Pyrimidine Derivatives and Related Compounds. 31.[1] A New Photochemical Transformation of 6-Azido-1,3-dimethyluracil to 6-Alkylamino-5-amino-1,3-dimethyluracils and Its Application to One-Step Synthesis of Lumazines and Fervenulins[2]

Shigeo Senda,* Kosaku Hirota, Tetsuji Asao, and Kazuo Maruhashi

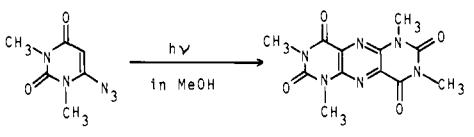
Contribution from Gifu College of Pharmacy, Mitahora-Higashi, Gifu 502, Japan.
Received April 4, 1978

Abstract: Irradiation of 6-azido-1,3-dimethyluracil (**1**) in the presence of primary or secondary alkylamines in THF gave 6-alkylamino-5-amino-1,3-dimethyluracils (**3**) in which the amines employed were introduced regiospecifically to the 6 position of uracils via a nitrene intermediate. This type of photochemical transformation was applied to a one-step synthesis of biologically interesting fused pyrimidines such as lumazines and fervenulins. Thus, irradiation of **1** in the presence of α-amino acid ethyl esters, α-amino ketones, acylhydrazines, or β-alanine ethyl ester gave 7-substituted 7,8-dihydrolumazines (**16**), 6-substituted 7,8-dihydrolumazines (**17**), fervenulins (7-azalumazines) (**20**), or pyrimido[4,5-*b*][5,9]diazepine (**18**), respectively.

Because of their biological importance, many investigators have directed their effort toward the synthesis of fused pyrimidines such as purines, pteridines, and flavines.[3] Since Traube synthesized guanine for the first time from 2,5,6-triaminopyrimidine-4(3*H*)-one and formic acid,[4] 5,6-diaminopyrimidine has been recognized to be the most important and useful key intermediate for preparing fused pyrimidines.

Such 5,6-diaminopyrimidines are generally synthesized stepwise from 6-aminopyrimidines by nitration or nitrosation followed by reduction[5] or by a Michael-type addition of diethyl azodicarboxylate.[6] A more convenient method overcoming such complicated procedures has not been reported yet. In fact, a simple and novel way to introduce a nitrogen source into the 5 and 6 positions of pyrimidines has long been desired.

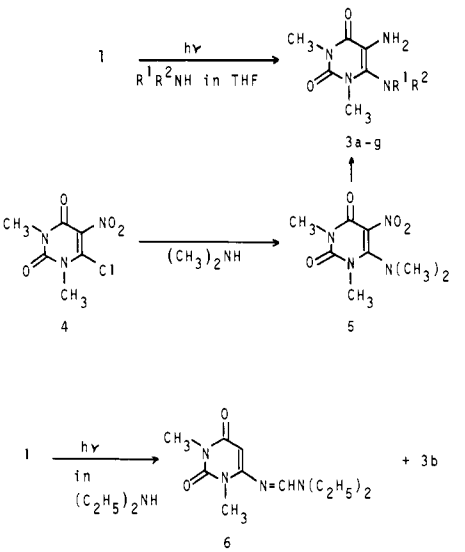
Incidentally, 6-azidopyrimidines are regarded as masked 6-aminopyrimidines and are expected as potential intermediates for preparation of fused pyrimidines, because the azido group possesses all the necessary properties as a starting group in organic synthesis;[7] for instance, aryl azides display a variety of thermochemical and photochemical reactivities.[8] However, only a few works concerning the chemistry of 6-azidopyrimidines have appeared in the literature[9] and, with reference to the photochemistry, quite a lot of attention has been paid. So far as we know, only Pfleiderer et al. reported the photolysis of 6-azido-1,3-dimethyluracil (**1**) in methanol giving 1,3,5,7-tetramethylpyrimido[4,5-*g*]pteridine-2,4,6,8(1*H*,3*H*,5*H*,7*H*)-tetrone (**2**) via a nitrene intermediate.[10]



1 **2**

From this viewpoint, we have investigated the photochemistry of **1** in the presence of various nucleophiles. This paper reports a new type of procedure to introduce a nitrogen source into both the 5 and 6 position of uracils by the photolysis of **1** with primary or secondary alkylamines. This paper also describes a one-step synthesis of biologically interesting fused pyrimidines such as lumazines and fervenulins by the reaction of **1** with amino acid esters, α-amino ketones, or acylhydrazines in place of alkylamines.

Scheme I



Results and Discussion

A solution of 6-azido-1,3-dimethyluracil (**1**) and dimethylamine in tetrahydrofuran (THF) was irradiated with a 100-W high-pressure mercury arc lamp through a Pyrex filter under nitrogen. After evaporation of the solvent, trituration of the residue with ether gave 5-amino-6-dimethylamino-1,3-dimethyluracil (**3a**) in 59% yield. Identification of the structure **3a** was established by an alternate synthesis of this compound from 6-chloro-1,3-dimethyl-5-nitrouracil (**4**). Thus, 6-dimethylamino-1,3-dimethyl-5-nitrouracil (**5**), prepared by condensation of **4** and dimethylamine, was converted to **3a** by catalytic hydrogenation (Scheme I). Similar photolysis of **1** with other primary or secondary alkylamines in THF gave the corresponding 6-alkylamino-5-amino-1,3-dimethyluracils (**3b–g**) in which the amines employed were introduced to the 6 positions (Table I). However, photolysis of **1** in the presence of arylamines such as aniline and *N*-methylaniline did not give the desired 5-amino-6-arylaminouracils.

In the course of the studies described above, we noticed that the formation of **3** was considerably affected by the solvents used. When irradiation was carried out in acetonitrile in place of THF, the yield of **3** was low and many byproducts were detected on TLC. Similar treatment of **1** in benzene, acetone,

0002-7863/78/1500-7661$01.00/0

Table I. Photochemical Formation of 6-Alkylamino-5-amino-1,3-dimethyluracils (3)

product	R^1	R^2	mp, °C[b]	yield, %	formula	anal.[c]
3a	CH_3	CH_3	142–143	59	$C_8H_{14}O_2N_4$	C, H, N
3b[a]	C_2H_5	C_2H_5	164–165	60	$C_{16}H_{21}O_9N_7$	C, H, N
3c	$(CH_2)_5$		128–130	64	$C_{11}H_{18}O_2N_4$	C, H, N
3d	$(CH_2)_2O(CH_2)_2$		220–221	83	$C_{10}H_{16}O_3N_4$	C, H, N
3e[a]	CH_3	H	189–190	42	$C_{13}H_{15}O_9N_7$	C, H, N
3f[a]	C_2H_5	H	245–246	30	$C_{14}H_{17}O_9N_7$	C, H, N
3g	i-C_3H_7	H	121–122.5	27	$C_9H_{16}O_2N_4$	C, H, N

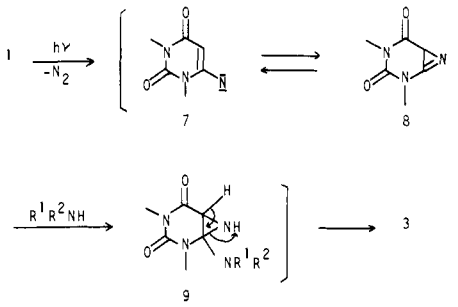
[a] Isolated as picrate. [b] Solvent of recrystallization: **3a**, ligroin: **3b,d,e,f**, MeOH; **3c,g**, EtOH. [c] Analyses were within 0.3% of theory.

Table II. Photochemical Formation of Lumazines (16)

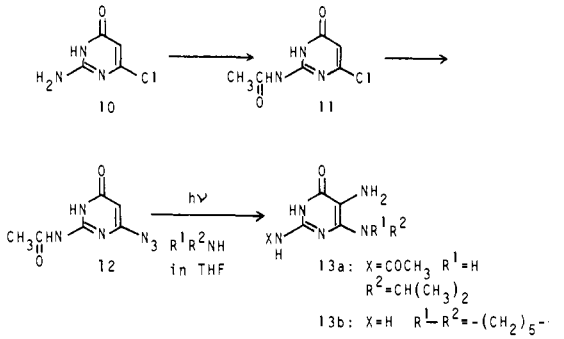
product	R	mp, °C[a]	NMR,[b] ppm	yield, %	formula	anal.[c]
16a	H	285	4.60 (2 H, s, 7-CH_2)	69	$C_8H_{10}O_3N_4$	C, H, N
16b	CH_3	270	4.78 (1 H, m, C7 H)	76	$C_9H_{12}O_3N_4$	C, H, N
16c	$C_6H_5CH_2$	223–225	4.25 (1 H, m, C7 H)	55	$C_{15}H_{16}O_3N_4 \cdot H_2O$	C, H, N
16d	$CH_3S(CH_2)_2$	197–200	4.75 (1 H, m, C7 H)	61	$C_{11}H_{16}O_3N_4S$	C, H, N

[a] Solvent of recrystallization: **16a,c**, H_2O; **16b,d**, MeOH. [b] Solvent: **16a,b,d**, CF_3CO_2H; **16c**, Me_2SO-d_6. [c] Analyses were within 0.3% of theory.

Scheme II



Scheme III



or methanol in the presence of alkylamines did not afford the expected 6-alkylamino-5-aminouracils. Photolysis of **1** in alkylamines without solvent (THF) caused a side reaction giving an unexpected product. Thus, **1** was irradiated in diethylamine under nitrogen to afford 6-(*N,N*-diethylaminomethylene)amino-1,3-dimethyluracil (**6**, 13%) together with **3b** (70%) (Scheme I). The formation of **6** can be explained by the mechanism proposed by Tišler et al.[11] On the other hand, thermolysis of **1** with amines in a variety of solvents did not give the expected 5,6-diaminouracils.[12] It indicates that the formation of **3** requires photochemical activation.

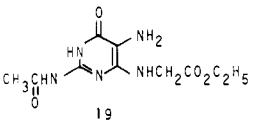
A plausible mechanism for the formation of **3** is presented in Scheme II. Photochemically induced loss of nitrogen from **1** gives a nitrene (**7**), which is in equilibrium with an azirine intermediate (**8**) as discussed previously.[13] Nucleophilic addition of the alkylamine to **8** affords an aziridine intermediate (**9**) which is followed by electrocyclic ring cleavage to give the product (**3**).

We have also tried photolysis of 2-acetamido-6-azidopyrimidin-4(3*H*)-one (**12**), prepared from 2-amino-6-chloropyrimidin-4(3*H*)-one (**10**) in two steps (Scheme III), with isopropylamine to afford 2-acetamido-5-amino-6-isopropylaminopyrimidin-4(3*H*)-one (**13a**). The irradiation of **12** with piperidine gave a deacetylation product, 2,5-diamino-6-piperidinopyrimidine-4(3*H*)-one (**13b**).

After having established a new type of photochemical transformation of **1** in the presence of alkylamines giving 5,6-diaminouracils, we turned our attention to the application of this method to the synthesis of fused pyrimidines. Photolysis of **1** and *N*-methylglycine ethyl ester gave 7,8-dihydro-1,3,8-trimethyllumazin-6(5*H*)-one (**14**) in 73% yield. The structure of **14** was determined from the spectral data and the ultimate proof was provided by a comparison of authentic **14** prepared by another route. Thus, **4** was treated with *N*-methylglycine ethyl ester and the resulting 6-(*N*-ethoxycarbonylmethyl-*N*-methyl)amino-1,3-dimethyl-5-nitrouracil (**15**) was subjected to a reductive ring closure to give lumazine **14** which was found to be identical with the product obtained above (Scheme IV).

The photolysis of **1** and various α-amino acid ethyl esters gave the corresponding 7-substituted lumazines (**16a–d**) in a single step and, furthermore, in good yields (Table II). Additionally, 6-substituted lumazines (**17a,b**) were prepared from **1** and α-aminoketones. Upon using β-alanine ethyl ester, the product was 7,8-dihydro-1,3-dimethyl-9*H*-pyrimido[4,5-*b*]-5,9-diazepine-2,4,6(1*H*,3*H*,5*H*)-trione (**18**) (Scheme V).

For the further application of the one-step synthesis to pterins, we applied this method to azidopyrimidine **12**. Thus, irradiation of **12** with glycine ethyl ester did not give the expected pterin, but 2-acetamido-5-amino-6-(*N*-ethoxycarbonylmethyl)aminopyrimidin-4(3*H*)-one (**19**) was obtained



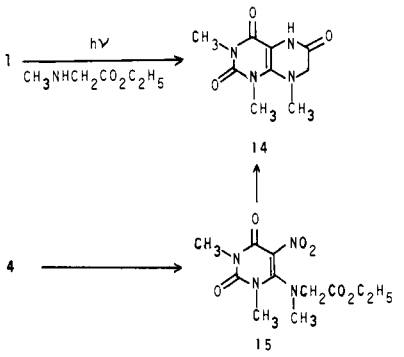
in quantitative yield. All attempts to convert **19** into pterin were unsuccessful.[14]

This type of photochemical conversion of azidopyrimidines is not only useful for preparation of lumazines **16** and **17** and their analogue **18** as described above, but also widely applicable as a general method for synthesis of 7-azalumazines (fervenulins). Thus, a solution of **1** and various acylhydrazines such as formylhydrazine, acetylhydrazine, benzoylhydrazine, phenylacetylhydrazine, and isonicotinoylhydrazine in THF was irradiated with aeration to afford antibiotic fervenulin

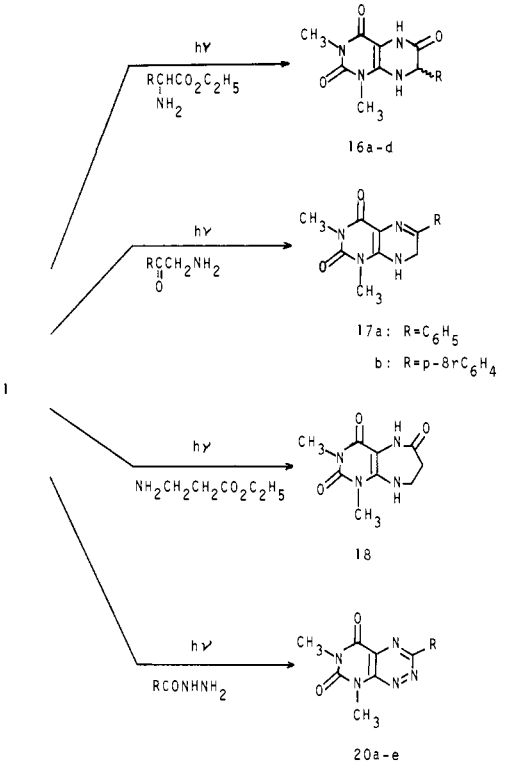
Table III. Photochemical Formation of Fervenulins (**20**)

product	R	yield, %
20a	H	55
20b	CH_3	68
20c	C_6H_5	81
20d	$C_6H_5CH_2$	72
20e	4-pyridyl	60

Scheme IV



Scheme V



(**20a**)[15] and its 3-substituted derivatives (**20b–e**)[16] (Scheme V, Table III). This reaction involves an oxidation process.[17] Further application of new synthetic routes to other heterocycles, i.e., purines, azapurines, and flavines, employing the 6-azidouracils is under study.

Experimental Section

All melting points were determined on a Yanagimoto micro melting point apparatus and were uncorrected. Elemental analyses were carried out at the Microanalytical Laboratory of our college. Proton magnetic resonance spectra (60 MHz) were recorded on a Hitachi Perkin-Elmer R-20B spectrometer, with tetramethylsilane (Me_4Si) as internal reference. Chemical shifts are reported in parts per million (δ) and signals are quoted as s (singlet), d (doublet), t (triplet), q (quartet), or m (multiplet); and J values are first order. Infrared spectra were taken on a Hitachi 215 instrument as KBr pellets. Ultraviolet spectra were obtained from a diluted ethanol solution on a Hitachi 323 spectrophotometer. Irradiation was carried out at 25–30 °C in a flask equipped with a Pyrex-jacketed immersion lamp until the spot of **1** on TLC completely disappeared. The light source was a Riko-UVL 100-W high-pressure mercury arc lamp. Prior to irradiation, the solution was flushed with nitrogen and nitrogen was bubbled through the solution at a constant rate during irradiation unless specified otherwise. Column chromatography was carried out in silica gel (Wakogel C-200) using chloroform as eluent. TLC was performed on plastic sheets coated with silica gel (Merck 60 F 254).

6-Azido-1,3-dimethyluracil (1). The method of Pfleiderer et al.[18] was used with slight modification. A solution of 10 g (0.057 mol) of 6-chloro-1,3-dimethyluracil and 5.6 g (0.086 mol) of sodium azide in 100 mL of ethanol was refluxed for 1 h. Ethanol was removed by evaporation and the residue was washed with water. The separated crystals were recrystallized from methanol to give 9 g (87%) of **1** as pale yellow plates, mp 148 °C (lit.[18] mp 149–151 °C).

Photochemical Formation of 6-Alkylamino-5-amino-1,3-dimethyluracils (3a–g). A solution of 0.5 g (0.0028 mol) of **1** and 0.0084 mol of alkylamine in 250 mL of THF was irradiated for 3 h. After evaporation of the solvent, the residue was treated with ether to give the corresponding 6-alkylamino-5-aminouracils (**3a,c,d,g**). When the oily residue was not solidified, then it was dissolved in 5 mL of absolute ether and 5 mL of ether saturated with picric acid was added. The resulting precipitate was collected by filtration and recrystallized to give the picrate (**3b,e,f**) as yellow prisms (Table I).

5-Amino-6-dimethylamino-1,3-dimethyluracil (3a). A suspension of 0.5 g (0.002 mol) of 6-dimethylamino-1,3-dimethyl-5-nitrouracil (**5**) in methanol (200 mL) containing 5% palladium/carbon (0.2 g) was hydrogenated at 20 °C under 30 atm for 3 h. The reaction mixture was filtered and the filtrate was concentrated and allowed to stand overnight to give 0.18 g (45%) of **3a** which was identical in all respects with the product obtained by the photochemical formation: mp 142–143 °C; NMR ($CDCl_3$) δ 2.28 (6 H, s, $N(CH_3)_2$), 3.38 and 3.40 (each 3 H, each s, each NCH_3), 3.50 (2 H, s, NH_2, deuterium exchangeable); IR (KBr) 3340 and 3420 cm^{-1} (NH_2).

6-Dimethylamino-1,3-dimethyl-5-nitrouracil (5). To a solution of 2 g (0.009 mol) of 6-chloro-1,3-dimethyl-5-nitrouracil (**4**)[19] in 20 mL of chloroform was added dropwise, over a period of 10 min, 1.6 g (0.018 mol) of 50% aqueous dimethylamine. The reaction mixture was stirred for an additional 1 h at room temperature and then evaporated to dryness. The residue was triturated with ether, and the separated crystals were collected by filtration and recrystallized from methanol to give 1.6 g (80%) of **5** as yellow prisms: mp 206–207 °C; NMR ($CDCl_3$) δ 2.90 (6 H, s, $N(CH_3)_2$). Anal. ($C_8H_{12}O_4N_4$) C, H, N.

Photolysis of 1 in Diethylamine. A solution of 1 g (0.0056 mol) of **1** in 250 mL of diethylamine[20] was irradiated for 5 h. After removal of the solvent under reduced pressure, the residue was subjected to silica gel column chromatography. Elution with chloroform gave 0.88 g (70%) of 5-amino-6-diethylamino-1,3-dimethyluracil (**3b**) which was identical with an authentic sample obtained by the photolysis in THF. Successive elution with the same solvent gave 0.17 g (13%) of 6-(*N,N*-diethylaminomethylene)amino-1,3-dimethyluracil (**6**). Recrystallization from ligroin gave colorless needles of **6**: mp 141–142 °C; NMR ($CDCl_3$) δ 1.22 and 1.28 (each t, each CH_2CH_3, each J = 7 Hz), 3.55 and 3.43 (each 3 H, each s, each NCH_3), 3.46 and 3.48 (each 2 H, each q, each CH_2CH_3, each J = 7 Hz), 5.08 (1 H, s, C5 H), 7.75 (1 H, s, CH=N). Anal. ($C_{11}H_{18}O_2N_4$) C, H, N.

2-Acetamido-6-chloropyrimidin-4(3*H*)-one (11). A solution of 10 g (0.069 mol) of 2-amino-6-chloropyrimidin-4(3*H*)-one (**10**)[21] and 100 mL of acetic anhydride was refluxed for 4 h. After evaporation of the solvent, the residue was treated with water and allowed to stand overnight. The resulting precipitate was washed with water and recrystallized from water to give 8.6 g (66%) of **11** as pale yellow plates: mp 225–227°C; NMR (Me_2SO-d_6) δ 2.19 (3 H, s, CH_3), 5.48 (1 H, s, C5H). Anal. ($C_6H_6O_2N_3Cl$) C, H, N.

2-Acetamido-6-azidopyrimidin-4(3H)-one (12). A solution of 5 g of **11** (0.027 mol) and 2 g (0.03 mol) of sodium azide in 20 mL of dimethylformamide was warmed at 80 °C for 2 h. After evaporation of the solvent, the resulting precipitate was washed with water and recrystallized from water to give 4 g (77%) of **12**: mp 163–165 °C; NMR (Me_2SO-d_6) δ 2.18 (3 H, s, CH_3), 6.11 (1 H, s, C5H); IR (KBr) 2120 cm^{-1} (N_3). Anal. ($C_6H_6O_2N_6$) C, H, N.

2-Acetamido-5-amino-6-isopropylaminopyrimidin-4(3*H*)-one (13a). A solution of 0.5 g (0.0025 mol) of **12** and 0.456 g (0.0077 mol) of isopropylamine in 250 mL of THF was irradiated for 3 h. After

evaporation of the solvent, the residue was treated with ethanol and recrystallized from methanol to give 0.42 g (72%) of **13a** as yellow prisms: mp 235 °C; NMR (CF_3CO_2H) δ 1.58 (6 H, d, $CH(CH_3)_2$, J = 7 Hz), 2.67 (3 H, s, $COCH_3$), 4.80 (1 H, m, $CH(CH_3)_2$), 4.94 (2 H, br s, NH_2). Anal. ($C_9H_{16}O_2N_5$) C, H, N.

2,5-Diamino-6-piperidinopyrimidin-4(3*H*)-one (13b). A solution of 0.5 g (0.0025 mol) of **12** and 0.63 g (0.0075 mol) of piperidine in 250 mL of THF was irradiated for 5 h. After evaporation of the solvent, the residue was treated with ethanol and recrystallized from methanol to give 0.48 g (75%) of **13b** as a colorless powder, mp 241–245 °C. Anal. ($C_9H_{15}ON_5$) C, H, N.

7,8-Dihydro-1,3,8-trimethyllumazin-6(5*H*)-one (14). A. A solution of 0.5 g (0.0028 mol) of **1** and 0.66 g (0.0056 mol) of *N*-methylglycine ethyl ester in 250 mL of THF was irradiated for 3 h. After evaporation of THF under reduced pressure, the residue was treated with ether. The resulting precipitate was collected by filtration and recrystallized from methanol to give 0.46 g (73%) of **14** as colorless needles: mp 240–241 °C; UV λ_{max} (EtOH) 245 nm (log ϵ 6.1), 262 (5.9, sh), 313 (5.9); NMR ($CDCl_3$) δ 2.90, 3.44, and 3.48 (each 3 H, each s, each NCH_3), 3.78 (2 H, s, $COCH_2N$), 8.49 (1 H, br s, NH, deuterium exchangeable). Anal. ($C_9H_{12}O_3N_4$) C, H, N.

B. A suspension of 0.5 g (0.0017 mol) of 6-(*N*-ethoxycarbonyl-*N*-methyl)amino-1,3-dimethyl-5-nitrouracil (**15**) in 200 mL of methanol containing 5% palladium/carbon (0.15 g) was hydrogenated at 20 °C under 30 atm for 3 h. The reaction mixture was filtered and the filtrate was concentrated and allowed to stand overnight. The resulting precipitate was filtered and recrystallized from methanol to give 0.15 g (42%) of **14** which was identical in all respects with the product obtained by procedure A.

6-(*N*-Ethoxycarbonylmethyl-*N*-methyl)amino-1,3-dimethyl-5-nitrouracil (15). To a solution of 3 g (0.0137 mol) of 6-chloro-1,3-dimethyl-5-nitrouracil (**4**) in 10 mL of chloroform was added dropwise, over a period of 10 min, 3.2 g (0.0274 mol) of *N*-methylglycine ethyl ester. The reaction mixture was stirred for an additional 1 h at room temperature, and then evaporated to dryness. The residue was triturated with acetone, and the separated crystals were collected by filtration and recrystallized from ligroin to give 0.6 g (15%) of **15** as yellow prisms: mp 105–106 °C; NMR ($CDCl_3$) δ 1.30 (3 H, t, OCH_2CH_3, J = 7 Hz), 2.98, 3.40, and 3.60 (each 3 H, each s, each NCH_3), 3.75 (2 H, s, NCH_2CO), 4.28 (2 H, q, OCH_2CH_3, J = 7 Hz). Anal. ($C_{11}H_{16}O_6N_4$) C, H, N.

7-Substituted 1,3-Dimethyl-7,8-dihydrolumazin-6(5*H*)-one (16a–e). A solution of 0.5 g (0.0028 mol) of **1** and 0.0056 mol of amino acid ethyl esters in 250 mL of THF was irradiated for 3 h. After evaporation of THF, the residue was treated with ether to give the corresponding 7-substituted 7,8-dihydrolumazines (**16a–e**) (Table II).

1,3-Dimethyl-6-phenyl-7,8-dihydrolumazine (17a). To a stirred suspension of 0.96 g (0.056 mol) of phenacylamine hydrochloride in 250 mL of THF was added dropwise, over a period of 5 min, 0.57 g (0.056 mol) of triethylamine. The reaction mixture was stirred for an additional 30 min at room temperature and then the resulting triethylamine hydrochloride was filtered off. To the filtrate was added 0.5 g (0.0028 mol) of **1** and the mixture was irradiated for 3 h. THF was removed and the residue was triturated with ethanol. The resulting crystals were collected by filtration and recrystallized from water to give 0.54 g (75%) of **17a** as yellow prisms: mp 255–257 °C; NMR (CF_3CO_2H) δ 3.53 and 3.65 (each 3 H, each s, each NCH_3), 5.34 (2 H, s, 7-CH_2); IR (KBr) 3330 cm^{-1} (NH). Anal. ($C_{14}H_{14}O_2N_4$) C, H, N.

6-(*p*-Bromophenyl)-1,3-dimethyl-7,8-dihydrolumazine (17b). To a solution of 1.2 g (0.0056 mol) of *p*-bromophenacylamine (prepared from *p*-bromophenacylamine hydrochloride as described above) in 250 mL of THF was added 0.5 g (0.0028 mol) of **1** and the mixture was irradiated for 3 h. After evaporation of THF in vacuo, the residue was treated with ethanol and recrystallized from water to give 0.68 g (70%) of **17b** as yellow prisms: mp 260–262 °C; NMR (CF_3CO_2H) δ 3.08 and 3.18 (each 3 H, each s, each NCH_3), 4.84 (2 H, s, 7-CH_2). Anal. ($C_{14}H_{13}O_2N_4Br \cdot \frac{1}{2}H_2O$) C, H, N.

1,3-Dimethyl-7,8-dihydro-9*H*-pyrimido[4,5-*b*][5,9]diazepine-2,4,6(1*H*,3*H*,5*H*)-trione (18). A solution of 0.5 g (0.0028 mol) of **1** and 0.66 g (0.0056 mol) of β-alanine ethyl ester in 250 mL of THF was irradiated for 3 h. THF was removed by evaporation under reduced pressure. The residue was poured into 10 mL of water and the mixture was allowed to stand overnight. The resulting precipitate was filtered off and the filtrate was concentrated. The resulting precipitate was collected by filtration and recrystallized from water to give 0.37 g (59%) of **18** as a colorless powder: mp 200–201 °C; UV λ_{max} (EtOH) 267 nm (log ϵ 4.9), 297 (5.0); NMR (Me_2SO-d_6) δ 2.60 (2 H, m, $COCH_2$), 3.15 and 3.31 (each 3 H, each s, each NCH_3), 3.50 (2 H, m, $NHCH_2$), 6.90 and 7.40 (each 1 H, each broad, each NH, deuterium exchangeable). Anal. ($C_9H_{12}O_3N_4$) C, H, N.

2-Acetamido-5-amino-6-(*N*-ethoxycarbonylmethyl)aminopyrimidin-4(3*H*)-one (19). A mixture of 0.5 g (0.0026 mol) of **12** and 0.8 g (0.0078 mol) of glycine ethyl ester in 250 mL of THF was irradiated for 5 h. The resulting precipitate was collected by filtration and recrystallized from water to give 0.63 g (90%) of **19** as a pale yellow powder: mp 213–214 °C; NMR (Me_2SO-d_6) δ 1.20 (3 H, t, CH_2CH_3, J = 7 Hz), 2.11 (3 H, s, $COCH_3$), 3.80 (2 H, s, CH_2NH), 4.15 (2 H, q, CH_2CH_3, J = 7 Hz), 8.40 and 9.02 (each 1 H, each broad, each NH, deuterium exchangeable). Anal. ($C_{10}H_{15}O_4N_5$) C, H, N.

Photochemical Formation of 3-Substituted Fervenulins (20a–e). A solution of 0.5 g (0.0028 mol) of **1** and 0.0056 mol of acylhydrazine in 250 mL of THF was irradiated for 3 h with aeration. After evaporation of the solvent, the residue was subjected to column chromatography (silica gel–chloroform) to afford the corresponding 3-substituted fervenulins (**20a–e**) (Table III).

Supplementary Material Available: Complete analytical data for all new compounds (2 pages). Ordering information is given on any current masthead page.

References and Notes

(1) For part 30, see S. Senda, K. Hirota, and T. Asao, *Chem. Pharm. Bull.*, in press.
(2) Preliminary reports of some of this work have been published: (a) S. Senda, K. Hirota, M. Suzuki, T. Asao, and K. Maruhashi, *J. Chem. Soc., Chem. Commun.*, 731 (1976); (b) S. Senda, K. Hirota, T. Asao, and K. Maruhashi, *J. Am. Chem. Soc.*, **99**, 7358 (1977).
(3) (a) R. K. Robins, "Heterocyclic Compounds", Vol. 8, R. C. Elderfield, Ed., Wiley, New York, N.Y., 1967, pp 162–442; (b) J. H. Lister in "The Chemistry of Heterocyclic Compounds", Vol. XXIV, "Fused Pyrimidines", Part II, "Purines", D. J. Brown, Ed., Wiley-Interscience, New York, N.Y., 1971.
(4) (a) W. Traube, *Chem. Ber.*, **33**, 1371 (1900); (b) *ibid.*, **33**, 3035 (1900).
(5) (a) D. J. Brown in ref 3b, Vol. XVI, "The Pyrimidines", A. Wessberger and E. C. Taylor, Ed., Wiley-Interscience, New York, N.Y., 1962, p 138; (b) D. J. Brown in ref 3b, "The Pyrimidines", Supplement 1, Wiley-Interscience, New York, N.Y., 1970, p 94.
(6) E. C. Taylor and F. Sowinski, *J. Org. Chem.*, **39**, 907 (1974), and references cited therein.
(7) For a review, see A. Reiser and H. M. Wagner in "The Chemistry of Azido Group", S. Patai, Ed., Wiley-Interscience, New York, N.Y., 1971, p 331.
(8) W. von E. Doering and R. A. Odum, *Tetrahedron.*, **22**, 81, (1966); (b) B. Iddon, H. Suschitzky, and D. S. Taylor, *J. Chem. Soc., Chem. Commun.*, 879 (1974); (c) B. Iddon, N. W. Pickering, H. Suschitzky, and D. S. Taylor, *J. Chem. Soc., Perkin Trans. 1*, 1868 (1975); (d) B. Iddon, N. W. Pickering, and H. Suschitzky, *J. Chem. Soc., Chem. Commun.*, 759 (1974); (e) S. E. Hilton, E. F. V. Scriven, and H. Suschitzky, *ibid.*, 853 (1974); (f) S. E. Carroll, B. Nay, E. F. V. Scriven, and H. Suschitzky, *Synthesis*, 719, (1975); (g) J. Rigaudy, C. Igier, and J. Barcelo, *Tetrahedron Lett.*, 3845 (1975); (h) S. E. Carroll, B. Nay, E. F. V. Scriven, and H. Suschitzky, *ibid.*, 943 (1977); (i) S. E. Carroll, B. Nay, E. F. V. Scriven, H. Suschitzky, and D. R. Thomas, *ibid.*, 3175 (1977).
(9) (a) C. Temple, Jr., C. L. Kussner, and J. A. Montgomery, *J. Org. Chem.*, **33**, 2086 (1968); (b) F. Yoneda and Y. Sakuma, *J. Heterocycl. Chem.*, **10**, 993 (1973).
(10) W. Pfleiderer, K. H. Schündehütte, and H. Ferch, *Justus Liebigs Ann. Chem.*, **615**, 57 (1958).
(11) S. Polanc, B. Stanovnik, and M. Tišler, *J. Org. Chem.*, **41**, 3152 (1976).
(12) Thermal reaction of **1** will be published in a separate paper.
(13) (a) R. Huisgen, D. Vossius, and M. Appl, *Chem. Ber.*, **91**, 1 (1958); (b) R. Huisgen and M. Appl, *ibid.*, **91**, 12 (1958).
(14) H. Zondler, H. S. Forrest, and J. M. Lagowski, *J. Heterocycl. Chem.*, **4**, 12 (1967).
(15) See, for example, "The Merck Index", 9th ed., M. Windhols, Ed., Merck & Co., Inc., Rahway, N.J., 1976, p 528, and references cited therein.
(16) G. Blankenhorn and W. Pfleiderer, *Chem. Ber.*, **105**, 3334 (1972).
(17) Cheng et al. synthesized 6-methylpyrimido[5,4-*e*]-1,2,4-triazine-5,7(6*H*,8*H*)-dione via a 7,8-dihydro intermediate (A) which was easily oxidized with air: T. K. Liao, F. Baiocchi, and C. C. Cheng, *J. Org. Chem.*, **31**, 900 (1966).
(18) W. Pfleiderer and K. H. Schündehütte, *Justus Liebigs Ann. Chem.*, **612**, 158 (1958).
(19) W. Pfleiderer and K. H. Schündehütte, *Justus Liebigs Ann. Chem.*, **615**, 42 (1958).
(20) Freshly distilled diethylamine was used.
(21) H. S. Forrest, R. Hull, H. J. Rodda, and A. R. Todd, *J. Chem. Soc.*, 3 (1951).