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Synthesis of Imidazo[4,5-*e*]-*as*-triazine (6-Azapurine) Derivatives

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6-Benzylidenehydrazino-3-methyluracils were treated with sodium nitrite in acetic acid to give the corresponding 5-nitrosouracils. Dehydrative cyclization of the 5-nitrosouracils with acetic anhydride afforded 6-substituted 3-methyl-7-azalumazines, ethylation of which gave 6-substituted 1-ethyl-3-methyl-7-azalumazines.

Treatment of these 7-azalumazines thus obtained and 6-substituted 1,3-dimethyl-7-azalumazines with alcoholic sodium hydroxide caused a benzilic acid type rearrangement followed by decarboxylation and oxidation by air to give the respective 5*H*-imidazo-[4,5-*e*]-*as*-triazine-6(7*H*)-ones (6-azapurines). Prolonged hydrolysis of 3-substituted 7-ethyl-5-methyl-5*H*-imidazo[4,5-*e*]-*as*-triazine-6(7*H*)-ones with alcoholic sodium hydroxide caused the ring cleavage to give 3-substituted 6-ethylamino-5-methylamino-*as*-triazines, which were fused with benzamidine hydrochloride to give rise to 3-substituted 7-ethyl-6-phenylimidazo[4,5-*e*]-*as*-triazines.

Keywords——6-azapurine; imidazo[4,5-*e*]-*as*-triazine; ring transformation; ring contraction; pyrimido[4,5-*e*]-*as*-triazine; 7-azalumazine (7-azapteridine); benzilic acid type rearrangement; 6-ethylamino-5-methylamino-*as*-triazine

A number of 8-azapurine (*s*-triazolo[4,5-*d*]pyrimidine) derivatives[2] have been synthesized as potential purine antagonists since discovery of antitumor activity in 8-azapurines.[3] Also, 2-azapurine (imidazo[4,5-*d*]-*v*-triazine) derivatives[4] have been prepared and found to be highly cytotoxic, although they were not effective as anticancer agents.[5] Though the isomeric 6-azapurine (imidazo[4,5-*e*]-*as*-triazine) ring system is of interest from a chemical as well as from a potential biological point of view, any report concerning this type of substances has not been found until two laboratories reported recently two independent synthetic routes.[6,7] Kaji and coworker[7] have described the synthesis of 6-azapurines consisting of the cyclization of 5,6-diamino-*as*-triazine-3(2*H*)-ones with one-carbon reagents. We now present the detailed account of a new approach to 6-azapurine (imidazo[4,5-*e*]-*as*-triazine) derivatives which involves a benzilic acid type rearrangement of 7-azalumazine (pyrimido-[4,5-*e*]-*as*-triazine) derivatives.[6b]

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2) *a*) R.K. Robins, "Heterocyclic Compounds," Vol. 8, ed. R.C. Elderfield, John Wiley, and Sons, 1967, p. 162, and references cited therein; *b*) A. Albert, *J. Chem. Soc.* (*B*), **1966**, 427; *c*) J.W. Bunting and D.D. Perrin, *ibid.*, **1966**, 433; *d*) A. Albert and K. Tratt, *J. Chem. Soc.* (*C*), **1968**, 344; *e*) A. Albert, *ibid.*, **1968**, 2076; *f*) A. Albert, *ibid.*, **1969**, 152; *g*) H.U. Blank, I. Wempen, and J.J. Fox, *J. Org. Chem.*, **35**, 1131 (1970); *h*) Y. Maki, M. Suzuki, K. Izuta, and S. Iwai, *Chem. Pharm. Bull.* (Tokyo), **22**, 1269 (1974); *i*) K. Senga, Y. Kanamori, S. Nishigaki, and F. Yoneda, *ibid.*, **24**, 1917 (1976); *j*) K. Senga, M. Ichiba, and S. Nishigaki, *Heterocycles*, **6**, 1915 (1977).
3) For example, the antitumor activity of 8-azapurines has been reviewed by *a*) R.K. Robins, *J. Med. Chem.*, **7**, 186 (1964), and *b*) J.A. Montgomery, T.P. Johnston, and Y.F. Shealy, "Medicinal Chemistry," part I, ed. A. Burger, Wiley-Interscience, 1970, p. 728.
4) *a*) D.W. Woolley and E. Shaw, *J. Biol. Chem.*, **189**, 401 (1951); *b*) E. Shaw and D.W. Woolley, *ibid.*, **194**, 1641 (1952).
5) *a*) J.J. Biesele, *Cancer*, **5**, 787 (1952); *b*) A. Fjelde, *Z. Krebsforsch.*, **61**, 364 (1956).
6) *a*) F. Yoneda, T. Nagamura, and M. Kawamura, *J. Chem. Soc. Chem. Comm.*, **1976**, 658; *b*) F. Yoneda, M. Kawamura, and T. Nagamatsu, K. Kuretani, A. Hoshi, and M. Iigo, *Heterocycles*, **4**, 1503 (1976).
7) K. Kaji and M. Kawase, *Chem. Pharm. Bull.* (Tokyo), **24**, 2274 (1976).

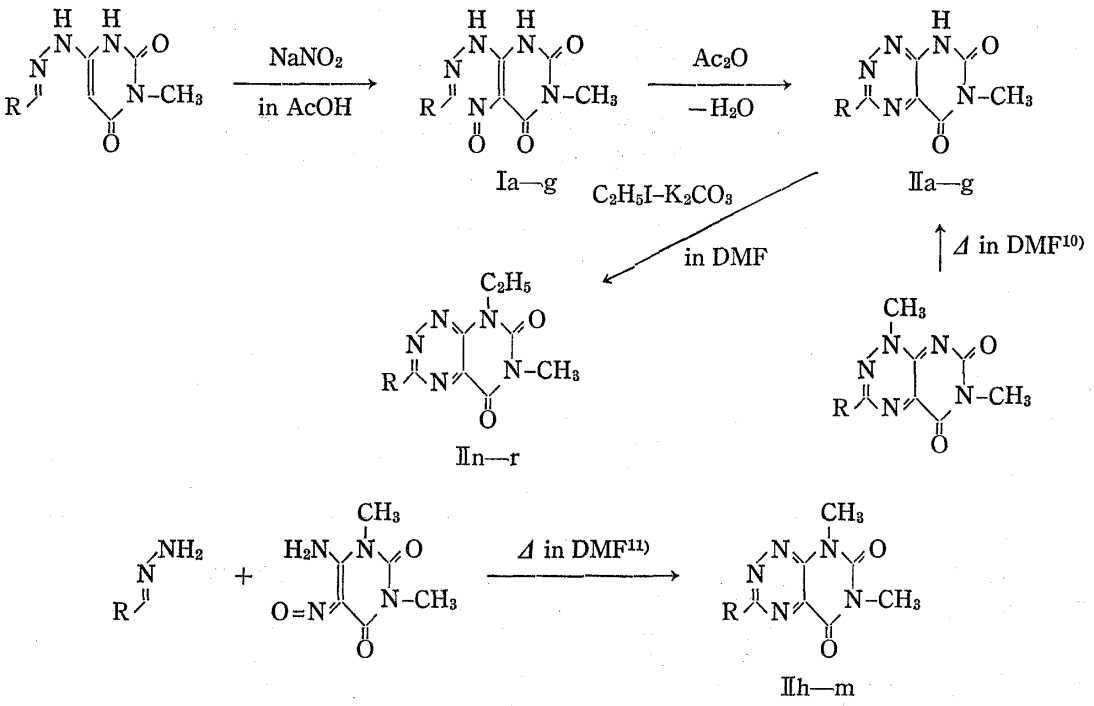
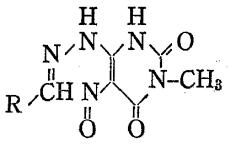


Chart 1

Syntheses of 7-Azalumazine (Pyrimido[4,5-*e*]-*as*-triazine) Precursors

It is known that the treatment of 6-benzylidenehydrazino-3-methyluracil in acetic acid with saturated aqueous sodium nitrite gives 6-benzylidenehydrazino-3-methyl-5-nitrosouracil (Ia).[8] By this method, 5-nitrosouracil derivatives (Ib—g) were obtained from the corresponding 6-benzylidenehydrazino-3-methyluracils[9] (Table I).

Table I. 6-Benzylidenehydrazino-3-methyl-5-nitrosouracils



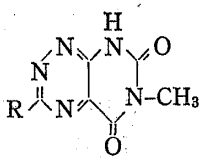
Compd. No.	R	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
Ia	C_6H_5	206	92	$C_{12}H_{11}N_5O_3$	52.74	4.06	25.63	52.68	4.12	25.47
Ib	4-Cl-C_6H_4	224	89	$C_{12}H_{10}ClN_5O_3$	46.84	3.28	22.76	46.93	3.28	22.46
Ic	3,4-Cl_2-C_6H_3	230	83	$C_{12}H_9Cl_2N_5O_3$	42.12	2.65	20.47	42.25	2.55	20.51
Id	4-CH_3O-C_6H_4	245	75	$C_{13}H_{13}N_5O_4$	51.48	4.32	23.09	51.55	4.30	23.34
Ie	3,4-CH_2O_2-C_6H_3	233	75	$C_{13}H_{11}N_5O_5$	49.21	3.49	22.08	49.07	3.46	21.79
If	4-$(CH_3)_2N$-C_6H_4	220	70	$C_{14}H_{16}N_6O_3$	53.16	5.10	26.57	53.22	5.19	26.48
Ig	4-CH_3-C_6H_4	236	81	$C_{13}H_{13}N_5O_3$	54.35	4.56	24.38	54.33	4.55	24.30

Refluxing of these 5-nitrosouracil derivatives (Ia—g) in acetic anhydride for 1 hr caused dehydrative cyclization to give the respective 6-substituted 3-methyl-7-azalumazines (3-substituted 6-methylpyrimido[4,5-*e*]-*as*-triazine-5,7(6*H*,8*H*)-diones) (IIa—g) in 40—70% yields,

8) F. Yoneda and T. Nagamatsu, *Chem. Pharm. Bull.* (Tokyo), **23**, 1885 (1975).
9) F. Yoneda and T. Nagamatsu, *Bull. Chem. Soc. Jpn.*, **48**, 1484 (1975).

which were in all respects identical with authentic samples[10] prepared by the demethylation of the corresponding toxoflavin derivatives (Table II).

Table II. 6-Substituted 3-Methyl-7-azalumazines (3-Substituted 6-Methylpyrimido[4,5-e]-*as*-triazine-5,7(6*H*,8*H*)-diones)

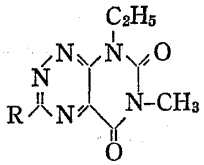


Compd. No.	R	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
IIa	C_6H_5	>320	46	$C_{12}H_9N_5O_2$	56.47	3.55	27.44	56.23	3.62	27.31
IIb	4-Cl-C_6H_4	>320	42	$C_{12}H_8ClN_5O_2$	49.75	2.78	24.18	49.69	2.77	24.04
IIc	3,4-Cl_2-C_6H_3	>320	68	$C_{12}H_7Cl_2N_5O_2$	44.46	2.18	21.61	44.38	2.19	21.40
IId	4-CH_3O-C_6H_4	>320	40	$C_{13}H_{11}N_5O_3$	54.73	3.89	24.55	54.49	3.73	24.24
IIe	3,4-CH_2O_2-C_6H_3	>320	47	$C_{13}H_9N_5O_4$	52.18	3.03	23.41	52.22	3.25	23.23
IIf	4-$(CH_3)_2N$-C_6H_4	>320	42	$C_{14}H_{14}N_6O_2$	56.37	4.73	28.18	56.22	4.65	28.23
IIg	4-CH_3-C_6H_4	>320	58	$C_{13}H_{11}N_5O_2$	57.99	4.09	26.02	58.13	4.00	26.10

6-Substituted 1,3-dimethyl-7-azalumazines (3-substituted 6,8-dimethylpyrimido[4,5-*e*]-*as*-triazine-5,7(6*H*,8*H*)-diones) (IIh—m) were obtained by the condensation of 6-amino-1,3-dimethyl-5-nitrosouracil with aldehyde hydrazones according to the procedure described previously.[11]

6-Substituted 1-ethyl-3-methyl-7-azalumazines (3-substituted 8-ethyl-6-methylpyrimido-[4,5-*e*]-*as*-triazine-5,7(6*H*,8*H*)-diones) (IIn—r) were obtained by ethylation of the corresponding 3-methyl-7-azalumazines (IIa—e) with ethyl iodide (Table III).

Table III. 6-Substituted 1-Ethyl-3-methyl-7-azalumazines (3-Substituted 8-Ethyl-6-methylpyrimido[4,5-*e*]-*as*-triazine-5,7(6*H*, 8*H*)-diones)



Compd. No.	R	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
IIn	C_6H_5	234	98	$C_{14}H_{13}N_5O_2$	59.35	4.63	24.72	59.28	4.64	24.39
IIo	4-Cl-C_6H_4	246	95	$C_{14}H_{12}ClN_5O_2$	52.92	3.81	22.04	53.01	3.80	21.85
IIp	3,4-Cl_2-C_6H_3	258	96	$C_{14}H_{11}Cl_2N_5O_2$	47.74	3.15	19.89	47.83	3.16	19.63
IIq	4-CH_3O-C_6H_4	225	95	$C_{15}H_{15}N_5O_3$	57.50	4.83	22.34	57.83	4.83	21.98
IIr	3,4-CH_2O_2-C_6H_3	230	94	$C_{15}H_{13}N_5O_4$	55.04	4.00	21.40	54.87	4.02	21.18

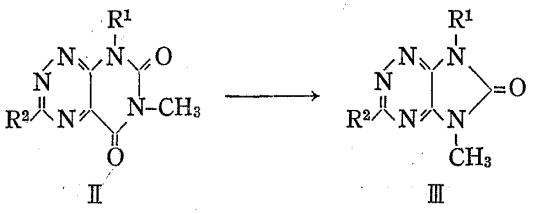
10) *a*) F. Yoneda and T. Nagamatsu, *Tetrahedron Lett.*, 1973, 1577; *b*) F. Yoneda and T. Nagamatsu, *Chem. Pharm. Bull.* (Tokyo), **23**, 2001 (1975).

11) *a*) F. Yoneda, M. Kanahori, K. Ogiwara, and S. Nishigaki, *J. Heterocycl. Chem.*, **7**, 1443 (1970); *b*) F. Yoneda and T. Nagamatsu, *Bull. Chem. Soc. Jpn.*, **48**, 2884 (1975).

Transformation of 7-Azalumazines into 6-Azapurines (Imidazo[4,5-*e*]-*as*-triazines)

Treatment of the 7-azalumazine derivatives (IIa—r) thus obtained with 10% alcoholic sodium hydroxide under the conditions indicated in Table IV, followed by acidification (evolution of carbon dioxide was observed here) with acetic acid, resulted in the formation of the respective 3-substituted 5-methyl- (IIIa—g), 3-substituted 5,7-dimethyl- (IIIh—m) and 3-substituted 7-ethyl-5-methyl-5*H*-imidazo[4,5-*e*]-*as*-triazine-6(7*H*)-ones (IIIn—r) (Table IV).

TABLE IV. Transformation of 7-Azalumazines into 6-Azapurines



II III

Starting material	Reaction conditions	6-Azapurine No.	R¹	R²	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd. (Found) C	H	N
IIa	Reflux 1 hr	IIIa	H	C_6H_5	283	61	$C_{11}H_9N_5O$	58.14 (58.20	3.99 4.01	30.82 30.64)
IIb	Reflux 1 hr	IIIb	H	4-Cl-C_6H_4	266	52	$C_{11}H_8ClN_5O$	50.49 (50.44	3.08 3.09	26.77 26.80)
IIc	Reflux 1 hr	IIIc	H	3,4-Cl_2-C_6H_3	284	49	$C_{11}H_7Cl_2N_5O$	44.61 (44.70	2.38 2.40	23.65 23.51)
IId	Reflux 1 hr	IIId	H	4-CH_3O-C_6H_4	292	42	$C_{12}H_{11}N_5O_2$	56.02 (55.88	4.31 4.51	27.23 27.21)
IIe	Reflux 2 hr	IIIe	H	3,4-CH_2O_2-C_6H_3	324	40	$C_{12}H_9N_5O_3$	53.14 (52.98	3.34 3.33	25.82 25.79)
IIf	Reflux 2 hr	IIIf	H	4-$(CH_3)_2N$-C_6H_4	281	51	$C_{13}H_{14}N_6O$	57.76 (58.02	5.22 5.25	31.10 30.09)
IIg	Reflux 1 hr	IIIg	H	4-CH_3-C_6H_4	296	53	$C_{12}H_{11}N_5O$	59.74 (59.68	4.60 4.45	29.03 28.83)
IIh	60° 10 min	IIIh	CH_3	C_6H_5	203	71	$C_{12}H_{11}N_5O$	59.74 (59.88	4.60 4.35	29.03 28.90)
IIi	60° 10 min	IIIi	CH_3	4-Cl-C_6H_4	251	65	$C_{12}H_{10}ClN_5O$	52.27 (52.30	3.66 3.62	25.40 25.28)
IIj	60° 30 min	IIIj	CH_3	3,4-Cl_2-C_6H_3	247	55	$C_{12}H_9Cl_2N_5O$	46.47 (46.59	2.93 2.88	22.58 22.42)
IIk	60° 30 min	IIIk	CH_3	4-CH_3O-C_6H_4	255	58	$C_{13}H_{13}N_5O_2$	57.56 (57.60	4.83 4.81	25.82 25.62)
IIl	60° 30 min	IIIl	CH_3	3,4-CH_2O_2-C_6H_3	330	51	$C_{13}H_{11}N_5O_3$	54.73 (54.75	3.89 3.85	24.55 24.20)
IIm	60° 30 min	IIIm	CH_3	4-$(CH_3)_2N$-C_6H_4	290	87	$C_{14}H_{16}N_6O$	59.14 (59.30	5.67 5.55	29.56 29.61)
IIn	Reflux 1 hr	IIIn	C_2H_5	C_6H_5	190	70	$C_{13}H_{13}N_5O$	61.16 (60.95	5.13 5.02	27.44 27.23)
IIo	Reflux 1 hr	IIo	C_2H_5	4-Cl-C_6H_4	225	68	$C_{13}H_{12}ClN_5O$	53.89 (54.02	4.18 4.17	24.17 23.79)
IIp	Reflux 1 hr	IIIp	C_2H_5	3,4-Cl_2-C_6H_3	206	58	$C_{13}H_{11}Cl_2N_5O$	48.16 (48.21	3.42 3.45	21.61 21.53)
IIq	Reflux 1 hr	IIIq	C_2H_5	4-CH_3O-C_6H_4	243	84	$C_{14}H_{15}N_5O_2$	58.93 (59.04	5.30 5.28	24.55 24.36)
IIr	Reflux 1 hr	IIIr	C_2H_5	3,4-CH_2O_2-C_6H_3	218	72	$C_{14}H_{13}N_5O_3$	56.18 (56.21	4.38 4.38	23.40 23.29)

The assigned structures of compounds III were deducel on the basis of elemental analyses, molecular weights as determined by mass spectrometry, IR (the presence of a carbonyl band at 1760 cm^{-1} region) and NMR data, and by consideration of their probable mode of forma-

tion (Chart 3). Furthermore, compounds IIIa—f were converted into the 5,7-dimethyl derivatives (IIIh—m) by methylation with methyl iodide and potassium carbonate in dimethylformamide for identification purpose.

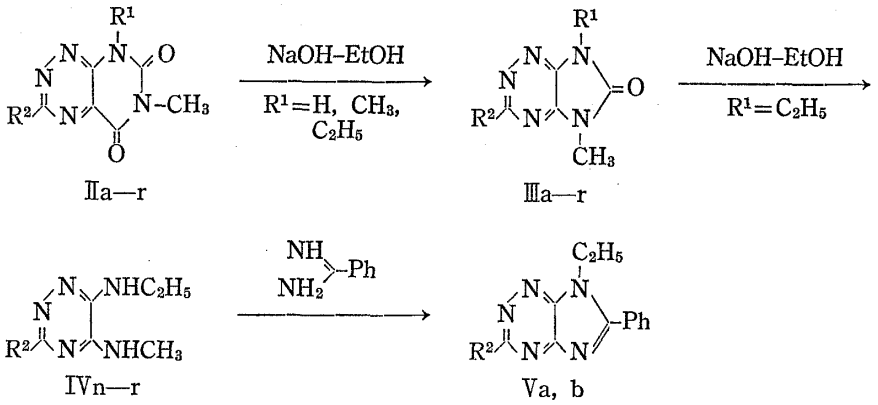


Chart 2

We suggest that these 6-azapurines are formed from 7-azalumazines by a benzilic acid type rearrangement, followed by decarboxylation and oxidation by air, as depicted in Chart 3. An analogous ring contraction was reported in the reaction of 1,3,7,9-tetramethylpy-

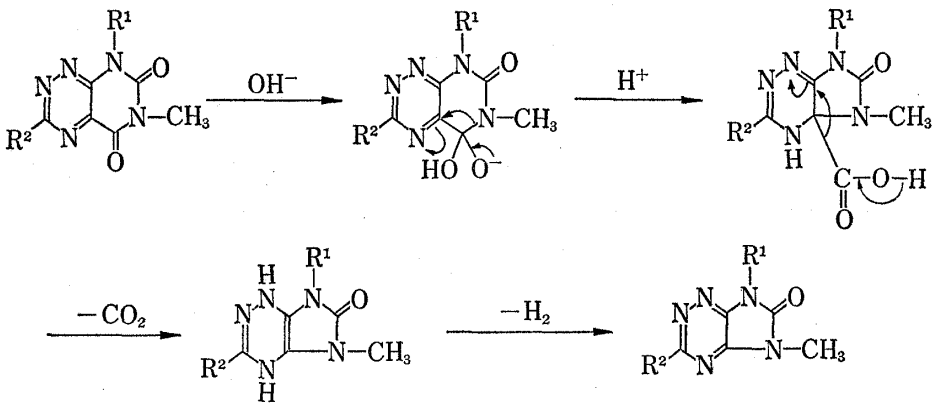
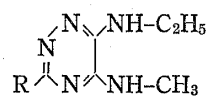


Chart 3

TABLE V. 3-Substituted 6-Ethylamino-5-methylamino-*as*-triazines



Compd. No.	R	mp (°C)	Yield (%)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N
IVa	C_6H_5	201	63	$C_{12}H_{15}N_5$	62.86	6.60	30.55	62.90	6.58	30.29
IVb	4-Cl-C_6H_4	220	56	$C_{12}H_{14}ClN_5$	54.65	5.35	26.56	54.62	5.29	26.19
IVc	3,4-Cl_2-C_6H_3	213	60	$C_{12}H_{13}Cl_2N_5$	48.33	4.39	23.49	48.41	4.35	23.38
IVd	4-CH_3O-C_6H_4	199	46	$C_{13}H_7N_5O$	60.21	6.61	27.01	59.99	6.60	26.73
IVe	3,4-CH_2O_2-C_6H_3	223	85	$C_{13}H_{15}N_5O_2$	57.13	5.53	25.63	57.21	5.54	25.55

rimido[5,4-*g*]pteridine-2,4,6,8(1*H*,3*H*,7*H*,9*H*)-tetrone 5-oxide with sodium hydroxide giving 1,3-dimethyl-5-methylaminocarbonyl-6-methylamino-1*H*-imidazo[4,5-*b*]pyrazin-2(3*H*)-one.[12]

When prolonged hydrolysis of compounds IIIn—r with 10% alcoholic sodium hydroxide was carried out, the corresponding ring-opened products, 6-ethylamino-5-methylamino-*as*-triazine derivatives (IVa—e) were obtained (Table V). The structures of IVa—e were ascertained by elemental analyses, molecular weight determination by mass spectrometry and by spectral data (the presence of two NH absorptions at 3270 and 3170 cm^{-1} regions and disappearance of a carbonyl band at 1760 cm^{-1} region).

Fusion of IVa and IVb with excess benzamidine hydrochloride at 180° caused the elimination of methylamine and ammonia and gave rise to 3-substituted 7-ethyl-6-phenylimidazo-[4,5-*e*]-*as*-triazines (2-substituted 7-ethyl-8-phenyl-6-azapurines) (Va and Vb). The elemental analyses and spectral data of Va and Vb (disappearance of two NH absorptions of IV in IR and survival of ethyl signals in NMR) were consistent with the assigned structures.

Table VI gives ultraviolet absorption data for some 6-azapurines, in which the expected hypochromic shifts were observed as compared with absorptions of the corresponding 7-azalumazines.[13]

Table VI. UV Maxima of 6-Azapurines

Compd. No.	λ_{max}^{EtOH} nm (log ε)
IIIa	306(3.68), 287 sh(3.69), 271 sh(3.74), 243(3.97)
IIIb	308(3.78), 289 sh(3.83), 278(3.84), 247(4.02)
IIId	320 sh(3.86), 279(4.25), 253(4.19)
IIIg	310 sh(3.60), 241(4.11)
IIIh	310(3.98), 271(4.08), 245(4.32)
IIIi	309(4.07), 275(4.25), 249(4.39)
IIIn	309(3.81), 270(3.88), 245(4.15)
IIIo	309(4.11), 289(4.25), 249(4.36)
Va	337(3.66), 270 sh(3.78), 259(3.87)
Vb	338(3.99), 289 sh(4.00), 264.5(4.26)
IIIh[a]	375(3.55), 278(4.45)

a) 1,3-Dimethyl-6-phenyl-7-azalumazine.[13]

Experimental[14]

6-Benzylidenehydrazino-3-methyl-5-nitrosouracils (Ia—g). General Procedure——To a stirred suspension of a 6-benzylidenehydrazino-3-methyluracil (0.01 mol) in AcOH (50 ml) was added saturated aqueous solution of $NaNO_2$ (0.015 mol) drop by drop under cooling at 5°. The reaction solution was then stirred at room temperature for 2 hr, during which time crystals were separated. The crystals were collected by filtration, washed with H_2O, and recrystallized from EtOH or DMF to give pale green microcrystalline powder of 5-nitrosouracil derivatives (Ia—g) (Table I).

6-Substituted 3-Methyl-7-azalumazines (3-Substituted 6-Methylpyrimido[4,5-*e*]-*as*-triazine-5,7(6*H*,8*H*)-diones) (IIa—g). General Procedure——The 5-nitrosouracil derivatives (Ia—g) (0.01 mol) thus obtained were refluxed in acetic anhydride (30 ml) for 3 hr. The reaction solution was evaporated into dryness under reduced pressure and the residue was treated with EtOH to cause the separation of yellow crystals which were filtered off and dried. Recrystallization from DMF–EtOH (1:1) gave yellow microcrystalline powder of the corresponding 7-azalumazines which were identical with authentic samples.[10]

6-Substituted 1-Ethyl-3-methyl-7-azalumazines (3-Substituted 8-Ethyl-6-methylpyrimido[4,5-*e*]-*as*-triazine-5,7(6*H*,8*H*)-diones) (IIn—r). General Procedure——A mixture of a 6-substituted 3-methyl-7-

12) E.C. Taylor, Y. Maki, and A. McKillop, *J. Org. Chem.*, **37**, 1601 (1972).
13) F. Yoneda, T. Nagamatsu, and K. Shinomura, *J. Chem. Soc. Perkin I*, **1976**, 713.
14) All melting points were uncorrected. NMR spectra were determined with a JEOL-PMX 60 spectrometer (tetramethylsilane as internal standard). Identity of compounds was confirmed by comparison of infrared spectra (Nujol mulls) with JASCO IR-1A spectrophotometer.

azalumazine (IIa—e) (0.1 mol), ethyl iodide (18.7 g, 0.12 mol) and K_2CO_3 (27.6 g, 0.2 mol) in DMF (150 ml) were refluxed for 2 hr. After cooling, the reaction mixture was diluted with H_2O (150 ml) to cause the separation of pale yellow crystals, which were filtered off, washed with H_2O and dried. Recrystallization from EtOH gave pale yellow needles (Table III).

Transformation of 7-Azalumazines (II) into 6-Azapurines (III). General Procedure——To 10% ethanolic sodium hydroxide (20 ml) was added a 7-azalumazine (0.004 mol) and the mixture was refluxed under the conditions indicated in Table IV. After cooling, the reaction mixture was acidified with AcOH and evaporated *in vacuo* into dryness. The residue was treated with H_2O and the separated crystals were filtered off and recrystallized from EtOH or DMF to give colorless needles of the respective 6-azapurines (Table IV).

3-Substituted 6-Ethylamino-5-methylamino-*as*-triazines (IVa—e). General Procedure——To 10% ethanolic sodium hydroxide (20 ml) was added a 7-ethyl-5-methyl-5*H*-imidazo[4,5-*e*]-*as*-triazine-6(7*H*)-one (IIIn—r) (0.004 mol) and the mixture was refluxed for 6 hr. After cooling, the reaction mixture was neutralized with AcOH to cause the separation of colorless crystals, which were collected by filtration, washed with H_2O and recrystallized from EtOH to give colorless microcrystalline powder of a 6-ethylamino-5-methylamino-*as*-triazine (IVa—e) (Table V).

3,6-Diphenyl-7-ethylimidazo[4,5-*e*]-*as*-triazine (2,8-Diphenyl-7-ethyl-6-azapurine) (Va)——A mixture of 6-ethylamino-5-methylamino-3-phenyl-*as*-triazine (IVa) (0.3 g, 0.0013 mol) and benzamidine hydrochloride (0.6 g, 0.0038 mol) was fused at 180° for 1 hr. After cooling, the reaction mixture was triturated in H_2O and the crystals were filtered off and dried. Recrystallization from DMF–EtOH (1: 1) gave colorless needles (0.3 g, 79%), mp 195°. *Anal.* Calcd. for $C_{18}H_{15}N_5$: C, 71.74; H, 5.02; N, 23.24. Found: C, 71.86; H, 5.11; H, 23.01.

3-(4-Chlorophenyl)-7-ethyl-6-phenylimidazo[4,5-*e*]-*as*-triazine [2-(4-Chlorophenyl)-7-ethyl-8-phenyl-6-azapurine] (Vb)——A mixture of 3-(4-chlorophenyl)-6-ethylamino-5-methylamino-*as*-triazine (IVb) (0.3 g, 0.001 mol) and benzamidine hydrochloride (0.6 g, 0.0038 mol) was treated as above to give colorless crystals (0.31 g, 81%), mp 198°. *Anal.* Calcd. for $C_{18}H_{14}ClN_5$: C, 64.38; H, 4.20; N, 20.86. Found: C, 64.39; H, 4.23; N, 20.48.

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