

The Range of Radical Processes in Nitration by Nitric Acid

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1 Introduction

The current emphasis on electron transfer processes has led to a number of reviews concerning nitration but these have, to some extent, concentrated on the special interests of their authors. Thus, the review of Ebersson and Radner¹ deals in particular detail with the electrochemical aspects of nitration and the application of Marcus theory; the more general review of Kochi² concentrates on the significance of charge transfer complexes in electrophilic substitution; and the writings of the Russian school^{3,4} have dealt mainly with the formation, properties, and reactions of radical cations. The present review emphasises more the information that can be obtained from kinetic studies and chemically induced dynamic nuclear polarization (CIDNP). The purpose is to complement the other material in the literature and to bring together the evidence on the extent to which radicals are formed during nitration by nitric acid in homogeneous aqueous or organic media.

The classical studies of Hughes, Ingold, and their co-workers* established two main mechanisms for such aromatic nitrations: one, occurring with all of the compounds studied, involving reaction through the nitronium ion and the other, limited to the more reactive aromatic compounds (amines, phenols, and alkyl substituted hydrocarbons), involving some form of nitrous acid catalysis. The reaction paths that they proposed are shown in Schemes 1 and 2. In Scheme 1, the rate-determining stage can be either reaction 2 or reaction 3 depending on the concentration and reactivity of the aromatic compound. In Scheme 2, the nitrosation stage was considered to be rate-determining under all conditions. In this Scheme, the final reaction regenerates the nitrous acid and so only trace amounts of the nitrous acid are required for the catalysis to operate.

The evidence for reaction through the nitronium ion came partly from the spectroscopic⁵ and cryoscopic⁶ studies on equilibria involving the nitronium ion in strongly acidic media and partly from the evidence for a zeroth-order kinetic form⁷ for nitration in organic solvents. This work, particularly when sup-

* The complete set of papers was published in *J. Chem. Soc.*, 1950, 2400–2684. Some of these are referred to individually below.

¹ L. Ebersson and F. Radner, *Acc. Chem. Res.*, 1987, **20**, 53.

² J. K. Kochi, *Acta Chem. Scand.*, 1990, **44**, 409.

³ Z. V. Todres, *Tetrahedron*, 1985, **41**, 2771.

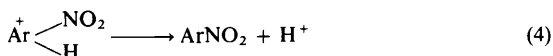
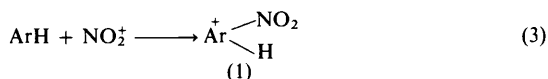
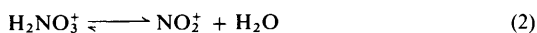
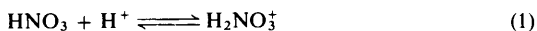
⁴ A. S. Morkovnik, *Russian Chem. Rev.*, 1988, **57**, 144.

⁵ C. K. Ingold, D. J. Millen, and H. G. Poole, *J. Chem. Soc.*, 1950, 2576.

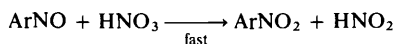
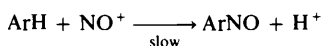
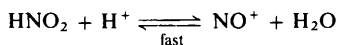
⁶ R. J. Gillespie, J. Graham, E. D. Hughes, C. K. Ingold, and E. R. A. Peeling, *J. Chem. Soc.*, 1950, 2504.

⁷ E. D. Hughes, C. K. Ingold, and R. I. Reed, *J. Chem. Soc.*, 1950, 2400.

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Scheme 1



Scheme 2

plemented by the studies of Bunton, Halevi, and Stedman⁸ on O¹⁸-exchange accompanying the formation of the nitronium ion, provided such strong evidence for the reaction path in Scheme 1 that the involvement of the nitronium ion in these reactions has rarely been questioned. The evidence for the second reaction path (Scheme 2) was, however, less complete: it came partly from the kinetic form (first-order with respect to nitrous acid) and partly from the formation of some nitroso-compounds under the conditions giving nitrous acid catalysed nitration.⁹ The effect of added nitrates on the reaction rate suggested that the initial nitrosation occurred in part by reaction with the nitrosonium ion and in part by reaction with molecular dinitrogen tetroxide.¹⁰

In recent years, alternative reaction paths have been supported for both the nitronium ion reaction and the reaction involving nitrous acid catalysis. The first form of the alternative to the mechanism in Scheme 1 predates the publication of the Ingold work for, in 1945, Kenner¹¹ suggested that the initial interaction of the nitronium ion with benzene could lead to electron transfer and hence to the formation of the benzene radical cation and nitrogen dioxide. This suggestion was rejected by Hughes, Ingold, and their co-workers¹² on the grounds that introduced nitrogen dioxide gave products that are not formed under normal conditions.

⁸ C. A. Bunton and E. A. Halevi, *J. Chem. Soc.*, 1952, 4917; C. A. Bunton and G. Stedman, *J. Chem. Soc.* 1958, 2420.

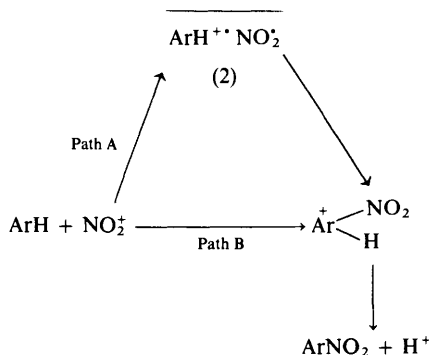
⁹ C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Jones, G. J. Minkoff, and R. I. Reed, *J. Chem. Soc.*, 1950, 2628.

¹⁰ E. L. Blackall, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.* 1952, 28.

¹¹ J. Kenner, *Nature*, 1945, 156, 369.

¹² G. A. Benford, C. A. Bunton, E. S. Halberstadt, E. D. Hughes, C. K. Ingold, G. J. Minkoff, and R. I. Reed, *Nature*, 1945, 156, 688.

The subsequent step of the Kenner mechanism,¹¹ involving proton loss from the intermediate benzene radical cation, would not now be considered plausible by anyone, but the proposal of an electron transfer followed by the formation of the Wheland intermediate (1) has been strongly supported in recent years. This electron transfer mechanism can be written as shown in Scheme 3, path A. The intermediate (2) in this Scheme is shown as a radical pair* in accord with the views of Kenner¹¹ who described the radicals as remaining 'within the sphere of each others action'.



Scheme 3

The currently accepted alternative to the Ingold mechanism for nitrous acid catalysed nitration was put forward in 1979 when Giffney and Ridd¹⁵ provided evidence that the nitrous acid catalysed nitration of *N,N*-dimethylaniline occurred through the oxidation of the aromatic compound to the corresponding radical cation followed by reaction with nitrogen dioxide. This mechanism (Scheme 4) was later shown to be more general¹⁶ and was supported by CIDNP effects,¹⁷ and kinetic studies.^{18,19} Either stage 1 or stage 3 of Scheme 4 can apparently be rate-determining depending on the conditions. In Scheme 4, the second stage is in

* In this review, the radical pair ($\text{ArH}^{\bullet+} \text{NO}_2^{\bullet}$) is treated as if it were a single chemical species. This may be an oversimplification, for some authors^{13,14} have suggested that several forms of this radical pair should be considered, depending on the relative positions of the two radicals.

¹³ W. N. White, H. S. White, and A. Fentiman, *J. Org. Chem.*, 1976, 41, 3166.

¹⁴ L. Ebersson and F. Radner, *Acta Chem. Scand. Ser. B*, 1985, 39, 357.

¹⁵ J. C. Giffney and J. H. Ridd, *J. Chem. Soc., Perkin Trans. 2*, 1979, 618.

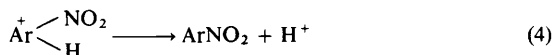
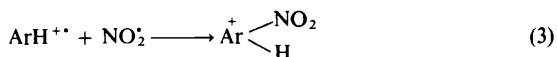
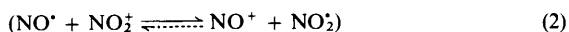
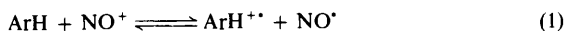
¹⁶ L. Main, R. B. Moodie, and K. Schofield, *J. Chem. Soc., Chem. Commun.*, 1982, 48.

¹⁷ (a) J. H. Ridd and J. P. B. Sandall, *J. Chem. Soc., Chem. Commun.*, 1981, 402; (b) A. H. Clemens, J. H. Ridd, and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2*, 1984, 1659; (c) *ibid.*, 1984, 1667; (d) A. H. Clemens, P. Helsby, J. H. Ridd, F. Al-Omran, and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1217; (e) A. H. Clemens, J. H. Ridd, and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1227.

¹⁸ M. Ali and J. H. Ridd, *J. Chem. Soc., Perkin Trans. 2*, 1986, 327.

¹⁹ U. Al-Obaidi and R. B. Moodie, *J. Chem. Soc., Perkin Trans. 2*, 1985, 467.

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Scheme 4

brackets since the reaction shown indicates only the stoichiometry of the process. The mechanism of this stage must be more complex since the rate of the nitrous acid catalysed reaction frequently exceeds the rate of formation of nitronium ions in the medium.

The two radical mechanisms have in common the fact that the product determining stage is the reaction of an aromatic radical cation with nitrogen dioxide. Before dealing with the evidence for and against the involvement of this radical pair as an intermediate in the reaction paths for uncatalysed and nitrous acid catalysed nitration, it is useful to look at the different types of argument that have been used and to consider whether, in principle, such arguments are permissive, persuasive, or compelling.

2 Possible Mechanistic Criteria

A. Calculations on the Electron Transfer Step.—In their first publication on this subject, Nagakura and Tanaka²⁰ pointed out that the energy of the LUMO of the nitronium ion (−11 eV) was below that of the HOMO of benzene (−9.24 eV) and that, in consequence:

‘in the course of the substitution reaction almost one π -electron should remove from benzene or other reactants toward the reagent.’

This point of view was developed in later publications²¹ and by other authors.²² However, any such arguments based on ionization potentials refer to what should happen in the gas phase and, in that phase, benzene and a number of other aromatic compounds are now known to react with nitronium ions by electron transfer or oxygen atom transfer followed by a slower reaction between the radical cation and nitrogen dioxide to give the Wheland intermediate.²³ The importance of the electron transfer step in such gas phase reactions is therefore not in dispute.

In solution, the solvation of the small nitronium ion should exceed that of the large aromatic radical cation and hence electron transfer should be less probable.

²⁰ S Nagakura and J Tanaka, *J Chem Phys*, 1954, **22**, 563

²¹ S Nagakura and J Tanaka, *Bull Chem Soc Jpn*, 1959, **32**, 734, S Nagakura, *Tetrahedron*, 1963, **19**, 361

²² R D Brown, *J Chem Soc*, 1959, 2224, 2232, T Takabe, K Takenaka, K Yamaguchi, and T Fueno, *Chem Phys Lett*, 1976, **44**, 65

²³ R J Schmitt, S E Buttrill, and D S Ross, *J Am Chem Soc*, 1984, **106**, 926

Table 1 Standard potentials (E^0) for the relevant electrophiles in different solvents (corrected, where necessary, to refer to the standard hydrogen electrode)

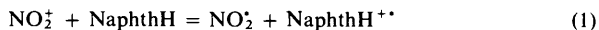
	E^0/V		
	CH_3CN	$(\text{CH}_2)_4\text{SO}_2$	CH_3NO_2
$\text{NO}_2^+/\text{NO}_2^+$	1.56 ^a	2.05 ^c	2.32 ^d
NO^+/NO^+	1.51 ^b	—	1.58 ^d

^a G. Cauquis and D. Serve, *C.R. Seances Acad. Sci., Ser. C*, 1968, **267**, 460. ^b G. Bontempelli, G.-A. Mazzocchin, and F. Magno, *J. Electroanal. Chem.*, 1974, **55**, 91. ^c A. Boughriet and M. Wartel, *J. Electroanal. Chem. Interfacial Electrochem.*, 1989, **262**, 183. ^d A. Boughriet and M. Wartel, *J. Chem. Soc., Chem. Commun.*, 1989, 809.

In principle, the use of the standard potentials for the $\text{ArH}/\text{ArH}^{++}$ and $\text{NO}_2^+/\text{NO}_2^+$ couples should be a much more accurate guide to the probability of electron transfer in solution, particularly since, when combined with the Marcus equation, a value for the second order rate coefficient for the electron transfer can be calculated.¹ The results of this approach are discussed in the following sections but some difficulties and complications should be noted.

First, the usual application of the Marcus equation assumes²⁴ that the interaction between the reactants before the electron transfer is less than 4 kJ mol⁻¹ (an outer-sphere reaction). Since this is less than the likely interaction within a π -complex formed from a nitronium ion and an aromatic compound, the treatment of electron transfer between a nitronium ion and an aromatic compound as an outer-sphere reaction may not be justified. The initial interaction should facilitate the electron transfer since the resulting bending of the nitronium ion should bring the structure nearer to that of the nitrogen dioxide radical and thus reduce the reorganization energy required.

A second complication comes from the marked solvent dependence of the standard potential for the $\text{NO}_2^+/\text{NO}_2^+$ couple. Evidence on this has only recently become available from the work of Boughriet and Wartel^{25,26} (Table 1) but it has led to calculations²⁵ that log K for the oxidation of naphthalene by nitronium ions (equation 1) has the following values in the solvents indicated: acetonitrile, -8.67; sulpholan, 0.8; nitromethane, 6.75.



It is curious that the very marked solvent dependence of the oxidizing power of nitronium ions has not been commented on previously but, if the above results are correct, it is clear that the rate of electron transfer to nitronium ions must also be very sensitive to the exact experimental conditions.

B. Kinetic Studies.—Kinetic studies are of only limited value in distinguishing

²⁴ L. Ebersson, 'Electron Transfer Reactions in Organic Chemistry', Springer-Verlag, Berlin, 1987, Chapter 11.

²⁵ A. Boughriet and M. Wartel, *J. Chem. Soc., Chem. Commun.*, 1989, 809.

²⁶ A. Boughriet and M. Wartel, *J. Electroanal. Chem. Interfacial Electrochem.*, 1989, **262**, 183.

between the classical and electron transfer paths in nitration by the nitronium ion. This is partly because the formation of the nitronium ion is frequently rate-determining but also because, when later stages of the reaction are rate-determining, the kinetic forms of the two reaction paths would normally be the same. The only possible kinetic distinction between the paths comes from the fact that aromatic radical cations are normally present to some extent as the dimer cations²⁷ $\{(\text{ArH})_2^{+*}\}$ and, if the second aromatic molecule facilitated the electron transfer or if the subsequent combination of the radical cation and nitrogen dioxide occurred through the dimer cation, the kinetic equation for path A (Scheme 3) could have a component that is second-order with respect to the aromatic substrate. Such a kinetic term has been found in the nitrous acid catalysed nitration of naphthalene²⁸ but not in nitration by the nitronium ion.

In contrast, the classical and radical mechanisms for nitrous acid catalysed nitration can have quite different kinetic forms for, in the classical mechanism (Scheme 2), the nitrosation of the aromatic compound is always rate-determining but, in the radical mechanism (Scheme 4), either stage 1 or stage 3 can be rate-determining depending, in part, on the concentration of nitrous acid. This leads to the curious consequence that, as the concentration of nitrous acid is increased, the order with respect to nitrous acid falls from one towards zero. This is not, perhaps, an obvious consequence of the reactions in Scheme 4 but comes from a conventional analysis using the steady state approximation¹⁸. The order with respect to nitrous acid in the catalysed nitration of *p*-nitrophenol was found to change in this way²⁹ although the change was not interpreted in terms of the radical mechanism until later¹⁸.

The correlation of rates of nitration with ionization potentials³⁰ has been taken as evidence of electron transfer in the transition state of the reaction although correlations with other reactivity indices are also satisfactory³¹. The interpretation of these correlations is also complicated by the fact that the experimental data³¹ were obtained without suppression of the nitrous acid catalysed mechanism and so the range of nitration reactions studied (with substrates benzene to diphenylamine) almost certainly encompasses a mechanistic change from nitronium ion nitration to the nitrous acid catalysed reaction. The nitronium ion can hardly be the reagent over the whole range of substrates since the stated reactivities of many of the compounds exceed that of mesitylene which is known to react with nitronium ions on encounter³².

C. Product Composition—Significance has been attached to the correlation between the orientation of nitration and the hyperfine coupling constants in the corresponding aromatic radical cations³⁰ but, for two reasons, this is of only

²⁷ M. A. J. Rodgers, *J. Chem. Soc., Faraday Trans. 1*, 1972, **68**, 1278.

²⁸ J. R. Leis, M. E. Peña, and J. H. Ridd, *Can. J. Chem.* 1989 **67**, 1677.

²⁹ A. P. Gosney and M. I. Page, *J. Chem. Soc. Perkin Trans. 2* 1980 1783.

³⁰ E. B. Pedersen, T. E. Petersen, K. Torsell, and S.-O. Lawesson, *Tetrahedron* 1973 **29**, 579.

³¹ M. J. S. Dewar, T. Mole, and E. W. T. Warford, *J. Chem. Soc.* 1956 3581; M. J. S. Dewar and D. S. Urch, *J. Chem. Soc.* 1958 3079.

³² K. Schofield, 'Aromatic Nitration', Cambridge University Press, 1980 Chapter 4.

limited value in distinguishing between paths A and B in Scheme 3. One reason is that the hyperfine coupling constants in the radical cation reflect the electron distribution in the frontier orbital of the neutral aromatic molecule and this electron distribution is known to be closely related to many other reactivity indices including, for example, the localization energy.³³ It is therefore difficult to know whether the correlation with hyperfine coupling constants is significant or accidental. The other reason is that any such correlation, even if significant, can only provide evidence on the degree of electron transfer in the transition state of the product determining step; it cannot distinguish between the one-step and two-step paths in Scheme 3. As many authors have recognized,^{21,22,30,33} the transition state of the one-step path may also have a major contribution from structures of the type $(\text{ArH}^{+\cdot} \text{NO}_2^-)$.

In contrast, any experimental evidence that, under essentially the same conditions, the reaction of the aromatic compound with nitronium ions and the reaction of the aromatic radical cation with nitrogen dioxide lead to different product compositions would be decisive evidence that the nitronium ion reaction did not occur through the conventional radical pair $(\text{ArH}^{+\cdot} \text{NO}_2^-)$. Such experiments are therefore very important but they are not easy to carry out without ambiguity, *e.g.*, with the exclusion of reaction between nitrogen dioxide and the neutral aromatic substrate.¹ One approach is to generate the radical cation electrochemically and here the work by Eberson and Radner³⁴ on the reaction of nitrogen dioxide with electrochemically generated naphthalene radical cations does appear to show that the product composition then differs from that obtained in nitration by nitronium ions (Section 3). Another way of generating the $(\text{ArH}^{+\cdot} \text{NO}_2^-)$ radical pairs, introduced by Kochi,² is by the specific irradiation of the charge transfer bands of complexes of aromatic compounds with nitrating agents such as tetranitromethane. Because of the very short lifetime of the radical anion of tetranitromethane, the photochemical electron transfer generates the encounter complex $(\text{ArH}^{+\cdot}, \text{NO}_2^{\cdot-}, \text{C}(\text{NO}_2)_3^-)$. What happens to this depends very much on the solvent. In acetonitrile, nitration predominates but, in dichloromethane, addition elimination processes occur leading, in part, to nitro-compounds.³⁵

D. Detection of Radical Cations.—The fact that nitrosonium tetrafluoroborate in acetonitrile is an excellent reagent for oxidizing aromatic compounds to their radical cations has been known³⁶ since 1977; with many substrates, solid tetrafluoroborate salts are obtained. The original work of Bandlish and Shine³⁶ on perylene and electron-rich heteroaromatic compounds has now been extended by Eberson and Radner³⁷ (using $\text{NO}^+ \text{BF}_4^-$ in CH_2Cl_2) to prepare a number of other radical cations including those from pyrene, anthracene, and chrysene. The

³³ K. Fukui, T. Yonezawa, and C. Nagata, *J. Chem. Phys.*, 1957, **26**, 831.

³⁴ L. Eberson and F. Radner, *Acta Chem. Scand. Ser. B*, 1980, **34**, 739.

³⁵ L. Eberson and F. Radner, personal communication.

³⁶ B. K. Bandlish and H. J. Shine, *J. Org. Chem.*, 1977, **42**, 561.

³⁷ L. Eberson and F. Radner, *Acta Chem. Scand. Ser. B*, 1984, **38**, 861.

last compound gave only slight conversion into the radical cation and, with naphthalene, no reaction was seen. However, the treatment of naphthalene with nitronium salts in trifluoroacetic acid gives rise to the dimer radical cation $(C_{10}H_8)_2^{+ \cdot}$ (detected by its UV spectrum) and the formation of polymers.³⁸

For a number of substrates,⁴ including naphthalene,³⁹ there is experimental evidence based on electronic and ESR spectra for the formation of the corresponding radical cations during nitration. The mechanism of formation of these cations is not known but it is probably mainly as a result of oxidation by the nitrosonium ion since, at least with naphthalene,³⁹ the evidence for the radical cation disappears when azide ions (a trap for nitrous acid) are present. There are two reasons why the nitrosonium ion could appear to be a much more effective oxidizing agent than the nitronium ion, particularly at relatively low acidities. First, from the relative equilibrium constants,⁴⁰ the proportion of the nitrous acid ionized to nitrosonium ions should be much greater than the proportion of the nitric acid ionized to nitronium ions. Secondly, oxidation by the nitrosonium ion should be the faster reaction since electron acceptance by the nitronium ion is accompanied by a particularly high reorganization energy because of the change in the geometry of the system.¹ However, there does appear to be at least one example in the literature⁴¹ where oxidation to the radical cation occurs *via* the nitronium ion, for mixtures of nitric acid and sulphuric acid oxidize 2,7-dinitrobenzo-1,4-dioxin to the corresponding radical cation whereas comparable mixtures of nitrous acid and sulphuric acid have no effect.

There is therefore no doubt that some radical cations are formed under the conditions of nitration although, where these are merely detected spectroscopically in trace amounts, they may not lie on the main reaction path for nitration.

E. CIDNP.—Reactions that occur through radical pairs can give rise to abnormal nuclear spin distributions as a result of the coupling of the electronic and nuclear spins; this can cause a marked increase in the intensity of the NMR signals which may also appear in emission instead of absorption. The theory of this effect (Chemically Induced Dynamic Nuclear Polarization) has been described in many reviews.⁴² Whether the effect can be detected depends on the magnitude of the enhancement and the persistence of the enhanced signals; the latter is determined by the relaxation time of the nucleus concerned.

Aromatic nitration carried out using ^{15}N labelled nitric acid is a particularly suitable reaction for observing this effect¹⁷ since, when reaction occurs through

³⁸ A S Morkovnik and O Y Okhlobystin, *J Gen Chem USSR (Engl Transl)*, 1985, **55**, 616

³⁹ A S Morkovnik, M M Levkovich, V D Stebletsova, N M Dobaeva, Z S Morkovnik, S I Testodova, and O Yu Okhlobystin, *Zh Obshch Khim*, 1988, **58**, 676

⁴⁰ N S Bayliss, R Dingle, D W Watts, and R G Wilkie, *Aust J Chem*, 1963, **16**, 933, M Sampoli, A De Santis, N C Marziano, F Pinna, and A Zingales, *J Phys Chem*, 1985, **89**, 2864

⁴¹ A S Morkovnik, *Khim Geterotsikl Soedin*, 1985, 274

⁴² S H Pine, *J Chem Educ*, 1972, **49**, 664, C Richard and P Granger, 'Chemically Induced Dynamic Nuclear and Electron Polarizations—CIDNP and CIDEP', Volume 8 of 'NMR Basic principles and Progress', ed P Diehl, E Fluck, and R Kosfeld, Springer-Verlag, Berlin, 1974

the $\text{ArH}^{+\cdot}\text{NO}_2$ radical pair, the enhancement of ^{15}N NMR signals is large (often by one or more powers of ten) and also unusually persistent (the relaxation time of the ^{15}N nitrogen atom in a nitro-group is about three minutes). It is also possible to determine whether this radical pair is formed by an electron transfer to a nitronium ion (as in Scheme 3) or by the diffusion together of the components (as in Scheme 4) since, from Kaptein's rules⁴³ (after modification⁴⁴ to apply to ^{15}N NMR spectra), the former should give enhanced absorption and the latter emission. This distinction* arises because of the necessary correlation of the electron spins in the radical pair formed by electron transfer as compared with that formed by diffusion. Evidence of nuclear polarization has also been found in ^{13}C NMR spectra taken during nitration⁴⁵ but the enhancements are then less than those observed in the ^{15}N spectra.

In this approach, one is looking at the main reaction product at a time when, from the abnormal nuclear spin distribution, it could be said to 'remember' not only that it was derived from a radical pair but also some details of how that radical pair was formed. This is unusually direct mechanistic evidence but there are still some difficulties in that the absence of nuclear polarization does not necessarily imply the absence of a radical pair on the reaction path since significant separation of the radical pairs must occur for CIDNP effects to be observed. Also, when only weak polarization is observed, it is necessary to check that it is not introduced into the nitric acid in some side-reaction and carried over into the main product.

Thus, of the above mechanistic criteria, the CIDNP effects can, in principle, provide the most compelling evidence for the presence of radical pairs on the reaction path, and the comparison of product compositions from conventional nitrations with those from the reactions of radical cations with nitrogen dioxide can, in principle, provide the most compelling evidence against such radical intermediates. For nitrous acid catalysed nitration, kinetic studies can also provide compelling evidence against the classical reaction path (Scheme 2). The application of these criteria to nitronium ion nitration and nitrous acid catalysed nitration will now be examined.

3 Nitration by the Nitronium Ion

Much of the current interest in electron transfer during nitration stems from a particularly forceful and well argued paper by Perrin⁴⁶ in 1977. Some years before, Coombes, Moodie, and Schofield⁴⁷ had demonstrated that the second-order rate coefficients for nitration in sulphuric acid reached a limit with compounds of reactivity equal or greater than that of the xylenes; this limit was ascribed to reaction on encounter of the aromatic compounds with nitronium

* The argument also depends on the g -values of the radicals and the signs of the hyperfine coupling constants. A discussion of this mechanistic distinction is given in reference 17b.

⁴³ R. Kaptein, *Chem. Commun.*, 1971, 732.

⁴⁴ N. A. Porter, G. R. Dubay, and J. G. Green, *J. Am. Chem. Soc.*, 1978, **100**, 920.

⁴⁵ M. Ali, J. H. Ridd, J. P. B. Sandall, and S. Trevellick, *J. Chem. Soc., Chem. Commun.*, 1987, 1168.

⁴⁶ C. L. Perrin, *J. Am. Chem. Soc.*, 1977, **99**, 5516.

⁴⁷ R. G. Coombes, R. B. Moodie, and K. Schofield, *J. Chem. Soc., B*, 1968, 800

ions. Intramolecular selectivity, *e.g.*, in 1,2,4-trimethylbenzene, was still observed.⁴⁸ Perrin⁴⁶ interpreted the limiting rate coefficient as an encounter-controlled electron transfer from the aromatic compound to the nitronium ion (Scheme 3, path A) and suggested that the intramolecular selectivity derived from the reactions of the resulting radical cations with nitrogen dioxide. He supported his interpretation by providing evidence that the product composition in the conventional nitration of naphthalene was the same as that observed in reactions of the electrochemically generated naphthalene radical cation with nitrogen dioxide.

This interpretation now appears much more doubtful since the supposed reaction of the naphthalene radical cation with nitrogen dioxide has been shown to involve a much more complex reaction path¹ including an acid catalysed reaction of the naphthalene molecule with nitrogen dioxide. The present position on this matter has been well summarized elsewhere.¹

The above arguments did, however, lead to a renewed interest in determining the boundary between conventional nitration by the nitronium ion and reactions *via* radical cations. On this matter, the ¹⁵N CIDNP experiments of Johnston, Ridd, and Sandall⁴⁹ provide a clear experimental distinction (Table 2). For nitration by nitric acid in mixtures of trifluoroacetic acid and nitromethane, the ¹⁵N NMR signals for the nitro products of mesitylene and *p*-xylene showed no enhancement, that from naphthalene showed slight enhancement, and that for the mononitro product from durene showed much stronger enhancement. This can be seen by the comparison of the signal for nitrodurene (A) with that of the standard (S) during and after reaction (Figure 1, a and b).*

The variation of the nuclear polarization with time was analysed to provide values of the enhancement coefficients^{49b} (the enhancement of the signals at the moment of forming the product) and the comparison of these with the values from a related reaction (the rearrangement of 4-methyl-4-nitrocyclohexadienone; enhancement coefficient *ca.* 1000)⁵⁰ known to proceed through such a radical pair suggested that, for naphthalene, nitration *via* the radical cation is only a few percent of the overall reaction. For durene, reaction through the radical cation is clearly more important but it is unlikely to be the major component. Hence, for nitration under these conditions, the borderline for the incursion of the radical cation pathway would appear to lie with aromatic substrates giving E^0 values of *ca.* 2.08 V (Table 2).

Durene and naphthalene have very similar standard potentials (Table 2) but one difference between them is that, with durene, much of the nitration is believed to arise from *ipso*-attack followed by rearrangement.^{17e} The much

* In this Figure, the emission signal for dinitrodurene presumably arises from the opposite polarization of the nitronium ions in the solution deriving from electron exchange with the nitrogen dioxide molecules that have escaped from the radical pair. When studied separately, the nitration of nitrodurene shows no CIDNP effect.^{17e}

⁴⁸ J W Barnett, R B Moodie, K Schofield, and J B Weston, *J Chem Soc, Perkin Trans 2*, 1975, 648

⁴⁹ (a) J F Johnston, J H Ridd, and J P B Sandall, *J Chem Soc, Chem Commun*, 1989, 244, (b) *idem*, *J Chem Soc, Perkin Trans 2*, 1991, 623

⁵⁰ J H Ridd, J P B Sandall, and S Trevellick, *J Chem Soc, Chem Commun*, 1988, 1195, S M Trevellick, Ph D Thesis, London, 1989

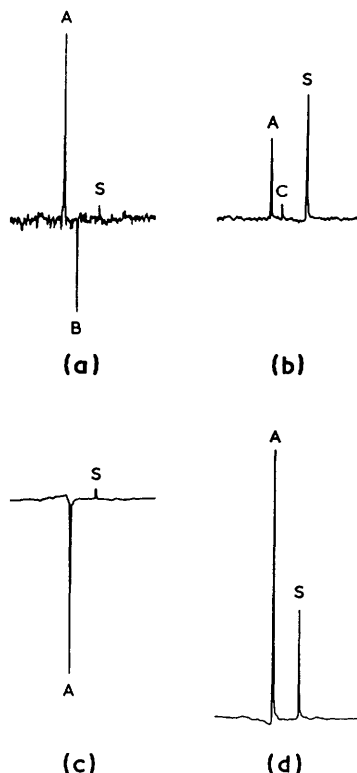


Figure 1 ^{15}N NMR spectra taken during nitration by H^{15}NO_3 and showing CIDNP effects. (a) the initial stage of the nitration of durene in $\text{CF}_3\text{CO}_2\text{H}/\text{CH}_3\text{NO}_2$ containing NaN_3 ; (b) the same reaction, after completion; (c) the initial stage of the nitrous acid catalysed nitration of mesitylene in $\text{CF}_3\text{CO}_2\text{H}$; (d) the same reaction after completion. Assignment of signals: A, main nitro-product; B, dinitrodurene; C, nitromethane (natural abundance); S, standard ($\text{C}_6\text{H}_5^{15}\text{NO}_2$) (Taken from A. H. Clemens, J. H. Ridd, and J. P. B. Sandall, *J. Chem. Soc., Perkin 2*, 1984, 1659; J. F. Johnston, J. H. Ridd, and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2*, 1991, 623; J. F. Johnston, Ph.D. Thesis, London, 1989)

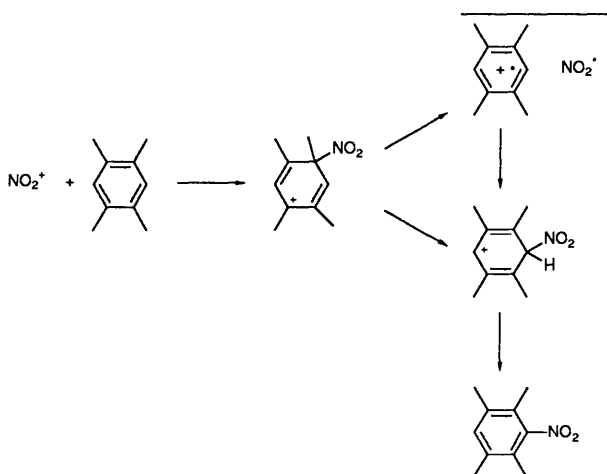
greater polarization observed in the nitration of durene (enhancement coefficient 76) compared with naphthalene (enhancement coefficient 8.7) and 2-methylnaphthalene (enhancement coefficient 25.1)^{49b} suggests that the polarization in the durene reaction comes mainly from the homolytic fission of the *ipso*-intermediate^{17e} (Scheme 5). This corresponds to the inner-sphere mechanism proposed for such electron transfers by Eberson and Radner.³⁷ An inner-sphere mechanism can have a lower reorganization energy because the part of the reorganization energy for the outer-sphere electron transfer that comes from the bending of the nitronium ion (estimated to be *ca.* 218 kJ mol⁻¹)¹ is no longer required.

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Table 2 Comparison of the standard potentials for the oxidation of aromatic compounds (E^0) with the ^{15}N CIDNP effects (A = enhanced absorption E = emission, N = no effect) for nitronium ion nitration and nitrous acid catalysed nitration. The enhancement coefficients are also shown in parenthesis

Substrate	Standard Potential		CIDNP ^a	
	Solvent	E^0/V	NO_2^+	HNO_2 cat
benzene	MeCN	3.03 ^b		
toluene	MeCN	2.61 ^d		
<i>m</i> -xylene	$\text{CF}_3\text{CO}_2\text{H}$	2.38 ^c		E
<i>o</i> -xylene	$\text{CF}_3\text{CO}_2\text{H}$	2.37 ^c		E
mesitylene	$\text{CF}_3\text{CO}_2\text{H}$	2.35 ^c	N	E
<i>p</i> -xylene	$\text{CF}_3\text{CO}_2\text{H}$	2.30 ^c	N	E
naphthalene	MeCN	2.08 ^b	A(8.8)	E
durene	MeCN	2.07 ^c	A(76)	E
2-methylnaphthalene	—	2.02 ^e	A(25)	
1-methylnaphthalene	—	1.99 ^e	A	
chrysene	MeCN	1.88 ^b		
anthracene	MeCN	1.61 ^b		
pyrene	MeCN	1.60 ^b		
perylene	MeCN	1.30 ^b		
<i>p</i> -nitrophenol			A	E
<i>N,N,N',N'</i> -tetramethylaniline				E

^a A H Clemens, J H Ridd, and J P B Sandall, *J Chem Soc, Perkin Trans 2*, 1985, 1227, and earlier papers in this series, J F Johnston, J H Ridd, and J P B Sandall, *J Chem Soc, Perkin Trans 2*, 1991, 623 ^b V D Parker, *J Am Chem Soc*, 1976, **98**, 98 ^c C J Schlesener, C Amatore, and J K Kochi, *J Am Chem Soc*, 1984, **106**, 3567 ^d L Ebersson, L Jonsson, and L-G Wistrand, *Acta Chem Scand*, 1978, **B32**, 520 ^e L Ebersson and F Radner, *Acta Chem Scand*, 1986, **B40**, 71



Scheme 5

The polarization observed in the nitration of naphthalene cannot, however, be ascribed to the homolytic fission of the corresponding Wheland intermediate since the polarization observed with naphthalene and d_8 -naphthalene is almost identical.⁴⁹ If the Wheland intermediate in the nitration of naphthalene were partitioned between homolytic fission and proton loss, the replacement of the protons by deuterons would necessarily increase the proportion of the reaction occurring by homolytic fission and hence increase also the polarization observed. This electron transfer must therefore occur before the formation of the Wheland intermediate. Whether such a process should be described as an inner-sphere or an outer-sphere electron transfer should presumably depend on the extent of the initial interaction between the nitronium ion and the aromatic substrate.

This conclusion that the reaction of naphthalene with nitronium ions occurs mainly by the classical mechanism is consistent with an earlier comparison³⁴ of the product compositions in dichloromethane as solvent from the nitration of naphthalene by nitronium tetrafluoroborate and from the reaction of the electrochemically generated naphthalene radical cation with nitrogen dioxide. The interpretation is complicated by the fact that both reactions are heterogeneous and, in principle, by the need to consider two forms of the naphthalene radical cation [$ArH^{+\bullet}$ and $(ArH)_2^{+\bullet}$] although, fortunately, the two forms appear to give essentially the same product composition.³⁴ From the α/β ratios (15 for $ArH + NO_2^+$ at $-30^\circ C$; 40 for $ArH^{+\bullet} + NO_2$ at -70 to $-20^\circ C$) (Table 3), it seems that the radical cation reaction is significantly more selective and hence that the direct nitration is unlikely to involve this species. This is supported by more recent work giving an α/β ratio of 65 for a reaction at $-45^\circ C$ in which the naphthalene radical cation is generated electrochemically in the presence of nitrogen dioxide.¹ Other evidence leading to the same conclusion comes from the comparison of the corresponding product compositions for the methyl naphthalenes (Table 3).

There is, however, some contrary evidence on the radical cation reaction for the recent work of Sankararaman and Kochi⁵¹ suggests that the reaction of the naphthalene radical cation with nitrogen dioxide gives a *lower* α/β ratio (5.5, MeCN, $-40^\circ C$; 7.4, MeCN, $25^\circ C$) than conventional nitration by NO_2^+ (Table 3). The similarity of these values to those for conventional nitration (and related studies on the methyl naphthalenes) has led these authors to suggest that the two reaction paths are very similar.

The discrepancy between the two sets of values for the orientation of substitution in the naphthalene radical cation presumably derives from the different ways of generating the reactive species. In the work of Eberson and Radner (Table 3), the naphthalene radical cation is generated electrochemically but, in the work of Sankararaman and Kochi,⁵¹ the radical pair ($ArH^{+\bullet} NO_2^-$) is generated by selective photoexcitation of the charge transfer complexes of naphthalene with either the nitropyridinium ion or tetranitromethane (Section

⁵¹ S. Sankararaman and J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2*, 1991, 1.

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Table 3 Comparison of the product compositions from the nitration of aromatic compounds by nitronium ions and from the reaction of the corresponding electrochemically generated radical cations with nitrogen dioxide

Substrate	Position	Percentage (a)	
		ArH + NO ₂ ⁺ ^b	ArH ^{•+} + NO ₂ [•] ^c
Naphthalene	1	93.8 ^d	97.5
	2	6.2 ^d	2.5
1-methylnaphthalene	2	31	8
	4	56	88
2-methylnaphthalene	1	56	84
	4	16	10
1,4-dimethylnaphthalene	2	6	95
	5	18	5
	4-CH ₂ NO ₂	76	<0.1
1,8-dimethylnaphthalene	2	70	<8
	4	30	>92

^a L. Ebersson and F. Radner, *Acta Chem. Scand. Ser. B*, 1980, **34**, 739; 1986, **40**, 71. ^b Reaction with nitric acid in acetic anhydride at -10°C unless specified otherwise. ^c Reaction of the aromatic radical cation hexafluorophosphate with nitrogen dioxide in dichloromethane at -70 to -20°C . ^d Reaction with nitronium tetrafluoroborate in dichloromethane at -30°C .

2C). It may be significant that these photonitrations can be complicated by addition-elimination reactions, at least with tetranitromethane in dichloromethane as solvent, and that these reaction paths lead to very low α/β ratios (*ca.* 1.5).³⁵ A small contribution from such a pathway could have a marked effect on the α/β ratio for the overall reaction.

A few years ago, the possibility that the nitration of naphthalene in nitromethane-trifluoroacetic acid could involve some reaction through the radical cation seemed improbable because of some calculations based on Marcus theory. Since the rate of nitration of naphthalene by nitronium ions is close to the encounter limit,³² the second-order rate coefficient for the overall reaction must be *ca.* $10^9 \text{ mol}^{-1} \text{ s}^{-1} \text{ dm}^3$ and that for the electron transfer step must be at least $10^7 \text{ mol}^{-1} \text{ s}^{-1} \text{ dm}^3$. The calculated rate coefficient for electron transfer from naphthalene to the nitronium ion has been given as $1.2 \times 10^{-6} \text{ mol}^{-1} \text{ s}^{-1} \text{ dm}^3$ using the E^0 values in acetonitrile.¹ However, the recognition that the E^0 value for NO₂/NO₂⁺ is very sensitive to the solvent (Section 2A) has changed the significance of that calculation; the value of the rate coefficient becomes $6.3 \text{ mol}^{-1} \text{ s}^{-1} \text{ dm}^3$ using the E^0 values in sulfolane²⁶ and should be much greater in nitromethane. It does not appear therefore that Marcus theory can completely rule out some contribution from electron transfer in the nitration of naphthalene, particularly if the initial π -complex interaction is considered to be sufficient to treat the electron transfer as an inner-sphere reaction.

From the above arguments, it appears that reaction through the radical cation is not a major component of the nitration reaction unless the standard potential for the oxidation of the aromatic compound is below 2.07 V. There is also a lower limit for this reaction to be significant since, with perylene ($E^0 = 1.3 \text{ V}$),

the stability of the radical cation prevents it from reacting cleanly with nitrogen dioxide,¹⁴ a large amount of the aromatic hydrocarbon being reformed.

4 Nitrous Acid Catalysed Nitration

Probably the most obvious evidence for the involvement of radicals in nitrous acid catalysed nitration comes from the very strong emission signal seen for the nitro-product in the ¹⁵N NMR spectrum.¹⁷ This emission signal is illustrated for the nitration of mesitylene in spectrum (c) of Figure 1; it can be 600 times as intense as the expected absorption signal^{17c} and so cannot easily be missed. One of the consequences of these ¹⁵N NMR studies has been to show how difficult it is to eliminate the nitrous acid catalysed mechanism in the nitration of aromatic compounds of the reactivity of mesitylene or naphthalene particularly when relatively high concentrations of the substrates are used (*ca.* 0.3 mol dm⁻³). Unless high concentrations of nitrous acid traps are used, most preparative nitrations of such compounds probably proceed mainly by the nitrous acid catalysed path.

In itself, the strong emission signal merely shows the presence of radical pairs on the reaction path and, in conjunction with the *g*-values and hyperfine coupling constants of the relevant radicals, that the radical pair is formed by the diffusion together of the components. This is entirely consistent with the mechanism given in Scheme 4, but stronger evidence for this mechanism comes from the kinetics observed. The expected kinetic form for reaction at a given acidity is shown in equation 2, and the two limiting forms in equations 3 and 4:

$$\text{Rate} = \frac{a[\text{ArH}][\text{HNO}_2]}{b + c[\text{HNO}_2]/[\text{HNO}_3]} \quad (2)$$

$$\text{'Low' } [\text{HNO}_2] \quad \text{Rate} = k[\text{ArH}][\text{HNO}_2] \quad (3)$$

$$\text{'High' } [\text{HNO}_2] \quad \text{Rate} = k'[\text{ArH}][\text{HNO}_3] \quad (4)$$

The limiting kinetic forms have been observed and also the transition between them.^{18,19,28} With the nitrous acid catalysed nitration of naphthalene, there is in addition a kinetic term that is second order with respect to the aromatic compound;²⁸ this is believed to derive from reactions involving the dimer radical cation $\{(\text{ArH})_2^+\}$.

This mechanism also receives support from the side-products formed during nitrous acid catalysed nitration for these are characteristic of reactions of the radical cations.^{4,17b-e} There is also plenty of evidence for the formation of radical cations in the reactions of nitrosonium ions with aromatic compounds and in nitrous acid catalysed nitration (Section 2D). Hence, although the details of the reaction in Scheme 4 may need modification and amplification, the main features now seem well established.

However, several questions remain, one concerning the range of this mechanism. This appears to be essentially the same as the range of nitrous acid

catalysed nitration, for the characteristic CIDNP effects have been seen in all of the examples studied so far. However, this does not imply that the classical mechanism is unimportant. Some careful kinetic studies by Moodie, Al-Obaidi, and Dix^{19,52} have established that nitrosation followed by oxidation (Scheme 2) plays a minor part in the nitrous acid catalysed nitration of phenol in 19–45% sulphuric acid¹⁹ and a major part in the nitrous acid catalysed nitration of anisole in 43–47% sulphuric acid.⁵² Reaction by the radical cation mechanism (Scheme 4) occurs with both substrates although, with phenol, the phenoxy radical (PhO[•]) is the species involved. As might be expected,⁵³ the nitrosation of phenol shows a kinetic isotope effect ($k_{o,H}/k_{o,D} = 3.5$)¹⁹ but the radical mechanism for the nitrous acid catalysed nitration of phenol does not.¹⁹

Some factors determining the relative importance of the classical and the radical pathways can be seen from the kinetic forms of these reactions. Since the nitrosation stage of the classical reaction is irreversible and the oxidation of the nitroso-compound is normally fast, the overall kinetic form should be first-order with respect to both the aromatic compound and nitrous acid. This accords with one of the limiting forms of the radical pathway (equation 3) but the relative importance of the classical reaction should decrease with acidity because of the rate-determining proton transfer now known to be present in nitrosation.⁵³ However, the radical pathway reaches a limiting rate as the concentration of nitrous acid is increased,¹⁸ and so the classical pathway should then be favoured. With the anisole work,⁵² the ratio $[\text{HNO}_2]/[\text{HNO}_3]$ was varied from 0.001 to 0.05; these values are appreciably greater than the traces of nitrous acid normally responsible for nitrous acid catalysed nitration.

The ease with which nitrous acid catalysis is observed in such compounds as mesitylene is in apparent conflict with the calculated rate of the electron transfer in the first stage of Scheme 4 (mesitylene, $k = 2 \times 10^{-5} \text{ mol}^{-1} \text{ s}^{-1} \text{ dm}^3$)¹ on the assumption of an outer-sphere reaction in acetonitrile as solvent. The calculations may be complicated by the initial interaction of the reactants (Section 2A) or by the variation of E^0 values with the medium (although the results in Table 1 suggest that this is less important for nitrosonium ions than for nitronium ions). Since aromatic nitrosation has an isotope effect (for benzene, $k_H/k_D = \text{ca. } 8.5$),⁵³ it is also possible that the first reaction of Scheme 4 is a true inner-sphere electron transfer, for the formation of the Wheland intermediate will not necessarily lead to nitrosation. The probability of this is increased by the observation of some concurrent reactions^{19,52} by the classical and radical pathways. In the nitrous acid catalysed nitration of phenols, another possible intermediate would be the aryl nitrite.¹⁹ An alternative mechanism for the electron transfer involving a more strongly electrophilic species ($\text{N}_2\text{O}_4\text{NO}^+$)⁵⁴ is unlikely as a general solution to this problem because, in nitrous acid catalysed nitration, the order with respect to nitrous acid has not so far been observed to exceed unity.

⁵² L. R. Dix and R. B. Moodie, *J. Chem. Soc., Perkin Trans. 2*, 1986, 1097.

⁵³ B. C. Challis, R. J. Higgins, and A. J. Lawson, *J. Chem. Soc., Perkin 2*, 1972, 1831.

⁵⁴ L. Ebersson and F. Radner, *Acta Chem. Scand. Ser. B*, 1985, 39, 343.

5 Conclusion

The above arguments point to three main conclusions. The first is that any discussions concerning the relative importance of paths A and B in Scheme 3 must pay great attention to the solvent involved. This comes from the marked solvent dependence of E^0 for $\text{NO}_2/\text{NO}_2^+$ (Table 1). What is true for reactions in nitromethane may not be true for reactions in acetonitrile and it is unfortunate that no information is available on the appropriate values of E^0 to use in various concentrations of mineral acids.

The second conclusion is that, as the reactivity of the aromatic compound is increased for nitration in $\text{CF}_3\text{CO}_2\text{H}/\text{CH}_3\text{NO}_2$, the direct electron transfer to the nitronium ion (Scheme 3, path A) is first seen with naphthalene, although the weakness of the CIDNP effect makes it unlikely that the bulk of the reaction then occurs by this mechanism. This is consistent with the different isomer proportions observed in the direct nitration of naphthalene and in the reaction of the electrochemically generated naphthalene radical cation with nitrogen dioxide (Table 3). This radical cation pathway appears therefore to be relatively unimportant in the reactions of the nitronium ion, for it appears limited to some but not all of the substrates which react with nitronium ions on encounter and probably also to those solvents (*e.g.*, nitromethane, Table 1) in which the oxidizing power of the nitronium ion is most strongly developed. In the direct reaction of the nitronium ion (Scheme 3, path B), the energy required for the bending of the ion is compensated by the formation of the C–N bond.¹ Radical cation formation almost certainly occurs more readily as a result of homolysis following *ipso*-attack (Scheme 5).

The third conclusion is that the nitrous acid catalysed nitrations normally occur through the radical cation pathway (Scheme 4) although the classical reaction path (Scheme 2) can also contribute to the reaction rate particularly when the acidity is relatively low and the concentration of nitrous acid relatively high. The greater importance of electron transfer to the nitrosonium ion compared with that to the nitronium ion can be linked to the different reorganization energies involved in these two steps.¹

In the above discussions, the references to the radical cation pathways refer to those reactions in which there is at least some separation of the radical pair $\text{ArH}^{+\cdot}\text{NO}_2$, for, without some such separation, no CIDNP effect would be observed. It is sometimes suggested that this radical pair is formed but that all of it passes immediately on to form the nitro-compound. This type of mechanism is very difficult to distinguish from a one-step mechanism in which the transition state closely resembles the radical pair and, as such, is outside the scope of this review. Some separation of a radical pair $\text{ArH}^{+\cdot}\text{NO}_2$ would, however, be expected since there is evidence that the reaction of the naphthalene radical cation with nitrogen dioxide is slower than a diffusion controlled process.³⁴

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