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SYNTHESIS OF [1,2,4]TRIAZOLO[4,3-*a*]PYRIMIDIN-7(8H)-ONE DERIVATIVES BY NUCLEOPHILIC SUBSTITUTION OF THE METHYLMERCAPTO GROUP IN 4-HYDROXY-6-METHYL-2-METHYLTHIOPYRIMIDINE

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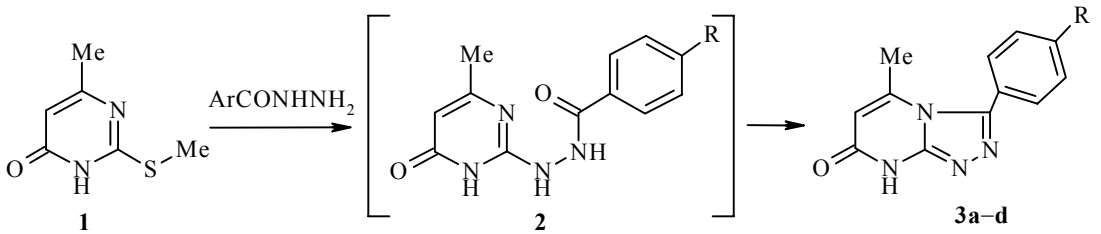
Keywords: 4-hydroxy-6-methyl-2-methylmercaptopyrimidine, [1,2,4]triazolo[4,3-*a*]pyrimidin-7(8H)-one, nucleophilic substitution, spontaneous cyclization.

Triazolopyrimidines display anti-inflammatory [1], vasodilative [2], and bactericidal activity [3].

In previous work [4], we showed that heating 2-arylidenehydrazones of 4-hydroxy-6-methylpyrimidines in nitrobenzene at reflux gives derivatives of [1,2,4]triazolo[4,3-*a*]pyrimidin-7(8H)-one. A method described in the literature for obtaining this system involves the reaction of 4-hydroxy-6-methyl-2-methylthiopyrimidine (**1**) with hydrazides of carboxylic acids in phenol [5, 6].



1 **2** **3a–d**

3 a R = H; **b** R = Cl; **c** R = Me; **d** R = CMe_3

We have found that the nucleophilic substitution upon fusing equimolar amounts of compound **1** and hydrazides of aromatic carboxylic acids at 200°C does not stop at formation of 2-benzoylhydrazines of 4-hydroxy-6-methylpyrimidine (**2**) but proceeds with spontaneous cyclization to give derivatives of 3-aryl-5-methyl[1,2,4]triazolo[4,3-*a*]pyrimidin-7(8H)-one (**3**). The NMR spectrum of compound **3b** is completely identical to the spectrum of the compound obtained by the oxidative cyclization of 2-(4-chlorobenzylidene)-hydrazone of 4-hydroxy-6-methylpyrimidine in nitrobenzene [4].

The structures of the compounds synthesized were supported by ^{1}H NMR spectral data obtained at 300 MHz, in DMSO-d_6 with TMS as the internal standard.

5-Methyl-3-phenyl[1,2,4]triazolo[4,3-*a*]pyrimidin-7(8H)-one (3a). Mixture of compound **1** (0.01 mol) and benzoic acid hydrazide (0.01 mol) was heated for 1 h at 200°C. Upon cooling, the reaction mixture was triturated in 2-propanol, filtered, and dried to give compound **3a** in 78% yield; mp >300°C (DMF). IR spectrum, ν, cm^{-1} (KBr pellets): 1610 (C=N); 1685 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.34 (3H, s, CH_3); 5.69 (1H, s, CH); 7.43-8.14 (5H, m, C_6H_5); 12.97 (1H, br. s, NH). Found, %: N 24.7. $C_{12}H_{10}N_4O$. Calculated, %: N 24.8.

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3-(4-Chlorophenyl)-5-methyl[1,2,4]triazolo[4,3-*a*]pyrimidin-7(8H)-one (3b) was obtained analogously to compound **3a** from equimolar amounts of pyrimidine **1** and 4-chlorobenzoic acid hydrazide. The yield of compound **3b** was 79%; mp >300°C (DMF). IR spectrum, ν, cm^{-1} (KBr pellets): 1600 (C=N); 1675 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.34 (3H, s, CH_3); 5.85 (1H, s, CH); 7.56 and 8.11 (4H, dd, C_6H_4); 13.2 (1H, br. s, NH). Found, %: N 21.3; Cl 13.3. $C_{12}H_9ClN_4O$. Calculated, %: N 21.5; Cl 13.6.

5-Methyl-3-(4-methylphenyl)[1,2,4]triazolo[4,3-*a*]pyrimidin-7(8H)-one (3c) was obtained analogously to compound **3a** from equimolar amounts of pyrimidine **1** and 4-methylbenzoic acid hydrazide. The yield of compound **3c** was 83%; mp >300°C (DMF). IR spectrum, ν, cm^{-1} (KBr pellets): 1600 (C=N); 1675 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.33 (3H, s, CH_3); 2.37 (3H, s, CH_3); 5.84 (1H, s, CH); 7.33 and 8.99 (4H, dd, C_6H_4); 13.2 (1H, br. s, NH). Found, %: N 23.5. $C_{13}H_{12}N_4O$. Calculated, %: N 23.3.

3-(4-*tert*-Butylphenyl)-5-methyl[1,2,4]triazolo[4,3-*a*]pyrimidin-7(8H)-one (3d) was obtained analogously to compound **3a** from equimolar amounts of pyrimidine **1** and 4-*tert*-butylbenzoic acid hydrazide. The yield of compound **3d** was 81%; mp >300°C (DMF). IR spectrum, ν, cm^{-1} (KBr pellets): 1600 (C=N); 1675 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.31 (9H, s, CH_3); 2.04 (3H, s, CH_3); 5.53 (1H, s, CH); 7.51 and 7.88 (4H, dd, C_6H_4); 10.2 (1H, br. s, NH). Found, %: N 20.2. $C_{16}H_{17}N_4O$. Calculated, %: N 19.9.

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