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Fused Pyrimidines. IV.¹⁾ Synthesis of 3-Alkyl(or Acyl)-aminopyrazolo[3,4-*d*]pyrimidine Derivatives from 6-Hydrazinouracils and Isothiocyanates²⁾

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1,3-Dialkyl-6-hydrazinouracils (I) reacted with alkyl and acyl isothiocyanates to yield 5,7-dialkyl-3-alkyl(or acyl)aminopyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-diones (II). This reaction was investigated in detail and it was found that the first product was a 6-[4-alkyl(or acyl)thiosemicarbazido]uracil (IV), which cyclized to II through two pathways. Acylation of II afforded the corresponding 2-acyl derivatives. Treatment of 1,3-diethyl-6-hydrazinouracil (Ia) with phosgeneimmonium chloride afforded 5,7-diethyl-3-dimethylamino[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (X).

Keywords—pyrazolo[3,4-*d*]pyrimidine; 6-hydrazinouracil; isothiocyanate; 6-thiosemicarbazidouracil; ring closure; acylation; phosgeneimmonium chloride; cyclic nucleotide phosphodiesterase inhibitor; diuretic activity

The preceding papers described the synthesis of isothiazolo[3,4-*d*]pyrimidines⁴⁾ and isoxazolo[3,4-*d*]pyrimidines¹⁾ from 6-aminouracils and 6-hydroxyaminouracils, respectively. This paper deals with a new procedure for the synthesis of 3-alkyl(or acyl)aminopyrazolo[3,4-*d*]pyrimidines from 6-hydrazinouracils and alkyl or acyl isothiocyanates.

1,3-Diethyl-6-hydrazinouracil (Ia)⁵⁾ was heated with three equivalents of methyl isothiocyanate (MeNCS) in dimethylformamide (DMF) at 100° for 8 hr to afford 5,7-diethyl-3-methylaminopyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (IIa) and 5,7-diethyl-3-methylamino-2-methylthiocarbamoylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (IIIa) in yields of 70 and 10 %, respectively (Chart 1).

Chart 1

The structure IIa was assigned on the basis of its elemental analysis ($C_{10}H_{15}N_5O_2$), nuclear magnetic resonance (NMR) (a doublet at δ 3.43 and a multiplet at δ 6.31 due to the $-NHCH_3$ group) and mass spectra (MS) (m/e 237, M^+). The structure IIIa was also established on the basis of its elemental analysis ($C_{12}H_{18}N_6O_2S$), NMR (two doublets at 3.19 and 3.52 due to the two $-NHCH_3$ groups) and MS (m/e 310, M^+). The methylthiocarbamoyl group was assumed to be located at the 2-position because acetylation of IIa took place at the 2-position, as

1) Part III: R. Marumoto and Y. Furukawa, *Chem. Pharm. Bull.* (Tokyo), **25**, 2974 (1977).

2) This work was presented at the 10th Congress of Heterocyclic Chemistry, Tsukuba, Japan, 1977; T. Naka and Y. Furukawa, *Heterocycle*, **9**, 101 (1978).

3) Location: Jusohonmachi, Yodogawa-ku, Osaka 532, Japan.

4) Y. Furukawa, O. Miyashita, and S. Shima, *Chem. Pharm. Bull.* (Tokyo), **24**, 970 (1976); Y. Furukawa and S. Shima, *ibid.*, **24**, 979 (1976).

5) G. Straus, *Ann.*, **638**, 205 (1960).

described later. Methylation of 5,7-dimethyl-3-phenylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione with methyl iodide was also shown to take place at the 2-position.⁶⁾

The following experiments i)–iii) were carried out to elucidate the mechanism of formation of IIa and IIIa. i) The treatment of Ia with one equivalent of MeNCS at 50° for 2 hr afforded 1,3-diethyl-6-(4-methylthiosemicarbazido)uracil (IVa) in 90% yield. Compound IVa was heated in dimethylformamide (DMF) at 100° for 8 hr to give IIa in 52% yield (path a). ii) The reaction of Ia with three equivalents of MeNCS at 100° was monitored by thin-layer chromatography (TLC) and it was found that IVa, IIIa and IIa appeared in this order, suggesting the formation of IIa from IIIa. iii) Heating of IIIa in DMF at 100° for 5 hr afforded IIa in 62% yield. In contrast, the treatment of IIa with three equivalents of MeNCS at 100° for 10 hr afforded IIIa in only 8% yield. These results indicate that the addition of IIa to MeNCS is reversible, the dissociation of IIIa to IIa and MeNCS being strongly favoured at high temperatures.

Thus, it is suggested that the formation of IIa and IIIa from Ia involves the two pathways outlined in Chart 2 (path a, IVa→IIa→IIIa, path b, IVa→V→IIIa→IIa) and the contributions of the two pathways may depend on the quantity of MeNCS used. Although

Chart 2

an attempt to isolate the intermediate (V) was unsuccessful, an analogous compound (VI) was formed in 57% yield by treatment of Ia with three equivalents of MeNCS in DMF at 100–110° for 4 hr. Compound VI was assigned the structure 1,3-diethyl-6-[2,2-bis(methylcarbamoyl)hydrazino]uracil on the basis of its elemental analysis ($C_{12}H_{20}N_6O_4 \cdot H_2O$), MS (m/e 312, M^+) and NMR (a doublet at δ 2.73 and a multiplet at δ 8.10 due to the two equivalent $-\text{CONHCH}_3$ groups) spectra. The latter signal ($-\text{NH}-$) was shifted to lower field by hydrogen bonding than the signal (δ 6.67) due to $-\text{CONHCH}_3$ of 1,3-dimethyl-6-methylsemicarbazido-uracil. Accordingly, the possibility of another structure (VI') was excluded (Chart 3).

Chart 3

6) F. Yoneda and T. Nagamatsu, *Bull. Chem. Soc. Jpn.*, **48**, 1484 (1975).

Similarly, treatment of 1,3-dialkyl-6-hydrazinouracils (I) with various alkyl and acyl isothiocyanates furnished the corresponding 3-alkyl(or acyl)aminopyrazolo[3,4-*d*]pyrimidine-4,6-(5*H*,7*H*)-diones (II), as summarized in Table I.

TABLE I. 3-Alkyl(or Acyl)aminopyrazolo[3,4-*d*]pyrimidine-4,6-(5*H*, 7*H*)-diones (II)

Series	R ^{1a)}	R ²	Yield (%)	mp (°C)	Cryst. ^{c)} solvent	Formula	Analysis (%)		
							Calcd. (Found)	C	H N
a	Et	Me	70	>280 (Sub.) ^{b)}	A	C ₁₀ H ₁₅ N ₅ O ₂	50.62 (50.34)	6.37 6.25	29.52 29.72
b	Me	Me	55	>300 (Sub.)	B	C ₈ H ₁₁ N ₅ O ₂	45.93 (45.78)	5.30 5.51	33.48 33.63
c	Me	Et	62	>300 (Sub.)	B	C ₉ H ₁₃ N ₅ O ₂	48.42 (48.80)	5.87 5.72	31.38 31.19
d	Me	i-Bu	36	238—239	A	C ₁₁ H ₁₇ N ₅ O ₂	52.57 (52.38)	6.82 6.54	27.87 28.03
e	Et	Et	70	261—262	B	C ₁₁ H ₁₇ N ₅ O ₂	52.57 (52.51)	6.82 6.77	27.87 27.93
f	Et	i-Bu	53	157—159	B	C ₁₃ H ₂₁ N ₅ O ₂	55.89 (55.71)	7.58 7.69	25.07 25.30
g	Et	Ac	30	254—255	A	C ₁₁ H ₁₅ N ₅ O ₃	49.80 (49.63)	5.70 5.76	26.40 26.57
h	Et	Pro	45	198—199	B	C ₁₂ H ₁₇ N ₅ O ₃	51.60 (51.51)	6.14 6.19	25.08 25.35
i	Me	Pro	42	276—277	B	C ₁₀ H ₁₃ N ₅ O ₃	47.80 (47.54)	5.22 5.22	27.88 28.01
j	Et	Bzo	30	262—264	A	C ₁₆ H ₁₇ N ₅ O ₃	58.70 (58.49)	5.23 5.07	21.40 21.62
k	<i>n</i> -Bu	Me	75	274—276	B	C ₁₄ H ₂₃ N ₅ O ₂	57.32 (57.20)	7.90 7.75	23.87 24.42
l	<i>n</i> -Bu	Ac	43	143—144	B	C ₁₅ H ₂₃ N ₅ O ₃	56.06 (56.19)	7.21 7.32	21.79 21.99

a) Me=methyl; Et=ethyl; Bu=butyl; Ac=acetyl; Pro=propionyl; Bzo=benzoyl.

b) Sub=sublime.

c) A=MeOH; B=EtOH.

Acetylation of IIe with acetic anhydride afforded 2-acetyl-3-ethylamino-5,7-diethylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (VIIb) in 68% yield. The location of the acetyl group was confirmed by the results of the following reactions. Acetylation of IVb with acetic anhydride in pyridine gave 6-(2-acetyl-4-ethylthiosemicarbazido)-1,3-diethyluracil (VIII) in 73% yield; the structure was established by the NMR: the signal of $-\text{CSNHet}$ of IVb appeared at δ 8.31 but that of VIII was shifted to δ 10.45, indicating hydrogen bonding as shown in Chart 4. Although an attempt to convert VIII to VIIb by heating in DMF at 110—120° for 8 hr was unsuccessful, treatment of VIII with N-chlorosuccinimide⁷⁾ in chloroform at room temperature furnished VIIb in 65% yield; this was identical with the product obtained by acetylation of IIe (Chart 4).

7) The oxidation of thiosemicarbazide derivatives with NCS will be described in the following paper (T. Naka and Y. Furukawa).

Chart 5

structure of X was assigned on the basis of elemental analysis ($C_{11}H_{17}N_5O_2$), and NMR [a singlet at δ 3.21 due to the $-N(CH_3)_2$] and MS (m/e 251, M^+).

The pyrazolo[3,4-*d*]pyrimidine ring system has been extensively studied¹⁰⁾ but the 3-substituted-amino derivatives described above have not been synthesized previously. Thus, we have found a new procedure for the synthesis of 3-substituted-

aminopyrazolo[3,4-*d*] pyrimidines from 6-hydrazinouracils and various isothiocyanates through the elimination of hydrogen sulfide by heating, and have found that acylation of these compounds affords only the 2-acyl derivatives. The cyclization of VIII to VIIb using NCS is an oxidative desulfurization.¹¹⁾ The application of this oxidative cyclization to the synthesis of heterocyclic compounds is in progress and will be reported elsewhere. Most of the compounds obtained above were inhibitors of cyclic nucleotide phosphodiesterase and showed diuretic activity.

Experimental

Melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. NMR spectra were recorded on a Hitachi R-24 spectrometer using tetramethylsilane as an internal standard. Ultraviolet (UV), infrared (IR) (nujol mull) spectra and MS were measured on Hitachi EPS-3T, 215 and RMS-4 machines, respectively. TLC was carried out on silica gel 60 F₂₅₄ plates (Merck).

1,3-Dialkyl-6-hydrazinouracil (I)—1,3-Dimethyl-6-hydrazinouracil^{10b)} and 1,3-diethyl-6-hydrazinouracil⁹⁾ were prepared by the known procedures.

1,3-Di-*n*-butyl-6-hydrazinouracil—A suspension of 1,3-di-*n*-butyl-6-chlorouracil¹³⁾ (10 g) in 100% hydrazine hydrate (30 ml) and methanol (60 ml) was heated at 70° for 1 hr. The solution was evaporated to a syrup, which was crystallized from MeOH-ether to give colorless crystals (8.5 g, 86%), mp 140–142°. NMR ($CDCl_3$) δ : 3.8 (2H, br. s, $-NHNH_2$), 5.30 (1H, s, H-5), 7.13 (1H, s, $-NHNH_2$). UV λ_{max}^{MeOH} nm: 270. λ_{min}^{MeOH} nm: 238. Anal. Calcd. for $C_{12}H_{22}N_4O_2$ (254.33): C, 56.67; H, 8.72; N, 22.03. Found: C, 56.96; H, 8.76; N, 21.91.

5,7-Diethyl-3-methylaminopyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (IIa) and 5,7-Diethyl-3-methylamino-2-methylthiocarbamoylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (IIIa)—a) A solution of 1,3-diethyl-6-hydrazinouracil (Ia) (4.0 g, 20 mmol) and MeNCS (4.4 ml, 60 mmol) in DMF (40 ml) was heated at 100–110° for 8 hr. The solution was evaporated to dryness and the residue was crystallized from methanol to yield IIa as colorless needles (3.3 g, 70%). The mother liquor was further cooled to give IIIa (0.5 g, 10%) as colorless needles. IIa: UV λ_{max}^{MeOH} nm (log ϵ): 218 (4.34), 245 (sh, 3.82), 274 (3.79). λ_{min}^{MeOH} nm (log ϵ): 261 (3.73). NMR (d_6 -DMSO) δ : 1.09 (6H, m, $>NCH_2CH_3$), 3.43 (3H, d, $-NHCH_3$), 3.84 (4H, m, $>NCH_2CH_3$), 6.31 (1H, m, $-NHCH_3$). IIIa: mp 160–162°. UV λ_{max}^{MeOH} nm (log ϵ): 258 (4.41), 278 (4.38), 324 (3.54). λ_{min}^{MeOH} nm (log ϵ): 232 (3.93), 271 (4.37), 306 (3.50). NMR (d_6 -DMSO) δ : 1.1–1.4 (6H, m, $>NCH_2CH_3$), 3.19 (3H, d, $-CSNHCH_3$), 3.52 (3H, d, $-NHCH_3$), 3.95 (4H, q, $>NCH_2CH_3$), 8.88 (1H, m, $-NHCH_3$), 10.44 (1H, m, $-CSNHCH_3$). Anal. Calcd. for $C_{12}H_{18}N_6O_2S$ (308.34): C, 46.43; H, 5.85; N, 27.08; S, 10.33. Found: C, 46.43; H, 5.75; N, 27.03; S, 10.31.

b) IVa (2.0 g) was heated in DMF (20 ml) at 100–110° for 8 hr and the resulting solution was worked up as described in a) to yield IIa (1.2 g, 53%).

c) A solution of IIa (1.0 g) and MeNCS (1.1 ml) in DMF (10 ml) was heated at 100–110° for 8 hr and worked up as described in a) to yield IIIa (0.1 g, 8%) and IIa (0.8 g, 80%).

d) A solution of Ia (1.0 g, 5 mmol) and MeNCS (0.4 ml, 5.5 mmol) in DMF (10 ml) was heated at 100–110° for 8 hr and worked up as described in a) to give IIa (0.5 g, 44%).

e) IIIa (0.1 g) was heated in DMF (5 ml) at 100–110° for 5 hr and the resulting solution was worked up as described in a) to give IIa (50 mg, 62%).

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- 11) Ring closure of thiosemicarbazide derivatives by heating with litharge has been reported.¹²⁾
- 12) G.W. Miller and F.L. Rose, *J. Chem. Soc.*, **1965**, 3357.
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1,3-Diethyl-6-(4-methylthiosemicarbazido)uracil (IVa)—A solution of Ia (5.0 g, 25 mmol) and MeNCS (5.0 ml, 68 mmol) in DMF (50 ml) was heated at 50–60° for 3 hr. After addition of water (50 ml), the solution was cooled to give crystals, which were recrystallized from aqueous DMF to afford colorless needles (6.2 g, 90%), mp 213–215°. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 245 (4.22), 267 (4.23). $\lambda_{\text{min}}^{\text{MeOH}}$ nm (log ϵ): 225 (3.88), 255 (4.12). NMR (d_6 -DMSO) δ : 1.0–1.4 (6H, m, $\text{>NCH}_2\text{CH}_3$), 2.90 (3H, d, --CSNHCH_3), 3.85–4.10 (4H, m, $\text{>NCH}_2\text{--CH}_3$), 4.67 (1H, s, H-5), 8.20 (1H, q, --CSNHCH_3), 8.90 (1H, s, --NHNHCS--), 9.35 (1H, s, --NHNHCS--). Anal. Calcd. for $\text{C}_{10}\text{H}_{17}\text{N}_5\text{O}_2\text{S}$ (271.34): C, 44.26; H, 6.32; N, 24.76; S, 14.17. Found: C, 44.29; H, 6.37; N, 24.77; S, 14.08.

1,3-Diethyl-6-(4-ethylthiosemicarbazido)uracil (IVb)—A solution of Ia (5.0 g) and ethylisothiocyanate (5.0 ml) in DMF (50 ml) was heated at 50–60° for 3 hr. After addition of water (30 ml), the solution was cooled to give crystals, which were recrystallized from aqueous DMF to afford colorless needles (6.0 g, 88%), mp 200–202°. NMR (d_6 -DMSO) δ : 1.0–1.4 (9H, m, $\text{>NCH}_2\text{CH}_3$), 3.20 (2H, m, $\text{--NHCH}_2\text{CH}_3$), 3.8–4.11 (4H, m, $\text{>NCH}_2\text{CH}_3$), 8.31 (1H, t, --NHCH_2), 8.95 (1H, s, --NHNHCS--), 9.40 (1H, s, --NHNHCS--). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 245, 267. $\lambda_{\text{min}}^{\text{MeOH}}$ nm: 224, 255. Anal. Calcd. for $\text{C}_{11}\text{H}_{19}\text{N}_5\text{O}_2\text{S}$ (285.37): C, 46.29; H, 6.71; N, 24.54; S, 11.24. Found: C, 46.48; H, 6.65; N, 24.31; S, 11.51.

1,3-Diethyl-6-[2,2-bis(methylcarbamoyl)hydrazino]uracil (VI)—A solution of Ia (1.0 g, 5 mmol) and MeNCS (1.0 ml, 14 mmol) in DMF (10 ml) was heated at 110° for 4 hr. The solution was evaporated to dryness and the residual yellow syrup was chromatographed on silica gel (30 g) using chloroform as an eluent to give colorless needles (850 mg, 57%), mp 202–205°. MS m/e : 312 (M^+). NMR (d_6 -DMSO) δ : 1.0–1.4 (6H, m, $\text{>NCH}_2\text{CH}_3$), 2.73 (6H, d, --NHCH_3), 3.8–4.1 (4H, m, $\text{>NCH}_2\text{CH}_3$), 4.61 (1H, s, H-5), 8.10 (2H, m, --NHCH_3), 8.83 (1H, s, --NHN--). Anal. Calcd. for $\text{C}_{12}\text{H}_{20}\text{N}_6\text{O}_4 \cdot \text{H}_2\text{O}$ (330.34): C, 44.85; H, 7.21; N, 26.15. Found: C, 44.43; H, 7.25; N, 25.91.

6-(4-Acetylthiosemicarbazido)-1,3-diethyluracil (IVc)—Acetylisothiocyanate (4.0 g, 40 mmol) was added dropwise to a suspension of Ia (5.0 g, 25 mmol) in dioxane (50 ml) and the mixture was stirred at room temperature for 1 hr. The precipitate formed was collected by filtration and washed with ether to give colorless needles (5.2 g, 70%), mp 202–204°. NMR (d_6 -DMSO) δ : 0.9–1.4 (6H, m, $\text{>NCH}_2\text{CH}_3$), 2.13 (3H, s, --NHCOCH_3), 3.6–4.1 (4H, m, $\text{>NCH}_2\text{CH}_3$), 9.18 (1H, s, --NHNHCS--), 11.5–11.7 (2H, br. s, --NHNHCS-- and --CSNHCO--). Anal. Calcd. for $\text{C}_{11}\text{H}_{17}\text{N}_5\text{O}_3\text{S}$ (299.35): C, 44.13; H, 5.72; N, 23.40. Found: C, 44.31; H, 5.55; N, 23.17.

3-Amino-5,7-dimethylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (IX)—Hydrazine hydrate (80%, 5 ml) was added dropwise to a suspension of 1,3-dimethyl-5-cyano-6-chlorouracil (5.0 g) in ethanol (30 ml) with stirring at room temperature. The precipitates formed were collected by filtration and crystallized from 50% ethanol to give colorless needles (3.0 g, 61%), mp 300°. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 216, 248, 272 (sh). $\lambda_{\text{min}}^{\text{MeOH}}$ nm: 237. NMR (d_6 -DMSO) δ : 3.22 and 3.34 (3H each, s, >NCH_3). Anal. Calcd. for $\text{C}_7\text{H}_9\text{N}_5\text{O}_2$ (195.18): C, 43.07; H, 4.65; N, 35.89. Found: C, 42.69; H, 4.39; N, 36.12.

2-Acetyl-3-ethylamino-5,7-diethylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (VIIb)—A mixture of IIe (1.5 g), acetic anhydride (3.0 ml) and pyridine (10 ml) was stirred at 50–60° for 1 hr. The solution was evaporated to dryness. The resulting syrup was chromatographed on silica gel (30 g) using chloroform as an eluent. The product was crystallized from methanol to give colorless needles (1.2 g, 68%). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 244 (4.32), 262 (4.17), 3.14 (3.67). $\lambda_{\text{min}}^{\text{MeOH}}$ nm (log ϵ): 220 (4.01), 258 (4.16), 287 (3.49). NMR (CDCl_3) δ : 1.0–1.4 (9H, m, $\text{>NCH}_2\text{CH}_3$), 2.54 (3H, s, >NCOCH_3), 3.8–4.2 (6H, m, $\text{>NCH}_2\text{CH}_3$), 8.68 (1H, m, $\text{--NHCH}_2\text{CH}_3$).

2-Acetyl-3-amino-5,7-dimethylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (VIIe)—A mixture of VIII (1.0 g), pyridine (10 ml) and acetic anhydride (3.0 ml) was heated at 100–110° for 2 hr. Water (10 ml) was added and the mixture was cooled to afford colorless crystals (1.0 g, 83%). UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm: 237, 264, 282 (sh). $\lambda_{\text{min}}^{\text{MeOH}}$ nm: 217, 250. NMR (d_6 -DMSO) δ : 2.52 (3H, s, >NCOCH_3), 3.16 and 3.28 (3H each, s, >NCH_3), 7.75 (2H, s, --NH_2).

6-(2-Acetyl-4-ethylthiosemicarbazido)-1,3-diethyluracil (VIII)—A suspension of IVb (1.0 g) in acetic anhydride (10 ml) was heated at 80° for 2 hr with stirring. The solution was evaporated to dryness and the residue was recrystallized from 70% ethanol to give colorless needles (0.8 g, 73%), mp 173–175°. NMR (d_6 -DMSO) δ : 1.0–1.4 (9H, m, $\text{>NCH}_2\text{CH}_3$), 2.25 (3H, s, >NCOCH_3), 3.5–4.1 (6H, m, $\text{--NHCH}_2\text{CH}_3$), 4.69 (1H, s, H-5), 9.59 (1H, s, --NHN--), 10.45 (1H, t, $\text{--NHCH}_2\text{CH}_3$). Anal. Calcd. for $\text{C}_{13}\text{H}_{21}\text{N}_5\text{O}_3\text{S}$ (327.40): C, 47.69; H, 6.46; N, 21.39; S, 9.79. Found: C, 47.58; H, 6.51; N, 21.46; S, 9.61.

Oxidative Cyclization of VIII with N-Chlorosuccinimide—N-Chlorosuccinimide (200 mg, 1.6 mmol) was added in portions to a suspension of VIII (400 mg, 1.2 mmol) in chloroform (10 ml) with stirring. After stirring at room temperature for 1 hr, the mixture was evaporated to dryness and the residue was crystallized from methanol to give colorless needles (245 mg, 65%), mp 137–139° (authentic VIIb, mp 138–139°).

5,7-Diethyl-3-dimethylaminopyrazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (X)—Phosgeneimmonium chloride (4.0 g, 25 mmol) was added to a solution of Ia (4.0 g, 20 mmol) in methylenedichloride (50 ml) and the mixture was stirred at room temperature for 1 hr. The resulting solution was evaporated to dryness to give yellow solids, which were triturated with water, collected by filtration, washed with 1 *N* NH_4OH and crystallized from 30% ethanol to give colorless needles (4.1 g, 82%), mp 203–204°. UV $\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ): 220 (4.29), 253 (3.81), 284 (3.83). $\lambda_{\text{min}}^{\text{MeOH}}$ nm (log ϵ): 244 (3.80), 265 (3.68). MS m/e : 251 (M^+). NMR (CDCl_3)

δ : 1.0—1.4 (6H, m, $\text{>NCH}_2\text{CH}_3$), 3.21 (6H, s, $-\text{NMe}_2$), 3.7—4.1 (4H, m, $\text{>NCH}_2\text{CH}_3$). *Anal.* Calcd. for $\text{C}_{11}\text{H}_{17}\text{N}_5\text{O}_2$ (251.29): C, 52.57; H, 6.82; N, 27.87. Found: C, 52.54; H, 6.84; N, 27.93.

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