



## Preparation and Characterization of New Compound by Electrochemical Oxidation of Methyl Catechol in the Presence of 2-Thiouracil

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### Abstract

The electrochemical oxidation of methyl catechol in the presence of 2-thiouracil (as a nucleophile) has been performed in aqueous solutions using cyclic voltammetry and controlled-potential coulometric techniques. The electrochemical behavior of methyl catechol in the presence of 2-thiouracil was investigated. The electrochemical synthesis of this compound has been successfully performed in an undivided cell in a good yield and purity and was characterized by IR, <sup>1</sup>H and <sup>13</sup>C NMR. According to the results obtained from <sup>1</sup>H NMR, <sup>13</sup>C NMR it is concluded that methyl o-quinones are attached in all probably only in the its C4 position to 2-thiouracil from S position leading to the formation of 2-(4,5-dihydroxy-2-methylphenylthio) pyrimidin-4(3H)-one (DMPTP).

**Keywords:** Methyl catechol; 2-Thiouracil; Electro-organic synthesis

### 1. Introduction

It should be noted that the electrochemical method is very suitable method for production of reactive species under mild conditions [1]. Electrosynthesis presents many advantages over classical routes such as high efficiency, lower prices of reagents and high reactivity of products [2]. The neutral organic compounds through electron transfer reactions are converted to cationic or anionic radicals. These reactive carbon species are utilized in various synthetic transformations, especially carbon-carbon bond formations [1,3]. Oxidation and reduction of functional groups are also important transformations in organic synthesis, and the electrochemical methods for such transformations are greener way [4]. Electrochemical oxidation of different

organic compound has been studied in the presence of various nucleophile in aqueous solution [5-9]. More recently, the use of catechol derivatives as precursors for electrogenerated electrophiles in 1,4-Michael additions has been described. Nematollahi and co-workers reported the electrochemical oxidation of catechol and 4-methylcatechol [10], 4-tert-butylcatechol and 3,4-dihydroxybenzaldehyde [11], 3-methylcatechol and 2,3-dihydroxybenzaldehyde [12], in methanol and also showed that these compounds undergo methoxylation reactions, to give the related methoxy-o-benzoquinone. A similar reaction was first exploited by Compton and co-workers to detect and quantify L-cysteine [13,14]. It has been shown that o- and p-diphenols can be oxidized electrochemically to o- and p-quinones, respectively. The quinones formed are quite reactive and can be attacked by a variety of nucleophiles such as,

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2-thiouracil [15] benzene sulfonate [16], 4-hydroxy-coumarin [17,18], 1,3-diethyl-2-thiobarbituric acid [12,19], and 4-hydroxy-6-methyl-2-pyrone [20] and were converted to the corresponding addition products. The importance of these compounds has encouraged us to synthesize a new compound named as, 2-(4,5-dihydroxy-2-methylphenylthio)pyrimidin-4(3H)-one. To the best of our knowledge, the electro-synthesis of such compound has not yet been reported in the literature. The present work has led to the development of a simple electrochemical method for the synthesis of this new compound by the electrochemical oxidation of methyl catechol in the presence of 2-thiouracil in the aqueous solutions. The mechanistic details of the reaction are analysed using electrochemical techniques. The synthesis of this new compound from thiadiazaflorenone group is performed in a high purity and selectivity and also in an excellent yield. In this work, first the electrochemical behavior of methyl catechol in the presence of 2-thiouracil is investigated. Then, the reactions involving the additions of this thiol to the electrochemically generated methyl o-quinone in a procedure with relatively high selectivity and purity is reported. IR, <sup>1</sup>H and <sup>13</sup>C NMR were used to characterize the new synthesized product.

## 2. Experimental

### Reagents

2-Thiouracil and methyl catechol were prepared from Merck and used as received. All other chemicals were of analytical reagent grade from Merck. All aqueous solutions were prepared with doubly distilled de-ionized water.

### Apparatus

Cyclic voltammetric experiments were performed with a Metrohm Computrace Voltammetric Analyzer Model 757 VA. A conventional three-electrode system was used with a glassy carbon disc (2 mm diameter), a saturated Ag/AgCl reference electrode, and

a platinum wire as the counter electrode. Controlled-potential coulometric experiments were performed using an Autolab potentiostat-galvanostat Model PGSTAT 30. The working electrode that used in controlled-potential coulometry and macro scale electrolysis was an assembly of four carbon rods (6 mm diameter and 4 cm length) and large platinum gauze constituted the counter electrode. The working electrode potential were monitored vs Ag/AgCl reference electrode (from Azar Electrode, Iran). NMR spectra were recorded on a Bruker DRX-500 Avance Instruments. Chemical shifts  $\delta$  are reported in ppm relative to DMSO (1H:  $\delta$ = 2.50/TMS) and DMSO-d<sub>6</sub> (13C:  $\delta$ =39.7/TMS) as internal standard. IR spectra were recorded on a Matson FT-IR Spectrophotometer Model 1000 R. A digital pH/mV/Ion meter (metrohm model 2500) was used for preparing of the buffer solutions, which were used as the supporting electrolyte in voltammetric and coulometric experiments.

### Electro-organic synthesis

In a typical procedure, 100 ml of phosphate buffer solution (0.15 M with pH 7.0) was pre-electrolyzed at the chosen potential (400 mV vs Ag/AgCl), in an undivided cell. In after step, 1 mmol methyl catechol (a) and 1 mmol 2-thiouracil (c) were added to the cell. The electrolysis was terminated when the decay of the current became more than 95%. During the electrolysis, the process was interrupted several times and graphite electrode was washed in acetone in order to reactivate it. At the end of electrolysis, a few drops of phosphoric acid were added to the solution and cell was placed in refrigerator overnight. The precipitated solid was collected by filtration and re-crystallized from a mixture of methanol/acetone (product yield 80%). After re-crystallization process, IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR were used for characterization of the product.

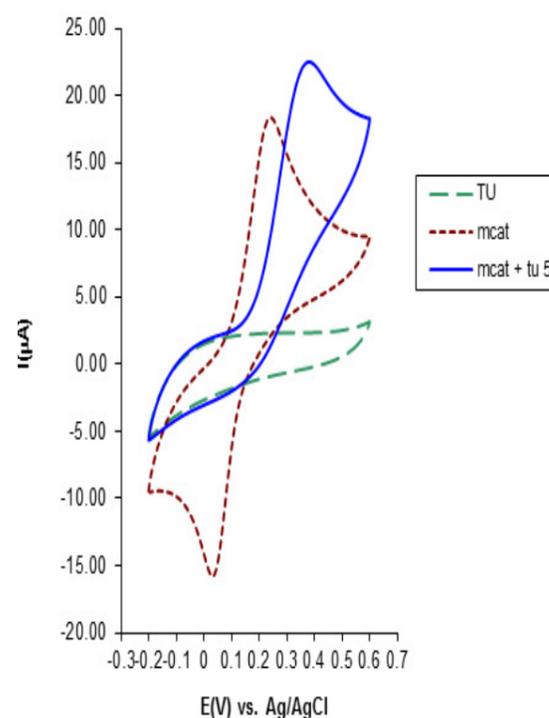
### Characteristics of the product

4,5-dihydroxy-2-methylphenylthio)pyrimidin-4(3H)-one. IR(KBr):3200, 3075, 1695,

1535, 1441, 1366, 1209.8, 1095.7, 928.9, 793.9 cm<sup>-1</sup>. <sup>1</sup>H NMR,  $\delta$  (500 MHz DMSO-d<sub>6</sub>): 2.1 (s, 3H); 5.8 (t, 1H); 6.37 (d, 1H); 6.53 (s, 1H); 6.58 (d, 1H); 7.36 (d, 1H); 8.59 (s, 1H); 12.37 (s, 1H). <sup>13</sup>C NMR,  $\delta$  (500MHz DMSO-d<sub>6</sub>): 21.2, 106.1, 116.3, 117.2, 120.3, 128.7, 142.9, 143.6, 145.8, 161.8 and 176.9

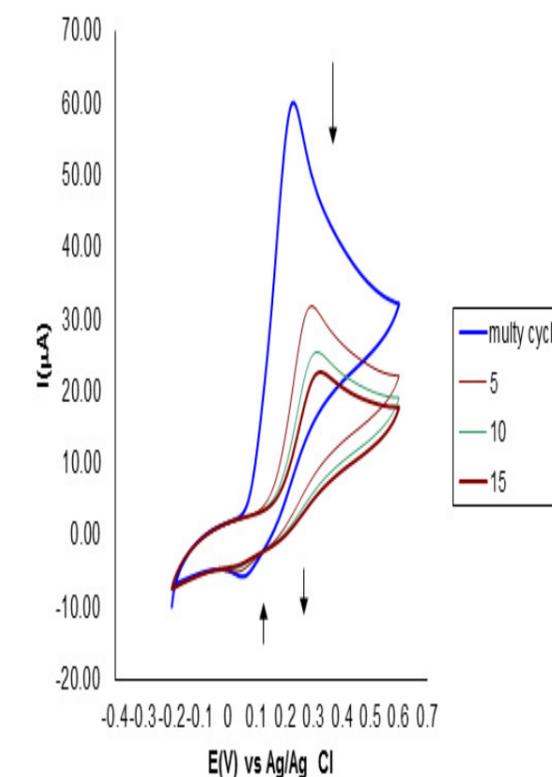
## 3. Result and Discussion

Cyclic voltammetry of 1 mM solution of methyl catechol, 1mM thiouracil and mixture of methyl catechol/thiouracil at the surface of glassy carbon electrode as working electrode and in an aqueous solution containing 0.15 M phosphate buffer (pH 7.0) as the supporting electrolyte have been shown in Fig. 1. As can be seen, one anodic and a corresponding cathodic peak was obtained, which corresponds to the transformation of methyl catechol to o-benzoquinone and vice versa within a quasi-reversible two-electron process. A peak current ratio (IPC /IPA) of nearly unity, particularly,



**Fig. 1.** Cyclic voltammograms of 1 mM methyl catechol (mcat), 1 mM 2-thiouracil (TU) and mixture of methyl catechol/thiouracil (mcat+tu 50) at a glassy carbon electrode (mcat-tu). Supporting electrolyte was 0.15 M phosphate buffer (pH 7.0); scan rate was 50 mV

during the repetitive recycling of the potential, can be considered as a criterion for the stability of methyl o-quinone produced at the surface of electrode under the experimental conditions. The electro-oxidation of 2-thiouracil was also studied. For thiouracil no redox peak observed. According to the voltammogram of 2-thiouracil, it was revealed that this compound is electrochemically inactive in the range of potential studied. The electro-oxidation of methyl catechol was studied in detail in the presence of 2-thiouracil as a nucleophile. The voltammogram exhibits an anodic peak at approximately same potential (250 mV). Under these conditions, the cathodic counterpart of the anodic peak completely disappeared. The multi-cyclic voltammetric studies of methyl catechol in the presence of 2-thiouracil show that the potential of anodic peak does not vary in consecutive cycles but, a new cathodic peak appears with an Epc value of 214 mV (Fig. 2). This new peak can

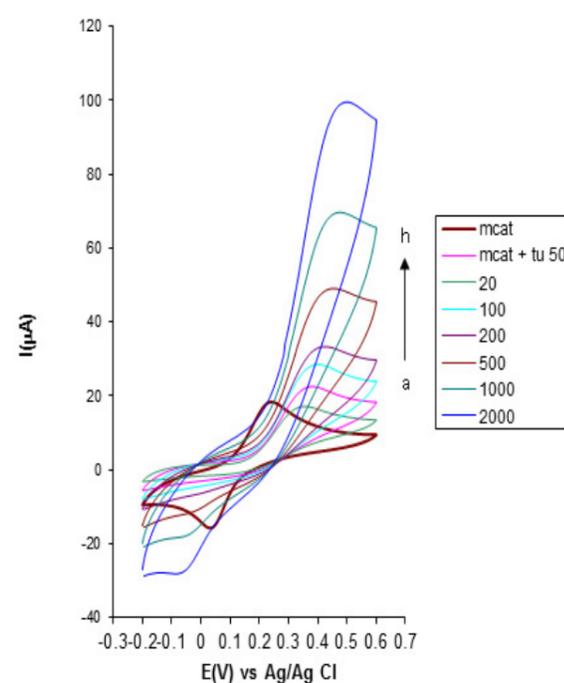


**Fig. 2.** Multi-cyclic voltammograms of 1 mM methyl catechol in the presence of 1 mM 2-thiouracil at a glassy carbon electrode. Supporting electrolyte was 0.15M .phosphate buffer (pH 7.0); scan rate was 50 mV/s

be related to electrochemical reduction of the product coming from the anodic oxidation of d, and was also investigated using the controlled-potential coulometric technique. The decrease in anodic current peak in next scans can be attributed to the consumption of methyl catechol in reaction with methyl o-quinone.

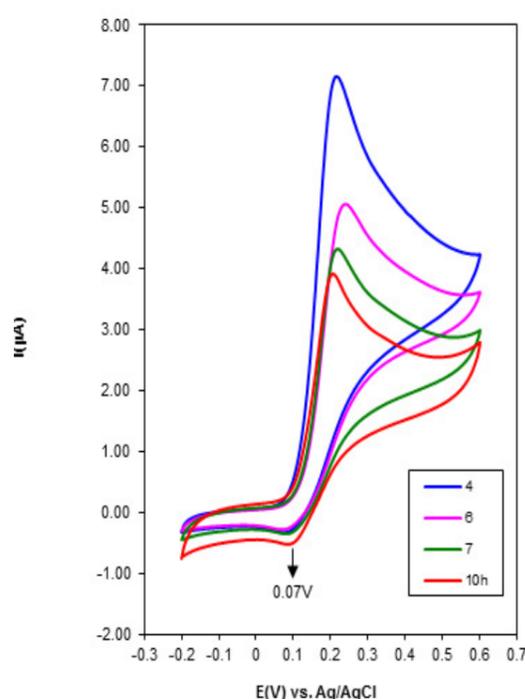
Further, it can be seen from Fig. 3 that anodic peak current (for oxidation of methyl catechol in the presence of 2-thiouracil) is increased with the addition of potential scan rate. On the other hand, the current function for this anodic peak ( $IP A / v^{1/2}$ ) decreases slightly with increasing the potential scan rate. Such a behavior is adopted as indicative of an ECE mechanism.

Nucleophilic attachment of 2-thiouracil is too rapid so that, even in very high sweep rates of potential (greater than 2000 mV/s), the cathodic peak for reduction of methyl o-quinone cannot be seen.

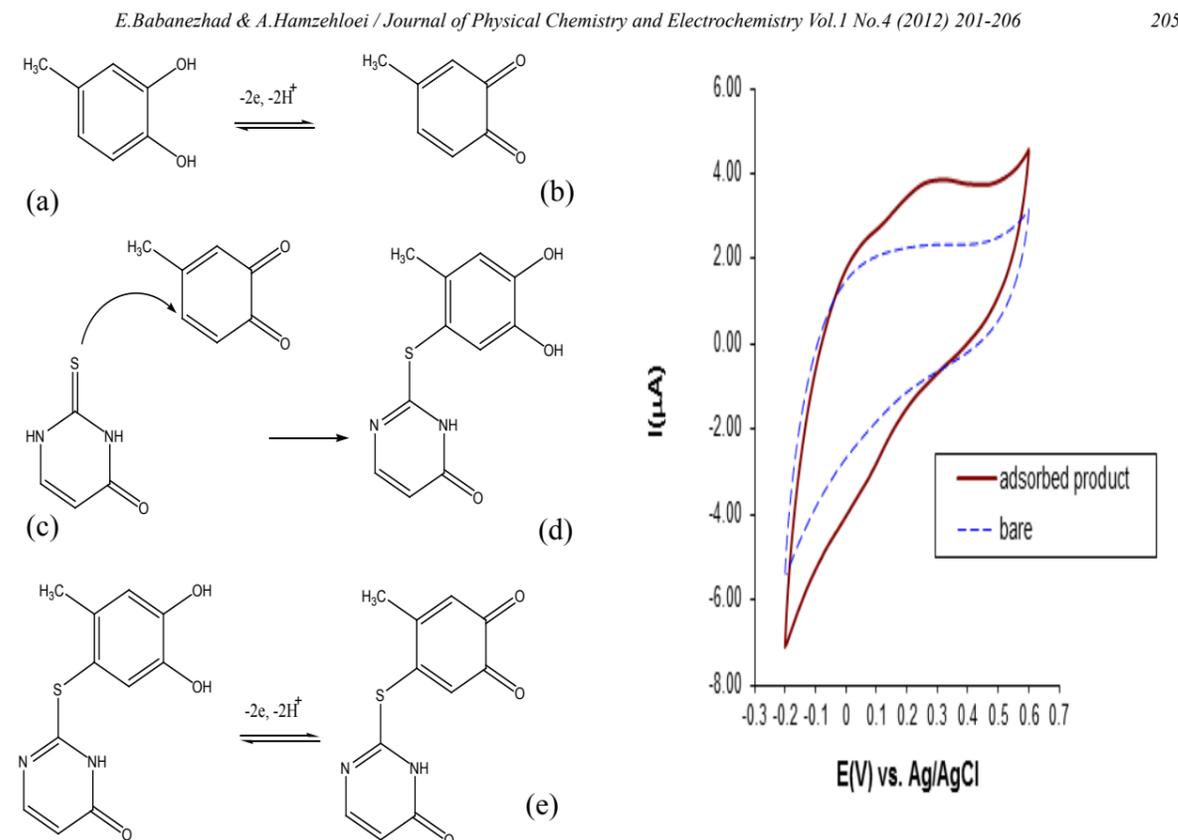


**Fig. 3.** Typical cyclic voltammograms of 1 mM methyl catechol, 1 mM methyl catechol in the presence of 1 mM 2-thiouracil at a glassy carbon electrode and at various scan rates. (a) methyl catechol at scan rate of 50 mV s<sup>-1</sup> and scan rates from (b) to (h) are: 20, 50, 100, 200, 500, 1000 and 2000 mV s<sup>-1</sup>, respectively. Supporting electrolyte was 0.15 M phosphate buffer (pH 7.0).

The controlled-potential coulometry was performed in buffered solutions (0.15 M phosphate pH=7) containing 1 mM of both methyl catechol and 2-thiouracil at the constant anodic potential of 0.400 V vs Ag/AgCl. The monitoring of electrolysis progress was carried out using cyclic voltammetry. It is shown that, proportional to the progress of coulometry, the anodic peak current for methyl catechol oxidation decreases (Fig. 4). As the coulometric process proceeded, a new cathodic peak is appeared at the potential of 214 mV. As the electrolysis time increases, the current of this new cathodic peak is increased and finally becomes constant. This is due to the limitation in the solubility of the product in aqueous solution. Stabilization of cathodic current peak, as the time of electrolysis is increased, can be another evidence for the saturation of solution by electrolytic product. As the coulometric process is terminated, the charge consumption becomes about per molecules of



**Fig. 4.** Cyclic voltammograms of 1 mM methyl catechol in the presence of 2-thiouracil at a glassy carbon electrode during controlled-potential coulometry at +0.40 V vs Ag/AgCl. CV curves are corresponding to solution after (a) 4, (b) 6, (c) 7, (d) 10 h. Potential scan rate was 50 mV s<sup>-1</sup>.



**Scheme 1**

methyl catechol. On the otherhand, as can be seen in Scheme 1 and also from NMR, the mechanism of interaction of methyl catechol with 2-thiouracil is based on a 4e reaction. Excess of two electrons in coulometric results corresponds to the ability of reaction product for anodic oxidation (d in Scheme 1). The result of cyclic voltammetric studies on the separated coulometric products shows that the potential of oxidation of this compound is similar to the methyl catechol (Fig. 5). At the end of coulometry, the ratio of  $IP_a = IP_c$  becomes 1, which reveals that the final product shows a reversible behavior. But these studies show that the reduction potential for this product is different from methyl catechol and appearance of a new cathodic peak at the potential of about 214 mV corresponds to this compound. These observations allow us to propose the pathway in Scheme 1 for the electro-oxidation of methyl catechol in the presence of 2-thiouracil (c). According to our results, it seems that the nucleophilic reaction

**Fig. 5.** Cyclic voltammogram of bar electrode and separated coulometric product (DMPTP) at glassy carbon electrode. Supporting electrolyte was phosphate buffer (0.15 M, pH=7.0) and scan rate was 50 mV s<sup>-1</sup>.

between 2-thiouracil (c) and methyl o-quinone (b) is fast enough and favors the progress of the subsequent reactions leading to the formation of product (d). There are two nitrogen atoms and a sulfur atom in the structure of 2-thiouracil. Sulfur is more nucleophilic than nitrogen, even though nitrogen is more basic than sulfur. Therefore, it seems that nucleophilic attachment must be performed from sulfur atom. Based on these observations, it is clear that very fast nucleophilic attachment of 2-thiouracil from S position to methyl o-quinone results in formation of the intermediate of (d), which with respect to presence of a donating group in its structure, more easily oxidized in the forward (anodic) scan in comparison to methyl catechol. According to the results obtained from <sup>1</sup>H NMR, <sup>13</sup>C NMR it is concluded that methyl o-quinones are attached in all probably only in the its C4 position to 2-thiouracil from S position (c) leading to the formation of only

one final product (d).

#### 4. Conclusion

The electrochemical oxidation has the potential for developing more green chemical synthesis. The reactivity of intermediates can be controlled more easily with electrochemical methods. The present results show the anodic oxidation of methyl catechol in the presence of a nucleophile agent (2-thiouracil). In the first step of this process, methyl catechol is electrochemically oxidized to methyl o-quinone in aqueous solutions. The methyl o-quinone is then attacked by 2-thiouracil (c) to produce DMPTP. The overall reaction mechanism for anodic oxidation of methyl catechol in the presence of 2-thiouracil (c) is presented in Scheme 1. The results showed that these compounds undergo 1,4 Michael addition reaction with 2-thiouracil (2-TU) according to ECE mechanisms, with consumption of four electrons per molecule, to give final product. From the results of this work one may conclude that the Michael reaction of this nucleophile (c) to electrolytically produced methyl o-quinone leads to the formation of 2-(4,5-dihydroxy-2-methylphenylthio) pyrimidin-4(3H)-one (DMPTP) as final product in a good yield (80%) and purity.

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