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REACTION OF 2-ALLYLOXY(THIO)-4-METHYLQUINOLINES WITH HALOGENS

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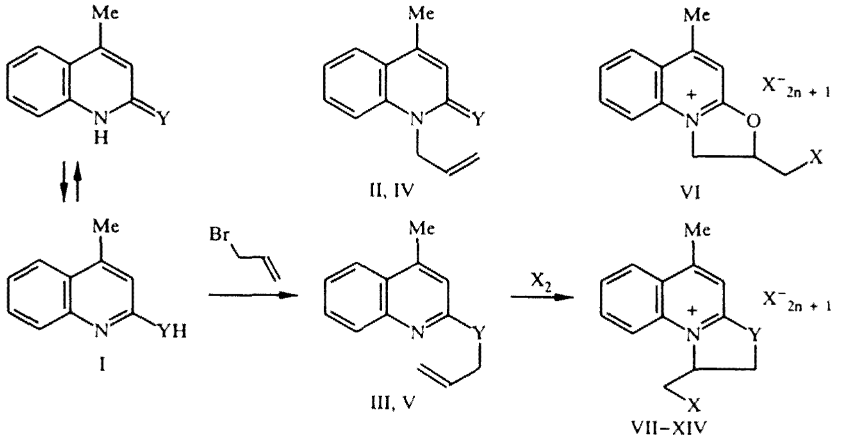
It was established that the halogenation of 2-allyloxy(thio)-4-methylquinolines leads to the formation of 3-halogenomethyl-2,3-dihydrooxazolo(thiazolo)[3,2-a]quinolinium halides.

The literature has contradictory data on the alkylation of 4-methyl-2-quinolinethione (I). It was shown in the work [1] that the reaction of the thione (I) with allyl bromide in the presence of alkali proceeds with the formation of 1-allyl-4-methyl-2-quinolinethione (II), with the mp 45-46°C, and it was shown in the work [2] that the reaction occurs with the formation of 2-allylthio-4-methylquinoline (III), which is a liquid with the bp 130°C (0.3 mm of Hg stem).

We studied the reaction of the thione (I) with allyl bromide in 2-propanol in the presence of NaOH, and established that the reaction proceeds, as was shown in the work [2], with the formation of the allyl sulfide (III). In contrast to the thione (I), the reaction of 4-methyl-2-quinolone with allyl bromide in the presence of alkali results in the formation of the mixture of 1-allyl-4-methyl-2-quinolone (IV) and 2-allyloxy-4-methylquinoline (V) with the predominance of the quinolone (IV).

It was previously shown in the works [1, 3, 4] that the halogenation of the quinolone (IV) proceeds by the scheme of the halogen cyclization reaction [5] with the formation of the 2-halogenomethyl-2,3-dihydrooxazolo[3,2-a]quinolinium halides (VI). We established that the iodination of the allyl compounds (III) and (IV) proceeds independently of the ratio of the starting reagents with the formation of the 3-iodomethyl-2,3-dihydrooxazolo(thiazolo)[3,2-a]quinolinium diiodoiodates (VII), (VIII).



Y = O, S; X = Br, I; n = 0, 1

The diiodoiodates (VII) and (VIII) react with sodium iodide and sodium thiosulfate to give the 3-iodomethyl-2,3-dihydrooxazolo(thiazolo)[3,2-a]quinolinium iodides (IX), (X). The reaction of the allyl compounds (III) and (V) with bromine using the equimolar ratio of reagents leads to the formation of the 3-bromomethyl-2,3-dihydrooxazolo(thiazolo)[3,2-a]quinolinium bromides (XI), (XII), and the excess of bromine gives the 3-bromomethyl-2,3-dihydrooxazolo(thiazolo)[3,2-

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a]quinolinium dibromobromate (XIII), (XIV). The dibromobromates (XIII), (XIV) are converted by acetone to the bromides (XI), (XII). The bromides (XI), (XII) react with sodium iodides to form the iodides (IX) and (X). The diiodoiodate (VIII) and dibromobromate (XIV) are also formed by the reaction of the allyl compound (III) with halogen, produced *in situ* from hydrogen halide acids and hydrogen peroxide (oxidative halogen cyclization).

The IR spectra of the compounds (III) and (V) contain bands at 1620 and 920 cm^{-1}, caused by vibrations of the double bond; they are absent from the spectra of compounds (VII)-(XIV). In the PMR spectra of the diiodoiodates (VII), (VIII), and the bromides (XI), (XII), the signals of the protons of the methyl group and the quinoline ring are shifted to low field by comparison with the initial allyl compounds; this is caused by the delocalization of the positive charge in the quinoline ring.

EXPERIMENTAL

The IR spectra were obtained on the Specord IR-75 spectrometer in Nujol. The PMR spectra were obtained on the Tesla BS-497 spectrometer (100 MHz), using $(CH_3)_2SO$ as the solvent and TMS as the internal standard. The course of reaction was monitored by the method of TLC on plates of Silufol UV-254.

The synthesis of 4-methyl-2-quinolinethione was performed according to the method of [5] by the fusion of 4-methyl-2-quinolone with P_2S_5 at 130-140°C.

2-Allylthio-4-methylquinoline (III). The mixture of 30 ml of 2-propanol, 0.45 g (2.5 mmole) of 4-methyl-2-quinolinethione, and 0.14 g (2.5 mmole) of KOH in 1 ml of water and 0.3 ml (3.7 mmole) of allyl bromide is stirred for 3 h. The residue of potassium bromide is filtered off, and the 2-propanol is distilled off. To the residue are added 20 ml of hexane and 4 g of Al_2O_3, and the mixture is stirred for 3 h. The mixture is filtered, and the hexane is distilled from the filtrate prior to the isolation of 2-allylthio-4-methylquinoline in the form of a light yellow liquid. The yield was 0.32 g (60%). Found, %: C 72.54, H 6.06, and S 14.93. $C_{13}H_{13}NS$. Calculated, %: C 72.51, H 6.09, and S 14.89.

2-Allyloxy-4-methylquinoline (V). The mixture of 15.9 g (0.1 mole) of 4-methyl-2-quinolone and 4.2 g (0.12 mole) of NaOH in 5 ml of water and 50 ml of 2-propanol is boiled for 1 h. To the resulting solution are added 10.4 ml (0.12 mole) of allyl bromide, and the mixture is boiled for 2 h. The solvent is distilled off, and acetone is added to the residue. The residue is filtered off, and the acetone is distilled off. The mixture of 1-allyl-4-methyl-2-quinolone and 2-allyloxy-4-methylquinoline is obtained. The total yield was 5.8 g (57%). The mixture is dissolved on heating in hexane; cooling results in precipitation of the residue of 1-allyl-4-methyl-2-quinolone. The hexane is distilled off, and the residue is chromatographed on Al_2O_3, using benzene as the eluent. The 2-allyloxy-4-methylquinoline is isolated in the form of a colorless liquid. The yield was 2.1 g (11%). The PMR spectrum was as follows: 2.52 ppm (3H, s, CH_3), 4.96 ppm (2H, m, OCH_2), 5.30 ppm (2H, m, $CH_2=$), 6.10 ppm (1H, m, $-CH=$), 6.72 ppm (1H, s, 3-H), and 7.1-7.9 ppm (4H, m, 5-, 6-, 7-, and 8-H). Found, %: C 78.15 and H 6.40. $C_{13}H_{13}NO$. Calculated, %: C 78.35 and H 6.59.

General Method for the Isolation of the Diiodoiodates (VII), (VIII). To the solution of 1 mmole of the allyl compound (III) or (V) in 5 ml of diethyl ether is added the solution of 0.5 g (2 mmole) of iodine in 5 ml of diethyl ether. After 2 h, the precipitated residue is filtered off, dissolved in acetone, and reprecipitated with diethyl ether.

3-Iodomethyl-2,3-dihydrothiazolo[3,2-a]quinolinium Diiodoiodate (VIII). The yield was 72%. The mp was 168-170°C (with decomposition). The PMR spectrum was as follows: 2.87 ppm (3H, s, CH_3), 3.5-4.3 ppm (4H, m, CH_2I, SCH_2), 6.46 ppm (1H, m, 3-H), and 7.8-8.5 ppm (5H, m, 5-, 6-, 7-, 8-, and 10-H). Found, %: S 4.40 and I 70.35. $C_{13}H_{13}I_4NS$. Calculated, %: S 4.43 and I 70.21.

3-Iodomethyl-2,3-dihydrooxazolo[3,2-a]quinolinium Diiodoiodate (VII). The yield was 64%. The mp was 72-74°C (with decomposition). The PMR spectrum was as follows: 2.93 ppm (3H, s, CH_3), 3.98 ppm (2H, m, CH_2I), 5.10 ppm (2H, m, OCH_2), 6.00 ppm (1H, m, 3-H), and 7.8-8.5 ppm (5H, m, 5-, 6-, 7-, 8-, and 10-H). Found, %: C 22.15, H 1.75, and I 71.33. $C_{13}H_{13}I_4NO$. Calculated, %: C 22.08, H 1.85, and I 71.81.

B. To the solution of 0.215 g (1 mmole) of the allyl compound (III) are added 1.42 ml (6 mmole) of the 54% solution of HI and 0.35 ml of the 30% solution of H_2O_2, and the mixture is stirred for 6 h. The resulting residue is filtered off, dissolved in acetone, and reprecipitated with diethyl ether. The yield of the diiodoiodate (VIII) was 52%.

General Method for the Isolation of the Bromides (XI), (XII). A. To the solution of 1 mmole of the allyl compound (III) or (V) in 5 ml of CH_2Cl_2 is added the solution of 0.1 ml (2 mmole) of bromine in 5 ml of CH_2Cl_2. After 2 h, the precipitated residue of the dibromobromates (XIII), (XIV) is filtered off prior to treatment with acetone to isolate the bromides (XI), (XII).

3-Bromomethyl-2,3-dihydrothiazolo[3,2-a]quinolinium Bromide (XII). The yield was 60%. The mp was 160-162°C. The PMR spectrum was as follows: 2.87 ppm (3H, s, CH_3), 3.8-4.4 ppm (4H, m, CH_2Br, SCH_2), 6.61 ppm (1H, m, 3-H), and 7.8-8.5 ppm (5H, m, 5-, 6-, 7-, 8-, and 10-H). Found, %: S 8.41 and Br 42.71. $C_{13}H_{13}Br_2NS$. Calculated, %: S 8.54 and Br 42.60.

3-Bromomethyl-2,3-dihydrooxazolo[3,2-a]quinolinium Bromide (XI). The yield was 54%. The mp was 162°C (with decomposition). The PMR spectrum was as follows: 2.93 ppm (3H, s, CH_3), 4.31 ppm (2H, m, CH_2Br), 5.27 ppm (2H, m, OCH_2), 6.32 ppm (1H, m, 3-H), and 7.8-8.5 ppm (5H, m, 5-, 6-, 7-, 8-, and 10-H). Found, %: C 43.35, H 3.55, and Br 44.62. $C_{13}H_{13}Br_2NO$. Calculated, %: C 43.48, H 3.65, and Br 44.50.

B. To the solution of 0.215 g (1 mmole) of the allyl compound (III) are added 1.2 ml (6 mmole) of the 40% solution of HBr and 0.35 ml of the 30% solution of H_2O_2, and the mixture is stirred for 6 h. The resulting residue is filtered off and treated with acetone for the isolation of the bromide (XII). The yield of the bromide (XII) was 0.18 g (48%).

General Method for the Isolation of the Iodides (IX), (X). A. To the solution of 1 mmole of the diiodoiodate (VII) or (VIII) in 5 ml of acetone are added 2 mmole of NaI in 3 ml of acetone. After 1 h, the precipitated residue is filtered off and washed with acetone.

3-Iodomethyl-2,3-dihydrothiazolo[3,2-a]quinolinium Iodide (X). The yield was 80%. The mp was 177°C (with decomposition).

B. The bromides (XI), (XII) (1 mmole) and 3 mmole of NaI are dissolved in 10 ml of 2-propanol, and the mixture is boiled using a reflux condenser for 1 h. The 2-propanol is distilled off, and the residue is washed with water and acetone. The yield of the iodide (IX) was 89%. The yield of the iodide (X) was 64%.

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