v-Triazolo[4,5-*d*]pyrimidines (8-Azapurines). Part XVI.[1] Preparation of 6-Amino-8-azapurines by heating 4-Amino-1,2,3-triazole-5-carbonitrile † (and its *N*-Alkyl Derivatives) with Amidines

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4-Amino-1,2,3-triazole-5-carbonitrile, and its 1-, 2-, and 3-methyl, and 3-benzyl derivatives (1a—e), reacted with formamidine, acetamidine, 2,2,2-trichloroacetamidine, and *NN'*-dibutylformamidine to give the corresponding 6-amino-, 6-amino-2-methyl-, 6-amino-2-trichloromethyl-, and 6-butylamino-8-azapurines (2), respectively. Yields were usually very good and the reaction has preparative value. 6-Amino-9-benzyl-2-methyl-8-azapurine was prepared also by the action of triethyl orthoacetate on 4-amino-3-benzyl-1,2,3-triazole-5-carboxamidine (3). A 2-trichloromethyl-8-azapurine was conveniently dehalogenated to the 2-dichloromethyl analogue.

4-Amino-3-benzyl-1,2,3-triazole-5-carbonitrile (1e) was converted by free guanidine into 1-(4-amino-3-benzyl-1,2,3-triazol-5-ylcarbonimidoyl)guanidine (7b), which could be cyclized thermally to 2,6-diamino-9-benzyl-8-azapurine (2p). The mechanisms of the amidine and guanidine reactions are compared.

I.r. and ^{1}H n.m.r. spectra are recorded and discussed.

6-AMINO-8-AZAPURINE (8-aza-adenine) has been found[2] to inhibit cancer cells that have become resistant to 2-amino-8-azapurin-6-one (8-azaguanine) during treatment with this drug. The 6-amino-compound also inhibits Gram-positive and -negative bacteria[3] by being incorporated into the RNA;[4] it greatly reduces

† In this series, the amino-group of aminotriazoles is consistently numbered 4, to facilitate comparisons.

[1] Part XV, A. Albert, *J.C.S. Perkin I*, 1974, 2030.

[2] D. Adomaitiene, T. N. Ignatova, D. Ya. Podgaetskaya, and V. A. Gershun, *Tsitologiya*, 1970, **12**, 457.

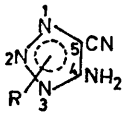
[3] R. O. Roblin, J. O. Lampen, J. P. English, Q. P. Cole, and J. R. Vaughan, *J. Amer. Chem. Soc.*, 1945, **67**, 290.

[4] J. D. Smith and R. E. F. Matthews, *Biochem. J.*, 1957, **66**, 323.

the rate of multiplication of tobacco mosaic [4,5] and potato [6] viruses, and it inhibits the synthesis of adenosine triphosphate in the fungus *Neurospora crassa*.[7] These inhibitions are typically reversed by adenine.[3,5]

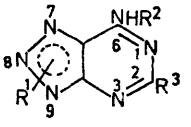
To assist similar biological studies, a convenient synthesis of 6-amino-8-azapurines with a variety of substituents was sought. A likely pathway seemed to be the condensation of 4-amino-1,2,3-triazoles with various amidines, analogous to the Taylor–Ehrhart reaction in which 4-aminopyrimidine-5-carbonitrile and formamidine, at 135°, gave 4-aminopyrimido[4,5-d]-pyrimidine.[8] This reaction, which has been extended to the pyrrole,[9] oxazole,[10] and imidazole [10] series, was reviewed [11] in 1970, and has since been used to convert 2-aminopyrazine-3-carbonitrile into 4-aminopteridine.[12]

In the present work, 4-amino-1,2,3-triazole-5-carbonitrile (1a) and its 1-, 2-, and 3-methyl derivatives (1b—d) were condensed with formamidinium acetate at 120° to give very good yields of 6-amino-8-azapurine



(1)

	R
a	H
b	1-Me
c	2-Me
d	3-Me
e	3-CH_2Ph



(2)

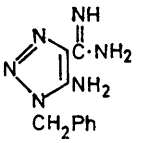
	R^1	R^2	R^3
a	H	H	H
b	7-Me	H	H
c	8-Me	H	H
d	9-Me	H	H
e	9-CH_2Ph	H	H
f	7-Me	H	Me
g	8-Me	H	Me
h	9-CH_2Ph	H	Me
i	7-Me	H	CCl_3
j	8-Me	H	CCl_3
k	9-CH_2Ph	H	CCl_3
l	8-Me	H	$CHCl_2$
m	7-Me	Bu^n	H
n	8-Me	Bu^n	H
o	8-Me	H	NH_2
p	9-CH_2Ph	H	NH_2

and its 7-, 8-, and 9-methyl derivatives, respectively (2a—d). The 9-benzyl analogue (2e) was prepared from the corresponding triazole (1e); the best yield (65%) came from a short, incomplete reaction, whereas longer heating gave a product contaminated by high-melting, feebly soluble material, different from the dimer [13] of the starting material, and suspected to arise from a Dains reaction (condensation of an amidine with a reactive methylene group, by elimination of ammonia).[14] To pursue this idea further, the *N*-4-acetyl and -formyl derivatives of the aminotriazole (1e) were treated similarly, but the former remained largely unchanged, and the latter was transformed mainly to the 8-azapurine (2e).

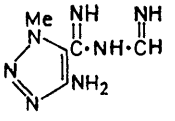
Some of the aminocyanotriazoles (1b—d) were condensed with acetamidinium acetate to give excellent yields of the correspondingly *N*-alkylated 6-amino-2-methyl-8-azapurines (2f—h). 6-Amino-9-benzyl-2-methyl-8-azapurine (2h) was also prepared by heating 4-amino-3-benzyl-1,2,3-triazole-5-carboxamidine [1] (3) with triethyl orthoacetate; when acetic anhydride was present also, the product was 6-acetamido-9-benzyl-2-methyl-8-azapurine. Moderate yields of three 6-amino-2-trichloromethyl-8-azapurines were obtained by condensing 2,2,2-trichloroacetamidinium acetate with the aminocyanotriazoles (1b—d); the yield could not be improved by increasing the reaction temperature (as had been done with acetamidine) because of decomposition.

6-Amino-8-methyl-2-trichloromethyl-8-azapurine (2j) was partly dehalogenated to 6-amino-2-dichloromethyl-8-methyl-8-azapurine (2l) by tin(II) chloride in cold acetone.

Mechanism of Condensations with Amidines.—The condensation (for example) for 4-amino-1-methyl-1,2,3-triazole-5-carbonitrile with formamidinium acetate could proceed through either the 5-carbonimidoylformamidine (4) or 4-aminomethyleneamino-1-methyl-1,2,3-triazole-5-carbonitrile (5a). That the latter route was preferred was indicated by the failure of 4-acetamido-1-methyl-1,2,3-triazole-5-carbonitrile to give the



(3)



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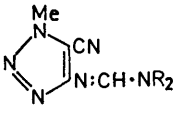
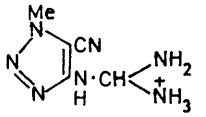


(5)
a; R = H
b; R = Me



(6)

4-acetamido-derivative of (4) when heated with formamidinium acetate under the conditions that converted the parent triazole (1b) into the 8-azapurine (2b). The most likely formation of the postulated intermediate (5a) is by addition of the 4-amino-group of the triazole to the double bond of the amidinium ion to give a tetrahedral intermediate [*e.g.* (6)], a course parallel to the addition [15] of ammonia to the cation of 4-dimethylaminomethyleneamino-1-methyl-1,2,3-triazole-5-carbo-

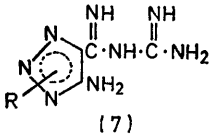
[5] I. R. Schneider, *Phytopathology*, 1954, **44**, 243.
[6] I. P. Zhuk, L. F. Didenko, and N. I. Gorbarenko, *Biol. Nauki*, 1970, 108.
[7] H. Urbanek, *Acta Soc. bot. Pol.*, 1967, **36**, 347.
[8] E. C. Taylor and W. A. Ehrhart, *J. Amer. Chem. Soc.*, 1960, **82**, 3138.
[9] E. C. Taylor and R. W. Hendress, *J. Amer. Chem. Soc.*, 1965, **87**, 1995.
[10] J. P. Ferris and L. E. Orgel, *J. Amer. Chem. Soc.*, 1966, **88**, 3829.
[11] E. C. Taylor and A. McKillop, 'The Chemistry of Cyclic Enaminonitriles and *o*-Aminonitriles,' Interscience, New York, 1970.
[12] A. Albert and K. Ohta, *J. Chem. Soc.* (*C*), 1971, 3727.
[13] A. Albert, *J. Chem. Soc.* (*C*), 1970, 230.
[14] F. B. Dains, O. O. Malleis, and J. T. Meyers, *J. Amer. Chem. Soc.*, 1913, **35**, 970; F. B. Dains, R. Irvin, and C. G. Harrel, *ibid.*, 1921, **43**, 613; F. B. Dains, R. Thompson, and W. F. Asendorf, *ibid.*, 1922, **44**, 2310; R. M. Roberts, *J. Org. Chem.*, 1949, **14**, 277.

nitrile (5b) as a preliminary to elimination of the dimethylammonium ion and ring closure to 6-amino-7-methyl-8-azapurine.[15]

However, the following experimental evidence opposes such a sequence of cationic forms here. The triazole (1e) failed to react with acetamidine hydrochloride under conditions where acetamidinium acetate gave a 65% yield. This result made it desirable to examine a free amidine. In place of free acetamidine (judged too unstable), trichloroacetamidine was heated with the triazole (1c) and gave a 28% yield of the corresponding 8-azapurine (2j) (much of this amidine survived the reaction); however the acetate gave a 61% yield, and the hydrochloride none at all. Thus acidity is helpful in one stage (and harmful in another) of the total reaction. The optimal acidity is too mild to force the eventual ring closure (addition of $-NH_2$ to $-CN$), which is most probably purely thermal. As an alternative to a tetrahedral intermediate, it may be assumed that a minute proportion of the aminotriazole is converted into its cation which combines with the (nucleophilic) neutral amidine much as equimolecular proportions of aniline and aniline hydrochloride react in the industrial synthesis of diphenylamine. However, there is an immense difference in the basic strengths of acetamidine (pK_a 12·4) and these aminotriazolenitriles (*e.g.* pK_a −1·4 for the 2-methyl derivative [16]). In the light of this discussion (which favours a tetrahedral intermediate), the severer conditions required for condensing acetamidine (compared to formamidine) seem to be mainly electronic, and those encountered with trichloroacetamidine mainly steric.

NN'-Dibutylformamidinium acetate and the triazoles (1b and c) at 200° eliminated butylamine to give 6-butylamino-7(and 8)-methyl-8-azapurine (2m and n) respectively, by a spontaneous Dimroth rearrangement of the first-formed 1-butyl-6-imino-1,6-dihydro-8-azapurine.[1] The hydrochloride of dibutylformamidine did not react.

Condensations with Guanidine.—In the literature, guanidine (always either free or as carbonate) has been used to annulate *o*-amino-nitriles to diaminopyrimido-aza-analogues; this has been done in the pyrroline, pyrimidine, and pyrazine series only.[11] Intermediates



(7)

a; R=2-Me
b; R=3-CH_2Ph

[namely 1-(2-aminopyrazin-3-ylcarbonimidoyl)guanidines] have been isolated only from the pyrazine ⟶ pteridine conversions.[17] Here, 4-amino-2-methyl-1,2,3-triazole-5-carbonitrile (1c) and free guanidine in boiling ethanol readily gave 1-(4-amino-2-methyl-1,2,3-triazol-5-ylcarbonimidoyl)guanidine (7a) which decomposed extensively when ring-closure to 2,6-diamino-8-methyl-8-azapurine (2o) was attempted in boiling butanol, acetic acid, N-hydrochloric acid, or ethanolic sodium hydroxide, or with guanidinium acetate in boiling butanol. 1-(4-Amino-3-benzyl-1,2,3-triazol-5-ylcarbonimidoyl)guanidine (7b), similarly prepared, readily cyclized (in boiling butanol) to 2,6-diamino-9-benzyl-8-azapurine (2p).

It was found that guanidinium acetate, unlike acetamidinium acetate, had little tendency to react with the aminocyanotriazoles (1). The greater success of *free* guanidine, and the different pathway selected by this reagent, must depend on the greater ease with which guanidine forms an anion, thanks to the electronic influence of the third amino-group. Such an anion would readily add to the electropositive carbon of the cyano-group, leading to intermediates of type (7).

Physical Constants.—I.r. spectra of 8-azapurines are in Table 1. The spectrum of 2,6-diamino-9-benzyl-8-azapurine is compatible with those of 2,6-diamino-7(and 8)-methyl-8-azapurine.[18] The 2-trichloromethyl

TABLE 1
I.r. spectra (Nujol)
$\nu_{max.}/cm^{-1}$

8-Azapurines	
6-Acetamido-9-benzyl-2-methyl	3220, 3150br,w (NH str.), 1690br,m (CO, amide I), 1590br,s (amide II), 1315s, 1300s (amide III), 1220m, and 715m
(2k)	3420m, 3315m, 3200m (NH str.), 1650br,s, 1575s, 1355m, 845s, and 795s (C—Cl str.)
(2i	3290br,m, 3210m, 1625br,s, 1225s, and 795m (C—Cl str.)
(2p)	3505w, 3370s, 3290m, 3260m, 3130m (NH str.), 1685m, 1610s (NH bend), 1585m, and 1430m
1,2,3-Triazoles	
4-Acetamido-3-benzyl-5-cyano	3230s, 3190s (NH str.), 2245m (C≡N str.), 1675br,s (CO str.), 1585m, 1520s, 1490s, 1325m, and 1245m
(7a)	3420m, 3310m (NH str.), 1600br,s, 1560m, 1430m, and 1185m
(7b)	3415m, 3355m, 3270m (NH str.), 1610br,s, 1530m, 1495m, 1425m, and 1180m

derivatives show a clear C–Cl stretching band at 795 cm^{-1}. The reversal of strength for amide I and amide II bands, as seen here in 6-acetamido-9-benzyl-2-methyl-8-azapurine, was discussed recently.[19] Spectra of some 1,2,3-triazoles, including the novel carbonimidoylguanidines, are given in the same table. ^1H N.m.r. spectra of six 6-amino-8-azapurines are given in Table 2. The chemical shifts of 2-H, 6-NH_2, and the various *N*-alkyl groups are very close to values determined for

[15] A. Albert, *J.C.S. Perkin I*, 1972, 461.
[16] A. Albert, *J.C.S. Perkin I*, 1973, 1634.
[17] J. H. Jones and E. C. Cragoe, *J. Medicin. Chem.*, 1968, **11**, 322.
[18] A. Albert and H. Taguchi, *J.C.S. Perkin I*, 1972, 449.
[19] A. Albert, *J.C.S. Perkin I*, 1973, 2659.

related 8-azapurines.[15] In the 2,7-dimethyl derivative, the 2-methyl signal occurs much further upfield than the 7-methyl signal, as may be expected. Other n.m.r. values are recorded in the Experimental section.

TABLE 2

^{1}H N.m.r. spectra [*ca.* 34°; solvent $(CD_3)_2SO$] of 8-azapurines

6-Amino-8-azapurine (2)			
R^1	R^2	R^3	τ Values [a]
7-Me	H	H	1·72 (1H, 2-H), 2·25br [b] (2H, NH_2), and 5·56 (3H, 7-Me)
7-Me	H	Me	2·38slbr [b] (2H, NH_2), 5·59 (3H, 7-Me), and 7·56 (3H, 2-Me)
9-CH_2Ph	Ac	Me	0·16 [b] (1H, CONH), 2·65 (5H, Ph), 4·19 (2H, CH_2), 7·36 (3H, 2-Me), and 7·47 (3H, Ac) [c]
7-Me	H	CCl_3	1·69br [b] (2H, NH_2), and 5·54 (3H, Me)
9-CH_2Ph	H	CCl_3	1·2vbr [b] (NH_2), 2·61 (5H, Ph), and 4·09 (2H, CH_2)
8-Me	H	$CHCl_2$	1·50br [b] (2H, NH_2), 3·05 (1H, $CHCl_2$), and 5·55 (3H, Me)

[a] Tetramethylsilane as internal standard; all signals were singlets. [b] Exchangeable in D_2O. [c] Assignments reversible for last two peaks.

EXPERIMENTAL

I.r. spectra were taken (for mulls) with a Perkin-Elmer 257 grating spectrometer. N.m.r. spectra were obtained with a Varian HA 100 (100 MHz) instrument. Specimens said to be identical were compared by (i) mixed m.p. determination where applicable, (ii) i.r. spectroscopy, and (iii) comparative chromatography on two Whatman No. 1 papers, developed in (a) aqueous 3% NH_4Cl, and (b) butanol–5N-acetic acid (7 : 3). Unless otherwise specified, material for analysis was dried at 80° in air. ' Pyridine trihydrate ' refers to the azeotrope, b.p. 92°.

4-Amino-1,2,3-triazole-5-carbonitrile,[20] and its 1-methyl,[16] 2-methyl,[16] 3-methyl,[21] and 3-benzyl [13] derivatives; also 4-acetamido-1-methyl-1,2,3-triazole-5-carbonitrile,[19] were prepared as indicated here. Condensations of these aminonitriles with amidines were carried out as specified in Table 3, with the results shown there.

Example of the Use of Formamidine.—4-Amino-1,2,3-triazole-5-carbonitrile (1a) (0·109 g, 0·001 mol), formamidinium acetate [8] (0·31 g, 0·003 mol), and sieve-dried butan-1-ol (2 ml) were heated under reflux at 125° (bath temp.) for 1 h. The solvent was removed at 90° and 25 mmHg. Water (1 ml) was added (pH 6·5); the suspension was refrigerated and the solid filtered off, triturated with N-hydrochloric acid (4 ml), and the mixture was filtered. The filtrate, mixed with M-sodium citrate (0·5 ml) and adjusted to pH 3 with 10N-sodium hydroxide, deposited 6-amino-8-azapurine (2a), identical with authentic material.

Example of the Use of Acetamidine.—4-Amino-1-methyl-1,2,3-triazole-5-carbonitrile (1b) (0·123 g, 0·001 mol), acetamidinium acetate [8] (0·354 g, 3 equiv.), and hexan-1-ol (2 ml) were heated under reflux for 4 h. The solvent was removed at 115° and 25 mmHg. The residue was slurried with boiling ethanol (2 ml), and set aside at −10° for 2 h. Filtration furnished 6-*amino*-2,7-*dimethyl*-8-*azapurine* (7-*amino*-1,5-*dimethyl*-v-*triazolo*[4,5-d]*pyrimidine*) (2f), m.p. 301°, after recrystallization from water with carbon to remove fluorescent material.

Alternative Syntheses of 2-*Methyl*-8-*azapurines* (5-*Methyl*-v-*triazolo*[4,5-d]*pyrimidines*).—4-Amino-3-benzyl-1,2,3-triazole-5-carboxamidine hydrochloride [1] (0·126 g, 0·0005 mol) and triethyl orthoacetate (3 ml) were strongly heated under reflux for 12 h. Volatiles were removed at 100° and 25 mmHg. The residue was boiled with N-acetic acid (2·5 ml) for 30 min, to effect a second stage of the reaction (as revealed by paper chromatography). The mixture deposited, on cooling, 6-*amino*-9-*benzyl*-2-*methyl*-8-*azapurine* (2h) (83%), m.p. 266° (from 55 parts of ethanol). When acetic anhydride (1 ml) was added initially, 6-*acetamido*-9-*benzyl*-2-*methyl*-8-*azapurine* (50%) was obtained, m.p. 153° (from 11 parts of ethanol) (Found: C, 59·4; H, 4·9; N, 29·7. $C_{14}H_{14}N_6O$ requires C, 59·6; H, 5·0; N, 29·8%).

Example of the Use of 2,2,2-*Trichloroacetamidine.*—4-Amino-2-methyl-1,2,3-triazole-5-carbonitrile (0·123 g), trichloroacetamidine [22] (0·483 g, 0·003 mol), acetic acid (0·18 g, 3 mol), and butanol (2 ml) were heated under reflux for 2 h. The solvent was removed at 90° and 25 mmHg; the residue triturated with water (2 ml) and filtered gave 6-*amino*-8-*methyl*-2-*trichloromethyl*-8-*azapurine* (7-*amino*-2-*methyl*-5-*trichloromethyl*-v-*triazolo*[4,5-d]*pyrimidine*).

Dehalogenation.—Tin(II) chloride dihydrate (0·45 g, 0·002 mol) dissolved in acetone (4 ml) was added dropwise to a stirred suspension of 6-amino-8-methyl-2-trichloromethyl-8-azapurine (0·534 g, 0·002 mol) in acetone (20 ml) at 24°. After 18 h, the clear solution was evaporated to dryness. N-Sodium hydroxide (16 ml) was added to dissolve the tin. The product was filtered off, boiled briefly with ethanol (15 ml), then set aside at 24°. Filtration re-

TABLE 3

Preparation of 6-amino-8-azapurines (2) from 4-amino-5-cyano-1,2,3-triazoles (1)

Product (2)			Starting triazole	Solvent [a]	Approx. temp. (°C)	Reflux time (h)	Recrystallization Solvent	(Parts)	M.p. (°C)	Yield (%)	Found (%)				Formula	Required (%)			
R^1	R^2	R^3									C	H	N	Cl		C	H	N	Cl
H	H	H	(1a)	B	120	1	H_2O	(350)		77 [b,c]									
7-Me	H	H	(1b)	B	120	2	H_2O	(110)		90 [b,d,e]									
8-Me	H	H	(1c)	B	120	2	H_2O	(50)		88 [b,e]									
9-Me	H	H	(1d)	B	120	2	H_2O	(400)		90 [b,e,f]									
9-CH_2Ph	H	H	(1e)	B	120	1	P [a]	(24)		65 [b,f]									
7-Me	H	Me	(1b)	H	160	4	H_2O	(60)	301 [g]	80	44·0	4·9	51·5		$C_6H_8N_6$	43·9	4·9	51·2	
8-Me	H	Me	(1c)	H	160	2	H_2O	(14)	220	82	44·3	5·2	50·7						
9-CH_2Ph	H	Me	(1e)	H	160	0·5	EtOH	(550)	266	83	60·3	5·2	35·3		$C_{12}H_{12}N_6$	60·0	5·0	35·0	
7-Me	H	CCl_3	(1b)	H	160	2	EtOH	(300)	>320	50	27·1	1·9	31·6	39·9	$C_5H_5Cl_3N_6$	26·95	1·9	31·4	39·8
8-Me	H	CCl_3	(1c)	B	120	2	EtOH	(120)	303 [h]	61	27·3	1·9	31·2	39·5					
9-CH_2Ph	H	CCl_3	(1e)	B	120	4	Benzene	(20)	186	42	42·3	2·9	24·2	30·6	$C_{12}H_9Cl_3N_6$	41·9	2·6	24·4	31·0
7-Me	Bu^n	H	(1b)	O	200	4	H_2O	(35)	167	54 [b,i]									
8-Me	Bu^n	H	(1c)	O	200	4	H_2O	(44)	126	20 [b,i]									

[a] B, butan-1-ol, H, hexan-1-ol, O, octan-1-ol, P, pyridine trihydrate. [b] Identical with authentic material. [c] Ref. 3. [d] A. Albert and K. Tratt, *J. Chem. Soc.* (*C*), 1968, 344. [e] Ref. 15. [f] A. Albert, *J. Chem. Soc.* (*C*), 1969, 152. [g] Slight decomp. [h] Much decomp. [i] Ref. 1.

[20] A. Albert and H. Taguchi, *J.C.S. Perkin I*, 1973, 1629.
[21] A. Albert, *J. Chem. Soc.* (*C*), 1969, 2379.
[22] A. Albert and B. Paal, *Chem. and Ind.*, 1974, 874.

moved some starting material (0·1 g). The filtrate was taken to dryness and the residue recrystallized from 100 parts of benzene (2 crops), giving *6-amino-2-dichloromethyl-8-methyl-8-azapurine* (*7-amino-5-dichloromethyl-2-methyl-v-triazolo*[4,5-d]*pyrimidine*) (66%), m.p. 202° prior to partial resolidification (Found: C, 30·8; H, 2·6; Cl, 30·5. $C_6H_6Cl_2N_6$ requires C, 30·9; H, 2·6; Cl, 30·4%).

Example of the Use of NN′*-Dibutylformamidine.*—4-Amino-1-methyl-1,2,3-triazole-5-carbonitrile (0·123 g), *NN′*-dibutylformamidine [8] (0·47 g, 3 equiv.), acetic acid (0·18 g, 3 equiv.), and octan-1-ol (2 ml) were heated under reflux for 4 h (the solution remained clear throughout). Solvent was removed at 135° and 25 mmHg. The crystalline residue was transferred to a filter with light petroleum, then recrystallized from a little water, giving 6-butylamino-7-methyl-8-azapurine, m.p. 167° (lit.,[1] 167°).

4-Acylamino-3-benzyl-1,2,3-triazole-5-carbonitriles.—4-Amino-3-benzyl-1,2,3-triazole-5-carbonitrile (1·0 g, 0·005 mol) and freshly prepared acetic formic anhydride (10 ml) were stirred at 22° for 17 h. The solvent was removed at 40° (*in vacuo*). The residual crystals, stirred with water (8 ml), then filtered off, gave *3-benzyl-4-formamido-1,2,3-triazole-5-carbonitrile* (91%) which, recrystallized from ethanol (6 parts), or benzene (280 parts), had m.p. 152° (Found: C, 58·4; H, 4·3; N, 31·0. $C_{11}H_9N_5O$ requires C, 58·1; H, 4·0; N, 30·8%), τ [$(CD_3)_2SO$] 1·57 (1H, CHO), 2·67 (5H, m, Ph), and 4·39 (2H, CH_2). The nitrile (1e) (1·0 g), acetic anhydride (1·0 g, 2 equiv.), and dried pyridine (10 ml) were heated under reflux for 4 h. The volatiles were removed at 100° and 25 mmHg. The residue, recrystallized from a little ethanol and then from 150 parts of benzene, gave *4-acetamido-3-benzyl-1,2,3-triazole-5-carbonitrile* (75%), m.p. 153° (Found: C, 59·5; H, 4·8; N, 29·4. $C_{12}H_{11}N_5O$ requires C, 59·7; H, 4·6; N, 29·0%).

Condensations with Guanidine.—Guanidine hydrochloride (0·24 g, 0·0025 mol) was boiled for 5 min with ethanolic 0·5M-sodium ethoxide (5 ml), cooled, and filtered from NaCl. The filtrate and 4-amino-2-methyl-1,2,3-triazole-5-carbonitrile (0·246 g, 0·002 mol) were heated under reflux for 1 h. The ethanol was removed *in vacuo* at 30°. The residue was stirred with water (2 ml) and filtered giving *1-(4-amino-2-methyl-1,2,3-triazol-5-ylcarbonimidoyl)guanidine* (7a) (85%) which, recrystallized from 150 parts of ethanol, softened at 177°, evolved ammonia, and melted about 300° [Found (for material dried at 24° and 25 mmHg): C, 33·1; H, 5·7; N, 61·6. $C_5H_{10}N_8$ requires C, 33·0; H, 5·5; N, 61·5%], $\lambda_{max.}$ (cation at pH 7) 231sh and 285 nm (log ε 2·97 and 3·92), τ(C_5D_5N), 3·74slbr (2H, 4-NH_2, exchangeable), 5·35mbr (5H, side-chain, exchangeable), and 6·15 (3H, 2-Me). *1-(4-Amino-3-benzyl-1,2,3-triazol-5-ylcarbonimidoyl)guanidine* (7b), prepared similarly, was triturated with N-acetic acid (6 ml), filtered from a little 2,6-diamino-9-benzyl-8-azapurine (13%), the filtrate adjusted to pH > 12 with N-sodium hydroxide, and the amidine (65%) filtered off; it softened, and evolved ammonia when heated, and melted at *ca.* 270° [Found (for material dried at 24° and 25 mmHg): C, 51·3; H, 5·5; N, 43·2. $C_{11}H_{14}N_8$ requires C, 51·15; H, 5·5; N, 43·4%]. This amidine (1 g) and butanol (8 ml) were heated under reflux for 1 h; the suspension, taken to dryness at 95° and 25 mmHg, gave *2,6-diamino-9-benzyl-8-azapurine* (*5,7-diamino-3-benzyl-v-triazolo*[4,5-d]*pyrimidine*) (2p) (91%) (from 80 parts of pyridine trihydrate, in 2 crops); very sparingly soluble in boiling ethanol (Found: C, 55·0; H, 4·6; N, 40·3. $C_{11}H_{11}N_7$ requires C, 54·8; H, 4·6; N, 40·6%).

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