Journal of Materials and Environmental Sciences
ISSN : 2028-2508
CODEN : JMESCN

J. Mater. Environ. Sci., 2020, Volume 11, Issue 1, Page 101-108

http://www.jmaterenvironsci.com

Diversity in Electrochemical Oxidation of Catechols in The Presence of Malononitrile: Application for Green, High Efficient and Simple Method for Synthesis of New Catechol and Quinone Derivatives

Donya Arefi, Raziyeh Sanavi Khoshnood * and Mahmoud Ebrahimi

Departeman of Chemistry, Mashhad Branch, Islamic Azad University, Mashhad, Iran

Received 05 July 2019,
Revised 24 Aug 2019,
Accepted 27 Aug 2019

Keywords
- ✓ Michael Addition,
- ✓ Quinone,
- ✓ Voltammetric Method

rskhoshnood@yahoo.com

Abstract

Electro-oxidation of catechol derivatives (1a-b) has been studied in the presence of malononitrile (3) as nucleophile in phosphate buffer solution (pH 7 and c = 0.2 mol L-1), using voltammetric methods. The results indicated that the o-benzoquinones derived from (1a-b) participates in 1,4-Michael addition reaction with malononitrile via ECE and ECEC mechanism that produces the relative new compounds (8a and 6b). this study has led to the development a simple method for the synthesis of new quinone and catechol derivatives.

1. Introduction

The term of quinone refers generally to a 1,4 or 1,2-diketone formally derived from dihydroxy aromatic compounds in which the two carbonyl groups are connected by a system of conjugated double bonds [1-3]. Naturally of properties quinones have captured human attention, because of their bright color with possible uses as dyes and drugs [4].

A large number of quinones with great structural diversity are provided by nature; some of them play a major role in the red-ox electron-transport chains of living systems [5]. Besides, *o*-quinones and *p*-quinones are of considerable interest because many drugs such as aclacinomycin A, adriamycin, carbazilquinone, daunorubicin, and mitomycin C in cancer chemotherapy contain quinines [6-9]. One of other applications of quinine is use in industry [10].

On the other hand, some of quinoes also exhibit anti-tumor and anti-malarial activities and many of them are also involved in enzyme inhibition and DNA cross-linking [11-13]. Also, it is demonstrated in comparison with simple catechols and quinones that highly oxygenated catechols [14-16] and quinines exhibit interesting biological activities [17,18].

Furthermore, catechol derivatives are a promising group of compounds which may lead to the discovery of selective acting, biodegradable agrochemicals having high human, animal and plant compatibility and, thus, worthwhile for further investigation [15].

Since, no report has been published until now about the electro-synthesis or synthesis and identification of such catechols or quinones, we have investigated the electrochemical oxidation of catechol derivatives in the

presence of malononitrile. We wished to study the effect of the existence of a methyl group in a reactive site of catechol. The work has led to the development of a simple, fast, green (without any toxic solventin) and catalyst-free method for the synthesis of new catechols and quinones with good yield and high purity.

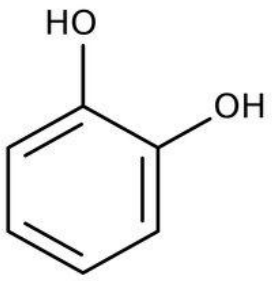
2. Experimental

Apparatus and reagents- Cyclic voltammetric experiments were performed using a Metrohm Voltammetric Analyzer Model 747 (Herisau, Switzerland) and controlled-potential coulometry was performed using a Behpajooh model 2062 galvanostat/potentiostat (Isfahan, Iran). The working electrode (WE) used in the voltammetry experiments was a glassy carbon disc (GC, 2 mm diameter) and platinum disk was used as a counter electrodes (CE). The working electrode (WE) used in controlled-potential coulometry was an assembly of 3 carbon rods (6 mm diameter and 8 cm length), and a sheet platinum (1 cm^2) constituted the counter electrode (CE). The working electrode potentials were measured versus Ag/AgCl. All electrodes were from AZAR Electrode Company (Urmia, Iran). NMR spectra were recorded on a Bruker DRX-400 Advance Instrument (Germany). Infrared (IR) spectra were recorded on a Shimadzu 8400S Fourier transform (FT)–IR spectrophotometer (Tokyo, Japan). All chemicals material was purchased from Merck (Darmstadt, Germany).

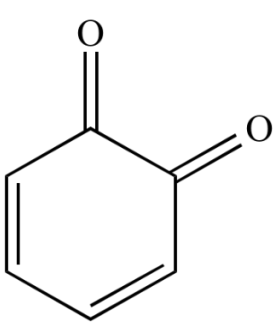
Typical method for the electrochemical synthesis of products (8a and 6b)- In this procedure, 100 ml of phosphate buffer solution (0.2 M, pH 7) as supporting electrolyte was pre-electrolyzed at the 0.45 V *vs*. Ag/AgCl in a two compartment cell. 0.5 mmol of catechol **(1a)** and 1 mmol of malononitrile **(3)** were then added to the cell (in the case of product **6b**, 0.5 mmol of catechol **1b** and 0.5 mmol of malononitrile). In continues, the coulometry under constant potential was performed using the 0.45 V *vs.* Ag/AgCl. The coulometry was terminated when the anodic current had been decreased more than 95%. The process was interrupted five times during the electro-organic synthesis of **8a** and **6b** compounds, to ensure complete electro-synthesis reaction. The carbon anodes were also washed in tetrahydrofuran to reactivate and clear the surface of working electrodes from formed side products such as polymers. At the end of electrochemical synthesis, the cell was placed in the refrigerator (3 ± 1^0C) for 12h. The precipitated solid was collected by centrifugation and washed with warm water to separate the remained catechols and malononitrile. Then, the products were sufficiently purified and the products were characterized using FT-IR, ^{1}H NMR, ^{13}C NMR and elemental analysis (CHN).

Catechol derivative (8a): yield: 84%. Mp >250 ºC (decomposed). FT-IR (KBr, cm^{-1}): 3520 (OH), 2190 (CN), 1573 and 1480. ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.87 (s, 1H, $CHCN_2$), 6.73 (s, 1H, aromatic), 8.78 (broad, 1H, OH). ^{13}C NMR (100 MHz, DMSO-d_6): δ 20.5, 110.3, 123.7, 127.5, 144.8. Anal. Calcd. for $C_{12}H_6N_4O_2$: C, 60.51; H, 2.54; N, 23.52. Found: C, 60.49; H, 2.52; N, 23.50.

Quinone derivative (6b): yield: 88%. Mp >250 ºC (decomposed). FT-IR (KBr, cm^{-1}): 2188 (CN), 1552 and 1471. ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.91 (s, 3H, CH_3), 3.88 (s, 1H, $CHCN_2$), 5.98 (s, 1H, quinone ring), 6.36 (s, 1H, quinone ring). ^{13}CNMR (100 MHz, DMSO-d_6): δ 19.7, 28.4, 110.4, 119.7, 122.1, 132.7, 137.9, 188.3, 188.6. Anal. Calcd. for $C_{10}H_6N_2O_2$: C, 64.52; H, 3.25; N, 15.05. Found: C, 64.49; H, 3.26; N, 15.07.



Cathecol



Quinone

3. Result and Discussion

Voltammetric studies- Electrochemical investigations of catechol **(1a)** in the presence and absence of malononitrile **(3)** as a nucleophile have been studied by cyclic voltammetry in a phosphate buffer solution (0.20 M, pH 7), under mild conditions. Typical cyclic voltammograms of **1a** are shown in Figure 1. It is clear from Figure 1 (curve a, section1) that, on the first anodic scan, one oxidation peak (A_1) at 0.14V was observed, while on the reverse scan a corresponding cathodic peak (C_1) at 0.11V appeared. These well-defined anodic and cathodic peaks are corresponding to the electrochemical oxidation of catechol **(1a)** to *o*-benzoquinone **(2a)** and *vice versa* within a quasi-reversible two-electron process [16]. The peak current ratio (IpC_1/IpA_1) is nearly equal to unity, which confirms the stability of *o*-benzoquinone produced at the surface of electrode under optimum condition, and the side reactions [17,18] which are too slow on the time scale of the cyclic voltammetry. The electro-oxidation of 2 mM of **1a** in the presence of 4 mM of **3** was investigated by cyclic voltammetry. Figure 1 (curve b, section 1), shows the cyclic voltammograms recorded for solution of 2 mM of **1a** in the presence of 4 mM of **3**. Under these optimum conditions, the cathodic counterpart of anodic peak A_1 decreases and a new cathodic peak (C_0) appears at potentials more with greater negative values than the cathodic peak (C_1) is related to electrochemical reduction of intermediate **6a** to **5a**. In addition, curve c (Figure 1, section 1) shows the cyclic voltammogram obtained for a solution of 2 mM of **3** in the absence of **1a**. On the other hand, electrochemical behavior of 4-methyl catechol **(1b)** in the absence and presence of malononitrile **(3)** was investigated (Figure 1, section 2).

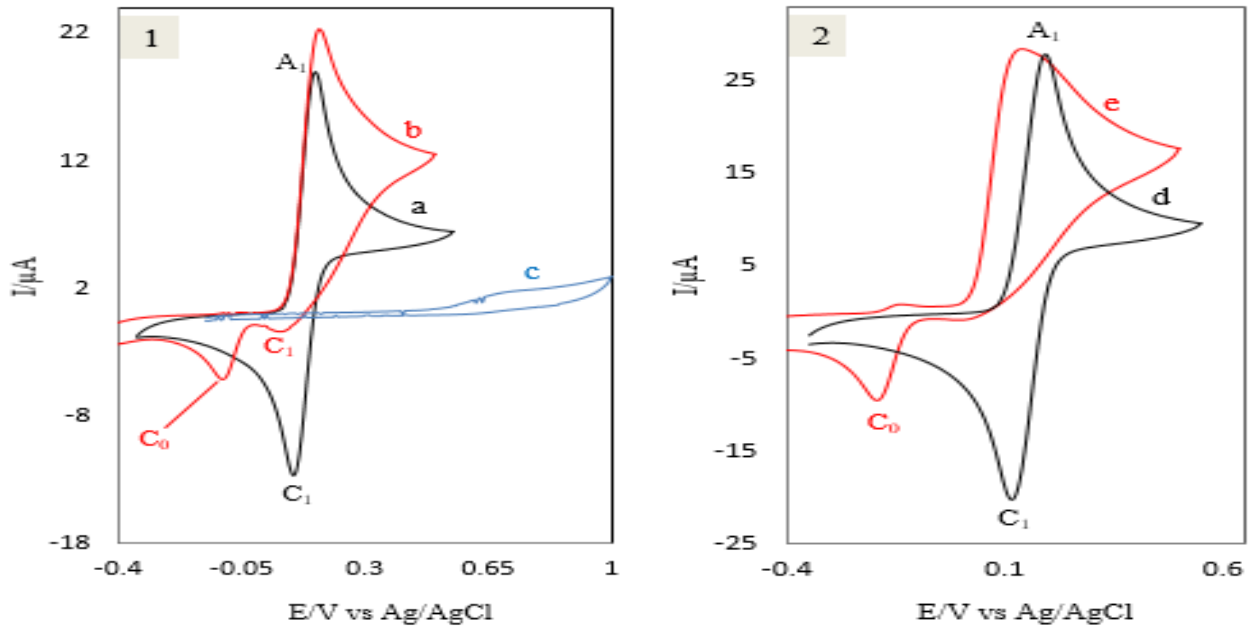


Figure 1. Cyclic voltammograms of 2 mM catechol (1a) in the absence (a), in the presence of 4 mM 3 (b), that of a 2 mM 3 in the absence of 1a respectively (c) and 2 mM 4-methyl catechol (1b) in the absence (d), in the presence of 2 mM 3 (e) at the glassy carbon electrode under optimum condition at a scan rate of 50 mVs^{-1}.

It is shown that, proportional to the increase of the potential scan rate and parallel with the decrease in height of C0, the height of C1 increases (Figure 2). The peak current ratios (I_{pC1}/I_{pA1}) and (I_{pC0}/I_{pC1}) versus potential sweep rate for a mixture of 2 mM of catechol **(1a)** and 4 mM of malononitrile **(3)** confirm the reactivity of **2a** towards **(3)** for 1,4- Michael addition reaction, appearing as an increase in the I_{pC1}/I_{pA1} (Figure 3) and a decrease in the I_{pC0}/I_{pC1} (Figure 3) at higher potential sweep rates.

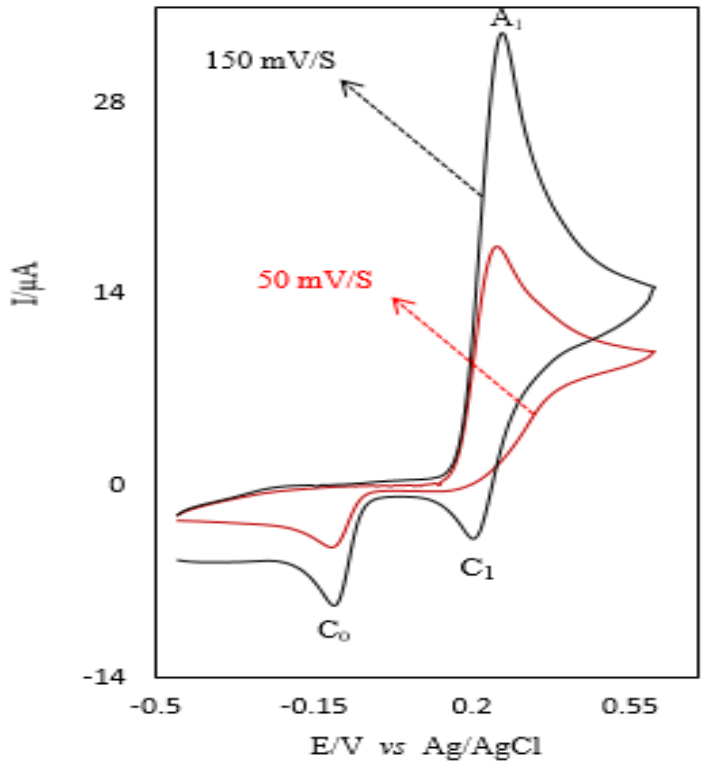


Figure 2. Typical cyclic voltammograms of 2 mM 1a in the presence of 4mM of 3 at the glassy carbon electrode, under experimental condition at various scan rates.

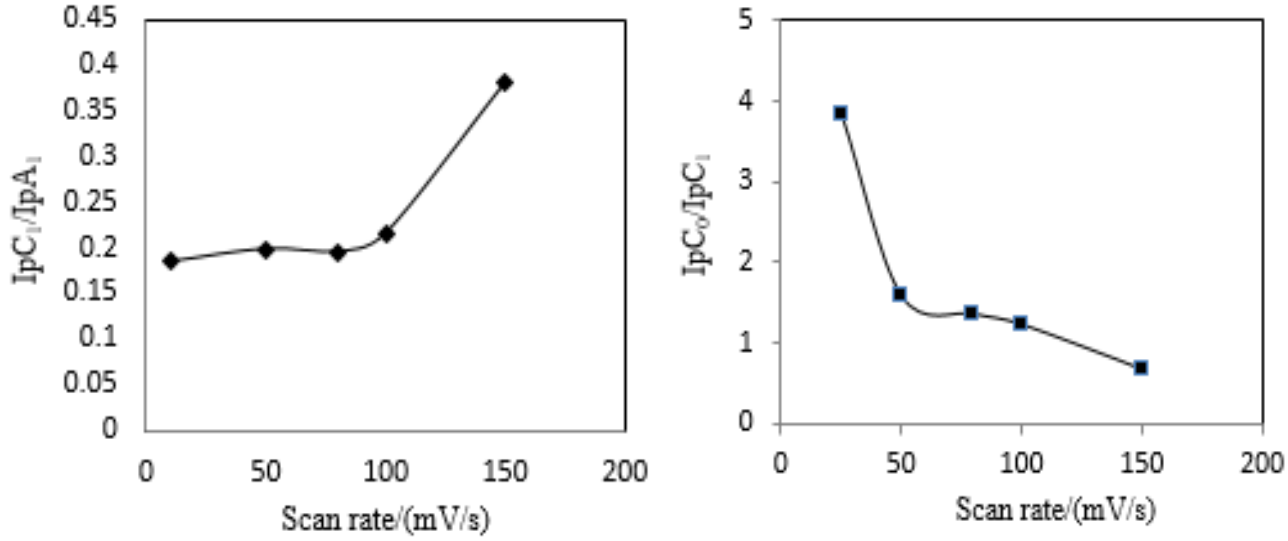


Figure 3. Variation of the peak current ratio I_{pC1}/I_{pA1} and I_{pC0}/I_{pC1} *versus* scan rate for 2 mM of catechol in the presence of 4 mM of 3 at the various scan rates under the optimum condition

The multi-cyclic voltammetry of **1a** in the presence of **3** shows that in the second cycles, parallel to the shift of the A1 peak in a positive direction, a new anodic peak (A0) appears (Figure 4). This new peak is related to electrochemical oxidation of intermediate **5a** to **6a**. The positive shift of theA_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 the electrode process [19]. According to our observation, it appears that the 1,4-Michael addition reaction of **3** to **2a** is much faster than other side reactions, leading to formation of intermediate **5a**.

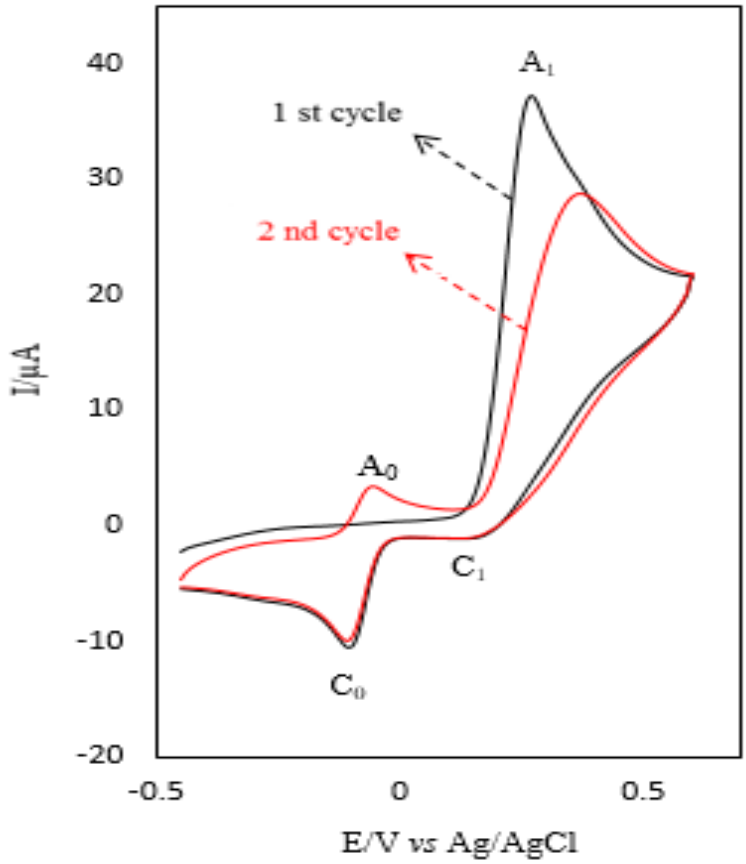


Figure 4. multi-cyclic voltammograms of 2 mM catechol (1a) in the presence of 4 mM 3 at glassy carbon electrode under experimental optimum condition, scan rate: 100 mVs^{-1}.

The electro-oxidation of this compound is easier than the electro-oxidation of the parent starting molecule **1a** due to the presence of an electron-donating group. After transformation of intermediate **5a** to **6a** the latter can be attacked with another **3** (Scheme 1). The product **8a** is insoluble in the phosphate buffer solution (pH 7, 0.2 M). Also, electro chemical oxidation of 4-methyl catechol **(1b)** in the presence of **3** was investigated (data in supporting information). According to our results, ECE mechanism was proposed for electro-oxidation of **1b** in the presence of **3** (Scheme 2).

Controlled-potential coulometry was performed in phosphate buffer solution (pH 7 and c = 0.2 mol L^{-1}) containing 4 mM of **1a** and 8 mM of **3** at 0.45 V *vs* Ag|AgCl electrode. The coulometry progress was carried out by cyclic voltammetry method (Figure 5). It is observed that, in proportion to the progress of coulometry, all of anodic and cathodic peaks have disappeared when the charge consumption becomes about $4e^-$ per molecule of **1a** in the presence of **3** (Figure 5, curve a-d).

Effect of pH- Electro-synthesis of **8a** and **6b** were performed in the acidic, natural and basic media (pH: 3 to 10) and maximum amount of pure product was obtained at pH 7, therefor pH 7 was selected as optimum pH value for electro-synthesis of our products (**8a** and **6b**).

According to the coulometric, voltametric and spectroscopic data, the *ECEC* mechanism is proposed for the electro-oxidation of catechols **(1a)** in the presence of malononitrile **(3)** and the *ECE* mechanism is proposed for the electrochemical oxidation of 4-methyl catechols **(1b)** in the presence of **3** (Scheme 1 and 2).

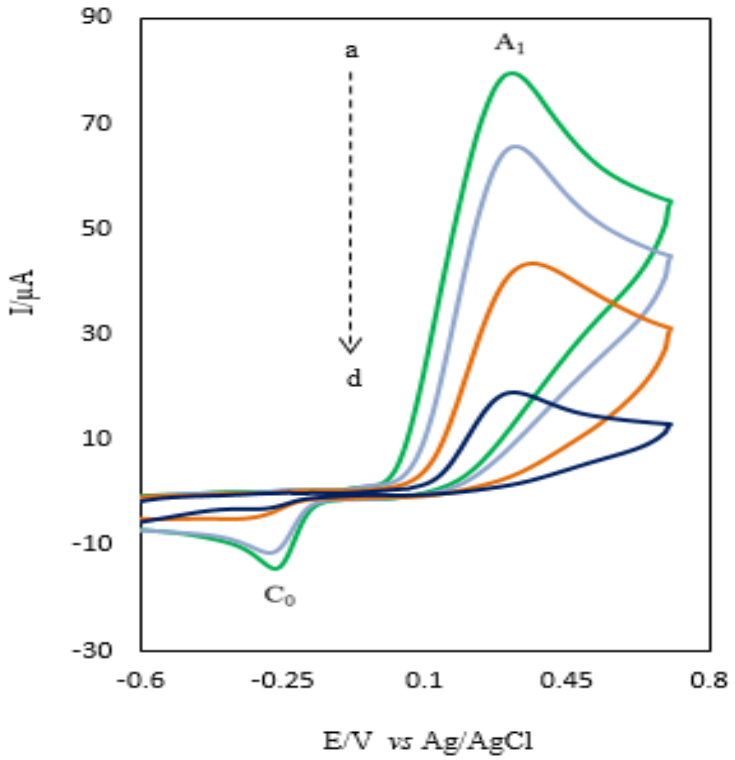
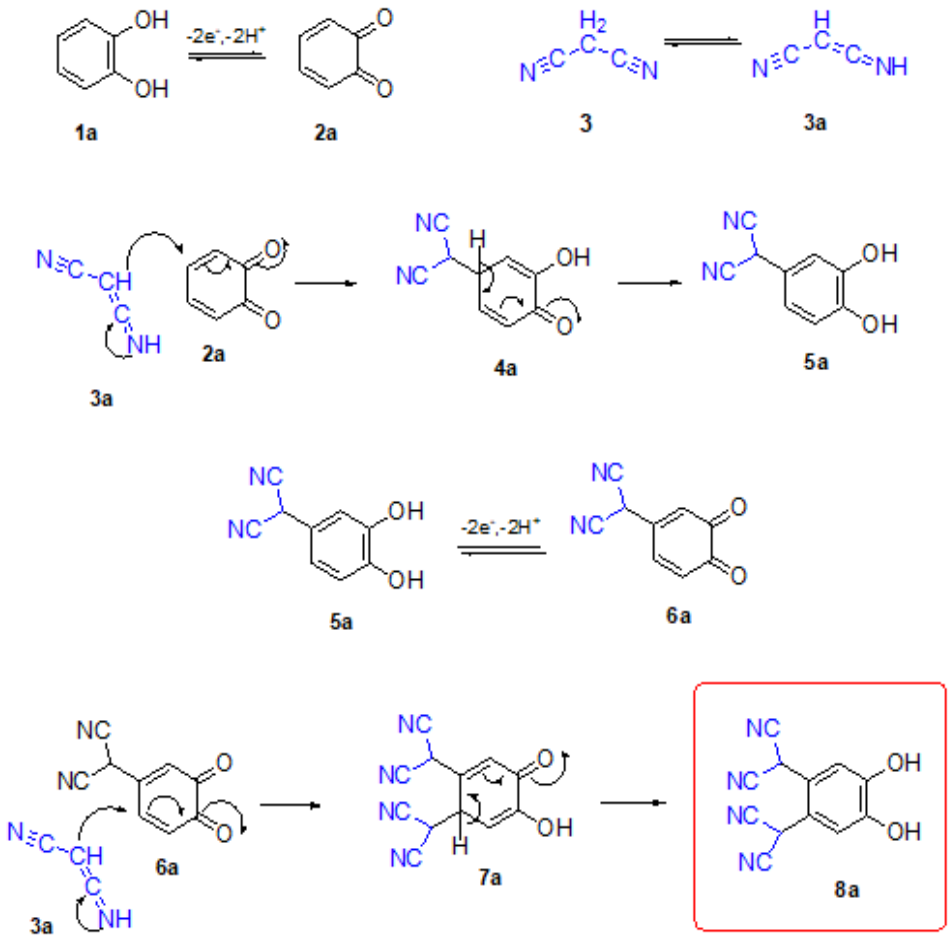
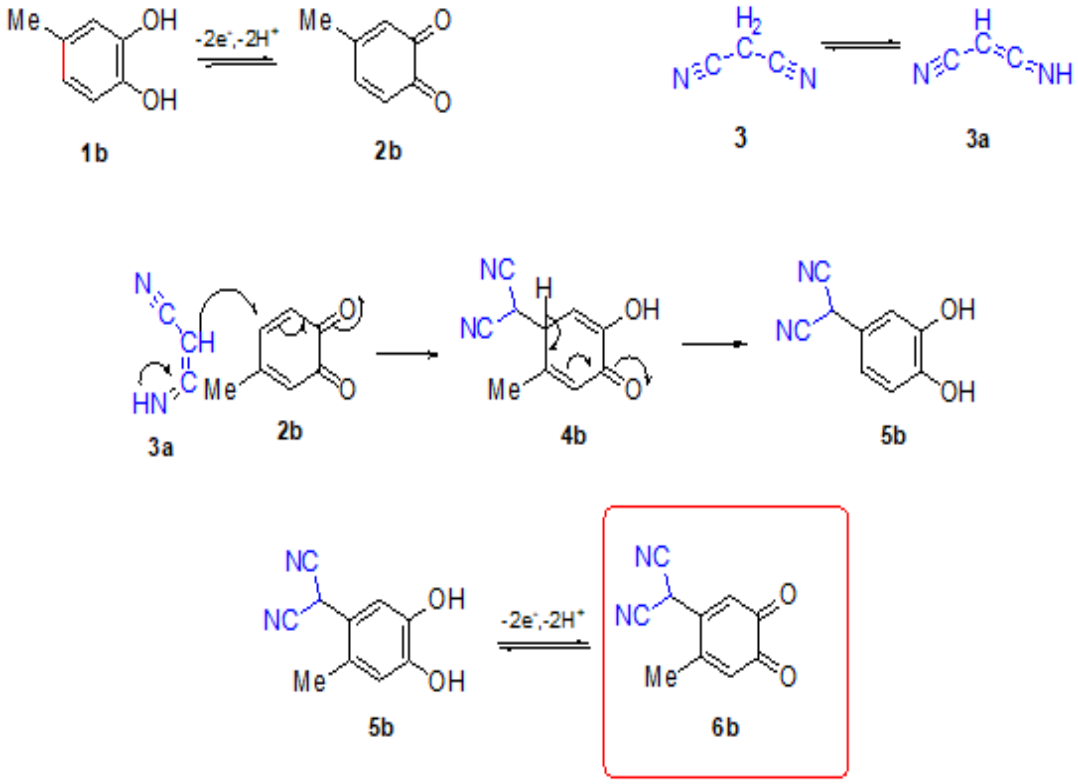


Figure 5. Cyclic voltammogram of 0.25 mmol catechol in the presenceof 0.5 mmol of malononitrile, at glassy carbon electrode under experimental conditions during electrolysis at 0.45 V *vs.* Ag/AgCl (scan rate: 50 mVs^{-1}). Progress of electrolysis is associated with decreased anodic peak (A1) current.



Scheme 1. Proposed of mechanism



Scheme 2. Proposed of mechanism

Conclusion

The present work is the first reported work in the electro-organic synthesis of compounds (**8a and 6b**) that have been produced efficiently and environmentally friendly from the electrochemical oxidation of catechols**(1a-b)** in the presence of malononitrile **(3)**. Safe waste and green synthesis, the use of electricity instead of chemical catalysts, mild conditions (room temperature and pressure), as well as a simple process conducted are marvelous features of this study. On the other hand, this study introduces electrochemistry as an *"efficient tool"* for the synthesis of new important organic compounds such as quinone and catechol derivatives.

Acknowledgment

The authors would like to thank from mashhad Azad University Research Council for financial supports of this work.

References

1. M. Florkin, E. H. Stozo, *comprehensive biochemistry* vol.9, pyrrole pigments, isoprenoid compounds and phenolic constituents; Elsevier publishing company, New York, eBook ISBN: 9781483222219 (1963).
2. Carmen Avendaño, J. Carlos Menéndez, Chap. 11 Drug Targeting in Anticancer Chemotherapy, in Medicinal Chemistry of Anticancer Drugs, ISBN:978-0-444-52824-7 (2008), https://doi.org/10.1016/B978-0-444-52824-7.00011-2
3. A. Mauger, C. Julien, A. Paolella, M. Armand, K. Zaghib, Recent Progress on Organic Electrodes Materials for Rechargeable Batteries and Supercapacitors, *Materials*, 12 (2019) 1770-1826; https://doi.org/10.3390/ma12111770
4. S. Patai, *The chemistry of quinonoid compounds* part I and II; John Wiley& Sons: New York, ISBN 0-471-91285-9 (Part 1), ISBN 0-471-91914-4 (Part 2), 1974. https://doi.org/10.1002/recl.19881071207
5. D. Nematollahi, M. Hesari, Electrochemical synthesis of amino-substituted 1,2-benzoquinone derivatives, *J. Electroanal. Chem.* 577 (2005) 197-203. https://doi.org/10.1016/j.jelechem.2004.11.031
6. R. H. Blum, S. K. Carter, Adriamycin. A new anticancer drug with significant clinical activity, *Ann. Intern. Med.* 80 (1974) 249-259. https://doi.org/10.7326/0003-4819-80-2-249

7. T. Komiyama, T. Kikuchi, Interactions of anticancer quinone drugs, aclacinomycin A, adriamycin, carbazilquinone, and mitomycin C, with NADPH-cytochrome P-450 reductase, xanthine oxidase and oxygen., *J. Pharmacobio-dyn.* 9 (1986) 651-664.
8. A. J. Shuhendler, P.J. O'Brien, A.M. Rauth, X.Y. Wu, On the synergistic effect of doxorubicin and mitomycin C against breast cancer cells. *Drug Metabol Drug Interact*.; 22(4) (2007) 201-33.
9. H. D. Beall and S. L. Winski, Mechanisms of action of quinone-containing alkylating agents I: NQO1-directed drug development, *Frontiers in Bioscience* 5(7) (2000) d629-638,
10. K. Kaleem, F. Chertok, S. Erhan, A novel coating based on poly(etheramine-quinone) polymers, *Prog. Org. Coating.* 15 (1987) 63-71. https://doi.org/10.1016/0033-0655(87)85004-5
11. D. Nematollahi, H. Shayani-Jam, Kinetic Study of Electrochemically Induced Michael Reactions of o-Quinones with Meldrum's Acid Derivatives. Synthesis of Highly Oxygenated Catechols, *J. Org. Chem.* 9 (2008) 3429-3434. https://doi.org/10.1021/jo800115n
12. G. T. Wondrak, Redox-Directed Cancer Therapeutics: Molecular Mechanisms and Opportunities, *Antioxid Redox Signal.* 11(12) (2009) 3013–3069. https://doi:10.1089/ars.2009.2541
13. B. Prabhu, A. Sivakumar, D. Balakrishnan, S. Sundaresan, Effect of lupeol on antioxidants and xenobiotic enzymes in N-Butyl-N-(4-hydroxybutyl) nitrosamine induced bladder carcinogenesis in experimental rats, *J. Exp. Ther. Oncol.*, 11(2) (2017) 139-416.
14. Y. Sawayama, T. Tsujimoto, K. Sugino, T. Nishikawa, M. Isobe, H. Kawagishi, Syntheses of Naturally Occurring Terphenyls and Related Compounds, *Biosci. Biotechnol. Biochem.* 70 (2006) 2998-3003. https://doi.org/10.1271/bbb.60389
15. Stacy H. DuVall Richard L. McCreery, Self-catalysis by Catechols and Quinones during Heterogeneous Electron Transfer at Carbon Electrodes, *J. Am. Chem. Soc.* 122(28) (2000) 6759-6764 https://doi.org/10.1021/ja000227u
16. L. Khalafi, M. Rafiee, M. Shahbak, and H. Shirmohammadi, Kinetic Study of the Oxidation of Catechols in the Presence of N-Methylaniline, *Journal of Chemistry*, Volume 2013, Article ID 497515, 5 pages http://dx.doi.org/10.1155/2013/497515
17. V. P. Bui, T. V. Hansen, Y. Stenstrøm, T. Hudlicky, Direct biocatalytic synthesis of functionalizedcatechols: a green alternative to traditional methods with high effectivemass yield, *Green Chem.* 2 (2000) 263. https://doi.org/10.1039/B006988O
18. Geoffrey A. Cordell, Hardcover ISBN: 9780123813411 eBook ISBN: 9780123813428, Academic Press, The Alkaloids, Volume 69 1st Edition Chemistry and Biology (2010)M.K. Bilonda and L. Mammino, Intramolecular Hydrogen Bonds in Conformers of Quinine and Quinidine: An HF, MP2 and DFT Study, *Molecules*, 22(2) (2017) 245; https://doi.org/10.3390/molecules22020245
19. AMICBASE-EssOil, Database on Natural Antimicrobials, Review Science, Germany, 1999-2002.
20. M. Arab Chamjangali, M. Bakherad, M. Ameri, Electrochemical oxidation of catechol derivatives in the presenceof 3-acetyldihydro-2(3H)-furanone: efficient and green methodfor synthesis of new butyrolactone derivatives, *Monatsh. Chem.* 146 (2015) 111-117 https://doi.org/10.1007/S00706-014-1286-6
21. M. D. Rayn, A, Yueh, C. Wen-Yu, The Electrochemical Oxidation of Substituted Catechols, *J. Electrochem. Soc.* 127 (1980) 1489-1495. http://dx.doi.org/10.1149/1.2129936
22. D. Nematollahi, M. Rafiee, A. Samadi-Maybodi, Mechanistic study of electrochemical oxidation of 4-tert-butylcatechol: A facile electrochemical method for the synthesis of new trimer of 4-tert-butylcatechol, *Electrochim. Acta.* 49 (2004) 2495-2502. https://doi.org/10.1016/j.electacta.2004.02.005
23. S. Golabi, D. Nematollahi, Electrochemical study of 3,4-dihydroxybenzoic acid and 4-tert-butylcatechol in the presence of 4-hydroxycoumarin application to the electro-organic synthesis of coumestan derivatives, *J. Electroanal. Chem.* 430 (1997) 141-146. https://doi.org/10.1016/S0022-0728(97)00134-4

(2020) ; http://www.jmaterenvironsci.com/