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Electrochemical Reduction of Phenazopyridine Hydrochloride in Dimetyl Sulfoxide

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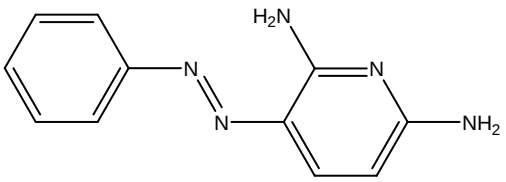
ABSTRACT

In the present work, the electrochemical reduction of phenazopyridine hydrochloride (PAP**)** was carried out on glassy carbon (GCE) electrode in different supporting electrolyte/solvent systems by cyclic voltammetric (CV) technique. The best results for PAP were obtained in 0.1 M tetrabutyammonium iodide/dimetyl sulfoxide (TBAI/DMSO) non-aqueous system by CV technique. In this media, three irreversible cathodic peaks were observed about -0.7 V, -1.7 V and - 2.0 V for PAP. With the scan rate measurements the process was found diffusion controlled. The possible reduction mechanism of PAP was also discussed.

Key words: *Phenazopypridine hydrochloride; Dimetyl sulfoxide; Glassy carbon electrode, Voltammetry*

1. INTRODUCTION

Phenazopyridine hydrochloride (PAP; Scheme 1) is an analgesic drug used to provide symptomatic relief of pain in conditions such as cystitis and urethritis [1-5]. The electrochemical reduction and determination of phenazopyridine hydrochloride were carried out at carbon paste electrode by osteryoung square wave voltammetry [5]. The electro-chemical properties of PAP were also investigated by adsorptive stripping voltammetric technique [6]. In addition, differential pulse polarography is convenient method for the analysis of nitrofurantoin and phenazopyridine in tablets [7].



Scheme1. The chemical structure of PAP

According to our literature investigation, there is no report yet except [8] on the electrochemical reduction of PAP in non-aqueous media. Therefore, in the present study, electrochemical reduction of PAP was investigated in **0.1** M tetrabutylammoniumiodide/ dimetyl sulfoxide (TBAI / DMSO) on glassy carbon electrode (GCE) by cyclic voltammetry (CV) [8].

2. EXPERIMENTAL

2.1. Apparatus

A Model Metrohm 757 VA Trace Analyzer (Herisau, Switzerland) was employed for the voltammetric measurements, with a three-electrode system consisting of a GCE (surface size φ = 7 mm, disc diameter R= 2 mm Metrohm) working electrode, a platinum wire auxiliary electrode and Ag/Ag+ (**0.01** M $AgNO_3$/ DMSO) reference electrode. Before each measurements was CGE polished manually with polishing alumina (prepared from φ = 0.01μm aluminium oxide) on alumina polish pad then rinsed with ultra pure deionize water, ethanol and DMSO. All measurements were carried out after the deoxygenating of the solutions with

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argon gas for 5 min for supporting electrolyte and 60 s for sample before each measurement.

2.2. Reagents

PAP was kindly supplied by Faco Inc. (Istanbul, Turkey). A stock solution of 1.0 $x10^{-1}$ M was prepared daily by dissolving an accurate mass of PAP. DMSO, TBAI (BDH Chemicals LTD, % 98), Alumina and silver nitrate were purchased from Merck (Germany).

3. RESULT AND DISCUSSION

3.1. Electrochemical Reduction of PAP

Electrochemical reduction of PAP was investigated in 0,1 M tetra TBAI / DMSO on GCE by CV technique. The sharp three irreversible cathodic peaks were observed for PAP (Figure1). As can be seen from Figure 1; first peak was -N=N- group, second peak was -C=N-group of adsorbed molecule and the third peak belongs to -C=N-group of molecule in the solution. To verify this, voltammograms of two different models of compounds were taken in the same experimental condition for this purpose, contained only -N=N-group of 1,1'-(4,4'-methylenebis(4,1-phenylene)bis(diazene-2,1-diyl)dinaphthalen-2-ol),(Scheme2) voltammogram was taken [9]. Only one reduction peak was observed about -1.0 V (Figure 2). However, the second (two shoulders) and third peak were no observed of PAP. Therefore, the observed peak is the result of the reduction of -N=N- group.

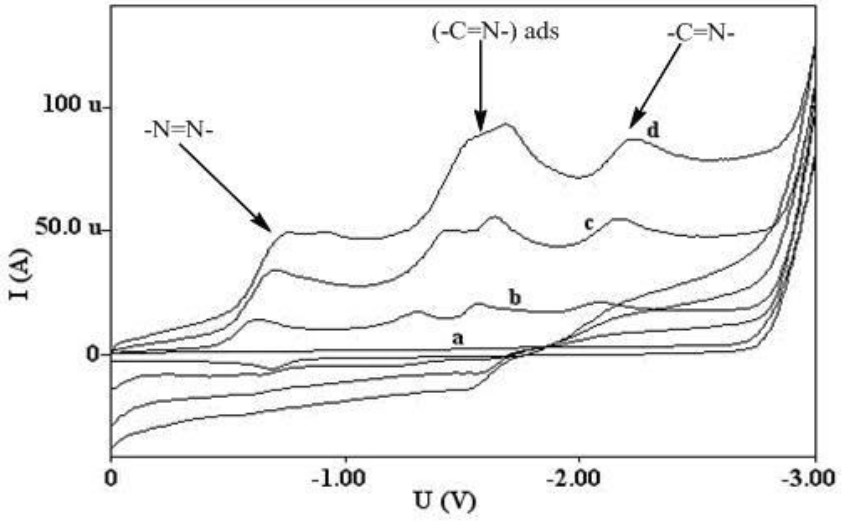
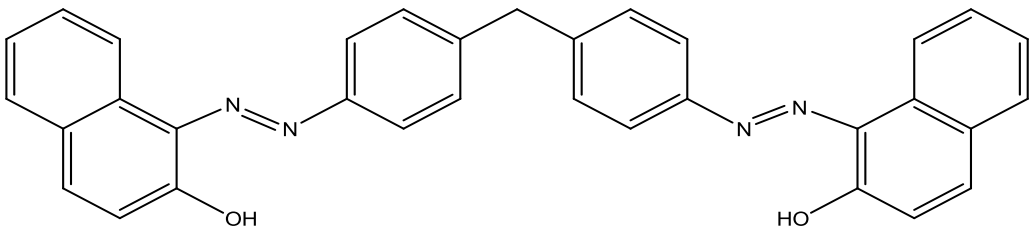


Figure 1. The cyclic voltammogram of 2×10^{-3} M PAP in 0.1 M TBAI/DMSO at GCE a) Supporting electrolyte, b-d) PAP, scan rate = 0.5; 1.0 ; 3.0 Vs^{-1} respectively



Scheme 2. The chemical structure of 1,1'-(4,4'-methylenebis(4,1-phenylene)bis(diazene-2,1-diyl)dinaphthalen-2-ol

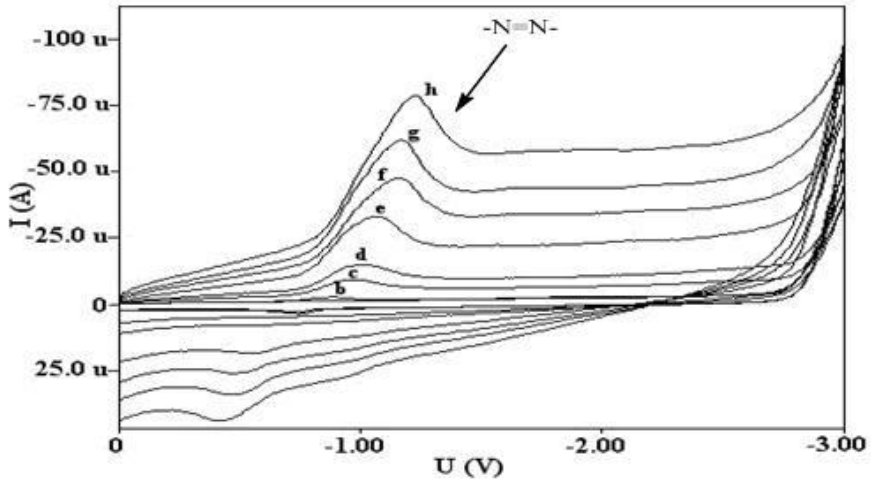
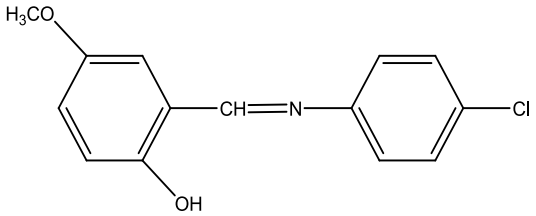


Figure 2. The cyclic voltammogram of 2×10^{-3} M 1,1'-(4,4'-metilenbis(4,1-fenilen)bis(diazen-2,1-diyl)dinaftalen-2-ol in 0.1 M TBAI/DMSO at GCE a) Supporting electrolyte , b) 0.1Vs^{-1} c) 0.5 Vs^{-1} d) 1.0 Vs^{-1} e) 3.0 Vs^{-1} f) 5.0 Vs^{-1} g) 7.0 Vs^{-1} h) 10.0 Vs^{-1} scan rate

Then, voltammogram of containing only -C=N- group of 2-((4-chlorophenylimino) methyl)-4-methoxyphenol as the second model compound (Scheme 3) were taken in the same conditions. Two reduction peaks for PAP were observed about **-1.5** V (two shoulders) and about -2.0 V (Figure 3). Therefore, the second peak was reduction of -C = N-group of adsorbed molecule, while the third peak was -C=N-group of molecule in the solution [10,11].



Scheme 3. The chemical structure of 2-((4-chlorophenylimino)methyl)-4-methoxyphenol

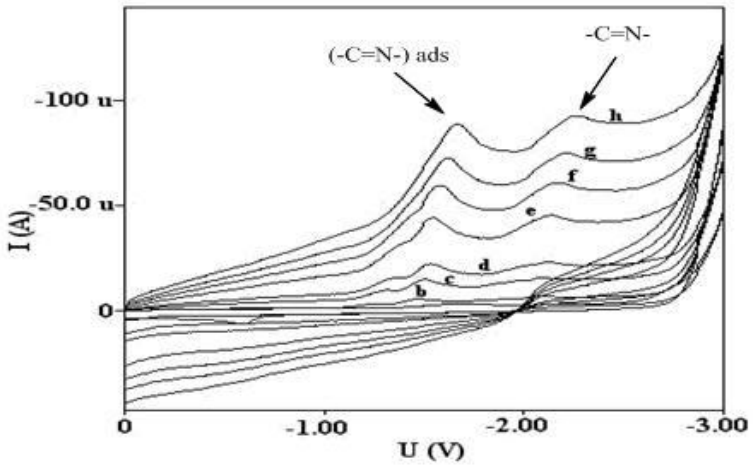


Figure 3. The cyclic voltammogram of 2×10^{-3} M 2-((4-chlorophenylimino)methyl)-4-methoxyphenol in 0.1 M TBAI/DMSO at GCE a) Supporting electrolyte b) 0.1Vs^{-1} c) 0.5 Vs^{-1} d) 1.0 Vs^{-1} e) 3.0 Vs^{-1} f) 5.0 Vs^{-1} g) 7.0 Vs^{-1} h) 10.0 Vs^{-1} scan rate

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The effects of various scan rates between 0.1-10Vs^{-1} on the peak potential and the peak current of 2×10^{-3} M PAP were evaluated. Scan rate studies were performed to assess whether the processes on GCE were under diffusion-or adsorption-control [12-21].

The cyclic voltammograms of 2×10^{-3} M PAP were obtained in **0.1** M TBAI/DMSO at GCE. The linear relationship existing between peak current and square root of the scan rate between 0.1-10Vs^{-1} (correlation coefficient about 0.99) showed that the oxidation process is predominantly diffusion-controlled in the whole scan rate range studied. In addition, a plot of logarithm of peak current versus logarithm of scan rate gave a straight line (Correlation coefficient about 0.99) with a slope of about 0.5, which is expected value for an ideal reaction of solution species [11-21]. Therefore, a diffusion component must be taken into account. Other studies were conducted in line with this phenomenon.

Table 1. Peak potential and peak current values of $2x10^{-3}$M PAP in 0,1 M TBAI/DMSO at GCE by CV. Scan rate = 3 Vs^{-1}

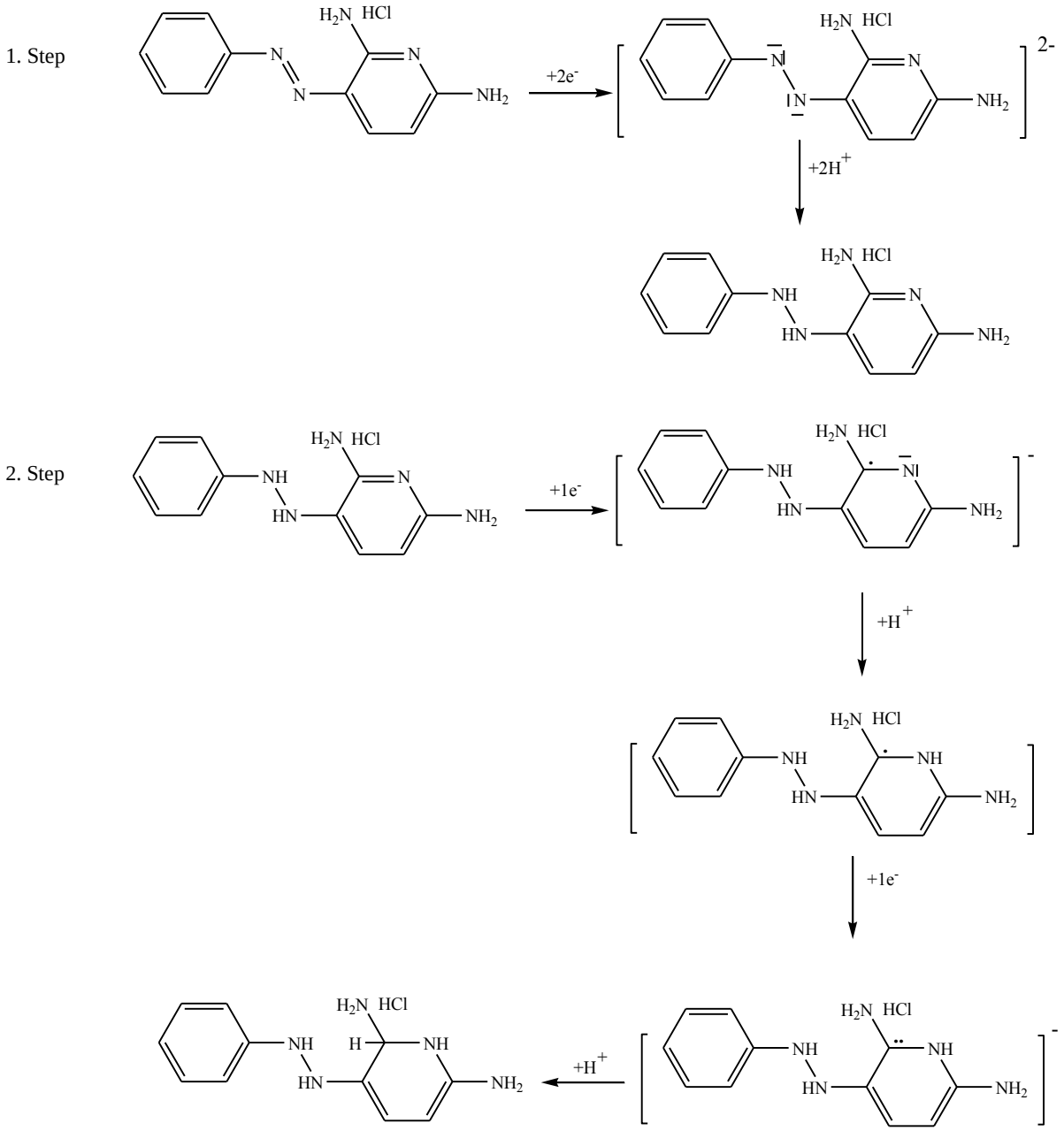
Compound	**Peak 1**		**Peak 2**		**Peak 3**	
	Ep_1 (V)	Ip_1 (uA)	Ep_2 (V)	Ip_2 (uA)	Ep_3 (V)	Ip_3 (uA)
PAP	–0.73	20.70	–1.68	31.00	–2.22	12.80

3.2. Proposed Reduction Mechanism of Electrode Reaction

When describing electrochemical reactions, an "*E*" and "*C*" formalism is often employed [11,12]. The *E* represents an electron transfer; sometimes E_O and E_R are used to represent oxidations and reductions respectively. The *C* represents a chemical reaction which, can be any elementary reaction step and often called a "following" reaction.

As can be seen from reduction mechanism: in the first stage, diazen group of PAP by taking two electrons, -N=N- bond open and the -N-N^{2-}- dianion occurs. Then, hydrazine anion binding $2H^+$, hydrazine compound (-NH-NH-) occurs. In the second stage, imine group of PAP taking one electron (C-$N^{\cdot-}$) radical anion occurs. Then, negative charged nitrogen atom binding $1H^+$, C$^{\cdot}$-NH occurs. In the third stage, this radical carbon atom takes one more electron and carbanion (C^--NH) occurs. The last step, carbanion takes a $1H^+$ ion from the solution and amine compound (CHNH) occurs. This reaction stages showed that the reduction runs according to EC mechanism [11,12].

Proposed mechanisms of electrode reaction as fallows (Schemes 4) :



Scheme 4. Proposed mechanism of electrochemical reduction of PA

4. CONCLUSION

In present work, electrochemical behaviors of PAP were first time investigated in non-aqueous media by voltammetric techniques. A simple, sensitive, selective CV technique was improved for the electrochemical reduction behaviors of PAP on GCE. Irreversible three sharp reduction peaks were observed for PAP.

The principal advantage of the electrochemical technique over the other techniques is that it may be applied directly to any sample without the need for extensive sample preparation, since there was no

interference from the excipients and endogenous substances. Another advantage is that the developed CV technique is rapid, requiring about 5 min to run any sample and involves no sample preparing other than dissolving, diluting, precipitating, centrifuging and transferring an aliquot to the supporting electrolyte.

5. ACKNOWLEDGEMENTS

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