

Synthesis, Structural, Spectroscopic and Electrochemical Properties of Novel S- and S,O-Substituted 1,4-Naphthoquinones

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New S- and S,O-substituted 1,4-naphthoquinone compounds **3**, **4** and **5** were synthesized from the reaction of 2,3-dichloro-1,4-naphthoquinone (**1**) with 2-mercaptobenzylalcohol (**2**) in ethanol with sodium carbonate for 2 h at room temperature. The structures of novel compounds were characterized by using micro analysis, FT-IR, UV/Vis, ¹H NMR, ¹³C NMR, mass spectra, cyclic voltammetry and fluorescence spectrophoto-tometer. The crystal structure of **3** was determined by X-ray diffraction method. The compound **3** was crystallized in the triclinic crystal system (space group P-1) with the unit cell parameters a = 7.9433(10) Å, b = 8.1707(11) Å, c = 10.5705(11) Å, α = 91.173(6)°, β = 93.564(6)°, γ = 106.115(6)°.

Key Words: 1,4-Naphthoquinone, Fluorescence, Cyclic voltammetry, Crystal structure.

INTRODUCTION

Recent chemical literature shows that the synthesis of quinoid natural products as synthetic intermediates and biologically active compounds have drawn a lot of attention. Quinones are well known in biological systems as a reactive center of transporting both electrons and protons accross biological membranes^{1,2}. Substituted 1,4-naphthoquinones are widespread among the natural quinones such as menaquinone (involved in the electron-transport chain of bacteria) and lawsone is the 2-hydroxy-1,4-naphthoquinone pigment found in the leaves of *Lawsonia alba*³. They have a great scale for biological activities from intercalating agents of the DNA double helix to respiration⁴. Some tetrathiabenzoquinone compounds are also used in the dye industry and were synthesized by our group⁵.

The redox chemistry of quinones and evaluation of their electrochemical parameters is a useful way for identifying of their biological evolutions. The biological activity of quinones results from their capacity for accepting one or two electrons. The relationship of the electrochemical parameters and the biological activity of important quinones have been investigated in literature^{6,7}. Quinone derivatives are an interesting group of model groups for voltammetry studies⁸. Electron-attracting

or -donating substituents also modulate the redox properties of quinones. They also have wide range of pharmacological properties including antibacterial^{9,10}, anticancer^{11,12}, antimalarial^{13,14}, antifungal^{15,16} and antiviral¹⁷.

The aim of this study is to synthesize the novel S- and S,O-substituted 1,4-naphthoquinone compounds and characterize them with spectral methods.

EXPERIMENTAL

Melting points were determined on a Buchi B-540 melting point apparatus and uncorrected. Microanalyses were performed on a Thermo Finnigan Flash EA 1112 Series elemental analyser. Infrared spectra were recorded in KBr pellets in Nujol mulls on a Perkin-Elmer precisely spectrum one FTIR spectrometer. UV spectra were recorded in Perkin-Elmer precisely Lambda 35 UV-VIS spectrometer. Fluorescence spectra were run on a VARIAN Cary eclipse fluorescence spectrophotometer. NMR spectra were recorded in CDCl₃ for ¹H NMR and ¹³C NMR on a Varian^{UNITY} INOVA operating at 500 MHz. Mass spectra were obtained on a Thermo Finnigan LCQ Advantage MAX LC/MS/MS spectrometer using ion-trap mass analyzer for ESI source. Crystal structure of **3** was determined on Rigaku R-Axis Rapid-S X-ray single crystal diffractometer.

Cyclic voltammetry measurements were performed in a conventional three-electrode cell using a computer controlled system of a Gamry Reference 600 Model potentiostat/galvanostat. A polished platinum disc was used as a working electrode with a 0.071 cm² surface area. The surface of the working electrode was polished with H₂O suspension of Al₂O₃ before each run. A platinum wire served as the counter electrode. The reference electrode was an saturated calomel electrode (SCE) isolated from the main cell by a double bridge filled with 0.1 M TBAP in DMSO. Electrochemical grade tetrabutyl ammonium perchlorate (TBAP) in extra pure DMSO was employed as the supporting electrolyte at a concentration of 0.10 M. Prior to each run solutions were purged with nitrogen. Measurements were made over a potential range between 0 and -2 V with a step rate of 0.1 V s⁻¹.

Products were isolated by column chromatography on silica gel (Fluka silica gel 60, particle size 63-200 μm). TLC plates silica 60F₂₅₄ (Merck, Darmstadt) and detection was carried out with ultraviolet light (254 nm). All reagents and solvents were of reagent-grade, obtained from commercial suppliers and used without further purification.

X-Ray structure determination: Red crystals of compound suitable for X-ray diffraction analysis were obtained by slow evaporation of an ethyl acetate solution at room temperature. A red crystal of compound **3**, C₁₇H₁₀O₃S₁, having approximate dimensions of 0.60 × 0.20 × 0.10 mm was mounted on a glass fiber. All measurements were made on a Rigaku R-Axis Rapid-S imaging plate area detector with graphite monochromated Mo-K_α radiation (λ = 0.71073 Å). The data were collected at room temperature to a maximum 2θ value of 50.3°. Experimental conditions are summarized in Table-1.

TABLE-1
CRYSTAL DATA AND REFINEMENT PARAMETERS FOR COMPOUND **3**

CCDC deposit number	CCDC 750251
Empirical formula	C ₁₇ H ₁₀ O ₃ S ₁
Crystal colour, habit	Red, chunk
Formula weight	294.32
Temperature	293(2)K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Cell dimensions	a = 7.9433(10) Å, b = 8.1707(1) Å, c = 10.5705(11) Å α = 91.173(6)°, β = 93.564(6)°, γ = 106.115(6)°
Volume	657.3(1) Å ³
Z	2
Density (calculated)	1.487 mg/m ³
Absorption coefficient	0.253 mm ⁻¹
F ₀₀₀	304.00
Index ranges	-9 ≤ h ≤ 9 -9 ≤ k ≤ 9 -12 ≤ l ≤ 12
Reflections collected	33926
Independent reflections	2354[R _{int} = 0.049]
Data/restraints/parameters	2153/0/190
Goodness of fit indicator	1.220
Final R indices [I > 3σ(I)]	R ₁ = 0.078, wR ₂ = 0.030
Largest diff. peak and hole	0.34 and -0.39 e. Å ⁻³

The structure was solved by SIR 92 and refined with CRYSTALS^{18,19}. The non-hydrogen atoms were refined anisotropically. H atoms were located in geometrically idealized positions C-H = 0.95(6) Å and treated as riding and U_{iso}(H) = 1.2 U_{eq}(C). The selected bond distances, bond and torsion angles for compound **3** are listed in Tables 2 and 3, respectively. Drawing were performed with the program ORTEP-III²⁰ with 50 % probability displacement ellipsoide²⁰ for compound **3** in Fig. 1. Crystallo-graphic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-750251 for **3**²¹.

General procedure: 1.0 g (4.43 mmol) 2,3-dichloro-1,4-naphthoquinone (**1**) and 1.0 g (4.42 mmol) 2-mercaptobenzyl alcohol (**2**) were stirred in 60 mL EtOH with Na₂CO₃ solution for 2 h at room temperature. The colour of the solution quickly changed to red and the reaction was monitored by TLC. Chloroform (30 mL) was added to the reaction mixture. The organic layer was washed with water (4 × 30 mL) and dried over Na₂SO₄. After the solvent was evaporated the residue was purified by column chromatography on silica gel.

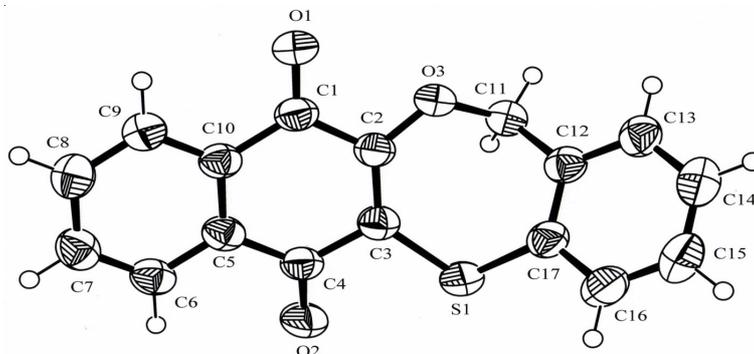


Fig. 1. Molecular structure of compound **3**. Displacement ellipsoids are plotted at the 50 % probability level

TABLE-2
SELECTED BOND DISTANCES (Å) FOR COMPOUND **3**

Atom	Distance	Atom	Distance
C2-C3	1.363(2)	C1-O1	1.215(2)
C4-O2	1.215(2)	C2-O3	1.339(2)
C3-S1	1.764(2)	S1-C17	1.763(2)
C5-C10	1.391(2)	O3-C11	1.454(2)

TABLE-3
SELECTED BOND AND TORSION ANGLES (°) FOR COMPOUND **3**

Atom	Bond angle	Atom	Torsion angle
C1-C2-C3	121.40(2)	C1-C2-C3-C4	14.7(3)
C2-C3-C4	118.70(2)	O1-C1-C2-C3	-1.8(3)
C3-C4-O2	119.10(2)	O2-C4-C3-C2	162.1(2)
C2-C1-O1	119.80(2)	C2-O3-C11-C12	-80.9(2)
S1-C3-C2	131.10(2)	C5-C4-C3-S1	166.1(2)
C3-S1-C17	104.87(8)	C1-C2-O3-C11	-164.3(1)
O3-C11-C12	111.20(2)	C3-S1-C17-C16	135.1(2)

[Cyclo-2-sulphonylbenzylalcoholyl] [2,3]-1,4-naphthoquinone (3): Yield 0.7 g (54 %); Red solid; m.p: 199-200 °C; $R_f = 0.5$ with CHCl_3 as an eluent; IR (KBr, ν_{max} , cm^{-1}): 3039 (CH_{arom}), 2986 (C-H), 1667 (C=O), 1590, 1552 (C=C); UV-vis [CHCl_3 , λ_{max} (nm) ($\log \epsilon$): 239 (3.6), 277 (4.2), 335 (3.3), 469 (4.1); UV-vis [THF, λ_{max} (nm) ($\log \epsilon$): 270 (4.4), 278 (4.3), 368 (2.4), 459 (3.3)]; ^1H NMR (499.74 MHz, CDCl_3): δ 5.5 (s, 2H, -OCH₂), 7.2 (t, $J = 6.84$ Hz, 2H, H_{arom}), 7.25 (t, $J = 6.84$ Hz, 1H, H_{arom}), 7.4 (dd, $J = 5.84$ Hz, $J = 6.81$ Hz, 1H, H_{arom}), 7.55 (t, $J = 5.84$ Hz, 2H, H_{arom}), 7.95 (dd, $J = 6.32$ Hz, $J = 5.84$ Hz, 2H, H_{arom}); ^{13}C NMR (125.66 MHz, CDCl_3): δ 71.88 (-OCH₂); 125.49, 125.75, 127.67, 128.82, 129.00, 129.95, 130.90, 132.72 (CH_{arom}), 122.96, 129.47, 130.35, 133.85 (C_{arom}), 136.82 (=C-S), 156.09 (=C-O), 176.55, 181.60 (C=O); MS (+ESI): m/z 295 ($\text{M}+\text{H}$)⁺; $\text{C}_{17}\text{H}_{10}\text{O}_3\text{S}$ (M, 294.32). Calcd. C, 69.37; H, 3.42; S, 10.89. Found C, 69.33; H, 3.22; S, 10.54.

(2-Sulphanylbenzylalcohol)-3-chloro-1,4-naphthoquinone (4): Yield 0.4 g (27 %); Red solid; m.p: 190-191 °C; $R_f = 0.4$ with CHCl_3 as an eluent; IR (KBr, ν_{max} , cm^{-1}): 3444 (-OH), 3038 (CH_{arom}), 2985 (C-H), 1673 (C=O), 1589, 1554 (C=C); UV-vis [CHCl_3 , λ_{max} (nm) (log ϵ): 239 (4.3), 277 (4.4), 390 (2.9), 471 (3.3); UV-vis [THF, λ_{max} (nm) (log ϵ): 238 (4.3), 273 (4.4), 368 (2.1), 460 (3.4); ^1H NMR (499.74 MHz, CDCl_3): 5.5 (s, 2H, $-\text{OCH}_2$), 7.25 (t, $J = 7.32$ Hz, 1H, H_{arom}), 7.3 (t, $J = 6.84$ Hz, 1H, H_{arom}), 7.45 (dd, $J = 7.81$ Hz, $J = 6.35$ Hz, 1H, H_{arom}), 7.6 (t, $J = 5.37$ Hz, 2H, H_{arom}), 8.0 (dd, $J = 6.84$ Hz, $J = 5.32$ Hz, 2H, H_{arom}); ^{13}C NMR (125.66 MHz, CDCl_3): δ 71.91 ($-\text{OCH}_2$); 125.54, 125.80, 127.70, 128.84, 129.02, 130.00, 132.75, 132.93 (CH_{arom}), 123.01, 124.12, 129.52, 130.42 (C_{arom}), 133.88 (=C-S), 136.85 (S-C), 156.11 (=C-Cl), 156.08 (=C-O), 176.63, 181.68 (C=O); $\text{C}_{17}\text{H}_{11}\text{O}_3\text{SCl}$ (M, 330.79). Calcd. C, 61.44; H, 3.40; S, 9.29. Found C, 61.73; H, 3.35; S, 9.69.

[2-Sulphanylbenzylalcohol][2,2'-dichloro [3,3']-bis(1,4-naphthoquinone) (5): Yield 0.3 g (13 %); Red solid; m.p: 190-191 °C; $R_f = 0.3$ with CHCl_3 as an eluent; IR (KBr, ν_{max} , cm^{-1}): 3015 (CH_{arom}), 2917 (C-H), 1672 (C=O), 1589, 1552 (C=C); UV-vis [CHCl_3 , λ_{max} (nm) (log ϵ): 240 (3.5), 277 (4.4), 336 (3.3), 468 (3.4); UV-vis [CHCl_3 , λ_{max} (nm) (log ϵ): 237 (4.8), 272 (4.9), 368 (3.2), 460 (3.8); ^1H NMR (499.74 MHz, CDCl_3): δ 5.5 (s, 2H, $-\text{OCH}_2$), 7.3 (t, $J = 5.32$ Hz, 3H, H_{arom}), 7.45 (t, $J = 5.32$ Hz, 3H, H_{arom}), 7.6 (dd, $J = 6.84$ Hz, $J = 7.32$ Hz, 3H, H_{arom}), 7.95 (dd, $J = 5.21$ Hz, $J = 4.85$ Hz, 3H, H_{arom}); ^{13}C NMR (125.66 MHz, CDCl_3): δ 71.89 ($-\text{OCH}_2$); 125.50, 125.76, 127.68, 128.82, 129.00, 129.96, 132.73, 132.91 (CH_{arom}), 122.97, 129.48, 130.37 (C_{arom}), 133.86 (=C-S), 136.83 (=C-Cl), 156.08 (=C-O), 176.57, 181.62 (C=O); MS (-ESI): m/z 522 (M-H) $^-$, 484 (M-Cl); $\text{C}_{27}\text{H}_{16}\text{O}_5\text{SCl}_2$ (M, 523.38). Calcd. C, 62.20; H, 2.71; S, 6.15. Found C, 62.16; H, 2.80; S, 6.55.

RESULTS AND DISCUSSION

The reaction of 2,3-dichloro-1,4-naphthoquinone (**1**) with 2-mercaptobenzyl alcohol (**2**) is yielded a series of new red coloured S- and S,O- substituted 1,4-naphthoquinone compounds (Fig. 2).

The first compound **3** was obtained by an interesting ring closure and is a S,O-substituted 1,4-naphthoquinone compound. The characteristic -OH band was disappeared in the IR spectrum of compound **3** because of the ring closure. In the ^1H NMR spectrum of **3**, the singlet at 5.5 was assigned to the $-\text{OCH}_2$. The ^{13}C NMR spectra of compound **3** gave two carbonyl signals at 176.55 and 181.60 ppm (C=O) in naphthoquinone unit. The mass spectra of compound **3** in the positive ion mode for ESI technique confirmed the proposed structure; molecular peak was identified at m/z 295 (Fig. 3).

The compound **4** is a S- substituted naphthoquinone and IR spectra of compound **4** showed a characteristic -OH band at 3444 cm^{-1} . The compound **5** is a S- and O-substituted dinaphthoquinone compound. The IR spectra of compound **5** showed characteristic carbonyl group's peak (C=O) at 1672 cm^{-1} as a result of conjugated

group effect. The characteristic -OH band was not observed in the IR spectrum of compound **5**. The fragmentation of molecular peak of compound **5** at m/z 522 in the negative ion mode for ESI gave a fragment ion at m/z 484 corresponding to the cleavage of a chlorine atom.

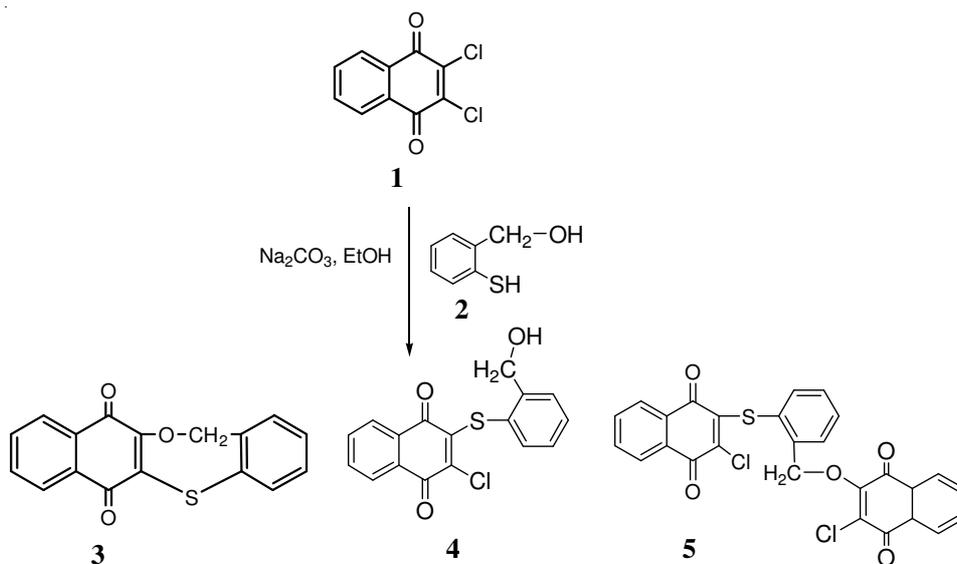


Fig. 2. Synthetic pathway of compounds **3**, **4** and **5**

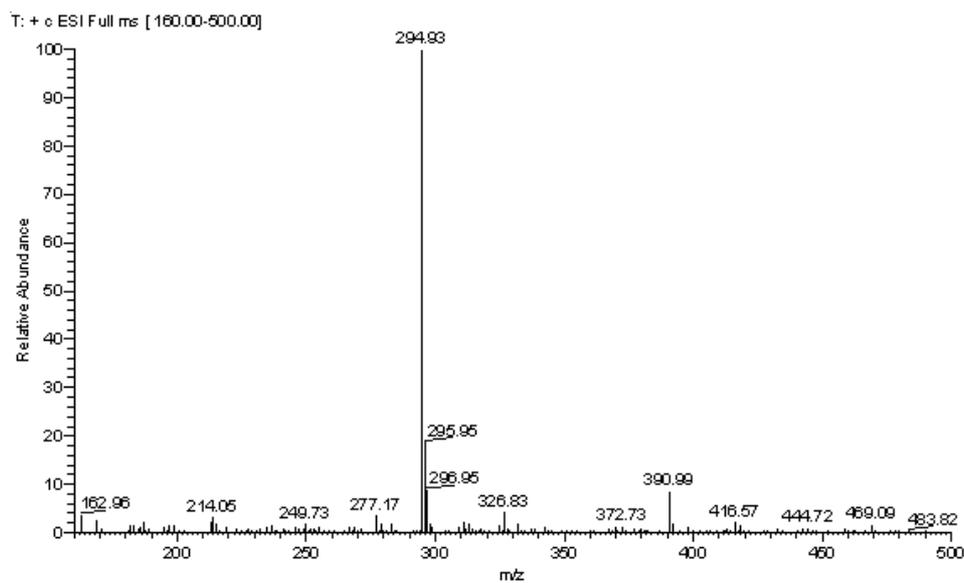


Fig. 3. Full mass spectrum of compound **3** for ESI technique

The UV-vis spectra of **3**, **4** and **5** were taken in chloroform and THF, respectively. The electronic absorption spectra of **3**, **4** and **5** showed the expected naphthoquinone bands in the UV region around 239-277 nm and 335-390 nm (π - π^* electronic transitions) in CHCl_3 (Fig. 4). A third energy transition also appeared as a broad band in the visible region between 459-471 nm (Table-4).

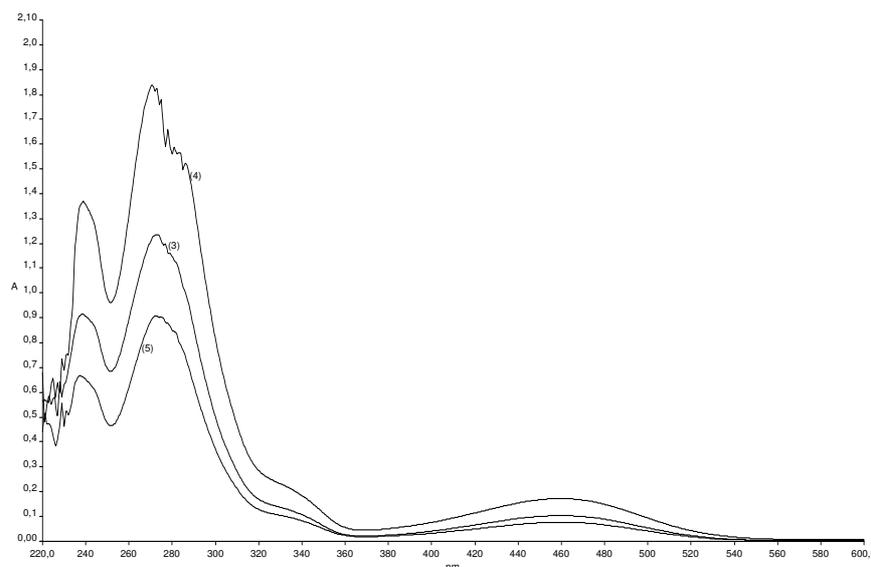


Fig. 4. UV-Vis spectra for 10^{-4} M **3**, **4** and **5** in THF

TABLE-4
UV-VIS DATA FOR DIFFERENT SOLVENTS

Compd.	Absorption		Molar absorptivity	
	$\lambda \text{ CHCl}_3$	$\lambda \text{ THF}$	$\log \epsilon \text{ CHCl}_3$	$\log \epsilon \text{ THF}$
3	239,277,335,469	270,278,368,459	3.6,4.2,3.3,3.4	4.4,4.3,2.4,3.3
4	239,277,390,471	238,273,368,460	4.3,4.4,2.9,3.3	4.3,4.4,2.1,3.4
5	240,277,336,468	237,272,368,460	3.5,4.4,3.3,3.4	4.8,4.9,3.2,3.8

Fluorescence is an important property of quinone compounds for the use of organic materials^{22,23}. The fluorescence properties of compound **3**, **4** and **5** were investigated in CHCl_3 for 10^{-4} M and excitation and emission wavelengths were given in Table-5. The excitation and emission spectra for compound **3** was shown in Fig. 5 as an example.

TABLE-5
EXCITATION AND EMISSION WAVELENGTHS OF COMPOUNDS **3**, **4**, **5** IN CHCl_3

Compound	$\lambda_{\text{ex.}} \text{ (max.)}$	$\lambda_{\text{em.}} \text{ (max.)}$
3	262, 471	648
4	263, 471	634
5	275, 471	635

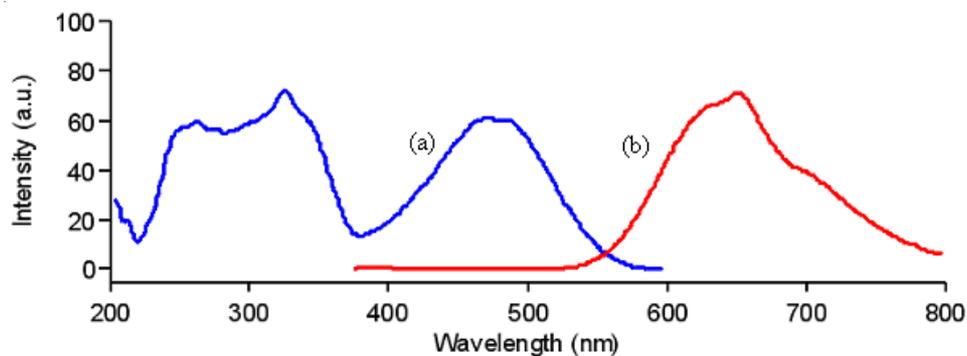


Fig. 5. Excitation (a) and emission (b) spectra for compound **3** (10^{-4} M) in CHCl_3 . Excitation and emission slit widths were set at 10 nm for all compounds

Voltammetry is a useful electrochemical technique for investigating electrochemical behaviours of organic compounds^{24,25}. Cyclic voltammograms of novel quinone compound **3**, **4** and **5** were obtained at 100 mV s^{-1} in DMSO for 0.1 M tetrabutyl ammonium perchlorate with a platinum electrode in the negative region of the CV (Fig. 6). These processes are attributed to the consecutive one-electron transfer to the naphthoquinone moiety, generating the semiquinone radical ($\text{Q}^{\bullet-}$) and the hydroquinone anion (Q^{2-}):

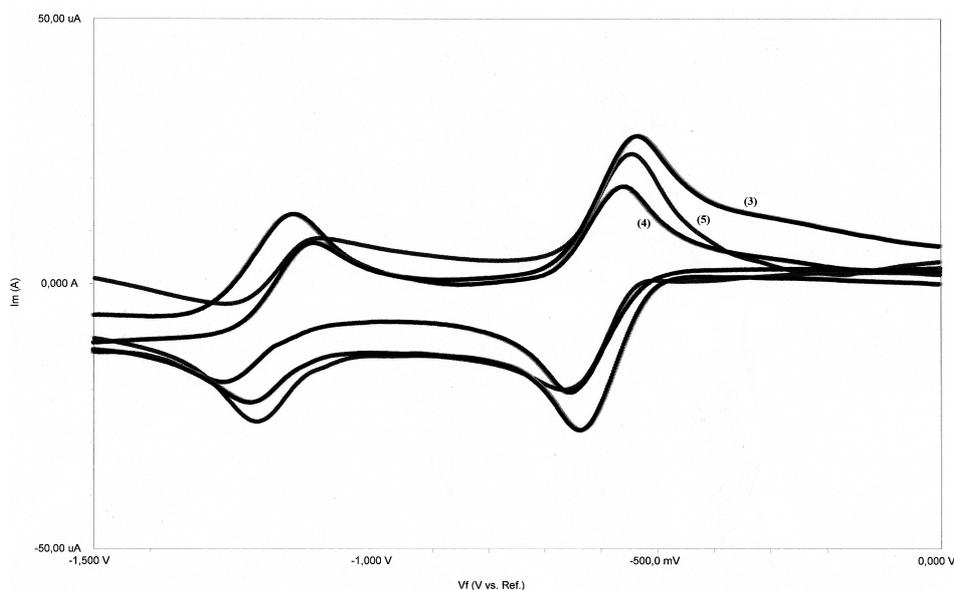
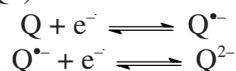


Fig. 6. Cyclic voltammograms of novel naphthoquinone derivatives **3**, **4** and **5**

The voltammetric data of these compounds; cathodic peak potentials (E_{pc_1} and E_{pc_2}), anodic peak potentials (E_{pa_1} and E_{pa_2}) *versus* saturated calomel electrode (SCE), half-wave peak potentials ($E_{1/2}$) and the difference between the first oxidation and reduction processes (ΔE_p) are shown in Table-6. As shown in Fig. 6 all compounds exhibit the same electrochemical behaviour of quinonoid system. Compound **3**, **4** and **5** have two reversible waves with fast electron transfer characteristics, ΔE_p near to 0.088 V and i_{pa}/i_{pc} equals 1.

TABLE-6
THE FIRST AND SECOND CATHODIC PEAK POTENTIALS (E_{pc_1} AND E_{pc_2}) AND THE ANODIC PEAK POTENTIALS (E_{pa_1} AND E_{pa_2}) *versus* SATURATED CALOMEL ELECTRODE (SCE) FOR NEW NAPHTHOQUINONE DERIVATIVES

Compd.	E_{pc} (V)	E_{pa} (V)	$E_{1/2}$ (V)	ΔE_p (mV)	i_{pa}/i_{pc}
3	-0.650 (E_{pc_1})	-0.562 (E_{pa_1})	-0.60	88	1.00
	-1.266 (E_{pc_2})	-1.148 (E_{pa_2})	-1.21	118	1.34
4	-0.633 (E_{pc_1})	-0.532 (E_{pa_1})	-0.58	101	1.03
	-1.221 (E_{pc_2})	-1.109 (E_{pa_2})	-1.16	112	0.95
5	-0.655 (E_{pc_1})	-0.550 (E_{pa_1})	-0.60	105	1.01
	-1.210 (E_{pc_2})	-1.110 (E_{pa_2})	-1.16	110	0.70

$$E_{1/2} = (E_{pa_1} + E_{pc_1})/2; \Delta E_p = (E_{pc_1} - E_{pa_1}).$$

X-ray study: The compound **3** was crystallized in the triclinic crystal system (space group P-1) with the unit cell parameters $a = 7.9433(10) \text{ \AA}$, $b = 8.1707(11) \text{ \AA}$, $c = 10.5705(11) \text{ \AA}$, $\alpha = 91.173(6)^\circ$, $\beta = 93.564(6)^\circ$, $\gamma = 106.115(6)^\circ$, $V = 657.3(1) \text{ \AA}^3$, $Z = 2$.

The bond lengths of C1-O1 and C4-O2 was $1.215(2) \text{ \AA}$, typical of C=O bonds. In the compound **3**, C-C-C and C-C-O angles were very close to 120° , as expected for sp^2 hybridized atoms. The double bond distance of C2-C3 was $1.363(2) \text{ \AA}$ in **3**, which was smaller than expected due to substituents such as =O. The double bond length of the quinone moiety agreed well with corresponding distance in a similar compound²⁴.

The compound **3** contains four ring systems which are naphthoquinone unit, phenyl and heterocyclic rings. Isolation and identification proved that a cyclization reaction had taken place yielding the compound **3**. Both rings of naphthoquinone unit and phenyl ring were planar with a maximum deviations of $0.0514(1) \text{ \AA}$ (plane 1 = C1-C2-C3-C4-C5-C10), $0.0024(1) \text{ \AA}$ (plane 2 = C5-C6-C7-C8-C9-C10) and 0.0025 \AA (plane 4 = C12, C13, C14, C15, C16, C17), respectively. The substituted heterocyclic ring was not planar with a maximum deviation of $0.2792(1) \text{ \AA}$ (plane 3 = C2-C3-S1-C17-C12-C11-O3). Dihedral angles were $21.52(1)^\circ$ between planes 2 and 3, $144.59(1)^\circ$ between planes 3 and 4.

Conclusion

The novel S- and S,O-substituted 1,4-naphthoquinone compounds **3**, **4** and **5** were synthesized. Their structures were determined using micro analysis, FT-IR,

UV/Vis, ^1H NMR, ^{13}C NMR, mass spectra, cyclic voltammetry and fluorescence spectrophotometer. The crystal structure of **3** was determined by X-ray diffraction method. These novel compounds possess high solubility in various organic solvents such as chloroform, dichloromethane, tetrahydrofuran and insoluble in water.

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