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## Voltammetric studies of 5-substituted isatins

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### ABSTRACT

In the present study, the electrochemical behavior of isatin, a potent endogenous neurochemical regulator in brain and some of its more effective 5-substituted analogues in DMF has been investigated at glassy carbon electrode (GCE) using cyclic (CV) and differential pulse voltammetry (DPV) techniques in 0.1 M LiCl solution. All the chosen substituted isatins (Ia-Ih) were found to exhibit two well-defined diffusion-controlled irreversible reduction waves. The number of electron transferred and the reduction products were identified using controlled potential electrolysis. Effect of scan rate and concentration of depolarizer on voltammetric response is also studied. An interesting correlation between half wave potential ( $E_{1/2}$ ) values of various substituents and Hammett substituent constant ( $\sigma$ ) has been interpreted. The kinetic parameter i.e. charge transfer coefficient ( $\alpha n$ ) and forward rate constant ( $K_{f,h}^0$ ) Diffusion constant ( $D_0^{1/2}$ ) have also been calculated. © 2008 Trade Science Inc. - INDIA

### KEYWORDS

5-Substituted isatins;  
Substituent effect;  
Kinetic parameters;  
Controlled potential  
electrolysis.

### INTRODUCTION

Isatin (indole 2, 3-dione) and its reduced species oxindole have been identified in urine of schizophrenic patients and suspected drug abusers<sup>[1-3]</sup>. Concentration of isatin in urine is to become a diagnostic marker for the clinical severity of Parkinson's disease in humans, however electrophysiology, synthetic and metabolic pathways of isatin in human system are not yet fully established<sup>[4,5]</sup>. Some 5-substituted isatin analogues which are more effective inhibitors of atrial natriuretic peptide (ANP) stimulated guanylyl cyclase (GC) in rat brain and heart membranes than isatin itself, may play a role as pharmacological tools for investigating the physiological roles of natriuretic peptides and their receptors<sup>[6]</sup>.

Due to their high sensitivity, voltammetric methods are now used for the determination of isatin in brain and

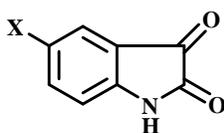
other tissues in mammals<sup>[7]</sup> but no reports are available on electrochemical behavior of substituted isatins on glassy carbon electrode (GCE) and the products identification<sup>[8]</sup>. In the present note, the electrochemical reduction of a series of substituted isatin (Ia-h) in DMF has been investigated using cyclic (CV) and differential pulse voltammetry (DPV) techniques at GCE in 0.1 M aqueous LiCl solution mainly to study the relation of half wave potential to Hammett substitution constant. The product of the two-electron reduction by conducting coulometry was mainly the alcohol, dioxindole. The kinetic parameter i.e. charge transfer coefficient ( $\alpha n$ ) and forward rate constant ( $K_{f,h}^0$ ) Diffusion constant ( $D_0^{1/2}$ ) have also been calculated.

### EXPERIMENTAL

Substituted isatins (Ia-h) were purchased from

TABLE 1: Electrochemical characteristics of substituted isatins in DMF at GCE in 0.1 M LiCl, concentration 1 mM, scan rate 100 mVs<sup>-1</sup>

Compd. no.	R	I <sup>st</sup> Cathodic peak			II <sup>nd</sup> Cathodic peak			
		-E <sub>pc/2</sub> (mV)	I <sub>pc1</sub> (μA)	E <sub>pc/2</sub> ' (mV)	I <sub>pc2</sub> (μA)	α <sub>na</sub>	K <sub>s</sub> (cms <sup>-1</sup> )	D <sub>o</sub> <sup>1/2</sup> (cm <sup>2</sup> s <sup>-1</sup> )
Ia	5-OCH <sub>3</sub>	610.6	12.1	1.026	7.27	0.563	2.6×10 <sup>-9</sup>	4.6×10 <sup>-5</sup>
Ib	5-CH <sub>3</sub>	604.1	11.07	0.987	6.23	0.546	2.16×10 <sup>-9</sup>	3.95×10 <sup>-5</sup>
Ic	5-H	598	12.58	0.924	5.84	0.569	3.58×10 <sup>-9</sup>	4.97×10 <sup>-5</sup>
Id	5-F	529.5	10.52	0.880	8.18	0.542	4.20×10 <sup>-9</sup>	5.22×10 <sup>-5</sup>
Ie	5-Cl	502.3	8.69	0.817	7.63	0.501	3.42×10 <sup>-8</sup>	4.89×10 <sup>-5</sup>
If	5-Br	489	10.68	0.782	8.49	0.547	3.93×10 <sup>-8</sup>	5.41×10 <sup>-5</sup>
Ig	5-I	495	8.02	0.725	6.38	0.598	4.52×10 <sup>-8</sup>	4.06×10 <sup>-5</sup>
Ih	5-COOH	467	9.87	0.692	8.46	0.577	4.39×10 <sup>-9</sup>	5.30×10 <sup>-5</sup>



Indole 2,3-dione (Isatin)

X=H, OCH<sub>3</sub>, CH<sub>3</sub>, Cl Br, I, COOH

Figure 1: Structure of Indole 2,3-dione (isatin)

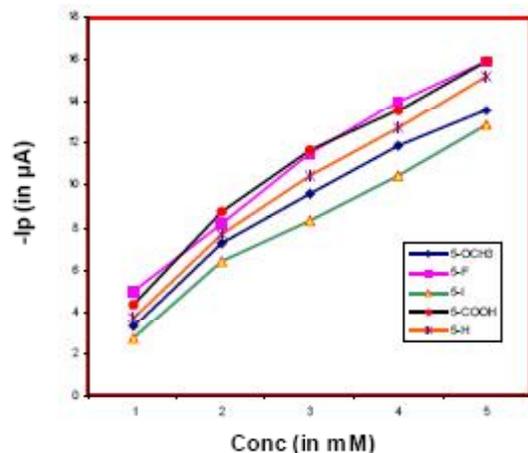


Figure 2: Plots of peak potential, I'pc (μA) vs. concentration for some 5 substituted isatins at scan rate 100 mVs<sup>-1</sup> at GCE

Sigma-Aldrich. 0.01M Stock solution of depolarizer was prepared by dissolving accurately weighed amount in purified DMF. More dilute solutions were prepared by accurate dilution with supporting electrolyte i.e. 0.1M LiCl solution in double distilled water.

A Potentiostat/Galvanostat electrochemical analyzer make princeton applied research model 263A was used for recording all voltammograms. The working electrode was a glassy carbon electrode (GCE) with diameter 2mm; the counter electrode was a platinum wire and reference electrode Ag/AgCl in 3M NaCl (E° = 0.209 volts vs. NHE).

All measurements were run in oxygen free environment. Purging and blanketing of nitrogen were done for analyte solution placed in the electrochemical cell of 15 ml capacity for 15 minutes prior to each experiment. Pretreatment of working electrode was done by mechanical polishing over a velvet micro cloth with a 0.05 α-alumina powder suspension and by keeping electrode at initial potential for 60 seconds before each scan. A Systronics model 106 Spectrophotometer was used to record UV-Visible spectra.

Controlled Potential Electrolysis (CPE) was carried out for calculating number of electrons involved in the reduction process. As the products of CPE were known to differ, electrolysis was carried out in a micro cell with a 7mm diameter graphite electrode as the working electrode, a platinum sheet as auxiliary electrode and an Ag/AgCl as reference electrode keeping a blanket of nitrogen over the surface of the solution. The number of electrons was calculated from the plot of amount of charge passed vs. t<sup>1/2</sup>.

## RESULTS & DISCUSSION

### Cyclic voltammetric studies

0.1M solution of LiCl was found to be a suitable supporting electrolyte for electro reduction studies of isatin in DMF on GCE as the peak of the electrolyte is well separated from depolariser reduction peaks. The α-carbonyl group in isatin is rendered electro-inactive at least before hydrogen evolution through mesomeric shift with the neighboring imino group<sup>[9]</sup> figure 1. So reduction of β-C=O group is found to be similar to other cyclic ketones<sup>[10,11]</sup>. All the isatins under study in 0.1 M LiCl show two separate well-defined one elec-

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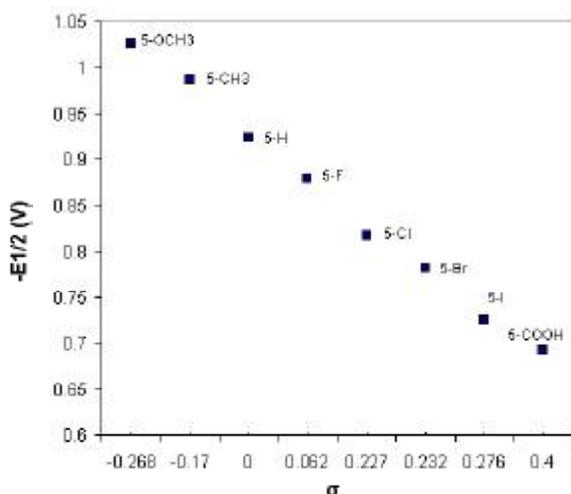


Figure 3: Plot of  $E_{1/2}$  and  $\sigma$  for 5-substituted isatins (Ia-h)

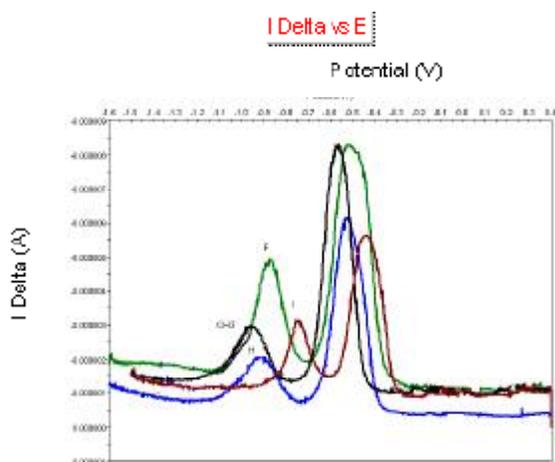


Figure 4: Differential pulse voltammograms for some substituted isatins at concentration  $1 \times 10^{-4} \text{M}$

iron reduction peaks at all concentration chosen for scan rates from 10 to  $250 \text{mVs}^{-1}$ . The linear dependence of peak current on the square root of the sweep rate ( $v^{1/2}$ ) and concentration indicates the diffusion-controlled nature of the electrode process<sup>[12,13]</sup> figure 2.  $E_{p2}$  values of second wave shift towards negative potential with increasing scan rate and concentration also confirming irreversible nature of the electrode process. Corresponding CV characteristics and kinetic parameters of substituted isatins (Ia-h), calculated by methods of Meites and Israel<sup>[14]</sup> are included in TABLE 1.

It is apparent from the data that the all compared compounds show diffusion controlled two electron reduction waves and values of  $\alpha n$  are practically in the same range for the entire series. Thus it is possible to

discuss the effects of substituents quantitatively in terms of Hammett equation figure 3. The values of the Hammett substituent constant ( $\sigma$ ) are used from the literature<sup>[15]</sup>.

### Differential pulse voltammetry

For isatins (Ia-h) at all chosen concentrations, two separate reduction peaks were observed in this medium at all selected scan rates figure 4. Experimental parameter chosen were: potential range 0.4 V to -1.6V, pulse amplitude 25mV, pulse duration 20ms, step height 2mV, step time 50ms, scan rate  $40 \text{mVs}^{-1}$  and equilibration time 10s.

### Controlled potential electrolysis (CPE)

CPE of all compounds (Ia-h) was carried out at the plateau potential of second irreversible reduction wave to determine the number of electrons transferred and the final product. The plot of  $\log I$  vs.  $t$  plot is linear and the value of 'n' was found to be 2. The progress of the electrolysis was monitored by recording UV-Vis spectra at different intervals of time and using TLC. For Ia, with the progress of the reaction, absorbance at 387nm systematically decreases and finally disappears. The product mixture obtained was evaporated to dryness in a rotary evaporator after electrolyses. The solid residue was triturated with diethyl ether several times and the ether soluble portion was subjected to preparative TLC on silica gel plates (Merck) using benzene and ethyl acetate (3:1, v/v) as the eluent. The eluent was separated and evaporated to dryness. While IR of isatin showed bands at  $1680$  and  $1720 \text{cm}^{-1}$  due to  $>\text{C}=\text{O}$  groups and NH band appeared at  $3200 \text{cm}^{-1}$ , formation of an alcohol, dioxindole, was indicated by the retention of  $\text{NHC}=\text{O}$  absorption band at  $1720 \text{cm}^{-1}$  and disappearance of another  $>\text{C}=\text{O}$  absorption of isatin moiety in IR spectra at  $1680 \text{cm}^{-1}$ . The band corresponding to OH group at  $\beta$ -position appeared at  $3620 \text{cm}^{-1}$  and NH of indole moiety at  $3250\text{-}3150 \text{cm}^{-1}$ .

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