[3,4]-Annulated pyrroles
1. Polynuclear heterocyclic systems based on pyrrolo[3,4-*d*]pyrimidine-2,4-dione

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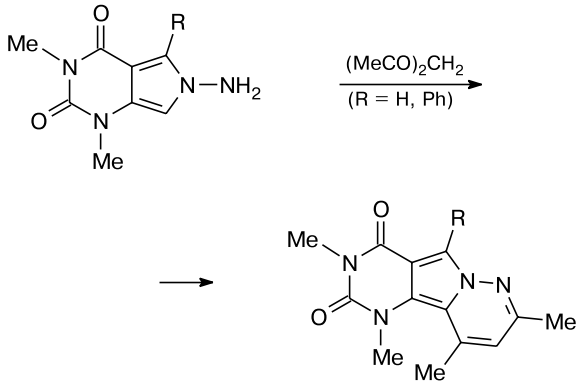
The intramolecular electrophilic substitution in 6-functionalized 1,3-dimethyl-1*H*-pyrrolo[3,4-*d*]pyrimidine-2,4(3*H*,6*H*)-diones was used for the synthesis of pyrimido[4′,5′:3,4]-pyrrolo[1,2-*a*]quinoxaline-8,10(7*H*,9*H*)-dione, pyrimido[4′,5′:3,4]pyrrolo[2,1-*c*][1,2,4]benzotriazine-8,10(7*H*,9*H*)-dione, and 2*H*-pyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]indole-2,4,11(1*H*,3*H*)-trione derivatives.

Key words: 1*H*-pyrrolo[3,4-*d*]pyrimidine-2,4(3*H*,6*H*)-diones, heterocyclization, electrophilic substitution, acylation, pyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]quinoxaline-8,10(7*H*,9*H*)-diones, diazotization, pyrimido[4′,5′:3,4]pyrrolo[2,1-*c*][1,2,4]benzotriazine-8,10(7*H*,9*H*)-diones, 2*H*-pyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]indole-2,4,11(1*H*,3*H*)-triones, ^{1}H NMR spectroscopy, anisotropic effect.

Among the known procedures for the construction of polynuclear heterocyclic systems, methods of synthesis involving the intramolecular electrophilic substitution in a heteroaromatic moiety as one of the steps, in particular, acylation and azo-coupling reactions, have great significance.[1—5]

Earlier,[6] we have reported that the reaction of 6-amino-1,3-dimethyl-1*H*-pyrrolo[3,4-*d*]pyrimidine-2,4(3*H*,6*H*)-diones with 1,3-diketones under mild conditions leads to spontaneous heterocyclization of intermediate enaminoketone at position 7 to form the pyridazine ring (Scheme 1).

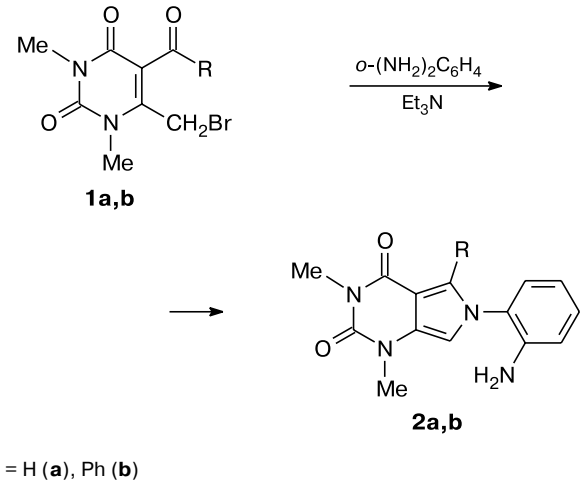
Scheme 1



Since the pyrrole moiety is highly π-excessive, pyrrolo[3,4-*d*]pyrimidine-2,4-diones would be expected to readily undergo other transformations of this type. This will enable the synthesis of more complex heterocyclic systems.

We performed condensation of 5-acyl-6-bromomethyluracils **1a,b** with *ortho*-phenylenediamine (Scheme 2) and obtained 6-(2-aminophenyl)-1,3-dimethylpyrrolo-[3,4-*d*]pyrimidine-2,4-diones (**2a,b**). The structures of these compounds are indicative of the possibility of intramolecular cyclization under the action of electrophiles.

Scheme 2



R = H (**a**), Ph (**b**)

Actually, treatment of amines **2a,b** with various strong acylating agents led to the pyrazine ring closure. This

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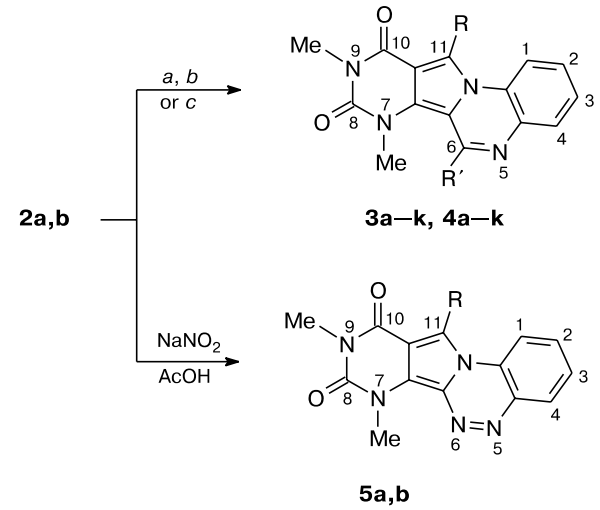
method was used for the synthesis of 7,9-dimethylpyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]quinoxaline-8,10(7*H*,9*H*)-diones (**3a—k** and **4a—k**) containing aliphatic or aromatic substituents at position 6.

Heating of pyrroles **2a,b** with formic acid in the presence of $HClO_4$ afforded perchlorates of 6-unsubstituted tetracyclic compounds **3a** and **4a** (Scheme 3). The treatment of compounds **2a,b** with acetic anhydride in the presence of $HClO_4$ in the cold gave rise to perchlorates of 6-methyl-substituted quinoxalines in high yields. Perchlorates of compounds **3a,b** and **4a,b** were transformed into the corresponding bases by the reactions of their solutions in DMSO with Et_3N. Heating of amines **2a,b** with an excess of carboxylic acid in $POCl_3$ followed by treatment of the reaction mixture with an aqueous NaOH solution proved to be the most convenient procedure for the synthesis of pyrroloquinoxalines **3c—k** and **4c—k** (see Scheme 3). 6-Trifluoromethyl-substituted pyrroloquinoxalines **3f** and **4f** synthesized under these conditions are characterized by the lowest basicity of all compounds **3** and **4** and were isolated from acidic solutions as free bases.

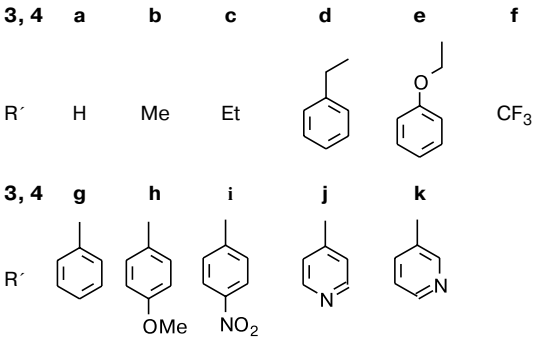
Diazotization of 6-(*o*-aminophenyl)pyrroles **2a,b** leads to annulation of the triazine moiety. For example, the reactions of compounds **2a,b** with $NaNO_2$ in an acetic acid solution gave intramolecular azo-coupling products, *viz.*, 7,9-dimethylpyrimido[4′,5′:3,4]pyrrolo[2,1-*c*]-[1,2,4]benzotriazine-8,10(7*H*,9*H*)-diones **5a,b**, in high yields (see Scheme 3).

Intramolecular acylation at position 7 allowed us also to perform annulation of a five-membered ring with the pyrrolopyrimidine system. The transformation of 2-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydro-6*H*-pyrrolo[3,4-*d*]pyrimidin-6-yl)benzoic acids **6a,b** on heating in $POCl_3$ afforded 2*H*-pyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]-indole-2,4,11(1*H*,3*H*)-trione derivatives **7a,b** as the major products (Scheme 4).

Scheme 3

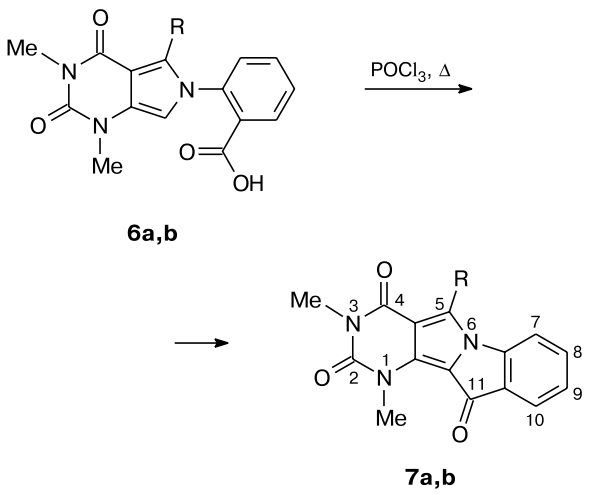


R = H (**3a—k, 5a**), Ph (**4a—k, 5b**)



Reagents: *a*. 1) HCOOH, $HClO_4$; 2) Et_3N; *b*. 1) Ac_2O, $HClO_4$; 2) Et_3N; *c*. 1) R′COOH, $POCl_3$; 2) H_2O, NaOH.

Scheme 4

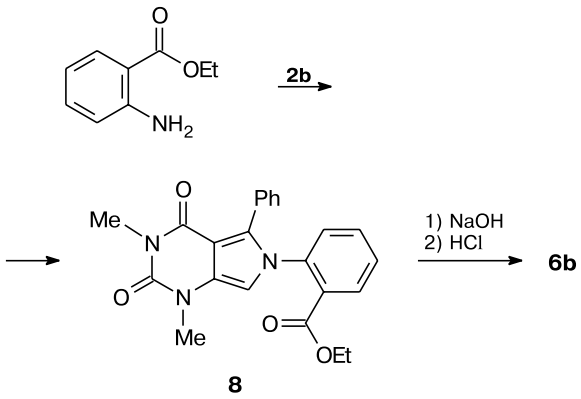


R = H (**a**), Ph (**b**)

Compound **6a** was synthesized by direct condensation of aldehyde **1a** with anthranilic acid. However, the reaction of ketone **1b** with anthranilic acid proceeded ambiguously, and, hence, we used ethyl anthranilate instead of the acid. The resulting ester **8** was subjected to alkaline hydrolysis to prepare the target acid **6b** (Scheme 5).

The conclusion that, in the absence of a substituent at position 5, heterocyclization occurs at position 7, was drawn based on a comparison of the ^1H NMR spectra of the products of analogous reactions of 5-unsubstituted pyrroles and 5-phenylpyrroles. The changes in the chemical shifts of the protons of the NMe group adjacent to the newly formed ring are particularly convincing. In molecules **3a**, **4a**, **5a,b**, and **7a,b**, these protons are deshielded due to the anisotropic effect of the aromatic ring (**3a**, **4a**) and the lone electron pairs of the N (**5a**,**b**) or O atom (**7a**,**b**). Hence, the corresponding signal in the

Scheme 5



spectra of these compounds is substantially shifted downfield (δ 3.85—3.90 for **3a**, **4a**, and **7a**,**b** and δ 4.10 for **5a**,**b**) compared to the signal of the 1-Me group in the spectra of the starting pyrrolopyrimidines (δ ~3.4—3.5). To the contrary, the protons of the NMe group in 6-arylquinoxalines **3g—k** and **4g—k** are additionally shielded, and the corresponding signal is observed at δ 2.6—2.7. This is associated with the anisotropic effect of the aromatic substituent at position 6 in a noncoplanar orientation. Earlier, we have observed[6] analogous phenomena in the spectra of pyrimidopyrrolopyridazines. In addition, the signal for the above-mentioned protons in the ^{1}H NMR spectra of trifluoromethyl-substituted compounds **3f** and **4f** is substantially broadened due apparently to the long-range spin-spin coupling with the ^{19}F nuclei.

To summarize, the use of the intramolecular electrophilic substitution in pyrrolo[3,4-*d*]pyrimidine-2,4-diones at position 7 enables the annulation of the pyrazine, triazine, and pyrrole rings.

Experimental

The IR spectra were recorded on a Specord IR-71 spectrophotometer in Nujol mulls. The ^{1}H NMR spectra were measured on Bruker Avance DPX-250 and Varian Unity-300 instruments in $CDCl_3$ or DMSO-d_6 with HMDS as the internal standard. The mass spectra were obtained on a Kratos instrument using a direct inlet system (electron impact, ionization energy was 70 eV, controlling voltage was 1.75 kV). Compounds **1a**,**b** were synthesized according to procedures described earlier.[6—9]

6-(2-Aminophenyl)-1,3-dimethylpyrrolo[3,4-*d*]pyrimidine-2,4-dione (2a). *ortho*-Phenylenediamine (4.51 g, 40.8 mmol) was added with stirring to a solution of aldehyde **1a** (5 g, 19 mmol) in EtOH (50 mL), which led to the formation of a voluminous orange precipitate of an intermediate compound (presumably, a Schiff base). The reaction mixture was stirred at ~20 °C for 30 min and then refluxed with stirring for 30 min. The crystalline compound that formed was filtered off and washed with EtOH and a small amount of $CHCl_3$. The yield was 4.81 g (93%), crystalline pale-gray powder, m.p. 275—277 °C (needles, from DMF). Found (%): C, 62.35; H, 5.16. $C_{14}H_{14}N_4O_2$. Calculated (%): C, 62.21; H, 5.22. ^{1}H NMR (DMSO-d_6), δ: 3.22 (s, 3 H, 3-Me); 3.32 (s, 3 H, 1-Me); 5.10 (s, 2 H, NH_2); 6.75 (t, 1 H, ArH(5), J = 7.9 Hz); 6.85 (d, 1 H, ArH(3), J = 7.6 Hz); 6.95 (d, 1 H, H(7), J = 2.3 Hz); 7.05—7.20 (m, 2 H, ArH(4), ArH(6)); 7.50 (d, 1 H, H(5), J = 2.3 Hz). IR, ν/cm^{-1}: 1660, 1690 (C=O); 3240, 3350 (NH_2).

6-(2-Aminophenyl)-1,3-dimethyl-5-phenylpyrrolo[3,4-*d*]-pyrimidine-2,4-dione (2b). A mixture of dispersed bromomethyl ketone **1b** (10 g, 30 mmol), *ortho*-phenylenediamine (3.9 g, 36 mmol), and Et_3N (5 mL, 3.6 g, 35.5 mmol) was refluxed with stirring in EtOH (50 mL) for 3 h. After cooling, the precipitate that formed was filtered off and washed on a filter successively with a small amount of EtOH and water. The yield was 7.4 g (72%), colorless finely crystalline compound, m.p. >310 °C (from DMSO). Found (%): C, 69.23; H, 5.16. $C_{20}H_{18}N_4O_2$. Calculated (%): C, 69.35; H, 5.24. ^{1}H NMR (DMSO-d_6), δ: 3.20 (s, 3 H, 3-Me); 3.35 (s, 3 H, 1-Me); 4.70 (s, 2 H, NH_2); 6.75 (t, 1 H, ArH(5)); 6.80 (m, 2 H, ArH(3), H(7)); 6.85 (d, 1 H, ArH(6)); 7.05 (t, 1 H, ArH(4)); 7.25, 7.35 (m, 5 H, Ph). IR, ν/cm^{-1}: 1665, 1680 (C=O); 3230, 3360 (NH_2).

7,9-Dimethylpyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]quinoxaline-8,10(7*H*,9*H*)-dione (3a). A 54% $HClO_4$ solution (0.22 mL, 2 mmol) was added to a solution of compound **2a** (300 mg, 1.1 mmol) in 95% HCOOH (3 mL). The solution was refluxed for 1 h. After cooling, water (10 mL) was added. The precipitate that formed was filtered off and washed with EtOH. The resulting crystalline bright-yellow compound, *viz.*, perchlorate **3a**, was transformed into the free base without purification. For this purpose, the precipitate was dissolved with heating in DMSO (4 mL), the solution was cooled to 70 °C, and Et_3N (0.26 mL, 1.87 mmol) was rapidly added. The suspension that formed was stirred until it became colorless and then diluted with EtOH (10 mL). The precipitate that formed was filtered off and washed with EtOH. Compound **3a** was obtained as colorless needles (Table 1).

7,9-Dimethyl-11-phenylpyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]-quinoxaline-8,10(7*H*,9*H*)-dione (4a) was synthesized analogously to compound **3a** from amine **2b** (380 mg, 1.1 mmol); pale-yellow crystalline compound (see Table 1).

6,7,9-Trimethylpyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]quinoxaline-8,10(7*H*,9*H*)-dione (3b). A 54% $HClO_4$ solution (0.22 mL, 2 mmol) was added to a suspension of finely dispersed compound **1a** (300 mg, 1.1 mmol) in Ac_2O (3 mL) cooled to −10 °C. Then cooling was stopped, the mixture was stirred at ~20 °C for 20 min, and ice water (1 mL) was added. After 20 min, the precipitate of perchlorate that formed was filtered off and washed with water and EtOH. The free base was isolated analogously to compound **3a**; colorless finely crystalline compound (see Table 1).

6,7,9-Trimethyl-11-phenylpyrimido[4′,5′:3,4]pyrrolo-[1,2-*a*]quinoxaline-8,10(7*H*,9*H*)-dione (4b) was synthesized analogously to compound **3b** from amine **2b** (380 mg, 1.1 mmol); pale-yellow crystals (see Table 1).

6-Substituted 7,9-dimethylpyrimido[4′,5′:3,4]pyrrolo-[1,2-*a*]quinoxaline-8,10(7*H*,9*H*)-diones 3c—k and 4c—k (general procedure). The corresponding carboxylic acid (2 mmol; 150 mg (1.2 mmol) in the case of pyridinecarboxylic acids) was added to a suspension of amine **2** (1 mmol) in $POCl_3$ (3 mL). The reaction mixture was refluxed until elimination of HCl ceased. The reaction time for aliphatic, substituted benzoic, and pyridinecarboxylic acids was 1, 2, and 6 h, respectively. In the

Table 1. Yields and elemental analysis data for pyrimidopyrroloquinoxalines **3** and **4**

Compound	Yield (%)	M.p. /°C	Found / Calculated (%) C	Found / Calculated (%) H	Molecular formula
3a	86	375—380	64.51 64.28	4.13 4.32	$C_{15}H_{12}N_4O_2$
3b	74	315—318	65.34 65.30	4.81 4.79	$C_{16}H_{14}N_4O_2$
3c	73	260—262	66.45 66.22	5.33 5.23	$C_{17}H_{16}N_4O_2$
3d	65	258—260	71.56 71.34	4.95 4.90	$C_{22}H_{18}N_4O_2$
3e	67	262—265	68.31 68.38	4.83 4.70	$C_{22}H_{18}N_4O_3$
3f	78	308—310*	54.88 55.18	3.20 3.18	$C_{16}H_{11}F_3N_4O_2$
3g	54	308—310	70.43 70.78	4.44 4.53	$C_{21}H_{16}N_4O_2$
3h	57	310—313	68.14 68.38	4.81 4.70	$C_{22}H_{18}N_4O_3$
3i	47	370—372	62.99 62.84	3.69 3.77	$C_{21}H_{15}N_5O_4$
3j	52	>360	67.10 67.22	4.15 4.23	$C_{20}H_{15}N_5O_2$
3k	59	>360	67.02 67.22	4.16 4.23	$C_{20}H_{15}N_5O_2$
4a	82	277—280	71.05 70.78	4.41 4.53	$C_{21}H_{16}N_4O_2$
4b	89	253—255	71.50 71.34	4.85 4.90	$C_{22}H_{18}N_4O_2$
4c	77	212—215	72.03 71.86	5.21 5.24	$C_{23}H_{20}N_4O_2$
4d	74	228—230	75.54 75.32	4.99 4.97	$C_{28}H_{22}N_4O_2$
4e	89	198—200	72.87 72.71	4.84 4.79	$C_{28}H_{22}N_4O_3$
4f	91	227—230	62.56 62.27	3.67 3.56	$C_{22}H_{15}F_3N_4O_2$
4g	72	237—240	74.90 74.99	4.62 4.66	$C_{27}H_{20}N_4O_2$
4h	77	243—245	72.81 72.71	4.72 4.79	$C_{28}H_{22}N_4O_3$
4i	59	>310*	67.73 67.92	4.09 4.01	$C_{27}H_{19}N_5O_4$
4j	51	280—283	72.23 72.04	4.48 4.42	$C_{26}H_{19}N_5O_2$
4k	35	235—237	72.15 72.04	4.46 4.42	$C_{26}H_{19}N_5O_2$

* With sublimation.

latter case, stirring was required. The course of the reactions was monitored by TLC on Silufol UV-254 plates ($CHCl_3$—EtOAc, 10 : 1, as the eluent) after hydrolysis and neutralization of the sample. The products and the starting amines were visualized with UV light (in the case of the starting amines, the plates were preliminary heated to 200 °C). After completion of the reaction, the mixture was cooled to ~20 °C and poured with stirring into a mixture of ice and water (~20 g). After complete hydrolysis with $POCl_3$ and cooling, the reaction mixture was neutralized with a 50% NaOH solution. The compound that remained undissolved was separated, triturated with a 10% NaOH solution (5 mL), filtered off, washed with water, dried, and recrystallized. Compounds **3c—g**,**k** and **4c—g**,**k** were purified by reprecipitation with EtOH from $CHCl_3$. All other compounds were purified by recrystallization from DMSO (see Table 1).

The IR spectra of all compounds **3** and **4** show two intense absorption bands of the carbonyl groups at 1655—1665 and 1685—1695 cm^{-1}. In addition, the spectra of 11-unsubstituted compounds **3** show a characteristic narrow band of the C—H bond at 3120—3125 cm^{-1}.

The ^1H NMR spectroscopic data for pyrroloquinoxalines **3** and **4** are given in Table 2. Unless otherwise indicated, the signals of 7-Me and 9-Me appear as three-proton singlets; the signal of 11-R for compound **3**, as a one-proton singlet. The spin-spin coupling constants of the signals of the substituent 6-R´ different from a singlet are typical of the corresponding groups. The coupling constants in the benzene ring are as follows: $J_{1,2}$ = 8.4—8.6 Hz, $J_{2,3}$ = 7.1—7.3 Hz, and $J_{3,4}$ = 7.9—8.2 Hz.

7,9-Dimethylpyrimido[4´,5´:3,4]pyrrolo[2,1-*c*][1,2,4]benzotriazine-8,10(7*H*,9*H*)-dione (5a). A solution of $NaNO_2$ (90 mg, 1.3 mmol) in water (0.5 mL) was added to a vigorously stirred suspension of finely dispersed aminopyrrole **2a** (270 mg, 1 mmol) in AcOH (5 mL). The reaction mixture was stirred for 0.5 h. The precipitate that formed was filtered off and washed with EtOH, after which the pure product was obtained. The yield was 240 mg (85%), orange finely crystalline compound, sublim. point > 360 °C (from DMSO). Found (%): C, 59.64; H, 3.81. $C_{14}H_{11}N_5O_2$. Calculated (%): C, 59.78; H, 3.94. ^1H NMR (DMSO-d_6), δ): 3.40 (s, 3 H, 9-Me); 4.05 (s, 3 H, 7-Me); 7.70 (t, 1 H, H(3), J = 7.5 Hz); 7.82 (t, 1 H, H(2), J = 7.9 Hz); 8.30 (d, 1 H, H(1), J = 8.0 Hz); 8.37 (d, 1 H, H(4), J = 8.1 Hz); 8.88 (s, 1 H, H(11)). MS, m/z: 281 $[M]^+$, 224 $[M - MeNCO]^+$, 196 [M – MeNCO – N_2], 169 [196 – HCN]. IR, ν/cm^{-1}: 1655, 1685 (C=O); 3120 (C—H .

7,9-Dimethyl-11-phenylpyrimido[4´,5´:3,4]pyrrolo[2,1-*c*]-[1,2,4]benzotriazine-8,10(7*H*,9*H*)-dione (5b) was synthesized analogously to compound **5a** from pyrrole **2b** (346 mg, 1 mmol). The yield was 332 mg (93%). Dark-orange needle-like crystals, m.p. 320—323 °C (sublim., from DMF). Found (%): C, 67.42; H, 4.30. $C_{20}H_{15}N_5O_2$. Calculated (%): C, 67.22; H, 4.23. ^1H NMR (DMSO-d_6), δ: 3.29 (s, 3 H, 9-Me); 4.10 (s, 3 H, 7-Me); 6.95 (d, 1 H, H(1), J = 8.3 Hz); 7.38 (t, 1 H, H(2), J = 7.2 Hz); 7.55—7.70 (m, 6 H, H(3) + Ph); 8.25 (d, 1 H, H(4), J = 7.9 Hz). IR, ν/cm^{-1}: 1655, 1690 (C=O).

2-(1,3-Dimethyl-2,4-dioxo-5-phenyl-1,2,3,4-tetrahydropyrrolo[3,4-*d*]pyrimidinyl-6)benzoic acid (6b). A solution of NaOH (160 mg, 4 mmol) in water (1 mL) was added to a solution of ester **8** (400 mg, 1 mmol) in EtOH (10 mL). The reaction mixture was refluxed until the sample ceased to turn turbid upon dilution with distilled water (1.0—1.5 h). Then the reaction mixture was diluted with water (10 mL), the major portion of EtOH was distilled off, and the mixture was acidified with concentrated HCl. The resinous substance solidified upon trituration with water and then it was used without additional purification. The yield was 255 mg (68%), powdered compound, m.p. 130—135 °C. Found (%): C, 67.71; H, 4.26. $C_{21}H_{17}N_3O_4$.

Table 2. ^{1}H NMR spectra of pyrimidopyrroloquinoxalines **3** and **4**

Compound	δ (*J*/Hz)							Solvent[a]
	7-Me	9-Me	6-R′	11-R	H(1)	H(2)	H(3)	H(4)	
3a	3.89	3.50	9.02	8.40	7.92 (d)	7.52 (m, 2 H)		7.85 (d)	C
3b	3.80	3.45	2.89 (s, 3 H)	8.40	7.82 (d)	7.48 (m, 2 H)		7.78 (d)	C
3c	3.65	3.30	3.12 (q, 2 H); 1,30 (t, 3 H)	9.03	8.38 (d)	7.50 (m, 2 H)		7.76 (d)	D
3d	3.62	3.35	4.5 (s, 2 H, CH_2); 7.15—7.25 (m, 5 H, Ph)	9.05	8.31 (d)	7.42 (t)	7.50 (t)	7.71 (d)	D
3e	3.68	3.37	5.42 (s, 2 H, CH_2); 6.95 (m, 3 H, H_o, H_p); 7.25 (t, 2 H, H_m)	9.10	8.35 (d)	7.50 (t)	7.55 (t)	7.80 (d)	D
3f	3.65[b]	3.37	—	9.32	8.47 (d)	7.58 (t)	7.70 (t)	7.91 (d)	D
3g	2.65	3.45	7.50 (m, 5 H)	8.50	7.95 (m)	7.66 (m, 2 H)		7.86 (m)	C
3h	2.70	3.35	3.90 (s, 3 H, OMe); 7.05, 7.65 (both d, 2 H each, C_6H_4)	9.10	8.35 (d)	7.50 (m, 2 H)		7.80 (d)	D
3i	2.75	3.35	7.90, 8.45 (both d, 2 H each)	9.00	8.45 (d)	7.50—7.65 (m, 2 H)		7.85 (d)	D
3j	2.75	3.50	7.62, 8.80 (both d, 2 H each, *J* = 5.9)	8.52	7.95 (d)	7.50—7.60 (m)		7.88 (d)	C
3k	2.60	3.55	7.52—7.64[c] (m, 1 H); 8.14, 8.76 (both d, 1 H each); 8.87 (s, 1 H)	9.19	8.47 (d)	7.48—7.62[c] (m)		7.86 (d)	D
4a	3.90	3.35	9.05 (s, 1 H)	7.40—7.60 (m, 5 H)	7.05 (m, 2 H)		7.34 (td)	7.82 (d)	C
4b	3.75	3.35	2.85 (s, 3 H)	7.52 (s, 5 H)	6.95 (d, 2 H)		7.32 (m)	7.75 (d)	C
4c	3.72	3.35	3.1 (q, 2 H), 1.45 (t, 3 H)	7.52 (s, 5 H)	6.95 (d, 2 H)		7.30 (m)	7.77 (d)	C
4d	3.61	3.27	4.45 (s, 2 H), 7.15—7.35[c] (m, 5 H)	7.54 (s, 5 H)	6.95 (d, 2 H)		7.30[c]	7.79 (d)	C
4e	3.60	3.25	5.40 (s, 2 H); 6.95 (m, 3 H, H_o, H_p); 7.27 (t, 2 H, H_m)	—	6.87 (d)	7.05 (t)	7.24 (t)	7.74 (d)	D
4f	3.65[d]	3.35	—	7.50—7.60 (m, 5 H)	6.98 (d)	7.12 (t)	7.39 (t)	7.90 (d)	C
4g	2.55	3.25	7.54—7.62 (m, 8 H); 7.75 (m, 2 H)	—	7.16 (d)	7.01 (t)	7.35 (t)	7.80 (d)	D
4h	2.70	3.25	7.06, 7.70 (both d, 2 H each)	7.50—7.70 (m, 5 H)	6.95 (m, 2 H)		7.32 (t)	7.77 (d)	D
4i	2.69	3.35	7.90, 8.40 (both d, 2 H each)	7.60 (s, 5 H)	7.08 (m, 2 H)		7.38 (m)	7.90 (d)	C
4j	2.70	3.35	7.66 (d, 2 H, *J* = 5.8); 8.82 (d, 2 H, *J* = 5.3)	7.60 (s, 5 H)	7.06 (m, 2 H)		7.38 (m)	7.88 (d)	C
4k	2.70	3.35	7.48 (dd); 8.05 (dt); 8.79 (d); 9.0 (s)	7.50—7.70 (m, 5 H)	7.05 (m, 2 H)		7.38 (m)	7.88 (d)	C

[a] C is $CDCl_3$ and D is DMSO-d_6.
[b] A broadened singlet.
[c] The signals overlap.
[d] A doublet with *J* = 1.5 Hz.

Calculated (%): C, 67.19; H, 4.56. ^{1}H NMR (DMSO-d_6), δ: 3.20 (s, 3 H, 3-Me); 3.32 (s, 3 H, 1-Me); 7.06 (s, 1 H, H(7)); 7.1—7.25 (m, 5 H, Ph); 7.33 (d, 1 H, H(6′), *J* = 7.1 Hz); 7.45—7.65 (m, 2 H, H(4′), H(5′)); 7.80 (d, 1 H, H(3′), *J* = 7.4 Hz). IR, ν/cm^{-1}: 1650—1690 (br, C=O); 3100—3300 (O—H).

1,3-Dimethyl-2*H*-pyrimido[4′,5′:3,4]pyrrolo[1,2-*a*]indole-2,4,11(1*H*,3*H*)-trione (7a). Anthranilic acid (333 mg, 2.33 mmol) and Et_3N (0.3 mL, 2.17 mmol) were added to a solution of aldehyde **1a** (467 mg, 1.80 mmol) in EtOH (15 mL). The reaction mixture was refluxed for 1 h, cooled, and acidified with concentrated HCl. The amorphous precipitate that formed was filtered off, washed with a small amount of water, and dried. The resulting 2-(1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrrolo[3,4-*d*]pyrimidinyl-6)benzoic acid (**6a**) was dried at 50 °C for 3 h and used without purification. The yield was 240 mg (45%), pale-gray powder, m.p. 260—265 °C (decomposition started at 235—240 °C).

A suspension of acid **6a** in $POCl_3$ (3 mL) was refluxed with stirring for 0.5 h, cooled, and poured into a mixture of water and ice (20 g). The reaction mixture was stirred for 30 min. The precipitate that formed was filtered off, washed with water, a 5% NaOH solution, and water, dried, and recrystallized from DMF. The yield was 183 mg (57%), yellowish needle-like crystals, m.p. 320—322 °C ($CHCl_3$). Found (%): C, 64.25; H, 4.09. $C_{15}H_{11}N_3O_3$. Calculated (%): C, 64.05; H, 3.94. ^{1}H NMR ($CDCl_3$), δ: 3.40 (s, 3 H, 3-Me); 3.90 (s, 3 H, 1-Me); 7.25—7.35 (m, 2 H, H(7), H(9)); 7.55 (t, 1 H, H(8), *J* = 7.2 Hz); 7.70 (d, 1 H, H(10), *J* = 7.1 Hz); 7.75 (s, 1 H, H(5)). IR, ν/cm^{-1}: 1660—1690 (br, s, C=O); 3125 (C—H).

1,3-Dimethyl-5-phenyl-2*H*-pyrimido[4′,5′:3,4]pyrrolo-[1,2-*a*]indole-2,4,11(1*H*,3*H*)trione (7b) was synthesized analo-

gously to indole **6a** from carboxylic acid **6b** (200 mg, 0.53 mmol). The yield was 128 mg (67%), yellow crystals, m.p. 328—330 °C ($CHCl_3$—EtOH). Found (%): C, 70.80; H, 4.16. $C_{21}H_{15}N_3O_3$. Calculated (%): C, 70.58; H, 4.23. ^{1}H NMR (DMSO-d_6), δ: 3.20 (s, 3 H, 3-Me); 3.85 (s, 3 H, 1-Me); 6.62 (d, 1 H, H(7), J = 7.9 Hz); 7.30 (t, 1 H, H(9), J = 7.4 Hz); 7.40 (t, 1 H, H(8), J = 7.7 Hz); 7.55—7.70, (m, 6 H, Ph + H(10)). MS, m/z: 357 $[M]^+$, 300 $[M - MeNCO]^+$, 271 $[300 - CO - H]^+$. IR, ν/cm^{-1}: 1650—1700 (br, s, C=O).

Ethyl 2-(1,3-dimethyl-2,4-dioxo-5-phenyl-1,2,3,4-tetrahydropyrrolo[3,4-*d*]pyrimidinyl-6)benzoate (8). Methyl anthranilate (0.52 mL, 3.1 mmol) and Et_3N (0.43 mL, 3.1 mmol) were added to a suspension of 5-benzoyl-6-bromomethyl-1,3,6-trimethyluracil **1b** (1 g, 3 mmol) in EtOH (10 mL). The reaction mixture was thoroughly stirred and then refluxed for 3 h. After cooling, the precipitate that formed was filtered off and successively washed with a small amount of EtOH and water. The yield was 0.75 g (62%), colorless needle-like crystals, m.p. 164—167 °C (from EtOH). Found (%): C, 68.75; H, 5.41. $C_{23}H_{21}N_3O_4$. Calculated (%): C, 68.47; H, 5.25. ^{1}H NMR (DMSO-d_6), δ: 1.05 (t, 3 H, Et); 3.35 (s, 3 H, 3-Me); 3.40 (s, 3 H, 1-Me); 4.10 (q, 2 H, Et); 6.5 (s, 1 H, H(7)); 7.2 (m, 5 H, Ph); 7.28 (dd, 1 H, H(6′)); 7.40 (td, 1 H, H(4′)); 7.51 (td, 1 H, H(5′)); 7.77 (d, 1 H, H(3′), J = 7.1 Hz). IR, ν/cm^{-1}: 1650—1695 (br, C=O).

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