SHORT COMMUNICATION

Synthesis of 5-amino salicylic acid at a Ti/TiO$_2$ electrode

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1. Introduction

5-Aminosalicylic acid (5-ASA) is known to be an effective anti TB drug. Also, it finds use in the manufacture of light sensitive paper and azo and sulphur dyes [1].

5-ASA is manufactured chemically by the reduction of 5-nitro-salicyclic acid (5-NSA) with zinc dust and HCl [2]. This method is expensive as the zinc has to be recovered by electrolytic means and, moreover, the yield is very poor. Honda *et al.* [3] have carried out the reduction of 4-NSA in HCl-ethanol medium using a tin cathode. Their reported yield was 74%. However, the method suffers from the point of view of environmental pollution and anode corrosion. Hence, alternatively, the reduction of 5-NSA has been tried in 50% ethanolic solutions containing 10–20% H_2SO_4. Here, pollution problems do not arise. The objective of the present investigation was to explore the possibility of using Ti/TiO$_2$ electrodes for the production of 5-ASA. Encouraging results were obtained as in the case of some compounds studied earlier [4–6]. The results on the cyclic voltammetric behaviour of 5-NSA at a Ti/TiO$_2$ electrode are also reported and compared with those obtained with the conventional glassy carbon electrode (GCE).

2. Experimental details

2.1. *Galvanostatic electrolysis*

The Ti/TiO$_2$ electrode was prepared at 550° C by the method employed earlier [4]. The cell consisted of a glass beaker of one litre capacity provided with a lead cover having holes for introducing a porous pot (diaphragm), the electrodes and an overhead stirrer. A stationary Ti/TiO$_2$ electrode served as the cathode and a lead sheet served as the anode. 200 ml of 10% or 20% H_2SO_4 containing 50% ethanol (by volume) with 5-NSA (amount indicated later) served as the catholyte and 25 ml of 10% H_2SO_4 containing 50% ethanol (by volume) served as the anolyte. The quantity of electricity consumed was $6\,\mathrm{F\,mol^{-1}}$. All the experiments were carried out at 35° C. Higher temperature was avoided in order to prevent loss of ethanol by evaporation.

Two experiments were carried out, the first employing 10% H_2SO_4 and the second 20% H_2SO_4. Other conditions which are the same for both experiments are a current density of $6\,\mathrm{A\,dm^{-2}}$ at 2.1 A current in the voltage range 3.5–4.5 V.

The high solubility of the amine sulphate in this medium and its stability afforded the possibility of re-use of electrolyte. The requisite amount of H_2SO_4 was added after each use after standard estimation in order to ensure that the same percentage of H_2SO_4 was made available. It was observed that the yield of the amine was not altered by re-use of the electrolyte for 3 to 4 runs. In Experiment 1 it was re-used for the third time by taking 13, 17 and 16 g of the nitro compound respectively (total 46 g). In Experiment 2 it was re-used for the fourth time by taking 11, 17, 3.5 and 6.5 g of the nitro compound respectively (total 38 g). Each of these amounts was added in instalments to ensure complete solubility of the nitro compound.

In the above experiments, as the concentration of the amine sulphate exceeded the saturation solubility, it separated out as a black solid. It was dissolved in water, decolourized with animal charcoal and then slowly neutralized with liquid ammonia in the presence of sodium metabisulphite to pH 3–4 when the free amine separated as a pale yellow powder. The spent electrolyte was also neutralized after charcoal treatment to recover the free base present in it.

The isolated compound was checked for its melting point, UV-visible and IR spectra and by paper chromatograph using 2 : 8 ethylacetate–ethanol mixture as the eluent. It was stored in an amber coloured bottle since longer exposure to light led to discolouration, yielding a reddish brown product.

2.2. *Cyclic voltammetric studies*

In cyclic voltammetric studies, an aqueous SCE and a platinum foil served as reference and counter electrodes respectively while a Ti/TiO$_2$ electrode (area $0.283\,\mathrm{cm^2}$) or a GCE (area $0.071\,\mathrm{cm^2}$) served as the working electrode. The depolarizer solution in the concentration range 1–25 mM was used. The experimental solution was deaerated using pure nitrogen gas.

3. Results and discussion

3.1. *Galvanostatic electrolysis*

The isolated yield and current efficiency for amine formation are 70% and 85.5% for Experiment 1 and 76% and 90.0% for Experiment 2, respectively. (The values reported are the average values of various runs for each of the two experiments). The increase in the yield of the amine with increase in acid strength is probably due to the fact that the amine, as soon as it

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Table 1. Cyclic voltammetric data for the reduction of 1×10^{-2} M *5-NSA in 50% ethanolic* 1 M H_2SO_4 *solution at a* Ti/TiO_2 *electrode and a GCE*

v(V s^{-1})	Ti/TiO$_2$ electrode			GCE		
	$-I_p$ (mA cm^{-2})	$-E_p$ (V)	$-I_p\, v^{-1/2}$	$-I_p$ (mA cm^{-2})	$-E_p$ (V)	$-I_p\, v^{-1/2}$
0.300	9.15	0.730	16.71	7.82	0.605	14.28
0.200	7.56	0.720	16.90	6.39	0.605	14.29
0.100	5.71	0.710	18.05	4.76	0.580	15.05
0.050	4.20	0.700	18.78	3.29	0.570	14.71
0.020	2.51	0.680	17.75	2.15	0.550	15.20
0.010	1.72	0.670	17.20	1.60	0.540	16.00
0.005	1.12	0.660	15.84	0.99	0.530	14.00

is formed, is removed from the vicinity of the electrode as the more soluble amine sulphate thus facilitating further reduction. Higher concentrations of H_2SO_4 were avoided since the salicylic acid part of the compound tends to resinify under these conditions.

The formation of the amine was confirmed from the fact that the product decomposed at 280° C as described in the literature, whereas the nitro compound melts sharply at 229° C [1]. Also, the amine exhibited a fluorescent green spot seen under long wavelengths in UV-light when spotted on a paper chromatograph. The UV-visible spectra of the amine (taken in methanol containing two drops of HCl) revealed a band at 304.6 nm due to n–π^* transition in the carbonyl group. An authentic sample of the amine gave a similar band at 304.5 nm under the same conditions. The main bands in the IR spectrum were observed for -OH stretching (very broad) at 3200–2500 cm^{-1} (3200–2500 cm^{-1}), carbonyl stretching (medium) at 1660 cm^{-1} (1665 cm^{-1}) and NH stretching 3500–3400 cm^{-1} (3500–3400 cm^{-1}) with the corresponding values of an authentic sample in parentheses. These results confirm the amine formation.

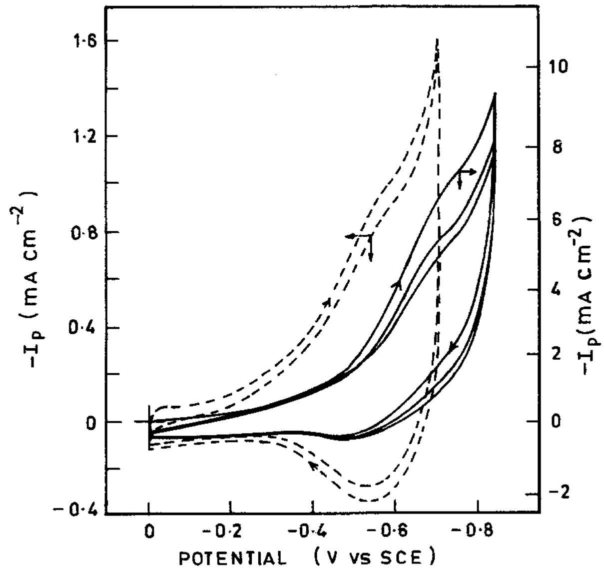

Fig. 1. Cyclic voltammetric behaviour of Ti/TiO$_2$ electrode in 50% ethanolic 1 M H_2SO_4 solution at a sweep rate of 0.1 V s^{-1}. (- - -) in the absence of 5-NSA; (——) in the presence of 5-NSA (1×10^{-2} M).

3.2. *Cyclic voltammetric studies*

The cyclic voltammogram for the thermally prepared Ti/TiO$_2$ electrode at 550° C in 50% ethanolic 1 M H_2SO_4 exhibiting surface redox behaviour is shown in Fig. 1 as dashed lines (- - -). The occurrence of the cathodic peak at −0.570 V and the corresponding anodic peak at −0.520 V are attributed to the following redox reaction:

$$TiO_2 + H_2O + H^+ + e^- \rightleftharpoons Ti(OH)_3 \quad (1)$$

Figure 1 also shows with continuous lines (——) the cyclic voltammogram obtained for the reduction of 5-NSA (1×10^{-2} M) under identical conditions. The disappearance of the anodic peak upon the addition of 5-NSA clearly illustrates the catalytic regeneration of Ti^{4+} at the electrode surface which is due to a fast reaction between the Ti^{3+} and the nitro compound, given by

$$6Ti(OH)_3 + RNO_2 \longrightarrow 6TiO_2 + RNH_2 + 8H_2O \quad (2)$$

Figure 2 shows the cyclic voltammogram of 5-NSA (1×10^{-2} M) obtained under identical conditions at a GCE. The cyclic voltammetric data on 5-NSA (1×10^{-2} M) in 50% ethanolic 1 M H_2SO_4 solutions at Ti/TiO$_2$ and glassy carbon electrodes are listed in Table 1.

From Table 1, it can be seen that at both the electrodes, the variation in the peak potentials with sweep

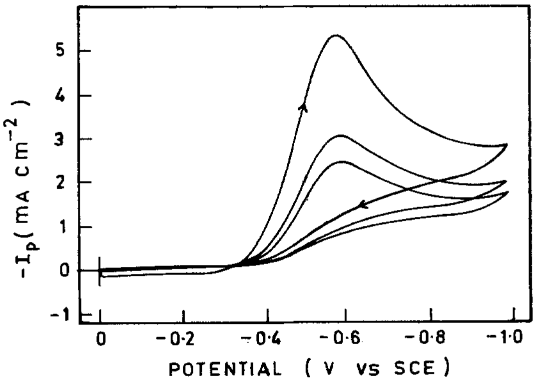

Fig. 2. Cyclic voltammogram of 5-NSA (1×10^{-2} M) in 50% ethanolic 1 M H_2SO_4 solution at GCE at a sweep rate of 0.1 V s^{-1}.

rate is identical. Also, the $I_p v^{-1/2}$ values suggest that at both the electrodes, a diffusion-limited irreversible electrode process is established. At a GCE, it is the ECE mechanism that is operative involving 'quinoneimine' as the electroactive intermediate. Due to the chemical reaction (involving the formation of quinoneimine by dehydration) being very fast in the time scale of cyclic voltammetric measurements, the response is that of a diffusion-limited one.

The reduction of 5-NSA at a Ti/TiO$_2$ electrode indicates clearly the catalytic regeneration of Ti^{4+} at the electrode surface from the observed amplification in the cathodic current with simultaneous disappearance of the anodic peak (Fig. 1). However, the cyclic voltammetric results (Table 1) show a diffusion-limited response in the sweep rate range of 0.3 to 0.005 V s^{-1}. This could be explained by considering that the reactions shown in Equations 1 (electroreduction of Ti^{4+} to Ti^{3+}) and 2 (chemical step involving the regeneration of Ti^{4+}) occur at a much faster rate compared to the diffusion of 5-NSA to the electrode surface. However, when the concentration of 5-NSA in the above experiment was increased tenfold, the $I_p v^{-1/2}$ values showed an increase at lower sweep rates, as expected for an electrochemical step with a follow up catalytic reaction. This is understandable since at higher concentrations of 5-NSA, the diffusion step becomes less important.

4. Conclusion

The Ti/TiO$_2$ electrode can be successfully used for the reduction of 5-NSA to 5-ASA and has advantages over the earlier chemical and electrochemical methods. Scale up of the above process and improvement in the yield of the amine are targets for future research.

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