Oxidation Potential as a Measure of the Effect of Environment on the Reactivity of Anionic Nucleophiles

Murat E. Niyazymbetov† **and Dennis H. Evans***
Department of Chemistry and Biochemistry, University of Delaware, Newark, DE 19716, USA

The irreversible anodic peak potential of anionic nucleophiles has been shown to be linearly correlated with various measures of their nucleophilic reactivity, including rates of S_N2 and S_NAr reactions as well as addition to Michael acceptors. The correlations incorporate both changes in the nature of the solvent and the identity of the counter ion. The nucleophiles considered were iodide, azide, cyanide, 4-cyanophenolate, the anion of 2-mercaptobenzoxazole and the anion of ethyl nitroacetate. It is suggested that the oxidation potential can be used as an easily measurable predictor of the effect of solution environment on nucleophilic reactivity.

In recent years in the field of electroorganic synthesis there has been increasing interest in the use of anionic nucleophiles that have either been produced by the action of an electrogenerated base on an acidic precursor or by direct generation of the anionic nucleophile by the cathodic reduction of the precursor.[1] The advantages of the electrochemical method of producing nucleophiles include the fact that stoichiometric quantities of strong chemical bases are not needed and the reactive anions can be generated in almost any solvent with free choice of counter ion. Nucleophilic reactivity is known to depend on both the solvent and the counter ion.

Of course, there continues to be a strong interest in the factors that govern nucleophilic properties in purely chemical solution-phase reactions[2] and the development of improved means of correlating and predicting reactivity will always be welcome.

It has long been recognized[3] that nucleophilicity is likely to be related to the oxidation potential of the nucleophile with high (positive) oxidation potentials associated with low reactivity. In theoretical treatments of S_N2 reactions,[4] the ionization potential of the nucleophile is a major factor governing the barrier height. Solution-phase oxidation potentials often show a linear correlation with gas-phase ionization potentials further strengthening the expectation of a strong relationship between oxidation potential and nucleophilic reactivity.

The relevant oxidation potential is the reversible potential of reaction (1). Direct experimental determination of the reversible

$$A^- \rightleftharpoons A^{\bullet} + e^- \qquad (1)$$

potentials of these one-electron oxidation reactions is difficult for most nucleophiles used in organic chemistry. Therefore, workers have resorted to thermodynamic cycles and other schemes for estimating the needed quantities for aqueous media[2b,5a] and a few other solvents.[5b,c]

In view of the uncertainties associated with estimation of one-electron oxidation potentials and the difficulties of measuring them directly, it would be useful to identify an easily measurable quantity that is related in a simpler manner to the reversible potential of reaction (1). One possibility is the anodic peak potential for the overall irreversible oxidation of A^-. In general, this peak potential is shifted[6] from the reversible potential by a kinetic term, X. The quantity X, which can be either negative or

$$E_{p,a} = E^{\circ} + X \qquad (2)$$

positive, will depend upon the scan rate and two kinds of kinetic processes, the rates of reactions that consume $A^{\bullet}$ (*e.g.*, dimerization) and the intrinsic rate of the heterogeneous electron-transfer reaction itself, $A^- \longrightarrow A^{\bullet} + e^-$.

Correlations of nucleophilicity with $E_{p,a}$ will be of quality equal to analogous correlations with E° if X is either constant for all nucleophiles and media or if nucleophilicity happens to correlate well with X. There is no basis, *a priori*, for predicting the likelihood of such behaviour though linear correlations have been observed.[7]

In a recent publication[8] it was found that literature values of the nucleophilicity parameter (N) showed an excellent correlation with irreversible oxidation half-wave potentials measured for twelve anionic nucleophiles in acetonitrile at a platinum electrode. The correlation spanned a very wide range of potentials (2.22 V) and nucleophilicity (N = 1.5–10). This work demonstrated the usefulness of oxidation potential as a predictor of nucleophilic reactivity. In this connection, it should be noted that a variety of parameters should provide good correlations including the anodic peak potential, the half-peak potential and the half-wave potential[8] (from hydrodynamic voltammetry) for the irreversible oxidation.

As mentioned above, the rates of the reactions of anionic nucleophiles are affected by the nature of the solvent and counter ion. The purpose of the present research was to determine whether reaction rates also correlated well with $E_{p,a}$ measured in various solution environments.

Results

The main experimental problem that accompanies the measurement of oxidation or reduction potentials in different solvents *vs.* a given reference electrode is the uncertainty in changes in liquid-junction potential on going from one solvent to another. It has been recommended[9] that potentials measured in non-aqueous media be reported with respect to a reference couple whose reversible potential is thought to be insensitive to changes in the solvent and electrolyte. We have used one of the recommended reference couples, ferrocene/ferrocenium (Fc/Fc^+), as an internal reference, *i.e.*, both ferrocene and the nucleophile were present in solution and the oxidation peak of ferrocene was recorded together with that of the anion under investigation. The reversible potential of the ferrocene/ferrocenium couple was taken as the average of the anodic and cathodic peak potentials. In some instances, when $E_{p,a}$ of the nucleophile was too close to the Fc/Fc^+ potential, cobaltocenium/cobaltocene (Cob^+/Cob) was used in an analogous fashion. It has been shown[10] that this couple is also apparently

---

† On leave from the N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky Prospect 47, Moscow 117913 Russia.

Table 1 Reversible redox potentials[a] for anion/neutral radical couple of 2,4,6-tri-*tert*-butylphenol in 0.10 mol dm^{-3} solutions of $MClO_4$ in different solvents

Entry	M^+	Solvent	Acceptor number	$E°$/V *vs.* Fc/Fc^+
1	Bu_4N^+	THF	8.0	−0.919
2		Diglyme	10.2	−0.872
3		HMPA	10.3	−0.797
4		DMA	13.6	−0.775
5		DMF	16.0	−0.747
6		MeCN	19.3	−0.707
7		CH_2Cl_2	20.4	−0.817
8		Pr^iOH	33.5	−0.685
9		EtOH	37.1	−0.451
10		MeOH	41.3	−0.328
11	Hep_4N^+	MeCN	19.3	−0.725
12	Et_4N^+	MeCN	19.3	−0.699
13	Me_4N^+	MeCN	19.3	−0.697
14	Na^+	MeCN + 10%DMF		−0.588
15	Li^+	MeCN	19.3	−0.459
16	Li^+	MeCN + 10%DMF		−0.513

[a] Determined at 25 °C on a Pt electrode; referred to the half-wave potential of ferrocene/ferrocenium in the same solvent and electrolyte.

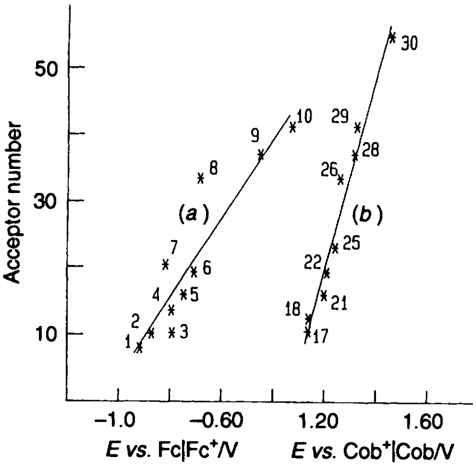

Fig. 1 Relationship between the Gutmann acceptor number and the reversible potentials for the anion/neutral radical couple of 2,4,6-tri-*tert*-butylphenol (*a*) and oxidation peak potentials for iodide ion (*b*). Numbers correspond to entry numbers in Tables 1 and 2. Regression equation for (*a*) AN = 63.26 + 59.58 ($E°$) (r = 0.914); (*b*) AN = − 154.2 + 144.9 ($E_{p,a}$) (r = 0.980)

an excellent reference couple as the difference between the half-wave potentials of Fc^+/Fc and Cob^+/Cob was almost constant (1.328 ± 0.004 V) for five solvents.

2,4,6-*Tri*-tert-*butylphenolate*.—We first set out to investigate the effect of solvent and electrolyte on the reversible potential for the one-electron oxidation of an anion. As noted earlier, electrode reaction (1) is irreversible for most anionic nucleophiles owing to the reactivity of the radical $A^{\bullet}$ (*e.g.*, dimerization, hydrogen-atom abstraction, *etc.*). The highly hindered anion formed by deprotonation of 2,4,6-tri-*tert*-butylphenol (TBP^-) is an exception, the corresponding phenoxyl radical being very stable.

Results are summarized in Table 1 where it may be seen that the reversible potential shifts in the positive direction by almost 600 mV on going from THF to MeOH solvents. This shift is caused principally by increased stabilization of the anion *via* solvation by the increasingly strong electron-accepting and hydrogen-bonding solvents. Differences in the solvation energy of the neutral radical are expected to be much smaller.

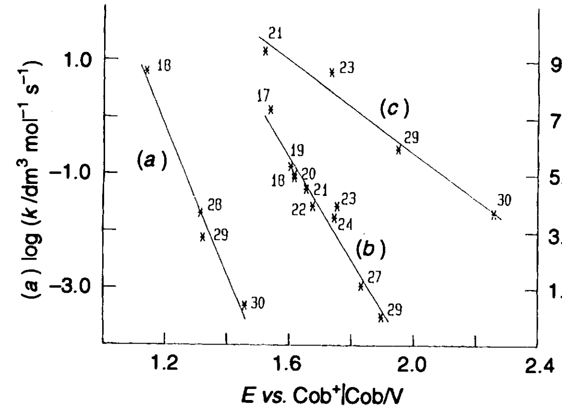

Fig. 2 Relationship between oxidation peak potentials of anionic nucleophiles and rate parameters of nucleophilic reactions in different solvents. Numbers correspond to entry numbers in Table 2. Rate parameters are: (*a*) I^-, log k where k is the second-order rate constant for the reaction of MeI with labelled iodide ions.[13] Regression equation: log k = 15.53 − 13.06($E_{p,a}$) (r = −0.990). (*b*) N_3^-, log ($k/k°$), relative rates for the reaction of azide-ion with *p*-fluoronitrobenzene;[14] $k°$ is the second-order rate constant for the reaction in methanol and k is for reaction in the given solvent. Regression equation: log (k/k_o) = 34.51 − 18.05 ($E_{p,a}$) (r = −0.969). (*c*) CN^-, N^+, Ritchie's nucleophilic parameter[15] based on cation–anion combination reactions in different solvents. Regression equation: N^+ = 21.99 − 8.098 ($E_{p,a}$) (r = −0.985).

There are several empirical approaches to account for the effects of solvent on the rates and equilibria of chemical reactions.[11] One of these is the acceptor number (AN) of Gutmann that characterizes the acceptor or electrophilic properties of the solvent. It has been shown[12] that rate constants of S_N2 reactions correlate with AN, with high AN associated with small rate constants.

The reversible potential for TBP^- gives a reasonably linear correlation with AN [Fig. 1(*a*)] for ten solvents with isopropyl alcohol showing the largest deviation. Similar correlations were seen for the neutral/anion radical couples of twenty-two nitrobenzene derivatives in five solvents.[10] The results in Table 1 also show small positive shifts in potential when smaller tetraalkylammonium cations were used, a result which might indicate weak ion pairing between TBP^- and the cation of the electrolyte. Ion pairing by lithium is very significant as indicated by the positive shift of about 250 mV.

Though TBP^- has the desirable property of reversible electrochemical reactions, it is a slowly reacting nucleophile, undoubtedly caused by steric bulk in the vicinity of the oxygen atom. Nevertheless, we were able to confirm that its very slow reactions with benzyl chloride had half-lives in the order MeOH > EtOH > MeCN > DMF ≈ *N,N*-dimethylacetamide. This order is the same as the order of decreasing (more negative) reversible potentials (Table 1), in qualitative agreement with expectation.

Iodide.—This nucleophile undergoes irreversible anodic oxidation. The peak potential for the first oxidation peak was measured (Table 2) and a good correlation was found with AN [Fig. 1(*b*)]. This correlation suggests that X in eqn. (2) either remains constant for this series of solvents or is also linearly correlated with AN.

Literature data[13] are available for the rate constants, k, for the S_N2 reaction of labelled iodide with methyl iodide for four of the solvents studied here. An acceptable linear correlation of log k with $E_{p,a}$ was observed [Fig. 2 (*a*)].

Azide.—This much-studied nucleophile also undergoes an

Table 2 Oxidation peak potentials,[a] V, of some anions and rate parameters[b] (in parentheses) of nucleophilic reactions in different solvents

Entry	Solvent	I^-	N_3^-	CN^-	ArO^-	$HetS^-$	$O_2N\bar{C}HR$
17	HMPA	1.137	1.538 (7.3)	—	1.396 (2.88)	1.406 (1.69)	1.655 (1.60)
18	Acetone	1.139 (0.80)	1.617 (4.9)	—	—	—	—
19	1-methyl-2-pyrrolidone	—	1.604 (5.3)	—	—	—	—
20	DMA	—	1.616 (5.0)	—	—	1.416 (1.79)	—
21	DMF	1.199	1.655 (4.5)	1.520 (9.33)	1.431 (2.97)	1.431 (1.91)	1.719 (1.90)
22	MeCN	1.210	1.676 (3.9)	—	1.513 (3.38)	1.463 (1.95)	1.767 (2.13; 2.95[c])
23	DMSO	—	1.755 (3.9)	1.734 (8.60)	—	—	—
24	$MeNO_2$	—	1.746 (3.5)	—	—	—	—
25	$CHCl_3$	1.242	—	—	—	1.523 (2.48)	—
26	Pr^iOH	1.259	—	—	—	—	—
27	MeNHCHO	—	1.833 (1.1)	—	1.592 (3.76)	—	—
28	EtOH	1.316 (−1.68)	—	—	—	1.566 (2.85)	1.943 (3.08)
29	MeOH	1.324 (−2.11)	1.897 (0)	1.950 (5.94)	1.622 (4.04)	1.620 (3.10)	2.096 (3.73)
30	H_2O	1.458 (−3.31)	—	2.258 (3.67)	—	—	—

[a] Determined at 25 °C on a Pt electrode in 0.10 mol dm^{-3} solutions of Bu_4NClO_4; referred to the half-wave potential of cobaltocenium/cobaltocene in the same solvent and electrolyte. In the aqueous solution the electrolyte was 0.10 mol dm^{-3} Me_4NClO_4. [b] The rate parameters are: for I^-: log k, where k is the second-order rate constant (dm^3 mol^{-1} s^{-1}) for the reaction of MeI with labelled iodide ions;[13] for N_3^-: log (k/k^0), relative rates for the reaction of azide ion with *p*-fluoronitrobenzene;[14] k^0 is the second-order rate constant for the reaction in methanol; k is for reaction in the given solvent; for CN^-: N^+, Ritchie's nucleophilic parameter[15] based on cation–anion combination reactions in different solvents; for anions of 4-cyanophenol (ArOH), 2-mercaptobenzoxazole (HetSH) and ethyl nitroacetate (O_2NCH_2R): log $t_{\frac{1}{2}}$, where $t_{\frac{1}{2}}$ is the half-life (s) for the pseudo-first-order reaction with benzyl chloride (ArO^- and $HetS^-$) or methyl iodide ($O_2N\bar{C}HR$). [c] For the anion of ethyl nitroacetate, log $t_{\frac{1}{2}}$ for its pseudo-first-order reaction with ethyl acrylate.

irreversible anodic oxidation (Table 2). The relative rates (referred to methanol) of its S_NAr reaction[14] with *p*-fluoronitrobenzene were found to correlate well with $E_{p,a}$ for nine solvents [Fig. 2(*b*)] with the greatest deviation occurring for DMSO.

Cyanide.—For cyanide ion we examined the relationship between $E_{p,a}$ (Table 2) and Ritchie's nucleophilic parameter, N^+, that was developed on the basis of cation–anion combination reactions in various solvents.[15] A satisfactory correlation was found [Fig. 2(*c*)], again with the solvent giving the lowest oxidation potential (DMF, easiest oxidation of cyanide) having the largest N^+.

Other Nucleophiles—4-Cyanophenolate, 2-Mercaptobenzoxazole Anion and the Anion of Ethyl Nitroacetate.—The results given above concerning rates and nucleophilicity parameters taken from the literature, indicate that $E_{p,a}$ can be used to describe the nucleophilic reactivity of anions in different solvents. In order to extend the concept to other nucleophiles, we studied both $E_{p,a}$ and reaction rates for three other nucleophiles with differing reaction centres, 4-cyanophenolate (oxygen), 2-mercaptobenzoxazole anion (sulfur) and the anion from ethyl nitroacetate (usually behaves as a carbanion). The results are presented in Tables 2 and 3 as oxidation peak potentials and half-lives of the pseudo-first-order reactions.

Excellent linear correlations are found for the reactions of 4-cyanophenolate [Fig. 3(*a*)] and 2-mercaptobenzoxazole anion [$HetS^-$, Fig. 3(*b*)] with benzyl chloride. In the latter case, we also studied the effects of varying the cation of the electrolyte for three solvents (entries 31 *vs*. 17; 34–38 and 41 *vs*. 22; 42 *vs*. 29). For HMPA and MeOH, changing from Bu_4N^+ to Li^+ had little effect on either the oxidation potential or the rate of the reaction of $HetS^-$ with benzyl chloride. Presumably, ion pairing is not prevalent in these solvents. However, the analogous change in MeCN caused a 0.12 V positive shift in oxidation potential and a tenfold reduction in rate. Ion pairing between $HetS^-$ and Li^+ in MeCN makes the anion more difficult to oxidize and less reactive as a nucleophile. Remarkably, both the effects of

Table 3 Oxidation peak potentials,[a] V, of anions of 2-mercaptobenzoxazole (HetSH) and ethyl nitroacetate (O_2NCH_2R) and log $t_{\frac{1}{2}}$ of the reaction of $HetS^-$ with benzyl chloride (number in parentheses) and anion of ethyl nitroacetate with methyl iodide (first number in parentheses) or addition to ethyl acrylate (second number in parentheses) in different $MClO_4$ solutions

Entry	Solvent	M^+	$HetS^-$	$O_2N\bar{C}HR$
31	HMPA	Li^+	1.383 (1.58)	—
32	DMF	Na^+	—	1.809 (2.18)
33	DMF	Li^+	—	1.906 (2.73; 4.24)
34	MeCN	Hep_4N^+	1.461 (1.88)	1.682 (1.78; 2.63)
35	MeCN	$(C_5H_{11})_4N^+$	1.455 (1.85)	1.755 (2.00)
36	MeCN	Et_4N^+	1.472 (2.00)	—
37	MeCN	Me_4N^+	1.500 (2.32)	1.812 (2.26; 3.01)
38	MeCN	Na^+	1.548 (2.60)	—
39	MeCN + 10%DMF	Na^+	—	1.968 (3.02)
40	MeCN + 20%DMF	Na^+	—	2.032 (—; 4.44)
41	MeCN	Li^+	1.586 (3.00)	2.216 (4.26; 5.14)
42	MeOH	Li^+	1.631 (3.19)	—

[a] Determined at 25 °C on a Pt electrode in 0.10 mol dm^{-3} solution of $MClO_4$; referred to the half-wave potential of cobaltocenium/cobaltocene in the same solvent and electrolyte.

changing the solvent and the counter ion are well accounted for by the same correlation line [Fig. 3(*b*)].

For the anion of ethyl nitroacetate, reaction with methyl iodide was chosen[1c] [Fig. 3(*c*)]. Once again, a very good linear correlation is found for twelve solvents and/or counter ions. The correlation spans 0.55 V and almost three orders of magnitude in the reaction rate and both the solvent dependence and the effect of counter ion are subsumed in the same correlation.

Finally, the reaction of the anion of ethyl nitroacetate with the Michael acceptor, ethyl acrylate, was studied [Fig. 3(*d*)]. This reaction gives good yields of the addition product, diethyl α-nitroglutarate.[1c] The correlation is satisfactory though not as strong as seen for the nucleophilic displacement reactions.

Discussion

From an analysis of the data of Tables 2 and 3 we can draw some conclusions that will be useful both in electrosynthesis and general organic synthesis.

In solvents like HMPA or DMF the influence of cation on $E_{p,a}$ and nucleophilic reactivity is not large because ion pairing is not prevalent in these solvents. In addition, the reactivity is quite high. There is also little effect of counter ion in alcohols, but in this case the reactivity of the anions is much lower so the reactions are not very practical from a synthetic point of view.

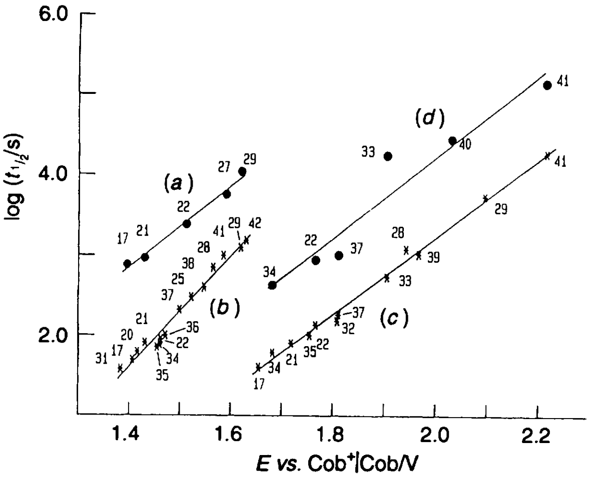

Fig. 3 Relationship between oxidation peak potentials of anions of 4-cyanophenol, 2-mercaptobenzoxazole and ethyl nitroacetate and log $t_{\frac{1}{2}}$ of their reactions. Numbers correspond to entry numbers in Tables 2 and 3. (*a*) Reaction of 4-cyanophenolate with benzyl chloride. Regression equation: $\log(t_{\frac{1}{2}}) = -4.219 + 5.047\,(E_{p,a})$ ($r = 0.993$). (*b*) Reaction of anion of 2-mercaptobenzoxazole with benzyl chloride. Regression equation: $\log(t_{\frac{1}{2}}) = -8.090 + 6.925\,(E_{p,a})$ ($r = 0.987$). (*c*) Reaction of anion of ethyl nitroacetate with methyl iodide. Regression equation: $\log(t_{\frac{1}{2}}) = -6.382 + 4.804(E_{p,a})$ ($r = 0.996$). (*d*) Reaction of anion of ethyl nitroacetate with ethyl acrylate. Regression equation: $\log(t_{\frac{1}{2}}) = -5.757 + 4.989\,(E_{p,a})$ ($r = 0.965$).

In MeCN, the reactivity is, in general, quite high and the influence of ion pairing on $E_{p,a}$ and reactivity of the anions is very strong. Here, there is a distinct advantage to using tetraalkylammonium salts as the supporting electrolyte in electrosynthesis because the greatest reactivity is seen with these weakly interacting counter ions.

As can be seen from the kinetic data, the reactivity of these anions in the presence of sodium salts in DMF (or DMA, HMPA) is large and very similar to the reactivity in the presence of tetraalkylammonium salts in acetonitrile. A practical advantage of the use of acetonitrile is its easy removal from the electrolysed solution by evaporation.

In general these conclusions are not new and only confirm that which is known qualitatively from other kinds of investigation. Nevertheless, the present approach offers an attractive way of evaluating reaction conditions for contemplated syntheses. The oxidation potentials are quickly and easily measured using equipment that is now widely available in chemistry laboratories. The screening process identifies those conditions (solvent and counter ion) that give the lowest (least positive) oxidation potential and, following the implication of the present work, that solution environment should lead to the most rapid reactions.

In summary, the present results, together with previous data,[8] lead to the conclusion that the irreversible oxidation potentials of anions can be used to predict their nucleophilic reactivity in different kinds of reaction such as S_N1, S_N2, S_NAr and addition reactions. It is noteworthy that the oxidation potential as a nucleophilic reactivity index describes the influence of both solvent and counter ion on the reactions.

Experimental

Materials.—Acetonitrile (MeCN), dimethylacetamide (DMA), dimethyl ether of di(2-hydroxyethyl) ether (diglyme), chloroform, isopropyl alcohol (Pr^iOH), nitromethane ($MeNO_2$), tetrahydrofuran (THF), methylene chloride, and potassium cyanide were from Fisher, hexamethylphosphoramide (HMPA), *N*-methylformamide (MeNHCHO), 2,4,6-tri-*tert*-butylphenol (TBPH), 2-mercaptobenzoxazole (HetSH), ethyl nitroacetate, benzyl chloride, 4-cyanophenol, methyl iodide, ethyl acrylate, ferrocene, cobaltocenium hexafluorophosphate, sodium perchlorate and lithium perchlorate were from Aldrich. Dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were from Burdick and Jackson whereas methanol (MeOH) and acetone were from EM Science, and 1-methyl-2-pyrrolidone was from Sigma. Ethanol (EtOH) was from Quantum, sodium azide from Johnson Matthey Electronics, tetrabutylammonium iodide and tetraethylammonium perchlorate from G. Frederick Smith and tetrabutylammonium perchlorate was supplied by Kodak. Tetraheptyl-, tetrapentyl- and tetramethyl-ammonium perchlorates were prepared by the method described.[16]

Standard samples of the reaction products ethyl 2-nitropropionate, diethyl α-nitroglutarate, *p*-(benzyloxy)benzonitrile and benzyl benzoxazol-2-yl sulfide were prepared as described elsewhere.[1c,17,18]

Instrumentation and Methods.—Voltammetric measurements and controlled potential electrolyses were carried out in a glass cell under nitrogen at 25 ± 1 °C. The working electrodes were a platinum (0.166 cm diameter) disk electrode for cyclic voltammograms (scan rate 0.100 V s^{-1}) and a platinum gauze electrode (*ca.* 10 cm^2) for electrolyses. The electrolyte concentration was 0.10 mol dm^{-3} and the volume of the test solution was 10 cm^3. The auxiliary electrode (platinum wire) compartment was separated from the working electrode compartment by two medium-porosity glass frits. The experiments were conducted using an EG&G Princeton Applied Research (PAR) Model 273 Potentiostat/Galvanostat. The silver reference electrode was composed of a silver wire in contact with 0.01 mol dm^{-3} AgNO$_3$, 0.10 mol dm^{-3} Et$_4$NClO$_4$ and acetonitrile and its potential was 0.043 ± 0.004 V negative of the ferrocene/ferrocenium couple and 1.287 ± 0.004 V positive of the cobaltocenium/cobaltocene couple in 0.10 mol dm^{-3} Bu$_4$NClO$_4$–MeCN.

The concentration of nucleophilic anions used in these studies was in the range 5–8 × 10^{-3} mol dm^{-3}. Tetrabutylammonium iodide, sodium azide and potassium cyanide were used to prepare solutions of iodide, azide and cyanide ions. The controlled cathode potential electrolysis of the corresponding non-ionized forms was used for generation* of the anions of 2,4,6-tri-*tert*-butylphenol (reduction peak potential in 0.10 mol dm^{-3} Bu$_4$NClO$_4$–MeCN is -2.24 V *vs.* Ag/Ag$^+$), 4-cyanophenol (-1.69 V), 2-mercaptobenzoxazole (-1.65) and ethyl nitroacetate (-1.82[1c]).

Studies of known concentrations of the anions showed that the anodic peak currents were proportional to concentration, providing a voltammetric method of monitoring anion concentration. The solutions of iodide, azide and cyanide were prepared by dissolving known quantities of pure salts and the solutions of the other anions were prepared by the electrochemical method or by treatment of solutions of the non-ionized forms with an equimolar quantity of tetrabutylammonium hydroxide or sodium hydride.

The reported oxidation peak potentials are averages of at least three measurements. The range of the values did not exceed 0.005 V. Between experiments the working electrode was polished with 0.05 μm alumina (Buehler), washed with distilled water, acetone and the appropriate solvent. The cyclic voltammograms in THF, diglyme, methylene chloride and Pr^{i}OH were recorded with IR compensation.

The kinetic measurements were carried out in the electrochemical cell. After production of the nucleophilic anions by electrolysis, the solution was stirred at constant speed with a magnetic stirrer and a hundredfold excess of alkyl halide was added to initiate the reaction. The decrease of the nucleophile concentration was monitored by chronoamperometry or, for reactions with slow rates, by cyclic voltammetry. For ethyl nitroacetate the reactions were monitored by GC except entries 17 and 20 which were monitored by cyclic voltammetry. Before analysis by chromatography, a fiftyfold excess of acetic acid was added to quench the nucleophilic reaction.

The formation of the expected alkylated products of the various nucleophilic reactions was generally confirmed by gas chromatography (comparison of retention time with standards). For 2-mercaptobenzoxazole, the product was identified by TLC (comparison of R_f with a standard) on silica-gel plates (Uniplate, Analtech) using a hexane–acetone mixture as the eluent. Other evidence that the alkylation reactions were proceeding was the appearance of oxidation peaks for chloride (0.8 V *vs.* Ag/Ag$^+$ in 0.10 mol dm^{-3} Bu$_4$NCl$_4$–MeCN) or iodide (0.08 V) in the voltammograms. These potentials were confirmed by recording voltammograms of trimethylbenzylammonium chloride and tetrabutylammonium iodide.

The reported half-lives ($t_{\frac{1}{2}}$) are averages of three successive values that were obtained from current–time or concentration–time curves.

Gas chromatographic analysis of the compounds was carried out with a Varian Model 3700 gas chromatograph with a 10% OV 101 Chrom GHP 100/120 column (0.5 m × 1/8 in) column and helium as the carrier gas. The column temperature for analysis of ethyl 2-nitropropionate was 60 °C for 1 min followed by a 25 °C min^{-1} increase to 80 °C; for *p*-(benzyloxy)benzonitrile it was 90 °C for 1 min followed by an 80 °C min^{-1} increase to 250 °C. A thermal conductivity detector was used at 250 °C. A working curve (peak height *vs.* concentration) was prepared by using solutions of known concentration of standard compounds in MeCN or DMF.

Acknowledgements

This research was supported by the National Science Foundation, Grant CHE9100281.

References

1 (*a*) For reviews see J. H. P. Utley, *Top. Curr. Chem.*, 1987, **142**, 131; M. M. Baizer, in *Organic Electrochemistry*, eds. H. Lund and M. M. Baizer, Marcel Dekker, New York, Basel, Hong Kong, 3rd edn., 1991, p. 1265; (*b*) T. Fushigami, K. Suzuki and T. Nonaka, *Electrochim. Acta*, 1991, **35**, 239, and papers cited therein; (*c*) M. E. Niyazymbetov and D. H. Evans, *J. Org. Chem.*, 1993, **58**, 779 and papers cited therein.
2 (*a*) J. M. Harris and S. P. McManus, eds., *Nucleophilicity*, American Chemical Society, Washington, DC, 1987 (*Advances in Chemistry Series*, No. 215); (*b*) R. G. Pearson, *J. Org. Chem.*, 1987, **52**, 2131; (*c*) C. D. Ritchie, *Can. J. Chem.*, 1986, **64**, 2239; (*d*) T. Kozaki, K. Morihashi and O. Kikuchi, *J. Am. Chem. Soc.*, 1989, **111**, 1547.
3 J. O. Edwards, *J. Am. Chem. Soc.*, 1954, **76**, 1540; 1956, **78**, 1819.
4 (*a*) A. Pross and S. S. Shaik, *J. Am. Chem. Soc.*, 1982, **104**, 2708; (*b*) S. S. Shaik, H. B. Schlegel and S. Wolfe, *Theoretical Aspects of Physical Organic Chemistry. The S$_N$2 Mechanism*, Wiley, New York, 1992.
5 (*a*) C. D. Ritchie, *J. Am. Chem. Soc.*, 1983, **105**, 7313; (*b*) C. D. Ritchie, in *Nucleophilicity*, eds. J. M. Harris and S. P. McManus, American Chemical Society, Washington, DC, 1987 (*Advances in Chemistry Series*, No. 215), p. 169; (*c*) L. Eberson, *Acta Chem. Scand., Ser. B*, 1984, **38**, 439.
6 A. J. Bard and L. R. Faulkner, *Electrochemical Methods. Fundamentals and Applications*, Wiley, New York, 1980, pp. 213–231; 429–487.
7 R. E. Dessy, *J. Am. Chem. Soc.*, 1966, **88**, 5121.
8 M. E. Niyazymbetov and V. A. Petrosyan, *Izv. Akad. Nauk SSSR., Ser. Khim.*, 1991, 2469.
9 G. Gritzner and J. Kuta, *Pure Appl. Chem.*, 1984, **56**, 461.
10 H. Shalev and D. H. Evans, *J. Am. Chem. Soc.*, 1989, **111**, 2667.

---

* It is known that the one-electron reduction of organic acids on a platinum cathode results in the formation of the corresponding anions with high efficiency; see ref. 1(*c*) and papers cited therein.

11 C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, VCH, Weinheim, 1988, p. 339.
12 V. Gutmann, *Electrochim. Acta*, 1976, **21**, 661.
13 E. R. Swart and G. J. LeRoux, *J. Chem. Soc.*, 1957, 406.
14 C. Reichardt, ref. 11, p. 219.
15 C. D. Ritchie, in *Solute–Solvent Interactions*, eds. J. F. Coetzee and C. D. Ritchie, Dekker, New York, 1976, Vol. 2, p. 260.
16 I. M. Kolthoff and J. F. Coetzee, *J. Am. Chem. Soc.*, 1957, **79**, 870.
17 C. Moussebois, J. F. Heremans, R. Merenyi, W. Rennerts, *Helv. Chim. Acta*, 1977, **60**, 237.
18 M. Yamato, Y. Takeuchi, K. Hashigaki, K. Hattori, E. Muroga, T. Hirota, *Chem. Pharm. Bull.*, 1983, **31**, 1733.

Paper 3/00799E
Received 9th *February* 1993
Accepted 23rd *March* 1993