J. Indian Chem. Soc.,
Vol. 73, April-May 1996, pp. 211-214

NOTE

Polarographic and Cyclic Voltammetric Studies on Potential Antibacterial 4-Hydroxy-2-methylthio-6-methyl-5-sulphonamoylazopyrimidine

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Manuscript received 18 August 1993, revised 10 August 1994, accepted 11 August 1994

Aromatic azo compounds have been the subject of many investigations[1]. However, heterocyclic azo compounds[2,3] have received much attention during the last decade. A literature survey reveals the absence of systematic electrochemical study on sulphonamoylazopyrimidines, a class of compounds which have several interesting applications in the field of medicine. In view of the fact that physiological activity of a molecule is closely related to its redox behaviour in the cell membrane, it was considered worthwhile to study the redox behaviour[4] of a representative member of the above class of compounds at the glassy carbon and dropping mercury electrodes.

Results and Discussion

The polarograms of 4-hydroxy-2-methylthio-6-methyl-5-sulphonamoylazopyrimidine were recorded in the pH range 2.0–12.0 in 30% acetonitrile solution. Electrochemical characteristics of the compound in concentration 1.0×10^{-4} *M* and at pH 5.6 are as follows : $-E_{1/2}$, 0.56 V; i_d, 0.45 μA; $-E_p$, 0.58 V; i_p, 2.95 μA; $dE_{1/2}/dpH$, 0.050; αn, 0.76, *I*, 3.29×10^3; *P*, 1.10. This compound displayed a single well defined polarographic wave, the height of which was practically constant within the whole pH range. The nature of the wave was investigated through the dependence of the limiting current on the height of the mercury column and temperature. The characteristics of the polarographic waves were evaluated at various temperatures and at different heights of mercury column. The limiting current was found to be diffusion-controlled as evident by the linear plots of i_d vs $\sqrt{h}$ and the low value of temperature coefficient (below 1.60%/°C). The shift of half-wave potential towards more negative values with increasing concentration of the depolariser (0.5×10^{-4}–2.0×10^{-4} *M*) and logarithmic analysis confirmed the irreversible nature of the electrode process.

The $E_{1/2}$ value shifted towards negative potential with the increase in pH of the solution. The plots of $E_{1/2}$ vs pH were linear upto pH 8.0 with slopes in the range 0.05–0.060 V/pH. After pH 8.0, there was practically no change in $E_{1/2}$ with pH. Two linear segments intersect at pH 8.0, a value which is in accord with the p*K* value. The shift of $E_{1/2}$ with increasing pH indicated the participation of protons in reduction and this leads to the conclusion that the proton transfer precedes the main electrode process. Above pH 8.0, $E_{1/2}$ becomes independent of pH. This indicates the reduction of de-protonated species. Similar dependence of half-wave potential on pH has also been reported in case of other azo compounds[5,6].

Controlled potential electrolysis of the compound at the plateau potential (1.2 V) using the mercury pool cathode consumed 2.0 electrons. The colour of the starting material faded out at the end of the electrolysis. A polarogram and cyclic voltammogram of the completely reduced solution did not show any reduction peak. This indicates that no electroactive species remained in the solution after complete electrochemical reduction of the compound.

The values of αn_a (product of transfer coefficient and number of electrons involved per molecule of

the reactant) and P (number of protons involved per molecule of the reactant in the rate-determining step) have been calculated using the following equation[6],

$$\alpha n_a = -0.0517/E_{1/4}-E_{3/4}$$

$$P = (dE_{1/2}/dpH)\ \alpha n_a/0.0591$$

Cyclic voltammetry of this compound was performed at glassy carbon electrode in the pH range 2.0–12.0. Some typical cyclic voltammograms are shown in Fig. 1. The voltammograms were recorded at various scan rates (50–200 mV s^{-1}) and scan

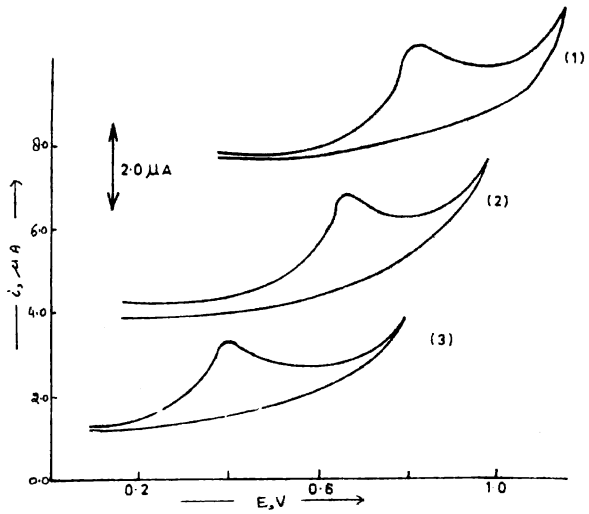
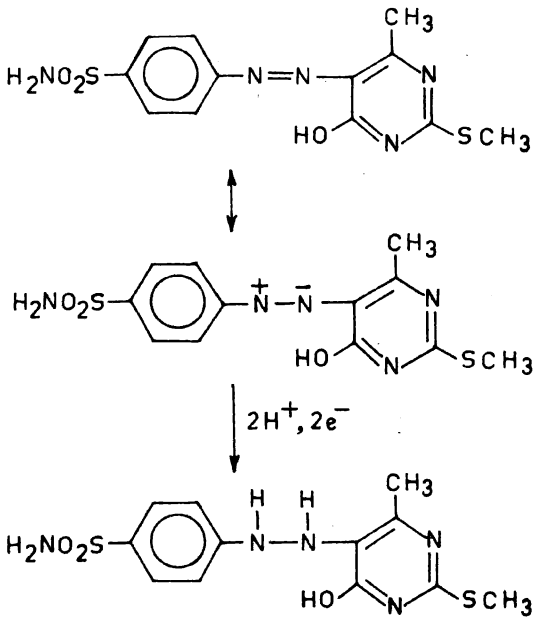


Fig. 1 Cyclic voltammograms of 4-hydroxy-2-methylthio-6-methyl-5-sulphonamoylazopyrimidine at pH : (1) 3.6, (2) 5.6, (3) 8.3; concn. = 1.0×10^{-4} M, v = 50 mVs^{-1}.

ranges. At different scan rates this compound showed only one voltammetric reduction peak at the glassy carbon electrode. The cathodic peak potential of the voltammograms were found to shift towards more negative potentials with increasing scan rate as expected for irreversible electron transfer step[7]. The plots of i_{pc} vs $v^{1/2}$ (scan rate) were found to be straight lines passing through the origin which indicate diffusion-controlled nature of the electrode process. Furgher, the effect of change of concentration of the depolariser on diffusion current has been examined. The plot of i_d vs concentration was a straight line indicating diffusion-controlled nature of the electrode process.

Keeping in view the feasibility[3] of the site of reduction it is concluded that –N=N– is more susceptible[6] to reduction as its reduction occurs at low potential. Hilson and Birnboun[8] and Tachi[9] reported that reduction of azo compounds takes place in a 2-electron wave at the –N=N– group giving the hydrazo derivative. Nygard[10] reported that reduction of azo benzene gives a reversible 2e wave at low concentration and low pH. The existence of a single irreversible wave observed for these compounds may be attributed to the bulky pyrimidine substituent in the molecule.

As the number of electrons involved in the reduction is two and the number of protons involved in the rate determining step is one, and only one product is obtained after exhaustive electrolysis, the mechanism shown in Scheme 1 may be proposed for the reduction of these compounds.



Scheme 1

The solution after controlled potential electrolysis gave negative test for amino group thereby showing that after reduction of –N=N– to –NH–NH– further reduction to aromatic amine does not take place (as also confirmed by the fact that the number of electrons involved is only two). Furthermore, the above mentioned electrolysed solution did not give any polarographic or cyclic voltammetric peak,

thereby confirming the above reduction mechanism. This mechanism is further supported by the work of others[11].

Effect of solvent composition : The nature and amount of the solvent can affect the half-wave potential and limiting current[12]. This behaviour was observed by observing changes both in $E_{1/2}$ and i_d in the present case. With the increase in the percentage of DMF, the $E_{1/2}$ value shifted towards more negative potential with simultaneous decrease in i_d (Table 1).

TABLE 1–EFFECT OF INCREASING PERCENTAGE OF DMF ON THE POLAROGRAPHIC REDUCTION OF 4-HYDROXY-2-METHYLTHIO-6-METHYL-5-SULPHONAMOYLAZOPYRIMIDINE

pH = 5 6, Concn = $1\ 0 \times 10^{-4}$ *M*

Sl no	DMF %	$-E_{1/2}$ V	i_d μA
1	30	0.56	0 45
2	40	0 58	0 41
3	50	0 63	0 38
4	60	0 67	0 35
5	70	0 68	0 32
6	80	(–)	(–)

(–) Drawn out waves.

An increase in the organic solvent content results in a rise in pH[13] and in an increase in the dissociation constant of the protonated species[14]. Both these factors lower the rate of protonation and consequently would lead to a shift in half-wave potential of the wave towards more negative value in all such cases where protonation precedes the electron transfer. It appears that only these two factors are not only responsible for the observed shift in $E_{1/2}$ because the resulted shift is greater than that what it would have been due to change in pH and the dissociation constant. An increase in percentage of DMF from 30 to 60% resulted in an increase of pH by 1.10 unit. This additional shift in $E_{1/2}$ may be ascribed to a decrease in adsorbability and hence surface concentration of the depolariser with an increasing percentage of DMF and acetonitrile in aqueous organic mixture[15]. Obviously, decreased surface concentration would retard the electrode process[16] resulting in decrease in $E_{1/2}$ and i_d.

Experimental

4-Hydroxy-2-methylthio-6-methyl-5-sulphonamoylazopyrimidine was synthesised[17] and its purity ascertained by recrystallisation and tlc. Stock solution (1.0×10^{-3} *M*) of the sulphonamolyazopyrimidine was prepared in acetonitrile[18]. All chemicals used were of A.R. grade.

Polarographic measurements were done on an Elico DC CL-25 polarograph. The capillary had a flow rate of 1.25 mg s^{-1} mercury and drop-time 2.66 s at zero applied potential vs S.C.E. in 1.0 *M* KCl solution at a height of 65 cm of mercury column. The polarograms were recorded at 25 ± 1.0°. The pH-metric measurements were made on an Elico LI-15 pH meter fitted with a glass electrode and saturated calomel electrode (reference electrode).

In order to evaluate the effect of varying acid strength on this compound, Britton-Robinson buffers[19] in the pH range 2.0–12.0, were prepared in double-distilled water using AnalaR grade chemicals. The solution for polarographic study was prepared by mixing depolariser (1.0 ml), acetonitrile (2.0 ml), necessary to keep the compound in solution, 1.0 *M* KCl (1.0 ml) and appropriate B.R. buffer (6.0 ml). The solution was deaerated[20] by passing purified nitrogen gas for about 10 min and corrections for residual current were made in all the cases. Temperature coefficient was calculated by Nejedly's method[21]

Cyclic voltammetric studies were carried out on a BAS CV-27 cyclic voltammograph in connection with a digital electronic 2000 Omnigraph *X-Y/t* recorder. The details of experimental set-up are described elsewhere[22]

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