effects such as low-amplitude librations. When direct detection of zero-field transitions with SQUID detectors[30] becomes routine, two-dimensional NMR should be particularly valuable for structure determinations. Extensions to spin decoupling and other multiple-pulse experiments are also imminent and will certainly extend the applicability of zero-field NMR. A number of laboratories are now engaged in such studies, and we look forward to a period of amusing and possibly useful developments.

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Electron-Transfer Mechanisms in Electrophilic Aromatic Nitration

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Nitration via Electron Transfer—A Longstanding Hypothesis

In 1980 Schofield[1] finished the introductory chapter of his magnificent textbook on aromatic nitration by the following passage: "Speculation about the mechanisms of nitration, which might be said to have started with Euler's nitronium ion hypothesis, is thus far from complete, nor is it ever likely to be. There are certainly surprises to come."

One piece of speculation that has recurred often in the history of aromatic nitration is the one-electron-transfer (ET)[2] mechanism of nitration by NO_2^+. Already in 1933 Hückel[3] quoted the suggestion of a radical cation mediated mechanism by Meerwein, Pfeiffer, and Wizinger,[4] but the accompanying reaction formula did not display a radical cation, but instead the Wheland intermediate. It was left to Kenner[5] and Weiss[6] to express the ET mechanism in modern nomenclature in the middle of the 1940s (eq 1 and 2), although the

$$\mathrm{ArH} + \mathrm{NO_2^+} \rightarrow \mathrm{ArH^{\bullet+}} + \mathrm{NO_2} \tag{1}$$

$$\mathrm{ArH^{\bullet+}} + \mathrm{HSO_4^-} \rightarrow \mathrm{H_2SO_4} + \mathrm{Ar^{\bullet}} \xrightarrow{\mathrm{NO_2}} \mathrm{ArNO_2} \tag{2}$$

proton abstraction step of eq 2 nowadays is considered a rather unlikely one. The ET mechanism was generalized by Weiss to be valid as well for other types of electrophilic aromatic substitution, such as halogenation and sulfonation. In general, the spirit of that period was happily tolerant of one-electron mechanisms or at least suggestions thereof; even the archetype of a two-electron-centered mechanism, that of the Diels–Alder reaction, was seriously expressed in an ET version by no less a person than R. B. Woodward![7]

Nagakura et al.[8] later developed these ideas theoretically and showed that in the gas phase the energy levels of the LUMO of typical charged electrophiles, like NO_2^+ (−11.0 eV), I^+ (−10.4 eV), and Br^+ (−11.8 eV), are lower than that of the HOMO of benzene (−9.24 eV); i.e., there is a strong driving force for ET from benzene to these cations. This was later confirmed in gas-phase studies,[9] ET being the predominant process for the reaction between benzene and substituted benzenes on the one hand and CH_3^+, NO_2^+, and NO^+ on the other. Further implications of the ET mechanism were explored by Pedersen et al.[10] They found correlations between log *k* for substitution and ionization potentials of substrates and between orientation of substitution and hyperfine coupling constants of the corresponding radical cations.

On the experimental side, a number of observations of radical cation formation in the reactions between aromatic or heteroaromatic compounds and NO_2^+ or $HNO_3/HClO_4$ were published.[11] Analogous results were obtained with NO^+ as the oxidant, and since the NO formed is easily removable, this method has turned out to be a good way of preparing radical cation salts.[12] It was also noted that side reactions during aromatic

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nitration by NO_2^+ often were of the oxidative substitution type[13] (eq 3 and 4; the product formed is dependent on the nature of the solvent/nucleophiles present), analogues of which were well-known from studies of anodic substitution reactions.[14]

$$ArH \xrightarrow{NO_2^+} \begin{cases} \text{quinone} \\ Ar'(OH)NO_2 \text{ via } ArONO_2 \\ Ar\text{-}Ar \end{cases} \qquad (3)$$

$$ArCH_3 \xrightarrow{NO_2^+} \begin{cases} ArCH_2ONO_2 \\ ArCH_2NO_2 \\ ArCH_2NHCOCH_3 \\ ArCH_2OAc \\ ArCH_2OCH_3 \\ ArCH_2Ar'CH_3 \end{cases} \qquad (4)$$

Revival of the ET Mechanism in 1977

An Experimental Approach to the Possible Coupling between Naphthalene Radical Cation and Nitrogen Dioxide. Time was eventually ripe for a forceful revival of the ET mechanism, reported by Perrin in a thought-provoking article[15] in 1977. This time the ET hypothesis was called upon to solve yet another problem, namely, the paradoxically strong intramolecular selectivity of nitration,[16] even when there is no intermolecular selectivity. A mechanism involving diffusion-controlled ET between ArH and NO_2^+ to give a radical pair, followed by its collapse to the usual σ-complex (eq 5), was postulated. It was then assumed that intermolecular selectivity would be absent for all ArH more reactive than toluene (diffusion-controlled rates), whereas intramolecular selectivity and positional orientation would be spin density controlled, as suggested by the results of Pedersen et al.[10] Arguments for this mechanism were based on (i) the high oxidizing power of nitronium ion, expressed in a high anodic half-wave potential, considered to be sufficient to make ET reactions between NO_2^+ and all aromatics more reactive than toluene exergonic and thus diffusion controlled, and (ii) an electrochemical experiment, in which naphthalene radical cation ($NaphH^{\bullet+}$) was generated at a controlled anode potential in the presence of nitrogen dioxide. The ratio of 1- to 2-nitronaphthalene formed in the coupling reaction between $NaphH^{\bullet+}$ and NO_2[17] was 9.2, within experimental error equal to that obtained in the NO_2^+ nitration of naphthalene in acetonitrile, 10.9.[15]

$$ArH + NO_2^+ \rightleftharpoons \overline{ArH^{\bullet+} + NO_2} \rightarrow Ar^+(H)NO_2 \qquad (5)$$

Difficulties with Electrochemical Nitration Experiments. This beautifully conceived experiment on closer inspection turned out to be marred with difficulties of practical nature.[18] First of all, a competing nitration process, namely by NO_2 itself, was shown to account for at least 60% and possibly all of the nitronaphthalenes formed. The uncertainty is due to the fact that the NO_2 nitration process is catalyzed by protons, which are formed during electrolysis via several processes, not the least from loss of the proton in the Wheland intermediate of eq 5. Besides, there is always a risk that the anodic oxidation of NO_2 to NO_2^+ can take place at the high potential used in these experiments.[19]

Table I.
Ratio of the Most Abundant α-Nitro Isomer to All Other Nitro Isomers in the Nitration of Naphthalene and Certain Methylnaphthalenes[22,23]

	nitration via		
compound	$AcONO_2$ in Ac_2O	N_2O_4 in CH_2Cl_2	$ArH^{\bullet+} + NO_2$ in CH_2Cl_2
naphthalene	11	25	>50
1-methylnaphthalene	1.3	1.9	7.3
2-methylnaphthalene	1.3	1.9	7.0
1,8-dimethylnaphthalene	2.3	7.3	>12
2,3-dimethylnaphthalene	3.3	3.3	9
2,6-dimethylnaphthalene	3.5	5.3	9

A consequence of eq 5 is that the formation of nitronaphthalenes should only depend on the amount of charge passed (the coupling between $ArH^{\bullet+}$ and NO_2 is assumed to be diffusion controlled) and be independent of temperature. Contrary to this, much lower yields of nitronaphthalenes were obtained at 5 °C than at 25 °C, again showing that a homogeneous process must be responsible for the major part of the product formation.[18]

Another difference from Perrin's experiment was noted in the ratios of 1- and 2-nitronaphthalene; larger ratios, in the range of 20–30, were consistently found in our anodic experiments. A ratio of 17 ± 3 was found by others in a later study.[20] This is characteristic of the NO_2 nitration process, as established in control runs. These discrepancies might be explained in either of two ways: there may be an unknown factor that makes this type of experiment difficult to reproduce—and organic electrochemistry has its fair share of irreproducible results—or we might have accidentally favored the homogeneous reaction so that the anodic reaction, as reported by Perrin, was completely overshadowed. Therefore, another approach was chosen.

Coupling between Preformed Radical Cation and Nitrogen Dioxide. The naphthalene radical cation can be prepared as its hexafluorophosphate by electrocrystallization from a dichloromethane solution at −45 °C.[21] The salt can be isolated and allowed to react with a solution of NO_2 in dichloromethane to give an almost quantitative yield of nitronaphthalenes with a very high 1- to 2-nitronaphthalene isomer ratio, between 35 and 60.[22] The experience gained in running these experiments eventually led to the almost perfect anodic experiment, oxidation of naphthalene at −45 °C in dichloromethane/tetrabutylammonium hexafluorophosphate in the presence of NO_2, which gave a 100% current yield of nitronaphthalenes with a 1-/2- ratio of 65. Thus, far from being a low-selectivity process, the coupling between $ArH^{\bullet+}$ and NO_2 displays high selectivity. This was confirmed[23] for a range of methylnaphthalene radical cations which were experimentally accessible with surprising ease and possessed unex-

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pectedly high stability in view of the possibility of proton loss from the side-chain position(s).[24] Table I shows that the $ArH^{\bullet+}/NO_2$ reaction is more selective than nitration by both $AcONO_2$ and N_2O_4. For 1,4-dimethylnaphthalene the difference is even more drastic; $AcONO_2$ gives the 5- and 2-nitro derivatives in a ratio of 5.8, N_2O_4 almost exclusively the side-chain nitro compound, and the radical cation reaction the 2-nitro isomer.[23]

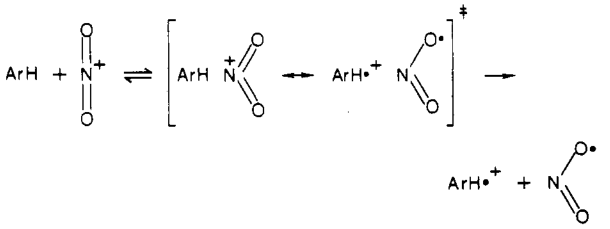
Perylene radical cation ($PeH^{\bullet+}$) is much easier to prepare and handle than $NaphH^{\bullet+}$, and we therefore undertook a similar study with $PeH^{\bullet+}$, allowing it to react with NO_2 under a variety of conditions.[25] Much to our surprise, the coupling reaction was not nearly as clean as that of $Naph^{\bullet+}$ and several side reactions were seen. The yields of $PeNO_2$ (3-/1- isomer ratio generally >100) were in the range of 3–70%; here the contribution from NO_2 nitration is significant.

The reaction between $ArH^{\bullet+}$ and NO_2 could also be studied in the gas phase,[9a] and it was shown that a number of $ArH^{\bullet+}$ corresponding to parent compounds of intermediate electron availability react with NO_2 to give the π-complex. $ArH^{\bullet+}$ from either electron-rich or electron-poor compounds (e.g., furan or pyridine, respectively) did not react, and naphthalene reacted very slowly. In methyl aromatics, coupling occurs predominantly at the ring. The low reactivity of $Naph^{\bullet+}$ is unexpected in view of the ease by which the corresponding solution reaction takes place, and clearly more work is needed to determine the origin of this difference.

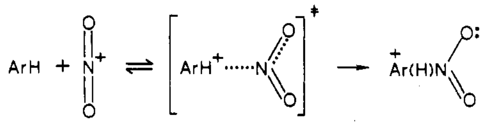
The results shown in Table I unambiguously show that the coupling between $ArH^{\bullet+}$ and NO_2 cannot lie on the pathway between ArH/NO_2^+ and the Wheland intermediate, unless we assume that the orientation within the radical pair immediately after electron transfer represents a unique state leading to an isomer distribution quite different from the one observed when $ArH^{\bullet+}$ and NO_2 diffuse together in solution. One possible reason for such control might be the existence of a structurally well-defined π-complex immediately preceding ET. Such an ad hoc hypothesis is always possible, and other ways of looking at the problem are therefore necessary.

Application of the Marcus Theory to the ET Step

The ET and polar pathways of the ArH/NO_2^+ reaction differ in one aspect only, namely, the degree of electronic interaction in the transition state. Equation 6 shows the ET pathway, as formulated on the basis of the Marcus theory for outer-sphere ET.[26] The important feature of this process is the attainment of the transition state by nuclear movements (bond reorganization) and solvent reorganization only; no electronic interaction between the reactants is allowed. This view of the ET transition state is a consequence of the Franck–Condon principle, which says that transfer of an electron is much faster than nuclear movements. Note that the outer-sphere transition state always includes two forms, one with the electronic description of the reactants and one with that of the products.

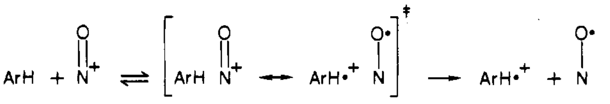

(6)

The usual polar transition state is shown in eq 7, where an appreciable electronic interaction is implicit in the dotted bonds of the transition state.


(7)

We now can get a grasp of the origin of the large difference between these two processes. In the ET transition state, the energy expended in bending the initially linear NO_2^+ moiety to a bent species, somewhere halfway to becoming an NO_2 molecule with an O–N–O bond angle of 134.3°, is very large.[27] This contribution to the bond reorganization energy, estimated to be 52 kcal mol^{-1}, is the factor responsible for making the ET step energetically difficult.[27] Minor changes take place within the ArH part of the transition state too, but they are negligible in this context (≤5 kcal mol).[28] Similar bond reorganization must occur during the attainment of the polar transition state, but here it is compensated by the electronic interaction (partial formation of a C–N bond) in the transition state.

It is instructive to view the nitrosonium ion oxidation of ArH in the same way. Equation 8 demonstrates that the bond reorganization necessary to reach the transition state is not nearly as extensive as in eq 6; again neglecting the part stemming from changes in ArH, the dominant change is the lengthening of the N–O bond, the full change in going from NO^+ to NO being ca. 0.09 Å. This contribution to the reorganization energy is only of the order of 10 kcal mol^{-1}.


(8)

In both the nitronium and nitrosonium ion effected ET reactions, the total reorganization energy also has a contribution from solvent reorganization, calculated by Kharkats' ellipsoidal model[29] to be 18 and 25 kcal mol^{-1}, respectively. This again neglects the very small contribution from solvent reorganization around ArH.

Apart from the reorganization energy, the other parameter of interest for the properties of an ET oxidant is its standard potential ($E°$). Reversible potentials for reduction of NO_2^+ and NO^+ in acetonitrile are known to be 1.56[30] and 1.51 V[31] (vs. normal hydrogen electrode;

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Table II.
Calculated log (k/M^{-1} s^{-1}) for Hypothetical Outer-Sphere ET Reactions between Aromatics or Heteroaromatics and NO^+ or NO_2^+ in Acetonitrile at 25 °C[27]

		$\Delta G°$/kcal mol^{-1}		log k for reaction with	
compound	$E°$/V[a]	NO^+	NO_2^+	$NO^{+\,b}$	$NO_2^{+\,c}$
benzene	3.03	35.0	33.8	−13.3	−16.4
toluene	2.61	25.4	24.1	−7.1	−11.5
mesitylene	2.43	21.2	20.9	−4.7	−9.5
naphthalene	2.08	13.1	11.9	−0.4	−5.9
dibenzo[1,4]dioxin	1.63	2.8	1.6	4.1	−1.7
anthracene	1.61	2.3	1.1	4.3	−1.5
perylene	1.30	−4.8	−6.0	6.8	0.9
Zn(II) tetraphenylporphyrin	0.95	−12.9	−14.1	9.1	3.4
phenothiazine	0.71	−18.4	−19.6	10.0	5.0
ferrocene	0.60	−21.0	−22.2	10.2	5.7

[a] $E°$ of NO^+ and NO_2^+ were taken to be 1.51[31] and 1.56 V,[30] respectively. [b] Reorganization energy set equal to 40 kcal mol^{-1}. [c] Reorganization energy set equal to 75 kcal mol^{-1}.

all potentials given in this paper are referred to this standard) and can be approximately equated with their $E°$ values. Thus, if one were to look at this parameter only, one would conclude that their powers as ET oxidants are roughly identical. However, the large difference in reorganization energy, qualitatively explained above, conspires to make NO_2^+ a much weaker oxidant. This can be put into quantitative terms by estimating outer-sphere ET rate constants via the Marcus treatment.[27] The details of this procedure will not be given here; it suffices to give the Marcus expression for $\Delta G^‡$ (eq 9) which shows that it is a function of both $\Delta G°$ [equal to $-23.06(E°_2 - E°_1)$, where $E°_1$ and $E°_2$ are the standard potentials for the $ArH/ArH^{\bullet+}$ and NO_2^+/NO_2 couples] and the reorganization energy (λ).

$$\Delta G^‡ = \lambda/4(1 + \Delta G°/\lambda)^2 \qquad (9)$$

We can use this expression in conjunction with a simple kinetic model to estimate log k values for ET between different ArH and NO^+ or NO_2^+ (Table II). Looking first at the NO_2^+ reaction, we see that even ferrocene, a very good ET reductant, is predicted to react at less than diffusion-controlled rate with NO_2^+. In fact, if one assumes that one can detect 1% of an ET reaction in competition with a polar process occurring at diffusion-controlled rate, the upper $E°$ limit for a reductant would be ca. 0.2 V, indeed an extremely easily oxidizable compound. (Examples with $E°$ around this limit would be decamethylferrocene and *N,N,N′,N′*-tetramethyl-*p*-phenylenediamine.) On the other hand, this treatment predicts nitrosonium ion to be a far stronger ET oxidant, perhaps by a rate factor of 10^6, and since it is a very weak electrophile,[36] it is indeed possible to find numerous examples of its role as an outer-sphere oxidant. Table III lists such reactions, and one can qualitatively note that chrysene, with an $E°$ of 1.88 V, seems to represent an upper limit for detection of radical cations upon treatment by NO^+. At this limit, the radical cations formed are so reactive that it is not possible to make quantitative measurements because of the instability of the solutions. Synthetic utility is shown by the fact that tris(4-bromophenyl)ammoniumyl tetrafluoroborate, a widely used catalyst for ET-catalyzed processes,[37] can be produced in a reasonably stable state by this procedure. Other methods, such as anodic oxidation or treatment by iodine/silver tetrafluoroborate of tris(4-bromophenyl)amine, give less stable preparations.[38]

Table III.
Nitrosonium Ion as an ET Oxidant Toward Organic Compounds

compound	$E°$ or $E_{1/2}$/V	result[a]	ref
triphenylene	2.12	no reaction	27
naphthalene	2.08	no reaction	27
chrysene	1.88	less the 1% of RC formed in solution[b]	27
dibenzo[1,4]dioxin	1.63	RC formed in solution	12
anthracene	1.61	RC formed in solution[b]	27
pyrene	1.60	RC formed in solution[b]	27
thianthrene	1.52	RC formed in solution	12
phenoxathiin	1.50	RC formed in solution	12
phenoxazine		RC isolated as salt	32
9,10-diphenylanthracene	1.44	RC formed in solution	27
9-phenylanthracene	1.34	RC formed in solution	27
perylene	1.30	RC formed in solution and isolated as salt	12, 27
tris(4-bromophenyl)-amine	1.30	RC formed in solution	33, 34
RC of 5,10-di-methyl-5,10-dihy-drophenazine	1.07	dication salt isolated	12
triphenylamine	0.99	RC formed in solution[b]	33
10-methylphenothiazine	0.94	RC isolated as salt	12, 33
1,5-dithiacyclooctane	0.88	RC formed in solution	35
RC of 1,5-dithia-cyclooctane		dication salt isolated	35
tris(4-methoxy-phenyl)amine	0.72	RC formed in solution	33
phenothiazine	0.71	RC isolated as salt	12
ferrocene	0.60	RC formed in solution	27
5,10-dimethyl-5,10-dihydrophenazine	0.35	RC salt isolated	12, 33[c]
N,N,N′,N′-tetramethyl-*p*-phenylenediamine	0.26	RC formed in solution	33

[a] RC = radical cation. [b] The RC solution was not stable upon standing. [c] The 5,10-methylphenyl and -diphenyl derivatives reacted in the same manner.

Inner-Sphere Electron Transfer in Nitration by Nitronium Ion. One phenomenon is however not explained by these calculations, and that is the actual detection of radical cations upon treatment of aromatic substrates with NO_2^+.[11] How are they formed, if we

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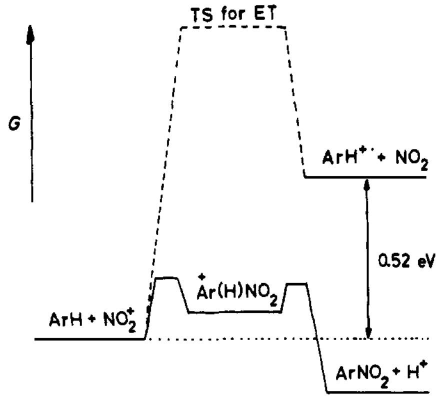


Figure 1. Schematic free energy diagram for a reaction between ArH and NO_2^+ where ET is endergonic. In this example ArH corresponds to naphthalene.

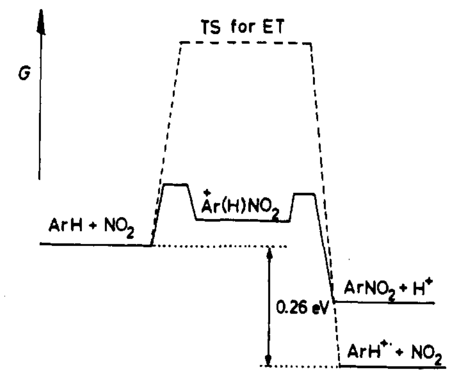


Figure 2. Schematic free energy diagram for a reaction between ArH and NO_2^+ where ET is exergonic. In this example ArH corresponds to perylene.

exclude the trivial possibility that NO^+ is somehow formed in catalytic amounts during the reaction? (Although trivial, this is certainly not unlikely, unless precautions are taken to add nitrous acid traps in the experiments.)

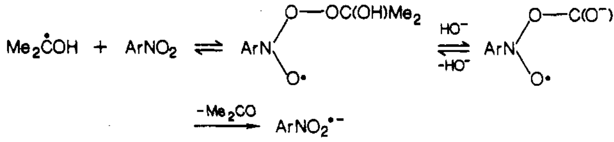
Inspection of energy diagrams for two extreme types of ArH/NO_2^+ reactions gives a reasonable explanation for several phenomena mentioned above.[25] The $NaphH/NO_2^+$ reaction (Figure 1) is endergonic by 0.52 V in the ET mode and has a very high lying transition state ($\log k = -5.9$; see Table II). The polar mechanism has a very low lying transition state (reaction proceeds at diffusion-controlled rate), and thus the coupling process between $ArH^{\bullet+}$ and NO_2 must be exergonic, and conversely, the homolytic cleavage of the Wheland intermediate endergonic. Thus, it is easily understood why presynthesized $NaphH^{\bullet+}$ reacts cleanly with NO_2 to give nitro products and why neither the ET nor the polar pathway will give any detectable concentration of the radical cation.

The situation is quite different for an ArH that *in principle* can undergo exergonic ET to NO_2^+. Figure 2 shows a schematic energy diagram for the perylene/NO_2^+ reaction. Here we still have a fairly high lying transition state for ET ($\log k = 0.9$; Table II), and as for naphthalene, a very low lying one for the polar pathway. However, the ET process is now overall exergonic which means that the homolytic cleavage of the Wheland intermediate necessarily must be exergonic too. This suggests two corollaries, namely, that (i) the radical cation *can* be a product from the initially polar pathway and (ii) the nitro product may be formed in a slightly endergonic reaction from $PeH^{\bullet+}/NO_2$, thus creating competition from possible side reactions of $PeH^{\bullet+}$, such as coupling, reaction with solvent, etc.

What then is proposed as the pathway for radical cation formation from ArH and NO_2^+ is no less than an *inner-sphere* ET mechanism (eq 10).[38] In this

$$ArH + NO_2^+ \rightleftharpoons Ar^+(H)NO_2 \rightleftharpoons ArH^{\bullet+} + NO_2 \qquad (10)$$

terminology, the association step to give the Wheland intermediate is equivalent to formation of the bridged intermediate (the precursor complex) and the dissociation step to give radical cation and NO_2 equivalent to the transfer of the electron from one site to the other. A similar association/dissociation mechanism was recently described for ET between hydroxyisopropyl radical and nitrobenzene to give acetone and (nitrobenzene)$^{\bullet-}$ (eq 11) and the analogy to the inner-sphere ET mechanism pointed out.[39] The formation of aromatic radical cations from the oxidation of ArH by hydroxyl radical has been interpreted analogously (eq 12).[40]



$$Me_2\dot{C}OH + ArNO_2 \rightleftharpoons ArN(O{-}OC(OH)Me_2)(\dot{O}) \underset{-HO^-}{\overset{HO^-}{\rightleftharpoons}} ArN(O{-}C(O^-)Me_2)(\dot{O}) \xrightarrow{-Me_2CO} ArNO_2^{\bullet-} \qquad (11)$$

$$ArH + HO^\bullet \rightleftharpoons \dot{A}rH(OH) \underset{-H^+}{\overset{H^+}{\rightleftharpoons}} \dot{A}rH(OH_2^+) \rightleftharpoons ArH^{\bullet+} + H_2O \qquad (12)$$

Thus, the simple provision to consider a bond equivalent to the bridging ligand in the inorganic variety of the inner-sphere ET mechanism immediately makes this useful concept available for use in organic mechanisms. In fact, this is exactly what is implied in Pross' recent proposal that all organic reactions mechanisms actually consist of one-electron *shifts*.[41]

Differences between Hydrocarbons. Ridd et al.[42-45] have studied possible ET mechanisms in the ArH/NO_2^+ system using ^{15}N-labeled nitronium ion. For mesitylene in trifluoroacetic acid (TFA, a very good solvent for radical cations) no nuclear polarization is seen in the product from the nitronium ion pathway.[42] This is in agreement with the results described above; mesitylene is a difficult compound to oxidize ($E° = 2.43$ V), so outer-sphere ET is prohibited for kinetic reasons (Table II) and inner-sphere ET for thermodynamic reasons. On the other hand, the nitrous acid catalyzed pathway gives nitromesitylene with very strong ^{15}N nuclear polarization (*emission* with a degree of enhancement of more than 200). This was attributed to the formation of the radical pair $ArH^{\bullet+}NO_2$ by diffusion together of the two components. The effect of nitrous acid catalysis was assumed to be generation of NO^+, which would act as an ET oxidant toward mesitylene.

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Side products isolated from these experiments, like nitrated diphenylmethane derivatives and the side-chain nitro product, could be rationalized as being derived from the radical cation.[13,44]

The difficulty with this interpretation is that the mesitylene/NO^+ reaction is endergonic according to estimates based on the standard potentials available. Since these refer to different solvents (mesitylene in TFA and nitrosonium ion in acetonitrile) and since it is a fairly general observation that oxidation potentials tend to increase in acidic media, it might well be that nitrosonium ion has a higher standard potential in TFA than in acetonitrile.

For durene, with an $E°$ of 2.07 V, the nitrous acid catalyzed reaction had the same characteristics as for mesitylene, but the nitronium ion reaction also exhibited nuclear polarization, the ^{15}N NMR signal showing enhanced *absorption*.[45] This indicates that the radical pair is formed via a dissociation step, and it was assumed that homolysis of the ipso intermediate was identical with this step (see eq 10, with $ArCH_3$ instead of ArH). Here we encounter the same difficulty as for the mesitylene/NO^+ reaction, in that the durene/NO_2^+ ET reaction is endergonic. Again a plausible explanation is that NO_2^+ has a higher standard potential in TFA than in acetonitrile. A recent measurement[46] of $E°(NO_2^+/NO_2)$ in sulfolane (around 1.9 V) at least shows that this value is solvent sensitive.

Related Problems

Reaction between Nitrite Ion and Radical Cations. Aromatic,[47] heteroaromatic,[48] and metalloporphyrin[49] radical cations are known to react with nitrite ion to give nitration products, believed to occur via direct nucleophilic attack of NO_2^- on the radical cation. The reactions were performed with either preformed radical cation and nitrite ion or parent compound and iodine/$AgNO_2$. In view of the findings reported above an alternative mechanism might be (i) ET between nitrite ion and the radical cation, followed by (ii) nitration of ArH by NO_2 which should be a fast process for the compounds reported (thianthrene, phenothiazine, dibenzo[1,4]dioxin, perylene, Zn(II) tetraphenylporphyrin, and Zn(II) octaethylporphyrin). The $E°$ value of the NO_2/NO_2^- couple is 1.0 V in water[50] and considerably lower in acetonitrile, estimated to be somewhere between 0.3 and 0.5 V.[51] Thus, ET between the above radical cations which all have $E° \geq 1.0$ V in acetonitrile and NO_2^- should be very fast and exergonic.

We first could establish that the iodine/$AgNO_2$ reagent in all probability acts as a source of NO_2 and does not induce a radical cation mechanism. This was shown simply by mixing $AgNO_2$ and iodine in acetonitrile and filtering off the solid AgI formed. The resulting solution had exactly the same characteristics as a nitration reagent as a solution of NO_2 in acetonitrile.[25] It is known that NO_2 is formed quantitatively from iodine and $AgNO_2$ in carbon tetrachloride.[52]

Secondly, it was shown that radical cations of naphthalene, 2-methylnaphthalene, pyrene, and perylene[22,23,25] react with nitrite in acetonitrile in 100% ET reactions, followed by nitration by NO_2 in cases of reactive parent compounds like perylene.[25] It is likely that this nitration mechanism prevails for systems with $E°$ values down to 1.0 V or possibly lower in acetonitrile or other badly anion solvating solvents.

Since the above radical cations react with nitrite ion in an exergonic, very fast ET process, the reverse reaction, ET oxidation of aromatics by NO_2, is not a feasible step. Such a mechanism was suggested recently for nitration of polycyclic aromatic hydrocarbons (PAH's) by NO_2 in dichloromethane,[53] but since the $E°$ values of the substrates studied were all >1.30 V, this proposal cannot be correct. An analysis by the Marcus treatment gave the same result in quantitative terms.[54]

The Mechanism of the NO_2 Nitration Reaction. This reaction is a fairly complex one,[54] and more work is needed to establish its mechanism with any degree of certainty. The reaction is catalyzed by protons and NO^+ and in many respects resembles the well-known nitrous acid catalyzed nitration,[1] in fact so much that the two reactions might well be identical. Preliminarily, we have suggested[54] that the nitrating species in the proton-catalyzed variety is protonated dinitrogen tetroxide, whereas in the NO^+-catalyzed reaction the nitrosated N_2O_4 species might be the attacking species. Analogous species are known.[55]

The Synthetic Potential of the NO_2 Nitration Process. This is a very mild nitration reaction, known from earlier work[56] but not explored fully for synthetic purposes. It is especially useful for easily oxidizable aromatics which tend to give extensive side reactions with the common nitronium ion based reagents. The reaction is carried out in dichloromethane, leading to very simple work-up procedures, not the least important in the synthesis of potentially mutagenic nitro derivatives of polycyclic aromatic hydrocarbons.[54,57] The reaction is more selective than nitronium ion effected ones, and yields are in the region of 90–95%. By addition of acid or nitrosonium ion, nitration of less reactive aromatics becomes possible, the practical limit being mesitylene and compounds of similar reactivity. Conversely, for very reactive substrates the reactivity of NO_2 can be decreased by addition of a hindered pyridine base, like 2,6-di-*tert*-butyl-4-methylpyridine. Thus, NO_2/dichloromethane should be the reagent of choice in the nitration of reactive aromatics.

Relation to Certain Environmental Problems. The mechanistic problems discussed above are not only of academic interest but have important connotations

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for the study of processes leading to the distribution of nitro derivatives of polycyclic aromatic hydrocarbons in the environment. These are formed in combustion processes, including smoking, and constitute a significant part of the carcinogenic compounds of airborne particulate matter.[58]

Conclusions

We do not claim that we have once and for all solved the problem of ET mediated nitration reactions, but we believe that two conclusions are presently possible to draw:

(i) If a radical cation is formed from an ArH/NO_2^+ reaction and the nitrous acid catalyzed pathway has been properly suppressed by addition of a nitrous acid scavenger, it is formed via an inner-sphere ET mechanism (eq 10).

(ii) If the nitrous acid catalyzed pathway has not been excluded by addition of a scavenger, the radical cation in all probability is formed via an outer-sphere ET mechanism with NO^+ as the oxidant.

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Polysaccharide Conformations and Kinetics

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Of the three classes of biopolymers—proteins, nucleic acids, and polysaccharides—the polysaccharides have been the Cinderella of the group. This is not to imply that proteins and nucleic acids are the Ugly Sisters, but simply that when biopolymers like insulin and DNA are compared with, for example, starch, most people would feel that polysaccharides are unworthy of close attention. This Account aims to show that polysaccharides are worthy of detailed study by chemists interested in structure and dynamics and that kinetics are useful in helping to establish the conformational states of these macromolecules in solutions.

We have been particularly interested in thermally reversible conformational transitions shown by a number of polysaccharides used as food hydrocolloids.[1]

(a) Xanthan (Figure 1) is an extracellular bacterial polysaccharide used widely as a thickener and a stabilizer to control the rheology of aqueous phases for a number of industrial applications. This is often referred to as giving "body" to fluids or emulsions. A 1% aqueous solution of xanthan has a viscosity 10 times that of water, and the pseudoplastic shear thinning behavior of xanthan solutions makes them particularly useful in food products such as sauces and salad dressings. Xanthan is used in the petroleum industry as a viscosifier for drilling fluids.[2] Its use may result in enhanced oil recovery since an increase in the viscosity of the aqueous solution used as a driver fluid to extract oil from a reservoir will delay the onset of water breakthrough into the oil being pumped out. A pilot plant has recently been commissioned in the U.K. to culture xanthan strains as biotechnological products.

(b) Carrageenans and agar (Figure 2) are a group of polysaccharides that are structural components of red seaweeds and are used in the food industry as gelling agents, particularly in cold-setting desserts. In food gels this type of polysaccharide, typically present at the 1% level, creates a three-dimensional network which gives the product the desired texture and shape. These gels are strongly dependent on the salt type and ionic strength, and clear gels are obtained by mixing polysaccharides such as agarose sulfate and ι- and κ-carrageenan with salts.

A principal aim of our work has been to determine the primary processes in salt-induced conformational changes and gelation. We first discuss polysaccharide conformations in the solid state and in solution, and then we describe the detailed information obtained from kinetic studies.

Polysaccharide Structures

A consequence of regularly repeating units in the backbone of polysaccharides is that they generally adopt geometrically regular spatial arrangements in the solid state. These have been categorized by Rees,[3] with

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