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Electrochemical synthesis of new organic compounds based on the oxidation of 1,4-dihydroxybenzene derivatives in the presence of primary and secondary amines

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ABSTRACT

An efficient method for the synthesis of 2-benzyl(4-hydroxyphenyl)amino)-6-(benzylamino)-*p*-benzoquinone derivatives and 2,5-bis-benzyl(methyl)amino)-*p*-benzoquinone based on the Michael type reaction is described. The electrochemically generated *p*-benzoquinone reacted with benzylamine derivatives (primary amines) and *N*-methylbenzylamine (a secondary amine), respectively, to produce the final products. In this work, some new symmetric and asymmetric *p*-benzoquinone derivatives are synthesized using green solvents with high yields.

1. Introduction

A vast number of structurally diverse quinones occur naturally; some of them play a major role in the redox electron-transport chains of living systems [1]. In addition, many drugs, such as doxorubicin, daunorubicin and mitomycin C in cancer chemotherapy contain quinones [2], whereas various other quinones have been used in industry [3]. Sayre and co-workers have investigated the behavior of quinone derivatives in the presence of benzylamine as a model for copper amine oxidases [4]. For example, the copper amine oxidases catalyze the oxidative deamination of primary amines to aldehydes at the expense of reduction of O_2 to H_2O_2 [5]. Similarly, quinone-mediated transamination of amines has precedent in the synthetically useful deamination of branched primary amines by 3,5-di-*tert*-butyl-1,2-benzoquinone [6] and in the deamination of benzylamine by pyrroloquinolinequinone. Sayre, Klinman and co-workers also showed that catalytic deamination of benzylamine and other amines proceeds with the addition of benzylamine to a carbonyl group of TPQ. This process forms a Schiff base, which hydrolyzes to release aldehyde and generates the reduced aminoresorcinol form of the cofactor. The Schiff base is subsequently reoxidized to the starting quinone with the release of NH_3 [7]. Amino derivatives of quinones are important building blocks in the synthesis of a variety of natural products, medicinal compounds [8] with antitumor and antimalarial activities [9]. Many of the alkylamino derivatives are involved in enzyme inhibition and DNA cross-linking [10].

The importance of interaction of amines, especially benzylamine derivatives, with quinones has motivated us to study the electrochemical oxidation of hydroquinone in the presence of various types of benzylamines. Aminoquinones are formed in the reactions of different amines with quinones [11]. For example 1,4-benzoquinone reacts with primary amines to give 2,5-diamino-1,4-benzoquinones. A

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similar reaction of 1,4-naphthoquinone with primary amines results in the formation of 2-amino-1,4-naphthoquinones [11d]. We previously studied the electrochemical oxidation of catechol derivatives in the presence of dibenzylamine [12]. It was shown that the electrochemically generated 1,2-benzoquinones participates in Michael type addition reactions with dibenzylamine, and converts to the amino or diamino substituted 1,2-benzoquinone derivatives. We also recently reported that electrochemical oxidation of 3,5-di-*tert*-butylcatechol in the presence of benzylamines produces 2-arylbenzoxazoles under green conditions [13]. In this work we describe a new route for the reaction of benzylamine derivatives with electrochemically derived *p*-benzoquinone.

2. Results and discussion

2.1. Electrochemical study of HQ in the presence of primary amines

The oxidation of hydroquinone (HQ) is pH dependent [14]. Similarly, the concentration of deprotonated benzylamine(s) (BA) depends on the pH [15]. Therefore, studying the effect of pH on the reaction of electrogenerated *p*-benzoquinone with benzylamines is essential to identify the optimum pH value. Fig. 1a shows the cyclic voltammogram of HQ at pH = 10.0. It is worth mentioning that the pk_{a1} of HQ is 9.85 [16], therefore the HQ monoanion (HQ^-) predominates at pH = 10. As can be seen, it shows one anodic peak (A_1) and its cathodic peak (C_1), which corresponds to the transformation of HQ^- to *p*-benzoquinone and vice versa [17]. The oxidation of HQ^- in the presence of BA as a nucleophile was also studied at pH = 10.0. Fig. 1b shows the cyclic voltammogram obtained for a solution of HQ^- in the presence of BA. The comparison of cathodic to anodic peak current ratio (I_{pC1}/I_{pA1}) in the absence and presence of BA shows a decrease of the I_{pC1}/I_{pA1} for the latter (Fig. 1b, pH = 10.0). The existence of a subsequent chemical reaction between *p*-benzoquinone and BA is supported by the following evidence: (a) The decrease in the I_{pC1}/I_{pA1} ratio indicates that *p*-benzoquinone is removed by a chemical reaction with BA. (b) The dependency of I_{pC1}/I_{pA1} on the potential sweep rate shows that with an increasing sweep rate, the peak current ratio (I_{pC1}/I_{pA1}) increases. It shows a departure from the intermediate region and arrival at the diffusion region [18]. It is worth mentioning that the same electrochemical results were obtained when methoxybenzylamine (MBA) (a benzylamine with an electron donating group) and chlorobenzylamine (CBA) (a benzylamine with an electron withdrawing group) were used.

It has been shown that in basic solutions the electrochemically generated quinones are unstable due to side reactions, such as hydroxylation [19] and/or dimerization reactions [20]. The rates of these reactions are pH dependent processes and enhanced by increasing pH [21]. Our result shows that the interference of these reactions is important especially at pH values ≥12. At these pHs, HQ^- shows an irreversible anodic process (Fig. 2).

Fig. 1 also shows the cyclic voltammograms of HQ in the presence and absence of BA at pH 7.5. There is little difference between the cyclic voltammograms of HQ in the absence (curve a) and presence (curve b) of BA. This is attributed to partial protonation of BA and its inactivation toward the Michael type addition reaction with *p*-benzoquinone. Therefore synthesis at alkaline pH has been

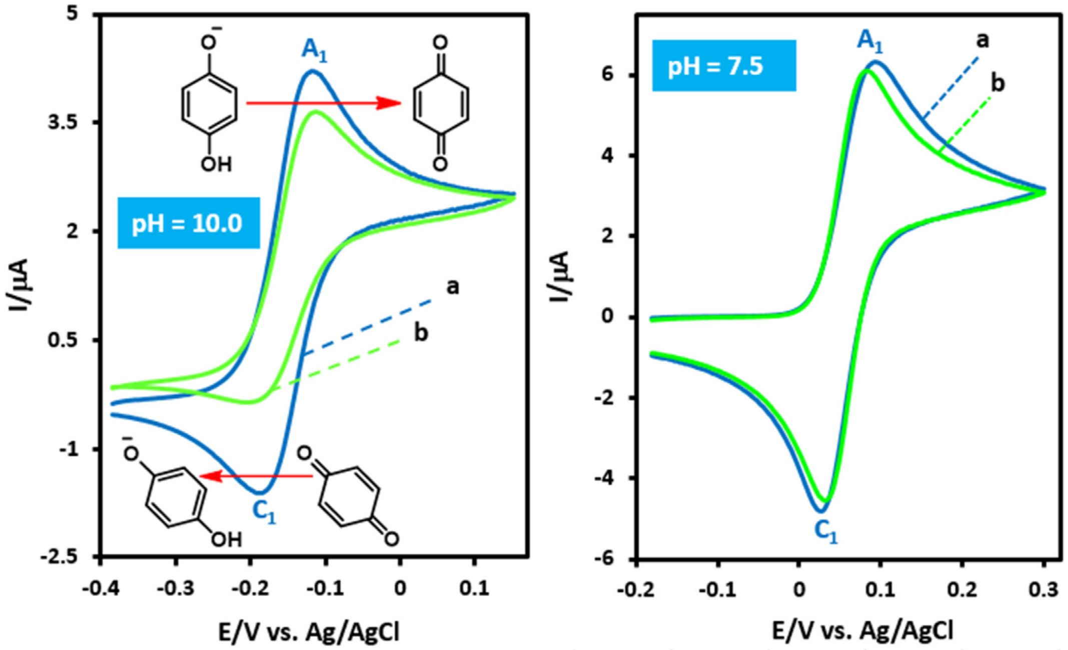

Fig. 1. Cyclic voltammograms of hydroquinone (1.0 mM) (a) in the absence, (b) in the presence of benzylamine (4.0 mM), at pH values 10.0 and 7.5, at a scan rate of 10 mV s^{-1}, on a glassy carbon electrode. Temperature = 25 ± 1 °C.

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