

## ELECTROCHEMICAL REDUCTION OF 2-HYDROXYPYRIMIDINE IN DIMETHYLSULFOXIDE

### INFLUENCE OF THE FATHER-SON REACTION

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#### ABSTRACT

In DMSO (0.1 M TEAP), 2-hydroxypyrimidine (2-HP) is reversibly reduced (1e process) to a radical anion, whose dimerization is slower than its attack (it is a strong base) on unreduced 2-HP to abstract a proton (father-son reaction), producing the neutral free radical, which dimerizes more rapidly than the radical anion, and the anion of 2-HP, which can be involved in a Hg(I)–Hg(0) couple; the apparent faradaic  $n$  is less than one. On addition of strong base to a 2-HP solution, the 2-HP is converted to the anion and the only electrochemical activity seen is that due to the mercury couple. On strong acid addition, the protonated 2-HP formed is more easily reduced than neutral 2-HP; the resulting current considerably exceeds that for 2-HP itself (faradaic  $n$  equals one); the anion-mercury reaction couple is not seen. The neutral free radical formed rapidly dimerizes. Weak acid addition produces an adduct due to hydrogen bridging between acid anion and pyrimidine reduction site; reduction to the neutral free radical is facilitated; the weak acid anion is involved in a Hg(I)–Hg(0) couple at a potential characteristic for the acid used; the mercury-pyrimidine anion couple occurs at a potential characteristic for 2-HP.

#### INTRODUCTION

The exact path for the polarographic reduction of 2-hydroxypyrimidine (2-(1H)-pyridone; pyrimidone-2) is an important factor in understanding the reduction path of the nucleic acid base cytosine (4-amino-2-hydroxypyrimidine), which is still uncertain [1].

There is general agreement [2–7] that, in aqueous solution, the 3,4 N=C bond in cytosine is initially reduced in a two-electron (2e) process to the 3,4-dihydro species; the latter rapidly deaminates to produce 2-hydroxypyrimidine (2-HP); the 2-HP is immediately reduced since it is more easily reduced electrochemically than cytosine itself. The disagreement is in respect to whether the 2-HP reduction is a 1e or 2e reaction, i.e., whether there is formed a free radical product, which dimerizes, or a 3,4-dihydro-2-hydroxypyrimidine.

In order to clarify the situation and to provide additional desired information,

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an investigation has been initiated of the electrochemical behavior of 2-HP, cytosine and related compounds in aqueous and non-aqueous media with particular attention to the roles of free radicals and anionic species (radical anions, carbanions, and dissociated conjugate bases) as reaction intermediates.

The present paper reports the results obtained in non-aqueous media (dimethylsulfoxide, DMSO) for 2-HP, which emphasize the importance of the reactivity of the free radical species produced on the initial 1  $e$  reduction of pyrimidines. The hydrochloride adduct derived from 2-hydroxypyrimidine (2-HP · HCl) was also examined in order to have an insured stoichiometric 1 : 1 pyrimidine-strong acid ratio. The effects were investigated of adding water, strong and weak acids, and strong base to DMSO solutions of 2-HP.

In aqueous media, a hydroxy substituent on a pyrimidine or purine carbon, which is part of a C=N bond, is largely, if not entirely, removed as a result of a keto-enol equilibrium; consequently, 2-HP in aqueous solution is predominantly in the keto form:



#### *Intersolvent comparison*

Polarographic currents observed in different solvents can be compared, as is subsequently done, on the following basis, where  $\eta$  represents the viscosity (usually expressed numerically in centipoise, 1 cP =  $10^{-3}$  kg m $^{-1}$  s $^{-1}$ ) and  $I_d$  the diffusion current constant. ( $I_d = \bar{i}_d/m^{2/3}t^{1/6}c$ , where  $\bar{i}_d$  is the average diffusion current in  $\mu$ A,  $m$  is the mercury flow rate in mg s $^{-1}$ ,  $t$  is the droptime in s, and  $c$  is the concentration of electroactive species in mmol l $^{-1}$ ).

If solvation effects are small to moderate (or generally similar) and if the solutes added do not appreciably alter the solvent viscosities, a diffusion-controlled current should be proportional to  $\eta^{1/2}$  and the  $I_d\eta^{1/2}$  product will be constant for a given electroactive species in different solvents (if the faradaic  $n$  is unchanged). The viscosities and the corresponding expected magnitudes per electron transferred per molecule (based on an  $I_d$  for average diffusion currents of 2.0 for  $n = 1$  in water, as is generally the case for small to moderate size molecules) are 0.89 and 2.0 for H $_2$ O, 0.35 and 3.2 for acetonitrile (AN), 0.80 and 2.1 for N,N-dimethylformamide (DMF), and 1.99 and 1.3 for dimethylsulfoxide (DMSO). For example, the observed  $I_d\eta^{1/2}$  products for the initial 1  $e$  reduction of pyrimidine itself are 2.01 in H $_2$ O, 1.99 and 2.10 in AN, and 2.00 in DMF [8].

The following data may be useful in interpreting the experimental results. The  $pK_a$  values in aqueous solution for proton gained and proton lost, respectively, are 2.2 and 9.2 for 2-HP;  $pK_a$  (solvent indicated) for benzoic acid is 4.2 (H $_2$ O), 12.0 (AN), 10.0 (DMSO) and 10.9 (DMF); for chloroacetic acid, it is 2.9 (H $_2$ O) and 9.8 (AN). Perchloric acid is essentially completely dissociated in all four solvents; HCl and TEAP are nearly completely dissociated in H $_2$ O and DMSO.

### Father-son reactions

Since the term, mother-daughter reaction, is a well established designation for a reaction series in which the product of one reaction becomes a reactant in a second reaction, use is suggested of the term, father-son reaction, to describe the situation where the principal product of a reaction reacts with the original reactant of interest, e.g.,



where the reagent may be an electron.

Reactions of this general type have been encountered — or, at least, postulated — in connection with the electrochemical behavior of inorganic and organic species, e.g., the reverse disproportionation reaction sequence such as the following:



In studies on the electrochemistry of heterocyclic nitrogen bases in non-aqueous media, the authors and their colleagues have encountered a number of cases where a compound, symbolized as RH, can serve as a proton source for neutralization of the radical anion, which it forms on 1 *e* reduction, i.e.,



Evidence for the occurrence of such acid-base father-son reactions is provided by studies published by Iversen, Baizer, Savéant and their coworkers.

Since such father-son reactions may be cause of many situations, where, for example, observed polarographic wave heights are less than expected for a 1 *e* process and coulometric faradaic *n* values are considerably less than one, it is worthwhile reviewing the mechanistic paths possibly involved under varying conditions in situations involving such reactions. The electrochemical patterns seen with 2-HP in non-aqueous medium are, consequently, illustrated in some detail.

## EXPERIMENTAL

### Chemicals

2-Hydroxypyrimidine hydrochloride (K & K) was used without further purification. 2-Hydroxypyrimidine (2-HP), prepared by neutralizing the hydrochloride with sodium hydroxide, was twice vacuum sublimed; its homogeneity was verified by n.m.r. and infrared absorption spectra, and m.p. (163–4°C) [9].

DMSO (Fisher Scientific), after drying over Linde 5A molecular sieves, was purified by on-line or off-line vacuum distillation. Tetraethylammonium perchlorate (TEAP), prepared following Kolthoff and Coetzee [10], was recrystal-

lized 4 times from water and then dried in a vacuum oven at 60°C. The background electrolyte system (0.1 M TEAP in DMSO) gave residual currents of less than  $-0.1$  and  $0.3 \mu\text{A}$  at  $+0.1$  and  $-2.7$ , respectively. A small wave, which appeared at about  $-2.1$  V, seemed to be due to an impurity; correction could readily be made for this wave, as subsequently discussed.

Other chemicals used were analytical reagent grade or the equivalent.

### Apparatus

Electrochemical measurements were made with a multipurpose instrument constructed from Philbrick operational amplifiers, and Moseley 135 and Houston 2000 XY recorders; for rapid-scan cyclic voltammograms, a Wavetek 112 function generator and a Tektronix 502 oscilloscope and C12 camera system were used. A Princeton Applied Research Model 174 polarograph was also used for DME polarography, and controlled-potential electrolysis and coulometry.

The vacuum line system and cell used have been described [11]; the simple cell arrangement, shown in Fig. 1, was also used.

Capillary constants of the DME in deoxygenated 0.1 M TEAP in DMSO at 25°C and open circuit were as follows (mercury column height,  $h$  in cm, uncorrected for back pressure; flow rate,  $m$ , in  $\text{mg s}^{-1}$ ; droptime,  $t$ , in s): 32, 0.837, 7.35; 42, 1.092, 5.65; 52, 1.359, 4.58; 62, 1.628, 3.87; 72, 1.917, 3.35; 82, 2.27, 2.94.

For the hanging mercury drop electrode used in cyclic voltammetry, one drop

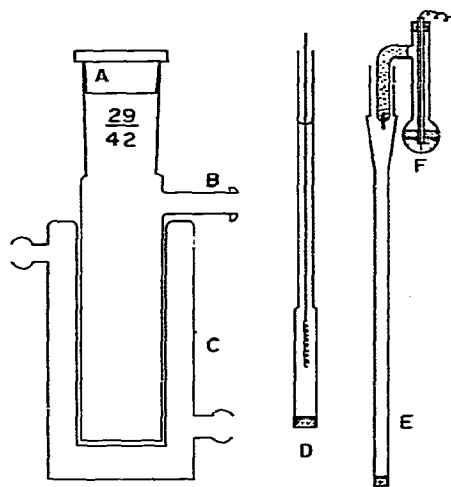


Fig. 1. Jacketed cell and component parts used for studies in DMSO, where small amounts of water (up to ca. 1% by volume) can be tolerated. Cell is constructed from a 29/42 standard taper outer joint. (A) Teflon stopper with six holes for inserting the dropping mercury and hanging mercury drop electrodes, counter and reference electrode compartments, the glass spoon for preparing the HMDE, and the nitrogen inlet; (B) 18/9 ball joint for connecting to vacuum line; (C) jacket through which thermostated water is circulated; (D) counter electrode compartment containing a platinum coil; (E) reference electrode compartment; (F) aqueous saturated calomel electrode; connecting arm is filled with a saturated KCl-agar gel and terminates in an asbestos fiber connection. Tubes D and E are filled with 0.1 M TEAP in DMSO and terminate in glass frits and methylcellulose bridges.

of mercury was collected from the DME ( $h = 62$  cm; open circuit) immersed in the electrolyte solution and hung on a mercury plated platinum disk (0.8 mm diameter) (electrode area = 2.6 mm<sup>2</sup>).

The counter electrode was a platinum coil (0.5 mm × 10 cm) or plate (1 cm<sup>2</sup>/side), which dipped directly into the test solution or was separated from it by a methylcellulose bridge and glass frits.

Potentials were measured against an aqueous saturated calomel electrode (SCE) by the following system: SCE | saturated KCl in water-agar bridge with asbestos fiber | 0.1 M TEAP in DMSO (20%)-methylcellulose bridge with medium porosity glass frits. To monitor the reference electrode potential, 0.5 mM RbCl in DMSO was polarographed;  $E_{1/2}$  was  $-2.044 \pm 0.002$  V over a period of four months (literature:  $-2.06$  V [12] and  $-1.96$  V [11]).

### Procedures

Vacuum line technics [11] were used for preparation of the test solution until it was confirmed that no significant effect results from the presence of less than 1% water or nitrogen bubbling. The test solution was then prepared by dissolving weighed quantities of compound and TEAP in freshly distilled DMSO and diluting to known volume. Water, strong and weak acids, and strong base were added with a pipet as the following solutions: 10% water in DMSO or pure water;  $5.8 \times 10^{-2}$  M perchloric acid in DMSO (containing 0.75% water);  $5 \times 10^{-2}$  M benzoic or chloroacetic acid in DMSO;  $6.8 \times 10^{-2}$  M tetraethylammonium hydroxide in DMSO (containing 9% water). Correction was made for dilution due to reagent solution addition; the effect of the minute amount of water added, which did not exceed 0.1% to 0.4% of the volume, was negligible, based on the study of the effect of water addition. Dissolved oxygen was removed by bubbling nitrogen (dried by passage through a 1 cm × 20 cm magnesium perchlorate column); nitrogen was passed over the solution during examination.

For controlled electrode potential electrolysis and coulometry, the PAR 174 and a simple cell were used with a mercury pool working electrode (ca. 5 cm<sup>2</sup> area), SCE, and platinum coil counter electrode (immersed in 0.1 M TEAP in DMSO, separated from the test solution by a methylcellulose bridge). Procedures were essentially as previously described [13]. Recorded current-time curves areas were integrated by the cut-and-weigh method.

## RESULTS AND DISCUSSION

The polarographic and voltammetric behavior in DMSO of 2-hydroxypyrimidine (2-HP) and of its hydrochloride (2-HP · HCl) are summarized in Table 1 and Fig. 2. Polarographic waves and cyclic voltammetric peaks are designated by Roman numbers; suffixes a and c designate their anodic or cathodic nature; I designates the wave or peak due to 2-HP itself, II that due to protonated 2-HP species, III due to 2-HP adduct with weak acid, IV due to 2-HP anion, V due to weak acid anion, and VI due to hydrogen reduction.

The principal electrode processes are mainly diffusion controlled, e.g., slopes of  $\log i - \log h$  plots for wave Ic are about 0.5 and the current functions ( $i_p /$

TABLE 1

Polarographic and voltammetric characteristics <sup>a</sup> of 2-hydroxypyrimidine in DMSO (0.1 M TEAP)

Compound	$-E_{1/2}/V$	$(E_{1/4} - E_{3/4})/mV$	$I_d^b$	$X^c$	$-E_p/V^d$			c.p.e. <sup>f</sup> <i>n</i>
					Ic, IIc	IVa	IVc	
2-HP <sup>g</sup>	1.67	140	0.77	0.51	1.80 (2.28)	0.17 (1.32)	0.22 (1.34)	0.58
2-HP · HCl <sup>g</sup>	0.78	42	1.58	0.58	0.84 <sup>e</sup> (6.12)			0.99

<sup>a</sup> Some of the values may be concentration-dependent; data are at the 2 mM level.

<sup>b</sup> Diffusion current constant:  $I_d = \bar{i}_d/cm^2/3t^{1/6}$ .

<sup>c</sup>  $\log i = X \log H_{Hg}$ .

<sup>d</sup> Numbers in parentheses are the corresponding cyclic voltammetric current functions,  $i_p/ACv^{1/2}$ , based on  $A = 2.6 \text{ mm}^2$ ; the values are 100 times as large for  $A$  in  $\text{cm}^2$ .

<sup>e</sup> An apparent cathodic-anodic peak couple is seen at more negative potential: cathodic,  $-1.82 \text{ V}$  (0.83); anodic,  $-1.70 \text{ V}$ .

<sup>f</sup> Controlled electrode potential electrolysis; faradaic  $n$  obtained by coulometry.

<sup>g</sup> Small cathodic waves appear at  $-2.15 \text{ V}$  for 2-HP ( $I_d = 0.14$ ) and at  $-2.19 \text{ V}$  for 2-HP · HCl ( $I_d = 0.39$ ), which seemed to be due to an impurity.

$ACv^{1/2}$ ) for peak Ic are relatively constant with variation in the scan rate ( $dE/dt$ ),  $v$ , e.g., less than 15% decrease between 0.07 and 161  $\text{V s}^{-1}$  for 2-HP. The diffusion current constant ( $I_d$ ) and the current function values for 2-HP · HCl — after adjustment for solvent viscosity — roughly coincide with those expected from  $I_d$  for pyrimidine in acetonitrile [8], and  $I_d$  and  $i_p/ACv^{1/2}$  for 2-HP in water [14],

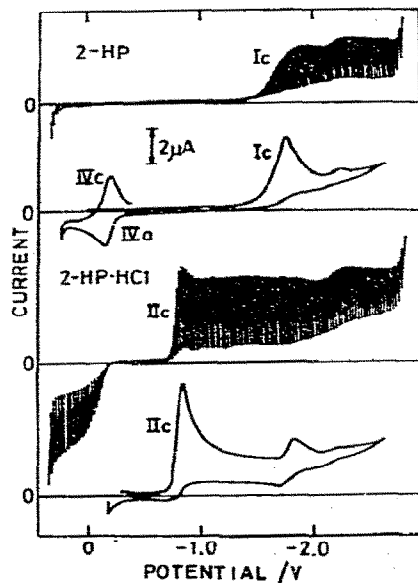


Fig. 2. DME polarograms and cyclic voltammograms of 2 mM 2-hydroxypyrimidine (2-HP) and of 2 mM 2-hydroxypyrimidine hydrochloride (2-HP · HCl) in DMSO (0.1 M TEAP). Scan rate on cyclic voltammetry = 69  $\text{mV s}^{-1}$ .

which involve 1  $e$  processes; however, the values for 2-HP are much lower. These facts suggest that the electrode reaction involves (a) a 1  $e$  process to produce a free radical followed by irreversible dimerization for 2-HP · HCl and (b) a 1  $e$  process followed or accompanied by a parent compound-consuming process for 2-HP, which causes the faradaic  $n$  to be less than one. The nature of the parent compound-consuming reaction is subsequently discussed.

It is also clear that (a) wave and peak Ic for 2-HP represents reduction of the original molecule, (b) peak IVa, which is only obtained on the return cycle after passing peak Ic, corresponds to an oxidation involving a product or products produced by the peak Ic process, and (c) peak IVc is due to reduction of the peak IVa process product. As subsequently discussed, the Ic process may produce dimeric forms of neutral and/or anionic free radicals, and an anionic form of the reactant molecule; the oxidation-reduction associated with the peak IVa–IVc couple involves the anionic form of the reactant molecule, e.g., peaks IVa and IVc grow on repeated scanning as would be expected from the generation of anion as a result of the peak Ic process. Wave IVa (cf. Effect of strong base addition) and peak IVa represent the same process.

#### *Effect of concentration*

An  $i_d$ – $c$  plot for 2-HP is linear up to at least 3 mM; plots of  $i_p$ – $v^{1/2}$  for peak Ic are linear up to at least 1.4 mM, while those for peaks IVa and IVc are linear at 0.4 mM, deviate slightly at 1.4 mM, and markedly at 2.9 mM ( $v$  range up to 160 V s<sup>-1</sup>).

The facts that  $E_{1/2}$  for 2-HP wave Ic becomes more positive with increasing concentration and that a complementary anodic peak Ia is not seen even at scan rates as high as 360 V s<sup>-1</sup> further support the notion that the initial 1  $e$  transfer is followed by a fast irreversible chemical reaction(s) of the second order.

#### *Effect of strong base addition*

Addition of Et<sub>4</sub>NOH to DMSO (0.1 M TEAP) produces an anodic wave at -0.09 V, whose height increases linearly with Et<sub>4</sub>NOH concentration; above ca. 1 mM Et<sub>4</sub>NOH, a second anodic wave appears at ca. -0.6 V, whose height also increases with Et<sub>4</sub>NOH concentration but to a lesser extent. On cyclic voltammetry, an apparently complementary cathodic peak also appears at ca. -0.2 V. These waves and peaks result from oxidation of mercury in the presence of an anion (hydroxide), which forms an insoluble compound with Hg(I).

With increasing Et<sub>4</sub>NOH concentration (Fig. 3), 2-HP wave and peak Ic — corresponding to reduction of the neutral molecule — decrease and then disappear at a molar base/2-HP ratio of 1.0. On the other hand, peaks IVa and IVc at -0.2 V (Table 1) are enhanced with increasing base concentration and appear even if the cathodic scan does not reach the potential at which peak Ic appears with subsequent reversal toward more positive potential. Waves IVa (portion beyond 2 mM Et<sub>4</sub>NOH) and VIIa in Fig. 3 correspond to the two waves seen on Et<sub>4</sub>NOH addition in absence of 2-HP.

The above and subsequent evidence indicate that peak IVa is due to an oxidation involving the dissociated form (anion) of 2-HP and peak IVc is due to reduc-

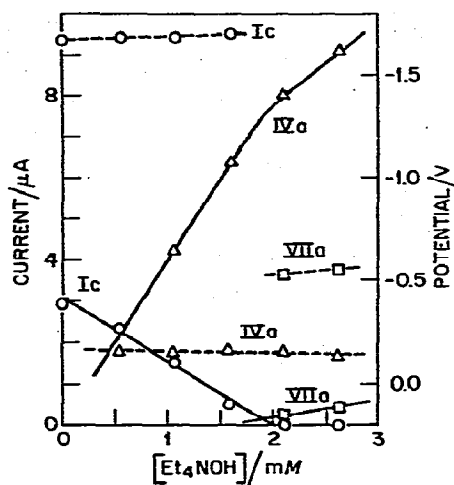


Fig. 3. Effect of addition of a strong base ( $\text{Et}_4\text{NOH}$ ) on the DME polarographic behavior of 2-hydroxypyrimidine (2 mM) in DMSO (0.1 M TEAP). (---) Potential, (—) current. Roman numbers: polarographic wave involved.

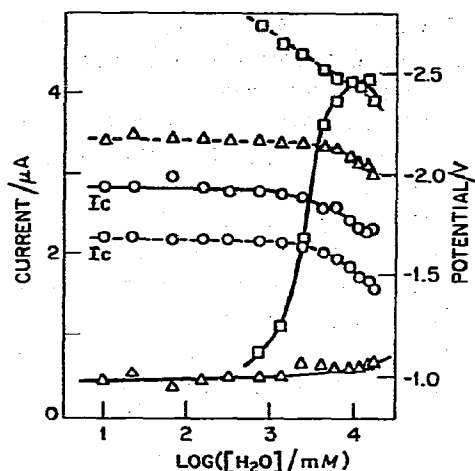


Fig. 4. Effect of addition of water on the DME polarographic behavior of 2-hydroxypyrimidine (2 mM) in DMSO (0.1 M TEAP). (---) Potential, (—) current. Roman numbers: polarographic wave involved. Water concentration is in millimolar units.

tion of the peak IVa product, which is probably a complex or insoluble compound of Hg(I) and the pyrimidine anion.

$\text{Et}_4\text{NOH}$  addition to a 2-HP · HCl addition produces concordant behavior, e.g., wave IIc decreases, and waves Ic and IVa (merged with Hg-Cl wave) appear and grow, followed by decrease in Ic.

#### Effect of water addition

The results on addition of water to DMSO solutions of 2-HP are summarized in Fig. 4. For comparison,  $E_{1/2}$  and  $i_a$  for the two waves seen in unbuffered aqueous solution (0.1 M TEAP) are  $-1.21$  V and  $4.3 \mu\text{A}$ , and  $-1.75$  V and  $2.6 \mu\text{A}$ ; the second wave is probably due to hydrogen ion reduction.

No effect is noticed when the water concentration is 1% or less. This phenomenon, which differs from the effect of water addition on pyrimidine [8] and the azabenzene [15] in AN, seems to be due to the 2-HP molecule functioning as a more effective proton donor than water at low water concentrations in DMSO. However, above 1% water, a new cathodic wave appears at more negative potential than the original wave (negative to ca.  $-2.5$  V). The new wave, whose current markedly increases and seems to level off (or perhaps to decrease) while its potential becomes more positive with increasing water content, may correspond to the second 2-HP wave observed in unbuffered aqueous medium.

With increasing  $\text{H}_2\text{O}$  concentration to 30%, the original wave at  $-1.67$  V shifts to more positive potential and decreases slightly in magnitude. The potential shifts seem to reflect the increasing proton activity. On cyclic voltammetry, with increasing  $\text{H}_2\text{O}$  concentration, the original peak at ca.  $-1.8$  V shifts posi-



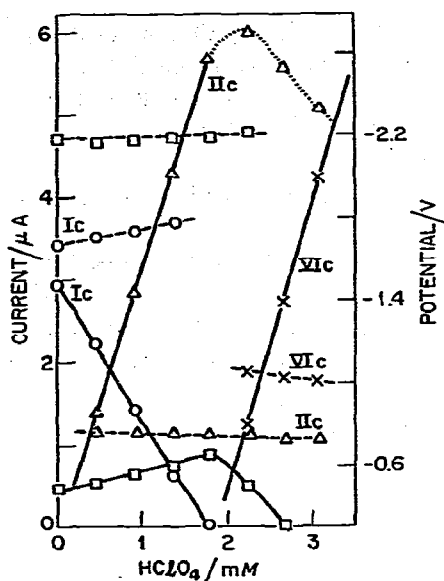


Fig. 5. Effect of addition of a strong acid (perchloric acid) on the DME polarographic behavior of 2-hydroxypyrimidine (2 mM) in DMSO (0.1 M TEAP). (---) Potential, (—) current. Roman numbers: polarographic wave involved.

tively and increases very slightly; the new peak behaves similarly to the corresponding wave. A pair of cathodic and anodic peaks seen near zero volt involve the redox behavior of the cathodic peak products. (The wave at ca.  $-2.2$  V is due to the impurity previously mentioned.)

#### *Effect of strong acid addition*

The effect of protonation was studied by examining 2-hydroxypyrimidine hydrochloride, 2-HP  $\cdot$  HCl, and the variation in behavior of 2-HP as perchloric acid was added.

A solution of 2-HP  $\cdot$  HCl gives a well defined polarographic wave (Fig. 2; Table 1), whose slope is near the 46 mV expected for a reversible 1  $e$  reduction followed by irreversible dimerization [16] and whose  $I_d$  slightly exceeds that expected for a 1  $e$  process. The cyclic voltammogram shows a correspondingly sharp peak at  $-0.8$  V; its current function decreases slightly with increase in  $v$  and its  $E_p$  becomes slightly more negative. An apparent redox couple appears at ca.  $-1.7$  V, whose cathodic peak height is 10 to 15% that of the  $-0.8$  V peak. An apparently similar cyclic voltammetric couple is observed in the region of 1 : 1 acid/2-HP when  $\text{HClO}_4$  is added to a 2-HP solution. The possible origin of the couple is subsequently discussed (cf. Reduction mechanisms).

Addition of  $\text{HClO}_4$  alone to DMSO (0.1 M TEAP) produces a wave at  $-1.03$  V (cyclic voltammetric peak at  $-1.15$  V), whose height is linearly proportional to  $\text{HClO}_4$  concentration. The effects of  $\text{HClO}_4$  addition to a 2-HP solution up to an acid : pyrimidine ratio of 1.5 are summarized in Fig. 5.

A new wave (IIc) appears at more positive potential than original wave Ic;

wave IIc grows at the expense of wave Ic, which has completely disappeared by an acid/pyrimidine ratio of 1.0, at which stage wave VIc due to reduction of  $\text{HClO}_4$  itself appears. It is difficult to measure the heights of the two waves at higher acid/pyrimidine ratios because of the maxima and drop-time irregularities which appear when the acid concentration reaches 3 mM.

The impurity wave at  $-2.2$  V seems to vary in magnitude with  $\text{HClO}_4$  concentration; a possible cause is considered subsequently.

The variations in the polarographic and voltammetric patterns are consistent with a prior protonation of 2-HP, probably at N(3), to give a species more easily reducible than the original molecule [8], and with the species  $2\text{-HP} \cdot \text{HCl}$  and  $2\text{-HP} \cdot \text{HClO}_4$  being largely to completely dissociated in DMSO to  $2\text{-HP} \cdot \text{H}^+$  and the anion.

Peak pair IVa–IVc at  $-0.2$  V, which involves mercury and an anionic form of the base, disappears on addition of strong acid.

### Effect of weak acid addition

Addition of a weak acid itself to DMSO (0.1 M TEAP) produces a wave at  $-1.8$  V (chloroacetic acid) or  $-2.1$  V (benzoic acid); each wave, which is presumably due to hydrogen ion reduction, is linearly proportional to concentration. As might be expected from chloroacetic acid being somewhat more highly dissociated than benzoic acid, the increase in current with concentration is somewhat greater for chloroacetic than for benzoic.

As benzoic or chloroacetic acid is added to a 2-HP solution up to an acid/base ratio of 2 (Figs. 6 and 7), a new wave (wave IIIc) appears at a potential corre-

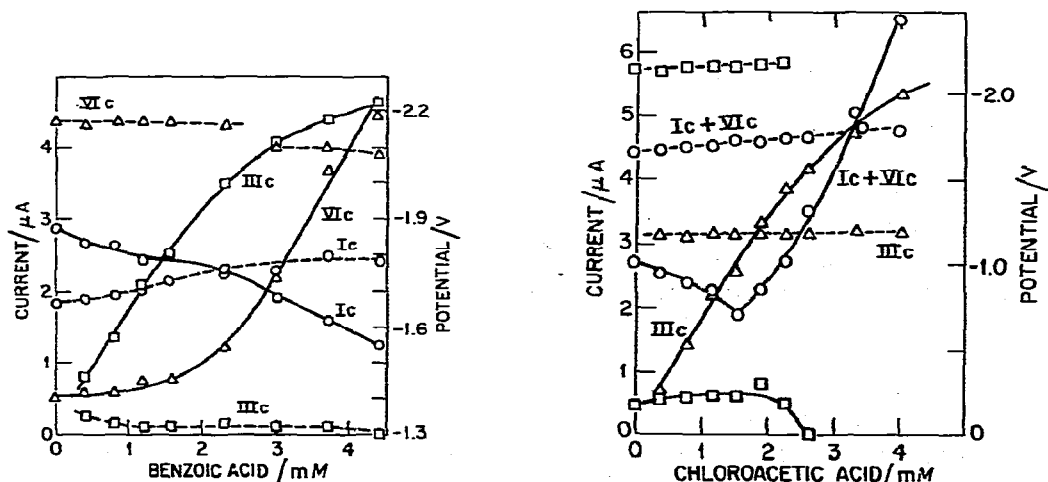


Fig. 6. Effect of addition of a weak acid (benzoic acid) on the DME polarographic behavior of 2-hydroxypyrimidine (2 mM) in DMSO (0.1 M TEAP). (---) Potential, (—) current. Roman numbers: polarographic wave involved.

Fig. 7. Effect of addition of a weak acid (monochloroacetic acid) on the DME polarographic behavior of 2-hydroxypyrimidine (2 mM) in DMSO (0.1 M TEAP). (---) Potential, (—) current. Roman numbers: polarographic wave involved.

sponding to the acid strength and grows, similar to the behavior on  $\text{HClO}_4$  addition; however, the wave patterns are more complicated and reflect the weaker protonating ability of the acids and the resulting equilibria involved, e.g., formation of adducts between the nitrogen base and the undissociated acid.

In the case of chloroacetic acid addition, the original 2-HP wave Ic seems to be merged with that due to chloroacetic acid (VIc); the merged wave decreases somewhat but starts to increase at an acid/base ratio of 0.8/1 while the new wave IIIc at more positive potential steadily increases. The  $-2.1$  V wave is due to the impurity.

On benzoic acid addition, where benzoic acid wave VIc seems to be superimposed on the impurity wave, the original 2-HP wave Ic has decreased by about a half at an acid/base ratio of 2 as a new wave IIIc at more positive potential grows and starts to level off by an acid/base ratio of 2.

Cyclic voltammograms show generally parallel behavior. In addition, a redox couple appears at about  $-0.1$  V in the case of benzoic acid and at about  $+0.2$  V in the case of chloroacetic acid, which is due to a  $\text{Hg(I)}-\text{Hg(0)}$  couple involving the anion of the acid.

#### *Controlled potential electrolysis and coulometry. Composition of electrolysis products*

Electrolyses were made at  $-2.0$  V for 2-HP and  $-1.0$  V for 2-HP · HCl. Coulometric  $n$  values are given in Table 1.

Electrolysis of a solution of 2-HP · HCl resulted in the decrease and eventual disappearance of wave IIc. There was no indication of wave IVa in the electrolyzed solution, e.g., the mercury-chloride ion oxidation wave was identical in the unelectrolyzed and electrolyzed 2-HP · HCl solutions.

Typical polarograms obtained during the course of electrolysis of 2-HP and the variation of current with time are shown in Figs. 8 and 9. Certain characteristics of these figures are immediately apparent. The sum of wave Ic at  $-1.7$  V, which decreases as electrolysis proceeds, and of wave IVa at  $-0.2$  V, which appears and grows, is constant within experimental error.  $E_{1/2}$  for wave IVa almost coincides with those of peak IVa (Fig. 2) and the oxidation wave obtained on strong base addition (Fig. 3). The anodic wave-height on completion of electrolysis almost equals that of the original reduction wave and one-half of the oxidation wave obtained on strong base addition. The  $\log i-t$  curve indicates the presence of interrelated processes. The first, which predominates during the early stage of electrolysis, is strongly dependent on 2-HP concentration and involves the father-son reaction. As the concentration of 2-HP decreases, the effect of the follow-up reaction on the effective rate of electrolysis decreases.

Increments of deoxygenated  $\text{HClO}_4$  were added to the completely electrolyzed solution of 2-HP; the resulting variation in the polarographic pattern is summarized in Fig. 10. On continued  $\text{HClO}_4$  addition, original wave Ic and the impurity wave grew at the expense of wave IVa; at a  $\text{HClO}_4$  to original 2-HP ratio of about 1 : 2, wave IVa disappeared and wave IIc — corresponding to reduction of protonated 2-HP — appeared and grew at the expense of wave Ic and, apparently, the impurity wave; the wave-height ratio between original wave Ic before electrolysis, and the maximum heights of oxidation wave IVa, regener-

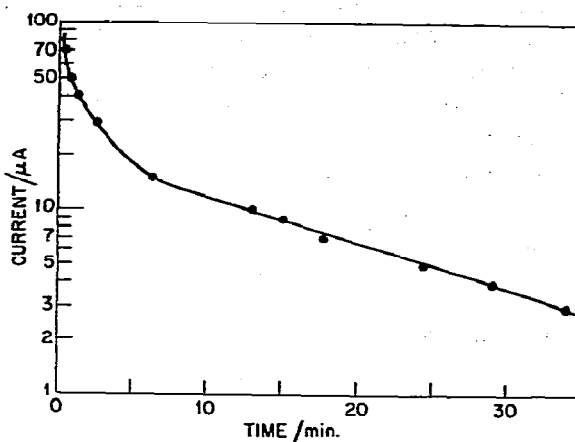
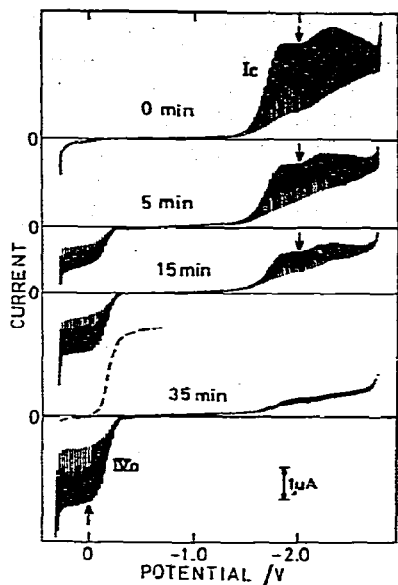


Fig. 8. Polarograms of 2-hydroxypyrimidine (2 mM) during its controlled electrode potential electrolysis at  $-2.0$  V in DMSO (0.1 M TEAP). Time in minutes after start of electrolysis is noted on each curve. Arrowheads indicate the original electrolysis potential ( $-2.0$  V) and the potential (0.0 V) applied to oxidize the reduced solution. The dashed line represents the essential feature of the DME polarogram of the reoxidized solution.

Fig. 9. Variation of the current (in arbitrary units) with time during the controlled potential electrolysis of 2 mM 2-hydroxypyrimidine in DMSO (0.1 M TEAP).

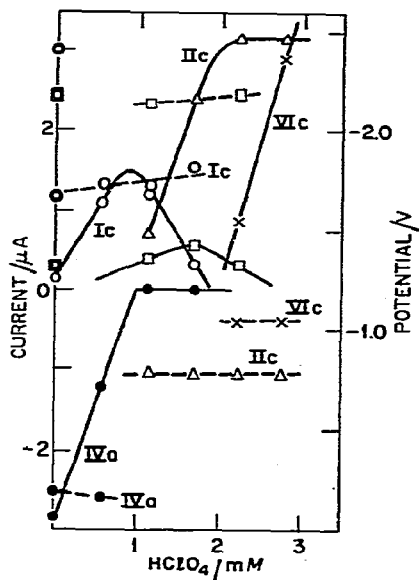


Fig. 10. Effect of  $\text{HClO}_4$  addition on an exhaustively electrolyzed solution of 2 mM 2-hydroxypyrimidine in DMSO (0.1 M TEAP). Positive currents are cathodic; negative currents are anodic. The double circles and double squares at 0 mM  $\text{HClO}_4$  show the currents and potentials of the 2-HP and impurity waves seen in the unelectrolyzed solution.

ated wave Ic, and protonated 2-HP wave IIc are approximately 1, 1, 0.5, and 1. Addition of  $\text{HClO}_4$  in excess of an acid-original base ratio of one produced the  $\text{HClO}_4$  reduction wave.

On electrolytic oxidation at zero volt of an exhaustively electrolyzed solution of 2-HP, a new reduction wave, whose  $E_{1/2}$  ( $-0.2$  V) was similar to those of wave IVa (Figs. 8 and 10) and peak IVc (Fig. 2), appeared and grew at the expense of wave IVa.  $E_{1/2}$  also coincided with that of the reduction wave seen after addition of mercurous perchlorate to a solution obtained on electrolysis at  $-2.0$  V of 2-HP, which should contain only the wave Ic products: (a) the dimer ( $\text{RH}_2-\text{RH}_2$ ) of the free radical ( $\dot{\text{R}}\text{H}_2$ ) produced on interaction of the radical anion ( $\dot{\text{R}}\text{H}^-$ ) formed on the initial  $1 e$  reduction with unelectrolyzed 2-HP ( $\text{RH}$ ) and (b) the anion of 2-HP resulting from the latter protonation reaction ( $\text{R}^-$ ). The last named anion reacts with the added  $\text{Hg(I)}$  to form  $\text{RHg}$ , which is also produced on oxidation of the reduced solution at a Hg electrode (wave IVa).

The variations in wave pattern during electrolysis and on subsequent  $\text{HClO}_4$  addition are elucidated in the section on Reaction mechanisms.

## REDUCTION MECHANISMS

The electrolytic redox reaction paths for 2-hydroxypyrimidine (2-HP) in DMSO ( $0.1 M$  TEAP), based on the available evidence and including accompanying chemical reactions, are summarized in Fig. 11, together with an indication of the waves and peaks, and of the approximate potentials associated with each electron-transfer process.

In the absence of added hydrogen ion or hydroxide ion source, 2-HP undergoes an apparently reversible  $1 e$  reduction (wave or peak Ic) to form a radical anion, which can dimerize to a dianion species. The latter reaction, however, is slower than attack of the radical anion, which is a strong base, on unreduced 2-HP to abstract a proton, producing the neutral free radical, which dimerizes much more rapidly than the corresponding radical anion, and the 2-HP anion.

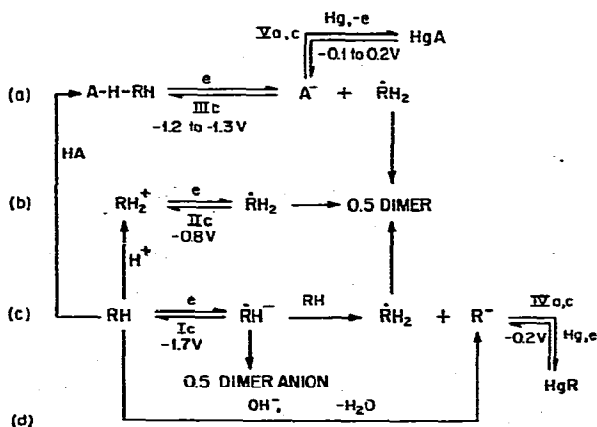


Fig. 11. Interpretation of the electrochemical and related chemical behavior observed for 2-hydroxypyrimidine (RH) in DMSO ( $0.1 M$  TEAP) solution in the presence of (a) weak acid (HA), (b) strong acid ( $\text{H}^+$ ), (c) no added acid or base, and (d) strong base (BOH).

The latter anion is involved in a Hg(I)—Hg(0) couple (IVa—IVc), whose current magnitude is, as expected, related to that of the pyrimidine reduction (Ic), i.e., the sum of the two magnitudes, Ic plus IVa, should approximate that expected for a 1 e faradaic process except that the nature of the IVa—IVc couple, which may involve film formation, introduces some complication.

A possible alternative or concurrent route, which does not alter the principal arguments involved in the previous statement or in those which follow, is that of the proton exchange involving in addition to reaction between the radical anion  $\dot{R}H^-$  and RH, reaction between the anionic dimeric species formed by  $\dot{R}H^-$  and RH. Favoring the latter reaction is the likelihood that the dimer anion is a stronger base than the radical anion itself. Favoring the anion radical being the proton acceptor is the apparently more favorable kinetics for reaction between  $\dot{R}H^-$  and RH as compared to reaction between  $\dot{R}H^-$  and  $\dot{R}H^-$ . The fact that only slightly more than half of the RH is reduced, also favors the radical anion being the proton acceptor.

The electrochemical reduction site, based on the reduction paths previously observed for pyrimidines in aqueous and non-aqueous media [3,7,8,17], is the 3,4 N=C double bond with the dimerization probably involving formation of a 4,4' or 6,6' C—C bond. The anionic species formed can neutralize their charge by ion-pairing with cationic Lewis acids such as protons from acid impurities or traces of metal ions.

On addition of a strong base (hydroxide ion) to a 2-HP solution, all of the pyrimidine is converted to the anion and the only electrochemical activity seen is that due to its couple with mercury (IVa—IVc), whose current approximately equals those of peaks Ic and IVa seen in the absence of the hydroxide ion.

The proton removed from 2-HP on its reaction with a strong base (e.g., its radical anion or hydroxide ion) is probably the proton on N(1).

On addition of a strong acid, i.e., a freely available hydrogen ion source, the protonated pyrimidine formed is more easily reduced (wave IIc) than the neutral species (Ic) with the resulting IIc current exceeding the Ic current; the couple due to reaction of the pyrimidine anion with mercury (IVa—IVc) is not seen.

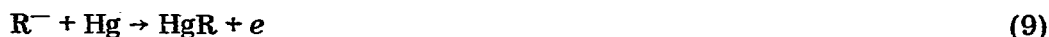
Based on the protonation patterns seen in aqueous media and the increased ease of reduction on protonation, the most likely protonation site is N(3).

Addition of a weak acid to a 2-HP solution results in formation of an adduct due to hydrogen bridging between the acid anion and the pyrimidine reduction site (probably at N(3)), since reduction of the pyrimidine in the adduct is facilitated (wave IIIc). The free radical produced can dimerize. The anion of the weak acid, liberated on reduction of the adduct, can produce a Hg(I)—Hg(0) couple similar to the pyrimidine anion; the resulting wave or peak couple Va—Vc, however, occurs at a potential characteristic for the acid used. On the other hand, the mercury-pyrimidine anion couple (IVa—IVc) occurs at a potential characteristic for the 2-HP.

The data obtained on controlled potential electrolysis (c.p.e.), coulometry, and subsequent treatment of the electrolyzed solution with  $HClO_4$  (cf. previous section) are explicable on the basis of the mechanisms discussed. During c.p.e., which involves the wave Ic process (RH represents 2-HP),



approximately half of the 2-HP is reduced to a free radical, which rapidly dimerizes; the remaining half is converted to the anion. The latter is the cause of wave IVa, e.g.,



whose height approximately equals that of wave Ic before electrolysis and one-half of the similar anodic wave produced on adding strong base to a 2-HP solution of the same concentration.

Addition of  $\text{HClO}_4$  converts  $\text{R}^-$  to  $\text{RH}$ , thus decreasing wave IVa (eqn. 9) and regenerating  $\text{RH}$ , which produces wave Ic (eqn. 8); however, as is evident from eqn. (8) and the fact that one-half of the original 2-HP has been converted to dimer during c.p.e., the maximum height of this wave is about one-half of that of wave Ic before c.p.e., which height is reached when the added  $\text{HClO}_4$  concentration equals one-half of the original 2-HP concentration (Fig. 10).

Further addition of  $\text{HClO}_4$  furnishes proton donor for protonation of regenerated 2-HP, i.e.,



The protonated 2-HP produces wave IIc,



which reaches a maximum magnitude when the added  $\text{HClO}_4$  concentration equals that of the 2-HP before c.p.e. or twice that of the  $\text{R}^-$  present after c.p.e. The maximum height of wave IIc is, accordingly, the same as that of 2-HP reduction before c.p.e. (wave Ic) or that of  $\text{R}^-$  oxidation (wave IVa) after c.p.e.

Continued addition of  $\text{HClO}_4$  does not alter wave IIc but does result in the appearance and growth of wave VIc due to reduction of the excess hydrogen ion. The constancy of wave IIc indicates that the neutral free radical dimerizes before it can be reduced, e.g., in an e.c.e. process, and supports the 1  $e$  reduction of 2-HP seen in aqueous medium [3].

On electrolysis of 2-HP  $\cdot$  HCl (protonated 2-HP), the reduction wave decreased but, as expected from the previous discussion, no anodic wave appeared. The electrolysis product, accordingly, is a dimer produced by the rapid chemical reaction of the neutral free radical, with oxidation of the dimer occurring at too positive a potential to be seen with a mercury electrode.

#### *Impurity wave*

Reference has been made to a wave seen at  $-2.05$  to  $-2.20$  V, which is most likely due to an impurity. Although it is difficult to measure this small wave precisely due to the large oscillations (noise current) of the DME current at such negative potentials, the effect of this wave on other waves in its immediate vicinity could usually be readily taken into account.

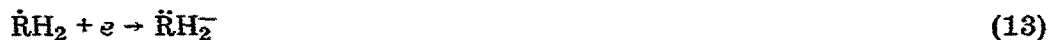
Solutions of 0 to 3 mM 2-HP gave maximum limiting currents of 0 to  $4.2 \mu\text{A}$  at  $-1.7$  V and 0 to  $0.7 \mu\text{A}$  at  $-2.1$  V (linear relations in both cases). The impurity wave was relatively greater in the case of 2-HP  $\cdot$  HCl. Addition of  $\text{Et}_4\text{NOH}$  to 2-HP  $\cdot$  HCl solution did not seem to affect the wave, but may have had some effect on 2-HP solutions. The general behavior patterns do not support the wave being due to reduction of an adsorbed or tautomeric form of 2-HP.

A cationic impurity, as previously indicated, could ion-pair with an anionic species produced on electrolysis. Thus, decrease of the wave during c.p.e. could be due to ion-pair formation with the 2-HP anion with its subsequent regeneration on  $\text{HClO}_4$  addition due to hydrogen ion being a more effective ion-pairing cation. However, the variations in the wave height may be due to the difficulties of measuring it.

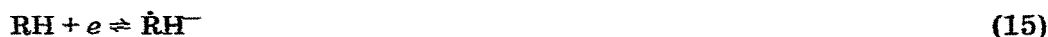
#### *Redox couple at $-1.7$ V*

It is tempting to assign the apparent redox couple observed at ca.  $-1.7$  V on cyclic voltammetry of a solution containing a strong acid : 2-HP ratio of one to reduction of 2-HP itself (RH) and oxidation of the resulting anion radical ( $\text{RH}^-$ ). The cathodic peak magnitude is ca. 0.1 that of the main 2-HP peak at  $-0.8$  V due to reduction of  $\text{RH}_2^+$ .

RH may be present in low concentration when the scan reaches  $-1.7$  V due to a slight deficiency in proton donor, to dissociation of the low concentration of unreduced  $\text{RH}_2^+$ , and/or to the occurrence to some extent of the following reaction sequence beyond  $-0.8$  V:



The small amount of RH thus generated would be reduced at  $-1.7$  V,



with the radical anion being sufficiently stable under the experimental conditions (e.g., low concentration and absence of proton donor) to produce a small anodic peak on the immediately initiated return scan.

#### ACKNOWLEDGMENTS

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