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Electrochemical behaviour of 2-hydroxy-5-methyl benzophenone benzoylhydrazone

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ABSTRACT

The electrochemical behaviour of 2-hydroxy-5-methyl benzophenone benzoylhydrazone (HMBPBH) has been studied in Britton-Robinson buffer solutions of pH 2.1, 4.1, 6.1, 8.1 and 10.1. The compound exhibits a single well defined diffusion controlled irreversible reduction wave in the entire pH range of study. In contrast to a single wave observed in the polarographic studies two peaks are observed in the cyclic voltammetric studies. Coulometric studies indicated the involvement of four electrons in the reduction process at pH 4.1 and eight electrons at pH 8.1. The single wave/two peaks observed in the pH range 2.1-6.1 are attributed to the four electron reductive cleavage of N-N bond. The single wave/two peaks observed at pH 8.1 and 10.1 are attributed to the four electron reduction of N-N bond and a four electron reduction of amide formed by the cleavage of N-N bond.

Keywords: Polarography, cyclic voltammetry, coulometry, electrochemical behaviour, 2-hydroxy-5-methyl benzophenone benzoylhydrazone.

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INTRODUCTION

The interest in the study of hydrazones and their derivatives has been growing due to their biological activity especially as potent inhibitors for many enzymes [1,2], in the treatment of tumor, tuberculosis, leprosy and mental disorder and their use in analytical chemistry [3] as metal extracting agents [4]. Some hydrazides are also found to exhibit antimalarial activity [5] while their chelates with Cu(II) have antifungal [6] effects against a number of pathogenic fungi. The development of agents which selectively inhibit the growth of certain types of cells is an area of much current interest. Aroyl hydrazines and many other hydrazine derivatives have been reported to inhibit many reactions catalyzed by pyridoxal 5-phospates as co-enzyme [7]. Hydrazides of organic acids and their arylidene derivatives are considered to function as antituberculous compounds [8, 9] and the mode of action was attributed to the formation of stable chelates with transition metal ions present in the cell.

A survey of the literature reveals very few benzoyl hydrazones were studies for their electrochemical behaviour [10] and studies on benzoyl hydrazones derived from aromatic ketones such as benzophenone are scarce. Hence because of the paucity of information on the electrochemical reduction of benzophenone hydrazones it has been thought worth while to synthesize and study the electrochemical behaviour of 2-hydroxy-5-methyl benzophenone benzoylhydrazone employing electrochemical techniques.

MATERIAL AND METHODS

2-hydroxy-5-methyl-benzophenone has been prepared by the method reported in the literature [11]. 2-hydroxy-5-methyl-benzophenone benzoylhydrazone (HMBPBH) was prepared by adopting the following procedure. 2-hydroxy-5-methyl-benzophenone (2.12 g.) was dissolved in 50 ml of alcohol. To this benzoylhydrazone (1.36 g.), crystallized sodium acetate (3 g.) dissolved in 10 ml of water was added. The flask was fitted with a reflux condenser and heated on a boiling water bath for 4 hr. The flask was allowed to cool down. The pale yellow crystals separated were filtered, washed with water and recrystallized from 50% aqueous alcohol; Yield 2.2 g.; mel. pt. 199-200^{o}C. The homogeneity and purity of the compound was tested through TLC and the structure confirmed by IR, NMR and Mass spectral studies.

Stock solution of the compound (1 x 10^{-3}) was prepared in dimethylformamide(AR). Other chemicals used were of analytical grade. Britton-Robinson buffers of pH 2.1 to 10.1 were prepared and used. Polarograms were recorded for deaerated solution containing 5 ml of the stock solution of the compound, 5 ml dimethylformamide [the minimum volume necessary to keep the compound in solution], 40 ml of the buffer solution of desired pH. A systronic polarograph model 1632 was used to record the polarograms with saturated calomel electrode as a reference electrode and platinum counter electrode. The polarographic console (1632) provides an accurately controlled and programmable DC ramp generator, a highly sensitive current monitor and facilities for controlling drop life of the mercury electrode. The pH measurements were made with digital pH meter (ELICO, India). Cyclic voltammograms were recorded for deaerated solution containing 1 ml of the stock solution of the compound, 1 ml dimethylformamide and 8 ml of the buffer solution of

desired pH with a Bio-analytical Systems CV-27 controller and conventional three electrode, Ag/AgCl reference electrode, glassy carbon working electrode and platinum counter electrode. Nitrogen gas was used as a purge gas.

The controlled potential electrolysis was carried out in a Lingane [12] H-type cell. 60 ml of the buffer solution of desired pH (4.1 or 8.1), 20 ml of DMF and 10 ml of 1M KCl are taken in the cathode compartment. A large pool of mercury is employed as the cathode at the bottom of the large compartment and a similar pool of mercury at the bottom of the smaller compartment is taken to serve as the anode. The solution in the cathode compartment is deaerated by bubbling pure nitrogen gas through it for about 15 minutes. The preelectrolysis is carried out for about 15 minutes with the cathode potential fixed at a value which is to be used for subsequent reduction of the oxidant. When the back ground current reached a constant value, 10 ml of the HMBPBH (1 mM) was added to the cathode compartment and the electrolysis continued at -1.15 V vs. S.C.E. at pH 4.1. The decrease in the limiting current with time was recorded at regular intervals of time and the number electrons involved in the reduction was calculated from the i-t curves following the procedure outlined by Lingane.

Controlled potential electrolysis was also carried out at pH 8.1 under similar experimental conditions at an applied potential of -1.65 V vs. S.C.E. The number of electrons involved in the reduction of HMBPBH is found to be four at pH 4.1 and eight at pH 8.1. The results are presented in **Table 1**.

Table 1: Coulometric data of 2-hydroxy-5-methyl benzophenone benzoylhydrazone

Concentration = 0.1 mM
Medium = Aqueous dimethylformamide (20% V/V)

pH	Current (μA)	Time (sec)	n-value
4.1	1.7	-	-
	1.2	7200	3.6
	1.0	10800	3.6
8.1	3.2	-	-
	2.4	7200	8.3
	2.0	10800	7.6

RESULTS AND DISCUSSION

Polarographic studies

The compound exhibits a single wave in the entire pH range of study. The half-wave potential of the wave increases with rise of pH in acidic pH's (2.1, 4.1 and 6.1) but remains unaltered in the alkaline pH range (8.1 and 10.1). The half-wave potential at different pH

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values are given in the Table 2 and the polarograms recorded at pH 4.1 and 8.1 are presented in Fig. . 1 and 2 respectively. Half-wave potential increases with pH in the acidic pH range. This observation suggests that protons are involved in the reduction. The $E_{1/2}$ is unchanged with the hydroxyl ion concentration and this may be attributed to the fact that both protonated (acidic) form and the unprotonated (basic) form of the depolarizer are electro active in the pH range of study. The half-wave potentials of both the forms (acidic and basic) are so close to each other that the waves merge [13] into a single wave. The shift of half-wave potential towards more negative values with rise in pH of the solution suggests that protons are involved in the reduction process. The values of $i_1/h^{1/2}$ are constant and the i_1 vs $h^{1/2}$ plots are linear passing through the origin. This confirms the diffusion controlled nature of the waves. E_{dme} vs log i / i_d - i graphs are linear but the slopes do not correspond to the values expected for two or four electron reversible reductions respectively. $E_{1/2}$ shifts towards more negative values with an increase in the concentration of the depolarizer. These observations suggest the irreversible nature of the waves. Limiting current vs concentration graph for 2-hydroxy–5-methyl benzophenone benzoylhydrazone is a straight line passing through the origin. Hence the polarographic method can be employed for the quantitative analysis of 2-hydroxy–5-methyl benzophenone benzoylhydrazone.

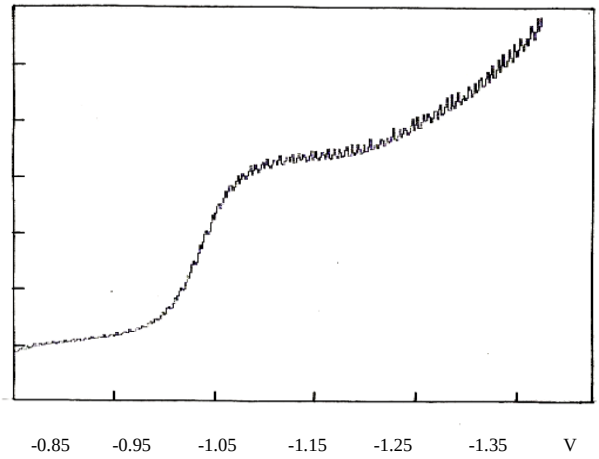

Fig. 1 Polarogram of 2-hydroxy-5-methyl benzophenone benzoylhydrazone at pH 4.1

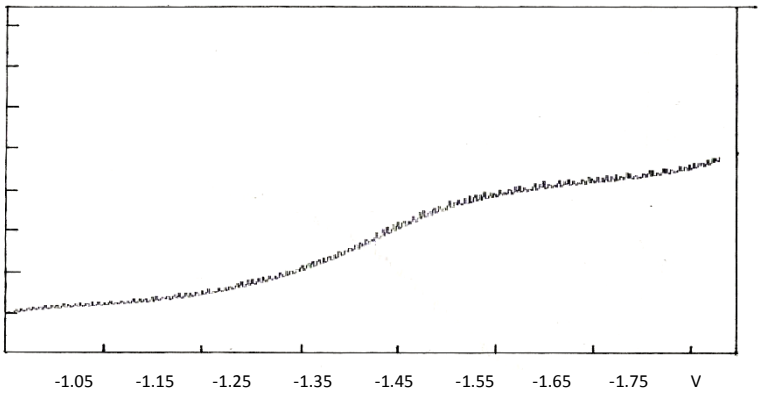

Fig. 2 Polarogram of 2-hydroxy-5-methyl benzophenone benzoylhydrazone at pH 8.1

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The effect of pH on the limiting current shows that the HMBPBH exhibit one wave in the entire pH range of study (2.1-10.1). The height of the wave in the acid pH range is found to about half of that of the wave in alkaline pH range. The variation of limiting current with change in pH may be ascribed to the difference in the number of electrons involved in the reduction of electroactive species.

Table 2: Polarographic data of 2-hydorxy-5-methyl benzophenone benzoylhydrazone
Concentration = 0.1 mM
Medium = Aqueous dimethylformamide (20% V/V)

pH	$-E_{1/2}$ V vs S.C.E	Limiting current (μA)
2.1	0.89	1.7
4.1	1.04	1.7
6.1	1.21	1.6
8.1	1.41	3.2
10.1	1.41	3.2

Kinetic parameters

Knowing the value of n (the number electrons involved in the reduction process), the values of diffusion coefficient (D) for the depolarizer is calculated using the Ilkovic equation. The values of heterogeneous forward rate constant have been evaluated by Meites-Israel [14] method. The values of $-E_{1/2}$ and αn_a are obtained from the intercept and slope of $E_{d.e.}$ vs log $[i/i_d-i]$ plot.

The activation free energy change ($\Delta G^{\#}$) has been determined by the relationship

$$k^{o}_{f,h} = \frac{kT}{h} r_o \exp\left(\frac{-\Delta G^{\#}}{RT}\right) \quad (1)$$

where k is the Boltzman constant, h the Plank's constant, r_o the mean distance between the depolarized ions in the bulk solution, R the gas constant and T the absolute temperature. In general the value of r_o is taken as 2×10^{-8} cm [15].

In acidic medium (pH 2.1 – 6.1), the variation of diffusion current with an increase in the pH of the supporting electrolyte influences the diffusion coefficient values also which vary in the same manner. The reason for slight decrease in diffusion coefficient values with increase in pH may be because of the decrease in the availability of protons. The rate constant values obtained decrease with increase in pH of the supporting electrolyte showing that the electrode reaction tends to become more irreversible. The values of $k^{o}_{f,h}$ are observed to be high in more acidic media indicating that the rate of reaction is fast in this medium as the protonated form is getting reduced. The values of activation free energy

change increase with the rise of pH. The trend confirms an increase in the irreversibility of the electrode process with increase in pH. The kinetic parameters observed in acidic media are not comparable with values observed in alkaline media as the number of electrons involved in the reduction process is different. The values obtained for transfer coefficient (αn_a), diffusion coefficient (D), heterogeneous forward rate constant ($k^o_{f,h}$) and the activation free energy change ($\Delta G^{\#}$) are given in Table 3.

Table 3: Polarographic characteristics and kinetic data of 2-hydroxy-5-methyl benzophenone benzoylhydrazone

Concentration = 0.1 mM.
Medium = Aqueous dimethylformamide (20% V/V)

pH	αn_a	Diffusion coefficient D x 10^6, cm^2 sec^{-1}	$k^o_{f,h}$ cm sec^{-1}	$\Delta G^{\#}$ kcal $mole^{-1}$
2.1	1.03	3.67	1.77×10^{-8}	17.77
4.1	1.01	3.67	1.94×10^{-9}	19.10
6.1	0.84	3.25	1.42×10^{-9}	19.28
8.1	0.30	3.25	3.58×10^{-6}	14.58
10.1	0.30	3.25	3.58×10^{-6}	14.58

Cyclic voltammetric studies

The compound exhibits two cathodic peaks at pH 4.1 and 8.1 at all the scan rates studied. The cathodic peak potentials shift to more negative values and the cathodic peak current increases with increase in the scan rate. The results are presented in Table 4 and the cyclic voltammograms recorded at pH 4.1 and 8.1 are presented in Fig. 3 and 4 respectively. i_{pc} vs $v^{½}$ is a linear plot passing through the origin and $i_{pc}/v^{½}$ values are nearly unaltered. This suggests that the reduction is diffusion controlled. The increase of the peak currents with the increase in concentration of the depolarizer confirms the diffusion controlled nature of the electrode process. The absence of anodic peak in the reverse scan and the shift in the values of E_{pc} towards more negative potentials with increase in the depolarizer concentration confirm the irreversible nature of the reduction. The cathodic peak potential shifts to more negative values with rise in the pH of the solution. The value of total peak currents also increases with rise in pH of the medium as in the case of polarographic studies. The number of peaks observed in the cyclic voltammetric studies is found to be different from that of the number of waves observed in polarography. The cyclic voltammetric results in general substantiate the results obtained in the polarography. Hence the reduction mechanism at glassy carbon electrode is assumed to be the same as at DME.

The compound exhibit two cathodic peaks at pH 4.1 and 8.1 at all the scan rates studied. But in contrast to this only a single reduction wave is observed in DC polarographic studies at pH 4.1 and 8.1. The single wave observed in polarographic studies at pH 4.1 is ascribed to the four electron reductive cleavage of N-N bond as shown in Scheme 1. The position of the two cathodic peaks on the potential axis at pH 4.1 suggest that the reduction of N-N is taking place in two steps. The peak potential data shows that these

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potentials are very close to each other. Hence the two steps seem to have been merged under low polarographic sweep rates. This is probably the reason for the presence of a single wave instead of two waves in DC polarography. At pH 8.1 the first peak observed may be assigned to the four electron reductive cleavage of N-N and the second peak to the reduction of amide to alcohol. The reason for the appearance of a single wave in polarography may due to fact that these steps are quite fast.

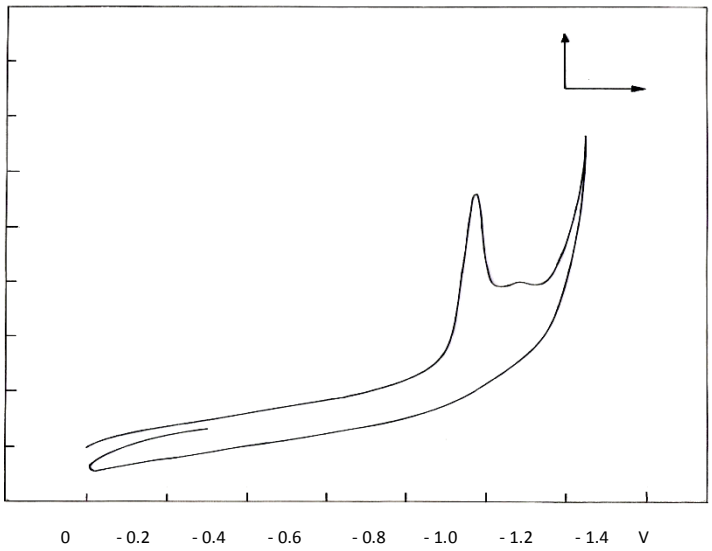

Fig. 3 Cyclic voltammogram of 2-hydroxy-5-methyl benzophenone benzoylhydrazone at pH 4.1.

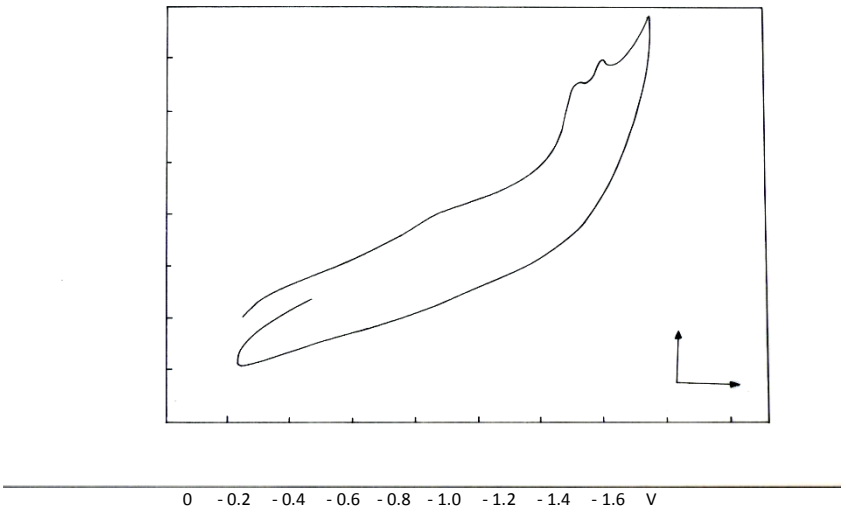

Fig. 4 Cyclic voltammogram of 2-hydroxy-5-methyl benzophenone benzoylhydrazone at pH 8.1.

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Table 4: Cyclic voltammetric data of 2-hydroxy-5-methyl benzophenone benzoylhydrazone
Concentration = 0.1 mM
Medium = Aqueous dimethylformamide (20% V/V)

pH	Scan rate VS^{-1}	Epc, V		i_{pc}, µA		$i_{pc}/v^{1/2}$	
		I	II	I	II	I	II
4.1	0.020	0.95	1.05	7.24	4.52	51.19	31.96
	0.050	0.97	1.07	11.75	7.59	52.54	33.94
	0.100	0.99	1.08	16.98	10.60	53.69	33.52
8.1	0.020	1.04	1.10	7.45	7.62	52.67	53.88
	0.050	1.06	1.12	11.25	12.37	50.31	55.32
	0.100	1.08	1.14	16.20	17.35	51.22	54.86

Mechanism of the polarographic reduction

The discussions presented above show that one wave is observed in the entire pH range of study. The increase in $E_{1/2}$ with rise in the pH in acidic solution suggests the involvement of protons in the reduction process. The coulometric studies show that 4 electrons are involved in the reduction process. Therefore the wave observed in acidic solutions of pH 2.1 – 6.1 is ascribed to the 4 electron reductive cleavage of the N-N bond to an amine. The wave expected to appear for the reduction of amide has not been observed which seems to have been merged with the decomposition potential of the buffer solution. Based on the results obtained the mechanisms shown in Scheme 1 may proposed for the reduction of HMBPBH in acidic solutions.

In alkaline solutions of pH 8.1 and 10.1 a single wave is observed. The coulometric studies indicate that the wave corresponds to 8 electron reduction process. The $E_{1/2}$ of the wave remains unchanged in alkaline solutions. This wave has been assigned to the 4 electron reductive cleavage of N-N linkage and the 4 electron reduction of the amide formed to alcohol. The $E_{1/2}$ potential of these two steps seems to be close to each other. Hence the two steps merge with each other and manifest as a single 8 electron reduction wave in polarographic studies. Thus the reduction mechanism shown in Scheme 2 is suggested for the reduction of HMBPBH at pH 8.1 and 10.1.

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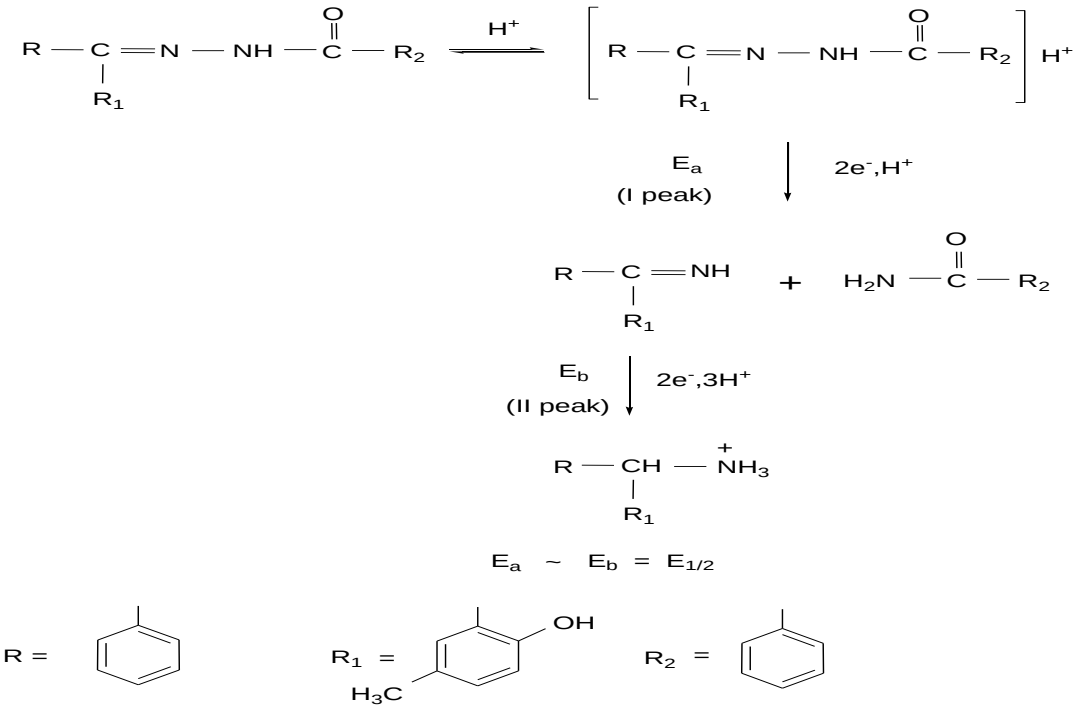
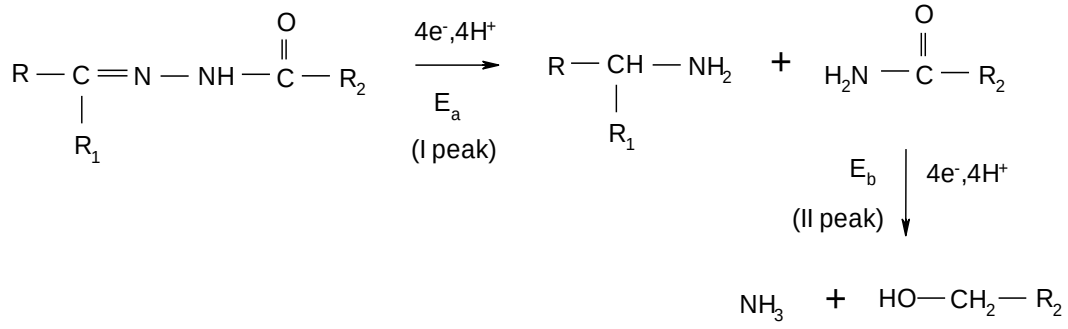
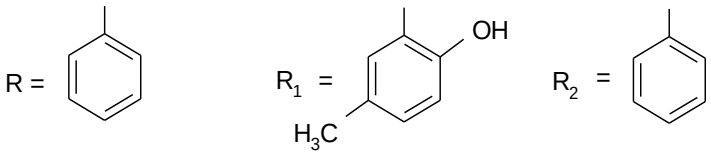


Scheme 1 Reduction mechanism of HMBPBH (pH 2.1 - 6.1)



$E_a \sim E_b = E_{1/2}$



Scheme 2 Reduction mechanism of HMBPBH (pH 8.1, 10.1)

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REFERENCES

[1] Alcock JF, Baker RJ, Diamantis AA. Aust J Chem 1972; 25: 289.
[2] Iskander MF, Zayan SE, Khalifa MA, El Sayed L. J inorg nucl Chem 1974; 36: 551.
[3] Katyal M, Dut Y. Talanta 1975; 22: 151.
[4] Gallego M, Garcia-Vargas M, Valcarcl M. Analyst 1979; 104: 613.
[5] Bohadour S, Pandey K. J Indian chem Soc 1980; 57: 447.
[6] Surage D, Gonekar MC. J Indian chem Soc 1980; 57: 95.
[7] Kurosawa A. Chem Pharm Bull, Tokyo 1969; 17: 49.
[8] Ma ST, Tien TM. Antibiotics and Chemotherapy 1953; 3: 491.
[9] Fox HH, Gibus JT, Motchane AM. J Org Chem 1956; 21: 356.
[10] Morsi MA, Helmy AMA, Fahmy HM. Indian J Chem 1979; 18A: 495.
[11] Dey BB, Sitaraman M. Laboratory Manual of Organic Chemistry, revised by. Govindachari TR. 4th revised edition, Allied publishers Ltd., New Delhi, 1992.
[12] Lingane JJ, J Amer Chem Soc1945; 67: 1916.
[13] Zuman P. The Elucidation of Organic Electrode Processes. Academic Press, New York, 1969, 25.
[14] Meites L, Israel Y. J Am Chem Soc 1961; 83; 4903.
[15] Delahay P. J Am Chem Soc 1951; 73: 4944.