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Electrochemical oxidation of catechols in the presence of 4-hydroxy-6-methyl-2-pyrone

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Abstract—Electrochemical oxidation of catechols (**1a**–**1c**) has been studied in the presence of 4-hydroxy-6-methyl-2-pyrone (**3**) as nucleophile in aqueous solution, using cyclic voltammetry and controlled-potential coulometry. The results indicate that the quinones derived from catechols (**1a**–**1c**) participate in Michael addition reactions with **3** to form the corresponding heterocyclic compounds (**6a**–**6c**). In this work we have proposed a mechanism for the electrode process. The electrochemical synthesis of **6a**–**6c** has been successfully performed on carbon rod electrodes and in an undivided cell.

1. Introduction

Previously we have shown that catechols can be oxidized electrochemically to *o*-quinones. The quinones formed are quite reactive and can be attacked by a variety of nucleophiles such as: methanol,[1–3] ethanol,[4] 4-hydroxycoumarin,[5–7] β-diketones,[8] barbituric acids,[9,10] 4-toluenesulfinic acid[11] and were converted to the corresponding alkoxyquinone, coumestan, benzofuran and pyrimidine derivatives, respectively. Compounds known as coumestans,[5–7] for example 6*H*-benzofuro[3,2-*c*][1]benzopyran-6-one, have the basic structure of many natural products such as wedelolactone, medicagol, psoraldin, isopsoraldin, erosnin and the estrogenic coumestrol, with interesting physiological activites.[12–14] The importance of these compounds has caused us to synthesize a number of new coumestan derivatives. In this work electrochemical oxidation of catechols (**1a**–**1c**) has been studied in the presence of 4-hydroxy-6-methyl-2-pyrone (**3**) as a possible nucleophile. The present work has led to the development of a facile electrochemical method for the synthesis of new coumestan derivatives (**6a**–**6c**), with similar structures to some melanizing agents such as: trioxsalen and methoxsalen.[15]

2. Results and discussion

Cyclic voltammetry of a 1 mM solution of catechol (**1a**) in an aqueous solution containing 0.15 M sodium acetate as supporting electrolyte, shows one anodic (A_1) and a corresponding cathodic peak (C_1) which corresponds 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_p^{Cl}/I_p^{Al}) of nearly unity, particularly during the repetitive recycling of potential, can be considered as a criterion for the stability of *o*-quinone produced at the surface of electrode under the experimental conditions. In other words, any hydroxylation or dimerization reactions are too slow to be observed on the time scale of cyclic voltammetry.[5–11] The oxidation of catechol (**1a**) in the presence of 4-hydroxy-6-methyl-2-pyrone (**3**) as a nucleophile was studied in some detail. Fig. 1, (curve b) shows the cyclic voltammogram obtained for a 1 mM solution of **1a** in the presence of 1 mM 4-hydroxy-6-methyl-2-pyrone (**3**). The voltammogram exhibits two anodic peaks at 0.24 and 1.15 V versus SCE, and the cathodic counterpart of the anodic peak A_1 decreases. In this figure, curve c is the voltammogram of **3**. Comparison of voltammograms b and c reveals that the peak A_2 (curve b), corresponds to the oxidation of **3**.

The multi-cyclic voltammetry of **1a** in the presence of **3** shows that in the second cycle, parallel to the shift of the A_1 peak in a positive direction, a new peak (A_0) appears with an E_p value of 0.25 V versus SCE (Fig. 1, curve d, 2nd. scan). This new peak is related to electro-oxidation of intermediate **4a**. The positive shift of the A_1 peak in the presence of **3** 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 electrode process.[5–11] Furthermore, it is seen that proportional to the augmentation of potential sweep rate, the height of the C_1 peak of **1a** increases (Fig. 2 curves a–f). A similar situation is observed when the 4-hydroxy-6-methyl-2-pyrone (**3**) to **1a** concentration ratio is decreased. A plot of peak current ratio (I_p^{Al}/I_p^{cl}) versus scan rate for a mixture of catechol (**1a**) and

Keywords: electrochemical oxidation; cyclic voltammetry; catechols; 4-hydroxy-6-methyl-2-pyrone.

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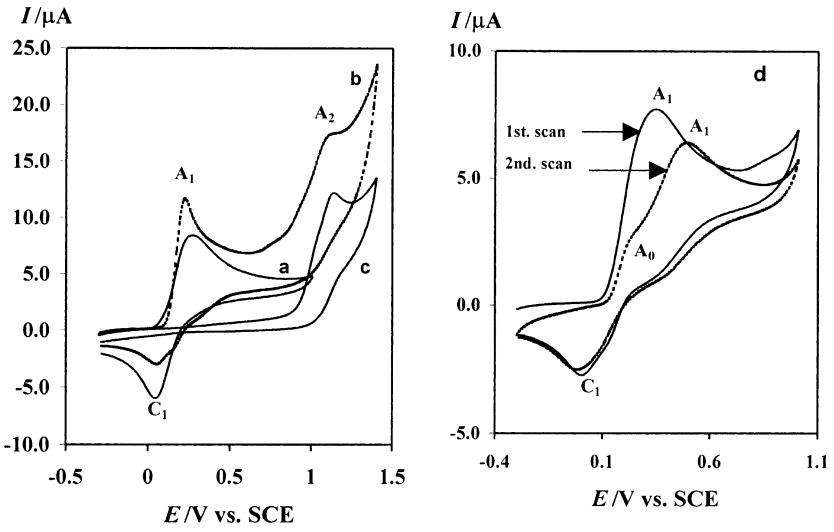


Figure 1. Cyclic voltammograms of 1 mM catechol (**1a**): (a) in the absence, (b) in the presence of 1 mM 4-hydroxy-6-methyl-2-pyrone (**3**), (c) 1 mM 4-hydroxy-6-methyl-2-pyrone (**3**) in the absence of catechol (**1a**) and (d) multi-cyclic voltammograms of **1a** in the presence of **3**, at glassy carbon electrode (1.8 mm diameter) in aqueous solution. Supporting electrolyte 0.15 M sodium acetate; scan rate: 50 mV s^{-1}; T=25±1°C.

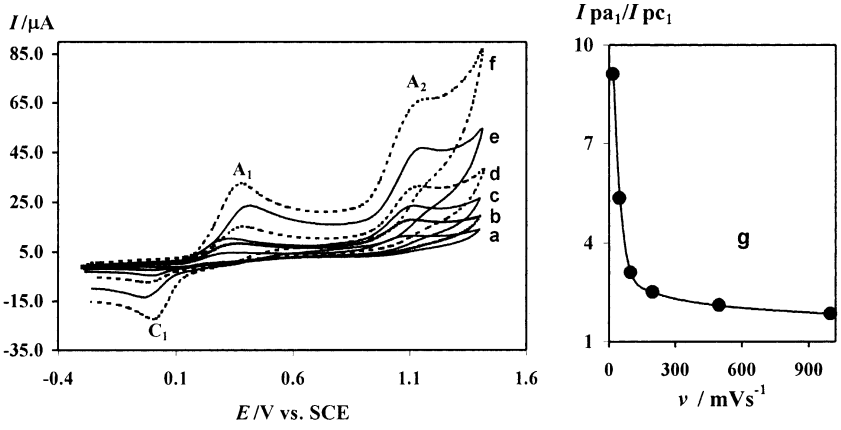


Figure 2. Typical voltammograms of 1 mM catechol (**1a**) in water in the presence of 1 mM 4-hydroxy-6-methyl-2-pyrone (**3**) at a glassy carbon electrode (1.8 mm diameter) and at various scan rates. Scan rates from (a) to (f) are: 20, 50, 100, 200, 500 and 1000 mV s^{-1}, respectively. Supporting electrolyte: 0.15 M sodium acetate. Curve g: variation of peak current ratio (I_p^{Al}/I_p^{Cl}), versus scan rate. T=25±1°C.

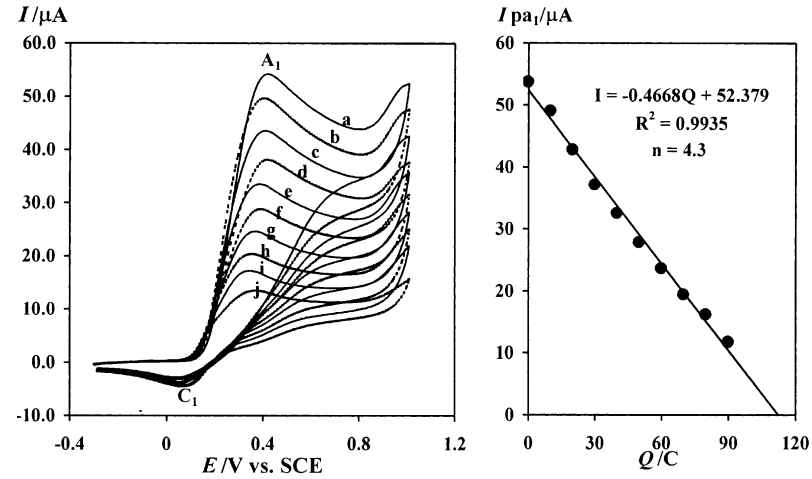
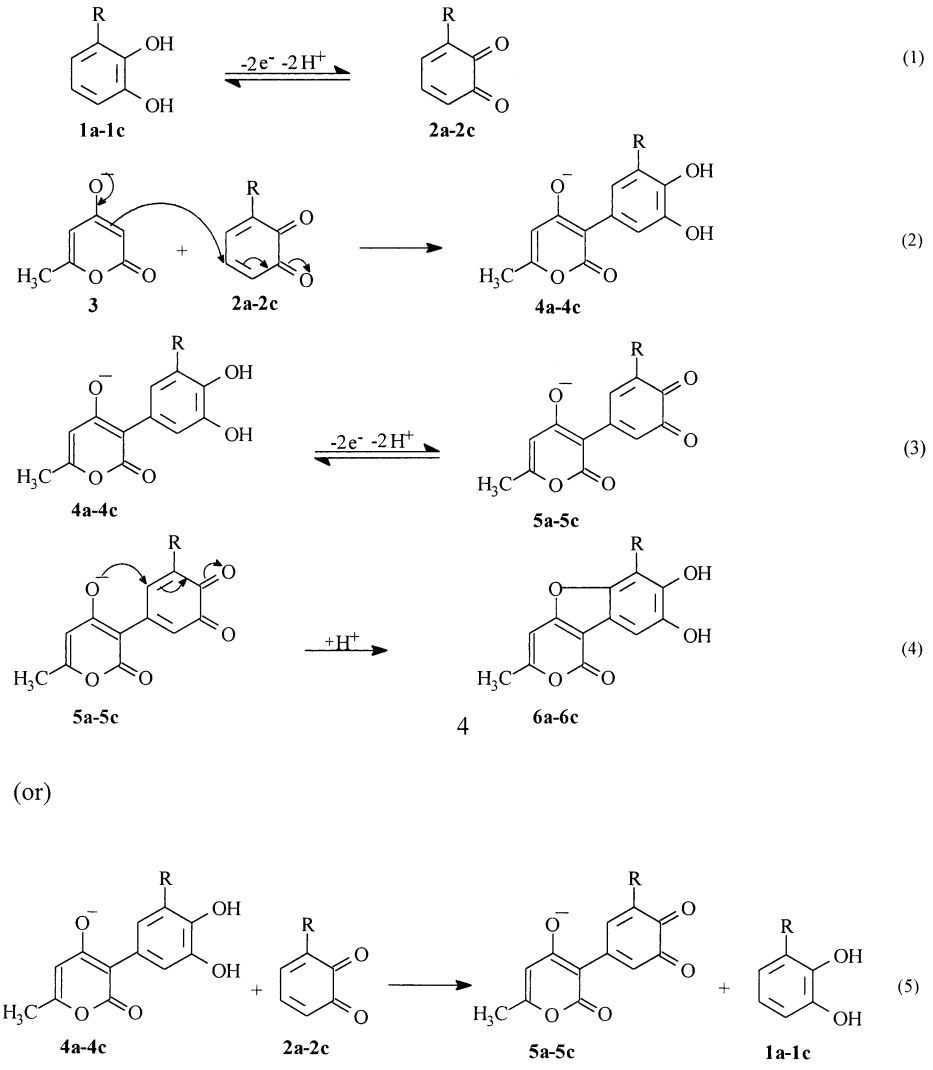


Figure 3. Cyclic voltammograms of 0.27 mmol catechol in the presence of 0.27 mmol 4-hydroxy-6-methyl-2-pyrone (**3**), at glassy carbon electrode (1.8 mm diameter) during controlled potential coulometry at 0.35 V versus SCE. After consumption of: (a) 0, (b) 10, (c) 20, (d) 30, (e) 40, (f) 50, (g) 60, (h) 70, (i) 80, (j) 90, C. Diagram: variation of peak current (I_p^{Al}) versus charge consumed. Scan rate 50 mV s^{-1}; T=25±1°C.



Scheme 1.

Table 1. Electroanalytical and preparative data

Conversion	Applied potential (V) (SCE)	Product yield %	Melting point (°C)
1a→6a[a]	0.35	63	265–267 (dec.)
1b→6b[b]	0.30	67	257–259 (dec.)
1c→6c[c]	0.30	69	225–227 (dec.)

[a] **Product 6a** $IR_{(KBr)}$: 3360, 3200, 2900, 1700, 1615, 1570, 1470, 1300, 1226, 1040, 968, 836 cm^{-1}. ^1H NMR, δ (90 MHz DMSO-d_6): 2.17 (s, 3H, methyl); 6.72 (s, 1H, pyrone); 6.92 (d, J=7.1 Hz, 2H, catechol); 9.27 (d, J=4.4 Hz, 2H, hydroxy). ^{13}C NMR, δ (90 MHz DMSO-d_6): 25.54, 101.38, 104.03, 108.90, 110.59, 119.03, 149.43, 150.91, 154.33, 164.66, 165.95, 168.45. MS: *m/e* (relative intensity); 232 (100), 217 (25), 203 (28), 189 (10), 162 (16), 69 (31). Anal. Calcd for $C_{12}H_8O_5$: C, 62.07; H, 3.45. Found: C, 61.86; H, 3.64.

[b] **Product 6b** $IR_{(KBr)}$: 3480, 3080, 2920, 1706, 1613, 1565, 1456, 1295, 1234, 1081, 976, 819 cm^{-1}. ^1H NMR, δ (90 MHz DMSO-d_6): 2.12 (s, 3H, methyl); 2.16 (s, 3H, methyl); 6.67 (s, 1H, pyrone); 6.90 (s, 1H, catechol); 8.60 (s, 1H, hydroxy); 9.52 (s, 1H, hydroxy). ^{13}C NMR, δ (90 MHz DMSO-d_6): 9.83, 20.70, 96.82, 102.53, 103.99, 109.25, 113.16, 144.24, 144.66, 148.96, 159.89, 161.98, 163.81. MS: *m/e* (relative intensity); 246 (100), 230 (18.5), 217 (29.6), 190 (14.1), 176 (22.6), 91 (22.1), 83 (22.2), 63 (36). Anal. Calcd for $C_{13}H_{10}O_5$: C, 63.41; H, 4.07. Found: C, 63.11; H, 4.32.

[c] **Product 6c** $IR_{(KBr)}$: 3333, 3091, 2930, 1685, 1612, 1571, 1498, 1361, 1296, 1231, 1094, 1045, 843, 786 cm^{-1}. ^1H NMR, δ (90 MHz DMSO-d_6): 2.38 (s, 3H, methyl); 4.10 (s, 3H, methoxy); 6.77 (s, 1H, pyrone); 7.08 (s, 1H, catechol); 8.65 (s, 1H, hydroxy); 9.60 (s, 1H, hydroxy). ^{13}C NMR, δ (90 MHz DMSO-d_6): 20.68, 61.13, 96.33, 100.25, 104.22, 114.95, 133.51, 137.02, 141.41, 145.06, 156.97, 161.30, 163.59. MS: *m/e* (relative intensity); 262 (100), 247 (72.4), 219 (20.4), 205 (14.3), 191 (12.1), 92 (23.6), 78 (36.5), 63 (62.8). Anal. Calcd for $C_{13}H_{10}O_6$: C, 59.54; H, 3.82. Found: C, 59.29; H, 4.09.

4-hydroxy-6-methyl-2-pyrone (**3**) confirms the reactivity of **2a** towards **3**, appearing as an increase in the height of the cathodic peak C_1 at higher scan rates (Fig. 2, curve g). On the other hand, the current function for the A_1 peak, ($I_p^{Al}/v^{1/2}$), changes on increasing the scan rate and such a behavior is adopted as indicative of an ECEC mechanism.[16]

Controlled-potential coulometry was performed in aqueous solution containing 0.27 mmol of **1a** and 0.27 mmol of **3** at 0.35 V versus SCE. The monitoring of electrolysis progress was carried out by cyclic voltammetry. It is shown that, proportional to the advancement of coulometry, anodic peak A_1 decreases (Fig. 3). All anodic and cathodic peaks disappear when the charge consumption becomes about $4e^-$ per molecule of **1a** (Fig. 3). These observations allow us to propose the pathway in Scheme 1 for the electro-oxidation of **1a** in the presence of **3**.

According to our results, it seems that the Michael addition reaction of anion **3** to *o*-quinone (**2a**) ((2) see Scheme 1) is faster than other secondary reactions, leading to the intermediate (**4a**). The oxidation of this compound (**4a**) is easier than the oxidation of the parent starting molecule (**1a**) by virtue of the presence of an electron-donating group. It can be seen from the mechanism shown in Scheme 1, that as the chemical reaction ((2) see Scheme 1) occurs, **1a** is regenerated through homogeneous oxidation ((5) see Scheme 1) and hence, can be reoxidized at the electrode surface. Thus, as the chemical reaction takes place, the apparent number of electrons transferred increases from n=2 to n=4 electrons per molecule. The reaction product (**6a**) can also be oxidized at a lower potential than the starting **1a** compound. However, overoxidation of **6a** was circumvented during the preparative reaction because of the insolubility of the product in the water/sodium acetate solvent medum.

The electro-oxidation of **1b** and **1c** in the presence of **3** as a nucleophile in sodium acetate solution proceeds in a similar way to that of **1a**. The existence of a methyl or methoxy group at the C-3 position of **1b** and **1c** probably causes these Michael acceptors (**2b** and **2c**) to be attacked by **3** at the C-4 and/or C-5 positions to yield two types of product in each case. However, according to thin layer chromatography (TLC) and ^{1}H NMR[17] results, we suggest that *o*-quinones **2b** and **2c** are attacked in all probability only in the C-5 position by **3** leading to the formation of the products **6b** and **6c**, respectively.

3. Conclusion

The present results complete the previous reports on the anodic oxidation of some catechols.[1–11] The results of this work show that catechols are oxidized in water to their respective *o*-quinones. The quinones are then attacked by anion **3** to form coumestan derivatives. The overall reaction mechanism for anodic oxidation of catechols in the presence of **3** as nucleophile is presented in Scheme 1. According to our results, it seems that the Michael reaction of this nucleophile to *o*-quinones formed leads to the formation of new coumestan derivatives as final products, in good yields and purity.

4. Experimental

4.1. Apparatus and reagents

Reaction equipment is described in an earlier paper.[10] All chemicals (catechols and 4-hydroxy-6-methyl-2-pyrone) were reagent-grade materials from Aldrich and sodium acetate was of pro-analysis grade from E. Merck. These chemicals were used without further purification.

4.2. Electroorganic synthesis of 4a–4c

In a typical procedure, 80 ml of sodium acetate solution in water (0.15 M) was pre-electrolyzed at the chosen potential (see Table 1), in an undivided cell; then 2 mmol of catechols (**1a**–**1c**) and 4-hydroxy-6-methyl-2-pyrone (**3**) (2 mmol) were added to the cell. The electrolysis was terminated when the decay of the current became more than 95%. The process was interrupted several times during the electrolysis and the graphite anode was washed in acetone in order to reactivate it. At the end of electrolysis, a few drops of acetic acid were added to the solution and the cell was placed in refrigerator overnight. The precipitated solid was collected by filtration and recrystallized from a mixture of methanol/acetone. After recrystallization, products were characterized by IR, ^{1}H NMR, ^{13}C NMR, MS and elemental analysis.

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