Electrochemical Oxidation of Ethyl 2,3-Dioxobutyrate 2-Phenylhydrazone

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The electrochemical oxidation of ethyl 2,3-dioxobutyrate 2-phenylhydrazone (I) has been studied in the pH range 3.0-10.0 at a pyrolytic graphite electrode. A single, 2e, 2H⁺ oxidation peak is observed. On the basis of cyclic voltammetric and coulometric studies and observed spectral changes a plausible mechanism for the electrochemical oxidation has been proposed.

A good amount of literature is available on the reduction of a variety of hydrazones on dropping mercury electrode. However, no attempt has so far been made to investigate the electrochemical oxidation of hydrazones. As most of the reactions involved in physiological systems are oxidation reactions, it was considered interesting to undertake the title investigation on electrochemical oxidation of a simple hydrazone, viz. ethyl 2,3-dioxobutyrate 2-phenylhydrazone (I), an important biologically active compound.

Materials and Methods

Ethyl 2,3-dioxobutyrate 2-phenylhydrazone was synthesised in the laboratory. The purity was ascertained by TLC. Oxidation at pyrolytic graphite electrode was carried out in phosphate buffers having an ionic strength of 0.5 M at 25 ± 1°C. SCE was used as the reference electrode. Equipments used for linear and cyclic sweep voltammetry, coulometry and spectral studies have been described elsewhere. Gas chromatographic analysis was done on an Aimil model 5700 gas chromatograph equipped with a glass column of 3% SE-30 on chromosorb W as adsorbent. The temperature of injector and detector were fixed at 250°C. The column was programmed at a rate of 6°C/min following the injection of sample (5 μl) at 60°C. TLC was carried out using silica gel G and benzene-methanol (70:30) as the developer.

The 2 mM stock solution of I was prepared in methanol (AR). The voltammograms were recorded after mixing 1.0 ml of stock solution with 9.0 ml of buffer solution and deaerated by passing a stream of purified nitrogen for about 10 to 15 min.

Isolation of electrooxidation products

In order to isolate the products of electrooxidation, compound I (4.5 mg) was oxidised at potentials more positive than that of peak la in the buffer of desired pH. The progress of electrolysis was monitored by recording the cyclic voltammograms at different intervals of time. When the peak in cyclic voltammogram completely disappeared, electrolysis was stopped and the electrolysed solution was transferred from the cell, lyophilised, extracted with ether (2 x 20 ml) and the ether extract concentrated and analysed by TLC and GC.

Results and Discussion

Linear sweep voltammetry of I at a scan rate of 5 mVs⁻¹ exhibited a well-defined oxidation peak (Ia) when the sweep was initiated in the positive direction. The peak potential was pH dependent and shifted towards less positive potentials with increase in pH in accordance with relation (1).

\[ E_p (pH 3.0-10.0) = [0.93-0.053 \ pH] V \ (vs \ SCE) \ ... (1) \]

In cyclic sweep voltammetry at a scan rate of 150 mVs⁻¹, a well-defined anodic peak was observed when the sweep was initiated in the positive direction. In the reverse sweep a cathodic peak was also observed. To check whether the anodic peak (Ia) was related to the cathodic peak (Ila), voltammograms were also recorded by initiating the sweep in the negative direction. It was interesting to observe that peak Iic appeared at exactly the same potential. Thus peak Ia and Iic were found as independent electrode reactions. Peaks Ia and Iic were sharp at low pH; however, at higher pH peak Ia was broad in nature when the sweep was initiated in the negative direction. Some of the typical cyclic voltammograms are presented in Fig. 1. The peak currents of peaks Ia and Iic were linear up to a concentration about 1.0 mM. At higher concentrations the peak current values were more or less constant. This behaviour suggests the involvement of adsorption in the electrode process.

Controlled potential electrolysis of compound (I) in a conventional three-compartment cell using pyrolytic graphite plates as working electrodes, platinum gauge as counter electrode and SCE as a reference...
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Fig. 1—Typical cyclic voltammograms of compound (I) in phosphate buffers at $\mu = 0.5 \text{ M}$[Scan rate = 150 V s$^{-1}$]

electrode gave the value of $n = 2.0 \pm 0.2$. The progress of electrolysis was also monitored by recording the UV-visible spectra (260-600 nm). Compound (I) exhibited a well-defined maxima at 360 nm at pH 3.0, 7.0 and 10.0. With progress of electrolysis the absorbance at 360 nm decreased systematically, and increased in the region 440-500 nm. After about 30 min of electrolysis absorbance at higher wavelength region decreased. This clearly indicated that the UV-visible absorbing species is generated during electrooxidation of I. The electrolysis was stopped when the absorbance at 360 nm decreased by about 95%.

Cyclic voltammograms were also recorded at different time intervals during controlled potential electrolysis of compound (I) to get information about electroactive species generated during electrooxidation. It was interesting to observe that peaks Ia and IIc started decreasing with progress of electrolysis (Fig. 2), and a redox-couple started appearing after about 1 hr of electrolysis. The redox couple IIc/IIla was clearly visible at low pH, even when the completely oxidised solution was allowed to stand at room temperature for a longer duration; whereas at higher pH the redox couple IIc/IIla was not visible during controlled potential electrolysis.

**Characterization of products**

The products of electrooxidation were characterised by electrolysis about 4.0 to 6.0 mg of compound (I) at potentials more positive than that of peak Ia. The concentrated ether extract gave two clear spots in TLC with $R_{f}$ 0.68 and 0.90. The gas chromatography of the ether extract gave three clear peaks with retention times: 0.0, 0.8 and 1.4 min. The peak with $R_{f} = 0.0$ min was due to the solvent used. The appearance of two spots in TLC and two peaks in the GC clearly indicated the formation of two products.

The peak with $R_{f} = 1.4$ min was identified as phenol by comparison with an authentic sample. The peak with $R_{f} = 0.8$ min was due to a ketonic product. Its $R_{f}$ and $R_{r}$ (0.90) were indicative that the product should be similar to ethyl 3-oxobutyrate.

Based on the available data we believe that the oxidation of I proceeds by a mechanism shown in Scheme 1.

![Scheme 1](image-url)

The above mechanism finds support from the observed increase in absorbance in the region 440-500 nm presumably due to the formation of phenylidimide (V), which has more extended π-conjugation than compound (I). As oxidation of III to V will be easier than oxidation of I, the peak IIIa at less positive
potential is observed in cyclic voltammetry. Compound (V) is also reducible in a reversible reaction to give peak IIIc. This redox couple was not observed at higher pH due to hydrolysis of compound (V) in a faster step to give the products of the reaction.

The mechanism proposed also finds support from the chemical oxidation of various hydrazones to give ketones. The formation of PhN=NH (V) has also been earlier reported in the literature.

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References