INVESTIGATIONS OF 2,3'-BIQUINOLYL. 7.* THIOLATION OF 1-ALKYL-3-(2-QUINOLYL)QUINOLINIUM HALIDES

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Thiolation of 1-alkyl-3-(2-quinolyl)quinolinium halides by a mixture of sulfur with KOH in DMF leads to formation of 1'-alkyl-1',4'-dihydro-2,3'-biquinolyl-4'-thiones, rearrangement of which in boiling ethylene glycol makes it possible to obtain 4'-alkylthio-2,3'-biquinolyls.

Keywords: 1'-alkyl-1',4'-dihydro-2,3'-biquinolyl-4'-thiones, 1'-alkyl-3-(2-quinolyl)quinolinium halides, 2,3'-biquinolyls, nucleophilic substitution, rearrangement, thiolation.

Continuing the investigation of the reactivity of 1-alkyl-3-(2-quinolyl)quinolinium halides (**1**) [1, 2], we have studied their thiolation. It is known [3] that elemental sulfur can be activated by Lewis bases with formation of relatively soft nucleophilic species, for generation of which we used the system DMF–sulfur–potassium hydroxide, where the sulfur probably is activated by the dimethylamine formed as a result of hydrolysis of DMF. Considering that soft nucleophilic reagents are added to salts **1** at the 4' position [2], we might expect formation of compounds **2**, fragmentation of which leads to thiones **3**.

In fact, boiling salts **1** with the reagent prepared by heating sulfur with KOH in DMF leads to formation of novel 1'-alkyl-1',4'-dihydro-2,3'-biquinolyl-4'-thiones **3** in 30%-85% yield (Scheme 1). The structure of the latter was confirmed by ^{1}H NMR spectroscopy (including experiments with 4'-D salts **1**).

Competing with the process of thiolation is formation of 2,3'-biquinolyl (**4**), the fraction of which increases in the order **1c** < **1b** < **1a** < **1d**. This is the main process in thiolation of salt **1d** (the ratio of compounds **4**:**3d** is 5:1.1). Compound **3d** cannot be isolated. The ^{1}H NMR spectrum ($CDCl_3$) of the mixture of biquinolines **3d** and **4** contains signals belonging both to compound **4** [9.76 (1H, d, J = 2.28 Hz, 2'-H), 8.86 ppm (1H, d, J = 2.28 Hz, 4'-H)] and **3d** [9.22 (1H, d, J = 8.09 Hz, 5'-H); 8.51 (1H, d, J = 8.54 Hz, 3-H); 5.48 ppm (2H, s, CH_2)]. 1-Phenacyl-2-(3-quinolyl)quinolinium bromide under the reaction conditions yields exclusively compound **4**. We also observed that when the sulfurization products of **3** are boiled in ethylene glycol, a 1,5-shift of the alkyl group occurs with formation of novel 4'-alkylthio-2,3'-biquinolyls **5**. The yield after recrystallization was 58%-75% (Scheme 2).

In the case of compound **3d**, in this reaction we used its mixture with the previously discussed 2,3'-biquinolyl **4**. In this case, we obtained a mixture of compounds **4** and **5d** with an amount of biquinolyl **4** equal to the original content, the ^{1}H NMR spectrum of which contained signals belonging both to compound **4** (see above) and **5d** [5.51 (2H, s, CH_2); 8.62 (1H, d, J_{56} = 8.4 Hz, 5'-H); 8.86 (1H, d, J_{34} = 8.7 Hz, 3-H); 9.06 ppm (1H, s, 2'-H)].

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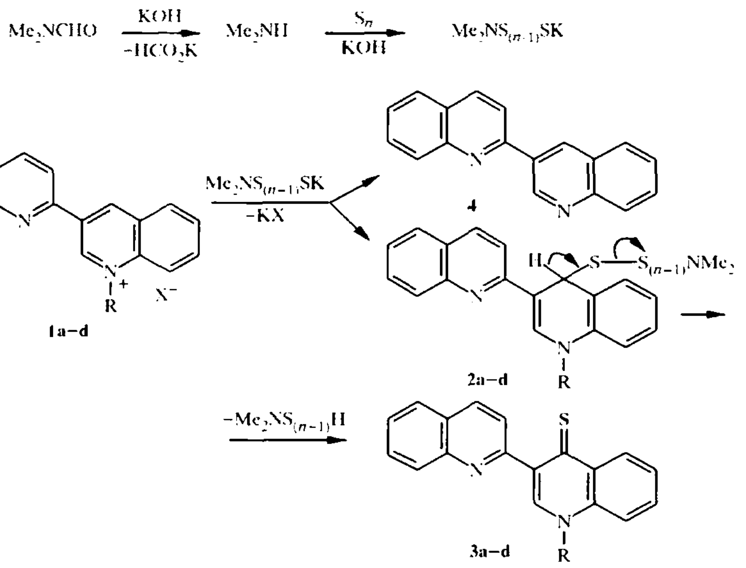
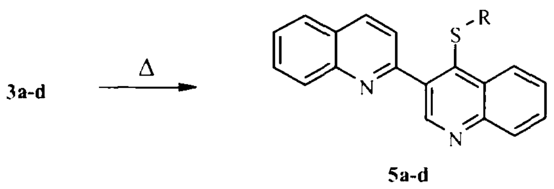
Scheme 1



1–3 **a** R = Me, **b** R = Et, **c** R = Bu, **d** R = CH_2Ph

Scheme 2



3, 5**a** R = Me, **b** R = Et, **c** R = Bu, **d** R = CH_2Ph

EXPERIMENTAL

The ^1H NMR spectra were recorded on Bruker WP-200 and Bruker AM-300 instruments using TMS as an internal standard. The course of the reactions and the purity of the synthesized compounds were monitored on Silufol UV-254 plates in ethylacetate. The DMF was purified by the procedure in [4].

1'-Alkyl-1',4'-dihydro-2,3'-biquinolyl-4'-thiones (3a-c). (General Procedure.) A mixture of elemental sulfur (1.28 g, 40 mmol) and KOH (1.68 g, 30 mmol) in DMF (70 ml) was boiled for 1 h. Then 1-alkyl-3-(2-quinolyl)quinolinium halide **1a-c** (20 mmol) was added, and the mixture was boiled for another 2.5 h. The reaction mixture was cooled and then poured into water (400 ml) containing KOH (4 mg). The precipitate was filtered off and recrystallized from aqueous alcohol.

1'-Methyl-1',4'-dihydro-2,3'-biquinolyl-4'-thione (3a). Yield 1.806 g (30.0%); mp 179-180°C. ^{1}H NMR spectrum (DMSO-d$_6$): 4.11 (3H, s, CH_3); 7.59 (1H, d, $J_{7'8'}$ = 7.76 Hz, 8'-H); 7.63 (1H, dd, $J_{5'6'}$ = 8.07, $J_{6'7'}$ = 7.07 Hz, 6'-H); 7.76 (1H, dd, $J_{6'7'}$ = 7.07, $J_{7'8'}$ = 7.76 Hz, 7'-H); 7.89 (1H, dd, J_{67} = 7.14, J_{78} = 8.26 Hz, 7-H); 7.92 (1H, dd, J_{56} = 7.96, J_{67} = 7.14 Hz, 6-H); 7.98 (1H, d, J_{56} = 7.96 Hz, 5-H); 8.07 (1H, d, J_{78} = 8.26 Hz, 8-H); 8.28 (2H, s, 3-H, 4-H); 8.48 (1H, s, 2'-H); 9.05 ppm (1H, d, $J_{5'6'}$ = 8.07 Hz, 5'-H). Found, %: C 75.67; H 4.59; N 9.21. $C_{19}H_{14}N_2S$. Calculated, %: C 75.50; H 4.64; N 9.27.

1'-Ethyl-1',4'-dihydro-2,3'-biquinolyl-4'-thione (3b). Yield 5.340 g (84.5%); mp 115-116°C. ^{1}H NMR spectrum (DMSO-d$_6$): 1.48 (3H, t, J = 7.28 Hz, CH_3); 4.59 (2H, q, J = 7.28 Hz, CH_2); 7.60 (1H, d, $J_{7'8'}$ = 7.78 Hz, 8'-H); 7.61 (1H, dd, $J_{5'6'}$ = 8.04, $J_{6'7'}$ = 7.12 Hz, 6'-H); 7.76 (1H, dd, $J_{6'7'}$ = 7.12, $J_{7'8'}$ = 7.78 Hz, 7'-H); 7.87 (1H, dd, J_{67} = 7.14, J_{78} = 8.29 Hz, 7-H); 7.97 (1H, dd, J_{56} = 7.71, J_{67} = 7.14 Hz, 6-H); 7.99 (1H, d, J_{56} = 7.71 Hz, 5-H); 8.08 (1H, d, J_{78} = 8.29 Hz, 8-H); 8.28 (2H, s, 3-H, 4-H); 8.50 (1H, s, 2'-H); 9.08 ppm (1H, d, $J_{5'6'}$ = 8.04 Hz, 5'-H). Found, %: C 76.12; H 5.03; N 8.76; $C_{20}H_{16}N_2S$. Calculated, %: C 75.95; H 5.06; N 8.86.

1'-Butyl-1',4'-dihydro-2,3'-biquinolyl-4'-thione (3c). Yield 5.979 g (86.9%); mp 122-123°C. ^{1}H NMR spectrum ($CDCl_3$): 1.01 (3H, t, J = 7.26 Hz, CH_3); 1.50 (2H, m, $CH_2CH_2\underline{CH_2}CH_3$); 1.98 (2H, m, $CH_2\underline{CH_2}CH_2CH_3$); 4.33 (2H, t, J = 7.11 Hz, $\underline{CH_2}CH_2CH_2CH_3$); 7.53 (1H, d, $J_{7'8'}$ = 7.78 Hz, 8'-H); 7.54 (1H, dd, $J_{5'6'}$ = 8.08, $J_{6'7'}$ = 7.12 Hz, 6'-H); 7.60 (1H, dd, $J_{6'7'}$ = 7.12, $J_{7'8'}$ = 7.78 Hz, 7'-H); 7.70 (1H, dd, J_{67} = 7.12, J_{78} = 8.26 Hz, 7-H); 7.76 (1H, dd, J_{56} = 7.73, J_{67} = 7.12 Hz, 6-H); 7.84 (1H, d, J_{56} = 7.73 Hz, 5-H); 8.11 (1H, d, J_{78} = 8.26 Hz, 8-H); 8.15 (1H, s, 2'-H); 8.18 (1H, d, J_{34} = 8.54 Hz, 4-H); 8.52 (1H, d, J_{34} = 8.54 Hz, 3-H); 9.29 ppm (1H, d, $J_{5'6'}$ = 8.08 Hz, 5'-H). Found, %: C 77.24; H 5.73; N 8.06. $C_{22}H_{20}N_2S$. Calculated, %: C 76.74; H 5.81; N 8.14.

4'-Alkylthio-2,3'-biquinolyls (5a-c). (General Procedure.) A solution of 1'-alkyl-1',4'-dihydro-2,3'-biquinolyl-4'-thione **2a-c** (1 mmol) in ethylene glycol (5 ml) was boiled for 16 h. The reaction mixture was poured into water (50 ml) containing KOH (0.5 mg). The precipitate was filtered off, washed with water (25 ml), dried, and recrystallized from a mixture of benzene and petroleum ether.

4'-Methylthio-2,3'-biquinolyl (5a). Yield 0.175 g (58.1%); mp 174-175°C. ^{1}H NMR spectrum ($CDCl_3$): 3.92 (3H, s, CH_3); 7.42 (1H, dd, $J_{7'8'}$ = 8.37, $J_{6'8'}$ = 1.01 Hz, 8'-H); 7.44 (1H, dt, $J_{5'6'}$ = 8.47, $J_{6'7'}$ = 7.99, $J_{6'8'}$ = 1.01 Hz, 6'-H); 7.46 (1H, dd, J_{56} = 8.09, J_{67} = 8.01, J_{68} = 1.11 Hz, 6-H); 7.64 (1H, dt, J_{67} = 8.01, J_{78} = 8.42, J_{57} = 1.53 Hz, 7-H); 7.67 (1H, td, $J_{6'7'}$ = 7.99, $J_{7'8'}$ = 8.37, $J_{5'7'}$ = 1.70 Hz, 7'-H); 7.79 (1H, dd, J_{56} = 8.09, J_{57} = 1.15 Hz, 5-H); 8.03 (1H, dd, J_{78} = 8.42, J_{68} = 1.11 Hz, 8-H); 8.16 (1H, d, J_{34} = 8.69 Hz, 4-H); 8.58 (1H, dd, $J_{5'6'}$ = 8.47, $J_{5'7'}$ = 1.70 Hz, 5'-H); 8.79 (1H, d, J_{34} = 8.69 Hz, 3-H); 8.84 ppm (1H, s, 2'-H). Found, %: C 75.71; H 4.58; N 9.19. $C_{19}H_{14}N_2S$. Calculated, %: C 75.50; H 4.64; N 9.27.

4'-Ethylthio-2,3'-biquinolyl (5b). Yield, 0.193 g (61.2%); mp 104-106°C. ^{1}H NMR spectrum (acetone-d$_6$): 1.60 (3H, t, J = 7.26 Hz, CH_3); 4.60 (2H, q, J = 7.26 Hz, CH_2); 7.48 (1H, dt, $J_{5'6'}$ = 8.11, $J_{6'7'}$ = 8.11, $J_{6'8'}$ = 1.28 Hz, 6'-H); 7.53 (1H, dd, J_{56} = 8.11, J_{67} = 8.11, J_{68} = 1.28 Hz, 6-H); 7.72 (1H, dt, J_{67} = 8.11, J_{78} = 8.11, J_{57} = 1.28 Hz, 7-H); 7.79 (1H, td, $J_{6'7'}$ = 8.11, $J_{7'8'}$ = 8.10, $J_{5'7'}$ = 1.71 Hz, 7'-H); 7.86 (1H, dd, $J_{7'8'}$ = 8.10, $J_{6'8'}$ = 1.28 Hz, 8'-H); 7.93 (1H, dd, J_{56} = 8.11, J_{57} = 1.28 Hz, 5-H); 8.03 (1H, dd, J_{78} = 8.11, J_{68} = 1.28 Hz, 8-H); 8.29 (1H, d, J_{34} = 8.54 Hz, 4-H); 8.54 (1H, dd, $J_{5'6'}$ = 8.11, $J_{5'7'}$ = 1.71 Hz, 5'-H); 8.98 (1H, d, J_{34} = 8.54 Hz, 3-H); 9.19 ppm (1H, s, 2'-H). Found, %: C 76.28; H 5.02; N 8.83; $C_{20}H_{16}N_2S$. Calculated, %: C 75.95; H 5.06; N 8.86.

4'-Butylthio-2,3'-biquinolyl (5c). Yield 0.256 g (74.4%); mp 109-110°C. ^{1}H NMR spectrum ($CDCl_3$): 0.99 (3H, t, J = 7.29 Hz, CH_3); 1.46 (2H, m, $CH_2CH_2\underline{CH_2}CH_3$); 1.93 (2H, m, $CH_2\underline{CH_2}CH_2CH_3$); 4.28 (2H, t, J = 7.24 Hz, $\underline{CH_2}CH_2CH_2CH_3$); 7.44 (1H, dt, $J_{5'6'}$ = 8.47, $J_{6'7'}$ = 7.99, $J_{6'8'}$ = 1.01 Hz, 6'-H); 7.49 (1H, dd, $J_{7'8'}$ = 8.37, $J_{6'8'}$ = 1.01 Hz, 8'-H); 7.54 (1H, dd, J_{56} = 8.09, J_{67} = 8.01, J_{68} = 1.11 Hz, 6-H); 7.65 (1H, dt, J_{67} = 8.01, J_{78} = 8.42, J_{57} = 1.53 Hz, 7-H); 7.67 (1H, td, $J_{6'7'}$ = 7.99, $J_{7'8'}$ = 8.37, $J_{5'7'}$ = 1.70 Hz, 7'-H); 7.82 (1H, dd, J_{56} = 8.09, J_{57} = 1.15 Hz, 5-H); 8.05 (1H, dd, J_{78} = 8.42, J_{68} = 1.11 Hz, 8-H); 8.22 (1H, d, J_{34} = 8.75 Hz, 4-H); 8.62 (1H, dd, $J_{5'6'}$ = 8.47, $J_{5'7'}$ = 1.70 Hz, 5'-H); 8.85 (1H, d, J_{34} = 8.75 Hz, 3-H); 8.97 ppm (1H, s, 2'-H). Found, %: C 77.48; H 5.71; N 8.05. $C_{22}H_{20}N_2S$. Calculated, %: C 76.74; H 5.81; N 8.14.

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