CHRONOPOTENTIOMETRIC STUDIES OF CERTAIN BIOLOGICALLY IMPORTANT COMPOUNDS AT TUBULAR GRAPHITE ELECTRODE

Ram PARKASH[a], Hari Om GUPTA[b] and Jatinder DUTT[b]

[a] *Department of Chemistry, Panjab University, Chandigarh 160 014, India*
[b] *Department of Chemical Engineering and Technology, Panjab University, Chandigarh 160 014, India*

Received February 19, 1990
Accepted November 9, 1990

Dedicated to the memory of Prof. J. Heyrovský on the occasion of his centenary.

The chronopotentiometric studies of certain phenothiazines in hydrodynamic systems at a solution flow-through tubular graphite electrode were carried out in sulfuric acid of different concentrations. A well-defined single wave (involving 2 electrons) in 0·1M H_2SO_4 and two waves (involving 1 electron each) in 2·0M H_2SO_4 were observed. Phenothiazines are oxidized through the formation of a monocation radical by the elimination of one electron from the lone pair of N-atom. The monocation radical is stable in sulfuric acid of a moderate concentration and is unstable in neutral or less acidic solutions. The cation radical undergoes instantaneous hydrolysis yielding sulfoxide, thus presenting an overall two-electron oxidation of the phenothiazine derivatives. The suitability of the chronopotentiometric technique for their determination was established.

Oxidative voltammetry of N-substituted phenothiazines has been carried out by various workers using different electrodes in stationary solutions and conflicting results have been obtained[1-6]. An experimental verification of the theory of chronopotentiometry at a tubular graphite electrode, through which the solution of the reactant flows, has been reported previously[7]. Chronopotentiometric study of these compounds in sulfuric acid of different concentrations is now undertaken with a view to understand the mechanism of anodic oxidation under better experimental conditions (well-defined hydrodynamics). An attempt has also been made to use chronopotentiometry in flowing solutions for a quantitative determination of these compounds in certain pharmaceutical preparations.

EXPERIMENTAL

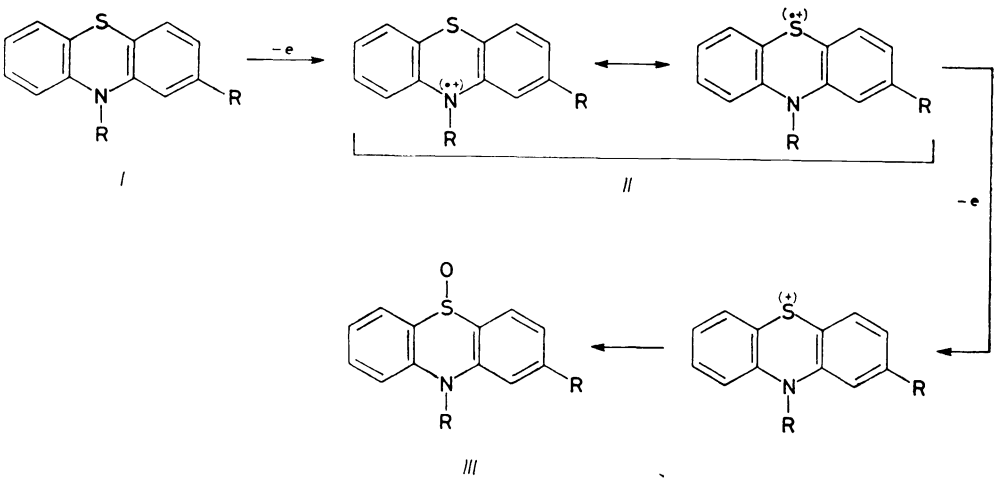
Most of the compounds were obtained from May and Baker Co. India unless otherwise specified, and were purified before use by usual methods. The electrode was fabricated from the spectroscopic grade compressed graphite rodes and had a length of 1·0 cm with an internal diameter of 0·2 cm.

Chronopotentiograms for the phenothiazines were recorded at the solution flow-rate of 0·5352 cm s^{-1} in a H_2SO_4 solution of concentration varying from 0·1 to 3 mol dm^{-3} by using an *X–Y* recorder attached to an equipment described earlier[7]. The *X*-axis of the recorder served as the time base. A thorough deaeration was carried out in order to avoid any complications due to the air-oxidation of the phenothiazines. The chronopotentiograms obtained in the case of promazine hydrochloride and chlorpromazine hydrochloride are presented in Figs 1 and 2. Similar chronopotentiograms were obtained for all other phenothiazines.

RESULTS AND DISCUSSION

These phenothiazines exhibit a single well-defined wave (involving 2 electrons) in 0·1M H_2SO_4 and two waves (involving one electron each) in 2·0M H_2SO_4. The reproducibility of all the waves is good; the repeated records superimpose on each other.

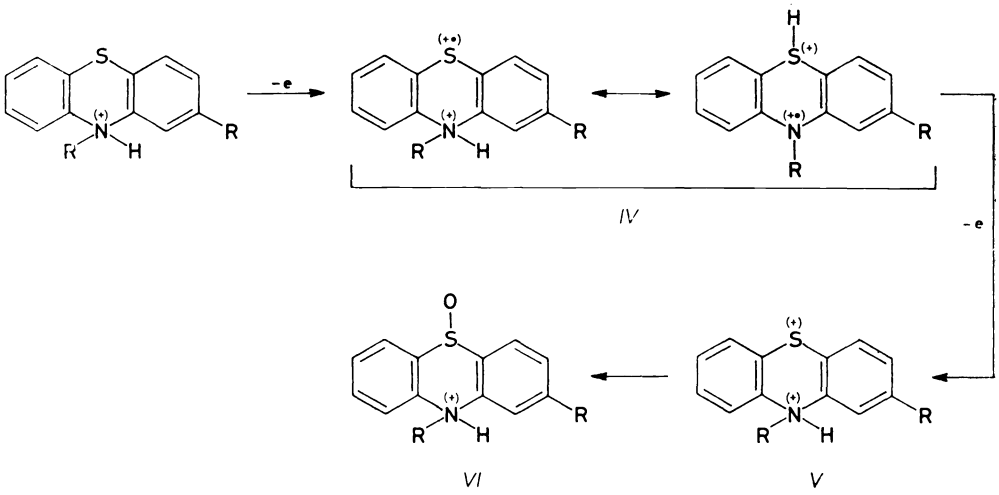
The appearance of the single oxidation wave during anodic oxidation of phenothiazine (*I*) in 0·1M H_2SO_4 suggests that the monocation (*II*) formed as an intermediate, with the loss of one electron from the lone pair of N-atom, is unstable in neutral to less acidic solutions. Under such conditions, there is a little or no protonation. The permitted resonance structures of the unprotonated monocation are unstable because of unsymmetrical charge distribution. The monocation undergoes oxidation and hydrolysis yielding sulfoxide (*III*) (Scheme 1). This mechanism



SCHEME 1

is in accordance with certain studies reported earlier[3,4]. The possibility of existence of such a free radical during the chemical oxidation of phenothiazines was shown by Michaeles et al.[1] and later on confirmed by several workers using ESR spectroscopy.

Two well-defined oxidation waves are formed in 2·0M H_2SO_4 indicating that the cation formed during the first oxidation stage with a loss of one electron is stable at this acid concentration and undergoes further oxidation at a higher potential losing another electron. Thus the oxidation of phenothiazines in 2·0M H_2SO_4 is a two-step process, involving one electron in each step. The transition time obtained in the second step is 2·5 times longer than the transition time in the first step. Sharma et al.[6] also attribute the stability of the monocation radical to the protonation of S and N atoms. The protonated dication radical permits stable resonance structures with a symmetrical charge distribution. This protonated stable dication (*IV*) undergoes anodic oxidation at higher potential and forms protonated trication (*V*) which is unstable and undergoes hydrolysis to give protonated sulfoxide (*VI*) (Scheme 2).



SCHEME 2

The stability of the monocation radical in 2·0M H_2SO_4 may also be confirmed from experimentally recorded chronopotentiograms (cf. Figs 1 and 2). The formation of the second oxidation wave provides sufficient evidence for the existence of monocation as a stable species in acidic medium. In 0·1M H_2SO_4, the monocation formed has little or no stability. Consequently, there is no indication of the second wave in this solution.

Billon[5] also reported two oxidation waves during the anodic oxidation of several phenothiazines in acetonitrile at platinum electrode. The first wave was attributed to the formation of the monocation free radical and the second to a dication free radical; the latter ultimately changing to the corresponding sulfoxide.

In order to confirm the chronopotentiometric observations, exhaustive electrolysis of prochlorperazine was carried out in 0·1M H_2SO_4 at 0·80 V vs SCE and in 2·0M H_2SO_4 at 0·1 V vs SCE. From both the solutions, sulfoxide was isolated in pure form by the method suggested earlier[4,6]. The samples of sulfoxide on being subjected to cathodic chronopotentiometry at the tubular graphite electrode under identical conditions give identical waves with almost the same value of half-wave potential

TABLE I

Estimation of phenothiazines in pharmaceutical preparations

Pharmaceutical preparation	Compound present	Amount (mg per tablet)	
		present	found
Largactil (May and Baker)	chlorpromazine hydrochloride	100·00	100·20
Thorazine (Smith, Kline and French Labs.)	chlorpromazine hydrochloride	50·00	50·40
Phenargan (Wyeth Ltd.)	promethazine hydrochloride	12·50	12·65
Temarial (Smith, Kline and French Labs.)	trimeprazine tartarate	2·50	2·60

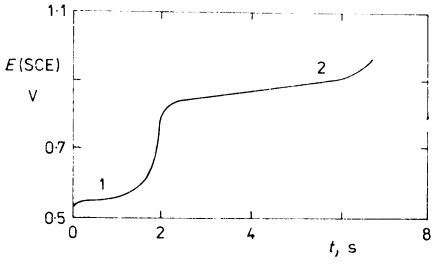


FIG. 1

Oxidation of promazine hydrochloride in 2·0M H_2SO_4 characterized by transition times τ and half-wave potentials $E_{\tau/2}$: 1 τ = 1·8 s, $E_{\tau/2}$ = 0·53 V; 2 τ = 4·5 s, $E_{\tau/2}$ = = 0·89 V

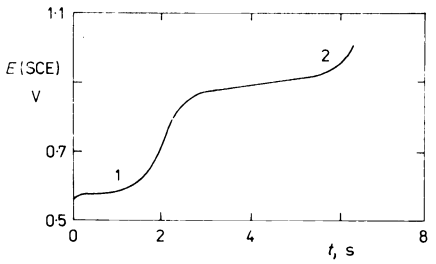


FIG. 2

Oxidation of chlorpromazine hydrochloride in 2·0M H_2SO_4 characterized by transition times τ and half-wave potentials $E_{\tau/2}$: 1 τ = 1·75 s, $E_{\tau/2}$ = 0·58 V; 2 τ = 4·2 s, $E_{\tau/2}$ = 0·90 V

($E_{1/2}$). These observations suggest the formation of sulfoxide on hydrolysis of unprotonated monocation.

Estimation of Phenothiazines in Pharmaceutical Preparations

For estimating phenothiazines present in certain commonly available pharmaceutical preparations, the test solution was forced to flow through the tubular graphite electrode at a constant rate and the potential–time curve was recorded. Under similar conditions, the potential–time curve for the solution of the phenothiazines of known concentration was also recorded. From the two values of transition time, the concentration of the test solution was calculated.

In order to establish the relationship between transition time and concentration, solutions of different concentrations ($1 \cdot 10^{-4}$ to $1 \cdot 10^{-3}$ mol dm^{-3}) were prepared for each of the phenothiazines in 0·1M H_2SO_4. The potential–time curve for each concentration was recorded keeping the solution flow-rate constant, the peak current was calculated, and the transition time function was plotted against concentration. The curve was a straight line in each case, indicating a linear relationship between transition time function and concentration.

The amount of phenothiazine per tablet determined chronopotentiometrically using the present method comes out to be quite close to the reported value (Table I). The accuracy also falls within the analytical range. Thus chronopotentiometric technique is highly dependable, more convenient and less time consuming than other methods available for the estimation of these materials.

REFERENCES

1. Michaelis L., Granick S., Schubert M. P.: J. Am. Chem. Soc. *63*, 351 (1941).
2. Gilman H., Nelson R. D.: J. Am. Chem. Soc. *75*, 5422 (1953).
3. Kabasakalian P., McGlotten J.: Anal. Chem. *31*, 431 (1959).
4. Merkle F. H., Discher C. A.: Anal. Chem. *36*, 1639 (1964).
5. Billon J. P.: Ann. Chim. *7*, 183 (1962).
6. Sharma L. R., Verma R. S., Sharma A., Singh G.: Indian J. Chem., A *23*, 642 (1984).
7. Dutt J., Gupta H. O., Singh T., Parkash R.: Analyst *113*, 493 (1988).
8. Dutt J., Singh T., Gupta H. O.: Analyst *109*, 755 (1984).