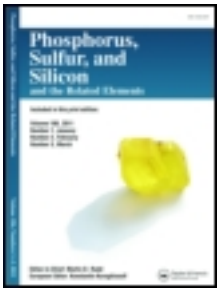

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Electrochemical Oxidation of Catechols in the Presence of Pyrimidine-2-thiol: Application to Electrosynthesis

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*The electrooxidation of catechols (**1a–d**) in the presence of pyrimidine-2-thiol (**3**) as a nucleophile in aqueous solution is described. The mechanistic investigations using cyclic voltammetry and controlled potential coulometry indicate that the quinone derived from catechols participates in a Michael addition reaction with pyrimidine-2-thiol to form corresponding catechol derivatives of **6a–d** (ECEC). The efficient electrosynthesis of **6a–d** has been performed at carbon rod electrodes in an undivided cell in good yield and purity.*

Keywords Catechol; cyclic voltammetry; electrosynthesis; Michael addition; oxidation

INTRODUCTION

The importance of catechols due to the presence of an *ortho*- or *para*-quinone ring as a reactive center of electron transfer in the structure of many natural compounds[1] and biological materials[2] caused many researchers to synthesize a number of catechol derivatives.[3–6] Many researchers have shown that *ortho*- and *para*-diphenols can be oxidized electrochemically to *o*- and *p*-quinones, which are quite reactive and can be attacked by a variety of nucleophiles.[7–11] In this direction, the electrosynthesis of various catechol derivatives such as coumestan,[12] benzofuran,[13] arylsulfonylbenzenediol,[14] pyrimidine,[15] and thio derivatives[16–19] have been reported. Indeed, in all of these investigations, attention was focused on both elucidation of the electron transfer

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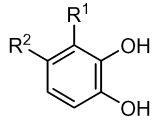
mechanism and proposal of an electrochemical route to led to the synthesis of compounds containing *ortho*- or *para*-quinone rings in their framework.[20]

The purpose of the work, in continuation of our interest in the electrochemistry of organic compounds,[21] is to investigate the electrooxidation of catechols in the presence of pyrimidine-2-thiol as a nucleophile. The study is based mainly on the cyclic voltammogram patterns of catechol in water on a glassy carbon electrode. We have also described a facile and efficient electrochemical method for the synthesis of some new pyrimidin-2-ylthio derivatives. A mechanism also proposed for electrode reactions and the effect of various parameters on the advancement of the electrode process is described.



R^1=H	R^2=H	**1a,** catechol
R^1=CH_3	R^2=H	**1b,** 3-methylcatechol
R^1=OCH_3	R^2=H	**1c,** 3-methoxycatechol
R^1=H	R^2=CH_3	**1d,** 4-methylcatechol

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. 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 macroscale 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 versus the 3M Ag/AgCl reference electrode (all electrodes were obtained from Metrohm). All experiments were carried out at room temperature.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DRX500 (500 MHz) spectrometer. TLC was carried out on alumina sheets precoated with silica gel 60 F 254 (Merck), and spots were visu-

alized with UV light. IR spectra were recorded on a Tensor 27 model HIO23502 FT IR spectrometer. 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.

RESULTS AND DISCUSSIONS

The cyclic voltammogram of a 1 mM solution of catechol (**1a**) in phosphate buffer solution (c = 0.2 M, pH = 7.2) shows one anodic (A_1) and a corresponding cathodic (C_1) due to the transformation of catechol (**1a**) to *o*-benzoquinone (**2a**) and vice-versa within a quasi-reversible, two-electrons process (Figure 1, curve a). The peak current ratio (I_p^{C1}/I_p^{A1}) of near unity, particularly in the repetitive recycling of potential, is a good indication of the stability of *o*-quinone to participitating in hydroxylation or dimerization side reactions.[22,23] As is shown in Figure 1 (curve b), 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 disappears. 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 electrode process.[7–11] In Figure 1, curve c is the voltammogram of **3**, which is inactive in this potential range.

The cyclic voltammograms of catechol **1a** in the presence of **3** at various scan rates are shown in Figure 2. 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 increasing current ratio I_p^{C1}/I_p^{A1} are a good indication of the reactivity of **3** toward **1a** in a following coupled chemical reaction (ECE). The appearance of an additional cathodic peak C_0 at high scan rate can be related to the formation of some polymeric species as final products.[24] For further mechanistic studies, the controlled potential coulometry was performed in phosphate buffer solution including 0.1 mmol **1a** and 0.2 mmol **3** at 0.22 V versus Ag/AgCl electrode. The coulometric results show the charge consumption of about 4e per molecule of **1a**. These observations allow us to propose the pathway in Scheme 1 for electro-oxidation of **1a** in the presence of **3**.

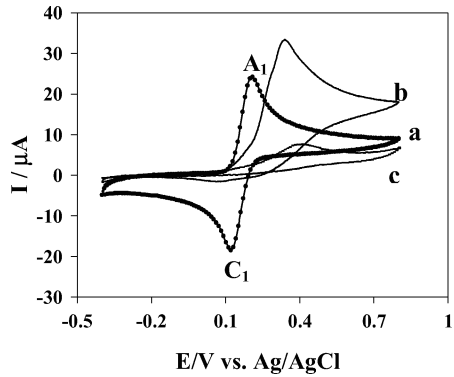


FIGURE 1 Cyclic voltammograms of 1 mM aqueous catechol **1a**: (a) in the absence, (b) in the presence of 1 mM pyrimidine-2-thiol **3**, (c) 1 mM pyrimidine-2-thiol **3** in the absence of catechol **1a** at the glassy carbon electrode in aqueous phosphate buffer (c = 0.2 M, pH = 7.2), scan rate: 100 mVs^{-1}.

According to the obtained results, it seems that **3** participates in a 1,4-Michael addition reaction with *o*-quinone (**2a**) (reaction 2) resulting intermediate **4a**. The oxidation of this compound (**4a**) is easier than the oxidation of the parent starting molecule by virtue of the presence of electro-donating group. Like *o*-quinone **1a**, *o*-quinone **5a** can also be attacked from the C-5 position by **3** to form the final production **6a**. The overoxidation of **6a** was circumvented during the preparative reaction

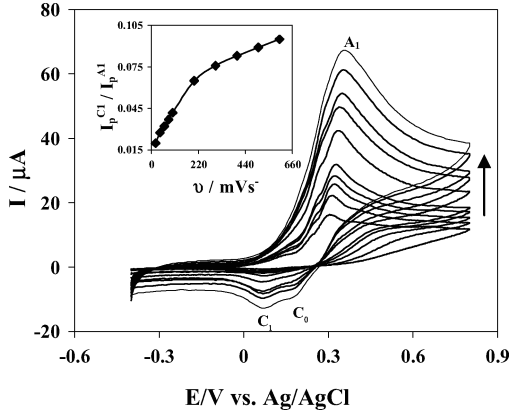
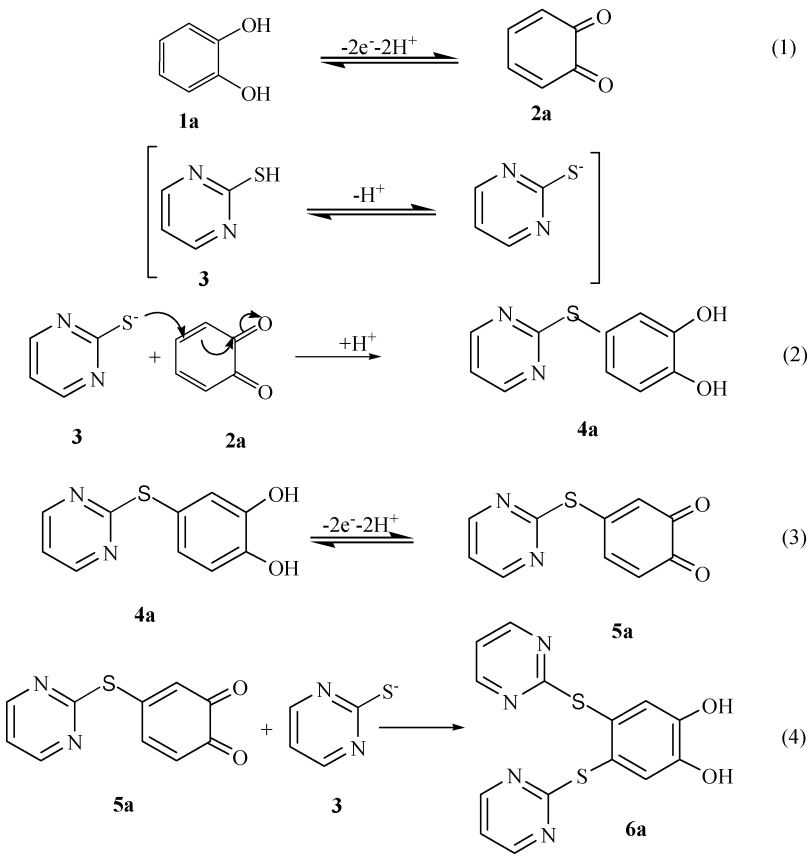


FIGURE 2 Typical voltammograms of 1 mM aqueous catechol **1a** in the presence of pyrimidine-2-thiol **3** at the glassy carbon electrode, in phosphate buffer (c = 0.2 M, pH = 7.2), scan rates: 20, 40, 60, 80, 100, 200, 300, 400, 500, 600 mVs^{-1}. Inset: variation of peak current ratio (I_p^{C1}/I_p^{A1}) versus scan rate.

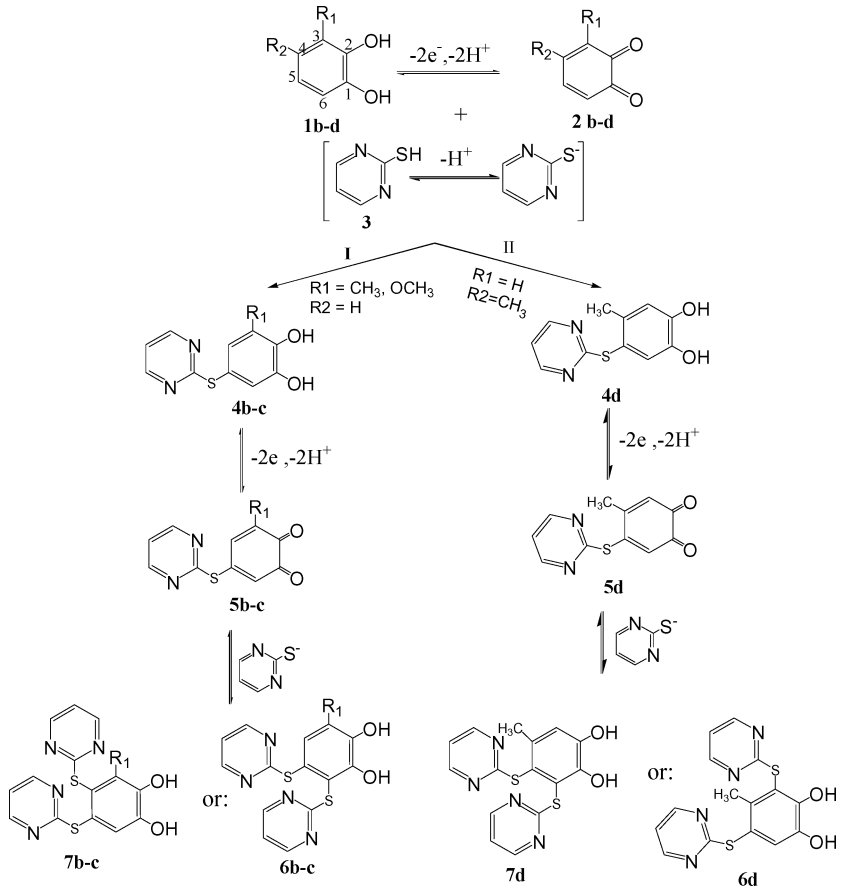


SCHEME 1

because of the insolubility of the product in phosphate buffer solution media. The ^{1}H-NMR spectrum of **6a** shows as a symmetric structure. The two aromatic protons of catechol appeared as a singlet, which confirms that the product of **6a** is 4,5-bis(pyrimidin-2-ylthio)benzene-1,2-diol rather than another symmetric structure of 3,6-bis(pyrimidin-2-ylthio)benzene-1,2-diol (Scheme 1).

Electrosynthesis of 6b–d

The first step of electro-oxidation of **1b-d** in the presence of **3** as a nucleophile in buffer solution proceeds in a way similar to that of **1a**. In the all cases the presence of methyl or methoxy groups as electron-donating substituents on the molecular ring causes a diminution in activity of



SCHEME 2

o-quinones **2b–d** as Michael acceptors toward the 1,4-addition reactions. However, the plot of peak current ratio versus scan rate confirms the reaction between *o*-quinones **2b–d** and **3**, appearing as an increase in peak current ratio, I_p^{C1}/I_p^{A1} with increasing scan rate.

After formation of *o*-quinone **5b,c** via 1,4-(Michael) addition reaction[7–19] and oxidation, it can be attacked by the **3** from C-4 or C-6, to yield two types of products (**6b,c** and **7b,c**) (Scheme 2). However, thin-layer chromatographic (TLC) results indicate the formation of one component in electrooxidation of **1b,c** in the presence of **3**.

The steric energy has been calculated for **6b,c** and **7b,c**, using the MM2 program after minimization of structures (Table I).[25] Results indicate that structures **6b, c** are energically more stable than the **7b,c**.

TABLE I Calculated Steric Energy by MM2 Program

Entry	Steric Energy (kcal/mol)
6b	9.31
7b	9.66
6c	9.72
7c	16.83
6d	8.51
7d	9.70

Therefore, because of less steric energy (about 0.35 and 7.11 kcal/mol for **6b** and **6c**, respectively) we think that *o*-quinone **5b,c** is attacked in all probability by the **3** from C-6 (path I, Scheme 2), leading to the formation of the products **6b,c**.

The existence of methyl group at C-4 position of *o*-quinone ring (**1a**) causes **5d** to probably be attacked by **3** from C-3 or C-6 positions to yield two types of products. As it can been seen from Table I, **6d** is the final product (path II, Scheme 2).

Data for 6a ($C_{14}H_{10}N_4O_2S_2$)

Mp >300°C, yield 74%. IR (KBr) υ (cm^{-1}): 3416 (-$H_{str.}$), 2925, 1557, 1379, 1290, 1182, 985, 863; ^{1}HNMR (TMS) δppm: 5.97 (s, 2H, catechol), 7.14 (t, 2H, pyrimidine-2-thiol), 8.62 (d, 4H, pyrimidine-2-thiol), 9.01 (b, 2H, hydroxy); MS (EI) *m*/*e* (relative intensity): 330 [$M^{+\cdot}$] (20), 313 (75), 297 (90), 279 (24), 258 (52), 219 (26), 190 (29), 132 (44), 79 (75), 53 (85).

Data for 6b ($C_{15}H_{12}N_4O_2S_2$)

Mp >300°C, yield 72%. IR (KBr) υ (cm^{-1}): 3325 (-$OH_{str.}$), 3121, 2924, 1587, 1490, 1380, 1283, 1190, 1034, 851; ^{1}HNMR (TMS) δppm: 2.21 (s, 3H, methyl), 7.09 (s, 1H, catechol), 7.15 (t, 2H, pyrimidine-2-thiol), 8.51 (d, 4H, pyrimidine-2-thiol); MS (EI) *m*/*e* (relative intensity): 344 [$M^{+\cdot}$] (12), 311 (20), 295 (8), 233 (85), 217 (12), 186 (8), 112 (8), 79 (12), 53 (20).

Data for 6c ($C_{15}H_{12}N_4O_3S_2$)

Mp >300°C, yield 81%. IR (KBr) υ (cm^{-1}): 3416 (-$OH_{str.}$), 3065, 2931, 1602, 1559, 1505, 1378, 1311, 1181, 958; ^{1}HNMR (TMS) δppm: 2.48 (s, 3H, methoxy), 6.65 (s, 1H, catechol), 7.17 (t, 2H, pyrimidine-2-thiol), 8.56 (d, 4H, pyrimidine-2-thiol), 8.56 (b, 2H, hydroxy); MS (EI) *m*/*e*

(relative intensity): 360 [$M^{+\cdot}$] (8), 329 [M-OCH_3] (11), 249 (100), 234 (25), 189 (15), 113 (18), 79 (25), 53 (50).

Data for 6d ($C_{15}H_{12}N_4O_2S_2$)

Mp>300°C, yield 76%. IR (KBr) υ (cm^{-1}): 3416 (-$OH_{str.}$), 1563, 1409, 1380, 1303, 1186, 1036, 808; ^{1}HNMR (TMS) δppm: 2.35 (s, 3H, methyl), 5.98 (s, 1H, catechol), 7.5 (t, 2H, pyrimidine-2-thiol), 8.45 (d, 4H, pyrimidine-2-thiol) ; MS (EI) *m*/*e* (relative intensity): 344[$M^{+\cdot}$] (8), 327 (6), 310 (12), 296 (14), 279 (30), 233 (44), 214 (28), 201 (74), 183 (10), 155 (26), 112 (34), 79 (42), 53 (84).

CONCLUSION

The results of this work show that catechols are oxidized to their respective *o*-quinones. The quinones are then attacked by **3**. Final products are obtained via an EC mechanism, after consumption of 4e per molecule of catechols (**1a–d**).

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