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SYNTHESIS OF BENZ-SUBSTITUTED 2-(2-MERCAPTOPHENYLAMINO)-4-METHYLQUINOLINES

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Interaction of 2-chloro-4-methylquinolines with o-mercaptoaniline under various conditions synthesis performed substituted in benzene ring 2-(2--aminophenylthio)-4-methylquinolines and 2-(2-mercaptophenylimino)-4-methyl--1,2-dihidroquinolines that by rearrangement or isomerization were respectively converted into 2-(2-mercaptophenylamino)-4-methylquinolines.

***Keywords*:** quinoline, o-merkaptoaniline, reactions of nucleophilic substitution.

Introduction. A quinoline ring containing compounds exhibit potent biological activities and has been proved by a number of recent reports [1, 2]. Quinoline derivatives were synthesized and explored for their analgesic activity [3], as antiallergetic agents [4], in treating alzheimer's disease (AD) [3], as anticancer [4, 5], antinephritic [6], antitumor [7] and anti-inflammatory activities.

Previously we studied the reactions of benz-substituted 2(4)-chloro-4(2)--methylquinolines with various nukleophiles [8–10].

Materials and Methods. Here we report reactions of nucleophilic substitution by o-mercaptoaniline of benz-substituted 2-chloro-4-methylquinolines (I, a–c) [6]. It was shown that the reaction between equivalent quantities of the above compounds by heating in ethanol in the presence of catalytic amount of hydrochloric acid during 5–6 *h* resulted in the formation of corresponding substituted 2-(2-mercaptophenylimino)-4-methyl-1,2-dihydroquinolines (II, a–c) with high yields, in the form of yellow crystals.

The same reaction in acetone solution was completed in two days at room temperature to produce the mixture of corresponding substituted 2-(2-aminophenylthio)-4-methylquinolines (III, a–c) and compounds II, a–c. By subsequent treatment of the resulting mixture with hydrochloride solution in water or ethanol the same yellow crystals of compounds II, a–c were also obtained.

The pest of compounds were transformed into colorless 2-(2-mercaptophenylamino)-4-methylquinolines (IV, a–c) by boiling in ethanol and aprotic polar solvents as well as during aging at room temperature evidently through isomerization according to the Scheme.

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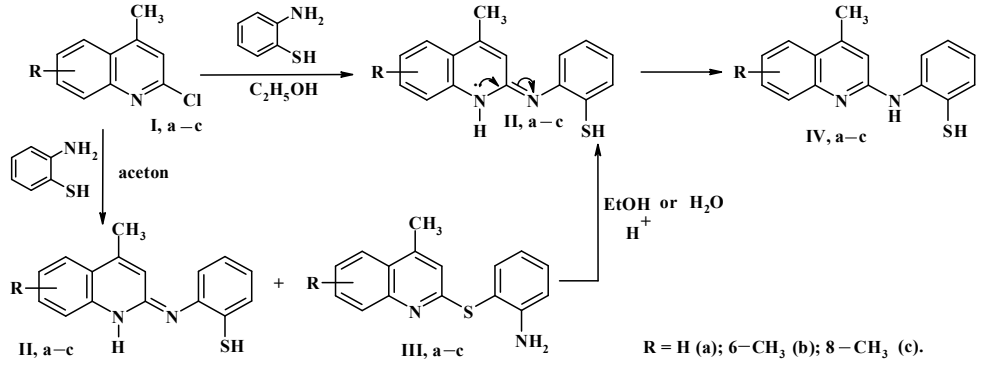

Scheme.

Experimental Part. ^{1}H NMR spectra were registered on a spectrometer Varian Mercury-300 from solutions in DMSO-d6. The purity of compounds obtained was checked by TLC on Silufol UV-254 plates (development in iodine vapor).

Substituted 2-(2-mercaptophenylimino)-4-methyl-1,2-dihydroquinolines (II, a–c) and 2-(2-aminophenylthio)-4-methylquinolines (III, a–c) as a mixture. A mixture of 0.01 *mol* of an appropriate substituted 2-chloro-4-methylquinoline [11] and 1.7 *mL* (0.01 *mol*) of o-mercaptoaniline in 5 *mL* of anhydrous acetone was stirred at room temperature for 2 days. The obtained crystals were filtered and washed with anhydrous acetone, after treatment with sodium hydroxide, substituted compounds II, a–c were isolated as mixtures with the corresponding substituted compounds III, a–c.

Substituted 2-(2-mercaptophenylimino)-4-methyl-1,2-dihydroquinolines (II, a–c).

a) A mixture of 0.01 *mol* of substituted 2-chloro-4-methylquinoline [11], 1.25 *g* (1.07 *mL*, 0.01 *mol*) of o-mercaptoaniline, 1 *mL* of conc. HCl in 30 *mL* of ethanol was heated on a water bath for 5–6 *h*. Then the reaction mixture was diluted with water and neutralized with water solution of NaOH to pH 7–7.5. The precipitated crystals were filtered, dried, the yield and melting point were estimated.

b) A mixture of 0.005 *mol* of an appropriate substituted compounds II, a–c and III, a–c, 10 *mL* of ethanol, and 0.75 *mL* of conc. HCl was heated on a water bath for 3–5 *h*. Then the reaction mixture was subjected to work up as in procedure a). Mixed samples of compounds III, a–c obtained by procedures a) and b) do not show depression of the melting point.

2-(2-Mercaptopheny)imino)-4-methyl-1,2-dihydroquinoline (II, a). Yield 2.61 *g* (98%) (*a*), 1.26 *g* (95%) (*b*), mp 253–255°*C*. Found, %: C 72.36; H 5.17; N 10.45; S 12.14. $C_{16}H_{14}N_2S$. Calculated, %: C 72.18; H 5.26; N 10.53; S 12.03.

2-(2-Mercaptophenylimino)-4,6-dimethyl-1,2-dihydroquinoline (II, b). Yield 2.69 *g* (96%) (*a*), 1.36 *g* (97%) (*b*), mp 261–263°*C*. Found, %: C 72.76; H 5.87; N 10.12; S 11.28. $C_{17}H_{16}N_2S$. Calculated, %: C 72.86; H 5.71; N 10.00; S 11.43.

2-(2-Mercaptophenylimino)-4,8-dimethyl-1,2-dihydroquinoline (II, c). Yield 2.60 *g* (93%) (*a*), 1.33 *g* (95%) (*b*), mp 237–239°*C*. Found, %: C 72.94; H 5.64; N 9.89; S 11.56. $C_{17}H_{16}N_2S$. Calculated, %: C 72.86; H 5.71; N 10.00; S 11.43.

Substituted 2-(2-mercaptophenylamino)-4-methylquinolines (IV, a–c). Compounds *III, a–c* (0.005 *mol*) at boiling in ethanol or aprotic polar solvents for ~0.5 *h* were converted into white crystals of compounds.

2-(2-Mercaptophenylamino)-4-methylquinoline (IV, a). Yield 1.01 *g* (76%), mp 222–223°*C*, R_f 0.54 (ethanol–toluene, 1:3). ^{1}H NMR spectrum, δ, ppm: 2.56 s (3H, CH3); 2.95 br. s (1H, SH); 6.64 s (1H, arom.); 6.95 t (1H, arom., *J*=7.1*Hz*); 7.25 t (1H arom., *J*=7.1 *Hz*); 7.29 t (1H arom., *J*=7.1 *Hz*); 7.47 t (1H arom., *J*=7.1 *Hz*); 7.49 d (1H arom., *J*=7.9 *Hz*); 7.57 d (1H arom., *J*=7.1 *Hz*); 7.63 d (1H arom., *J*=7.9 *Hz*); 7.75 d (1H arom., *J*=7.9 *Hz*); 8.36 d (1H, NH, *J*=7.9 *Hz*). Found, %: C 72.36; H 5.17; N 10.45; S 12.14. $C_{16}H_{14}N_2S$. Calculated, %: C 72.18; H 5.26; N 10.53; S 12.03.

2-(2-Mercaptophenylamino)-4,6-dimethylquinoline (IV, b). Yield 1.08 *g* (77%), mp 237–238°*C*, R_f 0.53 (ethanol–toluene, 1:3). Found, %: C 72.93; H 5.65; N 9.87; S 11.58. $C_{17}H_{16}N_2S$. Calculated, %: C 72.86; H 5.71; N 10.00; S 11.43.

2-(2-Mercaptophenylamino)-4,8-dimethylquinoline (IV, c). Yield 1.02 *g* (73%), mp 213–214°*C*, R_f 0.58 (ethanol–toluene, 1:3). Found, %: C 72.75; H 5.86; N 10.17; S 11.27. $C_{17}H_{16}N_2S$. Calculated, %: C 72.86; H 5.71; N 10.00; S 11.43.

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