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Mechanisms and Reactivity in Electron Transfer Induced Aromatic Nucleophilic Substitution. Recent Advances.

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Contents

1. INTRODUCTION

A wide class of substitution reactions at sp2 and sp3 carbons is induced or stimulated by light, by electrons dissolved in liquid ammonia, and by electrons transferred from an electrode or from homogeneous outer-sphere one-electron donors.[1-8] The mechanism commonly accepted[1-8] for these reactions, the "$S_{RN}1$" mechanism,[9] involves the following propagation loop shown in Scheme 1.

Scheme 1

$$RX^{\bullet-} \rightleftharpoons R^{\bullet} + X^{-} \qquad (1)$$

$$R^{\bullet} + Nu^{-} \rightleftharpoons RNu^{\bullet-} \qquad (2)$$

$$RX + RNu^{\bullet-} \rightleftharpoons RX^{\bullet-} + RNu \qquad (3)$$

The mechanism of the initiation depends on the nature and mode of production of the reducing species used to induce the reaction. In "thermally" induced $S_{RN}1$ processes, the nucleophile itself serves as the electron donor without external stimulation. In all cases, however, initiation involves generation, from the substrate RX, of the anion radical $RX^{\bullet-}$ or the radical $R^{\bullet}$ that then enters the propagation loop. The key-step of the substitution is reaction of radical $R^{\bullet}$ with the nucleophile to yield the anion radical, $RNu^{\bullet-}$. The latter intermediate may then transfer its unpaired electron to the substrate as in reaction 3 thus closing the propagation loop of the chain process depicted in Scheme I and producing the final substituted product, RNu. In the case of electrochemical induction, $RNu^{\bullet-}$ may also be concurrently re-oxidized at the electrode rather than by reaction with RX. Likewise, when the reaction is triggered by electron transfer to the substrate from the reduced form of a reversible redox couple, as in indirect electrochemical induction, $RNu^{\bullet-}$ may also concurrently lose its unpaired electron by transfer to the oxidized form of the redox couple.

Electron transfer reduction of $R^{\bullet}$ and H-atom abstraction from the solvent (in the case of organic solvents) by $R^{\bullet}$ have been identified as termination steps.[3,4,7] Determination of the nature and rate of the termination steps is essential not only for rational optimization of product distribution but also for establishment of the reaction mechanism, for estimation of the rate constant for combination of the $R^{\bullet}$ radical with the nucleophile and its correlation with molecular structure. Another widely employed strategy for study of mechanism, at least at a qualitative level, has been to observe the decrease of reactivity upon addition of radical traps, or, more frequently, redox traps able to interrupt the chain process.

Besides synthetic interest, the mechanistic and reactivity aspects of $S_{RN}1$ reactions have attracted considerable attention in connection with fundamental problems in chemical reactivity such as the relationship between one-electron transfer chemistry and radical chemistry, the respective role of one-electron vs electron-pair transfer in nucleophilic substitution,[7] and, more generally, in nucleophile-electrophile chemistry.

Another reason for sustained interest in $S_{RN}1$ reactions is the inherent difficulty of fully comprehending all the mechanism aspects owing to the large number of successive or competing steps involved; furthermore each mode of induction introduces its own peculiarities into the kinetics and even into the competition between steps that determines the product distribution. In spite of the large amount of mechanistic work devoted to this reaction, unsolved issues remain that raise questions about the validity of the $S_{RN}1$ mechanism and the possibility of looking for alternatives.

One of these is the possible occurrence of an "$S_{RN}2$" mechanism in which steps 1 and 2 would be concerted, i.e., replaced by a single bimolecular step :

$$RX^{\bullet-} + Nu^{-} \rightleftharpoons RNu^{\bullet-} + X^{-} \qquad (4)$$

In the framework of such a mechanism, the chain character of the reaction would be preserved and so would be the possibility that induction by any means (photochemistry, electrochemistry, heterogeneous or homogeneous one-electron donors) could trigger formation of the substrate anion radical as well as inhibition by redox traps.

These classical criteria for an $S_{RN}1$ mechanism are thus unable to distinguish it from "$S_{RN}2$".

There have not been many studies specifically aimed to distinguish these two mechanistic possibilities experimentally. One study concerns the relative reactivity in liquid ammonia of several nucleophiles of different electronic and steric characteristics toward a series of benzenes carrying different leaving groups .[10] Another deals with the electrochemically induced substitution of 2-chloroquinoline by thiophenoxide or 4-chlorothiophenoxide ions in liquid ammonia and with the substitution of 9-chloroanthracenes in dimethylsulfoxide.[11-13] In all these cases, in which the substrate anion radical was assumed to fragment rapidly, it was concluded that the reaction follows the $S_{RN}1$ mechanism rather than $S_{RN}2$.

The $S_{RN}2$ mechanism has been deemed to occur in several substitution reactions in which the anion radical of the substrate is relatively stable, such as in nitrophenyl or perfluoronitrophenyl substrates bearing, as leaving group, a halogen or another nitro group[14-22] as well as in p-nitrobenzophenone and p-nitrobenzonitrile where the leaving group is the nitrite ion.[23] Caution has been recommended in assigning the $S_{RN}1$ mechanism to all aromatic processes proceeding via a radical chain sequence.[24] In most of these cases, the assignment of $S_{RN}2$ was based on the stability of the anion radical in combination with the criteria of stimulation by light and inhibition by redox traps.

Furthermore, it has been recently claimed that all aromatic nucleophilic substitutions, so far thought to follow $S_{RN}1$, should rather be viewed in terms of the $S_{RN}2$ mechanism whatever the stability of the substrate anion intermediate.[22] This assertion was next challenged on the basis of a discussion of experimental facts and of the unlikelihood of the structure and properties of the transition state implied by the $S_{RN}2$ mechanism.[25,26] This is an important issue since its outcome is not merely to assign a reaction order of 1 or 2 to the keystep of the reaction but, more significantly, to decide whether such aromatic nucleophilic substitutions are essentially a manifestation of radical chemistry or of radical anion chemistry. Consequently, the present Report contains a detailed discussion of this problem. In the case of "stable" substrate anion radicals, we also examine whether or not the evidence presented so far is sufficient to support reliably an $S_{RN}2$ mechanism.

From a synthetic standpoint, photochemical induction appears superior to the other methods in terms of selectivity. It allows side-products arising from electron transfer to the $R^\bullet$ radical to be minimized as compared to direct or indirect electrochemical induction or to induction by solvated electrons. However, if one tries to base mechanistic analyses on precise quantitative kinetics, direct and indirect electrochemistry appears as the method of choice thanks to accurate control of the energy of incoming electrons by means of the electrode potential and the easy and precise determination of the overall reaction rate from the current flowing through the electrode surface.[27,28] Since mechanistic evidence based on electrochemical data may appear abstruse to readers not familiar with heterogeneous kinetics, the electrochemical sections in this Report are more detailed than the other sections.

One particularly puzzling feature of $S_{RN}1$ substitution is that the nature of the leaving group can affect the distribution of products, as clearly observed in light-induced and in solvated-electron induced reactions. At first sight, such an observation appears to contradict the $S_{RN}1$ mechanism since, at the stage where product selection takes place, the leaving group has already departed. This point will be discussed in section 5 with particular emphasis on recent analyses that have put on quantitative bases the early assumption[2,4] that, in reactions induced by solvated electrons, the initiation, propagation, and termination steps occur during mixing of solvated electrons with the substrate solution.

Kinetic data on the cleavage of aromatic anion radicals containing potential leaving groups as well as on the formation of anion radicals from aryl radicals and nucleophiles show that the rate constants of these two reactions depend strongly not only on the leaving group or the nucleophile, but also to a large extent on the aryl moiety. A quantitative model based on an extension of dissociative electron transfer theory to these reactions viewed as intramolecular one-electron transfers concerted with bond breaking or bond formation will be presented in section 6.

2. STABILITY OF ANION RADICALS CONTAINING POTENTIAL LEAVING GROUPS.

One important assumption underlying the reasoning in ref. 22 is that "the reactivity of the aryl radical (toward nucleophiles) should not be affected very much by a change in structure". This assertion, if true in the thermodynamic sense, would imply that the reverse reaction, i.e., the expulsion of an anion from an aromatic anion radical, would also be insensitive to the structure of the aryl moiety. Thus, in line with the reasoning in ref. 22, it would suffice to find particular aryl structures giving rise to stable anion radicals to infer that this should be the case for any other aryl structures. Since such aromatic anion radicals, stable towards cleavage, do exist[29,30] it would follow that all previous work is in error, in particular electrochemical studies that have concluded that aromatic anion radicals containing potential leaving groups can cleave. The ensuing determinations of cleavage rate constants would consequently be the result of an artifact.

Are these assertions consistent with experimental facts ? As will be shown below, electrochemical studies have demonstrated that lifetimes of aromatic anion radicals can span more than 10 orders of magnitude (from minutes or more to nanoseconds or less) just by change in the aryl moiety while the leaving group stays the same. In spite of the fact that similar variations have been observed with other techniques, such as pulse radiolysis, [31-36] how can one be sure that the electrochemical data on which these conclusions were based were not misinterpreted ?

Let us start with the halo nitrobenzenes[30] and halo benzophenones[29] that were taken (ref. 22) as examples of anion radicals stable toward cleavage. In liquid ammonia, at - 40°C, m- and p-chloronitrobenzene, m-bromonitrobenzene and m-fluorobenzophenone are typical cases where not only the anion radical but also the dianion are stable within the time-scale of the experiment defined by the value of the rate at which the electrode potential is scanned (linearly), 0.2 V/s in the present case. This is proved by the observation of two successive one-electron waves that are both reversible (see Figures 2, 4, 6 in ref. 30 and Figure 4a in ref. 29). In cyclic voltammetry, chemical reactions that follow electron transfers (for example monomolecular cleavages) modify the form of the wave, from reversible to irreversible, as a result of competition with diffusion. The rate of diffusion is itself a function of the scan rate (v). The parameter that governs the competition is thus :[27]

$$\lambda = \frac{RT}{F}\frac{k}{v} \quad \text{for a first order reaction ,} \qquad \lambda = \frac{RT}{F}\frac{kC^0}{v} \quad \text{for a second order reaction}$$

(R : gas constant, F : Faraday, T : absolute temperature, k : rate constant of the accompanying chemical step, C^0 : concentration of starting material in the bulk of the solution). Approximately, total reversibility is reached when $\lambda \leq 0.1$ and total irreversibility when $\lambda \geq 5$. Thus, the dianion lifetimes are, in all preceding cases, larger than 1s. The same is true a fortiori for the anion radicals. However they are not indefinitely stable : after 15 minutes electrolysis, 10% of the dianion of m-chlonitrobenzene and 100% of the dianion of p-chloronitrobenzene have disappeared. In the case of m-bromonitrobenzene the dianion is less stable; its decomposition is visible in cyclic voltammetry at low scan rates (0.05 V/s). The dianion is even more unstable in the case of m-chlorobenzophenone; the second wave is irreversible at 0.2 V/s, but reversibility is restored at

10 V/s.

Interestingly, in all cases where the two waves can be made reversible, the difference in standard potentials for generation of the anion radical and the dianion is very large : 800 mV with the nitro-compounds and 600 mV with the benzophenone derivatives in liquid ammonia at - 40°C. The same is observed at room temperature in solvents such as dimethylformamide (DMF) with aromatic molecules that do not bear leaving groups provided the cations of the supporting electrolyte (tetraalkylammoniums) do not give rise to strong ion-pairing.[37] The large separation between the two standard potentials reflects the strong coulombic repulsion between the two negative charges that is only partially compensated by interactions with the solvent and the counter-cations. The separation tends to decrease as the π^* orbital is able to spread over a more extended molecular framework.

For the iodonitrobenzenes in liq. NH_3,[30] the second wave, corresponding to the reduction of the anion radical into the dianion, is totally irreversible at 0.2 V/s and has a height corresponding to the transfer of two electrons per molecule. It is followed by a one-electron reversible wave that corresponds to the reduction of the nitrobenzene anion radical into the nitrobenzene dianion. The mechanism of the reaction is therefore as depicted in Scheme 2.

Scheme 2

$$RX + e^- \rightleftharpoons RX^{\bullet-} \qquad \text{1st wave}$$

$$RX^{\bullet-} + e^- \rightleftharpoons RX^{2-} \qquad RX^{2-} \rightleftharpoons R^- + X^- \qquad \text{2nd wave}$$

$$R^- + H^+ \text{ (solvent residual water)} \longrightarrow RH \qquad RH + e^- \rightleftharpoons RH^{\bullet-} \qquad \text{2nd wave}$$

$$RH^{\bullet-} + e^- \rightleftharpoons RH^{2-} \qquad \text{3rd wave}$$

With the para and meta isomers, the anion radical remains stable not only during the time scale of the cyclic voltammetric experiments (0.2 V/s) but also during coulometry (*ca.* 15 minutes). This is not the case with the ortho isomer where the anion radical disappears during coulometry giving rise to nitrobenzene.

The same occurs, but more rapidly, with para-bromobenzophenone.[29] At 0.2 V/s the first wave is irreversible and has a two-electron per molecule height (see Figure 2 in reference 29). It is followed by the two reversible waves of benzophenone ($RH + e^- \rightleftharpoons RH^{\bullet-}$, $RH^{\bullet-} + e^- \rightleftharpoons RH^{2-}$). Reversibility of the first wave is restored by decreasing slightly the temperature (-50°) and raising the scan rate (64 V/s). Under the latter conditions, the reduction wave of the anion radical is still irreversible and widely separated from the first wave (500 mV). The interpretation that was given for the irreversible and two-electron character of the first wave is summarized in the following "ECE-DISP" ("ECE" for a succession of electrode-chemical-electrode steps, "DISP" for a disproportion pathway) classical[27] scheme (Scheme 3).which implies that cleavage of the carbon-halogen bond takes place at the level of the anion radical rather than at that of the dianion. Could this conclusion be in error ?[22] It is true that cleavage of the dianion of p-bromobenzophenone is most likely faster

Scheme 3

$$RX + e^- \rightleftharpoons RX^{\bullet-}$$

$$RX^{\bullet-} \rightleftharpoons R^{\bullet} + X^-$$

$$\text{ECE :} \quad R^{\bullet} + e^- \rightleftharpoons R^- \qquad \text{and/or ,} \quad \text{DISP :} \quad R^{\bullet} + RX^{\bullet-} \rightleftharpoons RX + R^-$$

$$R^- + H^+ \text{ (solvent residual water)} \longrightarrow RH$$

than in the meta isomer. The faster the cleavage in the dianion the more positive the second wave; the positive shift would be at maximum (i.e. when the electron transfer is immeasurably fast) (RT/2F Ln 10) per decade of the rate constant (here, at - 40°C, 23 mV per decade). Thus, one may envision that the first two-electron reversible wave of p-bromobenzophenone is the result of a merging of the second wave (where the anion radical is reduced into the dianion) with the first wave (where the anion radical is generated). This is not what the experiment carried out at 64 V/s tells us since it would imply that the cleavage rate constant of the dianion has decreased by 19 orders of magnitude upon decreasing the temperature from - 40 to - 50°C !

More generally, starting from a standard potential E^0, the positive shift of the peak potential, (RT/2FLn10) log k, triggered by an increase of k, is limited by the kinetics of the electron transfer that creates the dianion as shown

$$RX^{\bullet-} + e^- \rightleftharpoons RX^{2-} \quad (k_s,\alpha) \qquad RX^{2-} \longrightarrow R^- + X^- \quad (k)$$

simply because the cleavage then prevents the reverse electron transfer. The maximum positive shift is then defined by : [27]

$$E_p = E^0 - 0.78\frac{RT}{\alpha F} + \frac{RT}{\alpha F}\mathrm{Ln}\left[\frac{k_s}{\left(\frac{\alpha F v D}{RT}\right)^{1/2}}\right]$$

(k_S : apparent standard rate constant of electron transfer, α : transfer coefficient, D : diffusion coefficient). One cm/s is certainly a maximum value of k_S for the electrochemical reduction of an anion radical.[38,39] Taking typical values for α (0.5) and D (10^{-5} cm^2 s^{-1}), one finds that the peak potential is at maximum (at 0.2 V/s) 144 mV positive to the standard potential. Since the difference in peak potentials between the reversible waves for generation of the anion radical and the dianion is of the order of 600 mV, the wave where the cleaving dianion is generated is 450 mV negative to that where the anion radical is generated (10.5 kcal, 10^{10} in terms of equilibrium constants). It is thus unambiguous that the first two-electron irreversible wave of p-bromo benzophenone is not the result of a merging of the dianion wave with the anion radical wave.

Another means by which the cleaving dianion could interfere in the first reduction wave of p-bromobenzophenone and make it irreversible and two-electron high might be by means of the homogeneous process depicted in Scheme 4.

Scheme 4

$$RX + e^- \rightleftharpoons RX^{\bullet-}$$

$$2\,RX^{\bullet-} \rightleftharpoons RX + RX^{2-} \qquad RX^{2-} \longrightarrow R^- + X^-$$

$$R^- + H^+ \text{ (solvent and/or residual water)} \longrightarrow RH$$

The most favorable conditions for this mechanism are those in which the third reaction is so fast that the forward step of the second reaction has become rate-determining. The second reaction is most effective when its reverse step is at the diffusion limit. This is indeed the case in practice since the forward step is strongly uphill ((RT/F) Ln K = - ΔE^0, ΔE^0 being of the order of 600 mV for the benzophenone derivatives, K is, in liq. NH_3 at - 40°C, of the order of 10^{-13}). The forward rate constant of the second reaction would then be 3 x 10^{-3} M^{-1}s^{-1}. At 0.2 V/s and with a typical concentration of 10^{-3} M, the kinetic factor λ, 3 x 10^{-7}, is extremely small, much too small for the proposed reaction to be efficient in making the first wave irreversible and two-electron high.[27]

We thus see that, even under the most favorable conditions, participation of the cleaving dianion at the level of the first irreversible two-electron wave of p-bromobenzophenone is totally excluded. This conclusion is more general as a consequence of the fact that the ΔE^0s of aromatic molecules are always large as already emphasized.

Since the cleaving dianion does not interfere, the irreversibility of the first wave is due to the cleavage of the anion radical and the ensuing production of the $R^{\bullet}$ radical. Its two-electron character is then a consequence of the fact that the $R^{\bullet}$ radical is easy to reduce, much easier to reduce than the starting material, thus giving rise to the "ECE-DISP" mechanism depicted in Scheme 3. Precise standard potentials for the $R^{\bullet}/R^{-}$ couple for aryl radicals are not available. However an approximate value of - 0.3 V vs SCE for the phenyl radical has been estimated from the oxidation of phenyl lithium in THF.[40] In liq. NH_3 a value of - 0.38 V vs 0.01 M Ag^{+}/Ag has been derived from thermochemical data (see section 6). For all aromatic substrates that have been used in $S_{RN}1$ reactions, the $R^{\bullet}/R^{-}$ standard potential is thus much more positive than the potential where the substrate is reduced. One needs a very easily reduced substrate such as an aromatic diazonium cation to observe something other than the reduction of the aryl radical, namely, in this particular case, the radical derivatization of the carbon surface used as electrode.[41]

In the reduction of p-bromobenzophenone in liq. NH_3 at - 40°C, an increase of the scan rate tends to restore the reversibility and to change the electron stoichiometry from 2e to 1e per molecule (see Figure 3 in reference 29). This points to a DISP mechanism ("DISP" from disproportionation between $R^{\bullet}$ and $RX^{\bullet-}$) rather than to an ECE mechanism. The factor that governs the competition between the heterogeneous (ECE) and the homogeneous (DISP) reduction of $R^{\bullet}$ is $k_D^{3/2}\,(FV/RT)^{1/2}/k^{3/2}$, where k is the cleavage rate constant and k_D the disproportionation rate constant; thus the DISP mechanism prevails over the ECE mechanism because k is not very large (for a more complete analysis of the ECE vs DISP competition, see ref. 42). Less rigorously, but more pictorially, with fast cleavages the $R^{\bullet}$ radical is formed close to the electrode surface and may then diffuse back rapidly to the electrode and be reduced with little chance to be intercepted reductively by $RX^{\bullet-}$. Conversely, with slow cleavages, the radical is formed far away from the electrode surface and has a high probability to be reduced by $RX^{\bullet-}$ before returning to the electrode. This type of variation of the wave characteristics with the scan rate has been used to measure the cleavage rate constant of a large number of anion radicals of aromatic substrates by cyclic voltammetry and related electrochemical techniques using standard millimetric electrodes or, more recently, micrometric electrodes up to 10^6 - 10^7 s^{-1}. [7,28,43]. For the reasons discussed above, there is no ambiguity that the rate constants determined in this manner do indeed refer to cleavage of the anion radical and have nothing to do with cleavage of the dianion.

Anion radicals having lifetimes below a few tenths of microsecond escape characterization by direct electrochemical techniques. "Redox catalysis", where the substrate is reduced by a mediator Q, electrochemically generated from a species P, instead of being directly reduced at the electrode (Scheme 5), is

Scheme 5

$$P + e^{-} \rightleftharpoons Q$$

$$Q + RX \rightleftharpoons RX^{\bullet-} + P \qquad (0)$$

A

$$RX^{\bullet-} \rightleftharpoons R^{\bullet} + X^{-} \qquad (1)$$

$$Q + R^{\bullet} \longrightarrow R^{-} + P \qquad (6)$$

B

$$Q + RX^{\bullet-} \longrightarrow R^{-} + X^{-} + P \qquad (5)$$

$$R^{-} + H^{+}\ \text{(solvent and/or residual water)} \longrightarrow RH$$

one of the most efficient of the indirect electrochemical methods devised so far.[27,28]The lower limit in lifetimes can then be pushed down to a few nanoseconds.[27,28,44] One built-in condition of the applicability of the redox catalysis method is that the standard potential of the mediator couple be positive relative to the reduction potential of RX. It follows that there is even less chance that the cleaving dianion could interfere in this reaction than in the direct reduction. If the anion radicals were stable and the mediator Q were to reduce the anion radical giving rise to the cleaving dianion, the rate constant governing the catalytic process would be at least ten orders of magnitude lower. No detectable increase of the current due to catalysis would then occur.

But let us be the devil's advocate. If on change in the structure of RX, the cleavage of anion radical becomes faster, the cleavage of the dianion will most likely become faster too. Suppose that acceleration of dianion cleavage is faster than acceleration of the anion radical cleavage. At the extreme, one may conceive that reduction of the anion radical and breaking of the R-X bond become concerted as in reaction 5 and faster than reaction 1. Do experimental facts exist that tell us whether or not reaction 1 (mechanism A) prevails over reaction 5 (mechanism B)? Analysis of the kinetic data provides the answer.

The kinetic terms coupled with diffusion toward and from the electrode that govern the catalytic increase of the current are as follows for mechanisms A and B respectively.

$$\begin{array}{cc} \text{A} & \text{B} \\ \dfrac{k_0\, k_1\, C_{RX}\, C_Q}{k_{-0}\,(C_P^0 - C_Q) + k_1} & \dfrac{k_0\, k_5\, C_{RX}\, C_Q^2}{k_{-0}\,(C_P^0 - C_Q) + k_5\, C_Q} \end{array}$$

i.e. in dimensionless terms :

$$\begin{array}{cc} \dfrac{k_0\, k_1\, (C_P^0)^2 \dfrac{C_{RX}}{C_P^0} \dfrac{C_Q}{C_P^0}}{k_{-0}\, C_P^0 \left(1 - \dfrac{C_Q}{C_P^0}\right) + k_1} & \dfrac{k_0\, k_5\, (C_P^0)^2 \dfrac{C_{RX}}{C_P^0} \dfrac{C_Q}{C_P^0}}{k_{-0} \left(1 - \dfrac{C_Q}{C_P^0}\right) + k_5 \dfrac{C_Q}{C_P^0}} \end{array}$$

(the C's are the concentrations of the subscript species and C_P^0 is the bulk concentration of the mediator P).

In the cases where the redox catalysis method was used to determine the lifetime of the $RX^{\bullet -}$ anion radical, i.e., for 2-chloroquinoline in DMF ($k_1 = 6 \times 10^5\ s^{-1}$), 9-bromoanthracene ($k_1 = 3 \times 10^5\ s^{-1}$), 1-chloronaphthalene ($k_1 = 5 \times 10^7\ s^{-1}$), 1-bromonaphthalene ($k_1 = 3 \times 10^8\ s^{-1}$) in dimethylsulfoxide (DMSO), 4-chlorobenzonitrile in CH_3CN ($k_1 = 5 \times 10^8\ s^{-1}$) at 20°C [44], chlorobenzene in liq. NH_3 at - 38°C ($k_1 = 4 \times 10^7\ s^{-1}$)[45], the observations that were made concerning the dependence of the catalytic increase of the cyclic voltammetric peak current upon C_P^0, which reflects the reaction orders, are consistent with mechanism A and not with mechanism B. When C_P^0 is decreased the kinetic response passes from independence vis-à-vis C_P^0 to a behavior indicative of a first-order dependency upon C_P^0 in agreement with the structure of the kinetic term given above (kinetic control passes progressively from reaction 1 to forward reaction 0). If mechanism B were followed, the first-order dependency should be observed whatever the range of values within which C_P^0 is varied.

It follows that the rate constants thus determined are unambiguously those of the anion radical cleavage with negligible interference from anion radical reduction.[46] Interestingly, for the fastest cleaving anion radicals of the series, cleavage would prevail over the dissociative reduction even if the latter were at the diffusion limit. For example, for 4-chlorobenzonitrile in CH_3CN and for 1-bromonaphthalene in DMSO, with a 1 mM concentration of mediator, $k_1/k_5C_P^0$ would then equal 25 and 75 respectively .[44]

For other compounds that have a higher π^* orbital energy such as chloro- and bromobenzene and 2- and

3-chloro and bromopyridines, the same type of redox catalysis carried out in DMF at 20°C [49] revealed that forward reaction 0 has become rate determining whatever the value of C_p^0, a result consistent with the expected acceleration of the anion radical cleavage. Since, for cleavages that are slower than in the present series, the anion radical cleavage was already faster than its dissociative reduction at the fastest limit, the same is a fortiori true here. We may thus conclude that the reduction of these halobenzenes and pyridines by outersphere electron donors such as stable aromatic anion radicals produces anion radicals that cleave very rapidly (rate constants close to or larger than 10^9 s^{-1}) overrunning their reduction by a second electron donor molecule. The aryl radical thus generated may then be reduced by a second electron donor molecule at a diffusion limited rate in most cases (because the aryl radicals are reduced at potentials much more positive than the standard potentials of the electron donors used). They may also be competitively trapped in other reactions, for example, H-atom abstraction from the solvent if it is a good H-atom donor (as are many of the organic solvents used in electrochemical studies)

With this background, we may now examine the critique made in reference 22 of the interpretation given in reference 50 of trapping experiments in the reduction of bromobenzene and 2-chloropyridine by the anion radical of benzonitrile with benzonitrile as solvent. *t*-Butylphenylnitrone was introduced in the solution and trapping of the aryl moiety was observed. In these experiments, the electrode potential was set up at the reduction "wall" of the solvent, and thus the electron donor was $PhCN^{\bullet-}$ ($E^0 = -2.24$ V vs SCE) rather than the electrode, since bromobenzene and 2-chloropyridine have more negative standard potentials (- 2.44 and - 2.40 V vs SCE respectively). The interpretation proposed in reference 50 is summarized in Scheme 6.

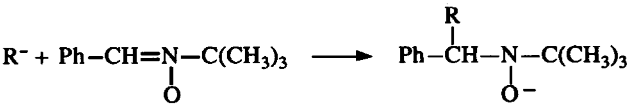
Scheme 6

$$PhCN + e^- \rightleftharpoons PhCN^{\bullet-}$$

$$RX + PhCN^{\bullet-} \rightleftharpoons PhCN + RX^{\bullet-} \qquad (0)$$

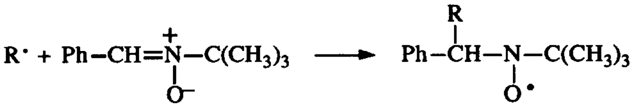
$$RX^{\bullet-} \longrightarrow R^{\bullet} + X^- \qquad (1)$$

$$R^{\bullet} + PhCN^{\bullet-} \longrightarrow R^- + PhCN \qquad (6)$$



$$R^- + Ph{-}CH{=}\underset{\underset{O}{|}}{N}{-}C(CH_3)_3 \longrightarrow Ph{-}\overset{\overset{R}{|}}{C}H{-}\underset{\underset{O^-}{|}}{N}{-}C(CH_3)_3 \qquad (7)$$

This mechanism was disputed on grounds that it is unlikely that reaction 6 is faster than either the trapping of the aryl radical by the nitrone leading directly to the nitroxide radical (reaction 8).

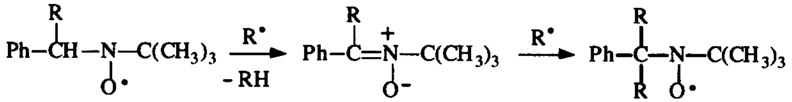


$$R^{\bullet} + Ph{-}CH{=}\underset{\underset{O^-}{|}}{\overset{+}{N}}{-}C(CH_3)_3 \longrightarrow Ph{-}\overset{\overset{R}{|}}{C}H{-}\underset{\underset{O^{\bullet}}{|}}{N}{-}C(CH_3)_3 \qquad (8)$$

or faster than its reaction with benzonitrile.[22] Instead, the formation of R^- was proposed to occur by dissociative reduction of the anion radical (reaction 5).

$$RX^{\bullet-} + PhCN^{\bullet-} \longrightarrow R^- + X^- + PhCN \qquad (5)$$

In fact, as seen earlier, reaction 5 cannot compete with the cleavage reaction 1. The possibility for reaction 6 to overrun reaction 8 is perfectly conceivable since reaction 6 has a driving force of the order of 1.7 eV and should therefore be at the diffusion limit. Note that the trapping method employed does not discriminate directly between reactions 7 and 8 (the anion formed in reaction 7 is detected after oxidative conversion to the nitroxide). The occurrence of reaction 7 rather than reaction 8 was inferred from the fact that, in other systems, when reaction 8 occurs it produces another nitroxide according to the following scheme.[51]



However this is not central to the point under discussion and should not detract from the conclusion that reaction 5 does not take place to any appreciable extent in this set of experiments contrary to what has been asserted.[22]

The rate constants obtained by the direct and indirect electrochemical methods exhibit a huge variation with the RX molecular structure. For example, $PhCl^{\bullet -}$ has a cleavage rate constant of $4 \times 10^7\ s^{-1}$ in liq. NH_3 at -38°C [45] (compare with o-, m- and p-chloronitrobenzenes which have a rate constant smaller than $10^{-3}\ s^{-1}$ [10]). The cleavage rate constants in chloroaromatic anion radicals thus span a range of at least 10 orders of magnitude under these experimental conditions. The same is true for chloro and bromoaromatics in DMF, DMSO, and CH_3CN at 20°C.[7,28,43] $PhI^{\bullet -}$ and $PhBr^{\bullet -}$ have so far escaped detection, their lifetimes being close to or smaller than one nanosecond.

The large rate constant variation in anion radicals of haloaromatics as a function of the aryl moiety is perfectly understandable were it only in terms of driving force (as will be discussed in section 6) and clearly shows that the dynamics of anion radical cleavage are extremely sensitive to structure. They should also be sensitive to interactions with the solvent and the counter-cations. The expulsion of the leaving anion indeed implies a redistribution of charge over the reacting system. Regarding the solvent, this is indeed what is found experimentally. Many aromatic anion radicals bearing strong electron-withdrawing substituents expel the anion less rapidly in water, as determined by pulse radiolysis,[31-33] than in aprotic organic solvents, as determined electrochemically (see refs. 7, 28 and 43 and references cited therein). The same is true with nitro and cyano substituted benzyl halides.[52-56] Variation of aromatic anion radical lifetimes with solvent have been observed by pulse radiolysis.[35,36] The variations were narrow however, presumably because the Lewis acidity of the solvent used spanned a narrow range too. A recent confirmation of the large solvent influence on the cleavage rate of anion radicals is as follows : m-Nitrobenzyl chloride exhibits a chemically irreversible cyclic voltammetric wave at low scan rate (0.1 V/s) in acetonitrile corresponding to a cleavage rate constant of $20\ s^{-1}$ as can be determined by restoring the reversibility by raising the scan rate.[56] Adding no more than 2-3% of water renders the 0.1 V/s wave totally reversible indicating that the cleavage rate constant has fallen below $0.5\ s^{-1}$.[57] Although some interpretation of these differences have been suggested (see section 6), a more systematic experimental analysis of environmental effects on the cleavage rate constants of anion radicals is clearly warranted, even though there is no doubt about the reality of the cleavage in contrast with suggestions in reference 22 made on the basis of such solvent effects.

A recent discussion[22] of the stabilities of the anion radicals of fluorobenzene and 4-fluorobenzonitrile similarly misinterprets previous experimental data[58-61] and leads to the claim that anion radicals are stable toward dissociation when all available data show they are not. In a pulse radiolysis study of a series of diversely substituted fluorobenzenes (including fluorobenzene itself) in water at 19°C, the anion radical of 4-fluorobenzonitrile could be detected whereas that of fluorobenzene could not.[58] The authors concluded that the lifetime of the latter species was less than fractions of microsecond. The reaction with fluorobenzene of electrons photoejected from sodium methoxide in liquid ammonia around - 50°C was reported later in a preliminary note lacking experimental details and not followed by a full paper.[59] This report indicated that the attachment rate of the electron increases when methanol is added and concluded that in the reaction sequence,

$$\mathrm{PhF} + e^- \rightleftharpoons \mathrm{PhF}^{\bullet -} \qquad \mathrm{PhF}^{\bullet -} \longrightarrow \mathrm{Ph}^{\bullet} + \mathrm{F}^- \quad ?$$

the reverse of the first step is faster than the second step, which is accelerated by methanol. This observation obviously does not prove that "the fluorobenzene anion radical does not dissociate to a phenyl radical and fluoride".[22] Presumably, the confusion arose from the parallel that was made between the fate of the fluorobenzene and 4-fluorobenzonitrile anion radicals under the tacit assumption that they should have similar reactivities toward cleavage. Two sources of information concern the reactivity of the latter anion radical. One comes from a pulse radiolysis study in water[58] in which the 4-fluorobenzonitrile anion radical was shown to protonate and cleave competitively. As expected, the latter reaction prevails in alkaline media leading to a rather high cleavage rate constant (6 x 10^5 s^{-1}). In two other studies[60,61] the anion radical was generated electrochemically in an aprotic solvent, acetonitrile. The anion radical appears in cyclic voltammetry and in double potential step chronoamperometry to have a lifetime (*ca* 10^{-2}s) larger than in water. At low concentration, the anion radical gives rise to benzonitrile implying the expulsion of the fluoride ion followed by reduction and protonation of the ensuing 4-cyanophenyl radical and/or H-atom abstraction from the solvent. At higher concentrations the product is the anion radical of 4,4'-dicyanobiphenyl, and the kinetics of its decay is second order. There has been two interpretations of the latter observations involving two different reaction sequences (Scheme 7).

Scheme 7

$$\mathrm{RX} + e^- \rightleftharpoons \mathrm{RX}^{\bullet -}$$

A

$$\mathrm{RX}^{\bullet -} \rightleftharpoons \mathrm{R}^{\bullet} + \mathrm{X}^-$$

$$2\mathrm{R}^{\bullet} \longrightarrow \mathrm{R{-}R}$$

B

$$2\mathrm{RX}^{\bullet -} \rightleftharpoons {}^-\mathrm{XR{-}RX}^-$$

$${}^-\mathrm{XR{-}RX}^- \longrightarrow \mathrm{R{-}R} + 2\mathrm{X}^-$$

$$\mathrm{R{-}R} + e^- \rightleftharpoons \mathrm{R{-}R}^{\bullet -}$$

Mechanism B has been supported by the second order kinetics observed. Mechanism A is also compatible with this reaction order if it is assumed that the dimerization step is an up-hill process, which is not unlikely in view of the rather larger lifetime of the 4-fluorobenzonitrile in the solvent used. A strong argument against mechanism A is the unlikelihood of the final dimerization step, which would have to compete against an easy reduction of the 4-cyanophenyl radical by $\mathrm{RX}^{\bullet -}$. Whatever the exact mechanism, and keeping in mind that simple cleavage takes place at low concentrations, nothing in all these facts supports the assertion that "very clearly the radical anion prepared under these conditions is different from the one prepared by pulse radiolysis".[22] The same anion radical may indeed react differently in different media and at different concentrations in the framework of a general competition between cleavage, protonation, and dimerization.

With respect to the stability of the fluorobenzene anion radical, another estimate of its lifetime may be derived from a previous indirect electrochemical investigation, by means of redox catalysis, (see Scheme 5) of the reduction of fluorobenzene in DMF at room temperature.[62] The direct electrochemical reduction of fluorobenzene in DMF occurs at very negative potentials, at which the reduction wave is almost completely merged with the supporting electrolyte discharge current. Redox catalysis with electrochemically generated aromatic anion radicals however allows the reduction of fluorobenzene to be observed and allows determination of its standard potential. Analysis of the kinetics of the direct and indirect electrochemical reduction then showed that the cleavage rate constant is larger than 10^6 s^{-1}. Fluorobenzene thus gives rise to a fast cleaving anion radical both in water and DMF. It is not difficult to understand why the anion radical of fluorobenzene is more unstable than that of 4-fluorocyanobenzene. As discussed in more detail in section 6, the main factor causing this difference in reactivity is the energy of the π^* orbital. A high π^* orbital energy favors the cleavage and vice versa. The π^* orbital is much lower in the latter case than in the former (by 0.6 eV as measured by the difference in standard potentials). Unlike anion radicals discussed earlier, the lifetime of the 4-fluorocyanobenzene anion radical is larger in acetonitrile than in water. However, at least in acetonitrile, it dimerizes rather than cleaves; and has been shown with the 9-cyanoanthracene anion radical that dimerization in aprotic solvent is accelerated by the addition of water.[63,64]

Three main conclusions emerge from the preceding discussion.

(i) The rate constants of aromatic anion radical cleavage that have been measured so far by direct and indirect electrochemical methods do represent the rate constants of the reaction :

$$RX^{\bullet -} \longrightarrow R^{\bullet} + X^{-}$$

These rate constants have nothing to do with the reduction of the anion radical into a fast cleaving dianion.

(ii) The cleavage rate constants not only vary with the nature of the leaving group but also with the nature of R (over more than 10 orders of magnitude with common leaving groups such as Cl^- and Br^-). A model exists (section 6) that reproduces correctly the existing data and may be used for predictions based on the energy of the π^* orbital (as measured by the standard potential of the $RX/RX^{\bullet -}$ couple), on the R-X bond dissociation energy, and on the standard potential of the $X^{\bullet}/X^{-}$ couple.

(iii) The rate constants of anion radical cleavages are also sensitive to solvent as shown by existing data and as expected from the redistribution of charges in the reaction.

3. H-ATOM ABSTRACTION BY ARYL RADICALS GENERATED FROM CLEAVAGE OF ANION RADICALS. H-ATOM ABSTRACTION BY ANION RADICALS ?

H-atom abstraction, after electron transfer to aromatic substrates containing a leaving group, is relevant to the present discussion in several respects. H-atom transfer to aryl radicals from organic substrates is fast and its rate varies with the nature of the H-atom donor.[65-67] It may thus be an efficient termination step in $S_{RN}1$ reactions. The electrochemical reduction of aromatic halides, RX, in aprotic polar organic solvents such as DMF, DMSO, and CH_3CN, generally gives the hydrogenolysis product RH. In view of their possible simultaneous interference in $S_{RN}1$ reactions, it was interesting to evaluate the competition, at the level of $R^{\bullet}$, between H-atom transfer leading directly to RH and a second electron transfer to $R^{\bullet}$ leading to R^- (and ultimately also to RH after protonation) as was done in previous electrochemical investigations. These can also serve to confirm the intermediacy of the aryl radical in the electrochemical reduction of aryl halides.

A related issue is whether H-atom abstraction would take place at the level of the anion radical rather than at the level of the aryl radical produced by the cleavage.[22] This debate is closely similar to the $S_{RN}1$ vs $S_{RN}2$ question : is H-atom abstraction after one-electron transfer to RX a manifestation of radical chemistry or of anion radical chemistry ? It should be emphasized that in none of the studies of the reaction of aromatic anion radicals with alcohols that are quoted in reference 22 [32,33,59,68,69] can one find any indication that hydrogenolysis products could result from the mechanism proposed in reference 22 (Scheme 8).

Scheme 8

$$RX^{\bullet -} + SH \longrightarrow HRX^{-} + S^{\bullet} \qquad (9)$$

$$HRX^{-} \longrightarrow RH + X^{-} \qquad (10)$$

For example reference 68 reports, for aromatic hydrocarbons not bearing any leaving group, pulse radiolysis reductions into anion radicals that are further protonated by the alcohols in the solution (the rate constants follow the acidities, and not the H-atom donor properties, of the alcohols). Not surprisingly aromatic anion radicals are much poorer H-atom scavengers than aryl radicals : aromatic C-H bonds are indeed much stronger than allylic C-H bonds (by *ca* 1 eV [70]) and the presence of a halogen should not change this situation dramatically.

Let us however examine whether or not quantitative data from electrochemical reduction in water / DMSO or acetonitrile mixtures of several aryl halides[71,72] provide evidence for the occurrence of reaction 9. Preparative scale experiments were carried out with 9-chloro-, bromo-, iodoanthracene, 1-chloro-, bromo-, iodonaphthalene in DMSO and 4-chloro-, bromo-, iodobenzonitrile in CH_3CN in mixtures of 10% H_2O - 90% perdeuterated solvent and of 10% D_2O - 90% light solvent so as to trace back the competition between H-(D) atom transfer from the organic solvent and electron transfer followed by $H^+(D^+)$ transfer from H_2O (D_2O) .[72] In all cases, the electron stoichiometry was 2e per molecule. The cross experiments gave consistent results taking into account the slight variation due to isotopic effects. In each series of experiments, deuterium incorporation strongly depended on the halogen and on the aromatic moiety. The results were shown to be in

Scheme 9

$$RX + e^{-} \rightleftharpoons RX^{\bullet -}$$

$$RX^{\bullet -} \xrightarrow{k} R^{\bullet} + X^{-} \qquad (1)$$

Electron transfer pathway

$$R^{\bullet} + e^{-} \rightleftharpoons R^{-}$$

and/or :

$$R^{\bullet} + RX^{\bullet -} \xrightarrow{k_D} R^{-} + RX$$

$$R^{-} + H_2O \longrightarrow RH + OH^{-}$$

H-atom transfer pathway

$$R^{\bullet} + SH \xrightarrow{k_H} RH + S^{\bullet}$$

$$S^{\bullet} + e^{-} \rightleftharpoons S^{-}$$

and/or :

$$S^{\bullet} + RX^{\bullet -} \xrightarrow{k_D} S^{-} + RX$$

$$S^{-} + H_2O \longrightarrow SH + OH^{-}$$

(SH : DMSO or CH_3CN)

agreement with the competition scheme 9, in which the second electron transfer can take place at the electrode and/or in solution according to the ECE-DISP competitive mechanism defined in section 2. The outcome of the competition, i.e., the relative amounts of RH formed through electron transfer and by H-atom transfer, is a function of two rate parameters :

$$\left(k_D[RX] / k^{1/2} k_H\right)\left(D^{1/2} / \delta\right) \qquad \text{and} \qquad k / k_H$$

(D, the diffusion coefficient, is assumed to be the same for all intervening species; δ is the thickness of the diffusion layer in the electrolysis experiment and decreases as the rate of agitation of the solution increases). The agreement of the competition scheme with the experimental data is demonstrated pictorially in Figure 10 in reference 7 (or Figure 1 in reference 72). Some remarkable features are worth noticing. With the naphthalene and benzonitrile derivatives, the relative amount of RH from H-atom transfer decreases from Cl to Br to I in accord with the acceleration of the anion radical cleavage in the competition between H-atom and electron transfer to $R^{\bullet}$at the electrode surface (ECE) where the competition parameter is simply k/k_H. For a halogen, the relative amount of RH from H-atom transfer is larger in the naphthalene series than in the benzonitrile series in keeping with anion radical cleavage being slower in the first case than in the second. The situation differs in the anthracene series where anion radical cleavage is markedly slower than in the other two series : the relative amount of RH from H-atom transfer increases from Cl to Br and then decreases from Br to I. The reason is that, because the cleavage of the anion radical of 9-chloroanthracene is relatively slow, the competition is between H-atom transfer and electron transfer from $RX^{\bullet-}$ to $R^{\bullet}$ (DISP) where the competition parameter is now $\left(k_D[RX] / k^{1/2} k_H\right)\left(D^{1/2} / \delta\right)$, the effect of k being therefore the opposite of what it is in the ECE case. In keeping with this interpretation is the observation that rate of deuterium incorporation was found to vary with C^0 and δ in the case of 9-chloroanthracene as predicted by this last expression whereas this was not the case for the compounds falling in the ECE-H-atom transfer competition domain.

Could these experimental observations, which have been shown to agree with the anion radical cleaving competition mechanism shown in Scheme 9, also be compatible with the alternative mechanism proposed in reference 22. If we were to believe that the anion radical is easier to reduce than the starting aromatic halide and that it may abstract H-atom from the solvent,[22] the competition mechanism would be that sketched in Scheme 10A. According to this mechanism, whatever the halogen and the aromatic group, there would be no deuterium incorporation in perdeuterated solvents containing 10% H_2O and total deuterium incorporation in light solvents with 10% D_2O.

Scheme 10

$$RX + e^- \rightleftharpoons RX^{\bullet-}$$

A

$$RX^{\bullet-} + e \rightleftharpoons R^- + X^-$$

$$R^- + H_2O \longrightarrow RH + OH^-$$

B

Electron transfer pathway

$$2RX^{\bullet-} \xrightarrow{k_d} RX + R^- + X^-$$

$$R^- + H_2O \longrightarrow RH + OH^-$$

H-atom transfer pathway

$$RX^{\bullet-} + SH \xrightarrow{k_H} HRX^{\bullet-} + S^{\bullet}$$

$$HRX^{\bullet-} \longrightarrow RH + X^-$$

$$S^{\bullet} + RX^{\bullet-} \longrightarrow S^- + RX$$

$$S^- + H_2O \longrightarrow SH + OH^-$$

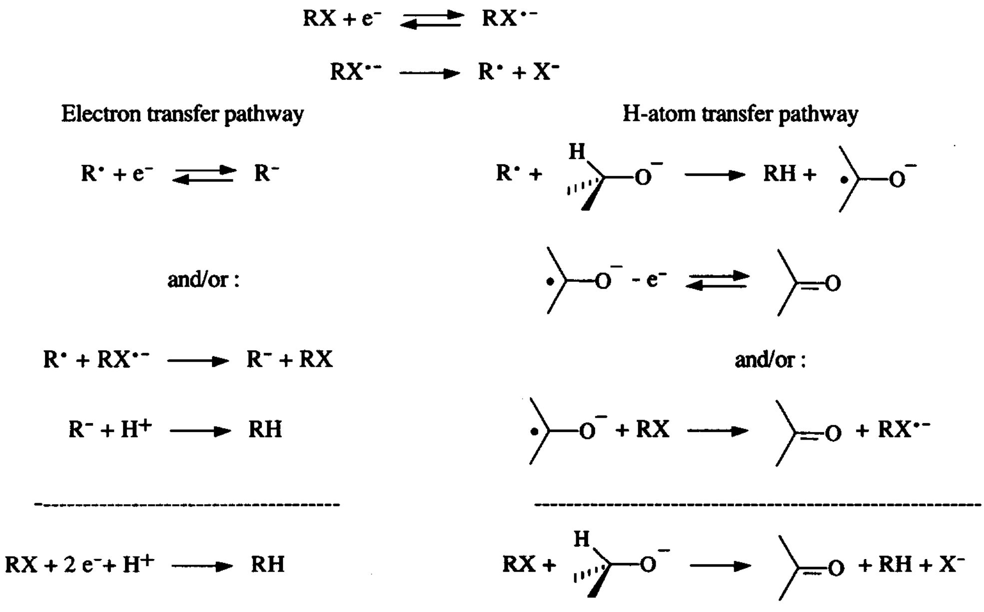
There is however another possibility for the reduction of $RX^{\bullet-}$ into the cleaving dianion (section 2), namely a direct disproportionation of two $RX^{\bullet-}$ molecules. The electron vs H-atom transfer competition would then be as depicted in Scheme 10B. In such a case, the competition parameter would be $k_d[RX]D^{1/2}/k_H^{3/2}\delta$. An increase in concentration should then favor deuterium incorporation in 10% D_2O - light organic solvent mixtures and disfavor deuterium incorporation in 10% H_2O - heavy organic solvent mixtures. This expectation is at variance with what is found experimentally in five cases out of six. The reason that electrode and solution electron transfer to $RX^{\bullet -}$ cannot compete in the present case, in contrast with what happens in Scheme 9 mechanism, is that a chemical step is interposed between the first and second electron transfers in the latter case and not in the former. We are thus led to conclude that direct H-atom transfer to $RX^{\bullet -}$ competing with its reduction into the cleaving dianion is not consistent with facts in these series of experiments.

The preceding study[72] also showed that the rate constants of hydrogen abstraction by the 9-anthracenyl, 1-naphthyl and 4-cyanophenyl radical from CH_3CN and DMSO are several orders of magnitude below the diffusion limit. The same conclusion may be drawn from the rate constants of hydrogen abstraction from DMSO, DMF and CH_3CN by 1-naphthyl radical obtained by an independent method.[73] Thus even if aryl radicals are good H-atom scavengers, there is no evidence that they should not show any selectivity toward different H-atom sources as asserted in reference 22 which quotes a study[74] that does not, in fact, provide any evidence of that sort. Significant variation of the H-atom abstraction reactivity of phenyl radical with the nature of the donor has been demonstrated in a study involving a considerable number of donors.[65]

Early work [75] has shown that, under stimulation by solvated electrons, H-atom abstraction by phenyl radicals from isopropoxide ions (when present together with acetone enolate ions) may compete with substitution. It was later proposed alternatively that H-atom abstraction from isopropoxide ions involves the anion radical rather than the aryl radical resulting from cleavage of the anion radical.[22] Of the two arguments used to fuel this proposition, one is the aforementioned inaccurate assertion of a lack of selectivity of phenyl radical toward H-atom donor. The other is that H-atom transfer from alkoxides to aromatic anion radicals is well known from the work described in reference 68. In fact, reference 68 describes protonation by alcohols of anion radicals not containing leaving groups and not H-atom abstraction.

A systematic study of the reaction of aryl halides with alkoxides in liq. NH_3 (where no hydrogen sources other than alkoxide ions are present) under electrochemical stimulation[76] has shown that the Scheme 11

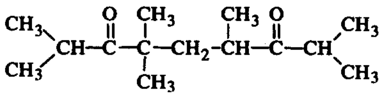
Scheme 11



mechanism based on H-atom abstraction by the aryl radical is perfectly consistent with the experimental data.

The overall reaction amounts to an oxidation of the alkoxide by the aryl halide and is a chain process of the same type as a $S_{RN}1$ substitution.[77] For the same reasons as developed above for the reduction of aryl halides in DMSO and CH_3CN, the mechanism proposed in reference 22 is not consistent with the kinetic data.

One last argument invoked[22] in favor of H-atom abstraction from the anion radical of the substrate and against its cleavage pertains to studies of the photostimulated reaction of 2,4-dimethyl-3-pentanone enolate ions in liquid NH_3 with iodobenzene,[80,81] on the one hand, and with 2-chloroquinoline and 2-bromopyridine[82, 83] on the other. The reaction is faster and the amount of side-products that are formed, besides the substitution product, is less in the latter two cases than in the former. The two side-products that are formed are RH and a dimer :



which results from the abstraction of an H-atom of the ketone enolate by the aryl radical as revealed by previous deuterium incorporation experiments.[84] This variation in side-product yields would contradict[22] the possibility of H-atom abstraction by the aryl radical and point to H-atom abstraction by the anion radical since structure changes should not affect the former reaction as opposed to the latter. In the competition, what changes in fact is the reactivity of the aryl radical toward nucleophilic attack rather than toward H-atom abstraction. The lower energy of the π^* orbital in quinolyl and pyridyl as compared to phenyl makes the nucleophilic attack faster (see section 6) and therefore provides a satisfactory explanation of the observed selectivity within the framework of H-atom abstraction by the aryl radical rather than by the anion radical.

We conclude this discussion of the role of H-atom transfer by noting that, (i) all available experimental facts do not provide any evidence for H-atom abstraction by anion radicals containing leaving groups as opposed to abstraction by aryl radicals derived from their cleavage; and (ii) in cases where kinetic investigations were carried out, the results accord with the latter alternative and contradict the former.

4. MECHANISTIC EVIDENCE FROM ELECTROCHEMICAL KINETIC AND PREPARATIVE-SCALE STUDIES.

Because precise kinetic investigations are time-consuming, most descriptions of $S_{RN}1$ reactions have been qualitative. Some quantitative studies were carried out with $S_{RN}1$ reactions triggered by direct or indirect electrochemical means. In fact, electrochemical initiation is far more easily controllable quantitatively than photochemical or solvated electron initiation. In spite of valuable case studies,[85,86] little is known quantitatively about reactions that, upon photochemical excitation, convert the initial aromatic substrate-nucleophile couple into $RX^{\bullet -}$ and/or $R^{\bullet}$ radicals that then enter the propagation chain as well as about the attending deactivations (non-radiative decay, back electron transfer, Etc.). Initiation by alkali metals in liquid ammonia are not amenable to quantitative kinetics because of experimental and theoretical difficulties. The latter are related to the strong reducing power of solvated electrons that makes initiation, propagation, and termination steps occur heterogeneously during the mixing time as will be discussed in section 5.

Typical examples of direct electrochemical kinetic investigations are provided by the cyclic voltammetric reduction, in liq. NH3 at -40°C, of 2-chloroquinoline in the presence of benzenethiolate or 4-

chlorobenzenethiolate ions and of 2-iodoquinoline in the presence of benzenethiolate ions.[12] In the absence of nucleophile, 2-chloro and 2-iodoquinoline, exhibit, as do most aryl halides, two successive waves, one irreversible two-electron wave and one reversible one-electron wave, corresponding respectively to the ECE-DISP reduction of the aryl halide RX into RH (Scheme 3) and to the reduction of RH into its anion radical $RH^{\bullet -}$. Upon addition of the nucleophile, these two waves decrease at the expense of a new reversible wave that appears between the two initial waves and corresponds to the $RNu/RNu^{\bullet -}$ couple. The kinetics of the substitution may thus be followed by monitoring the relative variations of the peak current of the first irreversible wave with the concentrations of RX and of Nu^- and with the scan rate, v. These variations reveal the efficiency of the substitution process and the kinetic orders of the competing reactions. In the context of $S_{RN}1$, these variations arise from the set of competing steps shown in Scheme 12.

Scheme 12

$$RX + e^- \rightleftharpoons RX^{\bullet -}$$

$$RX^{\bullet -} \xrightarrow{k} R^{\bullet} + X^-$$

$$R^{\bullet} + Nu^- \xrightarrow{k_{Nu}} RNu^{\bullet -}$$

ECE

$$RNu^{\bullet -} - e^- \rightleftharpoons RNu$$

$$R^{\bullet} + e^- \rightleftharpoons R^-$$

DISP

$$RNu^{\bullet -} + RX \xrightarrow{k_D} RNu + RX^{\bullet -}$$

$$R^{\bullet} + RX^{\bullet -} \xrightarrow{k_D} R^- + RX$$

$$R^{\bullet} + RNu^{\bullet -} \xrightarrow{k_D} R^- + RNu$$

$$R^- + H^+ \text{ (solvent, residual water)} \longrightarrow RH$$

The side-reactions leading to RH are only electron transfer reductions of $R^{\bullet}$ since, in liquid ammonia, H-atom transfer from the solvent can be neglected (since all three electron transfers below the DISP heading have large driving forces they can be regarded as diffusion-controlled).

From the cyclic voltammetric data in the absence of nucleophile, it appears that 2-chloroquinoline behaves in a DISP manner whereas 2-iodoquinoline is reduced according to the ECE mechanism, in keeping with the anion radical cleavage being faster in the latter case than in the former. The parameter that governs the competition between the DISP and ECE mechanism is $(k_D[RX]/k_1{}^{3/2})\ (Fv/RT)^{1/2}$.[12,13,27] Thus when k is large, all the electron transfers take place at the electrode surface, whereas when k is small they occur in the solution and involve all molecular electron donors present.

In the presence of the nucleophile, the relative height of the first peak is a function of two competition parameters, one (ρ) that governs the competition between substitution and reduction under DISP conditions, and the other (σ) that governs the competition between substitution and reduction under ECE conditions.

$$\rho = \frac{k_D}{k^{1/2} k_{Nu}} \frac{[RX]}{[Nu^-]} \left(\frac{Fv}{RT}\right)^{1/2} \quad , \qquad \sigma = \frac{k}{k_{Nu}[Nu^-]}$$

The ratio ρ/σ governs the competition between the DISP and ECE pathways. With 2-chloroquinoline, the kinetic results (Figures 9 and 10 in reference 12) agree with what is predicted for the $S_{RN}1$ scheme depicted in the right-hand side of Scheme 12 : the relative height of the first peak, $i_p/(i_p)_d$, varies with the scan rate and with the RX and Nu^- concentrations as predicted by the governing parameter ρ according to the theoretical variation $i_p/(i_p)_d$ vs ρ. These particular variations with v, [RX], and $[Nu^-]$ reflect the reaction orders of the competing steps.

With 2-iodoquinoline, the anion radical of which cleaves expectedly much faster than that of 2-chloroquinoline, the experimental results adhere to what is predicted for an ECE-substitution competition from the competition parameter σ, namely $i_p/(i_p)_d$ is independent of v and [RX] and is a decreasing function of $[Nu^-]$.

The question must now be raised whether these experimental results that conform to the $S_{RN}1$ mechanism would also be consistent with the $S_{RN}2$ mechanism. If we were to follow what is proposed in reference 22, the overall process would be that represented in Scheme 13, in which the bimolecular substitution competes with electron transfer from $RNu^{\bullet -}$.

Scheme 13

$$RX + e^- \rightleftarrows RX^{\bullet -}$$

Substitution :

$$RX^{\bullet -} + Nu^- \xrightarrow{k_{Nu}} RNu^{\bullet -} + X^-$$

$$RNu^{\bullet -} + RX \xrightarrow{k_D} RNu + RX^{\bullet -}$$

Electron Transfer :

$$RNu^{\bullet -} + RX^{\bullet -} \xrightarrow{k_R} RNu + R^- + X^-$$

$$R^- + H^+ \text{ (solvent, residual water)} \longrightarrow RH$$

As discussed in section 2, an ECE type situation is excluded because if $RX^{\bullet -}$ underwent easier reduction than RX at the electrode surface (in spite of the unlikelihood of such an event), no $RX^{\bullet -}$ could be produced at the electrode surface and therefore no substitution could occur. Reduction of $RX^{\bullet -}$ by $RNu^{\bullet -}$, if possible, should be much faster than disproportionation of two $RX^{\bullet -}$ molecules (as in Scheme 10), because in the present case $RNu^{\bullet -}$ is a much stronger reducing agent than $RX^{\bullet -}$ (the reduction potential of RNu is substantially negative to that of RX). The competition between reduction and substitution would then be governed by the parameter k_R/k_D and should not show the dependency toward $v^{1/2}\,[RX]/[Nu^-]$ found experimentally in the case of 2-chloroquinoline and toward $1/[Nu^-]$ found with 2-iodoquinoline. The same conclusion, namely, the inconsistency of the proposed version of the $S_{RN}2$ mechanism[22] and consistency of the $S_{RN}1$ mechanism with the experimental data,[12] can also be drawn for all systems investigated by the direct electrochemical method : PhS^- + 1-chloronaphthalene (DISP), + 2-bromoquinoline (ECE), $CH_3COCH_2^-$ + 2-chloroquinoline (DISP), + 2-iodoquinoline (ECE), $PhCOCH_2^-$ + 2-iodoquinoline (ECE) and $(EtO)_2PO^-$ + 2-chloroquinoline (DISP).

Another version of the $S_{RN}2$ mechanism, not mentioned in reference 22, may be envisaged (Scheme 14) in which the bimolecular substitution step would compete with the cleavage of the anion radical to $R^\bullet$, which would be reduced at the electrode or in the solution. Under both DISP and ECE conditions, the competition between reduction and substitution would then be governed by the parameter $k/k'_{Nu}\,[Nu^-]$. This expectation is at variance with what is found with 2-chloroquinoline but formally would be consistent, in terms of reaction orders, with the data pertaining to 2-iodoquinoline. More generally for all of the above-mentioned systems that behave in the DISP manner, analysis of the experimental data allows one to reject this other version of the $S_{RN}2$ mechanism and thus to show that $S_{RN}1$ is the only viable pathway. On the other hand, discrimination between the two mechanisms is not possible for the systems that behave in the ECE manner. However, as discussed below, the redox catalysis method allows one to reject also this $S_{RN}2$ mechanism for the latter systems.

The kinetics of several other $S_{RN}1$ substitutions have been investigated by means of the redox catalysis method in liq. NH3. The anion radical of the substrate is produced by means of electron transfer from an electrochemically generated aromatic anion radical, Q (serving as mediator) to the RX substrate. Variations of the mediator cyclic voltammetric wave are then used to probe the reaction. In the absence of nucleophile the mediator wave undergoes a catalytic increase with loss of reversibility as described in section 2 (Scheme 5). The introduction of the nucleophile decreases the catalytic wave, whose reversibility is eventually restored, according to Scheme 15 where an $S_{RN}1$ mechanism is assumed.

Scheme 14

$$RX + e^- \rightleftharpoons RX^{\bullet -}$$

Substitution : $$RX^{\bullet -} + Nu^- \xrightarrow{k'_{Nu}} RNu^{\bullet -} + X^-$$

Cleavage : $$RX^{\bullet -} \xrightarrow{k} R^\bullet + X^-$$

Propagation :

ECE

$$RNu^{\bullet -} - e^- \rightleftharpoons RNu$$

DISP

$$RNu^{\bullet -} + RX \xrightarrow{k_D} RNu + RX^{\bullet -}$$

Radical Reduction :

$$R^\bullet + e^- \rightleftharpoons R^-$$

$$R^\bullet + RX^{\bullet -} \xrightarrow{k_D} R^- + RX$$

$$R^\bullet + RNu^{\bullet -} \xrightarrow{k_D} R^- + RNu$$

$$R^- + H^+ \text{ (solvent, residual water)} \longrightarrow RH$$

In such circumstances, the decrease in the catalytic current is governed by the competition parameter $k_{Nu}[Nu^-]/k_D[P]$. The $S_{RN}1$ mechanism (Scheme 15) has been shown to agree fully with the experimental data in the following systems : PhS^- + 2-, 3-, 4-chloro, 4-bromo, 4-iodobenzonitrile, 1-chloro, 1-iodonaphthalene, 2-, 4-chloro, 3-bromo, 2-, 3-iodoquinoline[87,88], and chlorobenzene;[45] $(EtO)_2PO^-$ + chlorobenzene, diphenylsulfide.[45]

Scheme 15

$$P + e^- \rightleftharpoons Q$$

$$Q + RX \rightleftharpoons RX^{\bullet -} + P$$

$$RX^{\bullet -} \longrightarrow R^\bullet + X^-$$

$$R^\bullet + Nu^- \xrightarrow{k_{Nu}} RNu^{\bullet -}$$

$$RNu^{\bullet -} + P \xrightarrow{k_D} RNu + Q$$

$$Q + R^\bullet \longrightarrow R^- + P$$

$$R^- + H^+ \text{ (solvent and/or residual water)} \longrightarrow RH$$

Could the $S_{RN}2$ mechanism also be consistent with these experimental data ? As discussed in section 2, if the aryl halide anion radical were stable toward dissociation, as hypothesized in reference 22, the mediator wave should not show any catalytic increase in the absence of nucleophile. Indeed, since $RX^{\bullet -}$ cannot disproportionate, it could not, a fortiori, be reduced by Q, which is generated at a more positive potential than $RX^{\bullet -}$. Upon introduction of the nucleophile, the only possible event would be the appearance of a catalytic increase of the mediator wave according to the mechanism in Scheme 16 in the case where the reduction of

Scheme 16

$$\begin{array}{rcl} \mathrm{P} + e^- & \rightleftharpoons & \mathrm{Q} \\ \mathrm{Q} + \mathrm{RX} & \rightleftharpoons & \mathrm{P} + \mathrm{RX}^{\bullet -} \\ \mathrm{RX}^{\bullet -} + \mathrm{Nu}^- & \xrightarrow{k'_{Nu}} & \mathrm{RNu}^{\bullet -} + \mathrm{X}^- \\ \mathrm{RNu}^{\bullet -} + \mathrm{P} & \xrightarrow{k_D} & \mathrm{RNu} + \mathrm{Q} \\ \mathrm{RNu}^{\bullet -} + \mathrm{RX} & \longrightarrow & \mathrm{RNu} + \mathrm{RX}^{\bullet -} \\ \mathrm{RX}^{\bullet -} + \mathrm{RNu}^{\bullet -} & \longrightarrow & \mathrm{RNu} + \mathrm{R}^- + \mathrm{X}^- \\ \mathrm{R}^- + \mathrm{H}^+ \text{ (solvent, } \mathrm{H_2O}) & \longrightarrow & \mathrm{RH} \end{array}$$

$\mathrm{RX}^{\bullet -}$ by $\mathrm{RNu}^{\bullet -}$ would be faster than the $\mathrm{S_{RN}2}$ displacement (followed by two possible propagation steps : reaction of $\mathrm{RNu}^{\bullet -}$ with the oxidized form of the catalyst or with the substrate). In the opposite case, there will be no catalytic increase of the mediator wave. Such predictions obviously disagree with the experimental observations.

If we now consider, in the framework of redox catalysis, the same second possible version of the $\mathrm{S_{RN}2}$ mechanism as in direct electrochemistry (Scheme 17), a catalytic increase of the mediator wave should be observed as in the $\mathrm{S_{RN}1}$ case (Scheme 15). The catalytic wave should decrease, and eventually become reversible again, upon addition of the nucleophile. However the decrease of the catalytic current should then be a function of the competition parameter $k'_{Nu}[\mathrm{Nu}^-]/k$ instead of $k_{Nu}[\mathrm{Nu}^-]/k_D[\mathrm{P}]$ as in the $\mathrm{S_{RN}1}$ case. The experimental data in the above-mentioned systems accord with the latter prediction and not with the former.

Scheme 17

$$\begin{array}{rcl} \mathrm{P} + e^- & \rightleftharpoons & \mathrm{Q} \\ \mathrm{Q} + \mathrm{RX} & \rightleftharpoons & \mathrm{P} + \mathrm{RX}^{\bullet -} \\ \mathrm{RX}^{\bullet -} + \mathrm{Nu}^- & \xrightarrow{k'_{Nu}} & \mathrm{RNu}^{\bullet -} + \mathrm{RX} \\ \mathrm{RNu}^{\bullet -} + \mathrm{P} & \xrightarrow{k_D} & \mathrm{RNu} + \mathrm{Q} \\ \mathrm{RX}^{\bullet -} & \xrightarrow{k} & \mathrm{R}^{\bullet} + \mathrm{X}^- \\ \mathrm{R}^{\bullet} + \mathrm{Q} & \xrightarrow{k_D} & \mathrm{R}^- + \mathrm{P} \\ \mathrm{R}^- + \mathrm{H}^+ \text{ (solvent, } \mathrm{H_2O}) & \longrightarrow & \mathrm{RH} \end{array}$$

The main conclusion from the preceding discussion is that the kinetics of all substitutions investigated by direct and/or indirect electrochemical means follow expectations for the $\mathrm{S_{RN}1}$ mechanism and not for $\mathrm{S_{RN}2}$ (either the version proposed in reference 22 or the version discussed above where the $\mathrm{S_{RN}2}$ step would compete with cleavage of the anion radical rather than with its reduction). These conclusions apply to relatively short-lived substrate anion radicals with lifetimes ranging from 0.1 millisecond to less than 10 nanoseconds as in the above-mentioned studies. They may also apply to longer lived anion radicals, but that aspect has not been investigated so far.

In preparative scale electrochemical experiments, the competition between radical-nucleophile coupling and electron transfer, at the potential where the substrate is reduced, depends upon the parameter[89] $k_{Nu}[Nu^-]/k$ when electron transfer takes places at the electrode (ECE) and upon $(k^{1/2} k_{Nu}[Nu^-]/k_D[RX])(\delta/D^{1/2})$ when electron transfer occurs in the solution. The competition between electron transfer at the electrode (ECE) and electron transfer in the solution (DISP) is a function of $(k^{3/2}/k_D[RX])(\delta/D^{1/2})$. These parameters are similar to those governing the cyclic voltammetric responses (from which they can be obtained by replacing the expression of the diffusion rate, Fv/RT (section 2), by D/δ^2) and which have the same form as the parameters describing competition between H-atom transfer and electron transfer to electrochemically generated aryl radicals (section 3). From these expressions, we see that the magnitude of the cleavage rate constant plays a central role in the competition between coupling with the nucleophile and the two possible electron transfer pathways. With typical substrate concentrations, electron transfer reduction of $Ar^\bullet$ at the electrode and/or in the solution are the only side-reactions in solvents that are poor H-atom donors (e.g. liq. NH3). In organic solvents such as CH_3CN and DMSO, H-atom transfer is another competing reaction that produces RH as do the electron transfer reductions. Competition between this reaction and coupling with the nucleophile is governed by the parameter $k_H/k_{Nu}[Nu^-]$ where k_H is the pseudo-first order rate constant for H-atom abstraction.

These particular features of the electrochemical induction of $S_{RN}1$ reactions should be borne in mind when examining the experimental trends in product distribution that may be observed upon varying the aromatic substrate, the nucleophile, and the solvent.

For example, it has been claimed that comparisons of product distributions from the following four systems are not consistent with the $S_{RN}1$ mechanism.[22]

$$4\text{-}ClC_6H_4CN + CN^- \rightarrow \underset{\approx 20\%}{4\text{-}CNC_6H_4CN} + \underset{\approx 80\%\,*}{C_6H_5CN} \text{ (in DMF)}^{90}$$

(* as can be estimated from the cyclic voltammetric data of Figure 2 in reference 90).

$$4\text{-}IC_6H_4NO_2^* + CN^- \text{ (or } NO_2^-) \rightarrow \underset{\approx 90\%}{4\text{-}CNC_6H_4NO_2\ (4\text{-}NO_2C_6H_4NO_2)} + \underset{\approx 10\%}{C_6H_5NO_2}.\text{(in DMSO)}^{91}$$

(* not $4\text{-}ClC_6H_4NO_2$ as reported in ref. 22)

$$4\text{-}BrC_6H_4CN + PhS^- \rightarrow \underset{85\%}{4\text{-}PhSC_6H_4CN} + \underset{15\%}{C_6H_5CN}.\text{(in } CH_3CN)^{92}$$

$$4\text{-}IC_6H_4CN + PhS^- \rightarrow 20\%\ 4\text{-}PhSC_6H_4CN + 80\%\ C_6H_5CN.\text{(in } CH_3CN)^{92}$$

The explanation in references 90 and 92 for these variations in product distribution invoked the rate of decomposition of the anion radical in the framework of an ECE-DISP-substitution competition. Two points of concern arise from this explanation.[22] One involves the difference in yield in the last two experiments. As the nucleophile is the same and the 4-cyanophenyl radical is formed in both cases, the substitution yield should be the same and therefore the same radical could not be an intermediate. In fact, the explanation provided in reference 92 agrees with what is rigorously predicted for an ECE-DISP competition, namely, 4-bromo and 4-iodobenzonitrile give rise to fast cleaving anion radicals but with different cleavage rate constants ($\approx 2 \times 10^9$ and $2 \times 10^{10}\ s^{-1}$ in liq. NH3 at -40°C [91] respectively, in keeping with I^- being a better leaving group than Br^-). The ECE-DISP competition parameter favors the ECE pathway in both cases. Under these conditions, the ECE-substitution competition, and therefore the ratio of RH/RNu, is governed by the rate ratio $k/k_{Nu}[Nu^-]$. The difference in yields thus implies that the ratio of the anion radical cleavage rate constants of the iodo over the bromo derivative is of the order of 4, a quite reasonable figure.

In reference 90, the poor substitution yield in the first experiment as opposed to the second is explained by the fact that $4\text{-ClC}_6H_4CN^{\bullet -}$ cleaves rapidly, much more rapidly than $4\text{-IC}_6H_4NO_2^{\bullet -}$, and therefore that the coupling of CN^- with the radical competes more severely with electrode reduction in the first case than in the second (in line with what has been said above about the ECE-DISP-substitution competition). We now know that the reaction of CN^- with $^{\bullet}C_6H_5NO_2$ is likely to be more rapid than its reactions with $^{\bullet}C_6H_5CN$ for the reasons discussed in section 6. This additional factor favors substitution in the second system as compared to the first. Still another factor is that the first experiment was carried out in DMF and the second in DMSO, a poorer H-atom donor than DMF. Thus, besides competition with electron transfer, radical-nucleophile coupling may also compete with H-atom transfer under more unfavorable conditions in the first experiment than in the second.

Another point of concern regarding the first experiment would be[22] that nucleophiles other than CN^- ions give rise to significantly more substitution in their reaction with 4-chlorobenzonitrile in liq. NH3 (as in references 93-95 but also in references 88, 89 for liq. NH3 and reference 11 for DMSO and CH_3CN). There is in fact nothing mysterious in these reactivity differences. The reasons that make CN^- ions the less reactive nucleophile among those that have been used in $S_{RN}1$ substitutions are analyzed in detail in section 6.

A final point of concern comes from reported comparison among the first, third, and fourth experiments : "it is not reasonable to conclude that the reduction of one particular substrate is fast in one case and slow in the other".[22] In neither reference 91 nor reference 92 was the rate of "reduction of the substrate" mentioned as a rate-limiting factor. What is important is the cleavage rate constant, k, in that it governs the distance from the electrode at which $R^{\bullet}$ is formed (see section 2). Thus, why does 4-ClC_6H_4CN give a poor substitution yield in the first experiment whereas 4-BrC_6H_4CN, the anion radical of which certainly cleaves faster, gives a good substitution yield in the third experiment ? The answer is that the nucleophile is not the same in each case (CN^- in the first case vs PhS^- in the third). In the framework of an ECE-substitution competition the governing factor is $k/k_{Nu}[Nu^-]$. The increase of k from the first to the third experiment is overcompensated by the increase of k_{Nu}. When one compares 4-BrC_6H_4CN (third experiment) to 4-IC_6H_4CN (fourth experiment) with the same nucleophile, PhS^-, the substitution yield decreases, in agreement with the increase of k, while k_{Nu} remains the same ($4\text{-CNC}_6H_4^{\bullet} + PhS^-$).

H-atom transfers to aryl radicals are fast, so a change in the solvent or introduction of good H-atom donors are expected to modify the RX/RNu product ratio. One example of these variations is the decrease of the substitution yield in the reaction of p-bromobenzophenone with thiophenoxide ions in DMSO upon addition of 18-crown-6-ether (Na^+)[92] (crown ethers, as all ethers, are good H-atom donors).[65] The variations in product distribution upon change from DMSO to CH_3CN for various substrate-nucleophile couples[92] have been discussed in quantitative terms and shown to be consistent with the $S_{RN}1$ mechanism and with the independently established values of k, k_{Nu} and k_H.[11,96] We may thus conclude there is nothing inconsistent with the $S_{RN}1$ mechanism on the basis of product distribution under electrochemical induction.

The only termination steps to the $S_{RN}1$ chain process considered in the preceding discussions are homogeneous and heterogeneous electron transfer reduction of the intermediate aryl radical and H-atom transfer from donors in solution. The latter reactions, identified by deuterium incorporation experiments (section 3) clearly reveal the intermediacy of aryl radicals. But what about other radical reactions such as radical-radical coupling involving the aryl radicals ? One may think of the coupling of the aryl radical with itself or with the anion radicals $RX^{\bullet -}$ and $RNu^{\bullet -}$.

No coupling products have ever been found in the direct or indirect (by means of electrogenerated aromatic anion radicals) electrochemical reduction of the type of aromatic substrates used in $S_{RN}1$ substitution, whereas such coupling products have been obtained in reactions of aliphatic halides with aromatic anion radicals not containing leaving groups (e.g., sodium naphthenide[97,98] as well as many aromatic anion radicals generated electrochemically.[100-103]). Such studies, as well as other electrochemical investigations of the reduction potentials of alkyl radicals,[104-108] have allowed one to delineate the competition that opposes coupling and reduction of alkyl radicals by aromatic anion radicals ($A^{\bullet -}$) :

$$R^{\bullet} + A^{\bullet -} \longrightarrow RA^{-}$$

$$R^{\bullet} + A^{\bullet -} \longrightarrow R^{-} + A$$

It appears that the outcome of the competition depends both on the nature of R and of A, being essentially a function of the difference between the standard potential of the $A^{\bullet}/A^{\bullet -}$ couple and the reduction potential of $R^{\bullet}$. As noted earlier, reduction potentials of aryl radicals, unlike those of alkyl radicals, are considerably positive not only to the standard potentials of the $ArX/ArX^{\bullet -}$ couples but also to those of the $A/A^{\bullet -}$ couples used in these studies. The formation of coupling products between the aryl radical on the one hand and $RX^{\bullet -}$ or $A^{\bullet -}$ on the other is thus disfavored as compared to the reduction of the aryl radical either at the electrode surface or by $RX^{\bullet -}$ or $A^{\bullet -}$. The situation is as when an alkyl radical is generated by an aromatic anion radical having a standard potential much negative to the reduction potential of the alkyl radical.[101-104] Changes in reactant concentrations cannot modify the competition since the two reactions are bimolecular and involve the same reactants.

Until recently, no products from the coupling of two $Ar^{\bullet}$ radicals or of $Ar^{\bullet}$ with $ArX^{\bullet -}$ or $ArNu^{\bullet -}$ were found in electron transfer triggered aromatic nucleophilic substitution. The explanation of this observation was likewise based on the easy reduction of aryl radicals and/or their ability to abstract H-atoms from donors such as organic solvents. However, it has been recently reported that Ar-Ar dimers are produced in significant amount upon electrochemical induction (in liq. NH3 at - 40°C) of the reaction of 4-chloro, 4-bromo, 4-iodobenzonitrile and 4-chloropyridine with 2-pyridylthiolate ions and 4-iodobenzonitrile with thiophenoxide ions.[109,110] Dimer yields as high as 40% have been found in preparative scale runs but, in this case, part of the dimer may arise from combination of two $ArNu^{\bullet -}$ molecules followed by elimination of two Nu^{-} ions (as in the case of 4-fluorobenzonitrile according to Scheme 7B). Usually aromatic anion radicals do not dimerize, with the exception of those bearing an electron withdrawing substituent as might be the case for 4-fluorobenzonitrile and shown to be the case with 9-cyanoanthracene[63,64,113-118]. However, due to coulombic repulsion, the dimerization rate constants are not very large, of the order of 10^5 $M^{-1}s^{-1}$ for 9-cyanoanthracene anion radical and about the same for 4-fluorobenzonitrile anion radical as can be inferred from the data in reference 61. Dimerization of these $ArNu^{\bullet -}$ anion radicals is slow since the ArNu cyclic voltammetric wave remains reversible at scan rates as low as 0.1 V/s. It is thus remarkable that the formation of the dimer appears through its own reversible waves at the same scan rate provided the substrate concentration is sufficiently large. Thus it may be envisaged that, under these conditions, two Ar$^\bullet$ radicals could couple. This conclusion is provisional and should await confirmation from precise simulations of the rather complicated kinetics of these many-step processes.

5. INDUCTION OF S$_{RN}$1 REACTIONS BY LIGHT AND BY SOLVATED ELECTRONS. LEAVING GROUP EFFECTS.

Among the four main ways to induce S$_{RN}$1 reactions, photochemically, electrochemically, by solvated electrons, by outer-sphere single electron donors (usually generated electrochemically), photochemical induction appears more efficient that the other methods. In most cases, substitution occurs in excellent yield with little or no formation of hydrogenolysis product in contrast with what has often been observed for the same substrate-nucleophile couples with the other modes of induction.

Two examples serve to illustrate this difference in behavior. Photostimulated substitution by acetone enolate ions in liquid ammonia of a series of benzenes bearing as leaving group, I, Br, Cl, F, SPh, OPh produces mono and diphenylated acetone in high yields with very little formation of benzene.[119] When the reaction is triggered by solvated electrons, benzene is among the reaction products in amounts that vary with the nature of the leaving group and may be as high as 80 %.[120,121] Reaction of acetone enolate ions with 2-bromopyridine in liquid ammonia under photostimulation leads nearly quantitatively to the substitution product with no detectable formation of pyridine.[83] In contrast, when the reaction is triggered by solvated electrons in the same solvent the yield of substitution product is very low and pyridine is formed.[83]

There have been few quantitative studies of the photochemical induction process in S$_{RN}$1 reactions. [85,86,122]. Consequently knowledge is lacking of the modes of excitation (the substrate, the nucleophile, substrate-nucleophile adducts ?), of the rates of production of RX$^{\bullet-}$ and/or R$^\bullet$ that enter the propagation loop, of non-radiative decay of the excited states, of back electron transfer, etc. as functions of the structure of the nucleophiles and aryl substrates. However, whatever the exact induction mechanisms, it is clear that the steady-state concentrations of the excited state are so low that they cannot interfere in termination steps involving electron transfer to the aryl radical. Thus, in poor H-atom donor solvents, the only possible termination steps are electron transfers from the two anion radicals participating in the propagation loop :

$$R^\bullet + RX^{\bullet-} \longrightarrow R^- + RX$$

$$R^\bullet + RNu^{\bullet-} \longrightarrow R^- + RX$$

Their rate of generation from the photochemical process is small because the photon fluxes involved are small (the quantum yields for the production of RX$^{\bullet-}$ or R$^\bullet$ may also be small). Thus, if reactions 1 - 3 (Scheme 1) participating in the propagation loop are fast enough to prevent build-up of the RX$^{\bullet-}$ and RNu$^{\bullet-}$ concentrations, the two termination steps shown are inefficient even though they are very rapid, close to or at the diffusion limit in most cases because, as noted earlier, R$^\bullet$ is much easier to reduce than are both RX$^{\bullet-}$ and RNu$^{\bullet-}$. The situation is quite different in direct and indirect electrochemistry or with solvated electrons in the sense that the electrode, the redox mediator, or the solvated electrons provide large quantities of an electron donor able to reduce the key-intermediate R$^\bullet$, and also because the concentrations of RX$^{\bullet-}$ and RNu$^{\bullet-}$ may be much higher than in the case of photochemical induction.

The better selectivity of photochemical induction over induction by solvated electrons also allows one to refute an argument [22] given against the $S_{RN}1$ mechanism based on results on substitution by Ar_2As^-, Ar_2Sb^-, and $ArTe^-$ ions. When the phenyl nucleophiles are treated ***under photostimulation*** with an aryl halide, aryl group scrambling occurs. Thus all four possible substitution products are obtained in the case of As and Sb[123,124] and all three in the case of Te.[125] In the framework of the $S_{RN}1$ mechanism this scrambling is explained by the possibility of reversible cleavage of the initially formed substituted anion radical, which may give rise to a phenyl radical and to the $ArAs(Sb)Ph^-$ anion. The latter anion may then couple with $Ar^\bullet$ and so forth, leading to the four (or three) possible substitution products. On the other hand, Ph_3As and Ph_3Sb do not react appreciably with acetone enolate ions in liq. NH_3 in the presence of solvated electrons but rather produce benzene.[75] Although this result has been considered to contradict the above explanation of the aryl radical scrambling, [22] it is in fact perfectly conceivable in the framework of the $S_{RN}1$ mechanism for two reasons. One is that Ph_3As and Ph_3Sb are not easy to reduce, and thus the chain propagation through the $Ph_2As(Sb)CH_2COCH_3^{\bullet -} + Ph_3As(Sb) \rightarrow Ph_2As(Sb)CH_2COCH_3 + Ph_3As(Sb)^{\bullet -}$ reaction is not efficient (much less efficient than the reduction of the aryl iodide). The second is that Ph_2As^- and Ph_2Sb^- are not very good leaving groups in the $Ph_3As^{\bullet -}$ and $Ph_3Sb^{\bullet -}$ anion radicals, even though their reversible dissociation can produce the observed aryl group scrambling. As discussed above, these conditions favor the production of PhH rather than of substitution product when solvated electrons are used as reducing agent, much more so than under photostimulation.

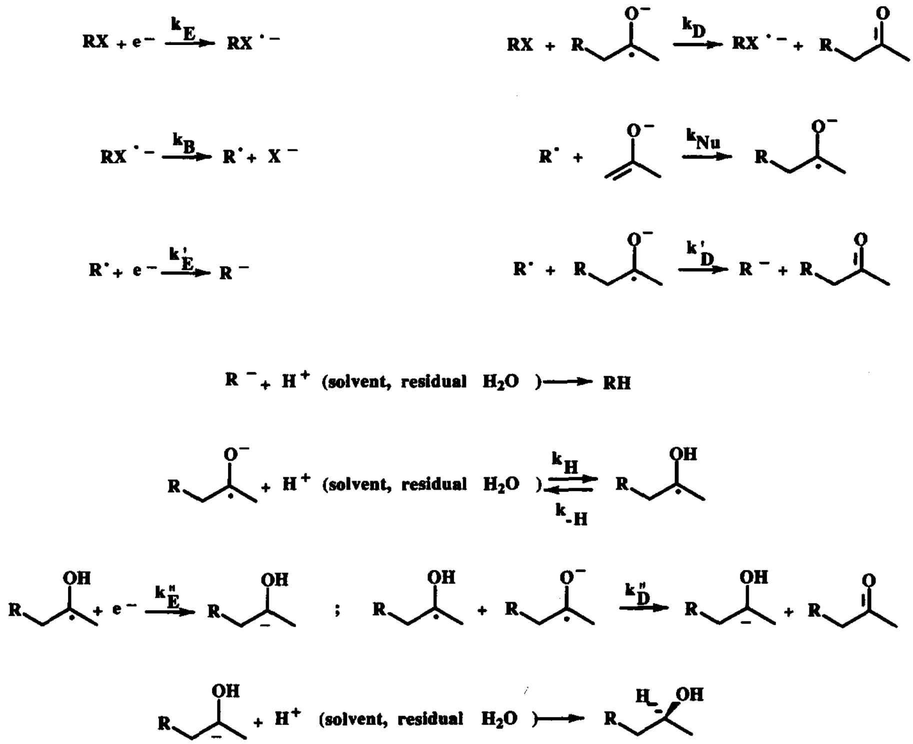
Significant leaving group effects appear in the overall rates of photoinduced $S_{RN}1$ reactions. A typical example is provided by the reaction of a series of monosubstituted benzenes (I, Br, Cl, F, SPh, $^+SPh_2$, SePh, OPh, NMe_3^+, $OPO(OEt_2)$) with acetone enolate ions in liq. NH_3.[119] They may be explained semi-quantitatively by variations in the speed at which the propagation loop repeats due to variations of the cleavage rate constant of the $RX^{\bullet -}$ anion radical (reaction 1) and/or the rate constant of the electron transfer between $RNu^{\bullet -}$ and RX (reaction 3), two reactions that are sensitive to the nature of the leaving group. A precise quantitative modeling of the overall rates is however precluded, at present, by the lack of data pertaining to the rate constants of the various initiation steps which may themselves depend upon the nature of the leaving group. It remains that the dependence of the overall reaction rates upon the nature of the leaving group is perfectly consistent with the $S_{RN}1$ mechanism.

In experiments where a pair of nucleophiles is treated with various substrates having the same R and different X s, there should be, in the $S_{RN}1$ framework, no effect of leaving group on the ratio of the two substitution products, provided the chain cycles fast enough to preclude hydrogenolysis. This expectation was borne out in a systematic study of the photostimulated reaction of substituted benzenes with diethyl phosphite and pinacolone enolate ions in liq. NH_3.[10] If substitution took place at the level of the anion radical ($S_{RN}2$ mechanism) a leaving group effect should be observed unless, as seems improbable, the rate constants of attack by the two nucleophiles vary in an exactly parallel manner from one leaving group to the other.

In the case of initiation by solvated electrons in liquid ammonia, product distribution is a better indication since, as noted earlier, reduction products compete more severely with substitution product. Indeed, striking leaving group effects on product distribution have been observed.[120,121,126] A typical example is the reaction of acetone enolate with a series of benzenes bearing as leaving groups I, Br, $^+N(CH_3)_3$, SPh, Cl, F and OPh.[120] Three main products are observed: the aryl ketone, the hydrogenolysis product, RH, and the aryl alcohol from reduction of the ketone (Scheme 18). The relative proportion of hydrogenolysis product and aryl alcohol increases from I to OPh in that series.

This observation may appear puzzling in that the $S_{RN}1$ mechanism would imply that product selection takes place at the level of the aryl radical, after the leaving group has departed. Indeed this observation was a leading argument against $S_{RN}1$ and in favor of the $S_{RN}2$ mechanism.[22] However, reductions by solvated electrons, introduced either by a piece of alkali metal or as solutions in liquid ammonia, are not homogeneous processes. As previously hypothesized[120,121] and demonstrated more rigorously in recent reports,[127,128] these reductions occur during mixing.

Scheme 18



Solvated electrons diffuse from the surface of the alkali metal to the solution containing RX or, when a saturated solvated electron solution in ammonia is mixed with the solution containing RX, electrons diffuse from the phase boundary to the RX solution. Conversely, RX can diffuse from bulk solution to the interphase. Since solvated electrons are potent reductants (E^0 = - 2.69 vs 0.1 M Ag^+/Ag[129]), they reduce most of the usual RX substrates quickly, but at rates that depend upon the nature of RX and, in particular, upon X. The reaction RX + e- --> $RX^{\bullet -}$ thus occurs within a very thin reaction layer itself located inside the diffusion layer as sketched in Figure 1.

Diffusion layer thicknesses under moderate stirring are of the order of 10^{-2} cm[130] and lead to a diffusion time for RX (diffusion coefficient ≈ 10^{-5} cm^2 s^{-1}) of the order of 10 seconds, whereas characteristic times for the reduction of RX in contact with solvated electron are of the order of 10^{-8} - 10^{-6} s under typical experimental conditions. It follows that initiation occurs during mixing. Since the termination steps (electron transfer to R$^\bullet$) are also fast and the steps of the propagation loop have to be fast if they are to compete with reduction, it follows that the entire $S_{RN}1$ process takes place within this thin reaction layer.

More quantitatively[127,128] the thickness of the reaction layer is approximately given by $\mu \approx \left(D\, l / k_E C_E^0\right)^{1/3}$ (l is the thickness of the diffusion layer (~10^{-2} cm.); D is the average diffusion coefficient of the intervening species; C_E^0 is the concentration of a saturated solution of solvated electrons (~10 M[131]) ; and k_E is the bimolecular rate constant for the reaction of RX with the solvated electrons). The rate constant k_E varies with the nature of R and X and thus influences the thickness of the reaction layer.

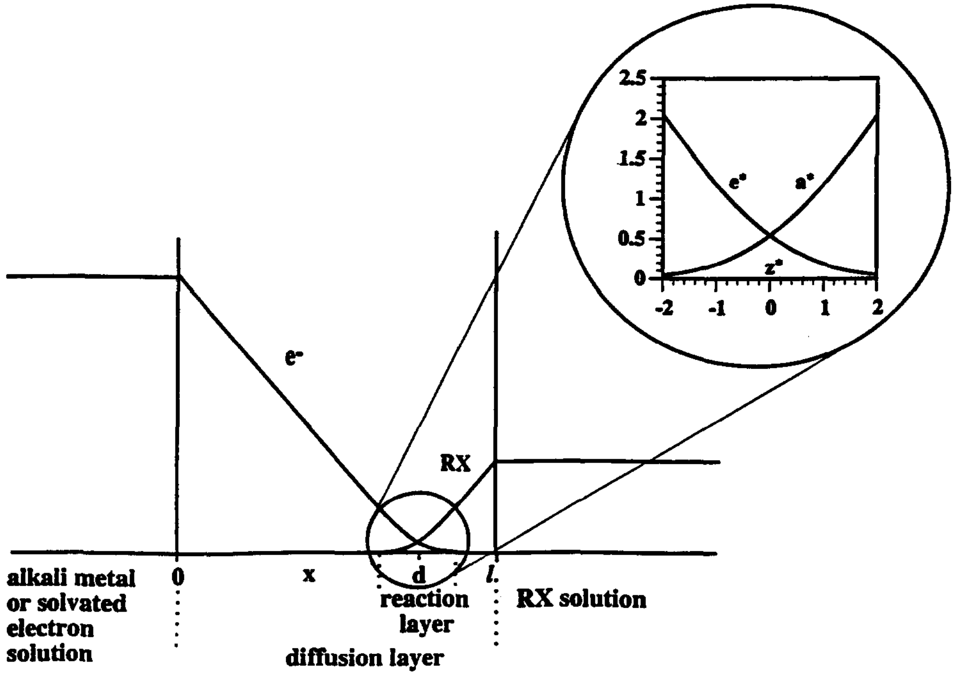
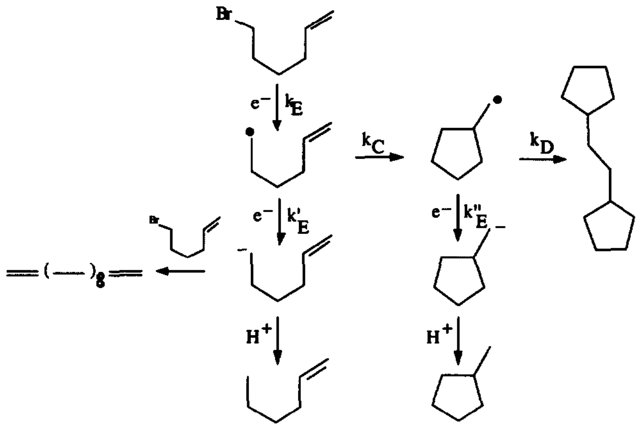


Fig.1. Concentration profiles for the reaction RX + solvated electrons --> product. $z^* = \frac{x-d}{l}\lambda_E^{1/3}$, $e^* = \frac{C_E}{C_E^0}\lambda_E^{1/3}$, $a^* = \frac{C_{RX}}{C_E^0}\lambda_E^{1/3}$ (C_E and C_{RX} are the space-dependent concentrations of the solvated electrons and of the substrate respectively).

The reactions in Schemes 19 and 20[132] help us comprehend $S_{RN}1$ substitutions initiated by solvated electrons. In Scheme 19, electron transfer to the substrate should be concerted with the breaking of the carbon-bromine bond as in all aliphatic halides.[7] In the reaction layer, competition is between cyclization of the open-chain alkyl radical and its reduction by solvated electrons (followed by protonation).

At the level of the cyclized radical, a second competition exists between dimerization and reduction by solvated electrons (followed by protonation). The distribution of products (open-chain reduction product, cyclized reduction product, cyclized dimer) is a function of the following parameters.[127,128]

Scheme 19



Cyclization vs reduction of the open-chain radical : $\left(k_C k_E^{1/3} / k'_E\right)\left(I^{2/3} / C_E^{0\,2/3} D^{1/3}\right)$

Reduction vs dimerization of the cyclized radical : $k''^{2}_E / k_D k_E$

(the various rate constants are those defined in scheme 19).

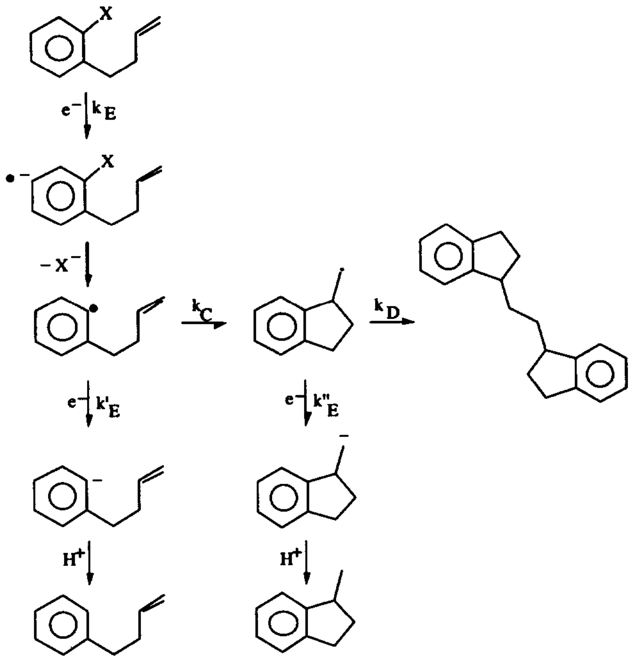
The high yield of open-chain reduction product reflects the fact that the cyclization of the 5-hexenyl radical is relatively slow[132] as compared to its reduction by solvated electrons, which is at or close to the diffusion limit since primary alkyl radicals are more easily reduced than the parent bromides.[104] No cyclized radical dimer is found, and the open-chain dimer arises from the combination between open-chain carbanion and starting bromide, as is known for aliphatic halides.

It should be emphasized that the magnitude of both competition parameters depend upon the value of k_E, the rate constant for reaction between *substrate* and solvated electrons. In this way the distribution of products can depend upon the substrate, in particular, upon the nature of the leaving group. The physical basis for this rigorous conclusion is that the concentration of solvated electrons in the reaction layer is a decreasing function of k_E : the faster the reaction between substrate and solvated electrons, the lower the concentration of the latter in the reaction layer and consequently the less efficient the reduction pathways. This is the key effect that allows one to understand how "departed" groups can influence product distribution in radical reactions where the initial radical is produced by a reductive cleavage involving the expulsion of a leaving group.

This leaving group effect is illustrated by the reactions sketched in Scheme 20. The three products are of the same type as in the preceding case.[132]

The main difference is that the anion radical of the substrate is an intermediate in the formation of the open-chain radical as has been observed for all aryl halides investigated so far.[7] Because of the intermediacy of the anion radical, reduction of the open-chain and cyclized radical can involve either solvated electrons or the substrate anion radicals. Since the former reduction pathway overruns the latter because the cleavage of the anion radicals in the series is fast, the product distribution depends upon the same competition parameters as in the preceding case. The observed leaving group effect (the ratio of cyclized over open-chain products increases in the series of halogen as F < Cl < Br < I) is explained straightforwardly by the fact that the rate at which the solvated electrons reduce the substrate increases in the same way as is well known from electrochemical studies of aryl halides. Quantitative application of the mixing model in Figure 1 showed an excellent correspondence to product distribution data for all leaving groups investigated (see Table I in reference 127).[133]

Scheme 20



Leaving group effects in aromatic $S_{RN}1$ substitutions triggered by solvated electrons in liq. NH_3 (Scheme 18) may be rationalized along the same lines, taking, in addition, account of the chain character of the reaction and of the fact that reduction of the aryl radical by the $RNu^{\bullet -}$ anion radical can compete much more effectively with the reduction by the solvated electrons than the reduction by the unstable $RX^{\bullet -}$ anion radicals. The distribution of the three products (aryl-ketone, aryl-alcohol and RH) is a function of the following three competition parameters (the rate constants are defined in Scheme 18).

$$\left(k_{Nu}\, k_E^{1/3} / k'\right)\left([Nu^-] / C_E^{0\ 2/3}\right) l^{2/3} / D^{1/3} \quad , \quad k'' / k_E \quad \text{and} \quad k_E / k_D$$

where $k' = k'_E = k'_D$ and $k'' = (k_H/k_{-H})\, k''_E = (k_H/k_{-H})\, k''_D$. The constants k''_D, k'_E, k'_D, k''_E, and k''_D are indeed all close to the diffusion limit in view that aryl radicals are reduced at rather positive potentials, much more positive than the potentials where solvated electrons and the $RNu^{\bullet -}$ anion radicals are generated. The amount of both aryl ketone and aryl alcohol formed at the expense of RH is an increasing function of the first parameter, whereas the relative amount of aryl alcohol and aryl ketone is an increasing function of the second parameter. The constants k_{Nu}, k', and k'' are independent of the leaving group, but k_E and k_D are not. The latter rate constants decrease in the order, I > Br > $^+N(CH_3)_3$ > S_{Ph} > Cl > F.[134] It is thus understandable that the total substitution product (ketone + alcohol) decreases in this same order whereas the yield of RH increases correspondingly. For the same reason, the relative amounts of alcohol and ketone increase in the same order. The essential reason behind these physically and mathematically rigorous predictions[127] is that the concentration of solvated electrons in the reaction layer is a decreasing function of k_E and thus the competition by reductions (formation of RH from R$^{\bullet}$ and of the substituted alcohol from the anion radical of the substituted ketone) is increasingly favorable as k_E increases. Quantitative application of the mixing model again led to satisfactory correlation of variations of product distribution with the leaving group (Figure 4 in reference 127).

We may thus conclude that the leaving groups effects observed in reactions triggered by photochemical or solvated-electron reduction of RX are completely consistent with radical mechanisms.

6. RELATIONSHIPS BETWEEN REACTIVITY AND STRUCTURE IN THE CLEAVAGE OF AROMATIC ANION RADICALS CONTAINING POTENTIAL LEAVING GROUPS AND IN THEIR FORMATION FROM ARYL RADICALS AND NUCLEOPHILES.

We have already seen that cleavage rate constants of aromatic anion radicals containing potential leaving groups, $RX^{\bullet-}$, can vary considerably with the nature of R and of X. The rate constants for the reverse process, namely formation of anion radical $RNu^{\bullet-}$ (from radical $R^{\bullet}$ and the nucleophile Nu^-) is also expected to vary with the nature of R and Nu^-. It is thus worth trying to relate reactivity and structure for these two reactions. One starting point is to examine main factors that govern their driving forces. The standard free energies of the two reactions may be expressed as in equation 1 (energies in eV, potentials in Volts) for the cleavage reaction (X^- designates the leaving group).

$$\Delta G^0_{RX^{\bullet-}\rightarrow R^{\bullet}+X^-} = E^0_{RX/RX^{\bullet-}} - E^0_{RX/R^{\bullet}+X^-} = D_{RX} + E^0_{RX/RX^{\bullet-}} - E^0_{X^{\bullet}/X^-} + T\,(\bar{S}_{RX} - \bar{S}_{R^{\bullet}} - \bar{S}_{X^{\bullet}}) \qquad [1]$$

and as in equation 2 for the radical-nucleophile reaction ($X^- = Nu^-$ designates the nucleophile in this case; the $\bar{S}$ s are the partial molar entropies of the subscript species).

$$\Delta G^0_{R^{\bullet}+X^-\rightarrow RX^{\bullet-}} = - E^0_{RX/RX^{\bullet-}} + E^0_{RX/R^{\bullet}+X^-} = - D_{RX} - E^0_{RX/RX^{\bullet-}} + E^0_{X^{\bullet}/X^-} - T\,(\bar{S}_{RX} - \bar{S}_{R^{\bullet}} - \bar{S}_{X^{\bullet}}) \qquad [2]$$

These driving forces depend on three main factors : (i) the strength of the bond being cleaved in the starting molecule or formed in the final substitution product as measured by the bond dissociation energy, D_{RX}; (ii) the standard potential for formation of the anion radical of the substrate or of the substituted product, $E^0_{RX/RX^{\bullet-}}$, which is a measure of the energy of the π^* orbital or any other low-lying orbital where the unpaired electron may be located; (iii) the standard oxidation potential of the nucleofugal group or of the nucleophile, $E^0_{X^{\bullet}/X^-}$.

Reactivity-structure trends in some experimental studies of the cleavage of anion radicals[7,43] (and in the converse formation of anion radicals from radicals and nucleophiles[45,88,135]) were previously discussed on the basis of these expressions as if reactivity were solely controlled by driving force. This presumption may not be generally valid and consequently a model of the dynamics of the two reactions has been proposed recently.[8,136,137] It has been previously suggested, from semi-empirical quantum mechanical calculations[7,43] or on intuitive grounds,[31-33,52-55] that the cleavage of anion radicals may be viewed as intramolecular concerted electron transfer-bond breaking processes . Thus, as the breaking bond stretches, the unpaired electron initially in a low energy orbital of the molecule (π * in the case of an aromatic anion radical) is transferred into the σ * orbital of the stretching bond concertedly with its cleavage when its energy has become low enough to match that of the orbital initially containing the unpaired electron (and vice versa for the formation of an anion radical from a radical and a nucleophile[4,138-140]).

Extending these ideas to a quantitative level, the Morse-curve model previously proposed for dissociative electron transfers,[7,8,137,141,142] has been adapted to the reactions under discussion.[8,136,137] The diabatic potential energy surfaces are functions of two main nuclear coordinates, the C-X distance and a coordinate representing solvent reorganization. The potential energy vs bond length profiles for the three systems, $RX+e^-$, $RX^{\bullet -}$, $R^\bullet+X^-$, are represented by equations 3-5.

$$G_{RX+e^-} = G^0_{RX+e^-} + D_{RX}\left\{1-\exp\left[-\beta\,(y-y_{RX})\right]\right\}^2 \qquad [3]$$

$$G_{RX^{\bullet -}} = G^0_{RX^{\bullet -}} + D_{RX^{\bullet -}}\left\{1-\exp\left[-\beta\,(y-y_{RX^{\bullet -}})\right]\right\}^2 \qquad [4]$$

$$G_{R^\bullet + X^-} = G^0_{R^\bullet + X^-} + D_{RX}\left\{\exp\left[-\beta\,(y-y_{RX})\right]\right\}^2 \qquad [5]$$

with :

$$\beta\,(y_{RX^{\bullet -}} - y_{RX}) = \mathrm{Ln}\left(\frac{D_{RX}}{D_{RX^{\bullet -}}}\right)^{1/2} \qquad [6]$$

In these expressions, $G^0_{RX+e^-}$, $G^0_{RX^{\bullet -}}$ and $G^0_{R^\bullet+X^-}$ are the ground state free energies of $RX+e^-$, $RX^{\bullet -}$ and $R^\bullet+X^-$ respectively; y is the R-X distance; y_{RX} and $y_{RX^{\bullet -}}$ the equilibrium values of y in RX and $RX^{\bullet -}$ ground states; D_{RX} the bond dissociation energy of RX ; $D_{RX^{\bullet -}}$ the bond dissociation energy of $RX^{\bullet -}$ into $(R^\bullet)^{\bullet -}$ and $X^\bullet$, or into $R^\bullet$and $(X^\bullet)^{\bullet -}$, according to whether the low energy orbital able to accommodate the unpaired electron belongs to R or to X; $\beta = \nu\left(2\pi^2\mu/D_{RX}\right)^{1/2}$ (ν is the R-X stretching frequency and μ the reduced mass of the two atoms of the R-X bond).

A quadratic activation-driving force relationship (as in Marcus-Hush theory of outer-sphere electron transfer[143-147]) ensues :

$$\Delta G^{\neq}_{RX^{\bullet -}\rightarrow R^\bullet+X^-} = \Delta G^{\neq}_{0,RX^{\bullet -}\leftrightarrow R^\bullet+X^-}\left(1+\frac{\Delta G^0_{RX^{\bullet -}\rightarrow R^\bullet+X^-}}{4\,\Delta G^{\neq}_{0,RX^{\bullet -}\leftrightarrow R^\bullet+X^-}}\right)^2 \qquad [7]$$

for the cleavage reaction, and,

$$\Delta G^{\neq}_{R^\bullet+X^-\rightarrow RX^{\bullet -}} = \Delta G^{\neq}_{0,RX^{\bullet -}\leftrightarrow R^\bullet+X^-}\left(1+\frac{\Delta G^0_{R^\bullet+X^-\rightarrow RX^{\bullet -}}}{4\,\Delta G^{\neq}_{0,RX^{\bullet -}\leftrightarrow R^\bullet+X^-}}\right)^2 \qquad [8]$$

for the radical-nucleophile coupling reverse reaction. The driving forces, $\Delta G^0_{RX^{\bullet -}\rightarrow R^\bullet+X^-}$ and $\Delta G^0_{R^\bullet+X^-\rightarrow RX^{\bullet -}}$ are given by equations 1 and 2 respectively. Equations 7 and 8 allows one to define the respective role of the driving force and of the intrinsic barrier in the determination of the activation barrier of each of the two reactions. The intrinsic barrier, $\Delta G^{\neq}_{0,RX^{\bullet -}\leftrightarrow R^\bullet+X^-}$, which is the same for both reactions, may be expressed as :

$$\Delta G^{\neq}_{0,R^\bullet+X^-\leftrightarrow RX^{\bullet -}} = \frac{D_{RX^{\bullet -}}+\lambda_0}{4} \qquad [9]$$

in which the two terms represent the contributions of bond breaking and solvent reorganization respectively. The latter has the same expression as in Marcus-Hush theory of outer-sphere electron transfer[143-147] and may be related to the geometrical parameters of the reacting system by :

$$\lambda_{0,RX^{\bullet -}\leftrightarrow R^\bullet+X^-} = e_0^2\left(\frac{1}{2a_{R^\bullet,X^-}}+\frac{1}{2a_{RX^{\bullet -}}}-\frac{1}{d}\right)\left(\frac{1}{D_{op}}-\frac{1}{D_s}\right) \qquad [10]$$

The major contribution is that of bond breaking. It is equal to one fourth of the bond dissociation energy in the anion radical. This may be related to accessible thermodynamic quantities in the following manner.

If the low energy orbital able to accommodate the electron belongs to the R portion of RX, as in the case of most aryl and arylmethyl substrates where it is the π^* orbital of the aryl group :

$$\Delta G^{\neq}_{0,\mathrm{RX}^{\bullet-}\leftrightarrow\mathrm{R}^{\bullet}+\mathrm{X}^-} = \frac{D_{\mathrm{RX}} + E^0_{\mathrm{RX/RX}^{\bullet-}} - E^0_{\mathrm{R}^{\bullet}/(\mathrm{R}^{\bullet})^{\bullet-}} + T\,(\bar{S}_{\mathrm{RX}} - \bar{S}_{\mathrm{RX}^{\bullet-}} + \bar{S}_{(\mathrm{R}^{\bullet})^{\bullet-}} - \bar{S}_{\mathrm{R}^{\bullet}})}{4} \qquad [11]$$

with :

$$E^0_{\mathrm{R}^{\bullet}/(\mathrm{R}^{\bullet})^{\bullet-}} \leq E^0_{\mathrm{R}^{\bullet}/\mathrm{R}^-}$$

where the notation $(\mathrm{R}^{\bullet})^{\bullet-}$ represents, starting from the radical $\mathrm{R}^{\bullet}$, the injection of one electron in the π^* orbital. In other words, $(\mathrm{R}^{\bullet})^{\bullet-}$ is an excited state of the carbanion R^- where one of the electron of the pair located in the σ orbital has been transferred to the π^* orbital.

With aliphatic substrates, the unpaired electron must be accommodated in an orbital belonging to the X portion of RX. Then :

$$\Delta G^{\neq}_{0,\mathrm{RX}^{\bullet-}\leftrightarrow\mathrm{R}^{\bullet}+\mathrm{X}^-} = \frac{D_{\mathrm{RX}} + E^0_{\mathrm{RX/RX}^{\bullet-}} - E^0_{\mathrm{X}^{\bullet}/(\mathrm{X}^{\bullet})^{\bullet-}} + T\,(\bar{S}_{\mathrm{RX}} - \bar{S}_{\mathrm{RX}^{\bullet-}} + \bar{S}_{(\mathrm{X}^{\bullet})^{\bullet-}} - \bar{S}_{\mathrm{X}^{\bullet}})}{4} \qquad [12]$$

with :

$$E^0_{\mathrm{X}^{\bullet}/(\mathrm{X}^{\bullet})^{\bullet-}} \leq E^0_{\mathrm{X}^{\bullet}/\mathrm{X}^-}$$

where $(\mathrm{X}^{\bullet})^{\bullet-}$ represents, starting from $\mathrm{X}^{\bullet}$, the injection of one electron in the low lying orbital (in most cases, although not necessarily, a π^* orbital), $(\mathrm{X}^{\bullet})^{\bullet-}$ being thus an excited state of X^-.

In terms of intrinsic barriers (equations 11, 12), weak R-X bonds and negative standard potentials for the generation of the anion radical are favorable to both the cleavage of the anion radical and its formation from the radical and the nucleophile.

In terms of driving forces (equations 1, 2), weak R-X bonds favor cleavage and disfavor coupling as expected intuitively. Negative values of $E^0_{\mathrm{RX/RX}^{\bullet-}}$ also favor the former reaction and disfavor the latter : a low energy π^* orbital containing the unpaired electron has a smaller tendency, in the cleavage reaction, to transfer the electron to the σ^* orbital with concomitant cleavage of the R-X bond. Conversely, in the coupling reaction, one of the electrons of the nucleophile electron-pair has a greater tendency to be transferred to the π^* orbital with concomitant formation of the R-X bond. Lastly, the contribution of the third term , $E^0_{\mathrm{X}^{\bullet}/\mathrm{X}^-}$, in equations 1,2 tells us that easy-to-oxidize nucleophiles produce easier coupling whereas nucleofugal groups that are difficult to oxidize promote easy cleavages.

The R-X bond dissociation energies are not extremely sensitive to the nature of the solvent and may therefore be estimated from existing gas-phase thermochemical data. The $E^0_{\mathrm{RX/RX}^{\bullet-}}$ can be derived simply from reversible, slow scan cyclic voltammetric waves when the $\mathrm{RX}^{\bullet-}$ anion radical is stable as in many coupling reactions. When $\mathrm{RX}^{\bullet-}$ is a fast cleaving anion radical, $E^0_{\mathrm{RX/RX}^{\bullet-}}$ can be measured by fast scan cyclic voltammetry or by indirect electrochemical techniques (redox catalysis) as discussed in section 2. The values of $E^0_{\mathrm{X}^{\bullet}/\mathrm{X}^-}$ are solvent-dependent mainly because of solvation of the X^- ion. They can be estimated from existing thermochemical and solvent transfer free energy data as summarized in Table I (the detailed derivations are given in reference 136).

From the estimation of the driving force according to equations 1 and 2 and of the intrinsic barrier using equations 11 and 12, the activation free energies of the cleavage and coupling reactions are obtained from equations 7 and 8 respectively, and then, the rate constants from equation 13 (A : pre-exponential factor).

$$\log k = \log A - \frac{F}{RT\,\mathrm{Ln}\,10}\,\Delta G^{\neq} \qquad [13]$$

TABLE I. Estimated $X^\bullet/X^-$ standard potentials in water, DMF, and liq. NH_3.

X	$E^0_{X\bullet/X^-,H_2O}$ [a]	$E^0_{X\bullet/X^-,DMF}$ [b]	$E^0_{X\bullet/X^-,NH_3}$ [c]
Cl	2.48	1.85	2.32
CN	2.28	-	2.12
Br	1.95	1.48	1.81
OH	1.82	-	1.52
I	1.34	0.99	1.24
t-BuO	1.18	-	0.97
PhO	0.94	-	0.80
PhS	0.74	-	0.63
CH_3COCH_2	0.68	-	0.49
NH_2	0.26	-	0.02
Ph	- 0.23	- 0.76	-0.38

a : at 25°C, in V.vs SHE . b : at 25°C, in V vs aq.SCE. c : at -40°C, in V vs 0.01M Ag^+/Ag .

As a first application one may examine the cleavage rates of anion radicals of aromatic chlorides and bromides as a function of the aryl group. It has already been noticed[7,43] that log k for this reaction correlates, as represented in Figure 2, approximately linearly with $E^0_{RX/RX\bullet^-}$ with a slope $-\partial(RT/F\,Ln10)\log k/\partial\Delta G^0 = \partial\Delta G^{\neq}/\partial\Delta G^0$ close to 0.5.

This correlation may be interpreted as resulting from a linearized version of the activation-driving force relationship depicted by equations 7 + 13 :

$$\log k_{RX\bullet^-\rightarrow R\bullet+X^-} = \log A - \frac{F}{RTLn10}\left(\Delta G^{\neq}_{0,RX\bullet^-\leftrightarrow R\bullet+X^-} + \frac{\Delta G^0_{RX\bullet^-\rightarrow R\bullet+X^-}}{2}\right) \qquad [14]$$

implying, as seems likely, that, given the halogen, the bond dissociation energy (and consequently, $E^0_{RX/R\bullet+X^-}$) does not vary much with R. The variation of the driving force, $\Delta G^0_{RX\bullet^-\rightarrow R\bullet+X^-}$, then essentially reflects that of the standard potential $E^0_{RX/RX\bullet^-}$ (equation 1). This interpretation also implies that the intrinsic barrier remains about constant when the structure of the R group changes, i.e., that the energies of the π* orbitals in RX and in the $R^\bullet$ radical vary in a parallel manner when R changes. That the correlation in Figure 2 appears approximate, with inversions for isomers of the same compound, is an indication of the approximate character of the constancy of the bond dissociation energy and of $E^0_{RX/RX\bullet^-} - E^0_{R\bullet/(R\bullet)\bullet^-}$ for small variations in R.

The $E^0_{RX/R\bullet+X^-}$, which can be estimated from existing thermochemical data, defines the zero driving force point from which, as depicted in Figure 2, the standard rate constant, k_0, (rate constant at zero driving force, i.e., the rate constant that corresponds to the intrinsic barrier) may be derived. Application of equation 13 then allows one to obtain a lower limit of the values of the pre-exponential factor ($\log A \geq 13$ for Cl, $\log A \geq 12$ for Br). [136] Since cleavage of these aromatic anion radicals involves transfer of one electron from the π* to the σ* orbital, one would expect the reaction to be symmetry forbidden. The large values of the pre-exponential factor indicate that some mechanism exists (out-of-plane vibration of the R-X bond, vibronic coupling ?) that circumvents the symmetry restrictions.

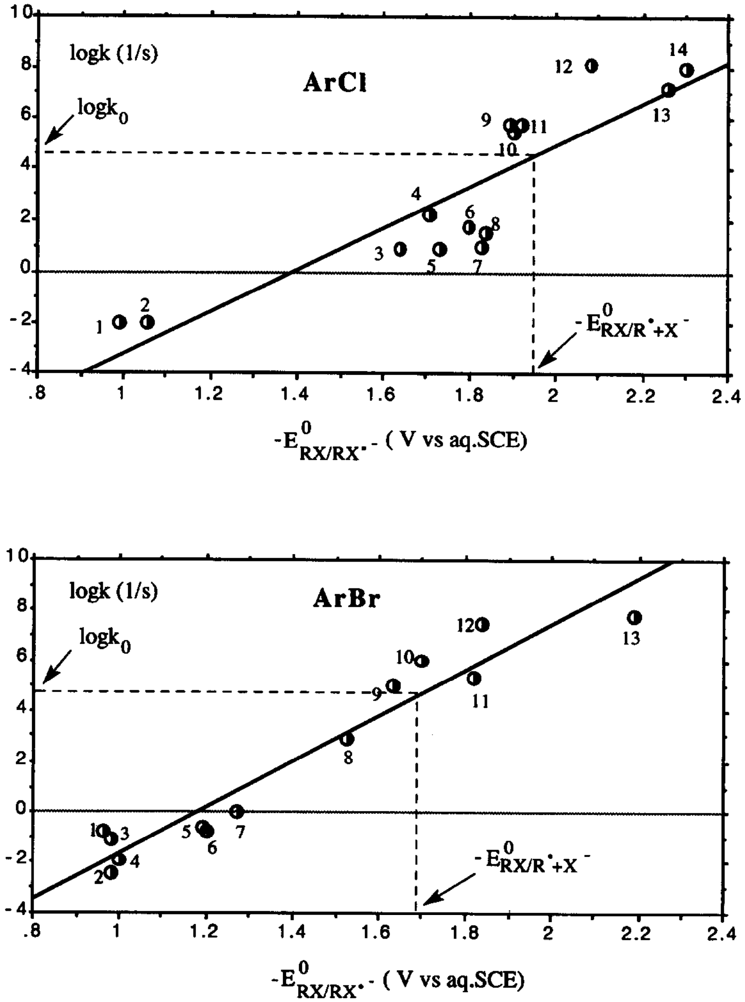


Fig.2. Cleavage rate constant, k, of aryl chlorides and bromides in DMF as a function of the standard potential $E^0_{RX/RX^{\bullet-}}$ (from the data in references 37). ArCl : 1: 4-nitrophenyl, 2: 2-nitrophenyl, 3: 4-benzoylphenyl, 4: 9-anthracenyl, 5: 1-anthracenyl, 6: 2-anthracenyl, 7: 4-(2-(4-pyridyl)vinyl)phenyl, 8: 3-acetylphenyl, 9: 4-quinolyl, 10: 4-acetylphenyl, 11: 2-quinolyl, 12: 4-cyanophenyl, 13: 1-naphthyl, 14: 2-naphthyl. ArBr : 1: 2-isopropyl-4-nitrophenyl, 2: 4-nitrophenyl, 3: 2-methyl-3-nitrophenyl, 4: 2-methyl-4-nitrophenyl, 5: 3-fluorenoyl, 6: 1-fluorenoyl, 7: 2,6-dimethyl-4-nitrophenyl, 8: 3-benzoylphenyl, 9: 4-benzoylphenyl, 10: 9-anthracenyl, 11: 3-acetylphenyl, 12: 4-acetylphenyl, 13: 1-naphthyl.

The reactivity of phenyl radicals toward classical $S_{RN}1$ nucleophiles, PhS^-, $CH_3COCH_2^-$, $(EtO)PO^-$, Ph_2PO^-, Ph_2P^-, has been determined in liq. NH3 at -40°C.[10,45] Diphenylsulfide is interesting because both the cleavage and the formation rate constants of the anion radical have been determined. Application of the model leads to a satisfactory agreement with the experimental data.[136] The other nucleophiles in the series have similar reactivities and are *ca* ten times more reactive than PhS^-; however all rate constants remain below the diffusion limit. The driving force is more favorable mainly because the R-X bond is stronger (equation 2), but this is compensated in part by an increase in the intrinsic barrier (equation 11).

Cyanide ions strikingly exemplify a nucleophile that is unreactive toward phenyl radicals in spite of a strong bond dissociation energy and therefore of a very favorable driving force ($\Delta G^0_{R\cdot+X^-\rightarrow RX\cdot^-} = -1.35$ eV as compared to 0.16 for PhS$^-$ and - 0.45 eV for CH$_3$CO-CH$_2^-$). It should be borne in mind that "unreactive" is a relative term. Because of competing electron transfer reduction of the phenyl radical, the coupling rate constant has to be larger than *ca* 10^5 M^{-1} s^{-1} for substitution to occur. It remains that CN$^-$ ions are much less reactive than the nucleophiles in the above series. This is the result of an increase of the intrinsic barrier due to the increased R-X bond strength (the D_{RX} term in equation 11), which is not compensated by the increased driving force. This apparently paradoxical situation, where a strongly down-hill reaction (CN$^-$) is slower than a slightly up-hill reaction (PhS$^-$), is best understood by examining equation 15, a linearized version of equation 8 where

$$\Delta G^{\neq}_{R\cdot+X^-\rightarrow RX\cdot^-} = \Delta G^{\neq}_{0,RX\cdot^-\leftrightarrow R\cdot+X^-} + \frac{\Delta G^0_{R\cdot+X^-\rightarrow RX\cdot^-}}{2}$$
$$= -\frac{D_{RX}}{4} + \frac{E^0_{X\cdot/X^-}}{2} - \frac{E^0_{RX/RX\cdot^-}}{4} - \frac{E^0_{X\cdot/(X\cdot)\cdot^-}}{4} + T\Delta S \qquad [15]$$

the two first terms prevail over the others on change from one nucleophile to the other. If all other factors were constant, an increase in D_{RX} should favor kinetically the coupling reaction with a factor 1/4 (1/2 in favor from the driving force, 1/4 in disfavor from the intrinsic barrier). However, the factor $E^0_{X\cdot/X^-}$ strongly plays against CN$^-$ ions, reverting the balance in favor of PhS$^-$ and CH$_3$COCH$_2^-$ ions (see Table I). An additional effect that plays against CN$^-$ is that the driving force is so strong that decrease in the activation barrier upon increasing the driving force is less than would be predicted by the linearized version (equation 15) of the quadratic relationship in equation 8. The above analysis allows one to place on quantitative grounds the intuition that CN$^-$ ion reacts poorly toward the phenyl radical because CN$^-$ is a hard, albeit strong, nucleophile.

Another striking feature of the reactivity of aryl radicals toward nucleophiles is the marked increase in rate for phenyl radicals carrying electron-withdrawing groups and for polyaromatic aryl radicals. For example, this reactivity increase occurs with nucleophiles such as thiophenoxide, diakylphosphite, acetone enolate and cyanide ions upon change from the phenyl radical to the 2-, 3-, 4- cyanophenyl, 1-naphthyl,3- and 4-quinolyl radicals (see Table I in ref. 7). In several cases, the acceleration reaches the diffusion limit. The origin of this increased reactivity is the lowering of the π* orbital accommodating the unpaired electron as measured by the positive shift of $E^0_{RX/RX\cdot^-}$ resulting in an increased driving force (equation 2). Overall, the situation is the reverse of the cleavage of aryl chlorides and bromides discussed earlier. As in the latter case, for each nucleophile, the bond dissociation energy and the intrinsic barrier do not vary much with the aryl structure making $E^0_{RX/RX\cdot^-}$ the sole important reactivity parameter.

With cyanide ions, the increase in reactivity is particularly remarkable. No coupling

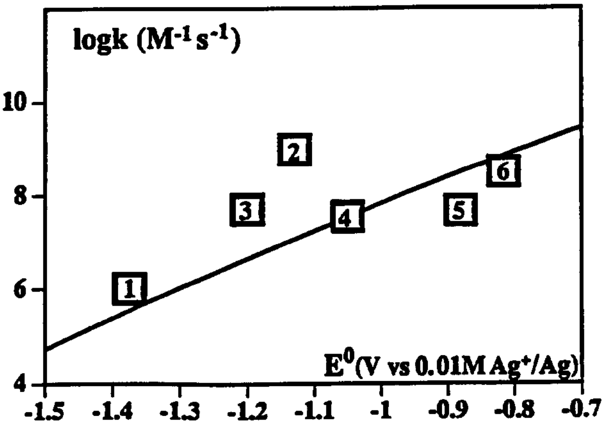


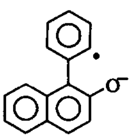
Fig.3 Coupling rate constant (from the data in refs. 135 and 148) of aryl radicals (1 : 1-naphthyl, 2 : 2-cyanophenyl, 3 : 3-cyanophenyl, 4 : 4-cyanophenyl, 5 : 4-benzoyl, 6 : 4-quinolyl) with cyanide ions as a function of the RX/RX$^{\cdot-}$ standard potential in liq. NH3 at - 38°C. Full line : predicted variation for log A = 15.

occurs with phenyl radicals, whereas it is observed with the substituted radicals mentioned above (see Figure 3 for the rate data [135,148]). As the driving force increases upon decrease in the height of the π^* orbital, substitution occurs and the coupling rate constant becomes measurable. The line in Figure 3 represents the predictions of the model discussed above.[136] With the exception of the ortho-substituted radical, the predictions agree satisfactorily with the experimental data. The plot in Figure 3 thus appears as the reverse of the plots in Figure 2. The two situations are however not exactly symmetrical. With the cleavage of the aryl chloride and bromide anion radicals, the point of zero driving force falls (within the range of experimental data) in line with a symmetry factor, α (equation 16), close to 0.5. This is not what happens in

$$\alpha = \frac{\partial \Delta G^{\neq}}{\partial \Delta G^{0}} = \frac{1}{2}\left(1 + \frac{\Delta G^{0}}{4\Delta G_{0}^{\neq}}\right) \qquad [16]$$

the present case where the zero driving force is reached for an extremely negative value (-3.26 V) of the $RX/RX^{\bullet-}$ standard potential. The set of experimental points covers a range of extremely strong driving forces, in accord with a symmetry factor (0.25) much lower than 0.5

Several other remarkable features of the reactivity of aryl radicals have been rationalized according to the same model.[136] For example, the fact that NH_2^- ions are reactive whereas OH^- ions are not results essentially from the less positive value of $E^0_{X\bullet/X^-}$ (Table I). Enolate ions couple with aryl radicals at carbon rather than at oxygen because the forming bond is the stronger and, to a lesser extent, because $E^0_{RX/RX\bullet^-}$ is less negative in the first case than in the second. The latter factor is responsible for the slight preference of ortho and para-carbon coupling over oxygen coupling in the case of aryloxide ions where carbon-oxygen coupling is expected to be slower than carbon-carbon coupling but not to a large extent. This outcome falls in line with the recent finding that carbon-oxygen coupling does occur intramolecularly in the radical shown[149,150] where carbon-carbon coupling is structurally disfavored.



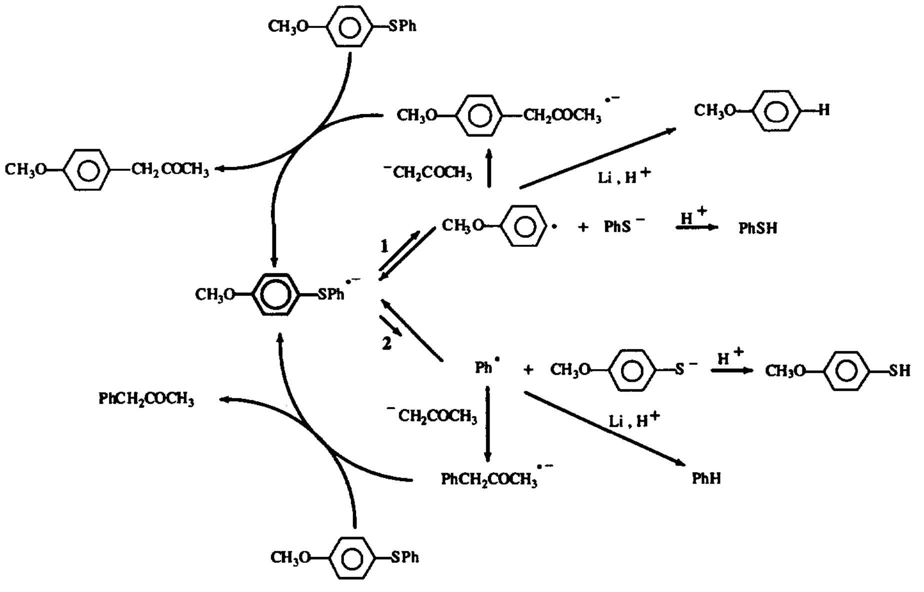
Another striking feature of the $S_{RN}1$ reaction is that benzyl radicals require strong electron-withdrawing substituents (one nitro group[1] or two cyano groups[151]) to couple with nucleophiles, whereas phenyl radicals do not. As discussed in more detail in reference 136, the essential reason for this difference in reactivity is the strength of the forming bond : with a large variety of groups, the bond dissociation energy is more than 1 eV larger with phenyl than with benzyl derivatives.[152] According to equation 15, an advantage of 4-5 orders of magnitude in terms of rate constant is expected. Since the reactions with the unsubstituted phenyl radical are not extremely fast (10^6-10^8 M^{-1} s^{-1}), it is therefore not surprizing that reactions of unsubstituted benzyl radical with the same nucleophiles are unable to compete with various side-reactions.

It is also noteworthy that aryl and arylmethyl radicals differ in their reactivity toward aryloxide ions. For example, 1-methyl-2-naphthoxide ions give efficient carbon-oxygen coupling in the reaction with α,p-dinitrocumene,[1] whereas carbon-carbon coupling occurs in the reaction of a similar nucleophile with p-iodoanisole and 1-iodonaphthalene.[153] An aryloxy substituent attached to the α-benzylic carbon has less influence on the π^* orbital of the phenyl ring than does an aryloxy substituent directly attached to the aryl ring. Therefore, the effect of the positive shift of $E^0_{RX/RX\bullet^-}$ favoring carbon-carbon coupling in the aryl case becomes negligible in the arylmethyl case.[136]

The structure-reactivity relationships that have been rationalized by the associative electron transfer model may also be used as diagnostic criteria in mechanism analysis. We may, for example, use them to remove remaining ambiguities about the $S_{RN}1$ and the $S_{RN}2$ mechanisms.[22] One of these appears in the comparison between decomposition of phenylazotriphenylmethane in DMSO in the presence of nitrite ions (to yield 5% nitrobenzene and 75% benzene) and electrolysis of 4-iodonitrobenzene in DMSO in the presence of nitrite ions that produces p-dinitrobenzene with no trace of nitrobenzene.[91] These results have been taken as evidence against the $S_{RN}1$ mechanism [22] under the tacit assumption that the phenyl radical and the 4-nitrophenyl radical should have the same reactivity toward nitrite ions. Based on our earlier discussion, this is obviously not the case. The strong electron-withdrawing para-nitro substituent is expected to accelerate, by several orders of magnitude, the reaction with the nucleophile. The results reported[91] do not therefore provide any evidence against the $S_{RN}1$ mechanism. The finding actually is consistent with what is known about the reactivity of aryl radicals toward nucleophiles : little nitrobenzene is obtained in the first case and much dinitrobenzene is obtained in the second case, because the phenyl radical is less reactive than the p-nitrophenyl radical toward nitrite ions.

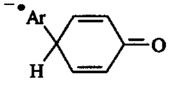
Another example concerns the product distribution in the reaction of 4-methoxyphenyl-phenyl sulfide with acetone enolate ions in liq. NH3 under photostimulation[154] which has been contrasted [22] with reduction of the same substrate by lithium metal in liquid methylamine.[155] The latter reaction leads almost exclusively to thiophenol which implies, in the framework of the anion radical cleavage mechanism depicted in the center of Scheme 21, that the 4-methoxyphenyl-sulfur bond cleaves in preference to the phenyl-sulfur bond. The formation of a small amount of benzene and of cyclohexane shows that the selectivity is most probably of the order of 100 : 1. The selectivity of substitution by acetone enolate ions is in the same direction, but the selectivity ratio benzyl methyl ketone/4-methoxybenzyl methyl ketone is significantly smaller, namely 3 : 1. This difference in selectivity was taken as evidence against the $S_{RN}1$ substitution mechanism .[22] In terms of driving forces, pathway 1 in Scheme 21 is more favorable than pathway 2 because the thiophenoxide ion is

Scheme 21

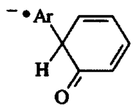


more difficult to oxidize than the 4-methoxythiophenoxide ion (corresponding to $E^0_{X\bullet/X^-}$ in equation 1) : a factor of 100 between the two dissociation constants corresponds to a difference of standard potentials of only 90 mV at -40°C. On the other hand, the phenyl radical is more reactive toward acetone enolate ions than is the 4-methoxyphenyl radical since the main reactivity factor in this case, $E^0_{RX/RX\bullet^-}$, is more negative in the first case than in the second again because of electron-donation by the 4-methoxy group. The cleavage reactions 1 and 2 in Scheme 21 are likely to be reversible uphill processes as is the cleavage of the $PhSPh^{\bullet-}$ anion radical. It follows that the selectivity in substitution is less than in reductive cleavage because the more favorable coupling of phenyl radical with acetone enolate ions as compared to the 4-methoxyphenyl radical partially compensates for its less favorable formation from the 4-methoxyphenyl-phenyl sulfide anion radical. (In terms of driving forces, the factor of 30 between the selectivity of the two reactions amounts to a difference in $E^0_{RX/RX\bullet^-}$ of only 70 mV). We may therefore conclude that the selectivities of the two reactions are consistent with the $S_{RN}1$ mechanism in the substitution reaction.

Anilide ions (see ref. 2, 4, 153 and citation therein) and phenoxide[93,149,156-158] ions are interesting nucleophiles in that they can give coupling involving the ortho and para carbons rather than the nitrogen or oxygen (meta coupling was not detectable[93,149,93,156-158]). It has been argued[22] that these results are incompatible with the $S_{RN}1$ mechanism since such regioselectivity "is not in accord with other phenylation reactions by phenyl radicals". In fact, previous results do indicate a strong regioselectivity in favor of the para and ortho-positions when the attaching radical bears an electron-withdrawing substituent (such as CN) and the aromatic acceptor contains an electron-donating substituent (such as OCH_3).[159] With O^- and NH^- substituents, the regioselectivity should be greatest because the usual cyclohexadienyl units of the coupling radical (here an anion radical) are further stabilized by charge delocalization (especially in the case of an electron-withdrawing substituent) as shown;

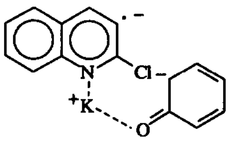


,

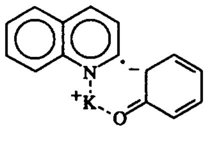


whereas such methylene quinone resonance structures cannot exist for meta-substitution.

It follows that the observed coupling selectivity does not contradict the $S_{RN}1$ mechanism. The issue may be viewed in another way. With substrates (like PhI or even 4-chlorobenzonitrile) whose anion radicals have lifetimes shorter than 10^{-8} s, the $S_{RN}2$ coupling, being limited by diffusion, cannot compete with cleavage as previously emphasized.[26] Since the nucleophile-anion radical reaction is excluded in these cases, the regioselectivity of the nucleophile-aryl radical coupling thus appears established. The earlier observation that "in no case has such regioselectivity been found for free radical arylation reactions"[22] was valid merely because such reaction with anionic oxygen or nitrogen nucleophiles were not attempted before. With 2-chloroquinoline as substrate, only the ortho isomer is obtained.[93] If structure A could explain this observation in the framework of an $S_{RN}2$ mechanism,[22] structure B provides an even better



A



B

explanation of the selectivity in the case of the $S_{RN}1$ mechanism.

Stereochemical clues to the mechanism of aromatic nucleophilic substitution may be found in the related field of substitution at vinylic carbons. Reaction of diphenyl phosphide ions and diphenyl arsenide ions with *cis* and *trans* dichloroethylene and *cis* and *trans* β-bromostyrene yields the corresponding substitution products with retention of configuration.[160-163] These observations have been taken[22] as evidence against an $S_{RN}1$ mechanism because the *cis-trans* interconversion of vinyl radicals is expected to be fast. In fact, stereospecificity has been observed in other reactions involving β-chloro and β-phenyl vinyl radicals.[164-166] It is true that coupling between the Ph_2P^- or the Ph_2As^- ions should be fast in order to compete with the rapid *cis-trans* equilibration of β-chloro and β-phenyl vinyl radicals. Such equilibration however is slower than with unsubstituted or with α-phenyl vinyl radicals.[164-166] Ph_2P^- and Ph_2As^- ions have been shown to be excellent nucleophiles is $S_{RN}1$ aromatic nucleophilic substitution.[4] Therefore it is perfectly plausible that their coupling with β-chloro and β-phenyl vinyl radicals may be at, or close to, the diffusion limit (as has been shown to be the case with many aryl radical-nucleophile couples) and thus might overrun the *cis /trans* equilibration of these radicals.

Interestingly, although alkylation of the anions of N,N-diethyl α-aminoproprionitrile, methyl acetylacetate, and phenylacetonitrile by optically active p-nitrobenzyl chloride or phosphonium cations involves sp3 rather than sp2 carbons, the $S_{RN}2$ mechanism appears unable to compete with the $S_{RN}1$ or the S_N2 mechanisms.[167]

7. REACTIONS OF "STABLE" (SLOWLY CLEAVING) ANION RADICALS WITH NUCLEOPHILES.

Several examples are known of substitutions involving aromatic substrates, whose anion radicals either appear to be stable within the time scale of slow scan cyclic voltammetry[23] or undergo reactions that may not involve expulsion of a leaving group (as in dimerization or reduction of the nitro group[21]). They are usually thermal reactions of nitro, cyano, or benzoyl aromatics in which the leaving group is a halogen or another nitro group (leaving as the nitrite ion) [14-22,168,169] as well as in p-nitrobenzophenone and p-nitrobenzonitrile where the leaving group is the nitrite ion.[23] These reactions are usually stimulated by light and, in one case,[21] by electrochemical reduction and are inhibited by redox traps.[21-23] Stimulation and inhibition are often weak.[23]

It has been argued[22,23] that the "stability" of the substrate anion radical in itself provides evidence against $S_{RN}1$ and in favor of the $S_{RN}2$ mechanism for these reactions. In fact the definition of the "stability" of these anion radicals lacks precision. Since the cleavages of these anion radicals are so slow, there is little doubt that they are energetically up-hill ($\Delta G^0_{R\cdot + X^- \rightarrow RX\cdot^-} \geq 0$). However, as seen earlier, several other aromatic anion radicals that fulfill this condition (see Figure 2) have been shown to be intermediates in $S_{RN}1$ rather than in $S_{RN}2$ substitutions. However, one might argue that they so behave because they are not stable enough toward dissociation. Indeed, as sketched in Figure 4, the more stable $RX^{\cdot-}$, the higher the probability for the $S_{RN}2$ mechanism to prevail over $S_{RN}1$. The problem is thus to distinguish between $S_{RN}2$ and $S_{RN}1$ when substrate anion radical cleavage would be up-hill, and possibly steeply up-hill, as in Scheme 22. The fact that the substrate anion radical appears kinetically stable within the time scale of slow scan cyclic voltammetry therefore does not, by itself, provide unequivocal evidence for an $S_{RN}2$ mechanism as tacitly assumed in a recent

Scheme 22

$S_{RN}1$ $\qquad\qquad\qquad\qquad$ $S_{RN}2$

$$RX^{\bullet -} \rightleftharpoons R^{\bullet} + X^{-} \quad (1) \qquad RX^{\bullet -} + Nu^{-} \rightleftharpoons RNu^{\bullet -} + X^{-} \quad (4)$$

$$R^{\bullet} + Nu^{-} \rightleftharpoons RNu^{\bullet -} \quad (2)$$

$$RX + RNu^{\bullet -} \rightleftharpoons RX^{\bullet -} + RNu \quad (3)$$

report.[23] Also aryl radicals, possibly produced from cleavage of such stable anion radicals, bear strong electron-withdrawing groups (nitro, fluorine, benzoyl, cyano) that make them particularly reactive toward nucleophilic attack (low energy π* orbitals). An unfavorable dissociation of the starting anion radical may thus be compensated by a favorable coupling of the aryl radical with the nucleophile in the framework of a $S_{RN}1$ mechanism.

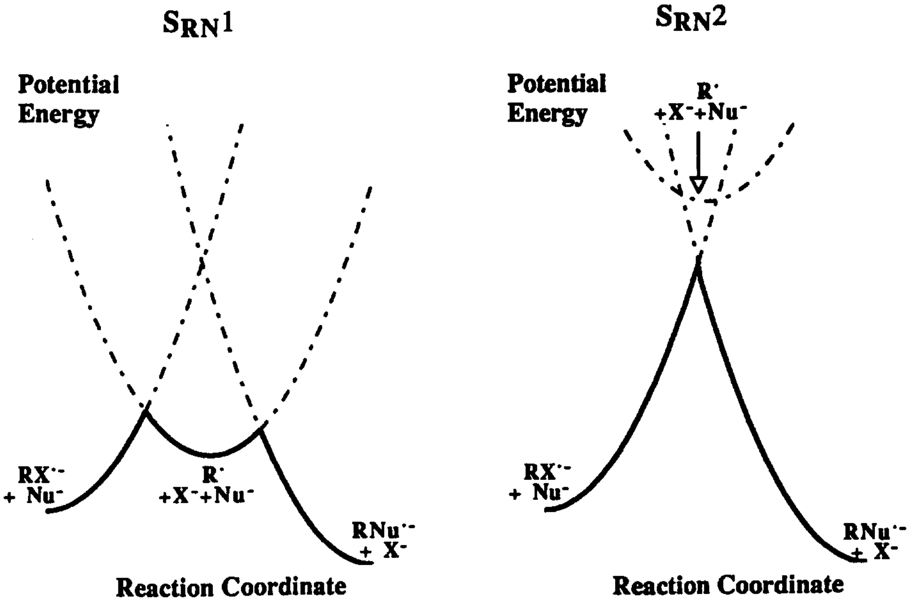
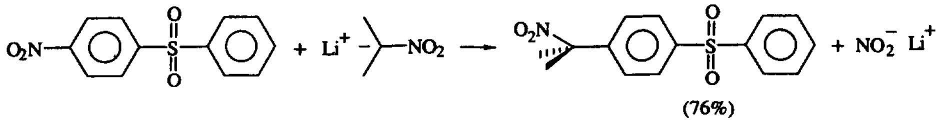
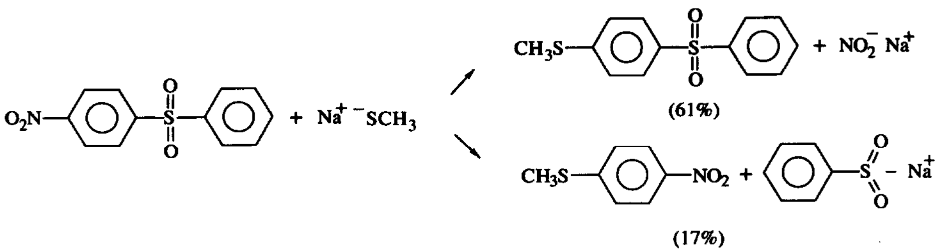


Fig.4. Schematic potential energy diagrams for the $S_{RN}1$ and $S_{RN}2$ mechanisms for thermodynamically unstable substrate anion radicals

Among the qualitative arguments supporting the $S_{RN}2$ mechanism for such slow cleaving anion radicals was the following observation[23], taken from previous work[170] that in the adjoining reactions, the selectivity appears to depend upon the nature of the nucleophile.



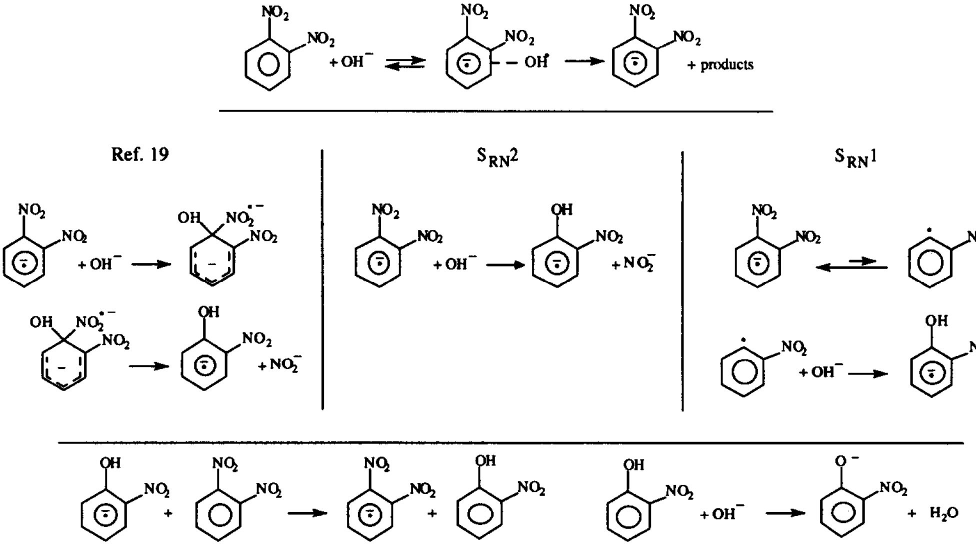


Although these results are compatible with the $S_{RN}2$ mechanism, they may not be inconsistent with $S_{RN}1$ (Scheme 22). Of the two possible up-hill reversible modes of dissociation of the substrate anion radical, loss of nitrite ion prevails over loss of benzenesulfinate ion presumably because bond dissociation is weaker in the first case than in the second. However, coupling of the methylmercaptide ion with the 4-nitrophenyl radical is likely to be more favorable than coupling of the same nucleophile with the 4-phenylsulfinylphenyl radical because $E^0_{RNu/RNu\bullet^-}$ is more positive in the first case than in the second. As in Scheme 21, this would favor more expulsion of benzenesulfinate ion than in the absence of nucleophile. Such an effect is likely to be much less pronounced when the nucleophile is the 2-nitropropane anion, since the difference in $E^0_{RNu/RNu\bullet^-}$ should be small because of the unpaired electron on the added nitro group.

A more converging set of arguments in favor of $S_{RN}2$ has been presented for the substitution (stimulated by light and electrochemical reduction) of the para fluorine in pentafluoronitrobenzene by MeO^-, PhO^- and PhS^- ions in water.[21] Besides the earlier argument based on the "stability" of substrate anion radical, three other pieces of evidence were offered. (i) The reaction half-life varies with the nucleophile ($RO^- > RS^-$). (ii) Methoxide ion gives substitution instead of H-atom transfer, unlike the reaction with unsubstituted phenyl radicals (see section 3 and ref. 79) and phenoxide ion couples at oxygen instead of carbon. (iii) The reaction is relatively insensitive to dioxygen, whereas it is depressed by classical redox traps such as galvinoxyl and 1,3-dinitrobenzene. When dioxygen acts as a radical trap rather than as redox trap (see p. 232 in ref. 4), its reaction with the perfluoronitrophenyl radical may be overrun by the coupling with the nucleophile, which is expected to be fast because of the strong electron-withdrawing substituents on the ring. For the same reason, coupling with the MeO^- ion may well be more favorable than H-atom abstraction. As discussed in section 6 (see also ref. 136), the balance between carbon and oxygen coupling in reactions with PhO^- ions depends essentially upon two factors : the bond dissociation energy, which slightly favors oxygen coupling; and the value of $E^0_{RNu/RNu\bullet^-}$ which favors carbon coupling because of electron-donation by the OPh oxygen. The latter effect is likely to be reduced dramatically by the presence of strong electron-withdrawing substituents possibly upsetting the balance. The situation would then resemble what happens with nitrobenzyl halide substrates, where oxygen coupling is often observed and has been rationalized similarly (see section 6 and ref. 136).If, in Scheme 22, coupling with the nucleophile (2) is slower than reverse reaction (1), the overall reaction rate may depend on the strength of the nucleophile. Consequently, although these observations are certainly compatible with the $S_{RN}2$ mechanism they are not sufficient to definitely rule out $S_{RN}1$. The recent observation that photodecomposition of 4-nitrotetrafluorophenyldiazonium ions in the presence of methanol yields only tetrafluoronitrobenzene (under conditions where pentafluoronitrobenzene gave substitution) is a strong argument against $S_{RN}1$ for the latter compound.[171]

Very few mechanistically revealing studies kinetic studies have been carried out with slow cleaving anion radicals. They concern thermal substitution of one nitro groups of 1,2- and 1,4-dinitrobenzene by OH^- in DMSO,[18-20] as sketched in Scheme 23 for the case of 1,2-dinitrobenzene. The mechanism favored by the

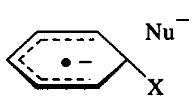
Scheme 23



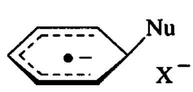
authors of references 19 and 20 is in fact not the $S_{RN}2$ process depicted in reference 22 but that shown on the left side of Scheme 23 which involves addition of OH^- to the anion radical. However, the key-observation that the decay of the substrate anion radical is pseudo-first order toward OH^-[19,20] may be accommodated by the $S_{RN}2$ mechanism as well. It is also consistent with an $S_{RN}1$ mechanism in which the dissociation of the substrate anion radical is reversible (as expected for a very slow cleaving anion radical) and serves as a pre-equilibrium to the rate-determining coupling of the radical with OH^-.

This analysis of the presently available data on the substitution of "stable" anion radicals shows that, even for these compounds, compelling evidence in favor or against the $S_{RN}2$ mechanism does not currently exist. For anion radicals having lifetimes above *ca* 10^{-4} s, solid evidence for or against the $S_{RN}1$ mechanism is lacking as well.

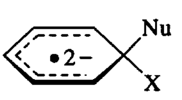
A possible theoretical argument against the $S_{RN}2$ path can be made on the basis of coulombic repulsion between two negatively charged reactants.[25,26] However, in a polar solvent, repulsion might not be to much of a handicap if, in the transition state, the incoming nucleophile and the leaving group bear most of the charge and are not too close to each other. Following a recently proposed structure for an S_NAr-like intermediate[25] in the $S_{RN}2$ reaction, one may envision the transition state as a resonance combination of structures A, B, and C. The contribution of C should be small since[25] its energy is likely to be much higher than that of the conventional



A



B



C

S_NAr intermediate.[172] All three structures involve a considerable bending of the C-X and/or C-Nu bonds out of the plane of the ring. It follows that, in the potential energy diagram of Figure 4, besides the C-X and C-Nu bond lengths and solvent reorganization parameters, the C-X and C-Nu bending angles should be included in the set of nuclear coordinates that constitutes the reaction coordinate. A substantial contribution of out-of-plane bending to the intrinsic barrier is thus expected. The experimental search for carefully demonstrated examples of $S_{RN}2$ reactions would then allow one to answer the question : Is there, in between $S_{RN}1$ and S_NAr mechanisms, any room for $S_{RN}2$ mechanisms for substrates with increasingly stable anion radicals ?

8. CONCLUSIONS AND PERSPECTIVES.

The main conclusions from the preceding discussion are as follows.

Among the many arguments developed in reference 22 in support of the $S_{RN}2$ mechanism as opposed to the $S_{RN}1$ mechanism for electron transfer induced aromatic nucleophilic substitutions, not one survives precise examination of experimental facts.

Moreover, in all investigated cases, the data pertaining to substitutions induced by direct or indirect electrochemical means are consistent with the $S_{RN}1$ mechanism and inconsistent with $S_{RN}2$. These conclusions concern relatively fast cleaving substrates anion radicals, having lifetimes below 10^{-4} s, and extend to photochemical and solvated electron induction experiments that have used the same substrate-nucleophile couples, i.e., practically all reactions previously deemed to follow the $S_{RN}1$ mechanism. In such cases, the substitution process is therefore the manifestation of radical chemistry rather than that of radical anion chemistry.

One of the most puzzling feature of $S_{RN}1$ reactions triggered by solvated electrons, namely the observation of leaving group effects seemingly acting after the group has left, has been explained satisfactorily at the quantitative level. These reactions are not homogeneous but take place during mixing of the reactants, and this view is supported by modeling of the ensuing kinetics. The model extends to other radical reactions triggered by solvated electrons. Such phenomena should probably be taken into account more generally when the initial step of a reaction is fast and when one of the reactants can partake a second time in the reaction sequence. The ensuing depletion of this reactant within the mixing reaction layer can then give rise to effects that might otherwise be assigned erroneously to particular chemical characteristics of the system.

Going to anion radicals that are increasingly stable toward cleavage in the thermodynamic sense should favor $S_{RN}2$ reactions. However, for the time being, there is no example where the occurrence of the $S_{RN}2$ mechanism rather than $S_{RN}1$ or other conceivable mechanisms, has been proved.

This does not mean that $S_{RN}2$ reactions do not exist. We already know that for several anion radicals that are thermodynamically stable toward cleavage (i.e. the reaction standard free energy is positive) the $S_{RN}1$ mechanism prevails over $S_{RN}2$. Why, in such cases, are the bond-breaking and bond-forming steps more efficient when successive than when concerted ? Future discovery of clear-cut examples of $S_{RN}2$ reactions would show that some room exists for a mechanism in between $S_{RN}1$ and S_NAr and would give additional impetus to the modeling of chemical reactivity at the border between single-electron and electron-pair chemistry.

H-atom transfer is important in the chemistry of aromatic anion radicals containing potential leaving groups. In spite of the suggestion that H-atoms are abstracted directly by the anion radical[22] rather than by the aryl radical resulting from its cleavage , analysis of existing data shows that they conform to the latter alternative and not to the former. Here also, there are presently no clear-cut examples of a direct H-atom transfer process that would significantly compete in the chemistry of aromatic anion radicals bearing potential leaving groups.

The cleavage rate constants for aromatic anion radicals containing potential leaving groups span an enormous range (lifetimes from minutes to less than one nanosecond) that not only depend upon the leaving group but also upon the aryl moiety. The recent suggestion[22] that the electrochemistry of the parent molecules could be interpreted in terms of an instability of the dianion derived from the uptake of two electrons rather than an instability of the anion radical itself does not agree with the facts. Likewise, the reverse reaction (coupling of nucleophiles with aryl radicals) depends of the structure of the two reactants. Recent extension of dissociative electron transfer theory to the modeling of the dynamics of the forward and reverse processes has allowed the rationalization of all available kinetic data and of the many semi-quantitative trends concerning $S_{RN}1$ substitution. Although approximate, this model provides a basis for relating reactivity and molecular structure in this field. Further work could include systematic experimental and theoretical analysis of the role of external factors such as solvation and ion-pairing.

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REFERENCES AND NOTES.

1. Kornblum, N. *Angew. Chem. Internat. Ed. Engl.* **1975**, *14*, 734.
2. Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.
3. Savéant, J-M. *Acc. Chem. Res.* **1980**, *13*, 323.
4. Rossi, R. A. ; Rossi, R. H. Aromatic Substitution by the SRN1 Mechanism. In *ACS Monograph 178*; The American Chemical Society : Washington D.C., 1983.
5. Russell, G. A. *Adv. Phys. Org. Chem.* **1987**, *24*, 271.
6. Bowman, W. R. *Chem. Soc. Res.* **1988**, *17*, 283.
7. Savéant, J-M. *Adv. Phys. Org. Chem.* **1990**, *26*, 1.
8. Savéant, J-M. Dissociative Electron Transfer . In *Advances in Electron Transfer Chemistry*; Mariano, P.S., Ed. ; JAI Press : New York, Vol. IV, in press.
9. Kim, J. K. ; Bunnett, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 7463.
10. Galli, C. ; Bunnett, J. F. *J. Am. Chem. Soc.* **1981**, *103*, 7140.
11. Amatore, C. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *J. Am. Chem. Soc* . **1982**, *104*, 817.
12. Amatore, C. ; Chaussard, J. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *J. Am. Chem. Soc.* **1979**, *101*, 6012.
13. Amatore, C. ; Savéant, J-M. ; Thiébault, A. *J. Electroanal. Chem.* **1979**, *103*, 303.
14. Chambers, J. Q. ; Adams, R. N. *J. Electroanal. Chem.***1965**, *9*, 400.
15. Shein, S. M. ; Bryukhovetskaya, L. V. ; Pischugin, F. V. ; Stavichenko, V. N. ; Voevodskii, V. V. *J. Structural Chem.* **1970**, *11*, 228.
16. Shein, S. M. ; Bryukhovetskaya, L. V. ; Ivanova, T. M. *Izv. Akad. Nauk. SSR,.Ser. Khim* . **1973**,

1594.

17. Blyumenfel'd, L. A. ; Bryukhovetskaya, L. V. ; Fomin, G. V. ; Shein, S. M., *Russ. J. Phys. Chem.* **1970**, *44*, 518.

18. Abe, T. *Chem. Lett* . **1973,** 1339.

19. Abe, T. ; Ikegamo, Y. *Bull. Chem. Soc. Japan.* **1976**, *49*, 3227.

20. Abe, T. ; Ikegamo, Y. *Bull. Chem. Soc. Japan.* **1978**, *51*, 196.

21. Marquet, J. ; Jiang, Z. ; Gallardo, I. ; Battle, A. ; Cayon, E. *Tetrahedron. Lett* . **1993**, *34*, 2801.

22. Denney, D. B. ; Denney, D. Z. *Tetrahedron* . **1991**, *47*, 6577.

23. Denney, D. B. ; Denney, D. Z. ; Perez, A. J. *Tetrahedron* **1993**, *49*, 4463.

24. Russell, G. A. ; Mudryk, B. ; Ros, F. ; Jawdosuik, M. *Tetrahedron* **1982**, *38*, 1059.

25. Bunnett, J. F. *Tetrahedron* **1993**, *49*, 4477.

26. Rossi, R. A. ; Palacios, S. M. *Tetrahedron* **1993**, *49*, 4485.

27. Andrieux, C. P. ; Savéant, J-M. "Electrochemical Reactions". In *Investigation of Rates and Mechanisms of Reactions, Techniques of Chemistry*; Bernasconi, C. F. Ed.; Wiley: New York, 1986; Vol. VI/4E, Part 2, pp 305-390.

28. Andrieux, C. P.; Hapiot, P. ; Savéant, J-M. *Chem. Rev.* **1990**, *90*, 723.

29. Savéant, J-M. ; Thiébault, A. *J. Electroanal. Chem.* **1978**, *89*, 335.

30. Teherani, T. ; Bard, A. J. *Acta Chem. Scand. B* **1983**, *37*, 413.

31. Behar, D. ; Neta, P. *J. Phys. Chem.* **1981**, *85*, 690.

32. Behar, D. ; Neta, P. *J. Am. Chem. Soc.* **1981**, *103*, 103.

33. Behar, D. ; Neta, P. *J. Am. Chem. Soc.* **1981**, *103*, 2280.

34. Kigawa, H. ; Takamuku, S. ; Toki, S. ; Kimura, N. ; Tsumori, K. ; Sakurai, H. *J. Am. Chem. Soc.* **1981**, *103*, 5171.

35. Kimura, N. ; Takamuku, S. *Bull. Chem. Soc. Japan.* **1986**, *59*, 3653

36. Kimura, N. ; Takamuku, S. *Radiat. Phys. Chem.* **1987**, *29*, 179.

37. Svensmark Jensen, B. ; Parker, V.D. *J. Am. Chem. Soc.* **1975**, *97*, 5211.

38. Reduction of anion radicals is slower than that of neutral aromatic molecules, $k_S = 1$ cm/s is among the largest rate constants for these neutral molecules.[39]

39. Kojima, H. ; Bard, A. J. *J. Am. Chem. Soc.* **1975**, *97*, 6317.

40. Jaun, B. , Schwartz, J. ; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 5741.

41. Delamar, M. ; Hitmi, R. ; Pinson, J. ; Savéant, J-M. *J. Am. Chem. Soc.* **1992**, *114*, 5883.

42. Amatore, C. ; Gareil, M. ; Savéant, J-M. *J. Electroanal. Chem.* **1984**, *176*, 377.

43. Andrieux, C. P. ; Savéant, J-M. ; Zann, D. *Nouv. J. Chim.* **1984**, *8*, 107.

44. Andrieux, C. P. ; Blocman, C. ; Dumas-Bouchiat, J-M. ; M'Halla, F. ; Savéant, J-M. *J. Am. Chem. Soc.* **1980**, *102*, 3806.

45. Amatore, C. ; Combellas, C. ; Pinson, J. ; Oturan, M.A. ; Robveille, S. ; Savéant, J-M. ; Thiébault, A. *J. Am. Chem. Soc.* **1985**, *107*, 4846.

46. The reliability of the redox catalytic method for determining rate constants of reactions following an outersphere single electron transfer has been recently demonstrated in a different field, namely oxidation of synthetic analogues of NADH, by comparison with laser flash photolysis and fast cyclic voltammetry.[47,48]

47. Anne, A. ; Hapiot, P. ; Moiroux, J. ; Neta, P. ; Savéant, J-M. *J. Phys. Chem.* **1991** *95*, 2370.

48. Anne, A. ; Hapiot, P. ; Moiroux, J. ; Neta, P. ; Savéant, J-M. *J. Am.Chem. Soc.* **1992**, *114*, 4694.

49. Andrieux, C. P. ; Blocman, C. ; Dumas-Bouchiat, J-M. ; Savéant, J-M. *J. Am. Chem. Soc.* **1979**, *101*, 3431.

50. Simonet, J. ; Chaquiq el Badre, M. ; Mabon, G. *J. Electroanal. Chem.* **1990**, *281*, 289.

51. Simonet, J. ; Chaquiq el Badre, M. ; Mousset, G. *J. Electroanal. Chem.* **1990**, *286*, 163.

52. Neta, P. ; Behar, D. *J. Am. Chem. Soc.***1980**, *102*, 4798.

53. Bays, J. P. ; Blumer, S. T. ; Baral-Tosh, S. ; Behar, D. ; Neta, P. *J. Am. Chem. Soc.* **1983**, *105*, 320.

54. Norris, R. K. ; Barker, S. D. ; Neta, P. *J. Am. Chem. Soc.* **1984**, *106*, 3140.

55. Meot-Ner, M. ; Neta, P. ; Norris, R. K. ; Wilson, K. *J. Phys. Chem.* **1986**, *90*, 168.

56. Andrieux, C. P. , Le Gorande, A. ; Savéant, J-M. *J. Am. Chem. Soc.* **1992**, *114*, 6892.

57. Andrieux, C. P. ; Robert, M. ; Savéant, J-M. , unpublished data.

58. Klever, H. ; Schulte-Frohlinde, D. *Ber. Bunsenges.Phys. Chem.* **1976**, *80*, 1259.

59. San Roman, E. ; Krebs, P. ; Shindewolf, N. *Chem. Phys. Letts.* **1977**, *49*, 98.

60. Rieger, P. H. ; Bernal, I. ; Reinmuth, W. H. ; Fraenkel, G. K. *J. Am. Chem. Soc.* **1963**, *85*, 683.

61. Houser, K. J. ; Bartak, D. E. ; Hawley, M. D. *J. Am. Chem. Soc.* **1973**, *95*, 6033.

62. Andrieux, C. P. ; Blocman, C. ; Savéant, J-M. *J. Electroanal. Chem.* **1979**, *105*, 413.

63. Amatore, C. ; Garreau, D. ; Hammi, M. ; Savéant, J-M. *J. Electroanal. Chem.* **1985**, *184*, 1.

64. Savéant, J-M. *Acta Chem. Scand. B* **1988**, *42*, 721.

65. Bridger, R. F. ; Russell, G. A. *J. Am. Chem. Soc.* **1963**, *85*, 3754.

66. Pryor, A. ; Echols, J. T. ; Smith, K. J. *J. Am. Chem. Soc.* **1966**, *88*, 1189.

67. Russell, G. A.. In *Free Radicals ;* Kochi, J., Ed., Wiley, New York : 1973, Vol. I ; , p. 275.

68. Arai, S. ; Dorfman, L. M. *J. Chem. Phys.* **1964**, *41*, 2190.

69. Anbar, M. ; Hart, E. J. *J. Am. Chem. Soc.* **1964**, *86*, 5633.

70. Handbook of Chemistry and Physics; 72nd Edition ; CRC; Cleveland, 1991-1992, p. 9/115.

71. M'Halla, F. ; Pinson, J. ; Savéant, J-M. *J. Electroanal. Chem.* **1978**, *89*, 347.

72. M'Halla, F. ; Pinson, J. ; Savéant, J-M. *J. Am. Chem. Soc.* **1980**, *102*, 4120.

73. Helgee, B. ; Parker, V. D. *Acta. Chem. Scand. B* **1980**, *34*, 7.

74. Kryger, R. G. ; Lorand, J. P. ; Stevens, N. R. ; Herron, N. *J. Am. Chem. Soc.* **1977**, *99*, 7589.

75. Rossi, R.A. ; Bunnett, J. F. *J. Am. Chem. Soc.* **1974**, *96*, 112.

76. Amatore, C. ; Badoz-Lambling, J. ; Bonnel-Huyghes, C. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *J. Am. Chem. Soc.*.**1982**, *104*, 1979.

77. A similar reaction was shown to occur with alcohols instead of with alkoxide ions.[78] The mechanism is then complicated by competition between deprotonation and reduction of the •>-OH radical formed by H-atom transfer from the alcohol to the aryl radical. The knowledge acquired on the reaction of alcohols and alkoxide ions with aryl radicals produced by electron transfer to aryl molecules containing leaving groups has been recently summarized.[79]

78. Andrieux, C. P. ; Badoz-Lambling, J. ; Combellas, C. ; Lacombe, D. ; Savéant, J-M. ; Thiebault, A. ; Zann, D. *J. Am. Chem. Soc.* **1987**, *109*, 1518.

79. Bunnett, J. F. *Acc. Chem Res.* **1992**, *25*, 413, 2.

80. Bunnett, J. F. ; Sundberg, J. E. *J. Org. Chem.* **1976**, *41*, 1702.

81. Wolfe, J. F. ; Moon, M. P. ; Sleevi, M. C. ; Bunnett, J.F. ; Bard, R. R. *J. Org. Chem.* **1978**, *41*, 1702.

82. Hay, J. V. ; Wolfe, J. F. *J. Am. Chem. Soc.* **1975**, *97*, 3702.

83. Komin, A.P. ; Wolfe, J. F. *J. Org. Chem.* **1977**, *42*, 2481.

84. Semmelhack, M. F. ; Bagar, M. T. *J. Org. Chem.* **1977**, *42*, 1481.

85. Hoz, S. ; Bunnett, J. F. *J. Am. Chem. Soc.* **1977**, *99*, 4690.

86. Fox, M. A. ; Yonnathan, J. ; Fryxell. *J. Org. Chem.* **1983**, *48*, 3109.

87. Amatore, C. ; Oturan M. A.; Pinson, J. ; Savéant, J-M. ; Thiebault, A. *J. Am. Chem. Soc.* **1984**, *106*, 6318.

88. Amatore, C. ; Oturan M. A. ; Pinson, J. ; Savéant, J-M. ; Thiebault, A. *J. Am. Chem. Soc.* **1985**, *107*, 3451.

89. Amatore, C. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *J. Electroanal. Chem.* **1981**, *123*, 231.

90. Bartak, D. E. ; Houser, K. J. ; Rudy, B. C. ; Hawley, M. D. *J. Am. Chem. Soc.* **1972**, *94*, 7526.

91. Bartak, D. E. ; Danen, W. C. ; Hawley, M. D. *J. Org. Chem.*.**1970**, *35*, 1206.

92. Pinson, J. ; Savéant, J-M. *J. Am. Chem. Soc.* **1978**, *100*, 1506.

93. Alam, N. ; Amatore, C. ; Combellas, C. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *J. Org. Chem.*, **1988**, *53*, 1496.

94. Amatore, C. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *J. Electroanal. Chem.* **1980**, *107*, 59.

95. Oturan, M. A. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *Tetrahedron. Lettt.* **1989**, *30*, 1373.

96. In the reaction of the α-naphthyl radical with PhS- in DMSO, a small discrepancy exists between the results from electrochemical reduction of α-bromonaphthalene (100±5% substitution) and rate constants derived from the generation of the radical from a diazonium salt, which predict 80% substitution.[73] The origin of the discrepancy is not clear, since reference 73 is a short note with no experimental details and no further full publication.

97. Garst, J. F. *Acc. Chem Res.* **1971**, *4*, 400.

98. However, in another study, a few percent of dimer has been reported in the reduction of iodo-, bromo-, and chlorobenzene.[99]

99. Sargent, G. D. *Tetrahedron Lett.* **1971**, 3279.

100. Andrieux, C. P. ; Gallardo, I. ; Savéant, J-M. ; Su K. B. *J. Am. Chem. Soc.* **1986**, *108*, 638.

101. Andrieux, C. P. ; Savéant; J-M. ; Su, K. B. *J. Phys. Chem.* **1986**, *90*, 3815.

102. Fuhlendorff, R. ; Occhialini, D. ; Pedersen, S. U. ; Lund, H. *Acta. Chem. Scand. B* **1989**, *43*, 803.

103. Occhialini, D. ; Pedersen, S. U. ; Lund, H. *Acta. Chem. Scand. B* **1990**, *44*, 715.

104. Andrieux, C. P. ; Gallardo, I. ; Savéant, J-M. *J. Am. Chem. Soc.* **1989**, *111*, 1620.

105. Wayner, D. D. M. ; Griller, D. *J. Am. Chem. Soc.* **1985**, *107*, 7764.

106. Sim, B. A. ; Griller, D. ; Wayner, D. D. M. *J. Am. Chem. Soc.* **1989**, *111*, 754.

107. Griller, D. ; Martino Simoes, J.A. ; Mulder, P. ; Sim, B. A. ; Wayner, D. D. M. *J. Am. Chem. Soc.* ,**1989**, *111*, 7832.

108. Sim, B. A. ; Milne, P. H. ; Griller, D. ; Wayner, D. D. M. *J. Am. Chem. Soc.* **1990**, *112*, 6635.

109. Ettayeb, R.; Savéant, J-M ; Thiébault, A. *J. Am. Chem. Soc.* **1992**, *114*, 10991.

110. Note that dimers have also been found in $S_{RN}1$ substitutions of 2-chloroquinoline and 2-chloropyridine induced by sodium amalgam.[111,112]

111. Austin, E. ; Alonso, R. ; Rossi, R. A. *J. Org. Chem.* **1991**, *56*, 4486.

112. Austin, E. ; Ferrayoli, C. G. ; Alonso, R. ; Rossi, R. A. *Tetrahedron* **1993**, *49*, 4495.

113. Yildiz, A. ; Baumgärtel, H. *Ber. Bunsenges. Phys. Chem.* **1977**, *81*, 1177.

114. Hammerich, O. ; Parker, V. D. *Acta. Chem. Scand. B* **1981**, *35*, 341.

115. Amatore, C.; Pinson, J. ; Savéant, J-M. *J. Electroanal. Chem.* **1982**, *137*, 143.

116. Savéant, J-M. *Acta. Chem. Scand., Ser. B* . **1983**, *37*, 365.

117. Hammerich, O. ; Parker, V. D. *Acta. Chem. Scand. B* **1983**, *37*, 379.

118. Eliason, R. ; Hammerich, O. ; Parker, V. D. *Acta. Chem. Scand. B* **1988**, *42*, 7.

119. Rossi, R. A. ; Bunnett, J. F. *J. Org. Chem.*.**1973**, *38*, 1407.

120. Bard, R. R. ; Bunnett, J. F. ; Creary, X. ; Tremelling, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 2852.

121. Tremelling, M. J. ; Bunnett, J. F. *J. Am. Chem. Soc.* **1980**, *102*, 7375.

122. Bethell, D. ; Compton, R. G. ; Wellington, R. G. *J. Chem. Soc. Perkin Trans. 2*, **1992**, 147.

123. Rossi, R. A. ; Alonso, R. A. ; Palacios, S. M. *J. Org. Chem.* **1981**, *46*, 2498.

124. Alonso, R. A. ; Rossi, R. A. *J. Org. Chem.*.**1982**, *47*, 77.

125. Pierini, A. B.; Rossi, R. A. *J. Org. Chem.* **1979**, *44*, 4667.

126. Rossi, R. A. ; Bunnett, J. F. *J. Am. Chem. Soc.* **1972**, *94*, 683.

127. Andrieux, C. P. ; Savéant, J-M. *J. Am. Chem. Soc.* **1993**, *115*, 8044.

128. Andrieux, C. P. ; Savéant, J-M. *J. Phys. Chem.* **1993**, *97*, 10879.

129. Teherani, T. ; Itaya, K. ; Bard, A. J., *Nouv. J. Chim.* **1978**, *2*, 481.

130. Andrieux, C. P. ; Savéant, J-M. Catalysis at Redox Polymer Electrodes. In *Molecular Design of Electrode Surfaces*; Techniques of Chemistry; Murray, R. W., Ed.; Wiley: New York, 1992; Vol. XXII, Chap.V, pp 207-270.

131. Lepoutre, G. ; Debacker, M. ; Demortier, A. *J. Chim. Phys.* **1974**, *71*, 113.

132. Meijs, G. F. ; Bunnett, J. F. ; Beckwith, A. L. J. *J. Am. Chem. Soc.* **1986**, *108*, 4899.

133. Because leaving group effects were observed in these reactions, the mechanisms in Schemes 19 and 20, where product selection takes place after the nucleofuge has left, has been disputed and instead a mechanism was proposed based on reactions involving the anion radical .[22] In the case of 19, this latter mechanism is strictly excluded by the fact that the anion radical is not an intermediate in the reduction of the halide since electron transfer and bond breaking are then concerted.

134. Amatore, C. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *J. Am. Chem. Soc.* **1981**, *103*, 6930.

135. Amatore, C. ; Combellas C. ; Robveille, S. ; Savéant, J-M. ; Thiébault, A. *J. Am. Chem. Soc.***1986**, *108*, 4744.

136. Savéant, J-M. *J. Phys. Chem.* **1994**, *98*, 3716.

137. Savéant, J-M. *Acc. Chem. Res.* **1993**, *26*, 455.

138. Rossi, R. A. *J. Chem. Educ.* **1982**, *59*, 310.

139. Villar, H. O. ; Castro, E. A. ; Rossi, R. A. *Can. J. Chem.* **1982**, *60*, 2525.

140. Villar, H. O. ; Castro, E. A. ; Rossi, R. A. *Z. Chem. Natureforsch.* **1984**, *A39*, 1984.

141. Savéant, J-M. *J. Am. Chem. Soc.* **1987**, *109*, 6788.

142. Savéant, J-M. *J. Am. Chem. Soc.* **1992**, *114*, 10595.

143. Marcus, R. A. *J. Chem. Phys.* **1956**, *24*, 4966.

144. Hush, N. S. *J. Chem. Phys.* **1958**, *28*, 962.

145. Marcus, R. A. ,Theory and Applications of Electron Transfers at Electrodes and in Solution. In *Special Topics in Electrochemistry*, Rock, P. A., Ed.; Elsevier: New York, 1977; pp. 161-179.

146. Marcus, R. A. *Faraday Discuss. Chem. Soc.* **1982**, *74*, 7.

147. Marcus, R. A. ; Sutin, N. *Biophys. Biochim. Acta* **1985**, *811*, 265.

148. Amatore, C. ; Combellas, C. ; Robveille, S. ; Savéant, J-M. ; Thiébault, A. *J. Electroanal. Chem.* **1985**, *184*, 25.

149. Baumgartner, M. T. ; Pierini, A. B. ; Rossi, R. A. *Tetrahedron Lett.* **1992**, *33*, 2323.

150. Baumgartner, M. T. ; Pierini, A. B. ; Rossi, R. A. *J. Org. Chem.* **1993**, *58*, 2593.

151. Kornblum, N. ; Fifolt, M. *Tetrahedron* **1989**, *45*, 1311.

152. Handbook of Chemistry and Physics; 72nd Edition ; CRC: Cleveland, 1991-1992, p. 9/121.

153. Pierini, A. B.; Baumgartner, M. T. ; Rossi, R. A. *J. Org. Chem..* **1991**, *56*, 580.

154. Bunnett, J. F. ; Creary, X. *J. Org. Chem.* **1975**, *40*, 3740.

155. Truce, W. E. ; Tate, D. P. ; Burdga, D. N. *J. Am. Chem. Soc.* **1962**, *82*, 2872.

156. Amatore, C. ; Combellas, C. ; Pinson, J. ; Savéant, J-M. ; Thiébault, A. *J. Chem. Soc. Chem. Commun.* **1988**, *7*.

157. Alam, N. ; Amatore, C. ; Combellas, C. ; Thiébault, A. ; Verpeaux, J. N. *Tetrahedron Lett.* **1987**, 28, 6171.

158. Beugelmans, R. ; Bois-Choussy, M. *Tetrahedron Lett.* **1988**, *29*, 1289.

159. Perkins, M. J. *Free Radicals*; Kochi, J. K. ; Ed., Wiley : New York, 1973, Vol. II, pp. 231-271.

160. Aguiar, A. M. ; Archibald, T. G. *J. Org. Chem..* **1967**, *32*, 2627.

161. Aguiar, A. M.; Mague, J. T.; Aguiar, H. G.; Archibald, T. G. ; Prejean, G. *J. Org. Chem.* **1968**, *33*, 1681.

162 Aguiar, A. M. ; Daigle, D. T. *J. Am. Chem. Soc.* **1964**, *86*, 2299.

163. Aguiar, A. M. ; Daigle, D. T. *J. Org. Chem.* **1965**, *30*, 2826, 3527.

164. Bentrude, W. G. *Annual Rev. Phys. Chem.* **1967**, *18*, 283.

165. Simamura, O. *Topics Stereochem.* **1969**, *4*, 1.

166. Singer, L. A. *Selective Organic Transformations.* Thyagarajan; Ed.; Wiley : New York, 1972, pp. 253-256.

167. Cabaret, D. ; Maigrot, N. ; Welwart, Z. *Tetrahedron* **1985**, *41*, 5357.

168. Sammes, P. G. ; Thitford, D. ; Voyle, M. *J. Chem. Soc. Perkin Trans. 1* **1988**, 3229.

169. Zhao, W. ; Huang, Z. *J. Chem. Soc. Perkin Trans. 2* **1988**, 1206.

170. Kornblum, N. ; Cheng, L. ; Kerber, K. C. ; Kestner, M. M. ; Newton, B. N. ; Pennick, H. N. ; Smith, R. G. ; Wade, P. A. *J. Org. Chem.* **1976**, *41*, 1560.

171. J. Marquet, personnal communication, March 1994.

172. Buncel, D. ; Crampton, M. R. ; Strauss, M. J. ; Terrier, F. , Electron Deficient Aromatic and Heteroaromatic - Base Interactions, the Chemistry of Anionic Sigma Complexes. In *Studies in Organic Chemistry 14*, Elsevier: Amsterdam, 1984.

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