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RELATIONSHIP BETWEEN THE PROPERTIES OF RADICAL CATIONS AND THE RATE CONSTANTS AND THE SUBSTITUTION PATTERNS IN ELECTROPHILIC AROMATIC SUBSTITUTION

E. B. Pedersen,* T. E. Petersen,†,‡ K. Torssell and S.-O. Lawesson
Department of Organic Chemistry, Chemical Institute, Aarhus University, DK-8000 Aarhus C., Denmark

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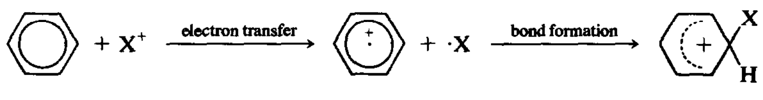
Abstract – By a charge transfer mechanism for electrophilic aromatic substitution the logarithmic plot of overall rate constants for substitution against ionization potentials is correctly predicted. Also, orientation of substitution is found to be correlated with the hyperfine coupling constants of the aromatic radical cation. The presence of radical cations under the conditions of electrophilic substitution is discussed.

INTRODUCTION

A number of indices of reactivity in electrophilic aromatic substitution has been suggested and used to explain the relative reactivities of the individual sites within a given molecule. In 1942 Wheland[1] presented the localization model of the reaction intermediate. In addition, several other theoretical studies have been carried out for interpreting chemical reactivity of aromatic substrate molecules, such as π-electron density,[2] free valency[3] and frontier electron density.[4,5] It is also well known by organic chemists that the relative reactivities have been predicted from the localization energy,[6,7] i.e. the difference in energy between the aromatic compound and the appropriate Wheland intermediate for substitution.

Less known by organic chemists is the charge transfer mechanism of electrophilic aromatic substitution (Eq. 1), which was proposed by Brown[8] and Nagakura.[9]



(1)

This theory was developed by the aid of Mulliken's conception of the resonance interaction between the nobond and charge transfer structures.[10,11]

$$\mathrm{Ar, E^+} \leftrightarrow \mathrm{Ar^{\cdot +}, \cdot E} \qquad (2)$$

Although Brown and Nagakura agreed that aromatic substitution involved charge transfer complexes as intermediates, they disagreed in factors introduced for explaining the observed orientation rule.

Another observation,[12] which is of interest for this paper, is that for even alternate hydrocarbons the Hückel theory predicts that the unpaired electron density ρ_i of radical ions is one half of the corresponding frontier electron density. Furthermore, ρ_i residing at an atom i of a radical ion is also related to the ESR hyperfine coupling constant a_i[13] by Eq 3.

$$a_i = Q\rho_i. \qquad (3)$$

This means that the hyperfine coupling constants of radical cations or anions should be indices of relative chemical reactivity rates at various sites in alternant polycyclic hydrocarbon molecules, and qualitative correlations[12] have been observed too. In this paper we wish to emphasize the close relationship between the charge transfer mechanism for aromatic substitution and the use of hyperfine coupling constants as reactivity indices.

Potential energy curve for the aromatic substitution

An example of an electrophilic substitution reaction is the nitration of benzene in strong acid solution. According to the work of Hughes, Ingold *et al.*[14] the essential steps are

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*To whom all correspondence should be directed.

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‡Present address: Dept. of Molecular Biology, Aarhus University, DK-8000 Aarhus C., Denmark.

$$C_6H_6 + NO_2^+ \rightarrow (C_6H_6NO_2)^+ \quad (4)$$

$$(C_6H_6NO_2)^+ + A \rightarrow C_6H_5NO_2 + HA^+ \quad (5)$$

In this reaction NO_2^+ is the electron-acceptor molecule and benzene is the donor molecule.[15] As the NO_2^+ approaches the benzene (Bz) molecule at first a loose outer complex may be formed. There may be no strong tendency for the NO_2^+ in this complex to localize near any particular atom of the benzene molecule. The loose outer complex, in which there is little expectation of electron transfer and no of σ-bond formation corresponds to the no bond structure (Bz, NO_2^+) in Fig 1.

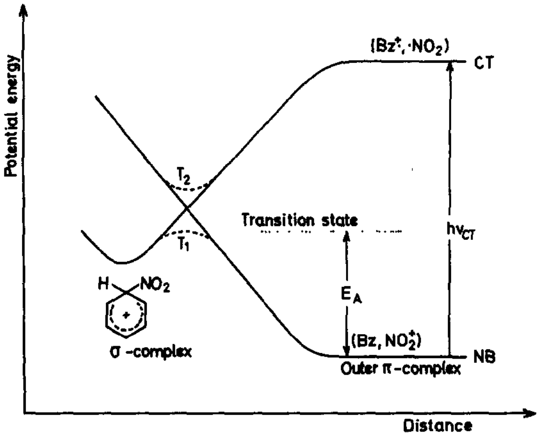

Fig 1.

If the outer complex is not the rate determining step in the aromatic electrophilic substitution, the energy increases as Bz and NO_2^+ approach each other (curve NB, Fig 1). On the other hand, curve CT is thought to be attractive because of bond formation between Bz^+ and NO_2. Therefore it may be expected that the energy difference between NB- and CT- structures decreases with an approach of substrate molecules and reagents. As is seen from the noncrossing rule,[16] the curves repel each other to some extent in the region of the crossing point, forming two resultant curves as indicated by the broken lines in Fig 1. T_1 represents the transition state described by Eq 2. If Bz^+ and NO_2 further approach each other the σ-complex is formed.

Prediction of relative rates from ionization potentials

For the reaction of different aromatic substrate molecules with the same reagent (for example NO_2^+) it would be reasonable to expect that the CT curves (Fig 1) would parallel to each other and Eq 6 should be valid.

$$E_A = \alpha h\nu_{CT} \quad (6)$$

(E_A is the activation energy and α is an empirical constant). But $h\nu_{CT}$ has been fitted by Eq 7 for charge-transfer complexes,

$$h\nu_{CT} = mI + n \quad (7)$$

(I is the vertical ionization potential[17,18] of the donor molecule and m and n are empirical constants). So from Eqs 6 and 7 Eq 8 is obtained

$$\ln k_{rel} = \frac{E_A}{RT} + a = \beta \cdot I + \gamma \quad (8)$$

where a, β and γ are empirical constants. This equation means that the logarithm of the relative overall rate constant k_{rel} for electrophilic aromatic substitution is directly proportional to the ionization potential of the used aromatic substrate.

In Fig 2 the logarithm of the overall rate constants relative to benzene for nitration of aromatic compounds with $AcONO_2$ in acetic anhydride,[19] is plotted against their corresponding ionization potentials. It was attempted to use ionization potentials from various sources, but the best plot (Fig 2) was obtained when they were determined from the excitation energies of charge-transfer bands.[20–22] However, this should be expected as I in Eq 8 in principle should be derived from the charge transfer energy, $h\nu_{CT}$, of the outer complex (Fig 1), whereas other methods for determination of the ionization constants do not have such a close relationship to electrophilic aromatic substitution. The only deviation from the straight line in Fig 2 was diphenyl amine. Similarly relative overall rates for hydrogen exchange[23] on the chlorination[24] of aromatic hydrocarbons are related to

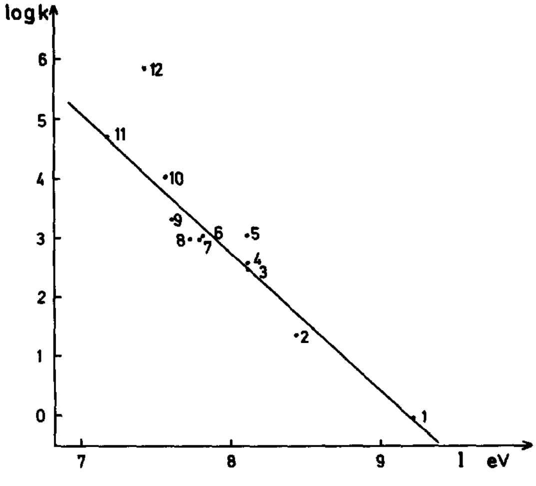

Fig 2. 1: benzene; 2: biphenyl; 3: naphtalene; 4: phenanthrene; 5: triphenylene; 6: chrysene; 7: fluorene; 8: fluoranthene; 9: coronene; 10: pyrene; 11: perylene; 12: diphenyl amine.

their ionization potentials in Figs 3 and 4, respectively. Considering that the ionization potentials are not determined in the solvent used for the electrophilic substitution reactions and that there is a relatively high uncertainty in their determination, a good linear fit is obtained between them and the relative overall rates in the three investigated cases for electrophilic substitution.

If the ionization potentials of even alternant hydrocarbons are plotted against their localization energies of the most reactive positions (calculated by PPP with fixed β and C—C bond length)[67] a straight line is obtained with a slope close to unity (Fig 5). This gives an evidence for the assumption that the CT curves should be parallel to each other for different aromatic substrate molecules.

On the other hand a good linear plot has been obtained of the logarithm of the basicity constant K_B and localization energy calculated by the SCF method for the most reactive positions.[25] According to this there should be a linear plot between ln K_B[23] and the ionization potentials (Fig 6). Finally, as both the reactivities and the basicity

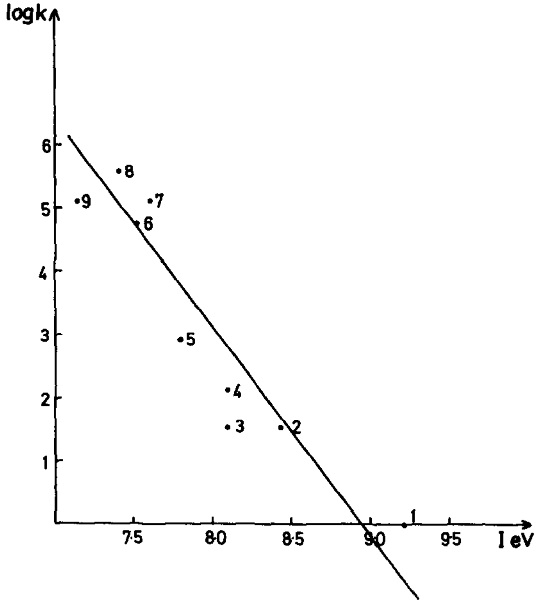

Fig 3. 1: benzene; 2: biphenyl; 3: triphenylene; 4: naphtalene; 5: chrysene; 6: pyrene; 7: 1,2-benzantracene; 8: anthracene; 9: perylene.

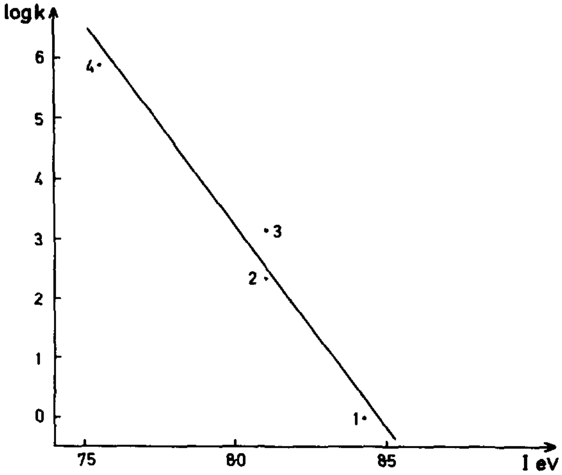

Fig 4. 1: biphenyl; 2: naphtalene; 3: phenanthrene; 4: pyrene.

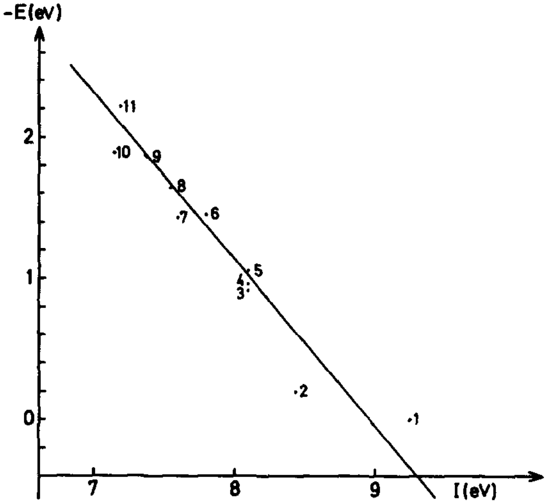

Fig 5. 1: benzene; 2: biphenyl; 3: naphtalene; 4: triphenylene; 5: phenanthrene; 6: chrysene; 7: coronene; 8: pyrene; 9: anthracene; 10: perylene; 11: benzo[a] pyrene.

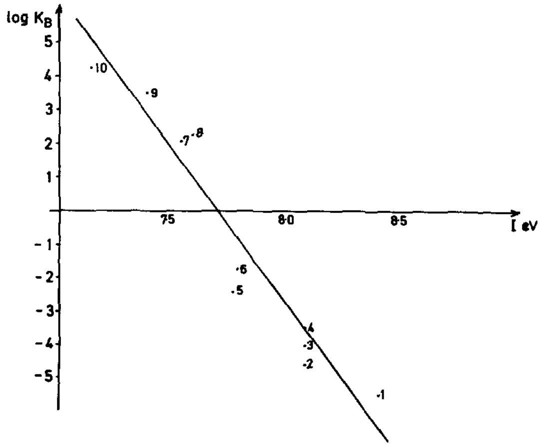

Fig 6. 1: biphenyl; 2: triphenylene; 3: naphtalene; 4: phenanthrene; 5: fluorene; 6: chrysene; 7: pyrene; 8: 1,2-benzanthracene; 9: anthracene; 10: perylene.

constants can be related linearly to the ionization potentials they should be expected to be related to each other which indeed has been found.[28]

Prediction of orientation from ESR-spectra

As mentioned before, a good description of the transition state for electrophilic aromatic substitution is the resonance structures given in Eq 2 where Ar is the aromatic substrate molecule and E an electrophilic reagent. The physical properties of the resonance structures are not easily available, but a reasonable approach for the determination of the reactive sites in an aromatic molecule should be to look for the properties of free Ar and $Ar^{\cdot +}$. Several authors[2–5] have already looked for the properties of the free aromatic molecule in order to explain the relative reactivities of the individual sites within a given molecule, but the other resonance structure $Ar^{\cdot +}$, E used for the description of the transition state seems to have been ignored until now. If this was the only reasonable resonance structure at the transition state, the mechanism for electrophilic aromatic substitution would be as suggested in Eq 1. This means that the substitution preferably should take place between the aromatic radical cation and the electrophilic reagent at the position where there is the greatest possibility for the single electron of the substrate and for the one of the reagent molecules to form a new bond, that is at the position of the radical cation with the highest unpaired electron density ρ_i. On the other hand it has been shown that the proton hyperfine splitting a_i^H at C atom i will vary linearly with the spin density in π for situations where the π spin density is distributed over more than one center (Eq 3). Consequently in electrophilic substitution reactions the order of the relative reactivities of the individual sites within an aromatic molecule should follow the order of the a_i^H's of the radical cation of the same molecule.

In Table 1 are given the order of the hyperfine coupling constants of aromatic radical cations as well as the order of reactivities within the same aromatic molecules. It is seen that the above statement is indeed correct. It is also interesting to note that Table 1 includes examples of alternant and non-alternant aromatic hydrocarbons, aromatic hydrocarbons with hetero-substituents, biphenyl systems and heterocyclic compounds. In all cases the order of reactivities within a given molecule follows the order of hyperfine coupling constants of the radical cation of the same aromatic molecule.

The description of the transition state gives direct understanding why the reactivities should be related to the hyperfine coupling constants of the radical cation and not of the radical anion contrary to an earlier investigation in this field.[12] Especially for non-alternant hydrocarbons this is essential as the hyperfine coupling constants of

Table 1.

Compound	Reaction	Order of Reactivity	Order of Hyperfine Coupling Constants of Radical Cation
Toluene	nitration	4 > 2 > 3[59]	4 > 2 > 3[60]
N,N-Dimethyl-aniline	bromination	4 > 2 > 3[61]	4 > 2 > 3[62]
N,N-Dimethyl-4-nitro-aniline	chlorination	2 > 3[63]	2 > 3[62, 64]
4-Dimethylamino-toluene	bromination	3 > 2[61]	3 > 2[64]
Naphtalene	nitration	1 > 2[26, 27]	1 > 2[66]
	detritiation	1 > 2[29]	
1,4-Dimethoxy-naphtalene	bromination	2 > others[30, 31]	2 > 5 > 6[32]
1,5-Dimethyl-naphtalene	bromination	4 > 2 > 3[33]	4 > 2 = 3[34]
1,8-Dimethyl-naphtalene	bromination	4 > 2[33]	4 > 2 > 3[34]
	detritiation	4 > 2 > 3[65]	
1,5-Difluoro-naphtalene	nitration	4 > others[35]	4 > 2 = 3[36]
Anthracene	acylation	9 > 1 > 2[13]	9 > 1 > 2[66]
Perylene	nitration	3 > others[26, 27]	3 > 1 > 2[66, 37]
Pyrene	nitration	1 > others[27]	1 > 4 > 2[38, 39]
	detritiation	1 > 4 > 2[29]	
Biphenylene	halogenation	2 > 1[40]	2 > 1[41]
	nitration	2 > 1[40]	
	detritiation	2 > 1[29]	
4,4′-Dimethyl-biphenyl	nitration	2 > 3[42]	2 > 3[43]
p-Quarterphenyl	nitration	4 > others[44]	4 > 3′ > 2 > 2′ > 3[45]
Azulene	nitration	1 > others[46, 47]	1 > 5 > 2 > 6 > 4[48]
Thianthrene	bromination	2 > 1[49]	2 > 1[50]
Dibenzo-*p*-dioxin	formylation	2 > 1[51]	2 > 1[53, 54]
	alkylation	2 > 1[52]	
10-Methyl-phenothiazine	acylation	3 > others[56]	3 > 1 > 2 > 4[57]

the radical anion of azulene[55] incorrectly would predict the order of electrophilic substitution to be 6 > 4 > 2 > 5 > 1.

Chemical consequences

From Fig 1 can also be predicted that if there is a small energy gap at the transition state between the NB- and CT-curve a thermically induced excitation from NB to CT should be possible. Thus the substrate molecule and the reagent again withdraw from each other, a free radical cation should be formed. This gives a simple relationship between the radical cation formation reactions (oxidation reactions) and electrophilic aromatic substitution reactions and it accounts for why aromatic radical cations for ESR investigations in many cases are generated under conditions similar to those of electrophilic aromatic substitutions.[58]

REFERENCES

[1] G. W. Wheland, *J. Am. Chem. Soc.* **64**, 900 (1942).

[2] C. A. Coulson and H. C. Longuet-Higgins, *Proc. Roy. Soc.* **A191**, 39; **A192**, 16 (1947).

[3] C. A. Coulson, *Disc. Faraday Soc.* **2**, 9 (1947).

[4] K. Fukui, T. Yonezawa and H. Shingu, *J. Chem. Phys.* **20**, 722 (1952).

[5] K. Fukui, T. Yonezawa and C. Nagata, *Bull. Chem. Soc. Japan* **27**, 423 (1954).

[6] A. L. H. Chung and M. J. S. Dewar, *J. Chem. Phys.* **42**, 756 (1965).

[7] M. J. S. Dewar and G. J. Gleicher, *J. Am. Chem. Soc.* **87**, 685, 692 (1965).

[8] R. D. Brown, *J. Chem. Soc.* 2224, 2232 (1959).

[9] S. Nagakura, *Tetrahedron 19 Suppl.* **2**, 361 (1963).

[10] R. S. Mulliken, *J. Phys. Chem.* **56**, 801 (1952).

[11] R. S. Mulliken, *J. Am. Chem. Soc.* **74**, 811 (1952).

[12] C. P. Poole, Jr., and O. F. Griffith, III, *J. Phys. Chem.* **71**, 3672 (1967).

[13] H. M. McConnell, *J. Chem. Phys.* **24**, 632 (1956).

[14] C. K. Ingold: *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, New York (1953).

[15] R. S. Mulliken and W. B. Person, *Molecular Complexes*, Wiley-Interscience (1969).

[16] C. A. Coulson, *Valence* p. 65. Oxford University Press, Oxford (1956).

[17] Ref. 15, p. 146.

[18] R. S. Mulliken and W. B. Person, *Annual Review of Physical Chemistry*, **13**, 107 (1962).

[19] J. G. Hoggett, R. B. Moodie, J. R. Penton and K. Schofield, *Nitration and aromatic reactivity*. Cambridge University Press (1971).

[20] G. Briegleb and J. Czekalla, *Z. für. Electrochem.* **63**, 6 (1959).

[21] J. B. Birks and M. A. Slifkin, *Nature, Lond.* **191**, 761 (1961).

[22] M. A. Slifkin and A. C. Allison, *Ibid.* **215**, 949 (1967).

[23] A. I. Shatenshtein, *Isotopic Exchange and the Replacement of Hydrogen in Organic Compounds*. Consultants Bureau, New York (1962)

[24] M. J. S. Dewar and T. Mole, *J. Chem. Soc.* 342 (1957).

[25] G. A. Olah and P. von R. Schleyer *Carbonium Ions II* p. 858. Wiley-Interscience (1970).

[26] M. J. S. Dewar and T. Mole, *J. Chem. Soc.* 1441 (1956).

[27] M. J. S. Dewar, T. Mole and E. W. T. Warford, *Ibid.* 3581 (1956).

[28] E. Berliner, Progr. *Phys. Org. Chem.* **2**, 253 (1964).

[29] R. Baker, C. Eaborn and R. Taylor, *J. C. S. Perkin* II 97 (1972).

[30] H. E. Ungnade and H. Hein, *J. Org. Chem.* **14**, 911 (1949).

[31] J. B. Data and R. D. Bennett, *Med. Pharm. Chem.* **4**, 327 (1961).

[32] P. D. Sullivan, *J. Phys. Chem.* **74**, 2563 (1970).

[33] J. B. Kim, C. Chen, J. K. Krieger, K. R. Judd, C. C. Simpson and E. Berliner, *J. Am. Chem. Soc.* **92**, 910 (1970).

[34] H. Yashima and K. Kuwata, *Mol. Phys.* **23**, 297 (1972).

[35] H. Zahn and H. Zuber, *Chem. Ber.* **86**, 172 (1953).

[36] P. H. H. Fischer and H. Zimmermann, *Tetrahedron Letters* 797 (1969).

[37] T. C. Chiang and A. H. Reddoch, *J. Chem. Phys.* **52**, 1371 (1970).

[38] J. T. Cooper and W. F. Forbes, *Canad. J. Chem.* **46**, 1158 (1968).

[39] O. W. Howarth and G. K. Fraenkel, *J. Chem. Phys.* **52**, 6258 (1970).

[40] W. Baker, J. W. Barton and J. F. W. McOmie, *J. Chem. Soc.* 2666 (1958).

[41] A. Carrington and J. D. Santos-Veiga, *Mol. Phys.* **5**, 285 (1962).

[42] E. E. J. Marlev and E. E. Turner, *J. Chem. Soc.* 2391 (1932).

[43] M. J. Shaw, J. A. Weil, H. H. Hyman and R. Filler, *J. Am. Chem. Soc.* **92**, 5096 (1970).

[44] M. L. Scheinbaum, *Chem. Comm.* 1235 (1969).

[45] M. K. Carter, *J. Phys. Chem.* **75**, 902 (1971).

[46] A. G. Anderson, J. A. Nelson and J. J. Tazuna, *J. Am. Chem. Soc.* **75**. 4981 (1953).

[47] D. H. Reid, W. H. Stafford and W. L. Stafford, *J. Chem. Soc.* 1118 (1958).

[48] R. M. Dessau and S. Shih, *J. Chem. Phys.* **53**, 3169 (1970).

[49] H. Gilman and D. R. Swayapati, *J. Am. Chem. Soc.* **77**, 5944 (1955).

[50] E. A. Lucken, *Theor. Chim. Acta* **1**, 397 (1963).

[51] G. Vasiliu and I. Baciu, *An. Univ. Bucuresti, Ser. Stiint. Natur.* **15**, (1) 125–8 (1966); *Chem. Abstr.* **68**, 59509e (1968).

[52] H. Gilman and J. J. Dietrich, *J. Org. Chem.* **22**, 1403 (1957).

[53] M. Tomita, S. Ueda, Y. Nakai, Y. Deguchi and H. Takaki, *Tetrahedron Letters*, 1189 (1963).

[54] M. Tomita and S. Ueda, *Chem. and Pharm. Bull. Japan* **12**, 33 (1964).

[55] A. H. Reddock, *J. Chem. Phys.* **41**, 444 (1964).

[56] M. H. Litt, J. W. Summers and T. M. Shimko, *J. Org. Chem.* **37**, 1045 (1972).

[57] P. D. Sulivan and J. R. Bolton, *J. Magnetic Res.* **1**, 356 (1969).

[58] E. T. Kaiser and L. Kevan, *Radical Ions* p. 202. Wiley-Interscience (1968).

[59] C. K. Ingold, A. Lapworth, E. Rothstein and D. Ward, *J. Chem. Soc.* 1959 (1931).

[60] T. Komatsu, A. Lund and P.-O. Kinell, *J. Phys. Chem.* **76**, 1721 (1972).

[61] J. E. Dubois and R. Uzan, *Tetrahedron Letters* 2397 (1964).

[62] B. G. Pobedimskii, A. L. Buchachenko and M. B. Neiman, *Russian J. Phys. Chem.* **42**, 748 (1968).

[63] K. H. Pausacker and J. G. Scroggie, *Austr. J. Chem.* **12**, 430 (1959).
[64] B. M. Latta and R. W. Taft, *J. Am. Chem. Soc.* **89**, 5172 (1967).
[65] B. N. McMaster, M. C. A. Opic and G. J. Wright, *Tetrahedron Letters* 2191 (1972).
[66] I. C. Lewis and L. S. Singer, *J. Chem. Phys.* **43**, 2712 (1965).
[67] M. J. S. Dewar and C. C. Thompson, Jr., *J. Am. Chem. Soc.* **87**, 4414 (1965).