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Electrochemical oxidation of clonazepam drug in the presence of arylsulfinic acid in aqueous solutions: A green method for synthesis new sulfonamide derivatives

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Abstract

The electrochemical oxidation of clonazepam (CLNP) has been studied in presence of some aryl sulfinic acids as nucleophiles in aqueous buffered solution by means of cyclic voltammetry, and controlled- potential coulometry. Voltammetric studies of electrochemical behavior of clonazepam have also been investigated in different pH values (pH 1.0 to 10.0) in absence and presence of toluenesulfinic acid (1a) as well as benzenesulfinic acid (1b). The results indicated that peak current and peak potential depends on the level of pH. Finally, the synthetizing new sulfonamide derivatives was conducted through constant current electrolysis of clonazepam in presence of arylsulfinic acids at carbon rod electrodes, employing a green electrochemical protocol. CLNP which has cathodically produced hydroxylamine species is oxidized at the anode to generate nitroso species, participate in reaction with the arylsulfinic acids, converts it to the corresponding new sulfonamide derivatives. The new products have been characterized by IR, MS, ^{1}H NMR and ^{13}C NMR methods.

Keywords: Clonazepam; Arylsulfinic acids; Sulfonamide derivatives; Cyclic voltammetry; Electrochemical oxidation.

1. Introduction

Sulfonamide compounds have attracted surmounting attention essentially as a result of an extensive range of biological as well as pharmaceutical features. The therapeutic and pharmaceutical characteristics of sulfonamides have been published, including anti-inflammatory [1,2], anticancer [3], antimicrobial [4,5], antiproliferative [6,7], cysteine protease inhibitors [8,9], antimalarial [10], thyroid receptor ntagonist [11], PI3K/Akt/mTOR signaling pathways inhibitors [12], EPAC2 antagonist [13], and γ-secretase inhibitors [14].

It should be noted that, the significance of sulfonamides has raised the attention of many researchers towards synthetizing these compounds. In this line, an extended number of derivatives of sulfonamide have accordingly been synthesized and many of them have been tested regarding their clinical value in various bacterial, protozoal, and viral diseases [15–18]. The most typical synthetic strategy resorted to for synthetizing sulfonamide compounds is the chemical synthesis [19–29].

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Nevertheless, some of the mentioned methods involve the use of high temperature, toxic transition metal, tedious workup, hazardous organic solvents as well as application of oxidative, which would result in unfavorable by-products other than environmentally hazardous remaining's. Furthermore, as a result of the on-the-rise need for the organic synthesis under green conditions, a great deal of attention has recently been focused on the employment of environmentally-friendly methods.

It is, on one hand, known that electrochemical methods are widely applied to the electrochemical synthetizing of both organic and inorganic compounds, kinetic and mechanistic studies of electron transfer reactions [30-39]. On the other hand, electrochemical synthesis can be regarded as an optimal method for green synthesis of the new organic compounds without presence any catalyst or additional reagents. The employment of mild reaction conditions, ease of control of the reaction, achievement of high atom economy, use of electricity instead of chemical reagents, decreased energy requirement, and unique selectivity due to in situ formation of an active species at the interface are among some of the advantages of electrosynthesis [40, 41].

Clonazepam, 5-(2-chlorphenyl)-1,3-dihydro-7-nitro-2H-1,4-benzodiazepin-2-one, is one of the benzodiazepine derivatives, used for many medical applications, including anxiolytic, anticonvulsant, sedative, muscle relaxant, hypnotic, and treatment of epilepsy for both adults and children [42,43]. Benzodiazepines are widely metabolized by cytochrome P-450 enzymes, particularly by CYP3A4 and CYP2C19. Consequently, inhibitors of these enzymes may impact the metabolism of mentioned class of drugs [44, 45]. Clonazepam is metabolized primarily to 7-aminoclonazepam by nitro reduction via hepatic cytochrome P450 and then N-acetylated to produce 7-acetamido clonazepam, which is excreted in the urine and feces following extensive biotransformation [46].

The main reason behind studying the anodic oxidation of clonazepam in the presence of various nucleophiles is that electrochemical oxidation very often parallels the cytochrome P450 catalyzed oxidation in liver microsomes. Therefore, regarding the resemblance between biological and electrochemical reactions, it can be proposed that the mechanism performed at the electrode surface inherits the same milestones as it does in the body. In this line, the researchers investigated the electrochemical reduction of clonazepam in both absence and presence of arylsulfinic acids (1a and 1b) as nucleophiles in aqueous solutions. In the next stage of the study, the obtained electrochemical data was used in the electrochemical synthesis of new sulfonamide derivatives using the same precursors by constant-current coulometry.

This method represents a simple one-pot electrochemical process for synthetizing some new sulfonamide derivatives (2a and 2b) under green conditions, without the presence of any toxic reagents or solvents by employing an environmentally friendly method which in itself enjoys a high atom economy. The concept of atom economy means the percentage of reactants that get permission into the final product

2. Experimental

2.1. Apparatus and reagents

Cyclic voltammetry was conducted employing an Autolab model PGSTAT 12 potentiostat/golvanostat. Next, controlled-potential coulometry besides constant current electrolysis were implemented imitating the Behpajooh model 2062 potentiostat/galvanostat (Isfahan, Iran). The working electrode applied in the voltammetry experiments was a glassy carbon electrode (1.8 mm diameter). For the counter electrode, a platinum wire was used. A collective bundle of four graphite rods (6 mm diameter and 8 cm length) was used in both controlled-potential coulometry and constant current electrolysis as anode. The analogous configuration carbon constitutes the cathode electrode. The working electrode potentials were measured

versus a saturated Ag/AgCl electrode (all electrodes from AZAR electrode).

Melting points, which were left uncorrected, were taken on a Stuart SMP3 melting point apparatus. IR spectra were obtained on a Ray Leigh Wqf-510 Fourier Transform Infrared (FT-IR) spectrophotometer. The remaining already-employed apparatus are described in the previous paper [38].

Clonazepam, a pharmaceutical grade material (purity > 99.9%), was attained from Sobhan pharmaceutical company, Iran. Toluenesulfinic acid, benzenesulfinic acid, phosphate salts and acetone were obtained from commercial sources. All remaining chemicals employed in this study enjoyed an analytical grade. Further, distilled water was used for preparing all solutions and subsequent dilutions.

2.2 General guideline for electrochemically synthetizing of sulfonamide derivatives

To do electro-organic synthesis of sulfonamide derivatives (2a and 2b), a solution (80 mL) of phosphate buffer (pH 6.0, C=0.2 M)/ acetone mixture (80/20, v/v) containing 0.4 mmol of CLNP, 0.4 mmol of 1a or 1b and 1 mmol $K_4Fe(CN)_6$ was electrolyzed under constant current density at 0.7 mA/cm2 and ambient temperature in an undivided cell. Following consumption of the theoretical amount of the charge consume the electrolysis was ended. Next the cell was placed in a refrigerator overnight. Employing filtration, the precipitated product was collected and rinsed in presence of distilled water several times, and then was recrystallized from ethanol. The resulting products were characterized by IR, MS, 1H and ^{13}C NMR.

2a: M·p = 189–191 °C. IR (KBr) = 3369, 3114, 2931, 2041, 1696, 1339, 1098, 743 cm−1. MS: m/z (relative intensity); 439 (M+, 4.6), 426 (5.1), 389 (2.3), 360 (4.2), 324 (17.2), 315 (28.4), 296 (21.5), 280 (31.2), 271 (37.2), 243 (16.3), 222 (15.4), 194 (100), 152 (13.7), 143 (17.3). ^{1}H NMR (400 MHz, DMSO-d6): δH (ppm) 2.5 (3 H, s, CH3), 4.3 (2H, s, CH2), 7.4-7.9 (11H, m, H-Ar), 8.4 and 11.1 (2H, NH). ^{13}C NMR (100 MHz, DMSO-d6): δC (ppm) 21.5, 55.4, 121.8, 124.5, 125.9, 126.3, 126.8, 127.2, 128.3, 128.5, 128.9, 129.3, 131.6, 132.2, 132.4, 137.2, 142.1, 144.8, 167.5, 169.7.

2b: M·p = 186–188 °C. IR(KBr) =3367, 3104, 2930, 2047, 1693, 1339, 1098, 747 cm^{-1}. MS: m/z (relative intensity); 425 (M+, 5.2), 396 (4.3), 369 (25.6), 313 (35.14), 298 (15.4), 280 (51.3), 269(48.2), 240 (35.2), 236 (100), 208 (21.5), 178 (16.3), 152 (17.9), 140 (13.2), 111 (18.5). ^{1}H NMR (400 MHz, DMSO-d6): δH (ppm) 4.9 (2H, s, CH_2), 7.2-7.8 (12H, m, H-Ar), 8.2 and 10.6 (2H, NH). ^{13}C NMR (100 MHz, DMSO-d6): δC (ppm) 57, 122.1, 124.8, 126.4, 126.6, 127.5, 127.8, 128.2, 128.5, 129.7, 130.6, 131.4, 131.5, 131.7, 137.9, 141.5, 144.2, 167.8, 169.2.

3. Results and discussions

The first and second cycles of cyclic voltammograms of 1.0 mmol/L of CLNP in aqueous phosphate buffer solution (c=0.2 M, pH 7) at a glassy carbon electrode are displayed in Fig. 1. During the first negative-going scan (starting potential, -0.15 V), it manifests a sharp cathodic wave (C0) at -0.6 V which corresponds to the reduction of CLNP (nitro group) to hydroxylamine group within an irreversible 4e−, 4H+, -H2O process [42, 47, 48]. Also, in the positive-going scan from -1.0 to +0.5 V, the voltammogram demonstrates an anodic peak (A1) at 0.15V, while in negative sweep from +0.5 to starting potential, it exhibits a new cathodic peak (C1) at -0.055V which can be regarded as a counterpart of oxidation peak, A1. The oxidation peak (A1) equals the oxidation of the hydroxylamine to a nitroso group within 2e−, 2H+. This is while reduction peak C1 is related to the reduction of the nitroso group back to the hydroxylamine group [47-50] (Scheme 1). The peak current ratio (IC1p /IA1p) is nearly close to the unity which could be attributed to the stability of nitroso group produced at the surface of the electrode in the time scale of cyclic voltammetry. In the second cycle, however, the voltammogram demonstrated that the peak current of C0 underwent decrease.

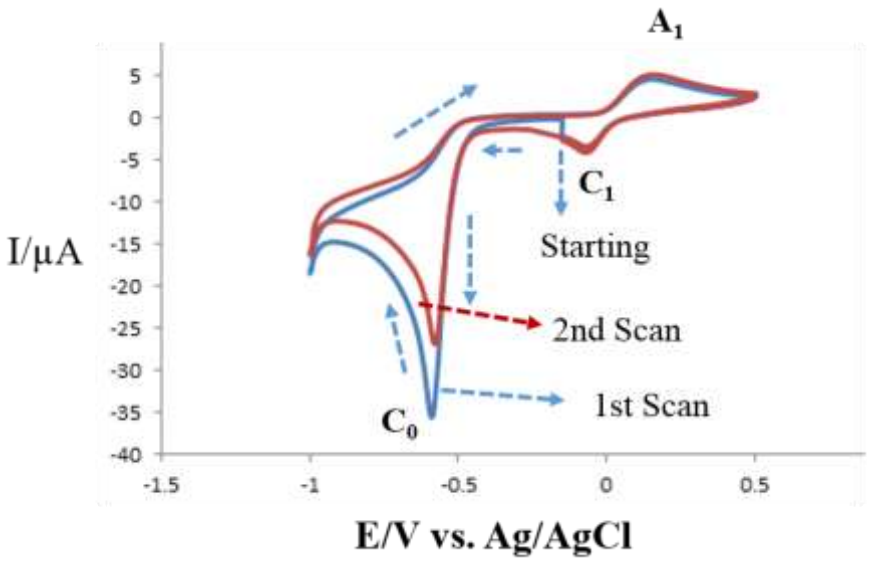
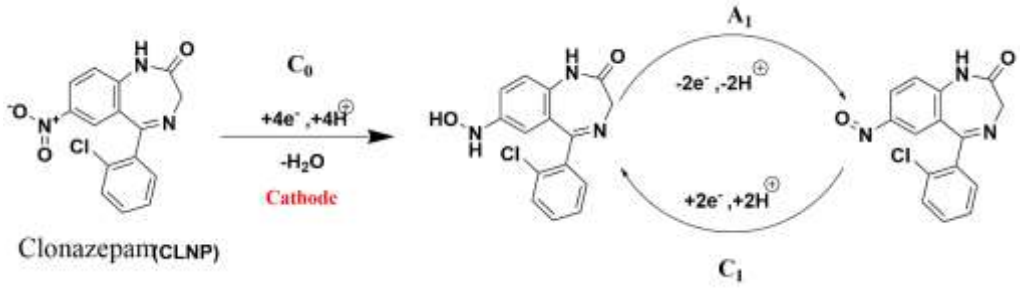


Figure 1. Cyclic voltammograms of 1.0 mM CLNP (First and second) in phosphate buffer solution /acetone (80/20) mixture (pH 6.0, C=0.2 M) at glassy carbon electrode; scan rate: 100 mV/s.



Scheme 1. Electrochemical behavior of **CLNP**.

Further, the recorded cyclic voltammograms of CLNP in aqueous solutions with various pHs (1 to 10) are displayed in Fig. 2. The cyclic voltammetry responses indicate peak current as well as the potential peak of all the peaks (C0, A1 and C1) which are pH-dependent. As can be seen in the Figure, in proportion to increasing pH, the potential peaks of all of peaks shifts to negative potentials which is pertinent to the participation of proton(s) in the redox processes.

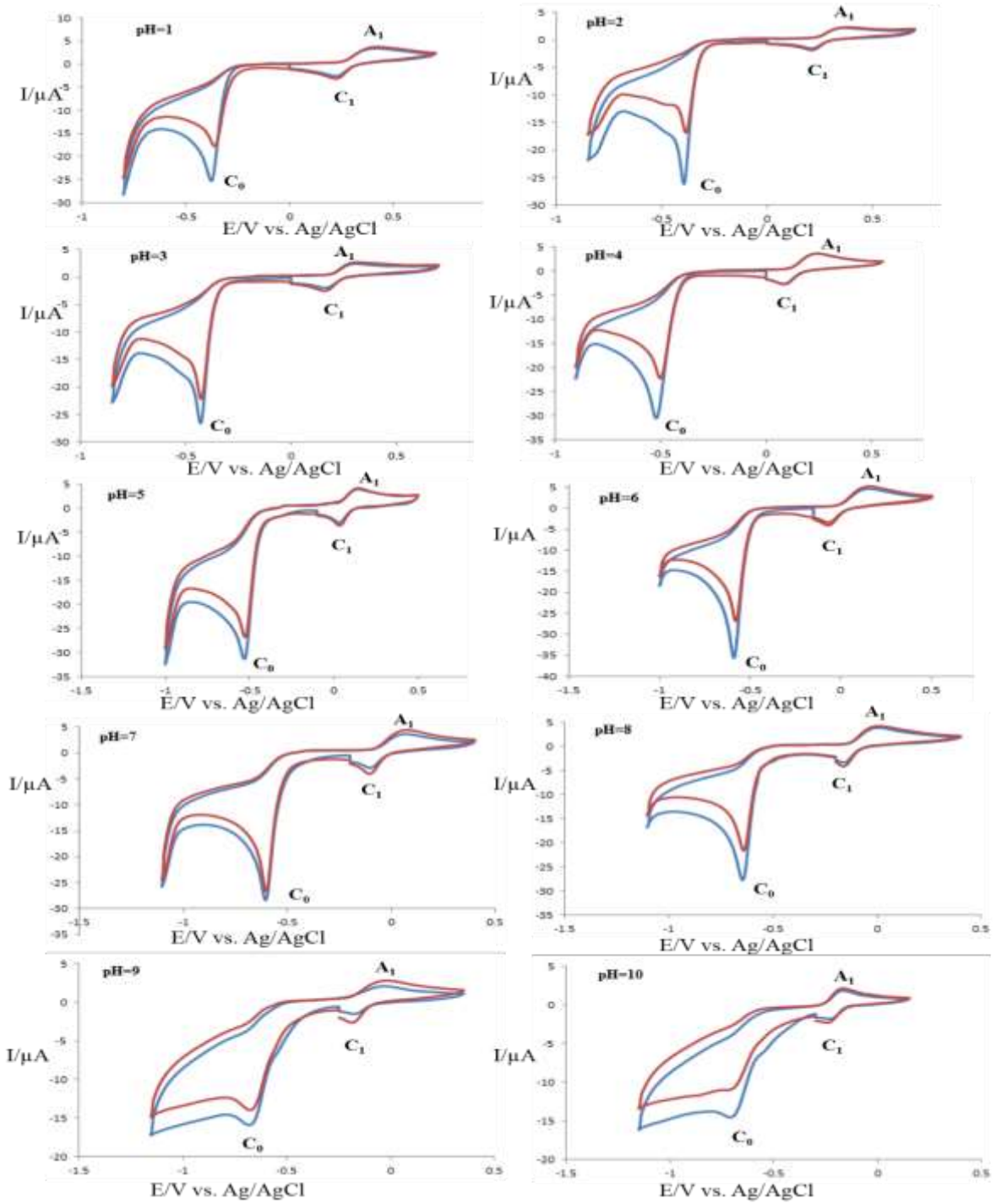


Figure 2. Cyclic voltammograms of 1.0 mM CLNP in phosphate buffer solution/acetone (80/20) mixture with various pH values at glassy carbon electrode, glassy carbon. Scan rate 100 mV/s.

The E-pH diagram for C0 and A1 peaks is plotted and displayed in Fig. 3. Considering Ep-pH diagrams (Fig. 3), the EpC0 and EpA1 values shift by -0.504 and -0.584 mV per pH, denoting that the reduction of CLNP to hydroxylamine group comprises the same number of electrons and protons. It also manifests that electrons and protons are equal in the electrochemical oxidation of the hydroxylamine to a nitroso group. It is interesting to note that the same outcome for electrochemical behavior had been reported previously by other researchers [47-50]. Regarding the results, pH 6 was regarded as an appropriate medium for the electrochemical investigation as well as for the synthesis of new sulfonamide derivatives.

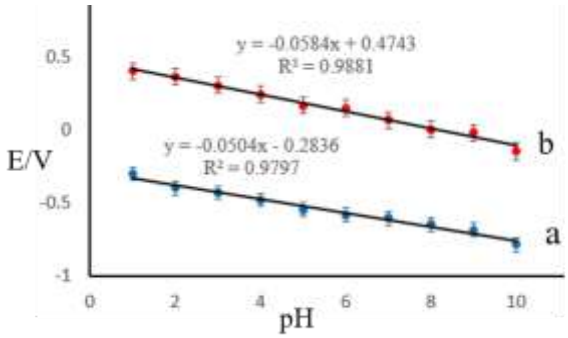


Figure 3. The E-pH diagram of CLNP; (a) Plot of the anodic peak potential (C_1) versus pH and (b) Plot of the cathodic peak potential (A_1) versus pH of the solution.

3.1. Electrochemical studies of CLNP conducted in Presence of 1a and 1b

Fig. 4, curves b and a demonstrate the cyclic voltammograms of CLNP already conducted in both presence and absence of 1a in phosphate buffer solution (C=0.2 M, pH 6). Comparing these voltammograms, one can observe that the main change is significant decrease of cathodic peak current (IpC1), which represents reaction of electro-generated nitroso group of CLNP with 1a. Also curve c, in Fig. 4, represents the cyclic voltammogram of 1a in the absence of CLNP.

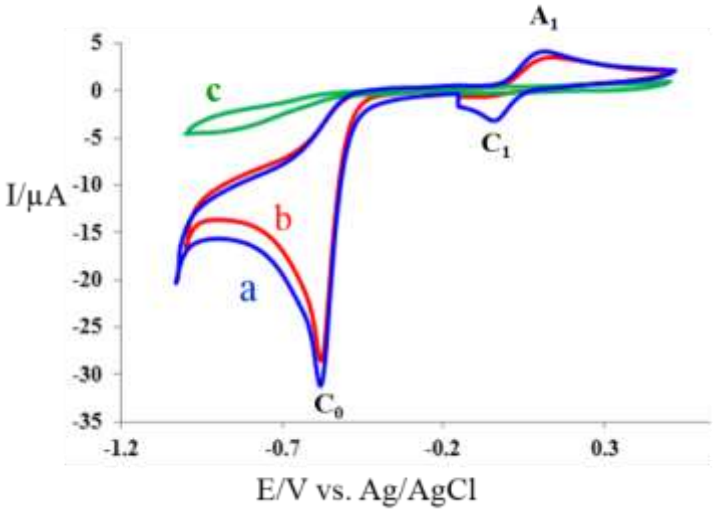


Figure 4. Cyclic voltammograms of 1.0 mM CLNP; (a) in absence and (b) in presence of 1.0 mM 1a; (c) 1.0 mM 1a in absence of CLNP at glassy carbon electrode in phosphate buffer solution (pH 6.0, C=0.2 M); scan rate: 100 mV/s.

To obtain more data, the electrochemical reduction of CLNP in the presence of both toluenesulfinic acid (1a) and benzenesulfinic acid (1b) as nucleophiles has been studied. Fig.5I displays the impact of various types of concentration of 1a on the cyclic voltammetric response of CLNP. The comparison of voltammograms indicates that, in proportion to the amplification of concentration of 1a, the significant change in voltammograms is decrease of IpC1 and IpC0 which represents the reaction between electro-generated nitroso group with 1a. Also, to have handy data for more studies, cyclic voltammograms of a solution containing CLNP (1.0 mM) and 1a (1.0mM) were recorded at various scan rates (Fig. 5II). It was

observed that the peak current ratio (IpC1/IpA1) increased parallel to the amplification of potential sweep rate (Fig. 5II inset). These observations, on one hand, confirm the reactivity of nitroso group towards 1a or 1b. On the other hand, growth of IpC1/IpA1 with potential increases of sweep rate, indicate that the time required for the reaction of CLNP with 1a is not enough; subsequently, with increase in scan rate, the ratio of it (IpC1/IpA1) increases.

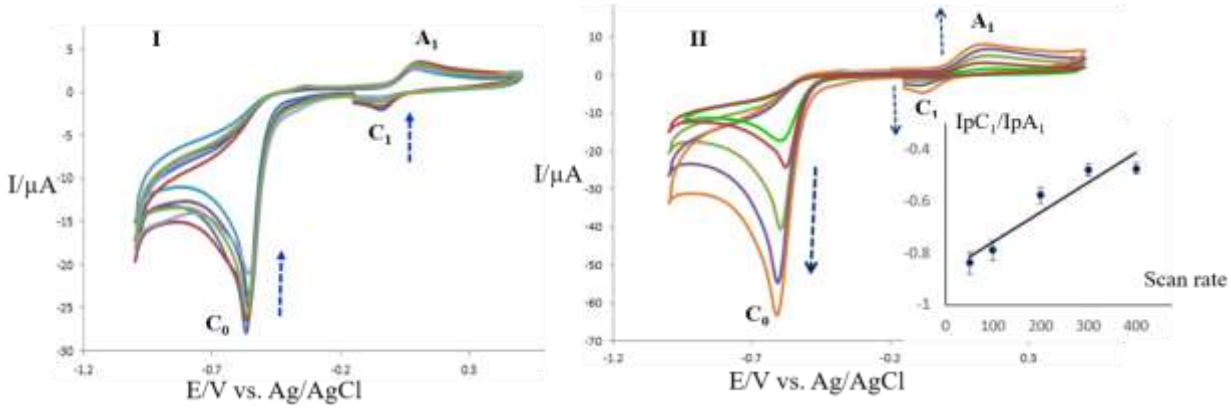


Figure 5. Part I, Cyclic voltammograms of 1.0 mM CLNP in presence of various concentrations of 1a. Concentrations of 1a include: 0.0, 0.2, 0.5, 0.8, and 1.0 mM, respectively. Scan rate: 100mV/s. Part II, Cyclic voltammograms of 1.0 mM CLNP in presence of 1.0 mM 1a at various scan rates. Scan rates consist of: 50, 100, 200, and 400 mV/s, respectively, at glassy carbon electrode in phosphate buffer solution (pH6.0, C = 0.2 M). Inset: variation of peak current ratios (IpC_1/IpA_1) versus scan rate.

In subsequent studies, to obtain more information on the reaction process and the number of electrons involved in reaction, controlled potential coulometry could be performed by a solution containing 1.0 mM of CLNP and 1.0 mM 1a or 1b at -0.6 V vs. Ag/AgCl. In addition, the electrolysis progress was followed by cyclic voltammetry (Fig. 6). As can be seen in the voltammograms, parallel with the progression of electrolysis, the reduction peak C0 decreased in a way that their current reached to about zero following the consumption of about 4e- per molecule of CLNP (Fig. 6, inset).

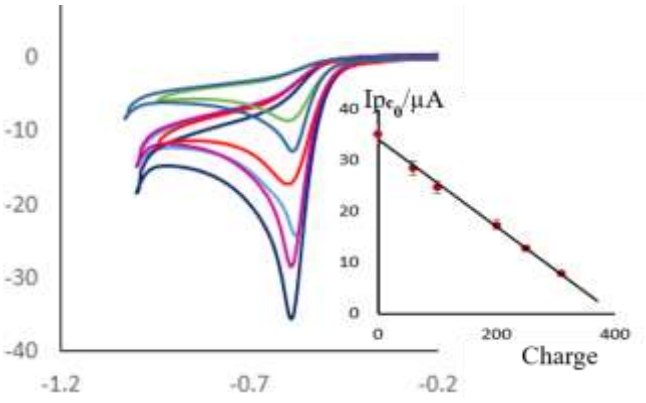
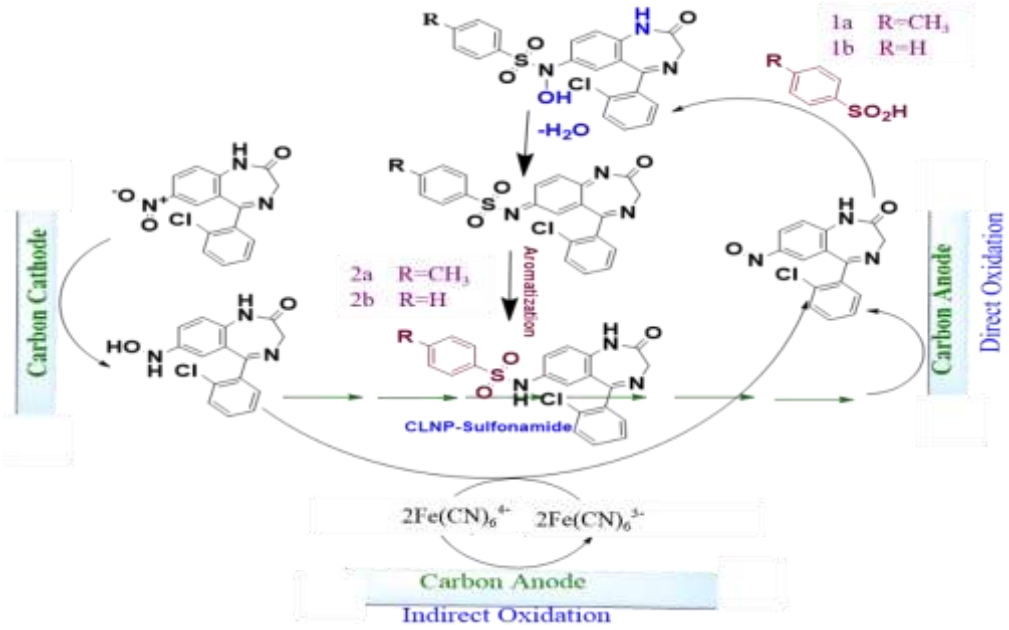


Figure 6. Cyclic voltammograms of 1.0 mM CLNP in the presence of 1.0 mM 1a, in phosphate buffer solution (pH 6.0, c = 0.2 M), during controlled- potential coulometry at -0.65 V. Inset: variation of Ip_{C0} versus charge consumed. Scan rate 100 mV/s.

The synthesis of 2a and 2b products was performed by constant-current electrolysis of CLNP in presence of 1a and 1b. To reach to better yields of products, an indirect method, mediated by [Fe(CN)6]4− ions (indirect oxidation), was employed. Based on coulometry and voltammetry results, the 1H NMR and 13C NMR data as well as MS of final products, EEC electrochemical mechanism was suggested for the electro reduction of

CLNP in the presence of 1a or 1b (Scheme 2). Regarding Scheme 2, in cathode, hydroxylamine group is generated from the CLNP, then it oxidized at the anode (direct oxidation) to convert hydroxylamine group to nitroso group of CLNP. In what comes next, the generated nitroso group from CLNP reacts with 1a or 1b, and then following aromatization, it results in 2a and 2b as the final products. The structure of products has been characterized using FT-IR, MS, ^{1}H NMR and ^{13}C NMR (**Figure 7** and **8**), the details of which are described in the experimental section.



Scheme 2. Electrochemical oxidation of **CLNP** in the presence of **1a or 1b**.

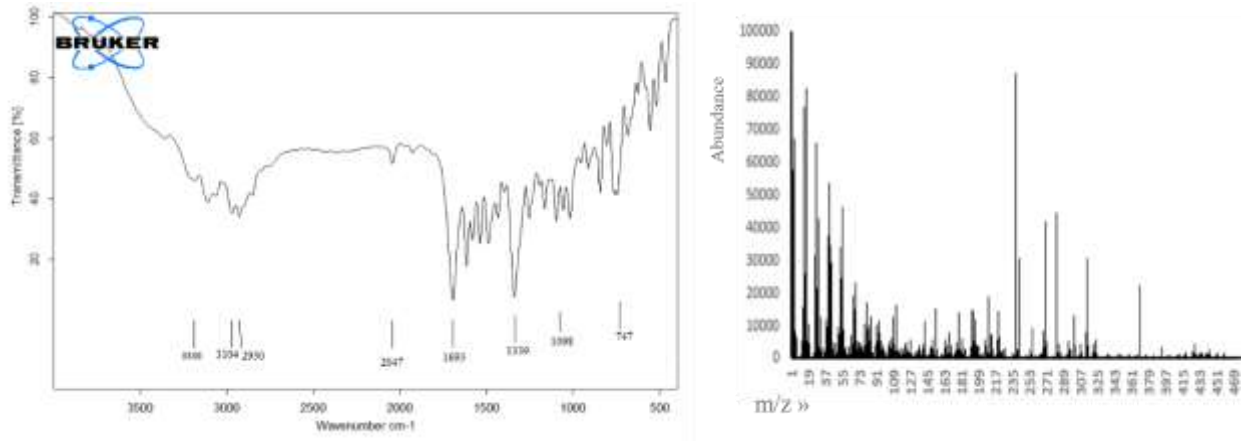


Figure 7. FT-IR spectra in pure dried KBr and Mass spectrum of 2b.

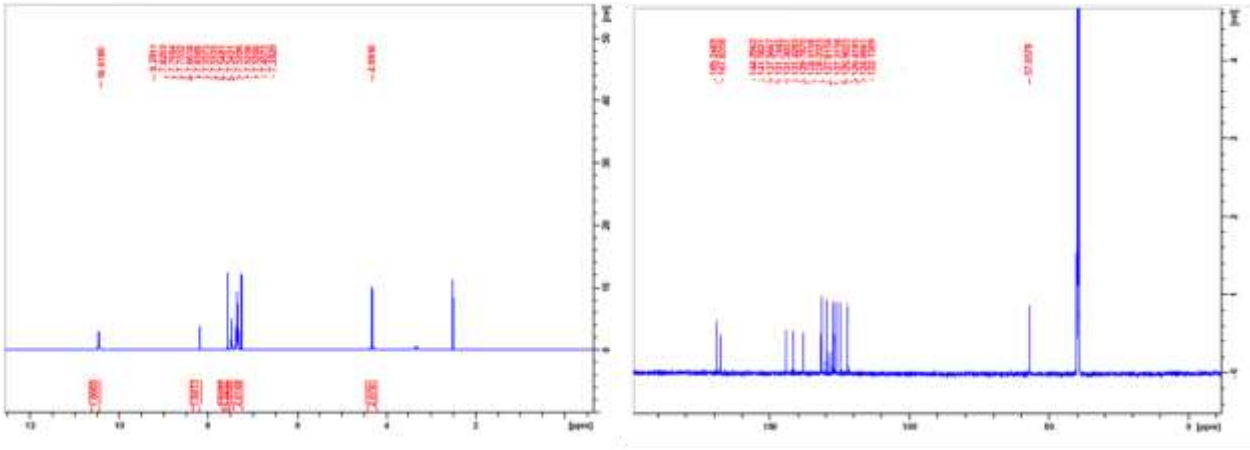


Figure 8. ^{1}H NMR and ^{13}C NMR spectrum of 2b in DMSO-d6.

4. Conclusions

In this work, electrochemical reduction of CLNP has been studied in the presence of arylsulfinic acids (1a and 1b). Also synthesis of some sulfonamide derivatives (2a and 2b) were performed in water/acetone mixture using a paired electrolysis in undivided cell under constant current conditions. For this purpose, the researchers used an indirect method, mediated by Fe(CN)6 4−. The use of Fe(CN)6 4− ion as a mediator significantly enhances the efficiency and yield of 2a and 2b production. The EEC electrochemical mechanism is suggested for reaction of CLNP with 1a or 1b. The suggested mechanism for this reaction is presented in Scheme 2. In addition, the synthesized products were identified by spectroscopic methods. The landmark features of the discussed method used for the synthesis of CLNP- sulfonamide derivatives is that it requires no catalysis, can be done at room temperature as well as atmospheric pressure, just uses simple cell and common electrodes. Further, the electrodes can easily separate the electrodes from the reaction mixture while use of mild reaction conditions are always under way

References

[1] B. Tozkoparan, E. Kupeli, E. Yesilada, and M. Ertan, *Bioorg. Med. Chem*., **15** (2007) 1808.

[2] S. H. Hwang, K. M. Wagner, C. Morisseau, J. Y. Liu, H. Dong, A. T. Wecksler, and B. D. Hammock, *J. Med. Chem.*, **54** (2011) 3037.

[3] M. S. Al-Said, M. M. Ghorab, and Y. M. Nissan, *J. Chem Cent.*, **6** (2012) 1.

[4]K. V. Kudryavtsev, M. L. Bentley, and D. G. McCafferty, *Bioorg. Med. Chem.*, **17** (2009) 2886.

[5] B. Guruswamy, R. K. Arul, M. V. S. R. K. Chaitan, and S. S. P. K. Darsi, *Eur. J. Chem.*, **4** (2013) 329.

[6] A. Cohen, M. D. Crozet, P. Rathelot, N. Azas, and P. Vanelle, *Molecules*, **18** (2012) 97.

[7] A. R. Usera, P. Dolan, T. W. Kensler, and G. H. Posner, *Bioorg. Med. Chem.*, **17** (2009) 5627.

[8] Y. T. Chen, R. Lira, E. Hansell, J. H. McKerrow, and W. R. Roush, *Bioorg. Med. Chem. Lett.*, **18** (2008) 5860.

[9] B. R. Shenai, B. J. Lee, A. Alvarez-Hernandez, P. Y. Chong, C. D. Emal, R. J. Neitz, W. R.[Roush, and P. J. Rosenthal, *Antimicrob. Agents Chemother*, **47** (2003) 154.

[10] P. J. Lee, J. B. Bhonsle, H. W. Gaona, D. P. Huddler, T. N. Heady, M. Kreishman-Deitrick, A. Bhattacharjee, W. F. McCalmont,

L. Gerena, and M. Lopez-Sanchez, *J. Med. Chem.,* **52** (2009) 952.

[11] J. Y. Hwang, W. Huang, L. A. Arnold, R. Huang, R. R. Attia, M. Connelly, J. Wichterman, F. Zhu, I. Augustinaite, and C. P. Austin, *J. Biol. Chem.,* **286** (2011) 11895.

[12] M. E. Welker and G. Kulik, *Bioorg. Med. Chem.,* 21 (2013) 4063.

[13] H. Chen, T. Tsalkova, O. G. Chepurny, F. C.Mei, G. G. Holz, X. Cheng, and J. Zhou, *J. Med. Chem.,* **56** (2013) 952.

[14] D. Shaw, J. Best, K. Dinnell, A. Nadin, M. Shearman, C. Pattison, J. Peachey, M. Reilly, B. Williams, and J. Wrigley, *Bioorg. Med. Chem. Lett.,* **16** (2006) 3073.

[15] J.B. Grimm, M.H. Katcher, D.J. Witter, A.B. Northrup, *J. Org. Chem.* **72** (2007) 8135.

[16] N. Ozbek, H. Katircioglu, N. Karacan, T. Baykal, *Bio. Med. Chem.*, **15** (2007) 5105.

[17] X.H. Deng, N.S. Mani, *Green Chem.,* **8** (2006) 835.

[18] A.K. Gadad, C.S. Mahajanshetti, S. Nimbalkar, A. Raichurkar, *Eur. J. Med. Chem.,* **35** (2000) 853.

[19] R. Davis, Synth. Commun., **17** (1987) 823.

[20] K. Peseke and U. Schonhusen, *J. Prakt. Chem.,* **332** (1990) 679.

[21] J. M. Blanco, O. Caamano, F. Fernandez, G. Gomez, and C. Lopez, *Tetrahedron: Asymmetry,* **3** (1992) 749.

[22] M. Y. Chang, M. H. Wu, C. K. Chan, and S. Y. Lin, *Tetrahedron Lett.,* **54** (2013) 6971.

[23] B. M. Graybill, *J. Org. Chem.,* **32** (1967) 2931.

[24] N. Margraf and G. Manolikakes, J. Org. Chem., **80** (2015) 2582.

[25] D. Kumar, V. Arun, M. Pilania, and K. C. Shekar, *Synlett*., **24** (2013) 831.

[26] V. G. Pandya and S. B. Mhaske, *Org. Lett.,* **16** (2014) 3836.

[27] Y. Xi, B. Dong, E. J.McClain,Q.Wang, T. L. Gregg, N. G. Akhmedov, J. L. Petersen, and X. Shi, Angew. *Chem. Int. Ed.,* **53** (2014) 4657.

[28] S. Cacchi, G. Fabrizi, A. Goggiamani, L. M. Parisi, and R. Bernini, *J. Org. Chem.,* **69** (2004) 5608.

[29] B. Bandgar, S. V. Bettigeri, and J. Phopase, *Org. Lett.,* **6** (2004) 2105.

[30] H. Beiginejad, D. Nematollahi, S. Khazalpour, *J. Of Applied Chemistry*, **48** (1397) 75.

[31] B. Habibi, Z. Aiazi, J. Rostami, *J. Of Applied Chemistry*, **46** (1397) 9.

[32] E. Tammari, Sh. Lotfi, *J. Elec. Chem.,* **766** (2016) 162.

[33] E. Salahifar and D. Nematollahi, *New J. Chem.,* **39** (2015) 3852.

[34] C. Costentin, *Chem. Rev*. **108** (2008) 2145.

[35] Sh. Lotfi, *J. Of Applied Chemistry,* **59** (1400) 99.

[36] J. Yoshida, K. Kataoka, R. Horcajada, A. Nagaki, *Chem. Rev.***108** (2008) 2265.

[37] Sh. Lotfi, E. Tammari, A. Nezhadali, *Mat. Sci.e and Eng. C,* **76** (2017) 153.

[38] E. Tammari, A. Nezhadali, Sh. Lotfi, *Electroanalysis*, **27** (2015) 1693.

[39] H. Beiginejad, D.Nematollahi, Mo. Noroozi& Sh. Lotfi, *J. the Iranian Chem. Society*,**12** (2014) 325.

[40] T. Shono, Electroorganic Synthesis; *Academic Press: San Diego*, 1991.

[41] E. Tammari, M. Bashiri, F. Ganjeizadeh Rohani, *J. Of Applied Chemistry*, **51** (1398) 177 in Persian.

[42] B. Habibi, M. Jahanbakhshi, *Electrochimica Acta*, **118**(2014) 10.

[43] T.R. Browne, *Am. J. Hosp. Pharm.* **35** (1978), 1048.

[44] R. M. Azzam, L. J. Notarianni, and H. M. Ali, *J. Chromatogr, B.* **708** (1998) 304.

[45] S.G. Jezequel, J. Mol. Catal, B: *Enzymatic*., **5** (1998) 371.

[46] M. Munakata, and S. Tsuchiya, *Epilepsia*. **49** (2008) 1803.

[47] J.M. Zen, J.J. Jou, A.S. Kumar, *Anal. Chim. Acta*, **396** (1999) 39.

[48] J.C. Chen, J.L. Shih, C.H. Liu, M.Y. Kuo, J.M. Zen, Anal. Chem., **78** (2006) 3752.

[49] K.C. Honeychurch, J. Brooks, J.P. Hart, *Talanta*, **147** (2016) 510.

[50] Sh. Lotfi, H. Veisi, *Mater. Sci. Eng. C*, **103** (2019) 109754.