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REVIEW COMMENTARY

NEWER ASPECTS OF ELECTRON TRANSFER IN ELECTROPHILIC AROMATIC NITRATION. RADICAL PAIRS AS REACTIVE INTERMEDIATES BY TIME-RESOLVED SPECTROSCOPY

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Aromatic nitration is effectively carried out by the deliberate irradiation of the charge-transfer absorption band ($h\nu_{CT}$) of the transient electron donor–acceptor complex [ArH, NO_2Y^+], where NO_2Y^+ represents common nitrating agents. Time-resolved spectroscopy demonstrates that the charge-transfer nitration effected in this way proceeds via an electron-transfer mechanism, in which the collapse of the reactive triad, [$ArH^{+\cdot}$, $NO_2^{\cdot}$, Y] is critical to the formation of the Wheland intermediate. Comparative product analyses of toluene and anisole nitrations together with the 'non-conventional' products arising from NO^+ catalysis, *ipso* attack and addition/elimination show that the activation process leading to charge-transfer (photochemical) nitration is indistinguishable from that leading to electrophilic (thermal) aromatic nitration.

1. INTRODUCTION

Nitration is the most extensively studied of all electrophilic aromatic substitutions,[1] and it has been the focus of both preparative and mechanistic studies. From the mechanistic point of view, the question centers on why the various nitrating agents, such as nitronium salts, nitric acid in acidic and organic solvents, oxides of nitrogen, metal nitrates and nitrites, *N*-nitramines, etc., react with typical aromatic substrates (toluene or benzene) to yield a limited and predictable collection of nitroaromatic products. The conventional resolution of this paradox[2–5] – essentially a single product from diverse reagents – has invoked the agency of the nitronium cation, NO_2^+, as the critical electrophile formed from all of the various nitrating systems. The nitration of more complex aromatic compounds, however, is accompanied by a bewildering variety of side-reactions such as *ipso* substitution, biaryl coupling, adduct formation and oxidation. The term for such processes, 'unconventional,'[6] betrays an uneasiness as to whether these anomalous reactions can be placed in the context of the usual electrophilic paradigm for nitration. We believe that the resolution of these anomalies will eventually lead to a revision of such conceptions about the nitration process, with the expansion and enrichment of the field to include the 'difficult cases.' Thus, rather than exploring the prevailing consensus on the mechanism of aromatic nitration, which has been amply and well reviewed,[2–5,7] the intention of this survey is mainly to explore the mechanistic benefits of new methodology, particularly time-resolved spectroscopy. We inquire as to what light such techniques shed on the process of aromatic activation, particularly with regard to the role of electron transfer in nitration. In conjunction with this objective, we will show how 'unconventional' and 'special' nitrations can be exploited in the elucidation of the activation process.

2. THE THREE STAGES OF ELECTROPHILIC AROMATIC NITRATION

Aromatic nitration can be considered in three discrete stages: step (a) the formation from precursors of the active nitrating electrophile, NO_2Y^+; step (b), the rate-limiting reaction of the active electrophile with the aromatic substrate to form the σ-intermediate (the arene activation process); and step (c), the further reaction of the σ-complex to yield the nitrated arene and other products. These processes are schematically presented in Scheme 1 for the nitration of an aromatic substrate (ArH).

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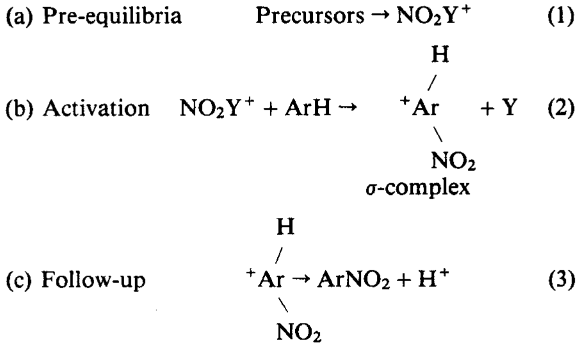


$$\text{(a) Pre-equilibria}\qquad \text{Precursors} \rightarrow \mathrm{NO_2Y^+} \qquad (1)$$

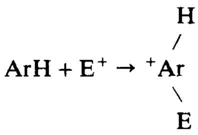
$$\text{(b) Activation}\qquad \mathrm{NO_2Y^+} + \mathrm{ArH} \rightarrow {}^{+}\underset{\diagdown\ \mathrm{NO_2}}{\overset{\mathrm{H}\ \diagup}{\mathrm{Ar}}} + \mathrm{Y} \qquad (2)$$

σ-complex

$$\text{(c) Follow-up}\qquad {}^{+}\underset{\diagdown\ \mathrm{NO_2}}{\overset{\mathrm{H}\ \diagup}{\mathrm{Ar}}} \rightarrow \mathrm{ArNO_2} + \mathrm{H^+} \qquad (3)$$

Scheme 1

Step (b) is believed to be common to all electrophilic substitution processes,[1] i.e.

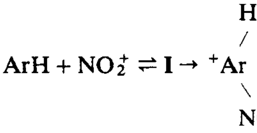


$$\mathrm{ArH} + \mathrm{E^+} \rightarrow {}^{+}\underset{\diagdown\ \mathrm{E}}{\overset{\mathrm{H}\ \diagup}{\mathrm{Ar}}} \qquad (4)$$

where E^+ is a generic representation of a variety of substituting electrophiles.

Productive mechanistic investigations have largely concentrated on the precursor step (a) and the follow-up step (c). The seminal work of Ingold,[2,8,9] for example, established the identity of the active nitrating agent NO_2^+ in a variety of acidic nitrations with HNO_3, a result confirmed by the isolation of nitronium salts and delineation of their nitrating ability.[10,11] Much mechanistic study, in turn, has focussed on how the σ-complex is converted into the final nitration products.[12] This pathway is not just a simple deprotonation, but may involve a plethora of different σ-complexes, cyclohexadienoid intermediates, adducts, etc. In particular, the absence of a kinetic isotope effect in the nitration of arenes[12a] clearly separates the activation process [step (b) in Scheme 1] from the rapid, irreversible loss of a proton from the σ-complex. This activation process is not easily addressed by classical physical organic techniques of kinetics and product studies that are applicable to the initial and follow-up processes (a) and (c). Arene activation is generally regarded mechanistically as a single and uncomplicated step.

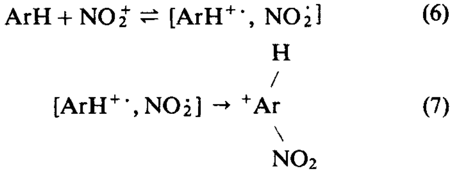
The need for appropriate methods to investigate the activation process in nitration has been made more acute by the revival of the electron-transfer mechanism for arene activation.[13] The problem stems in part from the demonstration by Olah and co-workers[14] of the necessity for an intermediate prior to the formation of the σ-complex. Nitration of reactive arenes, such as the xylenes and 1,2,4-trimethylbenzene, is diffusion limited (and therefore unselective), yet positional selectivity is maintained. A two-step mechanism was postulated by Olah *et al.*[5] to explain the anomaly. In this formulation, NO_2^+ reacts with the arene to generate an intermediate, **I**, in a step which determines the intermolecular reactivity. The subsequent transformation of **I** into the σ-complexes establishes the positional selectivity.



$$\mathrm{ArH} + \mathrm{NO_2^+} \rightleftharpoons \mathbf{I} \rightarrow {}^{+}\underset{\diagdown\ \mathrm{NO_2}}{\overset{\mathrm{H}\ \diagup}{\mathrm{Ar}}} \qquad (5)$$

Schofield and co-workers,[15] using similar arguments, also pressed for the necessity for an intermediate in the activation process. The problem thus became one of identifying this intermediate.

Since the formation of **I** in equation (5) is rate limiting, it must be a reactive (high-energy) intermediate. For this reason Olah *et al.*'s formulation of the intermediate as a π-complex and Schofield and co-workers' alternative formulation as an encounter complex are inadequate. Indeed, these complexes do exist (see below), but as relatively low-energy intermediates in equilibrium with the free arene and nitrating agent. The problem thus stood until Perrin,[16] in a provocative communication, suggested that the initial step occurs by electron transfer (ET) and that the critical intermediate is the [arene cation radical, $NO_2^{\bullet}$] pair (Scheme 2).



$$\mathrm{ArH} + \mathrm{NO_2^+} \rightleftharpoons [\mathrm{ArH^{+\bullet}}, \mathrm{NO_2^{\bullet}}] \qquad (6)$$

$$[\mathrm{ArH^{+\bullet}}, \mathrm{NO_2^{\bullet}}] \rightarrow {}^{+}\underset{\diagdown\ \mathrm{NO_2}}{\overset{\mathrm{H}\ \diagup}{\mathrm{Ar}}} \qquad (7)$$

Scheme 2

Suggestive experimental evidence for the involvement of arene cation radicals in equation (6) includes their observation under typical conditions of nitration. Moreover, side-chain coupling to give diarylmethanes and the formation of biaryls are frequently encountered side-reactions.[17,18] Since these products are also found on anodic oxidation of arenes, their presence in the nitration mixture points to a one-electron oxidation of the aromatic substrate by the nitrating agent. [The energetics of the electron transfer in equation (6) are discussed in Section 8.1.] The feasibility of the coupling reaction, [equation (7)] has also been experimentally tested. Isolated cation radical salts derived from naphthalene,[19] phenothiazine,[20] dibenzo-*p*-dioxin,[20] pyrene and perylene[19] react with $NO_2^{\bullet}$ and N_2O_4 to generate nitroarenes, often in high yields. [Owing to rapid and reversible homolytic dimerization, N_2O_4 and $NO_2^{\bullet}$ are equivalent reagents, and considered hereafter interchangeably]. Since these studies establish the *possibility* that some nitrations proceed by way of the mechanism in Scheme 2, there is a call for an assessment of the more general possibility of ET nitration with a variety of nitrating agents.

3. NITRATING AGENTS AS OXIDANTS

The combination of kinetics and spectroscopy has established the intermediacy of the nitronium cation, NO_2^+, in nitrations with nitric acid in concentrated sulfuric and perchloric acid. Its agency in these media is regarded as 'fully established' by Olah *et al.*[21] and it has rarely been questioned by Ridd.[22] Evidence for NO_2^+ as the active nitrating species in organic solvents is subject to more dissent,[23–26] but the isolation and utilization of nitronium salts have established NO_2^+ as a nitrating agent *par excellence*. Nevertheless, NO_2^+ can be regarded as one extremum of a continuum of nitrating agents, NO_2Y^+, where Y is an anionic or uncharged base. These were originally characterized by Ingold[2] as nitronium 'carriers' (and by Olah *et al.*[27] as 'transfer nitrating agents') and they can exhibit widely varying activity. For neutral Y, these carriers are exemplified by the family of *N*-nitropyridinium cations,[28] $XPyNO_2^+$, where the reactivity of NO_2^+ is modulated by the pyridine base (XPy).[29] Thus, 4-methoxy-*N*-nitropyridinium is inert to benzene and toluene at room temperature while 4-cyano-*N*-nitropyridinium nitrates these substrates in a few seconds.[29] Wheland intermediates and σ-complexes such as 9-nitroanthracenium[30] and nitrohexamethylbenzenonium[31] also fall into this category.

For anionic nucleophiles, NO_2Y^+ describes a set of uncharged nitrating agents such as nitryl chloride ($Y = Cl^-$) and fluoride ($Y = F^-$), nitrate esters ($Y = OR^-$), nitric acid ($Y = OH^-$), dinitrogen pentoxide ($Y = NO_3^-$), acyl nitrates ($Y = OCOR^-$) such as benzoyl, acetyl and trifluoroacetyl nitrates, and tetranitromethane [$Y = C(NO_2)_3^-$]. The question of whether these transfer nitrating agents are true nitrating agents in their own right or simply precursors of NO_2^+ frequently arises, but it can seldom be definitively answered. Spontaneous or Lewis acid-promoted heterolysis is always a conceivable process.

$$NO_2Y^+ \rightarrow NO_2^+ + Y \qquad (8)$$

Some transfer nitrating agents such as dinitrogen pentoxide (N_2O_5) or possibly nitronium perchlorate exist predominantly in ionic form in polar solvents (or in the solid state), but they are covalent species in non-polar solvents (or in the gas phase).[32] Since the nitronium ion itself has a very high energy of solvation, even 'free' NO_2^+ can be considered as nucleophilically solvated and thus an example NO_2Y^+. [The solvation enthalpy of NO_2^+ is given by $\Delta G_s = E^0 - IP + 4 \cdot 44$,[33] in which E^0 is the formal reduction potential of NO_2^+ and IP is the ionization potential of $NO_2^{\cdot}$.[34] For NO_2^+ dissolved in acetonitrile $\Delta G_s = -88$ kcal mol^{-1} (1 kcal = 4·184 kJ).]

For neutral nitrating agents (e.g. NO_2Cl) in solution, a series of electrophilic agents may exist in equilibrium:

$$NO_2^+ \underset{-Cl^-}{\overset{+Cl^-}{\rightleftharpoons}} \underset{\text{ion pair}}{NO_2^+, Cl^-} \rightleftharpoons O_2N{-}Cl \qquad (9)$$

where the generic designation 'ion pair' represents all the various contact and solvent-separated ion pairs extant in solution. All of these species can potentially serve as nitrating agents, and the rigorous identification of the active reagent could present problems in any particular case. Occasionally, nitration kinetics allows a distinction to be made. Thus the essentially second-order reaction kinetics (first order in arene and NO_2Y^+) observed for nitrations of arenes with *N*-nitropyridinium cations ($XPyNO_2^+$) rules out dissociation of NO_2^+ as the rate-limiting step.[29] Even in this unambiguous case, in which NO_2Y^+ (and not NO_2^+) is identified as the active nitrating species, the distribution of isometric nitrotoluenes (*o*-: *m*-: *p*- = 61 : 6 : 39) is the same as that obtained from the nitration of toluene with $NO_2^+BF_4^-$ (59 : 2 : 39). It is the singular lack of sensitivity (in the product distribution) to the identity of the nitrating agent which makes the identification of the active species difficult.[29]

Electrochemical studies indicate that NO_2^+ is a viable oxidizing agent in solution. Its standard reduction potential shows a pronounced correlation with the donicity of the solvent. The lowest value of $E^0 = 1 \cdot 53$ V is observed in the strongest donor solvent, ethyl acetate (Gutmann donor number, $DN = 17$ kcal mol^{-1}), and the highest value of $E^0 = 1 \cdot 73$ V is obtained in the weak donor solvent dichloromethane ($DN = 0$).[34] [All potentials are referenced to the normal hydrogen electrode.] Exactly the same effect is noted for the nitrosonium acceptor, NO^+, the reduction potential of which varies from $E^0 = 1 \cdot 50$ V in DMF (DN = 27 kcal mol^{-1}) to 1·72 V in CH_2Cl_2.[35] The oxidizing power of NO_2^+ and NO^+ places these electrophiles in the same class as the halogens, Ag^+, and other potent one-electron oxidizing agents. The solvent variation in E^0 highlights the importance of donor–acceptor interactions in modulating the energetics of electron transfer to nitronium and nitrosonium cations.

Since the electron deficiency of NO_2^+ is partially compensated for by the bonded nucleophile (Y), transfer nitrating agents, NO_2Y^+, are weaker acceptors than the solvated nitronium cation. Modulation of the degree of electron deficiency depends on the basicity of the substituent Y. For example, the irreversible cyclic voltammetric potentials for reduction of a series of *N*-nitropyridinium nitrating agents (NO_2Y^+, with Y being a substituted pyridine) varies from $E_p = 0 \cdot 14$ V for the cation derived from the strong base, 4-methoxypyridine (pK_a for the conjugate acid = 6·58) to 0·74 for the corresponding *N*-nitro-4-cyanopyridinium cation

($\mathrm{p}K_a = 1{\cdot}86$). This variation in E_p parallels the trend in nitrating activity.[29]

4. ELECTRON TRANSFER AND THE EDA COMPLEX

Having identified nitrating agents as viable oxidants, our interest now turns to the arene nucleophile.[36] Aromatic compounds are quintessential electron donors, as reflected in their low ionization potentials and easily accessible anodic oxidations in solution (Table 1).[37–40] More importantly, aromatic compounds are known to interact with electrophiles such as nitrating agents,[37] halogens,[43] carbocations,[44] $\mathrm{OsO_4}$,[45,46] boranes,[47] lead, mercury and thallium salts,[48] diazonium cations,[49] etc., to form a series of electron donor–acceptor (EDA) complexes. The various colors of the EDA complexes arise from an electronic transition via the overlap of the frontier MOs (donor HOMO and acceptor LUMO).[50] The energy of the new transition is directly proportional to the energy difference between the orbitals, as described in the Mulliken relation in equation (10):[51,52]

$$h\nu_{\mathrm{CT}} = IP - EA + \text{constant} \qquad (10)$$

in which the CT band energy is expressed as the difference between the ionization potential (*IP*) of the donor D and the electron affinity (*EA*) of the acceptor A. In other words, the CT absorption band is the visible sign of the molecular orbital interaction that precedes the combination of the electrophile with the nucleophile.

For those electrophilic substitution reactions that are amenable to kinetic study, such as halogenation or metalation with Hg(II) and Tl(III) electrophiles, the second-order rate constants correlate well with CT band energies ($h\nu_{\mathrm{CT}}$).[53] The particular advantage of using the CT energies as a basis for linear free energy correlations is that differences in HOMO–LUMO overlap owing to steric effects, solvation and other details of complexation are directly reflected in the CT energies. Since the same considerations pertain to the nucleophilic and electrophilic reactivity, the CT band correlations have the advantage of taking into account *all* aspects of chemical reactivity.[54]

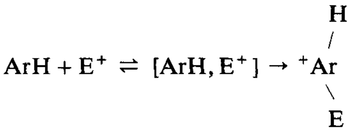
Table 1. Arenes as electron donors: oxidation potentials in solution and ionization energies in the gas phase

Arene	*IP* (eV)[a]	E^0 (V)[b]	
Benzene	9·23	3·01	
Toluene	8·82	2·64	
Mesitylene	8·42	2·35	
Durene	8·05	2·07	(1·99)[c]
Pentamethylbenzene	7·92	1·99	(1·93)[c]
Hexamethylbenzene	7·80	1·86	(1·82)[c]
Naphthalene	8·12	–	(2·06)
Anthracene	7·38	–	(1·66)
Phenanthrene	7·85	–	(2·02)
Anisole	8·39	–	–
1,4-Dimethoxybenzene	–	–	(1·54)

[a] Vertical ionization potentials in electron volts from Ref. 41.
[b] Standard oxidation potentials (vs NHE) of the indicated arene in trifluoroacetic acid from Ref. 41. Potentials in parentheses were recorded in acetonitrile (Ref. 42a).
[c] In acetonitrile from Ref. 42b.

Despite the applicability of the linear free-energy approach as a predictive tool for electrophilic reactivity,[54a] and as a stimulus to thinking,[54b] it has not provided the decisive evidence to distinguish the one-step mechanism [equation (4)] from the two-step electron-transfer mechanism (Scheme 2). Another aspect of EDA complexes does provide the unequivocal basis for the electron-transfer formulation of aromatic substitution as follows.

Since the activation step in nitration (and all electrophilic reactions) requires direct contact (and since such contact is accompanied by the formation of CT bands), the donor and acceptor in the EDA complex can be considered the obligatory precursors to the electrophilic combination. In this way, arene activation is represented as the (first-order) collapse of the complex, i.e.



$$\mathrm{ArH + E^+ \rightleftharpoons [ArH, E^+] \rightarrow {}^{+}Ar(H)(E)} \qquad (11)$$

where the brackets enclose the EDA complex. For the prototypical nitration reaction, the active electrophile E^+ is $\mathrm{NO_2^+}$, and the precursor complex is structurally identical with Olah and co-workers' π-complex or Schofield and co-workers' encounter complex. Unfortunately, the rapidity of the ensuing nitration of arene donors such as benzene and toluene precludes the spectroscopic detection of the transient charge-transfer bands. Hence a milder nitrating agent is needed for the actual detection and photostimulation of EDA complexes.

The uncertain behavior of $\mathrm{NO_2^+}$ in the EDA complex contrasts with that involving the related nitrosonium ($\mathrm{NO^+}$) electrophile. Owing to its substantially reduced electrophilic reactivity (e.g. the rates of nitrosation are estimated to be *ca* 10^{14} times slower than those of the corresponding nitration),[55] an extended series of EDA complexes of arene donors with $\mathrm{NO^+}$ can be observed in solution and isolated in the solid state.[56–59] These complexes are characterized by close non-bonded distances between ArH and $\mathrm{NO^+}$. The values of the formation constant, K_{EDA} in the equation

$$\mathrm{ArH + NO^+ \xrightleftharpoons{K_{EDA}} [ArH, NO^+]} \qquad (12)$$

increase with increasing electron richness of the aromatic donor. For the relatively electron-rich arenes such as mesitylene and hexamethylbenzene, IR and x-ray diffraction studies indicate that essentially complete charge transfer has occurred. This implies substantial contribution from resonance forms such as Ψ_{II} in the ground state of the EDA complex:

$$\underset{\Psi_I}{[\mathrm{ArH}, \mathrm{NO}^+]} \leftrightarrow \underset{\Psi_{II}}{[\mathrm{ArH}^{+\cdot}\ \mathrm{NO}^{\cdot}]}$$

Hence to the extent which NO^+ serves as a model for NO_2^+, the EDA complexes of the latter are expected to show the strong and variable bonding characteristics of the [arene, NO^+] complexes.

Tetranitromethane and *N*-nitropyridinium salts are sufficiently less active (relative to NO_2^+) to form persistent EDA complexes at convenient temperatures. [Tetranitromethane has been commonly used as a visual indicator of aromatic unsaturation owing to the vivid CT colors it forms when mixed with aromatic donors.[60]] These electrophiles serve as transfer nitrating agents, i.e. NO_2Y^+, with Y being either $C(NO_2)_3^-$ or pyridine (Py). The combination of various pyridine bases with NO_2^+ generates a series of nitrating agents ($XPyNO_2^+$) of varied electrophilic reactivity for direct comparison of the electrophilic and electron-transfer pathways.[29] The EDA complexes can be activated either (1) by allowing the nitration to proceed via the usual course of thermal activation (Δ) in solution or (2) by the direct photostimulation ($h\nu_{CT}$) of the charge-transfer bands:

$$\mathrm{ArNO_2} \xleftarrow{\Delta} [\mathrm{ArH}, \mathrm{NO_2Y^+}] \xrightarrow{h\nu_{CT}} \mathrm{ArNO_2} \quad (13)$$

[Note that the latter is carried out at (low) temperatures at which competition from the thermal process is unimportant.]

Photoactivation allows the utilization of time-resolved spectroscopy for the direct observation of the intermediates demanded by the ET mechanism in Scheme 2. Such an approach depends on (a) a combination of fast spectroscopic and classical chemical product studies to ascertain the course of the charge-transfer nitration and (b) a direct relationship between the photochemical and thermal (electrophilic) activation processes.

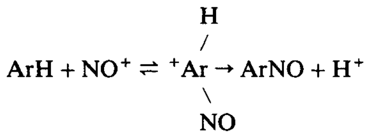
The major obstacle that impedes definitive research in arene activation (and prevents the resolution of the mechanistic dilemma) stems from the rapidity of the attack of NO_2^+ or NO_2Y^+ on the arene. For example, the rates of reaction of NO_2^+ with moderately reactive arenes such as toluene and mesitylene approach the diffusion-controlled limit. The relevant time-scales are thus of the order of nanoseconds. Nitration intermediates such as aromatic cation radicals and σ-complexes have similarly short (<1 μs) lifetimes in common organic solvents. The initial activation steps, which occur within the EDA complex, take place even faster, being on the picosecond or sub-picosecond time-scales. Experimental techniques with time responses of this order are therefore required to probe arene activation.

Classical physical organic chemistry is based on two primary investigative tools, neither of which will provide satisfactory answers to questions involving the process of arene activation. *Reaction kinetics* cannot distinguish the two activation processes in equation (4) and Scheme 2 even in the (unusual) cases in which the activation step is rate determining. Thus the kinetic form of the activation step is second order (first order in both arene and nitrating agent) in both cases. *Product analysis* by itself provides an uncertain guide owing to the plethora of intermediate steps between the initially formed σ-complex and the final product. Recent mechanistic investigations have shown that the mechanism of nitration, and particularly the formation of the nitration products, is complicated by the NO^+ catalysis, *ipso* attack and addition–elimination pathways.

5. NON-CONVENTIONAL NITRATION

5.1. NO⁺ catalysis

Nitrosation resembles nitration in that the active agent in nitrosation (in acidic media) is NO^+, which is structurally analogous to NO_2^+ as an electrophile. As such, the reaction is presumed to proceed via a σ-complex analogous to that of the Wheland intermediate in nitration:[61]



$$\mathrm{ArH} + \mathrm{NO}^+ \rightleftharpoons {}^+\mathrm{Ar}\begin{matrix} /\mathrm{H} \\ \backslash\mathrm{NO} \end{matrix} \rightarrow \mathrm{ArNO} + \mathrm{H}^+ \quad (14)$$

Although the acceptor properties of NO^+ and NO_2^+ (as assessed by electrochemical potentials[34,35]) are almost identical, they differ in their rates of anisole substitution by a factor of 10^{14}![55]

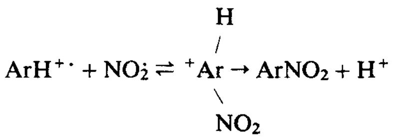
The nitrosonium cation has been implicated in the nitrite-catalyzed nitration of arenes such as mesitylene, *p*-xylene, naphthalene, anisole and various phenols. This nitration pathway was discovered by Ingold and co-workers,[62] who referred to it as 'special' nitration, and it has been principally elaborated for phenols. Nitrosophenol can be isolated from interrupted special nitrations.[63] The product distribution strongly favors *p*-nitrophenol,[64] which suggests that this nitration proceeds via a nitrosation–oxidation pathway:

$$\mathrm{ArH} \xrightarrow[\text{slow}]{\mathrm{NO^+}} \mathrm{ArNO} \xrightarrow[\text{fast}]{\mathrm{HNO_3}} \mathrm{ArNO_2} \quad (15)$$

Such a pathway is not applicable to less electron-rich substrates such as mesitylene or naphthalene,[65] since they are nitrosated too slowly for equation (15) to apply. On the basis of kinetics and CIDNP (see below), Giffney and Ridd[66] proposed the electron transfer mechanism shown in Scheme 3.

$$\mathrm{ArH + NO^{+} \rightleftharpoons ArH^{+\cdot} + NO^{\cdot}} \qquad (16)$$

$$\mathrm{NO^{\cdot} + NO_2Y^{+} \rightarrow NO^{+} + NO_2^{\cdot} + Y} \qquad (17)$$



$$\mathrm{ArH^{+\cdot} + NO_2^{\cdot} \rightleftharpoons {}^{+}Ar\overset{H}{\underset{NO_2}{\diagup}} \rightarrow ArNO_2 + H^{+}} \qquad (18)$$

Scheme 3

Nitration of some moderately electron-rich aromatics (*p*-nitrophenol,[67] mesitylene,[68] durene,[69] naphthalene[64,65]) in the presence of NO^+ yields essentially the same distribution of products as is found in nitrations with sodium azide or urea (added to the reaction mixture as NO^+ traps). In the absence of such traps, however, it is difficult to entirely exclude the possibility of NO^+ catalysis in nitrations as they are ordinarily carried out. Lower oxides of nitrogen are always present in nitric acid that is not specially purified,[70] and red fumes of $NO_2^{\cdot}$ are commonly observed in preparative nitrations. These can serve as sources of the NO^+ catalyst, particularly in nitrations of electron-rich aromatic substrates such as naphthalene and anisole. Indeed, Ridd[22] observed that 'unless high concentrations of nitrous acid traps are used, most preparative nitrations of such compounds probably proceed mainly through the nitrous acid pathway,' i.e. Scheme 3.

Nitrations of benzene, toluene and other aromatic hydrocarbons by N_2O_4 in solvents such as dichloromethane or nitromethane also appear to be NO^+-catalyzed nitrations. Mixtures of aromatics and N_2O_4 are red–brown,[71a] indicating the formation of the [arene, NO^+] complex by a CT induced disproportionation,[71b] i.e.

$$\mathrm{ArH + N_2O_4 \rightleftharpoons [ArH, NO^{+}]NO_3^{-}} \qquad (19)$$

The disproportionation and the follow-up nitration are promoted by Lewis acids that coordinate with the nitrate moiety. The critical step in the mechanism is the electron transfer in the equation

$$\mathrm{[ArH, NO^{+}] \rightarrow ArH^{+\cdot} + NO^{\cdot}} \qquad (20)$$

which can be thermally or photochemically promoted.[59] Nitration is effected by the subsequent reaction of the cation radical, $ArH^{+\cdot}$, with either $NO_2^{\cdot}$ or nitrate, since both processes give high yields of nitroaromatics.[20,71b] Even weak aromatic donors such as benzene and toluene are nitrated, so the endergonicity of the electron-transfer step in equation (20) imposes no strong restriction on ET nitration.

The direct autoxidation of the nitrosonium complexes of naphthalene, durene, toluene, etc. with dioxygen in solution also yields nitration products (e.g. α- and β-nitronaphthalenes, ring and side-chain nitrodurenes, *o*- and *p*-nitrotoluenes) with essentially the same product distributions as those obtained conventionally with nitric acid.[58] The activation step occurs by electron transfer, as demonstrated by the photopromotion of the nitrations by the deliberate irradiation of the CT absorption band of the EDA complexes, i.e.

$$\mathrm{[ArH, NO^{+}] \xrightarrow{h\nu_{CT}} ArH^{+\cdot} + NO^{\cdot}} \qquad (21)$$

Although the follow-up reactions of $NO^{\cdot}$ with O_2 are not fully elaborated, the activation step is the same for both the NO^+-catalyzed and autoxidative pathways. The latter includes aromatic donors such as toluene, with an even more endergonic ET activation step than mesitylene or naphthalene. These studies demonstrate the existence of an electron-transfer pathway for nitration and, in particular, the formation of the Wheland intermediate via the collapse of the [$ArH^{+\cdot}$, $NO_2^{\cdot}$] radical pair. Oxidation of aromatic hydrocarbons by NO^+ increases the likelihood of the corresponding activation by NO_2^+, i.e.

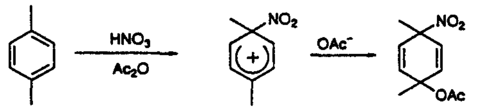
$$\mathrm{ArH + NO_2^{+} \rightarrow ArH^{+\cdot} + NO_2^{\cdot}} \qquad (22)$$

since the driving forces for electron transfer to NO^+ and NO_2^+ are essentially the same. On the other hand, electrophilic nitrations are usually carried out in the presence of adventitious nitrosonium. The significance of the distribution of products obtained from such reactions is unclear, since the possible incursion of the NO^+-catalyzed pathway has not always been taken into account. Even those nitrations effected with isolated nitronium salts (e.g. $NO_2^+BF_4^-$) may be catalyzed by NO^+, since these reagents are rarely prepared free of nitrosonium impurity.[70]

It should be noted that the first step in Ridd's mechanism is endergonic for arenes such as naphthalene and mesitylene ($\Delta G = +13$ and $+19$ kcal mol^{-1}, respectively). [The driving force, ΔG_{ET}, is calculated according to the equation, $\Delta G_{\mathrm{ET}} = -\mathcal{F}[E^0(\mathrm{NO^+}) - E^0(\mathrm{arene})]$, in which $\mathcal{F}$ represents the Faraday constant of 23·06 kcal mol^{-1} V^{-1}.] Such electron transfers are driven in part by the overall exergonicity of the nitration reaction, and partially by the decreased barrier to electron transfer that is a consequence of the EDA interaction.[33,72] These factors permit seemingly 'forbidden' electron transfers to occur.[73]

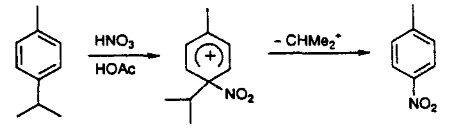
5.2. *Ipso* attack

Electrophilic attack by NO_2^+ at a substituent other than hydrogen (*ipso* attack)[74] is a significant feature of many nitrations of appropriately substituted aromatic compounds.[75] *Ipso* substitution is often detected by the trapping of the σ-intermediate by the nucleophile (often



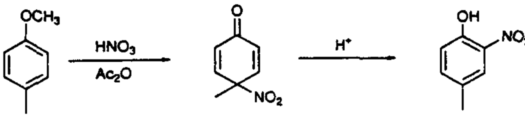
(23)

the nucleophilic Y from the nitrating agent NO_2Y^+) to yield cyclohexadiene derivatives (*ipso* adducts). Fischer and co-workers[75-79] have isolated several examples, including the adducts from *p*-xylene [equation (23)]. Other reactions of the *ipso* σ-complexes include nitrodealkylation[80] [equation (24)].



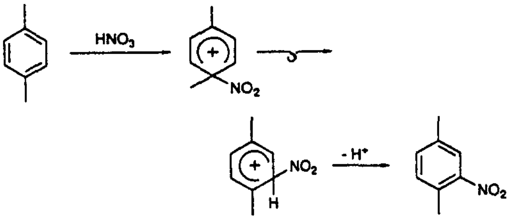
(24)

Nitrodehalogenations[81] and other group-loss processes[82] have been observed. *Ipso* attack *para* to a halogen, alkoxy or amine substituent yields nitrodienones which subsequently rearrange to nitrophenols, e.g. equation (25).[83] CIDNP studies indicate that the rearrangement proceeds through a [phenoxy radical, $NO_2^{\cdot}$] pair.[84]



(25)

The trapping and group transfer reactions, however, only establish a lower limit to *ipso* attack, since the nitro group can migrate to an unsubstituted position. Deprotonantion of the Wheland intermediate leads to the nitroaromatic product [equation (26)].[76] This rearrangement occurs by a 1,2-shift of the nitro group, as shown by an isotopic labelling experiment [equation (27)].[85]



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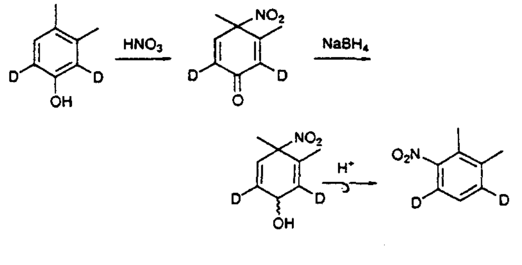

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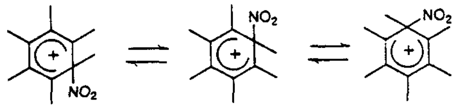
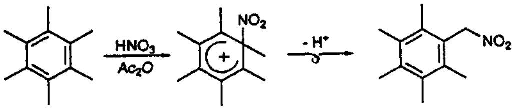


(28)

The nitrohexamethylbenzenonium cation undergoes degenerate rearrangement by a series of 1,2-shifts [equation (28)],[31] with low activation energy (16 kcal mol⁻¹). Intermolecular NO_2^+ transfer is established by the co-nitration of the added benzene or mesitylene. Side-chain nitration (and oxidation) occurs via the *ipso* intermediate, e.g. reaction (29).[6,86-88]



(29)

Ipso attack raises the question of whether the true reactivities and selectivities of arenes are at all established. In particular, it is doubtful whether accurate partial rate factors for substitution have been determined, since *ipso* complexes and their subsequent rearrangement to nitroarenes have not been taken into account quantitatively. A strong preference for *ipso* attack was demonstrated in the nitrations of *o*- and *p*-xylene, durene and other methylbenzenes commonly utilized as substrates.[7] As noted by Hahn and Groen,[89] '*True partial rate factors cannot be obtained without determination of the extent and consequences of ipso attack*' (emphasis in original).

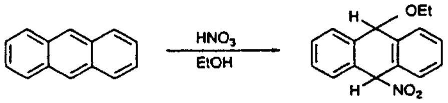
Since the *ipso* σ-complexes can serve as nitrating agents, competition studies must be conducted so as to take this factor into account. If this is not done, the results of such studies can be misleading. For example, durene was found recently to react more slowly than mesitylene in various electrophilic substitution reactions,[90,91] although no account was taken of the transfer reaction [equation (30)].

(30)

Since at least 90% of electrophilic attack on durene occurs at the *ipso* position,[7] the mechanistic conclusions drawn by the authors are invalid. Clearly, a full re-examination of reactant selectivities that are obtained by the competitive method is overdue.

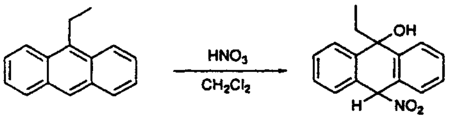
5.3. Addition–elimination

The isolation and characterization of the *ipso* adducts points to other complications which may lead to fallacious mechanistic interpretations. These *ipso* adducts frequently undergo elimination to yield nitroaromatic products. Electrophilic additions of nitrating agents



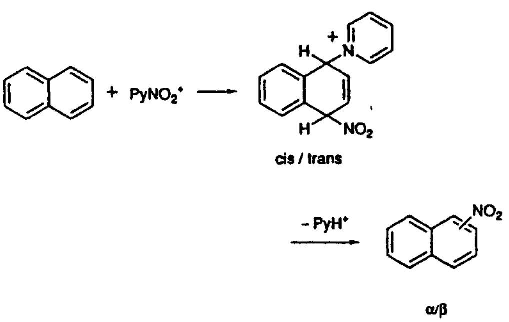
(31)

NO_2Y^+ to the π-systems of the aromatic compound have been observed with anthracene and alkyl nitrate, $RONO_2$ [equation (31)][92] or ethylanthracene and nitric acid [equation (32)].[93]



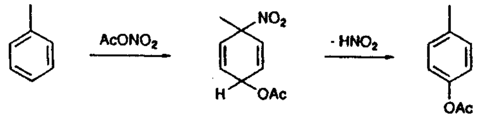
(32)

Nitration by the addition–elimination pathway occurs with naphthalene when it is nitrated with *N*-nitropyridinium cations [equation (33)].[94]



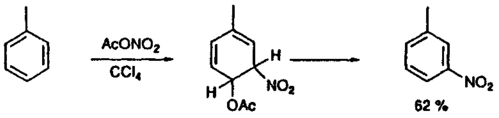
(33)

Photonitrations of various arenes with tetranitromethane are accompanied by nitrotrinitromethyl adducts.[95-98] Adduct formation has been inferred in the formation of *p*-cresyl acetate on treatment of toluene with acetyl nitrate [equation (34)].[99]



(34)

Addition can be inferred from an anomalous pattern of nuclear substitution, as in the nitration of toluene with acetyl nitrate in carbon tetrachloride [equation (35)].[100] The preferential *para*-nitration of anisole with this system may have a similar origin.[101]



(35)

Since the initially formed adducts undergo further reaction to form nitroarenes and other products, the absence of adducts in the reaction mixture is not conclusive evidence for their non-involvement in nitration. The large amount of *m*-nitrotoluene formed from $AcONO_2$–CCl_4 is an obvious sign of the anomalous reactivity.[100] However, addition–elimination pathways may affect product distribution more subtly. Obviously, the same points can be made for other substitution processes, and addition–elimination has also been implicated in aromatic chlorination and bromination reactions.[6,88]

The elucidation of NO^+ catalysis, *ipso* addition and addition–elimination pathways calls for the re-examination of many mechanistic conclusions about the aromatic nitration process, inasmuch as these are based on extrapolations from product distributions. The fact that these processes are not restricted to polycyclic or electron-rich substrates, but also include benzene and toluene, means that in no case can these complications be considered insignificant *a priori*. The assumption that the position of nitration reflects the initial position of electrophilic attack needs to be critically examined in each case, and mechanistic inferences from product ratios alone must be considered ambiguous. [Interpreting variations in the distributions of *minor* products (particularly using major/minor product ratios) is particularly hazardous, since accuracy in their quantification is limited by experimental factors. Thus a difference between a 3% and a 7% yield of minor product (for example, β-nitronaphthalene from the nitration of naphthalene) implies a change in the major/minor product ratio from 33 to 14, yet there is no truly significant change in the product distribution of *ca* 95:5. This elementary point must be emphasized, since differences in product ratios of this magnitude have been interpreted as being of major mechanistic significance.[19b]]

6. REACTIVE INTERMEDIATES IN AROMATIC NITRATION

6.1. Steady-state detection

Steady-state techniques such as the observation of radical cations on long time-scales (seconds or longer) are of limited use in deciding on the validity of Scheme 2. Since the electron transfer in equation (6) and the radical coupling in equation (7) are very rapid processes, each reaction step must be complete in (at most) a few microseconds. Steady-state techniques are restricted to the observation of intermediates which are generated and decay on the millisecond time-scale. These intermediates do not necessarily relate to the main (fast) reaction pathway. This problem was addressed by Morkovnik,[20] who deplored the necessity of using indirect methods of observation to study reactive cation radical intermediates in aromatic substitutions.

The indiscriminate use of ESR spectroscopy is particularly dangerous. Unambiguous identification and quantification of organic radical species are each difficult problems,[102] and mechanistic conclusions based on the observation of unknown radicals in unknown, and very low, concentrations are invalid. Interpretations of the absence of an ESR signal, or of relative intensities of steady-state signals are equally futile. [A recent publication,[103a] for example, proports to determine the relative rate of two fast reactions of $ArH^{+\cdot}$ (radical coupling to $NO_2^{\cdot}$ and nucleophilic attack by trinitromethide) by comparing the relative intensity of a set of uncertainly assigned ESR signals ($ArH^{+\cdot}$?) in the presence and absence of trifluoroacetic acid (TFA). Aside from the inherent problems of the time-scale of measurement discussed here, the researchers failed to take into account the dimerization of $NO_2^{\cdot}$ to N_2O_4 at their low reaction temperatures[103b] and (2) the special stabilization of aromatic cation radicals in the presence of TFA.[41]]

Transient techniques, on the other hand, permit firm conclusions to be drawn concerning the kinetics of the reactions in Scheme 2, because these reactions can be examined on the appropriate timescale. In particular, laser flash photolysis generates high concentrations of intermediates, and the separate processes of formation and decay can be studied. (Steady-state concentrations, on the other hand, represent an inseparable composite of formation and decay processes). Put bluntly, picosecond reactions are not amenable to investigation on a time-scale of minutes without serious oversimplifying assumptions. Since the intermediates in the nitration reaction are so short-lived, steady-state techniques are not useful for the study of electron-transfer mechanisms.

6.2. Gas-phase studies

Gas-phase studies, with a time resolution of 10–100 μs,[104] are the first to evoke clear evidence of nitration via the electron-transfer pathway. The two steps in the mechanism depicted in Scheme 2 can be established separately.[105] Nitronium cation reacts with benzene and toluene by competitive charge transfer:

$$ArH + NO_2^+ \rightarrow ArH^{+\cdot} + NO_2^{\cdot} \qquad (36)$$

and the atom transfer processes:

$$ArH + NO_2^+ \rightarrow ArHO^+ + NO^{\cdot} \qquad (37)$$

No evidence for the *direct* (one-step) formation of the Wheland intermediate (or any protonated arene) is found, even at relatively high pressures [100 Torr (1 Torr = 133·3 Pa)]. On the other hand, [arene–NO_2^+] complexes are readily generated by combination of benzene and toluene radical cations with $NO_2^{\cdot}$:

$$ArH^{+\cdot} + NO_2^{\cdot} \rightarrow Ar(H)NO_2^+ \qquad (38)$$

Since the complex can be deprotonated by pyridine, a protonated nitroarene structure was indicated. A later study, that utilized $MeOH(NO_2)^+$ as a transfer nitrating agent, also yielded protonated nitrobenzene, i.e.

$$C_6D_6 + MeOH(NO_2)^+ \rightarrow C_6D_6(H)NO_2^+ + MeOH \qquad (39)$$

The structure of the product can be probed by collisionally induced dissociation spectroscopy (on a time-scale of 10 μs). The structure corresponds to the *O*-protonated nitrobenzene (d_6), which is presumably formed via the isomerization of the Wheland intermediate. The formation of an intermediate prior to the σ-complex formation is strongly suggested by a leveling-off of the gas-phase rate constant as the substrate reactivity increases from benzene to toluene to mesitylene.[104] Further investigation of the intermediate is limited by the relatively long time-scale of this measurement technique. Nevertheless, for NO_2^+ at least, the results indicate that arene activation leading to nitration proceeds by the two-step ET reaction mechanism.

Unlike NO_2^+, nitrosonium reacts with benzene and toluene by a straightforward combination, i.e.

$$ArH + NO^+ \rightarrow Ar(H)NO^+ \qquad (40)$$

The product complex is not deprotonated by either pyridine or tetrahydrofuran, which implies that it is a π-complex.[106] However, in view of the appreciable barrier for deprotonation of the nitroso-substituted σ-complex in solution (k_H/k_D is greater than 3·0 for nitrosation of anisole),[55] such a conclusion may not be warranted.

6.3. Theoretical calculations

Theoretical calculations are not bound by the time constraints inherent in experimental observation, and can thus be used to probe very early (ps–fs) intermediates and transition states. For *ab initio* and MNDO calculations, the modeling of solvation is difficult, and thus the results relate mainly to the gas phase. MNDO calculations largely confirm the gas-phase experimental results, and thus indicate that the nitration of benzene and the alkylbenzenes with NO_2^+ proceeds through the radical pair,[107] a result which coincides with earlier lower level calculations based on ionization potentials.[108,109] This study particularly emphasizes the facile recombination of $NO_2^{\cdot}$ with $ArH^{+\cdot}$ to generate *ipso*-substituted σ-complexes (for example, with *p*-xylene cation radical) owing to the enhanced spin density on the *ipso* carbon atom. Theoretical analysis of the one-step electrophilic attack predicts no attack at the *ipso* position. This study supports earlier qualitative evidence that the substitution pattern in the nitration of substituted benzenes correlates well with the hyperfine coupling constants of the corresponding aromatic radical cations.[110]

Calculations clearly show that the π-complexes (EDA complexes) discussed in Section 4 are viable intermediates along the nitration pathway. Even for arenes and NO_2^+ that are restricted to their ground-state geometries, π-complex stabilization energies of 6·0 and 7·5 kcal mol^{-1} are calculated for the [benzene, NO_2^+] and [toluene, NO_2^+] complexes, respectively, with a degree of charge transfer from electrophile to arene corresponding to 0.04 (benzene) and 0.08 (toluene). The geometries of the complexes, as optimized by MNDO methods, consist of linear O—N—O moieties parallel to the plane of the aromatic ring and aromatic ring–NO_2 distances of 4·0–4·1 Å. No changes in bond distances and angles are apparent in either arene or NO_2 fragments. Thus these π-complexes correspond structurally to weak EDA complexes despite their appreciable stabilization energies.[111]

Another approach to the theoretical exploration of aromatic nitration reaction probes the feasibility of the initial ET step on the basis of Marcus theory.[112] Using this method, Eberson and Radner[19,113] calculate the rate constant for outer-sphere electron transfer from arenes (such as naphthalene) to NO_2^+ to be substantially too slow (by a factor of 10^{14}) to account for the diffusion-controlled rate of nitration. This striking result has been repeatedly cited as a hindrance to the reconciliation of ET mechanisms with the observed facts about nitration. However, the result should be accepted with some skepticism in light of the following observations. (1) The intermediacy of the [arene, NO_2^+] π-complex, with stabilization energies of several kcal mol^{-1} is established by gas-phase and theoretical studies, as well as by analogy with the corresponding isolated and characterized [arene, NO^+] complexes. Marcus theory is inadequate to treat electron transfer between strongly coupled ($-\Delta G_{\mathrm{EDA}} > 1$ kcal mol^{-1}) redox centers.[114] (2) Experimental evidence from gas-phase and CIDNP studies indicate that electron transfer from aromatic systems to NO_2^+ can occur at very fast rates. Reconciliation of such calculations with experimental results requires the abandonment of the outer-sphere model, and thus the quantitative aspects of Marcus theory. Indeed, the inapplicability of Marcus theory to most organic reactions[115,116] is now fully recognized.[117]

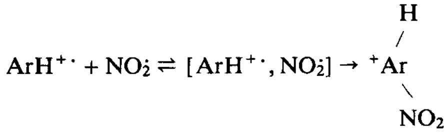
6.4. CIDNP

The discovery of chemically induced dynamic nuclear polarization (CIDNP)[118] in the products of aromatic nitration adds a powerful technique to the study of electrophilic aromatic substitution. Because the nuclear spins in a radical pair modulate the rate of (singlet–triplet) intersystem crossing, and the probability of reaction (combination or disproportionation) or cage escape, the products of these two pathways are formed with highly polarized, non-Boltzmann nuclear spin populations. The NMR spectra of such products, recorded during or immediately after reaction, will show emission (E) or enhanced absorption (A) lines. The characteristics of the radical-pair intermediates determine the sign (E or A) of these anomalous NMR spectral features. The recent work of Ridd[22] has focused on the interpretation of the CIDNP spectra of the ^{15}N nucleus (principally) of the products of nitrations with nitric acid. Thus, when mesitylene is nitrated with $H^{15}NO_3$, the ^{15}N NMR signal of nitromesitylene is observed in emission. The intensity of the polarization increases by a factor of 20 on addition of sodium nitrite to the solution.[67] Similar emissions from the nitroarene are observed when *p*-nitrophenol[68] and other phenols,[84] durene,[69] naphthalene[119] and aromatic amines[120] are nitrated. These CIDNP results, combined with earlier kinetic studies, enabled Ridd to clarify the nature of nitrous acid-catalyzed nitration in the following way.

The initial reaction is the oxidation of the arene by NO^+ to yield the cation radical and $NO^{\cdot}$. Nitric oxide reacts with NO_2^+ or NO_2Y^+ to regenerate NO^+ and form $NO_2^{\cdot}$, which subsequently couples with the cation radical in the CIDNP-generating step (Scheme 4). This radical pair, formed by diffusive encounter of free radicals and giving rise to a product of cage collapse, is predicted[121] to form nitroaromatics ($ArNO_2$) with emission in the ^{15}N NMR spectra.

$$\mathrm{ArH + NO^+ \rightleftharpoons ArH^{+\cdot} + NO^{\cdot}} \qquad (41)$$

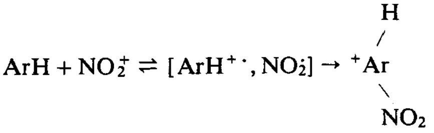
$$\mathrm{NO^{\cdot} + NO_2Y^+ \rightarrow NO^+ + NO_2^{\cdot} + Y} \qquad (42)$$



$$\mathrm{ArH^{+\cdot} + NO_2^{\cdot} \rightleftharpoons [ArH^{+\cdot}, NO_2^{\cdot}] \rightarrow \overset{H}{\underset{NO_2}{{}^{+}Ar}}} \qquad (43)$$

Scheme 4

When the NO^+-catalyzed nitration of durene is temporarily suppressed by the addition of sodium azide to the reaction mixture, the ^{15}N NMR signals of nitrodurene show enhanced absorption. Ridd interpreted this result as follows. The [$ArH^{+\cdot}$, $NO_2^{\cdot}$] pair is formed via an initial electron-transfer step, i.e.

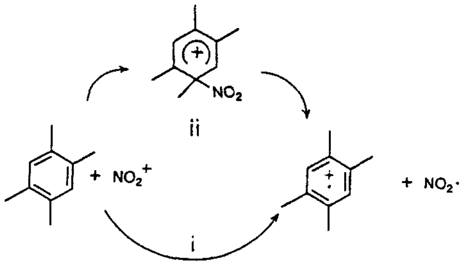


$$\mathrm{ArH + NO_2^+ \rightleftharpoons [ArH^{+\cdot}, NO_2^{\cdot}] \rightarrow \overset{H}{\underset{NO_2}{{}^{+}Ar}}} \qquad (44)$$

The radical pair in this case is formed from closed-shell precursors (the aromatic substrate and nitronium cation) rather than from freely diffusing $ArH^{+\cdot}$ and $NO_2^{\cdot}$ [as in Scheme 4, equation (43)]. Collapse of the radical pair in equation (44) will yield products with the opposite polarization to that observed in the products of the NO^+-catalyzed nitration.

Enhanced absorption signals are also observed from α-nitronaphthalene in the course of the nitration of naphthalene with $H^{15}NO_3$–NaN_3. However, no polarization of nitromesitylene is observed during the nitration of mesitylene in the presence of azide. It is concluded that the nitrations of naphthalene and durene with HNO_3 proceed in part through the $[ArH^{+\cdot}, NO_2^{\cdot}]$ radical pair in Scheme 2, but the nitration of mesitylene proceeds via the classical (one-step) electrophilic mechanism.

The presence of CIDNP in a reaction product is decisive evidence that at least part of the nitration occurs by way of a radical-pair intermediate.[122] Unfortunately, the phase of the polarization (E or A) merely imposes certain *restrictions* on the identity of the radical pair, and an unambiguous assignment is not always possible. Even if the radical pair is identified satisfactorily, the mechanism of its formation may still be ambiguous. For example, the polarization of nitrodurene formed by nitration of durene with HNO_3 in the presence of azide is consistent with a radical pair formed either by direct electron transfer [path (i), Scheme 5] or by homolysis of the *ipso* intermediate [path (ii)], since the same radical pair is formed in both cases. For these reasons, CIDNP provides us so far with only limited information concerning processes on the time-scale (ps) relative to the initial electron-transfer step.



Scheme 5

A more fundamental problem with CIDNP is that the generation of the polarization requires that (a) some radical pairs undergo diffusive escape and (b) the products arising from the escape and the recombination pathways be different [otherwise the equal and opposite polarizations will cancel in the final product(s)]. These conditions are not fulfilled for all nitrations. For example, mesitylene is ring nitrated in high yield in both the presence and absence of the nitrite catalyst. In this case, conventional nitration and free-radical combination give the same nitromesitylene product, and condition (b) is violated. In addition, it is certainly possible that some nitrations can occur without any cage escape [violating condition (a)]. No CIDNP is expected under this condition. For these reasons, the absence of CIDNP cannot be regarded as strong negative evidence for the absence of a radical-pair pathway in any reaction. [This point has been noted several times.][122–124] Thus, the inference that electron transfer is not operative in the NO_2^+-promoted nitrations of mesitylene and *p*-xylene is not warranted. Moreover, quantitative conclusions about the partitioning of reactions between radical and non-radical reactions based on the degree of polarization observed (enhancement ratios, etc.) should be treated with caution in view of the many factors (cage escape ratios, relaxation times, reaction rates, etc.) which determine the presence and intensity of the CIDNP.

Two intriguing CIDNP observations remain incompletely understood at present. (1) The nitration of durene in the absence of NO^+ generates a polarized signal attributed to dinitrodurene.[69] This signal is in emission, in contrast to the enhanced absorption observed from nitrodurene (therefore, it cannot arise from a simple non-radical pair nitration of durene, which would generate dinitrodurene with the same polarization as nitrodurene). The authors suggested that $NO_2^{\cdot}$ escaping from the $[\text{durene}^{+\cdot}, NO_2^{\cdot}]$ radical pair is reoxidized to a nitrogen(V) species, which nitrates nitrodurene by a non-radical process. In this case, however, emission polarization of the incoming nitro group would be expected to cancel the enhanced absorption of the mononitrodurene and yield no net CIDNP in the dinitrodurene product. (2) A recent publication from Ridd's group reports the results from the NO^+-catalyzed nitration of phenols.[84] In one case the ^{13}C NMR signals of the starting material, 2-methyl-6-nitrophenol, are observed in emission. The observation of CIDNP in the arene substrate, ArH, implies the existence of a pathway leading from a radical pair (either $[ArH^{+\cdot}, NO_2^{\cdot}]$ or $[ArH^{+\cdot}, NO^{\cdot}]$) back to the starting material. It seems more likely that this pathway is the reverse of the initial step in Scheme 4 [oxidation of the phenol with NO^+ in equation (41)], rather than reversal of all three steps (as suggested by the authors). The phase of the polarization, however, permits either interpretation.

Despite the ambiguities associated with CIDNP arising from the NO^+-catalyzed nitration process, the persistence of polarization in the absence of NO^+ catalysis indicates that a radical-pair intermediate is applicable to at least part of the nitration. This evidence for radical-pair intermediates is particularly valuable, since CIDNP is observed in ordinary organic solvents under typical conditions of preparative nitration.

The gas phase, theoretical and CIDNP approaches with the time resolutions that are relevant to the activation step all give support to the two-step ET mechanism for nitration. The logical next objective is the direct observation of the intermediates on the pertinent (ps–ns) time-scales.

7. CHARGE-TRANSFER NITRATION

Newly developed short-pulse lasers and concomitant advances in fast spectroscopic detection techniques allow our understanding of both simple and complex *reaction networks* to be vastly expanded, owing to access times of picoseconds and femtoseconds.[125-131] The application of these techniques to chemical problems has hitherto been restricted to the examination of simple single-step chemical reactions, such as electron transfer[132], bond homolysis,[133] proton transfer,[134] ligand dissociation and reassociation[135] and double-bond isomerization.[136] It should be noted, however, that a number of complicated biochemical problems, such as the visual cycle,[137] photosynthesis[138] and the mitochondrial respiratory chain,[139] have been successfully attacked by a combination of time-resolved and other spectroscopic approaches. The complexity of the system is no deterrent to the use of the new techniques. Thus the initiation of nitration by charge-transfer activation provides an opportunity to observe directly the relevant intermediates in the following way.

7.1. Arene cation radicals as critical intermediates

Owing to the enhanced electrophilic reactivity of nitronium salts even at low temperature, they are impractical as photonitrating agents. On the other hand, nitronium carriers (NO_2Y^+) such as tetranitromethane and *N*-nitropyridinium cations are sufficiently unreactive to form persistent EDA complexes with a wide range of aromatic nucleophiles. Direct CT activation of the EDA complexes is effected by the irradiation of their charge-transfer bands, which are spectrally separated (red shifted) from the local bands of either arene or nitrating agent. As a result, local excitation of the uncomplexed donor or acceptor does not interfere with the CT photostimulation process.[54a]

Photoinduced electron transfer has been shown by picosecond and sub-picosecond spectroscopy to be the initial step in all charge-transfer excitations,[132,140-142] i.e.

$$\underset{\text{EDA complex}}{[D, A]} \xrightarrow{h\nu_{CT}} \underset{\text{radical pair}}{[D^{+\cdot}, A^{-\cdot}]} \qquad (45)$$

This transformation was first observed on irradiation of the charge-transfer band of the EDA complexes formed from various anthracene donors (AN) with the tetracyanoethylene (TCNE) acceptor.[140] Anthracene radical cations ($AN^{+\cdot}$) and the radical anion of tetracyanoethylene ($TCNE^{-\cdot}$) are both observed within the rise time (25 ps) of the mode-locked Nd:YAG laser. Since these initial results appeared, further studies carried out on the picosecond and sub-picosecond timescales[141-143] have confirmed the original Mulliken formulation in equation (45).

The $[AN^{+\cdot}, TCNE^{-\cdot}]$ pair formed by CT irradiation is highly transient, and it decays to the original spectral baseline within 60 ps, owing to the rapid back-electron transfer (k_{BET}) to form the original EDA complex, i.e.

$$[AN, TCNE] \underset{k_{BET}}{\overset{h\nu_{CT}}{\rightleftharpoons}} [AN^{+\cdot}, TCNE^{-\cdot}] \qquad (46)$$

The rapidity of back electron transfer in equation (46) effectively precludes the diffusive separation of the radicals or other reactions of the individual radical ions. In contrast, the irradiation of the corresponding complexes of anthracenes with tetranitromethane (TNM) results in the immediate ($\tau < 10$ ps) formation of the trinitromethide anion (with $\lambda_{max} = 350$ nm) to indicate the fast fragmentation of the anion radical, $C(NO_2)_4^{-\cdot}$,[141,144] i.e.

$$[AN^{+\cdot}, C(NO_2)_4^{-\cdot}] \rightarrow [AN^{+\cdot}, NO_2^{\cdot}, C(NO_2)_3^{-}] \qquad (47)$$

The formation of $NO_2^{\cdot}$, which cannot be directly observed by time-resolved UV–visible measurements (owing to its diffuse absorption[145]), is inferred from the stoichiometry of the fragmentation and the observation of $NO_2^{\cdot}$ in the radiolytic reductions of TNM.[146] The radical cation of 9-methylanthracene (MA) is also formed by CT activation of the [MA, nitropyridinium] complex, and it persists unchanged throughout the time of observation (5 ns).[147] Back electron transfer is thus obviated by fast fragmentation of the *N*-nitropyridyl radical, $MeOPyNO_2^{\cdot}$, i.e.

$$[MA^{+\cdot}, MeOPyNO_2^{\cdot}] \rightarrow [MA^{+\cdot}, NO_2^{\cdot}, MeOPy] \qquad (48)$$

Even relatively electron-poor aromatic donors, such as naphthalene or benzene, are efficiently oxidized to their cation radicals by the process of CT activation (Figure 1).

The initial CT photoinduced electron transfer from aromatic donors to either TNM or nitropyridinium in equations (47) and (48) generates a triad of potentially reactive intermediates consisting of the aromatic cation radical, $NO_2^{\cdot}$, and pyridine or trinitromethide. Triad formation prevents back electron transfer, and it thus allows productive photonitration to take place.

Efficient formation of arene radical cations ($ArH^{+\cdot}$) by CT activation of a wide variety of aromatic donors (Table 2) with tetranitromethane or nitropyridinium has confirmed the generality of triad formation, i.e.

$$[ArH, NO_2Y^+] \xrightarrow{h\nu_{CT}} [ArH^{+\cdot}, NO_2^{\cdot}, Y] \qquad (49)$$

Transient quantum yields (Φ_{ArH^+}) provide a quantitative measure of the efficiency of the formation of the triad (Table 3). The magnitudes of Φ_{ArH^+}, combined with the quantum-efficient formation of products ($\Phi_P = 0{\cdot}2$–$0{\cdot}8$), leave no doubt that photonitrations proceed via the triad in equation (49).[101]

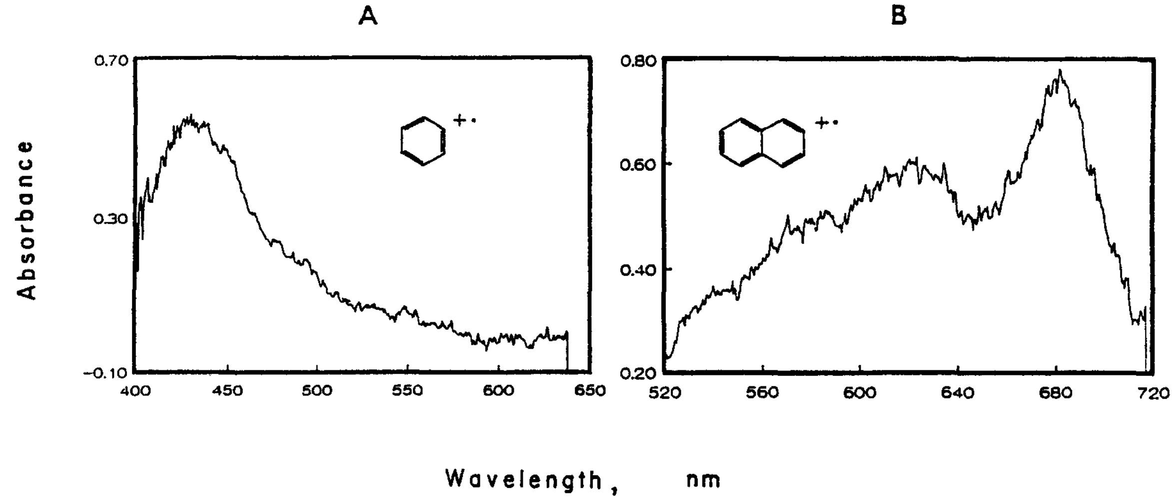


Figure 1. Transient spectra of the cation radicals of (A) benzene and (B) naphthalene acquired at 60 ps following the application of a (355 nm) 30 ps laser pulse to a solution of the aromatic EDA complex with (A) *N*-nitropyridinium and (B) 4-methoxy-*N*-nitropyridinium in acetonitrile

Table 2. Picosecond spectra of aromatic cation radicals generated via CT photoactivation of aromatic EDA complexes with nitrating agents[a]

Arene	Nitrating agent[b]	λ_{max} (nm)
Benzene	$\mathrm{MeOPyNO_2^+}$	428
Toluene	$\mathrm{MeOPyNO_2^+}$	430
p-Xylene	$\mathrm{MeOPyNO_2^+}$	440
Mesitylene	$\mathrm{MeOPyNO_2^+}$	455
Durene	$\mathrm{MeOPyNO_2^+}$	465
Hexamethylbenzene	$\mathrm{MeOPyNO_2^+}$	495
Anisole	$\mathrm{MeOPyNO_2^+}$	435
Naphthalene	TNM	690
	$\mathrm{MeOPyNO_2^+}$	690
1,4-Dimethylnaphthalene	TNM[c]	710
	$\mathrm{MeOPyNO_2^+}$	710
Anthracene	TNM[d]	710
9-Methylanthracene	$\mathrm{MeOPyNO_2^+}$	690

[a] Observed 50 ps after photoactivation with a mode-locked Nd:YAG laser of the EDA complex of the arene with tetranitromethane (TNM) or 4-methoxy-*N*-nitropyridinium ($\mathrm{MeOPyNO_2^+}$ as the $\mathrm{BF_4^-}$ salt) in MeCN or $\mathrm{CH_2Cl_2}$.

[b] Taken from Ref. 101 except where indicated.

[c] Ref. 149b.

[d] Ref. 141.

[e] Ref. 147.

Table 3. Quantum yields for the generation of aromatic cation radicals[a]

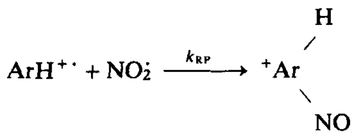
Aromatic donor	λ_{mon} (nm)	ε ($\mathrm{l\ mol^{-1}\,cm^{-1}}$)	$\Phi^{b}_{\mathrm{ArH}^{+\cdot}}$[b]
Anthracene	715	12500	0·72
Naphthalene	580	3600	0·82
Anisole	435	4800	0·80
Hexamethylbenzene	495	1800	0·56
Durene	465	1800	0·56
p-Xylene	440	2050	0·25
Toluene	435	2000	0·14

[a] Generated by CT activation of the aromatic EDA complexes with $\mathrm{MeOPyNO_2^+}$ in MeCN. Taken from Ref. 101.

[b] At 100 ns following the 10 ns laser flash.

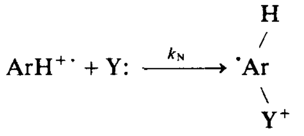
7.2. Fate of the reactive triad

Aromatic cation radicals generated by the CT activation of $[\mathrm{ArH, NO_2Y^+}]$ complexes persist for several microseconds, which is much longer than the lifetime of (geminate) radical or radical-ion pairs in acetonitrile and dichloromethane. Since the original triad undergoes diffusive separation, the subsequent reactions represent the recombination of free (transient) species. The contribution of geminate processes[148] is negligible. This conclusion is quantitatively exemplified by the second-order kinetics observed for cation-radical decay in polar solvents (MeCN or $\mathrm{CH_2Cl_2}$) in the absence of additives.[101,149–151] The latter directly indicates that the radical cation decays by reaction with one of the other triad components, either $\mathrm{NO_2^{\cdot}}$ via radical-pair collapse,



$$\mathrm{ArH^{+\cdot} + NO_2^{\cdot}} \xrightarrow{k_{RP}} {}^{+}\mathrm{Ar}\begin{matrix}\diagup\mathrm{H}\\ \diagdown\mathrm{NO_2}\end{matrix} \qquad (50)$$

or Y via nucleophilic attack on ArH$^{+\cdot}$,



$$ArH^{+\cdot} + Y: \xrightarrow{k_N} {}^{\cdot}Ar\begin{matrix} /H \\ \\ \backslash Y^+ \end{matrix} \quad (51)$$

[For an anionic nucleophile, such as trinitromethide, equation (51) constitutes an ion-pair collapse.] The ambiphilic reactivity of aromatic cation radicals (as radicals and as electrophiles) gives rise to this mechanistic dichotomy. Since equation (50) duplicates the second step in the two-step (ET) mechanism for aromatic nitration in Scheme 2, CT photoactivation provides a means of directing the course of the reaction along the ET pathway. In this way thermal activation can be directly compared with the (enforced) ET activation, provided that the competing reactivity with the cogenerated nucleophile, Y, is recognized and controlled.

7.3. Radical-pair collapse: dialkoxybenzenes

Electron-rich dialkoxybenzenes are easily photonitrated in high yield by CT activation of the EDA complexes with tetranitromethane, as indicated in Table 4. Nitration is accompanied by one equivalent of nitroform, according to the stoichiometry in the equation

$$ArH + C(NO_2)_4 \xrightarrow{h\nu_{CT}} ArNO_2 + HC(NO_2)_3 \quad (52)$$

Time-resolved spectroscopy shows the rapid (<25 ps) formation of the dialkoxybenzene cation radical (with spectral absorption between 400 and 500 nm) simultaneously with trinitromethide ($\lambda_{max} = 350$ nm). The subsequent decay of ArH$^{+\cdot}$ on the millisecond time-

Table 4. Charge-transfer nitration of dialkoxybenzenes[a]

Aromatic donor	Solvent	Isomer distribution (%) 2-NO_2^-	3-NO_2^-	4-NO_2^-
1,4-Dimethoxybenzene	MeCN	100	–	–
	CH_2Cl_2	100	–	–
1,2-dimethoxybenzene	MeCN	–	0	100
	CH_2Cl_2		0	100
4-Methoxyphenoxyacetic acid	MeCN	30	70	
	CH_2Cl_2	30	70	
3,5-Dimethoxyphenylacetonitrile	CH_2Cl_2	100	–	0
2-(4-methoxyphenoxy)ethanol	MeCN	60	40	0

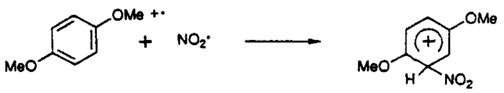
[a] Taken from Ref. 149b.

Table 5. Second-order rate constants for the disappearance of aromatic cation radicals[a] in CT nitration

Aromatic donor	Solvent[b]	Nitrating agent, NO_2Y^+	k_2 ($l\ mol^{-1} s^{-1}$)
1,4-Dimethoxybenzene	CH_2Cl_2[c]	TNM	$5{\cdot}0 \times 10^7$
	MeCN[c]	TNM	$5{\cdot}7 \times 10^7$
4-Methylanisole	MeCN[d]	MeOPyNO$_2^+$	$1{\cdot}6 \times 10^9$
	MeCN	TNM	$1{\cdot}3 \times 10^9$
	CH_2Cl_2	TNM	$9{\cdot}3 \times 10^9$
	CH_2Cl_2[e]	TNM	$1{\cdot}7 \times 10^9$
4-Chloroanisole	MeCN	TNM	$1{\cdot}4 \times 10^9$
	MeCN[d]	MeOPyNO$_2^+$	$1{\cdot}4 \times 10^9$
	CH_2Cl_2	TNM	$1{\cdot}6 \times 10^{11}$
4-Bromoanisole	MeCN	TNM	$2{\cdot}0 \times 10^9$
	MeCN[d]	MeOPyNO$_2^+$	$2{\cdot}0 \times 10^9$
	CH_2Cl_2	TNM	$2{\cdot}9 \times 10^{11}$

[a] Generated by CT activation of the aromatic EDA complex with NO_2Y^+.
[b] Taken from Ref. 150 except where indicated.
[c] Ref. 149.
[d] Ref. 101.
[e] Containing 0·1 M tetrabutylammonium perchlorate.

scale occurs by second-order kinetics with a rate constant, k_2, the value of which is the same in both acetonitrile and dichloromethane (Table 5). Moreover, it is unaffected by added inert salt. These results rule out ion-pair collapse, and the high yields of nitration products signify the decay process as radical-pair collapse, i.e.



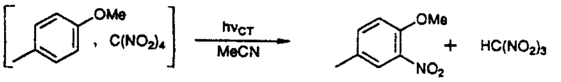
(53)

followed by the deprotonation of the σ-complex.[149] [The radical pair collapse in equation (53) is probably not simple and may involve *ipso* intermediates.]

7.4. Competing radical pair and nucleophilic reactions

7.4.1. *Anisoles*

A more intricate reaction pattern pertains when the photonitration is extended to weaker arene donors such as the anisoles. For example, 4-methylanisole (Ma) is quantitatively nitrated on CT activation of the [Ma, TNM] complex in acetonitrile according to equation (54).[150] On the other hand, the same reaction carried out in dichloromethane yields the product of trinitromethylation [equation (55)], which is diagnostic of the incursion of the nucleophilic attack. Trinitromethylation is completely replaced by nitration if an inert salt (tetra-*n*-butylammonium perchlorate, TBAP) is added to the reaction mixture prior to photoactivation (entry 4 in Table 6). The solution to this mechanistic conundrum is revealed by kinetic investigation on the microsecond time-scale. Thus, the cation radical from 4-methylanisole ($Ma^{+\cdot}$) decays in dichloromethane by second-order kinetics with a rate constant $k_2 = 9{\cdot}3 \times 10^9\,\mathrm{l\,mol^{-1}\,s^{-1}}$. Addition of the inert salt TBAP leads to a decrease in the rate constant (by a factor of six) to a value essentially the same as that observed in acetonitrile (Table 5). The solvent effect on the products, combined with the rate data, points to the predominance of the ion-pair collapse process in dichloromethane, as shown in equation (56).



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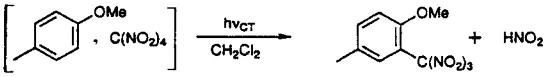
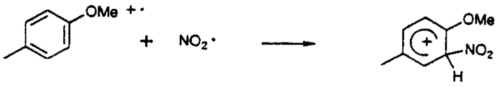


(55)

(56)

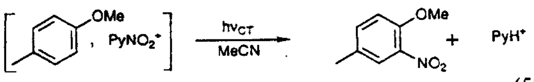
In contrast, the principal pathway for the disappearance of $Ma^{+\cdot}$ in the polar solvent, acetonitrile, involves radical-pair collapse [equation (57)].



(57)

Added salt suppresses the ion-pair collapse in equation (56), and it causes the process to revert to the radical-pair collapse in equation (57) with a rate constant $k_2 \approx 10^9\,\mathrm{l\,mol^{-1}\,s^{-1}}$, which is largely insensitive to solvent polarity. [The effect of added salt arises from the reduced reactivity of the ion pairs $Bu_4N^+C(NO_2)_3^-$ and $ArH^{+\cdot}ClO_4^-$ compared with the free ions.[151,152]] The key to promoting the desired nitration reaction in this system, and minimizing the competing ion-pair collapse, lies in the choice of a polar solvent (MeCN) and the addition of salt.[150]

Nitration can also be effected by the CT activation of the EDA complex of 4-methylanisole with *N*-nitropyridinium cation according to the stoichiometry in equation (58).



(58)

The rate constant for the second-order decay of the radical cation of 4-methylanisole is $k_2 = 1{\cdot}6 \times 10^9\,\mathrm{l\,mol^{-1}\,s^{-1}}$, which is the same as that observed for $Ma^{+\cdot}$ generated via CT activation of the [Ma, TNM] complex in acetonitrile, or in dichloromethane with added TBAP (Table 5, entries 3, 4 and 6). Similarly, the rate constants for the decay of the haloanisole cation radicals in acetonitrile is the same whether tetranitromethane or $XPyNO_2^+$ is employed as the nitrating agent. In all these systems, high yields of nitroanisoles are obtained. Since the rate constant for cation radical decay is invariant, a common pathway of radical-pair [$ArH^{+\cdot}$, $NO_2^\cdot$] collapse is readily deduced for nitrations in these diverse systems.[101]

The incursion of nucleophilic attack by pyridine bases (inherent to the reactive triad) is evident when weaker donor arenes are subjected to CT activation with *N*-nitropyridinium cations.[101] For example, the activation of the EDA complex of mesitylene with 4-methoxy-*N*-nitropyridinium yields products from both pyridine attack on the cation radical and radical pair ($MES^{+\cdot}$, $NO_2^\cdot$) collapse [equation (59)].

Table 6. Competition between nitration and trinitromethylation following the CT activation of 4-methylanisole[a]

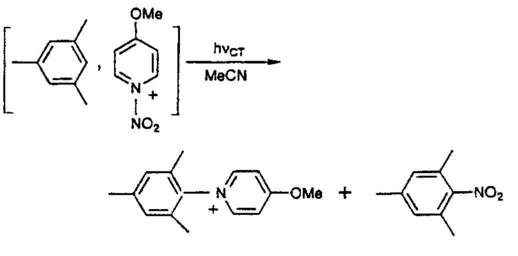
Solvent	Added salt	Product distribution (%)	
		Nitration[b]	Trinitromethylation[c]
MeCN	–	95	5
MeCN	$\mathrm{TBA^+ClO_4^-}$[d]	100	0
$\mathrm{CH_2Cl_2}$	–	5	95
$\mathrm{CH_2Cl_2}$	$\mathrm{TBA^+ClO_4^-}$[d]	95	5
$\mathrm{C_6H_6}$	–	15	85
$\mathrm{C_6H_6}$	$\mathrm{TBA^+ClO_4^-}$[d]	25	75

[a] From CT photolysis of the EDA complex of 4-methylanisole with tetranitromethane in Ref. 150.

[b] Yield of 2-nitro-4-methylanisole.

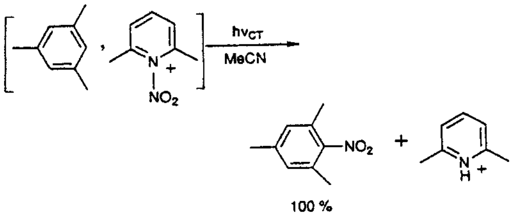
[c] Yield of 2-(trinitromethyl)-4-methylanisole.

[d] Tetra-*n*-butylammonium perchlorate.



(59)

The extent of pyridination is reduced by the addition of trifluoroacetic acid, and it is wholly eliminated by the use of the sterically hindered *N*-nitro-2,6-lutidinium ($\mathrm{LutNO_2^+}$) cation as the nitrating agent [equation (60)].



(60)

Nucleophilic attack by pyridine is manifested more subtly in the CT nitration of anisole with nitropyridinium cations. Anisole is converted into a mixture of *o*- and *p*-nitroanisoles on CT activation of the EDA complexes with nitropyridinium or TNM. *para*-Substitution predominates when $\mathrm{MeOPyNO_2^+}$ (or any other unhindered nitropyridinium cation) is the nitrating agent (entries 1–3 in Table 7), but the sterically hindered $\mathrm{LutNO_2^+}$ gives a more or less statistical distribution ($\frac{1}{2}\ o = p$) of *ortho*/*para* isomers. The suspicion that nucleophilic attack by pyridine on the cation radical influences the product distribution is confirmed by direct measurement of the relevant rate constants using time-resolved techniques. Thus the anisole cation radical ($\mathrm{An^{+\cdot}}$) generated in the presence of either added pyridine (lutidine) or added $\mathrm{NO_2^{\cdot}}$ decays by pseudo-first-order kinetics, to yield the second-order rate constants for nucleophilic collapse (k_N) and radical-pair collapse (k_{RP}). The rate constant for reaction of $\mathrm{An^{+\cdot}}$ with pyridine ($k_N = 2{\cdot}5 \times 10^9\ \mathrm{l\,mol^{-1}\,s^{-1}}$) is comparable to the rate of its reaction with $\mathrm{NO_2^{\cdot}}$ ($k_{RP} = 1{\cdot}5 \times 10^9\ \mathrm{l\,mol^{-1}\,s^{-1}}$). By contrast, the rate of lutidine attack is considerably diminished ($k_N = 0{\cdot}3 \times 10^9\ \mathrm{l\,mol^{-1}\,s^{-1}}$). This decrease in k_N reflects the steric hindrance of the lutidine nucleophile to addition. (For alkyl-substituted arenes, deprotonation of the cation radical may become important, particularly with hindered bases.[73,153])

Table 7. Photonitration of anisole in acetonitrile[a]

Nitrating agent, $\mathrm{NO_2Y^+}$	λ_{exc} (nm)	Isomer distribution (%)		
		ortho	*para*	$(\frac{1}{2}o/p)$
$\mathrm{MeOPyNO_2^+}$[b]	350	37	63	0·29
$\mathrm{MePyNO_2^+}$[c]	350	51	49	0·51
$\mathrm{PyNO_2^+}$[d]	350	51	49	0·51
TNM	425	43[e]	53	0·40
$\mathrm{LutNO_2^+}$[f]	400	65	35	0·93
$\mathrm{MeOPyNO_2^+}$	dark	69	31	1.1

[a] By CT activation of the [anisole, $\mathrm{NO_2Y^+}$] complex using light of wavelength longer than λ_{exc}. Taken from Ref. 101.

[b] 4-methoxy-*N*-nitropyridinium as the $\mathrm{BF_4^-}$ salt.

[c] 4-Methyl-*N*-nitropyridinium fluoroborate.

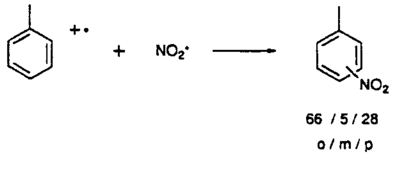
[d] *N*-Nitropyridinium fluoroborate.

[e] *Meta* isomer, 4%.

[f] 2,6-dimethyl-*N*-nitropyridinium.

7.4.2. *Toluene and* tert-*butylbenzene*[152]

Photonitration of toluene with the hindered nitrating agent ($\mathrm{LutNO_2^+}$) derived from 2,6-lutidine affords a mixture of nitrotoluenes that consists of an approximately statistical mixture of *ortho* and *para* isomers, together with a small amount (*ca* 5%) of the *meta* isomer (Table 8). *m*-Nitrotoluene predominates when the CT nitration of toluene is effected by sterically unencumbered nitropyridinium salts or with TNM. The addition of $\mathrm{NO_2^{\cdot}}$ (as $\mathrm{N_2O_4}$) leads to the restoration of the *ortho–para* isomer distribution. Since this pattern of substitution is found when excess $\mathrm{NO_2^{\cdot}}$ is added, it clearly derives from the radical-pair collapse in equation (61).



(61)

Table 8. Photonitration of toluene and *tert*-butylbenzene

Arene	Nitrating agent, $\mathrm{NO_2Y^+}$	Product distribution (%)[a]			
		ortho	*meta*	*para*	*ipso*[c]
Toluene	$\mathrm{PyNO_2^+}$	24	60	16	
	$\mathrm{MeOPyNO_2^+}$	14	59	27	
	$\mathrm{MePyNO_2^+}$	23	54	23	
	$\mathrm{MeOPyNO_2^+}$[b]	66	5	28	
	$\mathrm{LutNO_2^+}$	70	2	28	
tert-Butylbenzene	$\mathrm{MeOPyNO_2^+}$	5	73	22	40
	$\mathrm{MePyNO_2^+}$	4	64	32	27
	$\mathrm{PyNO_2^+}$	6	71	23	16
	$\mathrm{MeOPyNO_2^+}$[d]	7	15	78	17
	$\mathrm{MeOPyNO_2^+}$[b]	16	22	62	2
	$\mathrm{LutNO_2^+}$	6	12	82	2

[a] Isomer distribution of nitrotoluenes and nitro-*tert*-butylbenzenes formed on CT activation of the [arene, $\mathrm{NO_2Y^+}$] complex. Taken from Ref. 101.

[b] In the presence of excess nitrogen dioxide.

[c] Yield of isomeric di-*tert*-butylbenzenes.

[d] In the presence of excess trifluoroacetic acid.

A value of $k_{\mathrm{RP}} = 1{\cdot}0 \times 10^9\,\mathrm{l\,mol^{-1}\,s^{-1}}$ is obtained from the pseudo-first-order decay of $[\text{toluene}]^{+\cdot}$ in the presence of added $\mathrm{NO_2^{\cdot}}$. The predominant nitration at the *meta*-position probably occurs by an addition–elimination[75] pathway analogous to the *meta*-nitration of toluene with acetyl nitrate in carbon tetrachloride.[100] CT nitration with the hindered nitrating agent ($\mathrm{LutNO_2^+}$) provides nitrotoluenes with the normal (electrophilic)[154] substitution pattern, which reflects the inefficiency with which 2,6-lutidine undergoes nucleophilic addition.[73]

Photonitration of *tert*-butylbenzene with $\mathrm{MeOPyNO_2^+}$, $\mathrm{PyNO_2^+}$ or $\mathrm{MePyNO_2^+}$ is characterized by high *meta* content of the isomeric nitrated products (as in the case of toluene). Significant amounts of nitrobenzene and di-*tert*-butylbenzene are products of transalkylation.[80] If the nucleophilic activity of pyridine is eliminated, either by the use of $\mathrm{LutNO_2^+}$ as the nitrating agent or the addition of trifluoroacetic acid or the use of excess $\mathrm{NO_2^{\cdot}}$, the normal pattern of nitration is reinstated.[101]

7.5. Activation of arenes with nitrosonium

In contrast to the efficient photonitrations of arenes with $\mathrm{NO_2Y^+}$, the CT activation of the EDA complexes with the nitrosonium acceptor is chemically unproductive.[155] An investigation using time-resolved spectroscopy noted bimodal decays, on the picosecond and microsecond time-scales. The return of the photogenerated cation radicals to the spectral baseline is attributed to back electron transfer between geminate (ps) and freely diffusing (μs) $\mathrm{ArH^{+\cdot}}$ and $\mathrm{NO^{\cdot}}$ radicals. Kinetic analysis indicates that the $[\mathrm{ArH^{+\cdot}}, \mathrm{NO^{\cdot}}]$ radical pair is held together by bonding forces with $-\Delta G_{\mathrm{RP}}$ ranging from $0{\cdot}5\,\mathrm{kcal\,mol^{-1}}$ for $[\text{toluene}^{+\cdot}, \mathrm{NO^{\cdot}}]$ to $3\,\mathrm{kcal\,mol^{-1}}$ for $[\text{hexamethylbenzene}^{+\cdot}, \mathrm{NO^{\cdot}}]$. Spectral features of the cation-radical absorptions that indicate a significant electronic perturbation of $\mathrm{ArH^{+\cdot}}$ are observed during the *ca* 5 ns lifetime of the bound radical pair.[155] The $[\mathrm{ArH^{+\cdot}}, \mathrm{NO_2^{\cdot}}]$ pair is also be expected to show progressively stronger bonding features on changing the donor from benzene to hexamethylbenzene.

The arene cation radicals generated by the CT activation of the $[\mathrm{ArH}, \mathrm{NO^+}]$ complex in Table 9 decay to the spectral baseline without the formation of nitrosoarenes or other substitution products. This result indicates that the σ-complex is either not formed via $[\mathrm{ArH^{+\cdot}}, \mathrm{NO^{\cdot}}]$ pairs or is inefficiently converted to the nitrosation product. Substrates such as durene or *p*-xylene are activated towards *ipso*-substitution, however, and they may be unsuitable models as typical substrates for nitrosation such as mesitylene and anisole. The cation radicals can be trapped by photolysis of the corresponding *N*-nitrosopyridinium complexes, e.g. equation (62).[156] Electrophilic collapse occurs at

Table 9. EDA complexes of arenes with nitrosonium: first-order rate constants[a] for radical-pair collapse

Arene	E^{0}[b] (V)	$-\Delta G_{\mathrm{RP}}$[c] (kcal mol^{-1})	K_{EDA}[d] (l mol^{-1})	k_{RP}[e] (s^{-1})
Toluene	2·64	26	5	2×10^{10}
p-Xylene	2·35	19	30	1×10^{9}
Durene	2·07	15	450	7×10^{9}
Pentamethylbenzene	1·99	14	5000	4×10^{8}
Hexamethylbenzene	1·86	12	31000	1×10^{8}

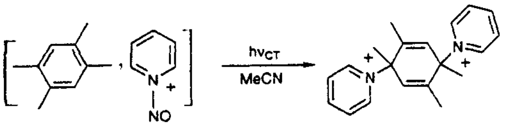
[a] Taken from Ref. 155.

[b] Standard potential (vs NHE) for oxidation in MeCN.

[c] Driving force for radical pair collapse (back electron transfer).

[d] Formation constant of the aromatic EDA complex with nitrosonium cation in acetonitrile, taken from Ref. 59.

[e] Rate constant for collapse of the radical pair.

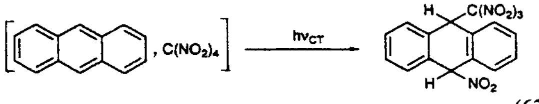

(62)

the *ipso* positions, which are the sites of greatest charge and spin density.[111,157] In all likelihood, the reason for the disparity in rates between NO$^+$ and NO$_2^+$ lies not in the activation steps, but in the differing rates of the follow-up (deprotonation) steps.

Rate constants for combination of NO$^\cdot$ and NO$_2^\cdot$ with cation radicals correspond to essentially diffusion-controlled reactions yet the fate of the [ArH$^{+\cdot}$, NO$_2^\cdot$] pair (nitration) is entirely different from that of the [ArH$^{+\cdot}$, NO$_2^\cdot$] pair (back electron transfer). Deprotonation of the nitroso-substituted Wheland intermediate is associated with an appreciable barrier, and the σ-complex can revert to the starting π-complex. This implies that electron transfer between ArH and NO$^+$ is reversible.[155] It is interesting to note that *ipso* nitrosation does occur readily with arenes substituted by electropositive groups such as —Hg(OCOR),[158] —Tl(OCOR)$_2$[159] and —SiR$_3$,[160] which are better (electrophilic) leaving groups than hydrogen. Thus the photochemical stability of [arene, NO$^+$] complexes is paralleled by the unreactivity of NO$^+$ in electrophilic substitution, despite the efficient activation of the arene by electron transfer.

7.6. Charge-transfer addition of NO$_2$Y$^+$

The formal addition of nitrating agents NO$_2$Y$^+$ to aromatic systems discussed in Section 5.3 can also be brought about in the course of CT activation. For example, anthracene reacts with tetranitromethane by addition of the elements of O$_2$NC(NO$_2$)$_3$ across the 9,10 positions [equation (63)].[96] Naphthalenes react with both tetranitromethane[95,161,162] and nitropyridinium cations[94,161] to yield a mixture of 1,4-adducts and nitronaphthalenes, e.g. equation (64).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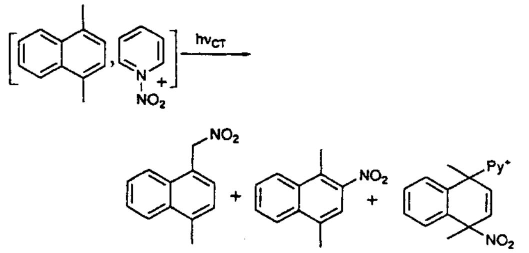

(64)

Table 10 includes the varying distributions of adducts, nitronaphthalenes and side-chain nitration products. Since the adduces undergo rearomatization

Table 10. Nitration and adduct formation in the CT activation of naphthalenes with NO$_2$Y^{+a}

Naphthalene	Solvent	NO$_2$Y$^+$	Product distribution (%)		
			ArNO$_2$^{b}	Adducts^c	Ar′CH$_2$NO$_2$^{d}
1,4-Dimethylnaphthalene	MeCN	TNM	10	40	50
	MeCN^e	TNM	10	67	23
	CH$_2$Cl$_2$	TNM	10	50	40
	MeCN	MeOPyNO$_2^+$	6	61	33
	MeCN^f	MeOPyNO$_2^+$	95	0	5
	MeCN^g	MeOPyNO$_2^+$	8	26	66
	MeCN	LutNO$_2^+$	16	16	68
Naphthalene	MeCN	TNM	18	82	
	MeCN^f	TNM	78	22	
	MeCN	MeOPyNO$_2^+$	71	29	
	MeCN^f	MeOPyNO$_2^+$	>99	<1	
	MeCN^g	MeOPyNO$_2^+$	90	10	
	MeCN	LutNO$_2^+$	>99	<1	

[a] Irradiated at 23 °C with focused light unless specified otherwise. Taken from Ref. 94.
[b] 2-Nitro-1,4-dimethylnaphthalene from 1,4-DMN and 1- and 2-nitronaphthalene from naphthalene.
[c] Isomeric mixture of *ipso*-adducts.
[d] 1-Nitromethyl-4-nitronaphthalene.
[e] Photolyzed at 0 °C.
[f] Contains 5 vol.% trifluoroacetic acid.
[g] Photolysis effected with diffuse light.

under typical preparative (work-up) conditions to yield nitronaphthalenes, the adducts must be examined *in situ* by NMR techniques. Three experimental variables control the yield of adducts relative to nuclear nitration: (1) addition of trifluoroacetic acid diverts the course of the reaction from adduct formation to nuclear nitration (entries 5, 9 and 11 in Table 10), (2) irradiation with diffuse light (rather than a focused beam) increases the yields of side-chain nitrated 1,4-dimethylnaphthalene (entry 6) and ring-nitrated naphthalene (entry 12) at the expense of the adducts; and (3) the sterically hindered *N*-nitro-2,6-lutidinium affords either diminished or no yield of adducts. Facets (1) and (3) point to the involvement of the pyridine (or trinitromethide) nucleophile in adduct formation. Accordingly, the fate of the cation radical is studied directly by time-resolved spectroscopy to resolve the mechanistic dilemma inherent to these addition–substitution reactions.

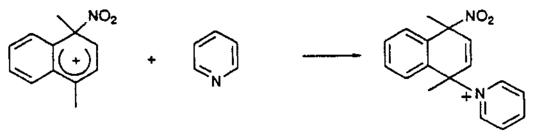
When generated by the CT activation of EDA complexes with either $MeOPyNO_2^+$ or TNM, the decay of the arene cation radical follows second-order kinetics. The strong effect of added salt on the decay of 1,4-dimethylnaphthalene cation radical ($DMN^{+\cdot}$) in dichloromethane (Table 11, entries 5–7) establishes the prevailing process as ion-pair annihilation of [$DMN^{+\cdot}$, trinitromethide] ion pairs, comparable to the alkylation process with the anisoles (see above). The decay rates of $DMN^{+\cdot}$ in acetonitrile are considerably diminished (compare entries 1 and 5) compared with the value of the rate constant obtained in dichloromethane (entry 5). Despite the considerable effect of added trifluoroacetic acid on the distribution of products, the decay of the cation radical is essentially unaffected (compare entries 1 and 3 with 2 and 4). Accordingly, the decay of the cation radicals in acetonitrile is ascribed to radical-pair collapse (k_{RP}). This assignment is confirmed by direct measurement of k_N and k_{RP}. Pseudo-first-order decays of $NAPH^{+\cdot}$ in the presence of $NO_2^{\cdot}$ yield a rate constant $k_2 = 4{\cdot}0 \times 10^9\,l\,mol^{-1}\,s^{-1}$, which is identical (within experimental error) with that observed from its second-order decay when generated from TNM or $MeOPyNO_2^+$. The corresponding rate constant for reaction with pyridine is slower by an order of magnitude.[94] Indeed, the addition of trinitromethide (as the tetrabutylammonium salt) left the decay of the naphthalene cation radical in acetonitrile unaffected, to emphasize the unimportance of ion-pair collapse in this solvent.[94] (Picosecond studies have established that the geminate ion pairs of various anthracene cation radicals with trinitromethide undergo 100% cage escape with no component of ion-pair collapse in acetonitrile.[151,152])

High yields of side-chain nitro compounds and adducts (up to 70%) are characteristic of the reaction of 1,4-dimethylnaphthalene with TNM or *N*-nitropyridinium.[95,161] The presence of the *ipso* σ-intermediate is indicated, and the minor 2-nitro-1,4-dimethylnaphthalene product results from deprotonation of the 2-nitro-substituted (Wheland) intermediate. The fate of the *ipso* intermediate is critically dependent on the role of pyridine. Nucleophilic addition of pyridine yields adducts such as those illustrated in equation (65). If the addition is frustrated by steric hindrance, deprotonation yields the sidechain nitroproduct. Finally, removal of both the side-chain deprotonation and the nucleophilic addition pathways (by the

Table 11. Second-order rate constants for the spectral decay of naphthalene cation radicals[a]

Cation radical[b]	NO_2Y^+	Solvent	Additive	k_2 ($10^8\,l\,mol^{-1}\,s^{-1}$)
1,4-$DMN^{+\cdot}$	TNM	MeCN	–	3·0
	TNM	MeCN	TFA[c]	5·0
	$MeOPyNO_2^+$	MeCN	–	6·0
	$MeOPyNO_2^+$	MeCN	TFA[c]	3·0
	TNM	CH_2Cl_2	–	440[d]
	TNM	CH_2Cl_2	TBAP[f]	55[d]
	TNM	CH_2Cl_2	TBAP[g]	10[d]
$NAPH^{+\cdot}$	TNM	MeCN	–	33[e]
	$MeOPyNO_2^+$	MeCN	–	30[e]

[a] Generated by CT activation at 23 °C of the EDA complexes derived from the naphthalene derivative and either tetranitromethane (TNM) or 4-methoxy-*N*-nitropyridinium ($MeOPyNO_2^+$). Taken from Ref. 161 except where indicated.
[b] 1,4-Dimethylnaphthalene and naphthalene cation radicals.
[c] Trifluoroacetic acid (5% v/v).
[d] Ref. 95.
[e] Ref. 94.
[f] Contains 0·005 M tetra-*n*-butylammonium perchlorate.
[g] Contains 0·02 M tetra-*n*-butylammonium perchlorate.



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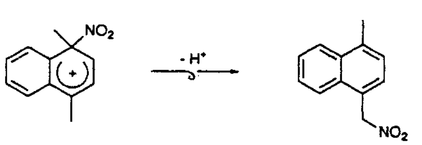

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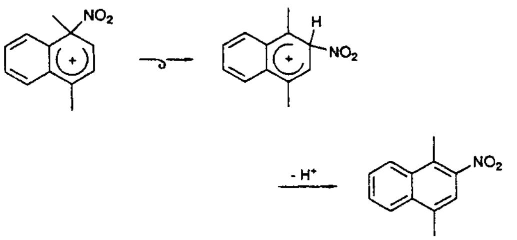
addition of trifluoroacetic acid) allows the (relatively slow)[31] rearrangement of the σ-intermediate to the Wheland intermediate, which yields 2-nitro-1,4-dimethylnaphthalene [equation (67)].



(67)

The effect of light intensity operates chiefly by modulating the steady-state concentration of photogenerated pyridine. The high photon-flux density obtained from a focused beam of light generates high local concentrations of pyridine. Efficient interception of pyridine by the σ-intermediate forms the *ipso*-adduct [equation (65)]. Low light levels imply low concentrations of pyridine, which permit the incursion of the deprotonation [equation (66)].[161]

8. IMPLICATIONS OF CHARGE-TRANSFER ACTIVATION FOR ELECTROPHILIC AROMATIC NITRATION

The foregoing experiments demonstrate that the mechanism of photonitration of arenes with NO_2Y^+ via CT activation proceeds according to the two-step mechanism: initial electron transfer, followed by radical–radical coupling of the [$ArH^{+\cdot}$, $NO_2^{\cdot}$] fragments. Interference from the combination of $ArH^{+\cdot}$ with the cogenerated nucleophile has been accounted for, and the means for neutralizing its effect, by solvent, salt and steric effects, can be successfully employed. The absence of a kinetic isotope effect on the reaction of the cation radicals of anisole[101,149,150] and naphthalene[94,95] derivatives accords with the kinetic distinction of CT activation from the follow-up reactions of the σ-complexes. In this respect photonitration parallels the electrophilic activation process.

When photonitrations are compared with nitrations effected under more usual electrophilic conditions, the arene substrates fall into two classes: (1) for reactive arenes such as the dimethoxybenzenes, the product distributions are the same, independent of whether they are formed by charge transfer or electrophilic activation (Table 12); and (2) for less electron-rich arenes such as the naphthalenes, anisole, substituted anisoles, toluene, *tert*-butylbenzene, and the polymethylbenzenes in Table 13, the product distributions are the same, provided that measures are taken to circumvent attack by the pyridine or trinitromethide nucleophile. It must be emphasized that this generalization applies to 'anomalous' or 'non-conventional' nitration products as well as those involving nuclear nitration. Thus, processes such as the transfer halogenation of 4-bromoanisole, hydrolytic demethylation of 4-methylanisole,[150] alkyl-group transfer from *tert*-butylbenzene and side-chain reactions of durene, pentamethylbenzene and hexamethylbenzene[101] are all indicative of the intermediacy

Table 12. Electrophilic and charge-transfer nitrations of dimethoxybenzenes

		Isomer distribution (%)		
Arene	Activation	2-NO_2	3-NO_2	4-NO_2
1,4-Dimethoxybenzene	CT	100	–	–
	EL	100	–	–
1,2-Dimethoxybenzene	CT	–	0	100
	EL		0	100
4-Methoxyphenoxyacetic acid	CT	30	70	–
	EL	30	70	–
2-(4-Methoxyphenoxy)ethanol	CT	60	40	–
	EL	55	45	–

[a] Nitration effected by either the photoactivation of the [arene, TNM] complex in MeCN (CT) or treatment with HNO_3 in acetic acid in the dark at 25 °C (EL). Taken from Ref. 149b.

Table 13. Products of the electrophilic and charge-transfer nitration of aromatic substrates[a]

Arene	Nitrating agent, NO$_2$Y$^+$	Activation mode[b]	Product distribution			Ref.
4-Bromoanisole			ArNO$_2$[c]		*ipso*[d]	
	LutNO$_2^+$	CT	62		38	101
	PyNO$_2^+$	CT	62		38	101
	TNM	CT	55		45	101
	LutNO$_2^+$	EL	70		30	101
	HNO$_3$	EL	61		39	74
Naphthalene			1-NO$_2$		2-NO$_2$	
	LutNO$_2^+$	CT	95		5	94
	MeOPyNO$_2^+$[f]	CT	93		7	94
	TNM[f]	CT	95		5	94
	MeOPyNO$_2^+$	CT	93		7	94
	LutNO$_2^+$	EL	88		12	94
	MeO$_2$CPyNO$_2^+$	EL	91		9	94
	PyNO$_2^+$	EL	93		7	94
	HNO$_3$[g]	EL	94		6	163
	HNO$_3$[g]	EL	95		5	27
Anisole			*ortho*		*para*	
	LutNO$_2^+$	CT	65		35	101
	MeOPyNO$_2^+$	EL	68		32	101
	MeO$_2$CPyNO$_2^+$	EL	71		29	101
	HNO$_3$[h]	EL	70		30	163
	HNO$_3$[i]	EL	60		40	163
	NO$_2^+$BF$_4^-$[h]	EL	69		31	163
Toluene			*ortho*	*meta*	*para*	
	LutNO$_2^+$	CT	70	2	28	101
	MeOPyNO$_2^+$[j]	CT	67	5	28	101
	PyNO$_2^+$	EL	62	5	33	29
	NCPyNO$_2^+$	EL	63	4	33	29
	MeO$_2$CPyNO$_2^+$	EL	62	4	34	29
	ClPyNO$_2^+$	EL	64	4	32	29
	NO$_2^+$BF$_4^-$	EL	68	3	29	154
tert-Butylbenzene			*ortho*	*meta*	*para*	
	LutNO$_2^+$	CT	6	12	82	101
	MeOPyNO$_2^+$[f]	CT	7	15	78	101
	MeOPyNO$_2^+$[j]	CT	16	22	62	101
	MeOPyNO$_2^+$	EL	13	15	72	29
	MeO$_2$CPyNO$_2^+$	EL	12	14	74	29
	NCPyNO$_2^+$	EL	11	14	75	29
	HNO$_3$	EL	10	10	80	164
	HNO$_3$[k]	EL	12	8	80	27
Pentamethylbenzene			Side-chain[l]		Ring	
	PyNO$_2^+$	CT	86		14	101
	MeO$_2$CPyNO$_2^+$	CT	8		20	101
	PyNO$_2^+$	EL	71		29	29
	MeO$_2$CPyNO$_2^+$	EL	7		30	29

continued

Table 13. Continued

Arene	Nitrating agent, NO_2Y^+	Activation mode[b]	Product distribution		Ref.
Durene			Side-chain[l]	Ring	
	$PyNO_2^+$	CT	83	17	101
	$PyNO_2^+$	El	85	15	29
Mesitylene					
	$LutNO_2^+$	CT	0	100	101
	$MeO_2CPyNO_2^+$	EL	0	100	29

[a] Nitrations conducted in MeCN unless indicated otherwise.
[b] Thermal electrophilic (EL) or charge-transfer (CT) activation.
[c] 2-Nitro-4-bromoanisole.
[d] 2,4-dibromoanisole with equimolar 4-nitroanisole.
[e] Acetic acid solvent.
[f] Acetonitrile containing 5% (v/v) trifluoroacetic acid.
[g] Acetic anhydride solvent.
[h] Sulfolane solvent.
[i] Sulfuric acid solvent.
[j] In the presence of excess N_2O_4.
[k] Nitromethane solvent.
[l] Total side-chain activation (dimers, side-chain nitro, alcohol, aldehydes, etc.).

of the *ipso*-σ-complexes in both the electrophilic and the charge-transfer processes. The conclusion can be drawn that when nitration is compelled, by CT activation, to proceed by the electron-transfer pathway the results, as reflected in product distributions, are not distinguishable from those obtained by following the electrophilic route.

8.1. Electron-transfer step

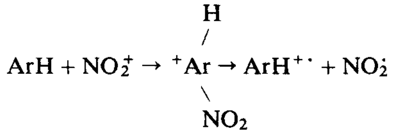
The first step in CT activation is the absorption of light of sufficient energy to effect the electron transfer. For electrophilic reactions, this initial electron transfer step appears too unfavourable thermodynamically to be consistent with the observed rates of nitration. For example, the substantial energy barrier of $\Delta G_{ET} = 11 \cdot 5$ kcal mol^{-1} does not seem compatible with a rate-determining ET step in the (diffusion-controlled)[165] reaction of NO_2^+ with naphthalene. Electron transfer is even more unfavorable with the less electrophilic transfer nitrating agents NO_2Y^+ since their reduction potentials are diminished relative to that of the unbound NO_2^+.[29] Since there is substantial experimental evidence that electron transfer does occur from naphthalene to NO_2^+ in solution,[22,119] it is clear that (thermodynamic) electrode potentials do not tell the entire story.

If electron transfer is a component of the nitration mechanism, it occurs within the EDA complex. The significant overlap between donor HOMO and acceptor LUMO implies a bonding interaction, with substantial reduction in the barrier to electron transfer between the components. Such a facilitation of electron transfer in an EDA complex has been demonstrated by quantitative analysis of charge-transfer band energies.[33,54,72] Indeed, inner-sphere electron transfer of this type is always characterized by faster rates of electron transfer than can be predicted from a consideration of thermodynamic driving forces alone. Since there appear to be no certain limits on the degree of inner-sphere facilitation of electron transfer, electron transfer cannot be ruled out solely on the basis of exergonicity even in the nitrations of benzene and toluene by NO_2^+.

An inner-sphere mechanism for electron transfer from arenes to NO_2^+, for example, constitutes a compromise between the two extreme forms of 'pure' outer-sphere electron transfer on the one hand, i.e.

$$ArH + NO_2^+ \rightarrow ArH^{+\cdot} + NO_2^{\cdot} \qquad (68)$$

and (net) electron transfer effected by a bond formation-homolysis process on the other, i.e.



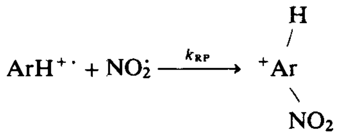
$$ArH + NO_2^+ \rightarrow {}^{+}Ar\begin{matrix}/H\\ \backslash NO_2\end{matrix} \rightarrow ArH^{+\cdot} + NO_2^{\cdot} \qquad (69)$$

with varying contributions from the two 'components.' In this respect, NO^+ serves as a model for electrophilic nitrating agents since its substantial (and variable) bonding interaction with arene donors and facile electron-transfer reactions (even endergonic ones) illustrate the inner-sphere ET behavior expected of NO_2^+ and its carriers.[166]

8.2. Collapse of the radical pair

The second factor pertinent to the charge-transfer activation of arenes is the radical-pair collapse of the cation radical with $NO_2^{\cdot}$ to generate the various σ-complexes.

Evidence for the reaction is found in the gas-phase experiments and the direct interaction of cation radicals with $NO_2^{\cdot}$. CT activation of the [ArH, $MeOPyNO_2^+$] complexes generates $ArH^{+\cdot}$, which in the presence of $NO_2^{\cdot}$ decays by pseudo-first-order kinetics on the microsecond–nanosecond timescale, to provide an unequivocal method for obtaining rates of reaction (70).



$$ArH^{+\cdot} + NO_2^{\cdot} \xrightarrow{k_{RP}} {}^{+}Ar(H)(NO_2) \qquad (70)$$

A range of arene cation radicals from 9-phenylanthracene to toluene react with $NO_2^{\cdot}$ at a uniform rate of $0{\cdot}5 \times 10^9$–$4 \times 10^9\,l\,mol^{-1}\,s^{-1}$ with no correlation with the radical cation stability (as measured by E^0)[101] (Figure 2). In this regard, the reaction resembles a straightforward radical–radical combination process. Indeed, the uniform value of *ca* $2 \times 10^9\,l\,mol^{-1}\,s^{-1}$ corresponds to that for a diffusion-controlled (spin-limited) reaction rate constant.[148b] Thus, $ArH^{+\cdot}$ behaves essentially like an ordinary free radical.[167]

This situation can be contrasted with the coupling of cation radicals with added pyridine. Here the electrophilic reactivity, k_N, is inversely correlated with stability (E^0) of the cation radical.[101] The reactive cation radicals of anisole, mesitylene and toluene react electrophilically with pyridine at rates comparable to that of the $NO_2^{\cdot}$ coupling reaction. On the other hand, cation radicals of polymethylbenzenes (durene, hexamethylbenzene) anthracenes and naphthalene react more slowly with pyridine than with $NO_2^{\cdot}$. (Ion-pair collapse of $ArH^{+\cdot}$ with trinitromethide is uniformly fast, with rate constants exceeding $10^{10}\,l\,mol^{-1}\,s^{-1}$ for arenes in dichloromethane. This reflects the efficiency of the ion-pair annihilation process and the enhanced nucleophilicity of anions in non-polar media.[168]) Thus arenes can be roughly divided into electron-poor, in which pyridine plays an important role, and electron-rich arenes in which radical-pair coupling occurs without significant competition from the nucleophilic reaction with pyridine.[169]

The collapse of the radical pair to the various σ-complexes determines the positional selectivity in nitration (including *ipso* substitution), largely according to the spin density at the various ring positions in the radical cation. It is the radical pair, then, that functions as Olah *et al.*'s π-complex intermediate to determine the overall arene reactivity. It should be noted that the original formulation is not incorrect, since $[ArH^{+\cdot}, NO_2^{\cdot}]$ is probably bound as a tight radical pair, analogous to the $[ArH^{+\cdot}\ NO^{\cdot}]$ complex discussed in Section 7.5. As such, the electron transfer mechanism in Scheme 2 constitutes the most plausible modification of the Ingold concepts to include the two-

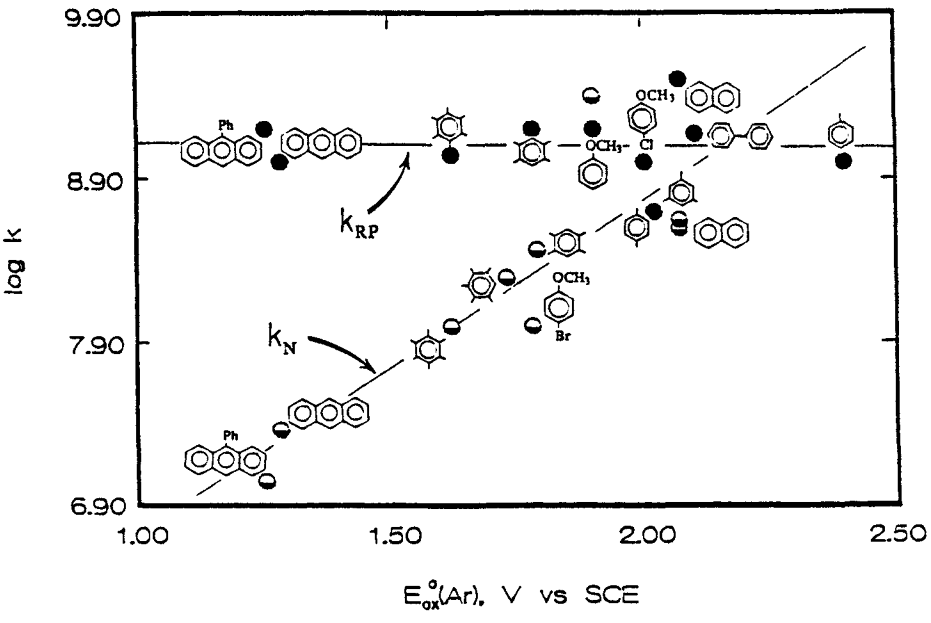


Figure 2. Variation of the rate constants k_{RP} (●) for radical-pair collapse of arene cation radicals with $NO_2^{\cdot}$ and k_N (◒) for attack of pyridine as a function of the oxidation potential of the arene donor

step activation process demanded by the reactivity–selectivity patterns in arene nitration.

9. SUMMARY AND CONCLUSIONS

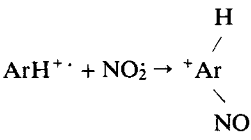
Transfer nitrating agents, especially those derived from substituted pyridines (XPy) in the form of *N*-nitropyridinium cations ($XPyNO_2^+$), can be effectively used to gain new mechanistic insight into the activation process for aromatic nitration by (1) providing a graded series of active nitrating agents with widely varying electrophilic reactivities which can approach that of the nitronium ion (NO_2^+); (2) forming pre-equilibrium amounts of transient aromatic EDA complexes, [ArH, $XPyNO_2^+$], that exhibit characteristic charge-transfer (CT) absorption bands; and (3) allowing aromatic nitration to take place by the deliberate photo-activation of the EDA complex (via the CT absorption).

Time-resolved spectroscopy in two time domains provides unequivocal evidence that charge-transfer activation ($h\nu_{CT}$) of the EDA complex on the picosecond time-scale occurs by electron transfer to form the reactive triad, i.e.

$$ArH + XPyNO_2^+ \overset{K_{EDA}}{\rightleftharpoons} [ArH, XPyNO_2^+] \quad (71)$$

$$[ArH, XPyNO_2^+] \xrightarrow{h\nu_{CT}} [ArH^{+\cdot}, NO_2^{\cdot}, XPy] \quad (72)$$

The subsequent diffusive separation and recombination of the triad on the nanosecond–microsecond time-scale leads to the Wheland intermediate by radical-pair collapse, i.e.



$$ArH^{+\cdot} + NO_2^{\cdot} \rightarrow {}^{+}Ar\begin{smallmatrix}H\\ NO_2\end{smallmatrix} \quad (73)$$

Together with the side-reaction, which diverts some of the aromatic cation radical by nucleophilic reaction with XPy, this sequence constitutes the complete mechanistic description of charge-transfer activation.

Charge-transfer activation of [ArH, $XPyNO_2^{\cdot}$] leads to the nitration of a wide variety of aromatic substrates, including toluene, anisole, mesitylene and durene, with high photoefficiencies. Aromatic nitrations carried out thermally with $XPyNO_2^+$ (in the dark) follow the same pattern of electrophilic activation previously established for nitrating agents such as nitric acid, acetyl nitrate and nitronium salts. The direct comparison of the products derived from the thermal (electrophilic) and the photochemical (charge-transfer) activation shows that the two processes are indistinguishable. This conclusion encompasses not only conventional (nuclear) nitration but it also includes side-chain substitution and *ipso* attack. The unity among the diverse array of products from 'non-conventional' nitrations (transalkylation, nitrodehalogenation, etc.) constitutes a particularly sensitive test of the essential identity of the two activation processes. Since the EDA complex is the common precursor to both, we conclude from the common terminus (i.e. product distributions) that electrophilic and charge-transfer nitrations also share reactive intermediates in common.

From a much broader perspective, the study of nitration as described here delineates a new approach to the elucidation of organic reaction mechanisms. Time-resolved spectroscopy is critical to the direct study of reactive intermediates with picosecond lifetimes that cannot otherwise be examined in the course of electrophilic (adiabatic) activation. (The charge-transfer paradigm is applicable to a wide variety of electrophilic reagents, including carbocations,[44] halogens,[53] quinones,[142,170] mercury acetate,[48] thallium trifluoroacetate,[48] osmium tetroxide,[46] titanium[171] and tin[172] tetrachlorides, cyanoalkenes[173] and others[50,174,175]).

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REFERENCES

1. R. Taylor, *Electrophilic Aromatic Substitution*, p. 263. Wiley, New York (1990).
2. C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, 2nd ed. Cornell University Press, Ithaca, NY (1969).
3. P. B. D. De La Mare and J. H. Ridd, *Aromatic Substitution: Nitration and Halogenation*. Butterworths, London (1959).
4. J. G. Hoggett, R. B. Moodie, J. R. Penton and K. Schofield, *Nitration and Aromatic Reactivity*, Cambridge University Press, Cambridge (1971).
5. G. A. Olah, R. Malhotra and S. C. Narang, *Nitration: Methods and Mechanisms*. VCH, New York (1989).
6. S. R. Hartshorn, *Chem. Soc. Rev.* **3**, 167 (1974).
7. K. Schofield, *Aromatic Nitration*, Cambridge University Press, Cambridge (1980).
8. R. J. Gillespie, J. Graham, E. D. Hughes, C. K. Ingold and E. R. A. Peeling, *Nature* (London) **158**, 480 (1946).
9. E. D. Hughes, C. K. Ingold and R. I. Reed, *J. Chem. Soc.* 2400 (1950).
10. A. Hantzsch, *Chem. Ber.* **58**, 941 (1925).
11. (a) D. R. Goddard, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.* 2559 (1950); (b) G. A. Olah and S. J. Kuhn, in *Freidel–Crafts and Related Reactions*, edited by G. A. Olah, Vol. III, Part II, p. 1393. Wiley, New York (1964).
12. (a) L. Melander and W. H. Saunders, Jr, *Reaction Rates of Isotopic Molecules*, pp. 162*ff*. Wiley, New York

(1980); (b) G. A. Olah, *J. Tenn. Acad. Sci.* **40**, 77 (1965); (c) V. A. Koptyug, *Top. Curr. Chem.* **122**, 203 (1984).

13. J. Kenner, *Nature* (London) **156**, 369 (1945).
14. (a) G. A. Olah, S. J. Kuhn and D. Mlinko, *J. Chem. Soc.* 4257 (1956); (b) G. A. Olah and S. J. Kuhn, *J. Am. Chem. Soc.* **83**, 4564 (1961); (c) G. A. Olah, S. J. Kuhn and S. H. Flood, *J. Am. Chem. Soc.* **83**, 4571, 4581 (1961).
15. R. G. Coombes, R. B. Moodie and K. Schofield, *J. Chem. Soc. B* 800 (1968).
16. C. L. Perrin, *J. Am. Chem. Soc.* **99**, 5516 (1977).
17. I. Puskas and E. K. Field, *J. Org. Chem.* **31**, 4204 (1966).
18. (a) H. Suzuki and K. Nakamura, *Bull. Chem. Soc. Jpn.* **43**, 473 (1970); (b) S. B. Hanna, E. Hunziker, T. Saito and H. Zollinger, *Helv. Chim. Acta* **52**, 1537 (1969).
19. (a) L. Eberson and F. Radner, *Acta Chem. Scand., Ser B* **40**, 71 (1986) (b) L. Eberson and F. Radner, *Acct. Chem. Res.* **20**, 53 (1987).
20. A. S. Morkovnik, *Russ. Chem. Rev.* **20**, 2144 (1988).
21. G. A. Olah, R. Malhotra and S. C. Narang, *Nitration: Methods and Mechanisms*, p. 144. VCH, New York (1989).
22. J. H. Ridd, *Chem. Soc. Rev.* **20**, 149 (1991).
23. J. H. Ridd, in *Studies on Chemical Structure and Reactivity*, edited by J. H. Ridd, p. 133. Wiley, New York (1966).
24. W. M. Weaver, in *The Chemistry of the Nitro and Nitroso Groups*, Vol. II, edited by H. Feuer, pp. 15ff. Wiley, New York (1970).
25. L. M. Stock, *Prog. Phys. Org. Chem.* **12**, 21 (1976).
26. J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2* 1689 (1992).
27. G. A. Olah, S. C. Narang, J. A. Olah and K. Lammertsma, *Proc. Natl Acad. Sci. USA* **79**, 4487 (1982).
28. G. A. Olah, S. C. Narang, J. A. Olah, R. L. Pearson and C. A. Cupas, *J. Am. Chem. Soc.* **102**, 3507 (1980).
29. E. K. Kim, K. Y. Lee and J. K. Kochi, *J. Am. Chem. Soc.* **114**, 1756 (1992).
30. G. A. Olah, S. C. Narang, R. Malhotra and J. A. Olah, *J. Am. Chem. Soc.* **101**, 1805 (1979).
31. G. A. Olah, H. C. Lin and Y. K. Mo, *J. Am. Chem. Soc.* **94**, 3667 (1972).
32. (a) A. Klemenc and A. Schiller, *Z. Anorg. Allg. Chem.* **141**, 231 (1924); (b) E. Grison, K. Eriks and. J. L. DeVries, *Acta Crystallogr.* **3**, 290, (1950); (c) D. J. Miller, in *Studies on Chemical Structure and Reactivity*, edited by J. H. Ridd, p. 157. Wiley, New York (1966); (d) L. E. Sutton, *Tables of Interatomic Distances and Configurations in Molecules and Ions*. Chemical Society, London (1958).
33. D. Bethell and V. D. Parker, *J. Phys. Org. Chem.* **5**, 317 (1992).
34. K. Y. Lee, C. Amatore and J. K. Kochi, *J. Phys. Chem.* **95**, 1285 (1991).
35. K. Y. Lee, D. J. Kuchynka, and J. K. Kochi, *Inorg. Chem.* **29**, 4196 (1990).
36. J. M. Harris and S. P. McManus, *Nucleophilicity*, p. 1. American Chemical Society, Washington, DC (1987).
37. J. K. Kochi, *Adv. Free Rad. Chem.* **1**, 53, (1990).
38. R. D. Cannon, *Electron Transfer Reactions*. Butterworths, London (1980).
39. N. Sutin, *Inorganic Biochemistry*, edited by G. L. Eichhorn, Vol. I, p. 611. Elsevier, Amsterdam (1973).
40. K. Yoshida, *Electrooxidation in Organic Chemistry*. Wiley, New York (1984).
41. J. O. Howell, J. M. Goncalves, C. Amatore, L. Klasinc, R. M. Wightman, and J. K. Kochi, *J. Am. Chem. Soc.* **106**, 3968 (1984).
42. (a) V. D. Parker, *J. Am. Chem. Soc.* **98**, 98 (1976); (b) C. Amatore and C. Lefrou, *J. Electroanal. Chem.* **325**, 239 (1992).
43. (a) R. L. Strong, S. J. Rand, and J. A. Britt, *J. Am. Chem. Soc.* **82**, 5053 (1960); (b) K. D. Raner, J. Lusztyk, and K. U. Ingold, *J. Phys. Chem.* **93**, 564 (1989).
44. Y. Takahashi, S. Sankararaman and J. K. Kochi, *J. Am. Chem. Soc.* **111**, 2594 (1989).
45. P. R. Hammond and R. R. Lake, *J. Chem. Soc. A* 3819 (1971).
46. J. M. Wallis and J. K. Kochi, *J. Am. Chem. Soc.* **110**, 8207 (1988).
47. E. N. Guryanova, I. P. Goldshtein, and I. P. Romm, *Donor–Acceptor Bond*, pp. 298*ff*. Wiley, New York (1975).
48. W. Lau and J. K. Kochi, *J. Am. Chem. Soc.* **108**, 6720 (1986).
49. H. M. Niemeyer, in *The Chemistry of Diazonium and Diazo Groups, Part 1*, edited by S. Patai, pp. 231ff. Wiley, New York (1978).
50. J. K. Kochi, *Pure Appl. Chem.* **63**, 255, (1991).
51. R. S. Mulliken, *J. Am. Chem. Soc.* **74**, 811 (1952).
52. R. S. Mulliken and W. B. Person, *Molecular Complexes. A Lecture and Reprint Volume*. Academic Press, New York (1969).
53. S. Fukuzumi and J. K. Kochi, *J. Am. Chem. Soc.* **103**, 7240 (1981).
54. (a) J. K. Kochi, *Acta Chem. Scand.* **44**, 409 (1990); (b) J. K. Kochi, *Angew. Chem., Int. Ed. Engl.* **27**, 1227, (1988).
55. B. C. Challis, R. J. Higgins and A. J. Lawson, *J. Chem. Soc., Perkin Trans. 2* 1831 (1972).
56. Z. J. Allan, J. Podstata, D. Snobl and J. Jarkovsky, *Tetrahedron Lett.* 3565 (1965).
57. S. Brownstein, E. Gabe, F. Lee and A. Piotrowski, *Can. J. Chem.* **64**, 1661 (1986).
58. E. K. Kim and J. K. Kochi, *J. Org. Chem.* **54**, 1692, (1989).
59. E. K. Kim and J. K. Kochi, *J. Am. Chem. Soc.* **113**, 4962, (1991).
60. E. Heilbronner, *Helv. Chim. Acta* **36**, 1121 (1953).
61. D. L. H. Williams, *Nitrosation*, pp. 58*ff*. Cambridge University Press, Cambridge (1988).
62. 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.* 2628 (1950).
63. S. Veibel, *Chem. Ber.* **63**, 1579, (1930).
64. E. D. Hughes, G. J. Minkoff and R. I. Reed, *Nature* (London) **158**, 504 (1946).
65. A. S. Morkovnik, M. M. Levkovich, V. D. Strblesova, N. M. Nobaeva, Z. S. Morkovnik, Z. S. Testoedova and O. Yu. Okhlobystin, *Zh. Obsch. Khim. (Engl. Trans.)* **58**, 597 (1988).
66. J. C. Giffney and J. H. Ridd, *J. Chem. Soc., Perkin Trans. 2* 618 (1979).
67. A. H. Clemens, J. H. Ridd and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2* 1659 (1984).
68. A. H. Clemens, J. H. Ridd and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2* 1667 (1984).

69. A. H. Clemens, J. H. Ridd and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2* 1227, (1985).
70. R. L. Elsenbaumer, *J. Org. Chem.* **53**, 437 (1988).
71. (a) B. Milligan, *J. Org. Chem.* **48**, 1495 (1983); (b) E. Bosch and J. K. Kochi, *Res. Chem. Intermed.* **16**, 811 (1993).
72. V. D. Parker, K. L. Handoo and B. Reitstöen, *J. Am. Chem. Soc.* **113**, 6218 (1991).
73. C. J. Schlesener, C. Amatore and J. K. Kochi, *J. Am. Chem. Soc.* **106**, 3567 (1984).
74. C. L. Perrin and G. A. Skinner, *J. Am. Chem. Soc.* **93**, 3389 (1971).
75. (a) A. Fischer and D. R. A. Leonard, *Can. J. Chem.* **50**, 3367 (1972); (b) A. Fischer and A. L. Williamson, *Can. J. Chem.* **50**, 3988 (1972).
76. A. Fischer and J. N. Ramsay, *Can. J. Chem.* **52**, 3960 (1974).
77. A.Fischer and R. Röderer, *J. Chem. Soc., Chem. Commun.* 798 (1975).
78. A. Fischer, D. L. Fyles, G. N. Henderson and S. RayMahasay, *Can. J. Chem.* **64**, 1764 (1986).
79. A. Fischer, G. N. Henderson and S. RayMahasay, *Can. J. Chem.* **65**, 1233 (1987).
80. D. V. Nightingale, *Chem. Rev.* **40**, 117 (1947).
81. C. L. Perrin, *J. Org. Chem.* **36**, 420 (1971).
82. R. Taylor, *Electrophilic Aromatic Substitution*, pp. 413*ff*. Wiley, New York (1990).
83. C. E. Barnes, K. S. Feldman, M. W. Johnson, H. W. H. Lee and P. C. Myhre, *J. Org. Chem.* **44**, 3925 (1979).
84. J. H. Ridd, S. Trevellick and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2* 573 (1992).
85. C. E. Barnes and P. C. Myhre, *J. Am. Chem. Soc.* **100**, 475, (1978).
86. R. Astolfi, E. Baciocchi and G. Illuminati, *Chim. Ind. (Milan)* **53**, 1153, (1971).
87. E. Baciocchi and G. Illuminati, *Prog. Phys. Org. Chem.* **5**, 1 (1967).
88. H. Suzuki, *Synthesis*, 217 (1977).
89. R. C. Hahn and M. B. Groen, *J. Am. Chem. Soc.* **95**, 6128, (1973).
90. E. Baciocchi and L. Mandolini, *Tetrahedron* **43**, 4035, (1987).
91. E. S. Rudakov and V. L. Lobachev, *Kinet. Katal. (Engl. Transl.)* **31**, 1138, (1990).
92. E. deB. Barnett, J. W. Cook and H. A. Matthews, *J. Chem. Soc.* 1994 (1923).
93. H. Suzuki, H. Yoneda, T. Hanafusa and T. Sugiyama, *Bull. Inst. Chem. Res. Kyoto. Univ.* **54**, 176 (1976).
94. E. K. Kim, T. M. Bockman and J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2* 1879 (1992).
95. S. Sankararaman and J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2* 1 (1991).
96. J. M. Masnovi and J. K. Kochi, *J. Org. Chem.* **50**, 5245 (1985).
97. L. Eberson, M. P. Hartshorn, F. Radner and W. T. Robinson, *Acta Chem. Scand.* **47**, 410 (1993).
98. (a) L. Eberson, M. P. Hartshorn, F. Radner, M. Mérchan and B. O. Roos, *Acta Chem. Scand.* **47**, 176 (1993); (b) L. Eberson, M. P. Hartshorn and J. O. Svensson, *Acta Chem. Scand.* **47**, 925 (1993); (c) L. Eberson and M. P. Hartshorn, *J. Chem. Soc., Chem. Commun.* 1563 (1992).
99. A. Fischer and G. J. Wright, *Aust. J. Chem.* **27**, 217 (1974).
100. E. S. Rudakov, V. L. Lobachev and O. B. Savsunenko, *Kinet. Katal. (Engl. Transl.)* **31**, 938 (1991).
101. E. K. Kim, T. M. Bockman and J. K. Kochi, *J. Am. Chem. Soc.* **115**, 3091 (1993).
102. (a) J. K. Kochi, *Adv. Free Rad. Chem.* **5**, 189 (1975); (b) M. C. R. Symons, *Chemical and Biological Aspects of Electron Spin Spectroscopy*. Wiley, New York (1978).
103. (a) L. Eberson, M. P. Hartshorn and J. O. Svensson, *J. Chem. Soc., Chem. Commun.*, 1614 (1993); (b) A. Boughriet, M. Wartel, J. C. Fischer and C. Bremard, *J. Electroanal. Chem.* **190**, 103 (1985).
104. M. Attinà, F. Cacace and M. Yañez, *J. Am. Chem. Soc.* **109**, 5092 (1987).
105. R. J. Schmitt, S. E. Buttrell, Jr, and D. S. Ross, *J. Am. Chem. Soc.* **106**, 926 (1984).
106. W. D. Reents, Jr, and B. S. Freiser, *J. Am. Chem. Soc.* **102**, 271 (1980).
107. J. Feng, X. Zheng and M. C. Zerner, *J. Org. Chem.* **51**, 4531 (1986).
108. S. Nagakura and K. Tanaka, *J. Chem. Phys.* **22**, 563 (1954).
109. R. D. Brown, *J. Chem. Soc.* 2224, 2232 (1959).
110. E. B. Pedersen, T. E. Petersen, K. Torssell and S.-O. Lawesson, *Tetrahedron*, **29**, 579 (1973).
111. P. Politzer, K. Jayasuriya, P. Sjoberg and P. R. Laurence, *J. Am. Chem. Soc.* **107**, 1174 (1985).
112. R. A. Marcus, *Annu. Rev. Phys. Chem.* **15**, 155 (1964).
113. L. Eberson and F. Radner, *Acta Chem. Scand., Ser. B* **38**, 861 (1984).
114. L. Eberson, *Electron Transfer Reactions in Organic Chemistry*, p. 14. Springer, Berlin (1987).
115. S. Fukuzumi, C. L. Wong and J. K. Kochi, *J. Am. Chem. Soc.* **102**, 2928 (1980).
116. S. Fukuzumi and J. K. Kochi, *Bull. Chem. Soc. Jpn.* **56**, 969 (1983).
117. L. Eberson, *New J. Chem.* **16**, 151 (1992).
118. A. R. Lepley and G. L. Closs (Eds), *Chemically Induced Magnetic Polarization*. Wiley, New York (1973).
119. J. F. Johnstone, J. H. Ridd and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2* 623 (1991).
120. A. H. Clemens, P. Heltsby, J. H. Ridd, F. Al-Omran and J. P. B. Sandall, *J. Chem. Soc., Perkin Trans. 2* 1217 (1985).
121. R. Kaptein, *J. Chem. Soc, Chem. Commun.* 732 (1971).
122. R. Kaptein, *Adv. Free Rad. Chem.* **5**, 319 (1975).
123. (a) R. Z. Sagdeev and A. L. Buchachenko, in *Spin Polarization and Magnetic Field Effects in Radical Reactions*, edited by Yu. N. Molin, p. 330 . Elsevier, Amsterdam (1984); (b) D. Bethell and M. R. Brinckman, *Adv. Phys. Org. Chem.* **10**, 53 (1973).
124. A. R. Lepley, in *Chemically Induced Magnetic Polarization*, edited by A. R. Lepley and G. L. Closs, p. 324. Wiley, New York (1973).
125. E. F. Hilinski and P. M. Rentzepis, *Acc. Chem. Res.* **16**, 224 (1983).
126. N. Mataga, *Pure Appl. Chem.* **56**, 1255 (1984).
127. B. I. Green, R. M. Hochstrasser and R. B. Weisman, *J. Chem. Phys.* **70**, 1247 (1979).
128. S. M. Hubig and M. A. J. Rodgers, in *Handbook of Organic Photochemistry*, edited by J. C. Scaiano, Vol. I, pp. 315*ff*. CRC Press, Boca Raton, FL (1989).
129. T. W. Ebbesen, L. E. Manring and K. S. Peters, *J. Am. Chem. Soc.* **106**, 7400 (1984).
130. C. V. Shank, *Science* **219**, 1027 (1983).

131. (a) M. R. Wasielewski, M. P. Niemczyk, W. A. Svec and E. B. Pewett, *J. Am. Chem. Soc.* **107**, 5562 (1985); (b) K. G. Spears, T. H. Gray and D. Huang, *J. Phys. Chem.* **90**, 779 (1986).
132. T. Asahi and N. Mataga, *J. Phys. Chem.* **95**, 1956 (1991).
133. (a) C. A. Langhoff, K. Gnadig, and K. B. Eisenthal, *Chem. Phys.* **46**, 117 (1980); (b) N. A. Abul-Haj and D. F. Kelley, *J. Chem. Phys.* **84**, 1335 (1986); (c) A. L. Harris, M. Berg, and C. B. Harris, *J. Chem. Phys.* **84**, 788 (1986); (d) J. P. Bergsmaa, P. H. Berens, K. R. Wilson, D. R. Fredkur and E. J. Heller, *J. Phys. Chem.* **88**, 612 (1984).
134. T. C. Swinney and D. F. Kelley, *J. Phys. Chem.* **95**, 10369 (1991).
135. (a) A. G. Doukas, R. H. Callender and R. R. Alfano, in *Applications of Fluorescence in the Biomedical Sciences*, edited by D. L. Taylor, p. 69. A. R. Liss, New York (1986); (b) Y. Hirata, N. Mataga, Y. Mukai and Y. Koyama, *Chem. Phys. Lett.* **134**, 166 (1987).
136. K. S. Peters, S. C. Freilich and J. Lee, *J. Phys. Chem.* **97**, 5482 (1993).
137. Y. Mukai, Y. Koyama, Y. Hirata and N. Mataga, *J. Phys. Chem.* **92**, 4649 (1988).
138. (a) A. M. Nuijs, H. J. van Gorkom, J. J. Plijter and L. N. M. Duysensi, *Biochim. Biophys. Acta* **848**, 167 (1986); (b) M. R. Wasielewski and D. M. Tiede, *FEBS Lett.* **204**, 368 (c) C. C. Moser, J. M. Keske, K. Warncke and P. L. Dutton, in *Electron and Proton Transfer in Chemistry and Biology*, edited by A. Müller, H. Ratajczak, W. Junge and E. Diemann, pp. 111*ff.* Elsevier, New York (1992).
139. (a) N. W. Woodbury, M. Becker, D. Middendorf and W. W. Parson, *Biochemistry* **24**, 7516 (1985); (b) O. Einarsdottir, R. B. Dyer, D. D. Lemon, P. M. Killough, S. M. Hubig, S. J. Atherton, J. J. Lopez-Garriga, G. Palmer and W. H. Woodruff, *Biochemistry* **32**, 12013 (1993).
140. E. F. Hilinski, J. M. Masnovi, C. Amatore, J. K. Kochi and P. M. Rentzepis, *J. Am. Chem. Soc.* **106**, 6167 (1983).
141. J. M. Masnovi, J. K. Kochi, E. F. Hilinski and P. M. Rentzepis, *J. Am. Chem. Soc.* **108**, 1126 (1986).
142. S. Perrier, S. Sankararaman and J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2* 825 (1993).
143. S. Ojima, H. Miyasaka and N. Mataga, *J. Phys. Chem.* **94**, 7534 (1990).
144. J. M. Masnovi, J. C. Huffman, J. K. Kochi, E. F. Hilinski and P. M. Rentzepis, *Chem. Phys. Lett.* **106**, 20 (1984).
145. G. D. Gillispie and A. U. Kahn, *J. Chem. Phys.* **65**, 1624 (1976).
146. K. D. Asmus, in *Fast Processes in Radiation Chemistry and Biology*, edited by G. E. Adams, E. M. Fielden and B. D. Michael, p. 40. Wiley, New York (1975).
147. T. M. Bockman, K. Y. Lee, and J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2* 1581 (1992).
148. (a) R. M. Noyes, *Prog. React. Kinet.* **1**, 129 (1961); (b) T. Koenig and H. Fischer, in *Free Radicals*, edited by J. K. Kochi, Vol. I, p. 157. Wiley, New York (1973).
149. (a) S. Sankararaman and J. K. Kochi, *Recl. Trav. Chim. Pays-Bas* **105**, 278 (1986); (b) S. Sankararaman, W. A. Haney and J. K. Kochi, *J. Am. Chem. Soc.* **109**, 5235 (1987).
150. S. Sankararaman, W. A. Haney and J. K. Kochi, *J. Am. Chem. Soc.* **109**, 7824 (1987).
151. T. Yabe, S. Sankararaman and J. K. Kochi, *J. Phys. Chem.* **95**, 4177 (1991).
152. T. Yabe and J. K. Kochi, *J. Am. Chem. Soc.* **114**, 4491 (1992).
153. J. M. Masnovi, S. Sankararaman and J. K. Kochi, *J. Am. Chem. Soc.* **111**, 2263 (1989).
154. G. A. Olah, R. Malhotra and S. C. Narang, *Nitration: Methods and Mechanisms*, pp. 150*ff.* VCH, New York (1989).
155. T. M. Bockman, Z. J. Karpinski, S. Sankararaman, and J. K. Kochi, *J. Am. Chem. Soc.* **114**, 1970 (1992).
156. K. Y. Lee and J. K. Kochi, *J. Chem. Soc., Perkin Trans. 2*, 237 (1994).
157. D. N. R. Rao, H. Chandra, and M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2* 1201 (1984).
158. L. I. Smith and F. L. Taylor, *J. Am. Chem. Soc.* **57**, 2460 (1935).
159. S. Uemura, A. Toshimiti and M. Okano, *J. Chem. Soc., Perkin Trans. 1* 1076 (1978).
160. M. Hossani and R. Taylor, *J. Chem. Soc., Perkin Trans. 2* 187 (1982).
161. T. M. Bockman, E. K. Kim and J. K. Kochi, *Bull. Chim. Soc. Fr.* **130**, 323 (1993).
162. L. Eberson, M. P. Hartshorn and F. Radner, *J. Chem. Soc., Perkin Trans. 2* 1793 (1992).
163. P. Kovacic and J. J. Hiller, *J. Org. Chem.* **30**, 2871 (1965).
164. L. M. Stock, *J. Org. Chem.* **26**, 4120 (1961).
165. J. H. Ridd, *Adv. Phys. Org. Chem.* **16**, 1 (1978).
166. J. K. Kochi, *Acct. Chem. Res.* **25**, 39 (1992).
167. K. U. Ingold, in *Free Radicals*, edited by J. K. Kochi, Vol. I, pp. 37*ff.* Wiley, New York (1973).
168. F. G. Bordwell, T. A. Cripe and D. L. Hughes, in *Nucleophilicity*, edited by J. M. Harris and S. P. McManus, p. 137. American Chemical Society, Washington, DC (1987).
169. B. Reitstöen and V. D. Parker, *J. Am. Chem. Soc.* **113**, 6954 (1991).
170. T. M. Bockman, S. Perrier and J. K. Kochi, *J. Chem. Soc., Perkin Trans 2* 595 (1993).
171. K. Brüggerman, R. S. Czernuszewicz and J. K. Kochi, *J. Phys. Chem.* **96**, 4405 (1992).
172. K. Brüggerman and J. K. Kochi, *J. Org. Chem.* **57**, 2956 (1992).
173. J. J. Ko, T. M. Bockman and J. K. Kochi, *Organometallics* **9**, 1833 (1990).
174. J. K. Kochi, *Chimia* **45**, 277 (1991).
175. R. E. Lehmann and J. K. Kochi, *J. Am. Chem. Soc.* **113**, 501 (1991).