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HALOHETEROCYCLIZATION OF 2-METHALLYL(PROPARGYL)-THIOQUINOLINE-3-CARBALDEHYDES

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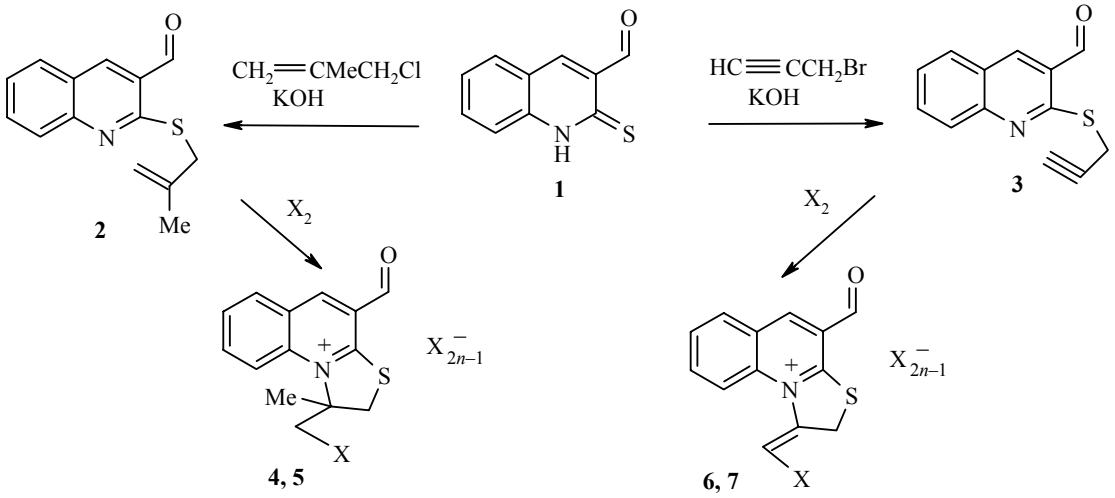
Interaction of 2-methallyl(propargyl)thioquinoline-3-carbaldehydes with halogens leads to the formation of 4-formyl-1-halomethyl(halomethylidene)-1,2-dihydrothiazolo[3,2-a]quinolinium halides.

Keywords: 3-formyl-2-methallylthioquinoline, 3-formyl-2-propargylthioquinoline, haloheterocyclization.

Haloheterocyclization reactions of unsaturated ethers and thioethers of quinoline are described in the literature [1, 2], as a result of which heterocyclic systems with oxa(thia)zolinium rings are obtained. In continuation of these investigations we chose the unsaturated thioethers 2-methallyl- and 2-propargyl-thioquinoline-3-carbaldehydes **2, 3** as model compounds for haloheterocyclization. The latter were obtained in good yield by the alkylation of 3-formylquinoline-2-thione (**1**) with the appropriate alkylating agents in the presence of alkali.



4, **6** X = Br; **5**, **7** X = I; **4**, **5**, **7** *n* = 2, **6** *n* = 1

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Bromine and iodine were used as electrophilic reagents for haloheterocyclization. Bromination was carried out in acetic acid or chloroform, and iodination in acetic acid with a twofold excess of halogen. As a result derivatives of 3-halomethyl(halomethylidene)-2,3-dihydrothiazolo[3,2-*a*]quinolinium halides **4-7** were obtained. It should be noted that on bromination of the methallyl thioether the tribromide **4** is formed, but in the case of the propargyl thioether, according to TLC data (in the system hexane–ether, 2:3), a mixture of the mono- and tribromides was formed. This was treated with acetone with the aim of obtaining the monobromide **6**. On iodination triiodides **5, 7** were obtained.

According to the spectral data, and also that of TLC, on halogenation of the propargyl thioether only one isomer is formed selectively, in difference to the haloheterocyclization of the analogous propargyl ether in [2].

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Varian VXR-300 spectrometer (300 MHz) in a mixture of DMSO-d_6 and CCl_4, internal standard was TMS.

3-Formylquinoline-2-thione (**1**) was synthesized by the procedure described in [3].

Preparation of Thioethers 2, 3 (General Method). A mixture of quinoline-2-thione **1** (1 mmol) and KOH (1.2 mmol) in water (3 ml) and 2-propanol (30 ml) was heated until dissolution was complete. The organic halide (1.5 mmol) (90% solution of methallyl chloride or 80% solution of propargyl bromide in toluene) was added to the obtained solution and the mixture heated for 0.5-1 h at 40-60°C. The solid was filtered off, and recrystallized from acetic acid or 2-propanol.

3-Formyl-2-methallylthioquinoline (2). Yield was 66%; mp 160-161°C (acetic acid). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.95 (3H, s, CH_3); 4.12 (2H, s, SCH_2); 4.96 (1H, s, $=CH_2$); 5.19 (1H, s, $=CH_2$); 7.50 (1H, t, *J* = 7.0, H-6); 7.75 (1H, d, *J* = 7.0, H-5); 8.10 (1H, t, *J* = 7.0, H-7); 8.25 (1H, d, *J* = 7.0, H-8); 8.93 (1H, s, H-4); 10.30 (1H, s, CHO). Found, %: N 5.84. $C_{14}H_{13}NOS$. Calculated, %: N 5.76.

3-Formyl-2-propargylthioquinoline (3). Yield was 64%; mp 118-120°C (2-propanol). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.99 (1H, s, ≡CH); 4.10 (2H, s, CH_2); 7.62 (1H, t, *J* = 7.0, H-6); 7.9 (1H, d, *J* = 7.0, H-5); 7.95 (1H, t, *J* = 7.0, H-7); 8.15 (1H, d, *J* = 7.0, H-8); 8.98 (1H, s, H-4); 10.11 (1H, s, CHO). Found, %: N 6.09. $C_{13}H_9NOS$. Calculated, %: N 6.16.

Preparation of Bromides 4, 6 (General Method). A solution of bromine (2 mmol) in chloroform or acetic acid (5 ml) was added with constant stirring to a solution of methallyl thioether **2** (1 mmol) or propargyl thioether **3** (1 mmol) in chloroform or acetic acid (10 ml). After 2 h the precipitated solid was filtered off.

1-Bromomethyl-4-formyl-1-methyl-1,2-dihydro[1,3]thiazolo[3,2-*a*]quinolinium Tribromide (4). Yield was 78%; mp 207-208°C (acetic acid). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.35 (3H, s, CH_3); 3.88 (2H, d, *J* = 7.0, CH_2Br); 4.22 (1H, d, *J* = 12.0, SCH_2); 4.53 (1H, d, *J* = 12.0, SCH_2); 7.96 (1H, t, *J* = 7.0, H-7); 8.19 (1H, d, *J* = 7.0, H-6); 8.52 (1H, t, *J* = 7.0, H-8); 8.66 (1H, d, *J* = 7.0, H-9); 9.65 (1H, s, H-5); 10.20 (1H, s, CHO). Found, %: N 2.45. $C_{14}H_{13}Br_4NOS$. Calculated, %: N 2.49.

1-Bromomethylidene-4-formyl-1,2-dihydro[1,3]thiazolo[3,2-*a*]quinolinium Bromide (6). Yield was 71%; mp 285-286°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.25 (1H, d, *J* = 7.0, SCH_2); 4.57, 4.69 (1H, d, *J* = 14.0, SCH_2); 7.56 (1H, t, *J* = 7.0, H-7); 7.65 (1H, d, *J* = 7.0, H-6); 7.72 (1H, t, *J* = 7.0, H-8); 8.05 (1H, d, *J* = 7.0, H-9); 8.35 (1H, s, =CHBr); 8.93 (1H, s, H-5); 10.55 (1H, s, CHO). Found, %: N 3.61. $C_{13}H_9Br_2NOS$. Calculated, %: N 3.47.

Preparation of Iodides 5, 7 (General Method). A solution of iodine (2 mmol) in acetic acid (20 ml) was added with constant stirring to a solution of allyl thioether **2** (1 mmol) or propargyl thioether **3** (1 mmol) in acetic acid (10 ml). After 2-3 h the precipitated solid was filtered off.

4-Formyl-1-iodomethyl-1-methyl-1,2-dihydro[1,3]thiazolo[3,2-*a*]quinolinium Triiodide (5). Yield was 85%; mp 125-126°C (acetic acid). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.27 (3H, s, CH_3); 4.07 (2H, d, *J* = 7.0, CH_2I); 4.40, 4.85 (2H, d, *J* = 12.0, SCH_2); 7.97 (1H, t, *J* = 7.0, H-7); 8.23 (1H, d, *J* = 7.0, H-6); 8.55 (1H, t, *J* = 7.0, H-8); 8.69 (1H, d, *J* = 7.0, H-9); 9.71 (1H, s, H-5); 10.24 (1H, s, CHO). Found, %: N 1.84. $C_{14}H_{13}I_4NOS$. Calculated, %: N 1.87.

1-Formyl-4-iodomethylidene-1,2-dihydro[1,3]thiazolo[3,2-*a*]quinolinium Triiodide (7). Yield was 71%; mp 240-242°C (DMF). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.95 (1H, d, *J* = 7.0, SCH_2); 4.28, 4.50 (1H, d, *J* = 9.0, SCH_2); 7.25 (1H, d, *J* = 8.0, H-7); 7.35 (1H, d, *J* = 8.0, H-6); 7.65 (1H, s, H-9); 7.95 (1H, s, =CHI); 8.50 (1H, s, H-5); 10.20 (1H, s, CHO). Found, %: N 2.00. $C_{13}H_9I_4NOS$. Calculated, %: N 1.91.

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