
Voltammetric and EQCM study of electrochemical oxidation of 5-substituted 1,3,4-oxadiazole-2-thiones

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The possibility to oxidise electrochemically 5-(6-methyl-2,4-dioxo-1,2,3,4-tetrahydro-3-pyrimidinyl)-methyl-1,3,4-oxadiazole-2-thione was investigated in order to synthesise its oxygen analogue. However, we have discovered that while using Pt electrodes the yield of the reaction is very low due to passivation of metal surface, caused by the irreversible adsorption of the products formed during electrochemical oxidation.

Key words: quartz microgravimetry, adsorption, electro-organic synthesis

INTRODUCTION

Electrochemical oxidation/reduction is one of the possible ways of heterogeneous synthesis. Presently it is rather widely applied for synthesis of organic compounds. On the other hand, by means of electrochemical technique it is possible to determine the mechanism of oxidation or reduction of a organic compound.

The object, 5-(6-methyl-2,4-dioxo-1,2,3,4-tetrahydro-3-pyrimidinyl)-methyl-1,3,4-oxadiazole-2-thione (compound **A**), chosen for the current study is a polyfunctional compound. Theoretically, 1,3,4-oxadiazole-2-thione atoms S or N(3) and pyrimidine ring atom N(1) or O atoms may take part in the reactions with electrophilic reagents [1]. Literature data show that 5-substituted 1,3,4-oxadiazole-2-thiones exhibit a their rather high biological activity. Namely, 5-pyrimidinyl substituted 1,3,4-oxadiazole-2-thiones (oxygen analogues to thiones) are known for their anti-inflammatory [2] or pesticidal action [3]. Taking all these facts into account, the first task set in this work was to investigate the electrochemical oxidation reaction of compound **A** and to evaluate the possibility of the electrochemical synthesis of its oxygen analogue.

Applying the method of the rotating ring-disk electrode, Bernstein and Hull [4] found that cyclic thiones dissolved in aqueous solutions can be oxidized up to an oxygen-containing analogue during the six-electron process. From voltammetric data, it has

been suggested that the oxidation of a thione compound occurs via formation of an intermediate disulfide di-cation. Woods [5] and later Moses [6] have proposed that the intermediate cation-radical formed in non-aqueous solutions may interact with a primary compound, what consequently leads to the formation of an oxygen analogue of thione.

EXPERIMENTAL

In this work, the methods of cyclic voltammetry (CV), electrochemical quartz crystal microbalance (EQCM) and chronoamperometry were used.

CV measurements were performed in a hermetic polytetrafluorethylene cell (volume 5 ml). Au wire 1 mm in diameter was used as working electrode. Only its cross-section area (geometric area 0.00785 cm²) was in contact with the solution. This type of construction of the working electrode enabled to easily prepare the Au surface before each experiment by polishing it with alumina powder and then washing with water in an ultrasound bath. The classical cyclic voltammetric curve obtained in H₂SO₄ solution served as a criterion of the purity of the Au surface. The real area of Au electrode surface was equal to 0.075 cm² as calculated from the measured oxygen adsorption-desorption charges. The reference electrode used in experiments was an Ag / AgCl / KCl(saturated) electrode placed into a separate vessel, which was isolated from the main cell by a Luggin capillary and a glass valve. All potentials are presented with respect to this electrode. Platinum foil was used as the counter electrode.

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For the synthesis of the oxygen analogue of compound **A** by means of electrolysis, the cell used was a closed 20 ml glass vessel containing two Pt electrodes of with an approximately 3 cm² geometrical area each. The cell solution was stirred by a magnetic stirrer.

For EQCM measurements, a hermetical cell similar to the one used for CV experiments was used. In this cell, one of the quartz sensor electrodes was used as the working electrode. Non-polished piezoelectric quartz crystals of 5 MHz main resonance frequency, coated with 200 nm thick platinum electrodes were used in this work. The area of the piezoelectric active surface was 0.283 cm². The evaluation of the purity of the Pt surface was the same as in the case Au surfaces – the classical CV curve obtained for the Pt electrode in H₂SO₄ solution served as the criterion of the Pt surface. The real area of the Pt surface is equal to 1.6 cm² as calculated from the measured hydrogen desorption charge.

All CV and EQCM measurement experiments were performed by using the measurement and control system built in the laboratory. The voltammetric system was centered around a single-amplifier type potentiostat, which allowed the working electrode to be grounded directly. In EQCM, harmonic oscillations of the quartz sensor were driven by a generator, which was built in our laboratory according to a scheme presented in [7]. The accuracy of measuring the resonant frequency of the quartz sensor was 1 Hz. The frequency was measured once a second by using a Ч3-32 frequency counter (Russia). The measurements were computer-controlled via 8 channel 16 bit A/D and 16 bit D/A converters (within the frame of IBM PC interface). The accuracy in measuring the current was 100 nA. All CV and EQCM measurements were controlled by software created at our laboratory.

Compound **A** and its separate components, namely, 5-methyl-1,3,4-oxadiazole-2-thione (compound **B**) and 6-methyl-2,4-dioxo-1,2,3,4-tetrahydro-3-pyrimidinyl (compound **C**), were synthesised and purified at the Department of Chemistry, Vilnius University [8]. 0.01 M aqueous solutions of these compounds were used for measurements. 0.1 M solution of twice-distilled H₂SO₄ was used as a supporting solution. Triple-distilled water was used for preparation of the solutions. Dissolved oxygen was removed from the solutions by bubbling purified N₂ prior to the measurements.

RESULTS AND DISCUSSION

At first, the oxidation potential of compound **A** was determined by measuring cyclic voltammetric curves in 0.1 M H₂SO₄ and 0.01 M compound **A** solution.

The obtained dependencies are presented in Fig. 1, where a solid line represents the first cycle of measurement and a dashed line after 10 cycles. In comparison with the CV measured in the supporting electrolyte (dotted line), one can observe an increase of the anodic current in the so-called oxygen adsorption area, *i.e.* in the positive potential region starting from ~1200 mV. It can be concluded that the oxidation of compound **A** begins at this potential along with the start of the gold electrode surface oxidation. The irreversibility of the oxidation process can be noted by comparing the anodic and cathodic currents, which shows that the charge consumed during the anodic process is about twice as large as the charge consumed during the cathodic process.

It is quite probable that the decrease of the current is related with the passivation of electrode surface due to formation of oxidation products. We also draw this assumption from the chronoamperometric measurements performed in the electrolysis cell. When a constant potential (1400 mV) is applied to the pure Pt electrode in the same solution (0.01 M compound **A** and 0.1 M H₂SO₄), the anodic current monotonous decreases and becomes negligible in 5 min whatever the intensity of stirring. At the beginning (the first hundred seconds when the potential is applied) the current is rather high (approximately 0.27 mA · cm⁻²). The possible explanation could be that the oxidized compound **A** remains adsorbed on the electrode surface.

A comparison of cyclic voltammograms shown in Fig. 2(a) and Fig. 1 shows that the oxidation potential of compound **A** in the case of Pt electrode remains close to the oxidation potential obtained for Au surface. Cycling the potential of Pt results in a decrease of the anodic current electrode

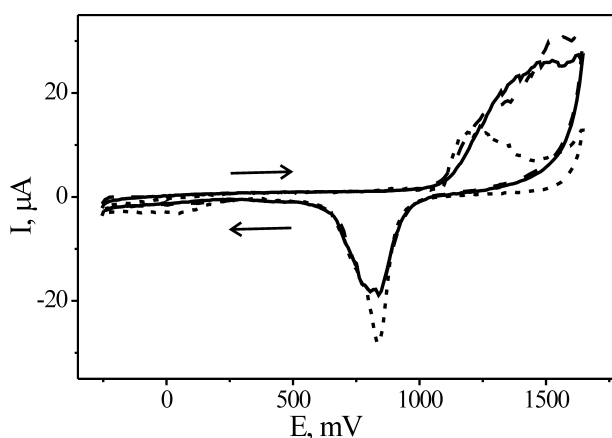


Fig. 1. Cyclic voltammograms of Au electrode in 0.1 M H₂SO₄ (dotted line) and in 0.01 M compound **A** + 0.1 M H₂SO₄: first scan (dashed line) and after 10 cycles (solid line). Potential sweep rate 100 mV/s

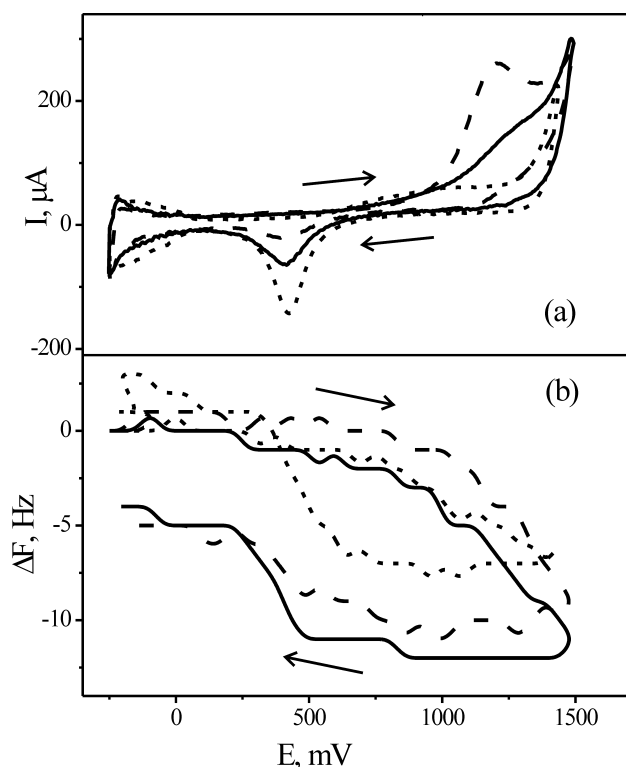


Fig. 2. Cyclic voltammograms (a) and resonance frequency change of Pt coated EQCM sensor (b) in 0.1 M H_2SO_4 (dotted line) and in 0.01 M compound **A** + 0.1 M H_2SO_4 solutions: first scan (dashed line) and after 10 cycles (solid line). Potential sweep rate 50 mV/s

(Fig. 2(a), curves shown by a dashed and a solid lines) similar to that observed for the Au electrode (Fig. 1). In addition, a decrease of the current in the hydrogen adsorption/desorption region from -250 mV to -50 mV (Fig. 2(a)) also supports the assumed passivation of the electrochemically active surface area.

In order to verify the possibility of the adsorption of compound **A** on a metal surface, an experiment of injection into an EQCM cell was performed. Figure 3 shows changes in the resonance frequency ΔF of quartz sensor with the Pt electrode during the time (no potential is applied). ΔF is observed only at the beginning of injection of the solution containing compound **A** into the supporting solution. Later, the frequency becomes constant and differs by approximately -20 Hz from the frequency measured before the injection. According to the Sauerbray equation ($\Delta m = -\text{const} \cdot \Delta F$), a increase / decrease of the electrode mass is directly related to a decrease / increase of frequency. Hence, some time following the injection the electrode mass becomes constant and larger than before the injection. Changes in solution viscosity, density and temperature can also influence the frequency, but these changes are too small to be of some impor-

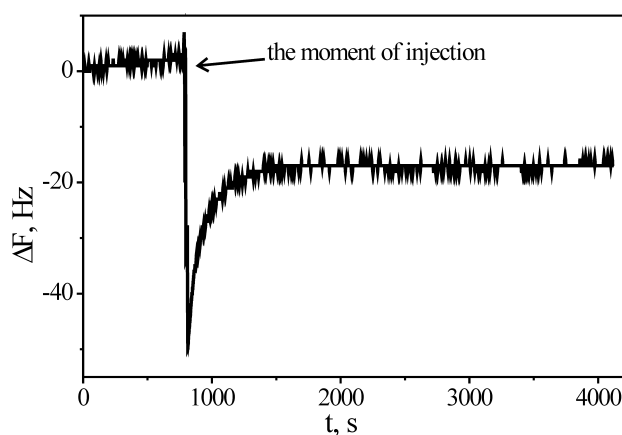


Fig. 3. Plots of frequency responses vs. the time during the injection of 0.01 M compound **A** + 0.1 M H_2SO_4 in 0.1 M H_2SO_4 solutions being in contact with the surface of EQCM sensor Pt electrode. Potential is not applied

tance for the injection experiment considered. First, the thermostatic conditions at 25 °C were the same for both the supporting and the injection solutions. Second, increase of the solution density-viscosity product $\rho\eta$ by a value of $0.1 \text{ kg}^2 \cdot \text{m}^{-4} \cdot \text{s}^{-1}$ may result in a decrease of resonant frequency by approximately 35 Hz [9]. In our case this change was much less than $0.1 \text{ kg}^2 \cdot \text{m}^{-4} \cdot \text{s}^{-1}$.

Figure 2 depicts the cyclic voltammograms and frequency dependencies on the potential, which were simultaneously measured by using a Pt-coated quartz sensor. The features of cyclic potential dependencies of quartz sensor resonant frequency (Fig. 2 (b)) obtained in the supporting solution (dotted line) and in the solution of compound **A** (dashed line) are rather similar, what should be related with the similarities in mass changes. The essential difference between these two dependencies is the fact that, when a solution contains an organic compound, the quartz sensor resonant frequency does not return to the initial value after each completed cycle. As the change of frequency is directly proportional to the change of mass (Sauerbray equation), it means that the mass of the electrode irreversibly increases after each oxidation–reduction cycle. For the sensor used, the sensitivity constant is equal to $4.8 \text{ ng} \cdot \text{Hz}^{-1}$, then during one cycle the mass increase is approximately 24 ng. This result is in agreement with our earlier assumption that the electrode passivation occurs due to the irreversible adsorption of the products of electrochemical reaction on the metal surface. During the oxidation / reduction cycles the features of the frequency curves do not change much (Fig. 2 (b), curves (dashed and solid lines)).

An accumulation of the products formed during oxidation of compound **A** was also observed under potentiostatic conditions. Changes of the current and

of the quartz resonator frequency with time were measured at 1200 mV. A monotonous decrease of both the current and the resonant frequency was observed (Fig. 4). The largest changes appeared within 130 s. After 600 s the total decrease in frequency was equal to 49 Hz. Such a decrease corresponds to the change of electrode mass equal to 235.2 ng. Assigning all mass change to the adsorption of compound A (molar mass 240 g/mol) gives 0.98 nmol. The density of surface atoms of polycrystalline platinum is $1.31 \cdot 10^{15} \text{ cm}^{-2}$ [10]. Hence, it can be concluded that the surface coverage is approximately 28%.

It has been already mentioned that according to literature data several functional groups of compound A may interact with electrophilic reagents [1]. In order to determine the most electrochemically active group, experiments were performed using different fragments of compound A – oxadiazole ring (compound B) and pyrimidine ring (compound C). Figure 5 depicts the simultaneously measured cyclic voltammograms (a) and cyclic potential dependencies of the change of quartz sensor resonant frequency (b) in solutions containing compound B (solid line) and compound C (dashed line). From the voltammograms, it is clear that the most active compound is oxadiazole-thione – its oxidation starts at a $\sim 600 \text{ mV}$ electrode potential. Referring to the data from the literature [4], one may conclude that at this potential the oxidation of thione group begins. As in the case of compound A, the cyclic potential dependent change of frequency has a similar mismatch of resonant frequency (approximately 2 Hz) at the start and at the end of a cycle. This also may be related to the irreversible adsorption of oxidation products on the Pt surface. When the solution contains compound C, the voltammogram

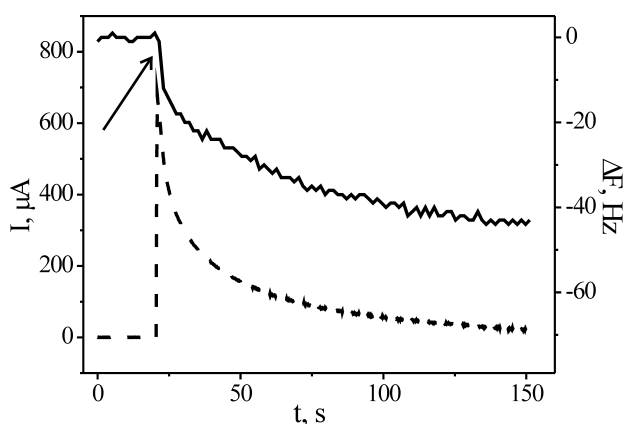


Fig. 4. Plots of current (dashed line) and frequency (solid line) responses vs. time in 0.01 M compound A + 0.1 M H_2SO_4 solution. Arrow denotes the time from which the potential equal to 1200 mV is applied

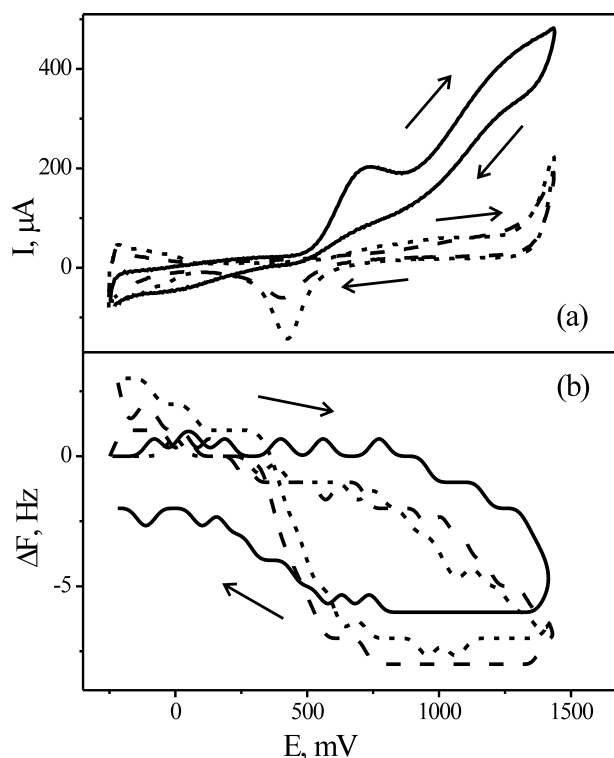


Fig. 5. Cyclic voltammograms (a) and resonance frequency change of Pt-coated EQCM sensor (b) in 0.1 M H_2SO_4 (dotted line), 0.01 M compound B + 0.1 M H_2SO_4 (solid line) and 0.01 M compound C + 0.1 M H_2SO_4 (dashed line) solutions. Potential sweep rate 50 mV/s

and frequency change are similar to those measured in the supporting electrolyte. However, in the case of compound C one can observe a decrease of hydrogen adsorption / desorption currents in a cyclic voltammogram. Probably it occurs due to passivation of electrode surface during the adsorption of the pyrimidine ring. The fact that the overall change of the resonant frequency during the whole potential cycle is slightly lower (8 Hz) than that obtained in compound A solution (12 Hz) might be related with the so-called electrode-aging effect [11], as there were made over 100 oxidation/reduction cycles inbetween the measurements, the results of which are presented in Fig. 2(b) (solid line) and Fig. 4(b) (solid line). A more detailed and quantitative evaluation of these effects could be carried out by applying the quartz sensor admittance technique and analysis [12].

CONCLUSIONS

One of the main factors that ensure a high yield of the reaction during electrochemical synthesis of organic compounds is the right choice of electrode material. The products produced during the reaction may interact specifically with the electrode sur-

face, thus “polluting” it. In the present work it is shown that the low yield of the electrochemical oxidation of pyrimidinyl-oxadiazole-thione (compound A) using inert Pt electrodes should be assigned to the passivation of metal surface. Such “poisoning” of the electrode can occur due to adsorption of the products formed during oxidation. The accumulation of these products was observed both in CV and potentiostatic experiments. In addition, CV measurements have shown that the pyrimidine fragment, which probably isn't involved in the electrochemical reaction, may also block the Pt surface to some extent.

The cyclic potential dependent change of resonant frequency shows that the desorption of oxidation products from the surface is rather negligible. Comparison of the data obtained in a pyrimidinyl-oxadiazole-thione solution with the data obtained in solutions containing fragments of the latter compound leads to the conclusion that only the oxadiazole-thione part is electrochemically active. Besides, it can be noted that the pyrimidine part of compound A increases the oxidation potential of thione group approximately from 600 mV to 1200 mV. However, to prove definitely that only thione groups take part in electrochemical oxidation further investigations are necessary.

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5-PAKEIŠTŲ OKSADIAZOL-2-TIONŲ
ELEKTROCHEMINĖS OKSIDACIJOS TYRIMAS
VOLTAMPEROMETRIJOS IR KVARCO
MIKROGRAVIMETRIJOS METODAIS

S a n t r a u k a

Tirta galimybė elektrochemiškai oksiduoti 5-(6-meti-2,4-dioksa-1,2,3,4-tetrahidro-3-pirimidinil)-metil-1,3,4-oksadiazol-2-tioną, tuo būdu susintetinant jo deguonies analogą. Tačiau nustatyta, kad taikant Pt elektrodus tokios reakcijos išeiga yra labai maža dėl metalo paviršiaus pasyvacijos. To priežastis yra produktų, susidariusių elektrocheminės oksidacijos metu, negrįžtama adsorbcija.