituents ($\pm I$), proceeds by two contemporaneous reaction routes, one of each polar type (compare Ingold and Patel, *loc. cit.*). In the case of ambipolar substituents ($- I + T$), both the inductive and the electromeric effect will influence both reaction routes, not only in opposite senses, but also by different mechanisms; it appears possible for either minima or maxima to occur, according to the relative degree to which the conflicting factors control the speeds of the reactions.

FIG. 4.
I>Br>Cl.

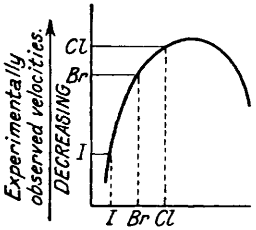


FIG. 5.
I<Br<Cl.

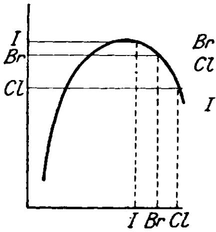


FIG. 6.
I>Cl>Br.

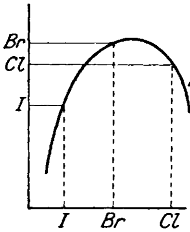


FIG. 7.
Br = F>Cl.

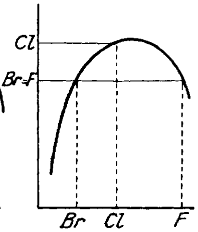


FIG. 4.—*Friedel-Crafts reactions between* p-Ar·SO_2Cl *and* C_6H_6 (*Olivier*, Rec. trav. chim., 1914, **33**, 244; 1922, **41**, 302).

FIG. 5.—*Acid hydrolysis of* p-*aryl β-chloroethyl sulphides* (*Baddeley and Bennett*, loc. cit.).

FIG. 6.—*Reduction of* p-Ar·NH·NH_2 (*Franzen*, J. pr. Chem., 1918, **97**, 61). *See also Baker* (loc. cit.).

FIG. 7.—*Acid hydrolysis of* m-Ar·CH_2Br (*Shoesmith and Slater*, loc. cit.).

The assumption of the complex mechanism of greatest simplicity (*i.e.*, a single reaction route involving two antipolar phases) leads to a reasonably satisfactory treatment for side-chain reactivity of "type B"; failure of this assumption in its application to the case of side-chain reactions of "type A" seems to indicate the probable existence of two or more reaction mechanisms (each possibly complex) for side-chain reactions in general, except in the case of the equilibria attained by anionotropic or prototropic systems activated by aryl groups.