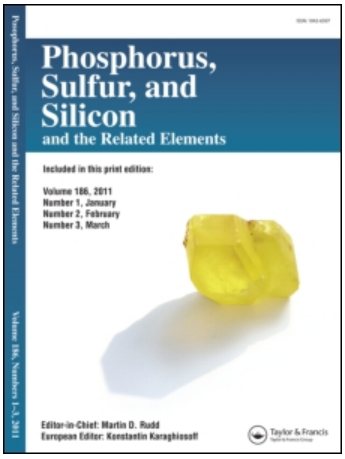

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4-Methoxy-3'-alkylsulfinyl-3,4'-diquinolinyl Sulfides--Synthesis and the Reaction with Sodium Methoxide

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4-METHOXY-3′-ALKYLSULFINYL-3,4′-DIQUINOLINYL SULFIDES—SYNTHESIS AND THE REACTION WITH SODIUM METHOXIDE[#]

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Reaction of 4-methoxy-3′-alkylthio-3,4′-diquinolinyl sulfides ***1a–d*** *with a nitrating mixture led to the title sulfoxides* ***2a–d****, but the same treatment of isopropylthio derivative* ***1e*** *resulted in S-dealkylation and oxidation with formation of 3,3′-diquinolinyl disulfide* ***3****. 3′-Alkylsulfinyl group promotes nucleophilic methoxy-desulfidation of 4′-quinolinyl sulfur bond in sulfoxides* ***2****, as compared to that in sulfides* ***1****, in which case it leads to 3-quinolinyl sulfoxides* ***6*** *and 3-quinolinethiolate* ***4-A****.*

Keywords: Nucleophilic heteroaromatic substitution; quinolinyl sulfides; quinolinyl sulfoxides; sulfides oxidation

INTRODUCTION

Although the electron attracting behavior of the sulfinyl group is well estabilished,[1] a literature review reveals only a few examples of the behavior of the sulfinyl group in nucleophilic aromatic substitution. Hammick and Williams showed that p-iodo-phenyl phenyl sulfoxide is hydrolyzed by alkali under conditions (5N KOH in 60% aqueous boiling ethanol) in which the *meta* isomer is not affected.[2] Oae and Khim studied in turn the hydrolysis of chloro-phenyl phenyl sulfoxides with potassium hydroxide in aqueous DMSO at 158°C and found that the phenylsulfinyl group activates the nucleophilic substitution in the *ortho* and *para* positions.[3] The latter effect was also demonstrated for amino-dechlorination of 4-chloro-3-propylsulfinylquinoline.[4] The promotion of nucleophilic aromatic substitution by an *ortho*-sulfinyl group also was demonstrated by an Italian group in the synthesis

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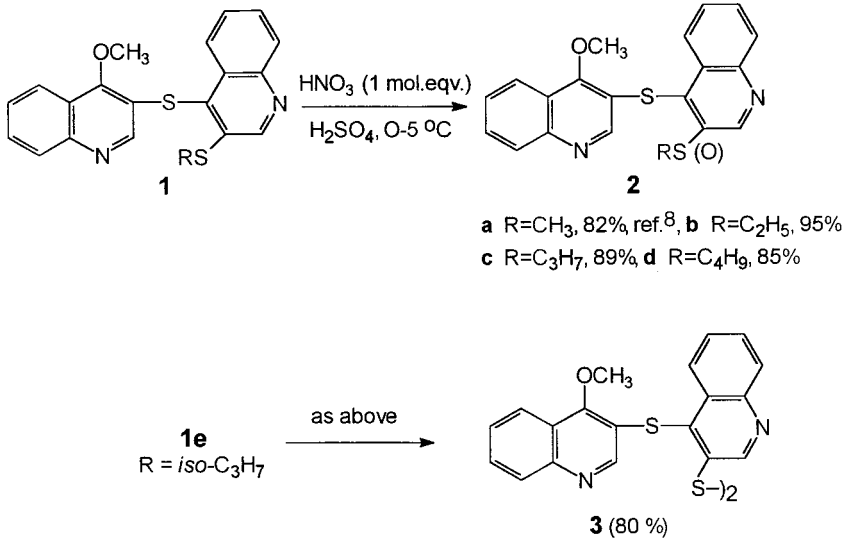
of antibiotic *rufloxacin* where nucleophilic substitution of chloride at C-10 in pyrido[1,2,3-de][1,4]benzothiazine system could only be obtained after oxidation of thiazinic sulfur to sulfoxide leaving the *meta*-fluorine substituent unaffected.[5,16]

A sulfinyl group can also act as leaving group during aromatic and heteroaromatic nucleophilic substitution in heterocycles such as pyridine, quinoline, or pyrazine.[6,7]

4-Substituted 3-alkylsulfinylquinolines exemplified by the dimethyl derivative **2a** and 4-methoxy-3-alkylsulfinylquinolines **6** could be prepared by careful oxidation with nitric acid of the corresponding β-quinolinyl sulfides.[8,9] In the present study we compared the ease of methoxy-desulfidation of the title 4-methoxy-3′-alkylsulfinyl-3,4′-diquinolinyl sulfides **2** with that of parent 3′-alkylthioquinolines **1** and demonstrate that this can be a new method of preparing 4-methoxy-3-alkylsulfinylquinolines **6**.

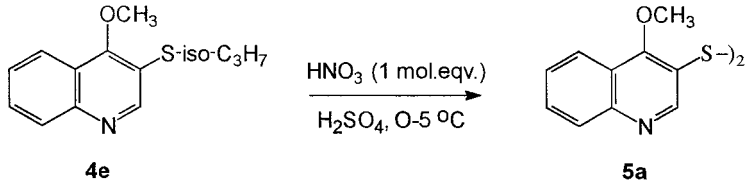
RESULTS AND DISCUSSION

Substitution at the *ortho* position in aromatic systems is strongly affected by the steric and electronic effects induced, that is, by the size of substituent which occupies the *ortho* position relative to the place of substitution.[10] Thus, to study the reaction of 4-methoxy-3′-alkylsulfinyl-3,4′-diquinolinyl sulfides **2** with sodium methoxide, substrates **1** with methyl, ethyl, n-propyl, n-butyl and *iso*propyl group were preliminary selected. Taking into account the ease of preparation of 3′-methylsulfinyl derivative **2a** by oxidation of 3′-methylthio derivative **1a** with a nitrating mixture[8] one would expect this procedure to be adaptable for the synthesis of sulfoxides **2**. In fact, treatment of sulfuric acid solution of ethylthio, propylthio, and butylthio derivatives **1b–1d** with nitrating mixture at 0–5°C proceeded as 3′-S-monooxidation and gave high yields of 3′-alkylsulfinyl-quinolines **2a–2d**. On the other hand, the same reaction with the isopropyl derivative **1e** did not lead to sulfoxide-type products as judged firstly from IR spectra. When the product was subjected to ^{1}H NMR analysis, the absence of the isopropyl group was observed. Relative to starting 3′-isopropylthio derivative **1e** the spectral positions of aromatic protons (benzene rings protons and H-2 one) remain almost unchanged, only the signal of H-2′ proton is shifted downfield by ca. 0.3 ppm up to the value $\delta = 9.21$ ppm. The same order of H-2 proton shift ($\Delta\delta = ca$ 0.2 ppm) was found for the couple 4-alkoxy-(3-methylthio)quinoline **4**/3,3′-bis(4-alkoxyquinolinyl) disulfide **5** (alkyl = methyl or propyl).[11] Taking into account the MS and ^{1}H NMR data one can conclude that disulfide **3** is the main product of the reaction of the *iso*propyl derivative **1e** with a nitrating mixture.



SCHEME 1

The same behavior of *S*-isopropyl group splitting followed by disulfide formation was observed for the reaction of 4-methoxy-3-(isopropylthio)quinoline **4e** with nitrating mixture and gave rise to 3,3′-bis(4-methoxyquinolinyl) disulfide **5a** (7%) accompanied by several unidentified products.



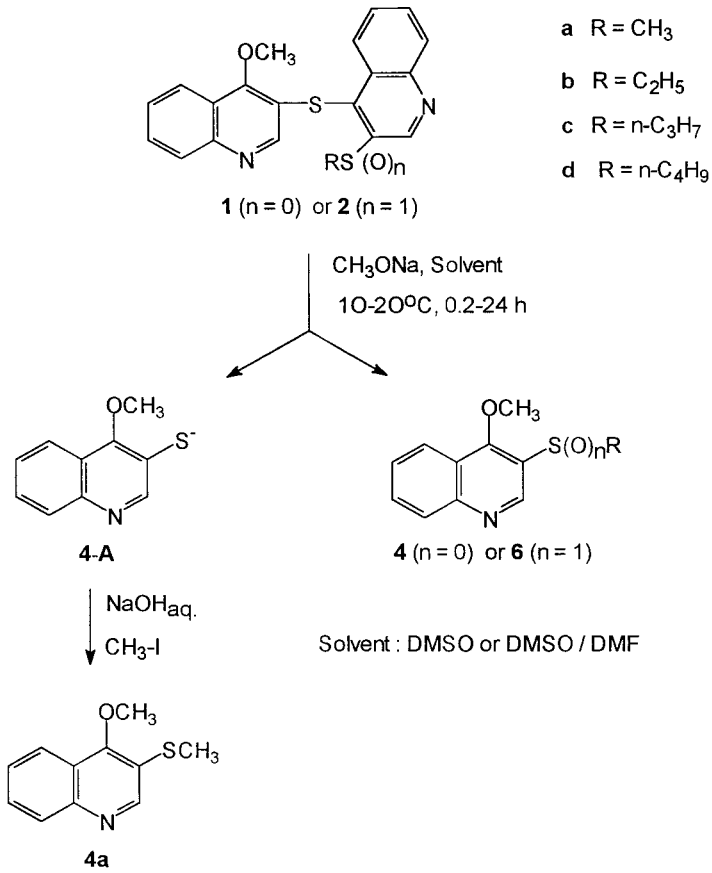
SCHEME 2

As in the case of diquinolinyl sulfides **1**, the reaction of 4-methoxy-3-n-alkylthioquinolines **4** with cold nitrating mixture led to the respective 4-methoxy-3-alkylsulfinylquinolines **6**.[9]

Reaction of 4-Methoxy-3′-alkylthio- and 4-Methoxy-3′-alkylsulfinyl-3,4′-diquinolinyl Sulfides 1a–d or 2a–d with Sodium Methoxide

4-Substituted 3′-alkylthio-3,4′-diquinolinyl sulfides, like the 4-methoxy derivatives **1**, reacted smoothly with nucleophiles (alkanethiolates and

alkanolates) in DMSO or DMF at 20°C.[11–13] These reactions proceeded usually by nucleophilic displacement of the 4′-quinolinyl-sulfur bond in **1** and formation of various 4-nucleophilo 3-(alkylthio)quinolines of type **4** and 4-substituted 3-quinolinethiolates of type **4-A**. The reaction mixture was then diluted with 5–15% aqueous sodium hydroxide.[11–13] The neutral products **4** were then isolated by extraction or filtration but the alkaline aqueous—DMSO (or DMF) layer containing thiolate **4-A** was alkylated to the same or another 4-substituted 3-(alkylthio)quinoline of type **4**[11–13] or oxidized to 3,3′-di(4-substituted-quinolinyl) disulfides.[11] This methodology, outlined in Scheme 3, was used to study the reaction of sulfoxides **2** with sodium methoxide.



SCHEME 3

When the experimental procedure typical for the reaction of **1** with sodium methoxide (20°C, DMSO, 40 min) was applied to the reaction of

dimethyl derivative **2a**, complete consumption of **2a** was accompanied by isolation of only 25% of 4-methoxy-3-methylsulfinylquinoline **6a** as a neutral product and ~6% of 4-methoxy-3-(methylthio)quinoline **4a** resulted from the methylation of thiolate fraction. However, when the reaction temperature was reduced to 5–10°C, sulfoxides **2** (in DMSO-DMF solution) were completely consumed within 40 min. Under the same conditions, the conversion of sulfides **1** reached 21–27%, while complete consumption of **1** required 4 h. In both cases the reaction brought (see Table I) high yields of the neutral products i.e. sulfoxides **6** or sulfides **4** as well as 4-methoxy-3-(methylthio)quinoline **4a** from methylation of thiolate **4-A** fraction.

The data collected in the Table I demonstrate that in methoxy-desulfidation of γ-quinolinyl sulfides **1**,**2** the transformation of *ortho* alkylthio substituents into alkylsulfinyl groups activates the γ-quinolinyl-sulfide bond toward nucleophilic heteroaromatic displacement. Competitive experiment with the (1:1) mixture of 3′-ethylthio- and 3′-ethylsulfinyl derivatives **1b** and **2b**, respectively, treated with 1.4 molar equivalent of sodium methoxide (10°C, 45 min.) enables a complete conversion of sulfoxide **2b**, leaving 84% of sulfide **1b** unaffected.

EXPERIMENTAL

Melting points were taken in open capillary tubes and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker MSL 300 spectrometer at 300 MHz in deuteriochloroform or in hexadeuteriodimethyl sulfoxide solutions with tetramethylsilane (δ 0.0 ppm) as internal standard. The ^{1}H and ^{13}C NMR spectra of **2b** were completely assigned using a previously described combination of 1D and 2D NMR techniques.[14] IR spectra were taken on an UR-10 apparatus (Carl Zeiss, Jena) in KBr pellets. EI MS spectra were determined on a LKB GC MS 2091 spectrometer at 15 or 70 eV and at temperatures ranging between 80 and 100°C. LSI mass spectra were obtained with the help of AMD-604 mass spectrometer (Cs^+, 15 keV, nba). Tlc analyses were performed employing Merck's silicagel 60 F_{254} plates and a solution of chloroform-methanol (25:2, v/v) as an eluent (system I) or Merck's aluminium oxide 60 F_{254} neutral (type E) plates using mixture of chloroform-methanol (60:1, v/v) as an eluent (system II). Chromatograms were visualized under UV light or with iodine vapour.

4-Methoxy-3′-alkylthio-3,4′-diquinolinyl sulfides 1a–1e were prepared from thioquinanthrene and sodium methoxide followed by *S*-alkylation with alkyl iodides, as described previously.[12,15]

TABLE I Formation of 4-Methoxy-3-Alkylthio- and 3-Alkylsulfinylquinolines **4** or **6** from the Sulfides **1** or Sulfoxides **2**, Respectively, According to the Reaction Sequences Shown in Scheme 3

Entry	Substrate	Solvent system	Reaction conditions	Conversion	Products from neutral fraction	**4a** from methylation of thiolate fraction
1	**1a** (R=Me)	DMSO/DMF	10°C, 40 min	27%	**4a**, 16%*	**4a**, 13%*
2	**1a** (R=Me)	DMSO/DMF	10°C, 4 h	100%	**4a**, 96%	**4a**, 71%
3	**1a** (R=Me)	DMSO	rt, 30 min	100%	**4a**, 86%	**4a**, 77%**
4	**1b** (R=Et)	DMSO/DMF	10°C, 40 min	21%	**4b**, 17%*	**4a**, 13%*
5	**1b** (R=Et)	DMSO/DMF	10°C, 4 h	100%	**4b**, 97%	**4a**, 65%
6	**1b** (R=Et)	DMSO	rt, 30 min	100%	**4b**, 85%	**4a**, 75%**
7	**1c** (R=Pr)	DMSO	rt, 30 min	100%	**4c**, 85%	**4a**, 69%
8	**1d** (R=Bu)	DMSO/DMF	10°C, 4 h	100%	**4d**, 94%	**4a**, 87%
9	**1d** (R=Bu)	DMSO	rt, 30 min	100%	**4d**, 86%	**4a**, 70%
10	**2a** (R=Me)	DMSO/DMF	10°C, 40 min	100%	**6a**, 89%	**4a**, 71%
11	**2b** (R=Et)	DMSO/DMF	10°C, 40 min	100%	**6b**, 97%	**4a**, 69%
12	**2c** (R=Pr)	DMSO/DMF	10°C, 40 min	100%	**6c**, 88%	**4a**, 72%
13	**2d** (R=Bu)	DMSO/DMF	10°C, 40 min	100%	**6d**, 87%	**4a**, 81%
14	**1b** (R=Et)	DMSO/DMF	10°C, 40 min	**1b**, 14%	**4b**, 10%	**4a**, 87%
	2b (R=Et)		1.4 molar eqvs of CH_3ONa	**2b**, 100%	**6b**, 97%	

*See Experimental: The reactions of **1** and **2** with sodium methoxide.
**Taken from ref.[12]

4-Methoxy-3′-butylthio-3,4′-diquinolinyl sulfide 1d: m.p. 77–79°C (ethanol). ^{1}H NMR ($CDCl_3$): δ 0.87 (t, $J = 7.4$ Hz, 3H, $C\underline{H}_3CH_2$), 1.42 (sextet, $J = 7.4$ Hz, 2H, $CH_3C\underline{H}_2CH_2$), 1.59–1.72 (m, 2H, $CH_2C\underline{H}_2CH_2$), 3.08 (t, $J = 7.4$ Hz, 2H, $SC\underline{H}_2CH_2$), 4.20 (s, 3H, CH_3O), 7.51–7.59 (m, 2H), 7.62–7.68 (m, 2H), 7.96–7.99 (m, 1H), 8.06–8.12 (m, 2H), 8.14 (s, 1H, H-2), 8.37–8.41 (m, 1H), 8.89 (s, 1H, H-2′). EI MS (70 eV) m/z (%): 406 (100, M^+). Anal. Calcd. for $C_{23}H_{22}N_2OS_2$ (406.12): C, 67.95; H, 5.45; N, 6.89; S, 15.77. Found C, 67.80; H, 5.28; N, 7.01; S, 15.49.

4-Methoxy-3-(butylthio)quinoline 4d and **4-methoxy-3-(isopropylthio)quinoline 4e** were prepared by treating 4-methoxy-3′-alkylthio-3,4′-diquinolinyl sulfides **1d** or **1e**,[15] respectively, with sodium methoxide followed by alkylation with butyl or isopropyl iodides according to the procedure d, ref.[12] and, finally, by purification using column chromatography.[12]

4-Methoxy-3-(butylthio)quinoline 4d: an oil. ^{1}H NMR ($CDCl_3$): δ 0.90 (t, $J = 7.2$ Hz, 3H, $C\underline{H}_3CH_2$); 1.48 (sextet, $J = 7.2$ Hz, 2H, $CH_3C\underline{H}_2CH_2$), 1.56–1.66 (m, 2H, $CH_2C\underline{H}_2CH_2$), 2.99 (t, $J = 7.4$ Hz, 2H, $SC\underline{H}_2CH_2$), 4.15 (s, 3H, CH_3—O); 7.53–7.58 (m, 1H); 7.66–7.72 (m, 1H); 8.05–8.08 (m, 1H); 8.10–8.13 (m,); 8.84 (s, 1H, H-2). EI MS (70 eV) m/z (%): 247 (100, M^+), 191(60). Anal. Calcd. for $C_{14}H_{17}NOS$ (247.36): C, 67.98; H, 6.93; N, 5.56; O, 6.47; S, 12.96. Found C, 67.89; H, 6.70; N, 5.38; S, 13.06.

4-Methoxy-3-(isopropylthio)quinoline 4e: an oil, b.p. 160–163°C/0.8 torr. ^{1}H NMR ($CDCl_3$): δ 1.28 [d, 6H, $J = 6.7$ Hz, $(C\underline{H}_3)_2CHS$)], 3.46–3.55 [m, 1H, $C\underline{H}(CH_3)_2$], 4.15 (s, 3H, CH_3—O), 7.53 (ddd, 1H, $J =$ 6.9 Hz, $J = 8.3$ Hz, $J = 1.2$ Hz, H-6), 7.68 (ddd, 1H, $J = 6.9$ Hz, $J = 8.4$ Hz, $J = 1.5$ Hz, H-7), 8.04 (ddd, 1H, $J = 8.4$ Hz, $J = 1.2$ Hz, $J = 0.7$ Hz, H-8), 8.11 (ddd, 1H, $J = 8.3$ Hz, $J = 1.5$ Hz, $J = 0.7$ Hz, H-5), 8.84 (s, 1H, H-2). EI MS (15 eV) m/z (%): 233 (97, M^+). Anal. Calcd. for $C_{13}H_{15}NOS$ (233.33): C, 66.92; H, 6.48; N, 6.00; O, 6.86; S, 13.74. Found C, 67.01; H, 6.50; N, 5.90; S, 13.60.

4-Methoxy-3′-alkylsulfinyl-3,4′-diquinolinyl sulfides 2a–2d were prepared by treatment of a sulfuric acid solution of 4-methoxy-3′-alkylthio-3,4′-diquinolinyl sulfides **1a–d** at 0–5°C with a nitrating mixture (containing up to 1 molar eqv. of HNO_3) as described previously (procedure A) for dimethyl derivative **2a**.[8]

4-Methoxy-3′-ethylsulfinyl-3,4′-diquinolinyl sulfide 2b: m.p. 119–122°C (ethanol). ^{1}H NMR ($CDCl_3$): δ 1.32 (t, $J = 7.3$ Hz, 3H, $C\underline{H}_3CH_2$), 3.06 (q, $J = 7.3$ Hz, 2H, $CH_3C\underline{H}_2$), 4.16 (s, 3H, CH_3O), 7.57 (ddd, 1H, $J = 8.1$ Hz, $J = 7.0$ Hz, $J = 1.1$ Hz, H-6), 7.59 (ddd, 1H, $J =$ 8.1 Hz, $J = 7.0$ Hz, $J = 1.1$ Hz, H-6′), 7.70 (ddd, 1H, $J = 8.4$ Hz, $J =$ 7.0 Hz, $J = 1.5$ Hz, H-7), 7.80 (ddd, 1H, $J = 8.4$ Hz, $J = 7.0$ Hz, $J = 1.5$ Hz,

H-7′), 8.01 (ddd, 1H, $J = 8.4$ Hz, $J = 1.1$ Hz, $J = 0.7$ Hz, H-8), 8.06 (ddd, 1H, $J = 8.1$ Hz, $J = 1.5$ Hz, $J = 0.7$ Hz, H-5), 8.24 (ddd, 1H, $J = 8.4$ Hz, $J = 1.1$ Hz, $J = 0.6$ Hz, H-8'), 8.27 (s, 1H, H-2), 8.29 (ddd, 1H, $J = 8.1$ Hz, $J = 1.5$ Hz, $J = 0.6$ Hz, H-5′), 9.40 (s, 1H, H-2′). ^{13}C NMR ($CDCl_3$): δ 6.3 ($\underline{C}H_3CH_2$), 49.2 (CH_2), 62.5 (CH_3O), 118.8 (C-3), 121.6 (C-5), 123.4 (C-4′a), 125.2 (C-5′) 127.4 (C-6′), 127.8 (C-4a), 128.8 (C-6), 129.8 (C-8′), 130.2 (C-7), 130.8 (C-8), 131.4 (C-7′), 137.7 (C-4′), 140.4 (C-3′), 146.2 (C-2′), 149.2 (C-8a), 149.6 (C-8′a), 150.6 (C-2), 161.2 (C-4). IR (KBr pellet) $\nu_{so} = 1044$, 1053 and 1081 cm^{-1}. LSI MS: 395 $(M + 1)^+$. Anal. Calcd. for $C_{21}H_{18}N_2O_2S_2$ (394.51): C, 63.94; H, 4.60; N, 7.10; S, 16.25. Found C, 64.01; H, 4.50; N, 6.85; S, 16.60.

4-Methoxy-3′-propylsulfinyl-3,4′-diquinolinyl sulfide 2c: m.p. 110–113°C (ethanol). ^{1}H NMR ($CDCl_3$): δ 1.01 (t, $J = 7.3$ Hz, 3H, $C\underline{H}_3CH_2$); 1.69–1.79 (m, 1H) and 1.88–1.98 (m, 1H) both from $CH_3C\underline{H}_2CH_2$ group, 2.88–2.93 (m, 1H) and 2.98–3.03 (m, 1H) both from $CH_2C\underline{H}_2S$ group, 4.15 (s, 3H, CH_3O), 7.57–7.61 (m, 2H), 7.69–7.72 (m, 1H), 7.79–7.82 (m, 1H), 8.00–8.02 (m, 1H), 8.04–8.06 (m, 1H), 8.23–8.25 (m, 1H), 8.28 (s, 1H, H-2), 8.29–8.31 (m, 1H), 9.42 (s, 1H, H-2′). IR (KBr pellet) $\nu_{so} = 1039$, 1061 and 1079 cm^{-1}. EI MS (70 eV) m/z (%): 408 (7.8, M^+), 366 (18, M—C_3H_6), 318 (53, M—C_3H_6SO). Anal. Calcd. for $C_{22}H_{20}N_2O_2S_2$ (408.53): C, 64.68; H, 4.93; N, 6.86; S, 15.70. Found C, 64.31; H, 4.80; N, 6.95; S, 15.35.

4-Methoxy-3′-butylsulfinyl-3,4′-diquinolinyl sulfide 2d: m.p. 132–135°C (ethanol). ^{1}H NMR ($CDCl_3$): δ 0.87 (t, $J = 7.3$ Hz, 3H, $C\underline{H}_3CH_2$); 1.31–1.47 (m, 2H, $CH_3C\underline{H}_2CH_2$), 1.61–1.70 (m, 1H) and 1.81–1.90 (m, 1H) both from $CH_2C\underline{H}_2CH_2$ group, 2.91–3.02 (m, 2H, $C\underline{H}_2S$), 4.15 (s, 3H, CH_3O), 7.57–7.60 (m, 2H), 7.69–7.72 (m, 1H), 7.79–7.82 (m, 1H), 8.00–8.02 (m, 1H), 8.04–8.06 (m, 1H), 8.23–8.25 (m, 1H), 8.28 (s, 1H, H-2), 8.29–8.31 (m, 1H), 9.41 (s, 1H, H-2′). IR (KBr pellet) $\nu_{so} = 1043$, 1060 and 1077 cm^{-1}. EI MS (70 eV) m/z (%): 422 (6.8, M^+), 406 (17.7, M—O), 318 (83, M—C_4H_8SO), 302 (71). Anal. Calcd. for $C_{23}H_{22}N_2O_2S_2$ (422.56): C, 65.38; H, 5.25; N, 6.63; S, 15.17. Found C, 65.17; H, 5.45; N, 6.45; S, 14.96.

Reaction of 4-methoxy-3′-isopropylthio-3,4′-diquinolinyl sulfide 1e with a nitrating mixture: 4-Methoxy-3′-isopropylthio-3,4′-diquinolinyl sulfide **1e** 0.98 g (2.5 mmol) was dissolved with stirring in 96% sulfuric acid (7.5 ccm) at 0°C. 1/3 Volume of the nitrating mixture (fuming nitric acid, d = 1.50 g/ccm, 0.4 ccm, ca. 9 mmoles of HNO_3 and 0.6 ccm of conc. sulfuric acid) was then added (1/3 volume) dropwise at 0–5°C within 30 min. The mixture was maintained at 0°C for 5 min. and then cautiously poured onto 125 g of ice, and neutralized at 0°C with conc.aqueous ammonia, up to pH 5.5. The solid was filtered off, washed twice with cold water and air-dried to give yellow-colored

product. It was recrystallized from methanol to give disulfide **3** (0.7 g, 80%).

3,3′-Bis[(4-methoxy-3-quinolinylthio)-4-quinolinyl] disulfide 3: m.p. 107–109°C. ^{1}H NMR ($CDCl_3$): δ 4.16 (s, 6H, 2 × CH_3O), 7.51–7.60 (m, 4H), 7.64–7.70 (m, 4H), 7.94–7.97 (m, 2H), 8.03–8.07 (m, 4H), 8.14 (s, 2 × 1H, H-2), 8.32–8.34 (m, 2H), 9.21 (s, 2 × 1H, H-2′). LSI MS: 699 $(M + 1)^+$. Anal. Calcd. for $C_{38}H_{26}N_4O_2S_4$ (698.10): C, 65.31; H, 3.75; N, 8.02; S, 18.35. Found C, 65.01; H, 4.05; N, 7.95; S, 18.60.

Treatment of 4-methoxy-3-(isopropylthio)quinoline 4e with a nitrating mixture, was performed in the same manner as for **1e**. It afforded after chloroform extraction a semi-solid material, which was subjected to column chromatography (silica gel with chloroform-ethanol, 50:1 /v/v/ as eluent). Due to instability of the components of the mixture separated, only 7% of 3,3′-bis(4-methoxyquinolinyl) disulfide **5a**[11] was isolated in a pure state. M.p. 81–83°C, ref.,[11] m.p. 83–84°C.

Reactions of 3,4′-diquinolinyl sulfides 1 and 2 with sodium methoxide. Sodium methoxide 0.33 g (ca. 6 mmol) was added to a suspension of sulfide **1** or **2** (2 mmol) in 10 ml of DMSO or the mixture of DMSO (8 ml) and DMF (2 ml). The mixture was stirred at 5–10°C or at 20°C for 0.5–4 h (for details see Table I). The solution was then poured into 20 ml of 5% aqueous sodium hydroxide)* and the neutral product **4** or **6** was extracted with chloroform (4 × 5 ml). The combined extracts were washed with water, dried with anh. sodium sulfate and evaporated to give crude 4-methoxy-3-(alkylthio)quinoline **4** or 4-methoxy-3-(alkylsulfinyl)quinoline **6**.

Compounds **4a–c** were purified by triple extraction with hot hexane (10 ml). Compound **6a** was recrystallized from ethanol to give material with m.p. 138–140°C (ref.[9] m.p. 138–140°C). Compounds **4d** and **6b–d** were purified by column chromatography on silica gel (100–200 mesh) using as eluent a mixture of chloroform (or methylene chloride) and 95% ethanol/50:1 v/v/. Properties of 4-methoxy-3-(alkylthio)quinolines **4a–c** were the same as those reported previously.[9] Structure of 4-methoxy-3-(butylthio)quinoline **4d** was confirmed by independent synthesis from **1d** (see above).

Aqueous-DMSO or aqueous-DMSO-DMF layer containing thiolate **4-A** was subjected to methylation with methyl iodide as described previously.[12] 4-Methoxy-3-(methylthio)quinoline **4a** was extracted with chloroform (4 × 10 ml) and then isolated and purified as above).

In the case of partially consumed substrates (Table I, entries 1 and 4) as well as for the competitive experiment (Table I, entry 14), the dilution of DMSO/DMF mixture with aqueous sodium hydroxide produced solid material. It was filtered off, washed with water, and air-dried. The filtrate and the aqueous washings were combined and then treated with

chloroform as above, forming a mixture of neutral compounds **1** and **4** (or **4** and **6**). Both the solid and the oily product mixtures were separately extracted with hot hexane. This permitted to recover non-consumed solid substrates **1a–c** and to separate the hexane-soluble **4a**,**b**. Aqueous layer was then methylated gradually with methyl iodide (up to 2.2 mmol).

4-Methoxy-3-butylsulfinylquinoline 6d: an oil. ^{1}H NMR ($CDCl_3$): δ 0.94 (t, $J = 7.3$ Hz, 3H, $C\underline{H}_3CH_2$); 1.38–1.55 (m, 2H, $CH_3C\underline{H}_2CH_2$), 1.59–171 (m, 1H) and 1.80–1.95 (m, 1H) both from $CH_2C\underline{H}_2CH_2$ group, 2.98–3.12 (m, 2H, $C\underline{H}_2S$), 4.16 (s, 3H, CH_3O), 7.62–7.67 (m, 1H), 7.80–7.85 (m, 1H), 8.11–8.14 (m, 1H), 8.18–8.21 (m, 1H), 9.24 (s, 1H, H-2). EI MS (15 eV) m/z (%): 263 (39.8, M^+), 207 (100, $M-C_4H_8$). Anal. Calcd. for $C_{14}H_{17}NO_2S$ (263.35): C, 63.85; H, 6.51; N, 5.32; S, 12.15. Found C, 64.01; H, 6.35; N, 5.15; S, 11.96.

[#]Part LXV in the series of Azinyl Sulfides.

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