Pyrimidines, Part XXXI [1]. Synthesis, Reactions and Properties of 6-Acyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-diones

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Acylations of 1,3-dimethyl- (**1**) and 1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**2**) with anhydrides in the presence of trifluoroacetic acid proceed well to give in good yields the corresponding 7-acyl derivatives **3-11**. The 6-trichloroacetyl derivatives **5** and **6** are sensitive towards nucleophiles, which displace the trichloromethyl group easily by formation of the corresponding 6-carboxylic acid derivatives **12-23**. The newly synthesized compounds have been characterized by elemental analysis, uv and ^{1}H nmr spectra and pK_a determinations.

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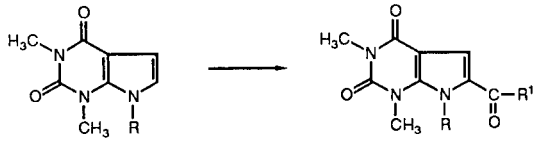
The 7*H*-pyrrolo[2,3-*d*]pyrimidine ring system can be regarded as a 7-deazapurine analog of interesting biochemical properties as indicated by the nucleoside antibiotics Tubercidin, Sangivamycin and Toyocamycin [2] as well as the tRNA component Queosine [3]. In order to investigate some electrophilic substitution reactions at the 7*H*-pyrrolo[2,3-*d*]pyrimidine nucleus have been chosen the 1,3-dimethyl- (**1**) and 1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**2**) [4] as substrates due to their structural relationships to theophylline and caffeine.

Compound **1** has already been subject to the Vilsmeier reaction, from which the 6-dimethylaminomethylene and 6-formyl derivatives [5] respectively were derived. These results indicate that the 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione reacts rather like pyrrole at the α-position than indole, which is preferentially substituted at the β-site.

Scheme 1



	R
1	H
2	CH_3

	R	R^1
3	H	CH_3
4	CH_3	CH_3
5	H	CCl_3
6	CH_3	CCl_3
7	H	CF_3
8	CH_3	CF_3
9	H	C_6H_5
10	H	$CH{=}CH{-}C_6H_5$
11	H	$C(CH_3)_3$

	R	R^1
12	H	OCH_3
13	H	OC_2H_5
14	CH_3	OC_2H_5
15	H	NH_2
16	CH_3	NH_2
17	H	$NHCH(CH_3)_2$
18	CH_3	$NHCH(CH_3)_2$
19	H	$NH(CH_2)_3CH_3$
20	CH_3	$NH(CH_2)_3CH_3$
21	H	$NHNH_2$
22	CH_3	$NHNH_2$
23	H	OH

Direct acylations of **1** and **2** could be achieved readily by the appropriate anhydrides under acid catalysis. Working in trifluoroacetic acid as the reaction medium and solvent at moderate elevated temperatures (25-50°) turned out to give the best results.

The acylation reaction can be applied quite generally using acetic, trichloroacetic, trifluoroacetic, benzoic, pivalic and cinnamic anhydrides to give the corresponding 6-acyl derivatives **3-11**.

Some of these compounds are quite labile and especially the 1,3-dimethyl-6-trichloroacetylpyrrolo[2,3-*d*]pyrimidine-2,4-dione showed a high sensitivity towards base, even at *p*H 9 by hydrolytic cleavage of the trichloromethyl group forming 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione-6-carboxylic acid (**23**) (Figure 1).

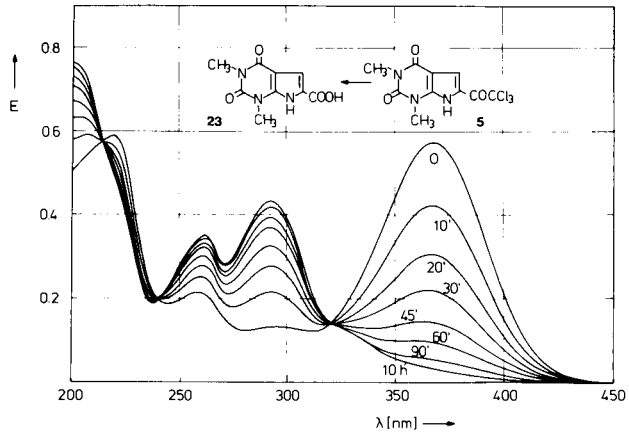


Figure 1. Hydrolytic cleavage of **5** to 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione-6-carboxylic acid (**23**) at *p*H 9.

Since also a methanolic solution of **5** showed a slow spectral change, the chemical behaviour of the 6-trichloroacetyl derivatives **5** and **6** towards nucleophiles was fur-

Table 1

Physical Data of 2,4-Dioxo-1,2,3,4-tetrahydropyrrolo[2,3-*d*]pyrimidines

No.	pK_a in H_2O	UV Absorption Spectra λ max (nm)				log ε				pH
1	11.35	212	244	276		4.31	3.81	3.85		7.0
			231	284			4.31	3.84		14.0
2		219	248	278		4.27	3.79	3.79		MeOH
3	9.10	207	[232]	269	310	4.37	[3.88]	3.78	4.39	5.0
		217	253	[274]	340	4.36	4.08	[3.59]	4.37	12.0
4		215		277	315	4.31		3.82	4.31	MeOH
5	7.54	206	243	[268]	346	4.30	3.84	[3.51]	4.36	5.0
		220	260	292	367	4.30	3.91	3.76	4.25	10.0
6		213	253		345	4.56	4.12		4.58	MeOH
7	7.23	206	241	[268]	340	4.31	3.90	[3.56]	4.36	5.0
		220	257		360	4.31	3.69		4.46	10.0
8		211	248	[270]	335	4.30	3.83	[3.46]	4.38	MeOH
9	8.65	206	242	[267]	337	4.41	4.02	[3.83]	4.47	6.0
		205	221	252	356	4.34	4.39	3.79	4.36	12.0
10	8.90		[250]	[286]	364		[3.91]	[3.98]	4.51	6.0
		206	226	285	394	4.36	4.38	4.21	4.43	12.0
11	10.06	207	[234]	270	316	4.28	[3.74]	3.66	4.27	6.0
		206	217	253	337	4.19	4.23	3.97	4.25	12.0
12		205	263	293		4.36	4.02	4.29		MeOH
13		204	263	293		4.35	4.03	4.29		MeOH
14		210	269	293		4.38	4.08	4.27		MeOH
15		203	263	291		4.41	4.10	4.25		MeOH
16		207	268	289		4.40	4.13	4.19		MeOH
17		207	263	291		4.26	3.97	4.09		MeOH
18		210	268	288		4.41	4.17	4.19		MeOH
19		207	263	291		4.42	4.15	4.27		MeOH
20		210	268	288		4.42	4.17	4.19		MeOH
21		205	263	294		4.33	4.00	4.21		MeOH
22		208	268	292		4.33	4.02	4.19		MeOH
23	3.24	202	262	296		4.39	4.02	4.31		1.0
	11.47	201	262	289		4.40	4.12	4.20		6.0
		240	[264]	307		4.36	[3.76]	4.15		14.0

[ ] Shoulder.

No.	^{1}H-NMR Spectra in DMSO-d_6 (δ in ppm) N-H	1-CH_3	3-CH_3	7-CH_3	5-H	6-Subst.
1	11.62	3.42	3.21	–	6.72 m	6.33 (m, 1H)
	–	3.68	3.19	3.86	6.62 m	6.29 (m, 1H)
2	12.34	3.48	3.21	–	7.44 s	2.40 (s, 3H)
3	–	3.70	3.23	4.06	7.54 s	2.43 (s, 3H)
4	12.81	3.54	3.24	–	7.63 s	–
5	–	3.75	3.26	4.06	7.80 s	–
6	13.08	3.50	3.22	–	7.50 s	–
7	–	3.71	3.21	4.09	7.50 s	–
8	11.18	3.68	3.40	–	7.22 s	7.40-7.9 m
9	12.38	3.45	3.17	–	7.50 m	7.30-8.00 m
10	12.03	3.51	3.22	–	7.32 s	1.36 (s, 9H)
11	12.46	3.46	3.19	–	7.02 s	3.80 (s, 3H)
12	12.75	3.49	3.21	–	7.04 s	4.28 q 1.29 t
13	–	3.72	3.22	4.10	7.15 s	4.23 q 1.29 t
14	12.09	3.48	3.20	–	7.18 s	7.68 (2H)
15	–	3.71	3.21	4.08	7.19 s	7.60 (2H)
16	12.06	3.48	3.20	–	7.21 s	4.00 (m, 1H) 1.15 (d, 6H)
17	8.06 d	3.69	3.20	4.04	7.12 s	4.03 (m, 1H) 1.11 (d, 6H)
18	12.09	3.49	3.21	–	7.17 s	3.16 (m, 2H) 1.35 (m, 4H) 0.8 (t, 3H)
19	8.27 t	3.70	3.20	4.04	7.08 s	3.15 (m, 2H) 1.37 (m, 4H) 0.85 (t, 3H)
20	12.25	3.49	3.21	–	7.24 s	10.01 (1H) 3.80 (2H)
21	–	3.70	3.20	4.05	6.99 s	9.55 (1H) 4.4 (2H)
22	12.37	3.48	3.21	–	7.02 s	–

ther investigated. Sodium methoxide converted **5** at room temperature into the methyl 1,3-dimethylpyrrolo[2,3-*d*]-pyrimidine-2,4-dione-6-carboxylate (**12**), which is not without precedence in the pyrrol series [6,7], and with concentrated ammonia the corresponding amides **15** and **16** were obtained. Treatment of the ethanolic solution of **5** and **6** respectively with ammonia gas at room temperature afforded no reaction, but at an elevated temperature of 70° the 6-ethoxycarbonyl derivatives **13** and **14** were formed rather than the expected primary amides. Neat primary amines such as isopropylamine and *n*-butylamine led to the secondary amides **17-20** and hydrazine also gave rise to a nucleophilic displacement reaction yielding the hydrazides **21** and **22** respectively. Several attempts to convert **5** and **6** with secondary amines into the tertiary amides were unsuccessful as well as the reactions with *C*-nucleophiles like sodium diethyl malonate. Surprisingly, also the 6-trifluoroacetyl analogs **7** and **8** did not react in the same manner and proved to be stable as seen from their recovery after refluxing in sodium methoxide solution.

The newly synthesized compounds have been characterized by their uv and nmr spectra (Table 1) as well as elemental analyses.

From the determination of several pK_a values it can be seen that the acidity of the starting 1,3-dimethylpyrrolo-[2,3-*d*]pyrimidine-2,4-dione (**1**) increases gradually with the introduction of more electronegative acyl groups. The 6-trifluoroacetyl derivative **7** possesses expectedly the most acidic properties in this series, which is also reflected in the low field chemical shift of the N-H function. It is also noteworthy that the 1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione-6-carboxylic acid (**23**) is a relatively strong acid with a pK_a of 3.24, whereas the second ionization takes place in basic medium as indicated by the pK_a 11.47. The carboxylate ion form counteracts the N-H deprotonation to some extent, since the acidity of the corresponding ester **12** is much higher due to the electron-attracting power of the methoxycarbonyl group.

A comparison of the uv spectra of the various molecular forms indicates that monoanion formation at the N-7H site is associated with a bathochromic shift of the long wavelength absorption band by 20-30 nm favouring a prolonged chromophoric system. In the carboxylic acid **23** monoanion formation causes a hypsochromic shift due to the internally stabilized carboxylate resonance, whereas conversion to the dianion reveals the normal spectral behaviour.

The peculiarities of the ^{1}H nmr spectra are illustrated by the comparisons of the N-7H with their corresponding N-7 methyl derivatives. N-7 methylation causes a downfield shift of one of the other two methyl signals, which allows an obvious assignment due to steric crowding of the peri-located substituents. An analogous effect has already been observed in the uric acid series [9], where a 3,9-dimethyl substitution is reflected in the same manner.

EXPERIMENTAL

The uv spectra were determined with a Cary, Model 118 (Applied Physics Corporation) and an Uvikon 820 (Kontron) recording spectrometer. The ^{1}H nmr spectra were obtained with a Bruker WM-250 spectrometer, with chemical shifts (δ) reported in ppm downfield from tetramethylsilane. DC was performed on silica gel plates F 1500 LS 254 and cellulose sheets F 1440 LS 254 of Schleicher & Schüll. The pK_a determinations were achieved by the spectrophotometric method [8]. Melting points were taken in capillary tubes in a Dr. Tottoli apparatus of Büchi Company and are uncorrected.

General Procedure for Acylation of 1,3-Dimethyl- (**1**) and 1,3,7-Trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**2**).

To a mixture of 0.01 mole of **1** or **2**, [4] and 20 ml of trifluoroacetic acid, the appropriate anhydride was added with stirring at room or slightly elevated temperatures. Stirring was continued until completion of the reaction, which was followed by tlc. The reaction solution was evaporated in vacuum to dryness and the residue treated with water or methanol to give the crude product. Purification was achieved by recrystallization from the appropriate solvent to give chromatographically and analytically pure material.

6-Acetyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**3**).

Treatment of 1.79 g of **1** with 20 ml of acetic anhydride at room temperature yielded after 4 days 1.7 g (77%) of colourless crystals from acetic acid of mp 313°.

Anal. Calcd. for $C_{10}H_{11}N_3O_3$ (221.2): C, 54.29; H, 4.97; N, 19.00. Found: C, 54.38; H, 5.02; N, 18.97.

6-Acetyl-1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**4**).

Stirring of 1.93 g of **2** with 20 ml of acetic anhydride at room temperature afforded after 2 days and on recrystallization from dichloromethane 2.0 g (85%) of colourless crystals of mp 219°.

Anal. Calcd. for $C_{11}H_{13}N_3O_3$ (235.2): C, 56.17; H, 5.53; N, 17.87. Found: C, 55.88; H, 5.72; N, 17.61.

6-Trichloroacetyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**5**).

Reaction of 1.79 g of **1** with 20 ml of trichloroacetic anhydride at 50° for 2 days gave a crude material, which was extracted with chloroform. Evaporation and recrystallization from dichloromethane gave 2.79 g (86%) of colourless crystals of mp 236°.

Anal. Calcd. for $C_{10}H_6Cl_3N_3O_3$ (324.5): C, 36.97; H, 2.46; N, 12.94. Found: C, 37.05; H, 2.44; N, 12.86.

6-Trichloroacetyl-1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**6**).

Treatment of 1.93 g of **2** with 20 ml of trichloroacetic anhydride at 50° for 20 hours, evaporation, hydrolysis and chloroform extraction yielded after recrystallization from dichloromethan 2.37 g (70%) of pinkish crystals of mp 173°.

Anal. Calcd. for $C_{11}H_{10}Cl_3N_3O_3$ (338.5): C, 39.02; H, 2.98; N, 12.41. Found: C, 39.11; H, 2.96; N, 12.38.

6-Trifluoroacetyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**7**).

Reaction of 1.79 g of **1** with 15 ml of trifluoroacetic anhydride at 45° for 1 day yielded on recrystallization from glacial acetic acid 2.01 g (73%) pale yellow crystals of mp 281°.

Anal. Calcd. for $C_{10}H_6F_3N_3O_3$ (275.2): C, 43.64; H, 2.91; N, 15.27. Found: C, 43.50; H, 2.84; N, 15.01.

6-Trifluoroacetyl-1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**8**).

Treatment of 1.93 g of **2** with 15 ml of trifluoroacetic anhydride at 40°

for 1 day gave on recrystallization from dichloromethane 1.88 g (65%) of pinkish crystals of mp 158°.

Anal. Calcd. for $C_{11}H_{10}F_3N_3O_3$ (289.2): C, 45.67; H, 3.46; N, 14.53. Found: C, 45.32; H, 3.39; N, 14.28.

6-Benzoyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**9**).

Reaction of 1.79 g of **1** with 6 g of benzoic anhydride at 50° yielded after 2 days 1.83 g (80%) of pinkish crystals from methanol of mp 269-271°.

Anal. Calcd. for $C_{15}H_{13}N_3O_3$ (283.3): C, 63.59; H, 4.63; N, 14.83. Found: C, 63.67; H, 4.57; N, 14.84.

6-Cinnamoyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**10**).

Treatment of 1.79 g of **1** with 7 g of cinnamic anhydride at 50° for 2 days gave 2.32 g (75%) yellow powder from DMF of mp 301-303°.

Anal. Calcd. for $C_{17}H_{15}N_3O_3$ (309.3): C, 66.01; H, 4.89; N, 13.59. Found: C, 65.78; H, 4.82; N, 13.54.

1,3-Dimethyl-6-pivaloylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**11**).

Reaction of 1.79 g of **1** with 4 g of pivalic anhydride at room temperature yielded 2.26 g (86%) of colourless crystals from methanol of mp 234-235°.

Anal. Calcd. for $C_{13}H_{17}N_3O_3$ (263.3): C, 59.30; H, 6.51; N, 15.96. Found: C, 59.41; H, 6.63; N, 15.91.

1,3-Dimethyl-6-methoxycarbonylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**12**).

To a solution of 0.5 g of sodium in 50 ml of absolute methanol was added 3.24 g (0.01 mole) of **5** and then stirred for 15 hours at room temperature. The mixture was neutralized with acetic acid and the precipitate collected. Recrystallization from methanol gave 1.85 g (78%) of colourless crystals of mp 265°.

Anal. Calcd. for $C_{10}H_{11}N_3O_4$ (237.2): C, 50.63; H, 4.67; N, 17.71. Found: C, 50.45; H, 4.70; N, 17.50.

1,3-Dimethyl-6-ethoxycarbonylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**13**).

To a solution of 0.5 g of sodium in 50 ml of absolute ethanol was added 3.24 g (0.01 mole) of **5** and then the mixture heated with stirring to 50° for 5 hours. On neutralization with acetic acid a precipitate separated, which was collected after cooling. Recrystallization from ethanol gave 2.03 g (81%) of colourless crystals of mp 274°.

Anal. Calcd. for $C_{11}H_{13}N_3O_4$ (251.2): C, 52.58; H, 5.22; N, 16.73. Found: C, 52.60; H, 5.24; N, 16.74.

6-Ethoxycarbonyl-1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**14**).

In a solution of 0.25 g of sodium in 75 ml of absolute ethanol was stirred 1.7 g (0.005 mole) of **6** at room temperature for 24 hours. It was neutralized with acetic acid, the precipitate collected and recrystallized from ethanol to give 0.90 g (68%) of colourless crystals of mp 190°.

Anal. Calcd. for $C_{12}H_{15}N_3O_4$ (265.3): C, 54.32; H, 5.69; N, 15.84. Found: C, 54.00; H, 5.72; N, 15.82.

6-Carbamoyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**15**).

In 40 ml of concentrated ammonia was refluxed 1.62 g (0.005 mole) of **5** for 5 minutes. The mixture was evaporated to dryness and the residue yielded on recrystallization from acetic acid, 0.89 g (80%) of colourless powder of mp 338°.

Anal. Calcd. for $C_9H_{10}N_4O_3$ (222.2): C, 48.65; H, 4.54; N, 25.21. Found: C, 48.53; H, 4.56; N, 25.05.

6-Carbamoyl-1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**16**).

To a mixture of 20 ml of dioxane and 10 ml of concentrated ammonia was added 1.7 g (0.005 moles) of **6** and then heated to 70° for 15 minutes. It was evaporated and the residue recrystallized from 50% aqueous acetic acid to give 0.97 g (82%) of colourless crystalline powder of mp 295°.

Anal. Calcd. for $C_{10}H_{12}N_4O_3$ (236.2): C, 50.83; H, 5.12; N, 23.72. Found: C, 50.81; H, 5.13; N, 23.41.

6-*N*-Isopropylcarbamoyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**17**).

In 15 ml of isopropylamine was heated 1.62 g (0.005 mole) of **5** to 40° for 3 days. After evaporation the residue was recrystallized from aqueous acetic acid to give 1.12 g (85%) of colourless crystals of mp 285°.

Anal. Calcd. for $C_{12}H_{16}N_4O_3$ (264.3): C, 54.55; H, 6.10; N, 21.20. Found: C, 54.38; H, 6.11; N, 20.96.

6-*N*-Isopropylcarbamoyl-1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**18**).

In 20 ml of isopropylamine was heated under reflux 0.85 g (2.5 mmoles) of **6** for 15 minutes. The mixture was then stirred overnight, evaporated and the residue recrystallized from ethanol to give 0.53 g (75%) of colourless crystals of mp 200°.

Anal. Calcd. for $C_{13}H_{18}N_4O_3$ (278.3): C, 56.10; H, 6.52; N, 20.13. Found: C, 55.91; H, 6.43; N, 20.11.

6-*N*-Butylcarbamoyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**19**).

In 15 ml of *n*-butylamine was heated 1.62 g (0.005 mole) of **5** to 80° for 30 minutes. The mixture was evaporated, the residue recrystallized from aqueous acetic acid to give 0.58 g (42%) of colourless crystals of mp 280°.

Anal. Calcd. for $C_{13}H_{18}N_4O_3$ (278.3): C, 56.10; H, 6.52; N, 20.13. Found: C, 55.89; H, 6.48; N, 20.04.

6-*N*-Butylcarbamoyl-1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**20**).

In 15 ml of *n*-butylamine was heated 1.7 g (0.005 mole) of **6** for 15 minutes under reflux. The precipitate was collected after cooling and gave on recrystallization from ethanol 1.1 g (75%) of colourless crystals of mp 190°.

Anal. Calcd. for $C_{14}H_{20}N_4O_3$ (292.3): C, 57.52; H, 6.90; N, 19.17. Found: C, 57.37; H, 6.92; N, 19.11.

6-Aminocarbamoyl-1,3-dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**21**).

In 15 ml of hydrazine hydrate was heated 1.62 g (0.005 mole) of **5** to 100° for 5 minutes. It was evaporated to dryness and the residue recrystallized from aqueous acetic acid to yield 0.9 g (76%) of a colourless powder of mp 345°.

Anal. Calcd. for $C_9H_{11}N_5O_3$ (237.2): C, 45.57; H, 4.67; N, 29.52. Found: C, 45.60; H, 4.80; N, 29.31.

6-Aminocarbamoyl-1,3,7-trimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione (**22**).

In 10 ml of hydrazine hydrate was heated 1.7 g (0.005 mole) of **6** to 100° for 5 minutes. The reaction solution was evaporated to dryness and the residue yielded on recrystallization from aqueous acetic acid 1.07 g (85%) of colourless crystals of mp 295°.

Anal. Calcd. for $C_{10}H_{13}N_5O_3$ (251.2): C, 47.80; H, 5.11; N, 27.88. Found: C, 47.71; H, 5.11; N, 27.68.

1,3-Dimethylpyrrolo[2,3-*d*]pyrimidine-2,4-dione-6-carboxylic Acid (**23**).

In 40 ml of 0.1 *N* sodium hydroxide was stirred at room temperature 1.62 g (0.005 mole) of **5** for 2 hours. The reaction solution was treated with charcoal, filtered and then acidified to *p*H 1. The precipitate was collected, washed with water and dried at 100° to give 0.85 g (76%) of greyish crystals of mp 262°.

Anal. Calcd. for $C_9H_9N_3O_4$ (223.2): C, 48.43; H, 4.06; N, 18.83. Found: C, 48.25; H, 4.17; N, 18.52.

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REFERENCES AND NOTES

[1] Part **XXX**: I. W. Southon and W. Pfleiderer, *Chem. Ber.*, **111**, 1006 (1978).

[2] T. Kondo, T. Ohgi and T. Goto, *J. Agric. Biol. Chem.*, **41**, 1501 (1977).

[3] H. M. Goodman, J. Abelson, A. Candy, S. Brenner and J. D. Smith, *Nature*, **217**, 1019 (1968).

[4] S. Senda and K. Hirota, *Chem. Pharm. Bull.*, **22**, 1459 (1974).

[5] S. Senda and K. Hirota, *Chem. Pharm. Bull.*, **22**, 2921 (1974).

[6] J. W. Harbuck and H. Rapoport, *J. Org. Chem.*, **37**, 3618 (1972).

[7] P. Belanger, *Tetrahedron Letters*, 2505 (1979).

[8] A. Albert and E. P. Serjeant, "The Determination of Ionization Constants", Chapman and Hall Ltd., London, 1971, p 44.

[9] W. Pfleiderer, *Ann. Chem.*, 2030 (1974).