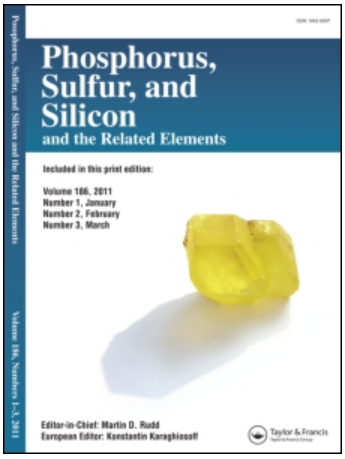


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# THE 1,4-DITHIIN RING OPENING IN ISOTHIOQUINANTHRENE

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# THE 1,4-DITHIIN RING OPENING IN ISOTHIOQUINANTHRENE†

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The 1,4-dithiin ring opening reactions in isothioquinanthrene **1** (1,4-dithiino[2,3-c;6,5-c']diquinoline) with selected S-, O- and Se-nucleophiles in DMSO or DMF at 20–70°C proceeded with cleavage of only one $C_{4\text{-quinolinyl}}$—S bond to give alkali metal salts of 4-substituted 4'-mercapto-3,3'-diquinolinyl sulfides **2a–2h** and **6** as primary products and after S-alkylation in aqueous sodium hydroxide solution 4-substituted 4'-alkylthio-3,3'-diquinolinyl sulfides **3–5** and **7** as the final products. In contrast to sulfides **2a–2h** sulfide **3a** reacted with S-nucleophiles (sodium alkanethiolates) with cleavage of the $C_{3\text{-quinolinyl}}$—S, $C_{4\text{-quinolinyl}}$—S and $CH_3$—S bonds to form 3,4-dialkylthioquinolines **8a–8e** as the main compounds. In the case of relatively bulky S-nucleophiles (the 2-methyl-2-propanethiolate and to some extent the ethanethiolate anions) the cleavage of the $C_{3\text{-quinolinyl}}$—S by a vicarious nucleophile (the methanethiolate anion, liberated in the cleavage of the $C_{4\text{-quinolinyl}}$—S bond) was observed.

*Key words:* 1,4-dithiinodiquinolines, 4-substituted 4'-alkylthio-3,3'-diquinolinyl sulfides, 3,4-dialkylthioquinolines, 1,4-dithiin ring opening, nucleophilic substitution, dealkylation.



## INTRODUCTION

Polycyclic 1,4-dithiin derivatives are useful as functional materials for electro-optical applications, $\pi$-donors for CT complexes, semiconductors and pigments.[1–4] Although there are known over 20 types of 1,4-dithiinodiheteroarenes and benzo-1,4-dithiinoheteroarenes, however, only four dithiins were explored in the 1,4-dithiin ring opening reactions. The first 1,4-dithiin ring opening reactions were carried out for 1,4-dithiino[2,3-b;5,6-b']dipyridazine and 1,4-dithiino[2,3-b;6,5-b']dipyridazine in the sixties and seventies.[5] The reaction of the former dithiinodipyridazine with phosphorus pentasulfide in boiling pyridine proceeded with cleavage of two C—S bonds to give 3,4,5-trimercaptopyridazine in 88% yield.[5a] Both dithiinodipyridazines reacted with sodium phenylmethanethiolate in boiling ethanol to give the product of cleavage of all the four C—S bonds—3,4-dibenzylthiopyridazine—in 36 and 41% yield and elemental sulfur.[5b] The most explored 1,4-dithiin ring opening reactions were performed with thioquinanthrene (1,4-dithiino[2,3-c;5,6-c']diquinoline—easy to obtain directly from the reaction of quinoline with elemental sulfur[6]). These reactions were carried out with various S-, O-, N- and C-nucleophiles in aprotic solvents to give the products of cleavage of one or both $C_{4\text{-quinolinyl}}$—S bonds.[7–15] The products were isolated after pouring the reaction mixture into aqueous sodium hydroxide solution and S-alkylation with alkyl halides and sulfates mainly as 4-substituted 3'-alkylthio-3,4'-diquinolinyl sulfides, 4,4'-dialkylthio-3,3'-diquinolinyl sulfides and 4-substituted 3-alkylthioquinolines. Only reactions with hydrochlorides of substituted anilines did not need aprotic solvents and S-alkylation to form various 12H-quinobenzo-1,4-thiazines.[16] Isothioquinanthrene **1** (1,4-dithiino[2,3-c;6,5-c']di-

†Part XXXIX in the series of Azinyl Sulfides. Part XXXVIII: A. Maślankiewicz, L. Skrzypek and A. Zięba, *Polish J. Chem.*, submitted.

quinoline—easy to obtain from thioquinanthrene via ring opening-ring closure reactions[12]) was examined only in a few cases.[7,12,13] Herein there are more examples of the 1,4-dithiin ring opening reactions in isothioquinanthrene **1** with nucleophiles including similarities and dissimilarities to the thioquinanthrene's reactions and examination of the cleavage of the $C_{3\text{-quinolinyl}}$—S and $C_{4\text{-quinolinyl}}$—S bonds by sodium alkanethiolates.

## RESULTS AND DISCUSSION

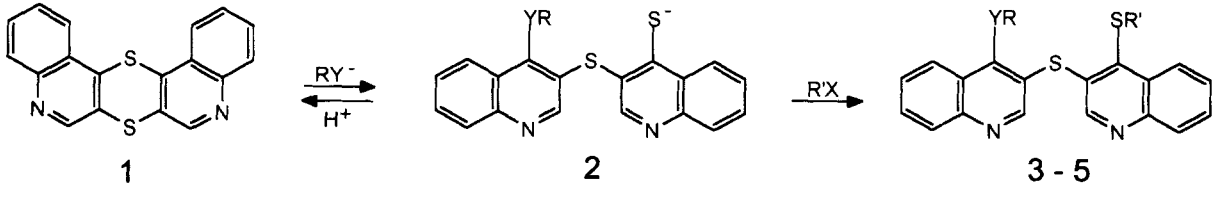
### A. *Cleavage of the $C_{4\text{-quinolinyl}}$—S Bond*

Reactions of isothioquinanthrene **1** with selected nucleophiles were performed in DMSO and DMF at room or elevated temperature (20–70°C). As isothioquinanthrene **1** is highly insoluble in organic solvents it was used as a suspension in the aprotic solvents for the 1,4-dithiin ring opening reactions. The progress of the reaction was followed by observation of the colour change of the reaction mixture (from yellow to deep red) and dissolution of dithiin **1** into solution during the course of the reaction (in the end of this stage the reaction mixture became a transparent red solution). The reaction mixture was poured into 3 volumes of 15% aqueous sodium hydroxide. Possibly unreacted isothioquinanthrene **1** was filtered off. The reported reactions proceeded with cleavage of only one $C_{4\text{-quinolinyl}}$—S bond to form appropriate alkali metal salts of 4-substituted 4′-mercapto-3,3′-diquinolinyl sulfides **2a–2h** and **6**. Attempts of isolation of these primary products as 4-substituted 4′-mercapto-3,3′-diquinolinyl sulfides **2H** by acidification were unsuccessful because of the tendency to intramolecular cyclization to form back isothioquinanthrene **1**. Therefore the filtrate was stirred with alkyl halides to form S-alkyl derivatives—4-substituted 4′-alkylthio-3,3′-diquinolinyl sulfides **3–5** and **7** as the final products (Scheme I, Table I).



1. *Reactions with sulfur nucleophiles.* In a previous paper[15] we found isothioquinanthrene **1** to be 15 times more reactive than thioquinanthrene towards sodium methanethiolate in the competitive reaction in DMSO at 20°C. Therefore the reactions of isothioquinanthrene **1** with sodium alkanethiolates in DMSO or DMF proceeded more smoothly than the thioquinanthrene's reactions (Table I). Although alkanethiol neat (i.e. phenylmethanethiol) was unreactive, however in the presence of alkali metal (lithium, sodium and potassium) hydroxides or potassium carbonate, the 1,4-dithiin ring in isothioquinanthrene **1** was opened very easily at 20°C to form sulfide **3d** in 85–92% yield. Disadvantage of the usage of alkanethiols and their alkali metal salts is the highly odorous smell of them. Instead of them S-alkylisothiouronium salts[13,15] can be used in the presence of alkali metal hydroxides or carbonates. These reactions needed elevated temperature (at least 30°C and 70°C, Table I) to produce alkanethiolate anions directly in the reaction mixture. It prompted us to examine thiourea alone or with alkyl halide in DMSO at 70°C. Although thiourea was unsufficiently nucleophilic to react with isothioquinanthrene **1**, equimolar amounts of thiourea and benzyl chloride (stirred for 30 minutes until isothioquinanthrene **1** and sodium hydroxide were added) opened the 1,4-dithiin ring to give after S-benzylation the sulfide **3e**. Owing to some amounts of unreacted benzyl chlo-

Scheme 1




1 2 3 - 5

| YR | YR |
|---|---|
| **2a** SMe | **2e** SPh |
| **2b** SEt | **2f** $SeCH_2Ph$ |
| **2c** St-Bu | **2g** OEt |
| **2d** $SCH_2Ph$ | **2h** Oi-Pr |

TABLE I

Reactions of isothioquinanthrene **1** with nucleophiles

| Entry | Nucleophile (equivalents) | Reaction conditions Temp./Time, Solvent | Alkylating agent | Product | YR | R' | Yield, % |
|---|---|---|---|---|---|---|---|
| 1 | MeSNa (2) | 20°/30 min., DMSO | MeI | **3a** | SMe | Me | 92 |
| 2 | MeSNa (2) | 20°/30 min., DMF | MeI | **3a** | SMe | Me | 90 |
| 3 | EtSNa (2) | 20°/30 min., DMSO | MeI | **3b** | SEt | Me | 84 |
| 4 | t-BuSNa (2) | 20°/30 min., DMSO | MeI | **3c** | St-Bu | Me | 85 |
| 5 | $PhCH_2SNa$ (2) | 20°/30 min., DMSO | MeI | **3d** | $SCH_2Ph$ | Me | 94 |
| 6 | $PhCH_2SH$ (2), MOH (2), M = Li, Na, K | 20°/30 min., DMSO | MeI | **3d** | $SCH_2Ph$ | Me | 88-92 |
| 7 | $PhCH_2SH$ (2), $K_2CO_3$ (4) | 20°/30 min., DMSO | MeI | **3d** | $SCH_2Ph$ | Me | 86 |
| 8 | $PhCH_2SC(NH_2)NH_2^+ Cl^-$ (3), NaOH (6) | 30°/60 min., DMSO | MeI | **3d** | $SCH_2Ph$ | Me | 92 |
| 9 | $PhCH_2SC(NH_2)NH_2^+ Cl^-$ (3), $K_2CO_3$ (6) | 70°/60 min., DMSO | MeI | **3d** | $SCH_2Ph$ | Me | 75 |
| 10 | $NH_2CSNH_2$ (3) | 70°/60 min., DMSO | - | -[a] | - | - | - |
| 11 | $NH_2CSNH_2$ (3), $PhCH_2Cl$ (3), NaOH (6) | 70°/30 min., DMSO[b] | $PhCH_2Cl$ | **3e** | $SCH_2Ph$ | $CH_2Ph$ | 79 |
| 12 | EtOCSSK (3) | 70°/30 min., DMSO | MeI | **3a** | SMe | Me | 79 |
| 13 | PhSNa (3) | 70°/60 min., DMSO | MeI | **3f** | SPh | Me | 53 |
| 14 | KSCN (3) | 70°/60 min., DMSO | - | -[a] | - | - | - |
| 15 | $NH_2CSeNH_2$ (3), $PhCH_2Cl$ (3), NaOH (6) | 70°/30 min., DMSO[b] | $PhCH_2Cl$ | **4** | $SeCH_2Ph$ | $CH_2Ph$ | 55 |
| 16 | NaOH (3) | 70°/60 min., DMSO | MeI | **7** | -[c] | Me | 71 |
| 17 | EtONa (3) | 70°/30 min., DMSO | MeI | **5a** | OEt | Me | 90 |
| 18 | i-PrONa (3) | 70°/30 min., DMSO | MeI | **5b** | Oi-Pr | Me | 84 |
| 19 | t-BuONa (3) | 70°/30 min., DMSO | MeI | **7** | -[c] | Me | 61 |
| 20 | PhONa (3) | 70°/60 min., DMSO | - | -[a] | - | - | - |
| 21 | $CH_3COONa$ (3) | 70°/60 min., DMSO | - | -[a] | - | - | - |
| 22 | t-$BuNH_2$ or cyclo-$C_6H_{11}NH_2$ (3) | 70°/60 min., DMSO | - | -[a] | - | - | - |
| 23 | $NaN_3$ (3) | 70°/60 min., DMSO | - | -[a] | - | - | - |
| 24 | NaX (3), X = F, Cl, Br, I | 70°/60 min., DMSO | - | -[a] | - | - | - |

[a] Isothioquinanthrene **1** recovered in at least 95%. [b] Thiourea or selenourea and benzyl chloride were stirred at 70°C for 30 minutes and then isothioquinanthrene **1** and sodium hydroxide was added. [c] The 1-methyl-4-oxo form.

ride in the reaction mixture this procedure can be applied only for the synthesis of symmetrical sulfides **3** i.e. where both alkyl groups were identical.

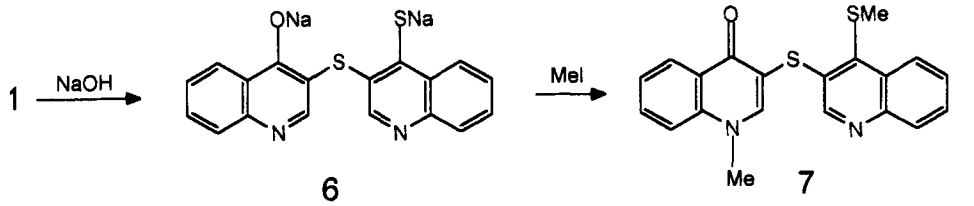
Potassium ethyl xanthate reacted with isothioquinanthrene **1** at 70°C to give after S-methylation the product of hydrolysis of the ROCSS group—sulfide **3a** in 79% yield. Similar hydrolysis was observed in the reaction of tetracyano-1,4-dithiin with potassium ethyl xanthate in acetone.[17] Potassium thiocyanide was unsufficiently nucleophilic to open the 1,4-dithiin ring.

Thioquinanthrene was reported[15] to be unreactive towards sodium benzenethiolate in DMSO at 70°C to cleave the $C_{4\text{-quinolinyl}}$—S bond. In contrast to it the more reactive isothioquinanthrene **1** reacted with sodium benzenethiolate to form after S-methylation sulfide **3f** in 53% yield.

2. *Reaction with selenourea and benzyl chloride.* The reaction of isothioquinanthrene **1** with equimolar amounts of selenourea and benzyl chloride (performed analogously as for thiourea and benzyl chloride) led to sulfide **4** in 55% yield. The yield was lower than for the thiourea reaction because of instability of the primary product which yielded red selenium.

3. *Reaction with oxygen nucleophiles.* Thioquinanthrene reacted with sodium hydroxide in a different way dependent on the reaction conditions to give products of the cleavage of one or both $C_{4\text{-quinolinyl}}$—S bonds: 4-oxo-1,4-dihydro-3′-methylthio-3,4′-diquinolinyl sulfide (70°C, 1 hour)[11] and 1-methyl-3-methylthio-4(1H)-quinolone (95°C, 24 hours).[8] In contrast the isothioquinanthrene **1** reacted with powdered sodium hydroxide in DMSO at 70°C for 1 hour to form after methylation unexpectedly not only the S- but also N-methylated product—1-methyl-4-oxo-1,4-dihydro-4′-methylthio-3,3′-diquinolinyl sulfide **7** in 71% yield (Scheme II).

Scheme 2




Reactions of isothioquinanthrene **1** with sodium ethoxide and 2-propoxide in DMSO at 70°C proceeded similarly as for sodium methoxide[12] giving after S-methylation sulfides **5a** and **5b**. In contrast to them the reaction with sodium *t*-butoxide carried out with the same conditions led to sulfide **7** instead of the expected *t*-butoxy derivative. This means that the *t*-butoxide anion was highly unreactive towards isothioquinanthrene **1** due to the steric hindrance and underwent probably a side reaction with the humidity in the air. However dealkylation during methylation in alkaline solution can not be excluded since methylation of the 4-methoxypyridine derivative with dimethyl sulfate gave the 1-methyl-4(1H)-pyridinone derivative.[18] It is worth noting that thioquinanthrene reacted reluctantly with sodium *t*-butoxide in DMF at 70°C with 34% conversion giving the *t*-butoxy derivative in 18.5% yield.[14]

Other oxygen nucleophiles—sodium acetate and phenoxide were insufficiently nucleophilic to open the 1,4-dithiin ring.

4. *Reactions with nitrogen nucleophiles.* Both reactions of isothioquinanthrene **1** with sodium azide and alkylamines (isobutylamine and cyclohexylamine) in DMSO at 70°C were unsuccessful.

5. *Reactions with halogen nucleophiles.* Reactions of isothioquinanthrene **1** with sodium fluoride, chloride, bromide and iodide were unsuccessful due to insufficient nucleophilicity of these reactants.

The most reactive 1,4-dithiin—tetracyano-1,4-dithiin—underwent facile addition reactions with many ionic nucleophiles at one of the carbon-carbon double bonds followed by ring opening.[17] Among succesfully used nucleophiles were acetate, phe-

noxide, azide and fluoride anions, however, they were unreactive towards isothioquinanthrene **1**.

### *B. The Cleavage of the $C_{3\text{-quinolinyl}}$—S Bond*

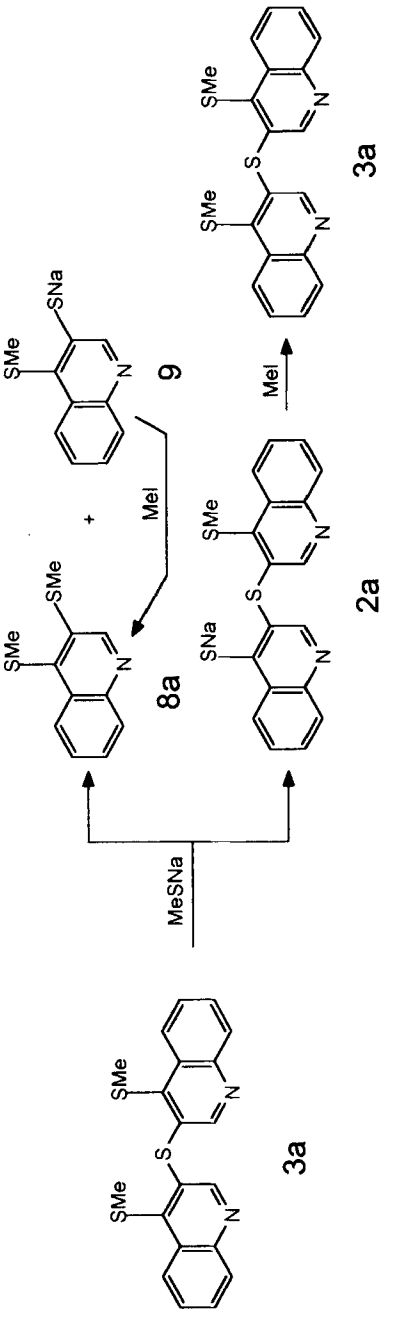
The higher reactivity of isothioquinanthrene **1** compared to thioquinanthrene was manifested in the reactions with sodium alkanethiolates and benzenethiolate. In our opinion the reactivity of isothioquinanthrene **1** is influenced by stabilization of the resulting 4′-quinolinethiolate **2a–2h** by electron delocalization between the sulfur atom (S′) and nitrogen (N′). In contrast to thioquinanthrene isothioquinanthrene **1** reacted with the cleavage of only one $C_{4\text{-quinolinyl}}$—S bond and the second $C_{4\text{-quinolinyl}}$—S bond was unaffected because of the partially negative sulfur atom (S′). The $C_{3\text{-quinolinyl}}$—S bonds in thioquinanthrene and isothioquinanthrene **1** remained untouched by nucleophiles.[7–15] It is well known that the C-3 carbon in quinoline (contrary to the C-2 and C-4 carbons) is not susceptible as a rule for nucleophilic attack because of lack of aza-activation.[19] Besides, the alkylthio and arylthio groups are not considered as good nucleofuges.[20] There are only a few reports involving nucleophilic substitution of the S-methyl or S-ethyl group in 2- and 4-alkylthiopyridines and quinolines.[21–23] Only the methylsulfonyl group in 2- and 4-methylsulfonylquinolines is as good a leaving group as the chlorine one.[24,25] There is no report on the nucleophilic displacement of the sulfide substituent in position 3 regardless of some examples of the Smiles rearrangement of the sodium salt of 4-alkylthio-3′-mercapto-3,4′-diquinolinyl sulfides.[12,13,15] It prompted us to examine the reactivity of the $C_{3\text{-quinolinyl}}$—S and $C_{4\text{-quinolinyl}}$—S bonds in the compound possessing the S-methyl function instead of the thiolate one i.e. in 4,4′-dimethylthio-3,3′-diquinolinyl sulfide **3a** towards sodium alkanethiolates.

Reaction of sulfide **3a** with 3 equivalents of sodium methanethiolate in DMSO at 70°C led unexpectedly after methylation to 3,4-dimethylthioquinoline **8a** in 48% yield and starting material **3a** in 29% yield. As the reaction was run until sulfide **3a** disappeared (the reaction was monitored by TLC) the presence of the substrate was due to methylation of the appropriate 4-quinolinethiolate **2a**. 3,4-Dimethylthioquinoline **8a** was formed not only as the direct product of the cleavage of the $C_{3\text{-quinolinyl}}$—S but also as the product of S-methylation of sodium 4-methylthio-3-quinolinethiolate **9** (Scheme III).

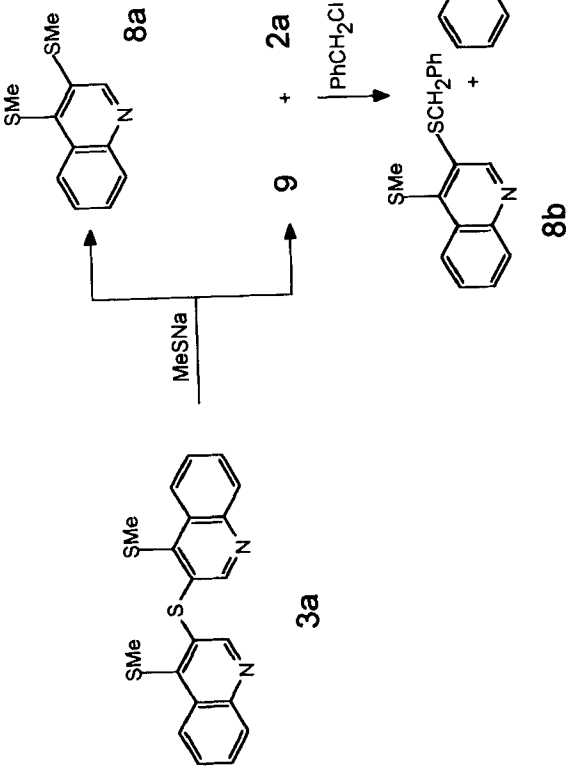
It means that the reaction proceeded with nucleophilic substitution at the C-3 carbon (the cleavage of the $C_{3\text{-quinolinyl}}$—S bond) and the methyl carbon (dealkylation, the cleavage of the $CH_3$—S bond).

To support this conclusion we made another experiment with sodium methanethiolate followed by alkylation with alkyl halide possessing other alkyl group than the methyl one. After pouring the reaction mixture into aqueous sodium hydroxide solution 3,4-dimethylthioquinoline **8a** (23%) was isolated by extraction with chloroform (Extract I). The aqueous layer was shaken with benzyl chloride and after 30 minutes extracted with chloroform (Extract II). Chloroform was distilled off and the residue was separated by column chromatography to give 3-benzylthio-4-methylthioquinoline **8b** (22%) and 4-benzylthio-4′-methylthio-3,3′-diquinolinyl sulfide **3d** (22%) as the product of the dealkylation of sulfide **3a** (Scheme IV). Dealkylation of

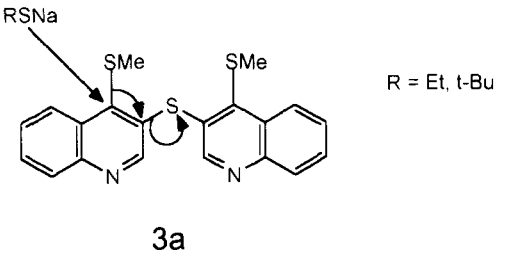
Scheme 3



Scheme 4

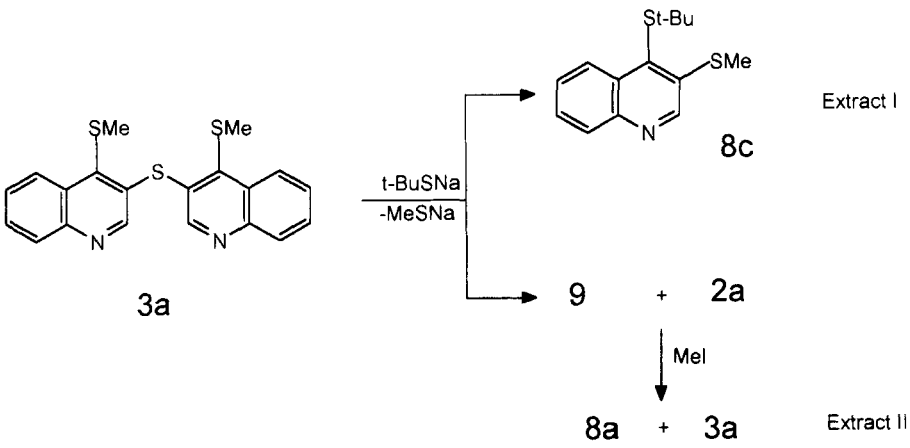


Scheme 5




3a

Scheme 6




alkylthioarenes and heteroarenes with an excess of sodium alkanethiolates (methanethiolate, ethanethiolate and 2-propanethiolate) in aprotic solvents (HMPA, DMF and DMA) was widely examined by Testaferri's and Tiecco's group. However dealkylation of 4-methylthio- and 4-ethylthioquinolines needed high temperature (100°C in HMPA and 154°C in DMF) and prolonged time (6 or 25 hours).[26,27]

Reactions of sulfide **3a** with other sodium alkanethiolates (for example ethanethiolate and 2-methyl-2-propanethiolate) were more complicated. First of all nucleophilic substitution at the C-4 carbon was observed. It turned out that the 2-methyl-2-propanethiolate anion was a too bulky nucleophile to cleave the $C_{3\text{-quinolinyl}}$—S bond. Instead of it this anion cleaved the $C_{4\text{-quinolinyl}}$—SMe bond liberating the methanethiolate anion which as a vicarious nucleophile cleaved the $C_{3\text{-quinolinyl}}$—S bond (Scheme V). It is a very unexpected result because there is no report on substitution of the one alkylthio group by another during dealkylation of alkylthioarenes and heteroarenes with an excess of sodium alkanethiolates.[28,29]

After pouring the reaction mixture into aqueous sodium hydroxide solution 3-methylthio-4-*t*-butylthioquinoline **8c** was isolated by extraction with chloroform (Extract I, 23%). The aqueous solution was shaken with methyl iodide and after 30 minutes was extracted with chloroform (Extract II). The similar work-up as described above gave two compounds: 3,4-dimethylthioquinoline **8a** (23%) and the substrate **3a** (24%) (Scheme VI).

The ethanethiolate anion which is not as bulky as the 2-methyl-2-propanethiolate

one reacted with isothioquinanthrene **1** giving a complex mixture of products. Extract I contained 5 compounds: 3-methylthio-4-ethylthioquinoline **8d**, 3-ethylthio-4-methylthioquinoline **8e**, 3,4-dimethylthioquinoline **8a**, 4-ethylthio-4′-methylthio-3,3′-diquinolinyl sulfide **3b** and 4,4′-diethylthio-3,3′-diquinolinyl sulfide **3g**. Since the mixture could not be separated the ratio of compounds was calculated from $^1$H NMR data comparing the intensities of the S-alkyl and H-2 proton signals with the proton signals in parent compounds[13,15,30] as follows: **8d** (20), **8e** (5), **8a** (1), **3b** (10) and **3g** (5). The aqueous layer was shaken with ethyl iodide and extracted with chloroform (Extract II). The work-up of the extract gave only two compounds: 3-ethylthio-4-methylthioquinoline **8e** (21%) and 4-ethylthio-4′-methylthio-3,3′-diquinolinyl sulfide **3b** (5%).

## CONCLUDING REMARKS

The 1,4-dithiin ring opening reactions in isothioquinanthrene **1** with selected nucleophiles proceeded with the cleavage of only one $C_{4\text{-quinolinyl}}$—S bond to give after S-alkylation 4-substituted 4′-alkylthio-3,3′-diquinolinyl sulfides **3–5** and **7**. The remaining $C_{4\text{-quinolinyl}}$—$S^-$ bond after the 1,4-dithiin opening and the newly formed $C_{4\text{-quinolinyl}}$—SR bond were cleaved by alkanethiolate anions only when the 4′-thiolate group was S-alkylated to form the 4′-alkylthio one. Reactions of 4,4′-dimethylthio-3,3′-diquinolinyl sulfide **3a** with sodium alkanethiolates proceeded as nucleophilic substitution at the C-3, C-4 and methyl carbons to give mainly 3,4-dialkylthioquinolines **8a–8e** and some amounts of 4,4′-dialkylthio-3,3′-diquinolinyl sulfides **3**. However, the yields of these reactions were significantly lower than for reactions of 3′,4-dialkylthio-3,4′-diquinolinyl sulfides with sodium alkanethiolates.[15,31] Only the methanethiolate and to some extent the ethanethiolate anions were able to cleave the $C_{3\text{-quinolinyl}}$—S bond. In the case of relatively bulky nucleophiles (the 2-methyl-2-propanethiolate and to some extent the ethanethiolate anions) the cleavage of the $C_{3\text{-quinolinyl}}$—S bond by the vicarious nucleophile—methanethiolate anion (liberated in the cleavage of the $C_{4\text{-quinolinyl}}$—SMe bond) was observed.



## EXPERIMENTAL

Melting points were determined in open capillary tubes on a Boetius melting point apparatus and were not corrected. The $^1$H NMR spectra were recorded on a Bruker MSL 300 spectrometer at 300 MHz in deuteriochloroform or DMSO-$d_6$ solvents. Mass spectra were run on LKB 9000S and Finnigan Mat 55Q 700 spectrometers using the electron impact method. Thin layer chromatography was performed on aluminium oxide (type E) and silica gel 60 254F plates (Merck) using methylene chloride and benzene-ethyl acetate (1:1) solutions as eluents. All new compounds gave satisfactory elemental analyses.

Isothioquinanthrene **1** was obtained from thioquinanthrene by the ring opening ring closure reaction.[12] Alkali metal alkanethiolates were commercial (Aldrich Chemical Co. or Merck) or prepared from commercial alkanethiols and sodium hydride in anhydrous benzene. Other reagents were commercial or prepared in common ways.

*Reaction of Isothioquinanthrene* **1** *with Nucleophiles. General Procedure*

To a suspension of isothioquinanthrene **1** (0.32 g, 1 mmol) in 10 ml of dry DMSO or DMF at ambient temperature (20–70°C) a nucleophile (2–3 mmols, Table I) was added. The mixture was stirred 30 or 60 minutes (Table I). The cooled mixture was poured into 30 ml of 15% aqueous sodium hydroxide. Possibly residual dithiin **1** was filtered and the filtrate was stirred with alkyl halide (1.5–3 mmols). The

solid was collected by filtration, washed with water and air-dried. The crude solids **3–5** and **7** were purified by column chromatography (silica gel 60, chloroform, chloroform/ethanol 20:1).

4,4′-Dimethylthio-3,3′-diquinolinyl sulfide **3a**, mp 142–143°C, lit[13] mp 142–143°C
4-Ethylthio-4′-methylthio-3,3′-diquinolinyl sulfide **3b**, mp 65–66°C, lit[13] mp 65–66°C.
4-*t*-Butylthio-4′-methylthio-3,3′-diquinolinyl sulfide **3c**, viscous oil.[12]
4-Benzylthio-4′-methylthio-3,3′-diquinolinyl sulfide **3d**, mp 112–113°C, lit[15] mp 112–113°C.
4,4′-Dibenzylthio-3,3′-diquinolinyl sulfide **3e**, mp 122–123°C, lit[13] mp 122–123°C.

4-Phenylthio-4′-methylthio-3,3′-diquinolinyl sulfide **3f**, mp 131–132°C. $^1$H NMR ($CDCl_3$): $\delta$ ppm, 2.46 (s, 3H, $SCH_3$), 7.08–7.21 (m, 5H, $C_6H_5$), 7.57, 7.64, 7.71 and 7.73 (m, 4H, H-6, H-6′, H-7 and H-7′), 8.06 and 8.09 (dd, 2H, H-8 and H-8′), 8.42 and 8.52 (dd, 2H, H-5 and H-5′), 8.57 and 8.59 (2s, 2H, H-2 and H-2′); MS (15 eV): m/z (%) 442 ($M^+$, 40.2); 395 (M-$SCH_3$, 6.1); 333 (M-$C_6H_5S$, 100); 318 (M-$C_6H_5SCH_3$, 33.9).

4-Benzylseleno-4′-benzylthio-3,3′-diquinolinyl sulfide **4**, mp 129–130°C. $^1$H NMR ($CDCl_3$): $\delta$ ppm, 4.20 (s, 2H, $CH_2$), 4.21 (s, 2H, $CH_2$), 7.02–7.16 (m, 10H, $2C_6H_5$) 7.59, 7.60, 7.69 and 7.71 (m, 4H, H-6, H-6′, H-7 and H-7′), 8.04 and 8.05 (dd, 2H, H-8 and H-8′), 8.38 and 8.43 (2s, 2H, H-2 and H-2′), 8.43 and 8.45 (dd, 2H, H-5 and H-5′), MS (70 eV): m/z (%) 580 ($M^+$, 1); 500 (M-Se, 9.4); 409 (M-$C_6H_5CH_2Se$, 58.0); 366 (M-$(C_6H_5CH_2)_2S$, 8.7); 318 (M-$(C_6H_5CH_2)_2Se$, 24.7); 91 ($C_6H_5CH_2^+$, 100).

4-Ethoxy-4′-methylthio-3,3′-diquinolinyl sulfide **5a**, mp 80–81°C. $^1$H NMR ($CDCl_3$): $\delta$ ppm, 1.44 (t, 3H, $CH_3$, $J$ = 7.0 Hz), 2.55 (s, 3H, $SCH_3$), 4.46 (q, 2H, $OCH_2$), 7.59, 7.64, 7.66 and 7.77 (m, 4H, H-6, H-6′, H-7 and H-7′), 8.02 and 8.12 (dd, 2H, H-8 and H-8′), 8.19 (dd, 1H, H-5), 8.29 (s, 1H, H-2′), 8.52 (dd, 1H, H-5′), 8.83 (s, 1H, H-2); MS (70 eV): m/z (%) 378 ($M^+$, 100); 302 (M-$C_2H_5SCH_3$, 54.7).

4-*i*-Propoxy-4′-methylthio-3,3′-diquinolinyl sulfide **5b**, viscous oil. $^1$H NMR ($CDCl_3$): $\delta$ ppm, 1.35 (d, 6H, $2CH_3$, $J$ = 6.1 Hz), 2.56 (s, 3H, $SCH_3$), 5.15 (m, 1H, OCH), 7.59, 7.65, 7.67 and 7.76 (m, 4H, H-6, H-6′, H-7 and H-7′), 8.01 and 8.09 (dd, 2H, H-8 and H-8′), 8.22 (dd, 1H, H-5), 8.27 (s, 1H, H-2′), 8.52 (dd, 1H, H-5′), 8.83 (s, 1H, H-2); MS (15 eV): m/z (%) 392 ($M^+$, 83.5); 350 (M-$C_3H_6$, 49.3); 303 (M-$C_3H_6$ and $SCH_3$, 36.7); 175 ($C_{10}H_9NS^+$, 100).

1-Methyl-4-oxo-1,4-dihydro-4′-methylthio-3,3′-diquinolinyl sulfide **7**, mp 252–253°C. $^1$H NMR (DMSO-$d_6$): $\delta$ ppm, 2.56 (s, 3H, $SCH_3$), 3.95 (s, 3H, $NCH_3$), 7.52, 7.70, 7.73 and 7.86 (m, 4H, H-6, H-6′, H-7 and H-7′), 7.80 and 7.95 (dd, 2H, H-8 and H-8′), 8.22 and 8.46 (dd, 2H, H-5 and H-5′), 8.31 (s, 1H, H-2), 8.76 (s, 1H, H-2′); MS (70 eV): m/z (%) 364 ($M^+$, 13.7); 333 (M-$SCH_3$, 100); 302 (M-$(CH_3)_2S$, 9.9).

*Cyclization of 4-Methylthio-4′-mercapto-3,3′-diquinolinyl Sulfide to Isothioquinanthrene* **1**

To a suspension of isothioquinanthrene **1** (0.32 g, 1 mmol) in 10 ml of dry DMSO at 20°C sodium methanethiolate was added (0.14 g, 2 mmoles). The mixture was stirred for 30 minutes to obtain the sodium salt of 4-methylthio-4′-mercapto-3,3′-diquinolinyl sulfide **2a**. The solution was neutralized with 5% hydrochloric acid to pH = 5. The resulting solid was filtered off, washed with water and air-dried to give isothioquinanthrene **1** 0.32 g (100%), mp 270–271°C, lit[12] mp 270–271°C. Methylation of the filtrate with methyl iodide did not give any S-methyl derivatives.

*Reaction of 4,4′-Dimethylthio-3,3′-diquinolinyl Sulfide* **3a** *with Sodium Methanethiolate*

*Alkylation with Methyl Iodide*: A solution of sulfide **3a** (0.38 g, 1 mmol) in 10 ml of dry DMSO at 70°C was stirred with sodium methanethiolate (0.21 g, 3 mmols) for 30 minutes. The mixture was cooled down to room temperature, poured into 30 ml of 15% aqueous sodium hydroxide and stirred with methyl iodide (0.42 g, 3 mmols) to give crude products. The products were purified by column chromatography (silica gel 60, chloroform) to give 3,4-dimethylthioquinoline **8a** (0.21 g, 48%, mp 93–94°C, lit[32] 93–94°C) and 4,4′-dimethylthio-3,3′-diquinolinyl sulfide **3a** (0.11 g, 29%, mp 142–143°C).

*Reaction of 4,4′-Dimethylthio-3,3′-diquinolinyl Sulfide* **3a** *with Sodium Methanethiolate*

*Alkylation with Benzyl Chloride*: A solution of sulfide **3a** (0.38 g, 1 mmol) in 10 ml of dry DMSO at 70°C was stirred with sodium methanethiolate (0.21 g, 3 mmols) for 30 minutes. The mixture was cooled down to room temperature, poured into 30 ml of 15% aqueous sodium hydroxide and extracted with chloroform (5 × 10 ml, Extract I). The extract was washed with water, dried with anhydrous sodium sulfate and evaporated to give crude product. The product was purified by column chromatography (silica gel 60, chloroform) to give 3,4-dimethylthioquinoline **8a** (0.10 g, 23%, mp 93–94°C).

The water layer was shaken with benzyl chloride (0.38 g, 3 mmols) and after 30 minutes extracted with chloroform (5 × 10 ml, Extract II). The extract was worked-up as described above to give 3-

benzylthio-4-methylthioquinoline **8b** (0.13 g, 22%, mp 71–72°C, lit[13] mp 71–72°C) and 4-benzylthio-4'-methylthio-3,3'-diquinolinyl sulfide **3d** (0.10 g, 22%, mp 112–113°C).

*Reaction of 4,4'-Dimethylthio-3,3'-diquinolinyl Sulfide* **3a** *with Sodium 2-Methyl-2-propanethiolate*

A solution of sulfide **3a** (0.38 g, 1 mmol) in 10 ml of dry DMSO at 70°C was stirred with sodium 2-methyl-2-propanethiolate (0.34 g, 3 mmols) for 30 minutes. The mixture was cooled down to room temperature, poured into 30 ml of 15% aqueous sodium hydroxide and extracted with chloroform (5 × 10 ml, Extract I). The extract was washed with water, dried with anhydrous sodium sulfate and evaporated to give crude product. The product was purified by column chromatography (silica gel 60, chloroform) to give 3-methylthio-4-*t*-butylthioquinoline **8c** (0.12 g, 23%, mp 105–106°C, lit[31] mp 105–106°C).

The water layer was shaken with methyl iodide (0.42 g, 3 mmols) and after 30 minutes extracted with chloroform (5 × 10 ml, Extract II). The extract was worked-up as described above to give 3,4-dimethylthioquinoline **8a** (0.10 g, 23%, mp 93–94°C) and sulfide **3a** (0.09 g, 24%, mp 142–143°C).

*Reaction of 4,4'-Dimethylthio-3,3'-diquinolinyl Sulfide* **3a** *with Sodium Ethanethiolate*

A solution of sulfide **3a** (0.38 g, 1 mmol) in 10 ml of dry DMSO at 70°C was stirred with sodium ethanethiolate (0.24 g, 3 mmols) for 30 minutes. The mixture was cooled down to room temperature, poured into 30 ml of 15% aqueous sodium hydroxide and extracted with chloroform (5 × 10 ml, Extract I). The extract was washed with water, dried with anhydrous sodium sulfate and evaporated to give crude products (0.22 g). Since the mixture could not be separated the ratio of compounds was calculated from $^1$H NMR data comparing the intensities of the S-alkyl and H-2 proton signals with the proton signals in parent compounds as follows:

3-Methylthio-4-ethylthioquinoline **8d**: δ ppm, 1.21 (t, 3H, $CH_3$), 2.66 (s, 3H, $SCH_3$), 2.96 (q, 2H, $CH_2$),[15] ratio 20.
3-Ethylthio-4-methylthioquinoline **8e**: δ ppm, 1.43 (t, 3H, $CH_3$), 2.45 (s, 3H, $SCH_3$), 3.16 (q, 2H, $CH_2$), 8.80 (s, 1H, H-2),[15] ratio 5.
3,4-Dimethylthioquinoline **8a**: δ ppm, 2.42 (s, 3H, 4-$SCH_3$), 2.65 (s, 3H, 3-$SCH_3$), 8.74 (s, 1H, H-2),[30] ratio 1.
4-Ethylthio-4'-methylthio-3,3'-diquinolinyl sulfide **3b**: δ ppm, 1.27 (t, 3H, $CH_3$), 2.56 (s, 3H, $SCH_3$), 3.10 (q, 2H, $CH_2$), 8.53 and 8.56 (2s, 2H, H-2 and H-2'),[13] ratio 10.
4.4'-Diethylthio-3,3'-diquinolinyl sulfide **3g**: δ ppm, 1.27 (t, 3H, $CH_3$), 3.10 (q, 2H, $CH_2$), 8.56 (s, 2H, H-2 and H-2'),[13] ratio 5.

The water layer was shaken with ethyl iodide (0.47 g, 3 mmols) and after 30 minutes extracted with chloroform (5 × 10 ml, Extract II). The extract was worked-up as described above to give 3-ethylthio-4-methylthioquinolines **8e** (0.10 g, 21%, mp 52–53°C, lit[15] mp 52–53°C) and 4-ethylthio-4'-methylthio-3,3'-diquinolinyl sulfide **3b** (0.02 g, 5%, mp 65–66°C).



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