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# A Simple and convenient one pot synthesis of aminoquinone derivatives via Electrochemical amination of benzoquinone with secondary amines

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**ABSTRACT**

*A simple and efficient method for the convenient synthesis of aminoquinones have been described on reaction with catechol and various secondary amines using lithium perchlorate as a supporting electrolyte in acetonitrile media at platinum electrode under constant potential electrolysis. The results revealed that the o-benzoquinone derived from the oxidation of catechol, participates in Michael addition reaction with secondary amines and convert it into the aminoquinones in a good yield with high purity.The method is cost-effective, high-yielding, clean, and selective. The products of electrosynthesis have been purified and characterized by FTIR, $^{1}$HNMR, $^{13}$CNMR and mechanism was deduced with cyclic voltammetric study.*

**Key Words**: Anodic oxidation, cyclic voltammetry, electrochemical synthesis, o-benzoquinone secondary amines.

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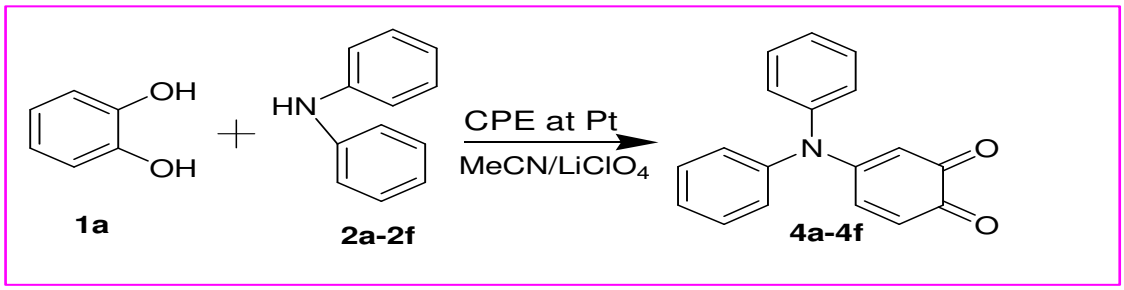
## INTRODUCTION

The anodic oxidation of a catechol generates a reactive o-benzoquinone that can be used to trigger a number of interesting reactions [1-5] and play an important role in the redox electron transport chains of living systems [6-8] for example, vitamine K is known to play an important role in blood coagulation mechanism and also in photosynthesis, vitamine E is important factor in electron transport and oxidative phosphorylation. More complex quinonoic compounds are used in medicine, as anticancer agents and their activity stems from their special ability to undergo one electron transfer reaction to form reactive radicals [9-10].

During recent years a number of methods have been developed to propose the synthesis of catechol derivatives. Among the most interesting and innovative chemical technologies, the electrochemical method provides a powerful means for the small-scale production of a number of value-added and high purity compounds [11-13]. Electroorganic reactions have found a wide application in industrial processes [14] and are of increasing interest with regard to the synthesis of complex molecules [15-18]. The major advantages of electrochemical methods include mild reaction conditions, the use of inexpensive electricity as a source of reduction equivalents, short reaction time, easy work up and high selectivity, resulting from the possibility to precisely tune the electrochemical potential at an

electrode. Furthermore, in some cases, electrochemical reactions can afford unexpected products that are difficult to prepare using chemical methods.

Aminoquinones have been found in many plants and their synthesis is regulated by stress conditions [19]. They are widely used in pharmaceutical preparations and in mammals; they are known to function as neurotransmitters with glycogen mobilizing ability [20]. The importance of biologically active compounds aminoquinone prompted to synthesize a number of these compounds by electrochemical oxidation of catechols in presence of various secondary amines [21]; such as diphenylamine, morpholine, piperazine and synthesized various biological and pharmaceutically active novel aminoquinone derivatives. Herein we wish to describe a one pot and straight forward protocol for synthesis of some aminoquinone derivatives in high yield and purity**. (Scheme 1)**




**Scheme 1:** Electrochemical synthesis of aminoquinones under constant potential electrolysis

## MATERIALS AND METHOD

### Instruments and reagents

Cyclic voltammetry, controlled potential coulometry and preparative electrolysis were performed using autolab model PGSTAT 20 Potentiostate/galvanostate. The working electrode used in the voltammetry experiments were a platinum electrodes and saturated calomel electrode (SCE) was used as reference electrodes. Melting points were obtained using a capillary melting point apparatus (Mel-Temp) and are uncorrected. IR spectra were registered with a Shimadzu 8201 PC spectrometer in KBr pellets. $^{1}H$ and $^{13}C$ NMR spectra were recorded with a Bruker DRX 400 (400 MHz) spectrometer in $CDCl_3$. Chemical shifts are reported in ppm downfield from TMS as internal reference. Mass spectra (EI, ionizing voltage 70 eV) were determined using a Thermofisher ITQ-900 DIP/GC-MS mass-selective detector. Elemental analyses were performed on a Perkin-Elmer model 240-B analyzer. IR spectra were measured using Bruker Alpha ATR spectrometer; samples were dissolved in $CHCl_3$. Chemicals used in reaction were reagent-grade, from Merck and Loba chemic. These chemicals were used without further purification. Water used for the experiment was double-distilled. All experiment were carried out in acetonitrile solution in presence of $LiClO_4$ as an electrolyte.

### Characteristics of products:

**4-(diphenylamino) cyclohexa-3, 5-diene-1,2-dione:**

brown colour solid, m.p 266-270˚C; $^{1}HNMR$ ($CDCl_3$); δ 6.6 (q, J 9.44, 1Har), 6.73 (t, J 14.56 ,1Har), 6.82 (t, J 15.24, 2Har), 7.1 (d, J 7.6, 2Har), 7.2 (d, J 15.72, 4Har), 8.30 (s, 1 Har), 8.8 (s, 1 Har); $^{13}CNMR$ ($CDCl_3$) 81.0, 118.4, 119.1,120.3, 128.7, 140.7, 144.0, 167.8, 180.5; GC-MS: $M^+$ (m/z = 275.09,100%); IR ($cm^{-1}$): 3044 ( ArC-H), 1715( 1,2 Benzoquinones) , 1594 (Ar-N), 1417 (ArC-C), 747 , 692; Anal. Calcd. (%) for $C_{18}H_{13}NO_2$: C, 78.54; H, 4.73; N, 5.09; O, 11.64; found C,

78.53; H, 4.76; N, 5.10; O, 11.61.

**4-(diethyl amino) cyclohexa-3, 5-diene-1, 2-dione:**

brown solid, m.p. 123-126˚C; $^{1}$H NMR ($CDCl_3$) δ 1.00 (t, J 21.88, 6H) , 2.59 (q, J 3.44, 4H), 5.00 (s, 1Har), 6.26 (s, 1 Har), 7.23 (s, 1Har); $^{13}$CNMR ($CDCl_3$) 15.0, 47.1, 80.2, 110.4, 140.0, 175.0, 182.5; GC-MS: $M^+$ (m/z = 179.09, 100%); IR ($cm^{-1}$) 3012 (ArC-H), 2125, 1632 (1,2 Benzoquinones) , 1489 (Ar-N), 1388 (ArC-C), 745; Anal. Calcd. (%) for $C_{10}H_{13}NO_2$; C, 67.04; H, 7.26; N, 7.82; O, 17.88; found C, 67.02; H, 7.31; N, 7.82; O, 17.85.

**4-(dimethylamino) cyclohexa-3, 5-diene-1, 2-dione:**

green solid, m.p.101-104˚C; NMR ($CDCl_3$) δ 2.47 (s, 6H), 5.25 (s, 1 Har), 6.66 (s, 1Har), 7.23 (s, 1Har $_r$); $^{13}$C NMR ($CDCl_3$) 43.1, 81.2, 115.4, 147.0, 178.4, 183.5; GC-MS: $M^+$ (m/z = 151.06,100%); IR ($cm^{-1}$) 3085, 1712 (1,2 Benzoquinones), 1539, 1145, 923, 712; Anal. Calcd. (%) for $C_8H_9NO_2$; C, 63.58; H, 5.96; N, 9.27; O, 21.19; Found C, 63.56; H, 6.00; N, 9.27; O, 21.17.

**4-(morpholino) cyclohexa-3, 5-diene-1, 2-dione:**

brown solid, m.p.162-165˚C; $^{1}$H NMR ($CDCl_3$) δ 2.45 (t, J 3.4, 4H), 3.47 (t, 4H), 5.15 (s, 1 Har), 6.20 (s, 1Har), 7.23 (s, 1Har); $^{13}$ CNMR ($CDCl_3$) 50.3, 67.3, 83.2, 118.4, 148.0, 175.4, 181.5; GC-MS: $M^+$ (m/z =193.07, 100%); IR ($cm^{-1}$) 3030, 1715, 1690, 1417, 1311, 1174, 956, 745; Anal. Calcd. (%) for $C_{10}H_{11}NO_3$; C, 62.18; H, 5.70; N, 7.25; O, 24.87; Found C, 62.17; H, 5.74; N, 7.25; O, 24.84.

**4-(piperazin-1-yl) cyclohexa-3, 5-diene-1, 2-dione:**

green powder, m.p.243-246˚C; $^{1}$H NMR ($CDCl_3$) δ 2.25 (m, 1H), 3.12 (t, 8H), 5.00 (s, 1Har ), 6.26 (s, 1Har), 7.23 (s, 1Har); $^{13}$CNMR ($CDCl_3$) 47.8, 58.7, 80.2, 117.4, 148.0, 175.4, 181.5; GC-MS: $M^+$ (m/z =192.09, 100%); IR ($cm^{-1}$) 3034, 2860, 1570, 1156, 933, 725; Anal. Calcd. (%) for $C_{10}H_{12}N_2O_2$; C, 62.50; H, 6.25; N, 14.58; O, 16.67; Found C, 62.49; H, 6.29; N, 14.58; O, 16.65.

**4-( piperidin-1-yl) cyclohexa-3,5-diene-1,2-dione:**

browm powder, m.p. 145-148˚C; $^{1}$H NMR ($CDCl_3$) δ 1.6(m, 6H), 2.7 (t, 4H), 5.10 (s, 1Har), 6.26 (s, 1Har), 7.23 (s, 1Har ); $^{13}$CNMR ($CDCl_3$) 26.0, 28.4, 48.8, 81.2, 116.4, 143.0, 175.4, 181.2GC-MS: $M^+$ (m/z =191.09, 100%); IR ($cm^{-1}$) 3089, 2870, 1565, 1170, 940, 720; Anal. Calcd. (%) for $C_{11}H_{13}NO_2$; C, 69.11; H, 6.81; N, 7.33; O, 16.75; Found C, 69.09; H, 6.85; N, 7.32; O, 16.73.

## RESULT AND DISCUSSIONS

In the course of our studies towards the synthesis of aminoquinones derivatives, we have reported the highly effective electrochemical technique for the oxidative conversion of catechol into *o*-benzoquinone in the presence of various secondary amines. Herein our interest is establishing a convenient, practical and general methodology for a variety of biologically active aminoquinones derivatives. In general, the efficiency of electrooxidation process can be enhanced by using a suitable solvent, supporting electrolyte and increasing the concentration of the intermediate.

In order to realize our goal, we commenced the study with a substrate (**1a**) was selected as a model substrate with appropriate amount and $LiClO_4$ as a supporting electrolyte. Both were dissolved in MeCN at room temperature. After electrolysis product (**4a**) was synthesized with complete consumption of the starting material in a 1-2 hours. No significant by products were detected by

TLC, $^{1}$HNMR, $^{13}$CNMR and mass spectroscopy. The protocol is economical and environmentally benign as it utilizes electrolysis and does not require any additives, heating or inert conditions.

Due to a number of advantages, in present one pot operation we used $LiClO_4$-acetonitrile as an ideal and also a non toxic pair.

- $LiClO_4$ is highly soluble in acetonitrile and do not form any complexes with solvent and substrate used, so maximum yield obtained during reaction.
- Due to co-catalyst nature it increases the rate of combination of benzoquinone with electrogenerated base and reaction goes on completion within a short time.
- Acetonitrile have a high dielectric constant so product form during reaction are soluble in solvent and media of reaction maintains.
- During electrolysis ionic activites increases in scheme so this pair maintain electrical neutrality of solution so avoid solution to make acidic or basic.

**Cyclic voltammetric study of catechol:**

Electrochemical properties of catechol investigated by cyclic voltammetry method. Cyclic voltammograms of 1mm catechol in acetonitrile solution at scan rate of potential 10 $mvs^{-1}$ is shown in Figure 1.

The voltammogram exhibits one anodic peak at 0.9 V potential respectively which corresponds to transformation of catechol (1a) to o-benzoquinone (2a) by two electron oxidation process, also a little amount of o-benzoquinone undergoes polymerization reaction.

Cyclic voltammogram of catechol in the presence of nucleophilic amines, show one anodic broad peak in the first scan of potential at scan rate of $10mVs^{-1}$ in Figure 2.

In lower concentration of secondary amines polymerization and catechol-secondary amine adduct formation take place in comparable degree, where as increasing the concentration of secondary amines make favorable nucleophilic attack toward o-benzoquinone generated at the surface of electrode. Consequently the amount of catechol- secondary amine adduct is more than polymer formation. On the basis of these observations we propose a plausible mechanism for the electrochemical oxidation of catechol in the presence of secondary amines.

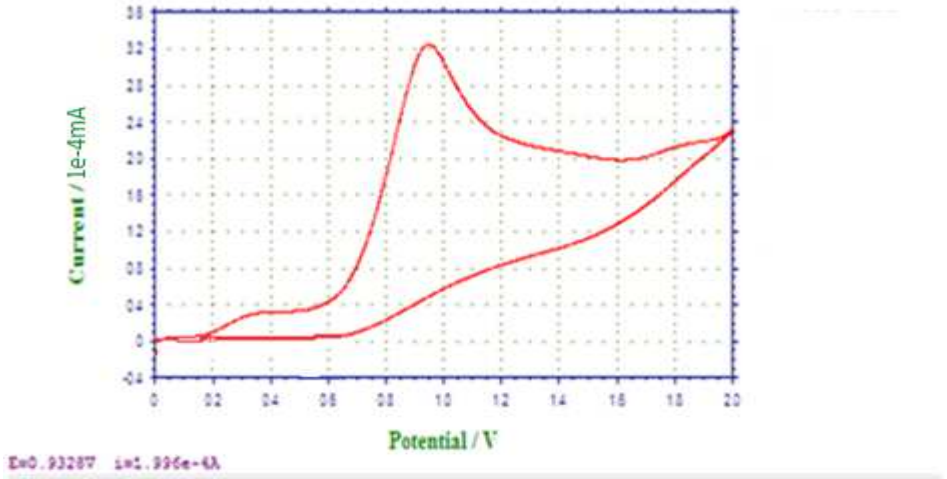


**Figure 1**: Cyclic voltammetry of catechol **(1a)** in the absence of nucleophiles at scan rate .01 m/s at potential within 0.0 V to 2.0 V

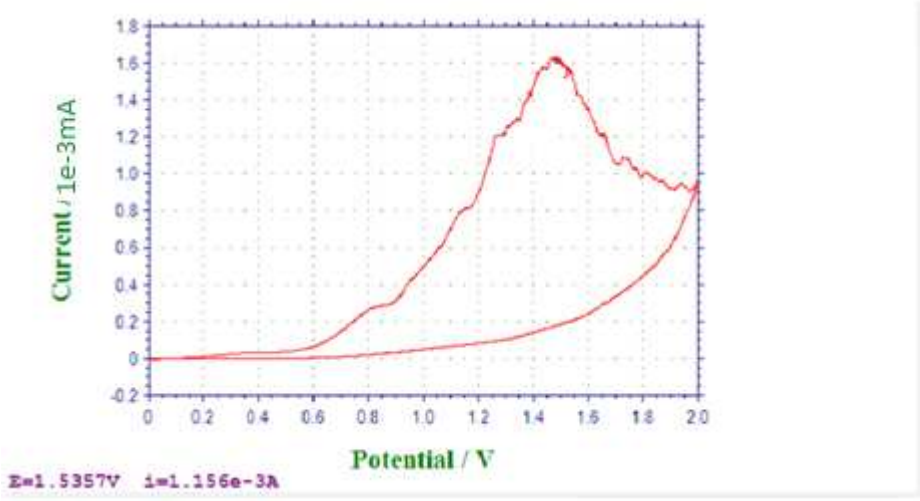


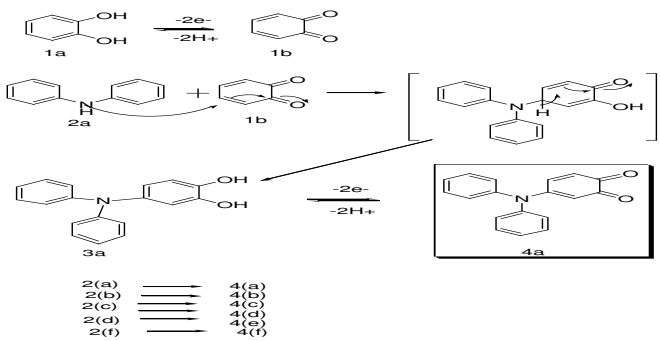

**Figure 2**: Cyclic voltammetry of catechol **(1a)** in the presence of nucleophiles at scan rate .01 m/s.

**Controlled potential electrolysis (CPE):**

Electroorganic synthesis of product (4a-4f): In a typical procedure, a solution of catechol (5mmol), secondary amines (Nitrogen nucleophile ) (10 mmol), $LiClO_4$ as an electrolyte (0.8g, 1N) in acetonitrile media was electrolyzed in an undivided cell [22-31] equipped with a magnetic stirrer under constant potential. The electrolysis was terminated when the decay of current became more than 95%. At the end of electrolysis the reaction mixture was removed from cell and extracted by simple solvent extraction method with chloroform (3×5 ml), brown color product was obtained. The structures of the synthesized products 4a-4f were clearly determined on the basis of their IR, $^{1}$HNMR, $^{13}$CNMR., Mass spectra and elemental analysis.

**Reaction mechanism:**

Adams et al. [32] and Nematollahi et al. [32-39] have demonstrated that the anodic oxidation of catechol leads to the formation of the corresbonding o-benzoquinone intermediates in the presence of different nucleophiles and synthesized products (4a-4f), are shown in scheme 2. Secondary nucleophilic amines attack on electrogenrated o-benzoquinone via a 1, 4 Michael addition reaction and aromatization to form intermediate 3a, which undergo further oxidation to give product 4a. The obtained aminoquinones were purified by recrystallization in chloroform and characterized by spectroscopic method.



**Scheme 2**: Proposed mechanism for electrochemical oxidation of catechol in presence of nucleophilic amines

**IR and NMR spectral analysis of compounds (4a-4f)**

Characteristic absorption of the Aminoquinone derivatives (4a-4f) are observed maxima in the region of 1714–1530 $cm^{-1}$ are characteristic of Ar-carbonyl (Ar-C=O) stretching frequency of benzoquinone function. The observed bands around 3045–3015 $cm^{-1}$ and 1690-1570 $cm^{-1}$ are due to ArC-H and Ar-N groups respectively. IR spectrum of compound 4(a) is shown in Fig. 3

For NMR spectral analysis, compound 4(a) was chosen as a representative. Proton NMR spectrum of this compound (Fig. 4) shows the presence of a Aromatic protons occur in the range of 8.8–5.15 ppm. Four sets of signals are observed for the aromatic protons. In product 4(b)-4(f) aliphatic proton occurred in the range 2.6-1.0 ppm.

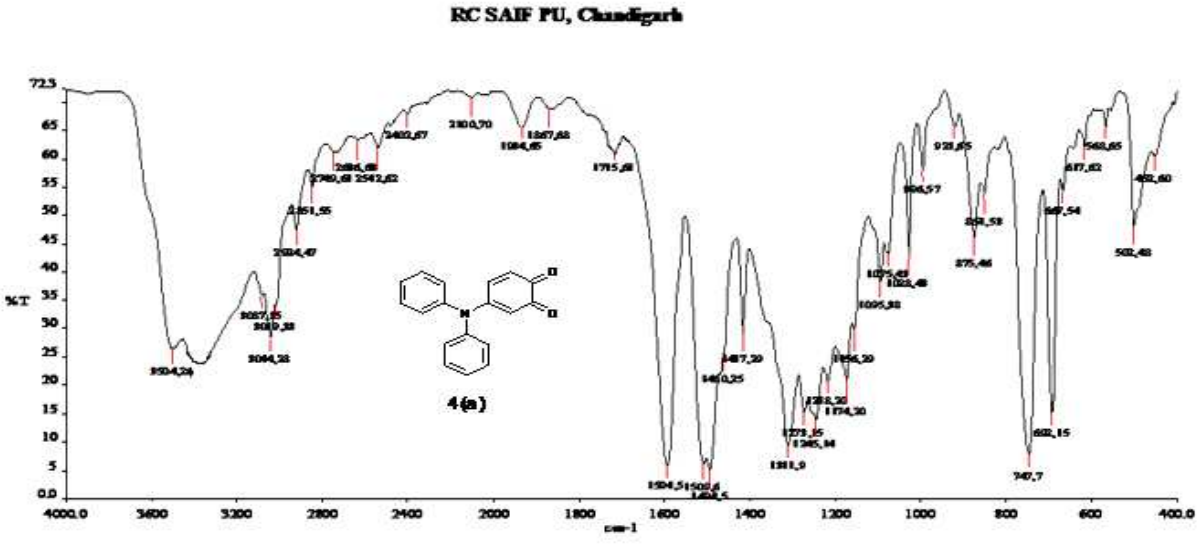



**Figure 3:** infrared spectrum of 4-(diphenylamine) cyclohexa-3,5-diene-1,2-dione 4(a)

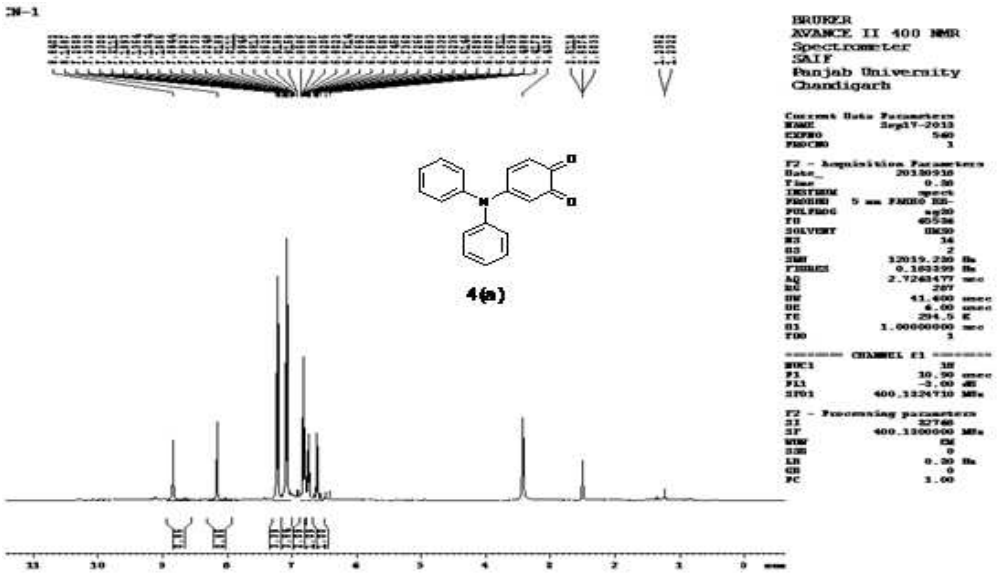


**Figure 4:** NMR spectrum of 4-(diphenylamine) cyclohexa-3, 5-diene-1, 2-dione

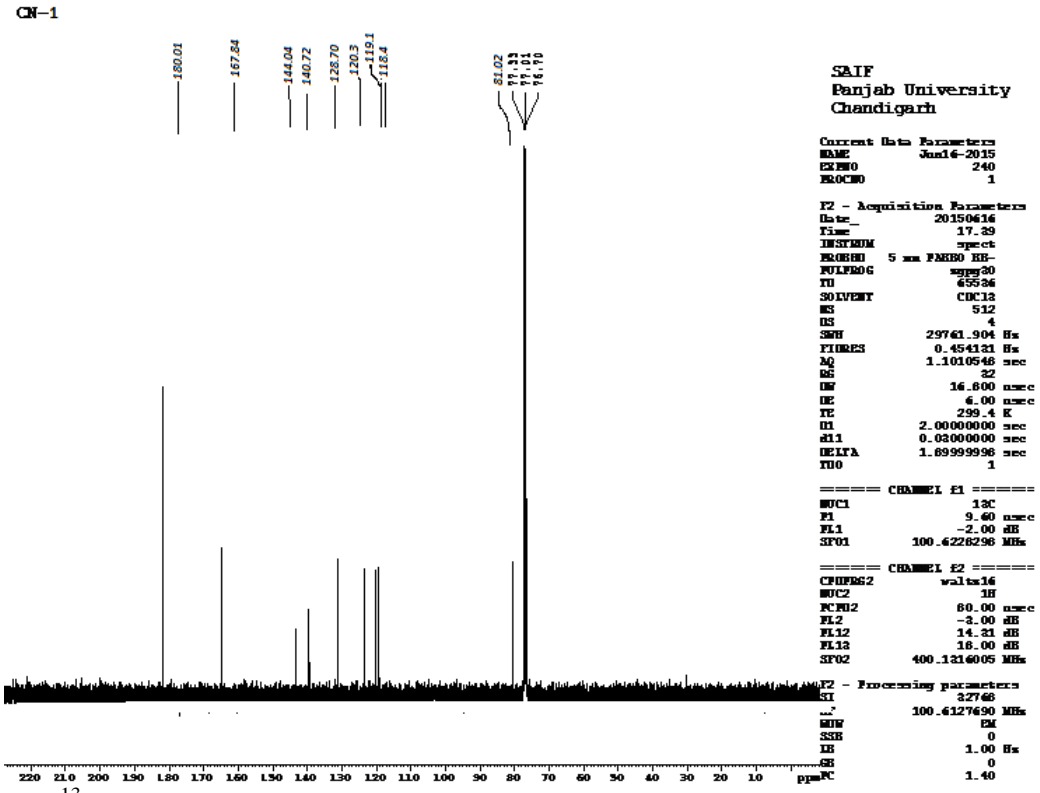



**Figure 5:** $^{13}$CNMR ($CDCl_3$) spectrum of 4-(diphenylamine) cyclohexa-3,5-diene-1,2-dione 4a

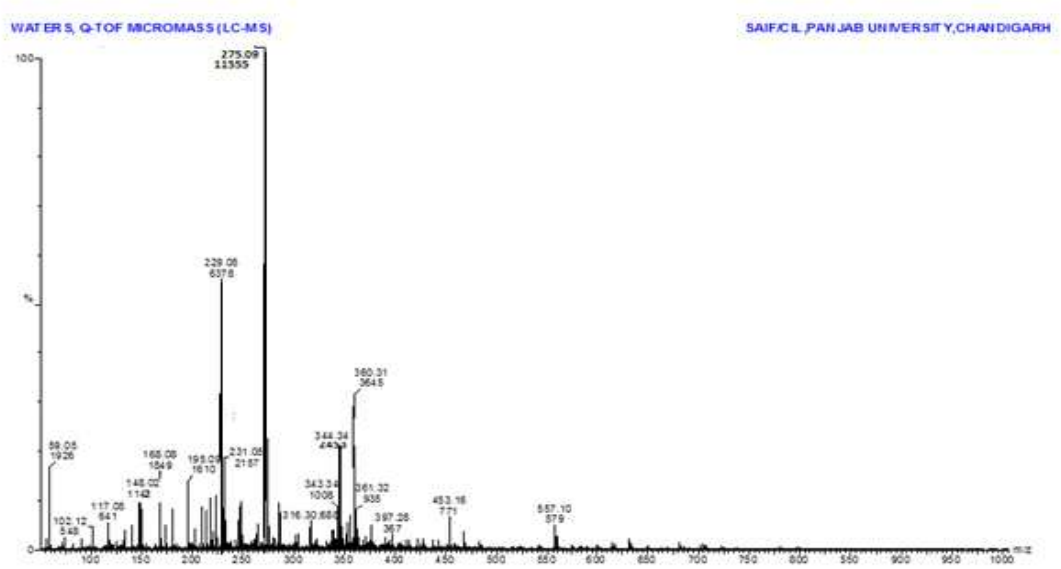
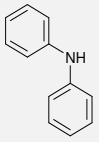
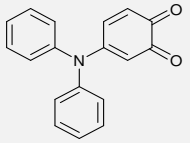
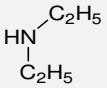
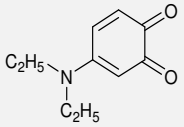
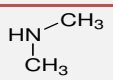
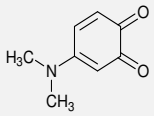
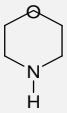
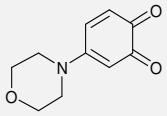
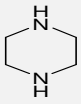
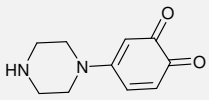


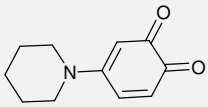

**Figure 6:** 4-(diphenylamine) cyclohexa-3,5-diene-1,2-dione 4(a) mass spectra

Diagnostic criteria of cyclic voltammetry and controlled potential coulometry accompanied by the

IR, NMR ($^{1}H$ and $^{13}C$) data, molecular mass of final product and elemental analysis allow us to propose the pathway in **scheme 2** for the electrochemical oxidation of catechol in the presence of nitrogen nucleophile formed (**4a-4f**) aminoquinone in high yield and purity.

**Table 1**: The Anodic oxidation of catechol **1a** in pressence of secondary amines (**2a-2f)** under constant potential electrolysis

| Entry | Substrate | Nucleophiles (2a-2f) | Potential (V) | Current density ($mA/cm^2$) | Time hrs) | Product (4a-4f) | Yield (%) |
|---|---|---|---|---|---|---|---|
| **1.** | 1(a) |  2(a) | 1.2 | 29 | 1.8 |  4(a) | 77 |
| **2.** | 1(a) |  2(b) | 1.1 | 29 | 1.6 |  4(b) | 72 |
| **3.** | 1(a) |  2(c) | 1.2 | 30 | 1.6 |  4(c) | 74 |
| **4.** | 1(a) |  2(d) | 1.2 | 38 | 1.8 |  4(d) | 79 |
| **5.** | 1(a) |  2(e) | 1.3 | 29 | 2.0 |  4(e) | 80 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **6.** | 1(a) |  2(f) | 1.4 | 27 | 2.0 |  4(f) | 78 |

## CONCLUSION

In summary, we have developed a convenient and novel method for the synthesis of aminoquinone by Michael addition of secondary amines with electrogenerated o-quinone at room temperature in acetonitrile. The remarkable features of this method are the one pot clean synthesis, use of electricity instead of chemical reagents, achievement of high atom economy, short reaction time, mild reaction conditions and easier workup. The present work extends the application of electrochemical synthesis of o-benzoquinone and its in situ transformation which would help to develop a general electrochemical approach for the aminoquinone synthesis.

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