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Synthesis and cyclization reactions of novel benzo[a]phenazine- and phenoxazine-5-ones derivatives

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In the present study we reported the cyclization reactions of 2-(alkylthio)-1,4-naphthoquinones to 6-(alkylthio)benzo[a]phenazine- and phenoxazin-5-ones derivatives **5a-c** and **7b-c**, respectively and their structural studies. The reactions of 2-(alkylthio)-3-chloro-1,4-naphthoquinone **3a-c** with phenyl-1,2-diamine **4** and 2-aminophenol **6** in ethanol in the presence of sodium carbonate (Na_2CO_3) were investigated. All new compounds were characterized on the basis of nuclear magnetic resonance spectroscopy (^{1}H- and ^{13}C-NMR), mass spectrometry (MS), and fourier transform infrared spectroscopy (FT-IR). A probable mechanism for the formation of all reaction products was presented and detailed spectroscopic data of all compounds were given.

Keywords Phenazine; Phenoxazine; Phenyl-1,2-diamine; 2-Aminophenol; Quinones

INTRODUCTION

Quinone imines are useful for medicine, dyestuffs and others in the wide of industries. Some phenoxazone and phenothiazone derivatives containing stable quinone imine systems have been synthesized to study the biological and pharmaceutical activities, e.g. antitumor activities, and to obtain the useful pigments [1-3]. Quinones are well known in biological systems as reactive centers of transporting both electrons and protons across biological membranes. The evaluation of the redox chemistry and electrochemical properties of quinones are a useful way for identifying their biological evolutions. Most of the reported methods for the synthesis of phenoxazones [4-6] from quinones and o-aminophenols involve the initial attack of the amino group of the o-aminophenol on the quinone substituent (OH, OCH_3, Cl, etc.) and subsequent ring closure. An *o*-aminophenol exchange reaction or a rearrangement leads finally to the phenoxazone system.

In this work, we synthesized novel 6-(alkylthio) benzo[a]phenazine-5(7H)-ones (compounds **5a-c**) and 6-(alkylthio)-5H-benzo[a]phenoxazine-5-ones (compounds **7b-c**) by the condensation of phenyl-1,2-diamine **4** or 2-aminophenol **6** with 2-(alkylthio)-3-chloro-1,4-naphthoquinone compounds (**3a-c**). The condensations between **3a-c** and **4** or **6** were carried out in ethanol in the presence of sodium carbonate (Na_2CO_3). The conversion of the substituents of the resulting products, the reduction and the dehalogenation were carried out. Their structures were characterizated by using micro analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR, MS spectroscopy.

EXPERIMENTAL

Reagents and apparatus

Micro analyses were performed on a Thermo Finnigan Flash EA 1112 Elemental analyser. Infrared (FT-IR) spectra were recorded in KBr pellets in Nujol mulls on a Perkin Elmer Precisely Spectrum One FTIR spectrometry. ^{1}H- and ^{13}C NMR spectra were recorded on VarianUNITYINOVA operating at 500 MHz. Chemical shifts δ (ppm) were reported relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard. ^{1}H- and ^{13}C NMR spectra in $CDCl_3$ refer to the solvent signal center at $\delta = 7.26$ and $\delta = 77.0$ ppm, respectively. Mass spectra were obtained on a Thermo Finnigan LCQ Advantage MAX LC/MS/MS spectrometer using an ESI probe. Products were isolated by column chromatography on Silica gel (Fluka Silica gel 60, particle size 63-200 μm). Melting points were measured on a Buchi B-540 melting point apparatus.

Analytical thin layer chromatography (TLC) was purchased from Merck KGaA (silica gel 60 F254) based on Merck DC-plates (aluminum based). Visualization of the chromatogram was performed by UV light (254 nm). Moisture was excluded from the glass apparatus using $CaCl_2$ drying tubes.

Solvents, unless otherwise specified, were of reagent grade and distilled once prior to use, and all

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other chemicals (reagent grade) were used without further purification.

General procedure for the synthesis 2-(alkylthio)-3-chloro-1,4-naphthoquinone compounds as a starting material ***(3a-c)***

2-(Ethylthio)-3-chloro-1,4-naphthoquinone (**3a**) [7], 2-(hexadecylthio)-3-chloro-1,4-naphtoquinone (**3b**) [8] and 2-(octadecylthio)-3-chloro-1,4-naphthoquinone (**3c**) [9] were synthesized from the reactions of compound **1** with **2a-c** for using as a starting material according to the literatures [7-9]

General procedure for the synthesis of new phenazine and phenoxazine compounds ***(5a-c** and **7b-c)***

Sodium carbonate was dissolved in ethanol (50 mL), and equimolar amounts of 2-(alkylthio)-3-chloro-1,4-naphthoquinone (**3a-c**) and nucleophilies (**4** and **6**) were added slowly. The mixture was heated at 40°C and stirred in a single reaction vessel for 18 h. The color of the solution quickly changed (from yellow to red color), 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.

6-(Ethylthio)-benzo[a]phenazine-5(7H)-one ***(5a)***

Compound **5a** was synthesized from reaction of 2-(ethylthio)-3-chloro-1,4-naphthoquinone **(3a)** (0.5 g, 1.978 mmol) with phenyl-1,2-diamine **4** (0.213 g, 1.978 mmol) according to the general procedure.

Orange solid. Yield: 18.4% (0.111 g). m.p.: 86.1-88.5°C. R_f [PET/$CHCl_3$(3:1)]: 0.52. FT-IR (KBr): υ (cm^{-1})= 2925-2853 (C-H_{aliph}), 3018 (C-H_{arom}), 1600 (C=N), 1588 (C=O), 1522 (C=C), 3295 (N-H). ^{1}H-NMR (499.74 MHz, $CDCl_3$): δ = 0.79-0.83 (t, 3H, *J*= 6.81 Hz, C***H***$_3$), 2.97-3.04 (q, 2H, *J*= 7.32 Hz, S-C***H***$_2$), 2.87 (bs, H, -N***H***), 7.00-7.07, 7.18-7.21 (m, 2H, C***H***$_{arom}$), 7.46-7.48, 7.27-7.29 (m, 2H, C***H***$_{arom}$), 7.73-7.78 (m, 2H, C***H***$_{naph}$), 8.29-8.33 ppm (m, 2H, C***H***$_{naph}$). ^{13}C-NMR (125.66 MHz, $CDCl_3$): δ = 13.5 (-***C***H$_3$), 28.8 (S***C***H$_2$-), 118.6 (S-***C***$_{naph}$), 141.6 (NH-***C***$_{naph}$), 131.3, 131.4, 131.9, 132.5 (***C***H$_{naph}$), 134.0, 135.1 (***C***$_{naph}$), 118.7, 127.9, 128.1, 129.3 (***C***H$_{arom}$), 135.2 (N-***C***$_{arom}$), 142.0 (NH-***C***$_{arom}$), 178.5 (***C***=O), 142.1 (***C***=N). MS [+ESI]: m/z = 307.1 $[M+H]^+$, Micro analysis: $C_{18}H_{14}N_2OS$, (M_A= 306.38 g/mol). Calculated: C, 70.56; H, 4.61; N, 9.14; S, 10.46% Found: C, 70.83; H, 4.92; N, 9.17; S, 10.45%.

6-(Hexadecylthio)benzo[a]phenazine-5(7H)-one ***(5b)***

Compound **5b** was synthesized from reaction of 2-(hexadecylthio)-3-chloro-1,4-naphtoquinone **(3b)** (0.2 g, 0.445 mmol) with phenyl-1,2-diamine **4** (0.048 g, 0.445 mmol) according to the general procedure.

Red solid. Yield: 10.4% (0.023 g). m.p.: 112.1-113.9°C. R_f [PET/$CHCl_3$(5:2)]: 0.60. FT-IR (KBr): υ (cm^{-1})= 2926-2854 (C-H_{aliph}), 3019 (C-H_{arom}), 1601 (C=N), 1590 (C=O), 1525 (C=C), 3335 (N-H). ^{1}H-NMR (499.74 MHz, $CDCl_3$): δ = 0.78-0.82 (t, 3H, *J*= 7.11 Hz, C***H***$_3$), 1.11-1.54 (m, 28H, C***H***$_2$), 2.97-3.00 (t, 2H, *J*= 7.31 Hz, S-C***H***$_2$), 2.84 ppm (bs, H, -N***H***), 7.74-7.84 (m, 2H, C***H***$_{arom}$), 8.23-8.28 (m, 2H, C***H***$_{arom}$), 8.30-8.36 (m, 2H, C***H***$_{naph}$), 9.32-9.34 ppm (m, 2H, C***H***$_{naph}$). ^{13}C-NMR (125.66 MHz, $CDCl_3$): δ = 14.1 (-***C***H$_3$), 22.7- 31.9 (-***C***H$_2$-), 35.2 (S***C***H$_2$-), 123.8 (S-***C***$_{naph}$), 142.7 (NH-***C***$_{naph}$), 129.2, 129.5, 129.9, (***C***H$_{naph}$), 130.0, 131.8 (***C***$_{naph}$), 123.9, 125.5, 128.8, 129.3 (***C***H$_{arom}$), 140.0 (N-***C***$_{arom}$), 144.0 (NH-***C***$_{arom}$), 174.4, (***C***=O), 140.1 (***C***=N). MS [+ESI]: m/z = 503.5 $[M+H]^+$, Micro analysis: $C_{32}H_{42}N_2OS$, (M_A= 502.75 g/mol). Calculated: C, 76.45; H, 8.42; N, 5,57; S, 6.38%; Found: C, 76.63; H, 9.01; N, 5,62; S, 6.35%.

6-(Octadecylthio)benzo[a]phenazine-5(7H)-one ***(5c)***

Compound **5c** was synthesized from reaction of 2-(octadecylthio)-3-chloro-1,4-naphthoquinone (**3c**) (0.4 g, 0.838 mmol) with phenyl-1,2-diamine **4** (0.090 g, 0.838 mmol) according to the general procedure.

Dark orange solid. Yield: 9.3 (0.041 g)%. m.p.: 117.6-118.4°C. R_f [PET/$CHCl_3$(5:2)]: 0.58. FT-IR (KBr): υ (cm^{-1})= 2920-2850 (C-H_{aliph}), 2957 (C-H_{arom}), 1649 (C=N), 1727 (C=O), 1591 (C=C), 3355 (N-H). ^{1}H-NMR (499.74 MHz, $CDCl_3$): δ = 0.81-0.84 (t, 3H, *J*= 7.46 Hz, C***H***$_3$), 1.13-1.61 (m, 32H, C***H***$_2$), 3.21 ppm (bs, H, -N***H***), 3.37-3.42 (t, 2H, *J*= 7.32 Hz, S-C***H***$_2$), 7.82-7.87 (m, 2H, C***H***$_{arom}$), 7.87-7.91 (m, 2H, C***H***$_{arom}$), 8.30-8.35 (m, 2H, C***H***$_{naph}$), 9.28-9.32 ppm (m, 2H, C***H***$_{naph}$). ^{13}C-NMR (125.66 MHz, $CDCl_3$): δ = 14.1 (-***C***H$_3$), 22.8-31.9 (-***C***H$_2$-), 38.7 (S***C***H$_2$-), 125.7 (S-***C***$_{naph}$), 143.1 (NH-***C***$_{naph}$), 129.5, 130.5, 130.7, 130.9 (***C***H$_{naph}$), 131.5, 132.5 (***C***$_{naph}$), 123.2, 125.9, 128.8, 129.8 (***C***H$_{arom}$), 141.6 (N-***C***$_{arom}$), 144.8 (NH-***C***$_{arom}$), 167.8 (***C***=O), 141.9 (***C***=N). MS [+ESI]: m/z = 553.3 $[M+Na]^+$, Micro analysis: $C_{34}H_{46}N_2OS$, (M_A= 530.33 g/mol). Calculated: C, 76.93; H, 8.74; N, 5,28; S, 6.04%, Found: C, 77.05; H, 8.99; N, 5,33; S, 6.01%.

6-(Hexadecylthio)-5H-benzo[a]phenoxazine-5-one ***(7b)***

Compound **7b** was synthesized from reaction of 2-(hexadecylthio)-3-chloro-1,4-naphthoquinone (**3b)** (0.4 g, 0.890 mmol) with aminophenol **6** (0.097 g, 0.890 mmol) according to the general procedure.

Red solid. Yield: 13.7% (0.061 g). m.p.: 80.6-81.9°C. R_f [PET/$CHCl_3$)(3:1)]: 0.61. FT-IR (KBr): υ (cm^{-1})= 2924-2852 (C-H_{aliph}), 3018 (C-H_{arom}), 1595 (C=N), 1633 (C=O), 1542 (C=C). ^{1}H-NMR (499.74 MHz, $CDCl_3$): δ = 0.89-0.91 (t, 3H, *J*= 7.09 Hz, C***H***$_3$), 1.21-1.68 (m, 28H, C***H***$_2$), 3.12-3.17 (t, 2H, *J*= 7.48 Hz, S-C***H***$_2$), 7.38-7.47 (m, 2H, C***H***$_{arom}$), 7.52-7.84 (m, 2H, C***H***$_{arom}$), 7.71-7.81 (m, 2H, C***H***$_{naph}$), 8.35-8.75 ppm (m, 2H, C***H***$_{naph}$). ^{13}C-NMR (125.66 MHz, $CDCl_3$): δ = 14.1 (-***C***H$_3$), 22.7-32.0 (-***C***H$_2$-), 33.4 (S***C***H$_2$-), 117.2 (S-***C***$_{naph}$), 146.5 (O-***C***$_{naph}$), 128.7, 129.6, 131.1, 131.8 (***C***H$_{naph}$), 132.1, 132.4 (***C***$_{naph}$), 115.9, 124.3, 125.7,127.0 (***C***H$_{arom}$), 133.0 (N-***C***$_{arom}$), 150.2, (O-***C***$_{arom}$), 183.0 (***C***=O), 144.0 (***C***=N). MS [+ESI]: m/z = 504.84 $[M+H]^+$, Micro analysis: $C_{32}H_{41}NO_2S$, (M_A= 503.74 g/mol). Calculated: C, 76.30; H, 8.20; N, 2.78; S, 6.37% Found: C, 76.72; H, 8.77; N, 2.84; S, 6.30%.

6-(Octadecylthio)-5H-benzo[a]phenoxazine-5-one ***(7c)***

Compound **7c** was synthesized from reaction of 2-(octadecylthio)-3-chloro-1,4-naphthoquinone **(3c)** (0.4 g, 0.838 mmol) with aminophenol **6** (0.091 g, 0.838 mmol) according to the general procedure.

Red solid. Yield: 11.9% (0.053 g). m.p.: 88-89°C. R_f [PET/$CHCl_3$(3:1)]: 0.62. FT-IR (KBr): υ (cm^{-1})= 2918-2849 (C-H_{aliph}), 3019 (C-H_{arom}), 1596 (C=N), 1628 (C=O), 1541 (C=C). ^{1}H-NMR (499.74 MHz, $CDCl_3$): δ = 0.87-0.91 (t, 3H, *J*= 7.09 Hz, C***H***$_3$), 1.21-1.68 (m, 32H, C***H***$_2$), 3.12-3.17 (t, 2H, *J*= 7.39 Hz, S-C***H***$_2$), 7.38-7.48 (m, 2H, C***H***$_{arom}$), 7.52-7.89 (m, 2H, C***H***$_{arom}$), 7.73-7.82 (m, 2H, C***H***$_{nafta}$), 8.35-8.75 ppm (m, 2H, C***H***$_{naph}$). ^{13}C-NMR (125.66 MHz, $CDCl_3$): δ = 14.1 (-***C***H$_3$), 22.7-32.0 (-***C***H$_2$-), 33.4 (S***C***H$_2$-), 116.1 (S-***C***$_{naph}$), 146.3 (O-***C***$_{naph}$), 129.6, 131.0, 131.5, 131.9, (***C***H$_{naph}$), 132.1, 132.2 (***C***$_{naph}$), 115.9, 124.7, 125.5, 126.5 (***C***H$_{arom}$), 132.8 (N-***C***$_{arom}$), 150,4 (O-***C***$_{arom}$), 181.2 (***C***=O), 144.4 ppm (***C***=N). MS [+ESI]: m/z = 532.5 $[M+H]^+$, Micro analysis: $C_{34}H_{45}NO_2S$, (M_A= 531.79 g/mol). Calculated: C, 76.79; H, 8.53; N, 2.63; S, 6.03% Found: C, 76.95; H, 8.84; N, 2.66; S, 5.98%.

RESULTS AND DISCUSSION

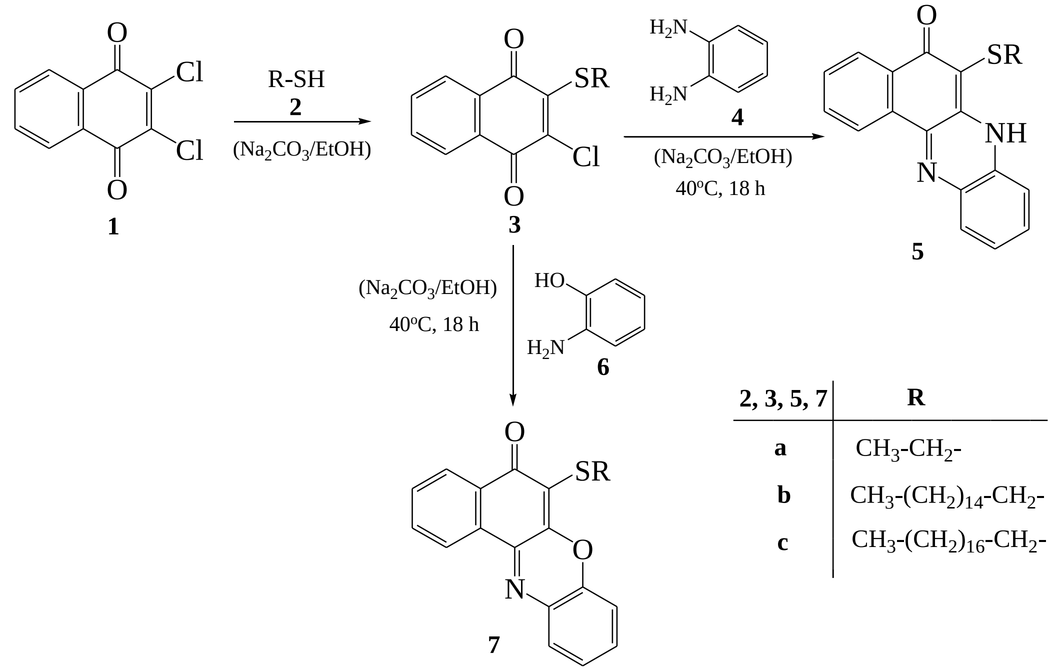
The aim of this work, the novel 6-(alkylthio) benzo[a]phenazine-5(7H)-ones (compounds **5a-c**) and 6-(alkylthio)-5H-benzo[a]phenoxazine-5-ones (compounds **7b-c**) were synthesized by the condensation reactions of phenyl-1,2-diamine **4** or 2-aminophenol **6** with 2-(alkylthio)-3-chloro-1,4-naphthoquinone compounds (**3a-c**), respectively. As shown in Scheme 1, the condensations between **3a-c** and **4** or **6** were carried out in ethanol in the presence of sodium carbonate (Na_2CO_3) at 40°C about 18 h.

The known compounds 2-(ethylthio)-3-chloro-1,4-naphthoquinone **(3a)**, 2-(hexadecylthio)-3-chloro-1,4-naphthoquinone (**3b)** and 2-(octadecylthio)-3-chloro-1,4-naphthoquinone **(3c)** were synthesized according to releated literatures [7-9]. These compounds were used for starting materials. All these new compounds were separated and purified by column chromatography and structures were established by micro analysis, FT-IR, ^{1}H- and ^{13}C-NMR, and mass spectra, chemical reactions, or comparison with authentic samples.

We assume that the reactions of **3a-c** and **4** or **6** in ethanol in the presence of sodium carbonate start with nucleophilic attack of the amino group of **4** or **6** on the halogen atom of **3a-c** with the elimination of hydrogen chloride to give B and D in schemes 2 and 3, respectively. In the formations of B and D, addition of the amino or hydroxyl group to the quinone carbonyl group in equilibrium reaction lead to the formation of the hemiketal, is etherified to the ketal. In addition to this, the open forms (B, D) and a hemiketal/ketal of B and D could not be isolated.

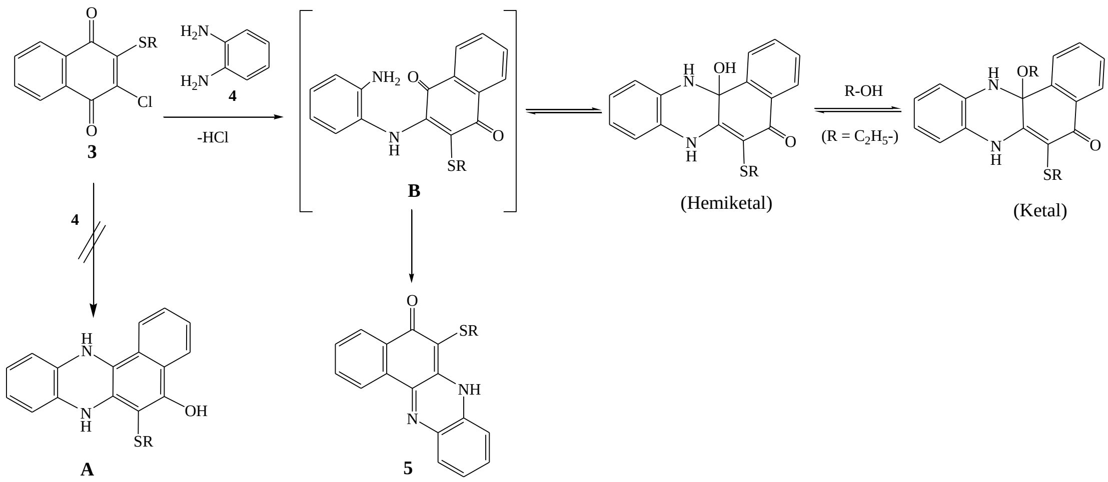
The formation of A and C in from the reactions of **3a-c** with **4** or **6** did not obtain reasonable because amino- and hydroxy-phenazines and phenoxazines were highly unstable [10]. These proposed mechanims in schemes 2 and 3 were agree well with the mechanism of the synthesis of similiar compounds [5].

The ^{1}H spectrum of the products in $CDCl_3$ displayed distinct signals with appropriate multiplets. ^{1}H NMR signal of the hydrogen atoms of the adjacent to the nitrogen atom (-NH) in compounds **5a-c** were shifted to a higher field and displayed singlet at 2.87, 2.84 and 3.21 ppm as single broad, respectively. The ^{13}C NMR spectra of compounds **5a-c** and **7b-c** gave just one carbonyl signals (C=O) at 178.5, 174.4 167.8, 183.0 and 181.2 ppm, respectively, in the naphthoquinone units of **5a-c** and **7b-c**. The carbonyl signals (C=O) in ^{13}C-NMR spectra of **5a-c** and **7b-c** are in close agreement with the spectral characteristic of analogous heterocycles [11-14]. In the ^{13}C-NMR spectra of compounds **5a-c** and **7b-c** carbon signals of (C=N) group appeared around at 144 ppm.

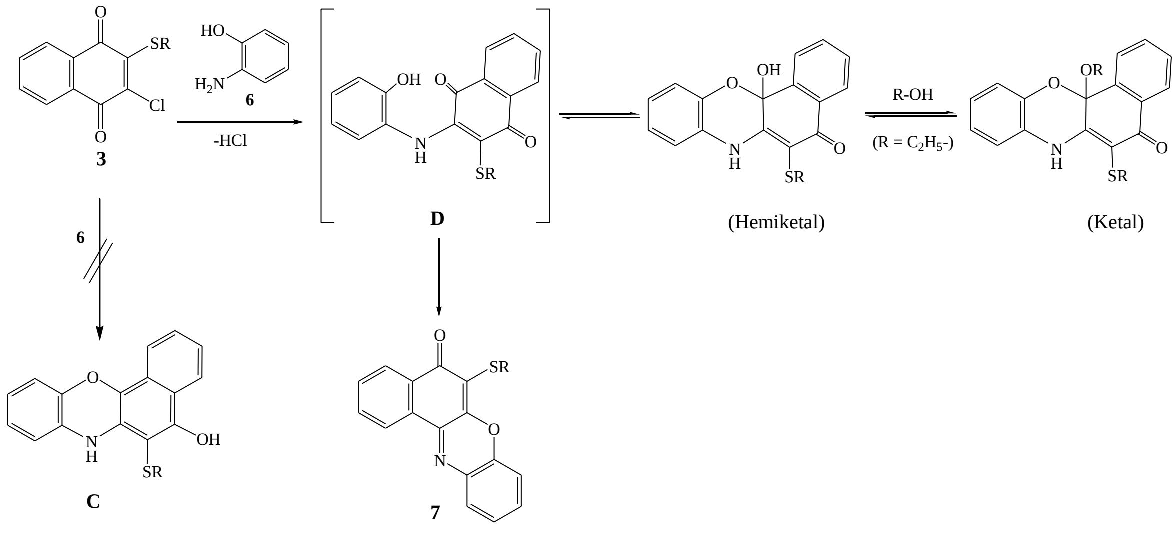


2, 3, 5, 7	R
a	CH_3-CH_2-
b	CH_3-$(CH_2)_{14}$-CH_2-
c	CH_3-$(CH_2)_{16}$-CH_2-

Scheme 1. The synthesis of phenazines and phenoxazines derivatives (**5a-c**, **7b-c**)



Scheme 2. Proposed mechanism of the synthesis of phenazine compounds (**5a-c**)



Scheme 3. Proposed mechanism of the synthesis of phenoxazine compounds (**7b-c**)

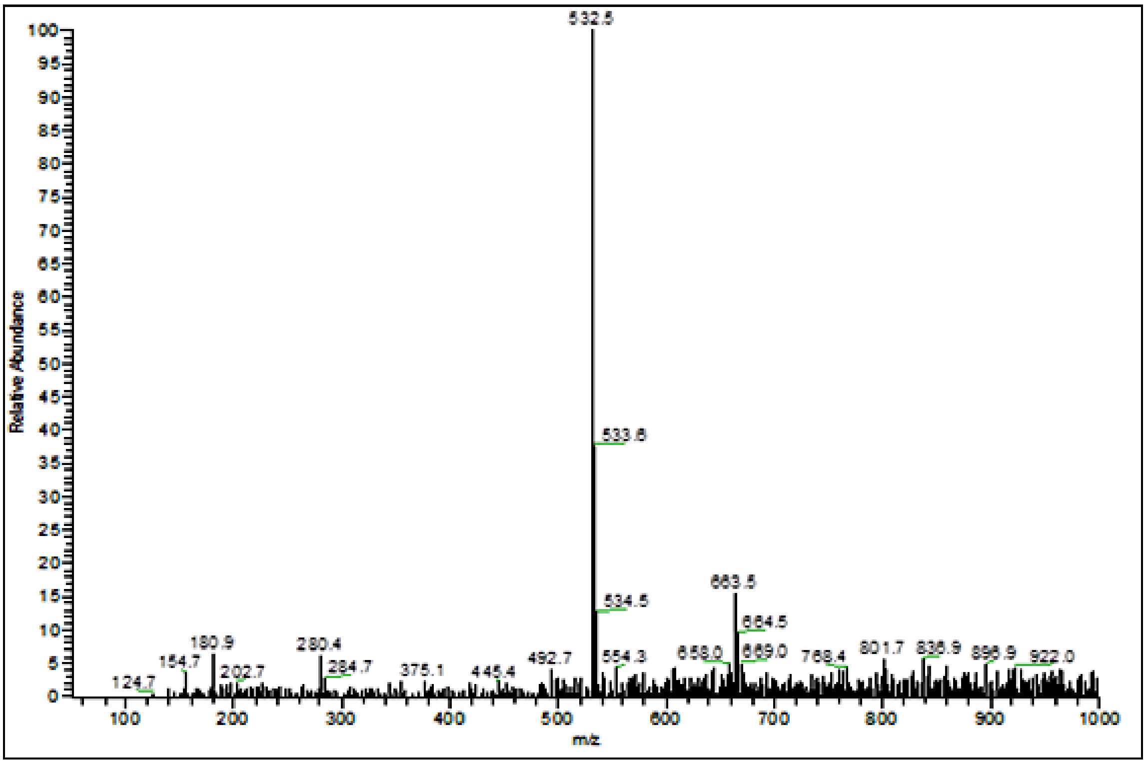


Fig. 1. The MS[+ESI] spectra of compound **7c**

The FT-IR spectra of compound **5a-c**, the characteristic (–NH) band appeared at 3295, 3335 and 3355 cm^{-1}, respectively. In the FT-IR spectrum of **7b-c** the characteristic (–OH) band disappeared, it is proved that intramolecular cyclization reactions had taken place, yielding the compounds **7b-c**. In the FT-IR spectra of compounds **5a-c** and **7b-c** typical strong quinonic carbonyl absorptions were observed at 1588, 1590, 1727, 1663 and 1628 cm^{-1}, respectively. The characteristic imine group (C=N) band of compounds **5a-c** and **7b-c** appeared at 1600, 1601, 1649, 1595 and 1596 cm^{-1}, respectively.

With the aid of the positive ion mode of electron spray ionization (ESI) mass spectrum of the compounds **5a-c**, the respective molecular ion peaks were observed at m/z (%) 307 (100) $[M+H]^+$, 503 (100) $[M+H]^+$, 553 (100) $[M+Na]^+$, respectively. The major fragment of compound **7c** in the MS [+ESI] spectrum was observed at m/z (%) 532 $[M+H]^+$.

CONCLUSION

In continuation of our investigations of quinone [11-16] chemistry, we have studied the reactions of naphthoquinones with phenyl-1,2-diamine **4** and 2-aminophenol **6**. The aim of this study was to the investigation of the cyclization reactions of 2-(alkylthio)-3-chloro-1,4-naphthoquinones **3a-c** with nitrogen- and oxygen-containing nucleophiles (**4**, **6**) and obtain to highly functionalized heterocyclic new compounds (**5a-c**, **7b-c**). The condensations between **3a-c** and compounds **4** or **6** were carried out in ethanol in the presence of sodium carbonate (Na_2CO_3). These reactions of **3a-c** and **4** or **6** proceeded at 40°C. A probable mechanisms for the formation of all reaction products was presented and detailed spectroscopic data of all compounds were given. All synthesized new compounds **5a-c** and **7b-c** were purified by the column chromatography. Their structures of new synthesized compounds were determined by micro analysis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and MS.

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REFERENCES

1. N. L. Agarwal, W. Schafer, *J. Org. Chem*., **45**, 5144 (1980).
2. A. Butenandt, U. Schiedt, E. Biekert, R. J. T. Cromartie, *Ann. Chem*., **75**, 590, (1954).
3. W. Schafer, I. Geyer, H. Schlude, *Tetrahedron*, **28**, 3811 (1972).
4. N. L. Agarwal, R. L. Mital, Z. *Naturforsch. B*., **31**, 106 (1976).

5. N. L. Agarwal, W. Schafer, *J. Org. Chem.*, **45 (11)**, 2155 (1980).
6. H. Hayakawa, S. Nanya, T. Yamamato, *J. Heterocyclic Chem.*, 1737 (1986).
7. L. F. Fieser, R. H. Brown, *J. Am. Chem. Soc*., **71**, 3609 (1949).
8. C. Sayil, C. Ibis, *Russian J. Org. Chem*., **46(10)**, 209 (2010).
9. C. Sayil, C. Ibis, *Bull. Korean Chem. Soc*., **31(5)**, 1233 (2010).
10. W. Schafer, *Prog. Org. Chem*., **6**, 135 (1964).
11. C. Ibis, N. G. Deniz, *J. Chem. Sci*., **124(3)**, 657 (2012).
12. C. Sayil, S. Kurban, C. Ibis, *Phosphorus Sulfur and Silicon.*, **188**, 1855 **(**2013).
13. N. G. Deniz, M. Ozyurek, A. N. Tufan, M. R. Apak, *Monatsh. Chem*., **146**, 2117 (2015)
14. C. Ibis, N. G. Deniz, *Phosphorus Sulfur and Silicon.,***185**, 2324 (2010).
15. N. G. Deniz, C. Ibis, Z. Gokmen, M Stasevych, V. Novikov, O. Komarovska-Porokhnyavets, M. Ozyurek, K. Guclu, D. Karakas, E. Ulukaya, *Chem. Pharm. Bull.*, **63(12)**, 1029 (2015)
16. C. Ibis, M. Yildiz, C. Sayil, *Bull. Korean Chem. Soc.*, 30(10), 2381 (2009).