Heterocyclic Free Radicals. Part 10.[1] Phenothiazine Cation-radicals as Probes of the Inductive Effect

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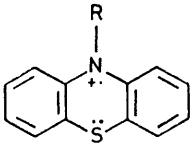
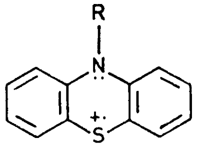
Phenothiazine cation-radicals, functionalised at nitrogen by polymethylene chains which terminate in polar substituents, exhibit nitrogen hyperfine splittings which vary regularly with the length of the polymethylene chain and with the polarity of the terminal substituent, as measured by σ_I. The cation-radicals are thus probes of the inductive effect which give quantitative insight into its transmission mechanisms and its attenuation by intervening bonds. For chain-lengths longer than a single methylene group, the field effects of the polar terminal substituents are correlated by a $\cos\theta/r^3$ function which implies that any terminal substituent may be modelled as a point-dipole whose mean orientation and mean separation from the radical aminium centre are determined by the conformational preferences of the polymethylene chain. Literature values of σ_I for certain substituents are questioned in the light of the results obtained and inductive substituent constants, in general, are discussed.

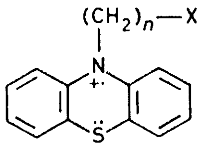
In an earlier Part,[2] devoted to an investigation of the influence of the structure and conformation of 10-alkyl substituents on the properties of phenothiazine cation-radicals, it was shown that alkyl side-chains larger than methyl, when appended to nitrogen, have strongly preferred conformations and influence the magnitude of the nitrogen hyperfine splitting by a classical through-bond inductive effect: the greater the polarisability of the alkyl group, the larger is the spin population which is stabilised at nitrogen *via* the concomitant positive charge. This is comprehended in terms of greater weightings for structure (1a) relative to (1b), the more polarisable is R.



(1a)



(1b)



(2)

The consequence of the introduction of polar groups into the alkyl substituent was also investigated to a limited extent: the nitrogen hyperfine splittings for a few radicals (1; R = CH_2X) were found to be correlated by σ_I for X. In the present work this aspect has been explored further. In particular, for (2) the polarity of X has been varied between alkyl and quaternary ammonium and the polymethylene chain separating the aminium centre of the radical from the polar substituent X has been varied from *n* 0—5.

RESULTS

(a) *E.S.R. Spectra.*—Previously, a failure was noted to obtain well resolved spectra from phenothiazine cation-radicals with *N*-alkyl groups longer than ethyl, when recorded for solutions in nitromethane at ambient temperature.[2] Now, however, we have obtained a satisfactorily resolved spectrum from (1; R = Pr^n) under these conditions. Spectra of better resolution than hitherto may be obtained at lower temperatures, *e.g.* (1; R = Et) exhibits splittings from *all* protons in the radical when spectra are recorded in nitromethane at −60 °C,[3] or at similar and lower temperatures in dichloromethane;[4] however, in the present work we are not concerned with detail of proton hyperfine structure but, rather, solely with the nitrogen splitting, *a*(N); also, we wish to make comparison with earlier results and therefore have retained nitromethane at ambient temperature as the solvent. The oxidants used on the parent phenothiazines in solution were either $AlCl_3$ or $Tl(OAc)_3$.

Introduction of a polar substituent X terminally into an alkyl group gives a cation-radical under the chosen conditions whose spectrum exhibits better general resolution than the corresponding alkylated radical where X = H. Thus we have obtained excellently resolved spectra for (2; X = $\overset{+}{N}Me_3$, *n* = 4) and spectra which are suitable for reliable measurement of *a*(N) for (2; X = $\overset{+}{N}Me_3$, *n* = 5). Substituents less polar than CN on a pentamethylene chain give radicals whose spectra are not adequately resolved, even for measurement of *a*(N). In general, any combination of X and *n* in (2), giving a radical expected to exhibit a nitrogen hyperfine splitting in excess of *ca.* 0.75 mT, fails to give a suitably resolved spectrum; a reason will be suggested subsequently.

In Table 1 are collected the nitrogen hyperfine splittings measured for (2) for the various *n* and X which are used in this work.

TABLE 1

Nitrogen hyperfine splittings (mT)[a] for (2) with various *n* and X

X \ *n*	0	1	2	3	4	5
H			0.751[b]	0.751	*c*	
Ph		0.710[b]	0.737[b]	0.750		
CHO		0.685				
CO_2Et	0.632[b]	0.685[b]	0.725			
Cl			0.700	0.735	0.750[d]	*c*
CN		0.648	0.692[b]	0.730	0.745	0.750
$\overset{+}{N}Me_3$			0.667	0.715	0.735	0.748

[a] ±0.005 mT. [b] Ref. 2. [c] Inadequately resolved spectrum. [d] Approximate value, resolution poor.

(b) *Correlations*.—(i) *Positive* σ_I. In Figure 1 the nitrogen hyperfine splittings are plotted against σ_I values for the substituents. Some data are used twice: *e.g.* the result for (2; X = CN, n = 2) is plotted using σ_I for CN on the n = 2 plot and also using σ_I for CH_2CN on the n = 1 plot; the result for (2; X = Cl, n = 3) is plotted using σ_I for Cl on the n = 3 plot and also using σ_I for CH_2Cl on the n = 2 plot, and so forth. The σ_I values used, given in Table 2 for convenience, are taken from Exner's [5] recent compendium and, where a choice of values is possible, those determined from the protolytic equilibria of quinuclidines have been preferred. The exceptions are the σ_I values used for CH_2CN, CHO, and $\overset{+}{N}Me_3$ which have not been determined in the quinuclidine system.

TABLE 2

Positive values of σ_I employed [5]

Substituent	σ_I	Substituent	σ_I
Ph	0.15	CO_2Et	0.31
CH_2Cl	0.16	Cl	0.48
CH_2CN	0.21	CN	0.57
CHO	0.25	$\overset{+}{N}Me$	0.93

The σ_I value taken for CH_2CN is interpolated from a value of σ_I for CN, all systems of measurement giving values for the latter which are essentially concordant; [5] the value for CHO is the only value listed and derives from ^{19}F n.m.r. shift measurements.[5] Exner [5] quotes several values of σ_I for $\overset{+}{N}Me_3$ ranging from 0.73 to 1.34. The value chosen lies near the middle of this range; it was measured on the protolytic equilibria of bicyclo-octanecarboxylic acids which are structurally similar to the quinuclidinium ions upon which preferred σ_I values were determined; [5] furthermore, allowance was made in its determination for the effect of ionic strength, an important factor recently re-emphasised; [6] additionally, the value coincides with that determined from ^{19}F n.m.r. shift measurements which is independent of ionic strength effects.[5]

Certain available [5] literature values of σ_I have not been used because these do not permit the self-consistent plotting of data within the array of Figure 1. In general, these are for substituents of type CH_2X. Thus, published σ_I values for CH_2CHO, CH_2CO_2Et, CH_2CH_2CN, and $CH_2\overset{+}{N}Me_3$ are rejected. We feel their exclusion to be justified for it permits the n = 0 and 1 lines of Figure 1 to cut the ordinate at intercepts coincident, within experimental error, with those of plots found previously for substituents at nitrogen with negative σ_I values,[2] and also shown in Figure 1 (dashed lines). We shall return to these rejected σ_I values in the Discussion section.

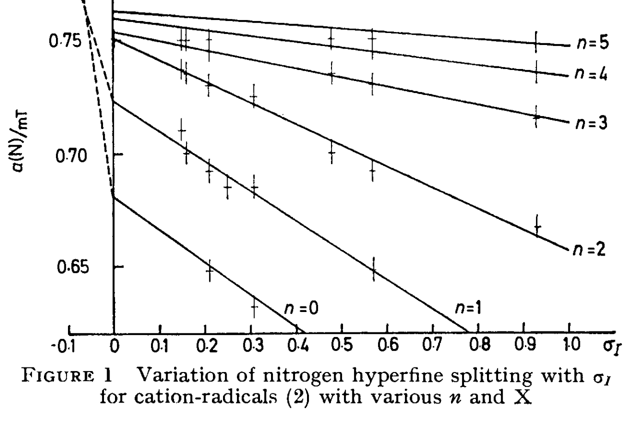


FIGURE 1 Variation of nitrogen hyperfine splitting with σ_I for cation-radicals (2) with various n and X

The least mean squares expressions for the n 1—3 lines are equations (1)—(3), respectively; the least mean squares expressions for the correlations involving negative σ_I values [7] are equations (4) (for n = 0) and (5) (for n = 1). (These have been recalculated for stricter comparison with the new data by excluding previous results for substituents attached to nitrogen by secondary carbon and by including the new result for chloroethyl, using σ_I −0.010 for the latter: [7] their coefficients thus differ somewhat from previous values.[2]) The n 0 line for positive σ_I is drawn arbitrarily from the intercept given by equation (4) with a slope of −0.145 mT for reasons to be explained subsequently; for want of data points, the n 4 and 5 lines are also arbitrarily drawn from the points appropriate to the $\overset{+}{N}Me_3$ substituent to intercepts on the ordinate calculated as follows.

$$a(N)_1 = 0.723 - 0.133\sigma_I \quad r\ 0.979 \qquad (1)$$

$$a(N)_2 = 0.750 - 0.094\sigma_I \quad r\ 0.993 \qquad (2)$$

$$a(N)_3 = 0.754 - 0.041\sigma_I \quad r\ 0.992 \qquad (3)$$

$$a(N)_0 = 0.681 - 1.440\sigma_I \quad r\ 0.969 \qquad (4)$$

$$a(N)_1 = 0.724 - 0.668\sigma_I \quad r\ 0.976 \qquad (5)$$

Levitt and Widing [7] showed that the curve which describes the variation of the inductive effects of simple linear alkyl groups with the number n of carbon atoms contained is a branch of a rectangular hyperbola. Since the intercepts, C_n, on the ordinate of Figure 1 correspond to nitrogen substituents of type $(CH_2)_nX$, where X has σ_I 0, they correspond to alkyl groups for $n \geqslant 1$ and to H for n 0.[2] Thus, following Levitt and Widing,[7] C_n should be given by equation (6) where C_∞ is the intercept expected (in Figure 1) for a radical with an infinitely long linear alkyl group and b is a constant. It follows that a graph of $C_n(n + 1)$ *versus* n should be linear with gradient C_∞. Figure 2 shows that this is indeed the case when the intercepts C_n of equations (1)—(4) are used; a least-squares value of C_∞ of 0.781 mT results which is in excellent agreement with the value, 0.780 mT, obtained from equation (4) using σ_I −0.0686, Levitt and Widing's [7] value of σ_I for an infinitely long alkyl group. A value of b of 0.865 also results. Using equation (6) with the values so determined for C_∞ and b, the intercepts of the n 4 and 5 lines of Figure 1 were calculated and their gradients obtained. The n 4 and 5 lines are thus expressed by equations (7) and (8), respectively.

$$C_n = C_\infty(n + b)/(n + 1) \qquad (6)$$

$$a(N)_4 = 0.760 - 0.027\sigma_I \qquad (7)$$

$$a(N)_5 = 0.763 - 0.016\sigma_I \qquad (8)$$

The form of the dependence upon n of the gradients m_n of equations (1)—(3), (7), and (8) is illustrated by the sigmoid curve of Figure 3. By trial and error, we find an expression which correlates the magnitudes of the gradients with n, within experimental error, to be equation (9). This gives a value of $|m_0|$ of 0.145 mT, the value used for the

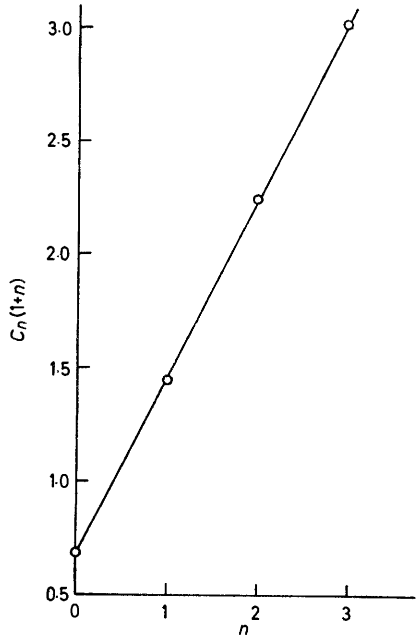


FIGURE 2 Plot of $C_n(n + 1)$ *versus* n

n 0 plot for positive σ_I in Figure 1. (A polynomial of degree

$$|m_n| = 0.071 - 0.074 \tanh[2(n - 2.4)/(n + 1)] \quad (9)$$

4 in n, will correlate the gradients m_n exactly, of course, but this takes small values for $0 < n < 1$ and is useless for interpolating a value for m_0.)

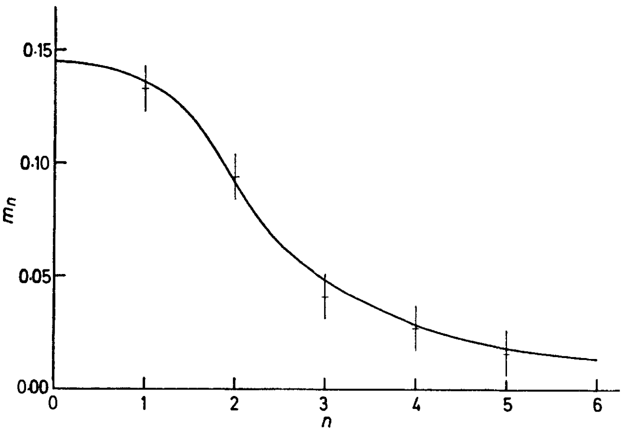


FIGURE 3 Curve: $|m_n|(\text{calc}) = 0.071 - 0.074\tanh[2(n - 2.4)/(n + 1)]$; experimental $|m_n|$ are also shown

Combining equations (6) and (9), permits equations (1)—(3), (7), and (8) to be expressed, generally, by equation (10) which reproduces essentially all the data of Figure 1, for $\sigma_I \geqslant 0$, within experimental error.

$$a(\mathrm{N})_n = \frac{0.781(n + 0.865)}{(n + 1)} - \sigma_I\left\{0.071 - 0.074\tanh\frac{[2(n - 2.4)]}{(n + 1)}\right\} \quad (10)$$

This expression indicates the effect on $a(\mathrm{N})$ of the total addend at nitrogen to comprise two components. The first varies only with n and we take it to reflect the polarisability of the polymethylene chain and its increase with the number of carbon atoms contained. The second term also depends on n, decreasing as n increases, and, additionally, on σ_I indicative of the polarity of the terminal substituent. Here, if σ_I measures the electrostatic field effect of the terminal substituent, the n dependence reflects its diminution with distance as the chain lengthens.

(ii) *Electrostatic field effects.* To elucidate further the distance dependence of the effect on $a(\mathrm{N})$ of a terminal polar substituent, theoretical calculations were performed on n-meric chains with the hypothetical structure N-$(\mathrm{CH_2})_n$-Cl, for values of n in the range $2 \leqslant n \leqslant 5$.[8] Chlorine was chosen as the model substituent as, being monatomic, it is the simplest of those actually studied and, further, its polarity as measured by σ_I lies in the middle of the range examined. The parameter $\langle r \rangle$, the average distance between the terminal nitrogen and chlorine atoms and the parameter $\langle \theta \rangle$, the average acute angle between the projection of the vector connecting the nitrogen and chlorine atoms and the projection of the terminal methylene-to-chlorine bond vector, were calculated using a rotational isomeric state model for polymethylene.[9,10] Each carbon–carbon skeletal bond was given three possible rotational states, ϕ_t 0(*trans*) and $\phi_{g\pm}$ $\pm 2\pi/3$ (*gauche* $\pm$). The bond lengths used were 1.53, 1.77, and 1.48 Å for the C–C, C–Cl, and N–C bonds, respectively; bond angle supplements of 68° were assigned to the carbon atoms. The values of r and θ for all possible conformations of the n-meric chain were calculated using vector methods; [11] these were then averaged by statistically weighting each conformation of the appropriate chain at 293 K, according to the weighting parameters described by Scales.[10] The resulting $\langle r \rangle$ and $\langle \theta \rangle$ are given in Table 3; the values quoted for the species N–$\mathrm{CH_2}$–Cl are discrete and were calculated using simple trigonometry.

TABLE 3

Electrostatic field data

n	$\langle r \rangle$/Å	$\langle \theta \rangle$ (°)	$\frac{10^3\cos\langle\theta\rangle}{\langle r \rangle^3}$	ξ_n (%)
1	2.70	32.56	42.82	18.39
2	3.65	35.11	16.82	12.53
3	4.69	37.50	7.69	5.44
4	5.63	41.62	4.19	3.55
5	6.54	44.14	2.56	2.10

It is a result of classical electrostatics that the electric field intensity in the direction PQ at a point Q a distance r from a point-dipole P is proportional to $\cos\theta/r^3$, where θ is the angle subtended between the direction PQ and that of the dipole.[12] In terms of our model, therefore, the average field due to the nett dipole of the terminal substituent, which is experienced by the aminium centre of a phenothiazine cation-radical bearing a terminally substituted polymethylene chain attached to nitrogen, is proportional to $\cos\langle\theta\rangle/\langle r\rangle^3$, on the assumption that the substituent may be represented as a point-dipole whose average orientation is the same as that of the bond between the substituent and the terminal methylene carbon and whose average separation from the aminium centre is determined by the conformational preferences of the polymethylene chain which tethers the substituent to the aminium centre, the latter preferences being unrestricted by the aromatic moiety of the radical.

For each length of polymethylene chain the electrostatic effect on a(N) of terminal substituents is expressed in Table 3 as ξ_n, the percentage decrease in a(N) per unit increase in positive σ_I, *i.e.* $\xi_n = 100|m_n|/C_n$. In Figure 4 the variation of ξ_n with $\cos\langle\theta\rangle/\langle r\rangle^3$ is shown. Points for all chain lengths where $n > 1$ are linearly correlated and the graph extrapolates to the origin implying similar correlation for $n \longrightarrow \infty$. Although $\cos\langle\theta\rangle$ does not vary greatly for the chain-lengths n = 1—5, nevertheless, the scatter of the correlated points is increased if the $\cos\langle\theta\rangle$ term is neglected. The scatter is also increased if terminal bond lengths less than 1.77 Å are used and, more importantly, the dependence of ξ_n on $\langle r\rangle$ takes non-integral powers of $\langle r\rangle$ between -2 and -3. It seems, therefore, that any of the substituents studied, which allow the evaluation of ξ_n and which vary widely in their actual geometries, may be modelled as point-dipoles orientated in the direction of the terminal methylene carbon–substituent bond and situated at a distance along this direction comparable with the C–Cl bond length.

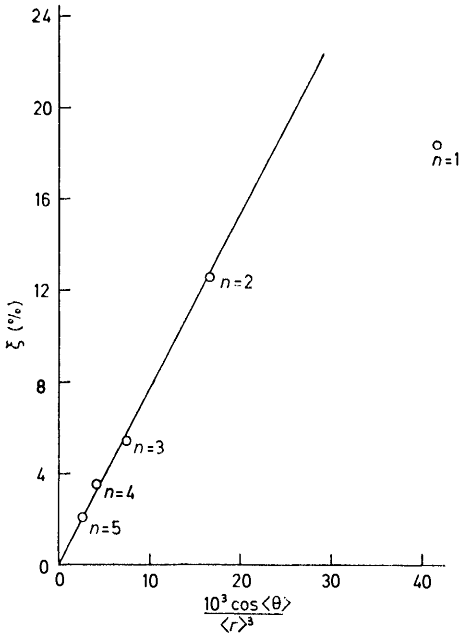


FIGURE 4 Variation of ξ_n with $10^3\cos\langle\theta\rangle/\langle r\rangle^3$

(iii) *Negative* σ_I. A family of plots appropriate to negative σ_I values and analogous to those given in Figure 1 for positive σ_I may be interpolated from the intercepts of Figure 1 and certain literature values [7] of σ_I for linear alkyl groups. Thus, for example, the intercept C_3 of 0.750 mT, given by equation (11) [*i.e.* equation (6) with constants evaluated], representing the nitrogen hyperfine splitting of the 10-propylphenothiazine cation-radical, may be plotted using σ_I for Et on the n = 1 plot, using σ_I for Me on the n = 2 plot, and using σ_I 0 on the n = 3 plot, and so forth yielding Figure 5. The plots so obtained are clearly curves as opposed to the lines of Figure 1. The algebraic form of the n = 0 curve of Figure 5 may be deduced by eliminating n between equation (11) and equation (12) which Levitt and Widing [7] found to relate the σ_I values of linear alkyl groups to the number of carbon atoms contained. The resulting expression is equation (13); equations of the same form, (14), differing merely in the coefficients, may be found for the remaining curves of Figure 5.

$$C_n \equiv a(\mathrm{N})_n = 0.781(n + 0.865)/(n + 1) \tag{11}$$

$$\sigma_I = -0.137n/(2n + 1) \tag{12}$$

$$a(\mathrm{N})_0 = (4.16\sigma_I + 0.676)/(7.30\sigma_I + 1) \tag{13}$$

$$a(\mathrm{N})_n = \frac{0.781\{[14.60(n + 0.865) - 7.30]\sigma_I + (n + 0.865)\}}{\{[14.60(n + 1) - 7.30]\sigma_I + (n + 1)\}} \tag{14}$$

We have previously assumed, and indeed observed,[2] a *linear* dependence of a(N) upon negative σ_I [*e.g.* equations (4) and (5), the broken lines in Figure 5]. There are various reasons for the apparent discrepancy. First, the range of negative σ_I values is narrow thus, necessarily, the line represented by equation (4) and the curve represented by equation (13) lie close together over the range of linear alkyl groups for which $n > 3$. Secondly, the value predicted by equation (13) for $a(\mathrm{N})_1$, the nitrogen hyperfine splitting of the 10-methylphenothiazine cation-radical (*i.e.* 0.728 mT), and which would be the most seriously divergent point from the linear correlation of equation (4), is in fact a hypothetical value. The real value (0.749 mT) is relatively elevated by the uniquely large capacity of the methyl group to perturb spin distribution by the hyperconjugative mechanism [2] and is consequently, though fortuitously, well correlated by equation (4). Thirdly, in defining equations (4) and (5) nitrogen side-chains other than linear alkyl groups were used. For certain groups, such as $PhCH_2$ and $Cl(CH_2)_2$, the σ_I values, although negative, are close to zero and therefore errors in them are likely to be proportionately large (see Discussion section). With only slightly different σ_I values, these points would be as well correlated by equation (13) as by equation (4). Thus we conclude that whereas correlation *curves* such as equation (13) and (14) are strictly appropriate the data can, with little detriment, be correlated by linear expressions such as equations (4) and (5). Certainly, the intercept for σ_I 0 of the correlation *lines* [equations (4) and (5)] upon which earlier argument is based [see (i) above], and those of the correlation *curves*

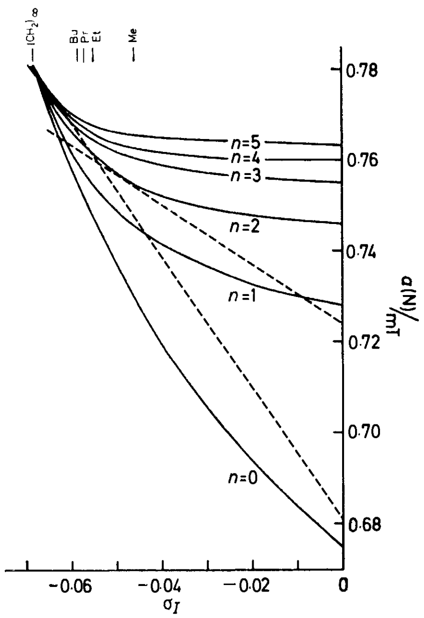


FIGURE 5 Plot of calculated intercepts, C_n *versus* negative σ_I for various n

[*e.g.* equation (13)] agree within the experimental error in the observable a(N) as internal consistency requires.

(iv) *Overview.* The correlations adduced in Figures 1 and 5 may be combined in a block diagram (Figure 6) where the three variables a(N), σ_I, and n are plotted in Cartesian co-ordinates. It may be seen that the experimental observable relates to the structure and general inductive character of the side-chain at nitrogen in terms of a surface with two curvatures. Both curvatures increase as n and σ_I approach zero; however, the dominant curvature of the surface takes opposite senses for the positive and negative ranges of σ_I with the consequence that the surface is 'creased' along a vertical section parallel to the n axis and corresponding to σ_I 0, the crease being especially marked for $n \leqslant 2$ but becoming negligible for larger n. In the limit of $n \rightarrow \infty$, the surface is planar, parallel to the n σ_I plane, with a(N) 0.781 mT. For negative σ_I, the surface has vertical sections parallel to the n axis which are hyperbolic curves except for the value σ_I -0.0686 where the section is rectilinear; vertical sections taken in the same direction for positive σ_I are curved, but the curvature is not hyperbolic: the rate of decrease of a(N) with n is less than a hyperbolic curvature would predict. Vertical sections of the surface parallel to the σ_I axis are hyperbolic curves when σ_I takes negative values but linear for positive σ_I. The surface is such that in most areas where $a(\mathrm{N}) > ca.$ 0.75 mT the gradients $\partial a(\mathrm{N})/\partial\sigma_I|_n$ and $\partial a(\mathrm{N})/\partial n|_{\sigma_I}$ are within the experimental error in a(N) so that a(N) is not susceptible to structural variation and unresolved spectra result for (2) above this value irrespective of the nature of n and X.

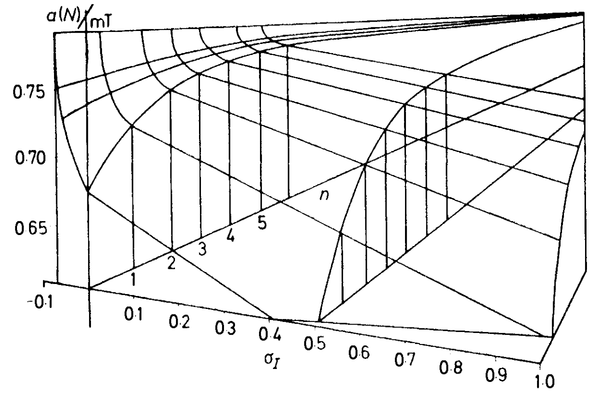


FIGURE 6 Block diagram showing variation of a(N) with n and σ_I

For $\sigma_I > 0$, the gradients $\partial a(\mathrm{N})/\partial n|_{\sigma_I} = s_n$ are obtained by differentiation of equation (10) with respect to n, *viz.* equation (15).

$$s_n = 0.105/(n + 1)^2 + 0.503\sigma_I\mathrm{sech}^2[2(n - 2.4)/(n + 1)]/(n + 1)^2 \quad (15)$$

Table 4 gives evaluations of s_0 and s_1 and their ratio $R = s_0/s_1$ for various σ_I. In Figure 7 is plotted R *versus* $(1 + \sigma_I)^{-1}$; the graph is linear with gradient 4, whence equation (16) is obtained.

$$R = 4/(1 + \sigma_I) \quad (16)$$

TABLE 4

Evaluation of gradients s_n to the surface of Figure 6 and their ratio

σ_I	$(1 + \sigma_I)^{-1}$	s_0/mT	s_1/mT	$R = s_0/s_1$
0	1.000	0.105	0.026	4.038
0.10	0.909	0.105	0.029	3.620
0.20	0.833	0.105	0.031	0.387
0.30	0.769	0.105	0.034	3.088
0.40	0.714	0.105	0.037	2.838
0.50	0.667	0.105	0.039	2.692
0.60	0.625	0.105	0.042	2.500
0.70	0.588	0.105	0.045	2.333
0.80	0.555	0.105	0.048	2.187
0.90	0.526	0.105	0.050	2.100
1.00	0.500	0.105	0.053	1.981

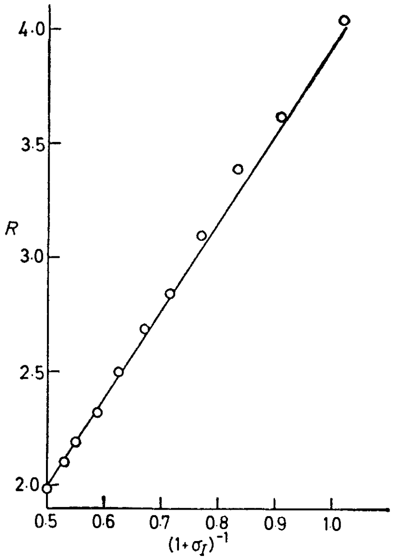


FIGURE 7 Plot of the gradients ratio R *versus* $(1 + \sigma_I)^{-1}$, $\delta_I \geqslant 0$

DISCUSSION

(a) *Ion-radicals as Detectors of Substituent Effects.*—The usual origin of substituent constants is in differences of pK_a between suitable substituted acids and their unsubstituted parent. For example, σ_I used in this work has been measured upon the protolytic equilibria of quinuclidinium ions[5,13] and bicyclo-octanecarboxylic[5,14] and acetic acids,[5,15] amongst other systems.[5] Thus four organic species are involved in the definition of a particular σ_I value: the substituted acid, the reference acid, and their respective conjugate bases. The inductive effect which σ_I purports to measure is differentially operative in two of these species. The fact that a relatively reliable scale of σ_I values has evolved indicates that, happily, errors frequently cancel. Nevertheless, it would be surprising if inconsistencies did not occur in the σ_I scale and particularly so for σ_I values which would be expected to be low in value, being small differences between pairs of similar pK_a values. Although σ values, generally, are thermodynamic quantities the very name *substituent* constant implies an interpretation at the molecular level, and the one usually made is that the constant reflects the electron displacement effected by the substituent in a particular molecular system.

The correlation by substituent constants of the changes in the hyperfine splittings of free radicals, which are induced by substitution, affords a very direct means of testing the validity of the constants. The hyperfine splitting manifested by a magnetic nucleus in the e.s.r. spectrum of a radical is directly related (proportionally, or approximately so [16]) to the spin population at the atom concerned and thus changes in the hyperfine splitting on substitution reflect the unpaired electron displacement wrought by the substitution. Previous experience shows that for charged aromatic radicals the influence of substituents on the radical involves principally interaction with the *charge*, as in diamagnetic ions; [2,17] only rarely does the substituent take upon itself a significant proportion of the spin and such cases are readily identified from the spectra. The e.s.r. experiment thus enables one to ' see ' the highest (singly) occupied MO in the radical and its distortion under substitution. Furthermore, when a substituent effect is detected by a radical only a single ground-state species is effectively involved; the two spin-states whose separation permits the e.s.r. experiment differ in energy by only that of a microwave quantum. Thus in a radical which experiences a substituent effect, the detecting system involves fewer chemical species than the more usual chemical detecting systems and the parameter observed bears a more direct relationship to the molecular quality which the substituent constants purport to reflect than the parameters used in any other detecting systems, whether chemical or physical in nature. These arguments, we feel, are justified by the order which has been discerned in the results presented here.

(b) *Inductive Effects in Phenothiazine Cation-radicals.*—In adducing the results, we have already shown that the effect of the combined addend at nitrogen comprises two parts [equation (10)] which have been identified as a polarisability component, determined by the number of carbon atoms in the side-chain and constants characteristic, no doubt, of the phenothiazine cation-radical system, and a field component determined by the number of carbon atoms, the nature of the terminal substituent, and characteristic constants. For side-chains containing two or more carbon atoms, confirmatory evidence that the second component of the total effect is indeed an electrostatic field effect is provided by the observation of the expected dependence of the experimental observable, for a given chain-length, on the average separation of the charge-bearing aminium centre and the substituent, viewed as a point-dipole, and on their average mutual orientation.

The failure of the $\cos\theta/r^3$ relationship (Figure 4) for radicals with single carbon side-chains is notable, ξ_1 taking considerably lower values than proportionality to $\cos\theta/r^3$ would require. Possible reasons for breakdown in this relationship are various. First, for $n = 1$ the $\cos\theta/r^3$ term may be inappropriate: for small r the approximation of the substituents to point-dipoles is expected to become invalid since the actual separation of charges in a substituent-dipole is then no longer negligible in comparison with r. In this case the dependence of ξ upon r^{-3} breaks down.[12] Additionally, if the separation of charges in the substituent-dipole *is* important, then the actual geometry of each substituent becomes significant and the orientations of the substituent-dipoles, which depend on individual geometry, may no longer be approximated by the orientation of the methylene carbon–substituent bond. The $\cos\theta$ term, as calculated, thus also becomes invalid. Alternatively, the failure of the proportionality may reside in a change in the character of ξ for $n = 1$, by comparison with that for greater values of n. Such change could stem only from a smaller than ' expected ' value of $|m_n|$ since C_n values are independent of the terminal substituents. The sigmoid form of Figure 3 demonstrates that the rate of increase of $|m_n|$ with decreasing n falls off for $n = 1$; evidently, the character of m_1 and hence ξ_1 does change. This change cannot arise from the operation of through-bond inductive effects of the terminal substituents since such effects would augment the field effects and result in larger than expected values, of m_1 and ξ_1. Apparently, the change reflects a ' saturation ' phenomenon in the experimental observable. No doubt there is a limit to the amount of positive charge and concomitant spin population that may be displaced from nitrogen in phenothiazine cation-radicals. In our previous work,[17] we have observed that *N*-unsubstituted cation-radicals undergo greater changes in a(N) on structural variation than do *N*-substituted cation-radicals. The greatest percentage reduction in a(N) observed in an *N*-unsubstituted radical was *ca.* 22%; the greatest percentage diminution in a(N) in the present *N*-substituted cation-radicals is 11% [for (2; $n = 2$, X = $\overset{+}{N}Me_3$)]. Correlation of all ξ_n with appropriate $\cos\theta/r^3$ would require ξ_1 in excess of 30%. It thus seems likely that the principal reason for the non-correlation of the results for $n = 1$ in Figure 4 derives from a physical limit to the amount of charge and spin density that may be displaced from the aminium centre. Although data are sparse, the similarity in slope of the $n = 0$ line of Figure 1 to that of the $n = 1$ line supports the idea that for polar substituents close to the aminium centre, there is a limit to the decrease in a(N) that is possible.

(c) *Generalisation.*—In principle, a surface comparable with that in Figure 6 should correlate any property, which is a function of energy, with molecular structure and general substituent polarity, although the curvatures and slopes on the surface would be expected to vary according to the nature of the electrical charges which interact, *e.g.* whether positive or negative, monopolar or dipolar, and with the intrinsic ability of the particular detector system to redistribute charges within itself. The range of substituent polarity has usually been calibrated (the σ_I scale) in terms of the vertical separation of two such surfaces, the one relating to the standard free energies of a family of undissociated acids, the other to those of the corresponding ionised forms. The fact that a coherent set of positive σ_I values has evolved using calibration systems as different in structure and charge-type as carboxylic acids and quinuclidinium ions implies that, over the range of heteroatomic substitution common in organic molecules, the convergence of these free energy surfaces, *i.e.* the difference in their gradients along sections parallel to the substituent polarity axis, takes constant values: it is the basis of *linear* free energy relationships.

There is controversy, however, over whether the σ_I and σ^* scales which have evolved to measure inductive effects meaningfully measure an electronic effect for alkyl groups or whether they are artefacts of residual steric effects or random errors.[7,15,18-24] Our successful use of Levitt and Widing's [7] σ_I values in correlations of nitrogen hyperfine splittings in phenothiazine cation-radicals, very directly electronic phenomena, confirms us in the view that these particular σ_I values do measure a real electronic phenomenon. This does not imply, however, that alkyl σ values reflect a coulombic field property like those of substituents containing heteroatoms; rather, we believe, the effect is one of polarisability: the more carbon atoms there are in an alkyl group the better able it is to supply σ-electron density through the bond which attaches it to an electron-deficient centre. It is significant that Levitt and Widing's alkyl σ_I scale which was calibrated using ionisation potential data also very precisely correlates gas-phase basicities of alkylamines [25] as well as our nitrogen hyperfine splittings in cation-radicals. All these systems discriminate between the various alkyl groups by making a high through-bond demand for electron density upon them. Those systems of calibration or reactivity which have led to the conclusion that all alkyl groups have σ_I (or σ^*) equal, or equal to zero, or inconsistent with the corresponding values of heteroatom-containing substituents, have usually involved the reactivity of acyl functions (protolytic equilibria of carboxylic acids or base-catalysed hydrolysis of their esters [14,22,24]) or have had the alkyl groups attached to sp^3 carbon atoms remote from the detector centre.[13,14] In each case no component of the system is able to polarise an attached alkyl group to the same degree as closely adjacent cationic charge; consequently, the discrimination between alkyl groups is low and may approach zero and lie within experimental error.

In any system used for calibrating the σ_I or σ^* scales, if the free energy surfaces whose separation measures the particular σ values do respond to the differential polarisabilities of alkyl groups but in a manner which leads to ***curved*** sections as in Figure 6, only fortuitously would the separation between such curved sections give a σ scale for alkyl groups comparable with that given for heteroatom-containing substituents by the separation of linear sections of the same surfaces; the alkyl σ values, whether σ_I or σ^*, would usually seem differently scaled from the corresponding values for heteroatom-containing substituents, as is observed.[14,19,20] We conclude that the curved and linear sections of the surface of Figure 6 occur because the σ_I values used in its definition reflect comparable curvature and linearity in the free energy surfaces used in ***their*** definition and that these different responses of the free energy surfaces to substituent-type relate directly to the different natures of the electronic effects of the substituents: a through-bond polarisability effect for alkyl groups, a through-space electrostatic field effect for polar substituents.

Consider now composite substituents of type $(CH_2)_nX$. It is commonly asserted that interposing a methylene group between a polar substituent X and a detector centre attenuates the substituent effect by a constant factor; [5,18,19] equation (17), which has been applied to both σ_I and σ^*, gives the factor a value of 1/2.8. Expression

$$\sigma_I(CH_2X) = \sigma_I(X)/2.8 \qquad (17)$$

(17) implies the attenuation factor to be independent of $\sigma_I(X)$ and it precludes $\sigma_I[(CH_2)_nX]$ from taking negative values. Equation (15), however, demonstrates that in the phenothiazine cation-radical system the variation of the experimental observable with n, for a particular value of σ_I, depends upon that value. In addition it must be recognised that when a methylene chain is lengthened the nature of the chain is changed as well as any terminal substituent being distanced. This change is one of polarisability: when an electron-deficient detector centre Y is separated from a polar substituent X by a single methylene group, the polarisation of the Y–C bond by Y is attenuated by the opposing polarisation of the same bond by X. On interposing further methylene groups the through-bond effect of X on Y–C dies off very rapidly [26] with the result that the polarisation of Y–C by Y increases sharply. (The sharp increase in the polarisability of the N–C bond in the phenothiazine cation-radical system is manifest in the change in slope of the lines of Figure 1 at the ordinate and in the ' crease ' which occurs for small values of n in the surface of Figure 6.)

For relatively weakly polar groups X, the increase in the polarisability of the chain upon extension can outweigh the weak field component of the combined effect with the result that σ_I for the composite substituent changes sign. For example, the substituent $(CH_2)_nPh$ has experimental σ_I values of 0.15, −0.026, −0.038, and −0.044 for respective values of $n = 0$—3 and the experimental σ_I values of $(CH_2)_nCl$ are 0.48, 0.16, and −0.01 for $n = 0$—2, respectively; [5,7] terminal substituents apart, replacement of H by C has its effect: witness the change of σ_I from zero for the H atom to −0.046 for the methyl group when a methylene group is interposed between H and a detector centre. These facts and equation (16) suggest that equation (18) should be preferable to equation (17) for estimating the σ_I value of a composite substituent CH_2X from that of X.

$$\begin{aligned}\sigma_I(CH_2X) &= -0.046 + \sigma_I(X)/R \\ &= -0.046 + \sigma_I(X)[1 + \sigma_I(X)]/4 \qquad (18)\end{aligned}$$

The divisor R is appropriate for $\sigma_I > 0$; since σ_I for alkyl groups is not independent of n [*cf.* equation (12)], a comparable divisor determined by differentiation of equation (14) fails to give an equation suitable for interpolating $\sigma_I(CH_2X)$ from negative $\sigma_I(X)$. However, a suitable expression [equation (20)] may be found by eliminating a common $a(\mathrm{N})$ from equation (14) applied to both $\sigma_I(\mathrm{X})$ with n 1 and to $\sigma_I(\mathrm{CH_2X})$ with $n = 0$. Thus, equation (19) applies. Cross-multiplying equation (19)

$$\frac{[4.16\sigma_I(\mathrm{CH_2X}) + 0.676]}{[7.30\sigma_I(\mathrm{CH_2X}) + 1]} = \frac{[15.56\sigma_I(\mathrm{X}) + 1.456]}{[21.90\sigma_I(\mathrm{X}) + 2]} \quad (19)$$

and collecting terms gives $22.55\sigma_I(\mathrm{X})\sigma_I(\mathrm{CH_2X}) + 2.31\sigma_I(\mathrm{CH_2X}) + 0.76\sigma_I(\mathrm{X}) + 0.105 = 0$, whence (20) is obtained.

$$\sigma_I(\mathrm{CH_2X}) = -0.046[1 + 7.31\sigma_I(\mathrm{X})]/[1 + 9.76\sigma_I(\mathrm{X})] \quad (20)$$

This expression permits the evaluation of $\sigma_I(\mathrm{CH_2X})$ from any negative $\sigma_I(\mathrm{X})$. It is noteworthy, however, that equation (21) which has the form of equation (18), except for one changed sign, gives results essentially identical to equation (20) for $-0.06 < \sigma_I(\mathrm{X}) < 0$, which range covers the range of negative σ_I values which are significant practically; *e.g.* it is unlikely that the composite substituent $(\mathrm{CH_2})_6\overset{+}{\mathrm{N}}\mathrm{Me_3}$ would be experimentally distinguishable from n-hexyl, both having σ_I -0.06.

$$\sigma_I(\mathrm{CH_2X}) = -0.046 + \sigma_I(\mathrm{X})[1 - \sigma_I(\mathrm{X})]/4 \quad (21)$$

(d) *Particular Substituents.*—Three of the σ_I values upon whose validity we cast doubt because they do not permit the correlation of present and earlier [2] results in Figure 1 pertain to substituents of type $\mathrm{CH_2X}$ where X is weakly polar [$\sigma_I(\mathrm{X}) <$ *ca.* 0.3]; the major part of the electronic effect of such groups, relative to hydrogen, derives from the methylene group rather than X [compare, for example, the relative contributions of the two terms of equation (10) in determining $a(\mathrm{N})$ of phenothiazine cation-radicals when $\sigma_I < 0.3$]. Such composite substituents are thus more comparable with alkyl groups than with highly polar heteroatom-containing substituents and, as with alkyl groups, it would be expected that carboxylic acid equilibria would be unsuitable for detecting their true electronic effects. From the $a(\mathrm{N})$ values observed for phenothiazine cation-radicals bearing these substituents at nitrogen we expect their σ_I values all to lie close to zero; actual values may be calculated using equations given earlier. The fourth doubted σ_I value is that for $\mathrm{CH_2}\overset{+}{\mathrm{N}}\mathrm{Me_3}$ *i.e.* 0.3; it was calculated by equation (17) from one of a wide range of values of σ_I for $\overset{+}{\mathrm{N}}\mathrm{Me_3}$; our data require σ_I *ca.* 0.4 for $\mathrm{CH_2}\overset{+}{\mathrm{N}}\mathrm{Me_3}$.

Ionic substituents differ from dipolar ones in the distance-dependence of their field effects and it has been shown that, as a consequence, their Hammett σ values should increase in magnitude with increase in molecular size.[27] Since mesomeric effects are of little significance for $\overset{+}{\mathrm{N}}\mathrm{Me_3}$ it is to be expected that its σ_I should follow a similar pattern of behaviour. Our results do not detect this directly and, indeed, the correlation of four separate ammonio-substituted radicals with the dipolar substituents implies, at first sight, that it is not true. There are at least two reasons for this. First, possibly through ion-pairing the ionic substituents were reduced effectively to dipoles; even though two of the phenothiazine salts used were perchlorates other nucleophilic anions were introduced *via* the oxidant. A second reason the actual results show no apparent inconsistency could stem from the particular σ_I value used for $\overset{+}{\mathrm{N}}\mathrm{Me_3}$. This was defined using the bicyclo-octanecarboxylic acid system where the substituent and detector-centre are separated by four carbon atoms.[14] Thus, if $\overset{+}{\mathrm{N}}\mathrm{Me_3}$ does require different σ_I according to the length of methylene chain to which it is attached, the value we have used is appropriate for the $n = 4$ correlation line in Figure 1. The gradients of the $n = 5$ and 3 lines are so similar that it is likely that the same σ_I is adequate (this is effectively equivalent to saying that when the separation r of the aminium centre and the substituent is sufficiently large, the distance dependence of the substituent effect, r^{-x}, is small and beyond experimental distinction for x being any small integer). Clearly, if our data are to show any internal anomaly for the ionic substituent it must be by examination of the results for *short* chain lengths. The result for (2; $\mathrm{X} = \overset{+}{\mathrm{N}}\mathrm{Me_3}$, $n = 2$) is correlated on the $n = 2$ line of Figure 1 on the limit of experimental error in $a(\mathrm{N})$: better correlation would be had using a marginally smaller σ_I value, but this alone is hardly substantial evidence that a smaller σ_I is appropriate for $\overset{+}{\mathrm{N}}\mathrm{Me_3}$ on short chains. However, equation (1), with σ_I 0.93, predicts the hypothetical radical (2; $\mathrm{X} = \overset{+}{\mathrm{N}}\mathrm{Me_3}$, $n = 1$) to have $a(\mathrm{N})$ 0.599 mT. To plot this value on the $n = 0$ line would require σ_I for $\mathrm{CH_2}\overset{+}{\mathrm{N}}\mathrm{Me_3}$ to be *ca.* 0.55 which is inconsistent with the value required for this substituent on all the other lines, *i.e.* 0.4. Conversely, the $n = 0$ line requires that a radical with an *N*-substituent having σ_I 0.4 will have $a(\mathrm{N})$ 0.623 mT. To plot this result on the $n = 1$ line would require σ_I 0.76 which is close to the value (0.73) determined for $\overset{+}{\mathrm{N}}\mathrm{Me_3}$ in the acetic acid system [15,28] and which, consistently, also has a single carbon atom between substituent and detector centre. Thus although we lack direct evidence, interpolation of our results may indicate that σ_I for $\overset{+}{\mathrm{N}}\mathrm{Me_3}$ takes a significantly lower value in systems where the substituent is separated from the detector centre by a single carbon atom than in others where more atoms are interposed. Caution is necessary in drawing this inference, however, since the pattern of behaviour which allows it could also be an artefact of the saturation effect in the experimental observable [see Discussion section (c)].

EXPERIMENTAL

The synthesis and characterisation of a number of the materials used has been described previously.[2] Terminally chlorinated 10-alkylphenothiazines were prepared according to established methods; their criteria of purity agreed with literature values.[29] Reaction of 10-(3-chloropropyl)-, 10-(4-chlorobutyl)-, and 10-(5-chloropentyl)-phenothiazine with NaCN in DMSO [30] gave the corresponding nitriles in high yield. Recrystallisation of the nitriles from n-hexane gave products melting, respectively, at 91—92, 88—89, and 36—40 °C. Phenothiazin-10-ylacetonitrile was prepared by the method of Hollins and Pinto;[31] *en route*, phenothiazin-10-ylacetaldehyde was obtained. M.p.s of both materials agreed with the literature values.[31] 10-(2-Dimethylaminoethyl)phenothiazine, m.p. 40—42 °C (lit.,[32] 44—44.5 °C), was prepared in the manner of 10-alkylphenothiazines [2] and was quaternised by reaction with an excess of iodomethane; promazine (Wyeth) was similarly quaternised. The resultant iodide salts were found, on oxidation in nitromethane to give iodine-coloured solutions which furnished poor quality e.s.r. spectra. The corresponding quaternary perchlorates were therefore prepared from the iodides by metathetical reaction with $AgClO_4$ in methanol. 10-(4-Chlorobutyl)- and 10-(5-chloropentyl)-phenothiazine were treated with an excess of trimethylamine in acetonitrile and their quaternary chlorides crystallised on standing for several days. M.p.s of the various (phenothiazin-10-yl)alkyltrimethylammonium salts are as follows: [2-(phenothiazin-10-yl)ethyl]trimethylammonium iodide, 256—260 °C (lit.,[33] 257 °C; perchlorate, 243—246 °C); [3-(phenothiazin-10-yl)propyl]trimethylammonium iodide, 255—258 °C (lit.,[34] 255—257 °C, perchlorate, 232—234 °C); [4-(phenothiazin-10-yl)butyl]trimethylammonium chloride, 190—193 °C; [5-(phenothiazin-10-yl)pentyl]trimethylammonium chloride, 122—125 °C. Ethyl 3-(phenothiazin-10-yl)propanoate was prepared by conjugate addition of phenothiazine to ethyl acrylate in a manner analogous to cyanoethylation of phenothiazine.[2,35] The material, recrystallised from ethanol melted at 58—61 °C (lit.,[29] 64 °C). Satisfactory elemental analyses and i.r. and n.m.r. spectroscopic data were obtained for all new compounds which were used to prepare radical-cations.

Nitromethane was refluxed for 1 h with calcium hydride and then distilled. Granular aluminium chloride (Fisons) and thallium triacetate sesquihydrate (Emanuel) were used as supplied.

The generation of cation-radicals and the conditions for the observation of their e.s.r. spectra have been described previously.[17]

We are indebted to Dr. G. Doggett for helpful discussions.

[1/615 *Received*, 15*th April*, 1981]

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