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Electrochemical activities of some heterocyclic compounds containing benzimidazole moiety

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Abstract - *A number of N-substituted benzimidazole derivatives have been synthesized and tested for their antibacterial activities. The chemical structures of the newly synthesized compounds were verified on the basis of spectral and elemental methods of analysis. Apart of this electrochemical analysis are performed on these derivatives. The electrochemical reduction of these compounds takes place in a single, two-electron transfer, diffusion- controlled, irreversible wave in the pH range 2.0-12.0 at dropping mercury and glassy carbon electrodes. A plausible reduction mechanism is suggested on the basis of cyclic voltammetric, polarographic and coulometric studies. Kinetic parameters, i.e., charge transfer coefficient (α_n) and forward rate constant ($K^0_{f,h}$) have also been calculated. In this paper we present new data on the electrochemical activities of 4,6-diphenyl-5[2-(2-methylprop-1-enyl)-1H benzimidazole-1yl] pyrimidene-2-(5H)-thione derivatives.*

Key Words- *Cyclic voltammetric, charge transfer coefficient (αn) and forward rate constant*

I. INTRODUCTION

Benzimidazole derivatives have diverse biological activity and clinical applications [1] and attract the attention of researchers in this decade. A good number of antiparasitic, fungicidal, anithelemintic and anti-inflammatory drugs contain such ring structures [2-5]. Furthermore, few benzimidazole nucleosides, particularly 5,6-dichlorobenzimidazole-1-β-D-ribofuranoside (DRB) and its 2-substituted derivatives show activity against human cytomegalovirus [6]. It is also known that 5,6-dinitrobenzimidazole can substitute 5,6-dimethylbenzimidazole in the vitamin B_{12} molecule in *Corynebacterium diphteriae* [7] and 2-trifluorobenzimidazoles are potent decouplers of oxidative phosphorylation in mitochondria. They are also inhibitors of photosynthesis, and some exhibit appreciable herbicidal activity [8]. Reference [9] reported antiprotozoal activity of substituted 2-trifluorobenzimidazoles recently, consistent with several earlier studies on the anti-giardial activity of various benzimidazole derivatives[10-11]. However, the general antimicrobial activity of benzimidazole derivatives has not been extensively investigated. In 1964[12], the antibacterial activity of these compounds appeared, and more recently two groups of substituted benzimidazoles, namely the 5,6-dinitro and 2-trifluoromethyl derivatives, to be promising candidates for antimicrobial drugs [13]. Synthesis and exploration of QSAR model of 2-methyl-3-[2-(2-methylprop-1-en-1-yl)-1H-benzimidazol-1-yl]pyrimido[1,2-a]benzimidazol-4(3H)-one and 5-[2-(2-methylprop1-enyl)-1H- benzimidazol-1-yl]-4,6-diphenyl-pyrimidin-2-(5H)-thione derivatives as potential antibacterial agents was reported by [14-15].

II. EXPERIMENTAL

All the chemicals used were of analytical grade purity. Melting points were taken in open capillary tubes using an electric melting point apparatus. All the melting points reported are uncorrected. ^{1}H NMR spectra were recorded at 300MHz with a Bruker advance DRX 300 instrument using TMS as an internal stranded. IR spectra were run on a Perkin Elmer model 377-spectrophotometer using KBr pellets. Analytical thin layer chromatography was performed using E. Merck Silica gel -G 0.50 mm plates (Merck No. 5700). Potentiometric studies were carried out using an expanded scale *p*H meter with glass electrode, which was previously standardized with buffer of known *p*H.

III. CHEMISTRY

The synthesis of 4,6-diphenyl-5[2-(2-methylprop-1-enyl)-1H-benzimidazole-1yl] pyrimidene-2-(5H)-thione derivatives **(3a-q)** was carried out under phase transfer catalysis condition as per **Scheme1**. The key intermediate 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)-thione] derivatives **(2a-q)** was prepared by condensation of 1,3-diphenyl-2-arylhydrazono propane-1,3-diones **(1a-q)** with phenyl thioura. Compound **2a-q** upon treatment with dimethylvinylidene carbine (which was generated *insitu* as an intermediate product of 3-chloro-3-methyl-1-butyne) in the presence of aqueous potassium hydroxide under phase transfer catalysis conditions resulted in the insertion-

cyclization of carbene fragment into N=N moiety of precursor to yield the required 4,6-diphenyl-5[2-(2-methylprop1-enyl)-1H-benzimidazole-1yl] pyrimidene-2-(5H)-thione derivatives **(3a-q)**.

IV. ELECTROCHEMICAL STUDIES

Controlled potential electrolysis (CPE) was carried out on Toshniwal Polarograph. A three–electrode cell system was used for the electrolysis. The working electrodes was dropping mercury electrode (DME), the reference electrode was Ag/AgCl and the auxiliary electrode was a platinum wire that was directly placed in a solution. Cyclic voltammograms and polarograms were recorded with a computerized VSM/EC/30-S potentiostat and Toshniwal Polarograph, respectively. For cyclic voltammetric studies, the working electrode was glassy carbon (GC), the reference electrode was Ag/AgCl and the auxiliary electrode was a platinum wire. The GC was polished with fine grade emery paper followed by polishing alumina (0.5 µm) and activated by triangular voltage sweeps from 0.2 to –2.0V at the rate of 20-200 $mVsec^{-1}$for ferricyanide/ferrocyanide system in 0.1 *M* KCl. The electrode area of GC was evaluated (0.02704 cm^2) from 0.6m*M* $K_4Fe(CN)_6$ aqueous solution, using diffusion coefficient of Fe $(CN)_6^{-4}$ as 0.65 x $10^{-5}cm^2$ sec^{-1}. The *p*H-metric measurements were made on Toshniwal *p*H meter. For identification of end products, the thin layer chromatography (TLC) was employed using readymade silica gel plates from E-Merck. The components of the electrolyzed solution on the TLC plate could be visualized with the help of a UV–vis spectrophotometer (Shimadzu160A). The rates of decrease in current with time were continuously monitored.

All the chemicals used were of analytical reagent grade. Stock solution (1.0x10^{-3}*M*) of 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)-thiones]**(2a-q)** was prepared in DMF. Tetraethyl ammonium bromide (TEAB) (0.01 *M*) was used as a supporting electrolyte. Britton – Robinson buffers in the *p*H range 4.0-11.0 were used to perform studies at various *p*H.

V. RESULTS AND DISCUSSION

5.1. Effect of *p*H and height

A single two-electron polarographic wave was observed in the B.R. buffer in the pH range 2.5 – 10.5. The diffusion-controlled nature of the diffusion current was established on the basis of the relations between i_d and $\sqrt{h}$ **(Table I)** and i_d *vs* concentration **(Table II).** The value of the temperature coefficient (below 1.6% deg^{-1}) further supported the diffusion-controlled nature of the reduction. The half-wave potentials were dependent on *p*H and shifted towards more negative potentials with an increase in *p*H **(Table III).** Since the wave character is irreversible, the value of charge transfer coefficient (α_n) and the rate constant have been calculated by the method [14].The value of α_n was obtained from the slope of the $E_{d.e}$ *vs* $\log\left(\frac{i}{i_d - i}\right)$ -0.546 log t, slope being equal to $\frac{-0.0542}{\alpha n}$. The intercept of the same plot gave the value of $E_{1/2}$, which was used to calculate $K^o_{f,h}$. The value of diffusion current was measured by extrapolation method. The value of diffusion current constant (I) was calculated using Ilkovic equation $I = i_d/C\ m^{2/3}t^{1/6}$ which were constant over wide concentration range: 1.0 x 10^{-4} – 1.0 x 10^{-3} M. Moreover, the value of electrons involved in the reduction 'n' was determined by $I \approx 1.67\ n$ and found to be 2 corresponding to azo moiety which is similar to the studies reported by others [9,10]. The number of protons (p) involved in the rate-determining step of reaction was determined by the slope of log plot expression.

$$\frac{dE_{1/2}}{d_{pH}} = \frac{0.05916}{\alpha n} \times P$$

5.2. Effect of sweep rate

Cathodic peak increases linearly with the concentration of the compound in the range of 1.0 x 10^{-4} to 1.0 x 10^{-3} M and square root of sweep rate ($\gamma^{1/2}$) in the range of 20 mVs^{-1} to 200 mV s^{-1}. The peak potential was found to shift cathodically with sweep rate and concentration. The behaviour clearly indicates the diffusion-controlled nature of the electrode process. The kinetic parameters were calculated by using the following equation and reported in **Table IV** which are in the same range as obtained by polarographic studies.

$$E_p = - RT / \alpha n F\ [0.780 + \ln \{D_o^{1/2} / K^0_{f,h}.\}] + \ln \{\alpha n\ F\nu^{1/2} / RT\}$$

$$i_p = 3.01 \times 10^5\ n\ (\alpha n)^{1/2}\ AC\ D_o^{1/2}\ \gamma^{1/2}$$

5.3. Redox Mechanism

Considering the feasibilities of different sites of reduction i.e., -N=N-, C=C or C=O and on the basis of DCP and CV, it was concluded that reduction site is -N=N- [11], since C=C and C=O requires higher potential for reduction. As the number of electrons involved in the reduction are two and the number of protons involved in the rate determining step is one and only one product is obtained after exhaustive electrolysis, the follow mechanism may be proposed for the reduction of of 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)-thiones]**(2a-q)** which are similar to that reported in

literature [12-13] .The solution after the controlled potential electrolysis gives negative dye test for amino group thereby showing that after reduction of -N=N-to -NH-NH- further reduction to aromatic amine does not take place.

VI. CONCLUSION

The reduction of of 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)-thiones] **(2a-q)** gives diffusion-controlled, irreversible and two-electron wave. The charge-transfer coefficient (αn) and forward rate constant ($K^{o}_{f,h}$) were calculated. Two electron and one proton are required for the reduction of –N=N- moiety. A plausible reduction mechanism is suggested.

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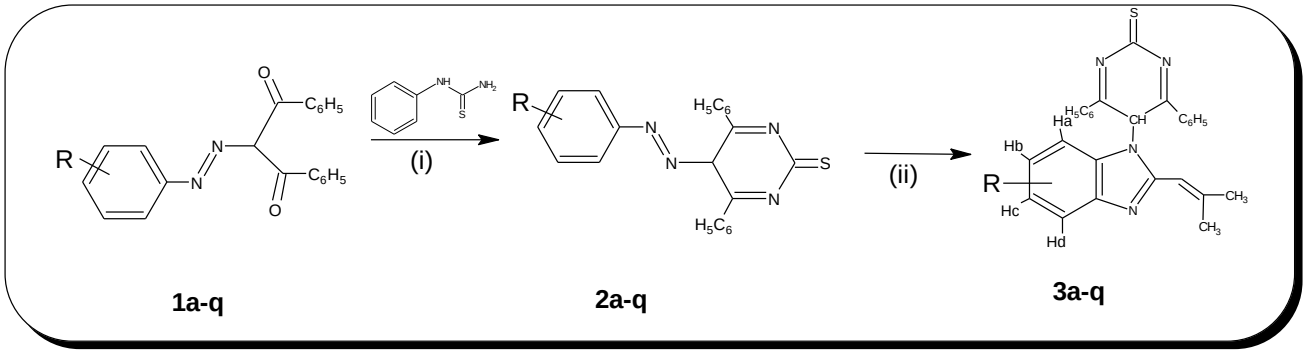
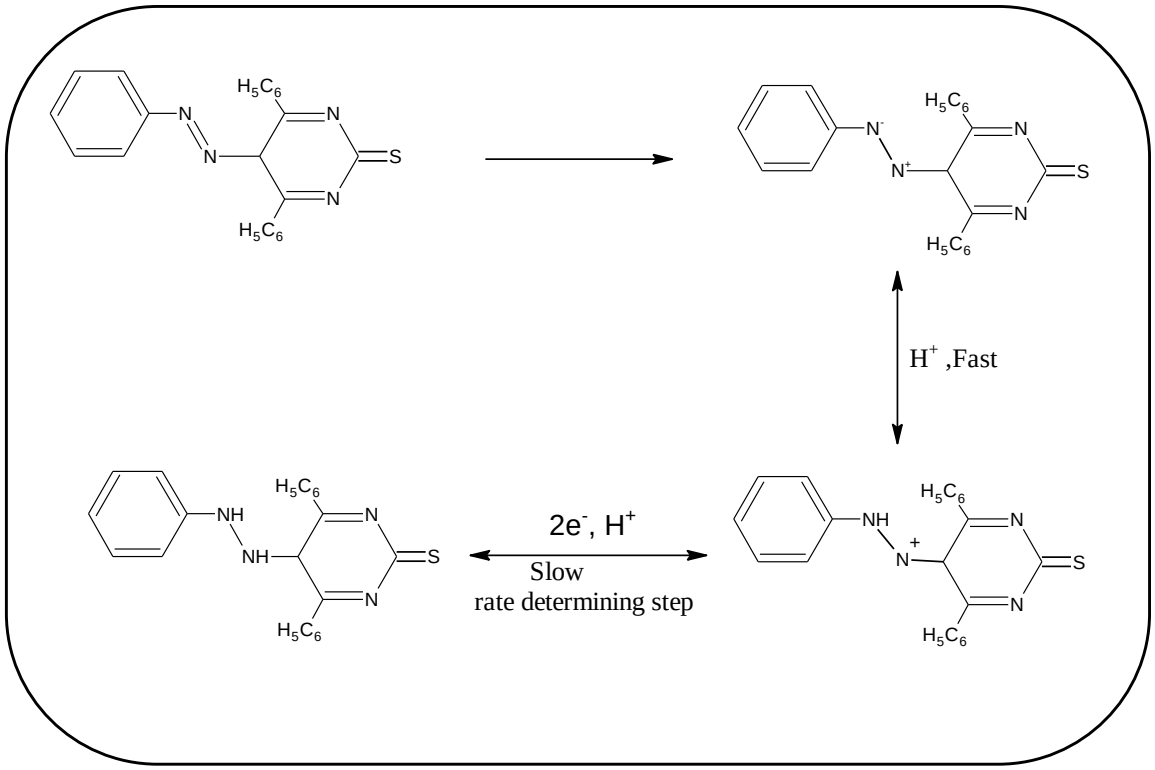


Scheme-I. Reagents and conditions: (i) C_2H_5ONa/C_2H_5OH, stirring, 1hr; (ii) 50% KOH, BTEAC, 3-chloro-3-methyl-1-butyne, benzene, stirring, 30 min.



Scheme-II. Electrochemical reduction of 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)- thiones] (2a-q).

Table 1 — Values of half-wave potential ($-E_{1/2}$,V) and diffusion-current (i_d, μA) at different pH values of 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)-thione] derivatives (2a-q). [C = 0.2 x10^{-3} M, h = 40.0 cm]

pH	$-E_{1/2}$(V)	i_d(μA)	$-E_p$(V)
2.4	0.05	2.12	0.11
4.0	0.14	2.16	0.20
5.2	0.26	2.20	0.26

6.2	0.38	2.38	0.32
8.0	0.50	2.39	0.38
9.4	0.62	2.40	0.44
10.0	0.62	2.40	0.44
11.2	0.62	2.40	0.44

Table 2 — Values of half-wave potential ($-E_{1/2}$,V) and diffusion-current (i_d, μA) 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)-thione] derivatives (2a-q) at different concentrations

Conc.(*M*)	$-E_{1/2}$,(V)	i_d(μA)
1.0×10^{-4}	0.36	1.14
2.0×10^{-4}	0.38	2.38
3.0×10^{-4}	0.39	3.41
4.0×10^{-4}	0.40	4.56
5.0×10^{-4}	0.41	5.68
6.0×10^{-4}	0.42	6.81
7.0×10^{-4}	0.44	7.94
8.0×10^{-4}	0.45	9.10

Table 3 — Values of half-wave potential ($-E_{1/2}$,V) peak potential ($-E_p$,V), peak current (i_p,μA)and diffusion current(i_d,μA) for 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)-thione] derivatives (2a-q) [$m^{2/3}t^{1/6} = 3.34\ mg^{2/3}\ s^{-1/2}$, n = 2, pH = 6.2, h = 40.0 cm., C = 0.2 x 10^{-3} M, A = 0.02704 cm^2]

Conc. (m*M*)	$-E_{1/2}$(V)	$-E_p$(V)	i_d(μA)	i_p(μA)	αn	Slope (mV)
0.1	0.36	0.42	1.14	1.05	0.694	78
0.2	0.38	0.44	2.38	2.10	0.677	80
0.4	0.40	0.46	4.56	4.05	0.660	82
0.6	0.42	0.48	6.81	6.10	0.645	84
0.8	0.45	0.51	9.10	8.03	0.630	86
1.0	0.47	0.53	11.35	10.10	0.615	88

Table 4 — Diffusion coefficient (αn) and forward rate constant ($K^o_{f,h}$) for 1-phenyl-5-[(2-phenyldiazenyl) pyrimidene-2(1H)-thione] derivatives (2a-q)

Conc. m*M*)	Polarography		Cyclic voltammetry	
	$D^0_{½}$ (cm^2s^{-1})	$K^0_{f.h}$ ($cm\ s^{-1}$)	$D^0_{½}$ (cm^2s^{-1})	$K^0_{f.h}$ ($cm\ s^{-1}$)
0.1	2.41×10^{-3}	4.17×10^{-8}	2.44×10^{-3}	1.03×10^{-7}
0.2	2.53×10^{-3}	2.77×10^{-8}	2.47×10^{-3}	8.04×10^{-8}
0.4	2.41×10^{-3}	1.74×10^{-8}	2.42×10^{-3}	6.20×10^{-8}
0.6	2.40×10^{-3}	1.15×10^{-8}	2.42×10^{-3}	4.86×10^{-8}
0.8	2.40×10^{-3}	6.14×10^{-9}	2.42×10^{-3}	3.13×10^{-8}
1.0	2.40×10^{-3}	4.30×10^{-9}	2.49×10^{-3}	2.59×10^{-8}