Reactions of 4-Dimethylamino-3-quinolinyl Sulfides with Nitrating Mixture and Transamination of 4-Dimethylamino-3-methylsulfinyl-6-nitroquinoline

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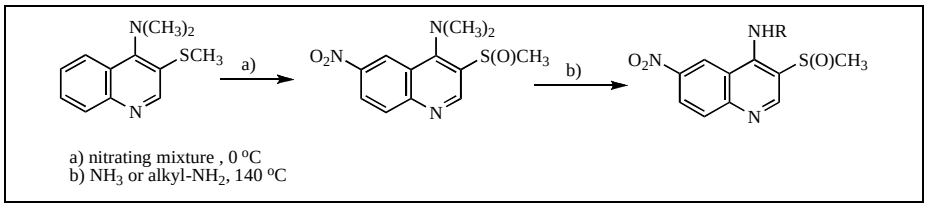

4-Amino-3-quinolinyl sulfides **4d-e** and **7a-c** were prepared by amination of 4-chloro-3-quinolinyl sulfides **4c** or **1c**, respectively, in methanol (140-160 ºC) or in boiling phenol with yields up to 95 %. Reaction of 4-dimethylamino-3-quinolinyl sulfides **7c** and **4e** with nitrating mixture proceeded simultanously as oxidation of the methylthio group to the methylsulfinyl one and as C6-nitration to form 6-nitro-β-quinolinyl sulfoxides **9c** or **10b**, respectively. 4-Dimethylamino-3-methylsulfinyl-6-nitroquinoline **9c** underwent acid catalysed transamination when reacting with primary aliphatic amines and ammonia.

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INTRODUCTION

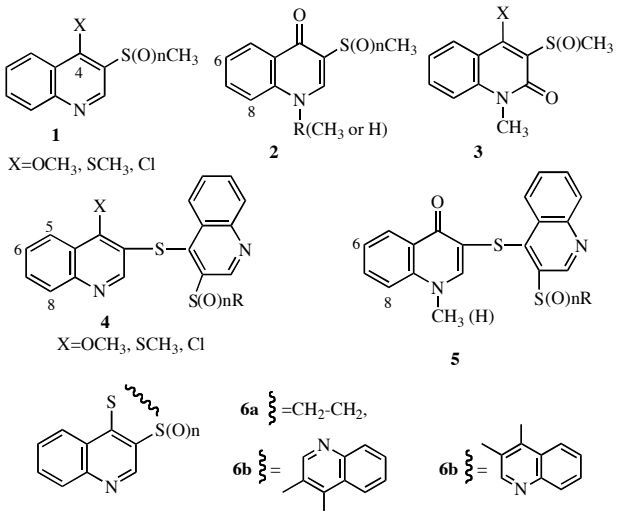
β-Quinolinyl sulfides of types **1-6** (n=0) were previously subjected to reaction with nitrating mixture. In all instances it led primarily to the formation of the respective β-quinolinyl sulfoxides **1-6** (n=1) [1-7]. Under further treatment with nitrating mixture (0-5 °C) some of them (**2-6**, n=1) underwent nitration at the $6_{quinolinyl}$, $8_{quinolinyl}$ [1,3] and even $5_{quinolinyl}$ positions [4], but 4-alkylthio derivatives of type **4** (X=SR) and **3** (X=SCH_3) were oxidized to the respective 4-alkylsulfinylquinolines of type **4** [X=S(O)R] or **3** [X=S(O)R], respectively [6,7] (Scheme 1). However, 4-methoxy- and 4-chloro-3-methylsulfinylquinolines **1**, (n=1) did not undergo any further transformation with nitrating mixture at 0-5 °C.

To complete the set of 4-substituted β-quinolinyl sulfides, we turned to 4-dimethylamino derivatives **7c** and **4e** [X=$N(CH_3)_2$, R=CH_3, n=0]. Treatment with nitrating mixture converted them to β-methylsulfinyl-6-nitro-derivatives **9c**, or **10a** and **10b**, respectively. Even a first insight into the structure of 4-dimethylamino-3-methylsulfinyl-6-nitroquinoline **9c** indicates that 4-dimethylamino substituent is strongly influenced by three electron-withdrawing groups: *endo*cyclic nitrogen-ring atom (*i.e.* by *aza*-activation), *ortho* 3-methylsulfinyl group and 6-nitro qroup [8]. This induced a study on nucleophilic displacement of 4-dimethylamino substituent in **9c** as a source of other 4-aminoquinolines as well as other quinoline derivatives.

RESULTS AND DISCUSSION

Synthesis of 4-amino-β-quinolinyl sulfides (7) and (4e). Direct and indirect *amino-de-chlorination* of

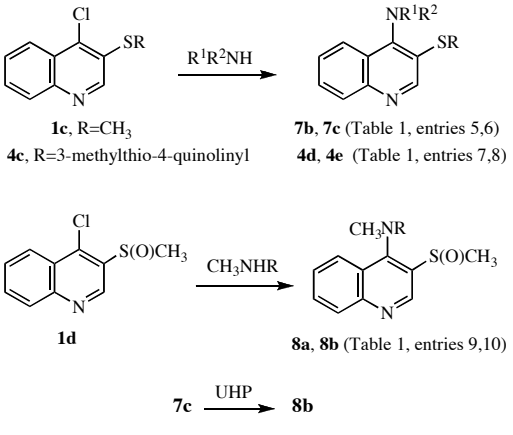
Scheme 1



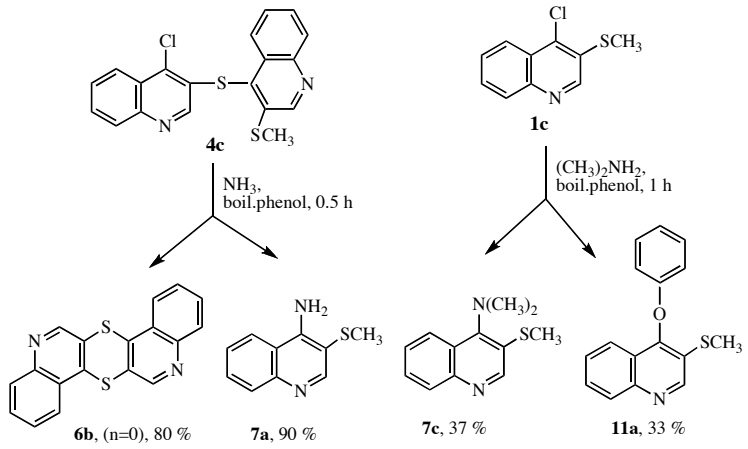
4-chloroquinolines was a matter of broad and numerous studies [9,12] due to potent biological activities of 4-aminoquinolines *e.g.* as antimalarial, [9] antirheumatic and antiinflammatory [10] or antiviral agents [11].

Some of literature indications were applied for preparation of 4-aminoquinolines (**7a**,**b**,**c**) from 4-chloroquinoline (**1c**) (see Schemes 2 and 3, Table 1). Best results with yields up to 95 % were obtained when treating chloroquinoline (**1c**) or (**4c**) with methanolic solution of amine in autoclave (140-160 ºC) in the presence of hydrochloric acid. (Table 1, entries 5-9). As methylsulfinyl group activates the *ortho* chlorine substituent towards nucleophilic displacement, amination of chloro-sulfoxide **1d** to **8a** and **8b** could be effectively

Scheme 2

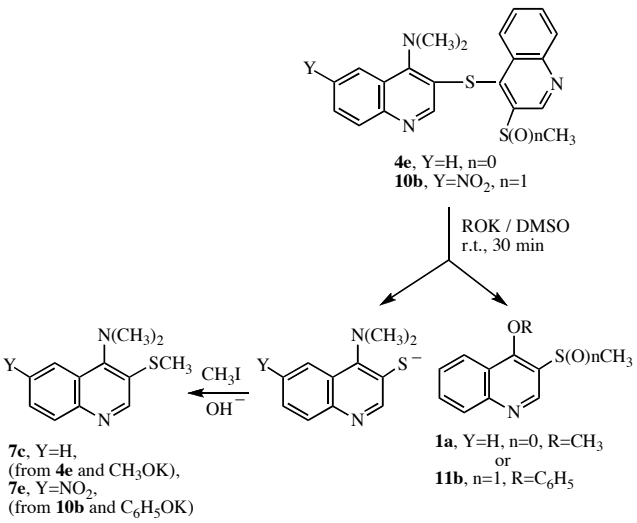


Scheme 3



performed at a lower temperature (Table 1, entries 9 and 10). Amination of 4-chloroquinoline **1c** in boiling phenol with ammonia led to the expected 4-amino-quinoline (**7a**) but that with dimethylamine yielded the 4-dimethyl-aminoquinoline (**7c**), which was accompanied by substantial amounts of 4-phenoxy-3-methylthio-quinoline (**11a**). Reaction of 4-chloro-3,4'-diquinolinyl sulfide (**4c**) with aqueous ammonia proceeded with breaking of the 4'-quinolinyl sulfur bond to give **7a**, which were accompanied by thioquinanthrene (**6b**) (n=0). 4-Dimethylamino-3-methylsulfinylquinoline (**8b**) could be also prepared by oxidation of **7c** with urea/hydrogen peroxide system (UHP).

Scheme 4



Dimethylamino-3-methylthioquinoline (**7c**) and its 6-nitroderivative (**7e**) (required for the transamination study presented below) were prepared from 3,4'-diquinolinyl sulfides (**4e**) or (**10b**) and ROK reagents: potassium methoxide for **4e** and potassium phenoxide for **10b**, as presented on Scheme 4

Table 1

Amination of 4-chloroquinolines **1cb**, **1d** and **4c** according to systems [a] or [b].

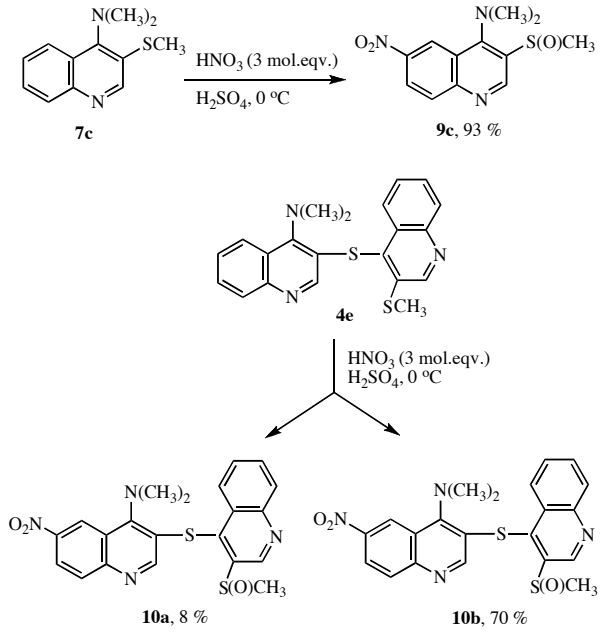
Entry	Substrate	Reaction conditions	Results, products [%]
1	**1c**, X=Cl, R=CH_3, n=0	NH_3, [a], 30 min	**7a**, R^1=R^2=H, 96 %
2	**1c**	$(CH_3)_2NH$, [a], 60 min	**7c**,R^1=R^2=CH_3, 37 % and **11a**, 33 %
3	**4c**, R=3-CH_3S-4-quinolinyl, n=0	NH_3, [a], 30 min	**7a**, R^1=R^2=H, 90 % and **6b** (n=0), 80 %
4	**1c**	DMF/KOH, [c] or boil. DMF, 18 h	**7c**, R^1=R^2=CH_3 , 60 % or 48 %
5	**1c**	$(CH_3)_2NH$,[b], 150 °C, 6 h	**7c**, R^1=R^2=CH_3 , 95 %, ref.[4].
6	**1c**	CH_3NH_2, [b] 140 °C, 6 h	**7b**, R^1=H, R^2=CH_3, 51 %
7	**4c**	CH_3NH_2, [b] 160 °C, 6 h	**4d**, R^1=H, R^2=CH_3, R=3'- CH_3S-4-quinolinyl, n=0, 64 %
8	**4c**	$(CH_3)_2NH$,[b], 160 °C, 6 h	**4e**, R^1=R^2= CH_3, R=3'-CH_3S-4-quinolinyl, n=0, 79 %
9	**1d**	CH_3NH_2, [b] 100 °C, 6 h	**8a**,R=H, 80 %
10	**1d**	$(CH_3)_2NH$,[b], 70 °C, 6 h	**8b**, R=CH_3, 80 %

[a] boiling phenol, [b] autoclave, methanol, HClaq.;[c] prepared as decribed for 4-chloroquinoline- ref [13].

Reactions of 4-dimethylamino-β-quinolinyl sulfides (7c) and (4e) with nitrating mixture. As discussed above (Scheme 1), action of nitrating mixture usually converts β-quinolinyl sulfides stepwise *via* β-quinolinyl

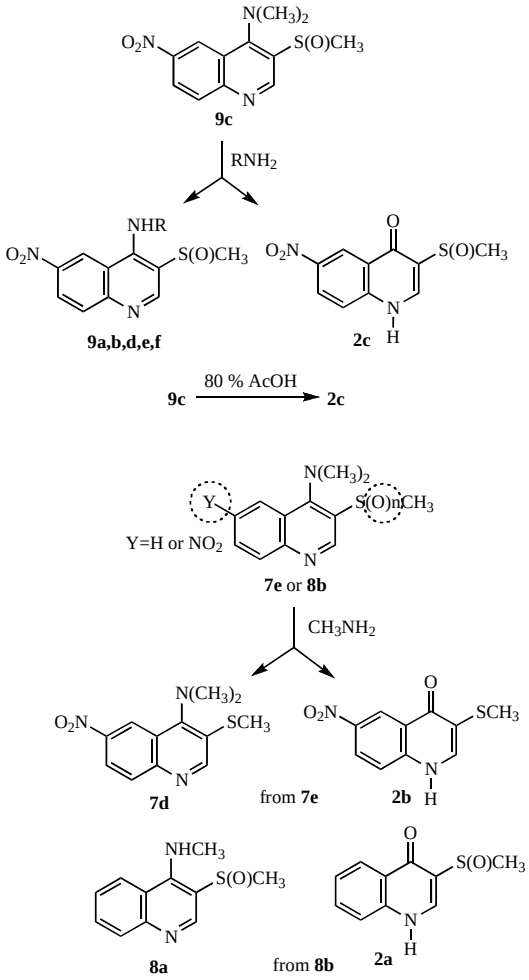
sulfoxides to nitro-β-quinolinyl sulfoxides. Similarly, reaction of 4-dimethylamino-3-methylthioquinoline (**7c**) with 3 mol. eqv. of HNO_3 (used in form of nitrating mixture) gave 4-dimethylamino-3-methylsulfinylo-6-nitroquinoline (**9c**) (93 %) but the same reaction performed even with use of 0.8 mol. eqv. of HNO_3 at 0 °C led to a mixture of **9c**, 4-dimethylamino-3-methylsulfinylquinoline (**8b**) and non-converted substrate **7c** in ratio 1:2:1. This may be due to high electron-donating properties of the 4-amino group, which significantly activate 4-aminoquinolines towards electrophilic substitution. Similarly, reaction of 4-dimethylamino-3'-methylthio-3,4'-diquinolinyl sulfide (**4e**) with nitrating mixture containing 3 molar eqv. of HNO_3 gave nitrosulfoxide (**10b**) (70 %) accompanied by its *N*-demethylated analog **10a** (8 %) and two unidentified products with lower R_f values. As nitration of 4-aminoquinolines was mentioned several times [14], 4-methylaminoquinoline (**4d**) was also subjected to the reaction with nitrating mixture, but it led to a multicomponent mixture of unstable products. IR spectra proved for the presence of sulfinyl groups and nitro groups in the molecules of **9c** and **10a**,**b**. Positioning of the nitro group in **9c** and **10a**,**b** was estabilished from ^{1}H NMR spectra based on coupling constant values $J_{H,H}$ and nitro group substituent effects, both being very close to data reported previously for 6-nitro-3-quinolinyl sulfides [1]. Structure of **10b** was additionally confirmed by its reaction with potassium phenoxide (Scheme 4).

Scheme 5



Transamination. 4-Dimethylamino substituent in the molecule of 4-dimethylamino-3-methylsulfinyl-6-nitroquinoline (**9c**) is strongly affected by three electron-withdrawing groups: *endo*cyclic nitrogen-ring atom, *ortho* 3-methylsulfinyl group and 6-nitro qroup [8]. All these groups strongly enhance susceptibility of 4-dimethylamino substituent towards nucleophilic displacement with the dimethylamino group acting as a leaving group. Although various nucleofuges have been used in activated aromatic [15-17] and heteroaromatic nucleophilic substitution reactions [18-19], the dialkylamino group has seldom been considered and is considered as a poor leaving group [18]. In spite of this, amine-amine group exchange, *i.e.* transamination, was observed in the reactions of 1-dialkylamino-2,4-dinitronaphtalenes with primary and secondary amines, in the case of 1-dimethylamino-2,4-di(trifluoroacetyl)naphthalene, [15-17] and also in the case of *aza*-aromatic systems *e.g.* for 2-dimethylaminoquinoline [18-19].

Scheme 6



Our study showed that the dimethylamino group in **9c** is readily replaced (aqueous methanol, 140-150 ºC) with methylamine and ammonia and then with butylamine

(Table 2). Acid catalysis accelerates transamination reactions of **9c**, however, since this reaction produces hydrogen chloride, the same yield of transamination product was obtained for both acid catalysed and non-catalysed reactions. The exchange of dimethylamino group is strongly affected by steric effects at the introductory amino group. We found for the case of primary alkylamines with some slightly bulkier isopropyl and cyclopropyl groups that the yields of transamination products **9d** or **9e** decrease to 30-38 % and that the transamination product is accompanied by a substantial amount of non-converted substrate (25-31 %) as well as by 6-nitro-3-methylsulfinyl-4(1*H*)-quinolinone (**2c**) (8-30 %). The latter could be also prepared by hydrolysis of **9c** with 80 % acetic acid. The same reactivity relative to amines was observed for the reaction of 4-dimethylamino-2,4-dinitronaphtalene [15].

Table 2

Transamination of dimethylaminoquinolines **9c**, **8b** and **7e**. (Scheme 6) [a].

No	Substrate	Amine	Products / Recovered substrate
1	**9c**	NH_3	**9a**, R=NH_2, 75 % / **9c**, 11 %.
2	**9c**	$MeNH_2$	**9b**, R=NH-Me, 90 % / **9c**, 0 %.
3	**9c**	$iPrNH_2$	**9d**, R=NH-iPr, 30 %; **2c**, 30 % / **9c**, 30 %.
4	**9c**	$cPrNH_2$	**9e**, R=NH-cPr, 39 %; **2c**, 8 % / **9c**, 31 %.
5	**9c**	n-$BuNH_2$	**9f**, R=NH-n-Bu, 60 %; **2c**, 18 % / **8b**, 13 %.
6	**8b**, R= $N(Me)_2$	$MeNH_2$	**8a**, R=NH-Me, 25 %; **2a**, 16 % / **8b**, 46 %.
7	**7e**, R= $N(Me)_2$	$MeNH_2$	**7d**, R=NH-Me, 31 %; **2b**, 22 % / **7e**, 31 %.

[a] Abbreviations: Me=methyl, iPr=*iso*propyl, cPr=cyclopropyl, n-Bu = n-butyl.

To compare the activating effect of 3-methylsulfinyl and 6-nitro groups, respective *desoxy* derivative **7e** (Y=NO_2, n=0) and *desnitro* derivative **8b** (Y=H, n=1) were subjected to reaction with methylamine. It indicates that activating effect of 6-nitro group is stronger for nucleophilic displacement of dimethylamino group at C4 in **9c** than that of the 3-methylsulfinyl one.

CONCLUSIONS

Reactions of 4-dimethylamino-β-quinolinyl sulfides (**4e**) and (**7c**) with nitrating mixture (3 molar eqv.) led directly to 4-dimethylamino-β-quinolinyl-6-nitro sulfoxides (**10b**) and (**9c**). Nitration of 3,4'-diquinolinyl sulfide (**4e**) proceeded in the 'left' quinoline unit being activated towards nitration by the 4-dimethylamino group.

4-Dimethylamino-3-methylsulfinyl-6-nitroquinoline (**9c**) underwent acid-catalysed transamination in the reaction with primary aliphatic amines and ammonia.

6-Nitro-4-aminoquinolines are most often prepared from the respective 4-chloroquinolines[9,12,21] and to less extent by nitration of 4-aminoquinolines.[14] Our approach open the third route to 6-nitro-4-aminoquinolines, *via* transamination of 4-dimethylamino-3-methylsulfinyl-6-nitroquinoline (**9c**) with primary aliphatic amines and ammonia leading to nitro derivatives of type **9** with amino and alkylamino groups at C4. It may be of interest as introduction of nitro group to the molecules of 4-aminoquinolines open access to numerous biologically active amino- and nitroquinoline derivatives [21].

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. 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 a mixture of CH_2Cl_2/ethanol, (19:1, v/v) (system II) and 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 III).

Preparation of 4-aminoquinolines 7b, 7c, 4d, 4e, 8a, 8b by amination of 4-chloroquinolines 1c, 4c and 1d in autoclave (Table 1, entries 5-10). The procedure described previously [6] was modified as follows:

4-Chloroquinoline (5 mmol), 15 mL of methanol, 4 mL of 20% aqueous methylamine or dimethylamine and one drop of conc. hydrochloric acid were placed in a steel autoclave. It was heated as described in Table 1. Volatile compounds were evaporated under vacuum at 50 °C and the residue was alkalized (if necessery) with few drops of 10% aqueous sodium hydroxide. 3,4'-Diquinolinyl sulfides **4d, 4e** were isolated by filtration and then recrystallized from ethanol.

4-Amino-3-thioquinolines **7b**, **7c**, **8a**, **8b** were isolated by extraction with methylene chloride (4 x 5 mL). Extracts were evaporated to dryness and the residue was recrystallized as indicated below. Properties of **7b** and **7c** were the same as reported previously [22,6].

4-Methylamino-3'-methylthio-3,4'-diquinolinyl sulfide (4d). This compound was obtained as bright yellow plates (ethanol), mp 173-175 °C; ^{1}H NMR ($CDCl_3$), δ: 2.69 (s, 3H, CH_3S), 3.41 (d, *J*=5.4 Hz, 3H, CH_3NH), 6.20-6.70 (broad, 1H, NH), 7.39-7.44 (m, 1H, H_{arom}), 7.58-7.68 (m, 3H, 3 x H_{arom}), 8.06-8.08 (m, 2H, 2 x H_{arom}), 8.13-8.16 (m, 1H, H_{arom}), 8.48-8.51 (m, 1H, H_{arom}), 8.68 (s, 1H, H-2), 8.79 (s, 1H, H-2'). *Anal.* Calcd. for $C_{20}H_{17}N_3S_2$: C, 66.08; H, 4.71; N, 11.56. Found: C, 65.80; H, 4.65 ; N, 11.29.

4-Dimethylamino-3'-methylthio-3,4'-diquinolinyl sulfide (4e). This compound was obtained as bright yellow plates (ethanol), mp 94-96 °C; ^{1}H NMR ($CDCl_3$), δ: 2.60 (s, 3H, SCH_3), 3.27 (s, 6H, $N(CH_3)_2$), 7.51-7.53 (m, 2H, H_{arom}), 7.57-7.59 (m, 1H, H_{arom}), 7.65-7.67 (m, 1H, H_{arom}), 7.92-7.95 (m, 1H, H_{arom}), 7.93 (s, 1H, H-2), 8.03-8.06 (m, 1H, H_{arom}), 8.10-8.12 (m, 1H, H_{arom}), 8.34-8.36 (m, 1H, H_{arom}), 8.83 (s, 1H, H-2'). *Anal.*

Calcd. for $C_{21}H_{19}N_3S_2$: C, 66.81; H, 5.07; N, 11.13; S, 16.99. Found: C, 66.48; H, 5.11; N, 11.12; S, 16.69.

4-Methylamino-3-methylsulfinylquinoline (**8a**)**.** This compound was obtained as white plates (ethanol), mp 165-167 °C; ^{1}H NMR ($CDCl_3$), δ: 2.96 (s, 3H, S(O)CH_3), 3.48-3.49 (d, *J*=5.6 Hz, 3H, N(CH_3), 7.42-7.46 (m, 1H, H_{arom}), 7.67-7.71 (m, 1H, H_{arom}), 7.87 (broad s, 1H, N*H*), 7.95-7.98 (m, 1H, H_{arom}), 8.27-8.29 (m, 1H, H_{arom}), 8.44 (s, 1H, *H*-2). IR (KBr pellet): $\nu_{S=O}$=1003 cm^{-1}. *Anal.* Calcd. for $C_{11}H_{12}N_2OS$: C, 59.97; H, 5.49; N, 12.72; S, 14.56. Found: C, 59.52; H, 5.91; N, 12.51; S, 14.61.

4-Dimethylamino-3-methylsulfinylquinoline (8b). This compound was obtained as white plates (ethyl acetate), mp 141-143 °C; ^{1}H NMR ($CDCl_3$), δ: 2.84 (s, 3H, S(O)CH_3), 3.16 (s, 6H, N(CH_3)$_2$), 7.57-7.59 (m, 1H, H_{arom}), 7.55-7.77 (m, 1H, H_{arom}), 8.05-8.07 (m, 1H, H_{arom}), 8.15-8.18 (m, 1H, H_{arom}), 9.30 (s, 1H, *H*-2). IR (KBr pellet): $\nu_{S=O}$=1047 cm^{-1}. *Anal*. Calcd. for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96. Found: C, 61.25; H, 6.01; N 12.01.

Amination in boiling phenol. Ammonia or dimethyl amine was passed through a mixture of phenol (5 g), 4-chloroquinoline **1c** or **4c** (5 mmol) and one crystal of ammonium chloride at 200 °C for 2 h. The mixture was then cooled down to rt, treated with 15 mL of 5 % aqueous sodium hydroxide and stirred with 15 mL of methylene chloride for 10 min. Further work-up depends on the products composition.

In the case of the reaction of **1c** with ammonia (Table 1, entry 1), organic layer was separated and dried over anhydrous Na_2SO_4. The solvent was then distilled off to give crude **7a** (~100 %) with mp. 123-125 °C. It was recrystallized from aqueous ethanol to results in product with mp. 124-126 °C.

In the case of the reaction of **1c** with dimethylamine (Table 1, entry 2), organic layer was worked-up as above to give a solution containing 4-dimethylamino-3-methylthioquinoline (**7c**) and 4-phenoxy-3-methylthioquinoline (**11a**). It was shaken with 5 mL of 5 % hydrochloric acid. The aqueous layer was washed twice with 5 mL of methylene chloride. The organic layers were combined, dried with anhydrous Na_2SO_4 and evaporated to dryness to give 0.44 g (33 %) of **11a** with mp 139-141 °C, ref. [23], mp 139-140 °C. Aqueous layer was alkalized with 5 % aqueous NaOH and extracted with chloroform (3 x 5 mL). Extracts were combined, dried and evaporated as above to give 0.40 g of **7c** with mp 86-88 °C, ref. [6], mp 86-88 °C.

In the case of the reaction of **4c** with ammonia (Table 1, entry 3) the solid [thioquinanthrene (**6b**)]) was collected by filtration. The solid was washed with water and dried on air to give 0.63 g (80 %) of the chromatographically homogenous yellow material with mp 314-315 °C being identical with thioquinanthrene (**6b**), ref. [24], mp 314-315 °C. Further work-up of organic layer gave crude **7a** (0.85 g, 100 %).

4-Amino-3-methylthioquinoline (**7a**)**.** This compound was obtained as white plates (aqueous ethanol), mp 124-126 °C; ^{1}H NMR (benzene-d_6) 1.79 (s, 3H, SCH_3), 4.75 (s, 2H, NH_2), 7.03 – 7.11 (m, 2H, H_{arom}), 7.28-7.34 (m, 1H, H_{arom}), 8.24-8.27 (m, 1H, H_{arom}), 8.97 (s, 1H, *H*-2). *Anal*. Calcd. for $C_{10}H_{10}N_2S$: C, 63.13; H, 5.30; N, 14.72; S, 16.85. Found: C, 63.09; H, 5.28; N, 14.58; S 16.75.

Oxidation of 4-dimethylamino-3-methylthioquinoline (7c) to 4-dimethylamino-3-methylsulfinylquinoline (8b) by means of UHP. Sulfide (**7c**) (0.22 g, 1 mmol) was added to a solution of UHP (*i.e*. urea-hydrogen peroxide complex [25], 0.55 g, 6 mmol) in 3 mL of methanol. The mixture was stirred at rt for 48 h. Then 6 mL of water was added and the mixture was extracted with chloroform (4 x 5 mL). The extracts were dried with anhydrous sodium sulfate and evaporated to dryness. The residue (190 mg, an oil containing the product **8b** and the substrate **7c**) was subjected to chromatographic separation (Al_2O_3 neutral, chloroform:ethanol, 30:1, v/v), which gave 0.03 g of substrate **7c** (the fraction with upper Rf value) and 0.16 g of product **8b**. The later was recrystallized from ethyl acetate to give 0.15 g (64 %) of pure **8b** with mp 142-143 °C being identical with the product prepared from amination od **1d** (Table 1, entry 10).

Reaction of 3,4'-diquinolinyl sulfides (4e) or (10b) with ROK reagents (Scheme 4). 3,4'-Diquinolinyl sulfide (1 mmol) was added at rt to 8 mL of DMSO and then on stirring, 3 mmol of ROK reagents [potassium methoxide for sulfide (**4e**) or potassium phenoxide for sulfide (**9b**)] was introduced in one portion. The mixture was stirred for 30 min at rt and then poured into 15 mL of 5% aqueous sodium hydroxide. 4-Phenoxy-3-methylsulfinylquinoline (**11b**) was filtered off and the residual part of **11b** was extracted with chloroform (3 x 5 mL), but 4-methoxy-3-methylthioquinoline (**1a**) was isolated by extraction (as above) only. The solid and extracts were combined (for **11b**), the solution was dried with anhydrous Na_2SO_4. The solvent was then distilled off to give crude **11b** or **1a**. **11b** was recrystallized from ethanol but **1a** was purified from impurities by extraction with hot hexane [23,5].

Aqueous DMSO solution was methylated on stirring (30 min) with 0.066 mL (1.1 mmol) of methyl iodide. 4-Dimethylamino-3-methylthioquinoline (**7c**) was extracted with chloroform (3 x 5 mL) and then isolated and purified as described previously [6]. 4-Dimethylamino-3-methylthio-6-nitroquinoline (**7e**) was isolated and purified in the same manner.

4-Dimethylamino-3-methylthio-6-nitroquinoline (**7e**)**.** This compound was obtained as yellow plates (ethanol), mp 120-122 °C; ^{1}H NMR ($CDCl_3$), δ: 2.56 (s, 3H, SCH_3), 3.22 (s, 6H, N(CH_3)$_2$), 8.11-8.13 (d, *J*=8.8 Hz, 1H, *H*-8), 8.34-8.37 (dd, *J*=8.82 Hz, *J*=2.4 Hz, 1H, *H*-7), 8.86 (s, 1H, *H*-2), 9.02-9.023 (d, *J*=2.4 Hz, 1H, *H*-5). IR (KBr pellet): ν_{NO2}=1337 cm^{-1} and 1505 cm^{-1}. *Anal.* Calcd. for $C_{12}H_{13}N_3O_2S$: C, 54.74; H, 4.98; N, 15.96. Found: C, 54.4; H, 5.12; N, 16.04.

Reactions of 3-methylthioquinolines (7c) and (4e) with nitrating mixture. The described procedure [6] was modified as follows:

3-Methylthioquinoline (5 mmol) was dissolved upon strirring in conc. sulfuric acid (11 mL) at 10 °C and the solution was cooled down to – 5 °C. Then, 1.25 mL of nitrating mixture (prepared from 1 mL of fuming nitric acid and 1 mL of conc. sulfuric acid) was added dropwise at -5 °C and kept at -5 °C for 15 min. The reaction mixture was poured on 110 g of crushed ice and then neutralized at 0 °C with conc. aqueous ammonia up to pH 6. The solid product was filtered off and dried on air. 4-Dimethylamino-3-methylsulfinyl-6-nitroquinoline (**8c**) was recrystallized from ethanol. Reaction products from **4e** were separated by column chromatography (silicagel 60, a mixture CH_2Cl_2/ethanol, 19:1 , v/v) to afford **10b** (R_f=0.32, system II), 1.54 g (70 %), **10a** (R_f=0.22, system II), 0.17 g (8 %).

4-Dimethylamino-3-methylsulfinyl-6-nitroquinoline (9c). This compound was obtained as yellow plates (ethanol), mp 160-162 °C; ^{1}H NMR ($CDCl_3$), δ: 2.85 (s, 3H, S(O)CH_3), 3.27 (s, 6H, N(CH_3)$_2$), 8.23-8.25 (d, *J*=9.2 Hz, 1H, *H*-8), 8.47-8.49 (dd, *J*=9.2 Hz, *J*=2.4 Hz, 1H, *H*-7), 9.04-9.05 (d, *J*=2.4 Hz, 1H,

H-5), 9.42 (s, 1H, *H*-2). IR (KBr pellet): $\nu_{S=O}$=1041 cm^{-1}, ν_{NO2}=1343 cm^{-1} and 1504 cm^{-1}. *Anal.* Calcd. for $C_{12}H_{13}N_3O_3S$: C, 51.60; H, 4.69; N, 15.04; S, 11.48. Found: C, 51.26; H, 4.71; N, 14.81; S, 11.16.

4-Methylamino-3'-methylsulfinyl-6-nitro-3,4'-diquinolinyl sulfide (10a). This compound was obtained as yellow solid (ethanol), mp decomposition from 189-193 °C; ^{1}H NMR ($CDCl_3$), δ: 2.86 (s, 3H, S(O)CH_3), 3.57 (d, *J*=5.4 Hz, 3H, NHCH_3), 6.41 (broad doublet, 1H, N*H*CH$_3$), 7.65-7.70 (m, 1H, H_{arom}), 7.81-7.86 (m, 1H, H_{arom}), 7.96-7.99 (m, 1H, H_{arom}), 8.21-8.24 (m, 1H, H_{arom}), 8.36-8.39 (m, 1H, H_{arom}),8.45-4.48 (m, 1H, H_{arom}), 8.68 (s, 1H, *H*-2), 9.18-9.19 (m, 1H, H_{arom}), 9.39 (s, 1H, *H*-2'). IR (KBr pellet): $\nu_{S=O}$=1035 cm^{-1}, ν_{NO2}=1336 cm^{-1} and 1590 cm^{-1}. *Anal.* Calcd. for $C_{20}H_{16}N_4O_3S_2$: C, 56.59; H, 3.80; N, 13.20. Found: C, 56.24; H, 4.03; N, 12.84.

4-Dimethylamino-3'-methylsulfinyl-6-nitro-3,4'-diquinolinyl sulfide (10b). This compound was obtained as yellow plates (ethanol), mp 218-220 °C; ^{1}H NMR ($CDCl_3$), δ: 2.91 (s, 3H, S(O)CH_3), 3.38 (s, 6H, N(CH_3)$_2$), 7.59-7.64 (m, 1H, H_{arom}), 7.83-7.89 (m, 1H, H_{arom}), 8.03-8.06 (m, 1H, H_{arom}), 8.06 (s, 1H, *H*-2), 8.20-8.23 (d, *J*=9 Hz, 1H, *H*-8), 8.27-8.30 (m, 1H, H_{arom}), 8.36-8.40 (dd, *J*=9 Hz, *J*=2.7 Hz, 1H, *H*-7), 9.02 (d, *J*=2.7 Hz, 1H, *H*-5), 9.51 (s, 1H, *H*-2'). IR (KBr pellet): $\nu_{S=O}$=1057 cm^{-1}, ν_{NO2}=1339 cm^{-1} and 1576 cm^{-1}. *Anal.* Calcd. for $C_{21}H_{18}N_4O_3S_2$: C, 57.52; H, 4.14; N, 12.78. Found: C, 57.44; H, 4.23; N, 12.54.

4-Methylamino-3-methylthio-6-nitroquinoline (7d). This compound was obtained as yellow plates (ethanol), mp 106-108 °C; EIMS (70 eV) m/z: 249 (100, M$^+$). ^{1}H NMR ($CDCl_3$), δ: 2.33 (s, 3H, SCH_3), 3.59-3.60 (d, *J*=6 Hz, 3H, NCH_3), 6.58 (broad, 1H, N*H*), 7.99-8.01 (d, *J*=9.3 Hz, 1H, *H*-8), 8.35-8.38 (dd, *J*=9.3 Hz, *J*=2.4 Hz, 1H, *H*-7), 8.78 (s, 1H, *H*-2), 9.29-9.3 (d, *J*=2.4 Hz, 1H, *H*-5). IR (KBr pellet): ν_{NO2}=1330 cm^{-1} and 1504 cm^{-1}. *Anal.* Calcd. for $C_{11}H_{11}N_3O_2S$: C, 53.00; H, 4.45; N, 16.86. Found: C, 52.86; H, 4.25; N, 16.68.

Transamination of 4-dimethylamino-3-methylsulfinyl-6-nitroquinoline (9c). 4-Dimethylaminoquinoline **9c** (0.28 g, 1 mmol), 16 mL of methanol, 3 mL of water, alkylamine (6 mmol) or 0.8 mL of 25 % aqueous ammonia or methylamine and one drop of conc. hydrochloric acid was placed in a steel autoclave. It was heated in an oil bath as described in Table 1. The volatile compounds were evaporated under vacuum at 80 °C up to volume of 3 mL and the residue was cooled down to rt. The solid was filtered off and the filtrate was extracted with $CHCl_3$ or CH_2Cl_2 (3 x 4 mL). The solid and the extracts were combined, dried with anhydrous Na_2SO_4. The solvent was distilled off. The residue was either recrystallized from ethanol (for **9a** and **9b**) or subjected to chromatographic separation (Al_2O_3, CH_2Cl_2 /ethanol, 35:1, v/v) (for the other experiments, Table 2, entries 3-5). The later give fractions of: transamination product **9d**,**e,f** (upper Rf value), substrate **9c** (middle Rf value), and 4(1*H*)-quinolinone **2c** (lower Rf value). Properties of **2c** were the same as described below.

In the same manner were performed transamination of **8b** and **7e** with methylamine (Table 2, entries 6,7).

Properties of 3-methylsulfinyl-4(1*H*)-quinolinone (**2a)** and 3-methylthio-6-nitro-4(1*H*)-quinolinone (**2b**) were the same as described earlier [5,23].

4-Amino-3-methylsulfinyl-6-nitroquinoline (9a). This compound was obtained as yellow solid (ethanol), mp 227-228 °C (decomp); ^{1}H NMR ($CDCl_3$), δ: 2.97 (s, 3H, S(O)CH_3), 6.9-7.05 (broad s, 2H, NH_2), 8.01-8.03 (d, *J*=9.2 Hz, 1H, *H*-8), 8.41-8.44 (dd, *J*=9.2 Hz, *J*=2.4 Hz, 1H, *H*-7), 8.45 (s, 1H, *H*-2), 8.78-8.84 (d, *J*=2.4 Hz, 1H, *H*-5). IR (KBr pellet): $\nu_{S=O}$=1019 cm^{-1}, ν_{NO2}=1336 cm^{-1} and 1499 cm^{-1}. *Anal.* Calcd. for $C_{10}H_9N_3O_3S$: C, 47.80; H, 3.61; N, 16.72. Found: C, 47.42; H, 3.70; N, 16.32.

4-Methylamino-3-methylsulfinyl-6-nitroquinoline (9b). This compound was obtained as yellow solid (ethanol), mp 210-212 °C; ^{1}H NMR ($CDCl_3$), δ: 3.00 (s, 3H, S(O)CH_3), 3.59-3.60 (d, *J*=5.6 Hz, 3H, NHCH_3), 8.01-8.03 (d, *J*=9.2 Hz, 1H, *H*-8), 8.42-8.45 (dd, *J*=9.2 Hz, *J*=2.4 Hz, 1H, *H*-7), 8.46 (s, 1H, *H*-2), 8.63 (1H, broad, N*H*), 9.35-9.36 (d, *J*=2.4 Hz, 1H, *H*-5). IR (KBr pellet): $\nu_{S=O}$=1031 cm^{-1}, ν_{NO2}=1335 cm^{-1} and 1557 cm^{-1}. *Anal.* Calcd for $C_{11}H_{11}N_3O_3S$: C, 49.80; H, 4.18; N, 15.84. Found: C, 49.52; H, 4.30; N, 15.58.

4-Isopropylamino-3-methylsulfinyl-6-nitroquinoline (9d). This compound was obtained as yellow solid (ethyl acetate), mp 156-158 °C; ^{1}H NMR ($CDCl_3$), δ: 1.47-1.49 (m, 3H, CH_3), 1.54-1.56 (m, 3H, CH_3), 2.99 (s, 3H, S(O)CH_3), 4.39-4.48 (m, 1H, C*H*), 8.02-8.04 (d, *J*=9.2 Hz, 1H, *H*-8), 8.14 (broad s, 1H, N*H*), 8.42-8.45 (dd, *J*=9.2 Hz, *J*=2.4 Hz, 1H, *H*-7), 8.51 (s, 1H, *H*-2), 9.16-9.17 (d, *J*=2.4 Hz, 1H, *H*-5). IR (KBr pellet): $\nu_{S=O}$=1053 cm^{-1}, ν_{NO2}=1340 cm^{-1} and 1503 cm^{-1}. *Anal.* Calcd for $C_{13}H_{15}N_3O_3S$: C, 53.23; H, 5.15; N, 14.32. Found: C, 53.48; H, 4.97; N, 14.25.

4-Cyclopropylamino-3-methylsulfinyl-6-nitroquinoline (9e). This compound was obtained as yellow solid (ethanol), mp 153-155 °C; ^{1}H NMR ($CDCl_3$), δ: 0.87-0.95 (m, 2H, CH_2), 1.19-1.29 (m, 2H, CH_2), 2.97 (s, 3H, S(O)CH_3), 3.24-3.33 (m, 1H, C*H*), 8.01-8.02 (d, *J*=9.2 Hz, 1H, *H*-8), 8.42 (s, 1H, *H*-2), 8.43-8.46 (dd, *J*=9.2 Hz, *J*=2.4 Hz, 1H, *H*-7), 8.98 (broad s, 1H, N*H*), 10.07-10.08(d, *J*=2.4 Hz, 1H, *H*-5). IR (KBr pellet): $\nu_{S=O}$=1011 cm^{-1}, ν_{NO2}=1348 cm^{-1} and 1498 cm^{-1}. *Anal.* Calcd. for $C_{13}H_{13}N_3O_3S$: C, 53.60; H, 4.50; N, 14.42; S, 11.01. Found: C, 53.41; H, 4.42; N, 14.12.

4-Butylamino-3-methylsulfinyl-6-nitroquinoline (9f). This compound was obtained as yellow solid (ethanol), mp 108-110 °C; ^{1}H NMR ($CDCl_3$), δ: 1.03-1.06 (m, 3H, CH_3), 1.59-1.63 (m, 2H, CH_2), 1.86-1.90 (m, 2H, CH_2), 3.01 (s, 3H, S(O)CH_3), 3.90-3.95 (m, 2H, CH_2), 8.01-8.03 (d, *J*=9.2 Hz, 1H, *H*-8), 8.41-8.44 (dd, *J*=9.2 Hz, *J*=2.4 Hz, 1H, *H*-7), 8.46 (broad s, 1H, N*H*), 8.47 (s, 1H, *H*-2), 9.26-9.27 (d, *J*=2.4 Hz, 1H, *H*-5). IR (KBr pellet): $\nu_{S=O}$=1011 cm^{-1}, ν_{NO2}=1323 cm^{-1} and 1504 cm^{-1}. *Anal.* Calcd for $C_{14}H_{17}N_3O_3S$: C, 54.71; H, 5.57; N, 13.67. Found: C, 54.72; H, 5.62; N, 13.60.

Hydrolysis of sulfoxide 9c to quinolinone 2c. Sulfoxide **9c** (0.28 g, 1 mmol) and 80 % acetic acid (3 mL) were stirred at 70 °C for 6 h. Volatile components were evaporated to dryness from water bath at vacuum. The residue was cooled to rt and mixed with 2 mL of water and then treated with saturated $NaHCO_3$. The solid was collected by filtration and dried on air. The resulted material was refluxed with the mixture of methylene chloride/ethanol (10-1, v/v) and quinolinone **2c** with mp 236-238 °C (0.176 g, 70 %) was hot filtered off. The filtrate was evaporated to dryness to give unreacted substrate (0.084 g, 30 %) Crude **2c** was recrystallized from DMF to yield the solid with mp 242-243 °C; lit. [5], mp 242-243 °C.

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