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SYNTHESIS OF A NEW HETEROCYCLIC SYSTEM – PYRIDO[3',2':4,5]THIENO-[2,3-*e*][1,2,3]TRIAZOLO[1,5-*a*]PYRIMIDINE

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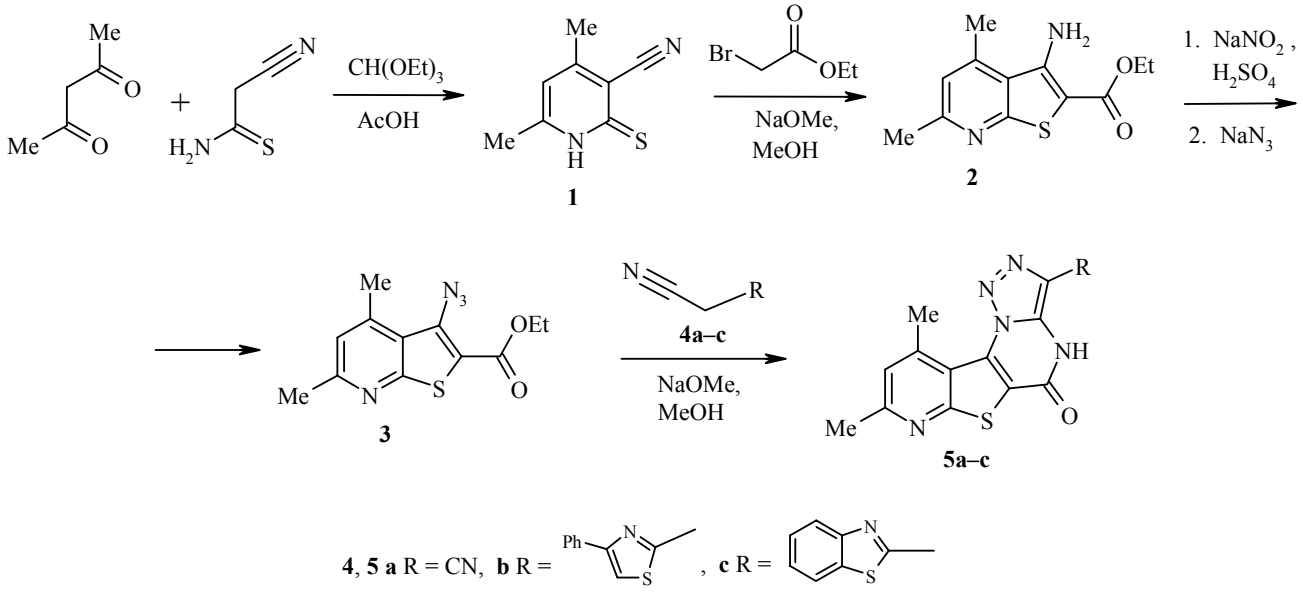
There has been considerable recent interest in polycyclic systems with a 1,2,3-triazole ring, in particular, [1,2,3]triazolo[1,5-*a*]pyrimidines, in light of the useful properties of these compounds [1]. The [1,2,3]triazolo[1,5-*a*]pyrimidine fragment fused with various heterocycles is conveniently constructed by the anionic domino reaction of *ortho*-substituted aryl and hetaryl azides. Such reactions have been described for compounds containing an azido group in pyrrole [2, 3], indole [4], pyrazole [5], imidazole [6], 1,2,3-triazole [7, 8], and thiophene rings [9]. Biological activity is noted for most of these compounds. In the present work, we propose a convenient method to synthesize a new polycyclic system, namely, pyrido[3',2':4,5]thieno-



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[2,3-*e*][1,2,3]triazolo[1,5-*a*]pyrimidine. 3-Cyanopyridine **1** [10] was used as the starting reagent and was converted to thienopyridine **2** [11] with the aim of subsequent transformation of the amino group into an azido group. We should note that, in many cases of such transformations, low basicity of the heterocyclic amine with an electron-withdrawing group in the position adjacent to the ring sharply diminishes the capacity of such compounds to react with a nitrosylating agent, thereby, hindering the synthesis of azides from available hetarylamines through diazonium salts. In our case, amine **2** undergoes diazotization by nitrososulfuric acid obtained by the reaction of $NaNO_2$ with concentrated sulfuric acid [11]. Subsequent treatment of the solution of the diazonium salt with sodium azide gives azide **3**, which readily undergoes an anionic domino reaction with nitriles **4a-c** possessing an active methylene group to give a new polycyclic system, namely, pyrimidines **5a-c**.

The reaction takes only a few minutes and products **5a-c** are obtained in high yields after crystallization from the reaction mixture without further purification.

This approach opens possibilities for the synthesis of representatives of this new heterocyclic system, namely, derivatives of pyrido[3',2':4,5]thieno[2,3-*e*][1,2,3]triazolo[1,5-*a*]pyrimidine. We also note that the synthesis of starting pyridine **1** [10] permits the introduction of a broad range of substituents in the ring [12] and, thus, in products **5**.

The ^{1}H NMR spectra were taken on a Varian Unity +400 spectrometer at 400 MHz in DMSO-d_6 with TMS as the internal standard. The mass spectra were taken on an Agilent 1100 LC/MSD with chemical ionization.

Ethyl Ester of 3-Azido-4,6-dimethylthieno[2,3-*b*]pyridine-2-carboxylic acid (3). Amine **2** (2.5 g, 0.01 mol) was dissolved in a mixture of concentrated sulfuric acid (2.5 ml) and water (7 ml) and cooled to 0°C. Then, a saturated solution of $NaNO_2$ (0.83 g, 0.012 mol) was added, maintaining the temperature below 5°C. The reaction mixture was maintained for 5 min. Then, a solution of NaN_3 (0.65 g, 0.01 mol) in water (5 ml) was added. The reaction mixture was maintained for 10 min at room temperature. The precipitate was filtered off to give azide **3** in 73% yield. This product was used without further purification, dec. 125-126°C. Mass spectrum, *m/z*: 277 $[M+H]^+$. Found, %: C 52.35; H 4.47; N 20.02. $C_{12}H_{12}N_4O_2S$. Calculated, %: C 52.16; H 4.38; N 20.28.

8,10-Dimethyl-5-oxo-4,5-dihydropyrido[3',2':4,5]thieno[2,3-*e*][1,2,3]triazolo[1,5-*a*]pyrimidine-3-carbonitrile (5a). Malononitrile **4a** (0.66 g, 0.01 mol) and azide **3** (2.76 g, 0.01 mol) were added with vigorous stirring to a solution of sodium methylate prepared from 0.3 g sodium and 20 ml methanol. The mixture was stirred at room temperature until a precipitate formed. The precipitate was filtered off to give compound **5a** in 87% yield; mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.58 (3H, s, CH_3); 3.00 (3H, s, CH_3); 7.07 (1H, s, H Py). Mass spectrum, *m/z*: 297 $[M+H]^+$. Found, %: C 52.78; H 2.54; N 28.28; S 10.98. $C_{13}H_8N_6OS$. Calculated, %: C 52.69; H 2.72; N 28.36; S 10.82.

Pyrimidones 5b and 5c were synthesized analogously.

8,10-Dimethyl-3-(4-phenyl-1,3-thiazol-2-yl)pyrido[3',2':4,5]thieno[2,3-e][1,2,3]triazolo[1,5-*a*]pyrimidin-5(4H)-one (5b) was obtained in 94% yield; mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.57 (3H, s, CH_3); 3.18 (3H, s, CH_3); 7.09 (1H, s, H Py); 7.31 (1H, t, ^3J = 7.6, H-4 Ph); 7.44 (2H, t, ^3J = 7.6, H-3, H-5 Ph) 7.77 (1H, s, H thiazole); 8.09 (2H, d, ^3J = 7.6, H-2, H-6 Ph). Mass spectrum, *m/z*: 431 $[M+H]^+$. Found, %: C 58.45; H 3.46; N 19.60; S 14.72. $C_{21}H_{14}N_6OS_2$. Calculated, %: C 58.59; H 3.28; N 19.52; S 14.90.

3-(1,3-Benzothiazol-2-yl)-8,10-dimethylpyrido[3',2':4,5]thieno[2,3-*e*][1,2,3]triazolo[1,5-*a*]pyrimidin-5(4H)-one (5c) was obtained in 97% yield; mp >300°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.59 (3H, s, CH_3); 3.18 (2H, s, CH_3); 7.12 (1H, s, H Py); 7.33 (1H, t, ^3J = 7.8, H-6 Ar); 7.45 (1H, t, ^3J = 7.8, H-5 Ar); 7.97-8.00 (2H, m, H-4, H-7 Ar). Mass spectrum, *m/z*: 405 $[M+H]^+$. Found, %: C 56.38; H 2.81; N 20.62; S 15.98. $C_{19}H_{12}N_6OS_2$. Calculated, %: C 56.42; H 2.99; N 20.78; S 15.86.

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