v-Triazolo[4,5-*d*]pyrimidines (8-Azapurines). Part XIV.[1] Synthesis of 6-Unsubstituted 8-Azapurines from Ring *N*-Alkylated 4-Amino-1,2,3-triazole-5-carbaldehydes

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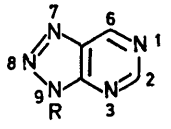
4-Amino-3-benzyl-1,2,3-triazole-5-carbaldehyde † (6c), on treatment with phosphoryl chloride and dimethylformamide, gave 3-benzyl-4-dimethylaminomethyleneamino-1,2,3-triazole-5-carbaldehyde (7), which was cyclised by ammonium acetate to give 9-benzyl-8-azapurine (1b). Likewise, 7-(and 8-)methyl-8-azapurine were obtained from 4-amino-1-(and 2-)methyl-1,2,3-triazole-5-carbaldehyde, respectively. The foregoing amino-aldehydes, heated with triethyl orthoformate, triethyl orthoacetate, and tetraethyl orthocarbonate, yielded (respectively) 4-ethoxymethyleneamino-, 4-(α-ethoxyethylideneamino)-, and 4-diethoxymethyleneamino-derivatives, which were cyclised by ammonia to give 7-methyl-, 9-benzyl-, 9-benzyl-2-methyl-, 2,7- and 2,8-dimethyl-, 9-benzyl-2-ethoxy-, and 2-ethoxy-8-methyl-8-azapurines.

Fission of 9-benzyl-2-ethoxy-8-azapurine gave 9-benzyl-8-azapurin-2-one. 2-Amino-8-methyl(and 2-amino-9-benzyl)-8-azapurine were made from the corresponding 2-ethoxy-derivatives and ammonia. 4-Amino-3-benzyl-1,2,3-triazole-5-carbaldehyde was converted into 4-amino-3-benzyl-5-dimethoxymethyl-1,2,3-triazole (13) and a condensed product (14). The amino-acetal (13) and ethyl chloroformate yielded 3-benzyl-4-ethoxycarbonylamino-1,2,3-triazole-5-carbaldehyde. An improved synthesis of 4-amino-2-methyl-1,2,3-triazole-5-carbaldehyde is given. I.r. and n.m.r. spectra are recorded and discussed.

THE potent and unique mutagenic action of 2-aminopurine on bacteria and phage [2] and its mild carcinostatic action in mice [3] have awakened interest in 6-unsubstituted 8-azapurines (1). These compounds also have special chemical interest because of the addition reactions readily undergone by an unhindered 1,6-double bond.[4-8] All known compounds of this type, synthesised mainly by cyclisation of 4,5-diaminopyrimidine derivatives (2), are either 9-alkylated [4] or else unsubstituted [4,9,10] in the triazole ring. Newer methods, using 4-amino-1,2,3-triazole-5-carboxamides [*e.g.* (3)], did not furnish any of the required 2-substituted derivatives, such as (4b) and (5c). The present work describes a new general method for making 7- and 8-methyl and 9-benzyl derivatives of 6-unsubstituted 8-azapurines, mostly substituted in the 2-position, from 4-amino-1,2,3-triazole-5-carbaldehyde (6) alkylated, in turn, on each of the three ring nitrogen atoms. The 3-benzyl- and 1-methyl-amino-aldehydes were prepared as in ref. 11; an improved preparation of the 2-methyl analogue is given.

The weakness as a nucleophile of the amino-group in the aldehydes (6) prevented *N*-acylation; hence Bischler's quinazoline synthesis [12] could not be applied. Even conversion into an acetal, which permitted *N*-acylation in the 2-aminopyrazine series,[13] sufficed in only one example. However (chloromethylene)dimethylammonium chloride [14] converted 4-amino-3-benzyl- into 3-benzyl-4-dimethylaminomethyleneamino-1,2,3-triazole-5-carbaldehyde (7) (see Table 1), cyclised by ammonium acetate to 9-benzyl-8-azapurine (see Table 2).

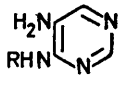
† In this series, the amino-group of aminotriazole has consistently been numbered **4**, to facilitate comparisons.



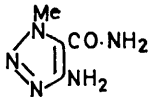
(1)

a; R = H

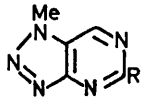
b; R = CH_2Ph



(2)



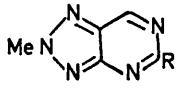
(3)



(4)

a; R = H

b; R = Me

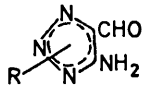


(5)

a; R = H

b; R = Me

c; R = OEt



(6)

a; R = 1-Me

b; R = 2-Me

c; R = 3-CH_2Ph

The constitution of the amidine aldehyde (7) was confirmed by strong i.r. absorption at 1690 and 1625 cm^{-1} (C=O and C=N str.) and by n.m.r. signals at τ [$(CD_3)_2SO$] −0·13 (s, CHO), 0·78 (1H, s, CH=N), and 6·80(s) and

[1] Part XIII, A. Albert and W. Pendergast, *J.C.S. Perkin I*, 1973, 1625.
[2] E. Freese, *J. Mol. Biol.*, 1959, **1**, 87; R. Rudner, *Biochem. Biophys. Res. Comm.*, 1960, **3**, 275; H. Gottschling and E. Freese, *Z. Naturforsch.*, 1961, **16b**, 515.
[3] R. K. Robins, *J. Medicin. Chem.*, 1964, **7**, 186.
[4] A. Albert, *J. Chem. Soc.* (*B*), 1966, 427.
[5] J. W. Bunting and D. D. Perrin, *J. Chem. Soc.* (*B*), 1966, 433.
[6] A. Albert and K. Tratt, *J. Chem. Soc.* (*C*), 1968, 344.
[7] A. Albert, *J. Chem. Soc.* (*C*), 1968, 2076.
[8] A. Albert and W. Pendergast, *J.C.S. Perkin I*, 1972, 457.
[9] G. M. Timmis, D. G. Felton, H. O. J. Collier, and P. L. Huskinson, *J. Pharm. Pharmacol.*, 1957, **9**, 46.
[10] F. Bergmann, G. Levin, and H. Kwietny, *Arch. Biochem. Biophys.*, 1959, **80**, 318.
[11] A. Albert and H. Taguchi, *J.C.S. Perkin I*, 1973, 1629.
[12] A. Bischler, *Ber.*, 1891, **24**, 506.
[13] A. Albert and K. Ohta, *J. Chem. Soc.* (*C*), 1971, 2357.
[14] H. Bredereck ,R. Gompper, K. Klemm, and H. Rempfer, *Chem. Ber.*, 1959, **92**, 837.

6·88(s) (NMe_2). 7- and 8-Methyl-8-azapurine (respectively) were obtained by adding aqueous ammonia to the reaction mixture of 4-amino-1-(and 2-)methyl-1,2,3-triazole-5-carbaldehyde with dimethylformamide and phosphoryl chloride. That an amidino-group was easily introduced into the amino-aldehydes (whereas acylation *failed*) is attributed to stabilisation of the product by conjugation with the nucleus (7).

the 4-(α-ethoxyethylideneamino)-derivative (8b) (see Table 1), which gave 2,7-dimethyl-8-azapurine (4b) with ammonia (see Table 2). The 3-benzyl- and 2-methyl-4-(α-ethoxyethylideneamino)-compounds (9b) and (10a), similarly prepared from the appropriate amino-aldehydes (6b or c), were readily cyclised to 2,8-dimethyl-8-azapurine (5b) and 9-benzyl-2-methyl-8-azapurine. Structures of the aldehyde derivatives were confirmed by

TABLE 1

Reactions of 4-Amino-1,2,3-triazole-5-carbaldehydes

R in starting material	Reagent	Reaction temp.[a]	Reaction time (h)	R′ in product	Purification[b]	M.p. (°C)[c]	Yield (%)	Analyses: Found (%) C	H	N	Formula	Required (%) C	H	N
1-Me	$Me_2N{\cdot}CHO{-}POCl_3$	A	24	N=CH·NMe_2	D									
2-Me	$Me_2N{\cdot}CHO{-}POCl_3$	A	24	N=CH·NMe_2	D									
3-CH_2Ph	$Me_2N{\cdot}CHO{-}POCl_3$	A	10	N=CH·NMe_2	E(I + J), M	95	83	61·0	5·9	26·9	$C_{12}H_{15}N_5O$	60·7	5·9	27·2
1-Me	$HC(OEt)_3$	B	3	N=CH·OEt	F(K)	70	72	46·3	5·55		$C_7H_{10}N_4O_2$	46·15	5·5	
3-CH_2Ph	$HC(OEt)_3$	C	7	N=CH·OEt	G	Viscous liq.	82[d]							
1-Me	$MeC(OEt)_3$	B	2	N=C(Me)·OEt	E(J), N	70	79	49·2	6·1		$C_8H_{12}N_4O_2$	49·0	6·2	
2-Me	$MeC(OEt)_3$	C	7	N=C(Me)·OEt	H	Liq. (O)	58	48·8	6·3	28·8	$C_8H_{12}N_4O_2$	49·0	6·2	28·6
3-CH_2Ph	$MeC(OEt)_3$	C	4	N=C(Me)·OEt	G, F(L)	64	65	62·0	5·9	20·9	$C_{14}H_{16}N_4O_2$	61·75	5·9	20·6
2-Me	$C(OEt)_4$	C	15	N=C(OEt)$_2$	G, H	Liq. (P)	40	48·1	6·5	24·8	$C_9H_{14}N_4O_2$	47·8	6·2	24·8
3-CH_2Ph	$C(OEt)_4$	C	8	N=C(OEt)$_2$	G	Viscous liq.	61[d]							

[a] A, 20—25; B, 120°; C, reflux. [b] D, cyclisation with ammonia performed without isolation; E, recrystallisation; F, sublimation; G, column chromatography on alumina [50 parts, eluted with 1 : 1 light petroleum (b.p. 60—80°)–diethyl ether]; H, distillation; I, benzene; J, light petroleum (b.p. 60—80°); K, 80° and 0·1 mmHg; L, 110° and 0·1 mmHg; M, dried at 33° and 0·01 mmHg; N sublimed at 50° and 0·05 mmHg. [c] O, b.p. 83—84° at 0·1 mmHg; P, b.p. 108—110° at 0·1 mmHg. [d] Crude product.

TABLE 2

Cyclisation to 8-azapurines

Starting material R	R′	Reagent[a]	Reaction temp.[b]	Reaction time (h)	Product R	R″	Purification[c]	M.p. (°C)	Yield (%)	Analyses: Found (%) C	H	N	Formula	Required (%) C	H	N
1-Me	N=CH·OEt	A	C	7	7-Me	H	E(G)	166—167 (lit.,[6] 167)	79	[d] (ref. 6)						
3-CH_2Ph	N=CH·OEt	A	C	7	9-CH_2Ph	H	E(H)	115—116 (lit.,[4] 117—118)	74	[d] (ref. 4)						
3-CH_2Ph	N=CH·NMe_2	B	D	8	9-CH_2Ph	H	E(I)	114—115	76	[d] (ref. 4)						
1-Me	N=C(Me)·OEt	A	C	7	7-Me	Me	F(J + K), M	147	73	48·0	4·7	47·3	$C_6H_7N_5$	48·3	4·7	47·0
2-Me	N=C(Me)·OEt	A	C	7	8-Me	Me	E(L)	143	71	48·1	4·95	46·9	$C_6H_7N_5$	48·3	4·7	47·0
3-CH_2Ph	N=C(Me)·OEt	A	C	7	9-CH_2Ph	Me	F(K), N	64	63	64·3	5·0	31·4	$C_{13}H_{11}N_5$	64·0	4·9	31·1
2-Me	N=C(OEt)$_2$	A	C	24	8-Me	OEt	F(K), O	121	66	47·0	5·3	39·5	$C_7H_9N_5O$	46·9	5·1	39·1
3-CH_2Ph	N=C(OEt)$_2$	A	C	34	9-CH_2Ph	OEt	F(K), N	88	64	61·5	5·3	27·5	$C_{13}H_{13}N_5O$	61·2	5·1	27·4

[a] A, ethanolic ammonia; B, ammonium acetate in methanol. [b] C, 20—25°; D, reflux. [c] E, sublimation; F, recrystallisation; G, 130° and 0·1 mmHg; H, 110° and 0·05 mmHg; I, 110° and 0·1 mmHg; J, benzene; K, light petroleum (b.p. 60—80°); L, 100° and 0·1 mmHg; M, sublimed at 120° and 0·05 mmHg; N, dried at 25° and 0·1 mmHg; O, dried at 65° and 0·1 mmHg. [d] Known compound.

Thus 4-amino-1-methyl-1,2,3-triazole-5-carbaldehyde was heated with triethyl orthoformate to give the 4-ethoxymethyleneamino-derivative (8a) (see Table 1), which cold ethanolic ammonia converted into 7-methyl-8-azapurine [6] (4a) (see Table 2). 9-Benzyl-8-azapurine [4] was obtained likewise from the 3-benzyl-amino-aldehyde (6c) *via* the 4-ethoxymethyleneamino-derivative (9a). (In contrast, the condensations [15] of *o*-ethoxymethyleneamino-carbonitriles with ammonia give fused 4-aminopyrimidines.)

Although orthoesters often form acetals,[16] this did not occur in the new reaction. 4-Amino-1-methyl-1,2,3-triazole-5-carbaldehyde and triethyl orthoacetate yielded n.m.r. (Table 3) and i.r. spectra (Table 4). There was no significant difference amongst the reactivities of the three amino-aldehydes with these orthoesters. The 2-methyl and 3-benzyl derivatives were stable, but the unstable 1-methyl derivatives (8a and b) were best submitted to ring closure with ammonia as quickly as possible.

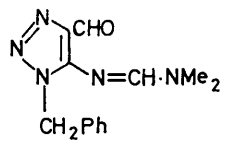
For making 6-unsubstituted 8-azapurin-2-ones (11), the ideal intermediates would be the 4-ethoxycarbonylamino-1,2,3-triazole-5-carbaldehydes [*e.g.* (12)]. Unfortunately, 4-amino-3-benzyl-1,2,3-triazole-5-carbaldehyde (6c) could not be induced to react with ethyl chloroformate or diethyl pyrocarbonate.[17] To increase the nucleophilicity of the amino-group, the amino-

[15] (*a*) E. C. Taylor and A. McKillop, 'The Chemistry of Cyclic Enamino-nitriles and *o*-Amino-nitriles,' Interscience, New York, 1970, pp. 238, 243; (*b*) A. Albert and K. Ohta, *J. Chem. Soc.* (*C*), 1971, 3727.

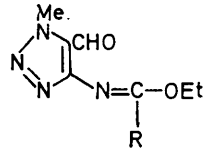
[16] R. H. De Wolfe, 'Carboxylic Ortho Acid Derivatives,' Academic Press, New York and London, 1970, p. 154.

[17] E. Dyer and H. Richmond, *J. Medicin. Chem.*, 1965, **8**, 195.

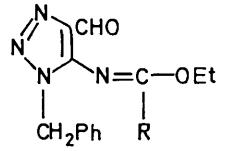
aldehyde (6c) was converted into an acetal (13) (with boron trifluoride–methanol complex; 53% yield). The acetal had strong i.r. absorption at 1050 and 1100 cm^{-1}



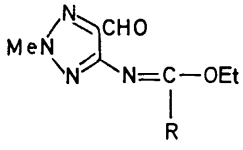
(7)



(8)
a; R=H
b; R=Me



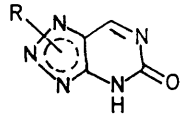
(9)
a; R=H
b; R=Me
c; R=OEt



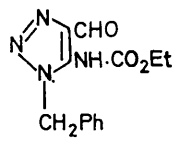
(10)
a; R=Me
b; R=OEt

(C–O–C) and no absorption around 1700 cm^{-1}. The n.m.r. spectrum showed singlets at τ 6·66 (6H, 2 × OMe) and 4·39 (1H, O·CH·O).

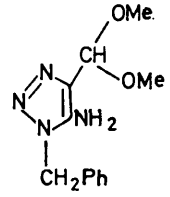
A dimeric by-product (14) of the acetalisation reaction (19%) showed u.v. absorption at 337 nm (log ε 4·30)



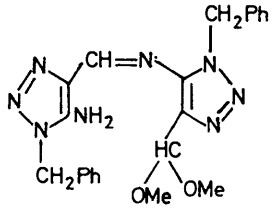
(11)



(12)



(13)



(14)

[*cf.* 248 nm (log ε 3·75) for the acetal (13)] and n.m.r. signals corresponding to two benzyl groups. A singlet at τ 6·60 (6H) was assigned to the two methoxy-groups, and two singlets at τ 4·45 (1H) and 0·84 (1H) were assigned to C*H*$(OMe)_2$ and C*H*=N systems, respectively.

The desired carbamate (12) was prepared from the amino-acetal (13) by the action of ethyl chloroformate in pyridine, followed by the hydrolysis of the acetal group, but in only poor yield. The following approach to 9-benzyl-8-azapurin-2-one was more successful.

Although a little is known about the reaction [18] of orthocarbonates with amines, they have never been used to prepare intermediates for ring closure. However, it was thought that they should condense with the amino-aldehydes (6) to give diethoxymethyleneamino-derivatives [*e.g.* (10b)], which could be cyclised readily to 2-ethoxy-8-azapurines, possible intermediates for making 8-azapurin-2-ones or 2-amino-8-azapurines. Tetraethyl orthocarbonate (made from chloropicrin by ethanolysis [19] with sodium ethoxide) was heated with 4-amino-2-methyl-1,2,3-triazole-5-carbaldehyde (6b) to give the 4-diethoxymethyleneamino-derivative (10b), identified by i.r. and n.m.r. spectra (see Tables 3 and 4). Stirring this compound (10b) in cold ethanolic ammonia gave a good yield of 2-ethoxy-8-methyl-8-azapurine (5c). Similar treatment of 4-amino-3-benzyl-1,2,3-triazole-5-carbaldehyde (6c) with the orthocarbonate afforded the 4-diethoxymethyleneamino-derivative (9c), as a viscous oil, which decomposed on distillation. Elemental analysis was not attempted, but the structure was confirmed by the n.m.r. spectrum, which showed the presence of two equivalent ethyl groups, an aldehyde, and a benzyl group. Stirring the compound (9c) in cold ethanol ammonia gave 9-benzyl-2-ethoxy-8-azapurine, the ethoxy-group of which was hydrolysed to give 9-benzyl-8-azapurin-2-one, [20] most satisfactorily with molten (moist) pyridine hydrochloride. [21]

2-Amino-8-methyl-(and 9-benzyl-)8-azapurine were obtained by heating these ethoxy-derivatives in ethanolic ammonia; moderately severe conditions were required. This replacement of an alkoxy- by an amino-group, although never observed in the 2-position of a purine nucleus, is facilitated here by the electron-attracting effect of the additional doubly-bonded nitrogen atom.

EXPERIMENTAL

I.r. spectra were measured with a Unicam SP 200 spectrometer calibrated with polystyrene at 1603 cm^{-1} (for mulls in Nujol or liquid films). ^1H N.m.r. spectra were determined with a Perkin-Elmer R10 instrument operating at 33·3° and 60 MHz, with tetramethylsilane as internal standard. The presence of an NH group was confirmed by exchange with D_2O. U.v. spectra were taken with a Unicam SP 800 spectrophotometer; the wavelength and intensity of each maximum were then checked with a Unicam SP 500 (series 2) manual instrument. N.m.r. and i.r. data for the 1,2,3-triazole-5-carbaldehyde derivatives obtained by the reaction of 4-amino-1,2,3-triazole-5-carbaldehydes with orthoesters are summarised in Tables 3 and 4.

Yields for substances without sharp m.p. refer to material giving only one spot on paper chromatograms run in (a) aqueous 3% ammonium chloride and (b) butan-1-ol–5N-acetic acid, or on t.l.c. (silica gel or alumina). Identity of compounds prepared by different routes was established by i.r. spectral, paper chromatographic, and (where possible) mixed m.p. comparisons.

[18] H. Tieckelmann and H. W. Post, *J. Org. Chem.*, 1948, **13**, 268; R. F. Meyer, *ibid.*, 1963, **28**, 2902; R. M. McDonald and R. A. Krueger, *Tetrahedron Letters*, 1965, **857**; *J. Org. Chem.*, 1966, **31**, 488.

[19] J. D. Roberts and R. E. McMahon, *Org. Synth.*, Coll. Vol. IV, Wiley, New York, 1963, p. 457.

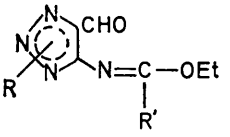
[20] A. Albert, *Chem. Comm.*, 1970, 858, and unpublished data.

[21] V. Prey, *Ber.*, 1941, **74**, 1219.

3-Benzyl-4-dimethylaminomethyleneamino-1,2,3-triazole-5-carbaldehyde (7).—4-Amino-3-benzyl-1,2,3-triazole-5-carbaldehyde [11] (0·61 g, 3·0 mmol) was added to a cooled mixture of phosphoryl chloride (0·57 ml) and dimethylformamide (1·5 ml) with stirring. The mixture was then stirred at 20—25° for 10 h, poured on ice (20 g), and set aside at 4°. The deposited crystals, collected and recrystallised from benzene–light petroleum (b.p. 60—80°), gave the *4-dimethylaminomethyleneamino-derivative* (see Table 1).

TABLE 3

^{1}H N.m.r. spectra (33·3° in $CDCl_3$) of 1,2,3-triazole-5-carbaldehyde derivatives



1,2,3-Triazole		τ Values			
R	R′	CHO [a]	R′ [a]	O·CH_2·CH_3 [b]	O·CH_2·CH_3 [c]
1-Me	H	−0·02	1·35	5·54	8·59
3-CH_2Ph	H	−0·10	0·91	5·59	8·61
1-Me	Me	0·18	7·75 [d]	5·71	8·62
2-Me	Me	0·00	8·06 [d]	5·70	8·65
3-CH_2Ph	Me	−0·02	8·37 [d]	5·75	8·66
2-Me	OEt	0·00		5·69 [e]	8·71 [e]
3-CH_2Ph	OEt	−0·01		5·75 [e]	8·75 [e]

[a] All are singlet peaks. [b] All are quartet peaks (*J* 7 Hz). [c] All are triplet peaks (*J* 7 Hz). [d] Assigned to CMe(3H). [e] Chemical shift modified by the second ethoxy-group R′; integration doubled.

TABLE 4

I.r. spectra of 1,2,3-triazole-5-carbaldehyde derivatives

1,2,3-Triazole [a]		$\nu_{max.}$/cm^{-1}						
R	R′	HC=O	C=N	C–O–C				Method [b]
1-Me	H	1680	1640	1260				A
3-CH_2Ph	H	1690	1620	1255	1220			B
1-Me	Me	1690	1665	1290				A
2-Me	Me	1700	1660	1280				B
3-CH_2Ph	Me	1700	1645	1290				A
2-Me	OEt	1700	1660	1305	1275	1075	1030	B
3-CH_2Ph	OEt	1695	1630	1310	1280	1065	1020	B

[a] Symbols having the same meaning as in Table 3. [b] A, Nujol mull; B, Liquid film.

3-Benzyl-v-triazolo[4,5-d]*pyrimidine* (*9-Benzyl-8-azapurine*) (1b).—The aldehyde (7) (0·13 g, 0·5 mmol) and ammonium acetate (0·30 g) in methanol (1 ml) were heated under reflux for 8 h. The cooled mixture was taken to dryness *in vacuo* and the residue was extracted with benzene (3 × 10 ml). The extract was taken to dryness under vacuum and the residue, when sublimed (see Table 2), gave 9-benzyl-8-azapurine (1b).[4]

4-Amino-2-methyl-1,2,3-triazole-5-carbaldehyde (6b) (improved synthesis, *cf.* ref. 11).—4-Amino-2-methyl-1,2,3-triazole-5-carbonitrile [20] (2·46 g, 0·020 mol) in 0·2N-hydrochloric acid (500 ml) was hydrogenated at 20° and 1 atm over 10% Pd–C (0·2 g) (uptake 0·02 mol. equiv.). The mixture was filtered and the filtrate adjusted to pH 7 with potassium hydrogen carbonate; this mixture was extracted with chloroform (3 × 200 ml). The extract was dried (Na_2SO_4) and taken to dryness *in vacuo*; the residue, sublimed at 70° and 0·01 mmHg, gave the aldehyde (74%), m.p. 100—101° (lit.,[11] 102°).

1-Methyl-1H-v-triazolo[4,5-d]*pyrimidine* (*7-Methyl-8-azapurine*) (4a).—4-Amino-1-methyl-1,2,3-triazole-5-carbaldehyde [11] (0·13 g, 1·0 mmol) was added to a cooled mixture of phosphoryl chloride (0·2 ml) and dimethylformamide (1·5 ml) with stirring. Stirring was continued for 24 h. Ice (10 g) was added to the mixture, which was then adjusted to pH 10·5 with aqueous 13N-ammonia, then stirred at 20—25° for 2 h and extracted with chloroform (3 × 20 ml). The extract was dried (Na_2SO_4) and taken to dryness *in vacuo*; the residue, purified by sublimation (see Table 2), gave 7-methyl-8-azapurine (48%), m.p. 165—166° (lit.,[6] 167°) (see Table 2 for a different synthesis). 4-Amino-2-methyl-1,2,3-triazole-5-carbaldehyde (6b) [11] similarly gave 8-methyl-8-azapurine (5a) (61%), m.p. 133° (lit.,[7] 133·5°).

General Procedure for the Reaction of 4-Amino-1,2,3-triazole-5-carbaldehydes with Orthoesters.—The appropriate 4-amino-1,2,3-triazole-5-carbaldehyde [11] (3·0 mmol), dissolved or suspended in the orthoester (10 ml), was heated (see Table 1 for temperature and time); the reaction mixture was then evaporated *in vacuo* [see Table 1 for m.p.s (or b.p.s) and yields].

Ring Closure of the Foregoing Compounds.—The appropriate triazole derivative (1·0 mmol), dissolved in ethanolic ammonia (10 ml), was stirred at 20—25° for the time given in Table 2. The mixture was taken to dryness *in vacuo* and the residue purified as in Table 2, which also gives m.p.s and yields.

Reaction of 4-Amino-3-benzyl-1,2,3-triazole-5-carbaldehyde with Boron Trifluoride–Methanol Complex.—4-Amino-3-benzyl-1,2,3-triazole-5-carbaldehyde [11] (1·0 g, 5·0 mmol), boron trifluoride–ether complex (0·7 ml), and methanol (12 ml) were stirred at room temperature for 6 h. The mixture was poured into water (30 ml) containing anhydrous sodium carbonate (3 g), then extracted with chloroform (3 × 10 ml). The extract was dried (K_2CO_3) and evaporated *in vacuo*. The residue was dissolved in benzene and passed through an alumina (30 g) column. Material eluted with diethyl ether was collected and rechromatographed. Elution with diethyl ether and recrystallisation of the product from benzene (20 parts), gave *4-amino-3-benzyl-5-dimethoxymethyl-1,2,3-triazole* (13), m.p. 110° [Found (material dried at 65° and 0·005 mmHg): C, 58·2; H, 6·3; N, 22·7. $C_{12}H_{16}N_4O_2$ requires C, 58·05; H, 6·5; N, 22·6%]. Material eluted with ethyl acetate after the elution with ether was collected and recrystallised from methanol (20 parts) to give *4-amino-3-benzyl-5-(1-benzyl-4-dimethoxymethyl-1,2,3-triazol-5-yliminomethyl)-1,2,3-triazole* (14), m.p. 168° (efferv.) [Found (material dried at 65° and 0·01 mmHg): C, 60·8; H, 5·55; N, 26·2. $C_{22}H_{24}N_8O_2$ requires C, 61·1; H, 5·6; N, 25·9%].

3-Benzyl-4-ethoxycarbonylamino-1,2,3-triazole-5-carbaldehyde (12).—Ethyl chloroformate (0·22 g) was added to a cooled solution of the acetal (13) (0·10 g, 0·4 mmol) in pyridine (0·5 ml) with stirring. The mixture was stirred at room temperature for 40 h, then the reagents were removed *in vacuo* (*ca.* 50°). The residue was mixed with 0·1N-hydrochloric acid (5 ml) and set aside for 2 h. The mixture was extracted with ethyl acetate (3 × 10 ml) and the extract was dried (Na_2SO_4) and evaporated *in vacuo*. The residue was submitted to t.l.c. (alumina; ethyl acetate). A band (R_F 0·4) which absorbed u.v. light of mainly 254 nm was collected and extracted with ethanol. Removal of solvent, followed by recrystallisation from benzene–light petroleum (b.p. 60—80°), gave the *carbamate* (12) (18%), m.p. 84—85° [Found (material dried at 65° and 0·01 mmHg):

C, 57·3; H, 5·15; N, 20·7. $C_{13}H_{14}N_4O_3$ requires C, 56·9; H, 5·15; N, 20·4%], $\nu_{max.}$ 3250m (NH), 1705vs (CHO and CO_2Et), 1540m, and 1265m (C–O–C) cm^{-1}.

3-*Benzyl*-v-*triazolo*[4,5-d]*pyrimidin*-5(4H)-*one* (9-*Benzyl*-8-*azapurin*-2-*one*).—A mixture of 3-benzyl-5-ethoxy-*v*-triazolo[4,5-*d*]pyrimidine (9-benzyl-2-ethoxy-8-azapurine) (0·13 g, 0·5 mmol) and pyridine hydrochloride (0·39 g) was heated at 135° (boiling xylene vapour) for 30 min. Water (1 ml) was added to the mixture, which was then cooled to 0°. The precipitate, recrystallised from water (360 parts), gave 9-benzyl-8-azapurin-2-one [20] (60%), m.p. 248° (decomp.), identical with a specimen made by oxidising 1,6-dihydro-9-benzyl-8-azapurin-2-one.[20] This product (and the following two compounds) fluoresced bright violet (on Whatman No. 1 paper).

5-*Amino*-3-*benzyl*-v-*triazolo*[4,5-d]*pyrimidine* (2-*Amino*-9-*benzyl*-8-*azapurine*).—A solution of 3-benzyl-5-ethoxy-*v*-triazolo[4,5-*d*]pyrimidine (9-benzyl-2-ethoxy-8-azapurine) (0·18 g, 0·7 mmol) in ethanolic ammonia (15 ml) was heated at 180° for 48 h. The mixture was taken to dryness *in vacuo* and the residue, recrystallised from ethanol (140 parts), gave 2-*amino*-9-*benzyl*-8-*azapurine* (43%), m.p. 206° [Found (material dried at 110° and 0·05 mmHg): C, 58·4; H, 4·8; N, 37·2. $C_{11}H_{10}N_6$ requires C, 58·4; H, 4·5; N, 37·15%].

5-*Amino*-2-*methyl*-v-*triazolo*[4,5-d]*pyrimidine* (2-*Amino*-8-*methyl*-8-*azapurine*).— 2-Methyl-5-ethoxy-*v*-triazolo[4,5-*d*]-pyrimidine (2-ethoxy-8-methyl-8-azapurine) (0·12 g, 0·7 mmol) in ethanolic ammonia (20 ml) was heated at 175° for 72 h. The mixture was taken to dryness *in vacuo* and the residue was triturated with ethanol. The precipitate was mixed with an equimolar amount of toluene-*p*-sulphonic acid in ethanol (0·5 ml). The tosylate was suspended in water (0·5 ml) and potassium hydrogen carbonate was added. The mixture was chilled and the deposited crystals, filtered off and recrystallised from ethanol (170 parts), gave 2-*amino*-8-*methyl*-8-*azapurine* (27%), m.p. 254° (decomp.) [Found (material dried at 110° and 0·01 mmHg): C, 40·0; H, 4·3; N, 55·75. $C_5H_6N_6$ requires C, 40·0; H, 4·0; N, 56·0%], $\nu_{max.}$ 3350m (NH), 3160s (NH), 1670m, 1610s (NH), 1560m, 1520m, 1435m, 1380m, and 1260m cm^{-1}.

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