INTRODUCTION
Phenothiazine derivatives exhibit interesting chemical properties and pharmaceutical activities.\textsuperscript{1} Many phenothiazine derivatives with the substituent attached to the thiazine nitrogen have been used as neuroleptic and antihistaminic drugs.\textsuperscript{2,3} In our earlier reports we described a two-step synthesis of 5-alkyl-12\textit{H}-quino[3,4-\textit{b}][1,4]benzothiazinium chloride\textsuperscript{4,5} from thioquanantrenediinium bis-salts\textsuperscript{6} via 1-alkyl-4-(phenylamino)quinolinium 3-thiolates (2) (Scheme 1). This reaction is a new method of synthesis of the 1,4-thiazine systems. Adaptation of the described procedure to obtain the 3-thiolates 4 and 12-substituted quino[3,4-\textit{b}][1,4]benzothiazine derivatives (5) in the reaction of thioquanantrenediinium bis-salts (1) with secondary amines was unsuccessful (Scheme 1).
The present study was aimed at using of 1-alkyl-4-(phenylamino)quinolinium 3-thiolates (2) as a source of 1-alkyl-4-(N-alkyl-N-phenylamino)quinolinium 3-thiolates (4). Cyclization of the 3-thiolates (4) could possibly lead to the expected 12-substituted quino[3,4-b][1,4]benzothiazine derivatives (5).

**RESULTS AND DISCUSSION**

The thiolate function in 1-alkyl-4-aminoquinolinium 3-thiolates can be protected as a thioester, from which it is regenerated by aminolysis reaction. The reactions of 1-alkyl-4-(phenylamino)quinolinium 3-thiolates (2) with benzoyl chloride (Scheme 2) occur easily as S-acylation and led to 1-methyl-3-benzoylthio-4-(phenylamino)quinolinium chlorides (6). The structure of compounds 6 was confirmed by $^1$H and $^{15}$N NMR spectra. In $^1$H NMR spectra of compounds (6a-b) in CDCl$_3$ solution, the signal of NH amine proton occurs in a typical range at $\delta = 11.80$ and 11.97 ppm. The $^{15}$N NMR spectrum of the compound (6a) in DMSO-$d_6$ revealed two resonances at $\delta_N = -220.3$ and $-254.4$. They were assigned with the help of the $^1$H–$^{15}$N HSQC and HMBC spectra. In the case of the quinoline endocyclic nitrogen atom ($\delta_N = -220.3$), a three-bond correlation with the H8 proton ($\delta_H = 8.24-8.29$) and a two-bond...
correlation with the H2 proton ($\delta_H = 9.12$) were observed. A one-bond correlation between the exocyclic nitrogen atom ($\delta_N = -254.4$) and the NH proton ($\delta_H = 11.52$, $^1J_{N-H} = 92$ Hz) was also detected. These results provided the evidence for NH group being present at the 4-position in the quinoline ring.⁸

Scheme 2

The reaction of salt 6 with aniline occurs via nucleophilic attack of the amine nitrogen atom on the carboxylic carbon atom and results in restitution of the thiolate function at the 3-position in the quinoline ring.
Table 1. Preparation of 1-alkyl-4-(phenylamino)quinolinium 3-thiolates (2) from 1-alkyl-3-benzoylthio-4-(phenylamino)quinolinium chloride (6).

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>6a</td>
<td>2a</td>
<td>74</td>
</tr>
<tr>
<td>6b</td>
<td>2b</td>
<td>62</td>
</tr>
</tbody>
</table>

In the presence of a base (DABCO), the compounds (6) were dehydrochlorinated to 1-alkyl-3-benzoylthio-1,4-dihydro-4-(phenylimino)quinoline (7) with quantitative yield. On the other hand, the reaction of 4-(phenylimino)quinolines (7) with hydrogen chloride led with quantitative yield to 4-(phenylamino)quinoline derivatives (6). The course of these reactions confirms the imine structure of compounds (7).

In our earlier report, we described reactions of 1-alkyl-3-alkylthio-1,4-dihydro-4-(phenylimino)quinolines with alkylating agents, which occurred as N-alkylation at the imine nitrogen atom and led to 1-alkyl-3-alkylthio-4-(N-alkyl-N-phenylamino)quinoline salts. We expected that 1-alkyl-3-benzoylthio-4-(N-ethyl-N-phenylamino)quinolinium bromide (8) can be obtained in the same way. A cleavage of the thioester group in the presence of aniline could possibly lead to the expected 3-thiolates (4).

Contrary to expectation the reactions of the 4-iminoquinolines (7) with ethyl bromide led to 1-alkyl-3-ethylthio-4-(N-benzoyl-N-phenylamino)quinolinium bromides (10). The reaction of compounds (10) with aniline led to 1-alkyl-3-ethylthio-1,4-dihydro-4-(phenylimino)quinolines (11) (Scheme 2).

A two-step reaction mechanism is proposed in order to explain the formation of compounds (10) following alkylation of compounds (7) with ethyl bromide. In the first step the compound (7) undergoes S-alkylation to give intermediate of the sulfonium salt structure (9). Then the sulfonium salt (9) undergoes intramolecular rearrangement to give compounds (10) by acylation at imine nitrogen atom. This hypothesis is supported by reaction 4-(phenylimino)quinolines (11) with benzoyl bromide. The structure of compounds (10) was studied using NOE ¹H-¹H homonuclear experiment (Scheme 3) as well as X-ray analysis (Figure 1).
Irradiation of methylene protons ($\delta = 3.34 - 3.40$) in MeCH$_2$ group of the compound (10a) increased the intensity of quinoline H2 signal ($\delta = 8.52, 1.8\%$) (Scheme 3). This rules out the expected compound (8) to be the product of the reaction considered as its ethyl group is linked to the exocyclic nitrogen atom in the 4-position of quinoline.

X-Ray analysis of the derivative (10a) demonstrated definitely that the examined compound has the structure of 1-methyl-3-ethylthio-4-(N-benzoyl-N-phenylamino)quinolinium bromide (Figure 1). The quinoline moiety is planar, maximum deviation from planarity is 0.024(4) Å for atom C3 and the methyl group at the endocyclic nitrogen atom is in the quinoline plane. The valence angle C8A-N1-C2 is equal to 121.8(3)$^\circ$ which is a value typical of azine salts. The bond length between the carbonyl carbon atom and exocyclic nitrogen atom N2 is equal to 1.383(5) Å.

Figure 1. View of 1-methyl-3-ethylthio-4-(N-benzoyl-N-phenylamino)quinolinium bromide 10a.

**EXPERIMENTAL**

Melting points are uncorrected. $^1$H NMR spectra (at 300 MHz) were recorded using a Varian VXR 300 spectrometer at 303 K. Proton chemical shifts are reported relative to TMS ($\delta = 0.0$) as internal standards. $^{15}$N NMR spectra were recorded in the DMSO solution using a Bruker AM 500 spectrometer at 50.698 MHz. NOE $^1$H-$^1$H homonuclear experiment was carried out for (10a) in the CDCl$_3$ solution at 500 MHz. EI MS spectra were recorded using an LKB GC MS 20091 spectrometer at 75 eV.

X-Ray data were collected on a Bruker Kappa ApexII diffractometer with graphite monochromated MoK$\alpha$ radiation ($\lambda = 0.71073$ Å). Diffractometer control program Collect, unit cell parameters and data reduction with Denzo and Scalepak. The structure was solved by direct methods SHELXS-97 and refined by full-matrix least-squares minimization based on all unique F$^2$ (SHELXL-97).
Crystal data: C₂₅H₂₃N₂OS⁺·Br⁻·H₂O, M = 497.44, light-yellow block, 0.50 × 0.30 × 0.30 mm, orthorhombic, space group Pbca, a = 13.26(3), b = 9.4976(5), c = 36.548(1) Å, V = 4605.8(3) Å³, Z = 8, Dc = 1.435 g/cm³, F(000) = 2048, µ = 1.900 mm⁻¹, T = 100(2)K, θmax = 55.0º. 23818 reflections collected, 5041 unique (Rint = 0.044). Final Goof = 1.08, R = 0.059, wR = 0.102, R indices based on 3975 reflections with I > 2σ(I) for 288 parameters and 0 restraints.

The crystallographic data for the structure (10a) have been deposited at the Cambridge Crystallographic Data Center (depository number CCDC-689038).

1-Alkyl-3-benzoylthio-4-(phenylamino)quinolinium chloride (6):
A. From 1-alkyl-4-(phenylamino)quinolinium 3-thiolates (2)
The mixture of 1-alkyl-4-(phenylamino)quinolinium 3-thiolates (2) (1 mmol) and benzoyl chloride (702 mg, 5 mmol) was mixed at rt for 2 h. The obtained chloride (6) was filtered off and washed with Et₂O. The raw product was purified through recrystallization from EtOH.
B. From 1-alkyl-3-benzoylthio-1,4-dihydro-4-(phenylimino)quinoline (7)
Hydrogen chloride was passed through the solution of 4-(phenylimino)quinoline (7) (1 mmol) in dry benzene (15 mL) at rt over 5 min. The solid product was filtered off and washed with dry benzene. The raw product was purified through recrystallization from EtOH.

1-Methyl-3-benzoylthio-4-(phenylamino)quinolinium chloride (6a): yield: (A) 92 %, (B) 89 %. ¹H NMR (CDCl₃) δ: 4.27(s, 3H, NMe), 7.02-7.16(m, 3H, Hₐrom), 7.18-7.26(m, 2H, Hₐrom), 7.29-7.42(m, 3H, Hₐrom), 7.49-7.58(m, 3H, Hₐrom), 7.82-7.93(m, 2H, Hₐrom), 8.61(s, 1H, H₂quinolinyl), 9.37-9.48(m, 1H, H₅quinolinyl), 11.80(s, 1H, NH). Anal. Calcd for C₂₃H₁₉ClN₂OS: C 67.89, H 4.71, Cl 8.71, N 6.88, S 7.88. Found: C 67.81, H 4.64, Cl 8.62, N 6.81, S 7.95.

1-Ethyl-3-benzoylthio-4-(phenylamino)quinolinium chloride (6b): yield: (A) 90 %, (B) 86 %. ¹H NMR (CDCl₃) δ: 1.62-1.81(t, J=7.5 Hz, 3H, NCH₂Me), 4.14-4.26(q, J=7.5 Hz, 2H, NCH₂Me), 7.05-7.23(m, 3H, Hₐrom), 7.25-7.48(m, 5H, Hₐrom), 7.52-7.64(m, 3H, Hₐrom), 7.85-8.07(m, 2H, Hₐrom), 8.75(s, 1H, H₂quinolinyl), 9.41-9.51(m, 1H, H₅quinolinyl), 11.97(s, 1H, NH). Anal. Calcd for C₂₄H₂₁ClN₂OS: C 68.48, H 5.03, Cl 8.42, N 6.65, S 7.62. Found: C 68.43, H 5.12, Cl 8.29, N 6.57, S 7.69.

1-Alkyl-4-(phenylamino)quinolinium-3-thiolate (2) from chloride (6):
Aniline (280 mg, 3 mmol) was added to the mixture of chloride (6) (1 mmol) in dry pyridine (10 mL) and the whole was mixed at 70 °C for 2 h. The solid product was filtered off and washed with dry Et₂O. The raw product was purified through recrystallization from EtOH.
1-Alkyl-3-benzoylthio-1,4-dihydro-4-(phenylimino)quinoline (7):
The solution of DABCO (135 mg, 1.2 mmol) in MeOH (5 mL) was added to the mixture of chloride (6) (1 mmol) in MeOH (10 mL) and the whole was mixed at rt for 1 h. The product was filtered off and washed with MeOH. The raw product was purified through recrystallization from EtOH.

1-Methyl-3-benzoylthio-1,4-dihydro-4-(phenylimino)quinoline (7a): yield 84%. oil. EI MS, (m/z): 370(M⁺, 60%), 265(M⁺-105, 65%). ¹H NMR (CDCl₃) δ: 4.17(s, 3H, NMe), 7.05-7.32(m, 7H, Hₐrom), 7.43-7.60(m, 3H, Hₐrom), 7.62-7.80(m, 3H, Hₐrom), 7.86-7.95(m, 1H, H₅quinolinyl), 9.12(s, 1H, H₂quinolinyl). Anal. Calcd for C₂₃H₁₈N₂OS: C 74.57, H 4.90, N 7.56, S 8.65. Found: C 74.55, H 4.97, N 7.48, S 8.72.

1-Ethyl-3-benzoylthio-1,4-dihydro-4-(phenylimino)quinoline (7b): yield 75%. oil. EI MS, (m/z): 384(M⁺, 72%), 279(M⁺-105, 68%). ¹H NMR (CDCl₃) δ: 1.73-1.88(t, J=7.1 Hz, 3H, NCH₂Me), 4.11-4.25(q, J= 7.1 Hz, 2H, NCH₂Me), 7.05-7.45(m, 7H, Hₐrom), 7.48-7.59(m, 3H, Hₐrom), 7.60-7.79(m, 3H, Hₐrom), 8.12-8.20(m, 1H, H₅quinolinyl), 9.17(s, 1H, H₂quinolinyl) (Anal. Calcd for C₂₄H₂₀N₂OS: C 74.97, H 5.24, N 7.29, S 8.34. Found: C 74.94, H 5.18, N 7.22, S 8.32.

1-Alkyl-3-ethylthio-4-(N-benzoyl-N-phenylamino)quinolinium bromide (10):
A. From 1-alkyl-3-benzoylthio-1,4-dihydro-4-(phenylimino)quinoline (7) The mixture of 1-alkyl-3-benzoylthio-1,4-dihydro-4-(phenylimino)quinoline (7) (1 mmol) and ethyl bromide (545 mg, 5 mmol) was mixed at 50 °C for 2 h. The mixture was cooled down to rt, the product was filtered off and washed with Et₂O. The raw product was purified through recrystallization from EtOH.
B. From 1-alkyl-3-ethylthio-1,4-dihydro-4-(phenylimino)quinolines (11) The mixture of compound (11) (1 mmol) and benzoyl bromide (555 mg, 3 mmol) was mixed at 70 °C for 4 h. The obtained bromide (10) was filtered off and washed with Et₂O. The raw product was purified through recrystallization from EtOH.

1-Methyl-3-ethylthio-4-(N-benzoyl-N-phenylamino)quinolinium bromide (10a): yield: (A) 87%, (B) 91%. ¹H NMR (DMSO-d₆) δ: 1.18-3.5(t, J=7.0 Hz, 3H, SCH₂Me), 3.34-3.40(q, J=7.0 Hz, 2H, SCH₂Me), 4.72(s, 3H, NMe), 7.06-7.66(m, 10H, Hₐrom), 7.93-8.10(m, 1H, Hₐrom), 8.12-8.19(m, 1H, Hₐrom), 8.28-8.36(m, 1H, Hₐrom), 8.52(s, 1H, H₂quinolinyl), 9.78-9.90(m, 1H, H₅quinolinyl). Anal. Calcd for C₂₅H₂₃BrN₂OS: C 62.63, H 4.84, N 5.84, S 6.62. Found: C 62.57, H 4.93, N 5.79, S 6.67.

1-Ethyl-3-ethylthio-4-(N-benzoyl-N-phenylamino)quinolinium bromide (10b): yield: (A) 91%, (B) 94%.
1H NMR (DMSO-d$_6$) $\delta$: 1.25-1.34(t, $J$=7.2 Hz, 3H, SCH$_2$Me), 1.54-1.79(t, $J$=7.5 Hz, 3H, NCH$_2$Me), 3.35-3.47(q, $J$=7.2 Hz, 2H, SCH$_2$Me), 5.05-5.24(q, $J$=7.5 Hz, 2H, NCH$_2$Me), 7.05-7.82(m, 10H, H$_{arom}$), 7.82-7.98(m, 1H, H$_{arom}$), 8.11-8.23(m, 1H, H$_{arom}$), 8.32-8.41(m, 1H, H$_{arom}$), 8.61(s, 1H, H$_2$quinolinyl), 9.69-9.86(m, 1H, H$_5$quinolinyl). *Anal. Calcd for C$_{26}$H$_{25}$BrN$_2$OS: C 63.28, H 5.11, N 5.68, S 6.50. Found: C 63.23, H 5.07, N 5.59, S 6.55.*

1-Alkyl-3-ethylthio-1,4-dihydro-4-(phenylimino)quinoline (11):
Aniline (140 mg, 1.2 mmol) was added to the mixture of bromide (10) (1 mmol) in dry pyridine (10 mL) and the whole was mixed at 70 °C for 4 h. After cooling down to rt the mixture was poured into water (50 mL). The resulting solid was filtered off and washed with water. The product was dehydrated in a vacuum exsiccator over calcium chloride. The raw product was recrystallized from EtOH.

1-Methyl-3-ethylthio-1,4-dihydro-4-(phenylimino)quinoline (11a): yield 76%. mp 106-108 °C. El MS, (m/z): 294(M$^+$, 82%). 1H NMR (CDCl$_3$) $\delta$: 0.99-1.04(t, $J$=7.4 Hz, 3H, SCH$_2$Me), 2.49-2.55(q, $J$=7.4 Hz, 2H, SCH$_2$Me), 3.66(s, 1H, NMe), 6.64-6.72(m, 2H, H$_{arom}$), 6.81-6.85(m, 1H, H$_{arom}$), 7.05-7.10(m, 1H, H$_6$quinolinyl), 7.14-7.19(m, 2H, H$_{arom}$), 7.40-7.43(m, 1H, H$_8$quinolinyl), 7.49-7.54(m, 1H, H$_7$quinolinyl), 7.64(s, 1H, H$_2$quinolinyl), 7.93-7.99(m, 1H, H$_5$quinolinyl). *Anal. Calcd for C$_{18}$H$_{18}$N$_2$S: C 73.43, H 6.16, N 9.51, S 10.89. Found: C 73.40, H 6.19, N 9.42, S 10.96.*

1-Ethyl-3-ethylthio-1,4-dihydro-4-(phenylimino)quinoline (11b): yield 84%. oil. El MS, (m/z): 308(M$^+$, 87%). 1H NMR (CDCl$_3$) $\delta$: 1.05-1.15(t, $J$=7.4 Hz, 3H, SCH$_2$Me), 1.40-1.49(t, $J$=7.5 Hz, 3H, NCH$_2$Me), 2.52-2.67(q, $J$=7.4 Hz, 2H, SCH$_2$Me), 4.01-4.12(q, $J$=7.5 Hz, 2H, NCH$_2$Me), 6.84-6.90(m, 2H, H$_{arom}$), 6.92-6.99(m, 1H, H$_{arom}$), 7.02-7.11(m, 1H, H$_{arom}$), 7.19-7.31(m, 3H, H$_{arom}$), 7.42-7.48(m, 1H, H$_{arom}$), 7.52(s, 1H, H$_2$quinolinyl), 8.02-8.19(m, 1H, H$_5$quinolinyl). *Anal. Calcd for C$_{19}$H$_{20}$N$_2$S: C 73.99, H 6.54, N 9.08, S 10.39. Found: C 73.94, H 6.49, N 9.01, S 10.34.*

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