cates the importance of the cyclic *oxycarbene* intermediate. It is certainly conceivable that the *oxycarbene* intermediate could be in equilibrium with the *diradical* intermediate. The quantum yield of these intermediates in the liquid phase can be much higher than 0.20 in *n*-C_7H_{16}, since we cannot be certain that the *oxycarbene* intermediate did not insert into the C–H bonds in *n*-C_7H_{16} before the intermediates decomposed to the C_2 and C_3 products. If one expects the quantum yield for the internal conversion process in the liquid phase to be about the same as in the gas phase, 0.6–*ca.* 0.7, then the total quantum yields of the observed products should be 0.3–0.4. Since the overall observed product quantum yields are less than 0.22, the unaccounted quantum yields are 0.1–0.2. It should be noted that the short-lived nature of the photoexcited cyclobutanone in the liquid phase is analogous to that of the photoexcited oxetanones previously studied.[20]

We hope to obtain further mechanistic insight into the roles played by the above proposed transient intermediates through the study of the thermal decomposition and the photochemical decomposition of *cis*- and *trans*-2,3-dimethylcyclobutanone as well as *cis*- and *trans*-2,4-dimethylcyclobutanone.[16b,19] One feature of cyclobutanone photochemistry worthy of attention is the rapid electronic relaxation process probably *via* a chemical isomerization route[12] which is responsible for the "predissociative" behavior.

Acknowledgment. Authors are grateful to Dr. D. C. Moule of Brock University for his kindness in giving us the spectral assignments from the high-resolution absorption spectra of cyclobutanone. Discussions with Drs. R. J. Campbell and R. F. Klemm have been helpful.

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Electrochemical Reduction of Pyrimidine in Acetonitrile. Behavior of the Anion Free Radical

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Abstract: The electrochemical reduction of pyrimidine, which is the model compound for the reduction of the biologically important purine–pyrimidine series, has been investigated in acetonitrile media. Pyrimidine is initially reduced in a one-electron, reversible, diffusion-controlled process at fairly negative potential to produce an unstable radial anion, which is quickly deactivated *via* two competitive pathways: (1) fast dimerization to form a pyrimidine anionic dimer (probably the 4,4′ species) with a rate constant of $8 \pm 5 \times 10^5$ l./(mol sec) and (2) proton abstraction from residual water [rate constant of *ca.* 7 l./(mol sec)], which is rapidly followed by a further one-electron reduction to produce ultimately 3,4-dihydropyrimidine. Addition of acid to pyrimidine solutions results in the appearance of a new wave at less negative potential, which is attributed to the one-electron reduction of an N-protonated pyrimidine species to produce a free radical which dimerizes very quickly, probably to the 4,4′ compound; this wave is very similar to the first one-electron wave of pyrimidine in aqueous media. Pyrimidine is the only aromatic system thus far systematically examined which shows initial one-electron reductions in both aqueous (proton rich) and nonaqueous (proton poor) media.

In recent years, much interest has developed in the electrochemical behavior of biologically important compounds.[1-3] As a result of our concern with purines, pyrimidines, and their nucleosides and nucleotides, considerable work has been done on pyrimidine (1,3-diazine) itself in aqueous solution[4-6] since it is the prototype compound for the purine–pyrimidine series; *e.g.*, the electrochemical reduction of purines occurs in the pyrimidine ring. Recent work has concentrated on the nature of the initial, rate-controlling, one-electron (1-e) reduction of pyrimidine, more definitive information on which should provide additional insight into the redox behavior of the biologically important purines and pyrimidines. Consequently, the electrochemical reduction of pyrimidine has been investigated in acetonitrile on the basis that the information obtained in an inert solvent would reflect, more directly, the properties of pyrimidine itself and not its solvent–solute interaction, as well as the properties and behavior of the anion free radical expected in proton-poor medium.

Another and more fundamental reason for investigating the pyrimidine reduction mechanism in a nonaqueous solvent is that it affords the unique opportunity of studying a 1-e reduction process in an aromatic system, which also undergoes 1-e reduction in aqueous media. Many organic compounds, *e.g.*, aromatic hydrocarbons, which exhibit a 1-e or two separate 1-e reduction steps in nonaqueous media, show only a 2-e reduction in aqueous media due to a fast ECE mechanism involving protonation of the electrogenerated radical anion. The development of information regarding the reduction of the C–N aromatic double bond

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Table I. Polarographic Data for Pyrimidine Reduction in Various Solvents

Solvent	$E_{1/2}$, V	$\lvert E_{3/4} - E_{1/4}\rvert$, mV	I_d	$\eta_{25°}$	$I_d\eta^{1/2}$	Ref
CH_3CN	-2.628^a	54	3.39	0.345	1.99	*e*
	-2.340^b	70	3.58		2.10	17
DMF	-2.340^c	70	2.24	0.802	2.00	14–16
H_2O	$-0.576-0.105\ pH^{b,d}$	43	2.12	0.894	2.01	4

[a] *Vs.* Ag|AgNO$_3$ (0.01 *M*) electrode in acetonitrile. [b] *Vs.* sce (aqueous). [c] *Vs.* Ag|AgCl electrode in DMF. [d] pH dependence of wave I. [e] Present study.

is another cogent reason for the study of pyrimidine in nonaqueous media.

Pyrimidine Reduction in Aqueous Media. In aqueous media, pyrimidine exhibits five reduction waves at mercury electrodes over the available pH range.[4,5] In acidic media, pH-dependent 1-e wave I is seen. At about pH 3, pH-independent 1-e wave II emerges from background discharge. These two waves merge near pH 5 to form pH-dependent 2-e wave III. Near pH 7.2, pH-independent 2-e wave IV emerges from background and, at pH 9.2, merges with wave III to form pH-dependent 4-e wave V. Wave I is due to the 1-e reduction of pyrimidine to the neutral radical; wave II is the 1-e reduction of the latter to a dihydropyrimidine, with wave III being the composite of these two steps. Wave IV is the 2-e reduction of the dihydro species to a tetrahydropyrimidine with wave V being the composite of waves III and IV.

Pyrimidine Reduction in Nonaqueous Media. Although a great deal of work has been done on the electrochemistry of nitrogen heterocyclic compounds in aqueous media,[7] study of their electrochemistry in nonaqueous media until quite recently has been primarily concerned with radical anion generation to observe electron paramagnetic resonance (epr) signals. Spectra were reported[8] for eight azine radical anions generated at a tungsten cathode coupled with a mercury pool anode; however, the "optimum anode–cathode voltage was determined empirically in each case" (30 V for pyrazine) so that no information can be gained about potential or current characteristics. The radical anions of pyrimidine and pyridine could not be generated, presumably because of rapid dimerization. No epr signal was observed on the electroreduction of pyrimidine in DMSO at a mercury pool electrode.[9]

More often, however, radical anions have been prepared using alkali metal in dimethoxyethane or tetrahydrofuran *in vacuo*.[10,11] A study[12] of the three diazine radical anions reported that pyrazine and pyridazine radical anions give a "normal" analyzable epr spectrum, but that pyrimidine gives a spectrum with profuse hyperfine splitting (>100 lines), qualitatively similar to that observed on alkali metal reduction of pyridine solutions. Since the spectrum of reduced pyridine was shown to be due to the bipyridyl radical anion,[13] it was concluded that a significant degree of coupling occurred and that the spectrum was due to the bipyrimidyl anion radical. However, no assignments were made and the spectrum was not analyzed to prove this hypothesis or to determine the structure of the dimer.

Several reports have recently appeared on the electrochemical reduction of nitrogen heterocycles in nonaqueous media. van der Meer[14–16] found a strong dependence between i_d and $E_{1/2}$, and the residual water level of the solvent for eight diazaaromatics including quinazoline in DMF, but not, surprisingly, for pyrimidine, whose reduction current was unaffected by as much as 1% water. The behavior of most azaaromatics was attributed to a fast ECE mechanism,[17] in which the electrogenerated radical anion is protonated and the resulting free radical is immediately reduced; it was concluded that protonation of the anion radical is the first step in the dimerization of pyrimidine and quinazoline. The behavior of some 20 azines in acetonitrile was surveyed,[18] using polarography and cyclic voltammetry.

Results and Discussion

DC Polarography. Pyrimidine gives a one-electron, diffusion-controlled, reversible reduction wave at very negative potential in acetonitrile–0.1 *M* TEAP; the data are compared with those for other solvents in Table I. The initial pyrimidine reduction wave is quite similar in acetonitrile and DMF, and is also similar to the initial 1-e reduction in water (wave I); *e.g.*, correction for the change in viscosity shows agreement in diffusion current constant to within 5% for the three solvents.

Although pyrimidine might be expected to be difficult to reduce in a nonaqueous solvent on the basis of the polarographic behavior of aromatic hydrocarbons in acetonitrile and of nitrogen heterocycles in water, since pyrimidine has only one ring about which to spread charge, the large difference between its ease of reducibility in aqueous and nonaqueous media merits further elaboration. On the basis of the rather tenuous extrapolation of half-wave potentials from water into acetonitrile, $E_{1/2}$ for the first 1-e reduction of pyrimidine in water at pH 13—if this process were to occur at pH 13—would be approximately −2.2 V.[19] Since

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(7) P. Zuman, "Substituent Effects in Organic Polarography," Plenum Press, New York, N. Y., 1967.

(8) J. C. M. Henning, *J. Chem. Phys.*, **44**, 2139 (1966).

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(14) D. van der Meer and D. Feil, *Recl. Trav. Chim. Pays-Bas*, **87**, 746 (1968).

(15) D. van der Meer, *ibid.*, **88**, 1361 (1969).

(16) D. van der Meer, *ibid.*, **89**, 51 (1970).

(17) An ECE mechanism for a single polarographic wave refers to one in which an electrochemical step involving electron transfer produces a species which undergoes a chemical reaction to produce a product which is unstable at the potential at which it is formed and thus rapidly undergoes a second electrochemical reaction.

(18) S. Millefiori, *J. Heterocycl. Chem.*, **7**, 145 (1970).

(19) (a) The autoprotolysis constant of acetonitrile[19b] is 3×10^{-27}, which corresponds to a 10^{-13} *M* proton concentration in acetonitrile. Actually, the "proton pressure" in acetonitrile is probably a few orders of magnitude greater than a pH of 13 would indicate owing to the presence in the solvent of minute traces of various acids, so that the esti-

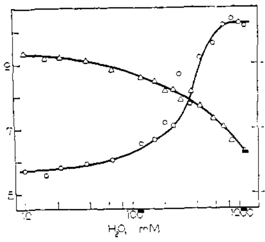

Figure 1. Effect of water on $E_{1/2}$ (Δ) and i_{max} (○) of the pyrimidine reduction wave in acetonitrile; pyrimidine, 1.47 m*M*.

the observed $E_{1/2}$ in acetonitrile is at least 400 mV more negative, it is reasonable to conclude that the solvent water markedly influences the reduction of pyrimidine, over and above the effect that proton concentration or solvation energy difference is known to have. On the assumption that the properties of the compound itself are more nearly seen in an "inert" solvent, drastically different behavior in water must, therefore, be due to water and proton participation in the electrode reaction. Although pyrimidine is a nonprotonated molecule over most of the pH range in water ($pK_a = 1.30$),[20] intimate proton participation in the first reduction step must be concluded; the slope of 0.105 V/pH for the $E_{1/2}$ *vs.* pH plot for pyrimidine would indicate involvement of two protons in the first reduction step.[4] Specific proton participation in the electrode reaction has been postulated for C—F bond fission and C—O double bond reduction *via* hydrogen bonding and concurrent electrode-C-X-H$^+$ bond polarization.[21] While the same type of hydrogen bonding cannot be postulated in the case of pyrimidine, the difference in behavior in the two solvents could be taken to indicate polarization by free or labile protons in water. It would appear that the behavior of pyrimidine in aqueous media will not be well understood until more emphasis is placed on the role of solvent participation (*cf.* Mechanism of Pyrimidine Reduction).

1. Effect of Water Addition. The effect of water and other possible proton donors on the electrochemical reduction mechanism of aromatic hydrocarbons is well known;[22-28] *e.g.*, the reduction of anthracene in the presence of proton sources can be treated on the basis of an ECE mechanism derived from reaction layer theory.[27,29,30] Since proton sources should have a much greater effect on azaaromatics than on aromatic hydrocarbons because of the basic nitrogen available for hydrogen bonding, their effect on the reduction of pyrimidine was investigated in detail.

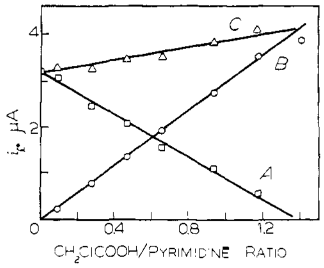

Figure 2. Effect of chloroacetic acid on the polarographic reduction of pyrimidine in acetonitrile; pyrimidine, 1.03 m*M*: (A) pyrimidine reduction wave, $E_{1/2} = -2.63$ V; (B) pyrimidine–acid wave, $E_{1/2} = 1.74$ V; (C) total current

Addition of water to acetonitrile solutions of pyrimidine produces rather large positive shifts in $E_{1/2}$ and increased reduction current (Figure 1). At 1.35% water (750 m*M*), $E_{1/2}$ has shifted about +110 mV, approximately the same magnitude as in DMF at this water concentration, but the diffusion current constant has also increased by some 75% over that in dry acetonitrile. At about 2% water, other waves appear, which may correspond to waves II and IV observed in aqueous solution (*cf.* the introduction). By 5–10% water, the polarographic behavior is close to that observed for pyrimidine in unbuffered aqueous solutions.

This behavior can be explained on the basis of the electrogenerated pyrimidine radical anion abstracting a proton from water to form a protonated radical which is more easily reduced than pyrimidine itself and, consequently, is reduced immediately on its formation at the electrode–solution interface. The resulting compound should eventually abstract a second proton from water to form a dihydro species, which is probably 3,4-dihydropyrimidine, the same product as is formed in aqueous solution. This type of ECE process is also invoked by van der Meer[14-16] to explain the reduction of other azaaromatics in DMF in which, as previously mentioned, pyrimidine did not exhibit an increase in current on addition of water; this behavior was attributed to the possibilities that very little R$^-$ ion or RH radical is formed or that another reaction mechanism had precedence with pyrimidine.

2. Effect of Acid Addition. In general, the addition of acids stronger than water produces a new, drawn-out wave at more positive potential than either the original pyrimidine reduction wave or a wave that can be attributed to reduction of the acidic proton itself. With increase in the acid/pyrimidine ratio at fixed pyrimidine concentration, the new wave increases and the original pyrimidine wave decreases, both approximately linearly (Figure 2), except in the case of the very weak acid phenol where the proximity of the two waves makes analysis of the current quite difficult. With increase in the acid/pyrimidine ratio, the new wave also becomes more drawn out and ill shaped, exhibiting one or more maxima and drop-time irregularities.

On addition of benzoic acid up to an acid/pyrimidine ratio of about 1.4, the original reduction wave is approximately constant in $E_{1/2}$ and slope, while $E_{1/2}$ of the new wave becomes some 20 mV more positive and its $E_{1/4} - E_{3/4}$ value increases from 90 to 200 mV. Plots of log *i vs.* log *h* for a solution of 1.46 m*M* pyrimidine and 0.94 m*M* benzoic acid (HA/py ratio = 0.64) have slopes of 0.70 and 0.79 for the new and original waves,

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mated difference between $E_{1/2}$ in water and in acetonitrile should be even larger by a few hundred millivolts. (b) J. F. Coetzee and G. R. Padmanabhan, *J. Phys. Chem.*, **66**, 1708 (1962).

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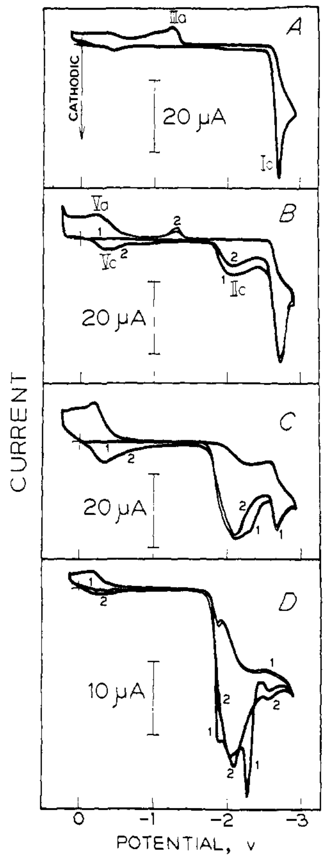

Figure 3. Effect of benzoic acid concentration on cyclic voltammograms of 1.46 mM pyrimidine in acetonitrile. Peaks identified in text. Arabic numerals refer to the number of the cycle on successive scans: (A) scan rate 200 mV/sec, acid concentration 0.0 mM; (B) scan rate 400 mV/sec, acid concentration 0.79 mM (HA/py ratio = 0.54); (C) scan rate 200 mV/sec, acid concentration 2.37 mM (HA/py ratio = 1.62); (D) scan rate 50 mV/sec, acid concentration 3.95 mM (HA/py ratio = 2.70).

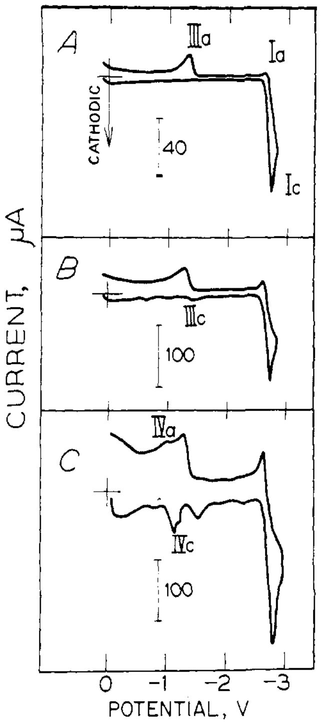

Figure 4. Steady-state cyclic voltammograms of 1.03 mM pyrimidine in acetonitrile at high scan rates: (A) 3.0 V/sec, (B) 15 V/sec, (C) 60 V/sec. Peaks identified in text.

respectively, indicating deviation from the simple diffusion control characteristic of pyrimidine reduction in dry acetonitrile (slope of 0.54). With increase in h from 20 to 60 cm, $E_{1/2}$ of the new wave becomes some 30 mV more negative.

Addition of the very strong acid, perchloric, results in the appearance of several waves prior to the main pyrimidine reduction wave, the most positive of which is at −0.80 V and is due to the pyrimidine–acid reduction process. The heights of the latter and original pyrimidine waves are difficult to measure because of maxima and drop-time irregularities. As perchloric acid is added, however, the original pyrimidine wave decreases and has completely disappeared by an acid/pyrimidine ratio of about 1.2, and the combined height of the two pyrimidine waves increases in approximately the same manner as for the other acids.

These results are consistent with a prior protonation of the pyrimidine molecule at one of the nitrogen atoms to give a species more easily reducible than the original pyrimidine molecule. The potential of the acid-produced pyrimidine reduction is more positive the stronger the acid added (Table II), which would indicate the involvement of either some equilibrium protonation step in the potential-determining reaction or some energetic barrier which would probably be dissociation of the proton from the acid. The nature of the pyrimidine–acid species formed on acid addition is most probably a hydrogen-bonded or ion-pair complex, *e.g.*, RN---H$^+$---A$^-$ or RNH$^+$A$^-$, in view of the weak dissociation of three of these acids in acetonitrile.

Table II. Correlation of Potential for the Pyrimidine–Acid Complex Reduction Wave with the Strength of the Added Acid

Acid added	pK_a^{AN}	pK_a^{aq}	$E_{1/2}$, V
Perchloric	*a*	*a*	−0.80
Chloroacetic	9.8[b]	2.8	−1.74
Benzoic	12.0[b]	4.2	−1.90
Phenol		10.0	−2.41

[a] Perchloric acid is completely dissociated in both acetonitrile and water. [b] From G. Charlot and B. Tremillon, "Les Réactions chimiques dans les Solvants et les Sels fondus," Gauthier Villars, Editeur, Paris, 1963, p 377.

Cyclic Voltammetry. At slow polarization rates (<200 mV/sec), pyrimidine first gives a cathodic peak (Ic) at −2.7 V, corresponding to the 1-e reduction of the pyrimidine moiety, whose height is proportional to concentration and the square root of scan rate (Figure 3A); on the return sweep, no anodic peak is seen until about −1.3 V (IIIa). On the second sweep, a small cathodic blip at about −1.3 V (IIIc) appears only at scan rates greater than 200 mV/sec. At moderate scan rates (>3 V/sec), anodic peak Ia appears at approximately the proper potential to indicate a couple with Ic and grows with increasing scan rate (Figure 4). Finally, at very fast scan rates (>20 V/sec), a fairly sharp doublet (IVc) and two small blips (IVa) on the positive potential side of peak IIa appear (Figure 4C).

Cyclic voltammetry of pyrimidine solutions containing benzoic acid (Figure 3) shows the irreversible pyrimidine–acid peak at about −2.1 V (IIc); this peak becomes quite distorted at higher acid concentrations—behavior analogous to the drawn-out, irregular wave obtained at the DME—and the second scan is markedly different from the first. At fairly high acid/pyrimidine ratios (Figure 3D), a sharp peak due to the reduction of benzoic acid itself is seen at about −2.3 V, which, however, does not appear on the second cycle, perhaps due to formation of the AHA$^-$ species by reaction of oncoming benzoic acid with benzoate anion remaining after proton reduction and proton loss due to the acid-assisted reduction of pyrimidine.[31] The variations in peak heights as a function of acid/pyrimidine ratio for the five waves observed at 200 mV/sec scan rate are summarized in Figure 5. On second and subsequent sweeps, a pair of peaks (Va and Vc) appear at −0.2 to −0.5 V, which are observed on reduction of acids in acetonitrile (*cf.* next subsection). A solution 1.46 m*M* in pyrimidine and 0.79 m*M* in benzoic acid showed a linear variation of i_p with $v^{1/2}$ for the various peaks for scan rates from 50 to 400 mV/sec, indicating diffusion control. At high scan rates, peak height IIc substantially decreases relative to peak Ic, as expected for an irreversible reaction with a preceding chemical reaction, *i.e.*, the rate of the chemical reaction is no longer able to keep up with the polarization rate.

Identification of Peaks. Peak Ic (−2.69 V), as indicated previously, corresponds to the 1-e reduction of the pyrimidine ring to the radical anion; peak Ia corresponds to the 1-e reoxidation of the latter. The fact that Ia is seen only at fast scan rates, and then with small peak height, indicates that the pyrimidine radical anion is very short lived, in agreement with the behavior postulated from epr work.[8,10–12]

Peak IIc—reduction of the pyrimidine–acid complex—probably corresponds most closely to the reduction process observed for pyrimidine in aqueous solution. Similar to the behavior in water, peak IIc is totally irreversible; no anodic peak could be identified that could serve for a couple with IIc, indicating that the product is stable to oxidation over the potential range scanned. In aqueous media, no anodic peaks at all could be seen which would be resultant from any of the pyrimidine reductions at the HMDE on slow or fast (36 V/sec) cyclic voltammetry.[6]

Epr data and the available voltammetric evidence (presented more fully later) indicate that the pyrimidine radical anion dimerizes readily. Voltammetric peak IIIa (−1.32 V), therefore, corresponds to the irreversible oxidation of a pyrimidine anionic dimer rather than of a free-radical species.

Peak IIIc (−1.37 V) probably corresponds to the reduction of the product of the oxidation producing peak IIIa. The following considerations support the argument that the species being reduced is free radical in nature, which implies a 1-e oxidation in IIIa. While the species responsible for peak IIIa is somewhat unstable (half-life probably not more than 10 sec), the species responsible for IIc is much less stable; peak height IIIc is quite small and disappears at scan rates less than 200 mV/sec. Addition of small amounts of benzoic acid (0.1–1 m*M*) markedly decreases IIIa, but IIIc disappears even at very fast scan rates. Peak Ia, due to oxidation of a free radical, also decreases more rapidly than IIIa on addition of protons. These facts also indicate that the species involved in Ia and IIIc are not protonated pyrimidine species such as might be produced on proton abstraction from the solvent. Recycling through the potential range of IIIa and IIIc produces only base current after the first sweep. The presence of a kinetic-controlled chemical step following the first electron transfer is supported by the fact that the shape, potential, and height of peaks IIIa and IIIc are affected by scan rate, cathodic switching potential, and the length of time spent at the latter.

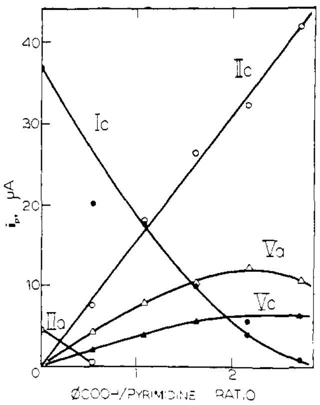

Figure 5. Effect of benzoic acid concentration on cyclic voltammetric peaks of pyrimidine (1.46 m*M*); scan rate 200 mV/sec. Peaks identified in text.

Multiple peaks IVa and IVc, which appear on steady-state cycling at very fast scan rates (>20 V/sec), do not seem to constitute redox couples, if only because of the discrepancy in current magnitude, and little can be said about the nature of the species producing them except that they are probably short-lived intermediates, possibly radical in nature, arising from the cyclic scanning and accompanying chemical reactions. Thus, peak IVa may simply result from oxidation of minor amounts of pyrimidine anionic dimers such as those observed on prolonged electrolysis at the HMDE at −2.9 V.

Peaks Vc and Va are an irregularly shaped peak pair seen on cyclic voltammograms of acids alone and of acids plus pyrimidine; clipping of the voltage sweep before the main pyrimidine reduction wave has essentially no effect on these peaks. Consequently, the peaks are connected with the reduction of acids in general and not specifically with the pyrimidine reduction.

Coulometry. Controlled electrode potential electrolysis at −2.75 V of five pyrimidine solutions (concentration 0.3–1.6 m*M*) gave an *n* value of 1.05 ± 0.04, thus providing proof for the 1-e nature of the initial pyrimidine reduction in dry acetonitrile. Plots of log *i*, corrected for residual current, *vs.* *t* display excellent linearity, indicating that the reduction is a clean 1-e process with little or no interference from follow-up reactions that produce reducible species; *i.e.*, in this concentration range, the pyrimidine dimerization reaction accounts for nearly 100% of the electrode process. Several solutions of very low pyrimidine concentration (0.03–0.08 m*M*) were electrolyzed to see if the protonation reaction would have an appreciable effect at the nominal water concentration (*ca.* 10 m*M*) present in the acetonitrile; *n* varied randomly between 1 and 2 with considerable deviation, probably indicating that small variations in the residual water level and experimental

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(31) I. M. Kolthoff, S. Bruckenstein, and M. K. Chantooni, *J. Amer. Chem. Soc.*, **83**, 3927 (1961).

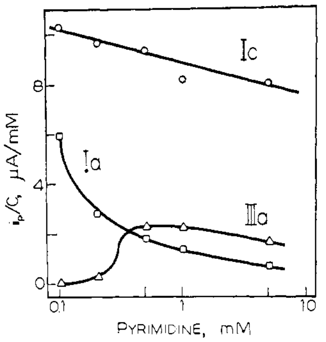

Figure 6. Peak currents (stationary state) for pyrimidine at a mercury-plated disk electrode as a function of concentration; scan rate 12 V/sec. Peaks identified in text.

conditions greatly affect the extent of the ECE process relative to the dimerization reaction.

Water was added to the electrolysis solution in an attempt to swamp out the dimerization reaction by enhancing the rate of the ECE process. Concentrations were chosen (1.22 mM pyrimidine and 960 mM water) at which polarography at the DME had indicated a complete 2-e reaction. Three electrolyses at -2.65 V resulted in an n value of 1.62 ± 0.05. Thus, under conditions of macroscale electrolysis at a mercury pool electrode with vigorous stirring of the solution, the 1-e dimerization reaction still accounts for nearly 40% of the total electrode process.

Experiments are currently underway involving macroscale electrolysis with spectrophotometric and voltammetric analysis of the electrolyzed solutions in an effort to isolate and positively identify the final pyrimidine electrolysis products and possible reaction intermediates. Various difficulties encountered in the experimental and interpretative parts of this work do not permit detailed statements to be made at this time.

The Pyrimidine Anion Free Radical

Since polarographic evidence indicates that pyrimidine is reduced in a 1-e process and since epr evidence indicates that the pyrimidine radical anion is so transient as not to be detected under certain experimental conditions, the electrogenerated pyrimidine radical anion must undergo one or more chemical reactions leading to its rapid disappearance. At least three more or less distinct kinetic possibilities can be visualized to account for such disappearance.

(A) Reversible electron transfer followed by a first-order chemical reaction, presumably either spontaneous fragmentation or reaction with the solvent (because of the high concentration of the latter, the reaction rate should be essentially zero order in solvent), may occur.

$$\mathrm{O} + ne \rightleftharpoons \mathrm{R} \tag{1}$$

$$\mathrm{R} \xrightarrow{k_1} \mathrm{Z} \tag{2}$$

(B) A second possibility is reversible electron transfer followed by reaction with protons and/or water due to residual impurities in the solvent.

$$\mathrm{O} + ne \rightleftharpoons \mathrm{R} \tag{3}$$

$$\mathrm{R} + \mathrm{X} \xrightarrow{k_1} \mathrm{Z} \tag{4}$$

(C) Reversible electron addition followed by dimerization is possible.

$$\mathrm{O} + ne \rightleftharpoons \mathrm{R} \tag{5}$$

$$2\mathrm{R} \xrightarrow{k_2} \mathrm{Z} \tag{6}$$

Calculation of Dimerization Rate. Nicholson and coworkers have presented theoretical treatments for observed cyclic voltammetric behavior due to reversible electron addition followed by a first-order chemical reaction[32] or by dimerization.[33] Since dimerization is a second-order reaction and the others are first order in pyrimidine concentration, a concentration study of peak Ia should give immediate insight into the nature of the following reaction. For case A, the ratio of the anodic and cathodic peak heights, i_a/i_c, should be unaffected by the pyrimidine concentration, all other conditions being equal. Although case B involves a second-order reaction, the latter is first-order in pyrimidine so that the i_a/i_c ratio should be relatively unaffected; moreover, since the reactant would presumably be a small and relatively constant concentration of residual protons or water, a small increase in the ratio might actually be expected with increase in pyrimidine concentration. For case C, the i_a/i_c should decrease with increased pyrimidine concentration.

Experimentally, the i_a/i_c ratio decreases markedly with increase in pyrimidine concentration from 0.1 to 7 mM (Figure 6). Pyrazine, which gives a rather stable epr spectrum and whose reduction seems to be clearly an ECE mechanism,[14-16] shows a remarkably constant (±2%) i_a/i_c ratio over the same concentration range.[34] At 7 mM pyrimidine, the anodic peak height is rather small even at a scan rate of 250 V/sec.

Analysis of i_a/i_c ratios at scan rates from 15 to 250 V/sec gave values for the dimerization rate constant k_2 of $10 \pm 4 \times 10^5$ and $6 \pm 2 \times 10^5$ l./(mol sec) for 0.103 and 1.03 mM pyrimidine solutions, respectively. Thus, a reasonable value for k_2 is $8 \pm 5 \times 10^5$ l./(mol sec). The accuracy of this value is limited by the following considerations. At higher scan rates, the effects of slowness of potentiostat response and of uncompensated ohmic resistance begin to be important. With increase in pyrimidine concentration, a slight shift of E_p for peak Ic to more negative potential, as opposed to the positive shift predicted by theory,[33] and an increase in peak separation, $E_p(\mathrm{Ic}) - E_p(\mathrm{Ia})$, are probably also associated with larger errors due to uncompensated resistance produced by the larger peak currents involved. Secondly, only a dimerization reaction is assumed to occur, with little or no contribution from other reactions that lead to disappearance of the radical anion; although the pyrimidine radical anion reacts with residual water, there is reason to believe that, particularly at higher scan rates, there is insufficient time for the reaction with water to occur to any appreciable extent.

The hypothesis that pyrimidine radical anions dimerize in nonaqueous solvents has been previously suggested[8,10,12,15] but the present study provides the first proof as well as a value for the dimerization rate constant.

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[32] R. S. Nicholson and I. Shain, *Anal. Chem.*, **36**, 706 (1964).

[33] M. L. Olmstead, R. G. Hamilton, and R. S. Nicholson, *ibid.*, 41, 260 (1969).

[34] J. E. O'Reilly and P. J. Elving, work in progress.

Calculation of Protonation Rate. As previously discussed, the pyrimidine radical anion can react with water to form a free radical which is immediately reduced, *i.e.*, an ECE mechanism. Addition of water leads to an increase in limiting current up to that expected for a 2-e reduction. Using the method of Nicholson, *et al.*,[35] involving the determination of the ratio of kinetic to diffusion current, i_k/i_d, a value for the second-order rate constant, k_1, for the protonation of pyrimidine radical anions by water was obtained of *ca.* 7 l./(mol sec). Since the theory of Nicholson, *et al.*, assumes a first-order reaction and there is the complicating effect of the concurrent dimerization reaction, this value was calculated at relatively high water concentrations (250–600 m*M*), where the current magnitude is fairly close to that for a 2-e process and first-order kinetics are approached.

van der Meer[16] reports a value for this same constant in DMF of *ca.* 32 l./(mol sec), apparently obtained by an extrapolation technique based on the experimental values of k_1 for pyrazine and pyridazine and molecular orbital calculations. He concluded that the first step in the deactivation of the pyrimidine radical anion is a first-order process, *i.e.*, protonation by the solvent. However, if the pyrimidine radical anion were protonated so rapidly, the product (pyrimidine free radical) would also be expected to be reduced, with a resulting increase in current as observed for pyrazine and pyridazine. It is more likely that the pyrimidine anion radical dimerizes very rapidly before protonation occurs (even at 1% water). Jezorek and Mark[28] have shown that the protonation effect of water in DMF is much less than in acetonitrile due to interaction of the water with DMF resulting in a viscosity increase and reduced water availability. It is also possible that the pyrimidine reduction mechanism in DMF differs from that in acetonitrile due to specific solvent influence as a result of DMF being a protophilic solvent whereas acetonitrile is weakly protogenic (the dielectric constants of both are about 37).

The Pyrimidine Anionic Dimer

The exact nature of the dianion formed on pyrimidine anion radical coupling cannot be confirmed at present. Although molecular orbital calculations[36] predict the order of reactivities of the positions to nucleophilic attack to be 2 > 4 (6) > 5, the facts that in acetonitrile cytosine is reducible and 4-methylpyrimidine is reduced at a more negative potential than is 5-methylpyrimidine[34] indicate that the 4 position is favored for initial electron transfer in acetonitrile as well as in water. Regardless of the position favored for initial electron attack, the preferred position for radical coupling may be different, since dimerization can occur after rapid electron rearrangement subsequent to electron addition. On reduction in dilute dimethoxyethane solution, pyridine couples at the 4 position,[10–12] so that the position para to a ring nitrogen seems favored; moreover, the 4 position is favored over the 2 position by a statistical factor of 2:1 in pyrimidine. Thus, the pyrimidine anionic dimer is likely to be the 4,4′ species, although small amounts of other dimers, such as the 2,4′, may be formed.[37]

Another question that cannot be fully answered is the state of protonation of the pyrimidine anionic dimer that is oxidized in peak IIIa. Since the pyrimidine dianion dimer, $(py)_2^{2-}$, would be quite basic and should readily abstract a proton from residual water or the solvent itself to form the monoanion, and since the i_p/C value for peak IIIa seems to reach a limiting value with increase in concentration (Figure 6), an intervening chemical reaction other than dimerization might be assumed. However, the relative constancy of the $i_p/Cv^{1/2}$ ratios for peak IIIa (8.1 ± 0.8) and peak Ic (35 ± 3) on scan rates from 3 to 200 V/sec for 1.03 m*M* pyrimidine solution at the hmde indicates that any protonation reaction which occurs must be very fast, which would tend to eliminate protonation by the small amount of water present, which reaction is relatively slow under the experimental conditions used. Moreover, the total absence of any anodic peak on cyclic voltammetry of pyrimidine in aqueous solution—except for oxidation of electrode mercury—emphasizes the fact that the anodic peaks observed for acetonitrile solutions of pyrimidine are probably due to nonprotonated species; *i.e.*, the ready availability of protons in water causes rapid protonation of various pyrimidine species, which are then not electrochemically oxidized. Thus, the species oxidized in peak IIIa is at least a monoanion and quite probably a dianion.

Mechanism of Pyrimidine Reduction

The mechanism for pyrimidine reduction in acetonitrile at mercury electrodes is summarized in Figure 7. Essentially, pyrimidine (I) undergoes a reversible one-electron reduction to produce an unstable radical anion II, which can then decompose *via* two competitive pathways: (1) a fast dimerization reaction which produces the pyrimidine dianionic dimer III and (2) a proton abstraction from residual water, the solvent, and/or traces of acids to produce the pyrimidine-free radical IV, which is immediately further reduced to produce ultimately a dihydropyrimidine VI.

Proton abstraction by the pyrimidine radical anion (reaction II → IV) probably occurs at the same carbon at which dimerization occurs. When the 4-carbon is blocked to dimerization reactions by a fairly high concentration of water (100 to 1100 m*M*), the alternate pathway leading to 3,4-dihydropyrimidine becomes dominant. The proton abstraction reaction is, of course, also a possible pathway with stronger acids, *i.e.*, acids at least as strong as phenols, and the acetonitrile solvent, which is present in 19 *M* concentration. However, the solvent does not appear to be a sufficiently good proton donor to permit this reaction to proceed to any great degree relative to the fast dimerization process, since the current in "dry" acetonitrile is quite close to that for a one-electron process, and the stronger acids are usually present in a fairly low concentration, *e.g.*, 0.01–2 m*M*, which minimizes the second-order process. The existence of the pyrimidine free radical (IV) is probably only transitory at best; the second elec-

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(35) R. S. Nicholson, J. M. Wilson, and M. L. Olmstead, *Anal. Chem.*, **38**, 542 (1966).

(36) R. D. Brown and M. L. Heffernan, *Aust. J. Chem.*, **9**, 83 (1956).

(37) As previously mentioned, the positive-potential side of peak IIIa is somewhat drawn out; prolonged (15–300 sec) electrolysis at the hmde at −2.9 V, followed by scan to positive potential, produces two more sharp peaks of variable height on the positive side of IIIa. The latter peaks could correspond to the oxidation of other pyrimidine dimers produced on prolonged electrolysis.

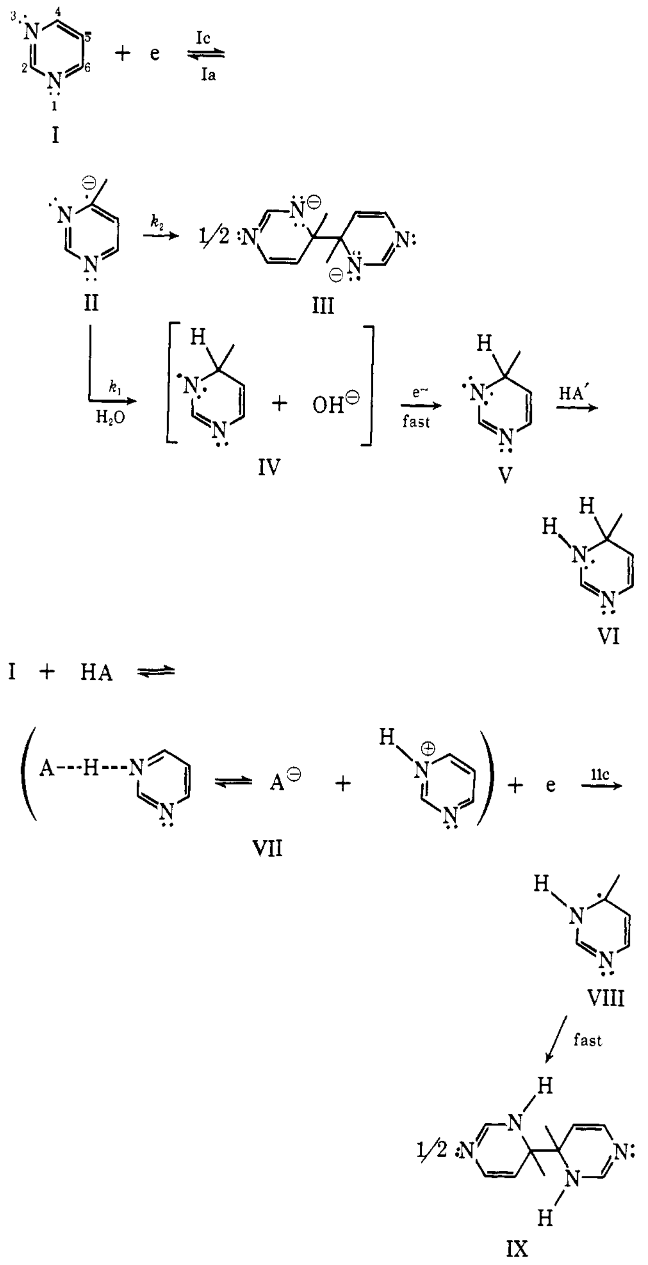

Figure 7. Interpretation of the electrochemical and chemical behavior observed for pyrimidine in acetonitrile media. HA refers to an acid as strong as phenols; HA′ refers to any proton source. Roman numerals above the reaction arrows refer to the cyclic voltammetric peaks produced by these reactions.

tron addition probably occurs almost instantaneously after proton abstraction.

When stronger acids are present, a preprotonation reaction can occur, leading to the formation of the same pyrimidine dimer IX, which is produced in the first one-electron reduction of pyrimidine in aqueous media. The pyrimidine–acid reduction wave obtained in acetonitrile at the DME appears to be only a one-electron process, based on the original pyrimidine concentration (Figure 2). Thus, the reaction sequence outlined for pyrimidine in acetonitrile (Figure 7) helps to explain the pyrimidine reduction mechanism in water; *e.g.*, wave I is observed in aqueous media only at relatively low pH, where there would be a sufficient concentration of labile protons to effect a preprotonation. At higher pH and more negative potential, a second reduction pathway becomes operative, in which the first step is electron addition followed by proton *abstraction* by the 4-carbon, leading to formation of the dihydro species. The second two-electron reduction wave in water is probably the result of a cascade effect: at quite high pH and negative potential, the third and fourth electrons are "funneled" into the pyrimidine molecule at the electrode surface.

It should be noted that the two postulated protonated pyrimidine free-radical species, IV and VIII, are different in nature, leading to the difference in mechanism. When the proton source is sufficiently acidic and of low concentration, prior protonation at a nitrogen atom occurs, leading to the formation of the pyrimidine dimer IX. When the proton source is of low acidity but of fairly high concentration (water at *ca.* 100 m*M*), proton abstraction by the pyrimidine anionic free radical at the 4-carbon position leading to 3,4-dihydropyrimidine begins to be the dominant reaction. If no effective proton sources are available, *e.g.*, acetonitrile with 10 m*M* or less residual water, the dominant reaction is anion radical coupling to give the pyrimidine anionic dimer III; this dimer should be a fairly basic species and, with time, should eventually react with available proton sources to produce a protonated dimer such as IX.

As noted on Figure 7, the pyrimidine–pyrimidine radical anion couple produces reversible waves and peaks Ic–Ia. Peak IIc is produced by the reduction of adduct VII to free radical VIII. Peak IIIa is due to the one-electron oxidation of the dimer III; peak IIIc represents reduction of the product.

Experimental Section

Chemicals. Chemicals were obtained from the following sources: pyrimidine, Mann Research Laboratories; benzoic acid, National Bureau of Standards; chloroacetic acid, Dow; phenol, Mallinckrodt; perchloric acid, G. F. Smith Chemical Co.; calcium hydride, Alfa Inorganics. Dinitrogen tetroxide was prepared by the thermal decomposition of lead nitrate.

Acetonitrile (Burdick and Jackson Laboratories) was purified essentially by the method of Sherman and Olson[38] and stored over Linde Type 4A molecular sieves. The purified acetonitrile gave between 0.4 and 0.6 μA of residual current at -2.5 V *vs.* the aqueous sce, of which at least 0.25 μA is purely capacitive, comparable to that previously reported.[38,39] Under the experimental conditions used, the solvent had a residual water level of about 0.02% (10 m*M*); this is termed the nominally "dry" solvent in the present paper.

Tetraethylammonium perchlorate (TEAP), used as background electrolyte, was prepared following Kolthoff and Coetzee,[40] and was recrystallized four times from water before drying in a vacuum oven at 60°.

Apparatus. Polarograms were recorded with a Leeds and Northrup Electro-Chemograph Type E, used in conjunction with an ir compensator;[41] zero damping was used. Cyclic voltammograms were obtained with a potentiostatic control loop of conventional design, constructed from Philbrick vacuum tube operational amplifiers, and a Moseley 7035A *X–Y* recorder. Fast-sweep cyclic voltammograms were obtained using a Hewlett-Packard 202A low-frequency function generator and a Tektronix 502 oscilloscope and C 12 camera system.

Capillary constants of the dme in deoxygenated 0.1 *M* TEAP in acetonitrile at 25° and open circuit were determined at the following

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[38] E. O. Sherman, Jr., and D. C. Olson, *Anal. Chem.*, **40**, 1174 (1968).

[39] J. F. Coetzee, G. P. Cunningham, D. K. McGuire, and G. R. Padmanabhan, *ibid.*, **34**, 1139 (1962).

[40] I. M. Kolthoff and J. F. Coetzee, *J. Amer. Chem. Soc.*, **79**, 870 (1957).

[41] R. Annino and K. J. Hagler, *Anal. Chem.*, **35**, 1555 (1963).

mercury column heights (cm, corrected for back pressure): 28 (m = 0.633 mg/sec, t = 11.31 sec), 38 (0.858, 8.36), 48 (1.078, 6.61), and 58 (1.305, 5.49). Drop times at potentials of interest were generally between 2 and 6 sec.

The jacketed three-compartment cell used for polarography and cyclic voltammetry has been described.[42] Temperature was regulated to 25.0 ± 0.1°. Salt bridges, inserted on the counter and reference sides of the medium-porosity glass frits separating the three compartments were prepared from dimethylformamide and methyl cellulose.[43] A cylindrical water-jacketed glass electrolysis cell, 4 cm in diameter, was used in coulometric studies; reference and counter electrodes, constructed in 0.5-in. glass tubes in the ends of which were glass frits and salt bridges, were suspended in the electrolysis solution.

Potentials were measured *vs.* a modified Pleskov[44] electrode constructed by dipping a coil of silver wire into a solution of 0.01 M $AgNO_3$ in acetonitrile–0.1 M TEAP contained in a 0.5-in. diameter glass tube having a medium-porosity glass frit and salt bridge at one end, which was suspended in background electrolyte in the reference compartment. The potential of this electrode is reported[45] to be 0.291 V *vs.* the aqueous sce; the potential, measured using a commercial calomel electrode and a potentiometer, was identical within experimental error: 0.293 ± 0.002 V. All reported potentials are *vs.* this electrode unless otherwise noted.

To monitor the reference electrode potential, polarograms were run on approximately 0.5 mM solutions of rubidium perchlorate on most days that polarograms were taken. Over a period of 10 months, using several reference electrodes and several stock solutions of rubidium perchlorate, no significant variation was found for either the half-wave potential or the diffusion-current constant for the rubidium ion reduction. The averages from well over 50 polarograms, not rejecting a single value, are: $E_{1/2} = -2.256 \pm 0.003$ V; $I_d = 3.27 \pm 0.05$; $|E_{3/4} - E_{1/4}| = 56 \pm 3$ mV. These values compare favorably with the data reported[40] for the reduction of rubidium iodide in acetonitrile (0.1 M tetra-*n*-butylammonium iodide).

Because of the good reproducibility of the Rb(I) reduction and the many reference electrodes that have been used in acetonitrile involving possibly substantial liquid junction potentials,[19,45,46] it is suggested that reports of polarographic studies in acetonitrile contain an experimental value obtained for Rb(I) to facilitate correlation of experimental data between different laboratories. Many authors[44,47,48] have suggested the use of Rb(I) as a reference ion owing to its insensitivity to solvent effects.

The counter electrode was a sheet of platinum foil (*ca.* 6 cm^2 in area) dipping into background electrolyte.

Polarographic Procedures. Stock solutions of pyrimidine and background electrolyte were prepared by dissolving weighed quantities in acetonitrile and diluting to known volume. Test solutions were prepared by pipeting appropriate volumes of stock solutions into 10-ml flasks and diluting to volume with acetonitrile; all solutions were 0.1 M in TEAP. High-purity argon (dried by passage through Drierite and saturated with acetonitrile vapor by being bubbled through a TEAP solution thermostated at 25°) was bubbled through the test solution for about 10 min; polarograms were recorded with argon passing over the solution.

For cyclic runs at the hanging mercury drop electrode (hmde), one drop of mercury was collected from the dme capillary and hung on the hanging drop assembly (Sargent S-29314-30). Occasionally, a mercury-plated disk electrode (mpde) was used for cyclic scans to eliminate the problem of mercury drop detachment at very negative potential just prior to background decomposition; this was prepared by attaching to the hanging drop assembly and then dislodging three or four mercury drops in succession. Generally, potentials were scanned in a negative direction from 0 V to some predetermined potential and then back to the starting potential; on occasion, this cycle was repeated one or more times.

Electrolyses were performed using a solid-state electrochemical unit as a potentiostat; *i–t* curves were recorded on an X–Y recorder and the area was integrated by means of a planimeter to obtain the number of coulombs passed. Electrolyses were performed by both (a) preelectrolysis of the background electrolyte solution and subsequent subtraction of a constant residual current and (b) without preelectrolysis of the background but with subtraction of the number of coulombs equal to the total passed during electrolysis of the background.

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