HETEROCYCLES, Vol. 65, No. 7, 2005, pp. 1577 - 1588
Received, 7th February, 2005, Accepted, 27th April, 2005, Published online, 28th April, 2005

4-SUBSTITUTED 3-METHYLSULFANYL-5-, 6-, AND 8-NITRO-QUINOLINES FROM NITRO DERIVATIVES OF 4-SUBSTITUTED 3'-METHYLSULFINYL-3,4'-DIQUINOLINYL SULFIDES [#]

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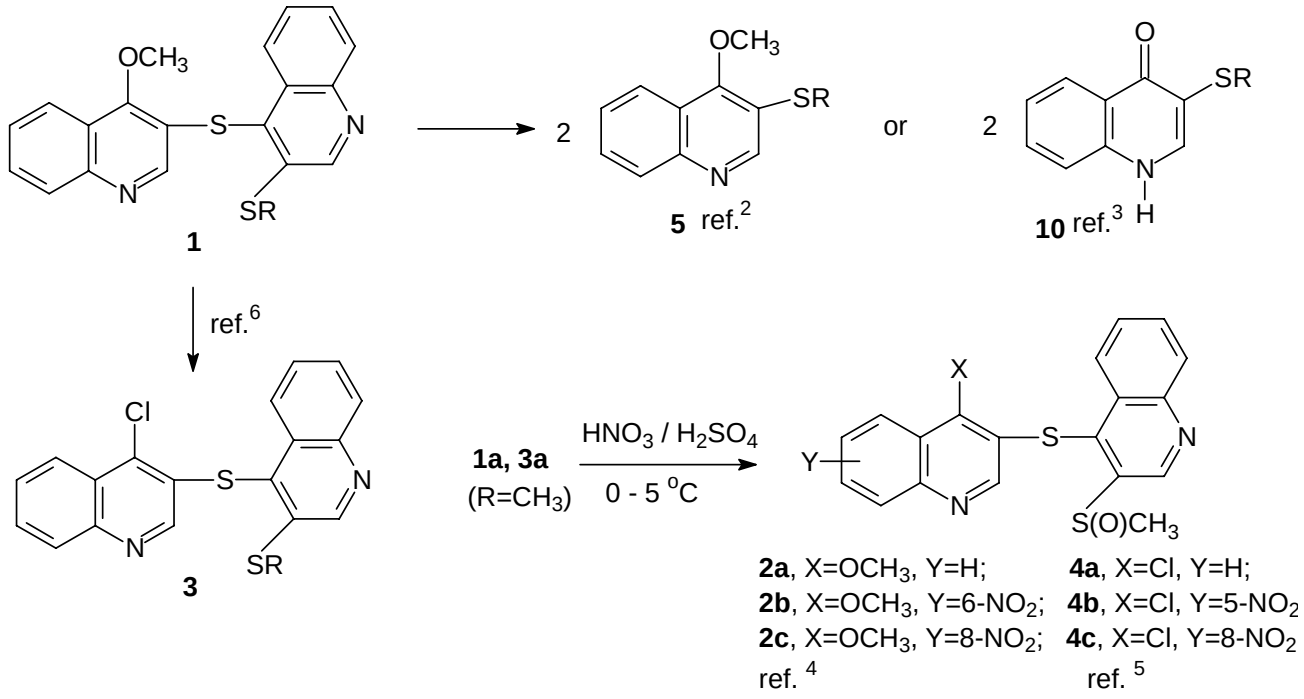
Abstract–Potassium phenoxide reacted with 4-substituted 3'-methylsulfanyl-3,4'-diquinolinyl sulfides (**1** or **3**) at the substituent at the C4 position. 3'-Methylsulfinyl group promotes nucleophilic substitution of 4'-quinolinyl sulfur bond in sulfoxides (**2**) and (**4**) in which case, after treatment with potassium phenoxide, it led to 4-phenoxy-3-methylsulfinylquinoline (**9**) and 4-substituted 3-quinolinethiolates (**5A**, **6A** or **7A**), trapped by methylation to form 4-substituted 3-methylsulfanylquinolines (**5a**), (**6a**) and (**7a**) or their 5-, 6- and 8-nitro derivatives (**5b,c**), (**6b,d**) and (**7b,d**), respectively. Synthesis of 5-, 6- and 8-nitro-3-methylsulfanyl-4(1*H*)-quinolinones (**10b**,**c**,**d**) was described.

INTRODUCTION

3,4'-Diquinolinyl sulfides of types (**1**) and (**3**) are easy available from thioquinanthrene (**12**) (the main quinoline sulfurization product).[1-3] Two types of transformations of compounds (**1**) and (**3**) were then elaborated. At first, the reactions of 3,4'-diquinolinyl sulfides (**1**) with sodium and potassium alkoxides led to the formation of 4-alkoxy-3-alkylsulfanylquinolines of type (**5**) [2] or to 3-alkylsulfanyl-4(1*H*)-quinolinones (**10**) [4] as the final products. Then, the treatment of compounds (**1**) or (**3**) with a nitrating mixture led to 6- and 8- or 5- and 8-nitro-3'-methylsulfinyl 3,4'-diquinolinyl sulfides (**2b**,**c**) [5] or (**4b**,**d**), [6] respectively (Scheme 1). It was of our interest to combine the above reactions and consider them a source of the title nitro derivatives of 4-substituted 3-methylsulfanylquinolines (**5**) or (**6**). (Scheme 4)

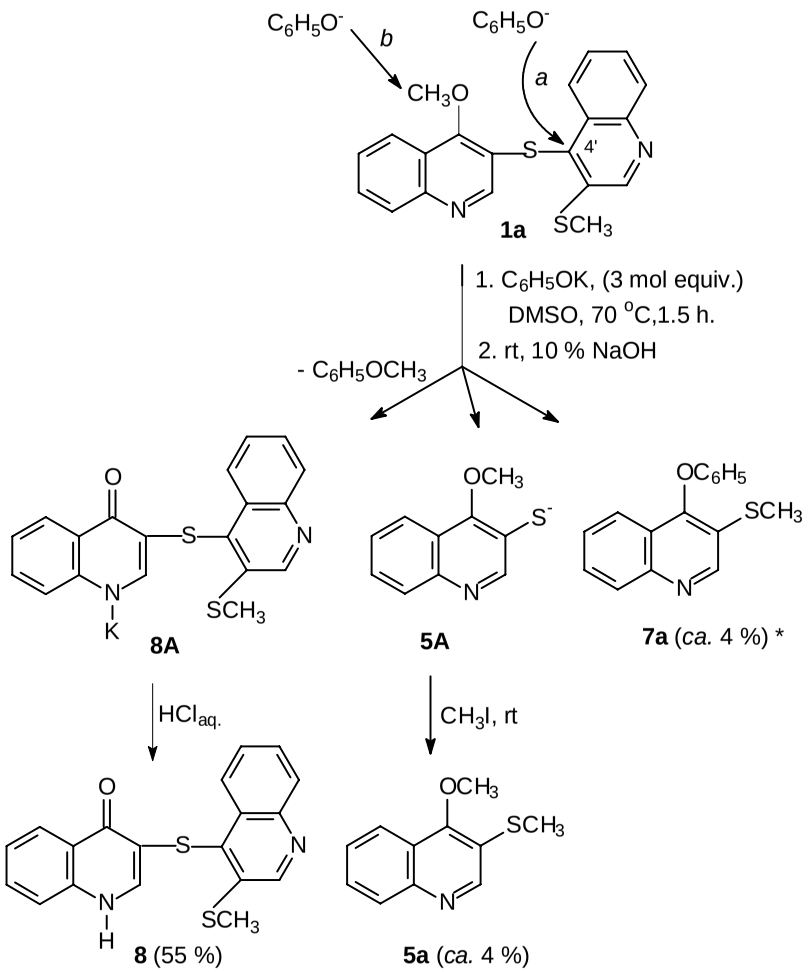
Scheme 1



RESULTS AND DISCUSSION

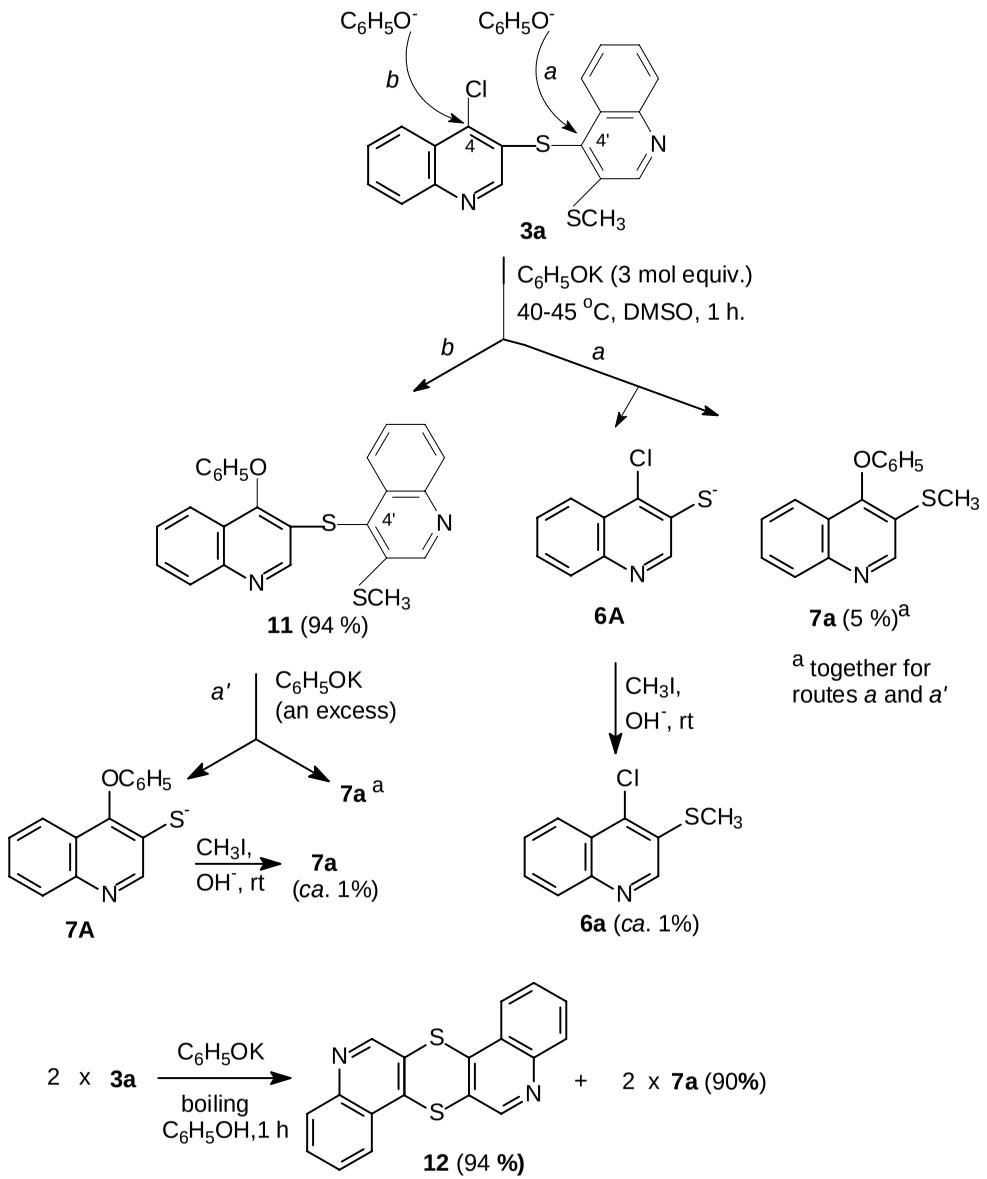
The cleavage of 4-methoxy-3'-alkylsulfinyl 3,4'-diquinolinyl sulfides (**2**) with sodium methoxide proceeded smoothly and gave the expected final products: 4-methoxy-3-methylsulfanylquinoline (**5a**) and 4-methoxy-3-alkylsulfinylquinolines. [7] However, the same reaction of nitro derivatives (**2b**,**c**) led to a complex mixture. Looking for more selective or milder *O*-nucleophile, we use the reactions of γ-quinolinyl sulfides with potassium phenoxide, although no reaction of thioquinanthrene (**12**) with sodium phenoxide (DMF/ 150 ^{o}C / 5h) was observed. At first, we decided to study the behavior of 3'-methylsulfanyl-3,4'-diquinolinyl sulfides (**1a**) and (**3**) in the reaction with potassium phenoxide, considering them the reference systems for the same treatment of 3'–methylsulfinyl derivatives (**2**) and (**4**) discussed below. It was found that phenoxide anion caused mainly *O*-demethylation of 4-methoxy-3'-methylsulfanyl-3,4'-diquinolinyl sulfide (**1a**) (DMSO, 1.5 h, 70 ^{o}C) to form anisole (40 %) and potassium salts (**8A**), after neutralization characterized as quinolinone (**8**) (55 %) (Scheme 2, route *a*). The competitive pathway (route *b*) leading finally to 4-phenoxy-3-methylsulfanylquinoline (**7a**) and 4-methoxy-3-methylsulfanylquinoline (**5a**) was observed in a much less extend (*ca*. 4 %). The products were accompanied by non-consumed sulfide (**1a**) (36%). As presented in Scheme 3, the action of phenoxide anion converts the molecule of 4-chloro-3'-methylsulfanyl-3,4'-diquinolinyl sulfide (**3**) into 4-phenoxy derivative (**11**) in high yield, the competitive reaction at C4' (route *b*) was observed in *ca*. 5 % only. Attempted *de-chloro-phenoxylation* of 4-chloroquinoline (**3**) with potassium phenoxide in boiling phenol proceeded with the cleavage of 4'-quinolinyl-sulfur bond and led to 4-phenoxy-3-methylsulfanylquinoline (**7a**) and thioquinanthrene (**12**).

Scheme 2



* removed by filtration together with non-consumed substrate (**1a**) (36 %)

Scheme 3



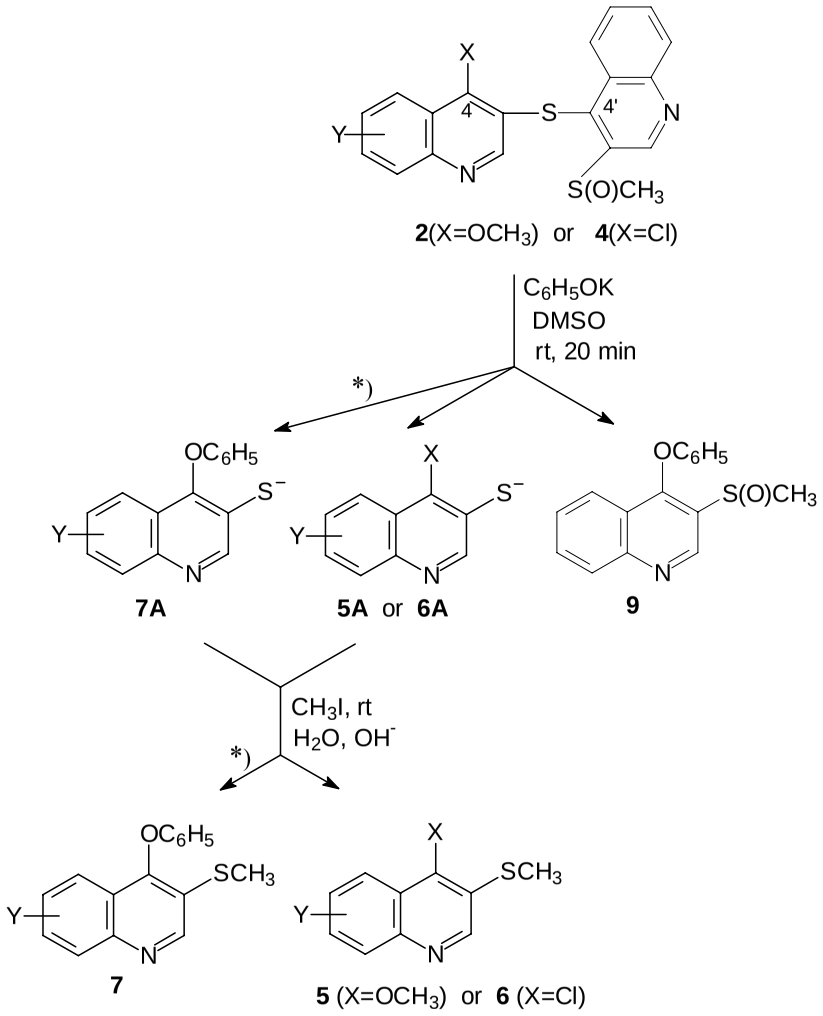
Literature review reveals that the sulfinyl group activates the nucleophilic aromatic substitution in the *ortho* and *para* positions, [7-10] therefore the action of phenoxide anion towards 3'-methylsulfinyl-3,4'-diquinolinyl sulfides (**2a,b**,**c**) and (**4a**,**b**,**d**) should cause the expected *phenoxy-desulfidation* at γ-quinolinyl-sulfur C4' bonds, as discussed in details below. (Scheme 4)

In the case of 4-methoxy-3'-methylsulfinyl derivative (**2a**) (3 mol equiv. of potassium phenoxide, DMSO, rt, 20 min) the reaction ran in a typical fashion to form 4-phenoxy-3-methylsulfinylquinoline (**9**) and 4-methoxy-3-quinolinethiolate (**5A**). After dilution with aqueous sodium hydroxide, the neutral compound (**9**) was isolated by filtration or extraction, but thiolate (**5A**) was trapped by methylation to **5a**. The same treatment of the mixture of nitro derivatives (**2b**) and (**2c**) afforded the mixture of 6- and 8-nitro-4-methoxy-3-methylsulfanylquinolines (**5c**) and (**5d**). The latter was easier separated by chromatography than the starting mixture of 6- and 8-nitro-4-methoxy-3,4'-diquinolinyl sulfides (**2b**) and (**2c**).

When the mixture of 4-chloro-5-nitro- and 4-chloro-8-nitrodiquinolinyl sulfides (**4b**) and (**4d**) was treated with potassium phenoxide (2-4 mol equiv.) (DMSO, rt), an exothermic reaction was observed. The neutral product (**9**) was isolated as above, but after methylation of the aqueous DMSO layer the mixture of 4-chloro-5-nitro- and 4-chloro-8-nitro-3-methylsulfanylquinolines (**6b**) and (**6d**) and 4-phenoxy-5- and 8-nitro-3-methylsulfanylquinolines (**7b**) and (**7d**) was obtained. Its composition could be evaluated by means of ^{1}H NMR spectra based on the intensity of H-2 and CH_3S proton signals. We were able to divide this mixture by chromatography only into the fraction with higher Rf value [8-nitro isomers (**6d**) and (**7d**)] and the fraction with lower Rf value [5-nitro isomers (**6b**) and (**7b**)] but not to individual components. To simplify the composition of mixture of nitro-3-methylsulfanylquinolines (**6**) and (**7**), the mixture was subjected to the reaction with potassium phenoxide (DMSO, 40 ºC, 0.5 h). It caused the *phenoxy-de-chlorination* of 4-chloroquinolines (**6b**) and (**6d**) to 4-phenoxyquinolines (**7b**) and (**7d**) and converted the starting four-component mixture into the two-component mixture of 4-phenoxyquinolines (**7b**) and (**7d**). The latter could be separated by chromatography into individual compounds (**7b**) and (**7d**).

In search for 4-chloro-3-methylsulfanyl-8-nitroquinoline (**6d**) we treated 4-methoxyquinoline (**5d**) with phosphorous oxychloride which gave the expected 4-chloroquinoline (**6d**) (88 %). (Scheme 5) Furthermore, the reaction of **6d** with potassium phenoxide afforded 3-methylsulfanyl-4-phenoxy-8-nitroquinoline (**7d**) (89 %). Similar reaction sequence permits to synthesize the 6-nitro isomers (**6c**) and (**7c**). The identification of 4-chloro-5-nitro-3-methylsulfanylquinoline (**6b**) was troublesome. Attempted hydrolysis of **6b** in the mixture with **7b** with hot hydrobromic acid failed. However, treatment of the mixture of **6b** and **7b** (i.e. the above-mentioned fraction with lower Rf value) with boiling 80% acetic acid caused hydrolysis of 4-chloroquinoline (**6b**) to 4-quinolinone (**10b**) leaving 4-phenoxyquinoline (**7b**) unaffected. It allows isolation of 5-nitro-3-methylsulfanyl-4(1*H*)-quinolinone (**10b**) which was chlorinated with phosphorous oxychloride to 4-chloro-5-nitroquinoline (**6b**). All interconversions among

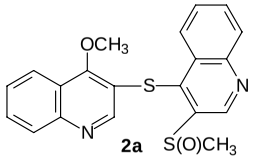
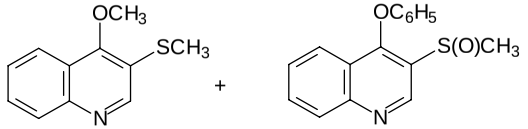
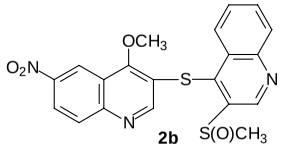
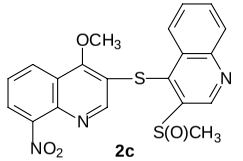
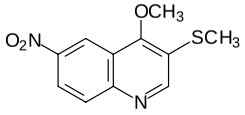
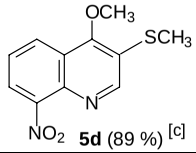
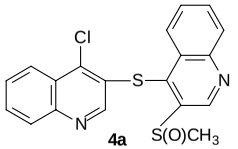
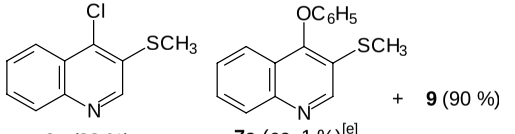
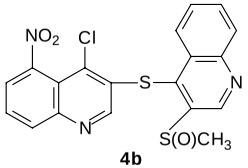
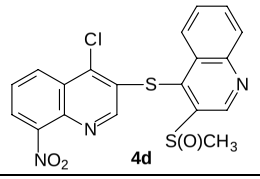
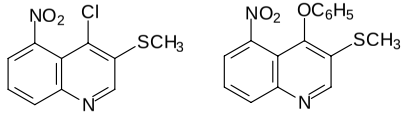
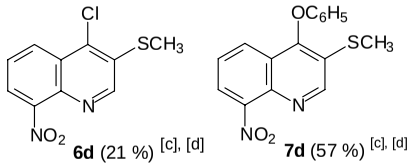
Scheme 4



Y = H, 5-NO_2, 6-NO_2 or 8-NO_2, for details see Table.

*) for 4-chloro compounds (**4**) only

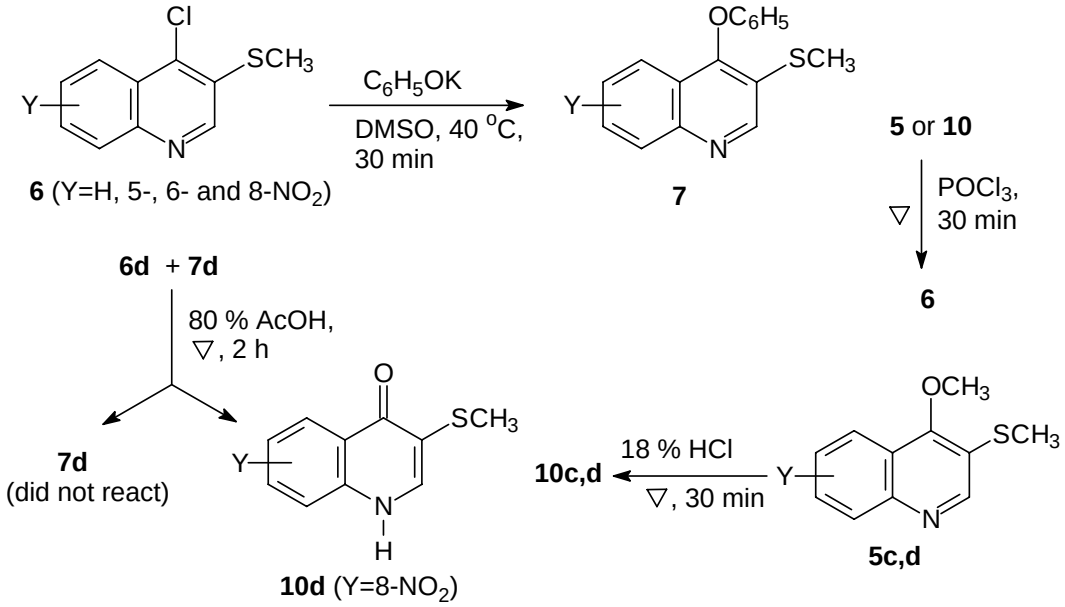
Table. Preparation of 4-substituted 3-methylsulfanylquinolines (**5**, **6**, **7**) from 3'-methylsulfinyl-3,4'-diquinolinyl sulfides (**2**) or (**4**)

No	Substrate(s)	Products, yield [%]
1	 **2a**	 **5a** (87 %) + **9** (88 %)
2 [a]	 **2b**  **2c**	 **5c** (87 %) [c] + **9** (92 %)  **5d** (89 %) [c]
3	 **4a**	 **6a** (88 %) **7a** (*ca.* 1 %)[e] + **9** (90 %)
4 [b]	 **4b**  **4d**	 **6b** (56 %) [c], [d] **7b** (30 %) [c], [d] + **9** (91 %)  **6d** (21 %) [c], [d] **7d** (57 %) [c], [d]

[a] Mixture of **2b** and **2c** in the ratio 3:2 was used. [b] Mixture of **4b** and **4d** in the ratio 2:1 was used. [c] Yield was calculated with respect to the content of 5-, 6- or 8-nitro isomer in the starting mixture. [d] The ratio **6b** : **6d** : **7b** : **7d** ~ 1.96 : 0.36 : 1.05 : 1 was evaluated by means of ^{1}H NMR spectra based on the intensity of H-2 and CH_3S proton signals. [e] Detected in mother liquor after recrystallization of **6a**.

4-substituted 3-methylsulfanylquinolines (**5**), (**6**), (**7**) and (**10**) were collected in Scheme 5.

S c h e m e 5



CONCLUSIONS

The molecules of 4-substituted 3'-methylsulfanyl- and 3'-methylsulfinyl-3,4'-diquinolinyl sulfides (**1** ,**2**, **3**, **4**) contain two *aza*-activated bonds at γ-quinolinyl carbons C4 and C4' both formally being susceptible to the action of nucleophile. Contrary to the reactions with alkoxide anions, [2] the reaction of phenoxide anion with 3'-methylsulfanyl derivatives (**1**) and (**3**) takes place mainly at the substituent at C4 to give potassium salt of 4(1*H*)-quinolinone (**8A**) or 4-phenoxy derivative (**11**), respectively. In both reactions (Schemes 2 and 3) the skeleton of 3,4'-diquinolinyl sulfide remains almost unaffected.

Due to the strong electron attracting properties, the 3'-methylsulfinyl substituent significantly activates the nucleophilic displacement at the *ortho* position and therefore C4' quinolinyl-sulfur bond in 3'-methylsulfinyl derivatives (**2**) and (**4**) appears to be more sensitive to the action of potassium phenoxide. It led to the splitting of the skeleton of 3,4'-diquinolinyl sulfide in the molecules of compounds (**2**) and (**4**) to 4-phenoxy-3-methylsulfinylquinoline (**9**) and 4-substituted 3-quinolinethiolates (**5A**, **6A** or **7A**), trapped by methylation to form of 4-substituted 3-methylsulfanylquinolines (**5a**), (**6a**) and (**7a**) or their 5-, 6- and 8-nitroderivatives (**5b,c**), (**6b,d**) and (**7b,d**).

EXPERIMENTAL

Melting points were taken in open capillary tubes and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker spectrometer at 400 MHz in deuterochloroform or in hexadeuterodimethyl sulfoxide solutions with tetramethylsilane (δ 0.0 ppm) as internal standard. EI MS spectra were determined on a Finnigan Mat 95 spectrometer at 70 eV and at a temperature of 80-100 °C. IR spectra were recorded with a Magma – IR 500 (Nicolet) spectrometer in potassium bromide pellets. TLC analyses were performed employing

Merck's silicagel 60 F_{254} plates and a solution of chloroform-ethanol (19 : 1, v/v) as an eluent (system I) or Merck's aluminium oxide 60 F_{254} neutral (type E) plates using mixture of chloroform - ethanol (19 : 1, or 10 : 1, v/v) as an eluent (system II).

Potassium phenoxide was prepared from potassium hydroxide and phenol according to the reported data. [11] 4-Substituted 3'-methylsulfanyl-3,4'-diquinolinyl sulfides (**1a**) (R=CH_3), [2] (**3a**) (R=CH_3) [6] and 6- and 8- or 5- and 8-nitro-3'-methylsulfinyl-3,4'-diquinolinyl sulfides (**2b**) + (**2c**) [4] and (**4b**) +(**4d**) [5] were prepared as described previously. The crude mixture (**2b**) + (**2c**) or (**4b**) +(**4d**) (1 g) was purified by dissolution in hot chloroform (10 mL), hot filtration of the insoluble material and evaporation of the solvent. In this form the above mixture exhibited mainly the presence of nitro isomers (**2b**) + (**2c**) or (**4b**) +(**4d**), and was used in the reactions with potassium phenoxide.

Reaction of 4-methoxy-3'-methylsulfanyl-3,4'-diquinolinyl sulfide (**1a**) with potassium phenoxide

A mixture of 3,4'-diquinolinyl sulfide (**1a**) (1.09 g, 3 mmol), 1.21 g (9 mmol) of potassium phenoxide and 15 mL of DMSO was stirred at 70 ^{o}C for 1.5 h and then cooled down to rt. It was next poured into 30 mL of 5% aqueous sodium hydroxide. The solid was filtered off, washed with water and dried on air. It was then separated by chromatography (SiO_2, chloroform : ethanol, 30 : 1, v/v) to give 0.4 g (36.7 %) of the non-converted substrate (**1a**) and 0.032 g (4 %) of 4-phenoxy-3-methylsulfanylquinoline (**7a**).

The filtrate was extracted with ether (3 x 10 mL), the extracts were dried with sodium sulfate and finally concentrated to give 0.13 g (40 %) of anisole. The alkaline aqueous DMSO layer was methylated on stirring with 0.06 mL (1 mmol) of methyl iodide within 30 min. The mixture was extracted with chloroform (3 x 5 mL), the extracts were dried with sodium sulfate. The solvent was distilled off and the residual volatile material was removed from boiling water bath under vacuum to give the oily material containing mainly 4-methoxy-3-methylsulfanylquinoline (**5a**) (0.025 g, *ca.* 4 %).

The aqueous DMSO layer was neutralized with 10 % hydrochloric acid at rt to precipitate 0.58 g (55 %) of quinolinone (**8a**) with mp 278-280 ^{o}C (DMF), lit., [2] mp 278-280 ^{o}C.

Reaction of 4-chloro-3'-methylsulfanyl-3,4'-diquinolinyl sulfide (**3a**) with potassium phenoxide

a) in DMSO solution leading to 4-phenoxy-3'-methylsulfanyl-3,4'-diquinolinyl sulfide (**11**)

A solution of sulfide (**3a**) in DMSO was prepared by heating sulfide (**3a**) (1.1 g, 3 mmol) in DMSO (15 mL) at 70 ^{o}C for 15 min. It was then cooled down to 40 ^{o}C. In the same manner was prepared the solution of potassium phenoxide (1.2 g, 9 mmol) in DMSO (4 mL). A solution of potassium phenoxide was added into the solution of sulfide (**3a**) and the mixture was stirred at 40-45 ^{o}C for 1 h. It was then cooled down to rt and poured into 60 mL of 15 % aqueous sodium hydroxide. The solid was filtered off, triturated with 2 mL of cold ethanol and dried on air to give the crude product. It was recrystallized from benzene to give

1.15 g (90 %) of pure 4-phenoxy-3'-methylsulfanyl-3,4'-diquinolinyl sulfide (**11**) with mp 130-132 °C. Mother liquors were concentrated to dryness, the residue was subjected to chromatographic separation (SiO_2, chloroform : ethanol, 30:1, v/v) which gave 4-phenoxy-3-methylsulfanylquinoline (**7a**) (40 mg, 5%) and sulfide (**11**) (55 mg, 4 %).

Aqueous DMSO filtrate was methylated with 0.03 mL (0.5 mmol) of methyl iodide to give 20 mg of the mixture of 4-chloro-3-methylsulfanylquinoline (**6a**) and 4-phenoxy-3-methylsulfanylquinoline (**7a**) in the ratio 1 : 1 as concluded from the ^{1}H NMR spectra.

b) in boiling phenol

A mixture of 4-chloro-3'-methylsulfanyl-3,4'-diquinolinyl sulfide (**3a**) (370 mg, 1 mmol), potassium phenoxide (130 mg, 1 mmol) and 600 mg of phenol was stirred at 185 °C for 6 h. It was then cooled to rt and treated with 25 mL of 5 % aqueous sodium hydroxide. The resulting mixture was stirred with 25 mL of methylene chloride for 10 min and the solid [thioquinanthrene (**12**)]) was filtered off. The solid was washed with water and dried on air to give 150 mg (94 %) of the chromatographically homogenous yellow material with mp 314-315 °C being identical with thioquinanthrene (**12**), lit., [1] mp 314-315 °C.

The filtrate was separated and the organic layer was dried over sodium sulfate. The solvent was removed to give 240 mg (90 %) of 4-phenoxy-3-methylsulfanylquinoline (**7a**) with mp 136-138 °C.

Synthesis of 4-phenoxy-3-methylsulfanylquinoline (**7a**) from 4-chloro-3-methylsulfanylquinoline (**6a**) in boiling phenol

A mixture of 4-chloro-3-methylsulfanylquinoline (**6a**) (210 mg, 1 mmol), potassium phenoxide (130 mg, 1 mmol) and 360 mg of phenol was stirred at 185 °C for 2 h. It was then cooled down to rt, treated with 15 mL of 5 % aqueous sodium hydroxide and the mixture was stirred with 15 mL of methylene chloride for 5 min. Organic layer was separated and dried over sodium sulfate. The solvent was distilled off to give 267 mg of 4-phenoxy-3-methylsulfanylquinoline (**7a**) with mp 133-135 °C. It was recrystallized from ethanol to give pure product (**7a**) (96 %).

The same treatment of 8-nitro-4-chloro-3-methylsulfanylquinoline (**6d**), or the mixture of **6b**, **6d**, **7b**, **7d** led to black insoluble polymeric products accompanied by some amounts of non-converted substrates.

4-Phenoxy-3-methylsulfanylquinoline (**7a**)

mp 139-140 °C (ethanol). EIMS (70 eV) (m/z): 267 (M^+, 100). ^{1}H NMR ($CDCl_3$), δ: 2.54 (s, 3H, CH_3), 6.83-6.87 (m, 2H, $H_{ortho\text{-phenyl}}$), 7.06-7.11 (m, 1H, $H_{para\text{-phenyl}}$), 7.28-7.33 (m, 2H, $H_{meta\text{-phenyl}}$), 7.50-7.55 (m, 1H, H_{arom}), 7.70-7.76 (m, 1H, H_{arom}), 7.90-7.94 (m, 1H, H_{arom}), 8.22-8.25 (m, 1H, H_{arom}), 8.93 (s, 1H, H-2). *Anal.* Calcd for $C_{16}H_{13}NOS$: C 71.88; H 4.90; N 5.24; S 11.99. Found: C 71.72; H 5.04; N 5.11; S 11.64.

4-Phenoxy-3'-methylsulfanyl-3,4'-diquinolinyl sulfide (**11**)

mp 134-135 °C (ethanol). ^{1}H NMR ($CDCl_3$), δ: 2.58 (s, 3H, CH_3), 6.70-6.73 (m, 2H, $H_{ortho\text{-phenyl}}$), 7.02-

7.06 (m, 1H, $H_{para\text{-phenyl}}$), 7.19-7.24 (m, 2H, $H_{meta\text{-phenyl}}$), 7.42-7.51 (m, 2H, $H_{arom.}$), 7.60-7.67 (m, 2H, $H_{arom.}$), 7.79-7.82 (m, 1H, $H_{arom.}$), 8.03-8.06 (m, 2H, $H_{arom.}$), 8.27-8.29 (m, 1H, $H_{arom.}$), 8.43 (s, 1H, H-2'), 8.73 (s, 1H, H-2). *Anal.* Calcd for $C_{25}H_{18}N_2OS_2$: C 70.40, H 4.25, N 6.57, S 15.03. Found: C 70.25, H 4.20, N 6.67, S 14.93.

Reaction of 4-substituted 3'-methylsulfinyl-3,4'-diquinolinyl sulfides (**2** or **4**) with potassium phenoxide

3,4'-Diquinolinyl sulfide (1 mmol) (**2a**) or (**4a**) or a mixture of 3,4'-diquinolinyl sulfides (**2b**,**2c**) or (**4b**,**4d**) (total amount, 1 mmol) was added at rt to 8 mL of DMSO and then on stirring, 0.4 g (3 mmol) of potassium phenoxide was introduced in one portion. The mixture was stirred for 20 min at rt and then poured into 15 mL of 5% aqueous sodium hydroxide.

4-Phenoxy-3-methylsulfinylquinoline (**9**) was filtered off. The residual part of **9** was extracted with chloroform (3 x 5 mL). The solid and extracts were combined, the solution was dried with sodium sulfate. The solvent was then distilled off to give crude **9**. It was recrystallized from ethanol.

Aqueous DMSO solution was methylated on stirring (30 min) with 0.066 mL (1.1 mmol) of methyl iodide. 4-Methoxy-3-methylsulfanylquinoline (**5a**) was extracted with chloroform (3 x 5 mL) and then isolated and purified as described previously. [6]

The precipitates containing the mixtures of 3-methylsulfanylquinolines: [(**5c**) + (**5d**)], [(**6a**) +(**7a**)] and [(**6b**) + (**6d**) + (**7b**) + (**7d**)] [for details see Table] were filtered off and air-dried to give the first crop (*ca.* 200-220 mg) of the products. The filtrates were extracted with chloroform (2 x 5 mL). The extracts were treated in a typical manner to give the second crop (~20 mg) of the mixture of 3-methylsulfanyl quinolines mentioned above. Both crops were combined and subjected to chromatographic separation (SiO_2, chloroform : ethanol, 30 : 1, v/v). The mixture of 4-methoxyquinolines (**5c**) + (**5d**) [Table, No. 2] could be separated into individual components.

Chromatographic separation (SiO_2, chloroform : ethanol, 50:1, v/v) of the mixture of 4-chloroquinolines (**6b**, **6d**) and 4-phenoxyquinolines (**7b**, **7d**) [Table, No. 4] gave only the fraction with higher Rf value [8-nitro isomers (**6d**) and (**7d**)] and the fraction with lower Rf value [5-nitro isomers (**6b**) and (**7b**)].

4-Phenoxy-3-methylsulfinylquinoline (**9**)

mp 111-113 ^oC (ethanol). ^1H NMR ($CDCl_3$), δ: 2.87 (s, 3H, CH_3), 6.87-6.89 (m, 2H, $H_{ortho\text{-phenyl}}$), 7.11-7.15 (m, 1H, $H_{para\text{-phenyl}}$), 7.31-7.35 (m, 2H, $H_{meta\text{-phenyl}}$), 7.51-7.55 (m, 1H, H_{arom}), 7.80-7.84 (m, 1H, H_{arom}), 7.84-7.86 (m, 1H, H_{arom}), 8.24-8.26 (m, 1H, H_{arom}), 9.41 (s, 1H, H-2). IR (KBr pellet): ν_{SO}=1060 cm^{-1}. *Anal.* Calcd for $C_{16}H_{13}NO_2S$: C 67.84; H 4.59; N 4.95; S 11.30. Found: C 67.72; H 5.04; N 5.01; S 11.02.

4-Methoxy-3-methylsulfanyl-6-nitroquinoline (**5c**)

mp 162-163 ^oC (ethanol). ^1H NMR ($CDCl_3$), δ: 2.61 (s, 3H, SCH_3), 4.24 (s, 3H, OCH_3), 8.17 (d, 1H,

J=9.2 Hz, H-8), 8.42 (d, 1H, *J*=2.5 Hz, H-7), 8.96 (s, 1H, H-2), 9.04 (d, 1H, *J*=9.2 Hz, H-5). *Anal.* Calcd for $C_{11}H_{10}N_2O_3S$: C 52.79; H 4.03; N 11.19; S 12.81. Found: C 52.42; H 4.14; N 11.49; S 12.82.

4-Methoxy-3-methylsulfanyl-8-nitroquinoline (**5d**)

mp 78-79 °C (ethanol). ^{1}H NMR ($CDCl_3$), δ: 2.60 (s, 3H, SCH_3), 4.15 (s, 3H, OCH_3), 7.61 (dd, 1H, *J*=7.5 Hz, *J*=8.5 Hz, H-6), 7.99 (dd, 1H, *J*=7.5 Hz, *J*=1.3 Hz, H-7), 8.30 (dd, 1H, *J*=8.4 Hz, *J*=1.3 Hz, H-5), 8.95 (s, 1H, H-2). *Anal.* Calcd for $C_{11}H_{10}N_2O_3S$: C 52.79; H 4.03; N 11.19; S 12.81. Found: C 52.76; H 4.05; N 11.97; S 13.09.

Preparation of 3-methylsulfanyl-4-phenoxyquinolines (**7a**, **7b**, **7c**, **7d**) from 4-chloro-3-methylsulfanylquinolines (**6a**, **6b**, **6c**, **6d**) and potassium phenoxide in DMSO solution

A mixture of 4-chloroquinoline (**6**) (1 mmol) and 10 mL of DMSO was heated up to 40 °C and then 0.13 g (1 mmol) of potassium phenoxide was added. The mixture was strirred for 0.5 h at 40 °C. It was then cooled down to rt and poured into 5 % aqueous sodium hydroxide (10 mL). Phenoxyquinoline (**7**) was extracted with methylene chloride (3 x 5 mL). The extracts were dried with sodium sulfate and then the solvent was evaporated to give almost quantitatively 3-methylsulfanyl-4-phenoxyquinolines (**7**). Crude (**7**) was recrystallized from ethanol.

This procedure was applied for the transformation of the mixture of 5- and 8-nitro-4-chloro-3-methylsulfanylquinolines (**6b**), (**6d**) and 5- and 8-nitro-3-methylsulfanyl-4-phenoxyquinolines (**7b**), (**7d**) to the mixture of 5- and 8-nitro-3-methylsulfanyl-4-phenoxyquinolines (**7b**), (**7d**). The mixture of **7b** and **7d** was separated by column chromatography (SiO_2, chloroform ethanol, 50 : 1, v/v) into individual components.

3-Methylsulfanyl-5-nitro-4-phenoxyquinoline (**7b**)

mp 139-141 °C (ethanol). ^{1}H NMR ($CDCl_3$), δ: 2.51 (s, 3H, SCH_3), 6.79-6.81 (m, 2H, $H_{ortho\text{-phenyl}}$), 7.09-7.13 (m, 1H, $H_{para\text{-phenyl}}$), 7.28-7.32 (m, 2H, $H_{meta\text{-phenyl}}$), 7.62-7.64 (dd, 1H, *J*=7.5 Hz, *J*=1.1 Hz, H-6), 7.69-7.73 (dd, 1H, *J*=7.5 Hz, *J*=8.4 Hz, H-7), 8.27-8.29 (dd, 1H, *J*=8.4 Hz, *J*=1.1 Hz, H-8), 8.96 (s, 1H, H-2). *Anal.* Calcd for $C_{16}H_{12}N_2O_3S$, C 61.53, H 3.87, N 8.97, S 10.26. Found: C 61.52; H 3.71; N 8.66; S 10.09.

3-Methylsulfanyl-6-nitro-4-phenoxyquinoline (**7c**)

mp 167-169 °C (ethanol). ^{1}H NMR ($CDCl_3$), δ: 2.57 (s, 3H, SCH_3), 6.85-6.88 (m, 2H, $H_{ortho\text{-phenyl}}$), 7.11-7.15 (m, 1H, $H_{para\text{-phenyl}}$), 7.31-7.35 (m, 2H, $H_{meta\text{-phenyl}}$), 8.24-8.26 (d, 1H, *J*=9.2 Hz, H-8), 8.41-8.44 (dd, 1H, *J*=9.2 Hz, *J*=2.5 Hz, H-7), 8.85-8.86 (d, 1H, *J*=2.5 Hz, H-5), 9.05 (s, 1H, H-2). *Anal.* Calcd for $C_{16}H_{12}N_2O_3S$, C 61.53, H 3.87, N 8.97, S 10.26. Found: C 61.45; H 3.72; N 8.76; S 10.10.

3-Methylsulfanyl-8-nitro-4-phenoxyquinoline (**7d**)

mp 93-94 °C (ethanol). ^{1}H NMR ($CDCl_3$), δ: 2.57 (s, 3H, SCH_3), 6.82-6.84 (m, 2H, $H_{ortho\text{-phenyl}}$), 7.09-7.12 (m, 1H, $H_{para\text{-phenyl}}$), 7.29-7.34 (m, 2H, $H_{meta\text{-phenyl}}$), 7.52-7.56 (dd, 1H, *J*=7.5 Hz, *J*=8.5 Hz, H-6), 7.97-

7.99 (dd, 1H, *J*=7.5 Hz, *J*=1.3 Hz, H-7), 8.09-8.11 (dd, 1H, *J*=8.5 Hz, *J*=1.3 Hz, H-5), 9.04 (s, 1H, H-2). *Anal.* Calcd for $C_{16}H_{12}N_2O_3S$: C 61.53, H 3.87, N 8.97, S 10.26. Found: C 61.33, H 3.80, N 8.78, S 9.97.

4-Chloro-3-methylsulfanyl-6- or 8-nitroquinolines (**6b**), (**6d**) from 4-methoxy-6- or 8-nitro-3-methylsulfanylquinolines (**5b**), (**5d**)

A mixture of 4-methoxyquinoline (**5**) (0.25 g, 1 mmol), 0.2 g (1.5 mmol) of triethylamine hydrochloride and 2 mL (63 mmol) of phosphorus oxychloride was boiled for 0.5 h and then cooled to rt. The mixture was then treated with ice (12 g) and then neutralized with ammonia. The solid was filtered off, dried on air and recrystallized from ethanol to give 4-chloroquinoline (**6**) (0.24 g, 94 %).

The same procedure was applied for the transformation of 5-nitro-3-methylsulfanyl-4(1*H*)-quinolinone (**10b**) to 4-chloro-3-methylsulfanyl-5-nitroquinoline (**6b**).

4-Chloro-3-methylsulfanyl-5-nitroquinoline (**6b**)

mp 148-150 °C (ethanol). ^{1}H NMR ($CDCl_3$), δ: 2.71 (s, 3H, SCH_3), 7.69 (dd, 1H, *J*=7.5 Hz, *J*=8.3 Hz, H7), 7.76 (dd, 1H, *J*=7.5 Hz, *J*=1.3 Hz, H-6), 8.26 (dd, 1H, *J*=8.3 Hz, *J*=1.3 Hz, H-8), 8.82 (s, 1H, H-2). *Anal.* Calcd for $C_{10}H_7N_2O_2ClS$: C 47.16; H 2.77; N 11.00; S 12.59. Found: 46.95; H 2.81; N 10.87; S 12.39.

4-Chloro-3-methylsulfanyl-6-nitroquinoline (**6c**)

mp 164-166 °C (ethanol). ^{1}H NMR ($CDCl_3$), δ: 2.73 (s, 3H, SCH_3), 7.74-7.76 (d, 1H, *J*=9.2 Hz, H-8), 8.42-8.45 (dd, 1H, *J*=9.2 Hz, *J*=2.5 Hz, H-7), 8.96 (s, 1H, H-2), 9.11-9.12 (d, 1H, *J*=2.5 Hz, H-5). *Anal.* Calcd for $C_{10}H_7N_2O_2ClS$: C 47.16; H 2.77; N 11.00; S 12.59. Found: C 47.01; H 2.59; N 10.85; S 12.37.

4-Chloro-3-methylsulfanyl-8-nitroquinoline (**6d**)

mp 142-144 °C (ethanol). ^{1}H NMR ($CDCl_3$), δ: 2.70 (s, 3H, SCH_3), 7.70 (dd, 1H, *J*=7.6 Hz, *J*=8.5 Hz, H6), 7.99 (dd, 1H, *J*=7.5 Hz, *J*=1.1 Hz, H-7), 8.39 (dd, 1H, *J*=8.5 Hz, *J*=1.1 Hz, H-5), 8.89 (s, 1H, H-2). *Anal.* Calcd for $C_{10}H_7N_2O_2ClS$: C 47.16; H 2.77; N 11.00; S 12.59. Found: C 46.98; H 2.67; N 10.91; S 12.40.

3-Methylsulfanyl-5-nitro-4(1*H*)-quinolinone (**10b**)

A mixture of 5-nitro-4-chloroquinoline (**6b**) and 4-phenoxy-5-nitroquinoline (**7b**) (0.33 g) [from chromatographic separation of the mixture of **6b**, **6d**, **7b** and **7d**] and 2 mL of 80% acetic acid was boiled for 3 h. After 45 min precipitation of yellow solid was observed. The volatile compounds were evaporated from water-bath under vacuum, then 2 mL of water was added and evaporated as above to dryness. The mixture was cooled down to rt and triturated with 2 mL of 5% aqueous sodium bicarbonate. The solid was filtered off, washed with water and dried on air. It was then boiled with chloroform (2 mL). Insoluble nitro-4-quinolinone (**10b**) was filtered off on hot and recrystallized from ethanol. Chloroform extract was concentrated to dryness to give 3-methylsulfanyl-5-nitro-4-phenoxyquinoline (**7b**) accompanied by small amount of 4-quinolinone (**10b**).

3-Methylsulfanyl-5-nitro-4(1*H*)-quinolinone (**10b**)

mp 300 °C (decomp). ^{1}H NMR (DMSO-d_6), δ: 2.33 (s, 3H, SCH_3), 7.53-7.55 (dd, 1H, *J*=7.1 Hz, *J*=0.9 Hz, H-6), 7.73-7.78 (dd, 1H, *J*=7.1 Hz, *J*=8.4 Hz, H-7), 7.79 (dd, 1H, *J*=8.4 Hz, *J*=0.9 Hz, H-8), 8.04 (s, 1H, H-2), 12.5 (br, 1H, N-H). *Anal.* Calcd for $C_{10}H_8N_2O_3S$: C 50.84; H 3.41; N 11.86; S 13.57. Found: C 50.75; H 3.24; N 11.80; S 13.35.

3-Methylsulfanyl-6-nitro-4(1*H*)-quinolinone (**10c**)

mp 300 °C (decomp). ^{1}H NMR (DMSO-d_6), δ: 2.37 (s, 3H, SCH_3), 7.74-7.76 (d, 1H, *J*=9.2 Hz, H-8), 8.01 (s, 1H, H-2), 8.38-8.41 (dd, 1H, *J*=9.2 Hz, *J*=2.6 Hz, H-7), 8.85-8.86 (d, 1H, *J*=2.6 Hz, H-5), 12.59 (br, 1H, N-H). *Anal.* Calcd for $C_{10}H_8N_2O_3S$: C 50.84; H 3.41; N 11.86; S 13.57. Found: C 50.69; H 3.34; N 11.79; S 13.29.

3-Methylsulfanyl-8-nitro-4(1*H*)-quinolinone (**10d**)

mp 230-235 °C (decomp). ^{1}H NMR (DMSO-d_6), δ: 2.35 (s, 3H, SCH_3), 7.53-7.55 (dd, 1H, *J*=8.0 Hz, *J*=8.0 Hz, H-6), 7.88-7.80 (d, 1H, *J*=6.1 Hz, H-2), 8.58-8.60 (d, *J*=8.0 Hz, H-5 or H-7), 8.66-8.68 (d, *J*=8.0 Hz, H-5 or H-7), 12.08 (br, 1H, N-H). *Anal.* Calcd for $C_{10}H_8N_2O_3S$: C 50.84; H 3.41; N 11.86; S 13.57. Found: C 50.68; H 3.21; N 11.71; S 13.37.

REFERENCES

Part LXXXV in the Series of Azinyl Sulfides

1. A. Maślankiewicz, *Polish J. Chem.*, 1985, **59**, 511.
2. A. Maślankiewicz and S. Boryczka, *Rec. Trav. Chim. Pays-Bas*, 1993, **112**, 519.
3. E. Bębenek, E. Chrobak, and A. Maślankiewicz, *Heterocycles*, 2003, **60**, 2065.
4. M. J. Maślankiewicz and A. Maślankiewicz, *J. Heterocycl. Chem.*, 1996, **33**, 1153.
5. M. J. Maślankiewicz, *J. Heterocycl. Chem.*, 2000, **37**, 697.
6. A. Maślankiewicz and S. Boryczka, *J. Heterocycl. Chem.*, 1993, **30**, 1623.
7. M. Rudnik and A. Maślankiewicz, *Heterocycles*, 1999, **51**, 2731.
8. S. Oae and Y. H. Khim, *Bull. Chem. Soc. Jpn.*, 1967, **40**, 1716.
9. V. Cecchetti, A. Fravolini, R. Fringuelli, G. Mascellani, P. Pagella, M. Palmioli, G. Segre, and P. Terni, *J. Med. Chem.*, 1987, **30**, 465.
10. V. Cecchetti, A. Fravolini, P. Pagella, A. Savino, and O. Tabarrini, *J. Med. Chem.*, 1993, **36**, 3449.
11. P. E. Weston and H. Adkins, *J. Am. Chem. Soc.*, 1928, **50**, 865.