Linear Free Energy Relations in Intramolecular Aromatic *ipso*-Substitutions by Substituted Methyl Radicals[1]

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Summary Reaction of the 1-arylsulphonyl-2-iodomethylpiperidines (**4**) with tri(n-butyl)stannane induces a 1,4-aryl radical rearrangement to (**5**) together with the formation of the thiazines (**6**) and methyl derivatives (**7**); plots of the relative rate constants against σ_m and σ_p values give good linear correlations with a V-shaped curve for the 1,4 process.

PRONOUNCED substituent effects have been found in a variety of free-radical reactions.[2] However, in spite of the sometimes excellent statistical correlations the interpretation of the results in terms of polar contributions is still disputed.[3] On the one hand in homolytic aromatic substitutions resonance structures of the type (**1**)—(**3**) would

$$[RCH_2\cdot + YPhX] \leftrightarrow [R\overset{+}{C}H_2\dot{Y}:\overset{-}{P}hX] \leftrightarrow [R\overset{-}{C}H_2:\dot{Y}\overset{+}{P}hX]$$
$$(\mathbf{1}) \qquad\qquad (\mathbf{2}) \qquad\qquad (\mathbf{3})$$

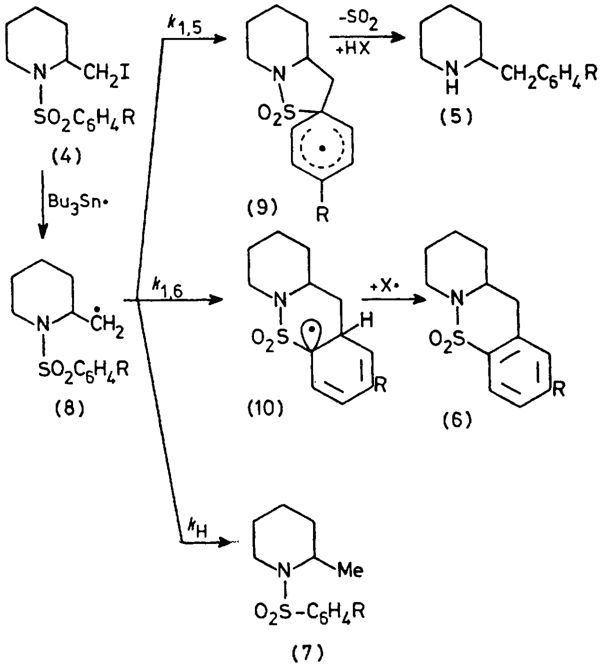
require the observation of different ρ values for a single process if the direction and magnitude of the resulting dipole depend on the nature of X and provided that contributions of (**2**) and (**3**) to the transition state are real.[4] On the other hand, the occurrence of two types of charged structures seems somewhat artificial when the same alkyl radical is involved. This seeming discrepancy is easily resolved by omitting one of the structures (**2**) or (**3**). Herein we present experimental evidence for the existence of two different types of ρ values in homolytic aromatic *ipso*-substitution reactions and also provide a rationale on a qualitative basis.

The tributylstannane induced reactions of the 1-arylsulphonyl-2-iodomethylpiperidines (**4a**—**i**)[5] affording the amines (**5a**—**i**), the thiazine *S*-dioxides (**6a**—**i**), and the methyl derivatives (**7a**—**i**) was investigated in anisole which had been distilled from $LiAlH_4$ and carefully degassed at 96 ±0·5 °C; 0·275 mmol of the iodide and 0·742 mmol of Bu_3SnH in 12·5 ml of anisole to which 12·5 mg of phenanthrene had been added as internal g.l.c. reference were stirred until the iodide had reacted completely (*ca.* 4 h for all reactions). Product analysis was carried out by g.l.c.† and independently confirmed *via* separation and determination by weight of the compounds formed. The relative percentages obtained are in the Table.

TABLE [a]

(4)		%(5)[b]	%(6)[b]	%(7)[b]
(a)	R = OMe	37	40	23
(b)	R = Me	32	45	23
(c)	R = F	30	49	21
(d)	R = H	27	48	25
(e)	R = Cl	41	34	25
(f)	R = Br	42	34	24
(g)	R = CO_2Et	53	27	20
(h)	R = COMe	57	25	18
(i)	R = CN	65	20	15

[a] Actual combined isolated yields range from 90 to 98%. For comparison all values have been normalized to 100%. [b] Satisfactory analytical data have been obtained for all new compounds.



SCHEME

The formation of the products can be accounted for by the mechanism in the Scheme which encompasses three separate types of reaction: *ipso* 1,5-addition of the methyl radical (**8**) to the aromatic nucleus with rate constant $k_{1,5}$; the corresponding *ortho* 1,6-addition, rate constant $k_{1,6}$; H abstraction from Bu_3SnH by (**8**), rate constant k_H. Simple expressions for the relative rate constants k_r can be derived when it is assumed firstly that a direct interrelation between (**9**) and (**10**) is energetically unfavourable because of the 1,2 alkyl shift involved[6] and secondly that k_H is independent of the substituent R because of the relatively large distance between reaction centre and substituent.[7] The relative rate constant k_r are given by equations (1) and (2).

$$k_r{}^{1,5} = [k_{1,5}]_R/[k_{1,5}]_H = [\%(\mathbf{5})/\%(\mathbf{7})]_R/[\%(\mathbf{5})/\%(\mathbf{7})]_H \qquad (1)$$

$$k_r{}^{1,6} = [k_{1,6}]_R/[k_{1,6}]_H = [\%(\mathbf{6})/\%(\mathbf{7})]_R/[\%(\mathbf{6})/\%(\mathbf{7})]_H \qquad (2)$$

Plotting of the log $k_r{}^{1,n}$ values against Hammett σ values gives good to excellent correlation as indicated in Figures 1 and 2. The 1,6 process gives a linear correlation with σ_m:[8] $\rho = -0{\cdot}31 \pm 0{\cdot}04$, $r = 0{\cdot}944$. Two straight lines are found for the *ipso*-substitution:[9] for (**4a**—**d**), $\rho = -0{\cdot}98 \pm 0{\cdot}18$, $r = 0{\cdot}937$ and for (**4d**—**i**), $\rho = +0{\cdot}92$

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† Varian Aerograph 2100, all glass, N_2 flow 44 ml/min, Gaschrom Q 80—100 m OV-17 (5%), temperature programming 100—250 °C.

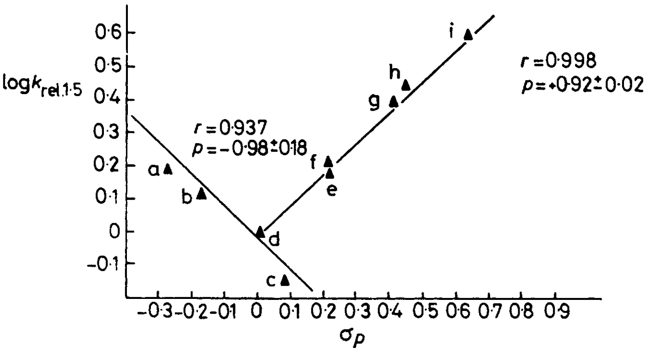

FIGURE 1. Hammett plot of log $k_{\text{rel}}^{1,5}$ vs. σ_p for *ipso* methyl radical attack [(**4**) → (**5**)]. See Table for identification of letters with substituents R.

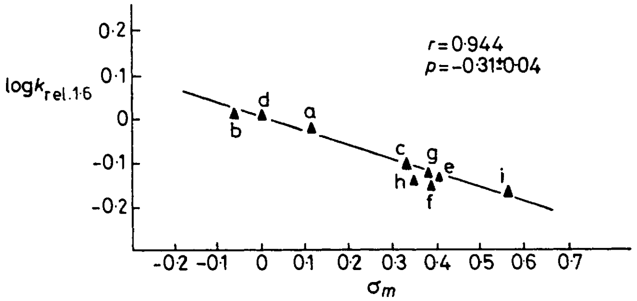

FIGURE 2. Hammett plot of log $k_{\text{rel}}^{1,6}$ vs. σ_m for *ortho* methyl radical attack [(**4**) → (**6**)]. See Table for identification of letters with substituents R.

$\pm 0{\cdot}02$, $r = 0{\cdot}998$, both with use of $\sigma_p{}^8$ parameters.‡ The latter ρ values are indicative of a substantial contribution of polar structures to the transition state.

Interpretation of these results on the basis of polar contributions would require a change in the polar character of the methyl radical, which is usually considered weakly nucleophilic,[10] depending on the R substituent. Although such behaviour cannot be excluded the following more realistic, albeit qualitative, explanation in terms of frontier orbitals can also be given.

When it is assumed that the interaction of a methyl radical with the π-electrons of an aromatic nucleus is determined to a major extent by the relative positions of highest occupied and lowest unoccupied MOs one might consider the possibility of a change in preference from singly occupied–highest occupied to singly occupied–lowest unoccupied MO interaction. Formally speaking the so-called electrophilic character of the methyl radical then changes into a nucleophilic one. This rationale is all the more likely in view of the considerable lowering of highest occupied and lowest unoccupied MO energy levels of a benzene molecule upon substitution with electron-withdrawing groups.[11] In the present case only disubstituted benzenes are involved which may account for the fact that this effect has not been observed previously in studies on homolytic alkyl substitutions in monosubstituted benzenes.[12]

Clearly a series of quantitative data on, *e.g.*, charge densities on *ipso* carbon atoms are needed before a more accurate description of the process can be given.

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‡ For σ° values (ref. 8) the following data were obtained: 1,6 process $\rho = -0{\cdot}29 \pm 0{\cdot}04$, $r = 0{\cdot}914$; 1,5 process $\rho = -1{\cdot}01 \pm 0{\cdot}07$, $r = 0{\cdot}994$ (**4a**—**d**), $\rho = +0{\cdot}91 \pm 0{\cdot}07$, $r = 0{\cdot}984$ (**4d**—**i**).

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