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Electrochemical Oxidation of Catechol and 4-tert-Butylcatechol in the Presence of 1-Methyl-1H-imidazole-2-thiol: Synthesis and Kinetic Study

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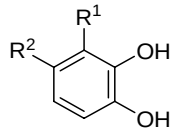
Electrochemical oxidation of catechol **1a** and 4-tert-butylcatechol **1b** has been studied in the presence of 1-methyl-1H-imidazole-2-thiol **3** as nucleophile in aqueous solution, using cyclic voltammetry and controlled-potential coulometry. The results indicate the participation of catechol **1a** and 4-tert-butylcatechol **1b** in Michael reaction with **3** to form the corresponding catechol thioethers **6a** and **4b**. Based on the observed EC mechanism, the homogeneous rate constants were estimated by comparing the experimental cyclic voltammetric responses with digital simulated results.

Keywords: Catechol, Oxidation, Cyclic voltammetry, Mechanism, Kinetic

INTRODUCTION

A vast number of quinones with great structural diversity are provided by nature, some of which play a major role in the redox electron-transport chains of living system [1-4]. In addition, many drugs such as doxorubicin, daunorubicin and mitomycin C in cancer chemotherapy contain quinones [5], whereas various other quinones have found uses in industry [6,7]. On the other hand, the existence of thiols (RSH) in biological media makes their investigations very important, particularly from their anti-oxidation and/or pro-oxidation properties when they attach to cellular species [8].

It is well-known that catechols can be oxidized electrochemically to *o*-quinones. The quinones formed are quite reactive and can be attacked by nucleophiles. In this connection, the electrochemical oxidation of catechols in the presence of a variety of nucleophiles such as thiotriazines [9-13], barbituric acids [14] and 4-hydroxy-6-methyl-2-pyrone [15] has been reported.



R^1 = H R^2 = H **1a**, catechol

R^1 = H R^2 = t-Bu **1b**, 4-tert-butylcatechol

Scheme 1

In order to develop a simple, fast and green method for the electrosynthesis of catechol thioethers, in this work, the oxidation of catechol **1a** and 4-tert-butylcatechol **1b** (Scheme 1, 2) has been studied in the presence of 1-methyl-1H-imidazole-2-thiol **3** as a nucleophile. In addition, the homogeneous rate constants (k_{obs}) for the reaction of *o*-quinone derived from catechol **1a** and 4-tert-butylcatechol **1b** with 1-methyl-1H-imidazole-2-thiol **3** have been estimated by digital simulation of cyclic voltammogram.

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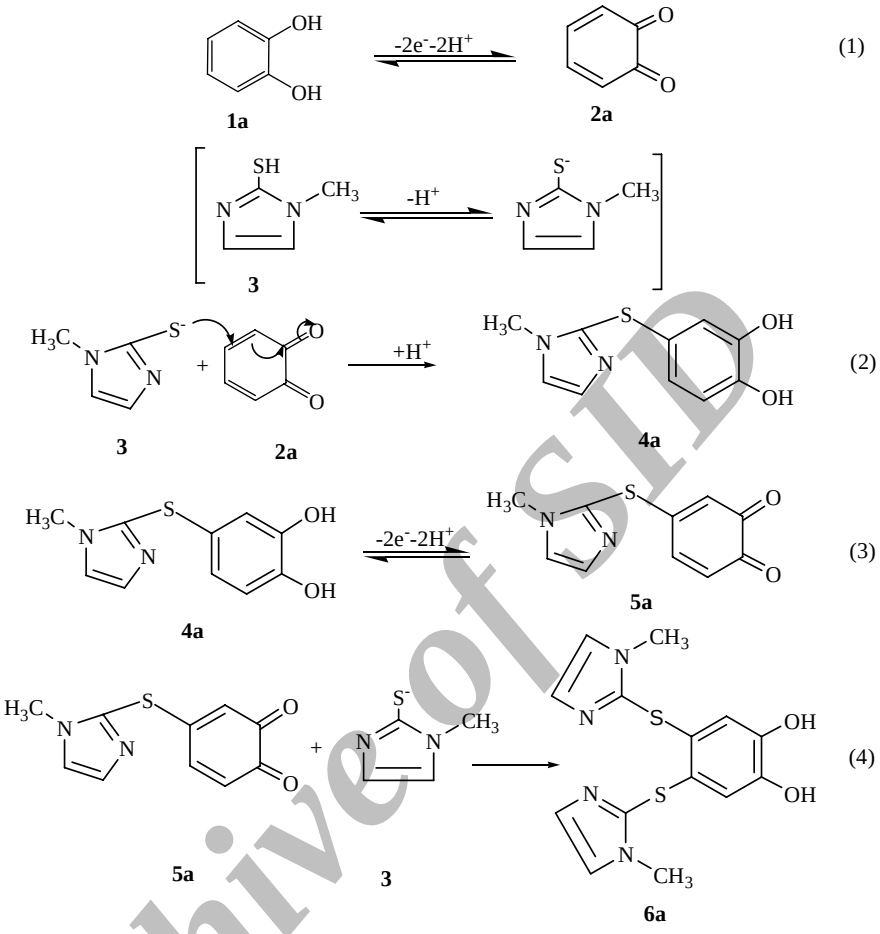


Scheme 2

EXPERIMENTAL

Apparatus

Cyclic voltammetry (CV) was performed using a Metrohm Computerized Voltammetric analyzer model 746 VA connected to a 747 VA stand. Controlled-potential coulometry and preparative analysis were performed using a potentiostat/galvanostat system model BHP 2061-C. All electrodes were obtained from Metrohm. The working electrode (WE) used in the voltammetry experiment was a glassy carbon disc (1.8 mm diameter) and platinum wire was used as the counter electrode (CE). The WE used in controlled -potential coulometry and macro scale electrolysis was an assembly of three graphite rods (8 mm diameter and 4 cm length) and a large platinum gauze constituted the CE. The WE potentials were measured *vs*. the 3 M Ag/AgCl reference electrode. All experiments were carried out at room temperature.

The ^{1}H NMR spectra were recorded on a Bruker AVANCE DRX500 (500 MHz) spectrometer. TLC experiments were carried out on alumina sheets pre-coated with silica gel 60 F 254 (Merck) and spots were visualized with UV light. The IR spectra were recorded on a Tensor 27 model HIO23502 FT IR spectrometer. The mass spectra were obtained using Agilent Technologies 6890 N Network GC system.

Chemicals

All chemical reagents were of pro-analysis grade from Merck and Flucka. These materials were used without further purification.

General Procedures

In a typical procedure, 80 ml aqueous solution containing

0.2 M phosphate buffer (pH 7.0) was pre-electrolyzed at 0.2 V *vs*. Ag/AgCl, in an undivided cell; subsequently, 2 mmol of each catechol **1a** and **1b** and 1-methyl-1H-imidazole-2-thiol **3** (4 mmol) were added to the cell. The electrolysis was terminated when the decay of the current became more than 95%. The process was interrupted during the electrolysis and the carbon anode was washed in acetone in order to make it reactive. At the end of electrolysis the precipitate was filtrated and washed with water. All products were characterized using the IR, ^{1}H NMR and MS spectra.

Compound 6a ($C_{14}H_{14}N_4O_2S_2$). m.p.: 172 °C, yield 84%. IR (KBr) υ (cm^{-1}): 693, 755, 855, 933, 1130, 1279, 1410, 1459, 1581, 2945, 3134, 3387; ^{1}H NMR (TMS) δ (ppm): 3.60 (s, 3H, methyl), 6.36-7.41 (m, 5H, aromatic); MS (EI) *m/e* (relative intensity): 334 ($M^{\cdot+}$, 14.5), 302(15.1), 222(20.2), 114(100), 72(48.5), 42(48.2).

Compound 4b ($C_{14}H_{19}N_2O_2S$). m.p.: 136 °C, yield 91%. IR (KBr) υ (cm^{-1}): 589, 747, 869, 1134, 1165, 1288, 1477, 2960, 3122, 3454; ^{1}H NMR (TMS) δ (ppm): 1.07 (s, 9H, -*tert*-butyl), 3.60 (s, 3H, methyl), 5.98 (s, 1H, aromatic), 6.67 (s, 1H, aromatic), 7.07 (s, 1H, aromatic), 7.42 (s, 1H, aromatic), 9.2 (broad, 2H, -OH); MS (EI) *m/e* (relative intensity): 279 ($M^{\cdot+}$, 8.5), 114(18.2), 166 (41).

RESULTS AND DISCUSSION

Cyclic voltammogram of 1 mM of catechol **1a** in aqueous solution containing 0.2 M phosphate buffer of pH 7.0 shows one anodic (A_1) and corresponding cathodic peak (C_1), corresponding to the transformation of catechol **1a** to *o*-benzoquinone **2a** and vice versa within a quasi-reversible two-electron process (Fig. 1, curve a). A peak current ratio (I_{C1}/I_{A1}) of nearly unity, particularly during the recycling of potential, can be considered as criteria for the stability of *o*-quinone produced at the surface of electrode under the experimental conditions. As it is shown in Fig. 1b, the presence of **3** as a nucleophile causes an anodic potential shift with increasing the anodic current of peak A_1, while the cathodic counterpart C_1 of the anodic peak A_1 is decreased. The positive shift of the A_1 peak in the presence of **3**, which is enhanced during the repetitive recycling of potential, is probably due to the formation of a thin film of product at the surface of the electrode inhibiting to a certain extent the performance of the

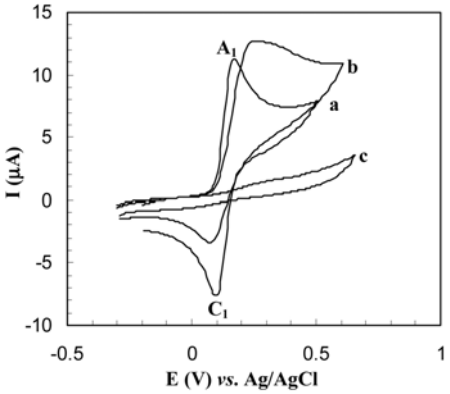


Fig. 1. Cyclic voltammograms of 1 mM aqueous catechol **1a** in the absence (a) and presence of 1 mM **3** (b), and that of a 1 mM **3** in the absence of catechol **1a** (c) at the glassy carbon electrode in 0.2 M aqueous phosphate buffer of pH 7.0 at a scan rate of 100 mV s^{-1}.

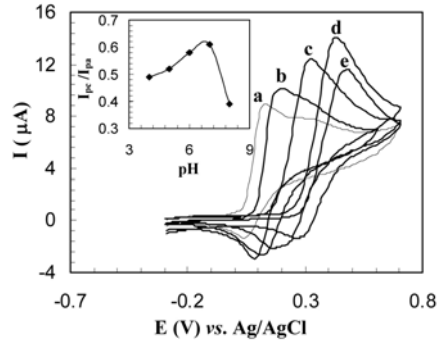


Fig. 2. Cyclic voltammograms of 1 Mm **1a** in the presence of 1 mM **3** at glassy carbon electrode at a scan rate of 100 mV $s^{-1}$and various pH: (a) 8, (b) 7, (c) 6, (d) 5, (e) 4. Inset shows the variation of peak current ratio (I_p^{C1}/I_p^{A1}) *vs*. pH.

electrode process [16]. In this Fig., curve c is the voltammogram of **3**.

The oxidation of catechol **1a** in the presence of **3** was studied by cyclic voltammetry at various pHs (Fig. 2). The results show that the peak current ratio (I_p^{C1}/I_p^{A1}) increases with increasing pH up to 7.0. This is related to protonation of **3** at lower pHs and its subsequent inactivation towards a Michael addition. On the other hand, the basic media increases

the rate of the coupling reaction between anion or dianione formed from deprotonation(s) of catechol and benzoquinone **2a** (dimerization reaction) [17]. Thus, because of the decreased rate of dimerization reaction and increased rate of the coupling reaction between deprotonated **3** and *o*-benzoquinone **2a,** a solution containing 0.2 M phosphate buffer of pH 7.0 was selected as solvent system for the electrochemical study and synthesis of these aminoquinone derivatives.

The cyclic voltammograms of catechol **1a** in the presence of **3** at various scan rates are shown in Fig. 3. It is seen that proportional to the augmentation of potential sweep rate, the height of the cathodic (C_1) peak of **1a** increases. A similar situation is also observed when the **3** to **1a** concentration ratio is decreased. On the other hand, the decreasing current function and decreasing current ratio I_p^{A1}/I_p^{C1} with increasing scan rate are good indications of the reactivity of deprotonated **3** toward *o*-quinone **2a**.

For further mechanistic studies, the controlled potential coulometry was performed in phosphate buffer solution including 0.2 mmol **1a** and 0.4 mmol **3** at 0.2 V *vs*. Ag/AgCl electrode. Monitoring of the progress of electrolysis was carried out by cyclic voltammetry (Fig. 4). As it is seen from inset of Fig. 4, the linear dependence of voltammetric currents with charge shows the charge consumption of about 4e per molecule of **1a**. These observations allowed us to propose the pathway in Scheme 1 for electro-oxidation of **1a** in the presence of **3**.

According to the obtained results, it seems that deprotonated form of **3** participates in a 1,4-Michael addition reaction with *o*-quinone **2a** (reaction 2) to result in the intermediate **4a**. The oxidation of **4a** is easier than the oxidation of parent starting molecule by virtue of the presence of electron-donating group. Like *o*-quinone **2a**, *o*-quinone **5a** can also be attacked from the C-5 position by deprotonated **3** to form the final product **6a** (ECEC mechanism). The overoxidation of **6a** was circumvented during the preparative reaction because of the insolubility of the product in phosphate buffer solution media (Scheme 2).

The electrooxidation of **1b** in the presence of **3** as a nucleophile in phosphate buffer (pH 7.0) solution shows an EC mechanism. The presence of t-Bu group as an electron-donating substitutent at the C-3 position on the molecular ring

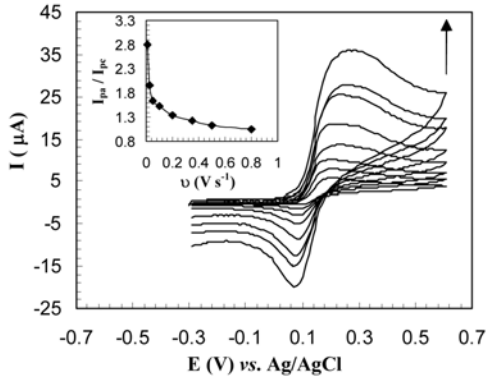


Fig. 3. Typical voltammograms of 1 mM aqueous catechol **1a** in the presence of **3** at the glassy carbon electrode, in 0.2 M phosphate buffer of pH 7.0 at scan rates of 10, 25, 50, 100, 200, 350, 500, 800 mV s^{-1}. Inset shows the variation of peak current ratio (I_p^{A1}/I_p^{C1}) *vs*. scan rate.

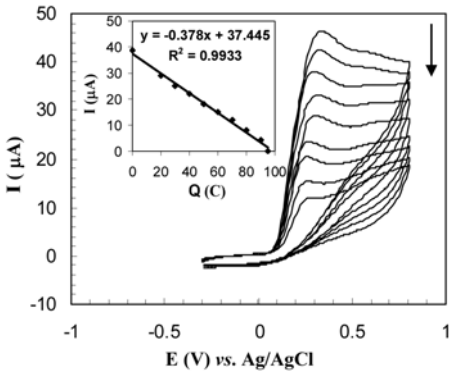
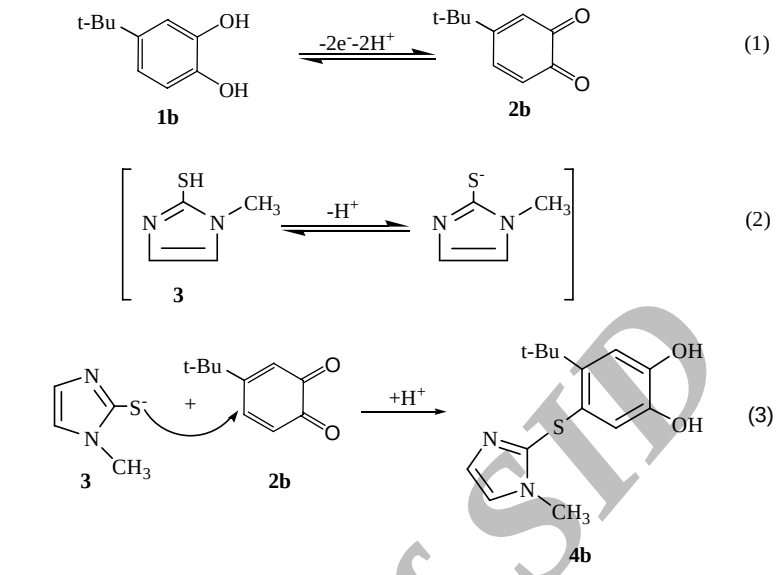


Fig. 4. Cyclic voltammograms of 0.2 mmol **1a** and 0.4 mmol **3** (1:2 ratio) at a scan rate of 50 mV s^{-1} during controlled potential coulometry at 0.2 V *vs*. Ag/AgCl. Inset shows variation of peak current *vs*. charge consumed.

causes the diminished activity of *o*-quinone **2b** as Michael acceptors toward the 1,4-addition reactions. However, the decreased peak current ratio with increasing scan rate confirms the reaction between *o*-quinones **2b** and deprotonated **3**. The coulometric results show 2e per each molecule of **1b**. These observations allowed us to propose the pathway in Scheme 3 for the electrooxidation of **1b** in the presence of **3**.

In order to obtain some kinetic information for the system, the scheme for the electrochemical oxidation of catechols **1a** and **1b** in the presence of **3** were proposed and tested by



Scheme 3

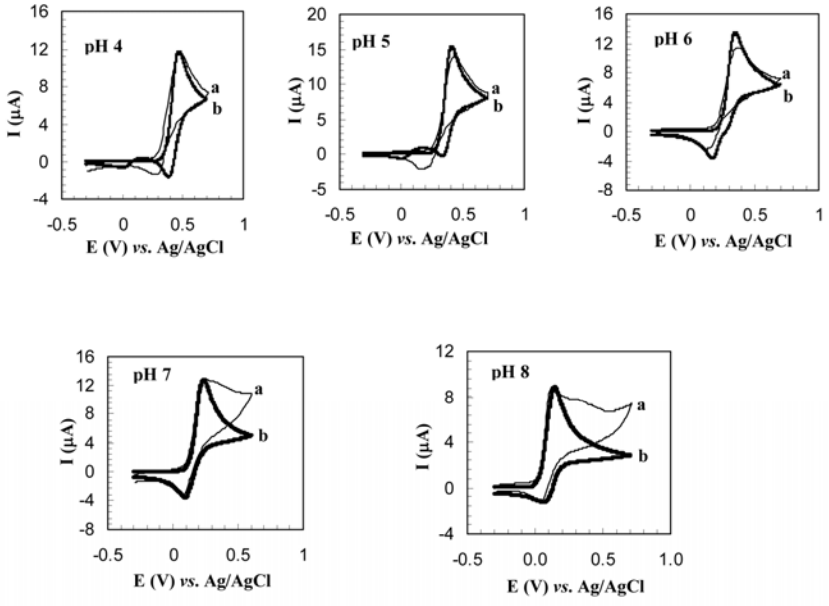


Fig. 5. Typical cyclic voltammograms of 1 mM **1a** and 1 mM **3** at various pH. (a) experimental; (b) simulated. Scan rates: 100 mV s^{-1}. Working electrode:glassy carbon electrode.

digital simulation. The simulation was carried out assuming a semi-infinite one-dimensional diffusion and planar electrode geometry. The transfer coefficients (α) were assumed to be 0.5 and the formal potentials were obtained experimentally as the midpoint potential between the anodic and cathodic peaks(E_{mid}). All parameters were kept constant through out the fitting of the digitally simulated voltammogram to the experimental data [18]. The observed homogeneous rate constant (k_{obs}) was allowed to change through the fitting processes. The k_{obs} values for the reaction of *o*-benzoquinone **2a** with **3** were estimated by comparison of the simulation results with experimental cyclic voltammograms at various pH and scan rates (Fig. 5). The simulation was performed based on an EC mechanism and the calculated values of observed

Table 1. Observed Homogeneous Rate Constants, k_{obs} (s^{-1}), for the Studied Catechols **1a** and **1b**. Scan rates are 10, 25, 50, 100 and 200 mV s^{-1}

pH	Catechol	4-tret-Butylcatechol
4	0.32 (±0.02)	0.17 (±0.03)
5	0.41 (±0.01)	0.35 (±0.02)
6	0.62 (±0.02)	0.50 (±0.01)
7	0.80 (±0.01)	0.61 (±0.01)
8	0.91 (±0.01)	0.75 (±0.02)

homogeneous rate constant (k_{obs}) for reaction of *o*-benzoquinone **2a**, **2b** with deprotonated **3** are shown in Table 1. As shown in Table 1, the magnitude of k_{obs} is dependent on the nature and position of the substituted group on the catechol ring. The presence of an electron-donating group such as tert-butyl on catechol ring causes a decrease in k_{obs}.

CONCLUSIONS

The overall reaction mechanism for electrochemical oxidation of catechols in presence of **3** is presented in Scheme 1. According to obtained results, the mechanism of electrooxidation reaction of catechol in the presence of **3** is two successive EC (ECEC) mechanisms, while 4-tert-butylcatechol shows an EC mechanism. The kinetics of the reactions of electrochemically generated *o*-benzoquinones **2a** and **2b** with **3** were studied by cyclic voltammetric technique and simulation of the obtained voltammograms under an EC mechanism. There is a good agreement between the simulated voltammograms with those obtained experimentally.

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