Review Article

On Radical Anions in Elucidation of Mechanisms of Organic Reactions†

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Radical anions have been used to investigate the role of electron transfer in nucleophilic reactions and to obtain reduction potentials of short-lived radicals. In the first type of investigation the radical anions have been used to establish the dependence of the rate of electron transfer from an outer-sphere electron donor to a given substrate, to establish the stereochemistry of a radical coupling with the substrate, and to find the entropy and enthalpy of activation of electron transfer reactions compared with polar reactions. The potentials of short-lived radicals have been obtained from the competition between coupling of a radical with a radical anion and the reduction of the radical by the radical anion. The potentials have been used to rationalize some reactions such as the occurrence of radicals in certain Grignard reactions and the photochemical pinacolization of benzophenone in 2-propanol.

Radical anions have inherently the possibility to react as radicals, nucleophiles, bases or electron donors, but the role of a radical anion in a reaction cannot always be placed in one of these categories. However, by suitable choice of substrates and reaction conditions it may be possible to have reactions where one of the properties mentioned may predominate. In the following the use of the electron donating properties of radical anions will be explored.

Electron transfer in the aliphatic nucleophilic substitution and related reactions. Radical anions of aromatic and heteroaromatic compounds have been suggested to react with alkyl halides through an initial transfer of an electron;[1–3] there is, however, not universal agreement on the electron transfer (ET) being an outer-sphere ET,[4] but some experimental evidence suggests that the inner-sphere component of the ET is of significance mostly for the ET to methyl chloride[5] but insignificant for ET to sterically more hindered alkyl bromides and iodides.[5]

ET has been shown to be involved in aliphatic nucleophilic substitution in some cases; derivatives of *p*-nitrobenzyl halides and 2-(4-nitrophenyl)-2-nitropropane[6] react with certain nucleophiles in an $S_{RN}1$ reaction

and ET has been suspected in other aliphatic nucleophilic substitutions.[7] Our interest in this reaction came from the observation that *tert*-butyl bromide and dimethyl-(*tert*-butyl)sulfonium iodide reacted in DMF with the electrogenerated anion of 4-methoxycarbonyl-1-methyl-1,4-dihydropyridine (1⁻) to 4-*tert*-butyl-4-methoxycarbonyl-1-methyl-1,4-dihydropyridine (2) [eqn. (1)].[8] The reaction could not be a classical S_N2 reaction for steric reasons, since the methyl groups in dimethyl-(*tert*-butyl)sulfonium would be attacked rather than the *tert*-butyl group, and an S_N1 reaction is unlikely, as the *tert*-butyl bromide did not form *tert*-butyl iodide in DMF in the presence of an excess of tetrabutylammonium iodide, at least not on the timescale of the experiment (hours, 25 °C). A reaction between the *tert*-butyl radical and 1⁻ in an $S_{RN}1$-like fashion is highly unlikely as the steady-state concentration of the nucleophile 1⁻ is negligible under the reaction conditions.
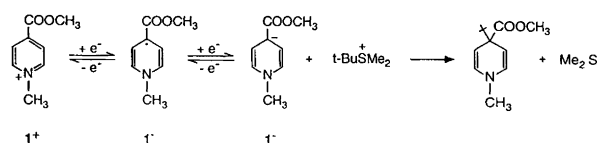
It was therefore suggested that the enolate ion 1⁻ had transferred an electron to the substrate which cleaved to a *tert*-butyl radical and the leaving group, and that the
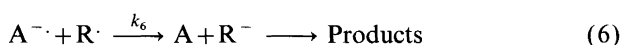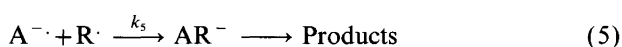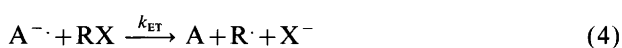
radical **1·** and *tert*-butyl radical coupled to give the product. It was also proposed[8] that there might be found reactions with transition states (TS) ranging from the classical S_N2 TS, with an approximately equal bonding of the central carbon to both the incoming nucleophile and the leaving group, to an ET TS, in which there is a negligible bonding (the limit is usually arbitrarily put to 1 kcal mol^{-1}) between the nucleophile and the central carbon. In such a TS the distance between the nucleophile and the central carbon would be greater than in the classical S_N2 TS and the nucleophile would not need to attack along the C–X axis. The reaction between **1**$^-$ and *tert*-butyl bromide could thus be described by eqn. (2).

$$1^- + t\text{-BuBr} \rightarrow [1^\cdot + t\text{-Bu}^\cdot + \text{Br}^-] \rightarrow 2 + \text{Br}^- \qquad (2)$$

ET in different organic reactions has been discussed by several authors[9-12] and Shaik and Pross[13] have pointed out that the net result of an S_N2 reaction is the transfer of one electron from the nucleophile to the leaving group rather than the electron pair depicted in most textbooks. They used the term 'electron shift' to distinguish the formal electron movement from that usually understood by electron transfer. It would, however, be of interest to investigate whether this formal electron shift under certain experimental conditions could represent an actual electron transfer. The reactions shown in eqns. (1) and (2) seemed to be representatives for such conditions, but in order to have arguments other than product studies, three types of experiment were carried out, *viz.*, kinetic measurements, stereochemical studies, and determination of thermodynamic parameters.[14]

1. Kinetic measurements. The reactions between radical anions of aromatic and heteroaromatic compounds and alkyl halides are described by the eqns. (3)–(6).

$$A + e^- \rightleftharpoons A^{-\cdot} \qquad (3)$$

$$A^{-\cdot} + RX \xrightarrow{k_{ET}} A + R^\cdot + X^- \qquad (4)$$

$$A^{-\cdot} + R^\cdot \xrightarrow{k_5} AR^- \longrightarrow \text{Products} \qquad (5)$$

$$A^{-\cdot} + R^\cdot \xrightarrow{k_6} A + R^- \longrightarrow \text{Products} \qquad (6)$$

The idea behind the kinetic test is to compare the rate constant k_{SUB} of the substitution of a nucleophile (e.g., **1**$^-$) on a certain alkyl halide with the rate constant (k_{ET}) of electron transfer from an outer-sphere electron donor with the same standard potential and reorganization energy (λ) as the nucleophile to the same alkyl halide. The ratio k_{SUB}/k_{ET} is a measure of the difference in activation energy between the substitution reaction and the outer-sphere ET TS. If $k_{SUB}/k_{ET} \sim 1$ then the rate determining step would be assumed to be the transfer of an electron from the nucleophile to the alkyl halide for this aliphatic nucleophilic substitution.[15]

2. Stereochemical probes. A classical S_N2 reaction would result in an inversion of the configuration at the central carbon, whereas in a radical reaction a stereochemical equilibration would be expected, although it has been argued that an inversion does not exclude a radical reaction.[16] Under all circumstances racemization would exclude an S_N2 mechanism.

3. Activation parameters. An S_N2 reaction would be expected to have, compared with an ET reaction, a relatively low enthalpy of activation due to the bonding stabilization in the TS, but a relatively more negative entropy of activation. The S_N2 TS is tighter than the ET TS, and it is generally assumed that strict stereochemical requirements in the TS result in a more negative $\Delta S\ddagger$.

Kinetic test for electron transfer. In the middle of the 1970s a revival of the use of indirect electrolysis[17-19] in organic chemistry occurred, especially with respect to the reduction of aromatic[17] and aliphatic[17,18] halides by radical anions of aromatic and heteroaromatic compounds. The occurrence of competition between coupling [eqn. (5)] and reduction [eqn. (6)] in the reaction between aromatic radical anions and aliphatic radicals, produced by reduction of alkyl halides, was established.[17]

For the kinetic test radical anions of aromatic hydrocarbons and heteroaromatic compounds were chosen as one-electron donors;[15] they are stable in the absence of proton donors and they have a relatively low reorganization energy connected with the electron transfer.

The rate of electron transfer from aromatic radical anions to the substrate may be measured by techniques such as cyclic voltammetry,[20] linear sweep voltammetry,[20] double potential step chronoamperometry[21] and homogeneous kinetic measurements using a rotating disc electrode or an ultra-microelectrode[22] to monitor the reaction. By these methods second order rate constants from about 10^{-3} M^{-1} s^{-1} to 10^6 M^{-1} s^{-1} may be measured. The results obtained are usually depicted in a plot with the driving force (proportional to the standard potential of the aromatic compound, E_A°) as the abscissa and the logarithm of the second order rate constant of ET as the ordinate.

The reaction between aromatic radical anions and alkyl halides probably involves a dissociative electron transfer which means that the electron transfer to the alkyl halide and the cleavage of the C–X bond are concerted. By applying Marcus theory[23] to the reaction between radical anions and alkyl halides Eberson[11] found empirically that the reorganization energy λ was large, which he attributed to a high degree of bond breakage in the TS. An important parameter in the determination of λ is thus the C–X bond strength. On the basis of Morse potential curves Savéant[24] later suggested that the sum of the bond strength and the solvent reorganization energy was a measure of λ_{dis}, thus $\lambda_{dis} = \lambda_o + D_{RX}$, where λ_o is the solvent reorganization energy.

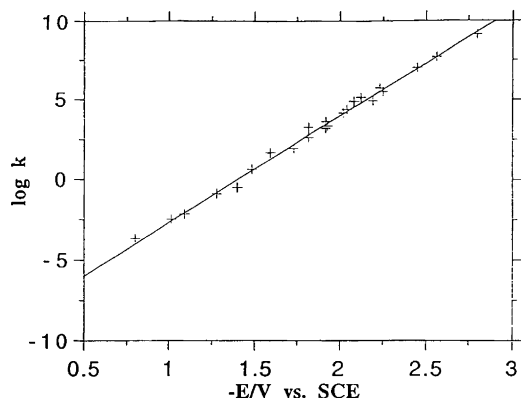In Fig. 1 log k_{ET} of the reaction between aromatic

Fig. 1. Logarithm of the rate constant (k_{ET}) of the reaction between t-BuBr and different aromatic anion radicals $(+)$ vs the redox potential of the aromatic compound $(-E_A^\circ$ vs. SCE). From Ref. 25.

radical anions and t-BuBr is shown as a dependence of the driving force;[25] the fastest reactions $(k_{ET} > 10^7 \text{ M}^{-1} \text{ s}^{-1})$ have been measured by pulse radiolysis.[26] In Fig. 1 a linear dependence is assumed, whereas theory suggests a parabola. Possibly an inner-sphere component becomes more significant when the ET becomes more endergonic and the reaction thus gradually develops more S_N2 character concurrently with the decrease of the rate of the ET. Together the range of rate constants spans 13 orders of magnitude, and as seen from Fig. 1 the points seem best represented by a straight line.[27]

The reactions between nucleophiles and alkyl halides have been followed with similar methods as used for the radical anions, and the rate constant of the substitution reaction, k_{SUB}, measured. The logarithm of the ratio of the rate constants, k_{SUB}/k_{ET}, is a measure of the activation energy of the substitution reaction compared with that
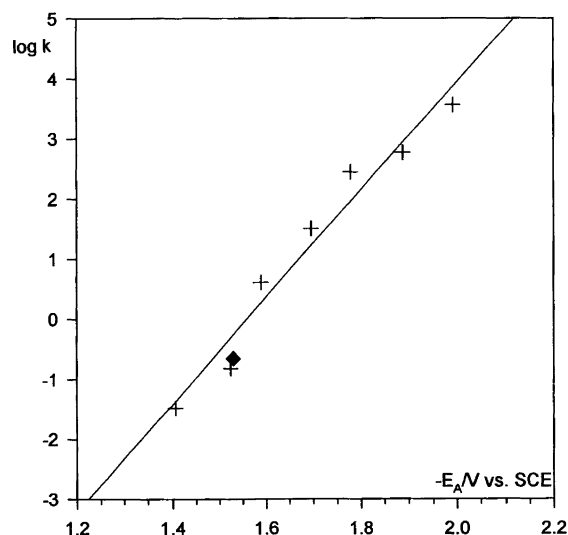
of the outer-sphere ET and is thus taken as an indication of the inner-sphere (S_N2) stabilization of the transition state.[15]

In Fig. 2 the crosses represent rate constants for the ET reaction of aromatic anion radicals with isobornyl bromide (3), and the diamonds the rate constant for the substitution reaction of 1^- with 3. As the k_{SUB} of 1^- falls on the straight line through the points for k_{ET}, $k_{SUB}/k_{ET} \sim 1$ in this case, the rate-determining step for this aliphatic nucleophilic substitution is assumed to be the transfer of an electron.

In Fig. 3 similar data are presented for the reaction of 1^- with 2-bromobutane (4). The ratio, k_{SUB}/k_{ET}, for 4 is 170 whereas it for ethyl bromide (5) it is 2500. These numbers may indicate some bonding stabilization in the transition state compared with the outer-sphere ET reaction, or they may be interpreted as a result of a competition between two reaction paths, outer-sphere ET and classical S_N2. We prefer the former point of view, but there is no compelling experimental evidence either way.

If one accepts the model that the ET TS and the classical S_N2 TS with significant bonding to both the incoming and leaving group leading to a stabilization (20–30 kcal mol^{-1}) in the TS are extremes and that there exist in between them transition states with different bonding stabilizations (in a somewhat similar way as is often advocated for the S_N1–S_N2 reactions), then the reactions between 1^- and 4 and 5 have transition states relatively close to the ET transition state with a rather low bonding stabilization (2–5 kcal mol^{-1}). A similar interpretation has been made on basis of the valence bond configuration mixing model (VBCM).[15]

In our investigations the standard nucleophile has been 1^-, but other easily oxidizable, delocalized anions, which
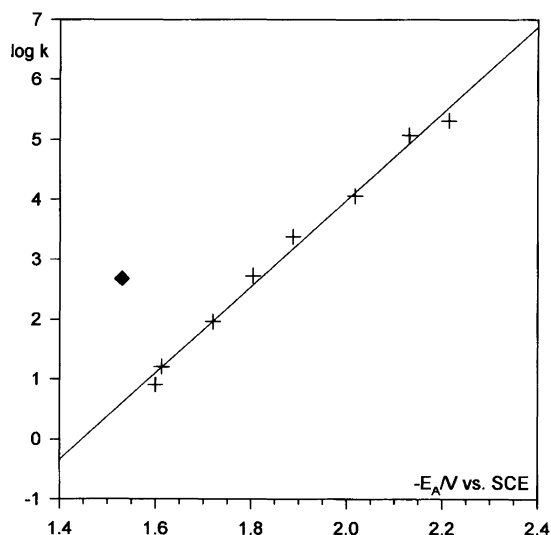

Fig. 2. Logarithm of the rate constant (k_{ET}) of the reaction between isobornyl bromide and different aromatic anion radicals $(+)$ or 1^- (k_{SUB}) $(\blacklozenge)$ vs. the redox potential $(-E_A^\circ)$ of the aromatic compound. The potentials are measured against SCE. From Ref. 14.

Fig. 3. Logarithm of the rate constant (k_{ET}) of the reaction between 2-bromobutane and different aromatic radical anions $(+)$ or 1^- (k_{SUB}) $(\blacklozenge)$ vs. the redox potential $(-E_A^\circ)$ of the aromatic compounds. The potentials are measured against SCE. From Ref. 14.

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give stable radicals on oxidation, behave similarly[28] in reactions with alkyl halides, and similar k_{SUB}/k_{ET} values are obtained. Examples have also been found of dianions[28] of aromatic compounds and neutral nucleophiles[15] reacting with alkyl halides with ET and similar values for k_{SUB}/k_{ET} are found.

It would be of interest to use nucleophiles other than 1^- (and similar compounds) in order better to bridge the gap between the ET TS and a classical S_N2 TS. Superoxide, $O_2^-\cdot$, may react as a nucleophile and an electron donor. The rate of the reaction between $O_2^-\cdot$ and alkyl halides[29] can be measured with the usual electrochemical techniques, but the interpretation of the k_{SUB}/k_{ET} values obtained is more difficult due to the lack of consistent data for the self-exchange reorganization energy $\lambda(0)$ for $O_2^-\cdot$; a value of about 45 kcal mol^{-1} is probably the most reliable.[30] The directly measured values for k_{SUB}/k_{ET} for the reaction between $O_2^-\cdot$ and some alkyl halides span a range from less than 0.6 for 1-iodoadamantane to 10^9 for butyl chloride; these k_{SUB}/k_{ET} values may have to be multiplied by a factor of ca. 500 due to the difference in the self-exchange reorganization energies between $O_2^-\cdot$ and the other ET donors. If so the corresponding stabilization energies range from below 4 kcal mol^{-1} to 17 kcal mol^{-1}. The results illustrate that the same nucleophile/electron donor may react mainly as an electron donor towards sterically very hindered alkyl halides and as a typical nucleophile with sterically less hindered electrophiles.

Stereochemical investigations. As is well known, the typical S_N2 reaction leads to inversion at the central carbon atom. Reduction of anthracene in DMF in the presence of bornyl and isobornyl bromide[31] gave the same 1:1 mixture of 9-(*exo*-2-bornyl)-9,10-dihydroanthracene and 9-(*endo*-2-bornyl)-9,10-dihydroanthracene. Curiously enough it happened to be an approximately 1:1 mixture of *exo* and *endo* product; a certain preference for the *exo*-substitution would have been expected. Small amounts of 1- and 2-substituted bornyldihydroanthracenes were detected by ^{1}H NMR and GC–MS.

The steric results indicate that, in the reaction between anthracene radical anion and bornyl and isobornyl bromide, the stereochemical information of the substrate is lost during the reaction and that the reaction is an outer-sphere ET. This finding together with the evidence presented above further indicates that some aliphatic nucleophilic substitutions with aromatic radical anions may proceed through outer-sphere ET and that the stabilization in the transition state is very small. In reactions with less sterically hindered alkyl halides an inner-sphere ET component may influence the stereochemical results.

Racemization in an aliphatic nucleophilic substitution with 1^- would be expected only in the cases when $k_{SUB}/k_{ET} \sim 1$, and the synthetic difficulties of making an optically pure chiral tertiary halide and to establish the degree of chirality in the substitution product made us turn to the *exo/endo* relation of the bornyl system.

Electrochemical reduction of 1^+ to 1^- in the presence of bornyl bromide in DMF gave two substitution products A and B in the proportion 1.4:1;[32] when isobornyl bromide and 1^- reacted, the same substitution products A:B = 1:1.3 were found. The results are explicable if it is assumed that the 2-bornyl radical is a common intermediate in the reaction of 1^- with both bornyl and isobornyl bromide. This suggests that when the kinetic results indicate $k_{SUB}/k_{ET} \sim 1$ then it may be expected that predominant racemization takes place during the substitution.

Whereas the reaction between bornyl bromide and 1^- gave the same ratio A:B at -40 and 50 °C, the reaction between isobornyl bromide and 1^-, although giving same mixture of A and B at 25 and 50 °C, at -40 °C gave a greater difference between the two stereoisomers A and B than at higher temperatures; it turned out that the major isomer was formed by inversion.[33] This suggests a certain inner-sphere component at low temperatures or perhaps that the leaving bromide ion hinders the approach of the nucleophile as is found in some S_N1 reactions.

Activation parameters. The entropy of activation for the S_N2 reaction should be more negative than that of the ET reaction; this is, among other things, caused by the strict geometrical requirements and associative character of the S_N2 TS. On the other hand, the enthalpy of activation of the S_N2 reaction would be expected to be smaller than that of the ET reaction due to the bonding stabilization in the TS. In order to obtain these parameters the dependence of the rate of reaction on the temperature was measured. For a 'well-behaved' reaction a linear connection between $\ln k$ and T^{-1} is expected from the Arrhenius equation.

In Fig. 4 the results for the reaction between the radical anion of anthracene and butyl bromide in the interval -50 °C to 50 °C are shown[25] and for this and all the
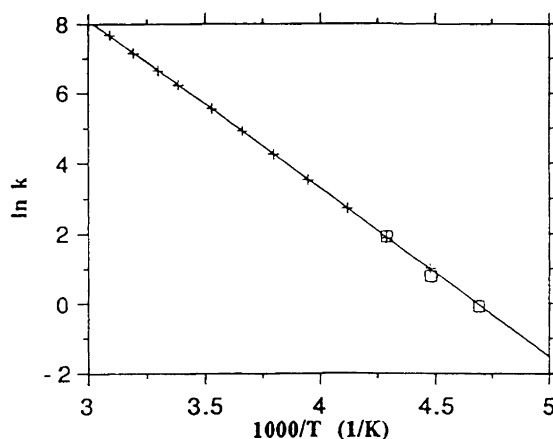

Fig. 4. Temperature dependence of the rate constants of the reaction between anthracene radical anion and 1-bromobutane in DMF–TBABF$_4$ measured by CV (+) and a potentiostatic method using a rotating disc electrode (□). From Ref. 25.

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Table 1. Some activation parameters from the reactions between aromatic anion radicals or 1^- with alkyl halides. $\Delta S^{\ddagger}$ in cal mol^{-1} K^{-1} and $\Delta H^{\ddagger}$ and $\Delta\Delta G^{\ddagger}_{\Delta S} = 298(\Delta S^{\ddagger}_{298,A^-} - \Delta S^{\ddagger}_{298,1^-})$ in kcal mol^{-1}.

Alkyl halide	$\Delta S^{\ddagger}_{298,A^-}$	$\Delta S^{\ddagger}_{298,1^-}$	$\Delta\Delta G^{\ddagger}_{\Delta S}$	$\Delta H^{\ddagger}_{298,A^-}$	$\Delta H^{\ddagger}_{298,1^-}$	$\Delta\Delta H^{\ddagger}_{298,A^-,1}$	$\dfrac{k_{SUB}}{k_{ET}}$
Butyl bromide	−16.4	−22.2	4.0	12.0	6.3	5.7	400
sec-Butyl bromide	−16.5	−21.2	3.7	11.6	7.4	4.2	170
tert-Butyl bromide	−8.4	−15.8	2.2	13.4	11.1	2.3	2.5
exo-Norbornyl bromide	−10.8	−16.2	1.6	15.4	13.2	2.2	1.7
1-Bromoadamantane	−7.6	−9.4	0.5	18.2	17.6	0.6	0.3
Bornyl bromide	−8.7	−8.9	0.1	17.7	17.2	0.5	0.2

other reactions between different radical anions and alkyl bromides investigated, we obtained a straight line. This we interprete to show *that in the temperature interval investigated (−50 °C to 50 °C) there is no change detectable, by this method, in the mechanism of the reaction between aromatic radical anions and alkyl bromides.*

From the Arrhenius plots the entropy and enthalpy of activation may be extracted.[25] In Table 1 are presented some values of entropy of activation $\Delta S^{\ddagger}_{298}$ for the reaction between radical anions and some alkyl halides together with corresponding values for the reaction between 1^- and the same alkyl halides.

In the reactions between radical anions and sterically hindered alkyl halides including t-BuBr approximately the same value for $\Delta S^{\ddagger}_{298}$ is found, and this value is taken as standard value of $\Delta S^{\ddagger}_{298}$ for an outer-sphere dissociative ET. The somewhat more negative values for $\Delta S^{\ddagger}_{298}$ for primary and secondary alkyl halides could be due to a bonding interaction in the TS, but other interpretations may be possible.

In the reaction with the enolate anion 1^- only the most sterically hindered alkyl halides, 1-bromoadamantane and bornyl bromide, have the same values for $\Delta S^{\ddagger}_{298}$ as the radical anions. This is in accordance with the above-mentioned stereochemical results and the $k_{SUB}/k_{ET} \sim 1$ which indicates that, for these sterically very hindered (against back-side S_N2 attack) alkyl halides, the substitution reaction may be described as an outer-sphere dissociative ET followed by a radical coupling. The sterically less hindered alkyl halides, even t-BuBr and exo-norbornyl bromide, show a more negative $\Delta S^{\ddagger}_{298}$, which may be interpreted as a slightly more S_N2-like TS. In the fourth column the difference between the values of the reaction with an outer-sphere electron donor $(\Delta S^{\ddagger}_{298,A^-} = −9 \text{ cal mol}^{-1} \text{ K}^{-1})$ and with 1^- is translated into differences in activation energy due to the entropy effect, $\Delta\Delta G^{\ddagger}_{\Delta S} = T(\Delta S_{298,A^-}) − (\Delta S_{298,1^-})$.

In Table 1 the values for the enthalpy of activation corresponding to the entropies are also given.[25] In the seventh column the difference $\Delta\Delta H^{\ddagger}_{298}$ between the values in columns 5 and 6 is given and in the last column the k_{SUB}/k_{ET} values are tabulated. As expected the primary and secondary alkyl halides have the highest values of $\Delta\Delta H^{\ddagger}_{298}$ indicating the higher stabilization of the TS in their reactions with 1^-. Again, only bornyl bromide and

1-bromoadamantane have the same enthalpy of activation in the reactions with 1^- and radical anions. A comparison of the numbers in columns 7 and 8 indicates the close connection between the two; a linear dependence between $\Delta\Delta H^{\ddagger}_{298}$ and $\log(k_{SUB}/k_{ET})$ is found; it suggests that k_{SUB}/k_{ET} is a good parameter to characterize the S_{ET}/S_N2 spectrum.

The results from the measurements of the activation parameters as well as those from the kinetic (k_{SUB}/k_{ET}) and stereochemical investigation show that there is a gradual change from the characteristics of a pure ET reaction to those of a classical S_N2 reaction. This may be interpreted in two ways; the observation may be caused by the competition between two distinct reaction routes, ET and S_N2, with only two types of TS, an outer-sphere dissociative ET followed by a radical coupling or a classical S_N2 TS; an alternative explanation is that there are transition states with structures with varying degrees of inner-sphere (bonding) stabilization ranging from the pure ET TS to the classical S_N2 TS. Although there is no definite evidence either way the fact that we find a linear dependence of ln k vs. T^{-1} for all the substitution reactions we have investigated suggests that there is no shift in reaction path in this interval. The observed difference in activation parameters would indicate that a break in the Arrhenius plot should be observed.

If one defines any TS which is not a pure outer-sphere ET TS as an S_N2 TS then nearly all the reactions discussed here are S_N2 reactions. In analogy with the S_N2–S_N1 and E1–E2–E1cb types of reaction it seems useful to have a special designation (e.g., S_{ET}/S_N2-hybrid) for reactions in the 'grey' area between ET and S_N2 TS in which the TS has characteristics of both model reactions. A description of the criteria to place a given reaction in a suitable category could be to use k_{SUB}/k_{ET}, or activation parameters, or reactions with some racemization as a characteristic of the 'grey area'; the most convenient criteria for an ET/S_N2-hybrid would probably be k_{SUB}/k_{ET}.

The results described above give hints on some of the important parameters which determine whether an ET, S_N2 or S_N1 type of reaction is likely to be favored. Besides the parameters, steric properties and standard potentials of the reaction partners, discussed below, other

properties of the system influence the reaction route. Our results suggest the following with regard to potentials and steric properties.[34]

(a) The S_N2 reaction is likely to take place, unless the steric hindrance prohibits an approach of the reagents to a distance at which some bonding stabilization can occur.

(b) If the steric conditions prevent bonding stabilization in the transition state and $\Delta E \leqslant 0$ V then the ET reaction is likely to occur; the ET reaction is favored by a delocalized HOMO of the donor.

(c) In the cases where steric factors inhibit the S_N2 reaction and ΔE is too positive to allow ET to proceed at a reasonable rate, then the classical S_N1 reaction may come into play by creating a planar carbocation R^+ with less steric hindrance than RX and which also is a much better electron acceptor than RX; this facilitates the bonding to the donor/nucleophile. Even then, if the nucleophile is very difficult to oxidize, the equivalent of being a very poor electron donor, the S_N1 reaction may fail to occur; e.g., in aqueous solution anions as perchlorate or tetrafluoroborate are practically unreactive in S_N1 reactions.

X-Philic reactions. In some aliphatic nucleophilic reactions with halogenated compounds, the nucleophile attacks the halogen rather than the carbon, and the carbon then becomes a leaving group in the form of a carbanion. The nucleophiles in such reactions are 'soft', that is, they are easily oxidizable. Such X-philic[35] or Z-philic[36] reactions have been less investigated than the classical S_N2 reaction. A special type of X-philic reaction is the reductive elimination of vic-dihalides by iodide, in which iodine and an alkene is formed.
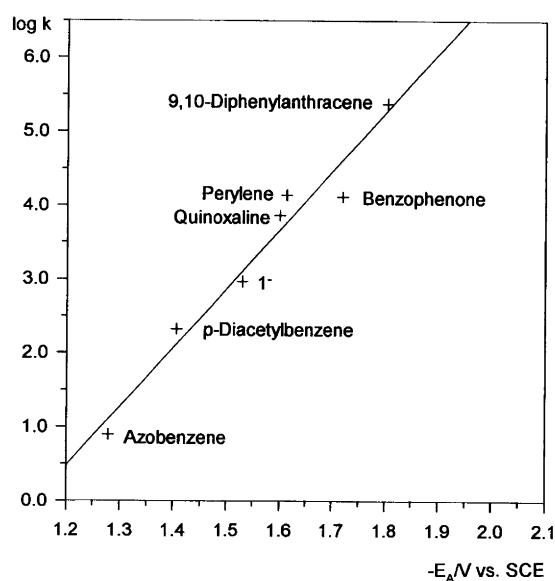
As such reactions proceed only when the nucleophile has a low oxidation potential it was of interest to investigate whether some X-philic reactions could proceed via an ET reaction with the transfer of an electron being the rate determining step.

The method used was similar to that described above; the rate constant of the ET from a series of radical anions to a given vic-dihalide was plotted against the oxidation potential of the radical anion and a parabola was drawn through the points (Fig. 5). The points of the rate constant for the reduction of the same dihalide by 1^- was found near the curve.[37] The rate-determining step was then assumed to be the transfer of an electron. Furthermore, measurement of the activation parameters, $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$, showed that the same activation entropy and enthalpy was found in the S_{ET} reaction and the reductive elimination. It remains to be seen which other nucleophilic reactions show examples of outer-sphere ET.

Redox potentials of short-lived radicals.[38] The thermodynamic properties of radicals are of interest for the understanding of many reactions, but relatively few redox potentials of short-lived radicals have been measured. Approximate oxidation potentials of anions have been obtained by anodic voltammetry.[39] Using fast CV at ultramicroelectrodes reversible oxidation potentials of fluorenide anions have been measured; the fluorenide radicals have life-times in the μs range.[40] The potentials of relatively long-lived (in the ms-range) radicals have been obtained by second harmonic ac-voltammetry[41] and photomodulated voltammetry[42] and by laser photoelectron spectroscopy.[43] Direct cyclic voltammetry may in some cases be used to estimate reduction potentials of short-lived radicals.[44]

Another method for the determination of redox potentials of short-lived radicals is based on the competition between coupling and reduction of radicals by radical anions. It was noticed early on[17] that the reaction between common aromatic radical anions (for example anthracene) and benzyl chlorides resulted in a catalytic

Fig. 5. Dependence of rate constants for the reaction between different electron donors including 1^- and meso-1,2-dichloro-1,2-diphenylethane on the reversible potential of the donors. Redrawn from Ref. 37.
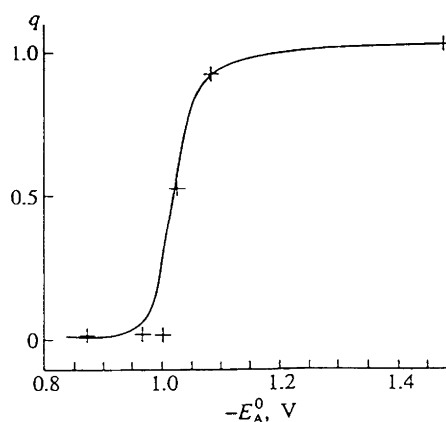

Fig. 6. q-Values for benzyl chloride vs. the redox potential (vs. Ag/AgI, $I^- = 0.1$ M) of some radical anions in DMF–TBABF$_4$. From Ref. 45.
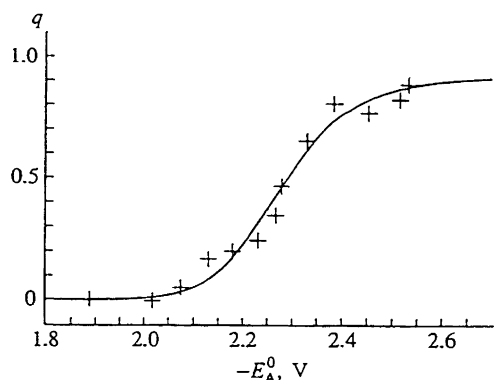
Fig. 7. q-Values of *exo*-norbornyl chloride vs. the redox potential (vs. SCE) of some aromatic radical anions in DMF–TBABF$_4$. From Ref. 49.

reduction of the halide [eqn. (6)], whereas the reaction with alkyl halides either gave a pure coupling [eqn. (5)] or coupling accompanied by a degree of catalytic reduction.

This observation has been interpreted as a competition between the coupling of the radical anion with the aliphatic radical [eqn. (5)] and the reduction of the radical by the radical anion [eqn. (6)]. When the reduction potential of the radical anion was more negative than the reduction potential of the radical, reduction took place, but when the opposite was the case the electron transfer from the radical anion to the aliphatic radical could not compete with the coupling reaction.[45-50]

The competition parameter $q = k_6/(k_6 + k_5)$ can be measured in different ways.[47] A plot of the q-values versus the standard potential of the different radical anions gives an S-shaped curve (Figs. 6 and 7). The midpoint of the curve, the reduction potential of the radical, $E_q^{\ddagger}$, characterizes the transition between follow-up reactions of a radical or carbanionic nature of an electrochemically produced radical.

From the potential $E_q^{\ddagger}$ the standard potential of the radical may be obtained if the reorganization energy $\lambda(0)$ of the radical is known. Direct determination of $\lambda(0)$ by, for instance, EPR is not possible due to the short life-time of these radicals, but an indication of its value can be gained from the width of the q versus E_A° plot[47,50] by fitting the plot to curves obtained on the basis of Marcus theory. As seen from the plots of benzyl

chloride (Fig. 6) and *exo*-norbornyl chloride (Fig. 7) the width of the S-shaped curve is much broader for the *exo*-norbornyl chloride than for benzyl chloride reflecting the larger $\lambda(0)$ for the unconjugated norbornyl radical compared with that of the conjugated benzyl radical.[51]

By measuring q-values and estimating the $\lambda(0)$ of the radicals, values for the standard potentials of a number of carbon-centered aliphatic,[48,49] allyl, [49] benzyl[45] and acyl[50] radicals have been obtained. The value of k_5 has been measured for some radicals[46] using 'radical clocks'.[52] The uncertainty of the potentials is caused mainly by the difficulty in obtaining exact values for $\lambda(0)$. This is not a serious problem for the benzyl radicals as indicated by the good correspondence with the results obtained by the Canadian group[42] (Table 2).

In Tables 2, 3 and 4, $E_q^{\ddagger}$ and E° for some alkyl, allyl, propargyl and acyl radicals are tabulated. Values for the butyl radicals have previously been obtained by Savéant *et al.*[44] Their values are in reasonable agreement with those in Table 3 . The uncertainty of the value of $\lambda(0)$ influences the standard potentials so much that for aliphatic radicals [$\lambda(0)$ estimated to be 50 kcal mol^{-1}] the potentials are uncertain by ±150 mV. When better values for $\lambda(0)$ of the radicals are known, more reliable standard potentials can be calculated from $E_q^{\ddagger}$ for which the uncertainty is about 50 mV.

Despite the uncertainty in the potentials of the alkyl radicals their relative values are less uncertain. As expected the *tert*-butyl radical has a more negative E° than *sec*-butyl and the *n*-butyl is less negative. The perhaps most surprising result is the potential obtained for the methyl radical, which by this method is found to be less negative even than the benzyl radical. However, estimation of the standard potentials of the methyl and some other aliphatic radicals in water[49] using thermodynamic data gives a similar result.

Radicals have often been described as 'nucleophilic' or 'electrophilic'. There is a clear connection between the estimated standard potentials of radicals and their nucleophilicity, that is, the more negative the standard potential of the radical, the greater the tendency of the radical to attack positions bearing a positive charge. It remains to be seen to what extent the nucleophilicity and electrophilicity of radicals can be expressed quantitatively by their standard potential.

Table 2. Reduction potentials $E_q^{\ddagger}$, standard potentials E°_{R/R^-}, half-wave potentials $E_{1/2}$ (V vs. SCE) and self-exchange reorganization energies $\lambda_{R/R}$-(0) of some substituted benzyl radicals in DMF–TBABF$_4$.

RX	$-E_q^{\ddagger}/V$	$-E^{\circ}_{R/R^-}/V$	$-E_{1/2}/V^a$	$\lambda_{R/R}$-(0)/kcal mol^{-1}
Benzyl chloride	1.42	1.40	1.45	10
1-Chloro-1-phenylethane	1.59	1.57	1.60	10
2-Chloro-2-phenylpropane	1.59	1.57	1.73	10
2-Chloro-2-phenylbutane	1.59	1.57	—	10
Benzhydryl chloride	1.09	1.07	1.14	10
4-Methoxybenzyl chloride	1.49	1.47	1.75	10
4-Chlorobenzyl chloride	1.42	1.40	1.40	10

^{a} From Ref. 45.

Table 3. Reduction potentials E_q^i, standard potentials E_{R/R^-}^o (V vs. SCE) and self-exchange reorganization energies $\lambda_{R/R^-}(0)$ for alkyl and allyl radicals in DMF–TBABF$_4$.

RX	$-E_q^i/V$	$-E_{R/R^-}^o/V^a$	$\lambda_{R/R^-}(0)/\text{kcal mol}^{-1}$
Methyl iodide	1.78	1.19	50
Ethyl bromide	2.23	1.64	50
Propyl bromide	2.22	1.63	50
Butyl chloride	2.20	1.62	50
2-Chlorobutane	2.30	1.72	50
2-Chloro-2-methylpropane	2.35	1.77	50
Chlorocyclopentane	2.30	1.72	50
Chlorocyclohexane	2.26	1.68	50
1-Chloro-2-methylpropane	2.15	1.57	50
2-Chloropropane	2.30	1.72	50
exo-Norbornyl chloride	2.26	1.67	50
Isobornyl chloride	2.26	1.67	50
Bornyl chloride	2.26	1.67	50
1-Bromo/chloroadamantane	2.24	1.81	40
trans-2-Methoxy(bromo)cyclohexane	1.98	1.39	50
cis-2-Methoxy(bromo)cyclohexane	1.98	1.39	50
trans-2-Methoxy(bromo)cyclopentane	1.96	1.37	50
Allyl chloride	1.54	1.39	20
3-Chloro-2-methyl-1-propene	1.54	1.39	20
3-Chloro-1-propyne	1.40	1.25	20
4-Chloro-2-pentene	1.87	1.72	20
3-Chloro-1-butene	1.70	1.55	20

Table 4. Reduction potentials E_q^i, standard potentials E_{R/R^-}^o (V vs. SCE) and reorganization energies $\lambda_{R/R^-}(0)$ for acyl radicals in DMF–TBABF$_4$.

| RX	$-E_q^i/V$	$-E^o{}_{R/R^-}/V$	$\lambda_{R/R^-}(0)/\text{kcal mol}^{-1}$
Acetic anhydride	2.03	1.75	30
Acetyl chloride	1.98	1.70	30
Succinic anhydride	2.03	1.75	30
Phenylacetyl chloride	1.91	1.63	30
Benzoic anhydride	1.41	1.13	30
Benzoyl chloride	1.42	1.14	30
4-Methoxybenzoyl chloride	1.44	1.16	30
3-Methoxybenzoyl chloride	1.43	1.15	30
4-Chlorobenzoyl chloride	1.30	1.02	30
4-Cyanobenzoyl chloride	1.30	1.02	30
1-Naphthoyl chloride	1.35	1.07	30

^{a} The uncertainty in the determination of E_q^i and E_R^o is estimated to be ± 50 mV and ± 150 mV, respectively.[49] The uncertainty in $\lambda_R(0)$ is ± 10 kcal mol^{-1}.

The reduction potentials of the allyl and propargyl radicals are, in general, only a little more negative than those of the benzyl radicals, but substantially more positive than those of the alkyl radicals. This is in accordance with the ability of allyl and benzyl radicals to delocalize charge, in contrast with the alkyl system. Also, the values of the self-exchange reorganization energy $\lambda_R(0)$ (~ 20 kcal mol^{-1}) for the allyl radicals are closer to $\lambda_R(0)$ for the benzyl radicals (~ 10 kcal mol^{-1}) than to $\lambda_R(0)$ for the alkyl radicals (~ 50 kcal mol^{-1}). Recent ab initio calculations of the reorganization energies of the benzyl and butyl radicals are in accordance with that.[51]

Some applications of redox potentials of radicals. In many thermochemical cycles electron transfer to or from a radical is one of the steps. A knowledge of the redox

potentials of the radicals involved makes it possible to calculate, for instance, bond dissociation energies and dissociation constants. An account of such procedures has recently been published.[53]

The photoreduction of benzophenone by 2-propanol with formation of benzopinacol and acetone is a textbook reaction. After the transfer of a hydrogen atom the two radicals $Ph_2\dot{C}OH$ and $(CH_3)_2\dot{C}OH$ are formed [eqn. (7)]; why do these two carbon centered radicals not couple to a mixed pinacol?

$$Ph_2C{=}O + (CH_3)_2CHOH + h\nu \rightarrow Ph_2\dot{C}OH + (CH_3)_2\dot{C}OH \tag{7}$$
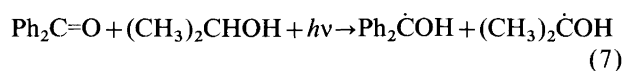
However, when acetophenone and methyl 1-phenylethyl ether are photolyzed, a similar hydrogen atom transfer occurs, but one obtains a product mixture close to the

statistical 1:2:1 of symmetric and crossed-coupling products.

If one calculates the energetics of the combined electron transfer and proton transfer from the redox potentials of the ketones and radicals involved, it turns out that in the former reaction the 2-hydroxy-2-propyl radical can reduce benzophenone whereas in the latter case the methyl 1-phenylethyl ether radical would not be able to reduce acetophenone and the radicals then couple without further redox reactions.[54]

From these results and the relevant redox potentials one would predict that photolyzing a mixture of p-methylacetophenone and 1-phenylethanol would give the three different coupling products but also, during the reaction, some acetophenone. The experiments are in accordance with that.[54]

The addition of Grignard reagents to ketones is generally described as a polar reaction in textbooks, but in some cases the product distribution indicates a radical reaction.[55] It is interesting that there is a good correspondence between the experimental results and the predictions made on basis of the redox potentials of the reactants, even if no steric and bonding interactions have been taken into account, the potentials are measured in DMF and not in diethyl ether, and the radical reaction may or may not be an outer-sphere electron transfer. In those cases the oxidation potential of the carbanion and the reduction potential of the ketone may be helpful for prediction of the reaction path. Reaction of benzophenone ($E° = -1.72$ V (SCE)) with tert-BuMgCl ($E°_{tBu·/t-Bu}- = -1.77$ V) and s-BuMgCl ($E_{s-Bu·/s-Bu}- = -1.72$ V) gives radical products whereas reaction with CH_3MgI ($E°_{CH_3·/CH_3}- = -1.19$ V) and $PhCH_2MgCl$ ($E°_{PhCH_2·/PhCH_2}- = -1.40$ V) gives no radical products. However, in the reaction with fluorenone ($E° = -1.19$ V) all of the Grignard reagents mentioned give the same products as formed when the radical anion of fluorenone reacts with the corresponding alkyl halides.[56]

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