Journal of Physical & Chemical Research

Journal homepage:

Superoxide Anion Radical Interaction With New Quinoline Compounds Measured By Cyclic Voltammetry

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Abstract

Cyclic voltammetry was used to study the interaction of four quinoline derivatives with superoxide anion radical ($O_2^{\cdot-}$). This method is based on the decrease of the anodic peak current of the superoxide anion radical $O_2^{\cdot-}$ generated electrochemically by the reduction of molecular oxygen O_2 dissolved in acetonitrile. The results obtained reveal that all derivatives showed a higher antioxidant activity than the standard used BHT. The binding parameters of the studied compounds were estimated in terms of binding constant (k_b), ratio of Binding Constants (K_{Red}/K_{Ox}) and binding Gibbs free energy ($\Delta G°$). From the results, it appears that the binding constant kb of the tested compounds is very high ranged from 15922 to 26181 L.mol^{-1} while negative values of $\Delta G°$ indicate the spontaneity of the antiradical reaction. It was also found that interaction of the reduced form $O_2^{\cdot-}$ with all derivatives is stronger than the oxidized form O_2 with ratio of binding constants values in the range 1.21-159.

1. Introduction

Quinoline derivatives are among the classical divisions of organic chemistry that have been widely studied in different fields of chemistry, including the chemical and pharmaceutical industries [1]. They are

excellent precursors in the synthesis of new systems that may present interesting biological properties related to the treatment of malaria, cardiovascular diseases, antifungal, anti-inflammatory, antibiotic, antitumor and antimicrobial [2–5]. They have shown a favorable pharmacological profile and a confirmed bactericidal power on sensitive strains. They are also used as corrosion inhibitors [1, 6, 7]. Several studies have shown that quinoline derivatives have a significant antioxidant activity and are able to scavenge several free radicals in vitro [8–11]. The present study aimed to determine electrochemically the binding parameters of a series of quinoline compounds having the formula {L= $RC_6H_4NHN=C(COCH_3)$ NHC_9H_6N, X= H, Br, F, NO_2} with superoxide anion $O_2^{\cdot-}$ radicals.

2. Experimental

2.1. Chemicals and reagents

All chemicals were purchased from Sigma-Aldrich and used without purification. Acetonitrile was used as solvent, tetrabutylammonium hexafluorophosphate ($TBuNPF_6$) was used as supporting electrolyte and its concentration was kept 0.1 $mol.L^{-1}$.

2.2. Synthesis

The four target compounds were synthesized according to the procedure described by M. El-Noaimi et al [12] by reacting an appropriate hydrazonyl chloride solution with 8-aminoquinoline and triethylaminel, scheme. 1.
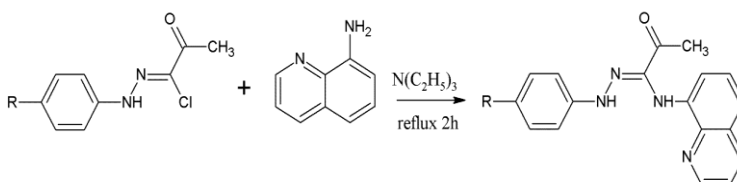
Scheme 1. Synthesis of $RC_6H_4NHN=C(COCH_3)$ NHC_9H_6N compound, H_2L-H: X= H,H_2L-Br: X=Br, H_2L-F: X= F, H_2L-NO_2: X= NO_2.

2.3. Scavenging Activity of Superoxide Anion $O_2^{\cdot-}$ radicals

The Electrochemical measurements were carried by a Voltalab 40 model PGZ301 (Radiometer Analytical) potentiostat / galvanostat) connected to an electrochemical cell with three electrodes. Saturated calomel electrode (SCE) as a reference electrode, a platinum wire as the counter electrode and a glassy carbon electrode (GCE) with a diameter of 2 mm as a working electrode. The potentiostat is piloted by a microcomputer with Volta Master 4 software, version 7.08. All measurements were carried

out at room temperature.

The in situ generation of $O_2^{\cdot-}$ was performed by the reduction of acetonirile solution of commercial molecular oxygen containing 0.1 mol.L^{-1} TBuNPF$_6$ at scan rate 100 mV.s^{-1}, in a potential window from -1.5 to 0.0 V. The superoxide radical scavenging activity is checked by successive addition of 0.1 ml of the solution of each compound, the voltammograms are then recorded under the same experimental conditions.

3. Results and discussion
3.1. Voltammetric Studies of H$_2$L-R– $O_2^{\cdot-}$ Interaction

Cyclic voltammetry is a useful method to generate $O_2^{\cdot-}$ without an enzyme system and to study its interaction with a molecule or extract, provided that the substrate is not active in the potential oxygen reduction range. The decrease of the anodic peak current of the radical $O_2^{\cdot-}$ with varying concentration of quinoline compounds was exploited to calculate the binding constant, whereas the shift of the peak potential was used to determine the modes of interaction [13,14]. Addition of first volume of all quinoline compounds causes a marked decrease of the anodic and cathodic peak currents accompanied by a shift in the peak potential (**Figure 1**). The reason of the peak current decrease is that both apparent diffusion coefficient and concentrations of superoxide anion radical are decreased due to the formation of $H_2L - X - O_2^{\cdot-}$ complex [15].
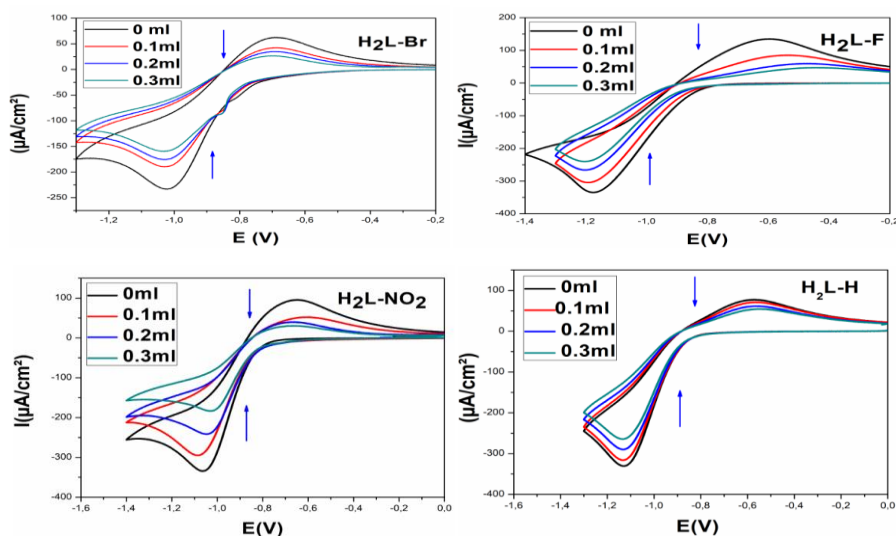

Figure 1. Cyclic voltammograms showing the scavenger effect of the $O_2^{\bullet-}$ radical recorded in the presence of different volumes of H$_2$L-Br, H$_2$L-H, H$_2$L-F and H$_2$L-NO$_2$

3.2. Scavenging activity and determination of IC50 values

The percent superoxide anion inhibition of the compounds studied is calculated using the following equation [16]:

$$\% \ O_2^{\cdot-} \ radical \ scavenging \ actuvity = \frac{I_{pa}^0 - I_{pa}}{I_{pa}^0} \times 100 \qquad (1)$$

Where I_{pa} and I_{pa}^0 present the oxidation peak current densities of $O_2^{\cdot-}$ in the presence and absence of the test compound, respectively. As shown in **Table 1**, the radical scavenging activity towards superoxide anion radicals increases with increasing the concentration.

Table 1. Percentage values of superoxide radical inhibition for H_2L-Br, H_2L-F, H_2L-H and H_2L-NO$_2$.

Compound	Additionnel volume (ml)	C (mol.L^{-1})	Current I_{pa} (µA)	RSA $_{o2\bullet-}$ %
	0	/	220.803	/
H$_2$L-H	0.1	9.9×10^{-6}	218.751	0929
	0 .2	1.94×10^{-5}	209.685	5.035
	0.3	2.83×10^{-5}	193.341	12.437
	0	/	225.442	/
H$_2$L-F	0.1	9.9×10^{-6}	208.654	7.446
	0 .2	1.94×10^{-5}	180.759	1.820
	0.3	2.83×10^{-5}	151.987	32.582
	0	/	220.803	/
H$_2$L-Br	0.1	4.34×10^{-5}	110.785	49.825
	0.2	4.95×10^{-5}	105.025	52.434
	0.3	5.46×10^{-5}	99.549	54.914
	0	/	227.527	/
H$_2$L-NO$_2$	0.1	9.9×10^{-6}	192.512	15.3892
	0.2	1.94×10^{-5}	168.414	25.980
	0.3	3.63×10^{-5}	131.849	42.051

The IC$_{50}$ values for all molecules were calculated by the plot of the percentage superoxide anion inhibition (% I) versus the molar concentrations (C) (**Figure 2**). The IC$_{50}$ values obtained are shown in **Figure 3**.
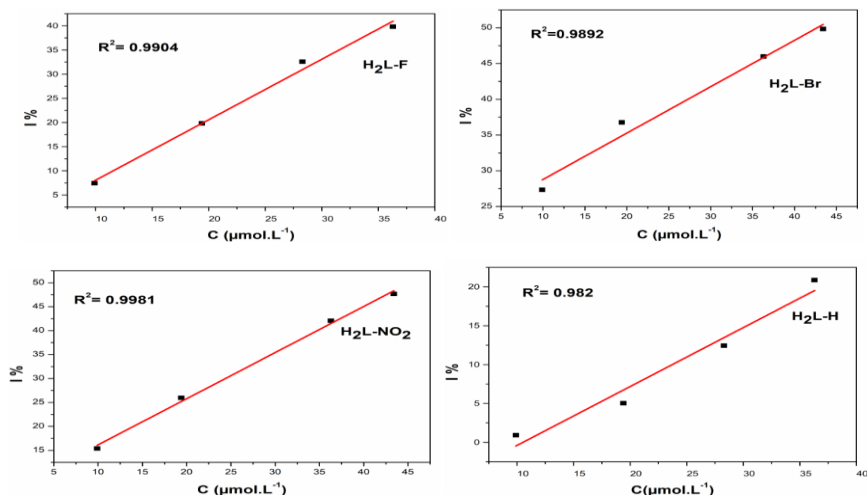
Figure 2. Plot of the ratio of percentage inhibition I % versus the concentration C of compounds H_2L-Br, H_2L-H, H_2L-F and H_2L-NO$_2$ for the calculation of the IC$_{50}$
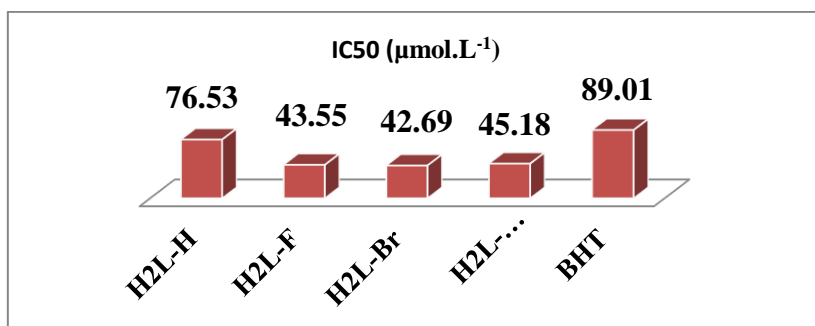
Figure 3. IC$_{50}$ values representing $O_2^{\bullet-}$ radical scavenging for the compounds H_2L-Br, H_2L-F, H_2L-H, H_2L-NO$_2$ and the BHT standard

From **Figure 3**, it can be seen that compounds H_2L-NO$_2$, H_2L-Br and H_2L-F present the lowest values for IC$_{50}$ in the order of 43.80±1.26 µmol. L^{-1} revealing the effect of electron-withdrawing groups (Bromo, Fluro and nitro) to increase the antioxidant activity, the lowest activity is represented by the compound H_2L-H with an IC$_{50}$ of the order of 76.53 µmol. L^{-1}. The present results are in good agreement with the results of the antioxidant activity evaluated by the three chemical techniques published previously [9], this confirms the valuable role of the electron withdrawing groups in the increase the antioxidant activity [17]. According to the histogram illustrated in **Figure 3**, we can classify the tested compounds by order of their decreasing reactivity:

$$H_2L\text{-Br} > H_2L\text{-F} > H_2L\text{-NO}_2 > H_2L\text{-H} > BHT$$
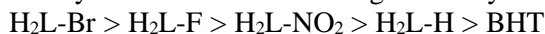
3.3. Thermodynamic parameters

The study of the interaction of the four quinoline compounds with superoxide anion was estimated in terms of binding constant (k_b), ratio of binding constants and standard Gibbs free energy ($\Delta G°$) (**Table 2**).
The k_b values are determined from the curves of the variation of log (1/C) versus log (i/i_0-i) plotted using the following equation [18]:

$$log\frac{1}{C} = logkb + log\frac{i}{i_0 - i} \tag{2}$$

Where C is the concentration of the tested compound (mol.L^{-1}), k_b is the binding constant (L.mol^{-1}), i and i_0 are the anodic current density in presence and absence of the tested compound, respectively.

Table 2. Values of k_b and $\Delta G°$ of the molecules H$_2$L-Br, H$_2$L-F, H$_2$L-NO$_2$, H$_2$L-H and the BHT standard.

Compound	Equation	R²	k_b (L.mol^{-1})	ΔG°(kJ/mol)
O$_2$·⁻-H$_2$L-NO$_2$	y = 0.795x+4.418	0.996	26181.83	-26.21
O$_2$·⁻-H$_2$L-H	y = 0.396x+4.202	0.998	15922.08	-24.93
O$_2$·⁻-H$_2$L-F	y = 0.591x+4.345	0.986	22134.94	-25.78
O$_2$·⁻-H$_2$L-Br	y = 1.402x+4.408	0.970	25585.85	-26.15
O$_2$·⁻-BHT	y = 0.369x+4.22	0.979	16595.86	-25.04

From **Table 2**, we can notice that the derivatives H$_2$L-Br, H$_2$L-F and H$_2$L-NO$_2$ present the highest values of k_b constants compared to the derivative H$_2$L-H and the standard BHT confirming their strong interactions with the superoxide radical. The negative values of the free energies $\Delta G°$ indicate the spontaneity of the antiradical reaction which is considered as clear evidence of the efficiency of the tested compounds.

The ratio of the equilibrium binding constants (K_{Red}/K_{Ox}) was determined from the shift of the value of the formal potential using the following equation [19]:

$$\Delta E^0 = E_b^0 - E_f^0 = 0,059 \, log\frac{K_{red}}{K_{ox}} \tag{3}$$

Where E_b^0 and E_f^0 are the formal potentials of the $O_2/O_2^{·-}$ redox couple in the bound and free forms. The values of the peak potential shift as well as the K_{red}/K_{ox} values for all the investigated compounds are summarized in **Table 3**.

The K_{Red}/K_{Ox} ratio values for compounds H₂L-H, H₂L-Br, H₂L-F and H₂L-NO₂ came out to be 1.42, 1.59, 1.21 and 1.53 respectively, which indicates that the interaction of the reduced form $O_2^{.-}$ with all derivatives is stronger than that of the oxidized form O_2.

Table 3. Electrochemical data of $O_2^{.-}$ bound form of H₂L-Br, H₂L-F, H₂L-NO₂ and H₂L-H.

Compound	EP_a(V)	EP_c((V)	E^0(V)	ΔE^0(mV)	Kr/Ko
$O_2^{.-}$	-0.587	-1.133	-0.86	-	
H₂L-H - $O_2^{.-}$	-0.573	-1.129	-0.851	9	1.42
$O_2^{.-}$	-0.678	-1.02	-0.849	-	
H₂L-Br - $O_2^{.-}$	-0.691	-1.032	-0.861	1.2	1.59
$O_2^{.-}$	-0.589	-1.175	-0.882	-	
H₂L-F - $O_2^{.-}$	-0.586	-1.189	-0.887	5	1.21
$O_2^{.-}$	-0.673	-1.066	-0.869	-	
H₂L-NO₂ - $O_2^{.-}$	-0.632	-1.084	-0.858	1.1	1.53

EP_c: cathodic potential; EP_a: anodic potential; $E^0 = \dfrac{EPa+EPc}{2}$; $\Delta E^0 = E^0$ (H₂L-R- $O_2^{.-}$)-E^0 (H₂L-R).

4. Conclusion

By using the electrochemically generated $O_2^{.-}$ in situ, the reactivities of the four quinoline compounds was evaluated by cyclic voltammetry method. All derivatives reacted similarly with $O_2^{.-}$, inducing decrease in anodic peak current. The magnitude of calculated free energy displayed the strong interaction between the $O_2^{.-}$ and the investigated compounds. The negative values of ΔG° suggested the spontaneity of the electrostatic interaction of $O_2^{.-}$ with H₂L-H, H₂L-Br, H₂L-F, H₂L-NO₂ compounds.

Acknowledgement

References

[1] Y.F. Baba, N.K. Sebbar, S. Hayani, F.O. Chahdi, E.M. Essassi, Moroc. J. Hetero. Chem. **17** (2018) 83-126.

[2] H. Breuer, Atlas de la chimie, (2000).

[3] A. Korolkovas, Essentials of medicinal chemistry, John Wiley & Sons, (2008).

[4] J.J. Pocidalo, F. Vachon, B. Regnier, Les nouvelles quinolones, Arnette, (1985).

[5] J.C. Bergh, T.H. Tötterman, B.C. Termander, K.A.-M. Strandgarden, P.O.G. Gunnarsson, B.I. Nilsson, Cancer Investig. **15** (1997) 204–211.

[6] Y.F. Baba, H. Elmsellem, Y.K. Rodi, H. Steli, F.O. Chahdi, Y. Ouzidan, N.K. Sebbar, E.M. Essassi, F. El-Hajjaji, B. Hammouti, J. Mater. Environ. Sci. **7 (7)** (2016) 2424-2434

[7] I. Benmahammed, T. Douadi, S. Issaadi, M. Al-Noaimi, S. Chafaa, J. Disp. Sci. Tech. **41** (2019) 1002-1021.

[8] K. Douadi, S. Chafaa, T. Douadi, M. Al-Noaimi, I. Kaabi, J. Mol. Struct. **1217** (2020) 128305.

[9] M.M. Kornet, O.A. Brazhko, M.P. Zavhorodniy, V.V. Tkach, O.S. Kruglyak, Y.G. Ivanushko, S.C. de Oliveira, P.I. Yagodynets, bio inter. Res. App. Chem. **11** (2021) 9148 - 9156.

[10] I. Bazine, Z. Cheraiet, R. Bensegueni, C. Bensouici, A. Boukhari, J. Hetero. Chem. **57** (2020) 2139–2149.

[11] A.A. Nagargoje, S.V. Akolkar, M.M. Siddiqui, D.D. Subhedar, J.N. Sangshetti, V.M. Khedkar, B.B. Shingate, Chem. Biodiver. **17** (2020) e1900624.

[12] M. Al-Noaimi, O.S. Abdel-Rahman, I.I. Fasfous, M. El-Khateeb, F.F. Awwadi, I. Warad, Spectrochim. Acta Part A: Mol. Biomol. Spect.**125** (2014) 375–383.

[13] T. Lanez, H. Hemmami, Current Pharm. Anal. **13** (2017) 110–116.

[14] N. Blanc, D. Hauchard, L. Audibert, E.A. Gall, Talanta. **84** (2011) 513–518.

[15] T. Lanez, M. Henni, J. Iran. Chem. Soc. **13** (2016) 1741–1748.

[16] C. Le Bourvellec, D. Hauchard, A. Darchen, J.-L. Burgot, M.-L. Abasq, Talanta. **75** (2008) 1098–1103.

[17] F.C. Torres, N. Brucker, S. Fernandes Andrade, D. Fabio Kawano, S. Cristina Garcia, G. Lino von Poser, V. Lucia Eifler-Lima, Cur. Top. Med. Chem. **14** (2014) 2600–2623.

[18] G.-C. Zhao, J.-J. Zhu, J.-J. Zhang, H.-Y. Chen, Anal. Chim. Acta **394** (1999) 337–344.

[19] X. Chu, G.-L. Shen, J.-H. Jiang, T.-F. Kang, B. Xiong, R.-Q. Yu, Anal. Chim. Acta **373** (1998) 29–38.