Homogeneous Electron Transfer to Alkyl Iodides, Bromides and Chlorides

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Rate constants have been measured for electron transfer from electrochemically generated anion radicals and the enolate anion of 4-methoxycarbonyl-1-methyl-1,4-dihydropyridine (1^-) to some alkyl iodides, bromides and chlorides. The ratio k_{SUB}/k_{ET} which indicates the ratio between the rate of substitution of 1^- with an alkyl halide and the rate of reaction of an anion radical having the same E° as 1^- with the same alkyl halide has been used as an indication of the ET-character of the reaction. The results show a small, but consistently higher ET-character in the reaction of the enolate ion with alkyl iodides than that with alkyl bromides which in turn shows more ET-character than the reaction with the chlorides. By far the most important factors in the polar/ET dichotomy in the nucleophilic substitution of alkyl halides with a given nucleophile is the steric hindrance in the transition state and the difference between the oxidation potential of the nucleophile and the reduction potential of the electrophile.

For a number of years there has been increasing interest in the role of electron transfer (ET) in organic chemistry, and one of the reactions which has been discussed in connection with the polar/radical dichotomy is aliphatic nucleophilic substitution. The idea of electron transfer has been supported by comparing the rate of reaction with that expected for an ET; the expected rate of ET has either been estimated from thermodynamic data and then calculated using the Marcus equation for the connection between the driving force and the activation energy,[1] or the rate of ET from some supposed outer-sphere electron donors to the substrate has been compared with the rate of the reaction investigated.[2]

A number of aliphatic nucleophilic substitution reactions has been studied in this manner, and the rate of substitution, k_{SUB}, and the expected rate of ET, k_{ET}, from a donor with the same standard potential, E_A°, as the nucleophile, E_{Nu}°, have been compared. In the reactions where k_{SUB}/k_{ET} was close to 1 it was assumed that the rate-determining step was an ET.[2]
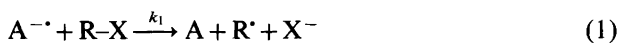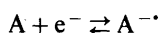
Some evidence has been presented[3] that for a given series of alkyl halides the importance of ET would be greatest for the iodide and smallest for the chloride, with bromide being in between. In most of the reactions studied by electrochemical methods alkyl bromides have been employed, and there have been only a few cases investigated in which the halide has been changed in a reaction between a nucleophile and a series of alkyl halides. In one such investigation the stereochemistry of the coupling products between anthracene anion radical and optically active 2-halooctanes was investigated.[4] The result was that the degree of racemization changed only slightly (2-iodooctane, 95% racemization, 2-bromooc-

tane 92% and 2-chlorooctane 89%), but in the direction expected. In another investigation[5] a comparison of the ratio k_{SUB}/k_{ET} for some substituted benzyl bromides and chlorides was made, and no definite conclusion as to the influence of the halide on the ratio could be made.

The purpose of this investigation is to compare k_{SUB}/k_{ET} for the standard nucleophile, the anion of 4-methoxycarbonyl-1-methyl-1,4-dihydropyridine (1^-), in its reaction with a number of alkyl iodides, bromides and chlorides. In the investigation are included butyl iodide (BuI), butyl bromide (BuBr), butyl chloride (BuCl), 2-butyl iodide (2-BuI), 2-butyl bromide (2-BuBr), 2-butyl chloride (2-BuCl), isobutyl iodide (iso-BuI), tert-butyl bromide (t-BuBr), tert-butyl chloride (t-BuCl), neopentyl iodide (1-iodo-2,2-dimethylpropane, neo-PeI), neopentyl bromide (neo-PeBr) and neopentyl chloride (neo-PeCl).

Results and discussion

We used anion radicals of aromatic hydrocarbons as electron donors, although it has been found that the reaction between such anion radicals and sterically less hindered alkyl halides may involve a certain degree of inner-sphere ET.[6] Previous investigations[2] have suggested that the reaction between aromatic anion radicals and alkyl halides may be formulated as shown in eqns. (1)–(3)

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

$$A^{-\bullet} + R\text{-}X \xrightarrow{k_1} A + R^\bullet + X^- \tag{1}$$

$$A^{-\bullet} + R^\bullet \xrightarrow{k_2} A\text{-}R^- \rightarrow products \tag{2}$$

$$A^{-\bullet} + R^\bullet \xrightarrow{k_3} A + R^- \rightarrow products \tag{3}$$

A–R$^-$ and R$^-$ will either be protonated by the solvent/ supporting electrolyte or will react with the substrate as a nucleophile in an S$_N$2 reaction. Whether reaction (2) or (3) is followed depends on the redox potentials of A$^{-\bullet}$ and R$^{\bullet}$.[7] The ET reaction (1) is practically irreversible because of the concerted R–X bond cleavage.

In Table 1 the rate constants are given for the electron transfer from electrochemically generated anion radicals to a number of alkyl iodides and chlorides; values for *tert*-butyl iodide have not been included, as it was not stable enough to be obtained sufficiently free of iodine and/or hydrogen iodide under the experimental conditions. The values for the bromides have previously been published.[2,8] The rate constants for the iodides were measured in MeCN rather than in DMF, as the iodides reacted to some degree with DMF. In the few cases where we measured ET rate constants for the same reaction in both DMF and MeCN the difference was found to be small. As an illustration of the dependence of the rate constant on the driving force the data for neo-PeI are depicted in Fig. 1. The experimental range is too narrow to decide whether the best curve would be a parabola[9] or a straight line; the curve is, in this investigation, used only for an estimation of the rate constant to be expected of an anion radical with the same standard potential as 1$^-$, and any parabola which would fit the data would be so flat, that the difference in the values of the expected rate constant would be insignificant whether a straight line or a parabola is used. In view of recent results[10,11] and for simplicity a straight line was chosen.

The rate of the reaction between benzophenone and 2-BuI is lower than expected, even when the measured value[12] ($\lambda = 14.7$ kcal mol^{-1}) of the reorganization energy of the self-exchange reaction is used rather than the value 10 kcal mol^{-1} which has generally been used for aromatic anion radicals. If an inner-sphere component were involved a faster, rather than a slower, reaction would be expected.

For the reaction between a given donor A$^{-\bullet}$ and the alkyl halides RX the rate constants k_{ET} decreases going from iodide through bromide to chloride, as expected from the reduction potentials and the bond strength of the R–X bond.

In Table 2 the rate of the reaction between 1$^-$ and the alkyl halides (k_{SUB}) has been compared with the rate expected for an electron transfer from an aromatic anion radical with the same standard potential as 1$^-$ (k_{ET}). The ratio k_{SUB}/k_{ET} diminishes drastically on going from sterically less hindered alkyl halides to the sterically hindered *tert*-butyl and neopentyl halides. For a given alkyl group there is a slight decrease in k_{SUB}/k_{ET} on passing from chloride through bromide to iodide.

The VBCM model[13] suggests that the ET reaction would be more important when the electron affinity of the acceptor is increased and thus the reaction with iodides should have more ET character than the reaction with the chlorides; however, a decrease in the carbon–halogen bond energy would lower the slope of the DA profile and thus give a later transition state with less ET character. The outcome of two opposing effects suggests a small overall effect which could go either way.

It has been argued[14] from considerations of the stabilization of the transition state that there is no general justification for the frequent assumption that the best

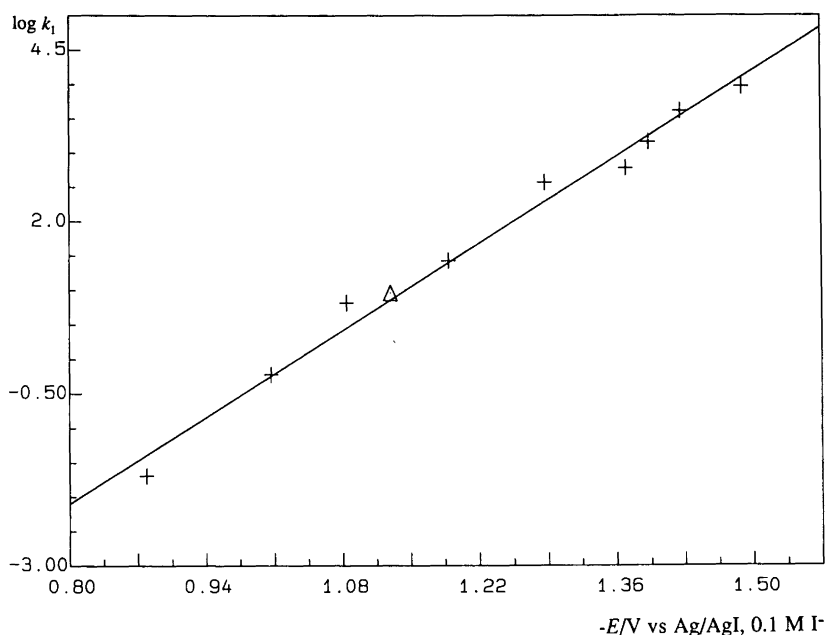*Fig. 1.* Logarithm of the rate of reaction (log k_1) in acetonitrile between neopentyl iodide and 1$^-$ and aromatic anion radicals vs. $-E_A^\circ$ (Ag/AgI, 0.1 M I$^-$) reference electrode; +, anion radicals; $\triangle$, 1$^-$.

Table 1. Rate constants for electron transfer from electrochemically generated anion radicals $(A^{-\cdot})$ to different alkyl chlorides and iodides (BX) measured potentiostatically at a rotating disk electrode or by cyclic voltammetry.

BX	A	$-E_{A^{-\cdot}/A}/V$ [a]	$k_{ET}/M^{-1}s^{-1}$	$\log k_{ET}$
Butyl chloride[b, c]	9,10-Diphenylanthracene[d]	1.394	0.023	−1.64
	Anthracene[d]	1.490	0.200	−0.70
	Pyrene[d]	1.618	0.68	−0.17
	Isoquinoline[d]	1.731	16	1.20
	Benzonitrile[f]	1.830	78	1.90
	p-Tolunitrile[f]	1.937	390	2.59
	Naphthalene[f]	2.057	1800	3.26
	1-Methoxynaphthalene[f]	2.137	5800	3.76
2-Butyl chloride[b, c]	9,10-Diphenylanthracene[d]	1.394	0.083	−1.08
	Anthracene[d]	1.490	0.55	−0.26
	Pyrene[d]	1.618	2.3	0.36
	Quinoline[f]	1.675	20	1.30
	Isoquinoline[f]	1.731	35	1.54
	Benzonitrile[f]	1.830	270	2.43
	p-Tolunitrile[f]	1.937	1400	3.15
	Naphthalene[f]	2.057	4900	3.69
	1-Methoxynaphthalene[f]	2.137	17000	4.23
Neopentyl chloride[c, d]	9,10-Diphenylanthracene	1.394	0.0021	−2.68
	9,10-Dimethylanthracene	1.506	0.011	−1.96
	Pyrene	1.618	0.029	−1.54
	Chrysene	1.782	0.33	−0.48
	p-Tolunitrile	1.937	7.5	0.88
	Triphenylene	1.988	29	1.46
	Naphthalene	2.057	64	1.80
Butyl iodide[e]	Azobenzene[d]	0.879	2.27	0.36
	p-Diacetylbenzene[d]	1.007	6.4	0.81
	1-Cyanoisoquinoline[d]	1.035	36	1.56
	p-Dicyanobenzene[f]	1.085	88	1.94
	2-Benzoylpyridine[d]	1.098	120	2.09
	3-Benzoylpyridine[f]	1.162	210	2.32
	Acenaphthylene[f]	1.190	440	2.64
	Perylene[f]	1.213	1060	3.03
	Fluoranthene[f]	1.288	2300	3.36
Isobutyl iodide[e]	Azobenzene[d]	0.879	1.684	0.23
	p-Diacetylbenzene[d]	1.007	2.69	0.43
	p-Dicyanobenzene[d]	1.085	35.8	1.55
	Acenaphthylene[f]	1.190	154	2.19
	Fluoranthene[f]	1.288	1100	3.04
2-Butyl iodide[e]	Azobenzene[d]	0.879	5.8	0.76
	p-Diacetylbenzene[f]	1.007	46	1.66
	p-Dicyanobenzene[f]	1.085	640	2.81
	Acenaphthylene[f]	1.190	1760	3.25
	Perylene[f]	1.213	4400	3.64
	Fluoranthene[f]	1.288	12900	4.11
	Benzophenone[f]	1.307	6500	3.81
Neopentyl iodide[e]	Azobenzene[d]	0.879	0.0203	−1.69
	p-Diacetylbenzene[d]	1.007	0.60	−0.22
	p-Dicyanobenzene[d]	1.085	6.6	0.82
	Acenaphthalene[f]	1.190	27	1.43
	Fluoranthene[f]	1.288	371	2.57
	p-Methoxybenzophenone[f]	1.371	600	2.78
	9,10-Diphenylanthracene[f]	1.394	1440	3.16
	9-Phenylanthracene[f]	1.427	4100	3.61
	Anthracene[f]	1.490	9300	3.97

[a]Measured against the $(Ag/AgI, I^- = 0.1 M)$ reference electrode. [b] From Ref. 19. [c] Medium DMF/0.1 M TBABF$_4$. [d] Obtained by the potentiostatic method at a rotating disk electrode. [e] Medium MeCN/0.1 M TBABF$_4$. [f] Obtained by cyclic voltammetry.

Table 2. Rate constants (k_{SUB}) for the substitution reaction between the anion of 4-methoxycarbonyl-1-methyl-1,4-dihydropyridine (1⁻) and some alkyl halides and the expected rate of ET (k_{ET}) from an electron donor with the same standard potential as 1⁻ to the same alkyl halides.

BX	$k_{SUB}/M^{-1}s^{-1}$	$k_{ET}/M^{-1}s^{-1}$	k_{SUB}/k_{ET}
Butyl chloride[a]	4.2	3.6×10^{-4}	11600
2-Butyl chloride[a]	0.48	1.34×10^{-3}	360
tert-Butyl chloride[b, 2]	1.6×10^{-2}	3.9×10^{-3}	4.15
Neopentyl chloride[a]	1.7×10^{-4}	2.12×10^{-5}	8.0
Butyl bromide[b, 2]	1420	3.5	400
2-Butyl bromide[b, 2]	480	2.8	170
tert-Butyl bromide[b, 2]	30	12	2.5
Neopentyl bromide[b, 2]	3.57×10^{-2}	1.12×10^{-2}	3.19
Butyl iodide[c]	20000	157	127
2-Butyl iodide[c]	10000	740	14
Neopentyl iodide[c]	9.2	7.3	1.25
Isobutyl iodide[b]	3700	60	61

[a] Obtained in DMF/0.1 M TBABF$_4$ ($T = 25\,°C$). [b] Obtained in DMF/0.1 M TBABF$_4$ ($T = 22\,°C$). [c] Obtained in MeCN/0.1 M TBABF$_4$ ($T = 20\,°C$).

electron acceptor among a group of alkyl halides reacts with the highest degree of ET; there should thus be no substantial difference between the degree of ET in the attack of a given nucleophile on an alkyl iodide or alkyl chloride.

Although the number of compounds investigated here is rather small, the results seem to show, that for the alkyl halides (not including benzyl halides) there is a small increase in the ET-involvement on going from alkyl chlorides to alkyl iodides. The ET-character is smallest in the reaction with BuCl which is expected from the relatively small steric hindrance in the transition state and the higher strength of the carbon–chlorine bond. The results show, however, that although a change in the kind of halide seems to have a small, but consistent influence on the ET-involvement in the aliphatic nucleophilic substitution, a much more important factor, in a reaction with a given nucleophile/donor, is the steric hindrance in the transition state. The electron transfer may play a deciding role when the classical polar transition state cannot be formed owing to steric hindrance and when the nucleophile is a sufficiently good electron donor.

Experimental

Reagents. The supporting electrolyte, Bu$_4$NBF$_4$, was recrystallized from ethyl acetate. The acetonitrile (MeCN) was distilled in a two-step procedure: (a) refluxed over $2\,gl^{-1}$ of P$_2$O$_5$ and then distilled slowly, discarding the first 5%, and then (b) distilled rapidly from $5\,gl^{-1}$ of anhydrous potassium carbonate. The aromatic and heteroaromatic electron donors were commercially available and used as received. Neopentyl iodide was

prepared as described in Ref. 15, and the other alkyl iodides, which were commercially available, were distilled and kept over pieces of copper at $-20\,°C$. The butyl chlorides were commercially available and were distilled before use; neopentyl chloride was made according to Ref. 16, except that a larger excess (3 equivalents) of lithium chloride was used.

Procedure. Measurements of the k_1 rate constants by CV were performed by the method described by Pedersen and Svensmark.[17] Values of k_1 of less than $10\,M^{-1}s^{-1}$ were measured by means of a potentiometric method using a rotating disk electrode following the procedure described in Ref. 18.

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