

# Electrochemical study of some 2-mercapto-5-R-amino-1,3,4-thiadiazole derivatives using carbon paste electrodes

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## Abstract

The electrochemical study of some 2-mercapto-5-R-amino-1,3,4-thiadiazole derivatives was made by cyclic and linear sweep voltammetry using a carbon paste electrode (CPE, graphite/solid paraffin ratio 2:1) as working electrode and an Ag/AgCl reference electrode. The current–potential curves were recorded in anodic polarisation in  $-0.1$  and  $+1.3$  V range using aqueous solutions and different buffers (between pH 1.2 and 10.0), with 20 or 50  $\text{mV s}^{-1}$  sweep rate. The oxidation peak appears between  $+0.65$  and  $+0.70$  V due to disulphides formation. The 5-phenyl derivative has two oxidation peaks, the first at  $+0.45 \pm 0.03$  V and the second at  $+0.65 \pm 0.03$  V. The oxidation potentials are pH dependent, decreasing from  $0.9 \pm 0.1$  V at pH 1.2 to  $0.6 \pm 0.1$  V at a pH between 8.0 and 10.0. In some potential ranges depending on  $\text{p}K_{\text{a}}$  of molecules the oxidation potential and oxidation current are pH independent. Simple, precise and accurate voltammetric methods for the determination of these compounds were developed and validated in  $2.5 \times 10^{-6}$ – $7.5 \times 10^{-4}$   $\text{mol l}^{-1}$  concentration ranges. The detection limits were 2.3  $\mu\text{mol l}^{-1}$  for 5-amino-, 12.3  $\mu\text{mol l}^{-1}$  for 5-acetyl-amino-, 11.6  $\mu\text{mol l}^{-1}$  for 5-allyl-amino-, and 1.2  $\mu\text{mol l}^{-1}$  for 5-phenyl-amino-2-mercapto-1,3,4 thiadiazole derivatives. © 1998 Elsevier Science B.V. All rights reserved.

*Keywords:* Mercapto-1,3,4-thiadiazoles; Linear sweep voltammetry; Cyclic voltammetry; Carbon paste electrodes

## 1. Introduction

The substantial progress concerning the development of electrochemical instrumentation, observed during the last decade and also the great number of papers dealing with fundamental and applicative research, presently brings electroana-

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lytical techniques to the attention of researchers, in competition with optical or magnetic analysis methods. The redox reactions investigated can provide information regarding concentration, kinetics, reaction mechanisms, chemical status and other behaviours of the chemical compounds in solutions, and at the surface of the electrode. The static and dynamic electroanalytical techniques with their alternatives (controlled potential-large or small amplitude, controlled current, controlled-charge) allow us, by adjusting potentials, current intensities or time, to obtain maximum information from the system at hand. Electroanalytical techniques are used in a large range of activities, from pharmaceutical and biomedical analysis to polymerisation kinetics or enzyme reactions and to trace detection in environmental or forensic analysis [1,2].

The different types of carbon paste electrodes (CPE) are presently the subject of a great interest, this explains the number of papers published, describing the use of these electrodes in a wide range of electroanalytical domains (including drug analysis, polluting compounds analysis or the analysis of biologically active molecules) [3–5]. The CPEs offer several advantages for the electrochemical study of inorganic and organic compounds. As well as being cheap and easy to prepare and use, their electroanalytical performances are very good, different from those of other solid electrodes: low noise and background currents in a wide range of potentials. Other advantages are, a low risk of irreversible degradation of the surface, the simple renewal of their surface, they allow the easy modification through several techniques and preconcentration through adsorption–extraction.

The important biological role of thiol functions and of the S compounds generally speaking, is due to the fact that they are sensitive to oxidation, they can be easily transformed into disulphides or even sulphones, sulphinic or sulphonic acids in more energetic conditions [6].

On the other hand this is due to their special coordinative properties, a great number of S ligands and their complex compounds with metallic ions being known and studied [7].

All these explain the interest that the scientists working in the coordinative chemistry and electrochemistry field show to the S compounds, beginning with the polarographic studies of thiolic and disulphide groups of cysteine, cystine, glutathion or thiobarbituric acids [8–10], the anodic differential pulse voltammetric determination of 6-mercaptapurine or 6-thioguanine [11], or the liquid chromatographic electrochemical detection of 2-thiothiazolidine-4-carboxylic acid [12], to the use of some 2-mercaptobenzthiazoles or 1,3,4-thiadiazoles for the preconcentration and the detection of different metal ions by various electroanalytical techniques [13–18].

The study of the electroanalytical behaviour of some 2-mercapto-5-*R*-ammino-1,3,4-thiadiazole derivatives, synthesised through the cyclisation of disubstituted dithiourea, by A. Silberg, et al. [19], is motivated by the analytical applications of these heterocyclic compounds and also by their biological properties (bacteriostatics, plant growth inhibitors). Another reason for choosing the 2-mercapto-5-*R*-ammino-1,3,4-thiadiazoles for our research is the great number of studies concerning different complexes with most of the powerful polarising and polarisable cations made in the last four decades, studies that have revealed their analytical properties. The results of these researches were used to develop different analytical methods: gravimetric ( $\text{Pb}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Cd}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Ag}^{+}$ ,  $\text{Tl}^{+}$ ) [20,21], photometric ( $\text{Bi}^{3+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Pd}^{2+}$ ) [20,22], potentiometric, conductimetric ( $\text{Ag}^{+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Hg}^{2+}$ ,  $\text{Cd}^{2+}$ ) [21,23,24], and entalpicimetric [25].

The analytical interest shown for 2-mercapto-5-*R*-ammino-1,3,4-thiadiazoles, even nowadays, is due to their acido-basic and redox properties, as they can have tautomer forms:

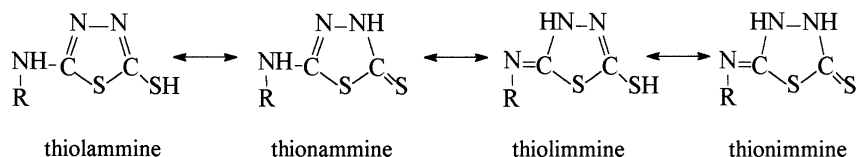
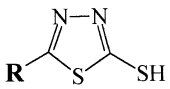


Table 1  
Structure and some physico-chemical properties of 2-mercapto-5-R-ammino-1,3,4-thiadiazoles

	R	Com- pound	M <sub>w</sub>	Melting point (°C)
	-NH <sub>2</sub>	MATD	133.2	245
	-NH-OC-CH <sub>3</sub>	MAcATD	175.2	294–296
	-NH-CH <sub>2</sub> -CH=CH <sub>2</sub>	MAIATD	173.2	133–134
	-NH-C <sub>6</sub> H <sub>5</sub>	MPATD	209.3	215–216
	-CH <sub>3</sub>	TDZ	132.2	182–186

The thiolic form cannot exist otherwise than solvated since the tautomeric thion-thiolic balance is shifted towards the thiolic form, when the polarity of the solvent and the pH increases.

Finally, the last reason for studying these compounds is their resemblance to a range of biologically-active molecules (enzymes, proteins) that have thiolic groups and molecules involved in cellular and tissular redox reactions. The 2-mercapto-5-R-ammino-1,3,4-thiadiazoles and other thiadiazoles can be used as models to establish some relations between their electrochemical properties and the pharmacological ones, or the biological action of structure related drugs or biochemically significant species.

## 2. Experimental

### 2.1. Apparatus

A Bruker E 100 potentiostat and XY Hewlett-Packard 7035 B recorder were used for linear sweep voltammetry, and a home-made wave generator (Institutul de Tehnologie Izo-topic si Moleculara, Cluj-Napoca) was added for the cyclic voltammograms. The measurements were performed with the use of a polarographic cell containing the CPE working electrode, SCE or Ag/AgCl (3 M NaCl) as ref-

erence electrodes and a platinum wire as the auxiliary electrode.

Samples were measured with 10, 100, and 500  $\mu$ l Hamilton syringes.

The pH of solutions was determined with a Chemcadet 5986-62 pH-meter (Cole Palmer) using a combined glass electrode.

All experiments were carried out at room temperature (22°C). The cyclic voltammograms were recorded in argon-deaerated solutions.

### 2.2. Reagents

All chemicals were of analytical grade (Merck or Reactivul Bucuresti) and were used as received. Glycocolle and citric acid were of pharmaceutical grade (FR X-Romanian Pharmacopoeia Xth ed.) and 2-mercapto-5-methyl-1,3,4-thiadiazole (TDZ Fw. 132.2) was obtained from ACROS Chemicals (Belgium).

The 2-mercapto-5-R-ammino-1,3,4-thiadiazole derivatives were prepared 'ex tempore', crystallised and purified in the organic chemistry laboratory using analytical grade ingredients (Merck). The identity of the four compounds was confirmed by elemental analysis, IR and NMR spectroscopy. Their structure and main physico-chemical properties are illustrated in Table 1. The stock solutions and buffer solutions were prepared using deionised water as follows.

### 2.2.1. $10^{-2}$ M 2-mercapto-5-R-amino-1,3,4-thiadiazole derivatives solutions

The following amounts: 0.03125 g 2-mercapto-5-amino-1,3,4-thiadiazole (MATD), 0.043 g 2-mercapto-5-acetylamino-1,3,4-thiadiazole (MAcATD), 0.040 g 2-mercapto-5-allylamino-1,3,4-thiadiazole (MAIATD), 0.050 g 2-mercapto-5-phenylamino-1,3,4-thiadiazole (MPATD), and 0.033 g TDZ, were weighed into 25 ml calibrated volumetric flasks; dissolved in ethylalcohol and diluted to the sign. The volumetric flasks were kept in darkness, to avoid photooxidation.

### 2.2.2. $10^{-1}$ M glycocole solution

Glycocole (7.505 g) and NaCl (5.850 g) were weighed into a 1 l calibrated volumetric flask, dissolved in deionised water and diluted to 1000 ml with deionised water.

### 2.2.3. Citric acid solution

A total of 21.002 g citric acid was weighed into a volumetric flask, dissolved in deionised water and diluted to 1000 ml with deionised water.

### 2.2.4. Disodium hydrogen phosphate solution

A total of 35.620 g  $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$  was weighed into a 1 l calibrated flask, dissolved in deionised water and diluted to 1000 ml with deionised water.

The buffer solutions were prepared by mixing into 100 ml calibrated flasks of different volumes of citric acid and disodium hydrogen phosphate solution (for pH 4.0–6.0 and 8.0), and glycocole solution, the pH being adjusted to the desired value by HCl (pH 1.0–3.0) or NaOH (pH 9.0 and 10.0). For the pH 7.0 we used a Radelkis (Hungary) buffer solution.

Two different CPEs were prepared, one based on paraffin oil and graphite from Metrohm (code 6280.1000) and one made by us with solid paraffin and graphite [5,26]. The paste or 'solid' paste was packed into the Teflon body of the electrode (1 mm i.d.). Before the measurements, the electrode was smoothed to a mirror finish using a clean paper card. The results obtained with the two pastes were quite similar but the

carbon paste prepared with solid paraffin had better mechanical properties. For that reason, in this paper we present and discuss only the results obtained with the 'solid paste'.

## 3. Results and discussion

### 3.1. Cyclic voltammetry

The study of the electrochemical behaviour of some 1,3,4-thiadiazole derivatives has been made by cyclic voltammetry at the carbon 'solid' paste electrode versus SCE reference electrode. The determination has been made by successively adding different volumes of  $1 \times 10^{-2}$  M alcoholic solutions of 1,3,4-thiadiazole derivatives in 50 ml phosphate buffer (pH 7.0), with a sweep rate of 20 and 50  $\text{mV s}^{-1}$ , at 500 nA and 1  $\mu\text{A}$  sensitivity.

The intensity-potential curves drawn in the potential range from  $-1.0$  to  $+1.0$  V revealed the fact that the main processes take place in the anodic range (Fig. 1a), and that is why further investigations have been made especially in this potential domain.

An irreversible oxidation peak at  $+0.48 \pm 0.02$  V can be seen in anodic polarisation. The second peak that appears at  $+0.95 \pm 0.02$  can be attributed to the further oxidation of the disulphide to sulphone [28], Fig. 1(b).

All the other 5-R-amino derivatives have behaved similarly, the first oxidation peak appears at  $+0.65 \pm 0.03$  V for MAcATD (Fig. 1c), at  $+0.50 \pm 0.02$  V for MAIATD (Fig. 1b), and at  $+0.45 \pm 0.02$  V for MPATD in agreement with previous results [27].

Close values of the oxidation potentials can be observed for the pairs MATD and MAIATD ( $+0.48$ , and  $+0.50$  V, respectively) (Fig. 1b), and MAcATD and TDZ ( $+0.62$ , and  $+0.60$  V, respectively) (Fig. 1c).

In the case of TDZ, there are two poorly defined oxidation peaks. (Fig. 1c).

### 3.2. Linear sweep voltammetry

The study of the electroanalytical behaviour of

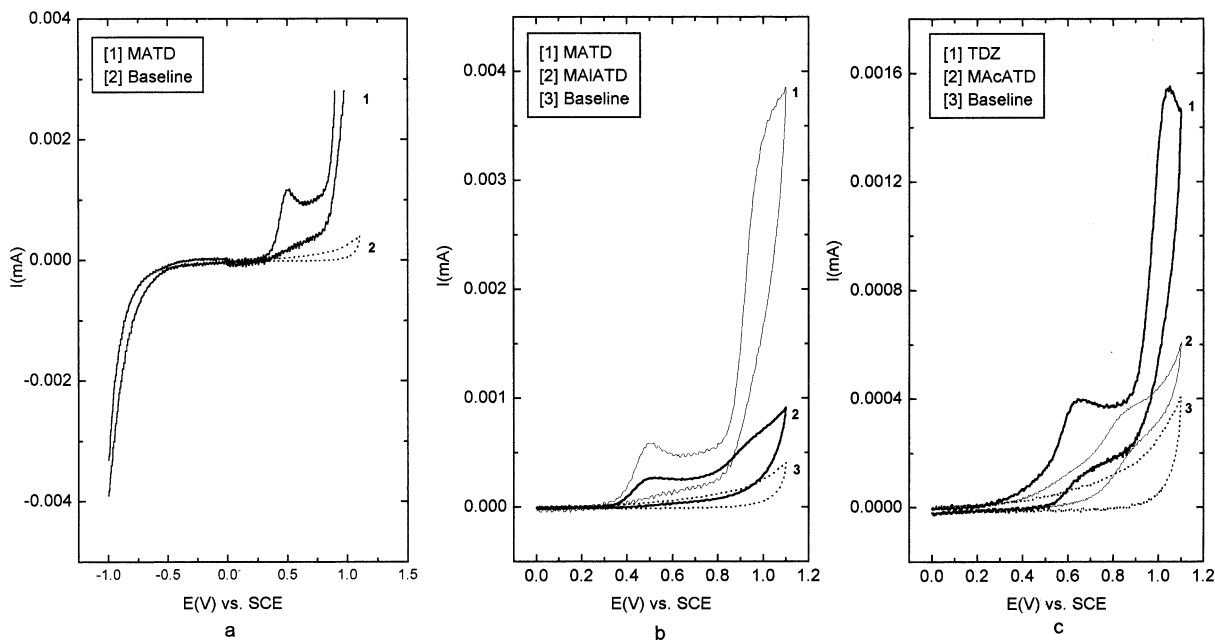


Fig. 1. Cyclic voltammograms of 1,3,4-thiadiazole derivatives. (a)  $6 \times 10^{-5} \text{ M l}^{-1}$  MATD;  $-1.0$  to  $+1.0$  V with CPE versus SCE, pH 7.0 buffer. (b)  $3 \times 10^{-5} \text{ M l}^{-1}$  MATD and  $3 \times 10^{-5} \text{ M l}^{-1}$  MAIATD;  $0$  to  $+1.0$  V with CPE versus SCE, pH 7.0 buffer. (c)  $1.3 \times 10^{-4} \text{ M l}^{-1}$  MAcATD and  $3 \times 10^{-5} \text{ M l}^{-1}$  TDZ;  $0$  to  $+1.0$  V with CPE versus SCE, pH 7.0 buffer.

the 1,3,4-thiadiazole derivatives has been performed by linear sweep voltammetry, using the solid-CPE.

The intensity/potential curves for MATD in water show an oxidation peak (Fig. 2a), whose potential decreases along with the raising of the pH values of the buffer, from  $+0.84$  V (pH 1.2) to  $+0.54$  V (pH 8.0). It is to be noted that the oxidation potential ( $E_{\text{ox}}$ ) is relatively pH independent ( $+0.82 \pm 0.02$  V) between 1.2 and 3.0, then it decreases in the pH range of 3.0–6.0 (60–70 mV per pH unit) and becomes stable again between 6.0–8.0 ( $E_{\text{ox}} = +0.56 \pm 0.03$  V) (Fig. 3a).

The current corresponding to the oxidation peak  $I_p$  also decreases within the pH range of 1.2–3.0, stays constant between pH 3.0–7.0 and then has a low increase at alkaline pHs (Fig. 4a).

In order to calculate the regression equation, oxidation curves were recorded using linear sweep voltammetry at pH 6.0. The electrodes are kept in the buffer solution about 60 s under stirring before each determination. Samples of 10–50  $\mu\text{l}$  of  $1 \times 10^{-2} \text{ M}$  MATD alcoholic solution we spiked;

in order to homogenise the solution the stirring was necessary after each replicate. The oxidation curves within the range of  $-0.1$  to  $+1.2$  V, at a speed of  $50 \text{ mV s}^{-1}$  on the 500 nA scale are illustrated in Fig. 2(a). Each determination was repeated three times, stirring the solution 60 s between replicates. The results have been statistically interpreted through the smallest square method.

The equation of the calibration curve in  $1.25 \times 10^{-5}$ – $7.5 \times 10^{-4} \text{ mol l}^{-1}$  concentration range is  $y = 1.72x + 12.5$  ( $r^2 = 0.998$ ) for the non-smoothed between replicates electrode, where  $y$  is in nA and  $x$  in  $\mu\text{l}$  (1  $\mu\text{l}$  contains 2.5 nmol MATD).

The reproducibility is good for the smoothed electrode and also without the smoothing of the surface of the electrode; there are no significant differences concerning the linearity, only a higher intensity of the oxidation current obtained.

For three series of six samples each, with concentrations between  $10^{-3}$  and  $10^{-5} \text{ mol l}^{-1}$ , done on 3 consecutive days, using each time

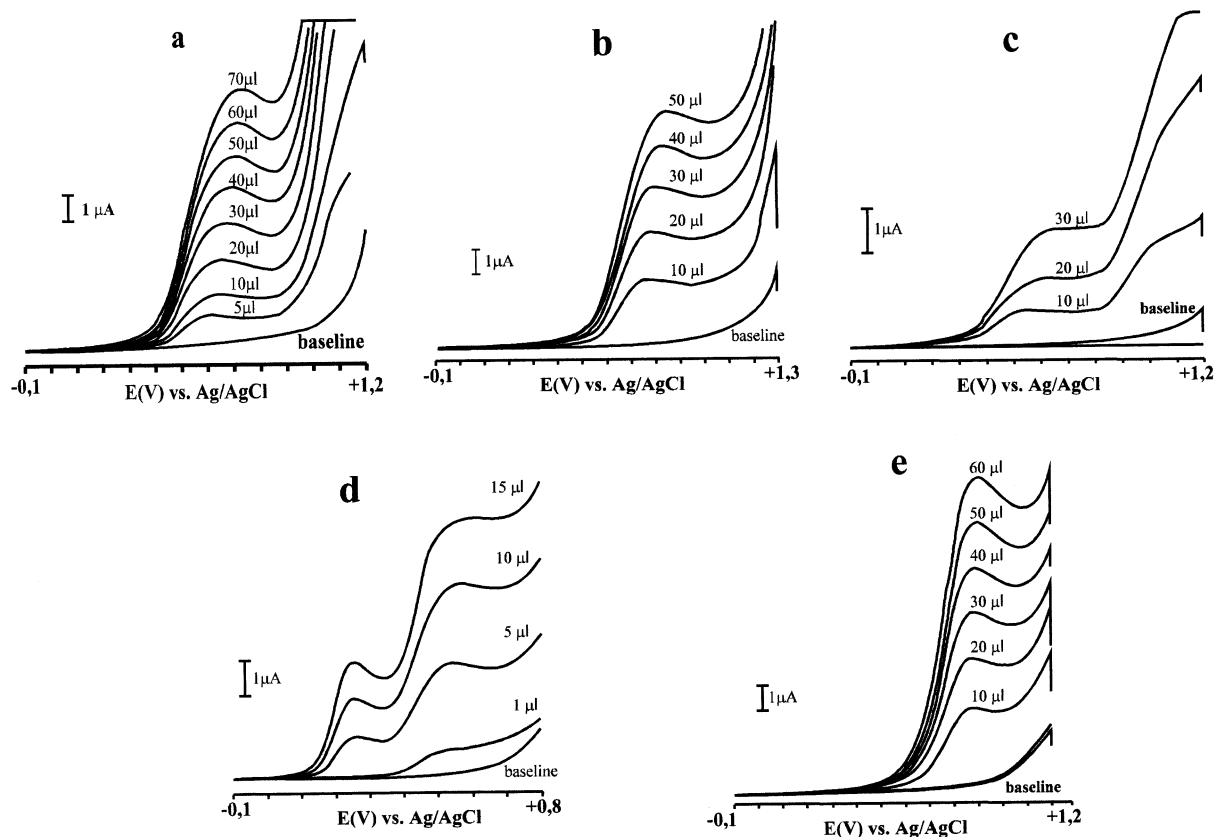


Fig. 2. Linear sweep voltammograms at different concentration ( $20 \text{ mV s}^{-1}$ ;  $1 \mu\text{A}$ ; 4 ml buffer pH 6.0) (a)  $1 \times 10^{-2} \text{ M}$  MATD alcoholic solution. (b)  $1 \times 10^{-2} \text{ M}$  MAcATD alcoholic solution. (c)  $1 \times 10^{-2} \text{ M}$  MAIATD alcoholic solution (500 nA). (d)  $1 \times 10^{-2} \text{ M}$  MPATD alcoholic solution ( $50 \text{ mV s}^{-1}$ ; 500 nA; pH 5.0). (e)  $1 \times 10^{-2} \text{ M}$  TDZ alcoholic solution (pH 5.0).

smoothed and renewed electrodes, the equation of calibration curve was  $y = 2.39x + 8.98$  ( $r^2 = 0.993$ ) where  $y$  is in nA and  $x$  in  $\mu\text{l}$  (1  $\mu\text{l}$  contains 2.5 nmol MATD) and the relative standard deviation (RSD) of the results 4.38%. The accuracy of the method was good and can be compared to other analytical methods,  $100 \pm 2\%$  and the detection limit is  $2.3 \mu\text{mol l}^{-1}$ . The equations of calibration curves, concentration ranges and validation parameters calculated for the studied 1,3,4-thiadiazoles are illustrated in Table 2.

For MAcATD in water there is an oxidation peak at  $+0.80 \text{ V}$  (Fig. 2b), that depends on the pH. Actually the oxidation potential showed three different domains: it is constant between pH 1.2 and 4.0, and has a value of  $0.95\text{--}1.0 \text{ V}$ , between pH 4.0 and 7.0 it decreases with a slope of  $75\text{--}80$

mV per pH unit and then it becomes pH independent again between pH 7.0 and 10.0 having a value of  $0.75 \pm 0.05 \text{ V}$  (Fig. 3b).

The current corresponding to the oxidation peak (Fig. 4b), decreases in a pH range of 1.2–2.0, has a relatively constant value in the pH range of 2.0–6.0 and decreases more at a pH  $> 6.0$ . At pH  $> 8.0$  the shapes of the oxidation curves are practically inoperable.

In order to calculate the regression line the recordings made were similar to MATD. The intensity-potential curves of samples between  $1.25 \times 10^{-5} \text{ M}$  and  $5 \times 10^{-4} \text{ mol l}^{-1}$  MAcATD, in the potential range of  $-0.1$  to  $+1.3 \text{ V}$ , in buffer solution (pH 6.0) and a sweep speed of  $20 \text{ mV s}^{-1}$ . The equations of the regression lines where  $y$  is in nA and  $x$  in  $\mu\text{l}$  (1  $\mu\text{l}$  contains 2.5

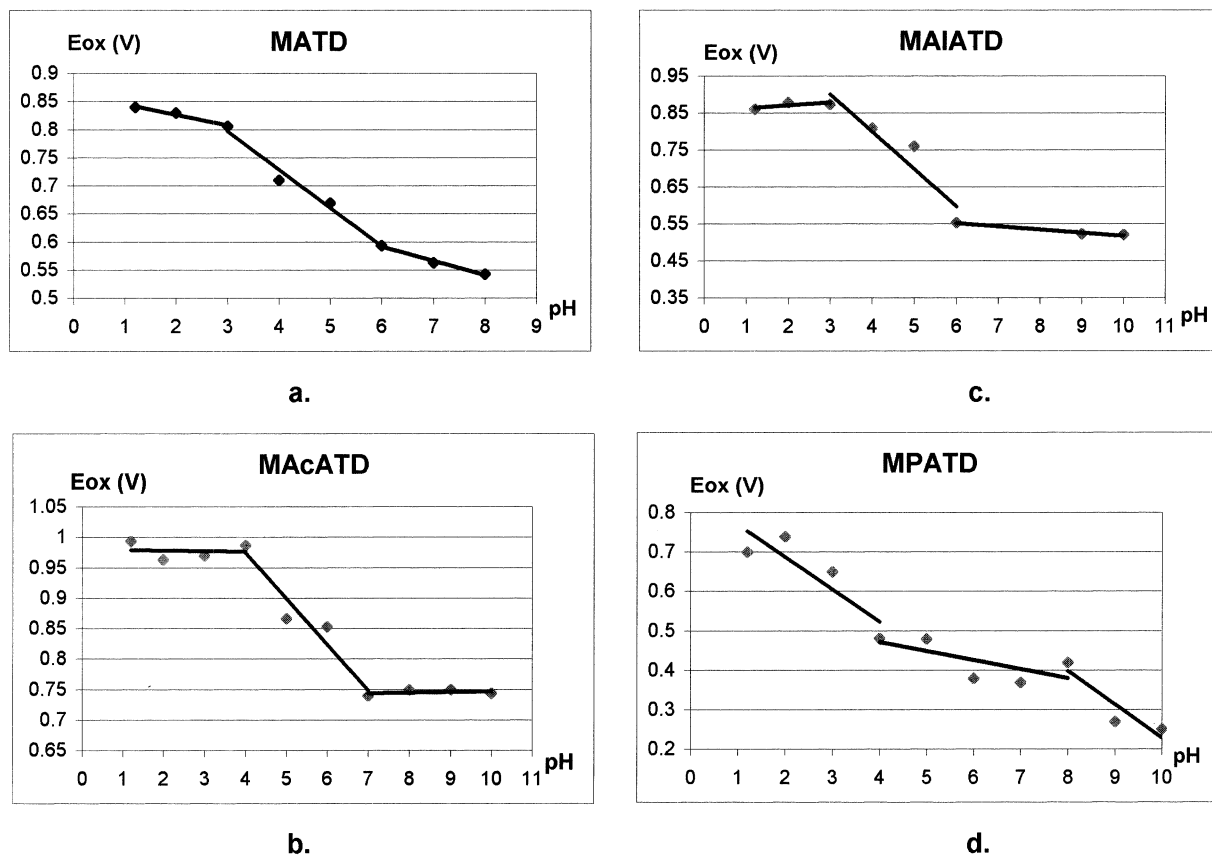


Fig. 3. Relative peak oxidation potential ( $E_{ox}$ ) versus pH ( $20 \text{ mV s}^{-1}$ ,  $500 \text{ nA}$ ) (a)  $2.5 \times 10^{-5}$ – $7.5 \times 10^{-5} \text{ M l}^{-1}$  MATD. (b)  $2.5 \times 10^{-5}$ – $7.5 \times 10^{-5} \text{ M l}^{-1}$  MAcATD ( $1 \mu\text{A}$ ). (c)  $2.5 \times 10^{-5} \text{ M l}^{-1}$  MAIATD. (d)  $3.7 \times 10^{-5} \text{ M l}^{-1}$  MPATD ( $50 \text{ mV s}^{-1}$ ).

nmol MAcATD) are  $y = 2.21x + 19.3$  ( $r^2 = 0.998$ ) for non-smoothed CPE and  $y = 3.36x + 1.99$  ( $r^2 = 0.999$ ) for a CPE smoothed before each determination, the differences being not significant (see Table 2).

For MAIATD in water, two oxidation peaks appear: the first one, at  $0.62 \pm 0.05 \text{ V}$ , well-shaped and the second one, at  $1.0 \pm 0.05 \text{ V}$ , as a shoulder (Fig. 2c). The oxidation potential of the first peak depends on the pH range as follows: for a pH range of 1.2–3.0 the potential is constant,  $+0.87 \pm 0.03 \text{ V}$ , in the pH range of 3.0–6.0 it decreases progressively and in the pH range of 6.0–10.0 becomes constant again,  $0.52 \pm 0.05$  (Fig. 3c). As a particularity we remarked the fact that the shape of the oxidation curves does not allow the measurement of the currents that correspond to the oxidation peak, except for the curves recorded at pH 6.0–7.0.

We can certainly claim that the current intensity decreases progressively with the increase of the pH, without giving the possibility to measure its amplitude, except for pH 6.0–7.0.

In order to calculate the regression line the same determinations as for MATD have been made in the case of MalATD. The intensity/potential curves in buffer with pH 6.0 of samples between  $2.3 \times 10^{-6}$  and  $4.6 \times 10^{-5} \text{ M}$  MAIATD in the potential range of  $-0.1$  to  $+1.3 \text{ V}$ , and a sweep speed of  $20 \text{ mV s}^{-1}$  on the  $500 \text{ nA}$  scale have been recorded (see Table 2).

The intensity-potential curves for MPATD [27], in the potential range  $-0.1$  to  $+1.3 \text{ V}$  confirmed the presence of the two oxidation steps (Fig. 2d), following researches being done in a limited domain of  $-0.1$  to  $+0.65 \text{ V}$ . In this range only the first step, the most stable and reproducible, can be

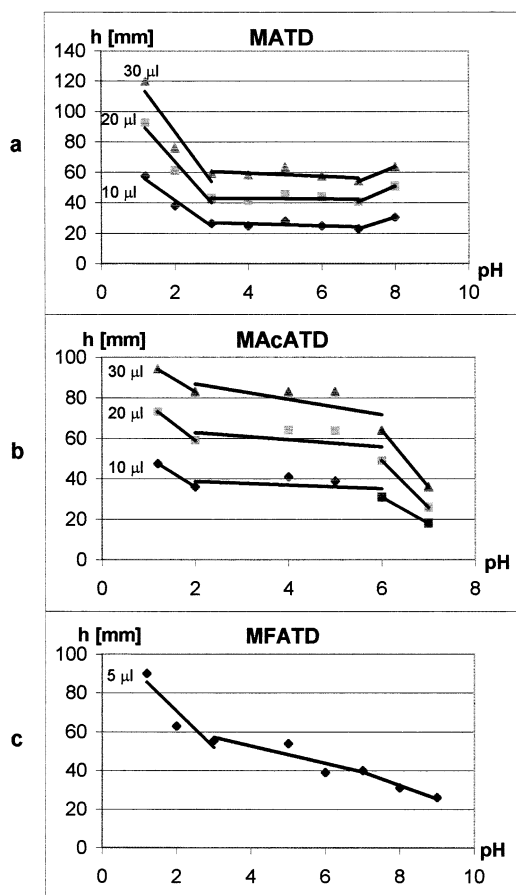
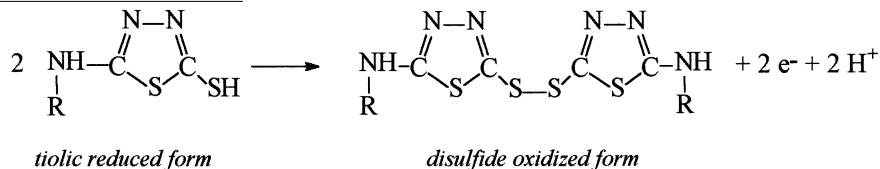


Fig. 4. Relative current intensity height (mm) versus pH ( $20 \text{ mV s}^{-1}$ ,  $500 \text{ nA}$ ). (a)  $2.5 \times 10^{-5}$ – $7.5 \times 10^{-5} \text{ M l}^{-1}$  MATD. (b)  $2.5 \times 10^{-5}$ – $7.5 \times 10^{-5} \text{ M l}^{-1}$  MAcATD ( $1 \mu\text{A}$ ). (c)  $1.25 \times 10^{-5} \text{ M l}^{-1}$  MPATD ( $50 \text{ mV s}^{-1}$ ).

observed. As for the other derivatives, if working in buffer solutions with a pH between 1.0 and 10.0 for a potential range  $-0.1 \text{ V}$  to  $+0.9 \text{ V}$ , a decrease of the oxidation potential from  $0.70 \pm 0.05$  to  $0.25 \pm 0.03 \text{ V}$  has been observed. The difference from the other three derivatives is that the oxidation potential decreases between pH 1.2 and 4.0 (slope of  $80 \text{ mV}$  per pH unit), and 7.0–10.0 (slope of  $80$ – $85 \text{ mV}$  per pH unit), respectively, having a



plateau in the region with a pH of 4.0–7.0 where  $E_{\text{ox}}$  is independent from the pH value (Fig. 3d). Also, in the pH range 1.2–4.0, only one oxidation peak appears, at  $0.67 \pm 0.03 \text{ V}$ ; above this pH value there is another oxidation peak, at  $0.6 \pm 0.05 \text{ V}$  (Fig. 2d). The current corresponding to the oxidation peak (Fig. 4c) decreases in three steps with different slopes, related to different pH values, 1.2–3.0, 3.0–7.0, and 7.0–9.0, respectively.

To calculate the regression line the same determination as for MATD have been made, recording the intensity-potential curves of samples between  $5 \times 10^{-6}$  and  $10^{-4} \text{ M}$  MPATD in a potential range of  $-0.1$  to  $+0.65 \text{ V}$ , in buffer solution pH 6.0, with a sweep speed  $50 \text{ mV s}^{-1}$  (see Table 2).

In order to elucidate the oxidation mechanisms we studied the electrochemical behaviour, in the same conditions, of TDZ, a compound that doesn't have an ammine-immine tautomerism.

The intensity-potential curves in water have similar shapes and an oxidation peak at  $0.93 \pm 0.03 \text{ V}$ . The value of the oxidation potential  $E_{\text{ox}}$  and the intensity of the signal depend on the pH, the shifts being similar to the ones of the amino-thiadiazoles; these facts suggest that the first oxidation peak is due to the thiol function. The shape of the intensity-potential curves at acid or alkaline pH values does not allow the measurement of the current intensity, the only valid results illustrated in Table 2, being the ones read for concentrations between  $5 \times 10^{-6}$  and  $10^{-4} \text{ mol l}^{-1}$  in buffer solutions with pH 5.0–6.0 (Fig. 2e).

The electrochemical behaviour of the five 1,3,4-thiadiazoles studied is similar, all the voltammetric observations suggest that the likely oxidation occurred at the thiol functionality as shown in the equation presented below. This should however be confirmed by performing large scale electrolysis and spectral characterisation of the oxidation products. For the same reasons the shift of the oxidation potentials and the variation of the current intensity are also similar.



Table 2  
Regression equation and statistical parameters of voltammetric determination of 1,3,4-thiadiazole derivatives

Com- pound	Calibration curve equation	$r^2$	Concentration (mol l <sup>-1</sup> )	RSD (%)		LOD ( $\mu$ mol l <sup>-1</sup> )	Accuracy
				Repeatability <sup>a</sup> ( <i>n</i> )	Reproducibility <sup>b</sup> ( <i>n</i> )		
MATD	$y = 17.2x + 12.5$	0.998	$1.25 \times 10^{-5}$ $-7.5 \times 10^{-4}$	3.92 (15)	4.38 (18)	2.3	100 $\pm$ 2%
MAcATD	$y = 3.36x + 1.99$	0.999	$1.25 \times 10^{-5}$ $-5 \times 10^{-4}$	4.13 (21)	4.94 (21)	12.3	101 $\pm$ 4%
MAIATD	$y = 5.71x - 1.32$	0.995	$2.5 \times 10^{-6}$ $-5 \times 10^{-5}$	5.29 (18)	5.74 (15)	11.6	100 $\pm$ 3%
MPATD	$y = 5.86x + 5.31$	0.998	$2.5 \times 10^{-6}$ $-1.25 \times 10^{-4}$	2.24 (41)	2.35 (36)	1.2	101 $\pm$ 2%
TDZ	$y = 1.98x + 14.7$	0.999	$5 \times 10^{-6}$ $-1 \times 10^{-4}$	1.78 (23)	2.08 (18)	2.8	100 $\pm$ 1%

<sup>a</sup> Same electrode surface, same day, same analyst, *n*, number of assays.

<sup>b</sup> Different electrode surfaces, different days, different analysts, *n*, number of assays.

All four 5-R-ammino-1,3,4-thiadiazoles have different behaviours concerning the oxidation potential within three pH ranges. Thus, the oxidation potentials of the 5-ammino-, 5-acetylammino- and 5-allylammino- derivatives are independent from the pH values in a domain that probably relates to the pK<sub>a</sub> values of the 5-immino- and 2-thiol- functions; excepting this domain,  $E_{ox}$  are decreasing together with the increase of the pH values due to the thiol-thiolate equilibrium.

The 5-phenylammino derivative has a completely opposite behaviour, probably explainable by the attractive electronic effects of the aromatic group. The difference in behaviour of the allyl derivative can be explained by the sensitivity to oxidation of the allyl radical and the ones of the 5-methyl derivative by the lack of ammine-immine tautomerism. The similarities of these two compounds could suggest either similar reducing properties or, better, similar electronic effects of the two substituents on the reducing thiol function.

#### 4. Conclusions

The electrochemical behaviour of the 5-methyl-, 5-ammino-, 5-acetyl-ammino-, 5-allyl-ammino- and 5-phenyl-ammino-2-mercapto-1,3,4-thiadiazoles has been studied, by cyclic and linear sweep voltammetry, with a CPE as a working electrode, an SCE, respectively, an Ag/AgCl as reference electrodes and an auxiliary Pt electrode.

Cyclic voltammetric studies of the five compounds revealed that the main oxidation processes due to the oxidation of the thiol function are irreversible.

The electrochemical study through linear sweep voltammetry within the potential range of  $-0.1$  to  $+1.3$  V, using different current densities, sweep rates, in buffer solutions with a pH range of 1.2–10.0, allowed the developing of some rapid, accurate and reproducible methods for the quantitative detection of these compounds. The CPE response was linearly related to the concentration of the 2-mercapto-1,3,4-thiadiazoles 5-substituted derivatives in the concentration range of  $10^{-5}$ – $10^{-6}$  mol l<sup>-1</sup>.

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