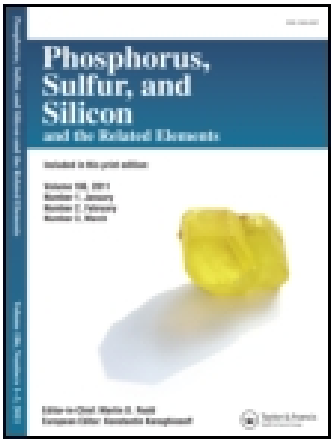

Phosphorus, Sulfur, and Silicon and the Related Elements

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The Synthesis, Characterization, and Electrochemical Investigation of Novel Thio- and Alkoxy-Substituted Benzoquinone Derivatives

Cemil Ibis [a] , Sibel Sahınler Ayla [a] & Senol Yavuz [a]

[a] Department of Chemistry, Faculty of Engineering , Istanbul University , 34320 , Avcilar , Istanbul , Turkey

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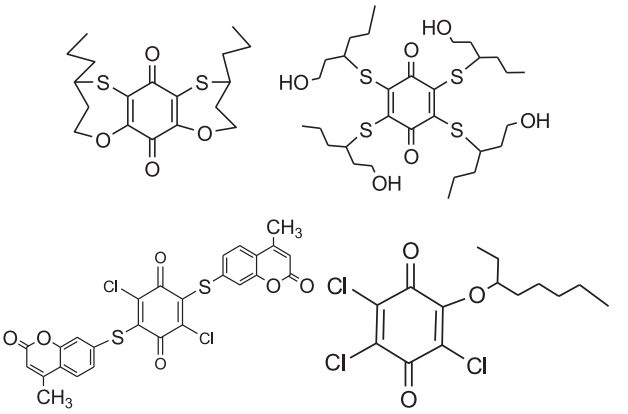
THE SYNTHESIS, CHARACTERIZATION, AND ELECTROCHEMICAL INVESTIGATION OF NOVEL THIO- AND ALKOXY-SUBSTITUTED BENZOQUINONE DERIVATIVES

Cemil Ibis, Sibel Sahınler Ayla, and Senol Yavuz
Department of Chemistry, Faculty of Engineering, Istanbul University, 34320 Avcilar, Istanbul, Turkey

GRAPHICAL ABSTRACT



Abstract *Novel thio- and alkoxy-substituted benzoquinone derivatives were synthesized from the reactions of* p-*chloranil* ***(1)*** *and related nucleophiles in a sodium carbonate (Na_2CO_3) solution of acetonitrile or in chloroform with Et_3N. The structures of novel compounds were characterized by using microanalysis, FTIR, ^1H NMR, ^{13}C NMR, MS, CV, and fluorescence spectroscopy.*

[Supplementary materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *for the following free supplemental files: Additional text and figures.]*

Keywords *p*-Chloranil; thioalcohols; mercaptans; coumarine

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We thank the Research Fund of Istanbul University for financial support to this work.
Address correspondence to Cemil Ibis, Department of Chemistry, Faculty of Engineering, Istanbul University, 34320 Avcilar, Istanbul, Turkey. E-mail: ibiscml@istanbul.edu.tr

INTRODUCTION

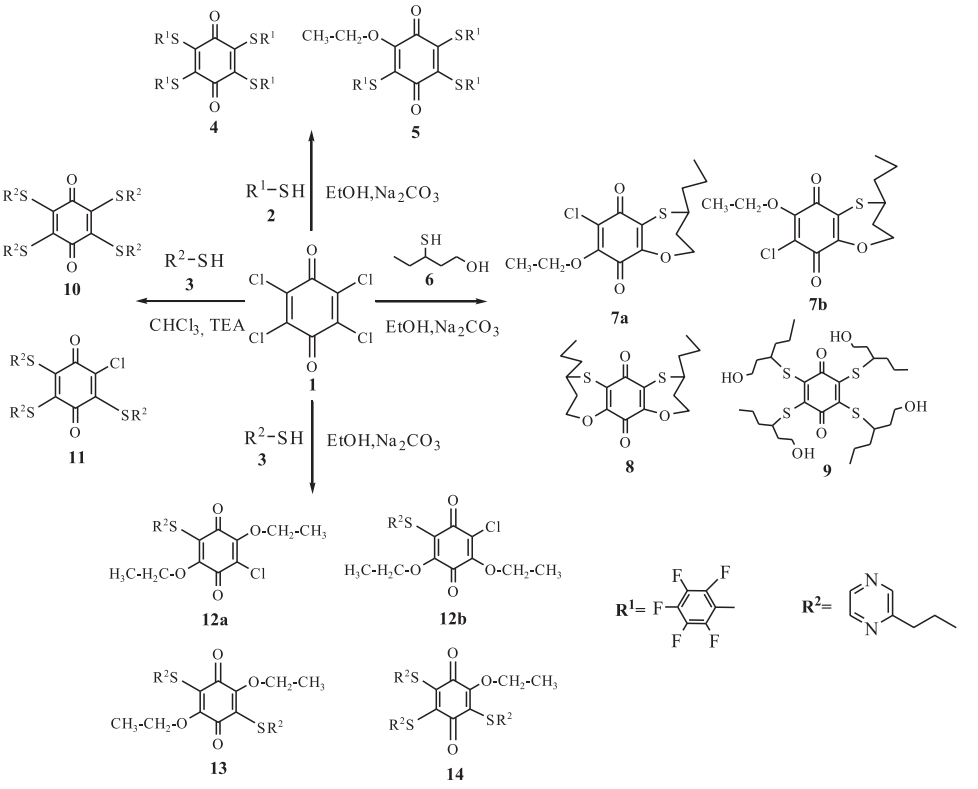
Nucleophilic additions to quinone structures have been widely studied in synthetic chemistry.[1–6] Heterocyclic ring quinone systems are found in biologically and pharmacologically active compounds.[7] It is also known from the literature that substitution of quinonoid structure with N-, S-, and O-nucleophiles leads to an observable increase in biological activity.[8] Many natural products from marine or plant sources involve quinonoid structures with important biological activity properties.[9–11]

Quinones also have been used in dye chemistry.[12] Quinone dyes have strong intramolecular charge-transfer chromophoric system. The compounds containing quinone structure have ability to undergo redox cycling to generate the reactive oxygen species (ROS) destroying the tumor cells.[13]

The aim of this study is to synthesize the novel benzoquinone compounds and characterize them with spectral methods.

RESULTS AND DISCUSSION

The novel benzoquinone derivatives **4** and **5** were obtained by the reaction of *p*-chloranil **1** and different molar equivalent of pentafluorothiophenol **2** in ethanol with sodium carbonate (Na_2CO_3) at room temperature (Scheme 1). The molecular ion peak of compound

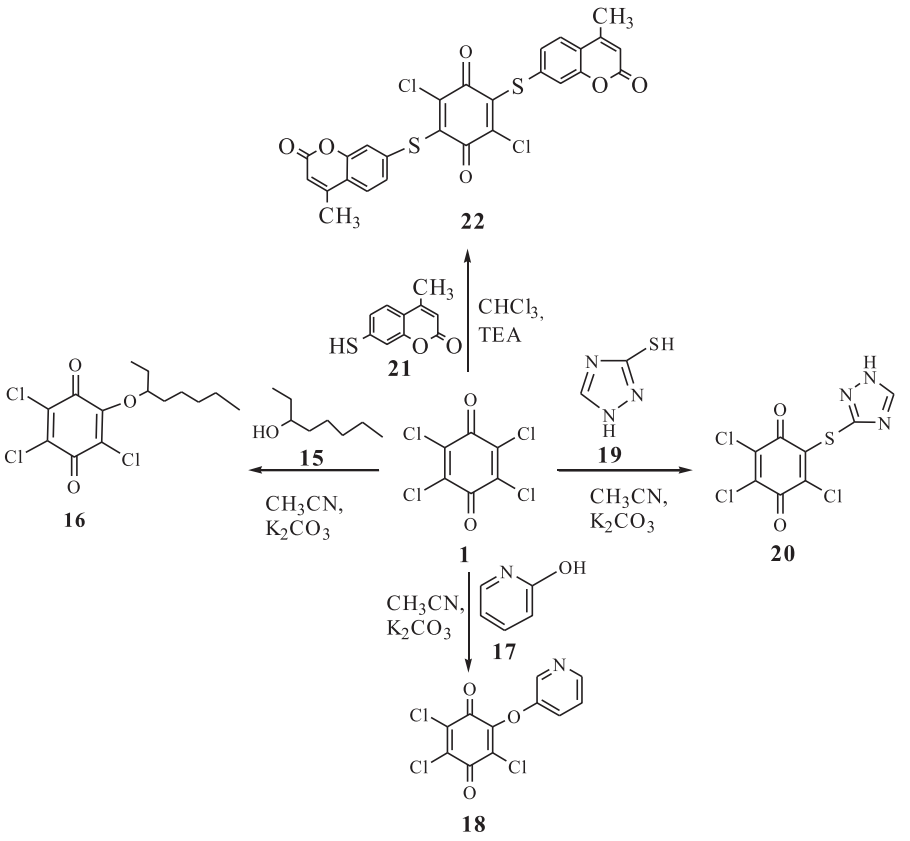


Scheme 1 Synthetic pathway of novel compounds.

4 was identified at m/z 900 in the negative ion mode for ESI technique. The $-OCH_2$ protons of compound **5** appeared at downfield region of ^1H NMR spectrum and showed triplets at 4.3 ppm.

The novel benzoquinone derivatives **7a**, **7b**, **8**, and **9** were obtained by the reaction of *p*-chloranil **1** and different molar equivalent of 3-mercapto-1-hexanol **6** in ethanol with sodium carbonate (Na_2CO_3) at room temperature. It is possible to say compounds **7a** and **7b** were obtained as an isomeric mixture and gave four carbon signals for C=O groups in benzoquinone unit resonating at 174.5, 175.1, 178.4, and 179.8 ppm. The ^{13}C NMR spectra of cyclic compound **8** gave only two carbonyl signals at 177.4 and 174.6 ppm as expected. The IR spectra of tetrakis-substituted compound **9** showed characteristic hydroxyl band (−OH) at 3334 cm^{-1} and gave one carbonyl signal at 173.1 ppm in ^{13}C NMR because of the symmetric structure of this compound.

The tetrakis-substituted compound **10** and tris-substituted compound **11** were obtained by the reaction of *p*-chloranil **1** and different molar equivalent of 2-(2-mercaptoethyl)pirazine **3** in chloroform with Et_3N. The ^{13}C NMR spectra of compounds **10** gave only one carbonyl signal at 172.6 ppm as a result of the symmetric unit. Furthermore, the tris-substituted compound **11** gave two carbonyl signals at 173.6 and 169.6 ppm. The mass spectra of compound **11** in the negative ion mode of ESI technique confirmed the



Scheme 2 Synthesis of novel O-, S-, and S,S-substituted chloranil compounds.

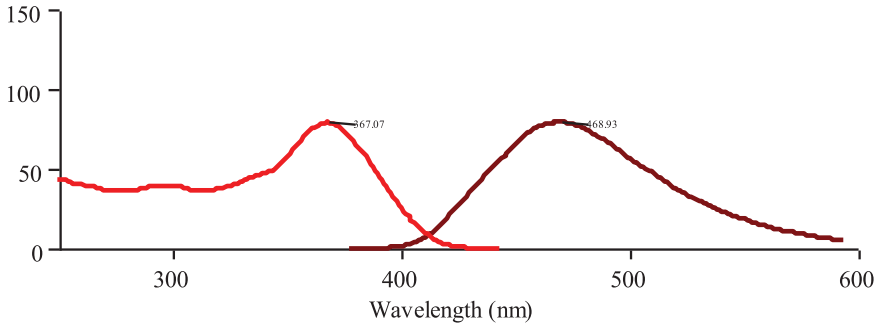


Figure 1 Excitation (367.07 nm) and emission (468.93 nm) spectra for compound **22** (10^{-4} M) in chloroform at room temperature. (Color figure available online).

proposed structure; the deprotonated molecular ion peak was identified at m/z (%) 556 (100).

The novel benzoquinone derivatives **12a**, **12b**, **13**, and **14** were obtained by the reaction of *p*-chloranil **1** and 2-(2-mercaptoethyl)pirazine **3** in sodium carbonate (Na_2CO_3) solution of ethanol at room temperature. It is possible to say compounds **12a** and **12b** were obtained as an isomeric mixture and gave four carbon signals for C=O groups in benzoquinone unit resonating at 178.0, 176.7, 174.5, and 173.9 ppm. The ^{13}C NMR spectra of compounds **13** gave only one carbonyl signal at 177.4, as a result of symmetric structure of compound **13**. The $-OCH_2$ protons of compound **14** appeared at downfield region of ^1H NMR spectrum and showed triplets at 4.2 ppm.

The novel alkoxy-substituted benzoquinone derivatives **16** and **18** were synthesized from the reactions of *p*-chloranil **1** and related alcohols in potassium carbonate (K_2CO_3) solution of acetonitrile (Scheme 2).

The mass spectra of compounds **16** and **18** in the negative ion mode of ESI technique confirmed the proposed structure; the molecular and deprotonated molecular ion peaks were identified at m/z (%) 338 (100) and 303 (100), respectively. The monothiosubstituted compound **20** was obtained from the reaction of *p*-chloranil **1** and 3-mercapto-1,2,3-triazole

Table 1 Half-wave potentials (for the 1st wave) and electrochemical data for some of the novel benzoquinone derivatives (10^{-3} M) in DMF/TBAP 0.1 M, $\upsilon = 100$ mV s^{-1}

Compound	E_p (Ic) (V)	E_p (IIc) (V)	ΔEp_1[a] (mV)	$E_{1,1/2}$[b] (V)
p-Chloranil **1**	0.200	−0.681	185	0.293
4	−0.152	−0.916	—	−0.076
8	−0.462	−1.048	74	−0.425
9	−0.162	−0.585	92	−0.116
10	−0.276	−0.968	—	−0.138
14	−0.317	—	—	−0.158
16	0.083	−0.798	102	−0.134
18	0.349	−1.116	66	0.331
20	0.2186	−0.356	94	0.265

[a] $\Delta Ep_1 = Epa_1 - Epc_1$.
[b] $E_{1,1/2} = (Epa_1 + Epc_1)/2$.

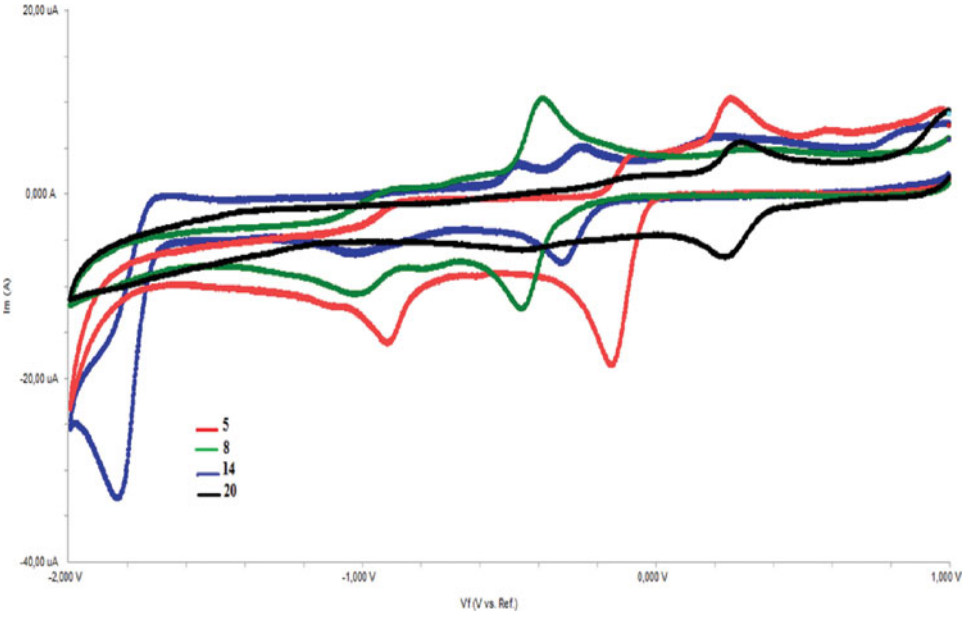


Figure 2 Cyclic voltammagram of some of the novel benzoquinone derivatives in DMF + 0.1 M TBAP on Glassy Carbon Electrode (ϕ^3mm) at 0.1 Vs^{-1}. (Color figure available online).

19 in potassium carbonate (K_2CO_3) solution of acetonitrile. The –NH proton of compound **14** showed doublets at 8.3 ppm. The 2,5-thiosubstituted compound **22** was obtained from the reaction of *p*-chloranil **1** and 7-mercapto-4-methyl-coumarine **17** in chloroform with triethylamine. The ^{13}C NMR spectra of compounds **22** gave only one carbonyl signal at 171.7 as a result of symmetric structure of compound **22**.

Quinones show shifts in UV-Vis and fluorescence spectra with a change of redox state.[14] Coumarin group also have fluorescence properties.[15,16] The fluorescence properties of compound **22** was investigated in chloroform solution at room temperature with a 5 nm slit width for fluorescence spectrometer. The excitation and emission bands were observed at 367.07 nm and 468.93 nm, respectively (Figure 1).

Quinone-hydroquinone systems are typical examples of organic redox reactions.[17,18] The electrochemical behaviors of compounds **1**(*p*-chloranil), **8**, **16**, **18**, and **20** have been studied in DMF using TBAP 0.10 M as supporting electrolyte at 100 mVs^{-1}. The *p*-chloranil **(1)** is reduced in two steps producing anion radical (semiquinone, Q^-) and the dianion (Q^{2-}). This behavior is typical for the reduction of quinones in aprotic conditions.[19,20] In Table 1, *p*-chloranil **1** was even reduced at positive potential in the first reduction step $E_p(Ic) = 0.200$ V. These can be related to the electron-attracting substituent (Cl atoms) attached to the ring causing the reduction potential at higher value. Two reversible pairs of peaks are also detected in compound **16**'s voltammogram. (Figure 2).

CONCLUSION

Novel substituted benzoquinone compounds were synthesized from the reactions of *p*-chloranil **(1)** and related nucleophiles in different reaction media. The structures of novel

compounds were characterized by using microanalysis, FTIR, ^{1}H NMR, ^{13}C NMR, MS, and CV.

EXPERIMENTAL

Material and Methods

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 analyzer. Infrared (IR) spectra were recorded in KBr pellets in Nujol mulls on a Perkin Elmer Precisely Spectrum One FTIR spectrometer. Fluorescence Spectra were run on a VARIAN Cary Eclipse Fluorescence Spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian UNITY INOVA spectrometer 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. 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 glassy carbon disc was used as a working electrode. The surface of the working electrode was polished before each run. A platinum wire served as the counter electrode. The reference electrode was an Ag/AgCl electrode. Electrochemical grade tetrabutylammonium perchlorate (TBAP) in extra pure DMF 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 Vs^{-1}.

Products were isolated by column chromatography on Silica gel (Fluka silica gel 60, particle size 63–200 μm). TLC plates silica $60F_{254}$ (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. Selected mass spectra, ^{1}H and ^{13}C NMR spectra, and cyclic voltammagrams are presented in the online Supplemental Materials (Figures S1–S11).

General Procedure 1

Sodium carbonate (1.52 g) was dissolved in ethanol (30 mL) and into the resulting solution, firstly *p*-chloranil and then thiol were added slowly in small portions. Without heating, the mixture was stirred for 8 h. The color of the solution quickly changed, and the extent of the reaction was monitored by TLC. Chloroform (30 mL) was added to the reaction mixture. The organic layer was separated, washed with water (4 $\times$ 30 mL), and dried with Na_2SO_4. After the solvent was evaporated, the residue was purified by column chromatography on silica gel.

General Procedure 2

Potassium carbonate (1.52 g) was dissolved in acetonitrile (30 mL) and into the resulting solution, firstly *p*-chloranil and then alcohol were added slowly in small portions. Without heating, the mixture was stirred for 12 h. The color of the solution quickly changed, and the extent of the reaction was monitored by TLC. Chloroform (30 mL) was added to the reaction mixture. The organic layer was separated, washed with water (4 $\times$ 30 mL), and

dried with Na_2SO_4. After the solvent was evaporated, the residue was purified by column chromatography on silica gel.

General Procedure 3

p-Chloranil and thiol were stirred in chloroform as a solvent (40mL). Triethylamine (1 mL) was added to reaction mixture slowly without heating, and the mixture was stirred for 12 h. The color of the solution quickly changed, and the extent of the reaction was monitored by TLC. Chloroform (30 mL) was added to the reaction mixture. The organic layer was separated, washed with water (4 × 30 mL), and dried with Na_2SO_4. After the solvent was evaporated, the residue was purified by column chromatography on silica gel.

2,3,5,6-Tetrakis(pentafluorophenylthio)-cyclohexa-2,5-diene-1,4-dione (4): Compound **4** was synthesized from the reaction of **1** (0.5g, 2.033 mmol) with **2** (1.04 mL, 8.1 mmol) according to the general procedure 1.

Orange solid; Yield: 0.26 g (14%); M.p.: 162–163°C; R_f = 0.52 (petroleum ether/$CHCl_3$ 3:1); Anal. Calcd for $C_{30}F_{20}O_2S_4$: C, 40.01; S, 14.24; Found: C, 39.75; S, 12.71. IR (KBr, cm^{-1}): $\nu = 3010$ (Ar−H), 2922, 2846 (C−H), 1665, 1638 (C=O), 1509, 1489 (C=C); ^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 108.3$ (S−*C*F), 146.4 (CO−*C*−S), 135.5, 137.5, 140.4, 141.4, 142.0, 144.0 (C_{arom}), 167.7 ppm (C=O); MS (*m*/*z*, (relative abundance,%)): 900 (M^-, 100)

6-Ethoxy-2,3,5-tris(pentafluorophenylthio)cyclohexa-2,5-diene-1,4-dione (5): Compound **5** was synthesized from the reaction of **1** (0.5 g, 2.033 mmol) with **2** (0.77 mL, 6.1 mmol) according to the general procedure 1.

Brown solid; Yield: 0.28 g (18%); M.p.: 102–103°C; $R_f = 0.8$ (petroleum ether/$CHCl_3$ 4:1); Anal. Calcd. for $C_{26}H_5F_{15}O_3S_3$: C, 41.83; H, 0.68; S, 12.89; Found: C, 41.83; H, 0.48; S, 12.20. IR (KBr, cm^{-1}): $\nu = 2990$, 2928 (C−H), 1674, 1651 (C=O), 1512, 1490 (C=C). ^1H NMR (499.74 MHz, $CDCl_3$): $\delta = 4.3$ (m, 2H, O−CH_2), 1.2 ppm (t, 3H, CH_3-).^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 15.3$ (−CH_3), 70.5 (O−*C*H_2), 106.4 (FC_{arom}–S), 125.2 (CO−C−S), 136.7, 138.7, 140.5, 142.2, 145.7, 147.5 (C_{arom}–F), 155.1 (CO−C−O), 174.9, 178.8 (C=O) ppm.

A mixture of isomer compounds [7-Chloro-8-ethoxy-3,4-dihydro-4-propyl-2*H*-benzo[*b*][1,4]oxathiepine-6,9-dione (7a) and 8-Chloro-7-ethoxy-3,4-dihydro-4-propyl-2*H*-benzo[*b*][1,4]oxathiepine-6,9-dione(7b)]: A mixture of isomer compounds 7a and 7b was synthesized from the reaction of 1 (1 g, 4.066 mmol) with 6 (0.55 mL, 4.02 mmol) according to the general procedure 1.

Red oil; Yield: 0.35 g (27%); $R_f = 0.67$ ($CHCl_3$); Anal. Calcd. for $C_{14}H_{17}ClO_2S$: C, 53.08; H, 5.41; S, 10.12; Found: C, 53.60; H, 6.02; S, 9.39. IR (KBr, cm^{-1}): $\nu = 2961$, 2928, 2872 (C−H), 1672, 1657 (C=O), 1561 (C=C). ^1H NMR (499.74 MHz, $CDCl_3$): $\delta = 4.8$ (m, 2H, C−O−CH_2), 4.4 (m, 2H, O−CH_2), 3.6 (m, 2H, OCH_2−CH_2−CH), 2.4 (m, 1H, CH_2−CH−S), 1.6 (m, 2H, SC−CH_2), 1.5 (m, 2H, C−CH_2−CH_3), 1.3 (m, 2H, O−CH_2−CH_3), 0.8 (t, 2H, CH_3-) ppm.^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 13.9$ (−CH_3), 16.1 (O−CH_2−*C*H_3), 20.2 (−CH_2−CH_2−CH_3), 34.6 (SCH−CH_2), 37.4 (S−CH−CH_2), 45.6 (O−CH_2−CH_2−CH), 70.8 (O−CH_2−CH_3), 71.6 (O−CH_2−CH_2), 123.9 (C−S), 126.4 (C−Cl), 152.7, 154.5 (=C−O), 174.5, 175.1, 178.4, 179.8 (C=O). MS (*m*/*z*, (relative abundance,%)): 317 ($M+H^+$, 42).

4,8-Dipropyl-3,4,9,10-tetrahydrobenzo[1,2-b:5,4-b′]bis([1,4]oxathiepine)-6,12 (2H,8H)-dione (8): Compound **8** was synthesized from the reaction of **1** (0.5 g, 2.033 mmol) with **6** (0.84 mL, 6.01 mmol) according to the general procedure 1.

Black oil; Yield: 0.08 g (9%); $R_f = 0.67$ (ethyl acetate/petroleum ether 1:3); Anal. Calcd. for $C_{18}H_{24}O_4S_2$: C, 58.67; H, 6.56; S, 17.40; Found: C, 59.01; H, 7.47; S, 17.24; IR (KBr, cm^{-1}): ν = 2958, 2926, 2869 (C−H), 1666, 1637 (C=O), 1596, 1555 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): δ = 4.4–4.8 (m, 4H, C−O−CH_2), 3.5 (m, 4H, OCH_2−CH_2−CH), 2.4 (m, 2H, CH_2−CH−S), 1.2, 1.4, 1.3, 1.7 (m, 8H, −CH_2), 0.8 ppm (m, 6H, CH_3-). ^{13}C NMR (125.66 MHz, $CDCl_3$): δ = 12.7 (−CH_3), 19.1 (−CH_2), 33.3 (SCH−CH_2), 36.1 (S−CH), 44.2 (O−CH_2−CH_2−CH), 70.4 (O−CH_2), 124.8 (C−S), 151.8 (=C−O), 172.9, 181.4 (C=O) ppm. MS (*m*/*z*, (relative abundance,%)): 369 ($M+H^+$, 100).

2,3,5,6-Tetrakis(1-hydroxyhexane-3-ylthio)cyclohexa-2,5-diene-1,4-dione (9): Compound **9** was synthesized from the reaction of **1** (1 g, 4.066 mmol) with **6** (2.24 mL, 16.2 mmol) according to the general procedure 1.

Brown oil; Yield: 0.17 g (6%); $R_f = 0.47$ (ethylacetate); Anal. Calcd. for $C_{30}H_{52}O_6S_4$:C, 56.57; H, 8.23; S, 20.14; Found: C, 57.07; H, 8.04; S, 18.02; IR (KBr, cm^{-1}): ν = 3334 (−OH), 2957, 2931, 2872 (C−H), 1658 (C=O), 1486, 1465 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): δ = 3.9, 3.8, 3.7, 3.6 (m, 8H, HO−CH_2), 1.9, 1.8 (m, 4H, S−CH), 1.7, 1.6, 1.5, 1.3, 1.2 (m, 24H, CH_2), 0.8 ppm (m, 12H, CH_3-). ^{13}C NMR (125.66 MHz, $CDCl_3$): δ = 12.9 (−CH_3), 18.9 (−CH_2−CH_3), 38.4, 36.4 (SCH−*C*H_2), 45.8 (O−CH_2−CH_2), 58.6 (O−CH_2), 145.8, 148.5, 149.7 (C−S), 173.1 (C=O) ppm. MS (*m*/*z*, (relative abundance,%)): 636 (M^-, 100).

2,3,5,6-Tetrakis(2-(pyrazin-2-yl)ethylthio)cyclohexa-2,5-diene-1,4-dione (10): Compound **10** was synthesized from the reaction of **1** (0.5 g, 2.033 mmol) with **3** (1 mL g, 8.1 mmol) according to the general procedure 3.

Brown oil; Yield: 0.5 g (37%); $R_f = 0.21$ (EtOH); Anal. Calcd. for $C_{30}H_{28}N_8O_2S_4$: C, 54.52; H, 4.27; N, 16.96; S, 19.41; Found: C, 54.53; H, 4.15; N, 16.35; S, 20.15; IR (KBr, cm^{-1}): ν = 3069, 3050, 3005 (Ar−H), 2926, 2837 (C−H), 1653 (C=O), 1634 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): δ = 8.4 (m, 12H, CH_{arom}), 3.4 (m, 8H, −CH_2-), 3.1 (m, 8H, S−CH_2) ppm. ^{13}C NMR (125.66 MHz, $CDCl_3$): δ = 33.4, 33.8, 35.1 (CH_2), 124.7 (−C−S), 141.8, 142.7, 143.9, 144.4, 153.7 (N−CH_{arom}), 172.6 ppm (C=O). MS (*m*/*z*, (relative abundance,%)): 661 ($M+H^+$, 100).

2,3,5-Tris(2-(pyrazin-2-yl)ethylthio)-6-cyclohexa-2,5-diene-1,4-dione (11): Compound **11** was synthesized from the reaction of **1** (1 g, 4.066 mmol) with **3** (1.5 mL, 12.2 mmol) according to the general procedure 3.

Brown oil; Yield: 1.36 g (60%); R_f = 0.6 (ethylacetate); Anal. Calcd. for $C_{24}H_{21}ClN_6O_2S_3$: C, 51.74; H, 3.80; N, 15.09; S, 17.27; Found: C, 51.75; H, 3.35; N, 14.55; S, 16.26; IR (KBr, cm^{-1}): ν = 3072, 3037 (Ar−H), 2958, 2923, 2853 (C−H), 1653 (C=O), 1577, 1527 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): δ = 8.4 (m, 9H, CH_{arom}), 3.6, 3.5 (m, 6H, −CH_2-), 3.3, 3.2, 3.1, 3.0 ppm (m, 6H, S−CH_2). ^{13}C NMR (125.66 MHz, $CDCl_3$): δ = 32.1, 33.5, 33.9, 34.9, 35.1 (CH_2), 120.9 (C−Cl), 122.3, 124.4, 126.4 (−C−S), 141.7, 143.1, 143.8, 153.8 (N−*C*H_{arom}), 173.6, 169.6 (C=O) ppm. MS (*m*/*z*, (relative abundance,%)): 556 (M^-, 100).

A mixture of isomer compounds [2-(2-(pyrazin-2-yl)ethylthio)-3-Chloro-5,6-diethoxycyclohexa-2,5-diene-1,4-dione (12a) and 2-(2-(pyrazin-2-yl)ethylthio)-6-chloro-3,5-diethoxycyclohexa-2,5-diene-1,4-dione (12b)]: A mixture of isomer

compounds 12a and 12b was synthesized from the reaction of 1 (1 g, 4.066 mmol) with 3 (1 mL, 8.1 mmol) according to the general procedure 1.

Red oil; Yield: 0.24 g (16%); $R_f = 0.3$ ($CHCl_3$); Anal. Calcd. for $C_{16}H_{17}ClN_2O_4S$: C, 52.13; H, 4.65; N, 7.60; S, 8.69; Found: C, 52.13; H, 5.32; N, 7.95; S, 8.87; IR (KBr, cm^{-1}): $\nu = 3010$ (Ar−H), 2987, 2977, 2939 (C−H), 1682, 1656 (C=O), 1625, 1576 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): $\delta = 8.4$, 8.3 (d, 3H, CH_{arom}), 4.4, 4.3 (m, 4H, −O−CH_2-), 3.4 (m, 2H, −CH_2-), 3.0 (m, 2H, S−CH_2-), 1.3, 1.2 ppm (m, 6H, −CH_3-). ^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 14.8$ (CH_3), 30.4 (S−CH_2), 34.6 (SCH_2−CH_2), 69.0 (O−CH_2), 122.5, 125.0 (C−Cl), 125.7, 128.9 (CO−C−S), 141.7, 143.1, 143.8, 153.8 (N−CH_{arom}, C_{arom}), 155.3 (CO−C−O), 173.9, 174.5, 176.7, 178.0 (C=O) ppm. MS (*m/z*, (relative abundance,%)): 369 ($M+H^+$, 100).

2,5-Bis(2-(pyrazin-2-yl)ethylthio)-3,6-diethoxycyclohexa-2,5-diene-1,4-dione (13): Compound **13** was synthesized from the reaction of **1** (1 g, 4.066 mmol) with **3** (1 mL, 8.1 mmol) according to the general procedure 1.

Brown oil; Yield: 0.07 g (3%); $R_f = 0.7$ (ethylacetate); Anal. Calcd. for $C_{22}H_{24}N_4O_4S_2$: C, 55.91; H, 5.12; N, 11.86; S, 13.57; Found: C, 55.90; H, 5.32; N, 11.68; S, 13.42; IR (KBr, cm^{-1}): $\nu = 3053$, 3034 (Ar−H), 2980, 2932, 2901 (C−H), 1650 (C=O), 1558 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): $\delta = 8.4$, 8.3 (d, 6H, CH_{arom}), 4.3, 4.2 (m, 4H, −O−CH_2-), 3.3, 3.1 (m, 8H, S−CH_2-), 1.3, 1.2 ppm (m, 6H-CH_3-). ^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 14.5$ (−CH_3), 30.4 (S−CH_2), 34.9 (SCH_2−CH_2), 69.3 (O−CH_2), 125.2 (C−S), 141.0, 142.6, 144.0, 153.7 (N−CH_{arom}, C_{arom}), 156.0 (CO−C−O), 177.4 (C=O) ppm. MS (*m/z*, (relative abundance,%)): 473 ($M+H^+$, 100).

2,3,5-Tris(2-(pyrazin-2-yl)ethylthio)-6-ethoxycyclohexa-2,5-diene-1,4-dione (14): Compound **14** was synthesized from the reaction of **1** (1 g, 4.066 mmol) with **3** (1 mL, 8.1 mmol) according to the general procedure 1.

Brown oil; Yield: 0.2 g (8%); $R_f = 0.33$ (Ethylacetate); Anal. Calcd. for $C_{26}H_{26}N_6O_3S_3$: C, 55.10; H, 4.62; N, 14.83; S, 16.97; Found: C, 54.84; H, 5.24; N, 14.47; S, 16.10; IR (KBr, cm^{-1}): $\nu = 3053$ (Ar−H), 2977, 2923 (C−H), 1647 (C=O), 1577 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): $\delta = 8.4$, 8.3 (d, 9H, CH_{arom}), 4.2 (m, 2H, −O−CH_2-), 3.4, 3.4, 3.3, 3.0 (m, 12H, −CH_2-), 1.3 ppm (m, 3H, −CH_3−). ^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 14.5$ (−CH_3), 32.0, (S−CH_2), 34.6 (SCH_2−CH_2), 68.4 (O−CH_2), 129.1 (C−S), 141.4, 142.7, 143.7, 145.3, 153.8 (N−CH_{arom}, C_{arom}), 155.7 (CO−C−O), 173.2, 177.7 (C=O) ppm. MS (*m/z*, (relative abundance,%)): 567 ($M+H^+$, 100).

2-(2-ethylhexyloxy)-3,5,6-Trichlorocyclohexa-2,5-diene-1,4-dione (16): Compound **16** was synthesized from the reaction of **1** (1 g, 4.066 mmol) with **15** (1.27 mL, 8.1 mmol) according to the general procedure 2.

Orange solid; Yield: 0.88 g (63%); M.p.: 82–83°C; $R_f = 0.5$ ($CHCl_3$/petroleum ether 1:2); Anal. Calcd. for $C_{14}H_{17}Cl_3O_5$:C, 49.51; H, 5.05; Found: C, 50.06; H, 6.02; IR (KBr, cm^{-1}): $\nu = 2955$, 2929, 2872 (C−H), 1685, 1660 (C=O), 1615, 1577 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): $\delta = 4.2$ (s, 2H, O−CH_2), 1.6, 1.4, 1.3, 1.2 (m, 9H, −CH_2), 0.8 (m, 6H, −CH_3) ppm; ^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 10.0$, 13.0 (−CH_3), 21.9, 22.4, 27.9, 28.9 (−CH_2-), 39.5 (O−CH_2), 124.4, 137.6, 139.4 (C−Cl), 153.8 (=C−O), 170.8, 171.8 (C=O) ppm; MS (*m/z*, (relative abundance,%)): 338 (M^-, 100).

2,3,5-Trichloro-6-(pyridine-3-yloxy)cyclohexa-2,5-diene-1,4-dione (18): Compound **18** was synthesized from the reaction of **1** (1 g, 4.066 mmol) with **17** (0.77 g, 4.066 mmol) according to the general procedure 2.

Brown solid; Yield: 0.08 g (6%); M.p.: 310–311°C; $R_f = 0.6$ (ethylacetate/petroleum ether 1:1); Anal. Calcd. for $C_{11}H_4Cl_3NO_3$: C, 43.39; H, 1.32; N, 4.60; Found: C, 43.70; H, 2.02; N, 3.87; IR (KBr, cm^{-1}): $\nu = 3059$ (Ar—H) 2923, 2851 (C—H), 1689 (C=O), 1569 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): $\delta = 7.3$ (m, 2H, —CH), 8.38 (dd, $J = 4.8$ Hz, $J =$ 3.4 Hz, 1H, CH—N), 8.32 (d, $J = 2.9$ Hz, 1H, OC—CH); ^{13}C NMR (125.66 MHz, $CDCl_3$): 123.6, 123.8, 130.2 (C—Cl), 137.6, 138.5, 139.9, 144.4, 149.8 (C_{arom}), 151.6 (OC—O), 169.9, 170.27 (C=O) ppm. MS (*m/z*, (relative abundance,%)): 303 (M^-, 100).

2-(1H-1,2,4-triazol-3-ylthio)-3,5,6-Trichlorocyclohexa-2,5-diene-1,4-dione (20): Compound **20** was synthesized from the reaction of **1** (1 g, 4.066 mmol) with **19** (0.82 g, 4.066 mmol) according to the general procedure 2.

Brown solid; Yield: 0.06 g (4%); M.p.: 208–209°C; $R_f = 0.72$ (ethylacetate/petroleum ether 1:1); Anal. Calcd. for $C_8H_2Cl_3N_3O_2S$: C, 30.94; H, 0.65; N, 13.53; S, 10.33; Found: C, 31.02; H, 0.46; N, 13.79; S, 10.37; IR (KBr, cm^{-1}): $\nu = 3043$ (Ar—H) 2920, 2847 (C—H), 1688 (C=O), 1568 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): 8.32 (dd, $J =$ 4.9 Hz, $J = 4.4$ Hz, 1H, NH), 7.3 (m, 1H, CH) ppm.^{13}C NMR (125.66 MHz, $CDCl_3$): 125.1, 139.0(*C*—Cl), 145.8 (N—C—N), 151.2 (SC—N), 152.9 (CO—CS), 170.9, 171.9 ppm (C=O); MS (*m/z*, (relative abundance,%)): 308 (M+, 100).

2,5-bis(4-methyl-oxo-2H-chromen-7-ylthio)-3,6-Dichlorocyclohexa-2,5-diene-1,4-dione (22): Compound **22** was synthesized from the reaction of **1** (1 g, 4.066 mmol) with **21** (0.78 g, 4.06 mmol) according to the general procedure 3.

Red solid; Yield: 0.11 g (10%); $R_f = 0.35$ with $CHCl_3$ as an eluent; Anal. Calcd. for $C_{26}H_{14}Cl_2O_6S_2$: C, 56.02; H, 2.52; S, 11.50; Found C, 56.25; H, 2.22; S; IR (KBr, cm^{-1}): 2960, 2923, 2853 (C—H), 1719 (ester C=O), 1673 (quinone C=O), 1529 (C=C); ^{1}H NMR (499.74 MHz, $CDCl_3$): δ 1.1 (s, 6H, $-CH_3$), 6.1 (s, 1H, CH_{vin}), 7.2–7.6 (m, 6H, H_{arom}); ^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 29.9$ ($-CH_3$), 125.4, 126.0, 141.0, 142.0, 151.5, 152.0, 153.8, 154.2, 160.0, 160.3 (CH_{arom}, C_{arom}, lactone C=O); 171.70 (quinone C=O); MS (*m/z*, (relative abundance,%)): 556 (M^-, 100).

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