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Full Paper

Electrochemical Studies of Aryl Hydrazones Containing 1,3,4-Oxadiazoles and Pyrazoline-3-one Moiety

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Abstract-The electrochemical behaviour of six aryl hydrazones containing 1,3,4-oxadiazole moiety and pyrazoline-3-one moiety was described by DC polarography. The obtained results were compared with those obtained in cyclic voltammetry (CV) employing hanging mercury drop electrode (HMDE) and modified carbon paste electrode (MCPE). Based on the results, mechanism for the electro-reduction process was proposed in acid as well in basic media. The structure of aryl hydrazones were characterized by elemental analysis, IR and ^{1}H NMR spectra**.**

Keywords- Aryl hydrazones, Polarography, Cyclic voltammetry, Hanging mercury drop electrode, Modified carbon paste electrode, Reduction mechanism

1. INTRODUCTION

Among heterocyclic compounds, pyrazolines have become important construction motif for the development of new drugs. They have been reported to possess various pharmacological activities such as antimicrobial [1-3], antiinflammatory [4], antihypertensive

[5], antiamoebic [6,7], antimycobacterial [8,9], antitumor [10], antidepressant [11], antidiabetic [12] and antibacterial [13] etc. Similarly a great number of compounds containing 1,3,4-oxadiazole core have a broad biological activity spectrum including antibacterial [14], antifungal [14], analgesic [15], antiinflammatory [15], antiviral [16], analgesic [16], antitumor [17], antioxidant [17], antitubercular [18], anticonvulsant [19] and hypoglycemic [20] activities. These reports demonstrate the relevance of pyrazolines and 1,3,4-oxadiazoles in heterocyclic and pharmaceutical chemistry.

The first systematic electrochemical study of hydrazones was reported by Laud [21]. Review of literature reveals that many scientists have reported [22-24] a four electron reduction for hydrazones in acid as well as in alkaline media with the formation of amino compounds. In their previous studies, the authors have reported that the azo group was reduced at the DME via usual sequence involving imine intermediate [25]. But a rationally different mechanism is proposed in the present studies.

The knowledge of electrochemical reduction/oxidation [26-28] of drugs is essential to characterize and identify reactive drug metabolites. In 1981 Shono et al. were the first to utilize direct electrochemical reduction/oxidation information successfully in the investigation of drug metabolites, for N-dealkylated metabolites of lisuride, diazepam, methysergide and imipramine [29]. Moreover, biological activities of drugs depend on the nature of the substituents [30,31]. The present article is aimed at exploring the application of electrochemistry in identifying the possible products of oxidation/reduction of aryl hydrazones that have potential pharmacological applications.

2. EXPERIMENTAL

2.1. Materials and Instruments

The chemicals employed in the studies were of analytical reagent grade and were procured from Merck India Limited. Britton-Robinson buffer solutions [32] were prepared from stock solutions of boric acid, phosphoric acid, acetic acid and sodium hydroxide. Analar mercury was further purified according to the procedure described in literature [33]. The surfactants used were of high purity grade and their aqueous solutions were employed in experiments. Infrared spectra of the compounds were recorded on Perkin-Elmer FT-IR spectrometer (υ_{max} in cm^{-1}). ^1H NMR spectra were recorded on a JOEL (300MHz) spectrometer using TMS as an internal standard (chemical shifts in δ). The pH measurements were made with pH meter, Model LI – 10, ELICO Private Limited, Hyderabad, India. A CL-25 Pen Recording Polarograph manufactured by ELICO Private Limited, Hyderabad, India was used to record current-voltage curves. The capillary having the characteristics 1.80 $mg^{2/3}$ $s^{-1/2}$ at h=80 cm was employed in the studies. The cyclic voltammeter used consists of a X–Y recorder (Model RE 0074), a PAR 175 Potentiostat and an PAR 175 Universal Programmer.

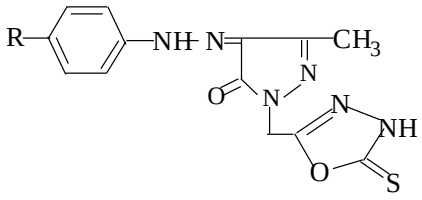
A stationary mercury drop electrode (SMDE 303) with a drop area 0.0096 cm^2 was used as working electrode.

2.2. Synthesis and characterisation of title compounds

Appropriate para substituted aniline was chosen to synthesize the respective compound under investigation by the procedure reported in literature [14].

The title compounds were characterized by elemental analysis, IR, ^{1}H NMR spectral data and the details are given below.

Table 1. Details of aryl hydrazones synthesized

Identification symbol	Structure of title compound	Substituent (-R)
a		H
b		4-CH_3
c		4-OCH_3
d		4- OC_2H_5
e		4-Cl
f		4-Br

(a): 5-methyl-4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one

Yield:65%; mp.:150^{0}C;
IR (KBr) ν_{max}(cm^{-1}): 3180 (NH), 3126 (Oxadiazole NH), 1670 (C=O), 1603 (C=N), 1134 (C=S); ^{1}HNMR (200 MHz, $CDCl_3$ + DMSO-d_6) δ (ppm): 2.3 (s, 3H, CH_3), 5.45 (s, 2H, N-CH_2), 6.6-7.2 (m, 5H, Ar H), 7.9 (s, H, Ar NH), 14.7 (s, H, thiol-thione tautomeric proton).
Molecular formula (mol wt.): $C_{13}H_{12}N_6O_2S$ (316).
Found (%): C 49.50, H 3.98, N 26.66, O 10.70, S 10.32.
Calcd (%): C 49.36, H 3.82, N 26.52, O 10.52, S 10.14.

(b): 5-methyl-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-4-(p-tolyl hydrazono)-2,4-dihydro-pyrazol-3-one

Yield: 67%; mp. : 152^{0}C;
IR (KBr) ν_{max} (cm^{-1}): 3160 (NH), 3110 (Oxadiazole NH), 1655 (C=O), 1600 (C=N), 1125 (C=S); ^{1}HNMR (200 MHz, $CDCl_3$ + DMSO-d_6) δ (ppm): 2.0 (s, 3H, CH_3), 2.26 (s, 3H,

CH_3), 5.40 (s, 2H, N-CH_2), 6.5-7.1 (m, 5H, Ar H), 7.5 (s, H, Ar NH), 14.3 (s, H, thiol-thione tautomeric proton).
Molecular formula (mol wt.): $C_{14}H_{14}N_6O_2S$ (330).
Found (%): C 51.09, H 4.42, N 25.60, O 9.74, S 9.89.
Calcd (%): C 50.90, H 4.27, N 25.44, O 9.69, S 9.71.

(c): 5-methyl-4-(4-methoxy phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one

Yield: 62%; mp. : 155^0C;
IR (KBr) ν_{max} (cm^{-1}): 3165 (NH), 3120 (Oxadiazole NH), 1660 (C=O), 1602 (C=N), 1130 (C=S); ^{1}HNMR (200 MHz, $CDCl_3$ + DMSO-d_6) δ (ppm): 2.2 (s, 3H, CH_3), 3.89 (s, 3H, OCH_3), 5.42 (s, 2H, N-CH_2), 6.6-7.2 (m, 5H, Ar H), 7.8 (s, H, Ar - NH), 14.5 (s, H, thiol-thione tautomeric proton).
Molecular formula (mol wt.): $C_{14}H_{14}N_6O_3S$ (346).
Found (%): C 48.70, H 4.25, N 24.43, O 14.03, S 9.40.
Calcd (%): C 48.55, H 4.07, N 24.26, O 13.86, S 9.26.

(d): 5-methyl-4-(4-ethoxy phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one

Yield: 63%; mp. : 160^0C;
IR (KBr) ν_{max} (cm^{-1}): 3160 (NH), 3115 (Oxadiazole NH), 1650 (C=O), 1600 (C=N), 1125 (C=S); ^{1}HNMR (200 MHz, $CDCl_3$ + DMSO-d_6) δ (ppm): 2.1 (s, 3H, CH_3), 1.8 (t, 3H, OCH_3), 3.16 (q, 2H, O-CH_2), 5.41 (s, 2H, N-CH_2), 6.5-7.1 (m, 5H, Ar H), 7.7 (s, H, Ar NH), 14.4 (s, H, thiol-thione tautomeric proton).
Molecular formula (mol wt.): $C_{15}H_{16}N_6O_3S$ (360).
Found (%): C 50.13, H 4.64, N 23.40, O 13.49, S 9.05.
Calcd (%): C 49.99, H 4.47, N 23.32, O 13.32, S 8.90.

(e): 5-methyl-4-(4-chloro phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one

Yield: 65%; mp. : 157^0C;
IR (KBr) ν_{max} (cm^{-1}): 3195 (NH), 3135 (Oxadiazole NH), 1680 (C=O), 1610 (C=N), 1140 (C=S); ^{1}HNMR (200 MHz, $CDCl_3$ + DMSO-d_6) δ (ppm): 2.4 (s, 3H, CH_3), 5.47 (s, 2H, N-CH_2), 7.0 (d, 2H, Ar H), 7.9 (s, H, Ar NH), 14.8 (s, H, thiol-thione tautomeric proton), 6.4 (d, 2H, Ar H).

Molecular formula (mol wt.): $C_{13}H_{11}ClN_6O_2S$ (350).
Found (%): C 44.67, H 3.34, N 24.12, O 9.20, S 9.31, Cl 10.27.
Calcd (%): C 44.51, H 3.16, N 23.96, O 9.12 S 9.14, Cl 10.11.

(f): 5-methyl-4-(4-bromo phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one

Yield: 68%; mp. : 162^0C;
IR (KBr) ν_{max} (cm^{-1}): 3195 (NH), 3140 (Oxadiazole NH), 1685 (C=O), 1615 (C=N), 1145 (C=S); ^{1}HNMR (200 MHz, $CDCl_3$ + DMSO-d_6) δ (ppm): 2.5 (s, 3H, CH_3), 5.48 (s, 2H, N-CH_2), 7.0 (d, 2H, Ar H), 7.9 (s, H, Ar NH), 14.9 (s, H, thiol-thione tautomeric proton), 6.4 (d, 2H, Ar H).
Molecular formula (mol wt.): $C_{13}H_{11}BrN_6O_2S$ (395).
Found (%): C 39.65, H 2.98, N 21.41, O 10.28, S 8.26, Br 20.39.
Calcd (%): C 39.51, H 2.81, N 21.26, O 10.11, S 8.11, Br 20.22.

2.3. General polarographic/cyclic voltammetric procedure

8.0 mL of the buffer solution of desired pH (1.1 – 10.1), 2 mL of the stock solution of the substrate (1.0×10^{-2} M) in dimethylformamide (DMF), 6 mL of DMF and 4.0 mL of distilled water were mixed thoroughly in the polarographic/cyclic voltammetric cell and the polarograms/cyclic voltammograms were recorded after deaeration. Gelatine was used as the maximum suppressor in all investigations except in experiments where the effect of surfactants was studied.

2.4. Preparation of chemically modified electrode

Thoroughly ground crown-ether (1,4,7,10,13,16-hexa oxacyclooxadecane) crystals, graphite powder and nujol in the ratio 36:10:54 (% w/w) were mixed. The paste was packed at the one end of a glass tube (3 mm bore, 1 mm wall) to make contact with a copper wire inserted into the tube.

3. RESULTS AND DISCUSSION

3.1. Polarographic behaviour of 5-methyl-4-(4-substituted aryl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-ones (a-f)

Literature survey [31, 34-36] reveals that not many benzene azo pyrazolines were studied for their electrochemical behaviour.

The polarographic investigations were carried out on 5-methyl-4-(4-substituted aryl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro- pyrazol-3-ones in Briton-Robinson buffer solutions of pH 1.1-10.1. The polarograms of 5-methyl-4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4] oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one are shown in the Fig. 1. The results are presented in the Table 2.

The compounds a-f exhibit a single wave in the pH range 1.1-6.1 and two waves in the pH range 8.1-10.1. An inspection of structure of the compounds showed that the sites vulnerable for reduction at the dropping mercury electrode were cyclic azomethine group (>C=N-), cyclic >C=0 group and the exocyclic azomethine group. It is well known that the exocyclic azomethine group is more proned for the reduction than the other groups. The reduction of the cyclic azomethine (>C=N-) group and cyclic >C=0 group generally occurs at higher negative potentials at the DME. The polarographic behaviour of 5-methyl-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one studied under similar experimental conditions revealed that the compound does not exhibit any reduction wave under the experimental conditions of study. This was probably because of the stabilization [37] of the pyrazoline ring by keto-enol tautomerism. This observation suggests that the waves observed with 5-methyl-4-(4-substituted aryl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-ones (a-f) were due to the reduction of exocyclic azomethine group.

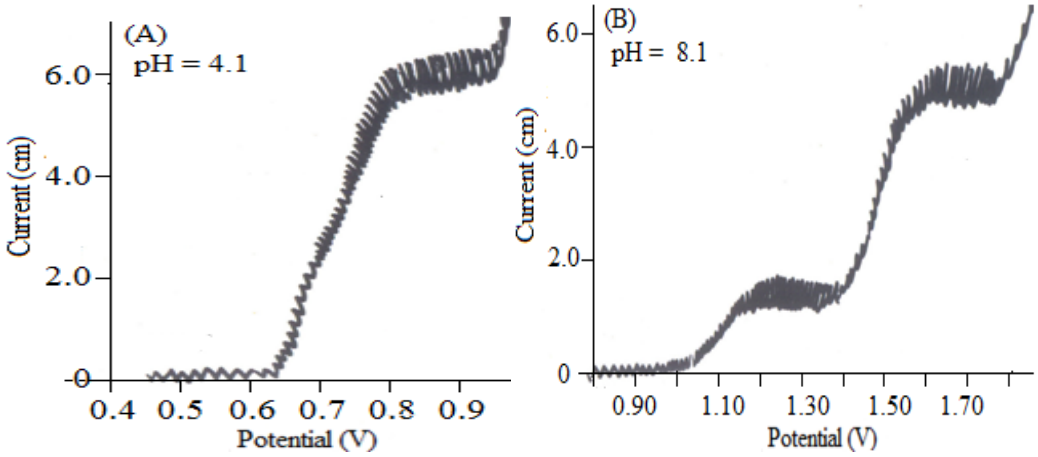


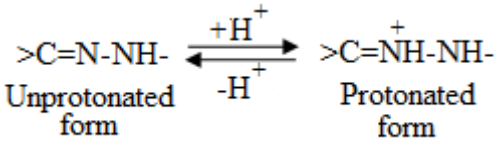
Fig. 1. (A) and (B) are the polarograms of 5-methyl-4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4] oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one (1×10^{-3}M). Medium: Aqueous dimethyl formamide (40% v/v)

3.1.1. Effect of pH on the half-wave potential

The results in the Table 2 showed that the half wave potential increase with increase in pH of the medium in the acidic pH range and it was unaltered in the alkaline pH range. The

graph drawn between half wave potential and pH was a straight line (up to pH 8.1). The slope of the straight lines lies between 180-230 mV. The half wave potential noticed in the present investigation was much more negative than that generally expected for the reduction of simple azo group [38]. The values of p, the number of protons (Table 2) were low and non-integers. This suggests that the process of proton transfer in the reduction was heterogeneous in nature. The shift in the half wave potential with pH of the solution can therefore be ascribed to the following reasons.

a) Both protonated and unprotonated forms of the depolarizer were electro active. There exists an equilibrium between protonated form and unprotonated form [39]. The unprotonated form of the azomethine group was reduced at more negative potential than the protonated form.



b) The pH dependence of the half wave potential was not only due to the antecedent acid-base reaction but also due to the consumption of protons in the reduction process.

c) The pH of the solution in bulk was different from pH at the electrode surface ($\Delta(pH_{surface}) < \Delta(pH_{bulk})$). $E_{1/2}$ remains constant as the equilibrium shifts towards the unprotonated form. It can be seen from Fig. 2 that above pH 8.1, the shift in half wave potential with pH was not so marked as it was in the acidic media.

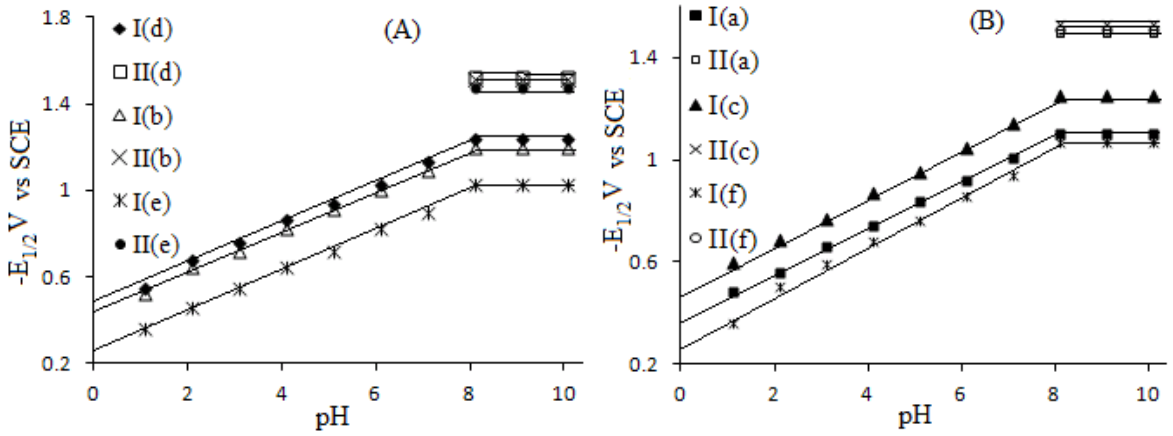


Fig. 2. Effect of pH on half wavepotential; [Arylhydrazone]=1×10^{-3}M; Medium = Dimethylformamide (40% by volume). I and II indicate first and second waves respectively of corresponding compound as shown in the figures (A) and (B)

$E_{1/2}$-pH plot was ⌐ shaped in the pH range of study. $E_{1/2}$ becomes practically constant in the alkaline media and was attributed to the electroactive nature of acidic and basic forms of

the depolarizer. But in the pH range where the protonation rate decreases, the half wave potentials of both the protonated form (acidic) and the unprotonated form (basic) were so close to each other that the waves merge [40] and a single wave was observed.

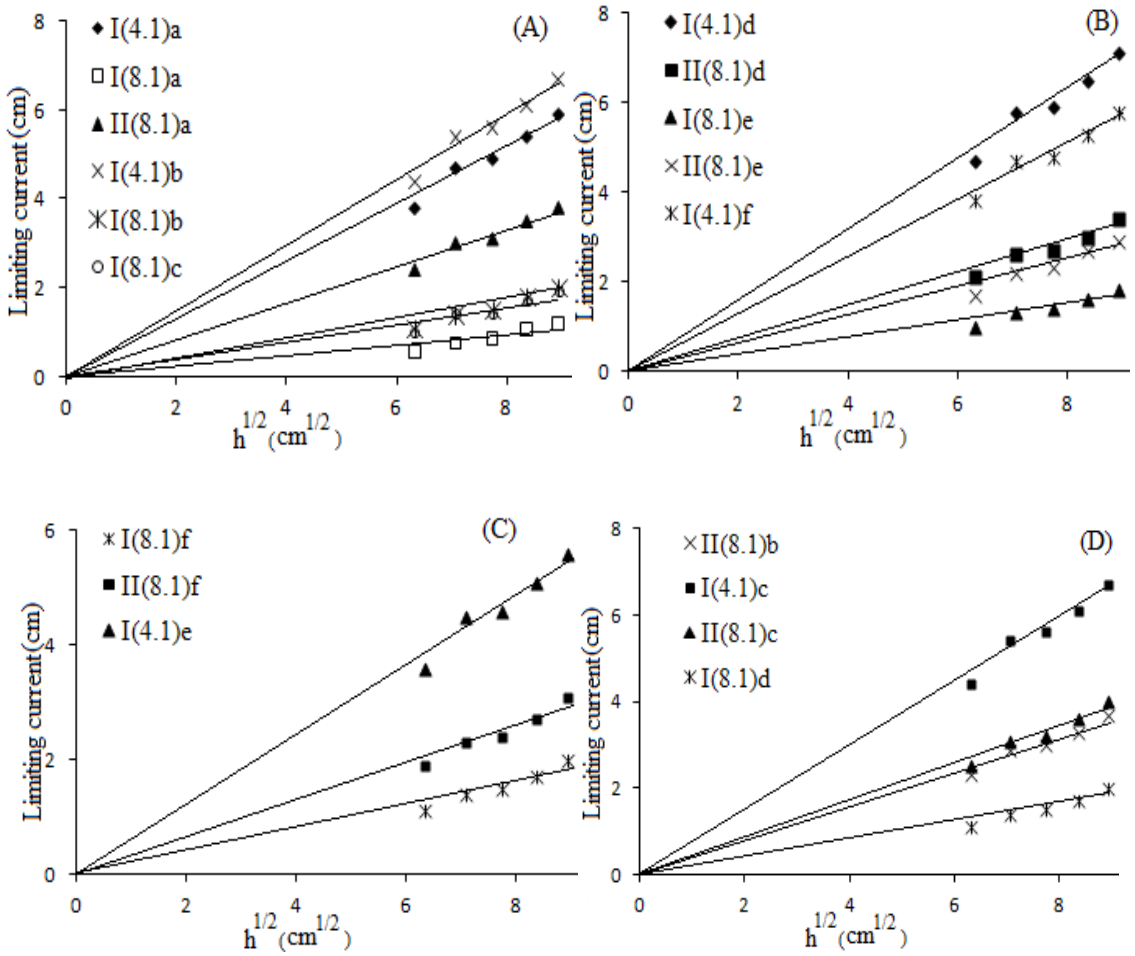


Fig. 3. Effect of mercury column height on limiting current; [Aryl hydrazone]=1×10^{-3}M; Medium = Dimethylformamide (40% by volume). I and II indicate first and second waves respectively of corresponding compound at indicated pH as shown in the figures (A), (B), (C) and (D)

3.1.2. Effect of the height of the mercury column head (h) on the limiting current (i_L)

The demonstrated influence [41] of mercury column height on the limiting current (Fig. 3) reveals the diffusion controlled nature of the polarographic wave. i_L *vs* $h^{1/2}$ plots were linear and were passing through the origin.

Table 2. Polarographic characteristics and kinetic parameters of 5-methyl-4-(4-substituted aryl hydrazono)-2-(5-thioxo-4,5-dihydro- [1,3,4] oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-ones (1×10^{-3} M); Medium: Aqueous dimethylformamide(40% by volume)

Compound	pH	$E_{1/2}$ / pH		α_{na}		No of protons		$D \times 10^{-6}$ cm s^{-1}		$I \times 10^{-6}$ cm s^{-1}		K^{o}_{fh} cm s^{-1}		$\Delta^{*}G$ Kcal $mole^{-1}$	
		I wave	II wave	I wave	II wave	I wave	II wave	I wave	II wave	I wave	II wave	I wave	II wave	I wave	II wave
a	2.1	0.09		0.43		0.65		8.84		3.61		0.61×10^{-5}		2.71	
	4.1	0.09		0.43		0.65		7.28		3.27		0.27×10^{-6}		3.06	
	6.1	0.09		0.39		0.59		0.923		1.16		0.13×10^{-7}		3.41	
	8.1	0.09		0.36		0.54		0.301	3.024	0.66	2.11	0.1×10^{-8}		3.71	
	10.1	0.09		0.36		0.54		0.301	3.024	0.66	2.11	0.1×10^{-8}		3.71	
b	2.1	0.09		0.48		0.31		10.55		3.94		0.80×10^{-6}		2.94	
	4.1	0.09		0.48		0.31		4.42		3.72		0.18×10^{-7}		3.44	
	6.1	0.09		0.43		0.65		4.24		2.5		0.1×10^{-8}		3.71	
	8.1	0.09		0.39		0.59		0.837	2.86	1.11	2.05	0.42×10^{-12}		4.59	
	10.1	0.09		0.39		0.59		0.837	2.86	1.11	2.05	0.42×10^{-12}		4.59	
c	2.1	0.09		0.48		0.31		11.77		4.16		0.33×10^{-6}		3.04	
	4.1	0.09		0.48		0.31		9.4		3.72		0.1×10^{-7}		3.44	
	6.1	0.09		0.43		0.65		1.52		1.5		0.69×10^{-11}		4.27	
	8.1	0.09		0.39		0.59		0.75	3.35	1.05	2.22	0.82×10^{-12}		4.52	
	10.1	0.09		0.39		0.59		0.75	3.35	1.05	2.22	0.82×10^{-12}		4.52	
d	2.1	0.09		0.48		0.31		11.46		4.11		0.39×10^{-6}		3.02	
	4.1	0.09		0.48		0.31		10.55		3.94		0.13×10^{-7}		3.41	
	6.1	0.09		0.43		0.65		1.76		1.61		0.1×10^{-8}		3.71	
	8.1	0.09		0.39		0.59		0.83	2.42	1.11	1.88	0.1×10^{-11}		4.49	
	10.1	0.09		0.39		0.59		0.83	2.42	1.11	1.88	0.1×10^{-11}		4.49	
e	2.1	0.1		0.54		0.91		7.28		3.27		0.11×10^{-4}		2.64	
	4.1	0.1		0.54		0.91		6.56		3.11		0.25×10^{-6}		3.07	
	6.1	0.1		0.48		0.81		3.52		2.27		0.15×10^{-3}		2.34	
	8.1	0.1		0.43		0.72		0.678	1.76	1.0	1.61	0.64×10^{-11}		4.28	
	10.1	0.1		0.43		0.72		0.678	1.76	1.0	1.61	0.64×10^{-11}		4.28	
f	2.1	0.1		0.56		0.94		7.78		3.38		0.37×10^{-5}		2.76	
	4.1	0.1		0.56		0.94		7.04		3.22		0.79×10^{-7}		3.21	
	6.1	0.1		0.50		0.84		3.87				0.4×10^{-8}		3.55	
	8.1	0.1		0.45		0.76		0.83	2.01	2.38	1.72	0.19×10^{-11}		4.42	
	10.1	0.1		0.45		0.76		0.83	2.01	2.38	1.72	0.19×10^{-11}		4.22	

3.1.3. Effect of concentration of the depolarizer on the diffusion current

The effect of concentration of the depolarizer on the diffusion current of aryl hydrazones in the range of 0.5–8.0 M has been studied in solutions of pH 4.1. i_L *vs* concentration plots were linear and passing through the origin as shown in the Fig. 4. The constant i_L/C values not only confirm the diffusion controlled nature of the wave but also indicate the applicability of the current polarographic method for the quantitative determination of aryl hydrazones (a-f) under study.

3.1.4. Effect of pH on the limiting current

It was observed from the Table 2 that the height of the wave decreases with increase in pH (Fig. 5) and this suggests that both the protonated form (acidic) and the unprotonated form (basic) were transported to the electrode surface and were electroactive. The decrease in limiting current with increase in pH may be due to acid-base equilibrium between the protonated form and unprotonated forms of the compound. The limiting current remains pH independent as long as the formation of acid form from the basic form was fast enough. As the pH increases, the rate of the protonation and hence the limiting current decreases.

3.1.5. Kinetic parameters of the electrode reaction

The kinetic parameters for the electrode reaction namely $k^o_{f,h}$ and ΔG^* were evaluated by Meites-Israel method [42]. The values at various pH media are shown in the Table 2. The $k^o_{f,h}$ values decrease and ΔG^* values increase with increase in pH of the medium. This trend shows that the electrode process was becoming increasingly irreversible with increase in the pH of the solution.

3.1.6. Nature of the electrode process

The results presented above revealed the diffusion controlled nature of the waves. The electrode processes were found to be irreversible in low acidic media unlike the reversible electrode process observed for simple azo and azomethine compounds [43] under similar conditions. The irreversible nature of the electrode process observed in the present investigations was further confirmed by

(a) the plots of $-E_{dme}$ *vs* log $(i/i_d - i)$ shown in Fig. 6 at typical pH 4.1 were linear and the values of slope (0.08-0.15) were not in agreement with the theoretical values (0.030 V and 0.015 V for 2-electron and 4-electron reduction respectively) expected for the reversible processes [44, 45].

(b) $E_{1/2}$ shifts towards more negative potentials with increase in the depolarizer concentration [31].

(c) The heterogeneous rate constant ($k^0_{f,h}$) calculated from the Meites–Israel equation were less than10^{-5}.

(d) ΔG* values increase with increase in pH in the range 1.1–6.1 and remain unaltered in alkaline pH range 8.1–10.1.

The irreversibility may be due to the bulky group present at the end of >C=N-NH- linkage [41].

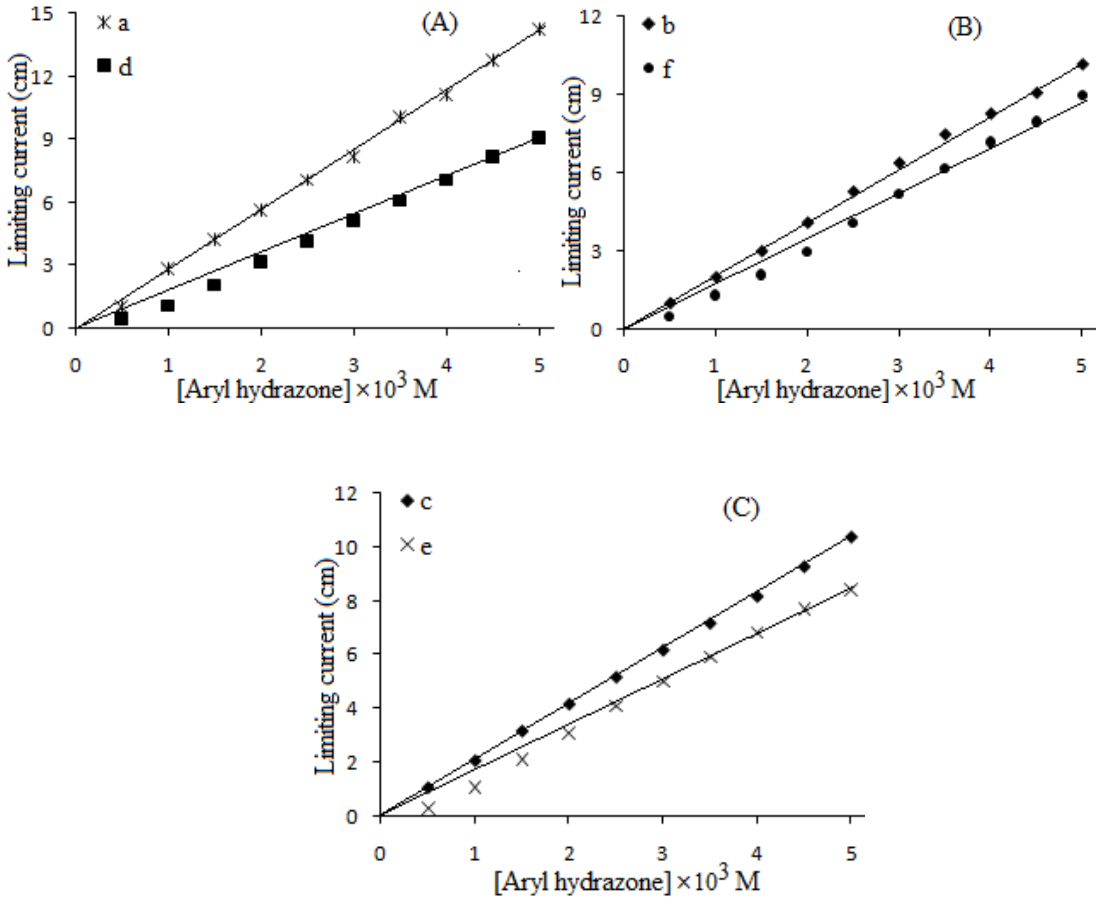


Fig. 4. Effect of concentration on limiting current; pH=4.1; Medium: Dimethylformamide (40% by volume). (A), (B) and (C) are plots of corresponding compounds as indicated in the figure

The slopes of $-E_{dme}$ *vs* log ($i/i_d - i$) plots further indicate that the tendency of the irreversibility increases with increase in the pH of the media. Irreversible nature of the polarographic wave was further confirmed by applying Tome's criteria [46]. αn_a values obtained were almost equal to the values obtained from conventional logarithmic plots (Table 2).

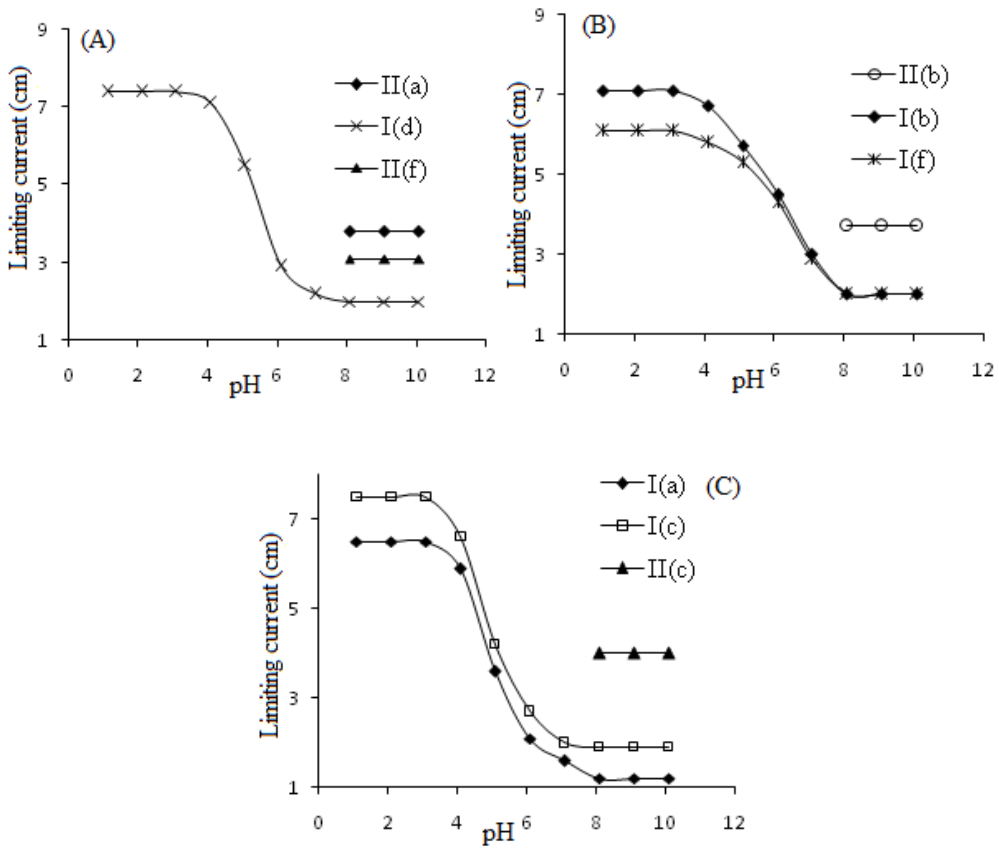


Fig. 5. Effect of pH on limiting current; [Aryl hydrazone]=1×10^{-3}M; Medium: Dimethylformamide (40% by volume). I and II indicate first and second wave respectively of corresponding compound as shown in the figures (A), (B), and (C)

3.1.7. Millicoulometric method

It is possible to determine the value of n by the method reported by DeVris and Kroon [47]. The results are reported in the Table 3.

3.1.8. Controlled potential electrolysis

The electrochemical reduction of 5-methyl-4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one (a) has been studied by the method of controlled potential electrolysis at pH 4.1.

The controlled potential electrolysis was carried out in a Lingane H-type cell. A large pool of mercury at the bottom of the large compartment was used as cathode and a similar pool of mercury at the bottom of the smaller compartment served as anode. The cathode compartment contains 10 mL of 0.01 M 5-methyl- 4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one **(**a), 30 mL of

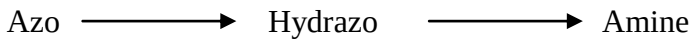
DMF, 20 mL of 1.0 M KCl and 40 mL of buffer solution (pH: 4.1). The electrolysis was followed at an applied potential of -1.1 V by recording decrease in current with time. The number of electrons per molecule was calculated from i-t curves by the procedure outlined by Lingane [48] and was found to be 4. After disconnecting the electrolysis cell, 1 mL of resulting solution was withdrawn and the presence of aniline in the solution was confirmed by standard spot test [49]. The remaining reaction mixture was partially evaporated to half its volume on a water bath, allowed to cool to room temperature and was extracted with ether. The ether layer was evaporated under diminished pressure and the yellow crystalline solid obtained was identified as 2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one**.**

Table 3. Millicoulometric data of 5-methyl- 4-(phenyl hydrazono)- 2-(5-thioxo- 4,5- dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one; Medium : dimethylformamide (40% by volume)

pH	Current (μA)		Time (s)		n value	
	I wave	II wave	I wave	II wave	I wave	II wave
4.1	6.5	--	0	--	--	--
	5.1	--	7200	--	3.9	--
	4.5	--	10800	--	3.9	--
8.1	1.2	3.8	0	0	--	--
	1.1	2.9	7200	7200	3.8	2.0
	1.3	2.4	10800	10800	3.8	1.8

3.1.9. Reduction mechanism

From the above discussion, it is clear that compounds a-f were reduced at dropping mercury electrode through a mechanism which involves the azo group and follows sequence different from the usual ones [25]. The sequence is given below.



This is further substantiated by following facts.

- The half wave potential of the wave was more negative than that expected for the reduction of the simple azo group [38,50].
- The aryl hydrazo pyrazoles [31] did not undergo reduction under the experimental conditions of study.
- Azo and hydrazo groups donot reduce at the same potential.

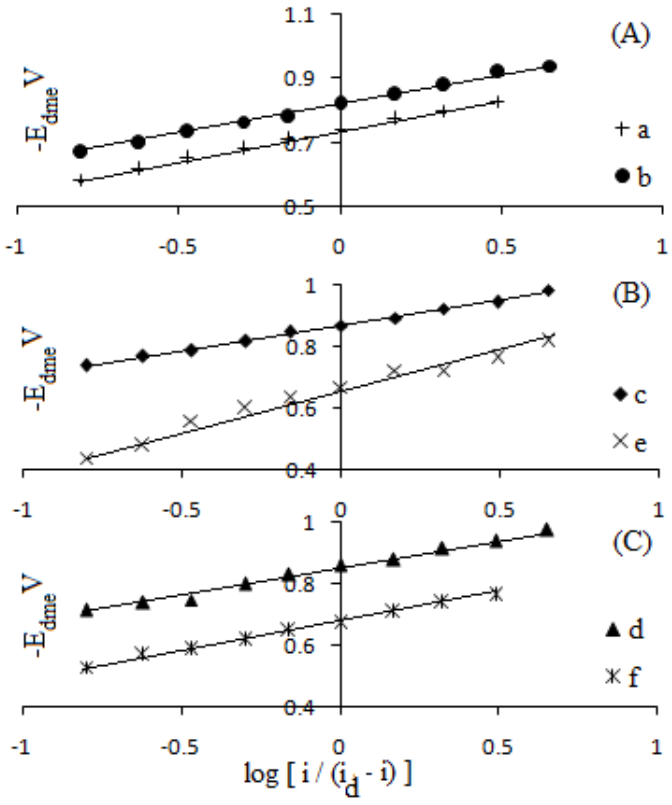


Fig. 6. Semi-log plots of aryl hydrazones; [Aryl hydrazone] = 1×10^{-3}M; pH = 4.1; Medium=Dimethylformamide (40% by volume).

- In strongly acidic aqueous solutions, the end products of the reduction of azobenzene are benzidine and diphenyline and were not electroactive [51].
- In strong acid solutions, the limiting current of azobenzene should therefore be very much less than that observed in weakly acidic solutions. In the present investigations, the limiting current decreases with increase in HCl concentration.
- Increase of half wave potential with increase in pH (Table 2) and positive shift of half wave potential with increase in HCl concentration confirmed that an acid-base equilibrium was playing a significant role in the reduction process. As the wave was not kinetic in nature, the said acid-base equilibrium was a fast process.

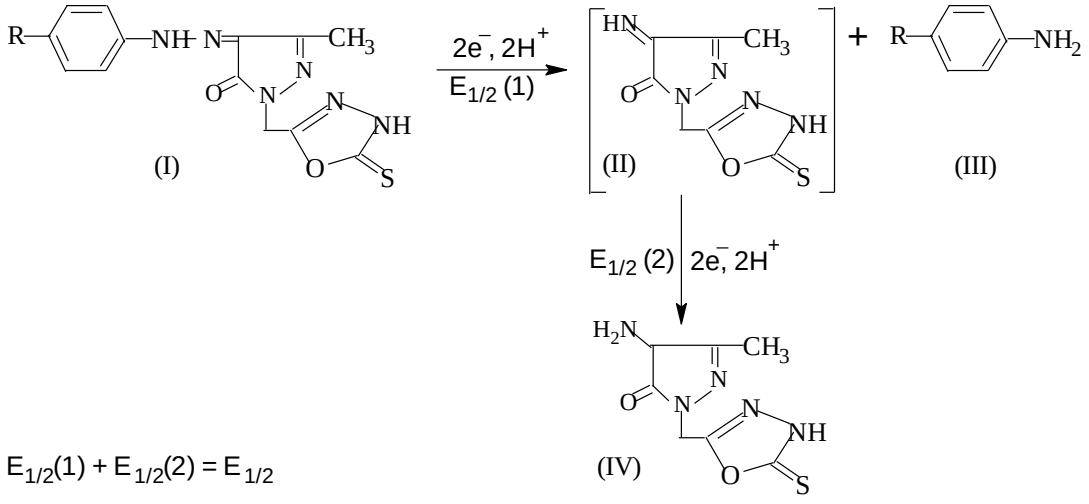
The above facts clearly indicated that a totally different sequence of mechanism must be operative in the present four electron reduction process. The aryl hydrazone pyrazoline-3-one (I) was protonated to yield the protonated form [52,53]. The weak (=N–NH-) single bond of the hydrazone was then cleaved [54,55] with the uptake of two electrons and two protons. As the strength of acid or alkaline medium employed for these reductions was approximately 0.4%, the amide linkage in the pyrazole nucleus was not affected. Moreover, it was found in a separate experiment that 2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one was not affected under stronger acidic or alkaline

conditions. The unstable intermediate (II, imine) produced in the above process was then reduced to amine (IV) in a 2 electron process. It was reported [56,57] that the above mentioned two steps of reduction occur at same potential resulting in a single four electron wave as shown in Scheme 1.

The large decrease in the half wave potential with the rise in HCl concentration from 0.2 to 1.0 was a noteworthy fact since the change in pH also corresponds to the enhanced influence of chloride ions. It was reported [58] that adsorption of the depolarizer plays a significant role in the reduction of the azomethine compounds in such environments. Hence the observed positive shift in the half wave potential was probably due to the adsorption favoring environment created due to the increased concentration of chloride ions.

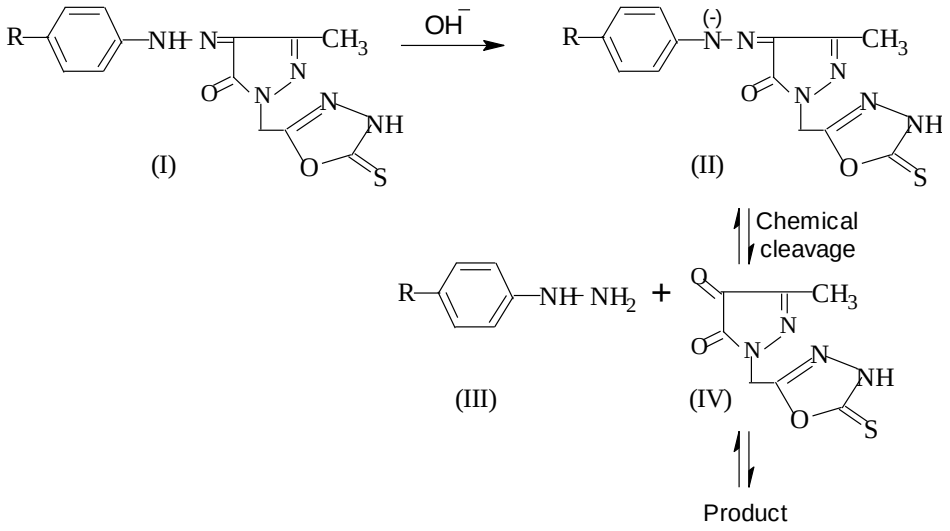
The results presented in Table 2 revealed that the compounds exhibit two waves in media of pH 8.1–10.1. In alkaline medium (pH > pK_a), 5-methyl-4-(4-substituted aryl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one exists in the azomethine anionic form (II) . The latter in alkaline media was susceptible to partial chemical cleavage into the corresponding carbonyl compound (IV) as shown in the Scheme 2. The carbonyl compounds were susceptible to reduction at the dropping mercury electrode. Therefore, the second wave observed in present studies has been ascribed to the two electron reduction of carbonyl compound and the first wave to the 4 electron reduction of azomethine anion. A decrease in the height of the first wave and an increase in the height of the second wave with increase in pH corroborate this conclusion. In strong alkaline solutions (0.2-1.0 M NaOH), a single wave whose height increases with the increase in alkali concentration was observed. Corresponding half wave potentials lie in the range –1.40 to –1.56 V. The wave was due to the 2 electron reduction of carbonyl group to alcohol.

Mechanism in acidic medium



Scheme 1. Reduction mechanism of title compounds in acidic medium

Mechanism in alkaline medium



Scheme 2. Reduction mechanism of title compounds in alkaline medium

3.2. Cyclic voltammetric studies of 5-methyl- 4-(4-substituted aryl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one a-f at hanging mercury drop electrode

3.2.1. General Voltammetric behavior at HMDE

The cyclic voltammetric experiments of aryl hydrazones (a-f) were conducted at HMDE in media of pH 2.1, 4.1, 6.1, 8.1 and 10.1 at different scan rates, 10 mV s^{-1}, 20 mV s^{-1}, 50 mV s^{-1}, 100 mV s^{-1}, 200 mV s^{-1}, 300 mV s^{-1} and 500 mV s^{-1}. The compounds (a-f) exhibit one cathodic peak in the pH range 2.1-6.1 and two cathodic peaks in the pH range 8.1-10.1 at all sweep rates. The cathodic peak potentials become more negative and the cathodic peak currents increase with the increase in scan rate. The cathodic peak potentials were shifted to more negative values and the peak currents decrease with the increase in pH. The data is given in the Table 4.

The irreversible nature of the electrode process [59] was characterized by dependence of peak potential on sweep rate, the absence of anodic peak in the reverse scan, the shape of $i_{pc}/\upsilon^{1/2}$ versus υ plot was in accordance with the Nicholson and Shain criteria [60] and the negative shift of peak potential with increase in sweep rate. A linear plot passing through the origin confirms the diffusion controlled nature of the electrode process. The cyclicvoltammograms of 5-methyl-4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4] oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one are shown in the Fig. 7.

3.2.3. Comparison between polarographic behaviour and cyclic voltammetric behaviour at HMDE

The plots of E_{Pc} *vs* pH were similar to $E_{1/2}$ *vs* pH plots observed in polarographic studies. The single polarographic wave noticed in DC polarography or cathodic peak noticed in CV in the pH range 2.1-6.1 was attributed to the four electron reduction of azomethine group to amine stage. DC polarographic studies revealed two polarographic waves and CV resulted in two cathodic peaks in alkaline media (pH 8.1–10.1). The first reduction step in DC polarography or the first cathodic peak in CV was attributed to 4 electron reduction of azomethine anionic form to amine stage (>C=N-N- to >C-NH-NH_2). The second reduction step in DC polarography or the second cathodic peak in CV was ascribed to two electron reduction of ketone to carbinol (Scheme 2).

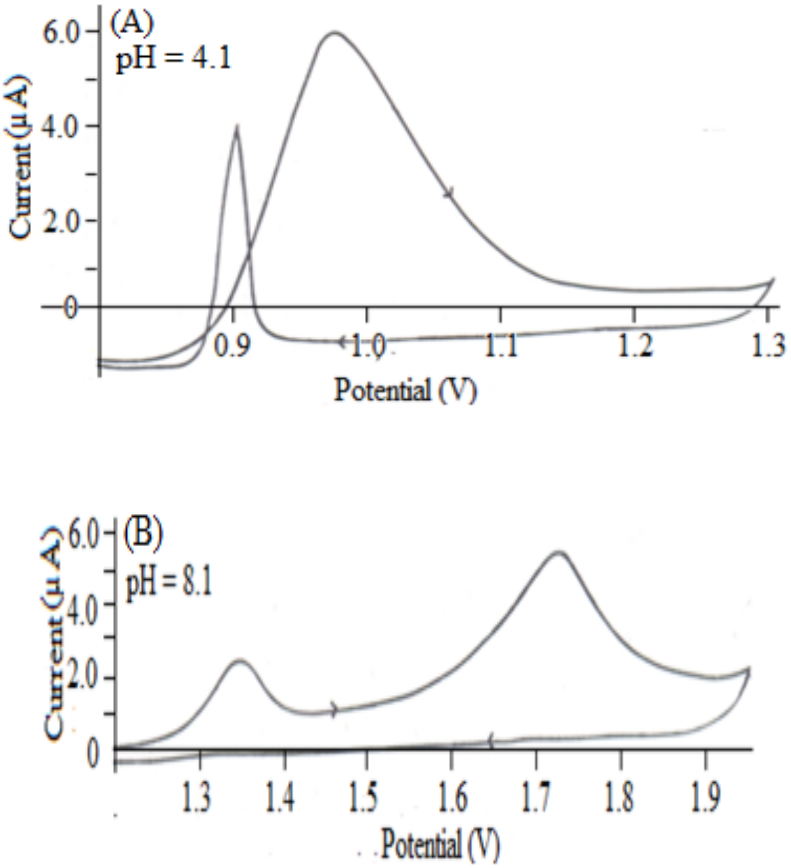


Fig. 7. (A) and (B) are the cyclic voltammograms (Sweep rate=100 mV s^{-1}) of 5-methyl-4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4] oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one (1×10^{-3}M) at HMDE. Medium: Aqueous dimethyl formamide (40% v/v)

3.2.4. Inverted peaks

The compounds under study a-f exhibit inverted peak in media of pH 2.1-6.1 [60-66]. The peaks potentials were unaltered in lower sweep rates (10-50 V s^{-1}) and increase in higher sweep rates (100-500 V s^{-1}). The peak current increases with increase in sweep rate. The inverted peak was due to the movement of the mercury surface due to uneven drop polarization [25].

3.3. Cyclic voltammetric studies of 5-methyl-4-(4-substituted aryl hydrazono) –2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazol-2-ylmethyl)-2,4-dihydro-pyrazol-3-one a-f using crown ether MCPE.

3.3.1 General voltammetric behavior at MCPE

The CV experiments of aryl hydrazones were conducted using a crown ether modified carbon paste electrode in Briton-Robinson buffer solutions of pH 2.1, 4.1, 6.1, 8.1 and 10.1 at different scan rates i.e. 10 mV s^{-1}, 20 mV s^{-1}, 100 mV s^{-1}, 300 mV s^{-1} and 500 mV s^{-1}. The cyclic voltammograms of 5-methyl-4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4] oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one are shown in the Fig. 8.The compounds a-f exhibit two cathodic peaks in buffer solutions of pH 2.1-6.1 and three cathodic peaks in alkaline buffer solutions of pH 8.1-10.1. However, an anodic peak was noticed in the solutions of pH 2.1-6.1 (Table 5).

The cathodic peak potential increases with increase in pH and was unaltered in alkaline solutions. The effect of variation of scan rates (γ) on electrochemical behavior of a-f was studied in the range of 10-500 mV s^{-1} in media of pH 2.1-10.1. The cathodic peak currents were proportional to square root of scan rates suggesting the diffusion controlled nature of the electrode process. The plots of i_{pc} *vs* concentration and i_{pc} *vs* $\upsilon^{½}$ fulfill the criteria for the diffusion controlled nature of the electrode process. In order to reconfirm this fact the concentration of the substrates was varied from 0.5×10^{-3}M to 5×10^{-3}M. As expected for a diffusion controlled process, a plot of i_{pc} *vs* concentration was linear passing through the origin. The absence of anodic peak in reverse scan suggests the irreversible nature of the process. A plot of $i_{pc}/ \upsilon^{1/2}$ versus sweep rate was a straight line parallel to sweep rate axis, it is contrary to behavior of a reversible system [60]. This not only confirms the irreversible nature of electrode process but also rules out the possibility of a fast electron transfer characteristic of a reversible behavior. The irreversible nature of the wave was further supported by negative shift in the peak potential with increase in sweep rate.

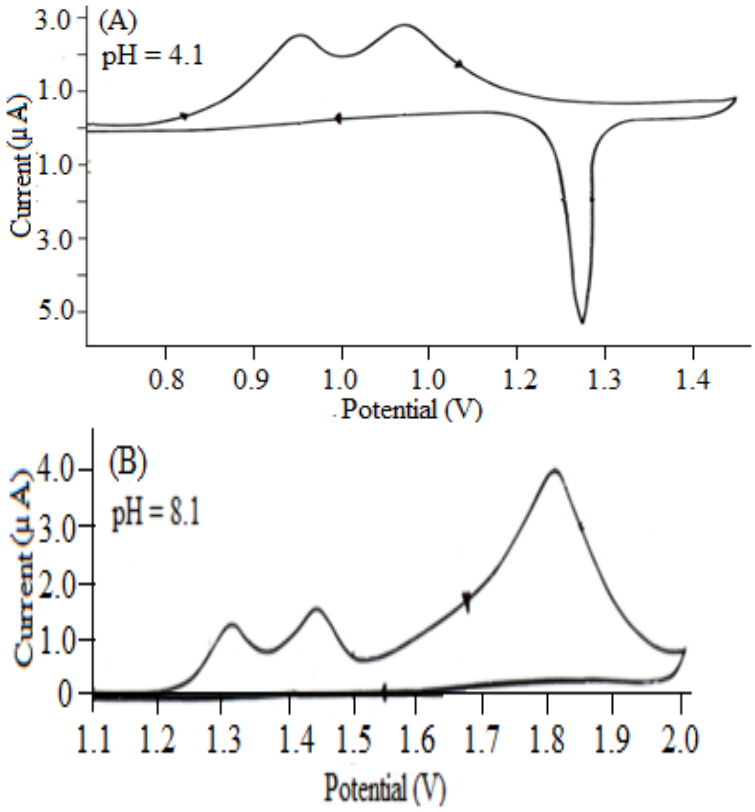


Fig. 8. (A) and (B) are the cyclic voltammograms (Sweep rate=100 mV/s) of 5-methyl-4-(phenyl hydrazono)-2-(5-thioxo-4,5-dihydro-[1,3,4] oxadiazole-2-ylmethyl)-2,4-dihydro-pyrazol-3-one (1×10^{-3}M) at MCPE. Medium: Aqueous dimethyl formamide (40% v/v)

3.3.2. Comparison between polarographic behavior and cyclic voltammetric behavior at MCPE

The first wave in polarographic studies (in media of pH 2.1-6.1) appear as two cathodic peaks in CV studies under similar experimental conditions at MCPE. On the basis of results noticed in CV, this was due to the four electron reduction of azomethine group (C=N-NH) in two steps through imine intermediate (Scheme 1). An anodic peak noticed in acidic solutions of pH 2.1-6.1 was due to oxidation of amine formed in the reduction process.

An inspection of the data (Table 5) suggests that the potential of the first peak was close to that of second peak. Therefore these two peaks were attributed to the two step reduction of anion of hydrazono group to the amine stage via imine intermediate. In polarographic studies, the pertaining peak potentials were so close to each other that the two waves merge and appear as a single wave. The third peak was ascribed to the two electron reduction of carbinol, which was formed as a result of partial chemical cleavage of azomethine anionic form.

Table 4. Cyclic voltammetric results aryl hydrazones at HMDE; [Aryl hydrazone] = 1×10^{-3} M; Medium: Aqueous dimethyl formamide (40 % by volume)

pH	Scan rate Vs^{-1}	$-E_{PCI}$ (V)	$-E_{PCI\,I}$ (V)	$-E_{PC}$ inv (V)	I_{PCI} (uA)	I_{PCII} (uA)	I_{PC} inv (uA)	$-E_{PCI}$ (V)	$-E_{PCI\,I}$ (V)	$-E_{PC}$ inv (V)	I_{PCI} (uA)	I_{PCII} (uA)	I_{PC} inv (uA)	$-E_{PCI}$ (V)	$-E_{PCI\,I}$ (V)	$-E_{PC}$ inv (V)	I_{PCI} (uA)	I_{PCII} (uA)	I_{PC} inv (uA)
Compound	a							b						c					
2.1	0.010	0.64		0.66	2.5		0.8	0.72		0.62	3.1		1.0	0.77		0.66	3.5		0.7
	0.050	0.72		0.74	5.6		1.8	0.80		0.70	6.9		2.2	0.85		0.74	7.8		1.5
	0.200	0.80		0.82	11.2		3.6	0.90		0.78	13.8		4.4	0.93		0.82	15.6		3.1
	0.500	0.92		0.94	17.7		5.6	1.02		0.90	21.9		7.0	1.05		0.94	24.7		4.9
6.1	0.010	0.96		0.93	1.1		1.8	1.12		0.93	3.5		1.7	1.17		0.99	1.7		1.4
	0.050	1.04		1.01	2.4		4.0	1.20		0.01	7.8		3.8	1.25		1.07	3.8		3.1
	0.200	1.12		1.09	4.9		8.0	1.28		1.09	15.6		7.6	1.33		1.15	7.6		6.2
	0.500	1.24		1.21	7.7		12.7	1.40		1.21	24.7		12.0	1.45		1.27	12.02		9.9
8.1	0.010	1.23	1.60		0.8	1.8		1.33	1.61		1.1	1.7		1.38	1.63		1.5	2.0	
	0.050	1.31	1.68		1.8	4.0		1.41	1.69		2.4	3.8		1.46	1.71		3.3	4.5	
	0.200	1.39	1.76		3.6	8.0		1.49	1.77		4.9	7.6		1.54	1.79		6.7	8.9	
	0.500	1.51	1.88		5.6	12.7		1.61	1.89		7.7	12.0		1.66	1.91		10.6	14.1	
Compound	d							e						f					
2.1	0.010	0.76		0.66	3.4		0.6	0.54		0.41	1.9		0.5	0.58		0.49	2.1		0.8
	0.050	0.84		0.74	7.6		1.3	0.63		0.49	4.2		1.1	0.66		0.57	4.7		1.8
	0.200	0.92		0.82	15.2		2.7	0.71		0.51	8.5		2.2	0.74		0.65	9.4		3.6
	0.500	1.04		0.94	24.0		4.2	0.83		0.69	13.4		3.5	0.86		0.77	14.8		5.6
6.1	0.010	1.15		1.01	1.9		1.5	0.94		0.78	3.1		1.3	0.98		0.82	3.3		1.3
	0.050	1.23		1.09	4.2		3.3	1.02		0.86	6.9		2.9	1.06		0.90	7.4		2.9
	0.200	1.31		1.17	8.5		5.3	1.10		0.94	13.8		5.8	1.14		1.0	14.7		5.8
	0.500	1.43		1.29	13.4		8.5	1.22		1.06	21.9		9.1	1.26		1.12	23.3		9.2
8.1	0.010	1.37	1.62		1.6	1.4		1.16	1.57		1.4	0.9		1.20	1.61		1.6	1.1	
	0.050	1.45	1.70		3.6	3.1		1.24	1.65		3.1	2.0		1.28	1.69		3.6	2.4	
	0.200	1.53	1.78		7.1	6.2		1.32	1.73		6.2	4.0		1.36	1.77		7.1	4.9	
	0.500	1.65	1.90		11.3	9.9		1.42	1.85		9.9	6.3		1.48	1.89		11.3	7.7	

Table 5. Cyclic voltammetric results of aryl hydrazones at MCPE; [Aryl hydrazone] = 1×10^{-3} M; Medium: Aqueous dimethyl formamide (40% by volume)

Comd.	pH	Scan rate Vs^{1}	E_{pcI} (V)	$-E_{pcII}$ (V)	$-E_{pcIII}$ (V)	$-E_{pa}$ (V)	I_{pcI} (µA)	I_{pcII} (µA)	I_{pcIII} (µA)	I_{pa} (µA)	E_{pcI} (V)	$-E_{pcII}$ (V)	$-E_{pcIII}$ (V)	$-E_{pa}$ (V)	I_{pcI} (µA)	I_{pcII} (µA)	I_{pcIII} (µA)	I_{pa} (µA)	Comd.
a	2.1	0.010	0.61	0.73		0.95	1.2	1.3		1.2	0.69	0.81		1.02	1.5	1.6		1.4	b
		0.050	0.69	0.81		1.03	2.7	2.9		2.7	0.77	0.89		1.10	3.3	3.6		3.1	
		0.200	0.77	0.89		1.11	5.3	5.8		5.3	0.85	0.97		1.18	6.7	7.1		6.2	
		0.500	0.89	1.01		1.23	8.5	9.2		8.5	0.97	1.09		1.30	10.6	11.3		9.9	
	6.1	0.010	0.93	1.05		1.27	0.5	0.6		2.2	1.09	1.23		1.42	1.7	1.8		2.1	
		0.050	1.01	1.13		1.35	1.1	1.3		4.9	1.17	1.29		1.50	3.8	4.0		4.7	
		0.200	1.09	1.21		1.43	2.2	2.7		9.8	1.25	1.37		1.58	7.6	8.0		9.9	
		0.500	1.21	1.33		1.54	3.5	4.2		15.5	1.37	1.49		1.70	12.0	12.7		14.8	
	8.1	0.010	1.20	1.32	1.69		0.3	0.4	1.3		1.30	1.42	1.70		0.5	0.6	1.2		
		0.050	1.28	1.40	1.77		0.7	0.90	2.9		1.38	1.50	1.78		1.1	1.3	2.7		
		0.200	1.36	1.48	1.85		1.3	1.8	5.8		1.46	1.58	1.86		2.2	2.7	5.3		
		0.500	1.48	1.60	1.97		2.1	2.8	9.2		1.58	1.70	1.98		3.5	4.2	8.5		
c	2.1	0.010	0.74	0.86		1.17	1.7	1.8		1.1	0.73	0.85		1.06	1.7	1.8		1.0	d
		0.050	0.82	0.94		1.25	3.8	4.0		2.4	0.81	0.93		1.14	3.8	4.0		2.2	
		0.200	0.90	1.02		1.33	7.6	8.0		4.7	0.89	1.01		1.22	7.6	8.0		4.4	
		0.500	1.02	1.14		1.42	12.0	12.7		7.7	1.01	1.13		1.34	12.0	12.7		7.0	
	6.1	0.010	1.14	1.26		1.47	0.8	0.9		1.8	1.12	1.24		1.45	0.9	1.0		1.9	
		0.050	1.22	1.34		1.55	1.8	2.0		4.0	1.20	1.32		1.53	2.0	2.2		4.2	
		0.200	1.30	1.42		1.63	3.6	4.0		8.0	1.28	1.40		1.61	4.0	4.4		8.5	
		0.500	1.42	1.54		1.75	5.6	6.3		12.7	1.40	1.52		1.74	6.3	7.0		13.4	
	8.1	0.010	1.35	1.47	1.72		0.7	0.8	1.5		1.34	1.46	1.71		0.7	0.8	0.9		
		0.050	1.43	1.55	1.80		1.5	1.8	3.3		1.42	1.54	1.79		1.5	1.8	2.0		
		0.200	1.51	1.63	1.88		3.1	3.6	6.7		1.50	1.62	1.87		3.1	3.6	4.0		
		0.500	1.63	1.75	2.0		4.9	5.6	10.6		1.62	1.74	1.99		4.1	5.6	6.3		
e	2.1	0.010	0.51	0.63		0.84	0.9	9.0		0.9	0.55	0.67		0.88	1.0	1.1		1.2	f
		0.050	0.59	0.71		0.92	2.0	2.2		2.0	0.63	0.75		0.96	2.2	2.4		2.7	
		0.200	0.67	0.79		1.0	4.0	4.4		4.0	0.71	0.83		1.04	4.4	4.9		5.3	
		0.500	0.79	0.91		1.12	6.3	7.0		6.3	0.83	0.95		1.16	7.0	7.7		8.5	
	6.1	0.010	0.91	1.03		1.24	1.5	1.6		1.7	0.95	1.07		1.28	1.6	1.7		1.7	
		0.050	0.99	1.11		1.32	3.3	3.6		3.8	1.03	1.15		1.36	3.6	3.8		3.8	
		0.200	1.07	1.19		1.40	6.7	7.1		7.6	1.11	1.23		1.44	7.1	7.6		7.6	
		0.500	1.19	1.31		1.52	10.6	11.3		12.0	1.23	1.35		1.56	11.3	12.0		12.0	
	8.1	0.010	1.13	1.25	1.66		1.2	1.3	0.4		1.17	1.29	1.70		0.7	0.8	0.6		
		0.050	1.21	1.33	1.74		2.7	2.9	0.9		1.25	1.37	1.78		1.5	1.8	1.3		
		0.200	1.29	1.41	1.82		5.3	5.8	1.8		1.33	1.45	1.86		3.1	3.6	2.7		
		0.500	1.41	1.53	1.94		8.5	9.2	2.8		1.42	1.57	1.98		4.9	5.6	4.2		

4. CONCLUSION

The article describes synthesis and electrochemical studies on a series of six 5-methyl-4-(4-substituted aryl hydrazono)–2-(5-thioxo-4,5-dihydro-[1,3,4]oxadiazol-2-ylmethyl)-2,4-dihydro-pyrazol-3-ones. The aryl hydrazones were characterized by elemental analysis, IR and ^{1}H NMR spectral data. Electrochemical behavior of these compounds were studied by two techniques namely polarography and cyclic voltammetry. Polarography was carried out at dropping mercury electrode and CV was carried out using HMDE and MCPE. Polarography in acid medium has resulted in a single reduction wave. In acid medium, CV at HMDE has resulted in a single cathodic peak and an inverted peak where as that at MCPE has resulted in two cathodic peaks. Polarography in basic medium has resulted in two waves. In alkaline medium, CV at HMDE has resulted in two cathodic peaks and an anodic peak where as that at MCPE led to three cathodic peaks. The results from both the techniques were compared and the reduction mechanism in acidic as well as basic medium was proposed.

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