"Thermal" $S_{RN}1$ Reactions: How Do They Work? Novel Evidence that the Driving Force Controls the Transition between Stepwise and Concerted Mechanisms in Dissociative Electron Transfers

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Abstract: In $S_{RN}1$ reactions, unlike in conventional nucleophilic substitutions, the nucleophile does not react directly with the electrophile but with a radical resulting from its reductive cleavage. Many $S_{RN}1$ substitutions require an external stimulation involving the injection of a catalytic amount of electrons. In "thermal" $S_{RN}1$ reactions, there is no other source of initiating electrons than the nucleophile which is usually a poor electron donor. Such reactions are unlikely to be initiated by a simple outersphere electron transfer from the nucleophile followed by the cleavage of the substrate anion radical. Rather, initiation follows a mechanism in which electron transfer and bond cleavage are concerted. These conclusions are based on a full analysis of a model system involving 4-nitrocumyl chloride as the substrate and the 2-nitropropanate ion as the nucleophile where all the pertinent thermodynamic and kinetic parameters were determined by direct or indirect electrochemical methods. They extend to other examples of thermal $S_{RN}1$ reactions reported earlier. These results provide new and unambiguous evidence that a decrease in driving force is able to change the mechanism of homogeneous reductive cleavage reactions from stepwise to concerted. The observation of this mechanism change was made possible by the kinetic amplification offered by the chain character of the $S_{RN}1$ process, which allows the investigation of very slow electron transfers resulting from very low driving forces, that would have otherwise escaped characterization.

$S_{RN}1$ substitutions (Scheme 1) form a well documented class of reactions.[1] Unlike in conventional nucleophilic substitutions, the nucleophile, Nu^-, does not react with the substrate, RX, but with the radical $R^\bullet$ resulting from the cleavage of the R—X bond (X is very often a halogen atom, but other leaving groups have been used). In a number of cases, the latter reaction involves the anion radical, $RX^{\bullet-}$, as intermediate as with aromatic substrates (Scheme 1a). With aliphatic substrates able to undergo $S_{RN}1$ substitutions rather than S_N2 or S_N1 substitutions,[1h] the mechanism depicted in Scheme 1b is followed instead since the anion radical does not exist and the cleavage therefore follows a concerted mechanism.[1g] The key step in the $S_{RN}1$ reaction is the coupling of the radical $R^\bullet$ with the nucleophile leading to the anion radical of the substitution

Scheme 1
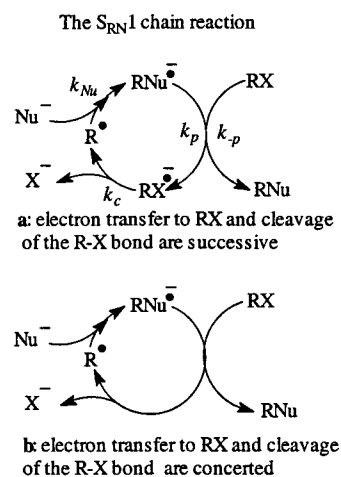
product, $RNu^{\bullet-}$. The chain process (Scheme 1) is completed by a reaction in which one electron is transferred from the product anion radical to the substrate, leading to the substitution product and closing the propagation loop.[2] This electron-transfer/bond-breaking reaction may be stepwise as in Scheme 1a or concerted (aliphatic substrates) as in Scheme 1b.

In most cases, the reaction requires an external stimulation in which a catalytic amount of electrons is injected into the

(1) (a) Kornblum, N. *Angew. Chem., Int. Ed. Engl* **1975**, *14*, 734. (b) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413. (c) Savéant, J.-M. *Acc. Chem. Res.* **1980**, *13*, 323. (d) Rossi, R. A.; Rossi, R. H. Aromatic Substitution by the $S_{RN}1$ Mechanism. In *ACS Monograph 1978*; The American Chemical Society: Washington, DC, 1983. (e) Russel, G. A. *Adv. Phys. Org. Chem.* **1987**, *24*, 271. (f) Bowman, W. R. *Chem. Soc. Rev.* **1988**, *17*, 283. (g) Savéant, J.-M. Single Electron Transfer and Nucleophilic Substitution. In *Advances in Physical Organic Chemistry*; Bethel, D., Ed.; Academic Press: New York, 1990; Vol. 26, pp 1–130. (h) Rossi, R. A.; Pierini, A. B.; Palacios, S. M. Nucleophilic Substitution by the $S_{RN}1$ Mechanism on Alkyl Halides. In *Advances in Free Radical Chemistry*; JAI Press: New York, 1990; Vol. 1, pp 193–252. (i) Savéant, J.-M. *Acc. Chem. Res.* **1993**, *26*, 455. (j) Austin, E.; Ferrayoli, C. G.; Alonso, R. A.; Rossi, R. A. *Tetrahedron* **1993**, *49*, 4495. (k) Savéant, J.-M. *J. Phys. Chem.* **1994**, *98*, 3716. (l) Savéant, J.-M. *Tetrahedron* **1994**, *50*, 10117. (m) Rossi, R. A.; Pierini, A. B.; Peñéñory, A. B. Recent Advances in the $S_{RN}1$ Reaction of Organic Halides. In *The Chemistry of Halides, Pseudo-Halides and Azides*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1995; Vol. 24, pp 1395–1485.
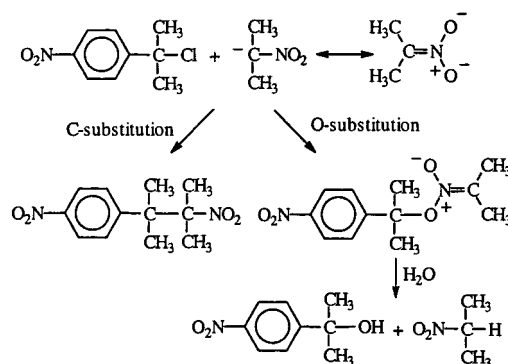
(2) When an electrode is used to inject the initiating electrons into the solution, the reoxidation of $RNu^{\bullet-}$ may also take place at the electrode.[1c]

solution. Solvated electrons in liquid ammonia,[1b] sodium amalgam in the same solvent,[1j] light,[1b,d,3] electrodes,[1c] electrogenerated electron donors,[1g,k] ferrous salts,[4] have been used for this purpose.

However, there are several examples where the reaction works without external stimulation. They mostly concern Kornblum reactions[1a] in which the substrates are benzyl or cumyl derivatives activated by one or more electron-withdrawing substituents on the phenyl ring (generally nitro groups). A few examples of similar reactions have been reported with aromatic iodides.[5] What is the mechanism of these reactions, the so-called "thermal" $S_{RN}1$ reactions? The only species that might provide stimulating electrons to the system is the nucleophile itself.[1a] However, in most cases, the nucleophile is such a poor electron donor that electron transfer from the nucleophile to the substrate is expected to be extremely slow, apparently too slow to serve as a viable initiation step. Previous attempts to discuss this question have come to the same conclusion even if the values used for the pertinent standard potentials were rather uncertain and if the kinetic factors controlling initiation, propagation, and termination were not precisely taken into account.[5a,6] So far, the reason thermal $S_{RN}1$ reactions work has thus remained mysterious.

The work reported below aimed at solving this enigma. Our strategy was to select one model pair of reactants, identify the reaction products, measure the reaction kinetics, determine all of the thermodynamic and kinetic factors of initiation, propagation, and termination that allow one to predict what should be the reaction kinetics if the nucleophile were the electron-donor initiator, and compare the result with experiment. The example we selected for this purpose was the reaction of 4-nitrocumyl chloride with the 2-nitropropanate ion. It will be shown that the results rule out the possibility that initiation could be a simple outersphere electron transfer from the nucleophile to the substrate, leading to an anion radical that would cleave in a successive step. The alternative is a dissociative electron transfer where the electron transfer from the nucleophile and the breaking of the carbon−halogen bond in the substrate are concerted. After estimation of the pertinent thermodynamic and kinetic parameters, it will be shown that the predicted kinetics satisfactorily reproduce the experimental results. Albeit with fewer details and less precision, we will see that the dissociative electron-transfer mechanism also explains the results gathered in previous studies of thermal $S_{RN}1$ reactions of 4-nitrocumyl chloride with other nucleophiles. Although, for phenyl iodide, the lack of pertinent thermodynamic and kinetic data precludes a detailed analysis of the reaction, it will be shown that the initiation step cannot be of the outersphere type in this case, too.

As shown below, the electrochemical reduction of 4-nitrocumyl chloride, a slightly uphill process, follows a stepwise mechanism, as does 4-nitrobenzyl chloride.[7] The same is true

(3) (a) Several possibilities have been envisaged for the mechanism of light initiation, in particular, the excitation of a nucleophile-charge-transfer complex.[3b,c] In the reaction of thiolates with 1-iodoadamantane, the initiating electron is photoejected from the thiolate ion.[3d] (b) Hoz, S.; Bunnett, J. F. *J. Am. Chem. Soc.* **1977**, *99*, 4690. (c) Fox, M. A.; Yonnathan, J.; Fryxell *J. Org. Chem.* **1983**, *48*, 3109. (d) Ahbala, M.; Hapiot, P.; Houmam, A.; Jouini, M.; Pinson, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1995**, *117*, 11488.
(4) Galli, C.; Gentili. *J. Chem. Soc., Perkin Trans. 2* **1993**, 1135.
(5) (a) Kim, J. K.; Bunnett, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 7463. (b) Scamehorn, R. G.; Bunnett, J. F. *J. Org. Chem.* **1977**, *42*, 1449. (c) Swarz, J. E.; Bunnett, J. F. *J. Org. Chem.* **1979**, *44*, 340. (d) Scamehorn, R. G.; Hardacre, J. M.; Lukanich, J. M.; Sharpe, L. R. *J. Org. Chem.* **1984**, *49*, 4881.
(6) (a) Eberson, L. *J. Mol. Catal.* **1983**, *20*, 27. (b) Eberson, L. *Acta Chem. Scand. B* **1984**, *38*, 439.
(7) Andrieux, C. P.; Le Gorande, A.; Savéant, J.-M. *J. Am. Chem. Soc.* **1992**, *114*, 6892.

Scheme 2

for the reaction with homogeneous electron donors, giving rise to a slightly uphill reaction. The observation that a concerted reaction is taking place with poor electron donors such as the 2-nitropropanate ion thus implies that a change in mechanism has occurred as a result of the attending change in driving force. This novel piece of evidence that the driving force controls the transition between stepwise and concerted mechanisms in dissociative electron transfers will be discussed in conjunction with previous observations pointing to the occurrence of the same phenomenon.

Results and Discussion

Reaction of 4-Nitrocumyl Chloride with 2-Nitropropanate Ion. Reaction Kinetics. The reaction was carried out under pseudo-first-order conditions (excess of 2-nitropropanate ions) in acetonitrile at 25 °C, under an argon atmosphere in a light-protecting vessel. The 2-nitropropanate ion was introduced as the tetramethylammonium salt. Two products were formed (Scheme 2). One is the expected C-substitution product. The other is an unstable compound which decomposes into the 4-nitrocumyl alcohol during workup and may thus be ascribed to O-substitution.[8] With 4-nitrobenzyl derivatives, the C-substitution product is considered to result from the $S_{RN}1$ reaction and the O-substitution product from a $S_{N}2$ substitution.[1a] Since steric hindrance at the reacting carbon prevents the $S_{N}2$ reaction to occur with 4-nitrocumyl chloride, we are led to conclude that both the C- and the O-substitution products result from a $S_{RN}1$ reaction.[9]

The concentrations of 4-nitrocumyl chloride and of the two substitution products vary with time as represented in Figure 1a. The half-reaction time is 41 min. Repeated runs showed a good reproducibility of the time variations.

The $S_{RN}1$ character of the reaction was ascertained by the effect of light irradiation and of the addition of a radical trap. Under light irradiation (Figure 1b), the half- reaction time is considerably shortened (3 instead of 41 min). Addition of di-*tert*-butyl nitroxide completely quenched the reaction: neither the C-substitution product nor the O-substitution product was observed after 4 h. This last experiment confirms the $S_{RN}1$ character of the reaction. Since the radical trap may only react with the R[•] radicals that have escaped the solvent cage where R[•], Nu[•], and X[−] have been formed, this experiment also indicates

(8) (a) The O-substitution product is also obtained, albeit in lesser yield, upon reaction with the lithium salt of 2-nitropropanate.[8b] Ion pairing of the negative end of the 2-nitropropanate ion by the countercation is expected to be stronger with Li^{+} than with $(CH_3)_4N^+$, thus explaining why the percentage of O-alkylation is less in the first case than in the second. (b) Kornblum, N.; Davies, T. M.; Earl, G. W.; Holy, N. L.; Manthey, J. W.; Musser, M. T.; Swiger, R. T. *J. Am. Chem. Soc.* **1968**, *90*, 6219.
(9) Ambident reactivity of nucleophiles is not unprecedented. For examples in aromatic $S_{RN}1$ reactions see ref 1k and references therein.
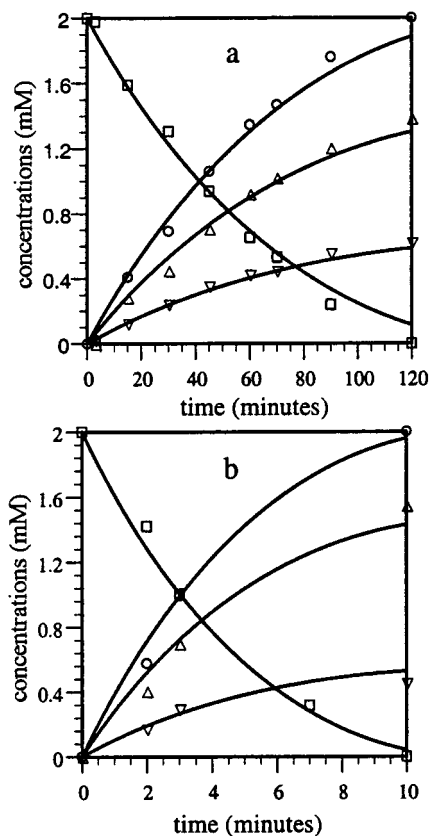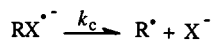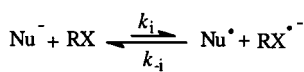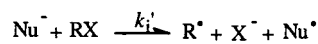
Figure 1. Reaction of 4-nitrocumyl chloride (2 mM) with tetramethyl-ammonium 2-nitropropanate (10 mM). Variation of the concentrations with time, ($\square$): 4-nitrocumyl chloride, ($\triangle$) C-substitution product, ($\triangledown$) O-substitution product, ($\bigcirc$) total of products. (a) In the dark. (b) Under light irradiation (wavelength > 300 nm).

Scheme 3

Initiation of the S_{RN}1 chain reaction

$$Nu^- + RX \underset{k_{-i}}{\overset{k_i}{\rightleftharpoons}} Nu^\bullet + RX^{\bullet-}$$

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

a: stepwise initiation

$$Nu^- + RX \xrightarrow{k_i'} R^\bullet + X^- + Nu^\bullet$$

b: concerted initiation

that, in the absence of radical quencher, the radical R$^\bullet$ does not react with Nu$^\bullet$ before diffusing out of the cage. They may however react outside of the cage. This observation will be used later when simulating the reaction kinetics. The fact that the formation of both the C- and the O-substitution products is quenched by the radical trap confirms that both species result from a S_{RN}1 reaction.

Can the S_{RN}1 Reaction Be Initiated by a Simple Outer-sphere Electron Transfer from the Nucleophile to the Substrate (Scheme 3a)? To answer this question, the determination of the standard potentials of the RX/RX$^{\bullet-}$ and Nu$^\bullet$/Nu$^-$ couples and of their intrinsic barrier is a first requirement for simulating the experimental kinetics. A second parameter of interest is the rate constant, k_c, of cleavage of the anion radical RX$^{\bullet-}$.

The *standard potential of the* RX/RX$^{\bullet-}$ *couple* and *the rate constant of cleavage* of RX$^{\bullet-}$ were determined by a combination of direct cyclic voltammetry and redox catalysis.
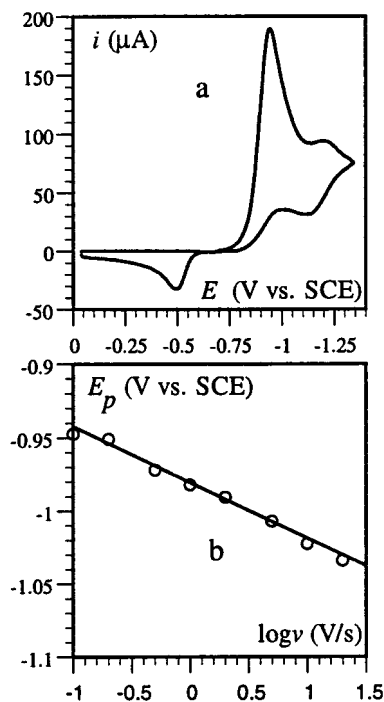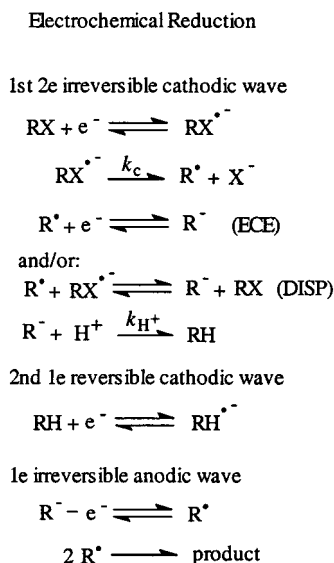
Figure 2. Cyclic voltammetry of 4-nitrocumyl chloride (2.68 mM) in CH$_3$CN + 0.1 M Et$_4$NBF$_4$. (a) Cyclic voltammogram at 0.2 V/s. (b) Variation of the peak potential of the first cathodic wave with the scan rate.

As shown in Figure 2a, the cyclic voltammogram of 4-nitro-cumyl chloride on a glassy carbon (GC) electrode exhibits an irreversible two-electron[10] wave. The variation of the peak potential with the scan rate (Figure 2b, slope: 38.2 mV per decade) indicates a mixed kinetic control of the reaction by the electron transfer and by a follow-up first-order reaction.[10b,c] These observations suggest the reduction mechanism depicted in Scheme 4. The anion radical formed upon electron transfer to the substrate cleaves to yield a radical that is easier to reduce than the starting material. The overall reduction is thus a two-electron process, the second electron being transferred from the electrode (ECE pathway[10c]) and/ or from RX$^{\bullet-}$ in the solution (DISP pathway[10c]). The reduction of the radical produces an anion which protonates rather slowly in the absence of purposely added acid, thanks to the presence of the *p*-nitro substituent on the phenyl ring. The carbanion gives rise to an irreversible one-electron anodic wave around -0.4 V vs SCE in which the radical is regenerated and further undergoes dimerization similarly to the oxidation of 2-nitropropanate ion that will be described further on. Thus, -0.4 V vs SCE is an approximate measure of the standard potential of the R$^\bullet$/R$^-$ couple. This observation confirms that the radical, when formed at the first cathodic wave, is immediately reduced, explaining why a global

(10) (a) From the comparison of the peak current with the peak current of the one-electron reversible wave of the C-substitution product, taking into account the variation of the peak height resulting from the change in kinetic control that occurs upon raising the scan rate.[10b,c] (b) Nadjo, L.; Savéant, J.-M. *J. Electroanal. Chem.* **1973**, *48*, 113. (c) Andrieux, C. P.; Savéant, J.-M In *Electrochemical Reactions in investigation of rates and Mechanism of Reactions, Techniques of Chemistry*; Bernasconi, C. F., Ed.; Wiley: New York, 1986; Vol. VI/4E, Part 2, pp 305−3910. (d) The choice of an ECE mechanism rather than a DISP mechanism is justified by the value of k_c thus found. Indeed, the competition between the two mechanisms is governed by the parameter[10c] $(Fv/RT)^{1/2}k_{disp}C^0/k_c^{3/2}$ (C^0 is the bulk concentration of substrate). The DISP solution electron transfer is a very downhill reaction (standard free energy of ca. -0.7 eV) and thus $k_{disp} = k_{dif} = 2 \times 10^{10}$ M^{-1} s^{-1}. It follows that, within the range of scan rates we explored (0.1−20 V/s), the above parameter ranges from 3×10^{-4} to 6×10^{-3}, i.e., values that are much in favor of the ECE pathway.

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Scheme 4

Electrochemical Reduction

1st 2e irreversible cathodic wave

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

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

$$R^\bullet + e^- \rightleftharpoons R^- \quad (ECE)$$

and/or:

$$R^\bullet + RX^{\bullet -} \rightleftharpoons R^- + RX \quad (DISP)$$

$$R^- + H^+ \xrightarrow{k_{H^+}} RH$$

2nd 1e reversible cathodic wave

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

1e irreversible anodic wave

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

$$2 R^\bullet \longrightarrow product$$

two-electron process is observed. The second one-electron reversible cathodic wave corresponds to the reduction of the hydrocarbon, RH, that resulted from partial protonation of R^- into its anion radical ($E^0_{RH/RH^{\bullet -}} = -1.18$ V vs SCE). As expected, the irreversible one-electron anodic wave increases at the expense of the second one-electron reversible cathodic wave upon increasing the scan rate, whereas the reverse is observed upon addition of a weak acid (phenol) to the solution. In the absence of purposely added acid, simulation of the cyclic voltammogram indicates that the pseudo-first-order rate constant of protonation of R^-, k_{H^+}, is of the order of 0.1 s^{-1}.

Coming back to Figure 2b, the value of the peak potential at each scan rate is a function of the two following parameters (assuming that the transfer coefficient is equal to 0.5).[10b,c]

$$E^0_{RX/RX^{\bullet -}} + \frac{RT}{2F} \ln\left(\frac{RT}{F}\frac{k_c}{v}\right)$$

(or alternatively

$$E^0_{RX/RX^{\bullet -}} + \frac{2RT}{F} \ln\left[k_S\left(\frac{2RT}{FvD}\right)^{1/2}\right]$$

and

$$p = \left(\frac{RT}{Fv}\right)^{1/2}\frac{k_S^2}{k_c^{1/2}D}$$

(k_S is the heterogeneous electron-transfer standard rate constant, v the scan rate and D the diffusion coefficient). Fitting the experimental data points with the theoretical curve for an ECE mechanism (solid line in Figure 2b) leads to two relationships between $E^0_{RX/RX^{\bullet -}}$, k_c and k_S. As seen below, from application of the redox catalysis method, $E^0_{RX/RX^{\bullet -}} = -1.12$ V vs SCE. It follows (taking $D = 10^{-5}$ cm^2 s^{-1}) that $k_c = 4 \times 10^7$ s^{-1} and $k_S = 1.07$ cm s^{-1}.[10d]

The *redox catalysis*[10c,11] experiments were carried out with duroquinone as the mediator. Duroquinone exhibits a one-
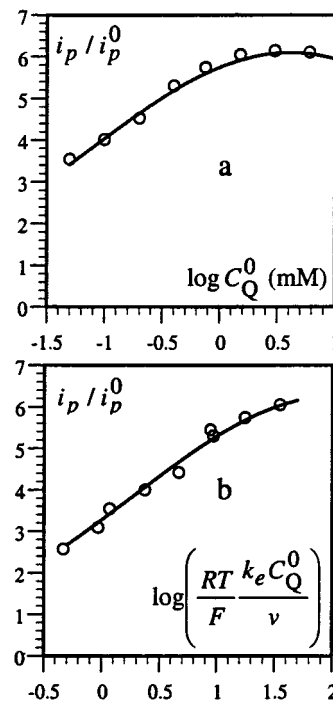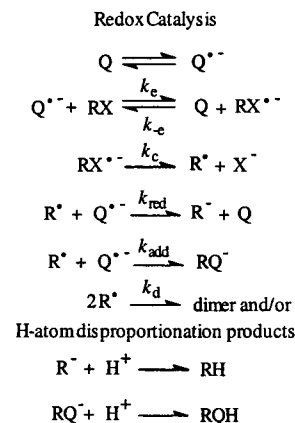
(11) (a) Andrieux, C. P.; Hapiot, P.; Savéant, J.-M *Chem. Rev.* **1990**, *90*, 723. (b) Andrieux, C. P., Blocman, C.; Dumas-Bouchiat, J.-M.; M'Halla, F.; Savéant, J.-M. *J. Am. Chem. Soc.* **1980**, *102*, 3806. (c) Andrieux, C. P.; Blocman, C.; Dumas-Bouchiat, J.-M.; M'Halla, F.; Savéant, J.-M. *J. Electroanal. Chem.* **1980**, *113*, 19. (d) Nadjo, L.; Savéant, J.-M.; Su, K. B. *J. Electroanal. Chem.* **1985**, *196*, 23.

Figure 3. Redox catalysis of the reduction of 4-nitrocumyl chloride by duroquinone in CH$_3$CN + 0.1 M Et$_4$NBF$_4$. (a) Variation of the duroquinone peak current with the duroquinone concentration at 0.2 V/s. (b) Variation of the duroquinone peak current with the duroquinone concentration and the scan rate in the domain where the reaction is under the kinetic control of the forward electron-transfer step. At 0.2 V/s, $C^0_Q = 0.05, 0.1, 0.2, 0.377, 0.4, 0.75, 1.5$ mM. At 1 V/s, $C^0_Q = 0.1, 0.2$ mM. For both a and b, the ratio of the concentrations of substrate and mediator is constant and equal to 2.9.

Scheme 5

Redox Catalysis

$$Q \rightleftharpoons Q^{\bullet -}$$

$$Q^{\bullet -} + RX \underset{k_{-e}}{\overset{k_e}{\rightleftharpoons}} Q + RX^{\bullet -}$$

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

$$R^\bullet + Q^{\bullet -} \xrightarrow{k_{red}} R^- + Q$$

$$R^\bullet + Q^{\bullet -} \xrightarrow{k_{add}} RQ^-$$

$$2R^\bullet \xrightarrow{k_d} dimer and/or$$

H-atom disproportionation products

$$R^- + H^+ \longrightarrow RH$$

$$RQ^- + H^+ \longrightarrow RQH$$

electron reversible cyclic voltammetric wave with a standard potential of -0.825 V vs SCE. Upon addition of RX, the cathodic peak increases, and the wave loses its reversibility as a result of the regeneration of the oxidized form of the mediator, Q, by reaction of its reduced form, $Q^{\bullet -}$, with RX (Scheme 5). The relative increase of the cathodic peak i_p/i_p^0 (i_p and i_p^0 are the peak currents in the presence and absence of substrate respectively) is the source of the kinetic information (Scheme 5) from which the parameters of interest will be derived. As seen in Figure 3a, i_p/i_p^0 increases with the concentration of the mediator, C^0_Q, for a constant value of the excess factor C^0_{RX}/C^0_Q, before reaching a plateau. This behavior is characteristic of a change in the rate-determining step which controls the catalytic process from the forward electron transfer (rate constant, k_e) to the cleavage (rate constant, k_c) with the preceding electron-
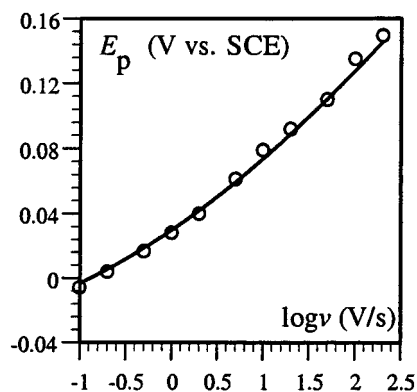
Figure 4. Cyclic voltammetry of tetramethylammonium 2-nitropropanate (2.4 mM) in CH$_3$CN + 0.1 M Et$_4$NBF$_4$. Variations of the anodic peak potential with the scan rate.

transfer acting as a preequilibrium in the latter case. It should also be taken into account that the catalytic process is counteracted by the coupling of the R$^\bullet$ radical with the anion radical of the catalyst (rate constant, k_{add}). In the range of mediator concentrations where the forward electron transfer is the rate-determining step, i_p/i_p^0 is a function of two dimensionless parameters, $(RT/F)(k_e C_Q^0/v)$ and $q = k_{red}/(k_{red} + k_{add})$. Under these conditions, the fitting of the experimental data points with the appropriate theoretical curve (solid line in Figure 3b) leads to $k_e = 1.8 \times 10^5$ M^{-1} s^{-1} and $q = 0.833$.[11d,12] The reduction of the R$^\bullet$ radical by the reduced form of the mediator has a driving force of ca. 0.4 eV. It may thus be considered to be at the diffusion limit ($k_{red} = k_{dif} = 2 \times 10^{10}$ M^{-1} s^{-1}). It follows that $k_{add} = 4 \times 10^9$ M^{-1} s^{-1}. If we assume that the electron transfer from RX$^{\bullet-}$ to the oxidized form of the mediator is also under diffusion limit ($k_{-e} = k_{dif} = 2 \times 10^{10}$ M^{-1} s^{-1}), derivation of the standard potential of the RX/RX$^{\bullet-}$ couple from

$$\frac{k_e}{k_{-e}} = \exp\left[\frac{F}{RT}(E^0_{RX/RX^{\bullet-}} - E^0_{Q/Q^{\bullet-}})\right]$$

leads to $E^0_{RX/RX^{\bullet-}} = -1.12$ V vs SCE. The assumption that $k_{-e} = k_{dif}$ is justified by the fact that this reaction is strongly downhill, with a driving force of ca. 0.3 eV. The data shown in Figure 3a allow, in addition, the determination of the cleavage rate constant k_c since, upon increasing the mediator concentration, the kinetic control passes from the forward electron transfer to the cleavage reaction. k_c has already been derived from the direct cyclic voltammetry of 4-nitrocumyl chloride. To test the agreement between these experiments and the redox catalysis experiments, we simulated the catalytic data displayed in Figure 3a using for k_c the cyclic voltammetric value, 4×10^7 s^{-1}. It is seen that the agreement between simulation and experimental data is excellent.

The *standard potential of the* Nu$^\bullet$/Nu$^-$ *couple* was determined by means of cyclic voltammetry. 2-Nitropropanate ions exhibit an irreversible one-electron anodic wave[13] which remains irreversible at the highest scan rate we have investigated (2500 V/s). The variation of the peak potential with the scan rate

(Figure 4) indicates that the electron-transfer step is followed by an irreversible second-order reaction (dimerization and/or H-atom exchange disproportionation, global rate constant, k_d). When the scan rate is increased, the kinetic control passes progressively from the follow-up reaction to the electron-transfer step.[10b] The variation of the peak width with the scan rate was also found to be consistent with this reaction scheme.

The value of the peak potential at each scan rate is a function of the following two parameters (assuming that the transfer coefficient is equal to 0.5).[10b]

$$E^0_{Nu^\bullet/Nu^-} + \frac{RT}{3F} \ln\left(\frac{RT}{F} \frac{2k_d C_{Nu^-}^0}{v}\right)$$

(or alternatively,

$$E^0_{Nu^\bullet/Nu^-} + \frac{2RT}{F} \ln\left[k_S\left(\frac{2RT}{FvD}\right)^{1/2}\right]$$

and

$$p = 3^{1/3}\left(\frac{RT}{Fv}\right)^{2/3} \frac{k_S^2}{k_d^{1/3} D(C_{Nu^-}^0)^{1/3}}$$

(k_S is the heterogeneous electron-transfer standard rate constant, v the scan rate and D the diffusion coefficient, $C_{Nu^-}^0$ the bulk concentration of 2-nitropropanate ions). Fitting of the experimental points with the appropriate working curve[10c] leads to two relationships between $E^0_{Nu^\bullet/Nu^-}$, k_d and k_S. The value of k_d may be derived from previous data concerning the *tert*-butyl and the 2-cyanopropanate radicals[14] and taken as equal to 10^9 M^{-1} s^{-1}. It follows that $E^0_{Nu^\bullet/Nu^-} = 0.077$ V vs SCE[15] and $k_S = 0.2$ cm s^{-1}.

The rate constant for the *coupling of the 4-nitrocumyl radical with the 2-nitropropanate ion*, k_{Nu}, was obtained both from direct cyclic voltammetry and redox catalysis experiments. In each case the experiment should be carried out quickly before the thermal reaction takes place to a significant extent. The direct method consists of observing the decrease of the substrate peak current upon addition of increasing amounts of the nucleophile.[16]

(12) Protonation of the two carbanions follows irreversible steps in both cases and therefore does not interfere in the overall kinetics. The second-order reactions undergone by R$^\bullet$ do not exert a significant influence because its concentration is very low. This was checked by simulation carried out in the absence of reactions and with a reaction rate constant equal to the diffusion limit which indeed gave the same result with a good precision.

(13) From the comparison of the peak current with the peak current of the one-electron reversible wave of ferrocene in the same solvent, taking into account the variation of the peak height resulting from the change in kinetic control that occurs upon raising the scan rate.[10b]

(14) (a) k_d for the *tert*-butyl radical is practically the same in benzene and in acetonitrile,[14b] and k_d for the 2-cyanopropanate radical is 0.9×10^9 M^{-1} s^{-1} in benzene.[14c] (b) Weiner, S. A.; Hammond, G. S. *J. Am. Chem. Soc.* **1969**, *91*, 986. (c) Schuh, H. H.; Fischer, H. *Helv. Chim. Acta* **1978**, *61*, 2130.

(15) (a) Somewhat different values of $E^0_{Nu^\bullet/Nu^-}$ have been reported in the literature for the tetramethylammonium salt of 2-nitropropanate.[15b] A value of 0.044 V vs SCE was obtained by treating low scan rate cyclic voltammetric data as if the oxidation were under complete electron-transfer kinetic control. The pitfalls of this procedure, previously applied to the reduction of NAD$^+$ analogues[15c,d] where a follow-up dimerization is also involved, have been previously analyzed.[15e] The second value, 0.1 V vs SCE, was obtained by the second harmonic AC technique using a BAS 100B instrument. Chemical reversibility of the system was claimed to be reached at a 50 Hz frequency.[15b] In cyclic voltammetry, there is no trace of reversibility at 200 V/s which corresponds to a frequency of 8000 Hz. There is, therefore, no possibility that reversibility could be reached at 50 Hz. The theoretical misconceptions and instrumental artifacts behind this apparent reversibility have been previously discussed.[15f] (b) Fukuzumi, S.; Fujita, M.; Maruta, J.; Chanon, M. *J. Chem. Soc., Perkin. Trans 2* **1994**, 1597. (c) Fukuzumi, S.; Kumitsu, S.; Hironaka, K.; Tanaka, T. *J. Am. Chem. Soc.* **1987**, *109*, 305. (d) Fukuzumi, S.; Kitano, T. *J. Chem. Soc., Perkin. Trans 2* **1991**, 41. (e) Hapiot, P.; Moiroux, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1990**, *112*, 1337. (f) Andrieux, C. P.; Hapiot, P.; Pinson, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1993**, *115*, 7783.

(16) (a) Amatore, C.; Chaussard, J.; Pinson, J.; Savéant, J.-M.; Thiébault, A. *J. Am. Chem. Soc.* **1979**, *101*, 6012. (b) Amatore, C.; Pinson, J.; Savéant, J.-M.; Thiébault, A. *J. Am. Chem. Soc.* **1982**, *104*, 817. (c) Amatore, C.; Oturan, M. A.; Pinson, J.; Savéant, J.-M.; Thiébault, A. *J. Am. Chem. Soc.* **1985**, *107*, 3451. (d) Amatore, C.; Savéant, J.-M.; Thiébault, A. *J. Electroanal. Chem.* **1979**, *103*, 303.
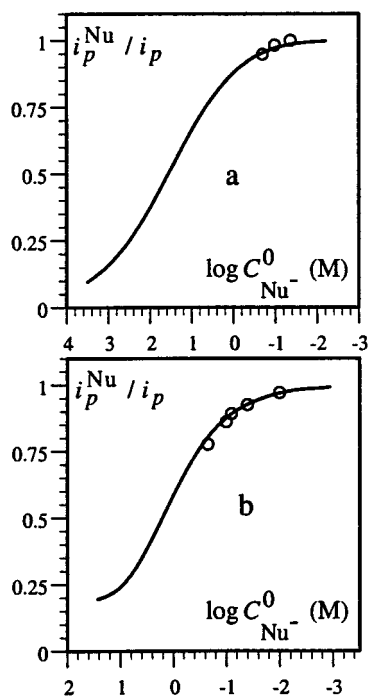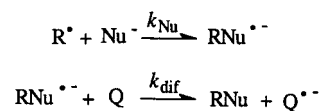
Figure 5. Determination of the rate constant, k_{Nu}, for the coupling between the 4-nitrocumyl radical and the 2-nitropropanate ion. (a) Cyclic voltammetry of 4-nitrocumyl chloride (1.2 mM) in CH$_3$CN + 0.1 M Et$_4$NBF$_4$ in the presence of increasing amounts of tetramethyl-ammonium 2-nitropropanate. (b) Cyclic voltammetry of duroquinone (0.425 mM) in CH$_3$CN + 0.1 M Et$_4$NBF$_4$ in the presence 4-nitrocumyl chloride (1.23 mM) and of increasing amounts of tetramethylammonium 2-nitropropanate. Scan rate: 0.2 V/s.

Scheme 6

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

$$RNu^{\bullet -} - e^- \rightleftharpoons RNu$$
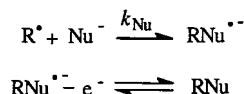
In the present case, the decrease is very small within the range of available nucleophile concentrations (Figure 5a) due to a rather modest coupling rate constant and to the severe competition with the reduction of the radical at the electrode in the framework of an ECE process (the mechanism involves the reactions composing the ECE version of Scheme 4 plus the reactions in Scheme 6). Under these conditions, the decrease of the peak current, defined as the ratio i_p^{Nu}/i_p of the peak currents in the presence and absence of nucleophile respectively, is a function of the parameter $k_{Nu}C_{Nu-}^0/[(k_{dif} + k_{add})C_Q^0]$.[16] Fitting of the experimental points leads to $k_{Nu}/k_c = 0.03$ M^{-1}, and thus to $k_{Nu} = 1.2 \times 10^6$ M^{-1} s^{-1}. As discussed above this value is not very accurate. Redox catalysis allows a more precise determination of k_{Nu}. It consists of observing the decrease of the catalytic peak current of the mediator in the presence of the substrate upon addition of increasing amounts of the nucleophile.[17] We used the same mediator, duroquinone, as in the previous experiments. Figure 5b shows the decrease of the ratio i_p^{Nu}/i_p of the peak currents in the presence and absence of nucleophile, respectively, upon addition of the nucleophile. The mechanism involves the reactions listed in Scheme 5 plus the reactions of Scheme 7. The decrease of the catalytic peak current results from the consumption of the oxidized form of the mediator by electron transfer from RNu$^{\bullet -}$. The latter reaction may be consider to be under diffusion control for it has a driving

(17) Amatore, C.; Oturan, M. A.; Pinson, J.; Savéant, J.-M.; Thiébault, A. *J. Am. Chem. Soc.* **1984**, *106*, 6318.

Scheme 7

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

$$RNu^{\bullet -} + Q \xrightarrow{k_{dif}} RNu + Q^{\bullet -}$$

force of ca. 0.3 eV. The standard potential derived from the one-electron reversible wave of an authentic sample of the C-substitution product is indeed −1.12 V vs SCE, exactly the same as the standard potential of 4-nitrocumyl chloride and very close to those of the corresponding alcohol, −1.16 V vs SCE (from the one-electron reversible wave of an authentic sample), and hydrocarbon, −1.18 V vs SCE (as reported above). These observations indicate that the main factor that governs the standard potential in this family of compounds is the energy of the π* orbital of the 4-nitrophenyl group with little influence of the substituents borne by the benzylic carbon. We may thus infer that the standard potential of the O-substitution product, which we cannot measure because of its instability, is very close to that of the C-substitution product[18] and therefore that the driving force of the electron transfer from RNu$^{\bullet -}$ to Q is practically the same in both cases. Under these conditions, the ratio i_p^{Nu}/i_p is a function of the parameter $kNuC_{Nu-}^0/[(k_{dif} + k_{add}) C_Q^0]$. Fitting of the experimental points in Figure 5b thus leads to $k_{Nu}/(k_{dif} + k_{add}) = 4.7 \times 10^{-5}$, and thus to $k_{Nu} = 1.1 \times 10^6$ M^{-1} s^{-1}, a value that is in agreement and more accurate than the value derived from the direct cyclic voltammetry. It should be emphasized that the rate constant thus obtained is a global value corresponding to both C- and O-substitutions. The rate of coupling between R$^\bullet$ and Nu$^-$ is relatively modest, significantly smaller than in the case of aryl radicals. As discussed earlier, this results from the fact that the C−Nu bond is weaker in benzylic derivatives (even more so for cumyl derivatives) than with phenyl derivatives and that this effect is not fully compensated by the activation of the radical due to the presence of the *p*-nitro group.[1k]

The *simulation of the overall kinetics for an outersphere electron-transfer initiation* requires the knowledge of the rate constants of the initiation step, of each step in the propagation loop, and of the termination steps.

For *initiation*, the forward and backward rate constants, k_i and k_{-i}, are obtained from the following equations:[19a−d]

$$\frac{1}{k_i} = \frac{1}{k_{dif}} + \frac{1}{k_{act}} + \frac{1}{k_{dif} \exp\left[\frac{F}{RT}(E^0_{RX/RX^{\bullet -}} - E^0_{Nu^\bullet/Nu^-})\right]}, \quad (1)$$

$$\frac{k_i}{k_{-i}} = \exp\left[\frac{F}{RT}(E^0_{RX/RX^{\bullet -}} - E^0_{Nu^\bullet/Nu^-})\right] \quad (2)$$

$$k_{act} = Z^{hom} \exp\left[-\frac{F}{RT}\frac{\lambda}{4}\left(1 + \frac{E^0_{Nu^\bullet/Nu^-} - E^0_{RX/RX^{\bullet -}}}{\lambda}\right)^2\right] \quad (3)$$

where the preexponential factor, $Z^{hom} = (a_{Nu} + a_{RX})^2(8\pi RT/\mu)^{1/2} = 4.27 \times 10^{11}$ M^{-1} s^{-1}. ($\mu = 61.065$ g is the reduced mass. $a_{Nu} = 3.88$ and $a_{RX} = 4.53$ Å are the radii of the

(18) This conclusion falls in line with the following observation. In the first stages of the substitution reaction, when the O-substitution product has not yet decomposed into the alcohol, the cyclic voltammetry of the solution exhibits a single one-electron reversible wave for the two substitution products.

(19) (a) Andrieux, C. P.; Savéant, J.-M. *J. Electroanal. Chem.* **1986**, *205*, 43. (b) Marcus, R. A. *J. Chem. Phys.* **1956**, *24*, 4966. (c) Hush, N. S. *J. Chem. Phys.* **1958**, *28*, 962. (d) Marcus, R. A. In *Special Topics in Electrochemistry*; Rock, P. A., Ed.; Elsevier: New York, 1977; pp 161−179.

equivalent sphere derived after a quantum chemical calculation where the geometries were optimized using the B3LYP density functional method). In view of the very low driving force, only the last two terms in the right-hand side of eq 1 are significant. The reorganization energy, λ, may be estimated as the sum of the solvent and intramolecular reorganization energies, λ_0 and λ_i. λ_0 is obtained from eq 4.[20]

$$\lambda_0 = 4 \left(\frac{1}{2a_{Nu}} + \frac{1}{2a_{RX}} - \frac{1}{a_{Nu} + a_{RX}} \right)$$

$$(\lambda_0 \text{ in eV, } a\text{'s in Å}) \quad (4)$$

We thus find: $\lambda_0 = 0.481$ eV. λ_i may be obtained from the electrochemical intramolecular reorganization energies for the two reactants according to eq 5.

$$\lambda_i = \lambda_{i,Nu^-}^{el} + \lambda_{i,RX}^{el} \quad (5)$$

The electrochemical reorganization energies may themselves be derived according to eq 6 from the previously determined electrochemical standard rates constants.[20]

$$k_S = Z^{el} \exp\left[-\frac{F(\lambda_0^{el} + \lambda_i^{el})}{4RT} \right] \quad (6a)$$

with

$$Z^{el} = \sqrt{\frac{RT}{2\pi M}} \text{ (M, molar mass)} \quad (6b)$$

and

$$\lambda_0^{el} \text{ (eV)} = 3/a \text{ (Å)} \quad (6c)$$

We thus find $\lambda_{0,Nu^-}^{el} = 0.773$ eV, $\lambda_{i,Nu^-}^{el} = 0.296$ eV, $\lambda_{0,RX}^{el} = 0.662$ eV, $\lambda_{i,RX}^{el} = 0.193$ eV. It is interesting to note that the value found for λ_{i,Nu^-}^{el} is close to the value, 0.253 eV, derived from B3LYP density functional quantum chemical calculations (see Experimental Section). Thus, $\lambda_i = 0.489$ eV. $\lambda = 0.97$ eV and therefore, from eqs 1–3, $k_i = 1.06 \times 10^{-10}$ M^{-1} s^{-1}, and $k_{-i} = 1.9 \times 10^{10}$ M^{-1} s^{-1}. As expected for such a poor driving force of the forward electron-transfer step, the backward electron-transfer step is practically under diffusion control.

For *propagation*, the rate constants of two among the three steps have already been determined. We now need to estimate the electron-transfer rate constants between the RX/RX$^{•-}$ and RNu/RNu$^{•-}$ couples (Scheme 1). The driving force of the reaction between RNu$^{•-}$ and RX is equal to zero. A reasonable estimate of k_p and k_{-p} is to take the self-exchange rate constant of the dinitrobenzene/dinitrobenzene anion radical, 6×10^8 M^{-1} s^{-1},[21] as a common value.

The termination steps are those depicted in Scheme 8. A reasonable estimate of k_{d1} is 4×10^9 M^{-1} s^{-1}, based on the value reported for the cumyl radical (8×10^9 M^{-1} s^{-1}),[14b] taking account of some delocalization of the unpaired electron on the nitro group. k_{d2} has already been estimated as equal to 10^9 M^{-1} s^{-1}. A reasonable estimate of k_{rc} is thus 2×10^9 M^{-1} s^{-1}. A second series of termination steps involves the reduction of the radical R$^{•}$ by the two anion radicals RX$^{•-}$ and RNu$^{•-}$. Both are very downhill reactions with a driving force of ca. 0.8 eV. We may thus consider that each of them is under diffusion control.
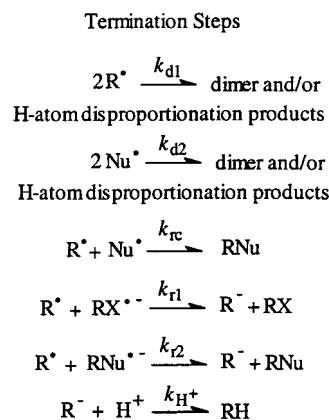
(20) Andrieux, C. P.; Savéant, J.-M.; Tardy, C.; Savéant, J.-M. *J. Am. Chem. Soc.* **1998**, *120*, 4167.
(21) Kojima, H.; Bard, A. J. *J. Am. Chem. Soc.* **1975**, *97*, 6317.

Scheme 8

Termination Steps

$$2R^{•} \xrightarrow{k_{d1}} \text{dimer and/or}$$
H-atom disproportionation products

$$2 Nu^{•} \xrightarrow{k_{d2}} \text{dimer and/or}$$
H-atom disproportionation products

$$R^{•} + Nu^{•} \xrightarrow{k_{rc}} RNu$$

$$R^{•} + RX^{•-} \xrightarrow{k_{r1}} R^{-} + RX$$

$$R^{•} + RNu^{•-} \xrightarrow{k_{r2}} R^{-} + RNu$$

$$R^{-} + H^{+} \xrightarrow{k_{H^+}} RH$$

Table 1. Reaction of 4-Nitrocumyl Chloride with the 2-Nitropropanate Ion. Pertinent Rate Constants[a] and Simulation of the Experimental Kinetics

Propagation
$k_c = 4 \times 10^7$,[b] $k_{Nu} = 1.2 \times 10^6$, $k_p = k_{-p} = 6 \times 10^8$

Termination
$k_{d1} = 4 \times 10^9$, $k_{d2} = 10^9$, $k_{rc} = 2 \times 10^9$, $k_{r1} = k_{r2} = 2 \times 10^{10}$

Initiation	
outersphere electron transfer	dissociative electron transfer
$E^0_{RX/RX^{•-}} = -1.12$[c]	$E^0_{RX/RX^{•}+X^-} = -0.26$[c]
$k_i = 1.09 \times 10^{-10}$, $k_{-i} = 1.9 \times 10^{10}$	$k_i' = 2.22 \times 10^{-6}$

Simulation (Experimental $t_{1/2} = 41$ min[d])	
outersphere electron transfer	dissociative electron transfer
$t_{1/2} = 4200$ min	$t_{1/2} = 30$ min

[a] In M^{-1} s^{-1} unless otherwise stated. [b] s^{-1}. [c] In V vs SCE. [d] Reaction of 2 mM 4-nitrocumyl chloride with 10 mM tetramethylammonium 2-nitropropanate in CH$_3$CN at 25 °C.

All of the pertinent rate constants are summarized in Table 1, thus allowing the simulation of the experimental kinetics.

It immediately appears that *the outersphere electron-transfer initiation mechanism cannot account for the observed kinetics*, the half-reaction time being more than 100 times larger than that observed. The chain process considerably enhances the global rate of the reaction (without a chain process, the half-reaction time would be 3 centuries) but the outersphere electron transfer between the nucleophile and the substrate is still too uphill a reaction to make it a viable initiation step.

The outersphere electrochemical reduction of 4-nitrocumyl chloride is a slightly uphill reaction (for example, at 0.2 V/s, the cyclic voltammetric peak potential is −0.95 V vs SCE whereas the standard potential is −1.12 V vs SCE, i.e., the driving force is −0.17 eV). It has been shown to consist of an outersphere electron transfer followed by the cleavage of the resulting anion radical. The same is true for the homogeneous reduction of 4-nitrocumyl chloride by the anion radical of duroquinone for which the driving force is −0.3 eV. It is predicted on theoretical grounds that a decrease in driving force should induce a change in the reductive cleavage mechanism from stepwise to concerted as illustrated in Figure 6.[19a] Experimental evidence of the correctness of this prediction has been reported in two electrochemical examples and for one homogeneous reaction.[22] We may thus expect that the very low driving force offered by the 2-nitropropanate ion may trigger

(22) (a) Andrieux, C. P.; Robert, M.; Saeva, F. D.; Savéant, J.-M. *J. Am. Chem. Soc.* **1994**, *116*, 7864. (b) Andrieux, C. P.; Savéant, J.-M.; Tardy, C.; Savéant, J.-M. *J. Am. Chem. Soc.* **1997**, *119*, 11546. (c) Antonello, F.; Maran, J. *J. Am. Chem. Soc.* **1997**, *119*, 12595. (d) Severin, M. G.; Farnia, E.; Vianello, E.; Arévalo, M. C. *J. Electroanal. Chem.* **1988**, *251*, 369.
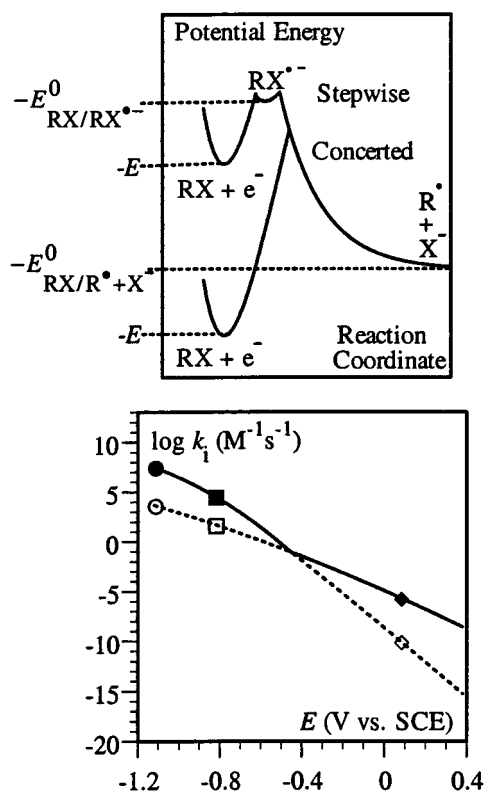
Figure 6. Passage from the stepwise to the concerted mechanism upon decreasing the driving force. (Top) Potential energy profiles. (Bottom) Reaction of 4-nitrocumyl chloride with homogeneous donors; diamonds: 2-nitropropanate ion, squares: duroquinone anion radical, circles: $RNu^{\bullet-}$. E: electrode potential or standard potential of a homogeneous donor.

the passage from the stepwise to the concerted mechanism (Scheme 3), thus resulting in an enhancement of the initiation rate (as illustrated in Figure 6).

We thus examine now whether a *dissociative electron-transfer initiation step matches* the experimental kinetics.

k_i' may be obtained from eq 7[1g,20,23]

$$k_i' = Z^{hom} \exp\left[-\frac{F}{RT}\frac{\lambda'}{4}\left(1 + \frac{E_{Nu^\bullet/Nu^-}^0 - E_{RX/R^\bullet+X^-}^0}{\lambda'}\right)^2\right] \quad \text{with}$$

$$\lambda' = BDE + \lambda_0' + \lambda_i' \quad (7)$$

where BDE is the R–X bond dissociation energy. For λ_0', the solvent reorganization energy, we may take the same value, 0.481 eV as already used in the outersphere case.[24] λ_i' is the intramolecular reorganization energy besides the cleavage of the R–X bond. It is equal to the electrochemical intramolecular reorganization energy for the oxidation of Nu^-, 0.296 eV.

The standard potential for the dissociative electron transfer may be expressed as $E_{RX/R^\bullet+X^-}^0 = -BDE + E_{X^\bullet/X^-}^0 + T(S_{R^\bullet} - S_{X^\bullet} - S_{RX})$. $E_{X^\bullet/X^-}^0$ is equal to 1.89 V vs SCE in acetonitrile.[25] BDE and the molar entropies have been estimated by means of B3LYP density functional quantum chemical calculations (see Experimental Section): $BDE = 2.6$ eV, $S_{R^\bullet} = 4.62$,

$S_{X^\bullet} = 1.65$, $S_{RX} = 4.76$ meV/K. We thus find $E_{RX/R^\bullet+X^-}^0 = -0.26$ V vs SCE. It follows from eq 7 that $k_i' = 2.2 \times 10^{-6}$ M^{-1} s^{-1}. From this value and the rate constants already determined for the propagation and termination steps, we find a half-reaction time of 30 min, in good agreement with the experimental value. We may thus conclude that the mechanism of the thermal $S_{RN}1$ substitution of 4-nitrocumyl chloride by 2-nitropropanate ions indeed involves as the initiation step the transfer of an electron from the nucleophile to the substrate but that electron transfer and bond breaking are concerted rather than successive. In other words, *the anion radical of 4-nitrocumyl chloride does not transpire along the initiation pathway although it is an intermediate during propagation*. Figure 6 illustrates the passage from the stepwise to the concerted mechanism in the homogeneous reductive cleavage of 4-nitrocumyl chloride as the driving force is made weaker and weaker. It is seen that this change of mechanism allows an acceleration of the initiation by the 2-nitropropanate ion by a factor of 20 000 resulting in an acceleration of the overall $S_{RN}1$ reaction by a factor of 140. The chains are long (chain length: 25 000), but the termination steps nevertheless play an important role (with no termination the half-reaction time would be 80 s instead of 1800 s) although the termination products are formed in very low amounts escaping detection; after the completion of the reaction of 2×10^{-3} M 4-nitrocumyl chloride with 10^{-2} M tetramethylammonium 2-nitropropanate, 3×10^{-8} M R–R dimer or H-atom disproportionation products are expected to be formed, 3×10^{-8} M RNu to be formed by coupling of $R^\bullet$ with $Nu^\bullet$ and 4.04×10^{-9} M RH, 4×10^{-9} M from the reduction of $R^\bullet$ by $RNu^{\bullet-}$ and 4×10^{-11} M from the reduction of $R^\bullet$ by $RX^{\bullet-}$.[26]

Reaction of 4-Nitrocumyl Chloride with Other Nucleophiles. The reactions of the same substrate, 4-nitrocumyl chloride, with a few other nucleophiles have been previously investigated, and the half-reaction times can be estimated from reported data.[27] Although all of the pertinent rate constants are not as precisely known as those with the 2-nitropropanate ion, we may attempt to see whether the same mechanistic conclusion is valid for these nucleophiles, too.

The experimental data as well as the available rate constants with the various parameters used to evaluate them are given in Table 2. We see that, in all cases and as for the 2-nitropropanate ion, the rate constant for outersphere electron-transfer initiation is much smaller than the rate constant for dissociative electron-transfer initiation. What is lacking for a simulation of the experimental kinetics, in the framework of the latter mechanism, is the value of the rate constants for the coupling of the radical with the nucleophile, k_{Nu}. We thus adjusted k_{Nu} so as to reproduce the experimental kinetics in the framework of the concerted mechanism. The values thus obtained (Table 2) are close to the value found for the 2-nitropropanate ion, 1.2×10^6 M^{-1} s^{-1}, ranging from 5×10^6 to 10^7 M^{-1} s^{-1}. As discussed earlier, the rate constants for radical–nucleophile coupling are expected to span a rather narrow range of values because of mutual compensation of the reactivity governing parameters.[1k] The fact that quite reasonable values of k_{Nu} are thus obtained is

(23) (a) Savéant, J.-M. Dissociative Electron Transfer. In *Advances in Electron-Transfer Chemistry*; Mariano, P. S., Ed.; JAI Press: New York, 1994; Vol. 4, pp 53–116. (b) Savéant, J.-M. *J. Am. Chem. Soc.* **1987**, *109*, 6788. (c) Savéant, J.-M. *J. Am. Chem. Soc.* **1992**, *114*, 10595.

(24) The solvation radius of RX decreases as the reaction proceeds, but this effect is likely to be compensated by the steric hindrance to solvation within a solvation shell crowded with three particles.

(25) Andrieux, C. P.; Differding, E.; Robert, M.; Savéant, J.-M. *J. Am. Chem. Soc.* **1993**, *115*, 6592.

(26) That much less RH is formed from the latter reaction than from the former results from the instability of $RX^{\bullet-}$ toward cleavage. That the reduction of $R^\bullet$ by $RNu^{\bullet-}$ is a less efficient termination step than the two other is a reflection of the fact that $RNu^{\bullet-}$ is formed relatively slowly as compared to its reoxidation by RX. In other words, the coupling of $R^\bullet$ with Nu^- is the slowest step in the propagation loop.

(27) Kornblum, N.; Cheng, L.; Davies, T. M.; Earl, G. W.; Holy, N. L.; Kerber, R. C.; Kestner, M. M.; Manthey, J. W.; Musser, M., T.; Pinnick, H. W.; Snow, D. H.; Stuchal, F. W.; Swiger, R. T. *J. Org. Chem.* **1987**, *52*, 196.

"Thermal" $S_{RN}1$ Reactions

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Table 2. Reaction of 4-Nitrocumyl Chloride with Other Nucleophiles[a]

	Nu⁻	PhS⁻	PhSO₂⁻	NO₂⁻
		Experimental Conditions and Data[v]		
[RX], [Nu⁻][b]		0.1, 0.1	0.1, 0.5	0.1, 0.5
solvent		DMF[c]	HMPA[d]	DMSO[e]
reaction time[f]		2 min	3 h[g]	300 h
		Propagation		
	$k_c = 4 \times 10^7, k_p = k_{-p} = 6 \times 10^8$			
		Termination		
	$k_{d1} = 4 \times 10^9, k_{rc} = 2 \times 10^9$			
k_{d2}		$9.6 \times 10^{9\,h}$	$9.6 \times 10^{9\,i}$	$10^{9\,j}$
$k_{e1} = k_{e2} = k_{dif}$		2×10^{10}	2×10^{10}	5×10^9
		Dissociative Electron Transfer Initiation		
	$a_{RX} = 4.53, BDE = 2.6, E^0_{RX/R\bullet+X^-} = -0.26$			
$E^0_{Nu\bullet/Nu^-}$		0.1^k	0.55^l	0.8^m
aNu^n		4.08	3.64	2.93
λ_i		0.363^o	0.363^p	0.873^q
λ_0^r		0.467	0.502	0.503
$Z^{hom\ s}$		4.2×10^{11}	3.5×10^{11}	4.3×10^{11}
$k_i'^{\ t}$		6.4×10^{-7}	1.3×10^{-11}	1.5×10^{-16}
predicted value of k_{Nu}		1.1×10^7	10^7	5×10^6
		Outersphere Electron Transfer Initiation		
	$E^0_{RX/RX^{\bullet-}} = 1.12$			
k_i^u		6.4×10^{-11}	10^{-18}	1.4×10^{-23}
predicted reaction time[f]		240 min	2400 h	100 000 h

[a] Monomolecular rate constants in s⁻¹, bimolecular rate constants in M⁻¹ s⁻¹, energies in eV, potentials in V vs SCE, radii in Å. [b] Concentrations in M. [c] N,N′-dimethylformamide. [d] Hexamethylphosphorotriamide. [e] Dimethylsulfoxide. [f] Half-reaction time unless otherwise stated. [g] Time for completion of the reaction. [h] Reference 15. [i] Assumed to be the same as for PhS⁻. [j] Guessed value; an increase or a decrease by 1 order of magnitude has no significant effect on the simulated kinetics. [k] Reference 15f. [l] Taken as equal to the value of the peak potential at 0.2 V/s in tetrahydrofuran.[28] [m] Taken as equal to the value of the peak potential at 0.5 V/s in DMSO as measured by us. [n] From B3LYP/6-31G* quantum chemical calculations. [o] From $k_S = 0.13$ cm/s[15f] and application of eq 6, which leads to $\lambda_0^{el} = 0.735$ eV. [p] Assumed to be the same as for PhS⁻. [q] From B3LYP/6-31G* quantum chemical calculations. [r] From eq 4. [s] $Z^{hom} = (a_{Nu} + a_{RX})^2 (8\pi RT/\mu)^{1/2}$. [t] From eq 7. [u] $k_i = k_{dif} \exp[(F/RT)(E^0_{RX/RX^{\bullet-}} - E^0_{Nu\bullet/Nu^-})]$. [v] Reference 27.

a strong indication of the correctness of the dissociative electron-transfer character of the initiation step. The simulation of the experimental kinetics according to an outersphere electron-transfer initiation step, using the above values of k_{Nu}, leads to reaction times that are considerably larger than the experimental data, thus ruling out this mechanism. Another way to reach the same conclusion is to attempt adjusting the values of k_{Nu} so as to reproduce the experimental kinetics. It is thus found that even with values of k_{Nu} much above the diffusion limit, the predicted reaction time remains larger than the experimental reaction time, in line with the fact that the cleavage of RX•⁻ then becomes the rate-determining step in the propagation loop.

As to the *aryl iodides* evoked in the Introduction, no sufficient supporting data are available to conduct the same type of analysis as in the 4-nitrocumyl chloride case. The occurrence of an outersphere electron-transfer initiation step is however extremely unlikely. Taking the standard potential of benzonitrile (−2.25 V vs SCE) as a higher limit of the phenyl iodide/phenyl iodide anion radical standard potential and −0.15 V vs SCE as the standard potential for the oxidation of a typical ketone enolate nucleophile, the standard free energy of the initiation reaction would be 2.10 eV, resulting in a rate constant of 3×10^{-36} M⁻¹ s⁻¹, obviously much too small for a viable initiation step, whatever the rate of the propagation and termination steps.

Conclusions

The solution of the riddle posed by Kornblum's thermal $S_{RN}1$ reactions is as follows. The nucleophile does work as a single electron-transfer initiator of the chain process. However, the mechanism of initiation does not consist of a mere outersphere electron transfer from the nucleophile to form the anion radical of the substrate. It rather involves a dissociative process in which electron transfer and bond breaking are concerted. The passage from a stepwise to a concerted mechanism is a consequence of the low driving force offered by the poor electron donor properties of the nucleophile.

The present study thus provides a new example of the governing role of the driving force in passing from one mechanism to the other. The possibility of investigating the reductive cleavage reaction under such low driving forces derives from the amplification of the initiation kinetics by the chain process, therefore giving access to very slow reactions that would otherwise escape kinetic measurements. The result obtained with 4-nitrocumyl chloride and the 2-nitropropanate ion provides a particularly unambiguous characterization of the passage to the concerted process as the driving force decreases since the dissociative reaction is then more than 4 orders of magnitude faster than the outersphere reaction.

The first illustration of the theoretical expectation that a decrease in driving force should drive the mechanism of reductive or oxidative cleavages from stepwise to concerted[19a] was found in the reduction of triphenylmethyl phenyl sulfide by a series of aromatic anion radicals in DMF.[22d] The conclusion was drawn with some caution because it was based on a rather modest deviation of a low driving force data point from the outersphere electron-transfer curve. Two examples of the same phenomenon were found later on in the electrochemical reduction of sulfonium cations in acetonitrile.[22a,b] That it is not a special feature of this particular class of compounds was further demonstrated by the finding that it also appears in the reduction of *tert*-butyl-*p*-cyanoperbenzoate in DMF,[22c] which was analyzed in even greater detail thanks to the use of the convolution voltammetric technique.[29] The present work provides a further, unambiguous, homogeneous example which confirms the validity of the concepts underlying the theoretical prediction.[19a] It also emphasizes the practical importance that this phenomenon may have.

Experimental Section

Chemicals. Acetonitrile (Merck Uvasol), the supporting electrolyte NEt₄BF₄ (Fluka, puriss), 2-nitropropane (Aldrich), nitrocumene (Aldrich), tetramethylammonium hydroxide pentahydrate (Aldrich), duroquinone (Fluka), di-*tert*-butyl nitroxide (Aldrich) were used as received. 4-Nitrocumyl chloride was prepared from nitrocumene as described elsewhere.[30] The tetramethylammonium salt of 2-nitropropane was prepared directly in the reaction vessel as follows. A deoxygenated solution of 2-nitropropane in acetonitrile is added, under argon, to a flask containing tetramethylammonium hydroxide pentahydrate. The solution is stirred for a few minutes and then transferred under argon in the reaction vessel. 2-Nitropropane is in small excess so that the quantity of nucleophile formed is equal to the quantity of tetramethylammonium hydroxide pentahydrate.

Silica gel (MN Kiesegel 60, 70−230 mesh, Macherey-Nagel) was employed for column chromatography. Analytical TLC was performed

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with 0.25-mm coated commercial plates (Macherey-Nagel, Polygram SIL G/UV$_{254}$). NMR spectra were taken in CDCl$_3$ using TMS as the internal standard for ^{1}H (200.132 Hz). Melting points are uncorrected. A 25-cm Kromasil C18 column, using 50% CH$_3$CN−50% H$_2$O as eluent was used for high-pressure liquid chromatography analysis.

Reactions of 4-Nitrocumyl Chloride with Tetramethylammonium 2-Nitropropanate. Identification of the Reaction Products. A 100 mL solution of the nucleophile (84 mM) is prepared as described above. It is then transferred, in the dark, under argon, into a 100 mL deoxygenated solution of 4-nitrocumyl chloride (42 mM) in acetonitrile. After stirring the solution during 10 h, HPLC analysis shows that 4-nitrocumyl chloride has completely disappeared and that two reaction products have been formed. Acetic acid (500 μL) was then added to the solution. After solvent evaporation and addition of CH$_2$Cl$_2$, the remaining white solid (most probably NMe$_4$Cl) is removed by filtration. Evaporation of the CH$_2$Cl$_2$ solution left a crude material which was shown to contain three products by HPLC. One of the two reaction products has been partially converted into a third product. The crude product was purified by silica gel chromatography (CHCl$_3$/CH$_3$CN, 95: 5), and two products were recovered and identified as the C-substitution product (one of the two reaction products) and 4-nitrocumyl alcohol which comes from hydrolysis of second reaction product.

C-substitution product: mp 210 °C (powder); ^{1}H NMR δ 1.56 (s, 12H, CH$_3$) δ 7.84 (m, 4H, H-arom). MS (CI,CH$_4$) 253 (M + H$^+$).

4-Nitrocumyl alcohol: ^{1}H NMR δ 1.62 (s, 6H, CH$_3$) δ 2.0 (s, 1H, OH) δ 7.65 (d, 2H, J = 9.0 Hz, H-arom) δ 8.17 (d, 2H, J = 9.0 Hz, H-arom); MS (CI,CH$_4$) 183 (M + H$^+$).

Kinetic Studies. A 20 mM solution of tetramethylammonium 2-nitropropanate in acetonitrile is prepared as described above. It is transferred, in the dark, under argon, into an equal volume of a deoxygenated solution of 4-nitrocumyl chloride (4 mM) in acetonitrile. The transfer duration is less than one minute. The solution is continuously stirred. At different reaction times, 100 μL of the solution is sampled and immediately added to 100 μL of an acetonitrile solution of acetic acid in order to quench the unreacted nucleophile. The resulting solution is then analyzed by HPLC.

The same reaction procedure was followed in the experiments where the reaction was carried out under irradiation (continuous irradiation with a 150-W xenon lamp). It was also employed in the experiments where the reaction was carried out, in the dark, in the presence of di-*tert*-butyl nitroxide (3.24 mM).

In all cases, the samples were analyzed by a high-pressure liquid chromatography (Gilson instrument) with UV detection at 270 nm. The concentrations of each product were determined by comparison with authentic samples.

Electrochemical Measurements. The working electrode was a 3 mm-diameter glassy carbon disk carefully polished before use. The counter-electrode was a platinum wire and the reference electrode an aqueous SCE electrode. The potentiostat, equipped with a positive feedback compensation and current measurer, was the same as previously described.[31]

The experiments devised for determining the rate constant of coupling between the 4-nitrocumyl radical and the 2-nitropropanate ion by direct cyclic voltammetry or redox catalysis must be carried out rapidly before the thermal reaction has time to take place to a significant extent. The following procedure was applied in this purpose. A 10 mL solution of 2 times the final concentration of 4-nitrocumyl chloride is prepared and divided into two 5 mL portions. Mixing one of these portions with 5 mL of a solution of pure supporting electrolyte and recording of the voltammogram allows the determination of the peak current in the absence of nucleophile, i_p^0. Rapid mixing, within a few seconds, of the second of these portions with 5 mL of a solution containing 2 times the final concentration of the nucleophile and immediate recording of the voltammogram allows the determination of the peak current in the presence of nucleophile, i_p.

Quantum Mechanical Calculations. The calculations were performed with the Gaussian 94 package[32a] using the B3LYP[32b] density functional method with a 6-31G*[32c] basis set. The geometries and electronic energies of 4-nitrocumyl chloride, 4-nitrocumyl radical, and of the chloride atom were calculated by full optimization of the conformations. The enthalpies and molar entropies were obtained after calculation of the frequencies. These values were corrected by a scaling factor (0.9804) applied to the zero-point energies and thermal energy corrections.[32d]

The radii of the equivalent spheres of the various species of interest were obtained by means of a volume calculation on the optimized geometries, meaning the volume inside a contour of 0.001 electrons/ bohr^3 density.

The heterogeneous internal reorganization factor of the nucleophile was calculated as follows.[33] The intramolecular reorganization factor for the electrochemical oxidation of the nucleophile, λ_i^{el} is obtained from

$$\lambda_i^{el} = \frac{E_2 - E_3 + E_4 - E_1}{2}$$

where E_1 and E_3 are the optimized energies of Nu$^-$ and Nu$^\bullet$, respectively, while E_2 is the energy Nu$^\bullet$ in the geometry of Nu$^-$, and E_4 is the energy of Nu$^-$ in the geometry of Nu$^\bullet$.

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