New Synthesis of Pyrrolo[3,2-*d*]pyrimidines (9-Deazapurines) by the 1,3-Dipolar Cycloaddition Reaction of Fervenulin 4-Oxides with Acetylenic Esters[1]

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The 1,3-dipolar cycloaddition reaction of fervenulin 4-oxides (6,8-dimethylpyrimido[5,4-*e*]-*as*-triazine-5,7(6*H*,8*H*)-dione 4-oxides) with dimethyl acetylenedicarboxylate and methyl propiolate which enables a new synthetic route to a variety of pyrrolo[3,2-*d*]pyrimidines (9-deazapurines) is described.

Because of the natural occurence of the pyrimido-[5,4-*e*]-*as*-triazine ring system as the triad of antibiotics (fervenulin, 2-methylfervenulone, and toxoflavin)[2] and because of the versatility of heterocyclic *N*-oxides as synthetic intermediates,[3] the pyrimido[5,4-*e*]-*as*-triazine *N*-oxides are of considerable theoretical interest. Although the chemistry of the pyrimido[5,4-*e*]-*as*-triazines has been extensively studied during the last two decades, only little is known about the *N*-oxides probably because of their relative inaccessibility. Of the five possible structural types of pyrimido[5,4-*e*]-*as*-triazine *N*-oxides, we have recently reported that the condensation of 6-hydrazino-1,3-dimethyl-5-nitrosouracil with various one-carbon reagents provides fervenulin 4-oxides [6,8-dimethylpyrimido-[5,4-*e*]-*as*-triazine-5,7(6*H*,8*H*)-dione 4-oxides (**1**)], one of which is particularly useful as an intermediate for the preparation of the antibiotics fervenulin and 2-methylfervenulone.[4]

In order to shed further light on the synthetic versatility of these heterocyclic *N*-oxides, we have been interested in studying their ability to undergo 1,3-dipolar cycloaddition reactions, since the *as*-triazine 4-oxide moiety of **1** is a cyclic nitrone with potential 1,3-dipolar reactivity.[5] The present paper describes the 1,3-dipolar cycloaddition reaction of **1** with dimethyl acetylenedicarboxylate (DMAD) and methyl propiolate which constitutes a new synthetic route to a variety of pyrrolo[3,2-*d*]pyrimidines (9-deazapurines).[6]

Treatment of fervenulin 4-oxide (**1a**) with 1.5 equiv of DMAD in toluene at 95 °C for 3 h resulted in the isolation of 7-(methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**6a**) in 62% yield. The structure of **6a** was tentatively assigned by analytical and spectral (IR, NMR, UV, and mass) data. Particularly, the UV spectrum (see Experimental Section) exhibited a marked analogy with that of the recently reported 7-(methoxycarbonyl)-3-methylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**7**)[6f] [λ_{max} (EtOH) 228 nm (log ϵ 4.45), 267 (3.80)]. In fact, the formation of the pyrrolo[3,2-*d*]pyrimidine ring system was proved by the successful hydrolytic decarboxylation of **6a** with 5 N HCl to the known pyrrolopyrimidine (**8a**).[6d] The structure of **6a** was eventually established by methylation with dimethylformamide dimethyl acetal (DMFDMA) to the 5-methyl derivative (**9a**), which was identical in all respects with the compound obtained by the exhaustive methylation of **7** with the same reagent. Additionally, the hydrolytic decarboxylation of **9a** with 5 N HCl afforded the known pyrrolopyrimidine **10**,[6d] which was alternatively obtained by the reaction of **8a** with DMFDMA.

In analogy with the above result, the reaction of 3-substituted fervenulin 4-oxides (**1b–d**) with DMAD in toluene gave the corresponding 6-substituted pyrrolo-[3,2-*d*]pyrimidines (**6b–d**) in 55–64% yields. Treatment of **6b,c** with DMFDMA yielded **9b,c**, while heating of **6b–d** with 5 N HCl furnished **8b–d**. Among the latter compounds, **8d** was identical with the sample prepared by the nitrene insertion reaction of 1,3-dimethyl-5-nitro-6-styryluracil (**11**) with triethyl phosphite according to Taylor's pyrrolo[3,2-*d*]pyrimidine synthesis.[7]

The reaction of **1a–d** with DMAD leading to **6a–d** can be best explained in terms of the initial formation of the tricyclic isoxazoline **2**. The cleavage of the isoxazoline ring of **2** to the 1,8-dipolar intermediate **3**, followed by the intramolecular cyclization to **4**, and subsequent extrusion of nitrogen would yield the intermediate **5**. The transformation of **5** into the final products **6a–d** probably occurs by liberation of the methoxalyl group as monomethyl oxalate due to water present in the solvent employed (Scheme I).

The participation of water in the conversion of **5** into **6a–d** is supported by the fact that the reaction of **1a** with DMAD in dry toluene under the same conditions afforded a 56% yield of 6-methoxalyl-7-(methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**14**) as the only isolatable product, and none of **6a** could be detected. The structure of **14** was surmised by the presence of an additional *O*-methyl group instead of the pyrrole proton at position 6 observed on **6a** in the NMR spectrum (see Experimental Section) and confirmed by the following reaction sequence. Heating of **14** with 5 N HCl gave the relatively stable α-keto acid **15**, which upon refluxing in dimethylformamide provided a quantitative yield of 6-formyl-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**16**), identical with the compound prepared by the alternative route (vide infra). Addi-

(1) Preliminary report: K. Senga, M. Ichiba, and S. Nishigaki, *Heterocycles*, **9**, 793 (1978).

(2) For a review on the chemistry and biology of pyrimido[5,4-*e*]-*as*-triazines, see D. J. Brown and R. K. Lynn, "Chemistry and Biology of Pteridines", W. Pfleiderer, Ed., Walter de Gruyter, New York, 1975, pp 575–601.

(3) (a) E. Ochiai, "Aromatic Amine Oxides", Elsevier, New York, 1967; (b) A. R. Katritzky and J. M. Lagowski, "Chemistry of Heterocyclic N-Oxides", Academic Press, New York, 1971.

(4) M. Ichiba, S. Nishigaki, and K. Senga, *J. Org. Chem.*, **43**, 469 (1978).

(5) For a review on the 1,3-dipolar cycloaddition reaction of nitrones, see D. St. C. Black, R. F. Crozier, and V. C. Davis, *Synthesis*, 205 (1975).

(6) (a) For a survey of methods for the synthesis of pyrrolo[3,2-*d*]-pyrimidines, see V. Amarnath and R. Madhav, *Synthesis*, 837 (1974); (b) H. Fenner and H. Motschall, *Tetrahedron Lett.*, 4185 (1971); (c) T. Murata and K. Ukawa, *Chem. Pharm. Bull.*, **22**, 240 (1974); (d) S. Senda and K. Hirota, *ibid.*, **22**, 2593 (1974); (e) Y. Okamoto and T. Ueda, *ibid.*, **24**, 547 (1976); (f) Y. Okamoto and T. Ueda, *Tetrahedron Lett.*, 2317 (1976); (g) S. Senda, K. Hirota, and M. Takahashi, *Heterocycles*, **4**, 461 (1976); (h) M. T. Garcia-López, F. G. de las Heras, and M. Stud, *J. Chem. Soc., Perkin Trans. 1*, 483 (1978); (i) R. S. Klein, Mu-ill Lim, S. Y.-K. Tam, and J. J. Fox, *J. Org. Chem.*, **43**, 2536 (1978).

(7) E. C. Taylor and E. E. Garcia, *J. Org. Chem.*, **30**, 655 (1965).

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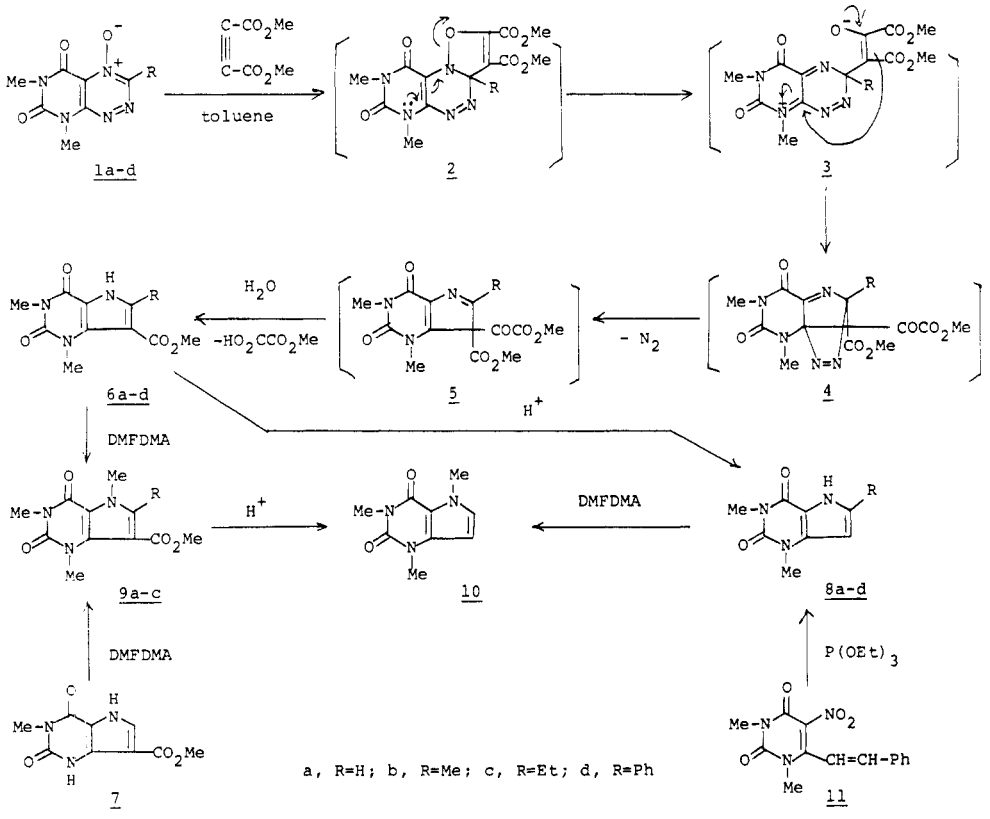
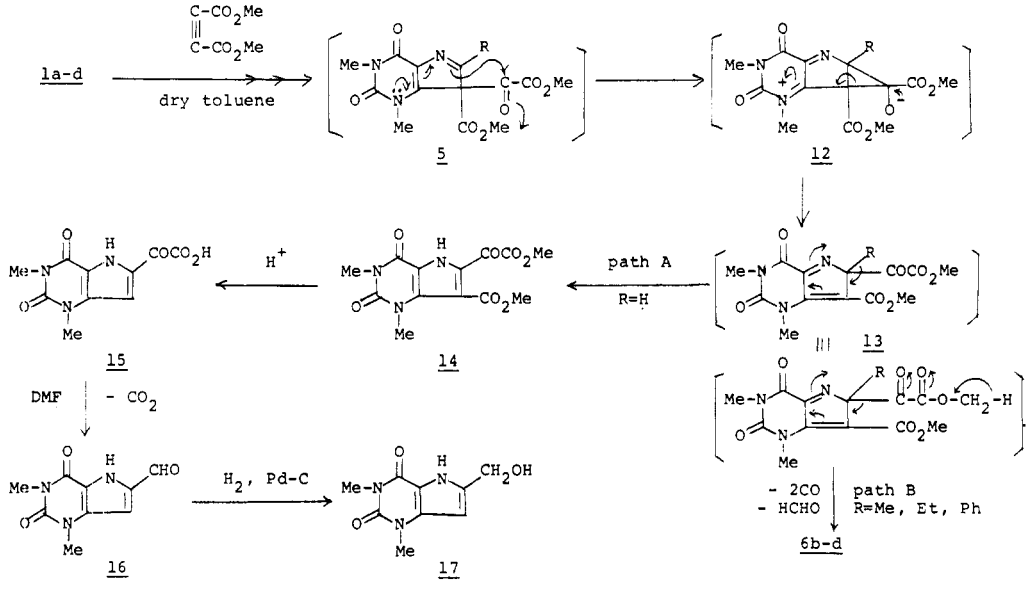
Scheme I



Scheme II



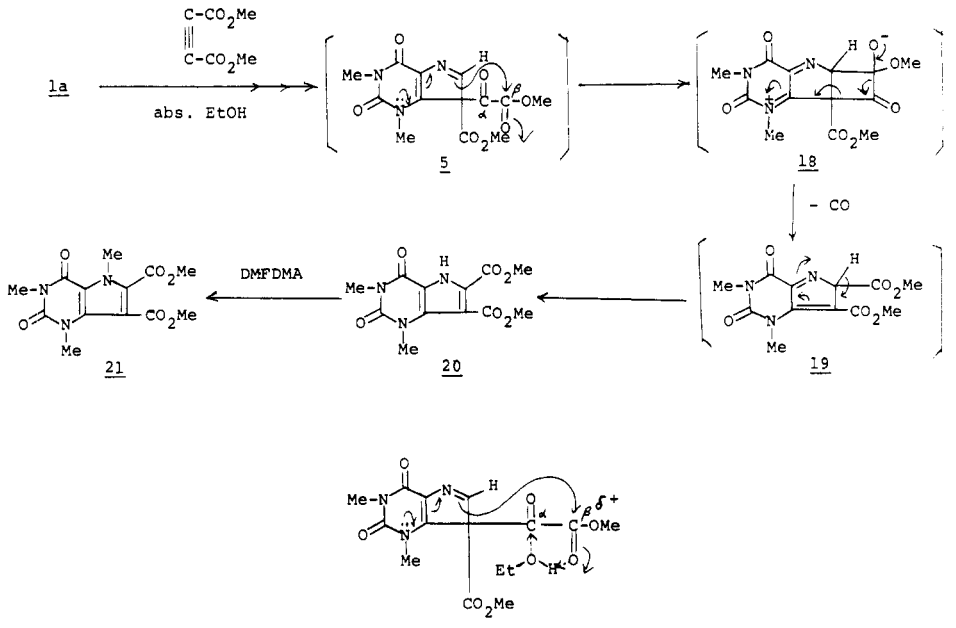
tionally, catalytic hydrogenation of **16** with palladium–charcoal in ethanol afforded the desired 6-(hydroxymethyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**17**). In contrast, the reaction of **1b–d** with DMAD in dry toluene again afforded **6b–d** in 40–80% yields even under carefully controlled anhydrous conditions.

A plausible mechanism for the formation of **14** would involve the 1,2-migration of the methoxalyl group of **5**. Thus an intramolecular nucleophilic attack of the enamine at the most nucleophilic α-carbonyl group of the methoxalyl substituent would yield the tricyclic intermediate **12**. Subsequent cleavage of the cyclopropane ring to **13** followed by the hydrogen transfer by path A would then produce **14**. The mechanism for the 1,2-migration of the methoxalyl group speculated above has close similarity to that proposed for the 1,2-migration of the methoxycarbonyl group in an indole.[8] On the other hand, the formation of **6b–d** would take place by hydrogen transfer of **13** by path B with the concomitant elimination of carbon monoxide and formaldehyde (Scheme II).

It is interesting to note that refluxing of **1a** with DMAD in absolute ethanol for 3 h gave the unexpected 6,7-bis-

(8) R. M. Acheson and J. M. Vernon, *J. Chem. Soc.*, 1907 (1963).

Scheme III



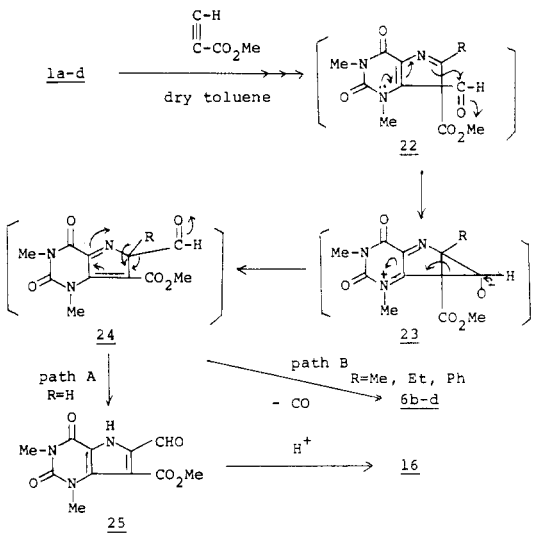
(methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**20**) in 34% yield with a recovery of a 29% yield of **1a**. The characterization of **20** was based on its methylation with DMFDMA to 6,7-bis(methoxycarbonyl)-1,3,5-trimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**21**) (vide infra). The conversion of **1a** into **20** can be rationalized by assuming intramolecular cyclization of **5** to **18**, followed by the cleavage of the cyclobutane ring to **19** by the loss of carbon monoxide and subsequent hydrogen transfer. The regiospecific cyclization of **5** to **18** (not to **12**) could be explained by the participation of the intermediacy of **5'** where the hydrogen bonding would make the β-carbonyl group more electrophilic than the α-carbonyl group. The possibility of the direct decarbonylation of **14** to **20** was excluded since refluxing of **14** in ethanol for a prolonged period resulted in the quantitative recovery of **14** (Scheme III).

The reaction of **1a** with 1.5 equiv of methyl propiolate in dry toluene at 95 °C for 3 h afforded a 53% yield of 6-formyl-7-(methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**25**) as the sole product. The structure of **25** was supported by the presence of a formyl proton in lieu of the pyrrole proton at position 6 observed on **6a** (see Experimental Section) and was established by its conversion into **16** with 5 N HCl. In contrast, the reaction of **1b–d** with methyl propiolate in dry toluene under the same conditions provided the respective **6b–d** in 72–80% yields.

The formation of both **25** and **6b–d** probably proceeds through the intermediacy of **22**, analogous to **5**. Thus the intramolecular nucleophilic attack of the enamine at the formyl carbonyl group would give the tricyclic intermediate **23**. The cleavage of the cyclopropane ring of **23** to **24** followed by the hydrogen transfer by path A would produce **25**, while the hydrogen transfer of **24** accompanying the loss of carbon monoxide by path B would yield **6b–d**. It should be noted that the reaction of **1a–d** with methyl propiolate to give **25** or **6b–d** is not affected by the presence of water (Scheme IV).

The structures of **14** and **25** described above were corroborated by the following results. Heating of **14** with DMFDMA at 95 °C for 5 min gave 6-methoxalyl-7-(methoxycarbonyl)-1,3,5-trimethylpyrrolo[3,2-*d*]pyrimi-

Scheme IV



a, R=H; b, R=Me; c, R=Et; d, R=Ph

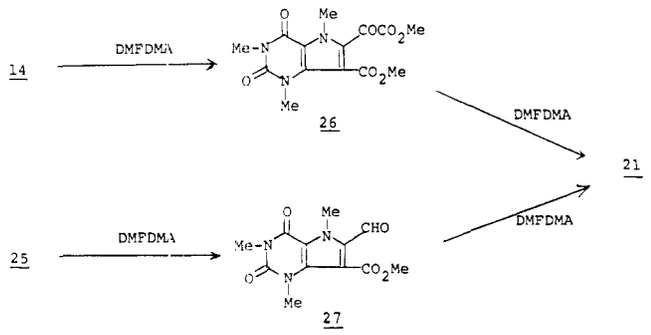
dine-2,4(1*H*,3*H*)-dione (**26**) in 65% yield; however, prolonged heating (8 h) of **14** with DMFDMA gave a 78% yield of **21**, which was identical with the compound prepared by the methylation of **20** with the same reagent. Analogously, the reaction of **25** with DMFDMA (6 h) provided **21** in 84% yield via 6-formyl-7-(methoxycarbonyl)-1,3,5-trimethylpyrrolo[3,2-*d*]pyrimidine (**27**). Although the conversion of both **26** and **27** into **21** seems somewhat analogous to the conversion of *p*-nitrophenyl isocyanate with dimethylformamide diethyl acetal into *N*-ethyl(*p*-nitrophenyl)urethane,[9] the mechanism for the formation of **21** is not yet clear (Scheme V).

Experimental Section

Melting points were taken on a YANACO micro-hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a JASCO IR-E spectrophotometer from samples

(9) H. Bredereck, G. Simchen, and E. Göknel, *Chem. Ber.*, **103**, 236 (1970).

Scheme V



mulled in Nujol. NMR spectra were determined at 60 MHz with a Varian T-60 spectrometer using tetramethylsilane as the internal standard. UV spectra were performed on a Hitachi 124 spectrophotometer in EtOH. The molecular weights for all compounds were correctly analyzed by mass spectroscopy with a JEOL JMS D-300 spectrometer by a direct-inlet system at 70 eV. Elemental analyses (C, H, and N) for all compounds were in agreement with the assigned structures to within ±0.4%. Results of mass spectra and elemental analyses were made available to the editor.

Fervenulin 4-Oxides (6,8-Dimethylpyrimido[5,4-*e*]-*as*-triazine-5,7(6*H*,8*H*)-dione 4-Oxides (1a–d)). Fervenulin 4-oxides **1a–c** were reported previously,[4] and 3-phenylfervenulin 4-oxide (**1d**) was prepared as follows. A mixture of 6-hydrazino-1,3-dimethyl-5-nitrosouracil[10] (0.3 g, 0.0015 mol) and trimethyl orthobenzoate (1 mL) was heated at 95 °C for 1 h. After the mixture was cooled, the precipitates were filtered, washed with EtOH, and recrystallized from dioxane to give **1d** (0.15 g, 38%), mp 229 °C (lit.[11] mp 229 °C).

7-(Methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-diones (6a–d). Method A (for 6a–d). A mixture of the appropriate **1a–d** (0.001 mol) and dimethyl acetylenedicarboxylate (DMAD; 0.213 g, 0.0015 mol) in toluene (2 mL) was heated at 95 °C for 3 h. After the mixture was cooled, the precipitates were filtered, washed with EtOH, and recrystallized from EtOH to give the corresponding **6a–d**.

6a (62%, mp 230–231 °C): IR 1723, 1690, 1630 (CO), 3100 cm^{-1} (NH); NMR (CF_3CO_2D) δ 3.64 (s, 3 H, NCH_3), 4.02 (s, 3 H, NCH_3), 4.03 (s, 3 H, OCH_3), 8.07 (s, 1 H, C^6H); (Me_2SO-d_6) δ 3.24 (s, 3 H, NCH_3), 3.68 (s, 3 H, NCH_3), 3.74 (s, 3 H, OCH_3), 7.73 (d, 1 H, C^6H, $J_{5,6}$ = 4 Hz), 12.83 (br, 1 H, NH, exchangeable with D_2O); UV λ_{max} (log ε) 232 nm (4.54), 273 (3.91).

6b (64%, mp 288–289 °C): IR 1720, 1700, 1645 (CO), 3160 cm^{-1} (NH); NMR (Me_2SO-d_6) δ 2.43 (s, 3 H, CH_3), 3.28 (s, 3 H, NCH_3), 3.54 (s, 3 H, NCH_3), 3.81 (s, 3 H, OCH_3), 12.60 (br, 1 H, NH, exchangeable with D_2O); UV λ_{max} (log ε) 233 nm (4.24), 275 (3.73).

6c (55%, mp 232–233 °C): IR 1720, 1690, 1640 (CO), 3160 cm^{-1} (NH); NMR (Me_2SO-d_6) δ 1.20 (t, 3 H, CH_3, J = 7 Hz), 2.87 (q, 2 H, CH_2, J = 7 Hz), 3.30 (s, 3 H, NCH_3), 3.53 (s, 3 H, NCH_3), 3.83 (s, 3 H, OCH_3), 12.52 (br, 1 H, NH, exchangeable with D_2O); UV λ_{max} (log ε) 234 nm (4.23), 275 (3.60).

6d (64%, mp 283–285 °C): IR 1715, 1670, 1635 (CO), 3140 cm^{-1} (NH); NMR (CF_3CO_2D) δ 3.60 (s, 3 H, NCH_3), 3.70 (s, 3 H, NCH_3), 3.77 (s, 3 H, OCH_3), 7.43–7.83 (m, 5 H, C_6H_5); UV λ_{max} (log ε) 238 nm (4.80), 290 (4.64).

Method B (for 6b–d). A mixture of the appropriate **1b–d** (0.001 mol) and DMAD (0.213 g, 0.0015 mol) in dry toluene (2 mL) was heated at 95 °C for 3 h. The reaction mixture was treated as described above to give the corresponding **6b–d**, identical with the samples prepared by method A, in 80, 40, and 61% yields, respectively.

Method C (for 6b–d). A mixture of the appropriate **1b–d** (0.001 mol) and methyl propiolate (0.126 g, 0.0015 mol) in dry toluene (2 mL) was heated at 95 °C for 3 h. The reaction mixture was treated as described above to give the corresponding **6b–d**, identical with the samples prepared by method A, in 75, 72, and 80% yields, respectively.

1,3-Dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-diones (8a-d). General Procedure. A suspension of the appropriate **6a–d** (0.001 mol) in 5 N HCl (5 mL) was heated at 95 °C for 8 h. The resulting solution was evaporated in vacuo, and the residue was triturated with 28% NH_3. The insoluble solid was filtered, washed well with H_2O, dried, and recrystallized from benzene (for **8a**) or EtOH (for **8b–d**) to give the respective **8a–d**.

8a [67%, mp 210–211 °C (lit.[6d] mp 210 °C)]: IR 1690, 1630 (CO), 3180 cm^{-1} (NH); NMR (Me_2SO-d_6) δ 3.27 (s, 3 H, NCH_3), 3.40 (s, 3 H, NCH_3), 6.15 (d, 1 H, C^7H, J = 2 Hz), 7.23 (d, 1 H, C^6H, J = 2 Hz), 12.00 (br, 1 H, NH, exchangeable with D_2O); UV λ_{max} (log ε) 225 (sh) nm (4.05), 266 (3.97).

8b (52%, mp 276–278 °C): IR 1690, 1635 (CO), 3180 cm^{-1} (NH); NMR (Me_2SO-d_6) δ 2.27 (s, 3 H, CH_3), 3.23 (s, 3 H, NCH_3), 3.33 (s, 3 H, NCH_3), 5.90 (d, 1 H, C^7H, J = 2 Hz), 11.73 (br, 1 H, NH, exchangeable with D_2O); UV λ_{max} (log ε) 220 (sh) nm (3.61), 273 (3.67).

8c (49%, mp 251–252 °C): IR 1690, 1640 (CO), 3160 cm^{-1} (NH); UV λ_{max} (log ε) 230 (sh) nm (4.17), 274 (4.25).

8d (25%, mp >300 °C): IR 1690, 1635 (CO), 3160 cm^{-1} (NH); NMR (Me_2SO-d_6) δ 3.27 (s, 3 H, NCH_3), 3.43 (s, 3 H, NCH_3), 6.70 (s, 1 H, C^7H), 7.33–8.00 (m, 5 H, C_6H_5), 12.33 (br, 1 H, NH, exchangeable with D_2O); UV λ_{max} (log ε) 242 nm (3.50), 310 (3.76).

The compound **8d** was alternatively prepared as follows. A mixture of 1,3,6-trimethyl-5-nitrouracil[12] (1.99 g, 0.01 mol) and benzaldehyde (1.06 g, 0.01 mol) in EtOH (45 mL) containing piperidine (1 mL) was refluxed for 2 h with stirring. After the mixture was cooled, the precipitates were filtered, washed with EtOH, and recrystallized from DMF–EtOH to give 1,3-dimethyl-5-nitro-6-styryluracil (**11**; 2.13 g, 74%), mp 190–192 °C. A suspension of **11** (1.435 g, 0.005 mol) in triethyl phosphite (5 mL) was refluxed at 170 °C for 5 h in a stream of nitrogen. After the mixture was allowed to stand overnight at room temperature, the precipitates were filtered, washed with EtOH, and recrystallized from EtOH to give **8d** (0.23 g, 18%), identical with the compound obtained above.

7-(Methoxycarbonyl)-1,3,5-trimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-diones (9a–c). General Procedure. A mixture of the appropriate **6a–c** (0.0005 mol) and dimethylformamide dimethyl acetal (DMFDMA; 1 mL) was heated at 95 °C for 30 min. The reaction mixture was evaporated in vacuo, and the residue was recrystallized from EtOH to give the corresponding **9a–c**.

9a (85%, mp 201–202 °C): IR 1725, 1700, 1645 cm^{-1} (CO); NMR (CF_3CO_2D) δ 3.47 (s, 3 H, NCH_3), 3.87 (s, 3 H, NCH_3), 3.90 (s, 3 H, OCH_3), 7.70 (s, 1 H, C^6H); UV λ_{max} (log ε) 234 nm (4.23), 272 (3.50).

9b (71%, mp 183–184 °C): IR 1715, 1700, 1650 cm^{-1} (CO); NMR (CF_3CO_2D) δ 2.63 (s, 3 H, CH_3), 3.63 (s, 3 H, NCH_3), 3.79 (s, 3 H, NCH_3), 4.13 (s, 6 H, NCH_3 and OCH_3); UV λ_{max} (log ε) 237 nm (4.34), 275 (3.90).

9c (77%, mp 145–146 °C): IR 1710, 1690, 1640 cm^{-1} (CO); NMR (Me_2SO-d_6) δ 1.12 (t, 3 H, CH_3, J = 7 Hz), 2.83 (q, 2 H, CH_2, J = 7 Hz), 3.21 (s, 3 H, NCH_3), 3.40 (s, 3 H, NCH_3), 3.79 (s, 3 H, NCH_3), 3.92 (s, 3 H, OCH_3); UV λ_{max} (log ε) 237 nm (4.38), 275 (3.74).

The compound **9a** was identical in all respects with the sample obtained by the following reaction. A mixture of 7-(methoxycarbonyl)-3-methylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**7**;[6f] 0.112 g, 0.0005 mol) with DMFDMA (2 mL) was heated at 130 °C for 3 h. The reaction mixture was treated as described above to yield **9a** (0.067 g, 53%).

1,3,5-Trimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (10). Method A. A mixture of **8a** (0.179 g, 0.001 mol) and DMFDMA (1 mL) was refluxed for 2 h. The reaction mixture was evaporated in vacuo, and the residue was recrystallized from MeOH to give **10** (0.1 g, 52%): mp 171–172 °C (lit.[6d] mp 170 °C); IR 1690, 1640 cm^{-1} (CO); UV λ_{max} (log ε) 225 (sh) nm (4.20), 262 (4.26).

Method B. A suspension of **9a** (0.08 g, 0.0032 mol) in 5 N HCl (3 mL) was refluxed for 3 h. The reaction mixture was evaporated in vacuo, and the residue was triturated with 28% NH_3. The insoluble crystals were filtered, washed well with H_2O, dried, and

(10) W. Pfleiderer and K.-H. Schündehütte, *Justus Liebigs Ann. Chem.*, **615**, 42 (1958).
(11) F. Yoneda, T. Nagamatsu, and K. Shinomura, *J. Chem. Soc., Perkin Trans. 1*, 713 (1976).
(12) S. Senda, A. Suzui, M. Honda, and H. Fujimura, *Chem. Pharm. Bull.*, **6**, 482 (1958).

recrystallized from MeOH to give **10** (0.05 g, 83%), identical with the compound prepared by method A.

6-Methoxalyl-7-(methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (14). A mixture of **1a** (0.209 g, 0.001 mol) and DMAD (0.213 g, 0.0015 mol) in dry toluene (2 mL) was heated at 95 °C for 3 h. After the mixture was cooled, the precipitates were filtered, washed with EtOH, and recrystallized from EtOH to give **14** (0.18 g, 56%): mp 233–234 °C; IR 1725, 1710, 1660, 1640 (CO), 3180 cm^{-1} (NH); NMR (CF_3CO_2D) δ 3.63 (s, 3 H, NCH_3), 3.73 (s, 3 H, NCH_3), 4.09 (s, 3 H, OCH_3), 4.12 (s, 3 H, OCH_3); UV λ_{max} (log ϵ) 228 nm (4.27), 255 (3.84), 347 (3.66).

6-Hydroxalyl-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (15). A suspension of **14** (0.323 g, 0.001 mol) in 5 N HCl (10 mL) was heated at 95 °C for 8 h. The resulting solution was neutralized with 28% NH_3. The precipitates were filtered, washed well with H_2O, dried, and recrystallized from EtOH to give **15** (0.14 g, 56%): mp 240 °C dec; IR 1710, 1685, 1640 (CO), 3160 cm^{-1} (NH); UV λ_{max} (log ϵ) 230 nm (3.34), 285 (3.30), 330 (3.06).

6-Formyl-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4-(1*H*,3*H*)-dione (16). Method A. A mixture of **15** (0.025 g, 0.0001 mol) and DMF (1 mL) was refluxed for 3 h. The reaction mixture was evaporated in vacuo, and the residue was recrystallized from EtOH to give **16** (0.02 g, 100%): mp >300 °C; IR 1710, 1680, 1640 (CO), 3120 cm^{-1} (NH); NMR (Me_2SO-d_6) δ 3.27 (s, 3 H, NCH_3), 3.40 (s, 3 H, NCH_3), 6.87 (s, 1 H, C^7H), 9.73 (s, 1 H, CHO); UV λ_{max} (log ϵ) 229 nm (4.36), 278 (4.29), 330 (3.88).

Method B. A suspension of 6-formyl-7-(methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**25**; 0.265 g, 0.001 mol) in 5 N HCl (5 mL) was refluxed for 6 h, and the resulting solution was neutralized with 28% NH_3. The precipitates were filtered, washed with H_2O, dried, and recrystallized from EtOH to give **16** (0.1 g, 49%), identical with the sample prepared by method A.

6-(Hydroxymethyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (17). A solution of **16** (0.207 g, 0.001 mol) in EtOH (30 mL) containing 10% Pd–C (0.2 g) was hydrogenated at room temperature and at atmospheric pressure. Hydrogenation was stopped when the theoretical volume (24 mL) of H_2 gas was consumed. The solution was filtered, and the filtrate was evaporated in vacuo. The residue was recrystallized from EtOH to give **17** (0.038 g, 18%): mp 235–238 °C: IR 1690, 1630 (CO), 3160 cm^{-1} (NH); UV λ_{max} (log ϵ) 220 nm (4.17), 273 (4.10).

6,7-Bis(methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]-pyrimidine-2,4(1*H*,3*H*)-dione (20). A mixture of **1a** (0.209 g, 0.001 mol) and DMAD (0.213 g, 0.0015 mol) in anhydrous EtOH (5 mL) was refluxed for 3 h. After the mixture was cooled, the precipitates were filtered, washed with a small amount of EtOH, and recrystallized from EtOH to give **20** (0.1 g, 34%): mp 248–249 °C; IR 1740, 1720, 1700, 1650 (CO), 3200 cm^{-1} (NH); NMR (CF_3CO_2D) 3.30 (s, 3 H, NCH_3), 3.37 (s, 3 H, NCH_3), 4.13 (s, 3 H, OCH_3), 4.17 (s, 3 H, OCH_3); UV λ_{max} (log ϵ) 230 nm (4.57), 273 (4.28), 307 (4.22).

The filtrate which removed **20** was evaporated in vacuo, and the residue was recrystallized from EtOH to give **1a** (29%).

6,7-Bis(methoxycarbonyl)-1,3,5-trimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (21). Method A. A mixture of **20** (0.03 g, 0.001 mol) and DMFDMA (1 mL) was heated at 95 °C for 5 min. The reaction mixture was evaporated in vacuo, and the residue was recrystallized from MeOH to give **21** (0.022 g, 71%): mp 149–150 °C; IR 1730, 1700, 1650 cm^{-1} (CO); NMR (Me_2SO-d_6) δ 3.26 (s, 3 H, NCH_3), 3.36 (s, 3 H, NCH_3), 3.83 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.17 (s, 3 H, NCH_3); UV λ_{max} (log ϵ) 230 nm (4.51), 275 (4.21), 310 (3.97).

Method B. A mixture of **14** (0.162 g, 0.0005 mol) and DMFDMA (1 mL) was heated at 95 °C for 8 h, and the reaction mixture was treated as described above to give **21** (0.12 g, 78%), identical with the compound obtained by method A.

Method C. A mixture of 6-formyl-7-(methoxycarbonyl)-1,3-dimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (**25**; 0.138 g, 0.0005 mol) and DMFDMA (2 mL) was heated at 95 °C for 6 h, and the reaction mixture was treated as described above to give **21** (0.13 g, 84%), identical with the compound prepared by method A.

6-Formyl-7-(methoxycarbonyl)-1,3-dimethylpyrrolo-[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (25). A mixture of **1a** (0.209 g, 0.001 mol) and methyl propiolate (0.126 g, 0.0015 mol) in dry toluene (2 mL) was heated at 95 °C for 3 h. After the mixture was cooled, the precipitates were filtered, washed with EtOH, and recrystallized from EtOH to give **25** (0.14 g, 53%): mp 249–251 °C; IR 1730, 1710, 1676, 1650 (CO), 3160 cm^{-1} (NH); NMR (CF_3CO_2D) δ 3.61 (s, 3 H, NCH_3), 3.83 (s, 3 H, NCH_3), 4.55 (s, 3 H, OCH_3), 10.20 (s, 1 H, CHO); UV λ_{max} (log ϵ) 230 nm (4.10), 277 (3.65), 335 (3.35).

6-Methoxalyl-7-(methoxycarbonyl)-1,3,5-trimethylpyrrolo[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (26). A mixture of **14** (0.162 g, 0.0005 mol) and DMFDMA (0.2 mL) was heated at 95 °C for 5 min. After the mixture was cooled, the precipitates were filtered, washed with a small amount of methanol, and recrystallized from MeOH to give **26** (0.11 g, 65%): mp 155–156 °C; IR 1740, 1710, 1680, 1655 cm^{-1} (CO); NMR (Me_2SO-d_6) δ 3.21 (s, 3 H, NCH_3), 3.46 (s, 3 H, NCH_3), 3.63 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 4.00 (s, 3 H, NCH_3); UV λ_{max} (log ϵ) 230 nm (4.43), 255 (3.97), 295 (3.83), 350 (3.43).

6-Formyl-7-(methoxycarbonyl)-1,3,5-trimethylpyrrolo-[3,2-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (27). A mixture of **25** (0.133 g, 0.0005 mol) and DMFDMA (0.5 mL) was heated at 95 °C for 5 min. The reaction mixture was evaporated in vacuo, and the residue was recrystallized from EtOH to give **27** (0.08 g, 56%): mp 166–167 °C; IR 1710, 1675 cm^{-1} (CO); NMR (CF_3CO_2D) δ 3.56 (s, 3 H, NCH_3), 3.69 (s, 3 H, NCH_3), 4.13 (s, 3 H, OCH_3), 4.38 (s, 3 H, NCH_3), 8.65 (s, 1 H, CHO); UV λ_{max} (log ϵ) 235 nm (4.14), 283 (3.68), 335 (3.10).

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