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Electrochemical synthesis of amino-substituted 1,2-benzoquinone derivatives

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Abstract

The electrooxidation of 3-substituted catechols (**1**) has been studied in the presence of dibenzylamine (**3**) in water + acetonitrile (90/10) solution, using electrochemical and spectroelectrochemical methods. The *o*-benzoquinones (**2**) derived from catechols (**1**) participate in Michael addition reactions with dibenzylamine (**3**) to form the corresponding monoamino-substituted *o*-benzoquinones (**5**). We propose a mechanism for the electrode process. An efficient electrochemical synthesis of amino-substituted 1,2-benzoquinone derivatives (**5**) has been performed at a carbon rod electrode in a two-compartment cell.

Keywords: Catechol; Dibenzylamine; Cyclic voltammetry; Amino-substituted 1,2-benzoquinone; Electrochemical synthesis

1. Introduction

A vast number of quinones with great structural diversity are provided by nature; some of them play a major role in the redox electron-transport chains of living systems [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]. In particular, alkylamino derivatives of quinones are of considerable interest because they exhibit antitumor and antimalarial activities [8–10] and many of them are also involved in enzyme inhibition and DNA cross-linking [11]. The 1,2-benzoquinone derivatives have been studied to a lesser extent than the 1,4-benzoquinone derivatives because they are generally more difficult to prepare in even moderate yields [9,10,12,13].

Previously, we have shown that catechols can be oxidized electrochemically to 1,2-benzoquinone. The in situ generated *o*-quinones are quite reactive and can readily react with a variety of nucleophiles including 4-hydroxycoumarin [14], 4-hydroxy-6-methyl-2-pyrone [15], barbituric acids [16,17], benzenesulfinic acid [18], dimedone [19], acetylacetone [20] and can be subsequently converted to the corresponding coumestan [14,15], pyrimidine [16,17], sulfone [18] and benzofuran [19,20] derivatives, respectively. Since no report has been published until now on the electrochemical synthesis of monoamino-substituted *o*-benzoquinones, we now report a new synthetic strategy involving the electrooxidation of catechols (**1**) in the presence of dibenzylamine (**3**) as a bulky *N*-nucleophile to generate monoamino-substituted *o*-benzoquinones (**5**) in a single step with good yields. In this work, we describe the electrooxidation of 3-substituted catechols (**1**) in the presence of dibenzylamine (**3**) in water + acetonitrile (90/10) solution using electrochemical and spectroelectrochemical techniques. We propose a mechanism for the electrode process. An efficient electrochemical synthesis of monoamino-substituted *o*-benzoquinones (**5**) has been performed at carbon rod electrodes in a two-compartment cell.

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2. Experimental

2.1. Apparatus

Cyclic voltammetry, controlled-potential coulometry and preparative electrolysis were performed using an Autolab model PGSTAT 20 potentiostat/galvanostat. The working electrode used in the voltammetry experiments was a glassy carbon disc (1.8-mm diameter) and a platinum wire was used as the counter electrode. The working electrode used in controlled-potential coulometry and macroscale electrolysis was an assembly of four carbon rods (6-mm diameter and 4-cm length), and a large platinum gauze constituted the counter electrode. The working electrode potentials were measured vs. SCE (all electrodes from AZAR Electrodes).

The homogeneous rate constants were estimated by analyzing the cyclic voltammetric responses using the simulation CVSIM software [21].

2.2. Reagents

All chemicals (catechols and dibenzylamine) were reagent-grade materials and phosphate salts were of pro-analysis grade. These chemicals were used without further purification.

2.3. Electroorganic synthesis of **5a–c**

A solution (ca. 80 mL) of phosphate buffer ($C = 0.2$ M, pH 7.0) in water + acetonitrile (90/10) solution, containing 1 mmol of catechol (**1a–c**) and 1 mmol of dibenzylamine (**3**), was electrolyzed in a two-compartment cell at 0.40 V vs. SCE. The electrolysis was terminated when the current decreased by 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 the electrolysis, the precipitated solid was collected by filtration. The products were purified by column chromatography (silica gel, ethyl acetate and dichloromethane). After purification, products were characterized by UV, IR, ^{1}H NMR, ^{13}C NMR and MS. The isolated yields of **5a–c** after chromatography are reported in Scheme 1.

2.4. Characteristics of 4-dibenzylamino-1,2-benzoquinone ($C_{20}H_{17}O_2N$) (**5a**)

M.p. 108–109 °C. $UV_{max}(CH_3CN)$ λ (nm): 500, 289. IR (KBr), ν (cm^{-1}): 1685, 1599, 1535, 1452, 1351, 1295, 1230, 1182, 803, 738, 697. ^{1}H NMR (500 MHz, DMSO-d_6), δ (ppm): 4.80 (broad, 4H), 5.45 (s, 1H), 6.35 (d, $J = 10.4$ Hz, 1H), 7.20–7.39 (m, 10H), 7.55 (d, $J = 9.8$ Hz, 1H). ^{13}C NMR (500 MHz, DMSO-d_6), δ (ppm): 183.3, 174.7, 156.3, 135.0, 131.5, 129.3, 129.0, 128.0, 127.0, 100.1, 55.3. MS: *m/e* (relative intensity); 305 (M + 2H) (70.4), 304 (M + H) (9.2), 303 (M) (4.1), 243 (14.3), 242 (5.1), 214 (36.7), 91 (100), 65 (27.6), 39 (28.6).

2.5. Characteristics of 5-dibenzylamino-3-methyl-1,2-benzoquinone ($C_{21}H_{19}O_2N$) (**5b**)

M.p. 140–142 °C. UV_{max} (CH_3CN) λ (nm): 503, 303. IR (KBr), ν (cm^{-1}): 1677, 1643, 1598, 1537, 1451, 1354, 1293, 1233, 884, 821, 768, 737, 696, 626. ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 1.98 (s, 3H), 4.72 (broad, 4H), 5.72 (s, 1H), 6.96 (s, 1H), 7.17–7.39 (m, 10H). ^{13}C NMR (500 MHz, $CDCl_3$), δ (ppm): 182.8, 175.7, 157.2, 141.3, 135.1, 129.3, 128.6, 128.2, 126.4, 99.2, 54.4, 16.4. MS: *m/e* (relative intensity); 319 (M + 2H) (99.2), 318 (M + H) (28.6), 317 (M) (10.2), 228 (99.3), 227 (46.9), 226 (27.6), 91 (100), 65 (83.7), 39 (54.1).

2.6. Characteristics of 5-dibenzylamino-3-methoxy-1,2-benzoquinone ($C_{21}H_{19}O_3N$) (**5c**)

M.p. 145–146 °C. UV_{max} (CH_3CN) λ (nm): 546, 334. IR (KBr), ν (cm^{-1}): 1702, 1689, 1630, 1600, 1525, 1495, 1437, 1352, 1288, 1241, 1222, 1078, 944, 827, 764, 733, 708, 693, 627. ^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 3.61 (s, 3H), 4.72 (broad, 4H), 5.68 (s, 1H), 6.02 (s, 1H), 7.19–7.39 (m, 10H). ^{13}C NMR (500 MHz, $CDCl_3$), δ (ppm): 178.2, 173.5, 159.4, 154.5, 134.48, 129.3, 128.3, 126.4, 101.5, 96.1, 55.9, 55.2. MS: *m/e* (relative intensity); 335 (M + 2H) (83.7), 334 (M + H) (8.3), 333 (M) (8.2), 244 (79.6), 243 (81.8), 242 (20.4), 91 (100), 65 (28.6), 39 (26.5).

3. Results and discussion

3.1. Voltammetric studies

A cyclic voltammogram of 1.0 mM catechol in water + acetonitrile (90/10) solution containing 0.2 M phosphate buffer (pH 7) shows one anodic peak (A_1) at 0.20 and the corresponding cathodic peak (C_1) at 0.15 V, which correspond 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^{C1}/I_p^{A1}) of nearly unity, particularly during the recycling of the potential, can be considered as a criterion for the stability of *o*-benzoquinone produced at the surface of the electrode under the experimental conditions. In other words, any hydroxylation [22–24] or dimerization [25–27] reactions are too slow to be observed on the time scale of cyclic voltammetry. The oxidation of catechol (**1a**) in the presence of dibenzylamine (**3**) was studied in some detail. Fig. 1 (curve (c)) shows the first cyclic voltammogram obtained for a 1 mM solution of **1a** in the presence of 1.0 mM dibenzyl-