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LETTERS TO THE EDITOR

Reaction of 7-Amino-3-*tert*-butyl-4-oxo-4,6-dihydropyrazolo[5,1-*c*]triazine-8-carboxamide with Carbonyl Compounds

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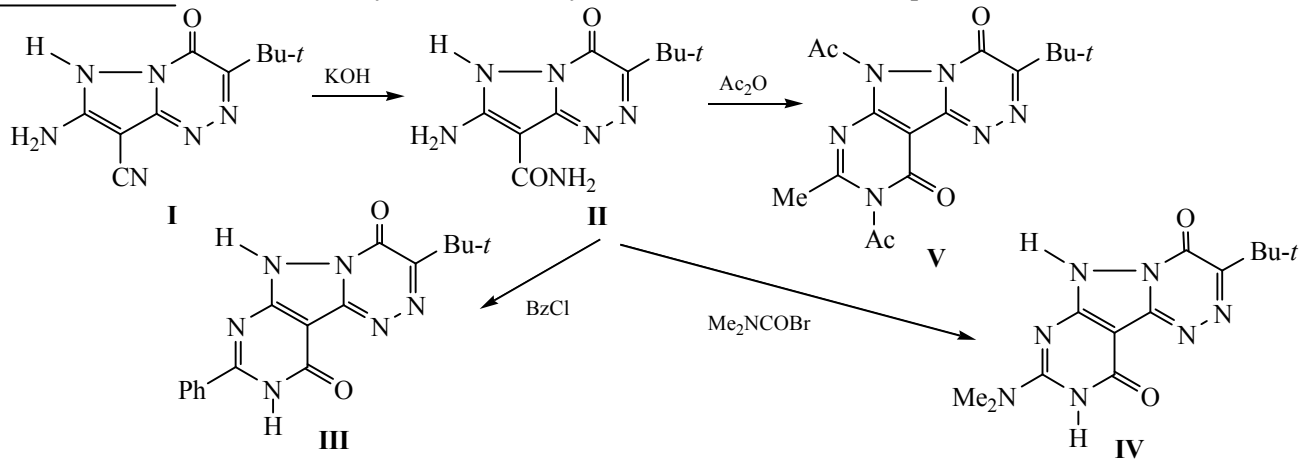
Reactivity of the 1,2,4-triazine derivatives containing pyrazole ring in the structure is now intensively studied. Thus, in a series of pyrazolo[5,1-*c*][1,2,4]triazines compounds were found with antibacterial, antiviral, fungicidal, and anti-cancer action [1, 2].

The presence of functional groups in the pyrazolo[5,1-*c*][1,2,4]triazine system opens the opportunity to use them for the synthesis of new compounds. Given the high practical value of the heterofused compounds of the 1,2,4-triazine series, it is relevant to develop the methods of the synthesis of new heterocyclic derivatives of 1,2,4-triazine.

We synthesized previously 7-amino-3-*tert*-butyl-4-oxo-4,6-dihydropyrazolo[5,1-*c*]triazine-8-carbonitrile (**I**) by the reaction of malonodinitrile with 4-amino-6-*tert*-butyl-3-methylsulfanyl-5-oxo-4*H*-1,2,4-triazine in the pyridine medium [3]. Compound **I** is insoluble in most organic solvents and water, making it difficult to perform further reactions. The aim of this work was to obtain related 7-amino-3-*tert*-butyl-4-oxo-4,6-dihydropyrazolo[5,1-*c*]triazine-8-carbamide (**II**) and to study its reactivity.

The hydrolysis of nitrile **I** in alkaline medium at reflux leads to amide **II**. The acylation of amide **II** with excess benzoyl chloride at reflux in the absence of a solvent led to 3-*tert*-butyl-4,11-dioxo-9-phenyl-6*H*,10*H*[1,3]pyrimidino[4',5':3,4]pyrazolo[5,1-*c*][1,2,4]-triazine (**III**) ([M^+] = 336). The acylation of amide **II** with dimethylcarbamoyl bromide in *N*,*N*-dimethylformamide (DMF) allowed us to isolate 3-*tert*-butyl-9-dimethylamino-4,11-dioxo-6*H*,10*H*[1,3]-pyrimidino-[4',5':3,4]pyrazolo[5,1-*c*][1,2,4]triazine (**IV**).

Acylation amide **II** with acetic anhydride at boiling does not stop at the formation of 3-*tert*-butyl-9-methyl-4,11-dioxo-6*H*,10*H*[1,3]pyrimidino[4',5':3,4]pyrazolo-[5,1-*c*][1,2,4]triazine (**IIIa**). This compound was not isolated under the experimental conditions, and 6,10-diacetyl-3-*tert*-butyl-9-methyl-4,11-dioxo[1,3]pyrimidino[4',5':3,4]pyrazolo[5,1-*c*][1,2,4]triazine (**V**) was obtained as the end product.



The structure of compounds **II–V** was established from the combined data of elemental analysis, IR and ^{1}H NMR spectroscopy, and mass spectrometry. In the ^{1}H NMR spectra of compounds **III–V** a singlet of the protons of amine group at 5.8 ppm and the singlets of the protons of the amide group at 6.6 and 7.52 ppm present in the specrum of the original amide **II** do not appear. There is a multiplet of protons of phenyl substituent at 7.45–7.6 ppm (**III**), and a singlets of protons at 1.3 ppm (**IV**) and 1.5 ppm (**V**), assigned to the substituent at 9 position of the heterocycle.

The synthesized compounds possess antimicrobial activity against gram-negative bacteria.

IR spectra were recorded on an UR-10 instrument from KBr tablets. ^{1}H NMR spectra were recorded on a Varian Mercury VX-200 instrument (200 MHz), solvent DMSO-d_6, internal reference HMDS (0 ppm). Mass spectra (EI, 70 eV) were obtained on the mass spectrometer MS-1302. The purity of products was monitored by TLC on Silufol UV-254 plates in the system of chloroform-methanol, 9:1.

Compound **I** was obtained by the method [3] (mp > 305°C).

7-Amino-3-*tert*-butyl-4-oxo-4,6-dihydropyrazolo-[5,1-*c*][1,2,4]triazine-8-carboxamide (II). 0.464 g (2 mmol) of compound **I** and 0.561 g (10 mmol) of KOH in 20 cm^3 of 2-propanol was refluxed for 20 min, the precipitate formed was filtered off and washed with cold methanol to give 0.451 g (90%) of a light yellow crystalline substance, mp 284–286°C (decomp.). IR spectrum, ν, cm^{-1}: 3444, 2960, 2928, 2870, 1700 (C=O), 1646 (C=O), 1634 (amide **I**), 1624, 1601 (amide **II**), 1549, 1515, 1495 , 1457, 1419, 1399, 1360, 1294, 1211, 1190, 1150, 1102, 1012, 967, 835, 789, 748, 705, 588. ^{1}H NMR spectrum, δ, ppm: 1.34 s (9H); 5.8 s (2H); 6.6 br.s (1H), 7.52 br.s (1H), 13.1 s (1H). Mass spectrum, *m/z* (I_{rel}, %): 250 (5.7) [M^+], 235 (1.5), 233 (2.0), 218 (4.5), 207 (4.2), 205 (3.4), 190 (3.6) , 141 (2.0), 127 (2.3), 121 (3.5), 119 (13.1), 117 (12.9), 97 (2.8), 87 (19.5), 85 (65.3) 83 (100), 82 (6.7) , 57 (24.5), 49 (8.3), 47 (21.6), 44 (61.9) 43 (25.6), 36 (30.7), 32 (15.8). Found, %: C 47.98, 47.96; H 5.62, 5.60; N 33.59, 33.61. $C_{10}H_{14}N_6O_2$. Calculated, %: C 47.99; H 5.64; N 33.58.

3-*tert*-Butyl-9-dimethylamino-4,11-dioxo-6*H*,10*H*-[1,3]pyrimidino[4',5':3,4]pyrazolo[5,1-*c*][1,2,4]triazine (IV). 0.5 g (2 mmol) of amide **II**, 0.61 g (4 mmol) *N*,*N*-dimethylcarbamoyl bromide in 15 cm^3 of DMF was heated for 10 h, then concentrated to 2/3 of volume, the separated precipitate was filtered off. Recrystallized from dioxane gave white crystalline substance, 0.44 g (74%), mp 195–200°C (decomp.). IR spectrum, ν, cm^{-1}: 2962, 2933, 1683 (C=O), 1660 (C=O), 1614, 1543, 1475, 1392, 1322, 1269, 1173, 1123, 1094, 967, 789, 740, 562, 523. ^{1}H NMR spectrum, δ, ppm: 1.3 s (6H); 1.4 s (9H); 11.95 s (1H); 14.7 s (1H). Mass spectrum, *m/z* (I_{rel}, %) 302 (1.2) [M^+], 260 (81.4), 246 (57.4), 218 (68.1), 217 (58.9), 205 (24.9), 190 (38.1), 150 (100), 137 (44.5), 126 (24.3), 96 (54.2), 68 (73.5), 67 (55.9), 66 (69.3), 57 (36.2), 45 (46.4), 41 (77.4). Found, %: C 51.46, 51.48; H 5.66. 5.63; N 32.31, 32.30. $C_{13}H_{17}N_7O_2$. Calculated, %: C 51.48; H 5.65; N 32.32.

3-*tert*-Butyl-9-phenyl-4,11-dioxo-6*H*,10*H*[1,3]-pyrimidino[4',5':3,4]pyrazolo[5,1-*c*][1,2,4]triazine (III). 0.5 g (2 mmol) of amide **II** and 10 cm^3 of benzoyl chloride was heated for 3 h, then cooled, the precipitate was filtered off, washed with hot 2-propanol, and dried in air. Yellow crystalline substance, 0.484 g (72%), mp 298–302°C (decomp.). IR spectrum, ν, cm^{-1}: 3280, 2934, 1792 (C=O), 1683 (C=O), 1628, 1550, 1481, 1454, 1366, 1332, 1266, 1174.1130, 1045, 1020, 998 , 961, 877, 759, 707, 618, 516. ^{1}H NMR spectrum, δ, ppm: 1.4 s (9H); 7.45–7.6 m (5H), 7.7 br.s (1H) 11.65 s (1H). Mass spectrum, *m/z* (I_{rel}, %): 336 (3.1) [M^+], 335 (2.2), 321 (3.4), 293 (2.8), 227 (4.6), 226 (2.3), 225 (2.1), 106 (24.7) 105 (100), 103 (6.7), 78 (3.2), 77 (43.0) 76 (3.6). Found, %: C 60.74, 60.72; H 4.81, 4.82; N 24.96, 24.98. $C_{17}H_{16}N_6O_2$. Calculated, %: C 60.71; H 4.79; N 24.99.

6,10-Diacetyl-9-acetylamino-3-*tert*-butyl-4,11-dioxo-[1,3]pyrimidino[4',5':3,4]pyrazolo[5,1-*c*]-[1,2,4]triazine (V). 0.5 g (2 mmol) of amide **II** was heated with 7–10 cm^3 of acetic anhydride for 3 h, the precipitate formed was filtered off and dried in air. The product was recrystallized from methanol to give a yellow crystalline solid, 0.45 g (63%), mp 285–290°C (decomp.). IR spectrum, ν, cm^{-1}: 2970, 2933, 1741 (C=O), 1709 (C=O), 1676 (C=O), 1636 (C=O), 1587, 1538, 1500, 1379, 1300 , 1241, 1150, 1097, 1028, 960, 869, 782, 613, 575. ^{1}H NMR spectrum, δ, ppm: 1.4 s (9H), 1.5 s (3H), 1.89 s (3H), 2.3 s (3H). Mass spectrum, *m/z* (I_{rel},%) 358 (11.6) [M^+], 316 (14.0) 275 (91.8) 274 (40.6), 260 (66.9) 249 (70.6), 234 (42.5), 232 (66.8) 217 (23.6), 207 (50.1), 205 (51.6), 190 (27.1), 165 (41.0) 151 (29.3), 123 (36.1), 109 (20.6), 96 (40.9), 93 (32.3), 82 (50.0) 67 (100), 66 (37.4), 57 (65.5). Found, %: C 53.61, 53.60; H 5.08, 5.07; N 23.46. 23.48. $C_{16}H_{18}N_6O_4$. Calculated, %: C 53.63; H 5.06; N 23.45.

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