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# PYRROLOPYRIMIDINES. 5*. REACTION OF 6-AMINO-1,3-DIMETHYL-PYRROLO[3,4-*d*]PYRIMIDINE-2,4(1H,3H)-DIONES WITH 1,3-DIKETONES

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*The reaction of 6-amino-1,3-dimethylpyrrolo[3,4-d]pyrimidine-2,4-dione with 1,3-diketones leads to formation of predominantly pyrimido[4',5':3,4]pyrrolo[1,2-b]pyridazine-2,4(1H,3H)-diones and, to a lesser extent, pyrimido[5',4':3,4]pyrrolo[1,2-b]pyridazine-1,3(2H,4H)-diones. The ease and direction of the cyclization reaction suggests a very π-electron rich pyrrole ring in the initial state, especially in the position 7.*

**Keywords:** N-aminopyrroles, acetylhydrazine, 1,3-diketones, pyrrolo[3,4-*d*]pyrimidine-2,4-diones, 1,3,6-trimethyluracil, Friedel–Crafts benzoylation, heterocyclization.

The reaction of 5-amino-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1H,3H)-dione (**1**) with 1,3-diketones $R^1COCH_2COR^2$ leads to formation of the corresponding enamino ketones, of which the compound with $R^1 = R^2 = Me$ in the presence of boron trifluoride etherate undergoes ring closure to form the pyrimidopyrrolopyridazine derivative [2].

In continuing this research, in this work we studied analogous conversions of the dione isomeric to **1**, 6-amino-1,3-dimethylpyrrolo[3,4-*d*]pyrimidine-2,4(1H,3H)-dione (**2)**, which has been described earlier in [3]. We established that, in contrast to compound **1**, reaction of amine **2** with 1,3-diketones did not stop in the step of formation of enamino ketones **3**, which are not observed even in trace amounts, but rather leads to cyclization products of the latter of the type **4** and **5**. This indicates high reactivity of the pyrrole ring in pyrrolo[3,4-*d*]-pyrimidinediones compared with their [3,2-*d*] isomers. So when amine **2** reacts with acetylacetone, two products are formed: the yellow pyrimido[4',5':3,4]pyrrolo[1,2-*b*]pyridazinedione **4a** (lmax for the long wavelength absorption band, 391 nm) and its isomeric colorless pyrimido[5',4':3,4]pyrrolo[1,2-*b*]pyridazinedione **5a** ($\lambda_{max}$ 352 nm). In this case, independent of the reaction conditions (the presence or absence of solvent and acid catalyst), the compound **4a** predominates in the mixture (**4a:5a** ≥ 10:1) (see Scheme 1).

Probably both isomeric products are formed as a result of spontaneous electrophilic cyclization of intermediate enamino ketones in the position 5 or 7 of the pyrrole ring. The reaction with benzoylacetone occurs analogously: the yield of the colored ($\lambda_{max}$ 410 nm) pyrimido[4',5':3,4]pyrrolo[1,2-*b*]pyridazinedione **4b** reaches 83%. In this case, its isomers **5b** and **4c** are also formed as minor products in 6% and 4% yields respectively;

* For Communication 4, see [1].

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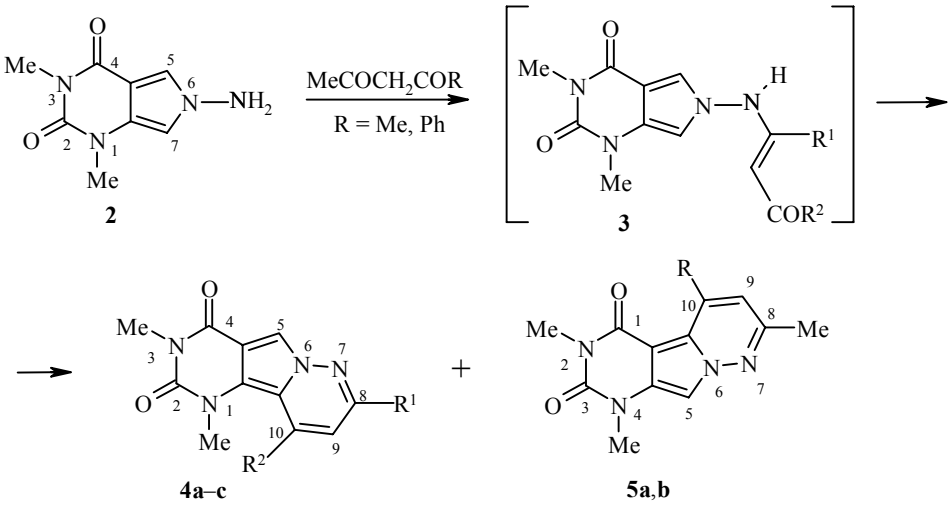
Scheme 1




**4 a** $R^1 = R^2 =$ Me; **b** $R^1$ = Me, $R^2$ = Ph; **c** $R^1$ = Ph, $R^2$ = Me; **5 a** R = Me; **b** R = Ph

they could not be separated due to their practically identical chromatographic mobility. However, there were no doubts about their identification in the mixture based on the $^1$H NMR spectrum (Table 1).

The structure of compounds **4a-c** and **5a,b** is supported by the following arguments. In the $^1$H NMR spectrum (Table 1) of compound **4b**, the signals from protons of one of the N-methyl groups is found at 2.55 ppm, while as usual in various 6-substituted pyrrolopyrimidines of type **2**, the N-methyl groups resonate in the 3.1-3.6 ppm region. Obviously such an appreciable paramagnetic shift may be due to the anisotropic effect of the spatially close 10-Ph substituent that is non-coplanar with the heterocyclic system, which is possible only in isomer **4b**. The similarity of the $^1$H NMR and UV spectra for compound **4b** and the major product of reaction with acetylacetone allows us to hypothesize that the latter has a structure related to compound **4a**. Accordingly, the colorless product with substantially different spectral characteristics is the isomer of the latter, **5a**.

Thus in the cyclization reaction, the 7 position in the molecule of compound **2** is much more active than the position 5 because it is more π-electron rich. In fact, the $C_{(7)}$ atom is conjugated with two electron-donor atoms $N_{(1)}$ and $N_{(6)}$, while the $C_{(5)}$ atom is conjugated with a donor $N_{(6)}$ and an acceptor $C_{(4)}$=O. The difference in reactivity of the indicated carbon atoms is also illustrated well by an experiment on acidic deuteron exchange of α-pyrrole protons in amine **2**, which showed that the ratio of the activities of the positions 7 and 5 is ~12:1 (Table 2). Evidence for this comes from quantum-chemical calculations of the effective atomic charges for the unsubstituted pyrrolo[3,4-*d*]pyrimidine-2,4-dione and the stabilization energies of σ complexes formed upon addition of $H^+$ and $HCO^+$ cations to it (Table 3). The chemical shifts of the $^1$H and $^{13}$C nuclei in the NMR spectra of amines **2** and **6** (Table 2) also reflect the familiar trend for heteroaromatic systems [4]: the more electron-rich positions on the ring correspond to lower values of δ.

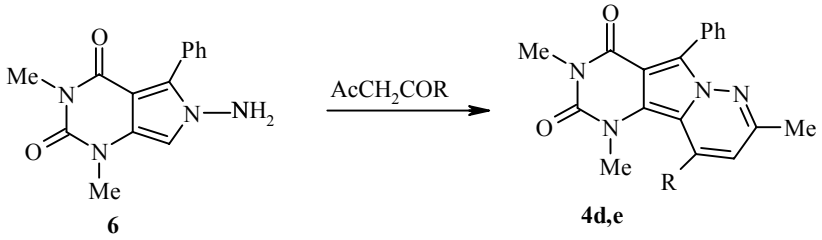
For the final experimental confirmation of the structure for the pyrimidopyrrolopyridazines obtained, using the same 1,3-diketones we reacted 6-amino-1,3-dimethyl-5-phenylpyrrolo[3,4-*d*]pyrimidine-2,4-dione (**6**), in the molecule of which cyclization is possible only at the position 7 (for synthesis of dione **6**, see below). In this case, we also could not detect formation of intermediate enamino ketones, and the only reaction product in both cases, as we expected, proved to be the yellow pyrimidopyrrolopyridazine of type **4**. However, we should note that reaction of amine **6** with acetylacetone and benzoylacetone in alcohol, in contrast to compound **2**, requires the presence of traces of acid. Acid catalysis is also necessary to obtain hydrazone **7**, while amine **2** reacts with benzaldehyde without a catalyst [3]. These data suggest decreased nucleophilicity of the N-amino group in compound **6** compared with compound **2**.

TABLE 1. $^1$H NMR Spectra of Synthesized Compounds

| Com-pound | Chemical shifts, δ, ppm (*J*, Hz)* |
|---|---|
| **4a** | 2.37 (3H, s, 8-$CH_3$); 2.61 (3H, d, *J* = 1.2, 10-$CH_3$); 3.45 (3H, s, 3-$CH_3$); 3.69 (3H, s, 1-$CH_3$); 6.22 (1H, br. d, *J* = 1.1, 9-H); 8.12 (1H, s, 5-H) |
| **4b** | 2.43 (3H, s, 8-$CH_3$); 2.58 (3H, s, 1-$CH_3$); 3.40 (3H, s, 3-$CH_3$); 6.24 (1H, s, 9-H); 7.38-7.50 (5H, m, Ph); 8.17 (1H, s, 5-H) |
| **4c** + **5b** | **4c** – 2.73 (3H, s, 10-$CH_3$); 3.47 (3H, s, 3-$CH_3$); 3.76 (3H, s, 1-$CH_3$); 6.79 (1H, s, 9-H); 7.93 (2H, dd, $J_1$ = 8.0, $J_2$ = 2.0, *o*-$H_{Ph}$); 8.30 (1H, s, 5-H)*$^2$<br>**5b** – 2.56 (3H, s, 8-$CH_3$); 3.27 (3H, s, 4-$CH_3$); 3.50 (3H, s, 2-$CH_3$); 6.74 (1H, s, 9-H); general signal: 7.35-7.55 [9H, m, 5-H and 5$H_{Ph}$ (**5b**) + 3$H_{Ph}$ (**4c**)] |
| **4d** | 2.30 (3H, s, 8-$CH_3$); 2.62 (3H, d, *J* = 1.0, 10-$CH_3$); 3.40 (3H, s, 3-$CH_3$); 3.72 (3H, s, 1-$CH_3$); 6.22 (1H, br. d, *J* = 1.0, 9-H); 7.38–7.51 (3H, m, *m*- and *p*-$H_{Ph}$); 7.69 (2H, d, *J* = 8.0, *o*-$H_{Ph}$) |
| **4e** | 2.39 (3H, s, 8-$CH_3$); 2.61 (3H, s, 1-$CH_3$); 3.38 (3H, s, 3-$CH_3$); 6.29 (1H, s, 9-H); 7.43-7.53 (3H, m, *m*- and *p*-$H_{Ph}$); 7.78 (2H, d, *J* = 8.1, *o*-$H_{Ph}$) |
| **5a** | 2.47 (3H, s, 8-$CH_3$); 2.93 (3H, d, *J* = 0.8, 10-$CH_3$); 3.42 (3H, s, 2-$CH_3$); 3.47 (3H, s, 4-$CH_3$); 6.61 (1H, br. d, *J* = 0.7, 9-H); 7.36 (1H, s, 5-H) |
| **6** | 3.16 (3H, s, 3-$CH_3$); 3.29 (3H, s, 1-$CH_3$); 6.14 (2H, s, $NH_2$); 6.82 (1H, s, 7-H); 7.40 (3H, m, *m*- and *p*-$H_{Ph}$); 7.60 (2H, m, *o*-$H_{Ph}$) |
| **7** | 3.23 (3H, s, 3-$CH_3$); 3.41 (3H, s, 1-$CH_3$); 7.45 (3H, m, *m*-, *p*-$H_{Ph}$); 7.63 (3H, m, *o*-$H_{Ph}$ and 7-H); 7.77 (1H, t, *J* = 8.0, *m*-$H_{Ar}$); 8.08 (1H, d, *J* = 7.7, *p*-$H_{Ar}$); 8.28 (1H, d, *J* = 8.1, *o*-$H_{Ar}$); 8.48 (1H, s, N=CH–Ph–H-2); 9.05 (1H, s, N=CH) |
| **8** | 2.20 (3H, s, 6-$CH_3$); 3.33 (3H, s, 3-$CH_3$); 3.47 (3H, s, 1-$CH_3$); 7.43 (2H, t, *J* = 7.4, *m*-$H_{Ph}$); 7.56 (1H, t, *J* = 7.3, *p*-$H_{Ph}$); 7.84 (2H, d, *J* = 7.0, *o*-$H_{Ph}$) |
| **9** | 3.33 (3H, s, 3-$CH_3$); 3.60 (3H, s, 1-$CH_3$); 4.22 (2H, s, $CH_2$); 7.45 (2H, t, *J* = 7.5, *m*-$H_{Ph}$); 7.58 (1H, t, *J* = 7.3, *p*-$H_{Ph}$); 7.83 (2H, d, *J* = 7.2, *o*-$H_{Ph}$) |
| **10** | 1.86 (3H, s, $COCH_3$); 3.17 (3H, s, 3-$CH_3$); 3.29 (3H, s, 1-$CH_3$); 6.96 (1H, s, 7-H); 7.35-7.45 (5H, m, Ph); 11.44 (1H, s, NH) |

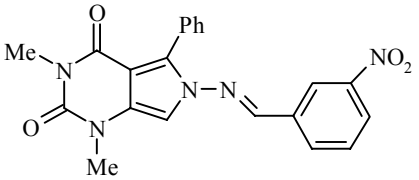
* The spectra of compounds **4a,b,d,e, 4c + 5b, 5a, 8, 9** were taken in $CDCl_3$, the spectra of compounds **6, 7**, and **10** were taken in DMSO-$d_6$.

*$^2$ The signals at 2.73 ppm and 6.79 ppm were broadened due to spin–spin coupling of the corresponding protons.




**6** **4d,e**

**4 d** R = Me, **e** R = Ph




**7**

The spectral characteristics of products **4d,e** ($\lambda_{max}$ 403 nm and 423 nm respectively) are very similar to those for pyrimidopyrrolopyridazines **4a,b**, which supports the structure of the latter, and are appreciably different from the characteristics of isomer **5a**. The quantum-chemical calculation of the electronic absorption

TABLE 2. Data for Acidic Deuteron Exchange (DMSO-$d_6$–$CD_3CO_2D$, 10:1, 100°C, 1 h) in Amine **2**, Chemical Shifts of Its $C_{(5)}$, $C_{(7)}$ Atoms and Protons Bonded With Them in $^1$NMR and $^{13}$C Spectra*

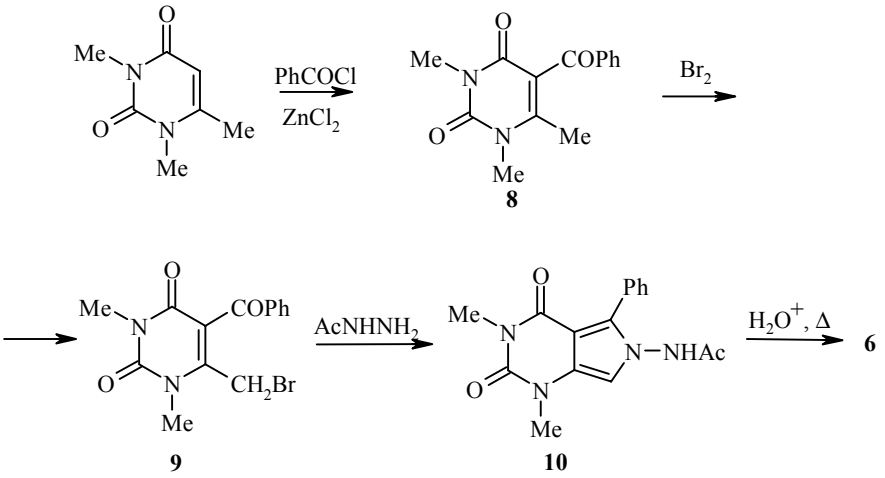
| Compound | % D | | $^1$H NMR spectrum, δ, ppm | | $^{13}$C NMR spectrum, δ, ppm | |
|---|---|---|---|---|---|---|
| | 5-H | 7-H | 5-H | 7-H | $C_{(5)}$ | $C_{(7)}$ |
| **2** | 4 | 49 | 7.25 | 6.60 | 119.5 | 104.4 |
| **6** | — | | — | 6.80 | 131.9*[2] | 104.9 |

* The signals were assigned based on comparison of the $^1$H and $^{13}$C NMR spectra of compounds **2** and **6**.

*[2] The downfield shift of the signal relative to the $C_{(5)}$ signal of compound **2** is explained by the electron-acceptor and anisotropic effect of the 5-Ph substituent.

spectra gives comparable results. The calculated values of the long wavelength $\lambda_{max}$ are 382 (**4a**), 388 (**4b**), 402 (**4d**), 407 (**4e**), 327, 358 nm (shoulder) (**5a**). The deeper color of diones **4a-d** compared with dione **5a** is obviously connected with the presence of an extended chromophore chain $N_{(1)}\cdots N_{(7)}$, where $N_{(1)}$ is the donor and $N_{(7)}$ is the acceptor. We note that in the $^1$H NMR spectra of compounds **4a,d** and **5a** we observe spin–spin coupling between the 9-H proton and protons of the 10-$CH_3$ group, which is apparent as doublets with $^4J_{Me,H}$ = 0.8-1.1 Hz (Table 1). An analogous phenomenon was observed previously for the pyrimidopyrrolo-pyridazine obtained from amine **1** [2].

Earlier we synthesized the previously unknown amine **6** from 1,3,6-trimethyluracil, which subsequently was benzoylated by a Friedel–Crafts reaction to form ketone **8**, brominated at the methyl group to the 6-bromomethyluracil derivative **9**, and then underwent ring closure when treated with acetylhydrazine to form amide **10**, which was subjected to acid hydrolysis.




Thus the reactivities of 6-aminopyrrolo[3,4-*d*]pyrimidinediones **2, 6** and the previously studied 5-aminopyrrolo[3,2-*d*]pyrimidinedione **1** are considerably different, which is due to the increased π-electron rich character of the pyrrole ring, especially for the 7 position, in diones **2**, **6** and consequently their higher activity with respect to electrophiles.

TABLE 3. Effective Charges $q_{eff}$ on $C_{(5)}$ and $C_{(7)}$ Atoms in the Pyrrolo-[3,4-*d*]pyrimidine-2,4-dione Molecule and the Stabilization Energies $E_{st}$ of the Corresponding σ-Complexes

| Atom | $q_{eff}$, e | $\|E_{st}\|$ for $H^+$, kcal/mol | $\|E_{st}\|$ for $HCO^+$, kcal/mol |
|---|---|---|---|
| $C_{(5)}$ | +0.102 | 206.69 | 49.67 |
| $C_{(7)}$ | -0.013 | 222.85 | 65.75 |

## EXPERIMENTAL

The IR spectra were obtained on a Specord-75 spectrometer in vaseline oil. The $^1H$ NMR spectra were recorded on a Bruker DPX-250 (250 MHz) (Table 1), the $^{13}C$ NMR spectra of amines **2** and **6** were taken in DMSO-$d_6$ on a Varian Unit-300 (75 MHz). The electronic absorption spectra of solutions of the compounds in methanol ($5 \cdot 10^{-5}$ mol/l) were recorded on a Specord M-40 spectrometer. The melting points were determined in open capillaries and were uncorrected. The course of the reactions and the purity of the compounds obtained were monitored using TLC on $Al_2O_3$ (Brockmann activity II-III), eluent $CHCl_3$ or $CHCl_3$–EtOAc, 5:1; visualization in UV light and iodine vapors. Amine **2** was obtained using the familiar procedure in [3]. We used the software package in [5] for the quantum-chemical calculations. The effective charges were calculated by the DGauss method in a 6-31G basis; the stabilization energies for the s complexes were calculated in a 3-21G basis; the electronic absorption spectra were calculated by the ZINDO CI method for optimized (AM1) conformation.

**1,3,8,10-Tetramethylpyrimido[4',5':3,4]pyrrolo[1,2-*b*]pyridazine-2,4(1H,3H)-dione (4a) and 2,4,8,10-Tetramethylpyrimido[5',4':3,4]pyrrolo[1,2-*b*]pyridazine-1,3(2H,4H)-dione (5a).** A mixture of amine **2** (1 g, 5.15 mmol) and acetylacetone (0.54 ml, 5.17 mmol) in alcohol (10 ml) was refluxed for 3 h. The precipitate forming after cooling was filtered out and carefully ground; the impurity of product **5a** was extracted with hot ethylacetate (3-6 times, ~5 ml each, TLC monitoring); the residue was recrystallized from DMF. Compound **4a** (950 mg, 72%) was obtained. Yellow prisms with yellow-green fluorescence in UV light; mp 235-237°C. IR spectrum, ν, $cm^{-1}$: 1575 (C=C), 1605, 1685 (C=O), 3120 ($C_{(5)}$–H). UV spectrum, $\lambda_{max}$, nm (log ε): 237.1 (4.54), 270.5 (4.21), 279.2 (4.22), 317 (3.71), 391 (3.44). Found, %: C 60.68; H 5.40. $C_{13}H_{14}N_4O_2$. Calculated, %: C 60.47; H 5.43.

The alcoholic mother liquor and the extract (EtOAc) with the precipitate forming from it were combined, the solvents were distilled off to dryness, the residue was chromatographed on a column ($l$ = 50 cm, $d$ = 1.5 cm) with $Al_2O_3$ (Brockmann activity III), eluent $CHCl_3$. From the eluate of the colorless band with blue fluorescence in UV light, after evaporation and recrystallization of the residue from alcohol we obtained 26 mg (1.9%) of compound **5a**. Colorless crystals with mp 278-280°C (sublimes). The solutions of compound **5a** have an intense blue fluorescence in UV light. IR spectrum, ν, $cm^{-1}$: 1375 (C=C), 1625, 1660, 1705 (C=N, C=O). UV spectrum, $\lambda_{max}$, nm (log ε): 264.8 (4.32), 318.5 (3.75), 351.6 (3.81). Found, %: C 59.88; H 5.62. $C_{13}H_{14}N_4O_2$. Calculated, %: C 60.47; H 5.43.

**1,3,8-Trimethyl-10-phenylpyrimido[4',5':3,4]pyrrolo[1,2-*b*]pyridazine-2,4(1H,3H)-dione (4b).** Benzoylacetone (260 mg, 1.60 mmol) was added to amine **2** (300 mg, 1.55 mmol) in boiling alcohol (3 ml), and the mixture was refluxed for 30 min. The precipitate forming after cooling was filtered out, washed with alcohol, and recrystallized from DMF. We obtained 402 mg (81%) of product **4b**. Yellow rhombic; mp 224-226°C. IR spectrum, ν, $cm^{-1}$: 1420 (C=C), 1540, 1680 (C=O). UV spectrum, $\lambda_{max}$, nm (log ε): 238.5 (4.39), 273.5 (4.26), 317.5 (3.50), 409.6 (3.35). Found, %: C 67.77; H 5.13. $C_{18}H_{16}N_4O_2$. Calculated, %: C 67.50; H 5.00.

The alcoholic mother liquor was evaporated to dryness; the residue was washed with ether (1-2 ml) and chromatographed on a column ($l$ = 50 cm, $d$ = 1.5 cm) with $Al_2O_3$ (Brockmann activity III), eluent $CHCl_3$. From the eluate of the band with the highest $R_f$ value (with blue fluorescence in UV light), after evaporation we obtained 50 mg of a mixture of compounds **5b** and **4c** (according to $^1$H NMR data, **5b:4c**, 3:2). Mixture of compounds **4c** and **5b**. Found, %: C 66.96; H 4.83. $C_{18}H_{16}N_4O_2$. Calculated, %: C 67.50; H 5.00.

**5-Benzoyl-1,3,6-trimethylpyrimidine-2,4-dione (8).** A mixture of 1,3,6-trimethyluracil (10 g, 64 mmol), benzoyl chloride (7.4 ml, 64 mmol), and $ZnCl_2$ (8.8 g, 64 mmol) in benzene (80 ml) was refluxed for 20 h; then water (50 ml) was added and the benzene was distilled off. After cooling, the precipitate was filtered out, triturated with ether (20 ml); the product **8** that did not dissolve was filtered out, recrystallized from 2-propanol, and washed on the filter with ether. Yield 7.5 g (45%). Colorless needles; mp 135-136°C. IR spectrum, ν, cm$^{-1}$: 1605, 1630 (C=N), 1660, 1700 (C=O). Found, %: C 65.32; H 5.26. $C_{14}H_{14}N_2O_3$. Calculated, %: C 65.10; H 5.43.

**5-Benzoyl-6-bromomethyl-1,3-dimethylpyrimidine-2,4-dione (9).** A solution of bromine (1.24 g, 7.75 mmol) in $CHCl_3$ (10 ml) was added dropwise to a solution of ketone **8** (2 g, 7.75 mmol) in dry $CHCl_3$ (10 ml) with stirring and heating on a water bath (50°C), the addition being made at such a rate that the reaction mixture could become colorless after each drop, and then the mixture was boiled until rapid evolution of HBr stopped (~1 h). The residue after distillation of the solvent was triturated with water (5 ml); the precipitate was filtered out, washed with water (50 ml), and recrystallized from 2-propanol. We obtained 2.05 g (79%) of product **9**. Colorless needles; mp 169-171°C. IR spectrum, ν, cm$^{-1}$: 1660, 1705 (C=O). Found, %: C 50.05; H 3.95; Br 23.81. $C_{14}H_{13}BrN_2O_3$. Calculated, %: C 49.85; H 3.85; Br 23.73.

**6-Acetylamino-1,3-dimethyl-5-phenylpyrrolo[3,4-*d*]pyrimidine-2,4(1H,3H)-dione (10).** Acetylhydrazine (134 mg, 1 mmol) and triethylamine (0.125 ml, 0.89 mmol) were added to a solution of compound **9** (300 mg, 0.89 mmol) in alcohol (10 ml); the mixture obtained was refluxed for 2 h, then cooled down to 0°C, and 192 mg (58%) of product **10** was filtered out that was sufficiently pure for further use. By recrystallization of the latter from alcohol, we obtained an analytical sample. Colorless prisms; mp 276-278°C. IR spectrum, ν, cm$^{-1}$: 1570, 1635 (C=N), 1670, 1700 (C=O), 3200 (N–H). Found, %: C 61.23; H 5.24. $C_{16}H_{16}N_4O_3$. Calculated, %: C 61.54; H 5.13.

**6-Amino-1,3-dimethyl-5-phenylpyrrolo[3,4-*d*]pyrimidine-2,4(1H,3H)-dione (6).** A suspension of amide **10** (463 mg, 1.48 mmol) in 10% aqueous HCl solution (4 ml) was refluxed with rapid stirring for 2 h 30 min and then cooled down; a 10% aqueous solution of KOH was added until the pH was about ~8, and the mixture was stirred for another 30 min. The precipitate was filtered out, washed with 5 ml water, and dried; it was heated twice with $CHCl_3$ (2 × 2 ml), each time filtering after cooling. We obtained 350 mg (83%) of pure (according to $^1$H NMR data) product **6**. Colorless crystals; mp 233-235°C. IR spectrum, ν, cm$^{-1}$: 1525 (C=C), 1595 (C=N), 1635, 1675 (C=O), 3300 ($NH_2$). Found, %: C 61.85; H 5.10. $C_{14}H_{14}N_4O_2$. Calculated, %: C 62.21; H 5.22.

**1,3-Dimethyl-6-(*m*-nitrobenzylidene)amino-5-phenylpyrrolo[3,4-*d*]pyrimidine-2,4(1H,3H)-dione (7).** *m*-Nitrobenzaldehyde (84 mg, 0.56 mmol) was added to ground amine **6** (150 mg, 0.56 mmol) in alcohol (2 ml) containing traces of HCl while boiling; the mixture was refluxed for another 10 min. After cooling, the precipitate was filtered out, washed with hot alcohol (3-5 ml), and recrystallized from DMF. Product **7** (135 mg, 60%) was obtained. Orange crystals; mp 278-280°C. IR spectrum, ν, cm$^{-1}$: 1630, 1675 (C=O), 3080 ($C_{(7)}$–H). Found, %: C 62.36; H 4.15. $C_{21}H_{17}N_5O_4$. Calculated, %: C 62.53; H 4.22.

**1,3,8,10-Tetramethyl-5-phenylpyrimido[4',5':3,4]pyrrolo[1,2-*b*]pyridazine-2,4(1H,3H)-dione (4d).** A mixture of amine **6** (180 mg, 0.67 mmol) and acetylacetone (0.1 ml, 0.8 mmol) in alcohol (3 ml) was refluxed for 1 h in the presence of traces of HCl. The precipitate forming after cooling was filtered out and recrystallized from DMF, and we obtained 176 mg (79%) of product **4d**. Yellow crystals; mp 267-269°C. IR spectrum, ν, cm$^{-1}$: 1510 (C=N), 1605, 1675 (C=O). UV spectrum, $\lambda_{max}$, nm (log ε): 246 (4.51), 335 (3.88), 403 (3.48). Found, %: C 68.18; H 5.60. $C_{19}H_{18}N_4O_2$. Calculated, %: C 68.32; H 5.69.

**1,3,8-Trimethyl-5,10-diphenylpyrimido[4',5':3,4]pyrrolo[1,2-*b*]pyridazine-2,4(1H,3H)-dione (4e)** was obtained similarly to dione **4d** from amine **6** (300 mg, 1.12 mmol) and benzoylacetone (190 mg, 1.20 mmol) in a yield of 413 mg (94%). Silky dark yellow crystals; mp 241-243°C. IR spectrum, ν, $cm^{-1}$: 1595 (C=N), 1660, 1690 (C=O). UV spectrum, $\lambda_{max}$, nm (log ε): 252.4 (4.48), 341 (3.82), 423 (3.40). Found, %: C 73.05; H 5.13. $C_{24}H_{20}N_4O_2$. Calculated, %: C 72.73; H 5.05.

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## REFERENCES

1. Yu. N. Tkachenko, E. B. Tsupak, and A. F. Pozharskii, *Khim. Geterotsikl. Soedin.*, 368 (2000).
2. Yu. N. Tkachenko, E. B. Tsupak, and A. F. Pozharskii, *Khim. Geterotsikl. Soedin.*, 375 (1999).
3. K. Hirota, Y. Yamada, T. Asao, and S. Senda, *Chem. Pharm. Bull.* **29**, 1525 (1981).
4. A. F. Pozharskii, *Theoretical Principles of Heterocyclic Chemistry* [in Russian], Khimiya, Moscow (1985), p. 62.
5. *CAChe 4.4 for Windows*, USA: CAChe Group, Fujitsu Systems Business of America, URL: http://www.cachesoftware.com.