DIFFERENTIAL ELECTROLYTIC POTENTIOMETRIC TITRATIONS OF SOME β-ADRENERGIC BLOCKING AGENTS IN NON-AQUEOUS MEDIA

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INTRODUCTION

The technique of direct current differential electrolytic potentiometry (d.c. DEP) consists of polarizing two identical electrodes with a stabilized small current and measuring the potential difference between them. Two types of differential titration curves can be obtained, depending on the speed of the electrode processes concerned [1]. For fast reactions, a symmetrical peak of type I results, but if one of the electrode processes is slow then the titration curve will have *Z*-shape (Type II). The d.c. DEP technique has been applied to acid–base reactions in both aqueous [2–4] and non-aqueous media [5]. Antimony electrodes have been employed as indicating systems in non-aqueous media like acetic anhydride–acetic acid mixed solvent [5]. This mixed solvent has been found to be suitable for the titration of weak bases that are not easily titrated in other solvents [6–8]. The addition of toluene, which is an aprotic solvent, to acetic anhydride has been found to improve the d.c. DEP titrations of certain weak bases like codeine, caffeine, and quinoline [5].

Compounds like propranolol practolol, metoprolol sotalol, and oxprenolol are nitrogen-containing compounds and can be considered as neutral molecules of basic character. These compounds belong to a family of drugs called β-adrenergic blocking agents which are competitive inhibitors of the effect of catecholamines at β-adrenergic sites. They have been prescribed for the treatment of many diseases such as hypertension, anxiety, convulsions, anginal effects, disfunctional labour, and migraine. Many techniques have been employed for their determination and these have been reviewed [9, 10].

This paper describes the results of a study of the applicability of d.c. DEP to acid–base titrations of the above mentioned β-adrenergic blocking agents in a mixture of acetic anhydride and toluene. The behavior of polarized antimony electrodes is also reported.

EXPERIMENTAL

The apparatus and titration processes have been described [2, 5].

REAGENTS

All of the chemicals used in this work were of analytical reagent grade unless otherwise stated.

Perchloric Acid Solution, 0.05 M

Perchloric acid (Aristar) 72% (w/w) was diluted with a mixture of acetic acid and acetic anyhydride (1:9 v/v). The resulting solution was standardized against a 0.01 M solution of potassium hydrogen phthalate in acetic anhydride.

Test Solutions

A 0.01 M solution of each of the following pure compounds was prepared by dissolvig the required amount in acetic anhydride. These compounds include propranolol and practolol (supplied by ICI), oxperenolol and metoprolol (supplied by Ciba-Geigy), and sotalol (supplied by Bristol Meyers).

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Lithium Perchlorate Solution, 0.05 M

This solution in acetic anhydride–toluene (1:1 v/v) was made by direct weighing of anhydrous lithium perchlorate, which serves as a supporting electrolyte.

RESULTS AND DISCUSSION

Acetic anhydride is a suitable solvent for the titration of weak bases, especially if perchloric acid is used as a titrant [8]. This is attributable to the absence of water which reduces the acidity of the solvated protons and to the formation of strong acidic species like the acetylium ion CH_3CO^+, which is a stronger acid than H_3O^+ [11, 12]. The addition of an aprotic solvent like toluene has been found to be effective in improving the titrations of weak bases like caffeine [5]. This is due to the fact that aprotic solvents usually have wide potential ranges. In addition, these solvents have low dielectric constants which are effective in suppressing the solubility of the resulting products. Hence, the buffer zones of the titration curves will be decreased and sharp peaks will be obtained even if weak bases are involved.

Compounds like propranolol, practolol, oxprenolol, sotalol, and metoprolol are β-blockers having a secondary amino group in their structures. Therefore, they are expected to be easily titrated with perchloric acid in a medium like acetic anhydride–toluene mixed solvent.

In an attempt to examine the behavior of the above mentioned compounds, propranolol was titrated with perchloric acid at various current densities. Figure 1 shows the differential curves obtained at for the titration of propranolol at current densities of 5, 10, and 20 μA cm^{-2}. It is obvious that these curves belong to type I [1] which indicates the reversibility of the electrode processes. Figure 1*a* shows the differential curve which was obtained at a current density of 20 μA cm^{-2}. It can be seen that this curve is almost symmetrical with a significant height. However, its breadth is quite obvious which indicates that the employed current density was above its optimum value. On decreasing the current density to 10 μA cm^{-2}, curve *b* resulted. It is clear that this curve is symmetrical and in the form of a peak which has an acceptable breadth. A similar peak, but with less height has also been obtained when a current density of 5 μA cm^{-2} was applied. This is shown from curve *c* in Figure 1. It is apparent from these curves that the optimum current density which gives a sharp peak can be selected to have any value between 10 μA cm^{-2} and 5 μA cm^{-2}.

Figure 2 presents the differential curves obtained from the titrations of practolol (curve *a*), metoprolol (curve *b*), sotalol (curve *c*), and oxprenolol (curve *d*) each at a current density of 5 μA cm^{-2}. It can be seen that these differential curves are almost symmetrical which indicates the normal behavior of antimony electrodes in both aqueous [3] and non-aqueous media. The slight asymmetry which is shown by curves 1–4 in Figure 2 is attributed to the overpotential of the electrode which acts as an anode. The increase of the overpotential of this electrode is probably due to the thickening of the oxide film at its surface.

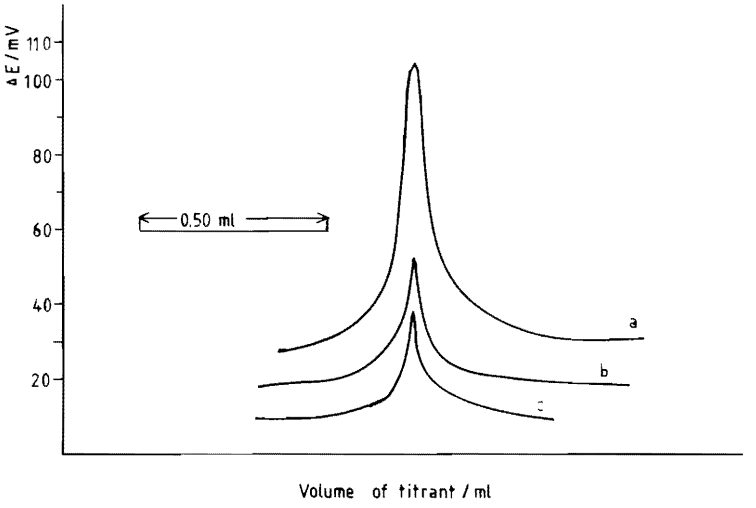

Figure 1. Titration of 5 ml of 0.01 M Propranolol with 0.05 M $HClO_4$ at Current Densities of: (a) *20 μA cm^{-2};* (b) *10 μA cm^{-2};* (c) *5 μA cm^{-2}.*

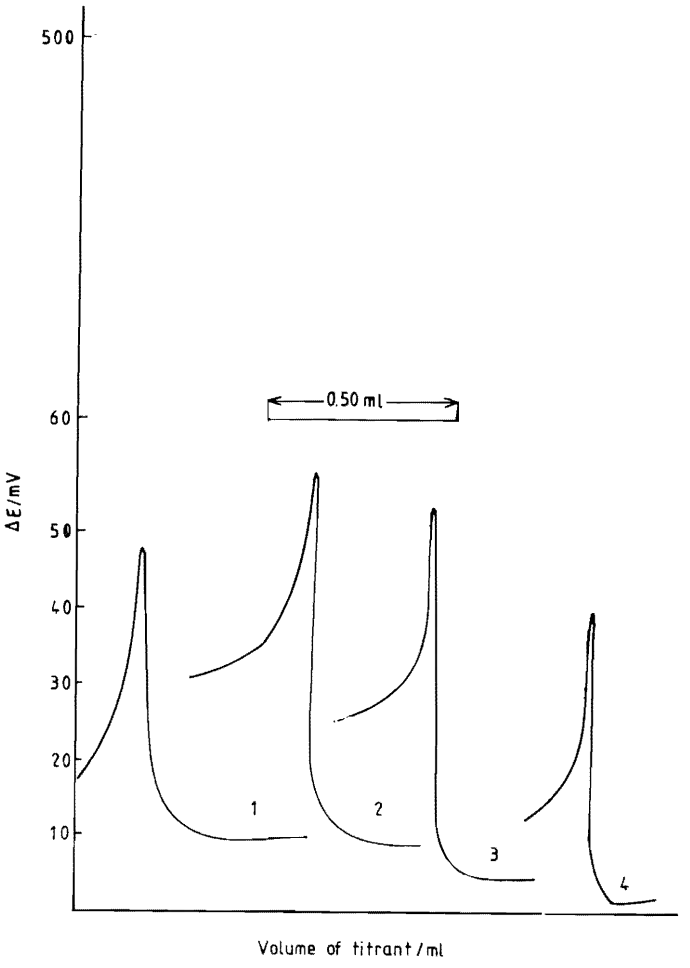

*Figure 2. Titration of 5 ml of 0.01 M of: Practolol **(1)**; oxprenolol **(2)**; sotalol **(3)**; and metoprolol **(4)** with 0.05 M $HClO_4$ at a current density of 5 $\mu A\ cm^{-2}$.*

The analytical validity of the d.c. DEP method was further investigated. Six identical samples of propranolol solution were titrated under almost the same conditions. A standard deviation of 7.07×10^{-3} ml was obtained which indicates the high precision of the d.c. DEP method.

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