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Electrochemical synthesis of quinones and other derivatives in biphasic medium

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ABSTRACT

Electrochemical synthesis of quinones has been attempted from phenols, 1,4-dihydroxybenzenes, 1,4-dihydroxynaphthalenes and related compounds using biphasic media. Excellent yields of quinones (98%) or brominated diols have been achieved with good current efficiency. Reuse of the electrolyte without any modification and quantitative conversion of substrate with theoretical amount of current are the advantages of this method.

Introduction

Quinones are the largest group of naturally occurring pigments coloured bright yellow or red. 1,4-Benzoquinone is the basic structure of quinonoid compounds. They are essential for many life processes in that they readily participate in biological redox processes. For example, the ubiquinones are the essential electron-transfer agents in our respiratory chain. Doxorubicin is one of the front-line cancer chemotherapy treatment agent. They function as intermediates in the biosynthesis of important antibiotics like tetracyclines, and exhibit a broad spectrum of biological activities with antioxidative, cytotoxic, anticancer, antidiabetic and enzyme inhibitory activities.[1–8]

The synthesis and study of quinones is therefore of immense importance given the biological activity associated with many such compounds, and hence it is an extremely active area of research worldwide.[1–4] Quinones also have importance as intermediates in organic synthesis and are among the most abundant substructures found in numerous naturally occurring bioactive molecules.[5–7]

2-Alkylanthraquinones are used in the industrial production of hydrogen peroxide. Benzoquinone is used as an oxidizing agent. Strongly oxidizing quinones include chloranil and 2,3-dichloro-5,6-dicyano-1,4 benzoquinone (DDQ). 9,10-Anthraquinone-2,7-disulphonic acid (AQDS) a quinone similar to one found naturally in rhubarb has been used as a charge carrier in metal-free flow batteries.[5]

1,4-Benzoquinones are often readily made from reactive aromatic compounds with electron-donating substituents such as i) Phenols with *t*-butyl hydrogen peroxide/Ru catalyst,[9] polymer supported vanadium salt,[10] supported heteropolycompounds,[11] potassium peroxomonosulfate catalysed by iron and cobalt phthalocyanine tetrasulfonate,[12] ii) By the selective demethylation of dimethoxy benzene or hydroquinone dimethyl ether with nitric acid,[13] silver oxide,[14] CAN in CH_3CN[15–28] and with H_2O_2/methyltrioxo rhenium.[29] iii) Direct oxidation of aromatic ring compounds to quinone also reported. For example 2-methylnaphthalene was quantitatively oxidized to quinones, 2-methyl-1,4-naphthoquinone 66% (vitamin-K_3) and 6-methyl 1,4-naphthoquinone 34% using Ce(IV)methanesulphonate as oxidant.[30] But the known pathways demonstrate disadvantages regarding selectivity and sustainability. iv) By the Oxidation of 1,4-dihydroxybenzene with ceric ammonium nitrate(CAN),[31,32] AgO,[33,34] HOCl[35] represent a useful alternative method. The oxidation of hydroquinone is a rapid and convenient method to get quinone due to formation of single isomer. Recently, Chaturvedi et al. reported the oxidation of phosphorylated 1,4-dihydroxynaphthalenes in THF to the corresponding 1,4-naphthoquinones in excellent yields using *N*-bromosuccin-

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imide (NBS).[36] The conventional method has the disadvantages of handling highly corrosive and costly oxidant and in the case of NBS, disposal of succinimide is an additional step involved. The electrochemical oxidation of quinol phosphate has been reported in aqueous solutions.[37] Linjin Ma et al. reported on the oxidation behaviours and the diffusion mechanism of hydroquinone at pre-anodized carbon paste electrode by cyclic voltametry.[38] Electro synthesis of benzoquinone from phenol was studied by Abaci et al.[39] by the potentiostatic electrolysis of a CH_3CN solution containing 20 mM phenol, 20 mM water, 10 mM $HClO_4$ and 100 mM TBAP using PbO_2 electrode. The maximum efficiency of 61% and 74% of conversion was observed with α & β-surfaces of the PbO_2 electrodes respectively at a potential of 1.6V versus Ag/AgCl. The benzoquinone decomposition products increased beyond 20 mM phenol concentration. Though the electrochemical oxidation of hydroquinone to quinone was examined by cyclic voltammetry by a number of authors the galvanostatic method was not reported to the best of our knowledge.[40–42]

In this communication, we report a convenient method for the oxidation of 1,4-dihydroxybenzene derivatives to the corresponding 1,4-benzoquinones by the galvanostatic biphasic electrolysis (Scheme 1). The aqueous NaBr containing H_2SO_4 present as aqueous phase and dichloromethane containing the aromatic diol as the organic phase. A charge of 2F/mol of the substrate were passed maintaining the temperature of the reaction mixture at 15 °C for quinone formation. However, in cases where quinones did not form, the nuclear brominated products were formed with the passage of 2 faraday charge and tribromo derivatives were formed as a single product after passing a charge of 6.5 F/mol.

Results and discussion

In this study, oxidation of 1,4-dihydroxybenzene derivatives to the corresponding 1,4-benzoquinones was investigated by electrolysis in biphasic media. Aqueous NaBr containing H_2SO_4 is the upper phase and CH_2Cl_2 containing 1,4-dihydroxybenzene is present in the lower organic phase. The electrolysis was carried out at 15 °C. During the electrolysis the substrate gets oxidised at the anode surface with the theoretical amount of current.[43] In the conventional two phase electrolysis the water insoluble reactant is present in the lower organic phase and the reactive species generated the by the electrolysis migrates from upper aqueous phase to the inter phase for the reaction to occur and the product can be isolated from the organic phase after evaporation of the organic solvent.

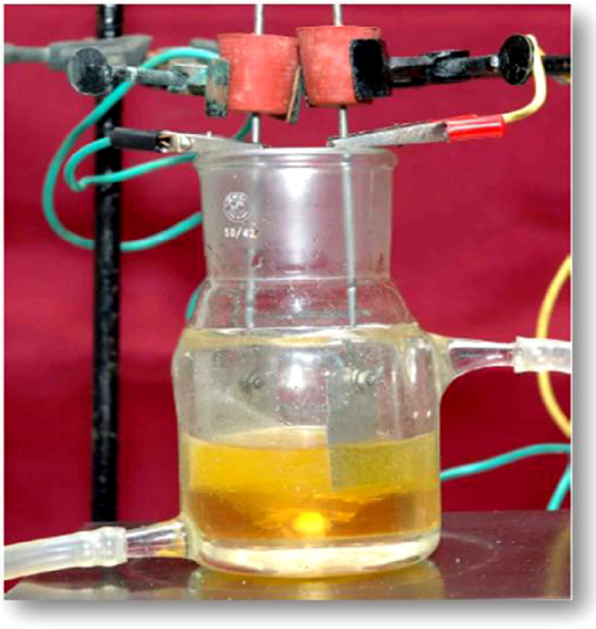


Fig. 1. Electrochemical cell for galvanostatic biphasic electrolytic oxidation.

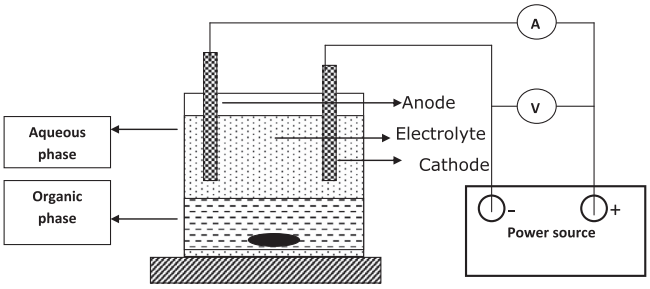
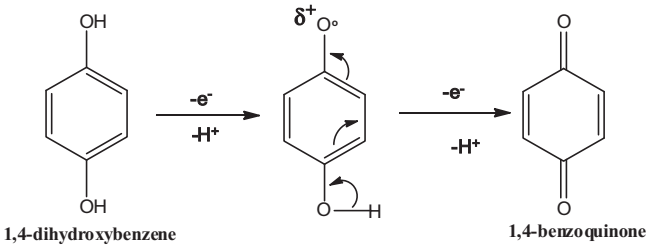


Fig. 2. Reaction set-up for galvanostatic biphasic electrolytic oxidation.



Scheme 1. General mechanism for the electro chemical oxidation of 1,4-dihydroxybenzene in a biphasic medium.

The advantage of the present method is that the utilization of theoretical amount of current for quantitative conversion of the substrate due to the existence of water soluble substrate (1,4-dihydroxybenzene) near the vicinity of electrode in the upper aqueous phase and the migration of the product to the more soluble organic phase avoids the over oxidation of highly reactive quinones. After removal of the product from the organic phase, the aqueous electrolyte could be reused several times for further synthesis of quinones or the nuclear brominated products as the case may be.

The possible reaction mechanism for the oxidation of 1,4-dihydroxybenzene is given in the Scheme 1. Initially water soluble 1,4-dihydroxybenzene forms a phenoxy radical ($HOC_6H_4O^{\cdot}$) at the vicinity of anode followed by the rearrangement of electrons to remove a proton from another phenolic group.

$$HOC_6H_4OH \rightarrow HOC_6H_4O^{\cdot} + H^+ + 1e^-$$

$$HOC_6H_4O^{\cdot} \rightarrow C_6H_4O_2(\text{benzoquinone}) + H^+ + 1e^-$$

The results on the electrochemical oxidation of aromatic diols using biphasic electrolysis are shown in Table 1. It has been shown that benzoquinone can be prepared with high efficiency from hydroquinone in 89–99% yield with >99% conversion. It can be seen that reactant 1–5, wherein the alcoholic groups present in 1,4-position, yielded quinones, i.e. 1,4-benzoquinone or 1,4-naphthoquinone as the case may be with yields in the range of 94–97% with high current efficiencies. However with reactant 6 (9,10-dihydroxyanthracene), no reaction occurred due to the quinol ring being highly deactivated due to adjacent benzene rings in either direction and hence resistant to oxidation. Whereas the reactant 7 to 9 (catechol and resorcinol), the corresponding bromo derivatives were formed as the products, instead of quinones with the passage of 2 F of charge. This is mostly probably due to steric effect which prevents quinone formation. With reactant 10, bromination occurs