[Chem. Pharm. Bull.]
31(11)3959—3966(1983)

Pyrimidine Derivatives and Related Compounds. XLVI.¹⁾ Thermal and Photochemical Transformation of 5-Substituted 6-Azido-1,3-dimethyluracils into Fused Pyrimidines such as Isoxazolo[3,4-*d*]pyrimidines, Pyrazolo[3,4-*d*]pyrimidines, and Pyrimido[4,5-*d*][1,2,3]triazine

KOSAKU HIROTA,* KAZUO MARUHASHI, TETSUJI ASAO,
NORIIHIKO KITAMURA, YOSHIFUMI MAKI,
and SHIGEO SENDA

*Gifu College of Pharmacy, 6-1, Mitahora-higashi
5-chome, Gifu 502, Japan*

(Received April 12, 1983)

Thermolysis and photolysis of 6-azido-1,3-dimethyluracils possessing certain substituents (formyl, benzoyl, hydrazonomethyl, phenyl, and benzyl groups) at the 5-position provided new methods for the preparation of fused pyrimidines. Irradiation and heating of 5-formyl- and 5-benzoyl-6-azidouracils (**3** and **7**) led to the formation of isoxazolo[3,4-*d*]pyrimidines (**4** and **8**). 2-(Substituted amino)pyrazolo[3,4-*d*]pyrimidines (**14**) were conveniently prepared by the reaction of 6-chloro-5-hydrazonomethyl-1,3-dimethyluracils (**12**) with sodium azide, followed by thermolysis of the resulting 6-azides. Upon thermolysis and photolysis of 5-phenyl- and 5-benzyl-6-azidouracils (**16** and **19**), pyrimido[4,5-*b*]indole (**17**) and pyrimido[4,5-*b*]quinoline (**10**) were obtained, respectively. Cyclization of **3** using triethyl phosphite and triphenylphosphine resulted in the formation of a new ring system, pyrimido[4,5-*d*][1,2,3]triazine (**5**).

Keywords—photolysis; thermolysis; azido group; isoxazolo[3,4-*d*]pyrimidine; pyrazolo[3,4-*d*]pyrimidine; pyrimido[4,5-*b*]indole; pyrimido[4,5-*b*]quinoline; pyrimido[4,5-*d*][1,2,3]triazine; 6-azido-5-formyl-1,3-dimethyluracil

A number of studies on the chemistry of azide compounds have been carried out because of the interesting reactivity and great utility of these compounds in organic synthesis.²⁾ For example, *o*-substituted phenylazide derivatives undergo intramolecular cyclization, which is frequently used for the preparation of benzoheterocycles.³⁾ Yoneda *et al.* have reported⁴⁾ that thermolysis of 6-azido-1,3-dimethyl-5-nitrouracil gave [1,2,5]oxadiazolo[3,4-*d*]pyrimidine *N*-oxide *via* cyclization between the 5-nitro and 6-azido groups with release of nitrogen (Chart 1).

Chart 1

We have demonstrated⁵⁾ that 6-azido-1,3-dimethyluracil (**1**) is a useful synthon for the synthesis of fused pyrimidines. Thus, photolysis of **1** in the presence of amino acid esters and acylhydrazines provides convenient methods for the preparation of 7,8-dihydrolumazines and fervenulins, respectively.

The present work was undertaken to explore further synthetic applications of 6-azido-1,3-dimethyluracils which possess appropriate substituents at the 5-position for intramolecular cyclization. We now wish to report new methods for the synthesis of fused pyrimidines such as isoxazolo[3,4-*d*]pyrimidines, pyrazolo[3,4-*d*]pyrimidines, and pyrimido[4,5-*d*]-[1,2,3]triazine.

5-Substituted 6-azidouracils used as starting materials in the present investigation were prepared either by introduction of a 5-substituent into 6-azido-1,3-dimethyluracil (**1**) or by reaction of the corresponding 5-substituted 6-chlorouracils with sodium azide.

The Vilsmeier reaction of **1** using a complex of dimethylformamide(DMF)– POCl_3 gave 6-azido-5-formyl-1,3-dimethyluracil (**3**) in 46% yield. Alternatively, **3** was obtained by the reaction of 6-chloro-5-formyl-1,3-dimethyluracil (**2**) with sodium azide in 73% yield.

Irradiation of **3** in methanol with a 100 W high pressure mercury arc lamp resulted in the formation of 5,7-dimethylisoxazolo[3,4-*d*]pyrimidine-4,6(5*H*,7*H*)-dione (**4**) in 74% yield. The structure of **4** was confirmed by comparison with an authentic sample.⁶⁾ Compound **4** was also obtained on heating of **3** in tetralin at 150–160 °C. In accordance with this observation, when the Vilsmeier reaction of **1** was carried out with heating, the isoxazolopyrimidine (**4**) could be obtained without isolation of **3**.

Chart 2

TABLE 2-(Substituted amino)-5,7-dimethylpyrazolo[3,4-*d*]pyrimidine-4,6(5*H*, 7*H*)-diones (**14a—e**)

No.	R	R'	mp (°C) (Recrystn. solvent)	Yield (%)	Formula	Analysis (%)			NMR (δ) C ₃ -H
						Calcd (Found)			
						C	H	N	
14a	C ₆ H ₅	H	225—228 (MeOH)	75	C ₁₃ H ₁₃ N ₅ O ₂	57.56 (57.30)	4.83 4.71	25.82 25.90	8.24 ^{a)}
14b	<i>p</i> -NO ₂ C ₆ H ₄	H	254—256 (MeOH)	70	C ₁₃ H ₁₂ N ₆ O ₄	49.37 (49.37)	3.82 3.96	26.57 26.24	8.58 ^{b)}
14c	C ₆ H ₅	CH ₃	157—158 (MeOH)	65	C ₁₄ H ₁₅ N ₅ O ₂	58.93 (58.79)	5.30 5.26	24.55 24.67	8.57 ^{b)}
14d	C ₆ H ₅	C ₆ H ₅	153—155 (DMF-H ₂ O)	73	C ₁₉ H ₁₇ N ₅ O ₂	65.69 (65.92)	4.93 4.87	20.16 20.20	8.60 ^{b)}
14e	CH ₃	CH ₃	198—200 (EtOH)	60	C ₉ H ₁₃ N ₅ O ₂	48.42 (48.30)	5.87 5.58	31.38 31.20	9.05 ^{b)}

a) In Me₂SO-*d*₆. b) In CF₃COOH.

hydrazines was carried out. Heating of **3** in neat aniline at 140—150 °C, however, gave an unexpected product, 1,3-dimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*, 3*H*)-dione (**10**),¹²⁾ in 45% yield. This reaction can be explained in terms of an initial nucleophilic substitution of the azido group at the 6-position by aniline. In fact, treatment of **3** with aniline and methylamine at room temperature gave 6-anilino- and 6-methylamino-5-formyl-1,3-dimethyluracils (**9a** and **9b**), respectively, in good yields. On heating, **9a** was easily converted into **10**.

When **3** was treated with hydrazines such as hydrazine hydrate, methylhydrazine, and phenylhydrazine at room temperature, 1*H*-pyrazolo[3,4-*d*]pyrimidines (**11a—c**)¹³⁾ rather than the expected hydrazone were obtained in good yields.

Next, 6-chloro-5-hydrazonomethyl-1,3-dimethyluracils (**12a—e**)^{13d)} prepared by condensation of **2** and hydrazines were employed for the preparation of the 6-azide derivatives (**13**). Treatment of *N*-methyl-*N*-phenylhydrazone (**12c**) with sodium azide at room temperature afforded the corresponding azide (**13c**). Irradiation of **13c** in methanol gave 5,7-dimethyl-2-(*N*-methylanilino)-2*H*-pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*, 7*H*)-dione (**14c**) in 54% yield. Cyclization of **13c** into **14c** also proceeded in 73% yield when **13c** was heated at 80 °C in DMF. Thus, when a suspension of the hydrazones (**12a—e**) and sodium azide in DMF was gradually warmed to 80 °C, 2-(substituted amino)-5,7-dimethyl-2*H*-pyrazolo[3,4-*d*]pyrimidines (**14a—e**) were directly obtained without isolation of the azide intermediates (**13**) (see Table).

The reaction of 6-chloro-1,3-dimethyl-5-phenyluracil (**15**) with sodium azide in refluxing water gave the corresponding azide (**16**) in 70% yield. Irradiation of **16** in methanol led to the formation of 1,3-dimethyl-9*H*-pyrimido[4,5-*b*]indole-2,4(1*H*, 3*H*)-dione (**17**).¹⁴⁾

A mechanism for the transformation of **16** into **17** could involve a well-known cyclization of a singlet nitrene.¹⁵⁾ On the other hand, the isoxazole and pyrazole formations (**4**, **8**, and **14**) could be explained in the terms of neighboring group participation (A) with concurrent loss of nitrogen without transient formation of the nitrene, as previously proposed in connection with the pyrolysis of arylazides.¹⁶⁾

Thermolysis of *o*-benzylphenylazide causes a ring expansion, giving rise to azepino[2,1-*a*]11*H*-indole.¹⁷⁾ 6-Azido-5-benzyl-1,3-dimethyluracil (**19**) was prepared by heating of 5-benzyl-1,3-dimethylbarbituric acid in phosphorus oxychloride, followed by treatment of the resulting chloride (**18**) with sodium azide. However, when **19** was refluxed in DMF, the product obtained was not an azepine derivative but pyrimido[4,5-*b*]quinoline (**10**). Irradiation

Chart 4

of **19** in tetrahydrofuran (THF) also afforded **10** in 15% yield. In both reactions, the expected azepine and other products could not be isolated.

Experimental

All melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were taken on a Hitachi 215 instrument from KBr pellets. Proton magnetic resonance spectra (NMR) were recorded on a Hitachi Perkin-Elmer R-20B spectrometer for solutions in CDCl_3 unless otherwise stated, with tetramethylsilane as an internal reference. Irradiation was carried out at 25–30 °C in a flask fitted with a Pyrex-jacketed immersion lamp. The light source was a Riko-UVL 100 W high-pressure mercury arc lamp.

6-Azido-1,3-dimethyl-5-formyluracil (3)—a) Phosphorus oxychloride (2.0 g) was added dropwise to a stirred suspension of **1**^{5b,18)} (2.0 g, 11 mmol) in DMF (14 ml) at 0 °C. The mixture was stirred at 0 °C for 3 h and then poured into ice water. The resulting precipitate was collected by filtration and recrystallized from MeOH to give 1.05 g (46%) of prisms, mp 137–138 °C. *Anal.* Calcd for $\text{C}_7\text{H}_7\text{N}_5\text{O}_3$: C, 40.19; H, 3.37; N, 33.48. Found: C, 39.95; H, 3.39; N, 33.33. IR (KBr): 2180 (N_3) cm^{-1} . NMR δ : 3.40 and 3.53 (each 3H, each s, each N-CH₃), 8.19 (1H, s, CHO).

b) A suspension of **2**¹⁹⁾ (2.0 g, 10 mmol) and sodium azide (0.78 g, 12 mmol) in EtOH (20 ml) was stirred at room temperature for 1 h. The resulting precipitate was collected by filtration and recrystallized from water to give 1.5 g (73%) of **3**, which was identical with the product obtained by procedure a).

5,7-Dimethylisoxazolo[3,4-d]pyrimidine-4,6(5H,7H)-dione (4)—a) A solution of **3** (0.5 g, 2.4 mmol) in MeOH (250 ml) was irradiated under nitrogen for 3 h. After evaporation of MeOH *in vacuo*, the residue was recrystallized from ligroin to give 0.32 g (74%) of prisms, mp 172–173 °C (lit.^{6a)} mp 170–171 °C; lit.^{6b)} mp 171–172.5 °C; lit.^{6c)} mp 172–173 °C). This compound was identical with an authentic sample.^{6c)} NMR δ : 3.41 and 3.56 (each 3H, each s, each N-CH₃), 9.06 (1H, s, C₃-H).

b) A solution of **3** (0.5 g, 2.4 mmol) in tetralin (5 ml) was heated at 150–160 °C for 5 min. The solution was diluted with petroleum ether (bp 30–70 °C). The resulting precipitate was collected by filtration and recrystallized from ligroin to give 0.28 g (65%) of **4** as colorless prisms, mp 172–173 °C; this product was identical with an authentic sample.^{6c)}

c) Phosphorus oxychloride (1.0 g) was added dropwise to a stirred suspension of **1** (0.5 g, 2.8 mmol) in DMF (5 ml) at 0 °C. The mixture was stirred at room temperature for 30 min and then heated to reflux for 1 h. The solvent was evaporated off under reduced pressure and the residue was triturated with a small amount of water. The resulting precipitate was collected by filtration and recrystallized from MeOH to give 0.26 g (60%) of **4**, mp 170–171 °C; this product was identical with an authentic sample.^{6c)}

6,8-Dimethylpyrimido[4,5-d][1,2,3]triazine-5,7-(6H,8H)-dione (5)—a) A solution of **3** (0.5 g, 2.4 mmol) and triethyl phosphite (0.4 g, 2.4 mmol) in hexane (10 ml) was stirred at 30–40 °C for 30 min. Excess water was added to the reaction solution. The mixture was allowed to stand overnight and extracted with CHCl_3 . The extract was dried over MgSO_4 . After removal of CHCl_3 , the residue was recrystallized from MeOH to give 0.25 g (55%) of plates, mp

168–169 °C. *Anal.* Calcd for $C_7H_7N_5O_2$: C, 43.52; H, 3.65; N, 36.26. Found: C, 43.57; H, 3.59; N, 36.28. NMR (DMSO- d_6) δ : 3.34 and 3.70 (each 3H, each s, each N-CH₃), 9.46 (1H, s, C₄-H). MS m/e : 193 (M^+), 165 ($M^+ - N_2$), 81 ($M^+ - CH_2NCO \times 2$).

b) A solution of **3** (0.5 g, 2.4 mmol) and triphenylphosphine (0.63 g, 2.4 mmol) in benzene (10 ml) was stirred at room temperature for 3 h. The resulting precipitate was collected by filtration and recrystallized from MeOH to give 0.34 g (75%) of **5**, which was identical with the product obtained by procedure a).

6-Amino-1,3-dimethyl-5-phenylhydrazonomethyluracil (6)—Phenylhydrazine (0.40 g, 3.9 mmol) was added to a solution of **5** (0.5 g, 2.6 mmol) in EtOH (5 ml), and the mixture was stirred for 5 min. The resulting precipitate was collected by filtration and recrystallized from water to give 0.5 g (70%) of **6**, mp 274–275 °C (lit.¹⁰ mp 273–277 °C). This compound was identical with an authentic sample prepared by the reported method.¹⁰

6-Azido-5-benzoyl-1,3-dimethyluracil (7)—A mixture of **1** (1.0 g, 5.2 mmol), benzoyl chloride (4 ml), and ZnCl₂ (0.75 g, 5.2 mmol) was heated at 90 °C for 5 h and then poured into water. The solution was extracted with CHCl₃. The extract was washed with 5% aqueous NaHCO₃ solution and then with water, dried over Na₂SO₄, and evaporated *in vacuo*. The residue was recrystallized from MeOH to give 0.15 g (10%) of needles, mp 154–156 °C. *Anal.* Calcd for $C_{13}H_{11}N_5O_3$: C, 54.73; H, 3.89; N, 24.55. Found: C, 54.65; H, 3.83; N, 24.55. NMR δ : 3.38 and 3.50 (each 3H, each s, each N-CH₃), 7.35–7.62 (3H, m, aromatics), 8.35–8.55 (2H, m, aromatics).

5,7-Dimethyl-3-phenylisoxazolo[3,4-*d*]pyrimidine-4,6(5*H*, 7*H*)-dione (8a)—a) A solution of **7** (0.5 g, 1.8 mmol) in THF (250 ml) was irradiated under nitrogen for 3 h. The solvent was removed by evaporation *in vacuo* and the residue was recrystallized from MeOH to give 0.32 g (70%) of prisms, mp 201–203 °C (lit.^{6a} mp 195–196 °C; lit.^{6b} mp 197–198 °C; lit.^{6c} mp 201–203 °C; lit.¹¹ mp 205 °C). The product was identical with an authentic sample.^{6c}

b) A solution of **7** (0.5 g, 1.8 mmol) in tetralin (15 ml) was heated at 150–160 °C for 5 min. The solution was diluted with petroleum ether (bp 30–70 °C) and the resulting precipitate was collected by filtration and recrystallized from MeOH to give 0.28 g (60%) of **8a**, mp 201–203 °C, which was identical with the product obtained by procedure a).

3,5,7-Trimethylisoxazolo[3,4-*d*]pyrimidine-4,6(5*H*, 7*H*)-dione (8b)—A mixture of **1** (0.25 g, 1.4 mmol), ZnCl₂ (0.15 g), and acetic anhydride (15 ml) was heated at 70–80 °C for 4 h. Acetic anhydride was evaporated off *in vacuo* and the residue was recrystallized from H₂O–MeOH to give 0.13 g (48%) of **8b**, mp 200 °C (lit.^{6c} mp 201–202 °C), which was identical with an authentic sample.^{6c} NMR δ : 2.75 (3H, s, C₃–CH₃), 3.37 and 3.50 (each 3H, each s, each N–NH₃).

6-Anilino-5-formyl-1,3-dimethyluracil (9a)—a) A mixture of **3** (0.5 g, 2.4 mmol) and aniline (5 ml) was stirred at room temperature for 10 min. Excess petroleum ether (bp 30–70 °C) was added to the mixture and the resulting precipitate was collected by filtration. Recrystallization from EtOH gave 0.44 g (70%) of needles, mp 176 °C. *Anal.* Calcd for $C_{13}H_{13}N_3O_3$: C, 60.22; H, 5.05; N, 16.21. Found: C, 60.24; H, 5.04; N, 16.36. NMR δ : 3.06 and 3.41 (each 3H, each s, each N–CH₃), 7.08–7.53 (5H, m, C₆H₅), 10.07 (1H, s, CHO), 12.45 (1H, brs, NH).

5-Formyl-1,3-dimethyl-6-methylaminouracil (9b)—An aqueous solution of 40% methylamine (5 ml) was added to a stirred solution of **3** (0.5 g, 2.4 mmol) in THF (10 ml). The mixture was stirred at room temperature for 10 min. The solvent was evaporated off *in vacuo* and the residue was recrystallized from EtOH to give 0.3 g (70%) of needles, mp 210–211 °C. *Anal.* Calcd for $C_8H_{11}N_3O_3$: C, 48.72; H, 5.62; N, 21.31. Found: C, 48.61; H, 5.56; N, 21.37. NMR δ : 3.26 (3H, d, 5.2 Hz, NH–CH₃), 3.38 and 3.63 (each 3H, each s, each N–CH₃), 9.90 (1H, s, CHO), 11.40 (1H, br, NH).

1,3-Dimethylpyrimido[4,5-*b*]quinoline-2,4(1*H*, 3*H*)-dione (10)—a) A mixture of **3** (0.5 g, 2.4 mmol) and aniline (5 ml) was heated at 140–150 °C for 10 min. The solution was diluted with petroleum ether (bp 30–70 °C). The resulting precipitate was collected by filtration and recrystallized from MeOH to give 0.26 g (45%) of prisms, mp 211–212 °C (lit.¹² mp 211–212 °C). *Anal.* Calcd for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.76; H, 4.55; N, 17.58. NMR δ : 3.51 and 3.80 (each 3H, each s, each N–CH₃), 7.25–8.07 (4H, m, aromatics), 9.00 (1H, s, C₅–H).

b) A solution of **9a** (0.26 g, 1 mmol) in DMF (5 ml) was refluxed for 20 min. The solvent was evaporated off *in vacuo* and the residue was recrystallized from EtOH to give 0.16 g (67%) of **10**, which was identical with the product obtained by procedure a).

c) A solution of **19** (0.5 g, 1.8 mmol) in THF (250 ml) was irradiated for 3 h. The solvent was removed by evaporation and the residue was triturated with ether. The resulting precipitate was collected by filtration and recrystallized from EtOH to give 0.065 g (15%) of prisms, mp 211–212 °C; this product was identical with the product obtained by procedure a).

5,7-Dimethyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*, 7*H*)-diones (11a–c): General Procedure—Hydrazines (2.9 mmol) *i.e.* hydrazine hydrate, methylhydrazine, phenylhydrazine, were added dropwise to a solution of **3** (0.5 g, 2.4 mmol) in EtOH (10 ml) with stirring at room temperature. After the solution had been stirred for 5 min, the resulting precipitate was collected by filtration and recrystallized from water to give the 1*H*-pyrazolo[3,4-*d*]pyrimidines (**11a–c**), which were identical with authentic samples.^{13c,d} **11a**: mp 277–279 °C (lit.^{13a,c} mp 277–279 °C), yield 90%. **11b**: mp 235–237 °C (lit.^{13a} mp 229–231 °C; lit.^{13c,d} mp 237–238 °C), yield 75%. **11c**: mp 218–220 °C (lit.^{13d} mp 219–220 °C), yield 80%.

6-Azido-1,3-dimethyl-5-*N'*-methyl-*N'*-phenylhydrazonomethyluracil (13c)—Sodium azide (1.32 g, 5 mmol) was added to a solution of **12c** (1.0 g, 3 mmol) in DMF (5 ml), and the mixture was stirred for 1 h. The resulting precipitate was collected by filtration and used for the next step without purification because of its instability. IR (KBr): 2150 (N_3) cm^{-1} . NMR δ : 3.38, 3.43, 3.48 (each 3H, each s, each $\text{N}-\text{CH}_3$), 7.23 (5H, br s, C_6H_5), 7.58 (1H, s, $\text{CH}=\text{N}$).

2-(*N*-Methylanilino)-5,7-dimethyl-2*H*-pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*, 7*H*)-dione (14c)—a) A solution of **13c** (0.6 g, 1.9 mmol) in DMF (5 ml) was heated at 80 °C for 1 h. The solvent was evaporated off *in vacuo* and the residue was triturated with a small amount of EtOH to give a crude product. Recrystallization from EtOH gave 0.4 g (73%) of prisms, mp 156–158 °C. The analytical and spectral data are shown in the Table.

b) A solution of **13c** (0.5 g, 1.6 mmol) in MeOH (250 ml) was irradiated for 3 h. The resulting precipitate was collected by filtration to give 0.25 g (54%) of **14c**, mp 155–157 °C, which was identical with the product obtained by procedure a).

2-(Substituted amino)-5,7-dimethyl-2*H*-pyrazolo[3,4-*d*]pyrimidine-4,6(5*H*, 7*H*)-diones (14a–e): General Procedure—A suspension of the hydrazones (**12**)^{13d} (2.0 mmol) and sodium azide (0.16 g, 2.4 mmol) in DMF (10 ml) was gradually warmed to 80 °C for 2 h. The solution was evaporated *in vacuo* and a small amount of water was added to the residue. The resulting precipitate was collected by filtration and recrystallized from an appropriate solvent (see Table).

6-Azido-1,3-dimethyl-5-phenyluracil (16)—A suspension of **15**²⁰ (2.0 g, 8 mmol) and sodium azide (0.62 g, 9.6 mmol) in water (20 ml) was refluxed for 1 h. The resulting precipitate was collected by filtration and recrystallized from MeOH to give 1.4 g, (70%) of needles, mp 139–140 °C. Anal. Calcd for $\text{C}_{12}\text{H}_{11}\text{N}_5\text{O}_2$: C, 56.02; H, 4.31; N, 27.23. Found: C, 56.12; H, 4.30; N, 27.15. IR (KBr): 2140 (N_3) cm^{-1} . NMR δ : 3.43 and 3.68 (each 3H, each s, each $\text{N}-\text{CH}_3$), 7.41 (5H, br s, C_6H_5).

1,3-Dimethyl-9*H*-pyrimido[4,5-*b*]indole-2,4(1*H*, 3*H*)-dione (17)—A solution of **16** (0.5 g, 1.9 mmol) in MeOH (250 ml) was irradiated for 3 h. The solvent was evaporated off *in vacuo*. Recrystallization of the residue from MeOH gave 0.33 g (75%) of **17**, mp > 300 °C (lit.¹⁴) mp > 300 °C), which was identical with an authentic sample.¹⁴

5-Benzyl-6-chloro-1,3-dimethyluracil (18)—Water (0.7 ml) was added to a solution of 5-benzyl-1,3-dimethylbarbituric acid (3.0 g, 2.2 mmol) in POCl_3 (24 ml). The solution was refluxed for 7 h and the excess POCl_3 was removed by evaporation *in vacuo*. The residue was triturated with ice water and the resulting precipitate was collected by filtration and recrystallized from EtOH to give 2.2 g (69%) of **18**, mp 86–87 °C. Anal. Calcd for $\text{C}_{13}\text{H}_{13}\text{ClN}_2\text{O}_2$: C, 58.98; H, 4.95; N, 10.58. Found: C, 58.82; H, 4.92; N, 10.61. NMR δ : 3.37 and 3.58 (each 3H, each s, each $\text{N}-\text{CH}_3$), 3.88 (2H, s, CH_2), 7.26 (5H, br s, C_6H_5).

6-Azido-5-benzyl-1,3-dimethyluracil (19)—A suspension of **18** (2.0 g, 7.6 mmol) and sodium azide (1.0 g, 15.2 mmol) in hexamethylphosphoramide (10 ml) was stirred at room temperature for 2 h. The reaction solution was diluted with water, and the resulting precipitate was collected by filtration and recrystallized from EtOH to give 1.1 g (54%) of the product (**19**), mp 75–76 °C. Anal. Calcd for $\text{C}_{13}\text{H}_{13}\text{N}_5\text{O}_2$: C, 57.56; H, 4.83; N, 25.82. Found: C, 57.49; H, 4.81; N, 25.74. IR (KBr): 2120 (N_3) cm^{-1} . NMR δ : 3.38 and 3.43 (each 3H, each s, each $\text{N}-\text{CH}_3$), 3.99 (2H, s, CH_2), 7.23 (5H, m, C_6H_5).

References and Notes

- 1) For Part XLV, see K. Hirota, Y. Kitade, K. Shimada, S. Senda, and Y. Maki, *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1293.
- 2) S. Patai (ed.), "The Chemistry of the Azido Group," Wiley-Interscience, New York, 1971.
- 3) E. F. V. Scriven, "Reactive Intermediates," Vol. 2, ed. by R. A. Abramovitch, Plenum Press, New York, 1982, pp. 1–54.
- 4) F. Yoneda and Y. Sakuma, *J. Heterocycl. Chem.*, **10**, 993 (1973).
- 5) a) S. Senda, K. Hirota, T. Asao, and K. Maruhashi, *J. Am. Chem. Soc.*, **99**, 7358 (1977); b) *Idem. ibid.*, **100**, 7661 (1978).
- 6) a) R. Marumoto and Y. Furukawa, *Chem. Pharm. Bull.*, **25**, 2974, (1977); b) S. Nishigaki, Y. Kanamori, and K. Senga, *ibid.*, **26**, 2497 (1978); c) K. Hirota, T. Asao, T. Fujioka, and S. Senda, *Nippon Kagaku Kaishi*, **1981**, 721.
- 7) A. G. Rowley, "Organophosphorus Reagents in Organic Synthesis," ed. by J. I. G. Cadogan, Academic Press, London, 1979, pp. 295–350.
- 8) No literature on the synthesis of a pyrimido[4,5-*d*] [1, 2, 3]triazine ring system has been found in *Chem. Abstr.*; see an excellent review of 1,2,3-triazines: R. J. Kobylecki, "Advances in Heterocyclic Chemistry," Vol. 19, ed. by A. R. Katritzky and A. J. Boulton, Academic Press, New York, 1976, pp. 215–278.
- 9) B. M. Adger, S. Bradbury, M. Keating, C. W. Rees, R. C. Storr, and M. T. Williams, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 31.
- 10) W. Pfeiderer and G. Strauss, *Justus Liebigs Ann. Chem.*, **612**, 173 (1958).
- 11) F. Yoneda, T. Yano, and M. Higuchi, *Chem. Lett.*, **1979**, 155.
- 12) a) K. Senga, K. Shimizu, S. Nishigaki, and F. Yoneda, *Heterocycles*, **6**, 1361 (1977); b) F. Yoneda, F. Takayama, and A. Koshiro, *Chem. Pharm. Bull.*, **27**, 2507 (1979); c) Y. Tominaga, H. Okuda, M. Tochiki, Y.

- Matsuda, and G. Kobayashi, *Heterocycles*, **15**, 679 (1981).
- 13) a) W. Pfeiderer and K.-H. Schündehütte, *Justus Liebigs Ann. Chem.*, **615**, 42 (1958); b) P. Schmidt, K. Eichenberger, and J. Druey, *Helv. Chim. Acta*, **41**, 1052 (1958); c) S. Senda, K. Hirota, and G.-N. Yang, *Chem. Pharm. Bull.*, **20**, 391 (1972); d) *Idem, ibid.*, **20**, 399 (1972).
- 14) S. Senda, K. Hirota, and M. Takahashi, *J. Chem. Soc., Perkin Trans. 1*, **1975**, 503.
- 15) J. M. Lindley, I. M. McRobbie, O. Meth-Cohn, and H. Suschitzky, *J. Chem. Soc., Perkin Trans. 1*, **1977**, 2194.
- 16) L. K. Dyllal and J. E. Kemp, *J. Chem. Soc., (B)*, **1968**, 976; L. K. Dyllal, *Aust. J. Chem.*, **30**, 2669 (1977).
- 17) L. Krbecek and H. Takimoto, *J. Org. Chem.*, **33**, 4286 (1968); G. R. Cliff and G. Jones, *J. Chem. Soc., Chem. Commun.*, **1970**, 1705.
- 18) W. Pfeiderer and K.-H. Schündehütte, *Justus Liebigs Ann. Chem.*, **612**, 158 (1958).
- 19) S. Senda, K. Hirota, G.-N. Yang, and M. Shirahashi, *Yakugaku Zasshi*, **91**, 1372 (1971).
- 20) G. Strauss, *Justus Liebigs Ann. Chem.*, **638**, 205 (1960).