Condensed Heteroaromatic Ring Systems. XVI.[1] Synthesis of Pyrrolo[2,3-*d*]pyrimidine Derivatives

Yoshinori KONDO, Ryô WATANABE, Takao SAKAMOTO, and Hiroshi YAMANAKA*

Pharmaceutical Institute, Tohoku University, Aobayama, Aoba-ku, Sendai 980, Japan. *Received April 5, 1989*

The synthesis of pyrrolo[2,3-*d*]pyrimidine derivatives was accomplished by the following two methods. One is the palladium-catalyzed reaction of terminal acetylenes with *N*-(5-halo-4-pyrimidinyl)methanesulfonamides prepared by the nucleophilic substitution of 4-chloro-5-halopyrimidines with methanesulfonamide. The other is the photocyclization of 4-azidopyrimidines containing an olefinic function at the 5-position. The synthesis of 4-azidopyrimidine derivatives is also described.

Keywords pyrrolo[2,3-*d*]pyrimidine; palladium-catalyzed reaction; *N*-(5-halo-4-pyrimidinyl)methanesulfonamide; acetylene; photochemical cyclization; 4-azidopyrimidine; nucleophilic substitution; 4-chloropyrimidine; methanesulfonamide

As a part of our investigation on the preparation of condensed heteroaromatic ring systems,[2] we have reported versatile methods for the synthesis of indole derivatives using the palladium-catalyzed cross-coupling reaction of 2-haloaniline derivatives with terminal acetylenes as a key reaction. Namely, ethyl 2-(1-hexynyl)phenylcarbamate, obtained by the palladium-catalyzed condensation of ethyl 2-bromophenylcarbamate with 1-hexyne, cyclized smoothly to give 2-butylindole under basic conditions,[3] and the palladium-catalyzed cross-coupling of *N*-(2-bromophenyl)methanesulfonamide with 1-hexyne is followed by spontaneous cyclization to give 2-butyl-1-methylsulfonylindole.[4] Through these two methods, a variety of pyrrolopyridines can be derived from the corresponding aminobromopyridines.[2,3] In spite of such utility in the pyridine series, these methods were accertained not to be applicable to the synthesis of pyrrolo[2,3-*d*]pyrimidine derivatives from 4-amino-5-halopyrimidines, for the following reasons: 1) the ethoxycarbonylation of 4-amino-5-halopyrimidines with ethyl chlorocarbonate was unsuccessful in general; 2) similarly, 4-amino-5-halopyrimidines do not react well with methanesulfonyl chloride under basic conditions.

Thus, we investigated alternative methods for the preparation of the pyrrolo[2,3-*d*]pyrimidine ring system from simple pyrimidine derivatives. In the present paper, we describe the synthesis of pyrrolo[2,3-*d*]pyrimidine derivatives from 4,5-dihalopyrimidines based on the combination of nucleophilic substitution at the 4-position and palladium-catalyzed cross-coupling reaction at the 5-position.

Cyclization of *N*-(5-Ethynyl-4-pyrimidinyl)methanesulfonamides When 4-chloro-5-iodo-2-methylthiopyrimidine (**1a**) was heated with methanesulfonamide in dimethylformamide (DMF) in the presence of sodium hydride, *N*-(5-iodo-2-methylthio-4-pyrimidinyl)methanesulfonamide (**2a**) was obtained. Similarly, 5-bromo-4-chloro-2-methyl-6-phenyl- (**1b**) and 4-chloro-5-iodo-2-isopropyl-6-methylpyrimidine (**1c**) were convertible to *N*-(5-bromo-2-methyl-6-phenyl-4-pyrimidinyl)- (**2b**) and *N*-(5-iodo-2-isopropyl-6-methyl-4-pyrimidinyl)methanesulfonamide (**2c**), respectively.

Unlike these 4-chloropyrimidine derivatives, 4-halopyridines, *e.g.* 3,4-dibromopyridine and its *N*-oxide, did not react with methanesulfonamide under similar conditions. Thus, the synthesis of *N*-(heteroaryl)methanesulfonamide through this approach was a consequence of the higher reactivity of the 4-chloro substituent of the pyrimidine ring toward nucleophilic substitution.

As well as the palladium-catalyzed reaction of *N*-(2-bromophenyl)methanesulfonamide with terminal acetylenes,[4] the reaction of **2a—c** with trimethylsilylacetylene, for example, was accomplished with intramolecular cyclization of the cross-coupling products (**3**), and the 2,4-disubstituted 6-trimethylsilyl-7-methylsulfonylpyrrolo[2,3-*d*]pyrimidine (**4a—c**) were isolated. 2,4-Disubstituted 6-butyl-7-methylsulfonylpyrrolo[2,3-*d*]pyrimidines (**5a—c**) were obtained by the similar reaction of **2a—c** with 1-hexyne. The results are listed in Table I.

Photochemical Cyclization of 4-Azido-5-ethenyl(or aryl)-pyrimidines When 4-chloro-2,6-dimethyl-5-phenylpyrimidine (**7a**), derived by the palladium-catalyzed cross-coupling reaction of 4-chloro-5-iodo-2,6-dimethylpyrimidine (**6**) with tributylphenylstannane,[5] was heatd with sodium azide in ethanol, 4-azido-2,6-dimethyl-5-phenylpyrimidine (**8a**) was obtained in considerable yield. 5-(2-Thienyl)- (**7b**), 5-ethenyl- (**7c**), 5-(2-trimethylsilyl)ethenyl- (**7d**), and 5-(2-ethoxycarbonyl)ethenyl-4-chloro-2,6-dimethylpyrimidine (**7e**)[6] reacted with sodium azide under the same conditions to give the corresponding 4-azidopyrimidines (**8b—e**), as expected. These 5-substituted 4-azidopyrimidines (**8a—d**) were also obtained by the palladium-cata-

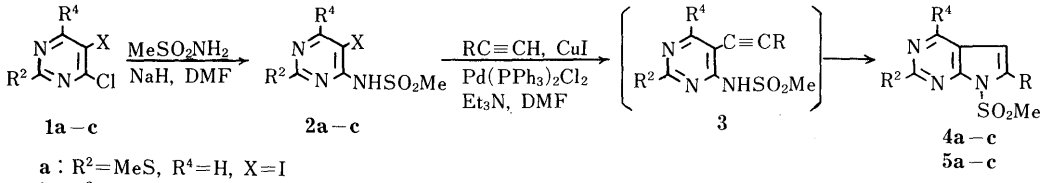

Chart 1

TABLE I. 7-Methylsulfonylpyrrolo[2,3-*d*]pyrimidines (**4** and **5**)

No.	Yield (%)	mp (°C) (Recryst. solvent)	^{1}H-NMR δ (ppm) [Solvent]	Formula	Analysis (%) Calcd (Found)		
					C	H	N
4a	46	133—134 (Hexane)	0.40 (9H, s), 2.63 (3H, s), 3.56 (3H, s), 6.77 (1H, s), 8.73 (1H, s) [$CDCl_3$]	$C_{11}H_{17}N_3O_2S_2Si$	41.88 (41.85	5.43 5.54	13.32 13.19)
4b	15	160—161 (Hexane)	0.39 (9H, s), 2.86 (3H, s), 3.65 (3H, s), 7.02 (1H, s), 7.4—7.6 (3H, m), 7.9—8.2 (2H, m) [CCl_4]	$C_{17}H_{21}N_3O_2SSi$	56.79 (57.05	5.89 5.78	11.69 11.32)
4c	23	92—94 (Hexane)	0.39 (9H, s), 1.49 (6H, d, J=7.0 Hz), 2.66 (3H, s), 2.9—3.5 (1H, m), 3.64 (3H, s), 6.73 (1H, s) [CCl_4]	$C_{14}H_{23}N_3O_2SSi$	51.66 (51.44	7.12 6.92	12.91 12.72)
5a	52	110—112 (Hexane)	0.8—1.9 (7H, m), 2.55 (3H, s), 2.8—3.1 (2H, m), 3.57 (3H, s), 6.15 (1H, s), 8.50 (1H, s) [CCl_4]	$C_{12}H_{17}N_3O_2S_2$	48.14 (48.22	5.72 5.85	14.03 14.15)
5b	31	115—117 (Cyclohexane)	0.8—2.1 (7H, m), 2.87 (3H, s), 2.9—3.3 (2H, m), 3.71 (3H, s), 6.58 (1H, s), 7.4—7.7 (3H, m), 7.9—8.1 (2H, m) [$CDCl_3$]	$C_{18}H_{21}N_3O_2S$	62.95 (62.95	6.16 6.26	12.23 12.29)
5c	60	68—70 (Hexane)	0.8—2.1 (7H, m), 1.37 (6H, d, J=7.0 Hz), 2.61 (3H, s), 2.7—3.5 (3H, m), 3.68 (3H, s), 6.27 (1H, s) [CCl_4]	$C_{15}H_{23}N_3O_2S$	58.22 (58.15	7.49 7.32	13.58 13.93)

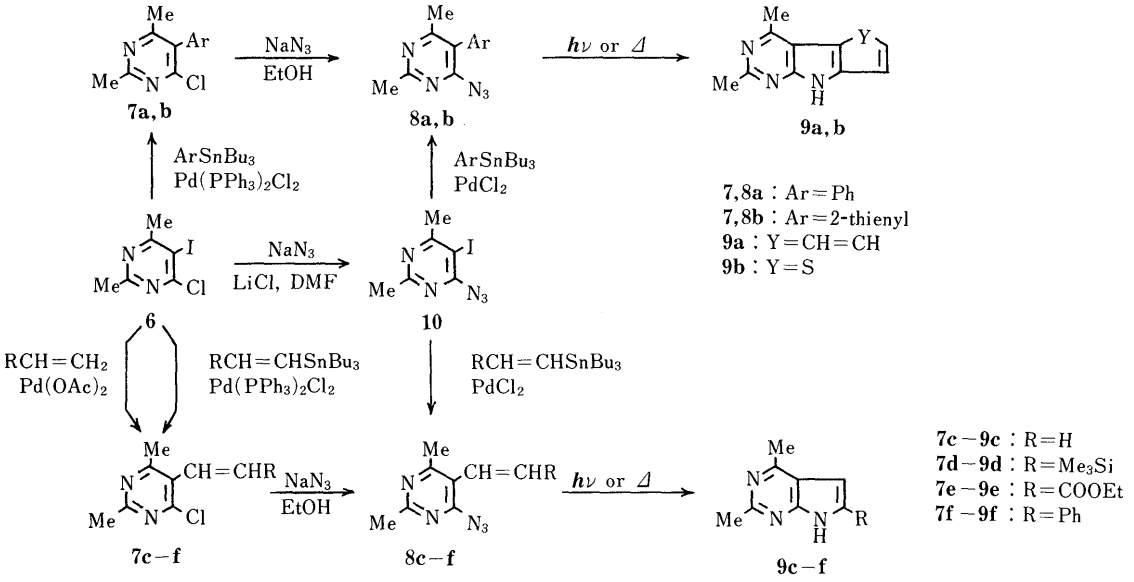

Chart 2

TABLE II. Photochemical Cyclization of 5-Substituted 6-Azido-2,4-dimethylpyrimidines (**8a—f**)

No.	Yield[a] (%) (Reaction time: h)	mp (°C) (Recryst. solvent)	IR ($CHCl_3$) cm^{-1} NH	^{1}H-NMR δ (ppm) [Solvent]	Formula	Analysis (%) Calcd (Found)		
						C	H	N
9a	90 (8) [0[b]]	270—271 (dec.) (AcOEt)	3450	2.67 (3H, s), 2.87 (3H, s), 7.1—7.7 (3H, m), 8.0—8.2 (1H, m), 11.9—12.2 (1H, br) [DMSO-d_6]	$C_{12}H_{11}N_3$	73.07 (72.78	5.62 5.77	21.30 21.39)
9b	73 (2) [—]	268—269 (dec.) (AcOEt)	3450	2.65 (3H, s), 2.70 (3H, s), 7.29 (1H, d, J=5.0 Hz), 7.75 (1H, d, J=5.0 Hz), 1.20—12.4 (1H, br) [DMSO-d_6]	$C_{10}H_9N_3S$	59.09 (59.00	4.46 4.51	20.67 20.76)
9c	58 (10) [51 (1)]	186—188 (AcOEt–C_6H_6)	3460	2.73 (3H, s), 2.81 (3H, s), 6.53 (1H, d, J=3.5 Hz), 7.42 (1H, d, J=3.5 Hz), 11.4—12.3 (1H, br) [$CDCl_3$]	$C_8H_9N_3$	65.29 (65.08	6.16 6.17	28.55 28.34)
9d	18[c] (10) [0[b] (2)]	153—154 (Cyclohexane)	3455	0.34 (9H, s), 2.72 (3H, s), 2.75 (3H, s), 6.73 (1H, br s), 9.0—9.5 (1H, br) [CCl_4]	$C_{11}H_{17}N_3Si$	60.23 (60.35	7.81 7.79	19.16 18.95)
9e	62 (16) [71 (1)]	191—192 (AcOEt)	3445	1.42 (3H, t, J=7.0 Hz), 2.75 (3H, s), 2.83 (3H, s), 4.46 (2H, q, J=7.0 Hz), 7.28 (1H, d, J=2.0 Hz), 10.6—11.2 (1H, br) [$CDCl_3$]	$C_{11}H_{13}N_3O_2$	60.26 (60.10	5.98 5.81	19.17 19.06)
9f	94 (3) [70[d] (0.5)]	215—216[e] (Ether)						

a) Yields in brackets are from the thermal cyclization. *b*) Multiple products were detected by thin-layer chromatography. *c*) Compound **9c** was isolated in 43% yield together with **9d**. *d*) Yield described in ref. 6. *e*) Lit.[6] mp 215—216 °C.

lyzed cross-coupling reaction of 4-azido-5-iodo-2,6-dimethylpyrimidine (**10**) with tributylstannanes, but the yields of **8a—d** were low.

The 4-azidopyrimidines (**8a—e**) thus obtained and 4-azido-2,6-dimethyl-5-styrylpyrimidine (**8f**)[7] were readily transformed into the corresponding pyrrolo[2,3-*d*]pyrim-

idine derivatives by photochemical cyclization in trifluoroacetic acid.[8] As listed in Table II, the yields of the products, except for that of 2,4-dimethyl-6-(trimethylsilyl)pyrrolo[2,3-*d*]pyrimidine (**9d**), were satisfactory. The photochemical cyclization of 4-azido-2,6-dimethyl-5-(2-trimethylsilyl)-ethenylpyrimidine (**8d**) in acidic medium gave the desilylated product, 2,4-dimethylpyrrolo[2,3-*d*]pyrimidine (**9c**), as a main product (43%) together with a small amount (18%) of **9d**.

We have already reported the thermal cyclization of **8f** in boiling 1,4-dibromobenzene, which gave rise to 2,4-dimethyl-6-phenylpyrrolo[2,3-*d*]pyrimidine (**9f**) in 70% yield.[7] When **8c**—**e** were heated in the reported manner, 2,4-dimethylpyrrolo[2,3-*d*]pyrimidine (**9c**) and ethyl 2,4-dimethylpyrrolo[2,3-*d*]pyrimidine-6-carboxylate (**9e**) were obtained in 51 and 71% yields, respectively, but no significant product was isolated from the thermal cyclization of **8d**.

On the basis of the experiments described above, it is clear that the photochemical transformation from **8a**—**f** to **9a**—**f** is advantageous for the preparation of the pyrrolo[2,3-*d*]pyrimidine system.

The present investigation, has opened a route to the pyrrolo[2,3-*d*]pyrimidine ring system from simple pyrimidine derivatives, by utilizing the reactivity of 4-chloropyrimidines. Although further improvement of these methods regards the reaction conditions and overall yields of the final products, the results of the present investigation suggest a wide generality of these methods.

Experimental

All melting points and boiling points are uncorrected. Infrared (IR) spectra were measured with a JASCO IRA-1 spectrometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were taken at 60 MHz with a JEOL JNM-PMX 60 spectrometer. Chemical shifts are expressed in δ (ppm) values, and coupling constants are expressed in hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, dd = double doublet, m = multiplet, and br = broad. Mass spectra (MS) were determined with a JEOL JMS-01SG-2 spectrometer.

5-Bromo-2-methyl-4-phenyl-6(1*H*)-pyrimidinone A solution of Br_2 (19.98 g, 0.125 mol) in AcOH (30 ml) was added to a solution of 2-methyl-4-phenyl-6(1*H*)-pyrimidinone (22.34 g, 0.12 mol) in AcOH (120 ml) at room temperature and the mixture was stirred for 1 h. After removal of the solvent, the residue was diluted with water and neutralized with Na_2CO_3. The resulting precipitate was filtered and recrystallized from acetone to give colorless prisms, mp 215—217 °C. Yield 22.09 g (69%). IR ($CHCl_3$): 1660 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 2.58 (3H, s), 7.4—8.0 (5H, m), 12.1—14.4 (1H, br). *Anal.* Calcd for $C_{11}H_9BrN_2O$: C, 49.84; H, 3.42; N, 10.57. Found: C, 49.80; H, 3.51; N, 10.44.

5-Bromo-6-chloro-2-methyl-4-phenylpyrimidine (1b) A mixture of 5-bromo-2-methyl-4-phenyl-6(1*H*)-pyrimidinone (2.65 g, 10 mmol) and $POCl_3$ (10 ml) was refluxed for 1 h. After removal of the excess $POCl_3$ *in vacuo*, the residue was poured onto ice, made alkaline with ammonia, and extracted with $CHCl_3$. The residue obtained from the $CHCl_3$ extract was purified by alumina column chromatography using C_6H_6 as an eluent. The procuct obtained from the C_6H_6 eluate was recrystallized from hexane to give colorless prisms, mp 82—84 °C. Yield 2.63 g (92%). ^{1}H-NMR (CCl_4): 2.63 (3H, s), 7.35 (5H, m). *Anal.* Calcd for $C_{11}H_8BrClN_2$: C, 46.59; H, 2.84; N, 9.88. Found: C, 46.60; H, 2.72; N, 9.87.

General Procedure for the Synthesis of *N*-(2,4-Disubstituted 5-Halo-6-pyrimidinyl)methanesulfonamides (2a—c) A suspension of 60% NaH (1.6 g, 40 mmol) and methanesulfonamide (5.70 mg, 60 mmol) in dry DMF (20 ml) was heated at 120 °C for 30 min. After cooling of the mixture to 80 °C, a 4-chloro-5-halopyrimidine (**1a**—**c**) (20 mmol) was added, and the whole was heated at 80 °C for 4—20 h. The DMF was removed under reduced pressure, and the residue was diluted with water and acidified (pH 3) with 3 N HCl. The resulting precipitate was collected by filteration and recrystallized.

N-(5-Iodo-2-methythio-6-pyrimidinyl)methanesulfonamide (**2a**) was obtained according to the general procedure (refluxing for 4 h) as colorless needles, mp 182—184 °C, from MeOH. Yield 5.13 g (74%). IR (KBr): 1150 cm^{-1}. ^{1}H-NMR (DMSO-d_6): 2.53 (3H, s), 3.31 (3H, s), 8.58 (1H, s), 7.3—9.8 (1H, br). *Anal.* Calcd for $C_6H_8IN_3O_2S_2$: C, 20.88; H, 2.34; N, 12.17. Found: C, 21.16; H, 2.16; N, 12.13.

N-(5-Bromo-2-methyl-4-phenyl-6-pyrimidinyl)methanesulfonamide (**2b**) was obtained according to the general procedure (refluxing for 4 h) as colorless prisms, mp 171—173 °C, from AcOEt. Yield 5.53 g (81%). IR (KBr): 1120 cm^{-1}. ^{1}H-NMR (DMSO-d_6): 2.67 (3H, s), 3.51 (3H, s), 7.3—7.8 (5H, m), 6.4—8.8 (1H, br). *Anal.* Calcd for $C_{12}H_{12}BrN_3O_2S$: C, 42.21; H, 3.53; N, 12.28. Found C, 41.99; H, 3.55; N, 12.26.

N-(5-Iodo-2-isopropyl-4-methyl-6-pyrimidinyl)methanesulfonamide (**2c**) was obtained according to the general procedure (refluxing for 20 h) as colorless prisms, mp 138—140 °C, from acetone. Yield 3.13 g (44%). IR (KBr): 1120 cm^{-1}. ^{1}H-NMR (DMSO-d_6): 1.28 (6H, d, J = 7.0), 2.54 (3H, s), 3.13 (3H, s), 2.6—3.2 (1H, m), 11.2—13.4 (1H, br). *Anal.* Calcd for $C_9H_{14}IN_3O_2S$: C, 30.43; H, 3.97; N, 11.83. Found: C, 30.61; H, 4.00; H, 12.02.

General Procedure for the Synthesis of 2,4,6-Trisubstituted 7-Methylsulfonylpyrrolo[2,3-*d*]pyrimidine (4a—c and 5a—c) A mixture of an *N*-pyrimidinylmethanesulfonamide (**2a**—**c**) (2 mmol), an acetylene (3 mmol), $Pd(PPh_3)_2Cl_2$ (32 mg), CuI (16 mg), Et_3N (0.60 g, 6 mmol), and DMF (1 ml) was heated at 80 °C for 24 h in a sealed tube. The reaction mixture was diluted with water and extracted with ether. The crude product obtained from the ethereal extract was purified by silica gel column chromatography using hexane–ether (9 : 1).

6-Azido-5-iodo-2,4-dimethylpyrimidine (10) A mixture of **6** (13.43 g, 50 mmol), NaN_3 (3.90 g, 60 mmol), LiCl (2.54 g, 60 mmol), and DMF (200 ml) was stirred at room temperature for 2 h. The mixture was poured

TABLE III. 5-Substituted 6-Azido-2,4-dimethylpyrimidines (**8a**—**e**)

No.	Yield[a] (%) (Reaction time: h)	mp (°C) (Recryst. solvent)	^{1}H-NMR δ (ppm) [Solvent]	Formula	Analysis (%) Calcd (Found)		
					C	H	N
8a	67 (12) [65 (3)]	68—69 (Cyclohexane)	2.55 (3H, s), 3.06 (3H, s), 7.2—7.7 (5H, m) [CCl_4]	$C_{12}H_{11}N_5$	63.99 (64.01)	4.92 5.07	31.09 31.05)
8b	90 (12) [45 (2)]	144—146 (Cyclohexane)	2.82 (3H, s), 3.13 (3H, s), 7.1—7.3 (1H, m), 7.58 (1H, dd, J = 1.5, 5.0 Hz), 7.78 (1H, dd, J = 1.5, 3.5 Hz) [$CDCl_3$]	$C_{10}H_9N_5S$	51.93 (52.28	3.93 3.94	30.28 30.40)
8c	80 (12) [11 (2)]	130—131 (Hexane)	2.98 (3H, s), 3.08 (3H, s), 5.89 (1H, dd, J = 4.0, 9.0 Hz), 6.6—7.3 (2H, m) [CCl_4]	$C_8H_9N_5$	54.85 (54.88	5.18 5.25	39.98 39.94)
8d	83 (12) [24 (2)]	82—84 (Hexane)	0.23 (9H, s), 2.66 (3H, s), 3.05 (3H, s), 7.02 (1H, d, J = 19.5 Hz), 7.81 (1H, d, J = 19.5 Hz) [CCl_4]	$C_{11}H_{17}N_5Si$	53.41 (53.62	6.93 7.04	28.31 28.47)
8e	55 (12) —	148—150 (Cyclohexane)	1.37 (3H, t, J = 7.0 Hz), 2.80 (3H, s), 3.13 (3H, s), 4.32 (2H, q, J = 7.0 Hz), 7.71 (1H, d, J = 16.0 Hz), 7.87 (1H, d, J = 16.0 Hz) [$CDCl_3$]	$C_{11}H_{13}N_5O_2$	53.43 (53.80	5.30 5.33	28.32 28.47)

a) Yields in brackets are from **10**.

into ice-water, and the resulting precipitate was collected, dried, and recrystallized from C_6H_6 to give pale yellow prisms, mp 150—151 °C. Yield 9.81 g (71%). ^{1}H-NMR ($CDCl_3$): 2.85 (3H, s), 3.10 (3H, s). *Anal.* Calcd for $C_6H_6IN_5$: C, 26.20; H, 2.20; N, 25.46. Found: C, 26.33; H, 2.19; N, 25.70.

General Procedure for the Palladium-Catalyzed Cross-Coupling Reaction of 10 with Tributylstannanes A mixture of **10** (2 mmol), a tributylstannane (3 mmol), $PdCl_2$ (17 mg), Et_4NCl (0.33 g, 2 mmol), and DMF (4 ml) was heated at 110 °C with stirring under a nitrogen atmosphere for an appropriate time (shown in Table III). The reaction mixture was diluted with water and extracted with water. The crude product obtained from the ethereal extract was purified by silica gel column chromatography using hexane–ether (9 : 1).

General Procedure for the Synthesis of 5-Substituted 6-Azido-2,4-dimethylpyrimidines (8a—e) from 5-Substituted 6-Chloro-2,4-dimethylpyrimidines (7a—e) A mixture of **7a—e** (0.5 mmol), NaN_3 (0.10 g, 1.5 mmol), EtOH (2.5 ml) was refluxed for 12 h. After removal of the EtOH, the residue was diluted with water, and the mixture was extracted with CH_2Cl_2. The product obtained from the CH_2Cl_2 extract was recrystallized from an appropriate solvent (shown in Table III).

General Procedure for the Photochemical Cyclization of 8a—f A mixture of **8a—f** (0.5 mmol) and CF_3COOH (10 ml) was irradiated in a Pyrex immersion apparatus equipped with a UVL-400P high-pressure mercury lamp under a nitrogen atmosphere for an appropriate time (shown in Tabl II). After removal of the solvent, the residue was diluted with water, neutralized with Na_2CO_3, and extracted with $CHCl_3$. The crude product obtained from the $CHCl_3$ extract was recrystallized from an appropriate solvent (shown in Table II).

General Procedure for the Thermal Cyclization of 8a—e A mixture of **8a—e** (1 mmol) and 1,4-dibromobenzene (2 g) was heated at 180 °C for an appropriate time (shown in Table II). The reaction mixture was diluted with C_6H_6 and extracted with 3 N HCl. The HCl extract was washed with C_6H_6, neutralized with Na_2CO_3, and extracted with $CHCl_3$. The crude product obtained from the $CHCl_3$ was recrystallized from an appropriate solvent (shown in Table II).

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References and Notes

1) Part XV: T. Sakamoto, M. An-naka, Y. Kondo, T. Araki, and H. Yamanaka, *Chem. Pharm. Bull.*, **36**, 1890 (1988).
2) T. Sakamoto, Y. Kondo, and H. Yamanaka, *Heterocycles*, **27**, 2225 (1988).
3) *a*) T. Sakamoto, Y. Kondo, and H. Yamanaka, *Heterocycles*, **24**, 31 (1986); *b*) T. Sakamoto, Y. Kondo, S. Iwashita, and H. Yamanaka, *Chem. Pharm. Bull.*, **35**, 1823 (1987).
4) T. Sakamoto, Y. Kondo, S. Iwashita, T. Nagano, and H. Yamanaka, *Chem. Pharm. Bull.*, **36**, 1305 (1988).
5) Y. Kondo, R. Watanabe, T. Sakamoto, and H. Yamanaka, *Chem. Pharm. Bull.*, **37**, 2814 (1989).
6) T. Sakamoto, Y. Kondo, and H. Yamanaka, *Chem. Pharm. Bull.*, **30**, 2410 (1982).
7) T. Sakamoto, Y. Kondo, and H. Yamanaka, *Chem. Pharm. Bull.*, **30**, 2417 (1982).
8) J. A. Hyatt and J. S. Swenton, *J. Org. Chem.*, **37**, 3216 (1972).