

On the Reaction between Alkyl Halides and Dianions of Aromatic Compounds

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The mechanisms of the aliphatic nucleophilic substitution reactions have been under active investigation for more than 50 years since Ingold¹ formulated the limiting mechanisms S_N1 and S_N2 . During the last 25 years evidence has accumulated that electron transfer (ET) may play a significant role under some conditions. It was recognized early on that the substitution reaction between aromatic anion radicals and alkyl halides involved ET,² and that sterically hindered *p*-nitrobenzyl halides reacted with some nucleophiles in an $S_{RN}1$ reaction.³ More recently, the reaction between sterically hindered alkyl halides and certain easily oxidizable anions have been suggested to have an ET as the rate-determining step,⁴ and stereochemical evidence has been presented in support of radicals as intermediates in the reaction.⁵ Measurements of the activation entropy and enthalpy of such reactions⁶ together with the above-mentioned results^{4,5} have been used to support the suggestion that the characteristics of an S_N2 reaction are gradually replaced by those of an electron-transfer reaction (S_{ET}) when the steric hindrance of approach of the reactants is increased.

Dianions of aromatic compounds, either obtained by addition of two electrons⁷ or two alkali-metal atoms⁸ to the molecule, have been shown to be good ET agents⁷ and in a few cases the reaction between an alkyl halide and a dianion has been suggested⁴ to involve ET as the rate-determining step.

In this communication the rate of the reaction, in *N,N*-dimethylformamide (DMF), between some electrochemically prepared dianions of aromatic compounds and some alkyl halides is investigated. The purpose is to compare the observed rate of substitution (k_{SUB}) with the rate expected for an electron transfer (k_{ET}). The latter is obtained by interpolation between observed values for the reaction between aromatic anion radicals and the same alkyl halides as described previously.⁴ From the ratio k_{SUB}/k_{ET} the importance of the electron transfer in the substitution reaction

can be inferred. The compounds used in the electrochemical investigation were chosen to give dianions which are not protonated by the medium on the timescale of the experiment; these included perylene (**1**), dicyclopenta[*ef,kl*]heptalene⁸ (isopyrene, **2**), 1,4-diacetylbenzene (**3**), and 9,10-anthraquinone (**4**).

Results

Three electrochemical techniques were used to measure the rate constants of the reactions between the dianions and the alkyl halides in DMF, cyclic voltammetry (CV), derivative cyclic voltammetry (DCV), and homogeneous kinetics using a rotating disc electrode to monitor the concentrations. CV was the most widely used technique, but the precision for the reactions with dianions was lower than in the reactions with anion radicals, as the background current was less well defined for measurements at the second peak owing to interference from the first voltammetric peak; the interference depended on the potential difference between the two peaks. For that reason the rate constants may differ by as much as a factor of two. DCV is, in such cases, preferable and it was used when it was deemed necessary. For relatively slow reactions ($1 > k > 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$) homogeneous kinetic measurements were made.

The results are presented in Table 1; k_{SUB} is the rate constant of the reaction between the dianion and the alkyl halide, whereas k_{ET} is the estimated rate of electron transfer from an aromatic anion radical with the same oxidation potential as the dianion; k_{SUB}/k_{ET} has been interpreted as an indication of the degree of ET participation;⁴ k_{SUB}/k_{ET} close to 1 is thus assumed to show that the rate of substitution is close to the rate expected for an outer-sphere electron-transfer reaction. In practice, k_{ET} of the reaction of a series of anion radicals with a given alkyl halide is measured, and k_{ET} at $E_{A^{2-}}^{\circ}$ is found by interpolation.

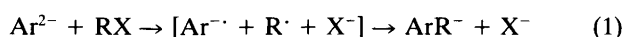
Table 1. Rate constants ($k_{\text{SUB}}/\text{M}^{-1} \text{s}^{-1}$) for the reaction between selected dianions and alkyl halides, together with the expected rate constant (k_{ET}) for ET obtained by inter-/extra-polation from data from the reaction between anion radicals and the alkyl halides. Medium: DMF containing 0.1 M tetrabutylammonium tetrafluoroborate, $T = 25^\circ\text{C}$.

Dianion	$E_{\text{Nu}}^{\circ}/\text{V}$ vs Ag/AgI	RX	k_{SUB}	k_{ET}	$k_{\text{SUB}}/k_{\text{ET}}$
Perylene ²⁻	-1.775	<i>t</i> -BuCl	170	87	2
		<i>s</i> -BuCl	280	51	5.4
		BuCl	380	31	12
		<i>exo</i> -Norbonyl Br	5.7×10^4	5.2×10^4	1
		<i>t</i> -BuBr	2.4×10^5	2.3×10^5	1
		<i>s</i> -BuBr	9.5×10^5	1.5×10^5	6.3
		BuBr	7.4×10^5	4.7×10^4	15
Isopyrene ²⁻	-1.748	<i>t</i> -BuCl	350	47	7.5 ^a
		<i>s</i> -BuCl	10 ³	28	36 ^a
		BuCl	6×10^2	16	37 ^a
		<i>exo</i> -Norbonyl Br	1.5×10^4	3.9×10^4	0.4 ^a
		<i>t</i> -BuBr	3.7×10^5	1.5×10^5	2.5 ^a
		<i>s</i> -BuBr	1.5×10^6	9.9×10^4	15 ^a
		BuBr	9.1×10^5	3.2×10^4	28 ^a
1,4-Diacetylbenzene ²⁻	-1.525	<i>s</i> -BuCl	13.5	0.34	40
		BuCl	33	0.14	2.3×10^2
		<i>t</i> -BuBr	1.4×10^4	6.4×10^3	2.3
		<i>s</i> -BuBr	3.7×10^4	3.0×10^3	12
		BuBr	4.8×10^4	1.6×10^3	30
Anthraquinone ²⁻	-1.123	<i>exo</i> -Norbonyl Br	0.17	0.22	0.8
		<i>t</i> -BuBr	400	12	34
		<i>s</i> -BuBr	485	2.8	173
		BuBr	1900	3.5	550

^aFrom Ref. 8.

Discussion

A nucleophilic substitution between a dianion of an aromatic hydrocarbon and an alkyl halide in which an electron transfer is the rate-determining step would involve the formation of an anion radical and a radical within a solvent cage and a very rapid coupling of these species [eqn. (1)].^{4,8}



The use of $k_{\text{SUB}}/k_{\text{ET}}$ as an indication of the importance of electron transfer in the substitution reaction rests on the assumption that the rate-determining step in the reaction between an anion radical of an aromatic hydrocarbon and an alkyl halide is the transfer of an electron. If there is, as suggested on theoretical grounds,⁹ certain stabilization in the transition state without stereochemical consequences for the product in the reaction between aromatic anion radicals and an alkyl halide, there might be similar stabilization in the transition state of the reaction between the dianion and the alkyl halide, even when $k_{\text{SUB}}/k_{\text{ET}}$ is close to 1. Measurements of the activation entropy of reactions between anion radicals and sterically very hindered alkyl halides suggest⁶ that such reactions are outer-sphere electron-transfer reactions, that is the bonding stabilization in the transition state (TS) is less than ca. 1 kcal mol⁻¹, but

that increased stabilization is present in the TS when the steric hindrance of approach between the reactants is diminished.

Another assumption behind the use of $k_{\text{SUB}}/k_{\text{ET}}$ is that the total reorganization energy λ of the reaction which according to Marcus theory for electron transfer is an important parameter in determining the rate of ET is similar for the anion radicals and the dianions. Presumably the solvent reorganization energy is somewhat larger for the dianion than for the anion radical, but it is not known how much. Measurement of the peak separation for the first [$E_p^1(a) - E_p^1(c)$] and the second reduction indicates that the heterogeneous rate constants for the first (k_p^1) and the second k_p^{11} reduction of **1** are 5 and 0.17 cm s⁻¹, respectively.^{10,11} These results suggest that the difference between the self-exchange reorganization energy connected with the first and second reduction of perylene is not very large. This is in accordance with the small difference (1.2 kcal) in self-exchange energies found for the divalent methyl viologen (MeV²⁺/MeV^{•+}) and its cation radical (MeV^{•+}/MeV).¹² The λ of cyclooctatetraene dianion (10.8 kcal) is not very different from that of aromatic anion radicals.¹³ In the reaction with alkyl halides the reorganization energy of the electron transfer is mainly determined by the alkyl halide, so the error introduced by using anion radicals as standard ET-reagents for **1**²⁻ seems not to be great. A large

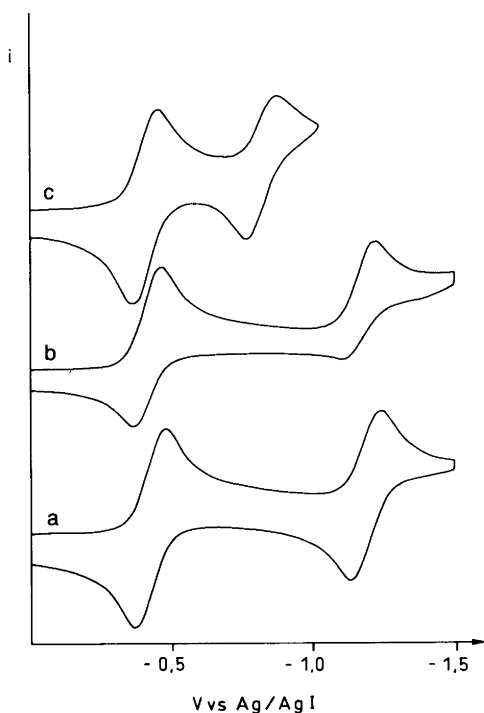


Fig. 1. Influence of lithium ion on the electron transfer, in DMF/TEABF₄, from the dianion of anthraquinone (4^{2-}) to benzyl chloride. (a) Anthraquinone (**4**; 3×10^{-3} M); (b) solution (a) + benzyl chloride (**5**; 0.01 M); solution (b) + lithium chloride (0.02 M). Gold electrode, sweep rate 400 mV s^{-1} .

difference between λ of the anion radicals and of the dianions would influence $k_{\text{SUB}}/k_{\text{ET}}$ in such a way that the reported values are too small.

Ion-pairing is known to have some influence on the peak potentials, although it was minimized by employing tetrabutylammonium ion as the counter ion. Lithium ion has a strong influence on the electron transfer from a dianion to an alkyl halide. In Fig. 1 the influence of lithium ion on the reaction between the dianion of anthraquinone (4^{2-}) and benzyl chloride (**5**) is shown. On addition of **5** (0.01 M) to 4^{2-} (3×10^{-3} M) the second reduction becomes irreversible; however, when lithium chloride (0.02 M) is added to the solution the second peak of **4** is shifted ca. 500 mV to less negative potentials and the reduction becomes (chemically) reversible; the ET from the ion pair [4^{2-} , 2 Li⁺] to **5** is then too slow to influence the voltammetric curve at the sweep rate used (400 mV s^{-1}).

The trend in $k_{\text{SUB}}/k_{\text{ET}}$ in the reaction between the dianions and alkyl halides is the same as between anions⁴ and alkyl halides, $k_{\text{SUB}}/k_{\text{ET}}$ is closest to 1 for sterically hindered alkyl halides (*exo*-norbornyl bromide, *t*-butyl bromide, and *t*-butyl chloride) and increases on going to secondary and primary halides. This was for anions interpreted as being due to increased bonding stabilization in the transition state on going from tertiary to secondary to primary alkyl halides, and a similar interpretation is proposed here. The finding that $k_{\text{SUB}}/k_{\text{ET}}$ in the reaction between 1^{2-} and both

norbornyl bromide and *t*-butyl bromide is close to 1 suggests that λ for these reactions are not significantly different from the standard reactions. The heterogeneous ET rate constant for $4^-/4^{2-}$ (0.10 cm s^{-1})¹¹ is slightly lower than that of $1^-/1^{2-}$ and λ is thus somewhat higher.

It has been suggested^{4,14} that the S_{ET}2 and S_N2 were limiting cases of reaction mechanisms with a gradual transition between the limiting cases; such a model would predict that some consequences of a bonding stabilization in the transition state would be found in the product. An example of a nucleophilic S_N2-like substitution of a dianion of an aromatic hydrocarbon is the reaction between 2^{2-} and dimethyl sulfate in acetonitrile which has $k_{\text{SUB}}/k_{\text{ET}} > 3500$.⁸

The data show that, except for *exo*-norbornyl bromide for which $k_{\text{SUB}}/k_{\text{ET}}$ is ca. 1, independently of the donor, there is a tendency in that the more negative the redox potential of the donor, the lower the ratio $k_{\text{SUB}}/k_{\text{ET}}$ and *vice versa*; the better the donor, the earlier the transition state in accordance with the predictions of the VBCM model.¹⁵ This is especially noticeable for 4^{2-} which has by far the most positive oxidation potential and in which the charge is more localized (on oxygen) than in the dianions of the aromatic hydrocarbons; this also explains the slightly higher λ value for 4^{2-} ; a higher degree of inner-sphere ET is then to be expected.

The similarities in the reactions between sterically hindered alkyl halides with aromatic anion radicals, certain easily oxidizable anions, or dianions of aromatic compounds suggest that in such reactions the oxidation potential of the donor and the reduction potential of the acceptor are the most important variables, and that it does not matter for the electron transfer whether the nucleophile is para- or dia-magnetic.

Experimental

The apparatus used for the determination of the rate constants has been described elsewhere.^{4,6}

Reduction of perylene. The reduction was performed as previously described; a yield of 56% of coupled products was obtained.⁴ The yields of the three coupling products, determined by GLC, were in a typical experiment A:B:C 7.5:1.4:1, but the ratio and especially the absolute yield depended on the absence of proton donors, as the dianion is a very strong base which is protonated rapidly; if the solution was not carefully dried most of the (reoxidized) perylene was recovered. The position of the *tert*-butyl group in the isomers was not determined. The products were characterized by GLC/MS. Major isomer A, MS (*m/z*, %): 309 (23), 308 (97), 294 (22), 293 (100), 277 (25), 276 (28), 253 (12), 252 (42), 132 (28). Isomer B (*m/z*, %): 308 (15), 276 (8), 255 (7), 253 (32), 252 (100), 250 (19), 249 (7), 248 (8), 126 (15), 57 (33). Isomer C (*m/z*, %): 308 (62), 292 (73), 276 (52), 253 (29), 252 (72), 250 (52), 249 (24), 138 (33), 57 (100).

Reduction of 1,4-diacetylbenzene. 1,4-Diacetylbenzene (153 mg) was reduced in 25 ml of deaerated DMF/0.1 M TBABF₄ at a mercury pool cathode at -1.6 V (Ag/AgI, 0.1 M I⁻) in presence of 0.6 ml of *tert*-butyl chloride. The reduction was complete after consumption of 197 C (*n* = 2.1). To the catholyte was added naphthalene (72 mg) as an internal standard for GC. The catholyte was then diluted with water (50 ml), extracted with diethyl ether (50 ml) which was washed free of DMF with water and dried over molecular sieves A4. GC showed one main product (80 %) and a dibutylated minor product (5 %). After evaporation of the solvent, the main product was identified as 2-(4-acetylphenyl)-3,3-dimethyl-2-butanol from ¹H and ¹³C NMR and MS spectra. ¹H NMR (CDCl₃): δ 0.90 (s, 9 H), 1.58 (s, 1 H), 1.59 (s, 3 H), 2.57 (s, 3 H), 7.53 (d, ³J 8.42 Hz, 2 H), 7.87 (d, ³J 8.38 Hz, 2 H). ¹³C NMR (CDCl₃): δ 24.9, 25.5, 37.9, 78.4, 127.0, 127.2, 135.2, 151.6, 198.0. MS (*m/z*, %): 165 (7.5), 164 (75), 163 (100), 147 (6.6), 121 (22), 105 (4), 77 (6), 57 (7), 43 (76). The 2-(4-acetylphenyl)-3,3-dimethyl-2-butanol used for the determination of the response factor in GC was prepared from **3** by reaction with *tert*-butylmagnesium bromide in THF.

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