Tetrahedron, 1965, Vol. 21, pp. 955 to 961. Pergamon Press Ltd. Printed in Northern Ireland

INFLUENCE OF SUBSTITUENT GROUPS IN THE ARYLATION OF SUBSTITUTED BENZENES BY ARYL RADICALS DERIVED FROM *p*-SUBSTITUTED N-NITROSOACETANILIDES

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(*Received* 1 *December* 1964; *in revised form* 15 *January* 1965)

Abstract—The partial rate factors for the homolytic arylation of substituted benzenes by substituted phenyl radicals generated from *p*-substituted N-nitrosoacetanilides are presented, and the influence of a substituent is shown to be divided into two parts which are attributable to the inductive and the conjugative effect respectively. Hammett's relations hold for the partial rate factors for the arylations at the *meta* position. The correlation of the ρ values with the inductive constants for the substituent groups in the arylating radicals indicates that the effect of a substituent in the radical is purely inductive in nature. The partial rate factors for arylations at the position *para* to a substituent in benzene are related to Hammett's substituent constant σ_p by the equation: $\log (k_p/k) = \rho\sigma_p + \tau_p$, where τ_p is a constant dependent on the nature of the substituent in the substrate and represents its conjugative capacity. On the assumption that the corresponding relation holds for the *ortho* position as well, very reasonable values of σ_0 and τ_0 are derived from the k_0/k and ρ values.

A CONSIDERABLE amount of work has been done on the influence of substituent groups on the reactivity and orientation of the homolytic arylation of benzene and its derivatives, largely with aroyl peroxides as the source of aryl radicals.[1]

We have begun work[2] in this field using aryl radicals produced from substituted N-nitrosoacetanilides,[3] and here summarize the results of our work, the experimental details of which have been published elsewhere,[4] on the effect of the substituents in the attacking radical as well as in the substrate molecule. In the early stages of our investigation, column chromatography, spectrophotometry etc. were used for product analysis, but the rather small variation in reactivity from compound to compound, which soon became apparent, necessitated improvement in the precision of the analytical method. We accordingly have adopted radioisotope dilution analysis as a more accurate and reliable method.[4] Thus, substituted acetanilides appropriately

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[1] G. H. Williams, *Homolytic Aromatic Substitution.* Pergamon Press, Oxford (1960). For earlier reviews see O. C. Dermer and M. T. Edmison, *Chem. Revs.* **57**, 77 (1957); D. R. Augood and G. H. Williams, *Ibid.* **57**, 123 (1957).

[2] O. Simamura, T. Inukai and M. Kanazashi, *Bull. Chem. Soc., Japan* **23**, 205 (1950); O. Simamura, T. Inukai and M. Kurata, *Ibid.* **25**, 76 (1952); O. Simamura and T. Migita, *Ibid.* **27**, 228 (1954); O. Simamura and T. Inukai, *Ibid.* **28**, 445 (1955).

[3] W. S. M. Grieve and D. H. Hey, *J. Chem. Soc.* 1797 (1934).

[4] T. Inukai, K. Kobayashi and O. Simamura, *Bull. Chem. Soc. Japan* **35**, 1576 (1962); T. Migita, N. Morikawa and O. Simamura, *Ibid.* **36**, 980 (1963); R. Itô, T. Migita, N. Morikawa, M. Okuni and O. Simamura, *Ibid.* **36**, 985 (1963); R. Itô, T. Migita, N. Morikawa and O. Simamura, *Ibid.* **36**, 992 (1963).

labelled with carbon-14 or with chlorine-36 have been converted into the N-nitroso-derivatives, and these have been allowed to decompose in mixtures of aromatic substrates with benzene, as a reference substance, at 20°. The products from these competitive arylations have been analyzed for substituted biphenyls by the dilution method, and the partial rate factors at the various nuclear positions of the substrates have been derived relative to a single nuclear position of benzene. The results are listed in Table 1.

Table 1. Partial rate factors

Substrate		Attacking radical				
		p-$NO_2C_6H_4\cdot$	p-$ClC_6H_4\cdot$	$C_6H_5\cdot$	p-$MeC_6H_4\cdot$	p-$MeOC_6H_4\cdot$
$PhNO_2$	k_0/k	0·93	4·35[a]	9·38	10·73	6·45
	k_m/k	0·35	0·61[a]	1·16	1·07	1·19
	k_p/k	1·53	6·18[a]	9·05	8·93	8·36
	k_x/k_H[b]	0·68	2·69[a]	5·02	5·50	3·94
PhCl	k_0/k	1·53	2·70	3·09	3·10	3·08
	k_m/k	0·65	0·87	1·01	1·04	1·82
	k_p/k	1·01	1·33	1·48	1·16	1·74
	k_x/k_H[b]	0·89	1·41	1·61	1·57	1·92
PhOMe	k_0/k	5·17	3·93[a]	3·56	3·69	3·68
	k_m/k	0·84	0·94[a]	0·93	1·09	1·03
	k_p/k	2·30	1·54[a]	1·29	1·52	1·31
	k_x/k_H[b]	2·39	1·88[a]	1·71	1·85	1·79
PhMe	k_0/k	3·28	2·97	3·30	3·27	3·09
	k_m/k	1·36	1·07	1·09	1·00	1·00
	k_p/k	1·51	1·32	1·27	1·33	1·18
	k_x/k_H[b]	1·80	1·56	1·68	1·65	1·56

[a] At 18° [b] $k_x = 2k_0 + 2k_m + k_p$ and $k_H = 6k$

The Table shows that, for all the aromatic compounds examined with the apparent exception of chlorobenzene in *p*-methoxyphenylation, the *ortho* and *para* positions are more reactive than the *meta* positions irrespective of the polar nature of the attacking aryl radicals. This substitution pattern is in keeping with what is already known as typical of the homolytic phenylation.[1]

The homolytic aromatic arylation is generally accepted as proceeding through the rate determining step of the addition of an aryl radical to an aromatic ring giving an arylcyclohexadienyl radical.[1] The widely observed *ortho-para* orientation suggests, as in the case of the phenylation itself, that the major factor controlling the orientation of the entering group ought to be the varying degree of the stabilization, due to delocalization of the odd electron, of the various transition states leading to the respective isomeric arylcyclohexadienyl radicals. Thus, when the addition takes place at the *ortho* or the *para* position to a substituent, the odd electron, in the transition state, can conjugate with the electrons in the substituent group through the π electron system of the the aromatic nucleus, and consequently the substituent contributes to the stabilization of the transition state. In substitution at the *meta* position the odd electron conjugates only with the π electrons in the aromatic ring and the conjugation does not extend further into the substituent group, and the stabilization due to the presence of the substituent does not therefore occur, with the result that all substituents direct the homolytic substitution preferentially to the *ortho* and the *para* position. In view of this, the conjugative effect in the transition state for the *meta* substitution will have nearly equal magnitude for monosubstituted benzenes as well as benzene itself, and accordingly the effect of the polar nature of the attacking radical will become significant enough to be reflected in the sequence of the reactivities of *meta* positions. Indeed, a plot of the logarithms of the partial rate factors for *meta* positions against Hammett's substituent constant σ_m fall on a straight line with the slope characteristic of the attacking aryl radical (Fig. 1). The Hammett reaction constants (ρ) obtained by means of the least squares method are shown in Table 2.*

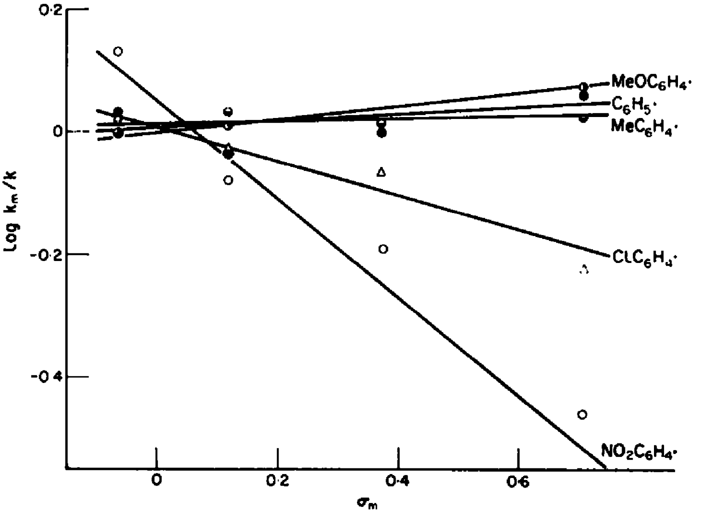


Fig. 1. The Hammett plots for arylations.

—⦶—⦶— *p*-Methoxyphenylation
—○—⊙— Phenylation
—⊖—⊖— *p*-Methylphenylation
—△—△— *p*-Chlorophenylation
—○—○— *p*-Nitrophenylation

The reaction constants for the *p*-chlorophenylation and *p*-nitrophenylation, —0·27 and —0·81, respectively, clearly show that the *p*-chloro- and *p*-nitro-phenyl radical are electrophilic, owing to the presence of an electron-attracting chlorine atom or a nitro group. The ρ values found for the phenyl, *p*-methoxyphenyl and *p*-methylphenyl radical indicate that the polarities of these radicals may be nearly the same or that at least the *p*-methoxyphenyl may have a very slight measure of nucleophilic character in comparison with the phenyl radical.

The Hammett substituent constants, σ_p, which are also included in Table 2 for comparison, may be taken more or less to represent the electronic influence of the substituent groups in the aryl radicals upon the carbon atom on which the odd electron is located. It is therefore plausible to suppose that the σ_p value may show correlation with the polar nature of arylation. In fact in the phenylation and *p*-nitro- and *p*-chlorophenylation, the numerical magnitudes of ρ and σ_p approximately coincide with each other. Although no theoretical significance can be attached to this numerical coincidence, if this correlation should hold throughout the entire range of σ_p values, it would predict much larger ρ values for the *p*-methyl- and *p*-methyoxy-phenylation than those

* The partial rate factor of 1·82 for the *meta* position of chlorobenzene in the *p*-methoxyphenylation seems to be anomalously high and has not been included in the calculation of the reaction constant. It is not clear whether this value is true or erroneous owing to some unknown experimental difficulty in the analysis for 3-chloro-4′-methoxybiphenyl.

actually found. In fact, the values for these arylations are practically indistinguishable from that for the phenylation. If we use σ_p^{n}[5] or σ_p^{o},[6] instead of σ_p, as a measure of the polar influence of a substituent for comparison, the parallelism becomes more noticeable. This fact evidently indicates that the influence on the arylation reaction exerted by a substituent group in the attacking radical is purely inductive in nature, since both σ_p^{n} and σ_p^{o} are thought to represent the inductive polar effect for the *para*-substituted phenyl group including the conjugative interaction between the substituent and the benzene ring. This view seems quite reasonable since the nature of the orbital which is occupied by the odd electron does not allow its conjugation with the π-electronic system of the benzene nucleus.

Table 2. Polar nature of aryl radicals in arylation

	Hammett's reaction constant	Substituent constant		
Aryl radical	ρ	σ_p	σ_p^{n}	σ_p^{o}
p-Nitrophenyl	−0·81	0·778	0·78	0·73
p-Chlorophenyl	−0·27	0·227	0·24	0·27
Phenyl	0·05	0	0	0
p-Methylphenyl	0·03	−0·170	−0·13	−0·15
p-Methoxyphenyl	0·09	−0·268	−0·11	−0·16

The Hammett relation does not hold for the *ortho* and *para* positions in keeping with the fact that the conjugative effect of a substituent is overwhelming at these positions. For the *para* positions, however, the following equation has been found to give a very good correlation with regard to the effect of the substituent:

$$\log(k_p/k) = \rho\sigma_p + \tau_p \qquad (1)$$

where k_p/k is the partial rate factor of the *para* position of a substituted benzene in an arylation; ρ, the Hammett reaction constant for this arylation as determined from the Hammett plot of partial rate factors of the *meta* position; and σ_p, the Hammett substituent constant for the *para* position. As shown in Table 3, the value for τ_p may be regarded as tolerably constant for each substituted benzene irrespective of the nature of the attacking radical and decreases in the order: $PhNO_2 \gg PhCl, PhOMe > PhMe$. Since the term $\rho\sigma_p$ obviously represents the polar effect consisting mainly of the inductive response in the presence of a polar attacking radical, τ_p may be considered to correspond to the conjugative effect. The approximate constancy of τ_p indicates that the magnitude of this effect is dependent only on the nature of the substituent group in the substrate and little affected by the polar nature of the attacking radical. The trend observed in the τ_p values may be regarded as reasonable in the light of the generally accepted qualitative notion about the conjugative nature of these substituent groups.

The conjugative effect, τ_p or, expressed in energy term, $2{\cdot}30 \times RT\tau_p$ may be identified with the difference in extra resonance energy, that is, the additional stabilization due to the conjugation of the substituent group with the π-electronic system, between the transition state and the initial state. Although the exact structure of the

[5] H. van Bakkum, P. E. Verkade and B. M. Wepster, *Rec. Trav. Chim.* **78**, 815 (1959).

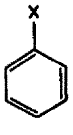
[6] R. W. Taft, *J. Phys. Chem.* **64**, 1805 (1960).

transition state is unknown, we may identify it with the structure of the arylcyclohexadienyl radical (II). The extra resonance energies in substituted benzenes have been evaluated by Matsen[7] by means of a perturbational treatment with simple molecular orbitals, and those for substituted cyclohexadienyls have now been estimated by the same method as in Matsen's treatment. The results are shown in Table 4, which also includes the values similarly calculated for the nitro group, it being assumed that the perturbing vacant molecular orbital of the nitro group has the energy $\alpha + \delta\beta$ ($\delta = -0{\cdot}5$ or $-0{\cdot}2$),* and that the coefficient of the atomic orbital of the nitrogen atom constituting the molecular orbital is $1/\sqrt{2}$. The trend seen in the differences in the calculated extra resonance energy between the substrate and the substituted cyclohexadienyl radical (II) shown in the fourth column is in satisfactory agreement with that in the τ_p values, considering the approximate nature of this molecular orbital treatment.

TABLE 3. CONJUGATIVE EFFECT OF A SUBSTITUENT GROUP IN THE SUBSTRATE, τ_p

	Substrate			
Arylation	$C_6H_5NO_2$	C_6H_5Cl	C_6H_5OMe	C_6H_5Me
p-Nitrophenylation	0·81	0·19	0·14	0·04
p-Chlorophenylation	1·00	0·19	0·12	0·07
Phenylation	0·92	0·16	0·12	0·11
p-Methylphenylation	0·93	0·06	0·19	0·13
p-Methoxyphenylation	0·85	0·22	0·14	0·09
Mean	0·90	0·16	0·14	0·09

In this connection, it is also to be noted that the extra resonance energies of the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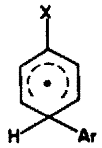
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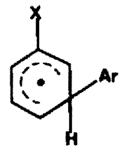
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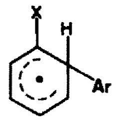
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TABLE 4. ESTIMATION OF THE CONJUGATIVE EFFECT

	Extra resonance energy[a]						
		ArC_6H_5X(II)		ArC_6H_5X(IV)			
X	C_6H_5X(I)		diff.[c]		diff.[c]	τ_p	τ_0
Me	0·24[b]	0·26	0·02	0·28	0·04	0·09	0·50
Cl	0·26[b]	0·29	0·03	0·31	0·05	0·16	0·48
OH(for OMe)	0·32[b]	0·37	0·05	0·40	0·08	0·14	0·57
$\delta = -0{\cdot}5$	0·29	0·48	0·19	0·54	0·25	0·90	0·88
NO_2							
$\delta = -0{\cdot}2$	0·35	1·01	0·66	1·08	0·73		

[a] In terms of the usual resonance integral value.
[b] Ref. 7.
[c] Difference from the value for C_6H_5X.

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* The energy of the vacant orbital of the nitro group may be estimated to be $a - 0{\cdot}15\beta$ ($\beta = -3$ ev) from the energy level values quoted by Nagakura and Tanaka[8] for the nitro group in nitromethane.

[7] F. A. Matsen, *J. Amer. Chem. Soc.* **72**, 5243 (1950).

[8] S. Nagakura and J. Tanaka, *J. Chem. Phys.* **22**, 236 (1954).

substituted cyclohexadienyl radicals (III) simulating the transition state of the arylation at the *meta* position are calculated to be the same as those in the corresponding substrates (Table 4, column 2), except for the case of the nitro group. Even in this case, however, the discrepancy is not serious, being 0·01 and 0·02 for $\delta = -0{\cdot}5$ and $-0{\cdot}2$, respectively. This result is very gratifying, since it implies that the conjugative effect is zero for every substituent in accordance with the fact that the Hammett relation has been found to hold for the partial rate factors at the *meta* position.

If the following equation, which is similar to equation 1, holds for the partial rate factors for the *ortho* position with σ_0 as the substituent constant

$$\log (k_0/k) = \rho\sigma_0 + \tau_0$$

it should express a straight line with a slope of σ_0 and an intercept of τ_0, when the values for log (k_0/k) are plotted against ρ as abscissa, that is, against the type of the arylation as variable (Fig. 2). The numerical values for σ_0 and τ_0 obtained by the least squares method are shown in Table 5. The σ_0 values are in fair agreement with those (σ_0^*) deduced by Taft[9] from his independent observation, when it is taken into account that the latter are expressed relative to the methyl group.

TABLE 5. CONJUGATIVE EFFECT AND SUBSTITUENT CONSTANT OF AN ORTHO SUBSTITUENT GROUP

	τ_0	σ_0	σ_0^*
$PhNO_2$	0·88	1·09	0·97
PhCl	0·48	0·34	0·37
$PhOCH_3$	0·57	−0·17	−0·22
$PhCH_3$	0·50	−0·01	0

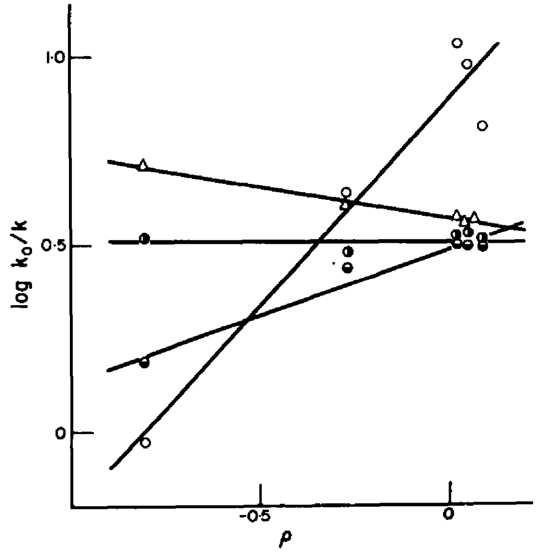

FIG. 2. Relation between the partial rate factors at the *ortho* position of a monosubstituted benzene and ρ values for various arylations.

—O—O—O— Nitrobenzene —⊕—⊕—⊕— Toluene

—⊖—⊖—⊖— Chlorobenzene —△—△—△— Anisole

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[9] R. W. Taft, *Steric Effects in Organic Chemistry* (Edited by M. S. Newman), p. 591. J. Wiley, New York (1956).

The conjugative effect τ_0 for the *ortho* position is found to be several times as large as the corresponding τ_p for the *para* position, except in the case of nitrobenzene. The extra resonance energies for substituted cyclohexadienyl radicals of structure IV corresponding to the arylation at the *ortho* position calculated by the same molecular orbital method as mentioned above are listed in Table 4 (column 5), and the differences (column 6) from the values for the substrates show that τ_0 should be about twice as large as τ_p. The fact that, for nitrobenzene, τ_0 has been found to be nearly the same as, or even smaller than, τ_p may suggest that steric hindrance is very important at the *ortho* position of nitrobenzene.