The Dimroth Rearrangement. Part XV.[1] Catalysis by Methylamine Salts. Preparation of 7-Methylamino- and 6,7-Dihydro-7-imino-*v*-triazolo[4,5-*d*]pyrimidines † *via* 4-Ethoxymethyleneamino-1,2,3-triazoles ‡

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The rearrangement of 1,6-dihydro-6-imino-1,*x*-dimethyl-8-azapurines (6,7-dihydro-7-imino-*y*,6-dimethyl-*v*-triazolo[4,5-*d*]pyrimidines), *e.g.* (3) and (4), to *x*-methyl-6-methylamino-8-azapurines (*y*-methyl-7-methylamino-*v*-triazolo[4,5-*d*]pyrimidines), *e.g.* (5), is found to be greatly facilitated by the use of methylamine salts, in contrast to the traditional use of free amines or inorganic bases. 9-Benzyl-6-methylamino-8-azapurine has been prepared similarly. The requisite imines [*e.g.* (3) and (4)], members of a new and relatively basic class of 8-azapurines, were prepared by the action of free methylamine on the corresponding 5-cyano-4-ethoxymethyleneamino-*x*-alkyl-1,2,3-triazoles, *e.g.* (1) and (2).

Ionization constants and u.v., i.r., and ^{1}H n.m.r. spectra are recorded and discussed.

THE Dimroth rearrangement (an isomerisation proceeding by ring fission of a heteroaromatic compound followed by recyclisation, whereby a ring nitrogen atom and its attached alkyl group exchange places with an imino-group in the position α to it) has hitherto been facilitated by bases such as sodium hydroxide or free aliphatic amines. A much more vigorous, and unexpected, facilitation by salts of an aliphatic amine is now reported. The preparation of the necessary intermediates will be described first.

4-Amino-5-cyano-1-methyl-1,2,3-triazole [2] was condensed with triethyl orthoformate and acetic anhydride to give the 4-ethoxymethyleneaminotriazole (1), the first member of a new class of triazole derivatives. A substantial amount of the 4-acetamido-analogue was formed as a by-product when equal volumes of the aliphatic reagents were used, and its nature was confirmed by synthesis. Use of a lower proportion of anhydride to ester improved the yield [of product (1)], but the yield was much lower when the anhydride was omitted. With this knowledge, the 2-methyl (2), 3-methyl, and 3-benzyl analogues of compound (1) were produced, in 70—90% yields, from the appropriately substituted 4-amino-5-cyanotriazoles; however the parent 4-amino-5-cyanotriazole [3] gave a mixture of products, difficult to separate. The ethoxymethyleneamino-compounds gave a ^{1}H n.m.r. signal (1H) near τ 1·4 (N:CH; *cf.* τ 1·11 for 3-cyano-2-ethoxymethyleneaminopyrazine [4]); the signal (3H) for the triazole ring methyl group (when present) appeared near τ 5·9.

† *v*-Triazolo[4,5-*d*]pyrimidines are commonly referred to as 8-azapurines to facilitate chemical and biological comparison with the corresponding purines.

‡ In this paper, the amino-group of aminotriazoles is consistently numbered 4, to facilitate the comparison of isomers.

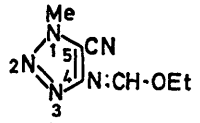
[1] Part XIV, D. J. Brown and B. England, *J. Chem. Soc.* (*C*), 1971, 2507.

[2] A. Albert, *J.C.S. Perkin I*, 1973, 1634.

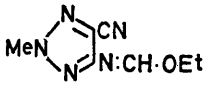
[3] A. Albert and H. Taguchi, *J.C.S. Perkin I*, 1973, 1629.

[4] A. Albert and K. Ohta, *J. Chem. Soc.* (*C*), 1971, 3727.

These ethoxymethylene compounds, being carboimidates, were readily hydrolysed by moisture, even when kept in 95% ethanol for 3 days at 25°, to the corresponding 5-cyano-4-formamido-analogues (of which the 1- and 2-methyl representatives were independently synthesised), and eventually to the *x*-alkyl-4-amino-5-cyano-1,2,3-triazoles.



(1)



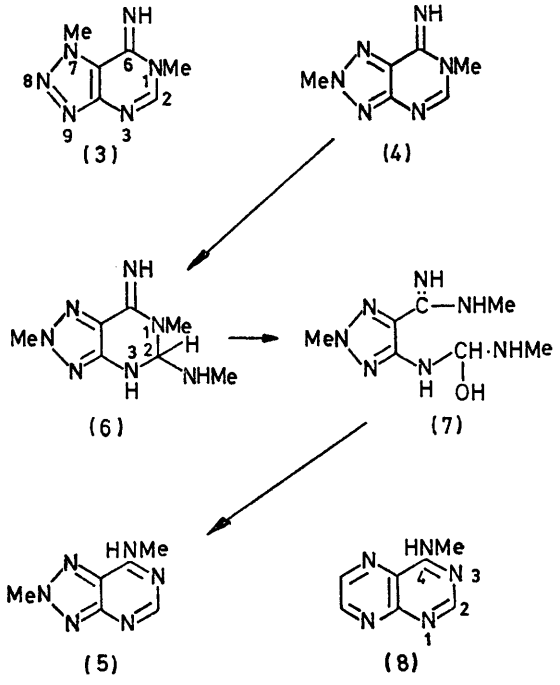
(2)

5-Cyano-4-formamido-1-methyl-1,2,3-triazole was unchanged when heated at 190°, or when heated under reflux with an excess of formic acid, but when set aside overnight in N-sodium hydroxide at 25°, it was hydrolysed to 4-amino-1-methyl-1,2,3-triazole-5-carboxylic acid.[5] 5-Cyano-4-formamido-2-methyltriazole, when boiled for 1 h with an excess of trifluoroacetic acid, gave 4-formamido-2-methyltriazole-5-carboxamide,[6] but, when set aside overnight (at 25°) in N-sodium hydroxide, afforded 4-amino-2-methyl-1,2,3-triazole-5-carboxamide.[6]

The imine (1) and ethanolic methylamine (at 0—25°) gave 1,6-dihydro-6-imino-1,7-dimethyl-8-azapurine (3). The 1,8- (4) and 1,9-dimethyl- and 9-benzyl-1-methyl analogues of this 8-azapurine were similarly made from the appropriate ethoxymethyleneamino-compounds, *e.g.* (2). These imines, obtained in 80—90% yield, constitute a new and unusually basic (see Table 1) type of 8-azapurine. They melted sharply, and were unchanged when heated for 1 h at 110°; however they slowly decomposed when boiled with water, and faster in boiling N-hydrochloric acid (ring opening). The analogue with a free 3-position (1,6-dihydro-6-imino-1-methyl-8-azapurine), for which no ethoxymethyleneamino-intermediate was available, was made by debenzylating the 9-benzyl analogue with sodium in ammonia [hydrogenation over palladium (70° and 4 atm) gave little of this product]. This appears to be the first example of an 8-azapurine successfully debenzylated with sodium; two examples[7] of success with catalytic hydrogen are recorded.

1,6-Dihydro-6-imino-1,8-dimethyl-8-azapurine was little changed when treated with methylamine (2 equiv.) in methanol for 50 h at 25°. However replacement of the free amine by its acetate effected almost complete isomerisation to 8-methyl-6-methylamino-8-azapurine (5) under these conditions. For preparative purposes, this reaction was carried out at 65°; under these conditions it was essentially complete in 2 h. The reaction was also effected in boiling water (yield 81% in 1 h), in order to observe the ambient pH range, which was found to be 6·1—6·4. [When boiling M-phosphate buffer (pH 6·3) replaced the methylamine solution, the yield was only 53%, and was even lower (32%) with pH 7·5 buffer.] Methylamine hydrochloride could replace the acetate without reducing the yield. By using methylamine acetate in boiling methanol, 7-methyl-, 9-methyl-, and 9-benzyl-6-methylamino-8-azapurine were produced in excellent yields from the appropriate imines, *e.g.* (3).

Dimroth rearrangements such as these, in which the imino-group is not situated between two ring nitrogen atoms, are often sluggish. For such cases. the use of amine salts should prove advantageous in preparative work. Only 1,6-dihydro-6-imino-1-methyl-8-azapurine, being a zwitterion (see later), was not



isomerised to 6-methylamino-8-azapurine by methylamine salts at 65°.

The likely reason for the improvement effected by substituting methylamine salts for methylamine will now be discussed. The mechanism of the Dimroth rearrangement is known from studies[8] with ^{15}N, and from kinetic work accompanied by the trapping of intermediates,[9] and has been reviewed.[10] The first step is a rapid addition of the facilitating agent across the most electronically delocalised C=N bond, thus endowing a ring carbon atom with three electron-withdrawing substituents, a situation which leads to hydrolytic ring fission. In a slower reaction, the ring closes after rotation of the (newly exposed) amidine group, and expulsion of the facilitating agent. By

[5] A. Albert and H. Taguchi, *J.C.S. Perkin I*, 1972, 449.
[6] A. Albert, *J. Chem. Soc.* (*C*), 1968, 2076.
[7] G. Nübel and W. Pfleiderer, *Chem. Ber.*, 1965, **98**, 1060.
[8] D. J. Brown, *Nature*, 1961, **189**, 828; J. Goerdeler and W. Roth, *Chem. Ber.*, 1963, **96**, 534.
[9] D. D. Perrin and I. H. Pitman, *J. Chem. Soc.*, 1965, 7071.
[10] D. J. Brown in 'Mechanisms of Molecular Migrations,' ed. B. S. Thyagarajan, Interscience-Wiley, New York, 1968, vol. 1, p. 209 (review).

analogy, in the experiments just described, 1,6-dihydro-6-imino-1,8-dimethyl-8-azapurine (4) should add methylamine across the 2- and 3-positions to give the triaminomethane derivative (6), the 1,2-bond of which should be opened by hydrolysis to produce the carbinolamine (7); this should finally close to give 8-methyl-6-methylamino-8-azapurine (5). (The results obtained with phosphate buffer suggest that the imine can function as its own nucleophile, but less efficiently.)

The superiority of methylamine salts in facilitating this reaction cannot be due to the 2,3-addition of amine cations, for these are not nucleophiles. Rather the methylamine cations may act as a source of hydrogen ions to convert the iminoazapurines into cations, which are of a charge type more susceptible to nucleophilic attack by free methylamine. Thus by maintaining the reaction mixture at pH 6·2, methylamine acetate keeps 74% of the imine (4) [pK_a 6·85 (Table 1)] as its cation. Similar considerations apply if the rate-limiting step is bond breaking in the adduct.

Ionisation and Spectral Data.—Ionisation constants and u.v. spectra are given in Table 1. The ethoxymethyleneaminotriazoles absorb at much shorter wavelengths than the corresponding dimethylaminomethyleneaminotriazoles.[11] The 6-imino-8-azapurines are stronger bases than the corresponding 6-methylamino-isomers by 2·4 to 4·3 pK units. The u.v. spectra of the cations of pairs of these isomers are distinct; hence the hydrogen ion, almost certain to be added to the =NH group of the imines, cannot reside on N-1 of the methylamino-isomers. Protonation of this position would give pairs of almost identical spectra; hence the proton is almost certainly on N-3. This allocation agrees with the behaviour of 4-methylaminopteridine (8), the cation of which spectrally resembles[12] that of 1,4-dihydro-4-imino-1-methylpteridine[12] and differs from that of 3,4-dihydro-4-imino-3-methylpteridine.[13]

1,6-Dihydro-6-imino-1-methyl-8-azapurine has a 'proton-gained' ionisation, pK_a 3·25 (see Table 1), related to that of the acidic group[14] (pK_a 4·84) in unsubstituted 8-azapurine; it also has a 'proton-lost' ionisation, pK_a 9·12 related to those of the three analogues in which further methylation has blocked the acidic function (Table 1). The increased strength of both acidic and basic functions (in the 1-methyl compound) indicates that the neutral species is zwitterionic, the acidic group being strengthened by the inductive effect of the cationic group in the same molecule, and *vice versa*, as in glycine.

I.r. spectra are given in Table 2. The 4-cyano-5-ethoxymethyleneaminotriazoles show characteristic peaks for C:N, C:N, and :C·O·C stretching. In a Nujol mull, the amide I signal of 4-acetamido-1-methyl-1,2,3-triazole-5-carboxamide is weaker than that of amide II, but the customary order is restored in acetonitrile solution. The imino-8-azapurines have a distinctive pattern of absorption, which contrasts with that of the 6-methylamino-isomers. Extra peaks in 1,6-dihydro-6-imino-1-methyl-8-azapurine indicate that it contains a high proportion of zwitterion in the solid state.

The n.m.r. spectra of the ethoxymethyleneaminotriazoles (Table 3) show consistent signals characteristic of the methyleneamino-proton and those in the various alkyl groups. The n.m.r. spectra of the 1,6-dihydro-6-imino-8-azapurines differ little from those of their

TABLE 1

Ionisation constants and u.v. spectra

Compound	Species[a]	Ionisation in water (20°) pK_a	Spread (±)	Concn. (M)	A.w.l.[b] (nm)	Spectroscopy in water[c] $\lambda_{max.}$/nm	log ε	pH
1,2,3-Triazoles								
5-Cyano-4-ethoxymethyleneamino-1-methyl	0					208, 255	4·05, 4·04	C[d]
5-Cyano-4-ethoxymethyleneamino-2-methyl	0					247	4·07	C
8-Azapurines								
1,6-Dihydro-6-imino-1-methyl	+	3·25	0·02	0·0001	280	261	3·96	1
	±					268	3·95	7
	−	9·12	0·05	0·0001	280	272	4·08	12
1,6-Dihydro-6-imino-1,7-dimethyl[e]	0					210, 277	4·07, 3·98	8·0
	+	5·10	0·02	0·0001	240	208, 277	4·25, 3·88	2·0
1,6-Dihydro-6-imino-1,8-dimethyl	0					210, 290	4·16, 4·05	9·0
	+	6·85	0·02	0·00005	290	211, *272*, 278	4·23, *3·97*, 3·98	4·0
1,6-Dihydro-6-imino-1,9-dimethyl	0					206, 273	4·15, 3·90	9·0
	+	6·84	0·04	0·0001	290	259—264	3·97	4·0
7-Methyl-6-methylamino[14]	0					210, 291	4·12, 4·02	
(for comparison)	+	2·74				*215*, *288*, 293, *303*	*3·86*, *4·14*, 4·14, *3·96*	
8-Methyl-6-methylamino	0					214, 250, 299	4·21, 3·38, 4·11	
(for comparison)	+	3·72				209, 287, 296, *308*	4·18, 4·12, 4·09, *3·84*	
9-Methyl-6-methylamino	0					210, *254*, 287	4·18, *3·59*, 4·13	5·0
	+	2·55	0·04	0·0001	290	*211*, *263*, 270	*4·19*, *4·12*, 4·14	0

[a] Neutral species (0), cation (+), anion (−), zwitterion (±). [b] Analytical wavelength for spectrometric determinations. [c] Shoulders in italics. [d] C, in cyclohexane. [e] Stable in water at pH 10.

[11] A. Albert, *J.C.S. Perkin I*, 1972, 461.
[12] D. J. Brown and N. W. Jacobsen, *J. Chem. Soc.*, 1960, 1978.
[13] D. J. Brown and N. W. Jacobsen, *J. Chem. Soc.*, 1965, 3770.
[14] A. Albert, *J. Chem. Soc.* (*B*), 1966, 427.

6-methylamino-isomers except that only the latter show coupling between the protons of the $HN{\cdot}CH_3$ substituent (abolished by deuteriation).

Improved preparations of 4-amino-3-benzyl-5-carbamoyl-1-methyl-1,2,3-triazolium toluene-*p*-sulphonate (necessary for preparing 4-amino-5-cyano-1-methyl-1,2,3-triazole), and of 6-methylamino-8-azapurine, are given in the Experimental section.

EXPERIMENTAL

U.v. spectra were measured with a Perkin-Elmer 450 recording spectrometer; wavelengths and intensities of maxima were determined more accurately with a Unicam SP 500 manual instrument. I.r. spectra were taken (for mulls in Nujol) with a Unicam SP 200 spectrophotometer. N.m.r. spectra were determined at 33·3° with a Perkin-Elmer R10 spectrometer (60 MHz). Specimens said to be identical were compared by mixed m.p. determination (where relevant), paper chromatography [developers (*a*) aqueous 3% NH_4Cl, (*b*) butanol–5N-acetic acid (7 : 3)], and i.r. spectroscopy.

5-Cyano-4-ethoxymethyleneamino-x-methyl-1,2,3-triazoles.—4-Amino-5-cyano-1-methyl-1,2,3-triazole [2] (0·5 g, 0·004 mol), acetic anhydride (1·3 ml), and triethyl orthoformate (4 ml) were boiled vigorously under reflux for 4 h. Volatile material was removed at 100° and 25 mmHg, giving *5-cyano-4-ethoxymethyleneamino-1-methyltriazole* (1) (78%) (from cyclohexane), m.p. 64·5° [Found (material dried at 24° and 0·05 mmHg): C, 47·1; H, 5·1; N, 39·0. $C_7H_9N_5O$ requires C, 46·9; H, 5·1; N, 39·1%]. The *2-methyl isomer* (2), prepared (70% yield) from the corresponding aminonitrile [2] similarly, had m.p. 60° (from 7 parts of cyclohexane) (Found: C, 47·1; H, 5·2; N, 39·0%). Similarly,

TABLE 2

I.r. spectra (ν in cm^{-1}, for mulls in Nujol)

5-Cyano-1,2,3-triazoles	
4-Ethoxymethyleneamino-1-methyl *	2230 (C⋮N str.), 1635s (C:N str.), 1270s (:C–O–C asym. str.), 1215m, and 1000w
4-Ethoxymethyleneamino-2-methyl	2250, 1635s, 1280s, 1195s, 1010m, and 915m
4-Ethoxymethyleneamino-3-methyl	2220, 1630s, 1285m, 1250s, 1195m, and 1000m
3-Benzyl-4-ethoxymethyleneamino	2250, 1635s, 1475m, 1265s, and 1200m
4-Acetamido-1-methyl	3230m (NH str.), 2270 (C⋮N), 1685m (amide I str.), 1575ms (amide II), 1355m, and 1305m (amide III) †
4-Formamido-1-methyl	3250m, 2250, 1680s, 1580s, 1440m, 1350s, and 1225m
4-Formamido-2-methyl	3250m, 2220, 1670s, 1560s, 1530s, and 1280m
1,6-Dihydro-6-imino-8-azapurines	
1,7-Dimethyl	3260ms (NH str.), 1665s (C:N str.), 1580ms, 1310ms, 1200m, and 1125m
1,8-Dimethyl	3330m, 1645s, 1585m, 1340m, 1300m, and 1205m
1,9-Dimethyl	3290m, 1655s, 1575m, 1345m, 1265m, 1180m, and 1100m
9-Benzyl-1-methyl	3290m, 1665s, 1565m, 1350m, 1260m, 1185m, 1100m, and 1050m
1-Methyl	3160br,m (NH), 1930br,w (:NH⁺ str.), 1700s (C:N⁺ str.), 1640s (C:N str.), 1575m, 1340m, and 1055m
6-Methylamino-8-azapurines	
7-Methyl	3310m (NH str.), 1625br,s, 1565m, 1345m, and 1200m
8-Methyl	3220br,w, 1635br,s, 1570m, 1340s, and 1300m
9-Methyl	3280br,m, 1635br,s, 1590m, 1335s, and 1325s

* *Cf.* spectrum of 3-cyano-2-ethoxymethyleneaminopyrazine.[6] † In acetonitrile solution, the amide I peak moved to 1707 cm^{-1} and was more intense than amide II (at 1535 cm^{-1}).

TABLE 3

^1H N.m.r. spectra [τ values; solvent $(CD_3)_2SO$; internal standard Me_4Si]

5-Cyano-1,2,3-triazoles	
4-Ethoxymethyleneamino-1-methyl	1·37 (1H, N:CH), 5·61 (2H, q, *J* 7 Hz, $CH_2{\cdot}CH_3$), 5·81 (3H, 1-Me), 8·62 (3H, t, *J* 7 Hz, $CH_2{\cdot}CH_3$)
4-Ethoxymethyleneamino-2-methyl	1·54 (1H), 5·66 (2H, q, *J* 7 Hz), 5·82 (3H, 2-Me), 8·67 (3H, t, *J* 7 Hz)
4-Ethoxymethyleneamino-3-methyl	1·44 (1H), 5·54 (2H, q, *J* 7 Hz), 6·11 (3H, 3-Me), 8·60 (3H, t, *J* 7 Hz)
4-Ethoxymethyleneamino-3-benzyl	1·59 (1H), 2·64 (5H, Ph), 4·56 (2H, CH_2Ph), 5·53 (2H, q, *J* 7 Hz), 8·57 (3H, t, *J* 7 Hz)
4-Acetamido-1-methyl	−1·4br * (1H, NH), 5·72 (3H, 1-Me), 7·83 (3H, COMe)
4-Formamido-1-methyl	1·57 (1H, CHO), 5·77 (3H, Me)
4-Formamido-2-methyl	1·56 (1H), 5·76 (3H)
1,6-Dihydro-6-imino-8-azapurines	
1,7-Dimethyl	2·00 (1H, 2-CH), 2·4br * (1H, NH), 5·63 (3H, 7-Me), 6·62 (3H, 1-Me)
1,8-Dimethyl	1·68 (1H, 2-CH), 1·9br * (1H, NH), 5·61 (3H, 8-Me), 6·46 (3H, 1-Me)
1,9-Dimethyl	1·73 (1H, 2-CH), 2·1br * (1H, NH), 5·96 (3H, 9-Me), 6·63 (3H, 1-Me)
6-Methylamino-8-azapurines	
7-Methyl ‡	1·38 (1H, 2-CH), 2·0br * (1H, NH), 5·42 (3H, 7-Me), 6·56 (3H, s, HN*Me*)
8-Methyl	1·1br * (1H, NH), 1·36 (1H, 2-CH), 5·44 (3H, 8-Me), 6·91 † (3H, d, *J* 6 Hz, HN*Me*)
9-Methyl	1·24br * (1H, NH), 1·62 (1H, 2-CH), 5·87 (3H, 9-Me), 6·58br * (N*H*Me), 6·96 † (3H, d, *J* 5 Hz, HN*Me*)
9-Benzyl	1·56 (1H, NH), 2·65 (5H, Ph), 4·22 (2H, CH_2), 6·96 † (3H, d, *J* 5 Hz, HN*Me*)

* D_2O removes this signal. † D_2O converts this signal to a singlet. ‡ Inserted for comparison; from ref. 11.

the 3-*methyl isomer* (from the corresponding aminonitrile in 70% yield,[15] m.p. 232° *) had m.p. 38° (from 20 parts of cyclohexane) [Found (material dried at 22° and 0·01 mmHg): C, 46·8; H, 4·9; N, 39·3%].

3-*Benzyl*-5-*cyano*-4-*ethoxymethyleneamino*-1,2,3-*triazole*.—4-Amino-3-benzyl-5-cyanotriazole[16] (0·6 g, 0·003 mol), acetic anhydride (1 ml), and triethyl orthoformate (3 ml) were vigorously boiled under reflux for 2 h. Volatile material was removed as before, giving the *ethoxymethyleneamino-compound* (90%) (from 25 parts of cyclohexane), m.p. 77° [Found (material dried at 20° and 0·05 mmHg): C, 61·4; H, 5·1; N, 27·8. $C_{13}H_{13}N_5O$ requires C, 61·2; H, 5·1; N, 27·4%].

4-*Acetamido*-5-*cyano*-1-*methyl*-1,2,3-*triazole*.—Acetic anhydride (0·8 g, 2 equiv.) was added dropwise to a stirred suspension of 4-amino-5-cyano-1-methyltriazole[2] (0·5 g) in dried pyridine (4 ml); the mixture was set aside overnight then warmed at 80° with ethanol (4 ml) for 1 h. Water (3 ml) was added and volatile material was removed at 50° and 25 mmHg, giving the *acetamido-compound* (93%), m.p. 222° (from 34 parts of water) (Found: C, 43·65; H, 4·4; N, 42·0. $C_6H_7N_5O$ requires C, 43·6; H, 4·3; N, 42·4%), soluble in N-sodium hydroxide.

5-*Cyano*-4-*formamido*-x-*methyl*-1,2,3-*triazoles*.—4-amino-5-cyano-1-methyl-1,2,3-triazole[2] (0·5 g) and acetic formic anhydride[17] (5 ml) were set aside at 25° for for 30 h. Removal of volatile material at 55° and 25 mmHg, left crystals which, rubbed with water (1 ml), gave 87% of 5-*cyano*-4-*formamido*-1-*methyl*-1,2,3-*triazole*, m.p. 156° (from 6 parts of methanol) [Found (material dried at 30° and 25 mmHg): C, 39·5; H, 3·3; N, 46·0. $C_5H_5N_5O$ requires C, 39·7; H, 3·3; N, 46·3%]. 5-*Cyano*-4-*formamido*-2-*methyltriazole*, similarly prepared (92%) from 4-amino-5-cyano-2-methyltriazole,[2] had m.p. 138° (from a little ethanol) (Found: C, 39·75; H, 3·5; N, 45·9%).

1,6-*Dihydro*-6-*imino*-1,x-*dimethyl*-8-*azapurines* (6,7-*Dihydro*-7-*imino*-y,6-*dimethyl*-v-*triazolo*[4,5-d]*pyrimidines*).—Ethanolic methylamine (30% w/w; 0·78 g, 2 equiv.) was added dropwise to a stirred suspension of 4-ethoxymethyleneamino-1-methyl-1,2,3-triazole (0·54 g, 0·003 mol) in ethanol (15 ml) at 0°. The mixture became clear, but soon deposited crystals. It was set aside at 20—25° overnight, then kept at −5° for 3—4 h and filtered. The crystals, washed with benzene, gave 1,6-*dihydro*-6-*imino*-1,7-*dimethyl*-8-*azapurine* (3) (85%), m.p. 217° (from 30 parts of methanol) [Found (material dried at 60° and 0·01 mmHg): C, 43·8; H, 5·1; N, 51·1. $C_6H_8N_6$ requires C, 43·9; H, 4·9; N, 51·2%]. The 1,8-*dimethyl isomer* (4), similarly prepared (87%), had m.p. 202° (from 15 parts of methanol) (Found: C, 43·6; H, 4·95; N, 51·2%), and is decomposed by hot, dilute acid. The 1,9-*dimethyl isomer*, made likewise (84%), had m.p. 206° (from 130 parts of benzene) [Found (material dried in air at 110°): C, 43·8; H, 5·0; N, 51·4%].

9-*Benzyl*-1,6-*dihydro*-6-*imino*-1-*methyl*-8-*azapurine* (3-*Benzyl*-6,7-*dihydro*-7-*imino*-6-*methyl*-v-*triazolo*[4,5-d]*pyrimidine*).—Ethanolic methylamine (30% w/w; 2·6 g, 2 equiv.) diluted with ethanol (20 ml) was added dropwise to a vigorously stirred solution (prepared at 60°, then cooled to 0°) of 3-benzyl-5-cyano-4-ethoxymethyleneamino-1,2,3-triazole (2·6 g, 0·01 mol) in ethanol (100 ml). The suspension, set aside at 20—25° overnight and filtered, gave the title *imine* (80%), m.p. 178° (from 30 parts of ethanol) [Found (material dried at 85° in air): C, 60·1; H, 4·95; N, 34·9. $C_{12}H_{12}N_6$ requires C, 60·0; H, 5·0; N, 35·0%].

1,6-*Dihydro*-6-*imino*-1-*methyl*-8-*azapurine* (6,7-*Dihydro*-7-*imino*-6-*methyl*-v-*triazolo*[4,5-d]*pyrimidine*.—Sodium (*ca.* 0·8 g) was added to 3-benzyl-1,6-dihydro-6-imino-1-methyl-8-azapurine (1·92 g, 0·008 mol) stirred in liquid ammonia (100 ml) until a faint blue colour persisted for 1 min. After evaporation of the ammonia, water (20 ml) was added, and the solution was clarified by stirring with kieselguhr and carbon. The filtrate, neutralised to pH 7 with phosphoric acid (*ca.* 1·1 ml), deposited 1,6-*dihydro*-6-*imino*-1-*methyl*-8-*azapurine* (70%). Purified from much boiling water, it suddenly charred and effervesced at *ca.* 295° [Found (material dried at 110° in air): C, 39·7; H, 4·1; N, 56·3. $C_5H_6N_6$ requires C, 40·0; H, 4·0; N, 56·0%]. It was unchanged by cold, but decomposed by boiling, 0·1N-sodium hydroxide.

x-*Methyl*-6-*methylamino*-8-*azapurines* (y-*Methyl*-7-*methylamino*-v-*triazolo*[4,5-d]*pyrimidines*).—1,6-Dihydro-6-imino-1,7-dimethyl-8-azapurine (0·165 g, 0·001 mol), methylamine acetate (0·18 g, 2 equiv.), and methanol (5 ml) were heated under reflux for 2 h. The solution, stirred at −5°, deposited 7-methyl-6-methylamino-8-azapurine (80%), m.p. 302° (from 80 parts of water) identical with an authentic specimen.[11] Similarly the 1,8-dimethyl-imine gave 8-methyl-6-methylamino-8-azapurine (90%), m.p. 255° (from 40 parts of water), identical with a specimen synthesised by another route.[11] Likewise the 1,9-dimethylimine gave 9-methyl-6-methylamino-8-azapurine (96%), m.p. 224° (slow decomp.), identical with authentic material[18] (Found: C, 43·8; H, 5·0; N, 51·4. Calc. for $C_6H_8N_6$: C, 43·9; H, 4·9; N, 51·2%).

9-*Benzyl*-6-*methylamino*-8-*azapurine* (3-*Benzyl*-7-*methylamino*-v-*triazolo*[4,5-d]*pyrimidine*).—9-Benzyl-1,6-dihydro-6-imino-1-methyl-8-azapurine (0·24 g, 0·001 mol), methylamine acetate (0·18 g), and methanol (7 ml), boiled for 90 min, chilled, and filtered, yielded 9-*benzyl*-6-*methylamino*-8-*azapurine* (93%), m.p. 204° [Found (material dried in air at 110°): C, 60·2; H, 5·1; N, 35·2. $C_{12}H_{12}N_6$ requires C, 60·0; H, 5·0; N, 35·0%].

4-*Amino*-3-*benzyl*-5-*carbamoyl*-1-*methyl*-1,2,3-*triazolium Toluene*-p-*sulphonate*.—4-Amino-3-benzyl-1,2,3-triazole-5-carboxamide[19] (20 g), methyl toluene-*p*-sulphonate (25 g), and dimethyl sulphoxide (10 ml) were rapidly heated to 150° (bath temp.) and stirred at that temperature for a few minutes until effervescence began to decrease and the solution became golden brown. The melt was cooled to 50°, ethanol (200 ml) was added, and the mixture was refrigerated then filtered. The product, recrystallised from water (9 parts) gave 70% of the triazolium salt, identical with authentic material.[20]

6-*Methylamino*-8-*azapurine* (*Improved Preparation*).—6-Methylthio-8-azapurine (0·8 g) and ethanolic methylamine (33% w/w; 4·8 ml) were heated in a sealed tube for 4 h at 100°. The solvent was evaporated off. The residual ammonium salt, dissolved in boiling water (200 ml) and adjusted to pH 3·7 with acetic acid, deposited pure

* New, higher m.p.

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6-methylamino-8-azapurine (83%), identical with authentic material.[18]

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