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REACTIONS OF SOME DITHIINODIQUINOLINE 7-OXIDES WITH POTASSIUM PHENOXIDE

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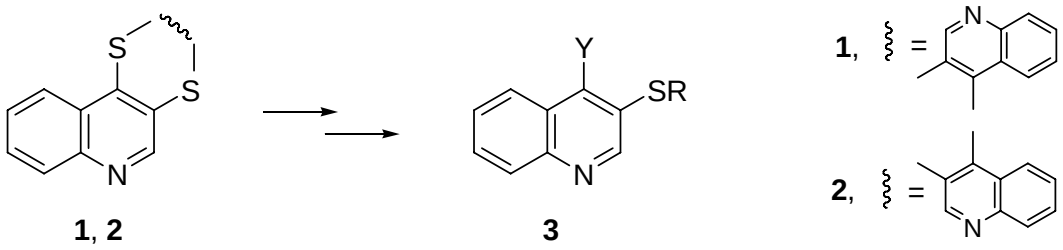
Abstract– *S*-Oxides of dithiinodiquinolines (**4**) and (**5**) react with potassium phenoxide at γ-quinolinyl-sulfur bond in two manners. Sulfinyl moiety at *non-aza*-influenced position in sulfoxide (**5**) significantly activates *ortho*-sulfanyl substituent towards nucleophilic *phenoxy-de-sulfidation* to form quinolinethiolate (**6A**). In the case of sulfoxide (**4**) with sulfinyl group in *aza*-activated position, nucleophilic *phenoxy-de-sulfinylation* occurs to form quinolinesulfenate anion (**7A**) trapped finally by methylation to products (**8**), (**9**) and (**10**).

INTRODUCTION

Transformations of thioquinanthrene (1,4-dithiino[2,3-*c*:5,6-*c*']diquinoline) (**1**) and isothioquinanthrene (1,4-dithiino[2,3-*c*:6,5-*c*']diquinoline) (**2**) induced by nucleophiles may serve as a source of numerous 4-substituted 3-quinolinyl sulfides (**3**)[1,2] (Scheme 1).

Scheme 1



1, **2** **3**

For example, reactions of dithiin (**1**) with sodium alkoxides proceeded easily (DMSO or DMF, 70 ºC, 0.5 h) with a 100 % conversion of **1** to results in 3,4'-diquinolinyl sulfides (**3**) (Y=alkoxyl, R=3-alkylsulfanyl-4-quinolinyl) (up to 92 %) after *S*-alkylation of the parent thiolates (R=3-thiolato-4-quinolinyl).[1] Transformations of the same type were also found for isothioquinanthrene (**2**).[2] No

reaction of dithiinodiquinolines (**1**) and (**2**) with other *O*-centred nucleophiles (potassium phenoxide, DMSO, 70 °C, 6h; boiling DMF, 6 h, and sodium acetate, DMSO, 70 °C, 6h) was observed.

Our previous studies showed that action of nitrating mixture converts dithiinodiquinolines (**1**) and (**2**) to corresponding 7-oxides (**4**) and (**5**).[3,4] The molecules of **4** and **5** contain sulfanyl and sulfinyl groups in the *ortho* positions. Since the sulfinyl group activates nucleophilic aromatic substitution in the *ortho* and *para* positions,[5-8] dithiinodiquinoline sulfoxides (**4**) and (**5**) were subjected to reaction with potassium phenoxide, which caused the expected *phenoxy-desulfidation* at γ-quinolinyl-sulfur bonds, as discussed in details below. (Schemes 2 and 3).

RESULTS AND DISCUSSION

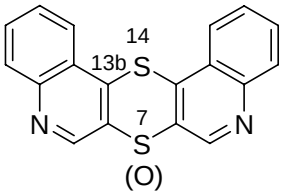
Due to electron attracting properties of the sulfinyl group it strongly affects nucleophilic substitution at aromatic and heteroaromatic systems.[5-8] Two effects were observed — x) sulfinyl group activates nucleophilic substitution in the *ortho* and *para* positions, xx) sulfinyl group acts as leaving group during nucleophilic substitution in *aza*-hetarenes such as pyridine, quinoline and pyridazine.[9] Taking this into consideration, we initiated the study described in this paper by the reaction between isothioquinanthrene 7-oxide (**5**) and potassium phenoxide because in the molecule of **5** the sulfinyl group should act as activating group only, and not as a leaving one. In fact, the reaction proceeded as *phenoxy-de-sulfidation* at *aza*-activated γ-quinolinyl C13b bond to form thiolate (**6A**) and gave 4-methylsulfanyl-4'-phenoxy-3,3'-diquinolinyl sulfoxide (**6**) after final *S*-methylation of **6A**. (Scheme 2)

According to general rules in *aza*-heteroaromatic nucleophilic substitution,[10] action of phenoxide anion towards dithiin *S*-oxide (**4**) should take place at *aza*-activated γ-quinolinyl C7a or C14a positions to give *thio*anions (**7A**) (when sulfinyl group acts as leaving group) or (**7B**) (when sulfinyl group acts as *ortho*-activating group). As sulfenate anion (**7A**) may undergo multidirectional transformations,[9] we decided to trap both of *thio*anions **7A** and (**7B**) by methylation. It revealed three products (separated by column chromatography). The main product — 3'-methylsulfinyl derivative (**9**) (41 %) was accompanied by 3'-methylsulfanyl derivative (**8**) (15 %) and 3'-methylsulfonyl derivative (**10**) (17 %). No formation of 3,4'-diquinolinyl sulfoxide derivative formed by methylation of thiolate (**7B**) was detected. This indicates that the sulfinyl group acts only as leaving group in the course of the reaction of dithiin *S*-oxide (**4**) with potassium phenoxide. (Scheme 3) Formation of sulfane (**8**) and sulfone (**10**) may be rationalized by disproportionation of sulfenate anion (**7A**) to mixture of the respective sulfanyl and sulfonyl anions trapped finally by methylation to products (**8**) and (**10**). Disproportionation of azinesulfenate anions was mentioned previously by Barlin and Brown.[9]

Scheme 4

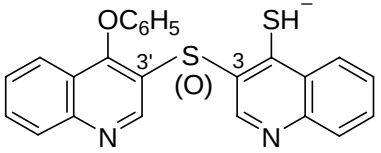
$$\underset{(\mathbf{7A})}{2\ QSO^-} \longrightarrow [QS^- + QSO_2^-] \xrightarrow{CH_3I} \underset{(\mathbf{8})}{QSCH_3} + \underset{(\mathbf{10})}{QSO_2CH_3}$$

Scheme 2



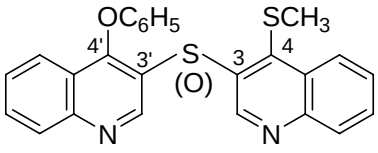
5

C_6H_5OK, (2 mol. eqv.)
DMF, -10 °C, 0.5 h



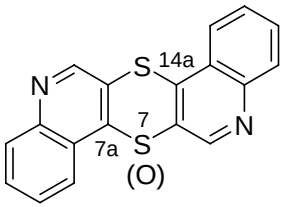
6A

CH_3I, 0 °C, 0.5 h



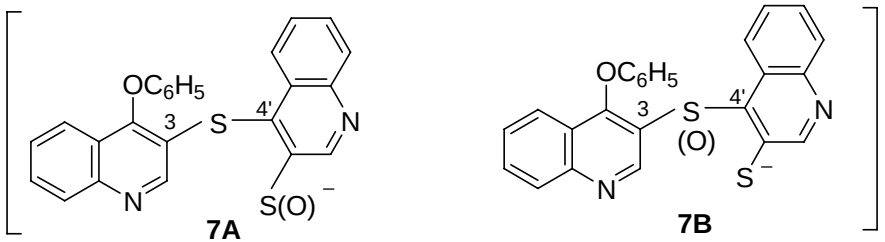
6

Scheme 3



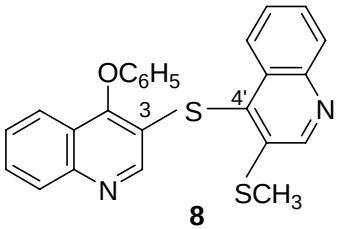
4

C_6H_5OK, (2 mol. eqv.)
DMF, -10 °C, 0.5 h

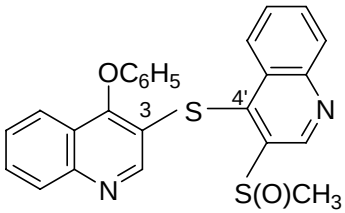


7A **7B**

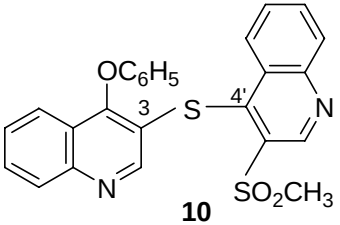
CH_3I, 0 °C, 0.5 h



8



9



10

Structure assignment of **8**, **9** and **10**. Properties of 3'-methylsulfanyl derivative (**8**) were identical with the sample of **8** prepared previously.[11] Structure of 3'-methylsulfinyl derivative (**9**) could be deduced from MS spectrum, elemental analysis and IR spectrum, the latter has shown strong band in sulfoxide region[12] at ν_{SO}=1051 cm^{-1}. However, the crutial data for structure assignment of methylsulfoxide (**9**) come from ^{1}H NMR spectra, because the H2' proton was deshielded by $\Delta\delta$=0.64 ppm and the CH_3S group protons were deshielded by $\Delta\delta$=0.24 ppm when compared to the δ_H values for methylsulfane (**8**). These changes are typical for the relation between 3-methylsulfanyl versus 3-methylsulfinylquinolines.[13] In the case of 3'-methylsulfonyl derivative (**10**), IR spectrum has shown strong band in sulfone region at ν_{SO2}=1141 cm^{-1} and positions of the H2' proton and the CH_3S group protons were shifted downfield when compared to sulfoxide (**9**) by $\Delta\delta$=0.07 ppm and by $\Delta\delta$=0.51 ppm, respectively, as deduced from ^{1}H NMR spectra.

CONCLUSION

S-Oxides of dithiinodiquinolines (**4**) and (**5**) reacted with potassium phenoxide at γ-quinolinyl-sulfur bond in two manners. In the case of sulfoxide (**5**) with sulfinyl moiety at *non-aza*-influenced position, significant activation of *ortho*-sulfanyl substituent towards nucleophilic displacement with potassium phenoxide was observed. However, in the case of sulfoxide (**4**) with sulfinyl group in *aza*-activated position, nucleophilic displacement of sulfoxide moiety by phenoxide anion occurred to form sulfenate anion (**7A**) trapped finally by methylation to products (**8**), (**9**), (**10**). These findings may serve as analytical tool in structure assignment of isomeric dithiinodiquinolines such as (**1**) and (**2**).

EXPERIMENTAL

Melting points were taken in open capillary tubes and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AVANCE 400 spectrometer operating at 400.22 MHz in deuterochloroform solutions with tetramethylsilane (δ 0.0 ppm) as internal standard. The COSY experiments were performed using standard Bruker program. 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 aluminium oxide 60 F_{254} neutral (type E) plates and using a mixture of carbon tetrachloride / aceton, 9 :1 , v/v as an eluent. Thioquinanthrene 7-oxide (**4**) and isothioquinanthrene 7-oxide (**5**) were prepared as described previously.[3,4] Potassium phenoxide was obtained from potassium hydroxide and phenol according to the reported data.[14] 4-Phenoxy-3'-methylthio-3,4'-diquinolinyl sulfide (**8**) was prepared from 4-chloro-3'-methylthio-3,4'-diquinolinyl sulfide and potassium phenoxide.[11]

Reaction of thioquinanthrene 7-oxide (**4**) and isothioquinanthrene 7-oxide (**5**) with potassium phenoxide

A mixture of sulfoxide (**4**) or (**5**) (0.67 g, 2 mmol) and DMF (12 mL) was stirred for 10 min and cooled down to –10 °C. 0.3 g (2.25 mmol) of potassium phenoxide was subsequently added and stirring was continued for 20 min. It leads to complete dissolution of the solid substrates.

The cherry-coloured solution was methylated on stirring at 0 °C with a solution of methyl iodide (0.13 mL, *ca.* 2 mmol) in 1 mL of DMF for 10 min and then allowed to warm to rt and stirred for additional 15 min. It was next poured into 30 mL of 5% aqueous sodium hydroxide. The solid was filtered off, washed with water and dried on air. Crude product formed from **5** was purified by recrystallization from ethanol. Mixture of products obtained from **4** was separated by column chromatography (Al_2O_3) using mixtures of tetrachloroethylene with 2.5 %, 5 % and 7.5 % of acetone, v/v as eluents to give sulfide (**8**) (Rf 0.81), sulfone (**10**) (Rf 0.49), and sulfoxide (**9**) (Rf 0.26).

3'-Methylsulfinyl-4-phenoxy-3,4'-diquinolinyl sulfide (**9**)

mp 212-213.5 ºC (EtOH). EIMS (70 eV) (m/z): 442 (9%, M^+), 426 (49%, M-O), 379 (10%, M-$SOCH_3$), 349 (8%, M-OC_6H_5). ^{1}H NMR ($CDCl_3$), δ: 2.83 (s, 3H, CH_3), 6.63-6.65 (m, 2H, $H_{ortho\text{-}phenyl}$), 7.04-7.07 (m, 1H, $H_{para\text{-}phenyl}$), 7.20-7.23 (m, 2H, $H_{meta\text{-}phenyl}$), 7.48 (ddd, 1H, *J*=8.1 Hz, *J*=6.9 Hz, *J*=0.8 Hz, H6), 7.56 (ddd, 1H, *J*=8.2 Hz, *J*=7.0 Hz, *J*=1.0 Hz, H6'), 7.71 (ddd, 1H, *J*=8.4 Hz, *J*=6.9 Hz, *J*=1.3 Hz, H7), 7.79 (ddd, 1H, *J*=8.3 Hz, *J*=6.9 Hz, *J*=1.3 Hz, H7'), 7.80 (dd, 1H, *J*=8.1 Hz, *J*=1.3 Hz, H5), 8.07 (dd, 1H, *J*=8.4 Hz, *J*=0.8 Hz, H8), 8.18 (dd, 1H, 1H, *J*=8.3 Hz, *J*=1.0 Hz, H8'), 8.25 (dd, 1H, *J*=8.2 Hz, *J*=1.3 Hz, H5'), 8.50 (s, 1H, H2), 9.37 (s, 1H, H2'). IR: ν_{SO}=1051 cm^{-1}. *Anal*. Calcd for $C_{25}H_{18}N_2O_2S_2$: C 67.87; H 4.07; N 6.33; S 14.48. Found: C 67.60, H 4.08; N 6.41; S 14.43.

3'-Methylsulfonyl-4-phenoxy-3,4'-diquinolinyl sulfide (**10**)

mp 172-173.5 °C (EtOH). EIMS (70 eV) (m/z): 458 (100%, M^+), 379 (50%, M-SO_2CH_3), 365 (10%, M-OC_6H_5). ^{1}H NMR ($CDCl_3$), δ: 3.33 (s, 3H, CH_3), 6.48-6.50 (m, 2H, $H_{ortho\text{-}phenyl}$), 7.00-7.04 (m, 1H, $H_{para\text{-}phenyl}$), 7.13-7.17 (m, 2H, $H_{meta\text{-}phenyl}$), 7.43 (ddd, 1H, *J*=8.2 Hz, *J*=6.9 Hz, *J*=1.0 Hz, H6), 7.47 (ddd, 1H, *J*=8.3 Hz, *J*=7.0 Hz, *J*=0.9 Hz, H6'), 7.66 (dd, 1H, *J*=8.2 Hz, *J*=1.2 Hz, H5), 7.70 (ddd, 1H, *J*=8.2 Hz, *J*=6.9 Hz, *J*=1.2 Hz, H7), 7.78 (ddd, 1H, *J*=8.2 Hz, *J*=7.0 Hz, *J*=1.2 Hz, H7'), 8.08 (dd, 1H, *J*=8.2 Hz, *J*=1.0 Hz, H8), 8.13 (dd, 1H, *J*=8.2 Hz, *J*=0.9 Hz, H8'), 8.21 (dd, 1H, *J*=8.3 Hz, *J*=1.2 Hz, H5'), 8.62 (s, 1H, H2), 9.45 (s, 1H, H2'). IR: ν_{SO2}=1143 cm^{-1}. *Anal.* Calcd for $C_{25}H_{18}N_2O_3S_2$: C 65.50; H 3.93; N 6.11; S 13.97. Found: C 65.12; H 3.99; N 6.01; S 13.64.

4-Methylsulfanyl-4'-phenoxy-3,3'-diquinolinyl sulfoxide (**6**)

Mp 144-146 °C (EtOH). EIMS (70 ev) (m/z): 442 (65%, M^+),425 (100, M –OH), 302 (30%, M-SCH_3-OC_6H_5). ^{1}H NMR ($CDCl_3$), δ: 2.32 (s, 3H, CH_3), 6.70-6.73 (m, 2H, $H_{ortho\text{-}phenyl}$), 6.88-6.92 (m, 1H, $H_{para\text{-}phenyl}$), 7.09-7.13 (m, 2H, $H_{meta\text{-}phenyl}$), 7.46 (ddd, 1H, *J*=8.2 Hz, *J*=6.9 Hz, *J*=1.0 Hz, H6), 7.65 (ddd, 1H,

J=8.2 Hz, *J*=7.0 Hz, *J*=1.1 Hz, H6'), 7.77 (dd, 1H, *J*=8.2 Hz, *J*=1.5 Hz, H5'), 7.78 (ddd, 1H, *J*=8.4 Hz, *J*=6.9.0 Hz, *J*=1.5 Hz, H7), 7.80 (ddd, 1H, *J*=8.4 Hz, *J*=7.0 Hz, *J*=1.3 Hz, H7'), 8.14 (dd, 1H, *J*=8.4 Hz, *J*=1.1, H8'), 8.18 (dd, 1H, *J*=8.4 Hz, *J*=1.0, H8), 8.30 (dd, 1H, *J*=8.2 Hz, *J*=1.3, H5'), 9.33 (s, 2H, H2 and H2'). IR: ν_{SO}= 1054 cm^{-1}. *Anal.* Calcd for $C_{25}H_{18}N_2O_2S_2$: C 67.87; H 4.07; N 6.33; S 14.48. Found: C 68.06, H 4.10; N 6.23; S 14.04.

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