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ANALYTICAL STUDY OF NEW CREATININIUM AND TETRAMETHYLAMMONIUM CATION SELECTIVE MEMBRANE ELECTRODES

KEY WORDS: electrode, creatininium, tetramethylammonium, titration

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ABSTRACT

Two new liquid membrane electrodes which respond to creatininium and tetramethylammonium cations are described. The creatininium cation electrode exhibits rapid and near Nernstian response to creatininium cation activity, at pH 3, in the 10^{-3}- 10^{-1} mol/L range. The useful concentration range extends to 10^{-4}mol/L. The tetramethylammonium cation electrode exhibits rapid and near Nernstian response to tetramethylammonium cation activity, at pH 2 - 11.5, in the $2x10^{-5}$ - 10^{-1} mol/L range. Major interferences for the creatininium electrode are Na^+, K^+, NH_4^+ and creatine. The pK_a of the creatininium cation was calculated. A method is described for the potentiometric precipitation titration of tetramethylammonium cation with sodium tetraphenylboron. Amounts of tetramethylammonium in the range 20-200 μmol have been determined using Gran´s plots, with an average error of about 0.6%.

INTRODUCTION

Potentiometry with ion selective electrodes has become a well established analytical method in the last few years. Several examples of organic anion sensitive electrodes have been recently reported in the literature [1-3]. Electrodes selective to organic cations have not received much attention and only scattered references have been made to the possibilities in this area[4]. Electrodes that respond to clinically relevant species are mainly those for Na^+, K^+, Ca^{2+}, H_3O^+, and those based on enzymic reactions coupled to ion selective indicator electrodes. Baum[4] described the first ion selective electrode specifically designed for the quantitation of acetylcholine cation.

In this paper, the performance characteristics of the first creatininium cation and tetramethylammonium cation selective membrane electrodes are described. The tetramethylammonium cation selective electrode has been used successfully in the potentiometric titration of tetramethylammonium with sodium tetraphenylboron.

EXPERIMENTAL

Apparatus

The creatininium cation(C^+) and tetramethylammonium cation (TMA^+) selective electrodes were used as the indicator electrodes, with a double junction silver-silver chloride electrode, Orion model 90-02-00, as the reference electrode. The outer chamber of the reference electrode was filled weekly with a 10% (w/v)NH_4NO_3 solution. The measurement system was the same as previously reported[2]. Test solutions were placed in 50-mL beakers and stirred magnetically.

Reagents

All solutions were prepared with deionized distilled water and reagent-grade substances, except where stated otherwise.

Creatinine solution 0.1000 mol/L was prepared by dissolving 1.131 g of pure creatinine (Merck) in water and diluting to 100.0 mL. The solution is kept in a refrigerator when not in use and is discarded after 10 days of use.

Tetramethylammonium bromide solution 0.1000 mol/L was prepared by dissolving 1.539 g of tetramethylammonium bromide (Eastman Organic Chemicals Co.) in water and diluting to 100.0 mL.

Sodium tetraphenylboron solution 0.1000 mol/L was prepared by dissolving 3.418 g of sodium tetraphenylboron (Merck) in water and diluting to 100.0 mL.

More dilute standard creatinine, tetramethylammonium bromide and sodium tetraphenylboron solutions were prepared by serial dilution.

Creatininium picrate was precipitated by mixing creatinine and acidified 0.1 mol/L sodium picrate solutions.

Preparation of the liquid ion exchanger:

(a) Creatininium electrode

Creatininium tetraphenylboron was precipitated by mixing 1.0 mL each of equimolar (0.1 mol/L) aqueous solutions of creatinine and sodium tetraphenylboron and acidifying the mixture with one drop of 5 mol/L HCl solution. The salt was extracted with 10 mL of 2-nitrotoluene, and the 2-nitrotoluene solution was washed twice with double-distilled water and dried thoroughly with anhydrous sodium sulfate.

(b) Tetramethylammonium electrode

Tetramethylammonium tetraphenylboron was precipitated by mixing 2.0 mL each of equimolar (0.1 mol/L) aqueous solutions of tetramethylammonium bromide and sodium tetraphenylboron. The salt was filtered in a G2 glass filter, washed thoroughly with water and dried in air for 24 hours. About 1/8 of the amount of this salt is dissolved in 20 mL of 2-nitrotoluene.

Construction of the electrodes

The body of an Orion 92 electrode equipped with Teflon membranes (Millipore 10-µm Teflon LCWPO 1300)[5] was used as the liquid membrane electrode. The electrode was assembled as described in the manufacturer´s instructions, and the internal reference and liquid ion exchanger solutions were injected into the appropriate ports in the electrode body.The internal reference solutions were 0.01 mol/L creatininium chloride-0.1 mol/L NaCl and 0.01 mol/L tetramethylammonium bromide-0.1 mol/L NaCl, for the creatininium and tetramethylammonium electrodes, respectively. The electrodes were conditioned by soaking in 0.01 mol/L creatininium chloride and tetramethylammonium bromide solutions, respectively, for 24 h before use,and were also stored in these solutions when not in use. The operative lifetime of the two electrodes was about two months.

RESULTS AND DISCUSSION

The salts tested for preparing the creatininium cation liquid ion exchanger were creatininium tetraphenylboron and creatininium picrate.

Solutions of creatininium tetraphenylboron in various organic solvents were tested as liquid ion exchangers. In the case of insoluble creatininium tetraphenylboron salts, saturated solutions were used. The results are presented in Table 1. The salt creatininium tetraphenylboron dissolved in 2-nitrotoluene was the most suitable to be used as a liquid ion exchanger in a creatininium electrode.

The salt creatininium picrate dissolved in 2-nitrotoluene was also tested as possible liquid ion exchanger but the resulting electrode was not responsive to creatininium cation.

In conclusion,it was decided to use the creatininium and tetramethylammonium tetraphenylboron salts dissolved in 2-nitrotoluene as liquid ion exchangers for the creatininium and tetramethylammonium electrodes.

Characteristics of the electrodes

Linear response range. Typical calibration graphs for the electrodes in stirred solutions are shown in Figures 1 and 2.The response of the creatininium electrode, at pH=3, is linear in the 10^{-3}-10^{-1} mol/L range with a slope of 57 mV/decade change in concentration at 20^{o}C. The slope decreases to 37 mV / decade in the 10^{-4} - 10^{-3} mol/L range. The response of the tetramethylammonium electrode is linear in the $2x10^{-5}$-10^{-1} mol/L range with a slope

TABLE 1

Solubility of creatininium tetraphenylboron in various organic solvents and response of the corresponding electrode

Solvent	Solubility	Comments
Cyclohexane	I*	Not responsive to C^+
1-Decanol	S**	Not responsive to C^+, may be due to strong H^+ interference
1,2-Dichloroethane	S	Very poor response to C^+
Bis(2-ethylhexyl)-phthalate	S	Not responsive to C^+
n-Butylacetate	S	Not responsive to C^+
Tri-n-butylphosphate	I	Not responsive to C^+
Dibutylphthalate	I	Poor response (10^{-4}-10^{-3} mol/L, slope=18 mV; 10^{-3}-10^{-2} mol/L, slope=35 mV).
Ethylacetate	S	Not responsive to C^+, may be due to strong H^+ interference
Isoamylacetate	S	Not responsive to C^+
2-Nitrotoluene	S	Satisfactory response

* I = insoluble
**S = soluble

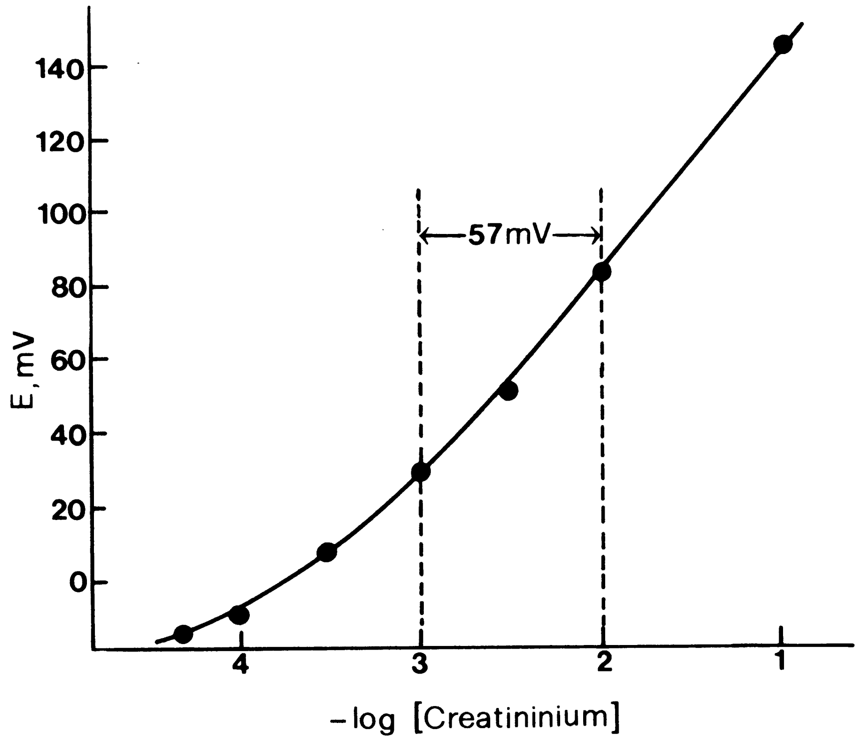

Figure 1. Calibration curve for the creatininium cation selective membrane electrode.

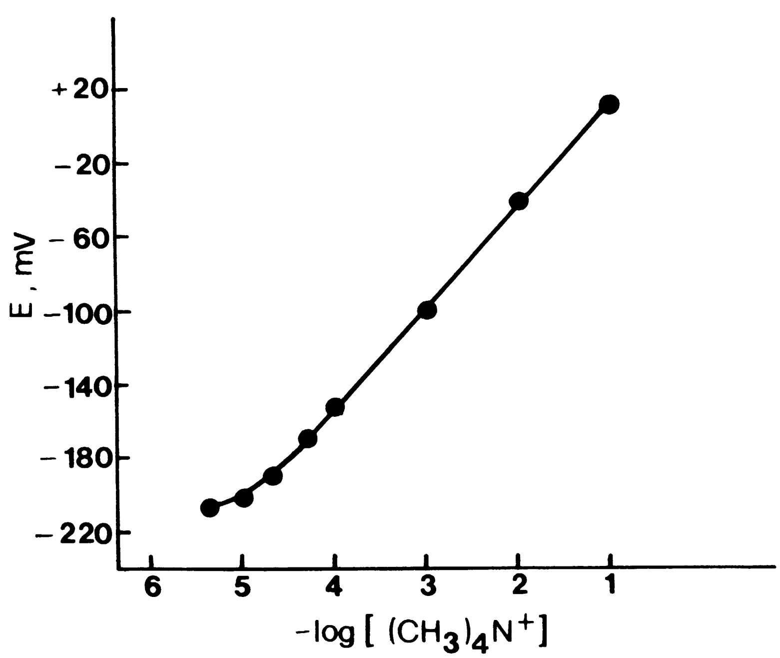

Figure 2. Calibration curve for the tetramethylammonium cation selective membrane electrode.

of 54 mV/decade. During one month the electrode readings were satisfactorily reproducible day-to-day, the slope of the electrode being 53.6 with a standard deviation of 3.0 mV.

Effect of pH. To check the pH-dependence of the potential of the creatininium cation selective electrode, potential-pH curves at various creatinine concentrations were constructed. The initial solution was made acidic by adding 3.00 mL of 1.00 mol/L HCl in 25.00 mL of creatinine solution (10^{-2} or 10^{-1} mol/L). The pH of the initial solution was altered by addition of small volumes of 18 mol/L NaOH and it was measured with a pH meter. The plots (Fig.3) show that between pH 2 and 3.9 the potential is practically independent of pH. At higher pH the potential decreases because of the decrease of the creatininium cation concentration which is converted to the neutral form. From the plots of Figure 3 it is possible to calculate the dissociation constant K_a of the creatininium acid. The pK_a is equal to the pH value where the initial creatininium cation concentration C^+ reduces to $C^+/2$, and this occurs when the potential of the electrode decreases by 17 mV. The pK_a value calculated in the present work is 4.99 at 20^oC and the value given in the literature is 4.88[6].

In the case of the tetramethylammonium electrode, a potential-pH curve was constructed at 10^{-2} mol/L te-

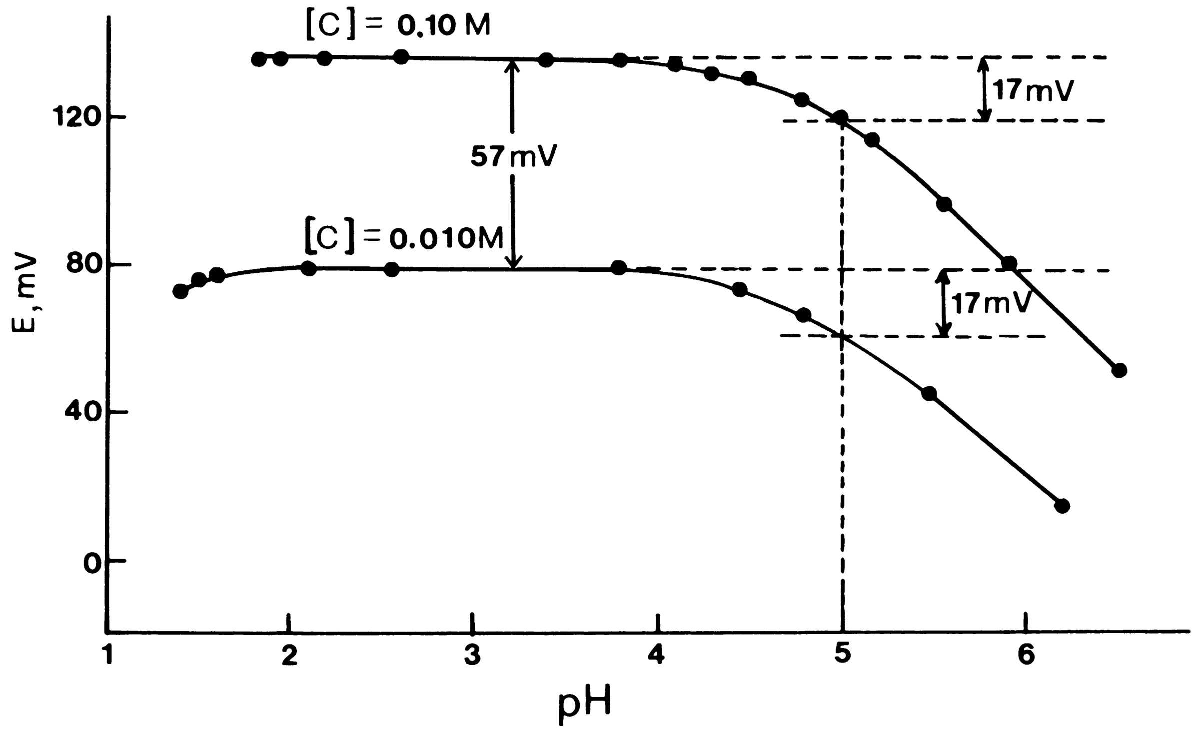

Figure 3. Effect of pH on the potential of the creatininium cation selective membrane electrode.

tramethylammonium concentration. The pH of the initial solution was altered by addition of very small volumes of NaOH and HCl solutions. It was found that the potential is practically independent of pH in the pH range 2-11.5.

Dyanamic response of the electrodes. The response times of the two electrodes were similar to those of the liquid ion exchanger electrodes described in previous communications[2,3], i.e. ≤ 10 s.

Potentiometric selectivity coefficients: (a) Creatininium electrode. The interference of various ions was studied by the mixed solution method and potentiometric selectivity coefficients, $K^{pot}_{C^+,j}$, were calculated from the formula

$$K^{pot}_{C^+,j} = \left[(10^{(E_2-E_1)F/2.303RT})\alpha_{C^+} - \alpha'_{C^+}\right] / \alpha_j^{1/z}$$

where E_1 is the potential in a creatininium cation solution of activity α_{C^+} , E_2 is the potential in a solution containing creatininium cation and interfering cation j of activities α'_{C^+} and α_j ,respectively, and z is the valency of the cation j[7]. Potentiometric selectivity coefficients are presented in Table 2. In all measurements,the pH was adjusted to 3.0 with HCl.

All concentrations were converted to activities by the expression: $\log f = -0.511\ z^2\left[\mu^{1/2} / (1+\mu^{1/2})\right]$, where f is the activity coefficient and μ is the ionic strength.

The interference of albumin, glucose and urea at final concentrations of 0.2 g/L, 20 g/L and 0.2 mol/L was negligible. Uric acid is precipitated at pH ≤ 3.

(b) Tetramethylammonium electrode. The selectivity of the tetramethylammonium electrode over the local anesthetic β-dimethylamino-α-tert-butyl-α-methyl benzoic acid ethylester was studied. It was found that in solutions where the anesthetic exists as a cation, it interferes strongly with the response of the tetramethylammonium electrode.

TABLE 2

Potentiometric selectivity coefficients of creatininium cation selective membrane electrode

Interferent, j	α_j mol/L	$\alpha'^{1}_{C^+}$ mol/L	$K^{pot}_{C^+,j}$
Mg^{2+}	5.24×10^{-3}	7.50×10^{-4}	6.3×10^{-3}
Ca^{2+}	5.24×10^{-3}	7.50×10^{-4}	6.5×10^{-3}
NH_4^+	4.29×10^{-2}	7.14×10^{-4}	2.8×10^{-2}
Na^+	8.02×10^{-2}	6.70×10^{-4}	1.2×10^{-2}
K^+	4.29×10^{-2}	7.14×10^{-4}	1.7×10^{-1}
Creatine	4.28×10^{-3}	8.93×10^{-4}	0.53

[1] α_{C^+} was 8.93×10^{-4} mol/L in all cases

Analytical applications

The clinical significance of creatinine is well known[8]. Numerous methods have been described for determining creatinine in biological fluids[9], some of which are based on potentiometric measurements[5,10,11]. The creatininium electrode was tested for the direct potentiometric determination of creatinine in urine. Unfortunately, the electrode is not specific enough and gives erroneous positive results. The application of the electrode to the determination of the activity of the enzyme creatininase[12] is under investigation.

The tetramethylammonium electrode can be used as an indicator electrode in potentiometric precipitation titrations[13]. As an example, the titration of tetramethylammonium was examined, based on the formation of the insolu-

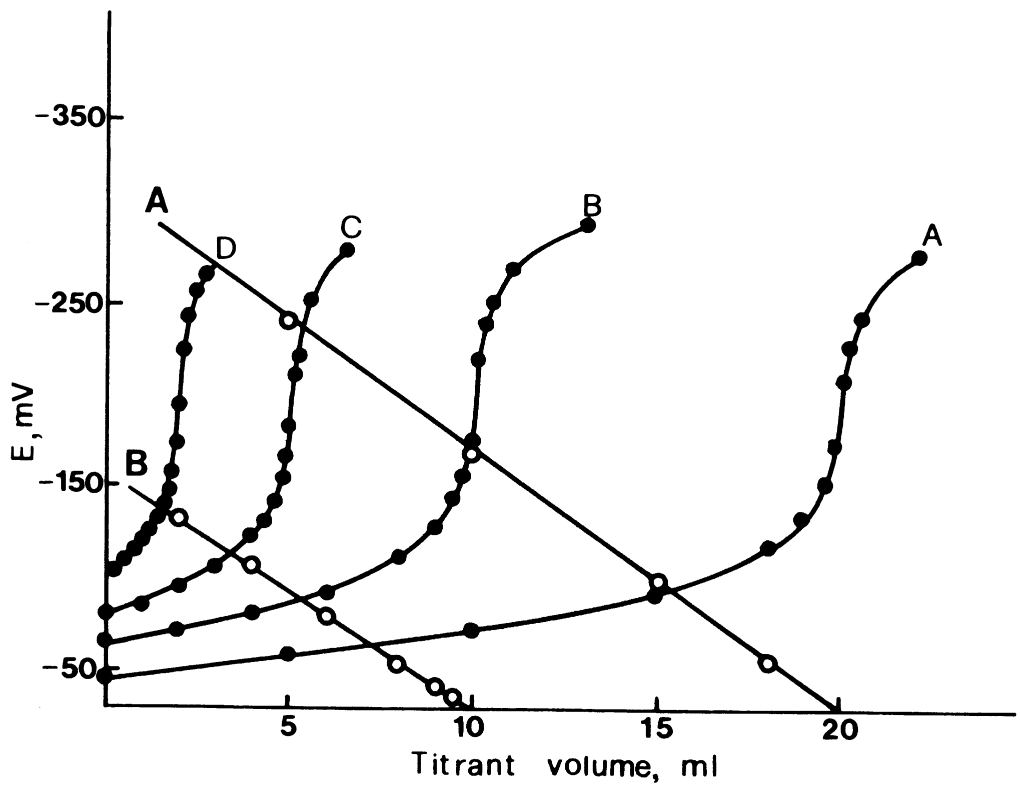

Figure 4. Titration curves for the potentiometric titration of 20 mL of tetramethylammonium with 1.00×10^{-2} mol/L sodium tetraphenylboron and two of the corresponding Gran's plots. (A) 10^{-2} mol/L, (B) 5×10^{-3} mol/L, (C) 2.5×10^{-3} mol/L, (D) 1×10^{-3} mol/L.

ble tetramethylammonium tetraphenylboron salt. For the titration, a 20.00 mL aliquot of the sample (10^{-3}-10^{-2} mol/L), was pipetted into a 50-mL beaker and titrated with standard 0.01000 mol/L sodium tetraphenylboron solution. Typical titration curves are shown in Figure 4. This figure also shows the Gran's plots constructed with experimental results taken before the equivalence point[14]. The end point was calculated by least squares extrapolation of the Gran's plot data[15]. For best accuracy, the Gran's plot data were taken in the 20 to 90% region of the titration curve.
The results are summarized in Table 3.

TABLE 3

Titrimetric determination of tetramethylammonium in aqueous solutions

μmol TMA^+		% Error
Taken	Found[a]	
20.00	20.06	+ 0.3
50.0	50.3	+ 0.6
100.0	98.9	- 1.1
200.0	199.0	- 0.5
		Av. 0.6

[a] Single Measurement.

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