Potential Dependence of Coupling vs. Reduction in the Reaction between Benzyl Halides and Anion Radicals

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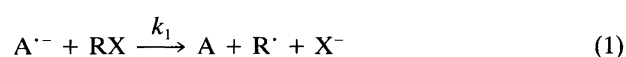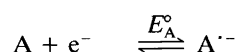
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Anion radicals of aromatic and heteroaromatic compounds with reduction potentials in a certain potential interval react with benzyl halides with dissociative electron transfer. The resulting benzyl radical $B^{\cdot}$ may either couple with or be reduced by another anion radical. If the reduction potential of the aromatic compound E_A° is more negative than a certain potential $E_{1/2}^q$ the anion radical $A^{\cdot-}$ will reduce the benzyl radical to the benzyl anion; if E_A° is less negative than $E_{1/2}^q$, coupling between $A^{\cdot-}$ and $B^{\cdot}$ will take place. The relation between $E_{1/2}^q$, which is defined as the potential at which half of the radicals are reduced and the other half couple, and the standard reduction potential $E^{\circ}(R^{\cdot}/R^-)$ for the benzyl radicals is discussed.

The reaction between chemically[1,2] and electrochemically[3–5] generated anion radicals and alkyl halides has been studied for several years, and it is generally agreed that the reaction involves an electron-transfer (ET) from the anion radical ($A^{\cdot-}$) to the alkyl halide (RX), although in some cases a competition between ET and an S_N2 reaction has been invoked to explain stereochemical results.[2]

The overall reaction between an anion radical and an alkyl halide is, in a number of cases, a reduction of RX rather than a coupling. The reactions may be formulated [eqns. (1)–(3)].

$$A + e^- \xrightleftharpoons{E_A^{\circ}} A^{\cdot-}$$

$$A^{\cdot-} + RX \xrightarrow{k_1} A + R^{\cdot} + X^- \tag{1}$$

$$A^{\cdot-} + R^{\cdot} \xrightarrow{k_2} AR^- \tag{2}$$

$$A^{\cdot-} + R^{\cdot} \xrightarrow{k_3} A + R^- \tag{3}$$

Reaction (1) is the rate-determining step; R^- and AR^- react further with electrophiles (HX, RX, etc.) to the final products.

Tertiary aliphatic alkyl halides have been observed to couple with anion radicals in most cases,[4] whereas benzyl chloride in many cases is reduced by anion radicals.[6] A reasonable hypothesis could be that the rate of reaction (3) for a given radical $R^{\cdot}$ depends on the redox potential of A; the more negative E_A° is, the higher the rate of reaction (3) is expected to be, and reaction (3) would thus be favoured in the competition with reaction (2).

The competition between (2) and (3) has been treated before with LSV (linear sweep voltammetry) and CV (cy-

clic voltammetry) by digital simulation;[7,8] a dimensionless competition parameter $q = k_3/(k_2 + k_3)$ was introduced.[7]

As the rate of reaction (3) is expected to be dependent on the redox potentials of both $A^{\cdot-}$ and $R^{\cdot}$, the latter is also of interest. Different techniques have been employed for the measurement of standard potentials of radicals. Pulse radiolysis has been used in connection with polarographic detection of radicals in aqueous solution.[9] Anodic oxidation potentials of several enolate ions[10] and potentials of the second voltammetric peak of some cations[11] have been measured by voltammetry, but the irreversibility of the reactions makes the thermodynamic significance of such potentials somewhat uncertain.

In cyclic voltammetry of *tert*- and *sec*-butyl iodides at a glassy carbon electrode, a second peak has been observed which allows the determination of an effective reduction potential for the *tert*- and *sec*-butyl radicals.[12] The standard potentials of the radicals have been estimated assuming a quadratic activation–driving force relationship. The standard potentials for these aliphatic radicals are found to be approximately one volt more positive than the observed peak potentials.

Recently a number of oxidation and reduction potentials of free radicals have been measured using modulated photolysis for the generation of radicals and phase-sensitive voltammetry for their detection.[13] In some cases the reduction potential of the radical could be compared with literature data for the oxidation of the corresponding anion and the potentials were close; it was concluded that the experimental values of $E_{1/2}$ were within 100 mV of $E^{\circ}(R^{\cdot}/R^-)$. By this method the reduction potentials of a number of benzyl radicals have been estimated.[13]

The competition parameter q may be found in different ways: preparative reduction and isolation of products, coulometry, polarography, and LSV. Coupling products from

reactions between benzyl chloride and some anion radicals have previously been described.[6] In this investigation LSV was used in most cases. Coulometry has been used when the rate of reaction (1) was too low for LSV.

In the investigation the following benzyl chlorides were included: benzyl chloride (1), 1-chloro-1-phenylethane (2), 2-chloro-2-phenylpropane (3), 2-chloro-2-phenylbutane (4), benzhydryl chloride (5), 4-methoxybenzyl chloride (6), and 4-chlorobenzyl chloride (7), representing primary, secondary, and tertiary benzyl radicals.

Results and discussion

LSV has been used to estimate the competition parameter q[7] for the reaction between a number of anion radicals and the benzyl chlorides. In this estimation of q the uncertainty is about 0.1. The data are shown in Table 1 and a plot of q vs. E_A° for **1** is shown in Fig. 1. In all cases q is a monotonic decreasing function of the redox potential of E_A°. The smooth passage for $q = 0$ (coupling) to $q = 1$ (reduction)

Fig. 1. Values of q for benzyl chloride vs. the redox potential E_A° of some anion radicals. The data are tabulated in Table 1.

Table 1. Competition parameters (q), in the reaction between anion radicals (A⁻·) and benzyl halides (BX) in DMF/0.1 M TBABF₄ measured by LSV.

BX	A	$-E_A^{\circ}/V$[b]	q
1	Azobenzene	0.879	0.0
	p-Diacetylbenzene	1.006	0.0
	1-Cyanoisoquinoline	1.034	0.5
	Tetracene	1.096	0.9
	Anthracene	1.488	1.0
2	p-Diacetylbenzene	1.006	0.0[a1]
	1-Cyanoisoquinoline	1.034	0.3
	Quinoxaline	1.200	0.5
	Perylene	1.213	0.9
3	p-Diacetylbenzene	1.006	0.0[a2]
	Acridine	1.131	0.1
	Quinoxaline	1.200	0.3
	Perylene	1.213	0.8
4	p-Diacetylbenzene	1.006	0.0[a3]
	1-Cyanoisoquinoline	1.034	0.3
	Quinoxaline	1.200	0.4
	Perylene	1.213	0.9
	Benzophenone	1.320	1.0
5	4-Methoxycarbonylazobenzene	0.615	0.0[a4]
	3-Chloroazobenzene	0.735	0.7
	4-Chloroazobenzene	0.783	0.8
	Azobenzene	0.879	1.00
6	1-Cyanoisoquinoline	1.034	0.0[a5]
	Tetracene	1.096	0.5
	Acridine	1.131	0.6
	Benzophenone	1.320	0.9
	9,10-Diphenylanthracene	1.404	1.0[a6]
7	p-Diacetylbenzene	1.006	0.0[a7]
	1-Cyanoisoquinoline	1.034	0.6
	Tetracene	1.096	0.9

[a]From preparative experiments: 1, $n = 2.0$; 2, $n = 2.2$; 3, $n = 2.1$; 4, $n = 2.2$; 5, $n = 2.3$; 6, $n = 16$; 7, $n = 2.0$. [b]Versus Ag/AgI.
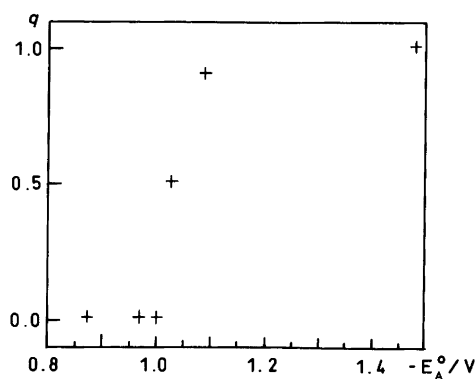
occurs usually within a potential range of approximately 100 mV. The redox potential for an imaginary compound for which $q = 0.5$ can be determined by interpolation and will in the following be referred to as $E_{1/2}^q$. The interpretation of $E_{1/2}^q$ in relation to the standard redox potential of R· will briefly be discussed.

The dependence of the competition between reactions (2) and (3) on the redox potential of A, E_A°, will be explained by assuming that the rate of reaction (3) depends on the potential difference between the redox potentials E_A° and $E^{\circ}(R·/R^-)$, whereas the rate of reaction (2) is assumed, to a first approximation, to be independent of these potentials. Coupling [reaction (2)] will thus occur when $E_A^{\circ} \gg E^{\circ}(R·/R^-)$ and reduction [reaction (3)] with $E_A^{\circ} \ll E^{\circ}(R·/R^-)$.

As $q = k_3/(k_2+k_3)$ the value of $E_{1/2}^q$ relative to $E^{\circ}(R·/R^-)$ will also depend on k_2. A knowledge of the reorganization energy λ connected with reaction (3) would be necessary to estimate the relation between $E_{1/2}^q$ and $E^{\circ}(R·/R^-)$.

Reaction (2) is an anion radical/radical coupling which generally is believed to be fast due to a negligible charge repulsion; the rate is probably near the diffusion limit. Garst and Barton[14] report $k_2 = 2\times10^9$ M^{-1} s^{-1} for the reaction between sodium naphthalene anion radical and 5-hexanyl radicals in THF. Although ion-pairing and solvation differ in DMF from that in THF, k_2 is probably of the same order of magnitude.

The reorganization energy $\lambda_a(0)$ is available for only a few radicals and carbanions due to their high reactivity. The 9-mesitylfluorenyl radical has been studied;[15] both the corresponding cation and anion are chemically sufficiently stable, so this redox reaction in CV gives rise to two reversible systems. The reorganization energy $\lambda_a(0)$ of the radical has been estimated[14] to be 2.5–10 kcal mol^{-1}, that[16] of fluorenyl radicals to be 43 kcal mol^{-1} and $\lambda_a(0)$ for alkyl radicals has been estimated[12] to be 45–54 kcal mol^{-1}.

A comparison of the measured $E_{1/2}^q$ values of the benzyl halides 1–7 with the half-wave potentials $E_{1/2}$ of the photochemically generated benzyl radicals[13] given in Table 2 show that for 1, 2, 5, and 7 the difference between $E_{1/2}^q$ and

Table 2. E°_A and $E_{1/2}$ values for some substituted benzyl radicals.

BX	$-E^q_{1/2}/V^a$	$-E_{1/2}/V^b$
Benzyl chloride (1)	1.03	1.06^c
1-Chloro-1-phenylethane (2)	1.20	1.21^c
2-Chloro-2-phenylpropane (3)	1.20	1.34^c
2-Chloro-2-phenylbutane (4)	1.20	–
Benzhydryl chloride (5)	0.70	0.75^c
4-Methoxybenzyl chloride (6)	1.10	1.36^c
4-Chlorobenzyl chloride (7)	1.03	1.01^c

^{a}Versus Ag/AgI. ^{b}The $E_{1/2}$ values are corrected from vs. SCE to vs. Ag/AgI by adding +0.39 V. ^{c}See Ref. 12.

$E_{1/2}$ is small (0–50 mV), whereas for 3 and 6 the difference is larger (130–250 mV).

Reaction (3) is an outer-sphere ET; Marcus' theory may be used to describe the relation between the driving force, reorganization energy, and rate. The diffusion-limited rate constant, k_d, is taken to be 1×10^{10} M^{-1} s^{-1}, and for the pre-exponential parameter, A, a value of 0.2 is chosen.[16] The measured rate constant, k_{obs}, can thus be expressed [eqn. (4)].

$$k_{obs} = 5 \times 10^{10} \exp\left[-\frac{\lambda}{4}\left(1 + \frac{\Delta G}{\lambda}\right)^2 \Big/ RT\right] \tag{4}$$

In eqn. (4) $\Delta G = -F[E^\circ_A - E^\circ(R\cdot/R^-)]$ and $\lambda = 1/2[\lambda_d(0) + \lambda_a(0)]$, where $\lambda_d(0)$ and $\lambda_a(0)$ are the reorganization energies for the self-exchange reactions for the donor and acceptor, respectively. The $\lambda_d(0)$ for aromatic anion radicals is typically 10 ± 2 kcal mol^{-1},[16] whereas $\lambda_a(0)$ for alkyl radicals has been reported to be about 50 kcal mol^{-1}. The flattening of the pyramidal structure of the benzyl anion allows delocalization of the charge and this decreases the solvent reorganization energy. $\lambda_a(0)$ for benzyl radicals are therefore considerably lower than for alkyl radicals, probably about 15–30 kcal mol^{-1}.

Table 3. The dependence on the potential range of the shift in q-values ($E^q_1 - E^q_3$) and the potential difference between $E^q_{1/2}$ and $E°(R\cdot/R^-)$ on λ and k_2. $\lambda = 1/2[\lambda_d(0) + \lambda_a(0)]$ and E^q are defined by $k_3 = 10\,k_2$ and $k_3 = k_2/10$, respectively.

λ/kcal mol^{-1}	k_2/M^{-1} s^{-1}	$(E^q_1 - E^q_3)$/mV	$[E^q_{1/2} - E°(R\cdot/R^-)]$/mV
10	10^6	−149	261
10	10^7	−168	182
10	10^8	−199	93
10	10^9	−258	−16
20	10^6	−218	114
20	10^7	−238	−4
20	10^8	−273	−123
20	10^9	−366	−277
30	10^6	−258	−98
30	10^7	−291	−234
30	10^8	−344	−389
30	10^9	−448	−578

The ^{13}C NMR spectrum in THF of the benzylic anion, 7-phenylnorbornane anion, has been interpreted to show that the lithium salt is pyramidal, whereas the potassium and cesium salts are planar.[17] This suggests that benzylic anions with TBA$^+$ counter-ions in DMF are planar with extended delocalization and that the solvent reorganization energy (Bz$^-$/Bz$\cdot$) is not much different from that of anion radicals of aromatic hydrocarbons (A$^{\cdot-}$/A). This is in accordance with recent calculations.[18]

When the reaction is a catalytic reduction of RX [reactions (1) and (3)] $q \simeq 1$, which means that $k_3 > 10\,k_2$, whereas when the reaction is a coupling [reactions (1) and (2)] $q \simeq 0$ and $k_3 < 0.1\,k_2$. In Table 3 the calculated potential range of the transition from $q \simeq 0$ to $q \simeq 1$ for several values of k_2 is shown as a function of the reorganization energy λ.

In Table 3 the difference between $E^q_{1/2}$ and $E°(R\cdot/R^-)$ is given as a function of λ and k_2. As seen from Table 3 an estimate of $E°(R\cdot/R^-)$ from $E^q_{1/2}$ requires an estimate of k_2 and λ. In principle λ may be estimated from the potential range in which q shifts from 0 to 1, if k_2 is known and is independent of the potential of the anion radical. We have here assumed that k_2 is, to a first approximation, independent of the potential differences between A$^{\cdot-}$ and R$\cdot$, which might not be a strictly valid assumption; furthermore, steric hindrance might also influence k_2, so parameters from apparently analogous systems may be misleading.

$E^q_{1/2}$ is analogous to the E^t,[12] the potential of the transition between radical and carbanion chemistry, in fact, preliminary investigations of $E^q_{1/2}$ for aliphatic alkyl radicals indicate $E^q_{1/2}$ to be close to the published values for E^t. The determination of $E^q_{1/2}$ does not require cyclic voltammograms with two separate waves and can thus be used to determine the potential useful for the prediction of the follow-up chemistry, but it cannot be used to obtain the standard reduction potential of the radicals without a knowledge of λ and k_2.

In conclusion, the reaction between benzyl radicals and anion radicals has been found to depend on the redox potential of the anion radical and a formal potential, $E^q_{1/2}$, of the radical. For $E^\circ_A \ll E^q_{1/2}$ a reduction of R$\cdot$ is observed, whereas a coupling is found for $E^\circ_A \gg E^q_{1/2}$. Further investigations are needed to establish the relation between $E^q_{1/2}$ and $E°(R\cdot/R^-)$.

Experimental

Materials. The mediators and some of the substrates were the same as previously reported.[5,6] 4-Chlorobenzyl chloride was used as received. Benzhydryl chloride was distilled at 155–159 °C (10 mmHg).

2-Chloro-2-phenylpropane was made by reaction of 2-phenylpropene with an excess of gaseous hydrogen chloride in diethyl ether; after washing of the organic phase twice with water and drying, and evaporation of the solvent, the NMR spectrum showed no impurities. The sup-

porting electrolyte, Bu_4NBF_4, and the solvent, DMF, were purified by standard procedures.[5]

Equipment. Instrumentation and data-handling procedures have been described previously.[19] The cells and the electrodes were of conventional type.

Procedures. Estimations of the competition parameter by LSV were performed by the method given by Pedersen.[7] In the preparative experiments, coulometric n-values of 2.0 ± 0.3 were characterized as coupling reactions ($q = 0.0$), while an n-value >10 was characterized as a catalytic reaction ($q = 1.0$).

As an example of a preparative coupling, the reduction of p-methoxybenzyl chloride by 1-cyanoisoquinoline anion radical is described. 1-Cyanoisoquinoline (0.25 g) was reduced in 50 ml deaerated DMF, 0.1 M $TBABF_4$ at a mercury cathode at -1.05 V (vs. Ag/AgI) in the presence of 2.19 ml of p-methoxybenzyl chloride. The electrolyte had been purified by being passed through a column of activated alumina. The reduction was complete after the consumption of 360 C. The catholyte was diluted with water (100 ml) and extracted with diethyl ether (100 ml), which was then washed with water (100 ml). After being dried (molecular sieves, 4A) the organic solvent was removed *in vacuo* and the residue was purified on a column of silica (100 g) with a 60:40 mixture of light petroleum/ethyl acetate as the eluent. Isolated was: 1,4-bis(4-methoxybenzyl) isoquinoline, ^1H NMR ($CDCl_3$): 3.71 (s, 3 H), 3.73 (s, 3 H), 4.28 (s, 2 H), 4.59 (s, 2 H), 6.78 (d, 4 H, J 5.4 Hz), 7.09 (d, 2 H, J 5.4 Hz), 7.19 (d, 2 H, J 5.4 Hz), 7.4–7.6 (m, 2 H), 7.89 (d, 1 H, J 4.5 Hz), 8.15 (d, 1 H, J 4.5 Hz), 8.33 (s, 1 H). MS (IP 70 eV, m/z): 369 (79), 368 (100), 338 (12), 121 (43), 91 (8), 77 (10).

References

1. Garst, J. F. *Acc. Chem. Res. 4* (1971) 400; Bank, S. and Juckett, D. A. *J. Am. Chem. Soc. 98* (1976) 7742.
2. Malissard, M., Mazaleyrat, J. P. and Welvart, Z. *J. Am. Chem. Soc. 99* (1977) 6933; Hebert, E., Mazaleyrat, J. P., Nadjo, L. and Savéant, J.-M. *Nouv. J. Chim. 9* (1985) 75.
3. Lund, H., Michel, M.-A. and Simonet, J. *Acta Chem. Scand., Ser. B 28* (1974) 900; Simonet, J., Michel, M.-A. and Lund, H. *Acta Chem. Scand., Ser. B 29* (1975) 489.
4. Lund, H. and Kristensen, L. H. *Acta Chem. Scand., Ser. B 33* (1979) 495; Kristensen, L. H. and Lund, H. *Acta Chem. Scand., Ser. B 33* (1979) 735.
5. Lund, T. and Lund, H. *Acta Chem. Scand., Ser. B 40* (1986) 470.
6. Lund, T. and Lund, H. *Acta Chem. Scand., Ser. B 41* (1987) 93.
7. Pedersen, S. U. *Acta Chem. Scand., Ser. A 41* (1987) 391.
8. Savéant, J.-M. and Su, K. B. *J. Electroanal. Chem. 196* (1985) 1.
9. Henglein, A. *J. Electroanal. Chem. 163* (1976) 9; Toffel, P. and Henglein, A. *Faraday Discuss. Chem. Soc. 63* (1977) 124.
10. Kern, J. M. and Federlin, P. *Tetrahedron 34* (1978) 661; Kern, J. M., Sauer, J. D. and Federlin, P. *Tetrahedron 38* (1982) 3023; Bank, S., Ehrlich, C. L. and Zubieta, J. A. *J. Org. Chem. 44* (1979) 1454; Bank, S., Schepartz, A., Giammatteo, P. and Zubieta, J. A. *J. Org. Chem. 48* (1983) 3458; Bordwell, F. G. and Bausch, M. J. *J. Am. Chem. Soc. 108* (1986) 1979.
11. Breslow, R. and Mazur, S. *J. Am. Chem. Soc. 95* (1973) 584; Wasielewski, M. R. and Breslow, R. *J. Am. Chem. Soc. 98* (1976) 4222; Breslow, R. and Grant, J. L. *J. Am. Chem. Soc. 99* (1977) 7745; Jaum, B., Schwartz, J. and Breslow, R. *J. Am. Chem. Soc. 102* (1980) 5741.
12. Andrieux, C. P., Gallado, I. and Savéant, J.-M. *J. Am. Chem. Soc. 111* (1989) 1620.
13. Wayner, D. D. M., McPhee, D. J. and Griller, D. *J. Am. Chem. Soc. 110* (1988) 132; Sim, B., Griller, D. and Wayner, D. D. M. *J. Am. Chem. Soc. 111* (1989) 754.
14. Garst, J. F. and Barton, F. E. *Tetrahedron Lett.* (1969) 587.
15. Andrieux, C. P., Savéant, J.-M. and Su, K. B. *J. Phys. Chem. 90* (1986) 3815.
16. Eberson, L. *Electron Transfer Reactions in Organic Chemistry,* Springer Verlag 1987.
17. Peoples, P. R. and Grutzner, J. B. *J. Am. Chem. Soc. 102* (1980) 4709.
18. Mikkelsen, K. V., Swanstrøm, P., Pedersen, S. U. and Lund, H. *To be published.*
19. Pedersen, S. U. and Svensmark, B. *Acta Chem. Scand., Ser. A 40* (1986) 607.