

Iodimetric Determination of 2-Mercaptothiazoline, 2,5-Dimercapto-1,3,4-thiadiazole and 2-Mercapto-4-methyl-5-thiazoleacetic Acid

WITOLD CIESIELSKI, ROBERT ZAKRZEWSKI* and URSZULA ZLOBIŃSKA†
Department of Instrumental Analysis, University of Łódź, Pomorska 163 90-236 Łódź, Poland
E-mail: robzak@chemul.uni.lodz.pl

In this paper a method of iodimetric determination of 2-mercaptothiazoline (1), 2,5-dimercapto-1,3,4-thiadiazole (2) and 2-mercapto-4-methyl-5-thiazoleacetic acid (3) in an alkaline media is presented. In the volumetric titration with potentiometric end-point detection, the determination ranges are: 10–500 μmol , 25–125 μmol and 10–1000 μmol for (1), (2) and (3), respectively. In the coulometric determination with biamperometric end-point detection, 0.20–10 μmol , 0.10–5 μmol and 0.10–10 μmol amounts of (1), (2) and (3), respectively, were successfully determined. Errors and relative standard deviations for all determinations were below 1 and 0.5%, respectively. For compounds (1) and (2) at higher concentration of sodium hydroxide, potentiometric titration curves were unusually shaped. An addition of iodine resulted in a significant potential drop. The examined systems do not reveal Nernstian behaviour.

Key Words: Iodimetry, Potentiometry, Coulometry, 2-Mercaptothiazoline, 2,5-Dimercapto-1,3,4-thiadiazole and 2-Mercapto-4-methyl-5-thiazoleacetic acid.

INTRODUCTION

Thiols have a wide application in various fields of industry, technology and medicine. 2-Mercaptothiazoline (1), 2,5-dimercapto-1,3,4-thiazole (2) and 2-mercapto-4-methyl-5-thiazoleacetic acid (3) are used as corrosion inhibitors^{1,2} and in photographic processing³. They are applicable as reagents in synthesis of antifungal compounds⁴, fungicides⁵, antiviral thazole⁶ and antibiotics⁷. 2,5-Dimercapto-1,3,4-thiadiazole (2) can be found in lithium batteries⁸ and lubricating oils⁹ and is also an important additive for copper pyrophosphate plating baths to control the finish¹⁰. 2-Mercaptothiazoline (1) was involved in cancer and inflammation treatment¹¹. The described thiols react with a number of metal ions to form complexes by means of mercapto group. This has become the basis of spectrophotometric methods of determination of palladium¹² and lead¹³, potentiometric methods of the determination of cobalt¹⁴, copper¹⁵, amperometric

†Technical Chemistry School, Sokolowska 2 95-100 Zgierz, Poland.

titration of iron, copper, cerium¹⁶, silver¹⁷ and voltammetric analysis of cadmium and zinc¹⁸.

Therefore, there is a demand for precise and reliable methods for determination of these substances. So far, mostly cyclic voltammetric^{19,20}, spectrophotometric²¹ and enzymatic^{22,23} methods and a potentiometric titration with silver ions²⁴ have been used for these purposes. Using induction properties of (2) in iodine-azide reaction, a determination method has been elaborated²⁵. However, these are mostly indirect methods that require standards. To avoid this drawback, the possibility of iodimetric titration of these thiols has been investigated. Yet, the iodimetric and iodometric determination of (1) have been worked out^{26,27}. The elaborated methods are based on the reaction of iodine with the thiol in non-aqueous medium. The first one applied thermometrical detection end-point and the second one was based on the quantitatively released iodide ions which were titrated with silver ions by using an ion-selective electrode as an indicator electrode. Since the described thiols react with iodine very slowly in aqueous acid or neutral conditions, there is a necessity to use organic solvents to apply direct titration with iodine.

In this paper, determination of 2-mercaptothiazoline (1), 2,5-dimercapto-1,3,4-thiadiazole (2) and 2-mercapto-4-methyl-5-thiazoleacetic acid (3) by their direct titration with iodine in an alkaline medium were described. Larger amounts of thiols were titrated volumetrically with potentiometric end-point detection (with a platinum indicator electrode and a saturated calomel reference electrode). For smaller amounts of these compounds, coulometric titration with biamperometric end-point detection was carried out.

EXPERIMENTAL

Potassium iodide, sodium hydroxide and iodine were purchased from POCH (Gliwice, Poland). 2-Mercaptothiazoline (1), 2,5-dimercapto-1,3,4-thiadiazole (2) and 2-mercapto-4-methyl-5-thiazoleacetic acid (3) from Aldrich (Steinheim, Germany) were used. The studied thiols were purified by dissolving them in sodium hydroxide solution (2 mol L⁻¹), precipitating with glacial acetic acid and washing the precipitates with large amounts of water. Doubly distilled water was used throughout. Standard iodine solutions of the concentration of 0.01, 0.02, 0.025, 0.05 and 0.1 mol L⁻¹ in potassium iodide solution were prepared. Stock solutions of thiols were obtained by dissolving weighed amount of reagent in sodium hydroxide.

A universal coulometric analyzer (Radelkis, Budapest, Hungary), type OH-404 was applied to coulometric titrations. An electrolysis cell²⁸ comprised two platinum electrodes of 5 cm² each, a working electrode in a generating circuit and an OH-9381 double electrode in a biamperometric circuit. Solutions were mechanically stirred. The pH-meter N-517 (Mera Elwro) with a saturated calomel electrode and a platinum or a gold electrode, was used. Indicator electrodes of variously shaped working surfaces (wire, plate) were applied for potentiometric titrations.

Potentiometric titration. The samples of the compounds were dissolved in 50 mL of sodium hydroxide solution of an appropriate concentration (Table-1) and titrated with iodine using potentiometric end-point detection with a platinum indicator electrode and a saturated calomel reference electrode. The equivalence point was estimated from the inflection point on the curve. The initial amount of the analyte was calculated using the equation

$$n = \frac{c(I) \times V}{z} \times 10^3$$

where n = amount of the analyte (μmol); $c(I)$ = titrant concentration (mol^{-1}); V = titrant volume at the end-point (mL); z = number of electrons transferred in the single reaction.

TABLE-1
THE RESULTS OF POTENTIOMETRIC DETERMINATION OF STUDIED
COMPOUNDS IN ALKALINE MEDIUM; $n = 6$

Compound	NaOH concentration (mol L^{-1})	Taken (μmol)	Found $\bar{x} \pm t_{0.95} \frac{s}{\sqrt{n}}$ (μmol)	RSD (%)
2-Mercaptothiazoline (1)	0.1	10.00	9.91 ± 0.03	0.26
		20.00	20.11 ± 0.06	0.30
		50.00	49.84 ± 0.07	0.14
		100.00	99.27 ± 0.33	0.33
		250.00	244.8 ± 0.67	0.27
		500.00	504.9 ± 0.67	0.13
2,5-Dimercapto- 1,3,4-thiadiazole (2)	0.1	25.00	25.10 ± 0.10	0.40
		50.00	50.35 ± 0.10	0.20
		125.00	126.0 ± 0.3	0.24
2-Mercapto-4-methyl- 5-thiazoleacetic acid (3)	0.5	10.00	9.95 ± 0.02	0.23
		20.00	19.92 ± 0.09	0.42
		50.00	49.98 ± 0.14	0.27
		100.00	99.43 ± 0.27	0.26
		250.00	248.8 ± 0.8	0.29
		500.00	498.4 ± 1.3	0.25
		1000.00	998.8 ± 1.4	0.13

Coulometric titration: Coulometric titration was carried out in the reagent solutions given in Table-2. A sample solution was added to 20 mL of the reaction solution in the anodic compartment of the electrolysis cell. The cathodic compartment of the electrolysis cell was filled up with the same solution. The polarization voltage applied was equal to 150 mV. Stabilizing current was passed through the solution after starting the mechanical stirrer. The current magnitude in the generating circuit (Table-2) depended on the amount of the analyte and

was adjusted appropriately to maintain the titration time at the level of several minutes. Charge (Q) was measured after completing the titration of thiol as soon as indicator current of 0.04 μA was obtained.

TABLE-2
THE RESULTS OF COULOMETRIC TITRATION OF THE STUDIED
COMPOUNDS; $n = 6$

Compound	Reaction solution	Taken (μmol)	Found $\bar{x} \pm t_{0.95} \frac{s}{\sqrt{n}}$ (μmol)	RSD (%)	Current (mA)
2-Mercaptothiazoline (1)	$c(\text{KI}) = 1 \text{ mol L}^{-1}$ $c(\text{NaOH}) = 0.1 \text{ mol L}^{-1}$	0.2000	0.2015 ± 0.0007	0.33	0.5
		0.5000	0.5015 ± 0.0017	0.32	1.0
		2.000	2.010 ± 0.007	0.33	2.0
		10.000	9.99 ± 0.04	0.42	10.0
2,5-Dimercapto-1,3,4-thiadiazole (2)	$c(\text{KI}) = 1 \text{ mol L}^{-1}$ $c(\text{NaOH}) = 0.05 \text{ mol L}^{-1}$	0.1000	0.0996 ± 0.0004	0.38	0.5
		0.5000	0.4977 ± 0.0022	0.42	1.0
		1.000	0.9945 ± 0.0011	0.10	2.0
		5.000	4.978 ± 0.008	0.15	10.0
2-Mercapto-4-methyl-5-thiazoleacetic acid (3)	$c(\text{KI}) = 1 \text{ mol L}^{-1}$ $c(\text{NaOH}) = 0.1 \text{ mol L}^{-1}$	0.1002	0.1003 ± 0.0005	0.48	0.5
		1.000	1.001 ± 0.003	0.29	2.0
		2.000	2.011 ± 0.006	0.29	2.0
		10.00	9.98 ± 0.04	0.36	10.0

The content (μmol) of the analyte in the tested sample was calculated according to Faraday's law:

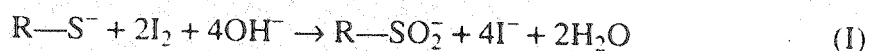
$$n = \frac{\Delta Q}{z \times F} \times 10^3$$

where $\Delta Q = Q - Q_0$ (mC); Q_0 = blank titration charge; z = number of electrons transferred in the single reaction; F = Faraday's constant (96485 C mol^{-1}).

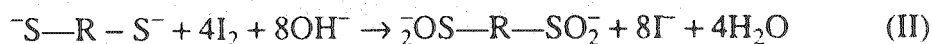
In order to calculate the electric charge Q_0 , which varied within the range 3–11 mC, a suitable amount of water instead of thiol was introduced into the reaction solution in the anodic compartment of the electrolysis cell.

RESULTS AND DISCUSSION

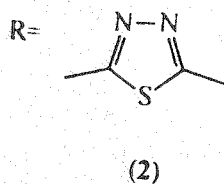
In acidic and neutral media, the studied thiols react very slowly with iodine, and thus iodimetric titration is impossible. However, in alkaline media the stoichiometry of the reactions is different. The reaction schemes between iodine and the studied thiols are given below:



where



where



Reactions (I) and (II) are fast, conduct quantitatively and direct iodimetric titrations are possible. Iodine disproportionates quickly in alkaline medium to give iodide and iodate(I) ions, and the latter being the virtual oxidizing agent. The titration in alkaline medium is only possible if the reaction of iodate(I) ions with thiol is faster than the decomposition of iodate(I) ions. The results of iodimetric determination of (1)–(3) are presented in Tables 1–2. When larger or smaller amounts of the studied compounds were titrated, the error increased above 1%. Exemplary potentiometric titration curves of (1) are shown in Fig. 1. The proposed potentiometric determination provides a high rise in potential near the end-point (above 200 mV/0.1 mL of the titrant).

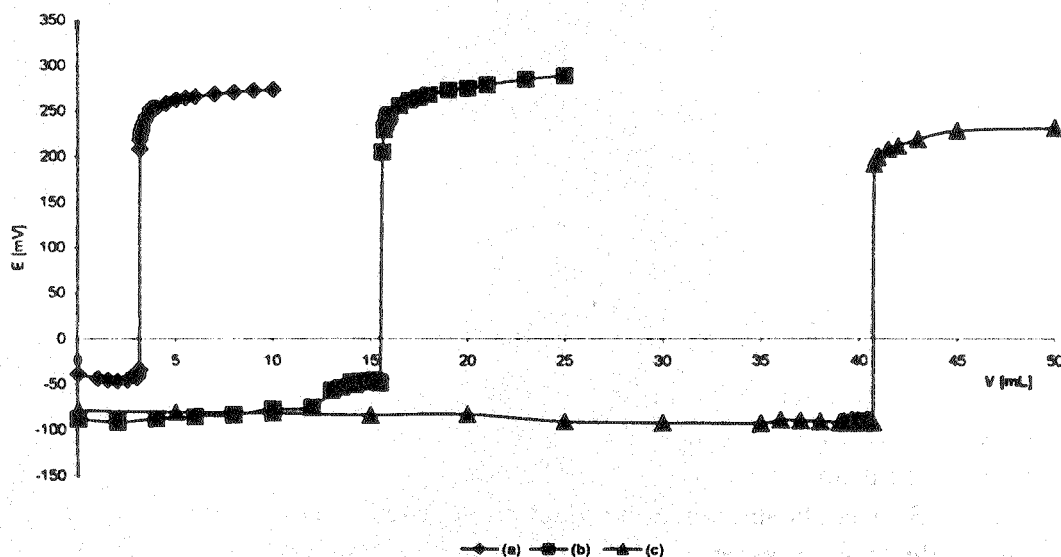
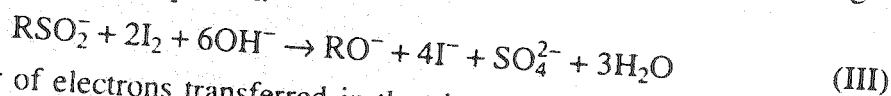


Fig. 1. Potentiometric titration curves of (a) 20 μmol , (b) 100 μmol and (c) 1000 μmol 2-mercapto-2-thiazoline (1) in 0.1 mol L⁻¹ sodium hydroxide solution; 0.025 (a and b) and 0.1 (c) mol L⁻¹ iodine solution

In the present research, the term "number of electrons transferred in the single reaction" is used as a tool for indication of reaction ratio of iodine and thiols in

an alkaline medium. According to reaction Scheme (I), the number of electrons transferred in the single reaction is exactly $z = 4$ for (1) and (3) when optimum sodium hydroxide concentration was applied to a reagent solution. In the case of (2), the number of electrons transferred in the single reaction is $z = 8$ ($z = 4$ per a mercapto group) in the optimum sodium hydroxide solution. At sodium hydroxide concentrations higher than optimum one, the sulphinates can be oxidized by iodine to give sulphate anion. Then, the following reaction might proceed according to the equation:



The number of electrons transferred in the single reaction (III) is also $z = 4$. In the previous report²⁹, it is found that 5,6-diamino-2,4-dimercaptopyrimidine is oxidizing by iodine in 3 mol L^{-1} sodium hydroxide solution with the number of electrons transferred in the reaction which is equal to $z = 16$ ($z = 8$ per one mercapto group). It has also been reported^{30, 31} that the 8-electron reaction occurs, when the excess of iodine is added to an alkaline thiopental solution and the unreacted iodate(I) is back-titrated after 15 min. Thiopental is oxidized to a proper RO^- derivative in a single step reaction. It means that some basic conditions (in direct or indirect titration) might be found which would lead to oxidization of the mercapto group into the final form: sulphate ion. In most cases, these conditions are not suitable for analytical purposes since the reaction is slow. Titration with iodine in alkaline medium was applied for determination of mercaptopyrimidines²⁹, 2-thiouracils^{32, 33}, mercaptopyridines³⁴, mercaptotriazoles and mercaptotetrazoles³⁵. In all cases mentioned above, the mercapto group is bounded with a heterocyclic ring containing a nitrogen atom. In the present report, a thiol group is connected to a heterocyclic ring containing not only a nitrogen atom but additionally a sulphur one. According to the results presented in Table-3, it is concluded that the cleavage of the heterocyclic ring of (1) and (2) by iodine in an alkaline medium takes part when high concentration of sodium hydroxide has been applied and the number of electrons transferred in the single reaction is more than $z = 8$ per a mercapto group (Table-3). The ring-opening reaction of thiazole³⁶ and penicillin ring³⁷⁻³⁹ by iodine in alkaline solution has also been reported. After the cleavage of the heterocyclic system, the sulphur atom might be oxidized to disulphide or sulphonate form³⁶⁻³⁹. In the present studies, the first step is oxidizing the mercapto group of (1)-(3) and the reaction (I) in case of (1) and (3) and reaction (II) for (2) are conducted in the sodium hydroxide solution (Table-1). The number of electrons transferred in the single reaction is exactly $z = 4$ per a mercapto group in 0.1 mol L^{-1} hydroxide sodium solution in volumetric titration. 0.5 mol L^{-1} sodium hydroxide solution for volumetric titration of (3) was chosen since the reaction is faster in the proposed media. The number of electrons transferred in the reactions of iodine with (1) and (2) depends on the concentration of sodium hydroxide. An increase of its concentration over 0.1 mol L^{-1} results in an increase in the number of electrons transferred in the reaction (Table-3). In strong alkaline conditions, further oxidation of RSO_2^- proceeds to give an RO^- derivative and sulphate ion when the total number of electrons transferred in the single reaction is $z = 8$ per a mercapto group.

Carbon-sulphur bond cleavage in heterocyclic ring appears in the next stage of the iodimetric reaction in case of (1) and (2) when his concentration of sodium hydroxide (Table-3) is applied and the number of electrons transferred in the single reaction increases above $z = 8$ per a mercapto group.

TABLE-3
THE INFLUENCE OF THE SODIUM HYDROXIDE CONCENTRATION ON
THE NUMBER OF ELECTRONS TRANSFERRED IN THE SINGLE REACTION

Compound	NaOH concentration [mol L ⁻¹]	Number of electrons transferred in the single reaction
2-Mercaptothiazoline (1)	0.05	3.98
	0.10	4.01
	0.50	4.05
	1.00	4.08
	5.00	4.45
	10.00	11.30
2,5-Dimercapto-1,3,4-thiadiazole (2)	0.05	7.89
	0.10	7.97
	0.50	14.10
	1.00	18.10
	5.00	20.10
	10.00	22.30
2-Mercapto-4-methyl-5- thiazoleacetic acid (3)	0.10	3.98
	0.50	3.98
	1.00	3.97
	5.00	3.97
	10.00	3.99

The oxidation reaction of (3) with iodine in an alkaline medium proceeds only according to equation (I) ($z = 4$). Moreover, the number of electrons transferred in the reaction of (3) is independent of the concentration of sodium hydroxide in the solution within the range 0.01–10 mol L⁻¹. The heterocyclic ring does not cleavage even in a strong alkaline solution.

In the volumetric titration of 10–500 μ mol of (1) and 25–125 μ mol of (2) with potentiometric end-point detection, the best results were obtained when the initial concentration of the sodium hydroxide solution was 0.1 mol L⁻¹. In case of (3), the most favourable outcome was achieved within the range 10–1000 μ mol when the 0.5 mol L⁻¹ sodium hydroxide solution was applied in the volumetric titration with potentiometric end-point detection.

Potentiometric end-point detection in coulometric titration of small amounts of (1–3) is impossible, owing to the slow response of the platinum indicator electrode at low concentration of the analyte. One can overcome this obstacle and improve the coulometric results by applying the biamperometric indicator system for the determination of (1–3).

The results of coulometric determination in alkaline medium were satisfactory in the presence of 0.1 mol L^{-1} sodium hydroxide and 1 mol L^{-1} potassium iodide for (1), (3) and (2), respectively. Under these conditions the reaction between thiols and iodine proceeds stoichiometrically within the range of 0.2–10, 0.1–5 and 0.1–10 μmol for (1)–(3), respectively, and the number of electrons transferred in the reaction of oxidized compounds (1) and (3) is $z = 4$ and of compound (2) is $z = 8$. In coulometric titration with iodine in an alkaline solution, 1 mol L^{-1} concentration solution of potassium iodide was required as a reagent solution⁴⁰. Such high concentration of potassium iodide solution ensured 100% current efficiency in the coulometric analysis.

Potentiometric titration curves of (1) and (2) were uniquely shaped at higher concentrations of sodium hydroxide (Fig. 2). A small addition of iodine resulted in a significant potential drop in the initial part of the curve, which did not occur at lower concentration of sodium hydroxide.

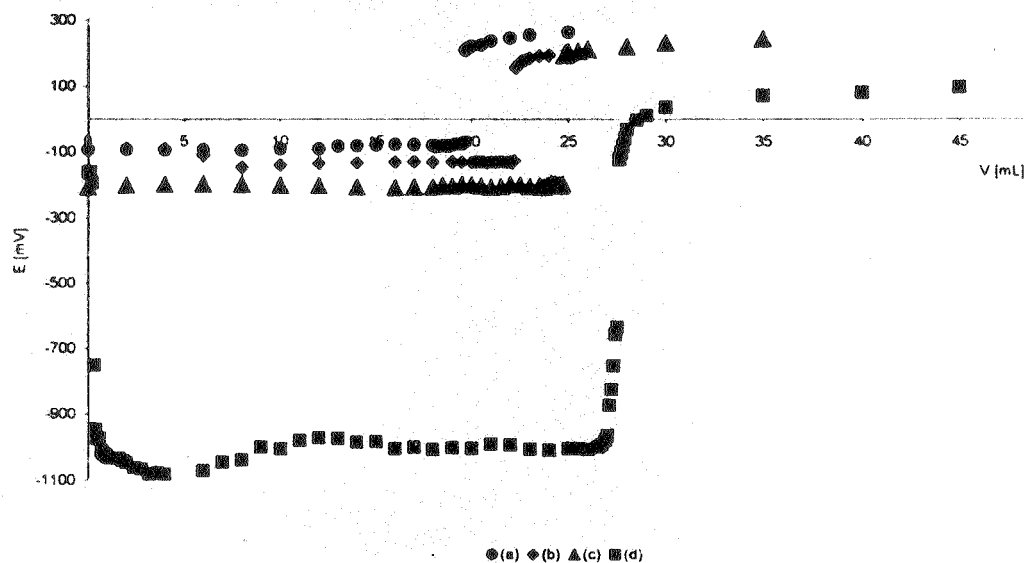


Fig. 2. Potentiometric titration curves of $125 \mu\text{mol}$ 2,5-dimercapto-1,3,4-thiadiazol (2) in (a) 0.1 , (b) 1 , (c) 5 and (d) 10 mol L^{-1} sodium hydroxide solution; 0.05 (a) and 0.1 (b, c, d) mol L^{-1} iodine solution

In case of potentiometric titration of (1) and (2), the potential drop appeared when a platinum or a gold indicator electrode was used. Moreover, when a gold wire indicator electrode was used for the potentiometric titration of (1) and (2), the shape of the response was typical (Fig. 3, curve a). With platinum indicator electrode (wire and plate) and a gold plate electrode the potential drop affected initial parts of the curves (Fig. 3, curves b–d).

In addition, the present research indicates that the preparation procedure of the electrodes used is not indifferent to the shapes of the obtained curves. The metal used for the preparation of the given electrode has different structures depending on how it is shaped—as a wire or as a plate. In the first case, the metal has been drawn in the second one it has been rolled. It has been found that the shapes of the titration curves obtained at high sodium hydroxide concentration depend on

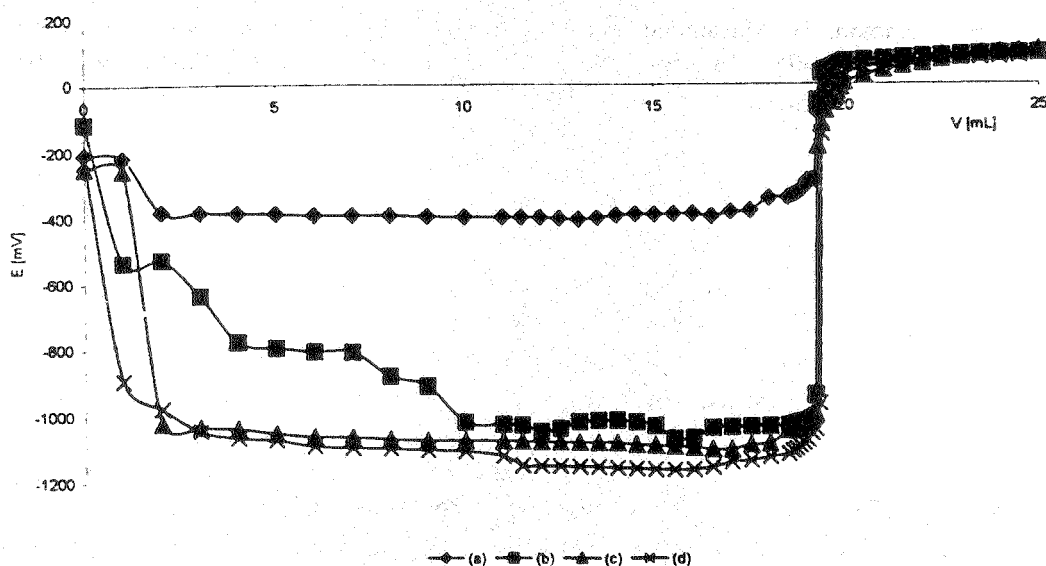


Fig. 3. Potentiometric titration curves of 100 μmol of 2-mercapto-2-thiazoline (1) with (a) gold wire, (b) gold plate, (c) platinum wire and (d) platinum plate indicator electrode

the material of the indicator electrode. This phenomenon is related to the adsorption processes and charging of the double layer, both occurring at the phase boundary of the indicator electrode.

Conclusion

Iodimetric analysis in alkaline solution is characterized by short analysis time, a high precision and accuracy, a simple procedure, commonly available reagent and the possibility of the determination over a wide order of magnitude. Moreover, alkaline medium provides stability of iodide ions in the presence of oxygen contrary to the acidic medium when iodide ions are oxidized in the presence of oxygen and light. The coulometric method is partly automated and as absolute one requires no use of standard solutions. Iodimetric analysis is the only direct method available for the determination of the described thiols in aqueous media.

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