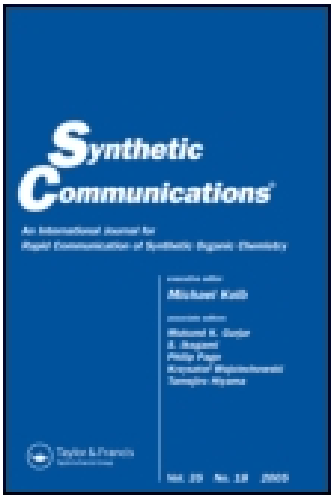

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SYNTHESIS AND CHARACTERIZATION OF NOVEL N-, S-, O-SUBSTITUTED P-CHLORANIL DERIVATIVES

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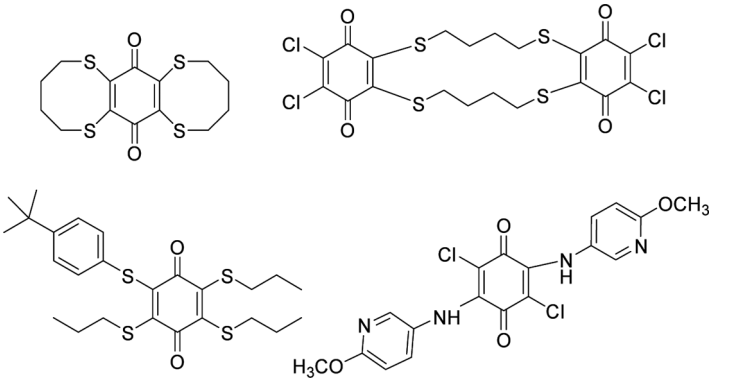
GRAPHICAL ABSTRACT



Abstract *A series of novel N-, S-, and O-substituted p-chloranil derivatives were synthesized from the reactions of* p-*chloranil* (***1***) *and related nucleophiles in sodium carbonate* (Na_2CO_3) *solution of acetonitrile or in chloroform with* Et_3N. *The structures of novel compounds were characterized by using microanalysis, Fourier transform–infrared,* ^1H *NMR,* ^{13}C *NMR, and mass spectrometry.*

Keywords Amine; p-chloranil; piperazine; thiol

INTRODUCTION

Many applications of quinone compounds can be found in synthetic organic chemistry.[1–3] Growing attention has been given to the quinone moiety because of important biologic activity properties such as anticoagulant,[4] antitumor,[5,6] and anticancer[7] activities. Another application area for *p*-chloranil derivatives is acceptors in charge-transfer complexes.[8]

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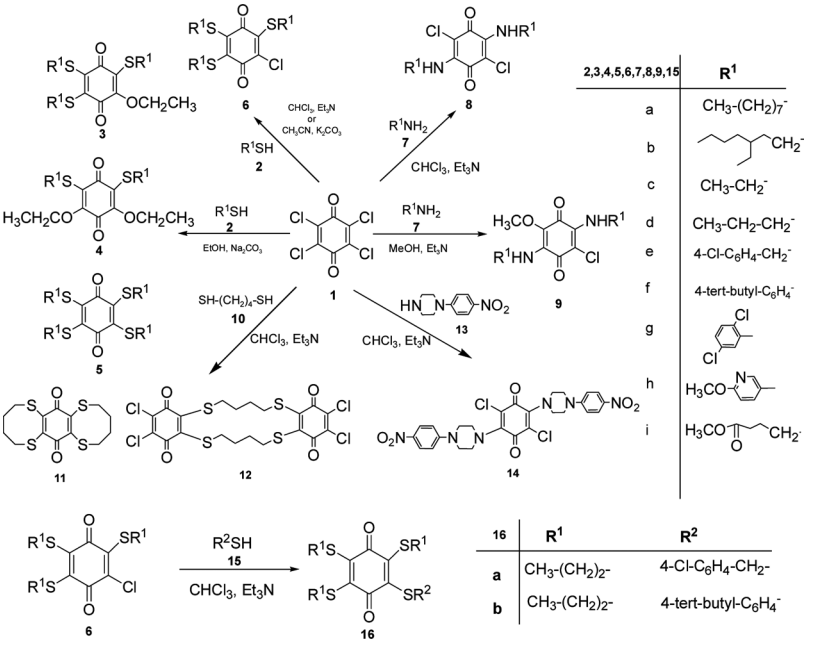
A large number of chemical derivatives with 1,4-naphthoquinone[9,10] and benzoquinone[11] have been synthesized by our group before. As a continuation of the synthesis of interesting cyclic thio(crown)ether structures, herein we report novel intermolecular compounds with diquinone moiety. The aims of this study are the synthesis of the novel benzoquinone compounds and characterization of them with spectral methods.

RESULTS AND DISCUSSION

In the formation of substituted quinone compounds, the nucleophiles containing sulfur or nitrogen atom attack the quinone structure and the addition reaction occurs.[12,13] Bis-, tris-, or tetrakis-substituted quinone adducts can be obtained in forward steps depending on the nucleophile structure.[14]

The novel ethoxy and tris(thio)substituted benzoquinone derivatives **3a** and **3b** were obtained by the reaction of *p*-chloranil **1** and 1-octanethiol (**2a**) and 2-ethylhexanethiol (**2b**) in ethanol with sodium carbonate (Na_2CO_3) at room temperature (Scheme 1). In this reaction ethanol behaved as a nucleophile and attacked the *p*-chloranile to give the addition reaction in the minority thiol nucleophile. These compounds were obtained as dark brown oils. In the ^{13}C NMR spectra of compound **3a** two carbonyl signals were seen at 173.64 and 177.69 as expected. The molecular ion peak of compound **3b** was identified at m/z (%) 585 (100) in the positive ion mode for electrospray ionization (ESI) technique.

Compounds **4e** and **5e** were synthesized by the reaction of p-chloranil (**1**) with 2 molar equivalents of 4-chlorobenzyl mercaptan (**2e**) in ethanol with sodium



Scheme 1. Synthetic pathway of novel substituted chloranile compounds.

carbonate (Na_2CO_3) at room temperature. In the ^{13}C NMR spectra of 2,6-thiosubstituted compound **4e** two carbonyl carbon signals were observed at 173.76 and 177.35 (*C*=O) ppm. The mass spectra of compound **5e** in the negative ion mode of ESI technique confirmed the proposed structure; the deprotonated molecular ion peak was identified at m/z (%) 734 (100).

The tetrakis(thio)-substituted compounds **5f** and **5g** were obtained by the reactions of p-chloranil (**1**) and related thiol nucleophiles **2f** and **2g** as black and orange powders, respectively. The ^{13}C NMR spectra of these compounds gave only one carbonyl signal at 175.33 and 171.8 ppm because of the symmetric structure of the quinone moiety. See Scheme 1.

The tris(thio)substituted novel benzoquinone derivatives **6b, 6c,** and **6d** were achieved by the reactions of *p*-chloranil **1** and different molar equivalent related thiols **2b, 2c,** and **2d** at room temperature. The infrared (IR) spectra of compound **6b** showed characteristic aliphatic bands (-CH) at 2959, 2928, 2872, and 2858 cm^{-1} and a carbonyl band (C=O) at 1671 cm^{-1}. The ^{13}C NMR spectra of compound **6c** gave carbonyl signals at 170.24 and 174.25 ppm. The molecular ion peak of compound **6d** was identified at m/z 364 in the negative ion mode for ESI technique.

The 2,5 N,N-substituted benzoquinone derivative **8h** was synthesized by the reaction of *p*-chloranil **1** and 5-amino-2-methoxypiridine (**7h**) in chloroform with triethylamine at room temperature. The IR spectra of compound **8h** showed characteristic amine band (-NH) at 3291 cm^{-1}. The reaction of *p*-chloranil **1** and B-alanine methyl ester hydrochloride (**7i**) in methanol with triethylamine at rt gave compound **9i**. The solvent methanol behaved as a nucleophile. The mass spectra of compound **9i** in the negative ion mode of ESI technique confirmed the proposed structure; the deprotonated molecular ion peak was identified at m/z (%) 377 (100).

The reactions of *p*-chloranil **1** with different molar equivalents of 1,4-butanedithiol (**10**) in chloroform with triethylamine at rt gave novel and interesting cyclic colored thio(crown)ethers **11** and **12**. The interesting cyclic compounds were obtained as thermodynamic products.[15] The ^{13}C NMR spectra of compound **11** and **12** gave only one carbonyl signal at 177.29 and 178.10 because of the symmetric structures. The mass spectra of compound **12** in the negative ion mode of ESI technique confirmed the proposed structure; the deprotonated molecular ion peak was identified at m/z (%) 589 (100).

The novel piperazine substituted benzoquinone derivative **14** was synthesized by the reaction of *p*-chloranil **1** and 1-(4-nitrophenyl)piperazine (**13**) in chloroform with triethylamine at rt. The ^{13}C NMR spectra of compound **14** gave carbonyl signals at 176.10 and 177.32 ppm.

The tetrakis(thio)-substituted benzoquinone derivatives **16a** and **16b** were syntesized by the substitution of thiol compound with one chlorine atom in tris(thio)-substituted compounds. The compound **16a** was obtained by the reaction of compound **6c** and 4-chlorobenzylmercaptan (**15e**) in chloroform with triethylamine at rt. The compound **16b** was obtained by the reaction of compound **6c** and 4-*tert*-butylthiophenol (**15f**) in chloroform with triethylamine at rt. The mass spectra of compounds **16a** and **16b** in the positive ion mode of ESI technique confirmed the proposed structure; the protonated molecular ion peaks were identified at m/z (%) 488 (100) and m/z (%) 495 (100), respectively.

EXPERIMENTAL

Synthesis of Cyclic (Thio)crown Ether Compound (12)

Compound **12** was synthesized by the reaction of **1** (p-chloranil (**1**) (0.5 g, 2.034 mmol) with 1,4-butanedithiol (**10**) (0.250 g, 2.045 mmol) in chloroform as solvent (40 mL). Triethylamine (1 mL) was added to the reaction mixture slowly. 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 thin-layer chromatography (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.

10,11,22,23-Tetra-chloro-2,7,14,19-tetra-tia-tricyclo[18,4,0,$0^{8,13}$]-tetra-kosa-1(20),8(13),10,22-tetra-en-9,12,21,24-tetraone (12)

Brown solid; mp: 128–129 °C; yield: 0.069 g (6%); R_f: 0.42 [$CHCl_3$]. IR (KBr): $\nu = 2959.25$, 2928.02, 2858.68 (C-H), 1655.63 (C=O), 1540.43 (C=C). ^{1}H NMR (499.74 MHz, $CDCl_3$): $\delta = 2.89$, 2.91, 2.95, 2.97 (m, $J = 7.32$ Hz, 4H, -S-C**H$_2$**), 1.89, 1.93, 1.97 (m, 4H, -S-CH_2- C**H$_2$**), 1.40 1.42, 1.43, 1.45 (m, $J = 6.83$ Hz, 4H -S-CH_2- CH_2- C**H$_2$**). ^{13}C NMR (125.66 MHz, $CDCl_3$): $\delta = 28.34$, 28.67, 29.04, 29.63 (*S*-***C**H$_2$*- ***C**H$_2$*-***C**H$_2$*-***C**H$_2$*-*S*-), 124.2 (=*C*-Cl), 153.1 (=*C*-S), 178.1 ppm (*C*=O); MS (-ESI): m/z 589 (M); $C_{20}H_{16}Cl_4O_4S_4$ (M = 590.41 g/mol). Calcd.: C, 40.69; H, 2.73; S, 21.72. Found: C, 40.50; H, 2.93; S, 24.32.

CONCLUSION

Novel substituted p-chloranil compounds were synthesized from the reactions of *p*-chloranil (**1**) and related nucleophilles in different reaction media. The structures of novel compounds were characterized by using microanalysis, FT-IR, ^{1}H NMR, ^{13}C NMR, and MS.

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SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher's website.

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