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SYNTHESIS AND HALOGENATION OF ALLYLTHIOETHERS OF PYRAZOLO[3,4-*d*]PYRIMIDINE

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The interaction of 6-allylthio-4-imino-1-methyl-3-methylthio-5-phenyl-1,5-dihydro-4H-pyrazolo[3,4-d]-pyrimidine with bromine leads to the formation of 8-bromomethyl-4-imino-1-methyl-3-methylthio-5-phenyl-4,5,7,8-tetrahydro-1H-pyrazolo[4,3-e][1,3]thiazolo[3,2-a]pyrimidinium tribromide.

Keywords: 6-allylthio-4-iminopyrazolo[3,4-*d*]pyrimidine, monobromide, pyrazolo[3,4-*d*]pyrimidine, tribromide, bromoheterocyclization.

With the aim of obtaining condensed pyrazolo[3,4-*d*]pyrimidine systems the condensation has been carried out of a substituted aminopyrazole, which contains a cyano group in the *ortho* position, with phenyl isothiocyanate and subsequent heterocyclization of the thiourea obtained. Analogous studies have been carried out using aminothiophene derivatives containing a cyano or an ethyoxycarbonyl grouping in the *ortho* position [1, 2].

5-Amino-4-cyano-1-methyl-3-methylthio-1H-pyrazole (**1**), which corresponds to the structural requirements, was used as the initial model aminopyrazole. It contains an amino and a cyano group in the *ortho* position, which is necessary for the synthesis of the condensed systems including pyrimidine.

A nonpolar high-boiling solvent, such as toluene or a mixture of the xylene isomers, was used as solvent for obtaining thioureas from aminocyanothiophenes and phenyl isothiocyanate [3]. We obtained thiourea **2** from pyrazole **1** and phenyl isothiocyanate in boiling ethanol in a yield of 809%. Thiourea **2** was cyclized into 4-iminopyrazolo[3,4-*d*]pyrimidine-6-thione **4** on heating with a twofold excess of alkali in 90% ethanol with subsequent neutralization with acetic acid.

Thioether **5** was obtained by the alkylation of potassium salt **3** with allyl bromide in 95% ethanol. Bromination of thioether **5** with a twofold excess of bromine in chloroform was effected, due to the presence of an unsaturated substituent and a nucleophilic nitrogen atom in the *ortho* position to heterocyclization, under the action of the electrophilic reagent to tribromide **6**, which was converted into the monobromide **7** by the action of acetone.

EXPERIMENTAL

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

1-[1,4-Dimethyl-3-(methylthio)-1H-pyrazol-5-yl]-3-phenylthiourea (2). Phenyl isothiocyanate (1.62 g, 0.012 mol) was added to a solution of pyrazole **1** (1.86 g, 0.01 mol) in ethanol (25 ml), and the mixture was boiled for 5 h. The bright yellow solid was filtered off, and recrystallized from ethanol. Yield 81%;

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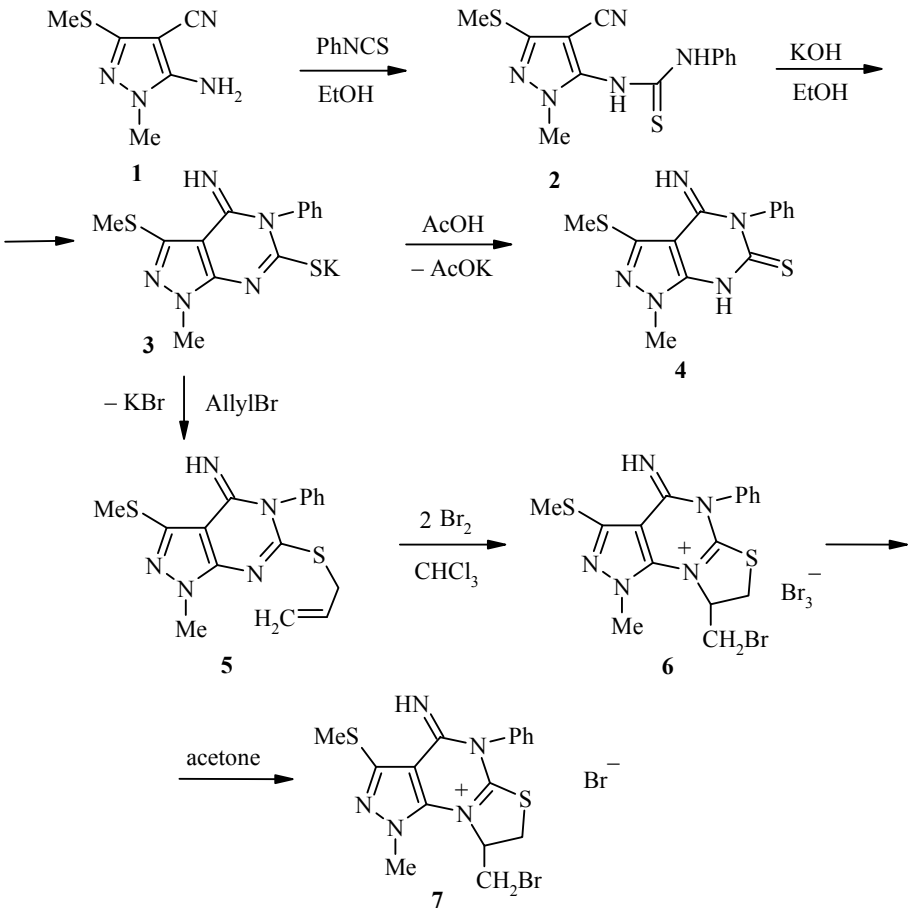

mp 113° C (from ethanol). ^{1}H NMR spectrum, δ, ppm: 2.55 (3H, s, NCH_3); 4.05 (3H, s, SCH_3); 7.45 (5H, m, C_6H_5); 13.15 (2H, s, 2NH). Found, %: N 22.75. $C_{13}H_{13}N_5S_2$. Calculated, %: N 23.08.

Potassium 4-Imino-1-methyl-3-methylthio-5-phenyl-4,5-dihydro-1H-pyrazolo[3,4-*d*]pyrimidine-6-thiolate (3). Potassium hydroxide (2.24 g, 0.02 mol) was added to a solution of thiourea **2** (3.01 g, 0.01 mol) in ethanol (20 ml), and the mixture boiled for 2 h. The white solid was filtered off, and washed with water. Yield 75%; mp 235°C. ^{1}H NMR spectrum, δ, ppm: 2.50 (3H, s, NCH_3); 4.12 (3H, s, SCH_3); 7.55 (5H, m, C_6H_5); 8.70 (1H, s, =NH). Found, %: N 20.12. $C_{13}H_{12}KN_5S_2$. Calculated, %: N 20.51.

4-Imino-1-methyl-3-methylthio-5-phenyl-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-*d*]pyrimidine-6-thione (4). Potassium salt **3** was dissolved in ethanol and acidified with 85% acetic acid solution. The white solid was filtered off, washed with water, and recrystallized from acetic acid. Yield 95%; mp >300°C. Found, %: N 22.88. $C_{13}H_{13}N_5S_2$. Calculated, %: N 23.08.

6-Allylthio-4-imino-1-methyl-3-methylthio-5-phenyl-1,5-dihydro-4H-pyrazolo[3,4-*d*]pyrimidine (5). A mixture of potassium salt **3** (3.42 g, 0.01 mol) and allyl bromide (1.72 g, 0.015 mol) in ethanol (20 ml) was heated at 60°C for 40 min, cooled, the white solid was filtered off, and recrystallized from ethanol. Yield 62%; mp 155-157°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.5 (3H, s, NCH_3); 3.8 (2H, d, J = 5, SCH_2); 4.15 (3H, s, SCH_3); 5.19 (2H, dd, J = 15, J = 9, $=CH_2$); 6.0 (1H, m, =CH); 7.1, 7.4, 7.8 (5H, m, C_6H_5); 8.75 (1H, s, =NH). Found, %: N 19.96. $C_{16}H_{17}N_5S_2$. Calculated, %: N 20.39.

8-Bromomethyl-4-imino-1-methyl-3-methylthio-5-phenyl-4,5,7,8-tetrahydro-1H-pyrazolo[4,3-*e*][1,3]-thiazolo[3,2-*a*]pyrimidinium Tribromide (6) and Monobromide (7). A solution of bromine (3.2 g, 0.02 mol) in chloroform (10 ml) was added slowly with constant stirring to a solution of thioether **5** (3.19 g, 0.01 mol) in

chloroform (20 ml). The solution was stirred for a further 3 h. The yellow solid tribromide **6** was filtered off, and recrystallized from DMF. Yield 45%; mp 192-193°C. Found, %: N 10.26; Br 47.45. $C_{16}H_{17}Br_4N_5S_2$. Calculated, %: N 10.56; Br 48.20.

Tribromide **6** was treated with acetone and monobromide **7** was obtained. Yield 85%; mp 223-225°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.66 (3H, s, NCH_3); 3.72 (2H, dd, *J* = 7, *J* = 8, SCH_2); 4.15 (2H, d, *J* = 5, CH_2Br); 4.25 (3H, s, SCH_3); 5.74 (1H, m, CH); 7.8 (5H, m, C_6H_5); 10.36 (1H, s, =NH). Found, %: N 13.68; Br 32.08. $C_{16}H_{17}Br_2N_5S_2$. Calculated, %: N 13.92; Br 31.75.

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