Polarographic & Cyclic Voltammetric Investigations on \( p-[(8\text{-Hydroxyquinolyl})\text{azo}] \) benzenesulphonamides

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The electrochemical behaviour of \( p-[(8\text{-hydroxyquinolyl})\text{azo}] \) benzenesulphonamides (1-9) has been studied at dropping mercury electrode and pyrolytic graphite electrode. Unlike most of the azo compounds, the reduction of these compounds occurs in a 4e, 4H\(^+\) process. In cyclic sweep voltammetry a reverse peak is also observed. The products of electroreduction have been characterised with the help of TLC and GC.

Like sulpha drugs, \( p-[(8\text{-hydroxyquinolyl})\text{azo}] \) benzenesulphonamides and analogous compounds have been reported to exhibit significant antibacterial activity. The azo group of these compounds has been reported to undergo reduction in liver and intestine to form sulphanilamide and 8-hydroxyquinoline, the products which inhibit the growth of bacteria. Most of the earlier studies on the electroreduction of azo compounds indicated a 2e, 2H\(^+\) process to give hydrazo products. In some recent studies on aromatic azo compounds having electron-releasing groups, such as \( p\text{-OH} \) or \( p\text{-NH}_2 \), the hydrazo derivative was found to be further reduced in a 2e, 2H\(^+\) process. In this paper we have investigated the electroreduction of various azo compounds (I) with sulpha drugs as substituents.

Materials and Methods
Benzenesulphonamide and \( p-[(8\text{-hydroxyquinolyl})\text{azo}] \) benzenesulphonamides (1-9) were synthesised by the method reported in literature. All the compounds (1-9) of the type (I) were recrystallised from ethanol and their purity checked by elemental analyses and spectral data.

Stock solutions (1mM) of 1-9 were prepared in N,N-dimethylformamide (AR, 99.9\%). Britton-Robinson buffers of pH 3.0-11.2 were prepared in doubly distilled water. Polarograms were recorded on a Cambridge pen recording polarograph. The capillary had the following characteristics: \( m = 1.25 \text{ mg s}^{-1} \); \( t = 3.92 \text{ s at } h = 70 \text{ cm} \) in 1.0M KCl at 0.0V. All the potentials refer to SCE as the reference electrode.

Linear and cyclic sweep voltammograms were recorded on a Micronics cyclic voltammeter. The graphite electrode had an area of 2mm\(^2\). The number of electrons (\( n \)) involved in the reduction was determined by coulometry using a mercury pool or pyrolytic graphite (PGE) as a working electrode and platinum gauze as a counter electrode. The change in current with time was monitored and the value of \( n \) was determined by the method suggested by Lingane. The spectral changes during the electroreductions were monitored using a UV-VIS (Carl Zeiss, Zena) spectrophotometer.

For the identification of products electrolysis was carried out by taking the starting compound (4-6 mg) in a buffer of desired pH. Mercury pool or PGE was used as working electrode. Nitrogen gas was bubbled throughout the electrolysis. The progress of electrolysis was monitored by recording cyclic voltammograms at different time intervals. Electrolysed solution was extracted with ether (3 \( \times \) 15 ml), to remove buffer constituents, concentrated under reduced pressure and the residual mass analysed with the help of an Amin Nucon gas chromatography (model 5700) using 3\% SE-30 on chromosorb W as an adsorbent. The temperature of injector and detector was maintained at 215\(^\circ\)C. The temperature of the column was raised from 70\(^\circ\)C to a final temperature of 215\(^\circ\)C, at a rate of 6\(^\circ\)C/min.

The solutions for recording polarograms and voltammograms were prepared by mixing the stock solution (1 ml) of the compound, dimethylformamide (2 ml), and appropriate buffer solution (7 ml) in a stream of purified nitrogen gas.
Results and Discussion

Polarographic behaviour

All the compounds (1-9) underwent reduction in a single well-defined wave in the pH range 3.0 - 11.8 (Fig. 1). The nature of the limiting current was found to be diffusion-controlled as evidenced by the linear plots of $i_d$ versus $\sqrt{t}$ and $i_d$ versus $C$ (concentration of depolariser). The limiting current was practically independent of pH in the range 3.0 - 11.8. It was observed that $E_{1/2}$ shifted to more negative potentials with increase in pH, indicating the involvement of protons in the electrode process. The plots of $E_{1/2}$ versus pH were linear. The nature of the waves was found to be irreversible by the log plot method in the entire pH range studied. The polarographic characteristics of these compounds are given in Table 1.

Cyclic voltammetric behaviour

Linear sweep cyclic voltammetry of compounds (1-9) exhibited a single reduction peak ($I_e$) in the pH range 3.0-11.8 at a scan rate of 5 mVs$^{-1}$. The peak potential of $I_e$ was linearly dependent on pH and shifted towards more negative potentials with increase in pH. At a scan rate of 200 mVs$^{-1}$, a well-defined cathodic peak ($I_c$) was observed (Fig. 1). In the reverse sweep an anodic peak ($I_a$) was also observed. Occasionally, a small hump close to the background was also noticed. The anodic peak was more clear at pH > 6.0. If the sweep was initiated in positive direction first, anodic peak was not observed, indicating that peak $I_c$ and $I_a$ are related to each other. The separation of potentials of peaks $I_c$ and $I_a$ clearly indicated that the electrode process was irreversible.

The possibility of peak $I_a$ as due to oxidation of the product formed was ruled out by monitoring the cyclic voltammograms after holding the potential (more negative to peak $I_e$) for different times. It was observed that the peak current of peak $I_a$ did not change. This indicates that peaks $I_a$ and $I_c$ form an irreversible couple.

Controlled potential electrolysis

Controlled potential electrolysis of the compound (1) at mercury pool cathode or at PGE (area 6 cm$^2$) consumed $4 \pm 0.2$ (average ± maximum deviation) electrons in the pH range 3.0-11.2.

The spectra of compound (1) at different pH values clearly indicate that the $\lambda_{max}$ shifts from 480 nm to 520 nm at pH > 6.8. Thus at pH < 6.8 these compounds exist as monoprotonated species and at pH > 6.8 as neutral species. UV-visible spectral changes with time during electroreduction were monitored at pH 3.0, 6.8 and 9.8 for the parent compound (1) to detect any intermediate formed during the reaction (see Fig. 2). It

Table 1—Polarographic and Cyclic Voltammetric Data of Reduction of p-[(8-Hydroxyquinolyl)azo]benzenesulphonamides (1-9)

<table>
<thead>
<tr>
<th>Compd</th>
<th>$-E_{1/2}$ (V)</th>
<th>$i_d$ (µA)</th>
<th>$dpH$ (mV/pH)</th>
<th>$\alpha_d$</th>
<th>$P$</th>
<th>$-E_d(1_e)$ (V)</th>
<th>$+E_d(1_i)$ (V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.43</td>
<td>0.925</td>
<td>71</td>
<td>0.98</td>
<td>0.96</td>
<td>0.48</td>
<td>0.62</td>
</tr>
<tr>
<td>2</td>
<td>0.44</td>
<td>1.100</td>
<td>53</td>
<td>0.92</td>
<td>1.28</td>
<td>0.52</td>
<td>0.61</td>
</tr>
<tr>
<td>3</td>
<td>0.32</td>
<td>0.900</td>
<td>62</td>
<td>0.98</td>
<td>1.03</td>
<td>0.43</td>
<td>0.68</td>
</tr>
<tr>
<td>4</td>
<td>0.38</td>
<td>1.100</td>
<td>55</td>
<td>0.87</td>
<td>0.94</td>
<td>0.48</td>
<td>0.64</td>
</tr>
<tr>
<td>5</td>
<td>0.44</td>
<td>0.950</td>
<td>60</td>
<td>0.92</td>
<td>0.98</td>
<td>0.50</td>
<td>0.66</td>
</tr>
<tr>
<td>6</td>
<td>0.32</td>
<td>0.975</td>
<td>67</td>
<td>0.78</td>
<td>1.05</td>
<td>0.43</td>
<td>0.68</td>
</tr>
<tr>
<td>7</td>
<td>0.39</td>
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<td>9</td>
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<td>1.100</td>
<td>62</td>
<td>0.96</td>
<td>1.13</td>
<td>0.46</td>
<td>0.50</td>
</tr>
</tbody>
</table>
is evident that upon application of potential more negative than that of peak \( I_e \), the absorbance at 480 nm decreases systematically and that at 262 nm increases. After about 90 min. the absorbance at 480 nm reaches a minimum value and the yellow colour of the solution fades out. The electrolysis was stopped at this stage.

The systematic decrease of absorbance at 480 nm and increase at 262 nm clearly points out that there is a decrease in the magnitude of \( \pi \)-chromophore system of starting material at the end of the electrolysis and the products absorb at shorter wavelength.

At \( \text{pH} \) 9.8 where compounds (1-9) exist as neutral species an entirely different behaviour is observed. Upon application of potential, absorbance systematically increases in lower wavelength region (260 nm) whereas at 520 nm, the absorbance increases for some time and then decreases systematically. Thus it is evident that at \( \text{pH} \) 6.8 an intermediate capable of absorbing at 520 nm is generated, which then decomposes to give final product of electroreduction.

**Product isolation and characterization**

A sufficient amount of compound (I) was electro-reduced at rough PGE at a constant potential in a buffer of desired \( \text{pH} \). At the end of electrolysis the solution was concentrated and analysed by TLC and GC. The TLC of solutions electrolysed at \( \text{pH} \) 3.0 and 9.8 gave two spots with \( R_f \) values 0.56 and 0.79 indicating the presence of two compounds. The product corresponding to \( R_f \) value 0.56 was identified as sulphanilamide by comparison with an authentic sample. The second product corresponding to \( R_f \) 0.79 could not be completely characterised. However, a comparison with 8-hydroxyquinoline (\( R_f \sim 0.81 \)) which has one amino group less than the product indicated that the second product is possibly be 5-amino-8-hydroxyquinoline. The ethereal extract of the electrolysed solution was also analysed by GC. Two well-defined peaks with retention times of 1.1 and 1.35 min were observed in addition to the solvent peak at 0.0 min. The reduction of azo group by \( 4e, 4H^+ \) process would lead to sulphanilamide and 5-amino-8-hydroxyquinoline as the final products of electro-reduction. As 5-amino-8-hydroxyquinoline was not available it was decided to use 8-hydroxyquinoline as the reference. The authentic samples of sulphanilamide and 8-hydroxyquinoline gave peaks with retention times of 1.1 and 1.35 min respectively, indicating thereby the formation of sulphanilamide and a product similar to 8-hydroxyquinoline.

On the basis of all these observed facts it is concluded that the reduction of the azo group in these compounds does not stop at the hydrazo stage but further reduction involving \( 2e, 2H^+ \) process occurs to give products.

Below \( \text{pH} \) 6.8 the nitrogen of the quinoline ring remains protonated due to which the participation of \( \pi \)-electrons of the naphthalene ring in \( \pi \)-chromophore system is inhibited and hence molecule absorbs at 480 nm. At \( \text{pH} > 6.8 \) the neutral molecule absorbs at 520 nm due to extensive conjugation.

The effect of substituents on the ease of reduction of the azo group was also studied. It was found that except compounds (3) and (6), the substituents do not appreciably affect the \( E_{1/2} \) of the parent compound. The aromaticity and basicity of the heterocyclic rings should affect the reduction of the azo group but as they are far removed from the reaction centre their effect is negligible. A similar behaviour is also observed for peak potentials. The quantitative treatment of the effect of substituents has not been possible because of the non-availability of Hammett substituent constants for these rings as substituents.

**References**