Free Radical Reactions in Solution. Part 7.[1] Substituent Effects on Free Radical Reactions: Comparison of the $\sigma^\cdot$ Scale with Other Measures of Radical Stabilization

By **Suphi Dinçtürk** and **Richard A. Jackson,*** School of Molecular Sciences, University of Sussex, Brighton BN1 9QJ

The $\sigma^\cdot$ scale of radical stabilization derived from the thermal decomposition of substituted dibenzyl mercurials is compared with other proposed scales. By using the $\sigma^\cdot$ scale, the parameter $\rho^\cdot$ can be used as a probe for the amount of radical character developed or destroyed in the transition state of a free radical reaction.

IN the preceding paper[1] we reported a novel scale of substituent constants $\sigma^\cdot$, which apply to stabilization of benzyl radicals at the *para*-position. In this paper we explore the advantages and disadvantages of our scale compared with other proposed and potential scales, and investigate the use of our $\sigma^\cdot$ scale as a probe for the amount of radical character generated or destroyed in the transition state of free radical reactions.

DISCUSSION

A number of criteria (see especially refs. 2—4) are important in choosing a model reaction system for evaluating the effects of substituents on a free radical reaction. (1) There must be a direct interaction between the substituent and the radical site. In practice, this is normally achieved by carrying out the reaction either at a benzylic centre α to an aromatic ring, or by attacking an aromatic ring itself, with the substituent concerned introduced at the *para*-position. (2) The mechanism of the reaction should be well understood. (3) Side reactions should be absent, as far as possible. (4) The kinetic effect involved should be large and an accurate method for its determination should be available. (5) Polar effects should be absent, minimized, or reliably separable from the radical stabilization effect. (6) A wide range of substituents should be studied, including ones which in polar situations are electron withdrawing and ones which are electron releasing. (7) Outside influences such as solvent effects and in particular steric effects should be minimized. (8) The model compounds should be easy to prepare.

The first attempt to separate polar and resonance effects in radical reactions was made by Alfrey and Price.[5] Copolymerization data were correlated on the basis of an empirical equation involving two parameters, a polar factor *e* and a radical stabilization factor *Q*. The main disadvantages of this scheme are its empirical character, and the fact that since *Q* for a particular compound depends on all the copolymerization data, addition of a new compound to the series involves re-evaluating all the other values.

Subsequent schemes have mainly relied on extended Hammett equations, essentially of type (1), where k_X and k_H refer to the rates of reaction of the substituted and unsubstituted compound, respectively;

$$\log k_X/k_H = \rho\sigma + \rho^\cdot\sigma^\cdot \qquad (1)$$

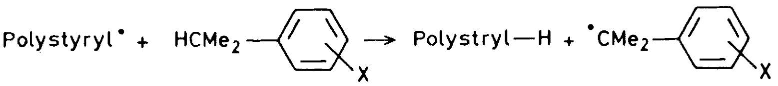
ρ is defined usually on the basis of *meta*-substituted compounds on the assumption that *meta*-substituents will not affect radical stability. Depending on the reaction concerned other scales of polar substituent constants such as σ^+ are sometimes used. $\rho^\cdot$ is usually defined as 1.0 for the reaction being studied, and $\sigma^\cdot$ values[1,4] are worked out for the *para*-substituents. Different symbolism has been used by different groups: the terms τ_p, E_D, and E_R were suggested in references 6, 7, and 8, respectively.

Bamford and Jenkins in 1963 suggested an alternative scheme[9] (' patterns of free radical reactivity ') but its application to simple substituents on a benzene ring in radical reactions is made difficult by the lack of data for chain transfer constants for substituted polystyryl radicals with toluene; we do not consider this scheme further in this paper. We include however in our discussion two model reactions which were not claimed by their authors as a basis for a ' $\sigma^\cdot$ ' scale, the copolymerization of methyl methacrylate with substituted styrenes by Walling and co-workers,[10] and the electrochemical reduction of substituted benzyl chlorides by Streitwieser and Perrin.[2]

All but one of these scales involve production of a benzylic radical in the transition state, either by hydrogen abstraction from a substituted cumene[8] [reaction (2)] or toluene[4] [reaction (3)], by addition of a radical to a substituted styrene[7,10] [reactions (4) and (5)], by electrochemical reduction of substituted benzyl chlorides[2] [reaction (6)], or by thermolysis of substituted dibenzylmercurials[1] [reaction (7)]. The other proposed reaction is a homolytic aromatic substitution reaction by phenyl radicals[6] [reaction (8)].

Reactions (2)—(5) all involve the production of a benzylic radical in the rate-determining step either by hydrogen transfer or by addition to a styrene double bond. In the transition state, benzylic radical character is only developed partially (*ca.* 30—50%, see later) and thus the kinetic effects will be smaller than they would be for more complete formation of benzylic character. The polar character of these reactions is often important, particularly when an electronegative radical such as $Br^\cdot$ or $CCl_3^\cdot$ is used, and indeed for brominations of substituted toluenes, the results can often be accommodated on a purely polar basis.[11] The question of what polar scale of σ constants should be used (σ, σ^n, σ^+, *etc.*) has often not been satisfactorily resolved, and Kieboom [12] has questioned the validity of the E_R scale [8] and by implication others of this type on this basis.

Fisher and Meierhoefer [4] attempted to reduce the polar character of radical brominations by introduction of a *meta*-cyano-group. However, this reaction still has a strong polar influence, the cyano-group introduces a steric complication which is absent in the other scales, and the fact that their scale uniquely of all the seven considered suggests destabilization of benzylic radicals by *para*-fluoro, -methoxy, and -methyl groups, suggests that this is far from an ideal model reaction. Probably the most satisfactory reaction in this group is the copolymerization of methyl methacrylate and substituted styrenes,[10] for which ρ is only 0.05, indicating that polar factors are almost negligible and thus arguments about which σ scale should be used are irrelevant. A remaining disadvantage of these reactions which produce benzylic radicals is that attack on substituent groups will take place to a greater or lesser extent. Even unreactive radicals such as benzyl will react for example with nitro-groups,[13] thereby affecting values of substituent constants.



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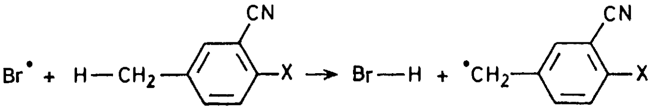

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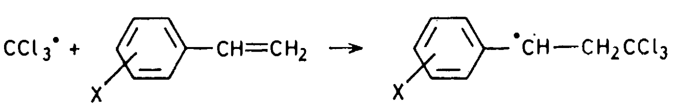

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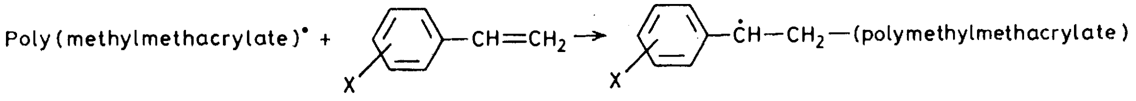

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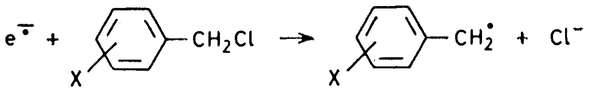

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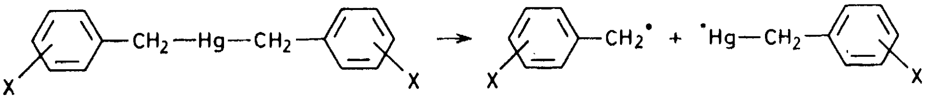

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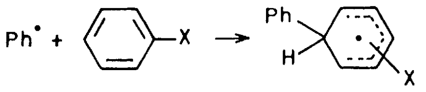


(8)

Advantages of the reduction of benzylic halides as a model reaction [2] include simplicity of operation and a polar effect in the opposite direction to the much studied halogenations of toluene. Disadvantages include the reduction of some substituent groups which makes it difficult to obtain values for substituents such as nitro, and the fact that the $E_{\frac{1}{2}}$ values for *meta*-substituents fall as a curve rather than as a straight line, making separation of polar from resonance effects uncertain.

The principal advantage of homolytic aromatic substitution [reaction (8)] as a model reaction is that a larger kinetic effect will be achieved, since *para*-substituents will be conjugated directly to a cyclohexadienyl radical rather than a benzyl radical and more radical character is developed on the former ($\frac{1}{3}$ compared with $\frac{1}{7}$ on a simple Hückel basis). Serious disadvantages are that τ_p values depend on the assumption that all (or the same proportion) of the intermediate adduct radicals end up as the substitution product $C_6H_5C_6H_4X$, and the reactive phenyl radicals used in this work will be even more prone to side reactions at the substituent groups.

We believe that our model reaction (7), though not perfect, offers significant advantages over the other schemes considered. Since homolysis of a benzyl–

mercury bond is involved, the full stabilizing effect of a *para*-substituent on a benzyl radical comes into play in the transition state, giving a reasonably large kinetic effect. Side reactions should be less important than for systems which depend on a radical–molecule reaction; provided that the solutions are dilute, the main fate of the benzyl radicals should be dimerization. The polar effect, though not absent, can be satisfactorily separated from the radical stabilization effect.[1] The main difficulties are experimental: some dibenzyl mercurials with conjugating electron-withdrawing groups are difficult to prepare, and some of the compounds have only a limited solubility in octane. A particular advantage of this model reaction is that since a benzyl radical is fully formed in the transition state, and $\rho^{\bullet}$ is defined as unity for this system, $\rho^{\bullet}$ values for other reactions, obtained by using our $\sigma^{\bullet}$ scale give a direct measure of the amount of radical character developed in the transition state of the reaction being considered. This is considered in more detail below.

TABLE 1

Correlations between various scales for radical stabilization by substituents

	$\sigma^{\bullet}$	$\sigma^{\bullet}_{\text{FM}}$	E_{R}	E_{D}	τ_{p}	log Q	Polymer	$E_{1/2}$	$a_{\text{H}}(\text{H}_2\text{O})$	$a_{\text{H}}(\text{org})$	Ref.
$\sigma^{\bullet}$	1.00	0.61	0.86	0.97	0.85	0.93	0.82	0.94	0.84	0.91	1
$\sigma^{\bullet}_{\text{FM}}$	*7*	1.00	0.68	0.69	0.92	0.62	0.27	0.27	0.90	0.73	4
E_{R}	*5*	*9*	1.00	0.81	0.99	0.82	0.86	0.67	0.92	0.93	8
E_{D}	*5*	*6*	*6*	1.00	0.82	0.98	0.95	0.92	0.98	0.96	7
τ_{p}	*5*	*6*	*5*	*5*	1.00	0.85	0.61	0.79	0.86	0.89	6
log Q	*5*	*8*	*9*	*6*	*5*	1.00	0.90	0.72	0.94	0.90	5
Polymer	*4*	*7*	*8*	*5*	*4*	*8*	1.00	0.79	0.93	0.86	10
$E_{1/2}$	*5*	*5*	*4*	*4*	*4*	*4*	*4*	1.00	0.96	0.95	2
$a_{\text{H}}(\text{H}_2\text{O})$	*5*	*7*	*6*	*5*	*4*	*5*	*5*	*5*	1.00	0.95	14
$a_{\text{H}}(\text{org})$	*5*	*6*	*5*	*5*	*4*	*5*	*5*	*5*	*6*	1.00	1

Correlation coefficients in top right half of table. Bottom left figures in italics are the number of pairs of data points used in calculating the correlation coefficients.

E.s.r. Data.—A non-kinetic alternative to the scales discussed above is the use of e.s.r. data on *para*-substituted benzyl radicals. Coupling constants for the α-hydrogen atoms reflect spin density on the α-carbon atom: *para*-substituents which stabilize the radical by delocalization of the unpaired electron should decrease the spin density on C_α and thus the α-H coupling constant. Neta and Schuler [14] γ-irradiated a number of *para*-substituted toluenes in aqueous solution at pH 13.7, and we have obtained data for substituted benzyl radicals in non-aqueous solution by radical abstraction of a hydrogen or a halogen atom from a substituted toluene or benzyl halide, respectively.[1] The two sets of data are in good agreement, in spite of the medium change, with r 0.95 for the six pairs of data points in common. The advantages of an e.s.r. based $\sigma^{\bullet}$ scale are that we are looking at a ground-state property of the radical, and there are no complications from side reactions. Disadvantages of such a scale are that the magnitudes of the substituent effect on a_{CH_2} are small (maximum 1.2 G in our work) leading to a coarsely graduated scale, and the difficulties of obtaining e.s.r. data for some radicals (for example *p*-nitrobenzyl) presumably because of side reactions at the substituent group, and the likely absence [1] of an exact linear relationship between stabilization energy and the $a_{\alpha\text{-CH}_2}$ coupling constant. For these reasons, the e.s.r. scale seems somewhat less desirable as a primary scale than our dibenzylmercury-based scale, but the general agreement (see below) adds to our confidence in the general validity of a $\sigma^{\bullet}$ scale.

Correlations between Scales.—We have correlated each of the scales discussed above, including the e.s.r. data, with each other and the correlation coefficients are shown in Table 1. The Fisher and Meierhoefer scale does not correlate well with the other scales on the whole because of the three substituents which have negative $\sigma^{\bullet}_{\text{FM}}$ values. The other scales correlate reasonably well with each other, with only two values in the matrix below 0.7. This seems a good indication that all the scales are trying to measure the same thing (*i.e.* radical stabilization), with variations caused by experimental error, side reactions, and incomplete separation of polar and resonance effects. The good correlation between $\sigma^{\bullet}$ and the a_{H} values obtained in non-aqueous solution is particularly noteworthy in showing agreement between the chemically based scales and a physical scale related directly to spin density.

In view of the broad overall agreement of all the scales (except for $\sigma^{\bullet}_{\text{FM}}$), we have used the correlations between the various scales (x) and $\sigma^{\bullet}$ (y) to give estimated $\sigma^{\bullet}$ values for substituents. These secondary $\sigma^{\bullet}$ values are collected in Table 2, and agree well with our primary values, though most of the other scales predict somewhat lower values for the methyl group than does our primary scale. We have also extended the scales to include secondary values for four substituents for which there is no primary value, provided that at least three values were available for a particular substituent. The scatter in these points is reasonably small, with the exception of cyano for which values ranging from 0.52 to 0.92 were calculated. Although in principle it would be possible to produce an ' average $\sigma^{\bullet}$ ' scale using the pooled data, we do not think it advisable at this stage since this would involve redefining the whole scale whenever new data is produced; use of a primary scale avoids this difficulty.

Use of $\rho^{\bullet}$ as a Probe of Radical Character in the Transition State.—Our proposed model reaction for defining the

$\sigma^{\bullet}$ scale involves the virtually complete formation of a free benzyl radical in the transition state, with associated stabilization by *para*-substituents: for other reactions, such as radical transfer reactions and additions to double bonds where only partial radical character is generated in the transition state, the effects of substituents will be smaller. Since $\rho^{\bullet}$ is defined as unity for the decomposition of substituted dibenzyl mercurials, reactions in which only partial radical character builds up in the transition state should have $\rho^{\bullet}$ values of less than unity. For reactions of substituted radicals where radical character is being destroyed in the transition state, negative $\rho^{\bullet}$ values should be found.

There is only a limited amount of literature data which can be analysed in these terms and much of it is concerned with the reactions already considered, which have been considered suitable as model reactions in their own right. We are not aware of any data showing a negative $\rho^{\bullet}$ value.

We would expect that other reactions which produce a benzylic radical in the transition state should have $\rho^{\bullet}$ values of about unity. Timberlake and his co-workers [15] studied the thermal decomposition of five-substituted phenylazoethanes $XC_6H_4CH_2\text{-}N{=}N\text{-}CH_2C_6H_4X$ at 150° but unfortunately they only chose *para*-substituents, so separation of polar and resonance effects is difficult. A least squares fit to an extended Hammett equation using σ° constants for the polar contribution and our $\sigma^{\bullet}$ values for the radical resonance contribution gives ρ° and $\rho^{\bullet}$ as 0.62 and 0.46, respectively. The polar component is in the opposite direction from our dibenzylmercury value as expected, but the $\rho^{\bullet}$ value is lower than would be expected for a reaction producing a free benzyl radical in the transition state. However, a greater range of substituents (some of them *meta*) would be needed to draw reliable comparisons between the two systems.

The majority of substituent effect studies have been on radical transfer reactions and additions to C=C double bonds, for which $\rho^{\bullet}$ values in the region of 0.5 would be anticipated, since in the transition state benzylic character is only partially generated. A value of 0.49 is obtained for $\rho^{\bullet}$ for the abstraction of hydrogen from substituted cumenes by the polystyryl radical [reaction (2)] in accord with this (though note Kieboom's criticism of the basis of the E_{R} scale [12]). A number of studies of hydrogen abstraction from substituted toluenes has been carried out, with considerable attention focused on the operation of polar factors. Particularly for electronegative radicals such as chlorine and bromine atoms, it is often difficult to disentangle polar from radical stabilization in the transition state, and for reactions of this type, competing aromatic substitution reactions can be a complicating factor.[16]

Addition of $CCl_3^{\bullet}$ radicals to substituted styrenes [reaction (4)] gives enhanced reactivity for *para*-substituents from which a value for $\rho^{\bullet}$ of 0.36 can be calculated, whilst values of $\rho^{\bullet}$ of 0.35 and 0.50 respectively can be derived from the reactivity of the growing polymer radicals $R\text{-}CH_2\text{-}\dot{C}HPh$ and $R\text{-}CH_2\text{-}\dot{C}(CH_3)\text{-}CO_2Me$ with substituted styrenes.[10] Thus available data are consistent with an interpretation of $\rho^{\bullet}$ as the measure of radical character built up in the transition state, but more examples would be very useful to have.

TABLE 2

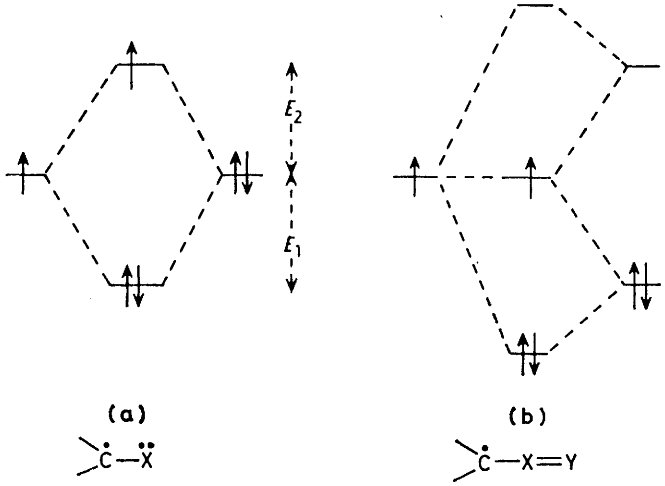
$o^{\bullet}$ Values

para Substituent	$\sigma^{\bullet}$ (primary)	$\sigma^{\bullet}$ (secondary) [a]	$\sigma^{\bullet}$ [from $(\lvert\sigma^{\pm} - \sigma\rvert)/n$]	$\dfrac{\lvert\sigma^{\pm} - \sigma\rvert}{n}$
H	0.00	0.09 ± 0.07 (8)	0.04	0.00
F	0.12	0.07 ± 0.05 (3)	0.15	0.065
Cl	0.18	0.25 ± 0.06 (8)	0.15	0.065
Ph	0.42		0.42	0.23
Me	0.39	0.27 ± 0.06 (8)	0.32	0.17
OMe	0.42	0.40 ± 0.09 (8)	0.45	0.25
NO_2	0.76	0.76 ± 0.02 (4)	0.77	0.44
Br		0.26 ± 0.06 (3)	0.13	0.055
I		0.31 ± 0.03 (3)	0.16	0.075
CN		0.71 ± 0.18 (6)	0.47	0.26
NMe_2		0.61 ± 0.08 (3)	0.93	0.535

[a] Number of values included in parentheses after standard deviation. [b] Substituent constant data taken from O. Exner in 'Correlation Analysis in Chemistry,' eds. N. B. Chapman and J. Shorter, Plenum, New York, 1978, p. 439.

Comparison with Schemes derived from Hammett Polar Parameters.—A number of schemes to quantify radical resonance effects in terms of Hammett polar parameters have been suggested. Since it is widely recognized that *para*-substituents, whether electron withdrawing or releasing, usually have a stabilizing effect on radicals, the use of σ^2 has been suggested.[17] The proponents of this scheme had, however, to exclude from the scheme substituents such as thiomethyl which has σ 0 but a large radical stabilizing effect and $\overset{+}{N}Me_3$ which has a large σ value but little radical stabilizing ability. A more sophisticated suggestion (but which suffers from the same defect) based on a theorem by Dewar [18] that electron-donors should be twice as effective at stabilizing a positive charge as an odd electron led to the definition [19] of the $\sigma^{\ddagger}$ scale as $\sigma/2$ for $\sigma < 0$ and $-\sigma$ for $\sigma > 0$.

We believe that conjugation effects are likely to be more important than inductive effects in stabilizing radicals: such conjugating effects in polar systems are measured by $\lvert\sigma^{+} - \sigma\rvert$ or $\lvert\sigma^{-} - \sigma\rvert$ depending whether the group is electron releasing or withdrawing. To relate radical-stabilization to ion-stabilization requires care, since stabilizing substituents are basically of two types, involving either (a) an electron pair, or (b) a double bond or equivalent π system (Scheme). For substituents of type (a) which include fluorine and methoxy, cations will be more effectively stabilized than radicals,



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and to a first approximation if $E_1 = E_2$ the stabilizing effect of the substituent will be only half as great on a radical as on a cation, since the extra electron has to go into the destabilized orbital. By contrast, the interaction with a double bond (or a larger π-system) involves interaction with both the filled π and the unfilled π^* orbital as shown, giving in effect an allylic system with a non-bonding orbital. The non-bonding orbital will be empty in the cation, half-filled in the radical, and filled in an anion, but to a first approximation the stabilization will be the same for all three.

Thus we suggest a scale $(|\sigma^{\pm} - \sigma|)/n$ to correlate radical stabilization with Hammett-type polar constants, where $\sigma^{\pm}$ is σ^+ or σ^- as appropriate, with $n = 2$ for electron-pair conjugating substituents [type (a)] and $n = 1$ for the type (b) substituents [methyl is considered a type (b) substituent].

In support of the assumptions made in setting up this scale, $(|\sigma^{\pm} - \sigma|)/n$ correlates excellently with $\sigma^{\bullet}$ (r 0.99) and this correlation suggests that for substituents for which $\sigma^{\bullet}$ has not been measured, values may be estimated using the regression equation (9). Values of $(|\sigma^{\pm} - \sigma|)/n$ and $\sigma^{\bullet}$ values estimated by the above regression equation are listed in Table 2 for comparison with the

$$\sigma^{\bullet}_{\text{estimated}} = 1.665\,(|\sigma^{\pm} - \sigma|)/n + 0.037 \qquad (9)$$

primary and secondary $\sigma^{\bullet}$ values discussed above. It must be stressed that the success of this relationship depends upon the assumptions about the orbital energy levels made earlier, and these may turn out to be unreliable in some cases, particularly for elements below the first row of the periodic table. More sophisticated calculations would be needed to obtain better approximations. However, the wide availability of Hammett polar substituent constant data makes the scale based on $(|\sigma^{\pm} - \sigma|)/n$ attractive to provide an estimate of radical stabilization, when the effect has not been measured directly.

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