Reactions of 4-Methoxy-3-quinolinyl and 1,4-Dihydro-4-oxo-3-quinolinyl Sulfides Aiming at the Synthesis of 4-Chloro-3-Quinolinyl Sulfides [1]

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The preparation of 1,4-dihydro-4-oxo-3'-alkylthio-3,4'-diquinolinyl sulfides **3** or 1,4-dihydro-4-oxo-3-(alkylthio)quinolines **4** by acid catalysed hydrolysis of 4-methoxy-3'-alkylthio-3,4'-diquinolinyl sulfides **1** or 4-methoxy-3-(alkylthio)-quinolines **2** is described. The reactions of 4-methoxy-3'-alkylthio-3,4'-diquinolinyl sulfides **1** or 1,4-dihydro-4-oxo-3'-alkylthio-3,4'-diquinolinyl sulfides **3** with phosphoryl chloride in DMF afforded 4-chloro-3'-alkylthio-3,4'-diquinolinyl sulfides **5**. Treatment of the title compounds **1** or **3** with boiling phosphoryl chloride systems:leads to 4-chloro-3-(alkylthio)quinolines **6** and thioquinanthrene but those of alkoxy- or oxo-quinolines **2** or **4** lead to 4-chloro-3-(alkylthio)quinolines **6**. The reactions of *N*-methyl-4(1*H*)-quinolinones **3n** and **4n** with phosphoryl chloride directed to 4-chloro-3-(alkylthio)quinolines **6** were studied as well.

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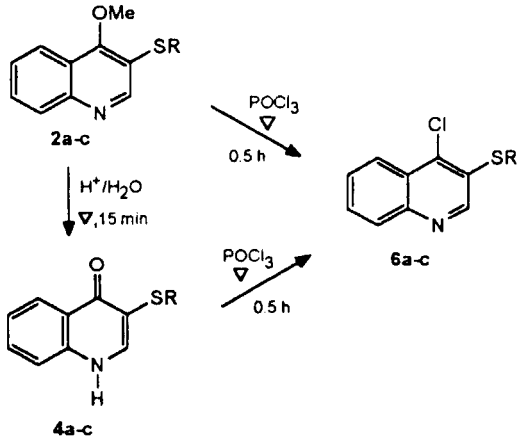
Introduction.

Typical transformations of the substituents being in the *aza*-activated positions in six-membered hetarenes were usually carried out from x-chloro-systems:to x-alkoxy ones [2-3]. However, our recent results made 4-alkoxy-3-quinolinyl sulfides **1** and **2** easily available [4-5]. It induced the present study on the reverse substituent replacement, *i.e.* from 4-alkoxyquinolines **1** and **2** to 4-chloroquinolines **5** or **6**, indirectly *via* 4-quinolinones **3** or **4** and then directly using phosphoryl chloride as a chlorine source. Two routes were elaborated: the first one was performed under mild conditions in DMF and at room temperature. It allowed for the simple direct replacement of the 4-alkoxy or 4-oxo- group for the 4-chloro one, both in quinolinyl sulfides **2** and **4** as well as in 3',4-diquinolinyl bis-sulfides **1** or **3**. Under more rigorous conditions, *i.e.* in the boiling phosphoryl chloride/triethylamine hydrochloride system, the replacement mentioned above took place also but the reaction of compounds **1** and **3** ran with the cleavage of both γ-quinolinyl-heteroatom bonds and led to 4-chloro-3-(alkylthio)quinolines **6** and thioquinanthrene. For a comparison, the reactions of selected *N*-methyl-4(1*H*)-quinolinones **3n** and **4n** with phosphoryl chloride were performed as well.

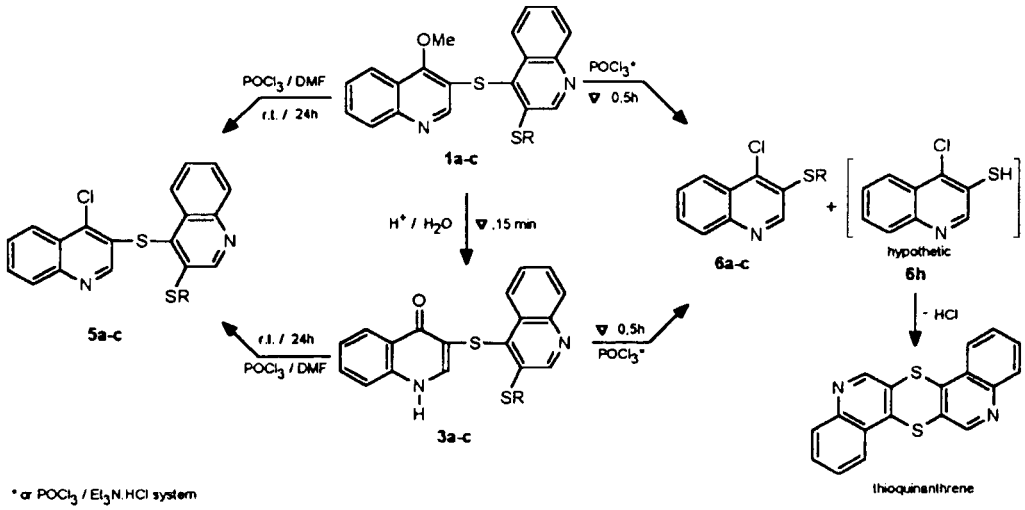
Results and Discussion.

The reactions of 4(1*H*)-quinolinones or quinoline *N*-oxides are the most often exploited methods for the preparation of 4-chloroquinolines [2,6]. Since 3-alkylthio-4(1*H*)-quinolinones **3** and **4** are easily available by the acid hydrolysis of 4-alkoxy-3-quinolinyl sulfides **1** [4] or **2** (see Schemes 1 and 2, and experimental), we started with the reactions of compounds **3** and **4** with boiling phosphoryl chloride. Compounds **4** gave pure 4-chloro-3-(alkylthio)quinolines **6** (78-89%). However, similar treatment of diquinolinyl sulfides **3a-c** led to 4-chloro-3-(alkylthio)-quinolines **6** (65-80%) and thioquinanthrene (86-90%). Most probably, under acid catalysis conditions, the reactions of compounds **3a-3c** run by the cleavage of both γ-quinolinyl-heteroatom bonds to form two 4-chloroquinolines **6h** and **6a-6c**. The first one should undergo cyclodehydrochlorination to form the 1,4-dithiin ring of thioquinanthrene as it was suggested or proved in the case of the formation of dithiinodipyridines [7], dithiinodiquinolines [8] and dithiinodipyridazines [9] from respective *ortho* chloromercaptoazines (see Scheme 2).

Scheme 1

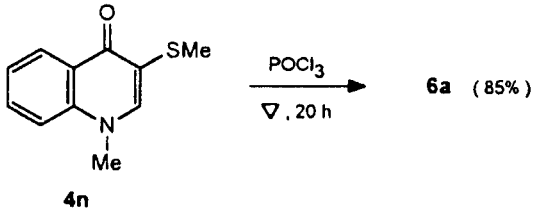


Scheme 2



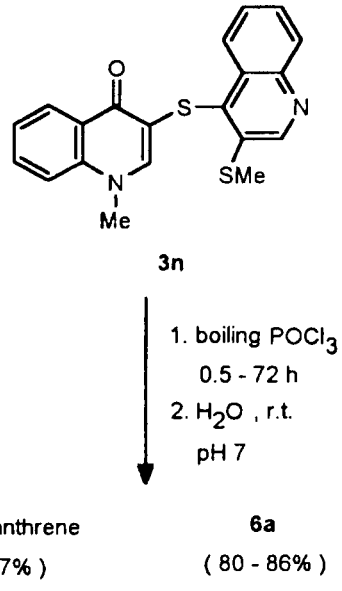
Since both *N*-non-substituted lactams [6] and (but more difficult) *N*-alkyl ones [6] can be transformed into the respective chlorolactim derivatives by the reactions with phosphoryl chloride, we attempted to carry out the reactions with *N*-alkyl-4(1*H*)-quinolinones **3n** and **4n**. However, complete consumption of 1-methyl-3-methylthio-4(1*H*)-quinolinone **4n** (directed in 85% in 4-chloro-3-(methylthio)quinoline **6a**) required 20 hours as compared to 0.5 hour for *N*-non-substituted 4-quinolinone **4a**.

Scheme 3



Furthermore, the reactions of 1-methyl-1,4-dihydro-4-oxo-3'-methylthio-3,4'-diquinolinyl sulfide **3n** with phosphoryl chloride up to 2 hours gave only 4-chloro-3-(methylthio)-quinoline **6a** as the sole isolated product (after treatment of reaction mixture with water followed by neutralization). Prolongation of the reaction time up to 72 hours gave both 4-chloro-3-(methylthio)quinoline **6a** (80%) and thioquinanthrene (37%). It indicates that the reactions of 3,4'-diquinolinyl sulfide **3n** having a *N*-methyl-4(1*H*)-quinolinone fragment also took place with the breaking of the γ-quinolinyl sulfur bond to give 4-chloro-3-(methylthio)quinoline **6a** as the product formed from the bis-sulfide part of the substrate **3n** and a thioquinanthrene as the product formed by *N*-demethylation of the *N*-methyl 4(1*H*)-quinolinone fragment of **3n**.

Scheme 4



Comparing the results of the conversion of *N*-non-substituted 4(1*H*)-quinolinones **4a-c** and *N*-methyl-4(1*H*)-quinolinone **4n** into 4-chloroquinolines of type **6** *versus* those in the transformation of the *N*-non-substituted 4(1*H*)-quinolinone fragment of **3a-c** and the *N*-methyl-substituted 4(1*H*)-quinolinone fragment of **3n** into thioquinanthrene one could conclude that the *N*-demethylation process seems to be the step limiting further transformation of *N*-methyl-4(1*H*)-quinolinones **3n** and **4n**. To explain the unsatisfactory balance of both the quinoline part of **3n** as well as the low yield in the formation of thioquinanthrene from **3n** in its reaction with phosphoryl

Table

Reactions of 4-Methoxy-3-quinolinyl Sulfides **1** and **2** and 1,4-Dihydro-4-oxo-3-quinolinyl Sulfides **3** and **4** with Phosphoryl Chloride.

Entry	Substrate	Chlorinating system	Temp. [°C]	Time [hour(s)]	The products, yield (%) 4-Chloroquinoline	Thioquinanthrene*
1	**1a** R=Me	A	reflux	0.5	6a (80)	95
2	**1a** R=Me	B	r.t.	24	5a (58)	
3	**1b** R=Et	A	reflux	0.5	6b (80)	95
4	**1b** R=Et	B	r.t.	24	5b (57)	
5	**1c** R=$PhCH_2$	A	reflux	0.5	6c (70)	96
6	**1c** R=$PhCH_2$	B	r.t	24	5c (57)	
7	**2a** R=Me	A	reflux	0.5	6a (94)	
8	**2b** R=Et	A	reflux	0.5	6b (91)	
9	**2c** R=$PhCH_2$	A	reflux	0.5	6c (87)	
10	**3a** R=Me	A	reflux	0.5	6a (80)	86
11	**3a** R=Me	B	r.t.	24	5a (82)	
12	**3b** R=Et	A	reflux	0.5	6b (72)	87
13	**3b** R=Et	B	r.t.	24	5b (76)	
14	**3c** R=$PhCH_2$	A	reflux	0.5	6c (65)	90
15	**3c** R=$PhCH_2$	B	r.t.	24	5c (69)	
16	**3n**	A or A1	reflux	0.5	6a (86)	0
17	**3n**	A or A1	reflux	5	6a (85)	4
18	**3n**	A or A1	reflux	30	6a (84)	21
19	**3n**	A or A1	reflux	72	6a (80)	37
20	**4a** R=Me	A	reflux	0.5	6a (89)	
21	**4a** R=Me	H	r.t.	24	6a (78)	
22	**4b** R=Et	A	reflux	0.5	6b (86)	
23	**4c** R=$PhCH_2$	A	reflux	0.5	6c (79)	
24	**4n**	A	reflux	5	6a (65)	
25	**4n**	A	reflux	20	6a (85)	

A - $POCl_3$(neat), A1 - $POCl_3$/ Et_3N•HCl, B - $POCl_3$ in DMF. * IUPAC name.

chloride we considered the occurence of 5,12-dimethylthioquinanthrenediinium bis-salts as a percursor of thioquinanthrene. However, treatment of 5,12-dimethylthioquinanthrenediinium bis-chloride with boiling phosphoryl chloride did not lead to thioquinanthrene although it exhibited high instability of the starting bis-salt, which was 50% consumed after 1 hour and completely consumed after 24 hours. In the last case only the formation of traces of thioquinanthrene was noted. (Further study of the behaviour of 5,12-dimethylthioquinanthrenediinium bis-salts in boiling phosphoryl chloride is now in progress).

The lability of the 4-alkoxy group in 4-alkoxyquinolines under acid catalysis conditions [10,4], and more generally, the sensitivity of the *aza*-activated ether linkage in alkoxy or aryloxyheteroarenes towards acid catalysed nucleophilic displacement [1 1] directed us to the reactions of 4-alkoxyquinolines **1** and **2** with phosphoryl chloride. In fact, treatment of 4-methoxy-3-(alkylthio)-quinolines **2a-2c** with boiling phosphoryl chloride during 0.5 hour afforded 4-chloro-3-(alkylthio)quinolines **6a-6c** in high yields (see Scheme 1). The reaction of 4-methoxy-3'-alkylthio-3,4'-diquinolinyl sulfides **1** with boiling phosphoryl chloride gave the same results as in the case of quinolinones **3a-3c**, *i.e.* 4-chloro-3-(alkylthio)quinolines **6** and thioquinanthrene were formed (Scheme 2). Also reactions of 4-alkoxydiquinolinyl sulfides **1a-1c** with the phosphoryl chloride/DMF system led to the same 4-chloroquinoline products **5a-5c** as for compounds **3**, however, with some lower yields (52-58%) (Scheme 2).

Differences in the reactivity of 4-methoxy-3'-alkylthio-3,4'-diquinolinyl sulfides **1** *versus* 1-methyl-1,4-dihydro-4-oxo-3'-methylthio-3,4'-diquinolinyl sulfide **3n** towards phosphoryl chloride also support our revision [4-5] that 4-alkoxy-3'-alkylthio 3,4'- diquinolinyl sulfides **1** but not 1-alkyl-1,4-dihydro-4-oxo-3'-alkylthio-3,4'-diquinolinyl sulfides **3** [16] are the products of the reaction of thioquinanthrene with sodium alkoxides followed by *S*-alkylation.

In conclusion, we have shown that 4-chloro-3'-alkylthio-3,4'-diquinolinyl sulfides **5** and(or) 4-chloro-3-(alkylthio)quinolines **6** can be easy obtained by an effective 3 or 4 step synthesis starting from quinoline *via* thio-

quinanthrene.

EXPERIMENTAL

Melting points were determined in open capillary tubes on a Boetius melting point apparatus and are uncorrected. The ^{1}H nmr spectra were recorded on a Bruker MSL 300 (300 MHz) spectrometer in deuteriochloroform or DMSO-d_6 solvents with tetramethylsilane as the internal standard and chemical shifts reported in ppm (δ) and J values in Hz. EI mass spectra were run on a LKB GC 2091 spectrometer at 70 eV and 15 eV. Thin layer chromatography was performed on silica gel 60 254F plates (Merck) using a mixture of chloroform and ethanol (15:1 v/v) as an eluent.

Thioquinanthrene was obtained by exhaustive sulfurization of quinoline with elemental sulfur [12]. 1-Methyl-1,4-dihydro-4-oxo-3'-methylthio-3,4'-diquinolinyl sulfide **3n** was prepared by methylation of the sodium salt of 1,4-dihydro-4-oxo-3'-methylthio-3,4'-diquinolinyl sulfide **3a** according to the method described earlier [4]. 1-Methyl-3-(methylthio)-4(1*H*)-quinolinone **4n** with mp 123-124° and ^{1}H nmr as in ref [4] was prepared by thermal rearrangement of 4-methoxy-3-(methylthio)quinoline **2a** [13]. 4-Methoxy-3-(methylthio)quinoline **2a**, 4-methoxy-3-(ethylthio)quinoline **2b**, 4-methoxy-3-(benzylthio)quinoline **2c**, were prepared from thioquinanthrene and sodium methoxide in DMF solution followed by treatment of sodium 4-methoxy-3-quinolinethiolate formed with alkylating agents according to the one-pot procedure described previously [5]. 5,12-Dimethylthioquinanthrenediinium bis-chloride was obtained from 5,12-dimethylthioquinanthrenediinium bis(methyl sulfate) [14].

4-Methoxy-3'-alkylthio-3,4'-diquinolinyl Sulfides (**1**).

Compounds **1** were prepared from thioquinanthrene [12] and sodium methoxide followed by *S*-alkylation of sodium 4-[(4-methoxy-3-quinolinyl)thio]-3-quinolinethiolate with alkyl iodides (in the case of compound **1c** with benzyl chloride) according to the general procedure reported previously [4,5].

4-Methoxy-3'-methylthio-3,4'-diquinolinyl Sulfide (**1a**).

Compound **1a** had mp 131-132°, yield 91%; ^{1}H nmr and ms spectra as in ref [4].

4-Methoxy-3'-ethylthio-3,4'-diquinolinyl Sulfide (**1b**).

This compound had mp 109-110°, yield 80% ; ^{1}H nmr (deuteriochloroform): δ 1.34 (t, 3H, J = 7.3 Hz, CH_3CH_2S), 3.11 (q, 2H, J = 7.3 Hz, CH_3CH_2S), 4.24 (s, 3H, CH_3O), 7.41-8.37 (m, 8H, Ar-H), 8.08 (s, 1H, H-2), 8.81 (s, 1H, H'-2); ms:(70 eV) m/z (relative intensity): 378 (37.8, M$^+$), 317 (6.3, M-C_2H_5S), 302 (7.4, M-C_2H_5S-CH_3).

Anal. Calcd. for $C_{21}H_{18}N_2OS_2$: C, 66.65; H, 4.80; N, 7.41 ; S, 16.91. Found: C, 66.72; H, 4.87; N, 7.37; S, 16.75.

4-Methoxy-3'-benzylthio-3,4'-diquinolinyl Sulfide (**1c**).

This compound had mp 99-100°, yield 88%; ^{1}H nmr (deuteriochloroform): δ 4.13 (s, 3H, CH_3O), 4.27 (s, 2H, CH_2S), 7.17-7.25 (m, 5H, Ar-H), 7.49-8.36 (m, 8H, Ar-H), 8.12 (s, 1H, H-2), 8.86 (s, 1H, H'-2); ms: (70 eV) m/z (relative intensity) 440 (72.9, M$^+$), 409 (18.9, M-CH_3O), 349 (19.4, M-$C_6H_5CH_2$), 318 (12.1, M-$C_6H_5CH_2$-CH_3O).

Anal. Calcd. for $C_{26}H_{20}N_2OS_2$: C, 70.89; H, 4.58; N, 6.36; S, 14.53. Found: C, 70.8; H, 4.47; N, 6.47; S, 14.4.

Hydrolysis of 4-Methoxy-3'-alkylthio-3,4'-diquinolinyl Sulfides **1** to 1,4-Dihydro-4- oxo-3'-alkylthio-3,4'-diquinolinyl Sulfides **3**.

A mixture of 4-methoxy-3'-alkylthio-3,4'-diquinolinyl sulfide (**1**) (3 mmoles) and azeotropic hydrochloric acid (20 ml) was heated at reflux for 15 minutes. The solution was then evaporated *in vacuo* to dryness. The residue was neutralized with 5% aqueous sodium bicarbonate solution (20 ml). The resultant solid was filtered off and air-dried to give crude 1,4-dihydro-4-oxo-3'-alkylthio-3,4'-diquinolinyl sulfide **3**, which was crystallized from DMF to yield pure **3**.

1,4-Dihydro-4-oxo-3'-methylthio-3,4'-diquinolinyl Sulfide (**3a**).

Compound **3a** had mp 270-272°, ref [4] mp 278-280°, yield 81%; ^{1}H nmr and ms spectra as in ref [4].

1,4-Dihydro-4-oxo-3'-ethylthio-3,4'-diquinolinyl Sulfide (**3b**).

This compound had mp 240-242°, yield 79%; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.47 (t, 3H, J = 7.3 Hz, CH_3CH_2S), 3.30 (q, 2H, J = 7.3 Hz, CH_3CH_2S), 7.44-8.54 (m, 8H, Ar-H), 7.77 (s, 1H, H-2), 8.96 (s, 1H, H'-2); ms: (70 eV) m/z (relative intensity) 364 (43.0, M$^+$), 303 (100, M-C_2H_5S).

Anal. Calcd. for $C_{20}H_{16}N_2OS_2$: C, 65.92; H, 4.43; N, 7.69; S, 17.56. Found: C, 65.98; H, 4.38; N, 7.62; S, 17.67.

1,4-Dihydro-4-oxo-3'-benzylthio-3,4'-diquinolinyl Sulfide (**3c**).

This compound had mp 130-132°, yield 74%; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 4.57 (s, 2H, CH_2S), 7.25-7.46 (m, 5H, C_6H_5), 7.61-8.57 (m, 8H, Ar-H), 7.79 (s, 1H, H-2), 8.98 (s, 1H, H'-2); ms: (70 eV) m/z (relative intensity) 426 (40.2, M$^+$), 335 (12.5, M-$C_6H_5CH_2$), 303 (100, M-$C_6H_5CH_2S$).

Anal. Calcd. for $C_{25}H_{18}N_2OS_2$: C, 70.41; H, 4.26; N, 6.57; S, 15.01. Found: C, 70.58; H, 4.20; N, 6.51; S, 15.20.

Hydrolysis of 4-Methoxy-3-(alkylthio)quinolines **2** into 1,4-Dihydro-4-oxo-3-(alkylthio)quinolines **4**.

The same procedure as in the case of transformation of 4-methoxy-3'-alkylthio-3,4'-diquinolinyl sulfides **1** to 1,4-dihydro-4-oxo-3'-alkylthio-3,4'-diquinolinyl sulfides **3** was applied for the conversion of 4-methoxy-3-(alkylthio)quinolines **2** into 1,4-dihydro-4-oxo-3-(alkylthio)quinolines **4**.

1,4-Dihydro-4-oxo-3-(methylthio)quinoline (**4a**).

This compound had mp 170-172°, ref [15] mp 173-175°, yield 93%; ^{1}H nmr (deuteriochloroform): δ 2.40 (s, 3H, CH_3S), 7.42-8.53 (m, 4H, Ar-H), 8.34 (s, 1H, H-2), 12.90 (broad singlet, 1H, NH); ms: (70 eV) m/z (relative intensity) 191 (100, M$^+$), 176 (35.2, M-CH_3), 158 (28.6, M-SH).

1,4-Dihydro-4-oxo-3-(ethylthio)quinoline (**4b**).

This compound had mp 158-159°, yield 92%; ^{1}H nmr (deuteriochloroform): δ 1.22 (t, 3H, J = 7.4 Hz, CH_3CH_2S), 2.85 (q, 2H, J = 7.4 Hz, CH_3CH_2S), 7.43-8.45 (m, 4H, Ar-H), 7.97 (d, 1H, J = 8.4 Hz, H-2), 12.96 (broad singlet, 1H, NH); ms: (70 eV) m/z (relative intensity) 205 (100, M$^+$), 191 (21.8, M-CH_2), 176 (37.5, M-C_2H_5).

*Anal.*Calcd. for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82; S, 15.62. Found: C, 64.45; H, 5.47; N, 6.71; S, 15.41.

1,4-Dihydro-4-oxo-3-(benzylthio)quinoline (**4c**).

This compound had mp 186-188°, yield 89%; ^{1}H nmr (deuteriochlorofrom): δ 3.87 (s, 2H, $C_6H_5CH_2$), 7.08 (s, 5H, $C_6H_5CH_2$), 7.39-8.47 (m, 5H, Ar-H), 12.42 (broad singlet, 1H, NH); ms:(70 eV) m/z (relative intensity) 267 (25.3, M^+), 234 (10.4, M-SH), 176 (8.4, M-$C_6H_5CH_2$).

Anal. Calcd. for $C_{16}H_{13}NOS$: C, 71.88; H, 4.90; N, 5.24; S, 11.99. Found: C, 71.96; H, 4.84; N, 5.18; S, 11.79.

Synthesis of 4-Chloro-3-(alkylthio)quinolines **6** from 4-Methoxy-3-(alkylthio)quinolines 2 or from 1,4-Dihydro-4-oxo-3-(alkylthio)quinolines **4**.

A mixture of 4-methoxy-3-(alkylthio)quinoline **2** (10 mmoles) or 1,4-dihydro-4-oxo-3-(alkylthio)quinoline **4** (10 mmoles) and phosphoryl chloride (20 ml) was refluxed for 0.5 hour. Then the excess of phosphoryl chloride was evaporated *in vacuo*. The residue was carefully poured onto ice (30 g) and then neutralized with conc. ammonia at 0-5°. The solid was filtered off, washed with water and air-dried. The product was purified by vaccum distillation (compound **6a**) or crystallized from ethanol (compounds **6b**, **6c**) to give 86-94% of final product **6**.

4-Chloro-3-(methylthio)quinoline **6a** had b.p. 164-166°/ 1 mm Hg, mp 104-105° (ethanol), ref [16] mp 104-105°.

4-Chloro-3-(ethylthio)quinoline **6b** had mp 49-50° (ethanol), ref [16] mp 49-50°.

4-Chloro-3-(benzylthio)quinoline **6c** had mp 96-97° (ethanol), ref [16] mp 96-97°.

Reaction of 4-Methoxy-3'-alkylthio-3,4'-diquinolinyl Sulfides **1** or 1,4-Dihydro-4-oxo-3'-alkylthio-3,4'-diquinolinyl Sulfides **3** with Boiling Phosphoryl Chloride or with Phosphoryl Chloride/Triethylamine Hydrochloride System.

A mixture of sulfide **1** or **3** (5 mmoles) triethylamine hydrochloride (2.2 g) and phosphoryl chloride (15 ml) was refluxed for 0.5 hour. Then the excess of phosphoryl chloride was evaporated *in vacuo*. The residue was carefully poured onto ice (30 g) and then neutralized with concentrated ammonia at 0-5°. The solid was filtered off, air-dried and boiled with tetrachloromethane (20 ml). The insoluble solid was hot-filtered, air-dried and crystallized from DMF to give thioquinanthrene (86-96%) with mp 310-311, ref [12] mp 314-315°

The tetrachloromethane filtrate was evaporated to dryness. The residue was crystallized from ethanol to give 4-chloro-3-(alkylthio)quinoline **6** in yields of 65-80%. Results are collected in the Table.

Reaction of 1-Methyl-3-[(3-methylthio-4-quinolinyl)thio]-4-oxo-1,4-dihydro- quinoline **3n** with the Phosphoryl Chloride/Triethylamine Hydrochloride System

A mixture of sulfide **3n** (1.82 g, 5 mmoles), triethylamine hydrochloride (2.2g) and phosphoryl chloride (20 ml) was refluxed in an oil bath at 140-145° for 0.5-72 hours. Then the excess of phosphoryl chloride was evaporated *in vacuo*. The residue was treated as in the case of the reaction of compound **3a** with phosphoryl chloride. Results are collected in the Table.

a) Synthesis of 4-Chloro-3'-alkylthio-3,4'-diquinolinyl Sulfides **5** from 1,4-Dihydro-4-oxo-3'-alkylthio-3,4'-diquinolinyl Sulfides **3**.

A mixture of 1,4-dihydro-4-oxo-3'-alkylthio-3,4'-diquinolinyl sulfide **3** (2 mmoles), phosphoryl chloride (0.55 ml) and dimethylformamide (10 ml) was stirred at room temperature under nitrogen atmosphere for 24 hours and poured into a mixture of water and ice (20 ml). The mixture was then neutralized with concentrated aqueous ammonia at 0°. The solid formed was filtered off, washed with water and air-dried. The crude product was then crystallized from dimethylformamide to give the compound **5** in the yields of 69-82%.

4-Chloro-3'-methylthio-3,4'-diquinolinyl Sulfide (**5a**).

This compound had mp 155-156°, yield 82%; ^{1}H and ^{13}C nmr spectral data were published previously [17]; ms: (15 eV) m/z (relative intensity) 370 (34.2, M + 2), 368 (51.8, M^+), 335 (13.0, M + 2-^{35}Cl), 333 (100, M-^{35}Cl and M + 2-^{37}Cl); 318 (59.5, M-CH_3Cl).

Anal. Calcd. for $C_{19}H_{13}N_2S_2Cl$: C, 61.95; H, 3.56; N, 7.61; S, 17.38; Cl, 9.50. Found: C, 61.80; H, 3.57; N, 7.57; S, 17.52; Cl, 9.61.

4-Chloro-3'-ethylthio-3,4'-diquinolinyl Sulfide (**5b**).

This compound had mp 116-117°, yield 76%; ^{1}H nmr (deuteriochlorofrom): δ 1.37 (t, 3H, J = 7.4 Hz, CH_3CH_2S), 3.15 (q, 2H, J = 7.4 Hz, CH_3CH_2S), 7.52-8.32 (m, 8H, Ar-H), 7.96 (s, 1H, H-2), 8.91 (s, 1H, H-2'); ms: (15 eV) m/z (relative intensity) 384 (14.5, M + 2), 382 (34.2, M^+), 346 (100, M-^{35}Cl and M + 2-^{37}Cl), 318 (91.3, M-Cl-C_2H_5).

Anal. Calcd. for $C_{20}H_{15}N_2S_2Cl$: C, 62.82; H, 3.96; N, 7.33; S, 16.74; Cl, 9.15. Found: C, 62.75; H, 3.91; N, 7.26; S, 16.85; Cl, 9.22.

4-Chloro-3'-benzylthio-3,4'-diquinolinyl Sulfide (**5c**).

This compound had mp 106-107°, yield 69%; ^{1}H nmr (deuteriochloroform): δ 4.31 (s, 2H, CH_2S), 7.20-7.29 (m, 5H, Ar-H), 7.50-8.29 (m, 8H, Ar.H), 7.91 (s, 1H, H-2), 8.90 (s, 1H, H-2'); ms: (15 eV) m/z (relative intensity) 446 (6.2, M+2), 444 (15.1, M^+); 409 (40.6, M-^{35}Cl and M + 2-^{37}Cl), 318 (14.1, M-Cl -$C_6H_5CH_2$).

Anal. Calcd. for $C_{25}H_{17}N_2S_2Cl$: C, 67.56; H, 3.86; N, 6.31; S, 14.40; Cl, 7.87. Found: C, 67.47; H, 3.87; N, 6.38; S, 14.51; Cl, 7.80.

b) Synthesis of 4-Chloro-3'-alkylthio-3,4'-diquinolinyl Sulfides **5** from 4-Methoxy-3'-alkylthio-3,4'-diquinolinyl Sulfides **1**.

The reactions of 4-methoxy-3'-alkylthio-3,4'-diquinolinyl sulfides **1** with phosphoryl chloride in dimethylformamide solution were performed in the same manner as above (procedure a), but in order to obtain pure **5**, crude product **5** (upper R_f value) should be separated from unreacted methoxy substrate **1** (lower R_f value) by column chromatography on silica gel 40 (70-230 mesh), using a mixture of chloroform and ethanol (10:1 v/v) as an eluent and finally purified by crystallization from DMF. The results in the preparation of 5 are collected in the Table.

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