

***v*-Triazolo[4,5-*d*]pyrimidines (8-Azapurines).† Part VIII.^{1,2} Synthesis, from 1,2,3-Triazoles,‡ of 1- and 2-Methyl Derivatives of 5,7-Disubstituted *v*-Triazolo[4,5-*d*]pyrimidines (7- and 8-Methyl 2,6-Disubstituted 8-Azapurines)**

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4-Amino-1-methyl-1*H*-1,2,3-triazole-5-carboxamide (1), fused with thiourea, gave 5-mercapto-1-methyl-1*H*-*v*-triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (2-mercapto-7-methyl-8-azapurin-6-one) (2a), which was methylated and oxidised to give the 5-methylsulphonyl derivative. This, when heated with sodium methoxide or ammonia, gave the 5-methoxy- and 5-amino-derivatives, respectively. 4-Amino-2-methyl-2*H*-1,2,3-triazole-5-carboxamide similarly gave various 5-substituted 2-methyl-2*H*-*v*-triazolo[4,5-*d*]pyrimidin-7(6*H*)-ones. 4-Amino-2-methyl-*N*-bis(methylamino)methylene-2*H*-1,2,3-triazole-5-carboxamide (5) was obtained as a by-product when the 2-methyl-5-methylsulphonyl derivative was heated with methylamine.

Alkaline hydrolysis of the two methylsulphonyl compounds gave the corresponding 5,7-diones, identical with products obtained by fusing the two triazoles with urea. A by-product of the first hydrolysis was 1-methyl-4-ureido-1*H*-1,2,3-triazole-5-carboxylic acid (3), which was further degraded to the 4-amino-derivative.

The two 5-mercapto-compounds were converted into the corresponding 5,7-bis(methylthio)-derivatives, which gave 7-amino-5-methylthio-compounds on heating with ethanolic ammonia. 5,7-Diamino-derivatives were made by heating the derived sulphones with ethanolic ammonia; in contrast, treatment with sodium methoxide and aqueous alkali gave 7-amino-5-methoxy- and 7-amino-5-oxo-derivatives, respectively. 5,7-Dichloro-2-methyl-2*H*-*v*-triazolo[4,5-*d*]pyrimidine (2,6-dichloro-8-methyl-8-azapurine) (made from the appropriate 5,7-dione) gave the 5,7-diamine with ethanolic ammonia.

The ionisation constants and the u.v., i.r., and n.m.r. spectra of these compounds are recorded and discussed.

AMONG the analogues of naturally occurring purines, probably the best known anti-cancer agent is '8-azaguanine' (2-amino-8-azapurin-6-one; 5-amino-*v*-triazolo[4,5-*d*]pyrimidin-7-one). It has been shown to be highly active in suppressing growth of several strains of transplantable adenocarcinomas of the breast in mice,^{3a-d} even strains that had become resistant to 6-mercapto-purine,^{3a} and it inhibited the Brown-Pearce squamous-cell carcinoma in rabbits' eyes.^{3b} In human patients this drug was, in part, degraded to the 2-oxo-analogue^{3c} (purine numbering) and, when the dose was raised, skin rashes limited its use.^{3d} These results suggested that derivatives methylated in the triazole ring might prove more useful, (a) by acting as depots for the liberation of '8-azaguanine' by normal biochemical *N*-demethyl-

ation,⁴ or (b) by blocking the deaminating enzyme (guanylase).

9-Alkyl-derivatives of '8-azaguanine' can easily be prepared from 5-amino-4-alkylaminopyrimidines, but synthesis of 7- and 8-alkyl derivatives has awaited the new methods⁵ which use 1,2,3-triazole intermediates, e.g. (1). The present work describes the first general method for making 7- and 8-methyl derivatives of 2,6-disubstituted 8-azapurines (1- and 2-methyl 5,7-disubstituted triazolopyrimidines), and includes the required alkylated analogues of '8-azaguanine', e.g. (2e).

Preparation of 7- and 8-Methyl-8-azapurin-6-ones

³ (a) G. W. Kidder, V. C. Dewey, R. E. Parks, and G. L. Woodside, *Science*, 1949, **109**, 511; (b) A. Gellhorn, M. Engelman, D. Shapiro, S. Graff, and H. Gillespie, *Cancer Res.*, 1950, **10**, 170; (c) K. Sugiura, G. H. Hitchings, L. F. Cavalieri, and C. C. Stock, *ibid.*, p. 178; (d) J. A. Montgomery, J. R. Johnson, and F. M. Schabel, *ibid.*, 1959, **19**, 425; (e) A. Gellhorn, *Cancer*, 1953, **6**, 1030.

⁴ A. Albert, 'Selective Toxicity,' Methuen, London, 4th edn., 1968, sections 2.3 and 2.4.

⁵ (a) A. Albert and K. Tratt, *J. Chem. Soc. (C)*, 1968, 344 (b) A. Albert, *ibid.*, p. 2076.

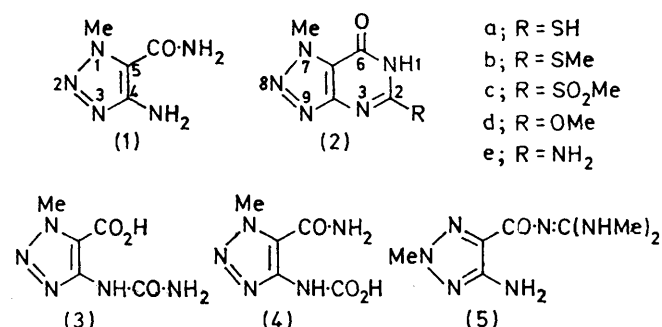
† This series was previously entitled '1,2,3,4,6-Penta-azadenes.'

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

¹ Part VII, A. Albert, *J. Chem. Soc. (C)*, 1969, 2379.

² Preliminary report, A. Albert and H. Taguchi, *Chem. Comm.*, 1971, 249.

with Various 2-Substituents.—4-Amino-1-methyl-1,2,3-triazole-5-carboxamide^{5a} could not be induced to react with guanidine or with guanidine carbonate under various conditions. However, fusion with thio-urea gave 2-mercapto-7-methyl-8-azapurin-6-one (2a), which was S-methylated (with methyl iodide in cold aqueous sodium hydroxide) to give the 2-methylthio-analogue (2b) in excellent yield. The ¹H n.m.r. spectrum



of the latter showed characteristic peaks for an *N*- and an *S*-methyl group. This methylthio-analogue, when stirred with potassium permanganate in dilute acetic acid, gave a good yield of the 2-methylsulphonyl compound (2c), showing *N*- and *S*-methyl n.m.r. signals, and i.r. bands at 1335s + 1320m, and 1180m + 1155m cm⁻¹ (S-O stretching, asymmetric and symmetric, respectively).⁶

Similarly 4-amino-2-methyl-1,2,3-triazole-5-carboxamide,^{5b} gave successively the corresponding 2-mercapto-, 2-methylthio-, and 2-methylsulphonyl-8-methyl-8-azapurinones. The sulphone was hydrolysed with cold aqueous potassium hydroxide to the 2,6-dione, identical with the product obtained by fusing 4-amino-2-methyl-1,2,3-triazole-5-carboxamide with urea. Both specimens were identical with the compound isolated in 20% yield⁷ from the methylation products of 8-azapurine-2,6-dione.

The isomeric sulphone (2c) similarly gave the 2,6-dione, identical with the substance obtained by condensing 4-amino-1-methyl-1,2,3-triazole-5-carboxamide (1) with urea, and with a specimen previously obtained by debenzylating 9-benzyl-7-methyl-8-azapurine-2,6-dione.⁷ Hydrolysis of the sulphone (2c) also gave a by-product, the proportion of which increased on longer exposure to alkali or on heating. This by-product was also obtained by stirring 7-methyl-8-azapurine-2,6-dione in aqueous potassium hydroxide. Elemental analysis indicated the empirical formula C₈H₇N₅O₃; the n.m.r. spectrum ([²H₈]dimethyl sulphoxide) showed three singlets, one at τ 5.75 (3H, NMe) and the others as broad peaks at τ 2.90 (2H) and 1.96 (1H) (exchangeable,

* All *N*-methyl-8-azaguanines are now known: namely the 1-methyl isomer (C. W. Noell, L. B. Townsend, and R. K. Robins, 'Synthetic Procedures in Nucleic Acid Chemistry,' ed. W. W. Zorbach and R. S. Tipson, 1968, Interscience-Wiley, New York, 1, 44), the 3-methyl isomer (L. B. Townsend and R. K. Robins, *ibid.*, p. 18), and the 9-methyl isomer [made by J. Davoll (London), unpublished, but tested against tumours by the Sloan-Kettering Institute as MHC-2164].

NH). The i.r. spectrum showed a carbonyl band at 1695s,br cm⁻¹. These data indicated structure (3) or (4); the latter seemed unlikely because the substance did not decarboxylate easily as a substituted carbamic acid should. In order to confirm structure (3), the stability of the carboxamide group to alkali was compared with that of the carboxamide group in 4-amino-1-methyl-1,2,3-triazole-5-carboxamide. The latter, under the conditions (1 h at 100°) used in the hydrolysis of the 2,6-dione, furnished 4-amino-1-methyl-1,2,3-triazole-5-carboxylic acid in 74% yield. This result suggested the presence of a stable urea (rather than an amide) group in the by-product, and confirmed the identification as 1-methyl-4-ureido-1,2,3-triazole-5-carboxylic acid (3). Further hydrolysis of this substance (3) in boiling aqueous potassium hydroxide eventually gave 4-amino-1-methyl-1,2,3-triazole-5-carboxylic acid.

As expected, the sulphone group in compound (2c) was easily replaced by nucleophiles. Thus 2-methoxy-7-methyl-8-azapurin-6-one (2d) was readily obtained when the sulphone (2c) was boiled with sodium methoxide in methanol. Likewise, the 2-amino-7-methyl derivative* (2e), of potential biological and biochemical interest as an analogue of guanine, was obtained in excellent yield by heating the sulphone (2c) with ethanolic ammonia at 160°. Similarly 8-methyl-2-methylsulphonyl-8-azapurin-6-one furnished 2-methoxy-, 2-ethoxy-, 2-amino-,* 2-methylamino-, and 2-dimethylamino-derivatives.

When 8-methyl-2-methylsulphonyl-8-azapurin-6-one was heated with methylamine at 90°, the expected 8-methyl-2-methylamino-derivative was obtained, accompanied by a by-product which was the main product at 120°. Elemental analysis of this by-product satisfied the empirical formula C₇H₁₃N₇O; the u.v. spectrum (neutral species at 260 nm and cation at 233 nm) indicated the presence of the triazole ring system.^{5b} The n.m.r. spectrum (CF₃·CO₂H) showed a singlet (NMe in the triazole ring) at τ 5.78 and a six-proton singlet at τ 6.89. This compound was much more strongly basic (p*K*_a 7.97) than other aminotriazoles,⁵ but the p*K*_a value was similar to that of an acylguanidine.⁹ These physical data indicated the compound to be 4-amino-2-methyl-*N*-bis(methylamino)-methylene-1,2,3-triazole-5-carboxamide (5).

Preparation of 7- and 8-Methyl-8-azapurines with a 6-Amino-group.—Because 2,6-diamino-8-azapurine possesses strong enzyme-inhibiting properties,⁸ modifications of the foregoing reactions were investigated

⁶ D. Barnard, J. M. Fabian, and H. P. Koch, *J. Chem. Soc.*, 1949, 2442; E. D. Amstutz, I. M. Hunsberger, and J. J. Chessick, *J. Amer. Chem. Soc.*, 1951, 73, 1220; C. C. Price and H. Morita, *ibid.*, 1953, 75, 4747; C. C. Price and R. C. Gillis, *ibid.*, 1953, 75, 4750.

⁷ G. Nübel and W. Pfeiderer, *Chem. Ber.*, 1965, 98, 1060.

⁸ H. G. Mandel, *Pharmacol. Rev.*, 1959, 11, 743; R. E. Handschumacher and A. D. Welch, 'The Nucleic Acids,' ed. E. Chargaff and J. N. Davidson, Academic Press, New York, 1955, vol. 3, p. 453.

⁹ A. Albert, R. Goldacre, and J. Phillips, *J. Chem. Soc.*, 1948, 2240.

in order to obtain similar agents by introducing a 6-amino-group.

2-Mercapto-7-methyl-8-azapurin-6-one (2a), heated with phosphorus pentasulphide in pyridine, gave the 2,6-dithione, which was methylated (with methyl iodide in cold aqueous sodium hydroxide) to give the 2,6-bis(methylthio)-compound. The n.m.r. spectrum (CDCl₃) showed singlets at τ 7.32 and 7.22 ($2 \times$ SMe) and at τ 5.48 (NMe). Heating this bis(methylthio)-derivative with ethanolic ammonia gave 6-amino-7-methyl-2-methylthio-8-azapurine without any by-product. The i.r. spectrum showed a band at 3350 cm⁻¹ (primary NH₂) and the n.m.r. spectrum ([²H₆]dimethyl sulphoxide) showed singlets (3H) at τ 7.40 and 5.52 (S- and N-Me, respectively) and a broad peak (2H) at τ 2.06 (NH₂, exchangeable). This methylthio-compound was oxidised with potassium permanganate to give the sulphone in excellent yield, ν_{\max} 1310s and 1140s cm⁻¹ (SO₂).

Again the methylsulphonyl group was reactive and gave the 2,6-diamine* (by the action of ethanolic ammonia) and the 6-amino-2-methoxy- (by heating with sodium methoxide in methanol) and 6-amino-2-oxo-derivatives (aqueous potassium hydroxide at 20°). The physical properties of the last named substance, different from those of 2-amino-7-methyl-8-azapurin-6-one, confirmed that ammonia selectively attacked the 6-position of the 2,6-bis(methylthio)-derivative. [Similarly in 2,6-bis(methylthio)purine, only the group in the 6-position could be replaced with dimethylamine,¹⁰ and 2,6-diaminopurine could not be obtained by heating 6-amino-2-methylthiopurine with ammonia.¹¹]

2,6-Bis(methylthio)-8-methyl-8-azapurine, similarly prepared from the 2-mercapto-6-one *via* the 2,6-dithione, was converted into the 6-amino-2-methylthio-derivative (by heating with ethanolic ammonia) which, on oxidation with potassium permanganate, gave the 6-amino-2-methylsulphonyl compound. 2,6-Diamino-8-methyl-* and 6-amino-2-methoxy-8-methyl-8-azapurine were made by heating the sulphone with ammonia and sodium methoxide, respectively. 6-Amino-8-methyl-8-azapurin-2-one was obtained by hydrolysis of the sulphone. 2,6-Bis(methylthio)-8-methyl-8-azapurine, with potassium permanganate, underwent oxidation and then partial hydrolysis to give 8-methyl-2-methylsulphonyl-8-azapurin-6-one, providing another example of the greater reactivity of the 6- over the 2-position.

Heating 8-methyl-8-azapurine-2,6-dione with phosphoryl chloride gave the readily hydrolysed 2,6-dichloro-derivative, which was easily converted, by

* For another isomer, 2,6-diamino-9-methyl-8-azapurine, see J. Davoll, *J. Chem. Soc.*, 1958, 1593.

¹⁰ J. A. Montgomery, L. B. Holum, and T. P. Johnston, *J. Amer. Chem. Soc.*, 1959, **81**, 3963.

¹¹ G. B. Elion, W. H. Lange, and G. H. Hitchings, *J. Amer. Chem. Soc.*, 1956, **78**, 217.

¹² D. Heinert and A. E. Martell, *J. Amer. Chem. Soc.*, 1959, **81**, 3933.

heating with ethanolic ammonia, into the 2,6-diamine; this route is more direct than that already given.

Physical Properties.—The i.r. spectra of all 8-azapurines (triazolopyrimidines) mentioned have weak or medium bands at 1030—1085, 1270—1310, 1380—1420, and *ca.* 1580 cm⁻¹, assignable to the heterocyclic nucleus (*cf.* spectra of pyrimidines¹² and 1,2,3-triazoles¹³). The carbonyl bands of the 6-ones appeared at rather high frequencies (1700—1730 cm⁻¹) [especially high in the 2-methylsulphonyl-6-ones (1730 cm⁻¹) because of strong electron-withdrawal by the sulphone group]. I.r. spectra of most of the 8-azapurines with sulphur substituents in the 2- and/or 6-positions showed medium or strong bands between 1140 and 1190 cm⁻¹, as found for other similarly substituted π -deficient heteroaromatic compounds¹⁴ [however these bands were not seen in the case of 6-amino-7-(or 8)-methyl-2-methylthio-8-azapurine].

N.m.r. spectra of the 6-amines ([²H₆]dimethyl sulphoxide) showed surprisingly sharp NH₂ signals ($W_{\frac{1}{2}}$ 6—10 Hz). However 2-aminopyrazine and 2- and 3-aminopyridine in the same solvent revealed signals that were almost as sharp ($W_{\frac{1}{2}}$ 9—10 Hz), whereas for solutions in the more commonly used [²H]chloroform these signals were much broader (20—27 Hz).

Ionisation constants of the 2- and 6-substituted 8-azapurines are shown as pK_a values in the Table. The effects of the 2-substituents on the ionisation (as acids) of the 6-ones are linearly correlated with Hammett's σ_m values¹⁵ for the substituents, and the slopes of lines (for the 7- and 8-methyl series) were similar. Each member of the 7-methyl-6-one series was more acidic (by 0.3—0.6 unit) than the 8-methyl isomer.

U.v. spectra of the 8-azapurines are shown in the Table. Comparison of the peak of longest wavelength for each 2-substituted 8-azapurin-6-one with that for the unsubstituted parent [7-Me-6-one 264 nm (0), 281 (—); 8-Me-6-one 267 nm (0), 286 (—); *ref.* 5], showed that it had shifted to a slightly longer wavelength in most examples, as expected; the λ_{\max} values of the neutral species (but not of the anion) of the 2-methylthio-derivatives had shifted slightly in the opposite direction. An unusually large hypsochromic shift (18—27 nm) was observed when most of the 2-amino-derivatives were converted into cations. However 6-amino-2-ones did not show this hypsochromic shift, but there were large bathochromic shifts (27—28 nm) when they were changed into anions.

Typical of the differences between the purine and the 8-azapurine series, 2-amino-7-methylpurin-6-one

¹³ E. Lieber, C. N. R. Rao, T. S. Cho, and H. Rubinstein, *Canad. J. Chem.*, 1958, **36**, 1441; E. Borello, A. Zecchina, and E. Guglielminotti, *J. Chem. Soc. (B)*, 1969, 307.

¹⁴ E. Spinner, *J. Org. Chem.*, 1958, **23**, 2037; M. Horák and J. Gut, *Coll. Czech. Chem. Comm.*, 1963, **28**, 3392.

¹⁵ H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. Trav. chim.*, 1959, **78**, 815; H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191; D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420; H. Zollinger and C. Wittwer, *Helv. Chim. Acta*, 1955, **39**, 347.

has acidic and basic pK_a values of 10.0 and 3.5, respectively, and is thus a weaker acid and a stronger base than 2-amino-7-methyl-8-azapurin-6-one (see Table). These large differences spring from the electron-withdrawing effect of the additional doubly-bonded nitrogen atom in the five-membered ring, which gives the 8-azapurines more of the electron disposition of pteridines than of purines (*cf.* 2-aminopteridin-4-one, pK_a 7.9 and 2.3).

When tested in mice against malignant tumours, 8-methyl-8-azaguanine inhibited the Ehrlich ascites

(series 2) spectrophotometer. 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 . I.r. spectra were taken (for mulls in Nujol and hexachlorobutadiene) with a Unicam SP 200 spectrophotometer, recalibrated at 2850, 1603, and 906 cm^{-1} (polystyrene standards).

Yields of substances which lacked a sharp m.p. refer to material sufficiently pure to give only one spot in chromatography on Whatman no. 1 paper developed with solvent A (aqueous 3% ammonium chloride) or B [butanol-5*N*-acetic

Ionisation constants and u.v. spectra

Compound	Ionisation in water (20°)					U.v. data (water) ^c		
	Species ^a	pK_a	Spread (±)	Concn. (M)	A.w.l. ^b (λ/nm)	λ_{max}/nm	$\log \epsilon$	pH ^d
8-Azapurin-6-one								
7-Methyl-2-methylthio	0					<235, 261	>3.5, 4.08	4
	—	6.73	0.04	4.0×10^{-5}	295	244, 295	4.30, 3.78	10
7-Methyl-2-methylsulphonyl	0					268	4.03	0
	—	2.96	0.04	3.0×10^{-5}	300	284	4.01	6
2-Methoxy-7-methyl	0					226, 277	3.65, 3.80	5
	—	7.17	0.04	3.9×10^{-5}	300	239, 284	3.66, 3.84	10
2-Amino-7-methyl	0					239, 297	3.85, 3.70	5
	—	8.25	0.03	4.7×10^{-5}	260	242, 299	3.76, 3.77	11
	+	1.58	0.03	3.3×10^{-5}	300	270	3.78	-2
8-Methyl-2-methylthio	0					234, 264	4.14, 4.04	4
	—	7.28	0.03	4.0×10^{-5}	300	244, 295	4.20, 3.99	10
8-Methyl-2-methylsulphonyl	0					<210, 272	>3.5, 4.05	1
	—	3.54	0.01	1.9×10^{-5}	300	221, 292	4.23, 4.05	7
2-Methoxy-8-methyl	0					227, 275	3.62, 3.87	5
	—	7.69	0.03	3.9×10^{-5}	300	248, 284	3.72, 3.91	10
2-Amino-8-methyl	0					243, 293	3.82, 3.80	6
	—	8.64	0.02	2.4×10^{-5}	300	251, 298	3.68, 3.90	12
	+	1.86	0.03	3.0×10^{-5}	300	268	4.00	-1
6-Amino-8-azapurine								
2-Amino-7-methyl	0					<230, 249, 309	>3.5, 3.78, 3.79	7
	+	4.27	0.04	2.4×10^{-5}	275	218, 258, 282	4.13, 4.07, 3.90	1
2-Amino-8-methyl	0					257, 307	3.77, 3.91	8
	+	5.17	0.05	1.9×10^{-5}	275	259, 284	4.11, 4.08	2
7-Methyl-2-oxo	0					255, 287	3.93, 3.83	6
	—	9.04	0.03	1.2×10^{-4}	275	251, 314	3.65, 3.77	12
	+	2.94	0.04	2.5×10^{-5}	260	295	3.76	0
8-Methyl-2-oxo	0					256, 285	4.03, 4.03	7
	—	9.98,	0.02	1.2×10^{-4}	280	257, 313	3.70, 3.90	13
	+	3.94	0.04	2.5×10^{-5}	250	289	3.99	1

^a Neutral species (0), cation (+), anion (-). ^b Analytical wavelength, for spectrometric determinations as in ref. 4. ^c Reflections in italics. ^d Negative values are solutions of sulphuric acid of acidity function H_0 (K. N. Bascombe and R. P. Bell, *J. Chem. Soc.*, 1959, 1096).

tumour and the Ridgeway osteogenic tumour at the highest tolerated dose (100 mg kg^{-1} day⁻¹). The 7-methyl isomer was relatively inactive at this dose and rather toxic to the mice.

EXPERIMENTAL

M.p.s were determined with an Electrothermal apparatus by the capillary method. As the m.p.s of most of the triazolopyrimidines were high, the thermometer was recalibrated with caffeine (m.p. 237°), phenolphthalein (m.p. 263°), benzophenone (b.p. 304° at 760 mmHg), and lead (f.p. 327.4°) (National Standards Laboratories specimens).

U.v. spectra were measured with a Unicam SP 800 spectrophotometer; the wavelength and intensity of each maximum were then checked with a Unicam SP 500

acid (7:3)], and viewed under 254 and 365 nm light. The identity of material from different reactions was established by comparison of i.r. spectra and R_F values, and also (where appropriate) by mixed m.p.

5-Mercapto-1-methyl-1*H*-*v*-triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (2-Mercapto-7-methyl-8-azapurin-6-one) (2a).—4-Amino-1-methyl-1,2,3-triazole-5-carboxamide ^{5a} (0.20 g) and thiourea (0.50 g) were heated at 176° for 150 min. The cooled mixture was dissolved in 2*N*-sodium hydroxide (5 ml) and refrigerated. The sodium salt was filtered off, washed with cold 2*N*-sodium hydroxide, and dissolved in warm water (3 ml); the solution was adjusted to pH 2 with 5*N*-sulphuric acid and chilled. The solid deposited, recrystallised from water (200 parts), gave the triazolopyrimidine (2a) (60%), m.p. 311° (decomp.) (Found: for material dried at 110° and 0.05 mmHg: C, 33.1; H, 2.9; N, 38.1; S, 17.5. $C_8H_5N_5OS$ requires C, 32.8; H, 2.8;

N, 38.2; S, 17.5%), ν_{\max} . 1750s (C=O str.), 1605s (NH), 1590s, 1300m, 1190m, and 1140m cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 6.60br (1H, NH), 5.69 (3H, s, NMe), and -2.75br (1H, NH).

1-Methyl-5-methylthio-1H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (7-Methyl-2-methylthio-8-azapurin-6-one) (2b).—To the thiol (2a) (2.30 g), dissolved in a solution of sodium hydroxide (1.52 g) in water (50 ml), cooled in ice, was added methyl iodide (2.04 g) with stirring. The mixture was stirred at 0° for 5 min more, and then at 20° for 20 min, and neutralised with acetic acid. The precipitate, recrystallised from ethanol (200 parts), gave the *methylthio-derivative* (2b) (89.5%), m.p. 305° (decomp.) (Found, for material dried at 110° and 0.05 mmHg: C, 36.8; H, 3.9; N, 35.5; S, 16.4. $\text{C}_6\text{H}_7\text{N}_5\text{OS}$ requires C, 36.5; H, 3.6; N, 35.5; S, 16.3%). ν_{\max} . 3350w, 3030m, 1700s (C=O str.), 1585m, 1300m, and 1170m cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 7.40 (3H, s, SMe), 5.63 (3H, s, NMe), and -3.05br (1H, NH).

1-Methyl-5-methylsulphonyl-1H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (7-Methyl-2-methylsulphonyl-8-azapurin-6-one) (2c).—Potassium permanganate (0.13 g) in water (3 ml) was added to a stirred suspension of the methylthio-compound (2b) (0.10 g) in aqueous 1% acetic acid (6 ml) at 20°. The mixture was stirred at 20° for 2 h longer, cooled in ice, and decolourised by passing sulphur dioxide. The needles deposited, recrystallised from ethanol (200 parts), gave the *sulphone* (2c) (74%), m.p. 231.5° (efferv.) (Found, for material dried at 110° and 0.05 mmHg: C, 31.6; H, 2.9; N, 30.4; S, 14.15. $\text{C}_6\text{H}_7\text{N}_5\text{O}_3\text{S}$ requires C, 31.4; H, 3.1; N, 30.6; S, 14.0%), ν_{\max} . 3030m, 2850m, 1730s (C=O str.), 1595m, and 1290m cm^{-1} , and sulphonyl bands (see Discussion section), $\tau[(\text{CD}_3)_2\text{SO}]$ 6.45 (3H, s, SMe), 5.55 (3H, s, NMe), and 2.28br (1H, NH).

5-Mercapto-2-methyl-2H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (2-Mercapto-8-methyl-8-azapurin-6-one).—4-Amino-2-methyl-1,2,3-triazole-5-carboxamide^{5b} (0.10 g) and thiourea (0.25 g) were heated at 176° for 180 min. The cooled mixture was dissolved in warm 5N-sodium hydroxide (0.6 ml) and refrigerated. The sodium salt was collected and dissolved in warm water (0.5 ml). This solution, adjusted to pH 2.5 with 5N-sulphuric acid, deposited a precipitate which, recrystallised from water (300 parts), gave the *5-mercapto-2-methyltriazolopyrimidin-7-one* (52%), m.p. 312.5° (efferv.) (Found, for material dried at 110° and 0.05 mmHg: C, 33.1; H, 2.8; N, 38.2; S, 17.1. $\text{C}_5\text{H}_5\text{N}_5\text{OS}$ requires C, 32.8; H, 2.8; N, 38.2; S, 17.5%), ν_{\max} . 3150m (NH), 1710s (C=O str.), 1605s (NH), 1300m, 1280m, 1165m, and 1150m cm^{-1} , $\tau(\text{CF}_3\text{-CO}_2\text{H})$ 5.54 (3H, s, NMe) and 1.70br (1H, NH).

2-Methyl-5-methylthio-2H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (8-Methyl-2-methylthio-8-azapurin-6-one).—To an ice-cold solution of the foregoing thiol (0.20 g) and sodium hydroxide (0.13 g) in water (4 ml) was added methyl iodide (0.17 g) with stirring. The mixture was further stirred for 10 min in an ice-bath and for 15 min at 20–25°, neutralised with acetic acid, and chilled. The crystals, collected and recrystallised from ethanol (120 parts), gave the *methylthio-derivative* (80%), m.p. 285.5° (Found, for material dried at 110° and 0.05 mmHg: C, 36.2; H, 3.9; N, 35.5; S, 16.1. $\text{C}_6\text{H}_7\text{N}_5\text{OS}$ requires C, 36.5; H, 3.6; N, 35.5; S, 16.3%), ν_{\max} . 1720s (C=O str.), 1580s, 1400m, 1300m, 1280m, and 1160s cm^{-1} , $\tau(\text{CF}_3\text{-CO}_2\text{H})$ 7.00 (SMe) and 5.47 (NMe).

2-Methyl-5-methylsulphonyl-2H-v-triazolo[4,5-d]pyrim-

idin-7(6H)-one (8-Methyl-2-methylsulphonyl-8-azapurin-6-one).—Potassium permanganate (0.26 g) in water (15 ml) was added at 20–25° with stirring to a suspension of the foregoing methylthio-derivative (0.20 g) in 1% acetic acid (12 ml) during 1 h. The mixture was stirred for 4 h longer, then cooled in ice and decolourised by passing sulphur dioxide. The needles deposited, recrystallised from ethanol (300 parts), gave the *sulphone* (78%), m.p. 223° (efferv.) (Found, for material dried at 110° and 0.05 mmHg: C, 31.3; H, 3.0; N, 30.9; S, 14.0. $\text{C}_6\text{H}_7\text{N}_5\text{O}_3\text{S}$ requires C, 31.4; H, 3.1; N, 30.6; S, 14.0%), ν_{\max} . 3380m (NH), 1730s (C=O str.), 1600m (NH), 1335s (SO_2 asym. str.), 1300m, 1280m, 1190m, and 1160m, and 1140m (SO_2 sym. str.) cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 6.71 (s, SMe) and 5.65 (s, NMe).

2-Methyl-2H-v-triazolo[4,5-d]pyrimidine-5(4H),7(6H)-dione (8-Methyl-8-azapurine-2,6-dione).—4-Amino-2-methyl-1,2,3-triazole-5-carboxamide (0.10 g) and urea (0.2 g) were heated at 176° for 160 min. The cooled mixture was dissolved in warm N-sodium hydroxide (3 ml) and refrigerated. The sodium salt was filtered off and dissolved in warm water (0.5 ml). The solution, adjusted to pH 2.5 with 5N-sulphuric acid, deposited crystals which [from water (80 parts)] gave the *dione* (63.5%), m.p. 352° (efferv.; unstandardised thermometer) (Found, for material dried at 110° and 0.05 mmHg: C, 35.7; H, 3.0; N, 41.9. Calc. for $\text{C}_5\text{H}_5\text{N}_5\text{O}_2$: C, 35.9; H, 3.0; N, 41.9%), ν_{\max} . 3170m (NH), 3060, 2890, and 2800m (NMe), 1700br,s (C=O str.), 1605m (NH), 1475m, 1385m, 1275m, and 1160m cm^{-1} .

Hydrolysis of 2-Methyl-5-methylsulphonyl-2H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (8-Methyl-2-methylsulphonyl-8-azapurin-6-one).—A solution of the *sulphone* (0.046 g) in N-potassium hydroxide (1 ml) was stirred at 20–25° for 20 h and adjusted to pH 2.5 with 5N-sulphuric acid. The solid deposited, recrystallised from water (80 parts) gave 2-methyl-2H-v-triazolo[4,5-d]pyrimidine-5(4H),7(6H)-dione (8-methyl-8-azapurine-2,6-dione) (58%), m.p. 352° (efferv.) (lit.,⁷ 326°).

1-Methyl-1H-v-triazolo[4,5-d]pyrimidine-5(4H),7(6H)-dione (7-Methyl-8-azapurine-2,6-dione).—4-Amino-1-methyl-1,2,3-triazole-5-carboxamide (0.10 g) and urea (0.20 g) were heated at 176° for 1 h. The cooled mixture was dissolved in 2N-sodium hydroxide (1.5 ml) and refrigerated. The sodium salt was collected, washed with cold 2N-sodium hydroxide, and dissolved in warm water (1 ml). The solution was adjusted to pH 2.5 with 5N-sulphuric acid. The solid deposited [recrystallised from water (100 parts)] gave the *triazolopyrimidinedione* (89%), m.p. 355° (decomp.; unstandardised thermometer; lit.,⁷ >350°) (Found, for material dried at 110° and 0.05 mmHg: C, 36.1; H, 2.95; N, 42.25. Calc. for $\text{C}_5\text{H}_5\text{N}_5\text{O}_2$: C, 35.9; H, 3.0; N, 41.9%), ν_{\max} . 1710s (C=O str.), 1620m, 1590m, 1350m, 1290m, and 1130m cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 5.73 (3H, s, NMe) and -1.67 (1H, s, NH).

Hydrolysis of the Sulphone (2c).—(a) A solution of the *sulphone* (0.023 g) in N-potassium hydroxide (0.5 ml) was stirred at 20–25° for 23 h and adjusted to pH 2 with 5N-sulphuric acid. The precipitate, recrystallised from water, gave 1-methyl-1H-v-triazolo[4,5-d]pyrimidine-5(4H),7(6H)-dione (7-methyl-8-azapurine-2,6-dione) (44%), m.p. 354° (decomp.).

(b) A solution of the *sulphone* (0.023 g) in N-potassium hydroxide (0.5 ml) was stirred at 20–24° for 84 h and adjusted to pH 2 with 5N-sulphuric acid. The deposited crystals [from water (300 parts)] gave 1-methyl-4-ureido-1H-1,2,3-triazole-5-carboxylic acid (3) (64.5%), m.p. 220.5°

(efferv.) (Found, for material dried at 110° and 0.05 mmHg: C, 32.3; H, 3.9; N, 37.55. $C_5H_7N_5O_3$ requires C, 32.4; H, 3.8; N, 37.8%), ν_{\max} 3350s (NH), 3200m (NH), 1695s (C=O str.), 1600s, 1310m, 1280m, 1210m, and 1160m cm^{-1} .

Hydrolysis of 1-Methyl-1H-v-triazolo[4,5-d]pyrimidin-5(4H),7(6H)-dione (7-Methyl-8-azapurine-2,6-dione).—(a) A solution of the dione (0.033 g) in *N*-potassium hydroxide (0.7 ml) was stirred at 20° for 96 h and adjusted to pH 1. The deposited crystals [recrystallised from water (300 parts)] gave the ureidotriazole (3) (67%), mp. 220° (efferv.).

(b) A solution of the dione (0.20 g) in *N*-potassium hydroxide (5 ml) was heated on a steam-bath for 1 h, adjusted to pH 1 with 5*N*-sulphuric acid, and cooled. The deposited crystals [from water (300 parts)] gave the ureidotriazole (3) (74%), m.p. 220.5° (efferv.).

Hydrolysis of 4-Amino-1-methyl-1,2,3-triazole-5-carboxamide (1).—A solution of the amide (0.40 g) in *N*-potassium hydroxide (10 ml) was warmed on a steam-bath for 1 h, adjusted to pH 2 with 5*N*-sulphuric acid, and cooled. The deposited crystals [recrystallised from water (50 parts)] gave 4-amino-1-methyl-1H-1,2,3-triazole-5-carboxylic acid (74%), m.p. 202–202.5° (efferv.) (Found, for material dried at 110° and 0.05 mmHg: C, 34.0; H, 4.0; N, 39.4. $C_5H_6N_4O_2$ requires C, 33.8; H, 4.3; N, 39.4%), ν_{\max} 3500m (NH), 3350s (NH), 2450w,br, 1695s (C=O str.), 1630m, 1320s, 1180s, and 775s cm^{-1} , $\tau[(CD_3)_2SO]$ 5.85 (3H, s, NMe) and 2.07br (2H, NH₂).

Hydrolysis of the Ureidotriazole (3).—A solution of the ureidotriazole (0.037 g) in *N*-potassium hydroxide (1 ml) was heated under reflux for 3 h, adjusted to pH 2 with 5*N*-sulphuric acid, and cooled. The deposited crystals (from water) gave 4-amino-1-methyl-1,2,3-triazole-5-carboxylic acid (43%), m.p. 202° (efferv.).

5-Methoxy-1-methyl-1H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (2d) (2-Methoxy-7-methyl-8-azapurin-6-one).—The sulphone (2c) (0.20 g) and methanolic sodium methoxide (0.06 g of sodium and 15 ml of methanol) were heated under reflux for 1 h. While cooling, the mixture was neutralised with acetic acid and evaporated to dryness under reduced pressure. The residue [from water (60 parts) and then from methanol (70 parts)] gave the *methoxy-derivative* (2d) (78%), m.p. 227° (Found, for material dried at 110° and 0.05 mmHg: C, 39.8; H, 3.6; N, 38.75. $C_6H_7N_5O_2$ requires C, 39.8; H, 3.9; N, 38.7%), ν_{\max} 3350m (NH), 3150m, 3100m, 1705s (C=O str.), 1620s, 1310s, 1060m (last two bands C–O–C str.), and 865m cm^{-1} , $\tau(CF_3 \cdot CO_2H)$ 5.75 (s) and 5.31 (s).

5-Amino-1-methyl-1H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (2e) (2-Amino-7-methyl-8-azapurin-6-one).—The sulphone (2c) (1.00 g) and saturated ethanolic ammonia (50 ml) were heated at 160° for 12 h. The mixture was evaporated to dryness under reduced pressure, water (20 ml) was added, and the suspension was chilled. The needles deposited were dissolved in 0.2*N*-sodium hydroxide (30 ml) and, after filtration, the solution was adjusted to pH 6 with 0.1*N*-hydrochloric acid. The precipitate, boiled with water (50 ml) for 15 min and filtered hot, gave the *amine* (2e) (85%), m.p. >360° [Found, for material recrystallised from water (4000 parts) and dried at 110° and 0.05 mmHg: C, 36.4; H, 3.6; N, 50.2. $C_5H_6N_6O$ requires C, 36.1; H, 3.6; N, 50.6%], ν_{\max} 3350s (NH), 3200m, 1705s (C=O str.), 1680s, 1630m, 1140m, and 880m cm^{-1} , $\tau(CF_3 \cdot CO_2H)$ 5.41 (3H, s, NMe) and 1.49br (2H, NH).

5-Methoxy-2-methyl-2H-v-triazolo[4,5-d]pyrimidin-7(6H)-

one (2-Methoxy-8-methyl-8-azapurin-6-one).—2-Methyl-5-methylsulphonyl-2H-*v*-triazolo[4,5-*d*]pyrimidin-7(6H)-one (8-methyl-2-methylsulphonyl-8-azapurin-6-one) (0.20 g) and methanolic sodium methoxide (0.06 g of sodium and 15 ml of methanol) were heated under reflux for 1 h. While cooling, the mixture was neutralised with acetic acid and evaporated to dryness under reduced pressure. The residue, crystallised from water (70 parts), gave needles which [from methanol (100 parts)] yielded the *methoxy-derivative* (84%), m.p. 232° (Found, for material dried at 65° and 0.05 mmHg: C, 39.75; H, 4.0; N, 39.0. $C_6H_7N_5O_2$ requires C, 39.8; H, 3.9; N, 38.7%), ν_{\max} 3400w, 3200m, 1710s (C=O str.), 1640s, 1560m, 1530m, 1340m, 1310s, 1285m, 1085m (last two C–O–C str.), 965m, and 880m cm^{-1} , $\tau[(CD_3)_2SO]$ 6.02 (3H, s, OMe), 5.67 (3H, s, NMe), and –2.3br (1H, NH).

5-Ethoxy-2-methyl-2H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (2-Ethoxy-8-methyl-8-azapurin-6-one).—Similarly, the methylsulphonyl derivative (0.10 g) and ethanolic sodium ethoxide (0.03 g of sodium and 15 ml of ethanol) were heated under reflux for 1 h. After chilling, the mixture was neutralised with acetic acid and evaporated. Water (50 parts), added to the residue, gave needles which [from ethanol (50 parts)] furnished the *ethoxy-derivative* (89%), m.p. 239.5° (Found, for material dried at 65° and 0.05 mmHg: C, 43.2; H, 4.8; N, 36.1. $C_7H_9N_5O_2$ requires C, 43.1; H, 4.65; N, 35.9%), ν_{\max} 3400w, 3200m (NH), 1720s (C=O str.), 1630s, 1530m, 1300s, 1290m, 1085m (last two C–O–C str.), and 1020m cm^{-1} , $\tau[(CD_3)_2SO]$ 8.64 (3H, t, *J* 7 Hz, O-CH₂-CH₃), 5.69 (3H, s, NMe), 5.55 (2H, q, *J* 7 Hz, O-CH₂-CH₃), and –2.3br (1H, NH).

5-Amino-2-methyl-2H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (2-Amino-8-methyl-8-azapurin-6-one).—Similarly, the sulphone (0.20 g) and saturated ethanolic ammonia (10 ml) were heated at 160° for 12 h and evaporated to dryness. Water (5 ml) was added to the residue; the solution was adjusted to pH 6 with acetic acid and chilled. The needles deposited [recrystallised from water (1000 parts)] gave the *amine* (90%), m.p. >350° (Found, for material dried at 110° and 0.05 mmHg: C, 35.8; H, 3.75; N, 50.2. $C_5H_6N_6O$ requires C, 36.1; H, 3.6; N, 50.6%), ν_{\max} 3380s (NH), 3210s (NH), 1710s (C=O str.), 1680s, 1630m, 1565s, 1320m, 1280m, and 900m cm^{-1} , $\tau(CF_3 \cdot CO_2H)$ 5.53 (3H, s, NMe) and 1.6br (2H, NH).

Reaction of 2-Methyl-5-methylsulphonyl-2H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (8-Methyl-2-methylsulphonyl-8-azapurin-6-one) with Methylamine.—The sulphone (0.20 g) and ethanolic 33% methylamine (10 ml) were heated at 90° for 12 h and evaporated to dryness under reduced pressure. Water (3 ml) was added to the residue, and the pH was adjusted to 6.5 with acetic acid. The prisms deposited [recrystallised from water (200 parts)] gave 2-methyl-5-methylamino-2H-*v*-triazolo[4,5-*d*]pyrimidin-7(6H)-one (8-methyl-2-methylamino-8-azapurin-6-one) (53.5%), m.p. >360° (Found, for material dried at 110° and 0.05 mmHg: C, 40.0; H, 4.3; N, 47.2. $C_6H_8N_6O$ requires C, 40.0; H, 4.5; N, 46.7%), ν_{\max} 3300s (NH), 3220s (NH), 1715s (C=O str.), 1630s, and 1550s cm^{-1} , $\tau(CF_3 \cdot CO_2H)$ 6.61 (NHMe) and 5.52 (NMe). The filtrate, adjusted to pH 8.5 with aqueous 2*N*-ammonia, deposited needles which [from methanol (200 parts)] gave 4-amino-2-methyl-*N*-bis(methylamino)methylene-2H-1,2,3-triazole-5-carboxamide (5) (40%), m.p. 275° (efferv.) (Found, for material dried at 110° and 0.05 mmHg: C, 40.0; H, 6.4; N, 46.6. $C_7H_{13}N_7O$ requires C, 39.8; H, 6.2; N, 46.4%), ν_{\max} 3460m, 3350m, 1670m,

1640s (C=O str.), 1610s, 1570s, 1530m, and 1425m cm^{-1} , $\tau(\text{CF}_3 \cdot \text{CO}_2\text{H})$ 6.89 (6H, s, NMe), 5.78 (3H, s, NMe), and 1.6—2.95 (4H, NH).

The same sulphone and ethanolic 33% methylamine were similarly heated at 120° for 12 h and evaporated to dryness under reduced pressure. The residue, crystallised from water and then from methanol (200 parts), gave the acylguanidine (5) (66%), m.p. 275° (efferv.).

5-Dimethylamino-2-methyl-2H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (2-Dimethylamino-8-methyl-8-azapurin-6-one).—The same sulphone (0.10 g) and ethanolic 33% dimethylamine (5 ml) were heated at 90° for 12 h, and evaporated to dryness under reduced pressure. Water (1 ml) was added to the residue and the pH was adjusted to 6 with acetic acid. The prisms deposited [recrystallised from water (100 parts)] gave the *dimethylamino-derivative* (80.5%), m.p. 322—323° (decomp.) (Found, for material dried at 110° and 0.05 mmHg: C, 42.9; H, 4.9; N, 43.5. $\text{C}_7\text{H}_{10}\text{N}_6\text{O}$ requires C, 43.3; H, 5.2; N, 43.3%), ν_{max} 3200m (NH), 1700s (C=O str.), 1605s (NH), and 1340m cm^{-1} , $\tau(\text{CF}_3 \cdot \text{CO}_2\text{H})$ 6.40 (s, NMe₂) and 5.49 (s, NMe).

5,7-Bis(methylthio)-1-methyl-1H-v-triazolo[4,5-d]pyrimidine [2,6-Bis(methylthio)-7-methyl-8-azapurine].—A solution of 5-mercapto-1-methyl-1H-v-triazolo[4,5-d]pyrimidin-7(6H)-one (2-mercapto-7-methyl-8-azapurin-6-one) (0.44 g) and phosphorus pentasulphide (1.07 g) in pyridine (10 ml) was heated under reflux for 5 h, and the mixture was evaporated under reduced pressure. Water (10 ml) was added to the residue and the deposited precipitate was collected and mixed with *N*-sodium hydroxide (5 ml). Filtration and acidification of the filtrate with 5*N*-sulphuric acid gave crude 1-methyltriazolopyrimidine-5,7-dithione (7-methyl-8-azapurine-2,6-dithione) (0.34 g), which decomposed on attempted purification. To a cooled solution of the crude material (0.34 g) in 0.5*N*-sodium hydroxide (7.5 ml), methyl iodide (0.75 g) was added; stirring was continued at 20—25° for 2 h. Deposited crystals were sublimed at 150° and 0.05 mmHg. Recrystallisation from methanol (50 parts) gave the *bis(methylthio)-derivative* (58%), m.p. 166—167° (sealed tube) (Found, for material dried at 65° and 0.05 mmHg: C, 36.7; H, 3.8; N, 30.5; S, 28.3. $\text{C}_7\text{H}_9\text{N}_5\text{S}_2$ requires C, 37.0; H, 4.0; N, 30.8; S, 28.2%), ν_{max} 1560s, 1450s, 1220m, and 1180m cm^{-1} .

7-Amino-1-methyl-5-methylthio-1H-v-triazolo[4,5-d]pyrimidine (6-Amino-7-methyl-2-methylthio-8-azapurine).—The foregoing bis(methylthio)-derivative (1.70 g) and saturated ethanolic ammonia (100 ml) were heated at 130° for 12 h and evaporated to dryness. Water (100 ml) was added to the residue. The deposited crystals [from water (250 parts)] gave the *amino-derivative* (88.5%), m.p. 287.5° (efferv.) (Found, for material dried at 65° and 0.05 mmHg: C, 36.8; H, 4.1; N, 42.4; S, 16.5. $\text{C}_6\text{H}_8\text{N}_6\text{S}$ requires C, 36.7; H, 4.1; N, 42.8; S, 16.3%), ν_{max} 3350m (NH), 1640s, 1580m, 1455m, 1270m, and 1220m cm^{-1} .

7-Amino-1-methyl-5-methylsulphonyl-1H-v-triazolo[4,5-d]pyrimidine (6-Amino-7-methyl-2-methylsulphonyl-8-azapurine).—Potassium permanganate (1.43 g) in water (30 ml) was added to a stirred suspension of the foregoing amino-derivative (1.10 g) in 1% acetic acid (60 ml). The mixture was stirred at 20—25° for 4 h longer, cooled with ice, and decolourised by passing sulphur dioxide. The crystals deposited [recrystallised from ethanol (300 parts)] gave the *sulphone* (87%), m.p. 262.5° (efferv.).

(Found, for material dried at 65° and 0.05 mmHg: C, 31.7; H, 3.6; N, 36.5; S, 14.3. $\text{C}_6\text{H}_8\text{N}_6\text{O}_2\text{S}$ requires C, 31.6; H, 3.5; N, 36.8; S, 14.05%), ν_{max} 3370m (NH), 1650s, 1620m, 1560m, 1435m, 1425m, 1310s (SO_2 asym.), 1140s (SO_2 sym.), and 775 m cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 6.59 (3H, s, SMe), 5.43 (3H, s, NMe), and 1.30br (2H, NH).

5,7-Diamino-1-methyl-1H-v-triazolo[4,5-d]pyrimidine (2,6-Diamino-7-methyl-8-azapurine).—The foregoing sulphone (0.34 g) and saturated ethanolic ammonia (20 ml) were heated at 150° for 12 h and evaporated to dryness under reduced pressure. Water (50 ml) was added to the residue; the crystals deposited were mixed with 0.1*N*-hydrochloric acid (solution clarified by filtration). The filtrate, made alkaline with aqueous 2*N*-ammonia gave the *diamine* (85%), m.p. >360° (Found, for material dried at 110° and 0.05 mmHg: C, 36.4; H, 4.7; N, 58.7. $\text{C}_5\text{H}_7\text{N}_7$ requires C, 36.4; H, 4.3; N, 59.4%), ν_{max} 3350m (NH), 3200s (NH), 1650s, 1600s (NH), and 1510m cm^{-1} , $\tau(\text{CF}_3 \cdot \text{CO}_2\text{H})$ 5.28 (s, NMe).

7-Amino-5-methoxy-1-methyl-1H-v-triazolo[4,5-d]pyrimidine (6-Amino-2-methoxy-7-methyl-8-azapurine).—The same sulphone (0.05 g) and methanolic sodium methoxide (0.015 g of sodium and 5 ml of methanol) were heated under reflux for 2 h. After chilling, the mixture was neutralised with acetic acid and evaporated to dryness under reduced pressure. Water (3 ml) was added to the residue; the crystals deposited [recrystallised from methanol (700 parts)] gave the *methoxy-amine* (78%), m.p. 282° (decomp.) (Found, for material dried at 110° and 0.05 mmHg: C, 40.2; H, 4.6; N, 46.8. $\text{C}_6\text{H}_8\text{N}_6\text{O}$ requires C, 40.0; H, 4.5; N, 46.7%), ν_{max} 3400m (NH), 3120m, 1660m, 1615m, 1590m, 1500m, 1450m, 1365m, 1340m, 1230s, and 1030m (last two bands C—O—C) cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 6.02 (3H, s, OMe), 5.52 (3H, s, NMe), and 2.08 (2H, NH₂).

7-Amino-1-methyl-1H-v-triazolo[4,5-d]pyrimidin-5(4H)-one (6-Amino-7-methyl-8-azapurin-2-one).—The same sulphone, finely powdered (0.05 g), and *N*-potassium hydroxide (1.5 ml) were stirred at 20—25° for 24 h. After chilling, the mixture was adjusted to pH 7 with *N*-acetic acid and the deposited crystals [recrystallised from water (1000 parts)] gave the *7-amino-5-one* (83%), m.p. 345° (decomp.) (Found, for material dried at 110° and 0.05 mmHg: C, 36.05; H, 4.0; N, 50.2. $\text{C}_5\text{H}_6\text{N}_6\text{O}$ requires C, 36.1; H, 3.6; N, 50.6%), ν_{max} 3340m (NH), 3190m (NH), 1680m, 1650s (C=O str.), 1620s, 1580m, 1480m, 1420m, 1390m, 1355m, and 1310m cm^{-1} , $\tau(\text{CF}_3 \cdot \text{CO}_2\text{H})$ 5.26 (s, NMe).

5,7-Bis(methylthio)-2-methyl-2H-v-triazolo[4,5-d]pyrimidine [2,6-Bis(methylthio)-8-methyl-8-azapurine].—5-Mercapto-2-methyltriazolopyrimidin-7(6H)-one (2-mercapto-8-methyl-8-azapurin-6-one) (0.50 g), phosphorus pentasulphide (1.25 g), and pyridine (10 ml) were heated under reflux for 1.5 h and the mixture was evaporated under reduced pressure. Addition of water (20 ml) to the residue formed a precipitate which was collected and mixed with *N*-sodium hydroxide (5 ml) (clarified by filtration). Acidification of the filtrate with 5*N*-sulphuric acid gave crude 2-methyltriazolopyrimidine-5,7-dithione (8-methyl-8-azapurine-2,6-dithione) (0.46 g). To a cooled solution of the dithione (0.46 g) in 0.5*N*-sodium hydroxide, methyl iodide (1.02 g) was added, and stirring was continued for 1 h at 20—25°. The deposited crystals were sublimed at 150° and 0.05 mmHg. Recrystallisation from ethanol (60 parts) gave the *bis(methylthio)-derivative* (43%), m.p. 197° (Found, for material dried at 110° and 0.05 mmHg: C, 37.3; H, 4.05; N, 31.1; S, 27.9. $\text{C}_7\text{H}_9\text{N}_5\text{S}_2$ requires

C, 37.0; H, 4.0; N, 30.8; S, 28.2%), ν_{\max} 1575m, 1550s, 1450s, 1380s, 1160s, 1050m, and 840m cm^{-1} , $\tau(\text{CDCl}_3)$ 7.35 (s, SMe), 7.27 (s, SMe), and 5.38 (s, NMe).

7-Amino-2-methyl-5-methylthio-2H-v-triazolo[4,5-d]-pyrimidine (6-Amino-8-methyl-2-methylthio-8-azapurine).—The foregoing bis(methylthio)-derivative (0.30 g) and saturated ethanolic ammonia (20 ml) were heated at 130° for 12 h and evaporated to dryness. Two recrystallisations of the residue from water (70 parts) gave the *amine* (91%), m.p. 209.5° (Found, for material dried at 110° and 0.05 mmHg: C, 36.9; H, 4.4; N, 43.0; S, 16.6. $\text{C}_6\text{H}_8\text{N}_6\text{S}$ requires C, 36.7; H, 4.1; N, 42.8; S, 16.3%), ν_{\max} 3500 (NH), 3250 (NH), 3130, 1660, 1610, 1570, 1445, 1380, and 1230 (all m) cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 7.50 (3H, s, SMe), 5.53 (3H, s, NMe), and 1.77br (2H, NH_2).

7-Amino-2-methyl-5-methylsulphonyl-2H-v-triazolo[4,5-d]pyrimidine (6-Amino-8-methyl-2-methylsulphonyl-8-azapurine).—Potassium permanganate (0.26 g) in water (5 ml) was added to a suspension of the foregoing amine (0.20 g) in 1% acetic acid (12 ml) at 20–25°, and stirring was continued for 2 h longer. The mixture was cooled in ice and decolourised by passing sulphur dioxide. The crystals deposited [recrystallised from ethanol (150 parts)] gave the *methylsulphonyl analogue* (89%), m.p. 232.5° (efferv.) (Found, for material dried at 110° and 0.05 mmHg: C, 31.6; H, 3.9; N, 36.3; S, 14.1. $\text{C}_6\text{H}_8\text{N}_6\text{O}_2\text{S}$ requires C, 31.6; H, 3.5; N, 36.8; S, 14.05%), ν_{\max} 3450s (NH), 3350s (NH), 3250m (NH), 1650s, 1610m, 1560m, 1380m, 1305s (S=O), 1145s (S=O), 1135s (S=O), and 945m cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 6.60 (3H, s, SMe), 5.42 (3H, s, NMe), and 0.95br (2H, NH_2).

5,7-Diamino-2-methyl-2H-v-triazolo[4,5-d]pyrimidine (2,6-Diamino-8-methyl-8-azapurine) from the 5-Methylsulphonyl Analogue.—The 5-methylsulphonyl compound (0.25 g) and saturated ethanolic ammonia (13 ml) were heated at 170° for 12 h and evaporated under reduced pressure. The residue, treated as described for the 1-methyl isomer, gave the *5,7-diamine* (70%), m.p. 326° (decomp.) (Found, for material dried at 110° and 0.05 mmHg: C, 36.05; H, 4.3; N, 58.9. $\text{C}_6\text{H}_8\text{N}_8$ requires C, 36.4; H, 4.3; N, 59.4%), ν_{\max} 3380s (NH), 3200s (NH), 1670s, 1645s, 1590s (NH), 1510m, 1400s, and 1310m cm^{-1} , $\tau(\text{CF}_3\cdot\text{CO}_2\text{H})$ 5.46 (s, NMe).

7-Amino-5-methoxy-2-methyl-2H-v-triazolo[4,5-d]pyrimidine (6-Amino-2-methoxy-8-methyl-8-azapurine).—The same 5-methylsulphonyl compound (0.23 g) and methanolic sodium methoxide (0.07 g of sodium and 20 ml of methanol) were heated under reflux for 1 h. The mixture, treated as the 1-methyl isomer, gave the *5-methoxy-7-amine* (84%), m.p. 243° (Found, for material dried at 110° and 0.05 mmHg: C, 40.0; H, 5.0; N, 46.2. $\text{C}_6\text{H}_8\text{N}_6\text{O}$ requires C, 40.0; H, 4.5; N, 46.7%), ν_{\max} 3400m (NH), 3100m, 2980m, 2950m (NMe), 1650m, 1610m (NH), 1580m, 1490m, 1430m, 1340m, 1300s, and 805m cm^{-1} , $\tau[(\text{CD}_3)_2\text{SO}]$ 6.11 (3H, s, OMe), 5.60 (3H, s, NMe), and 1.85br (2H, NH_2).

7-Amino-2-methyl-2H-v-triazolo[4,5-d]pyrimidin-5(4H)-one (6-Amino-8-methyl-8-azapurin-2-one).—The finely powdered 5-methylsulphonyl compound (0.18 g) and

n-potassium hydroxide (4 ml) were stirred at 20–25° for 3 h. The solution was chilled and adjusted to pH 7 with *n*-acetic acid. The deposited crystals [recrystallised from water (150 parts)] gave the *cyclic amide* (88%), m.p. 330° (efferv.) (Found, for material dried at 110° and 0.05 mmHg: C, 36.3; H, 3.8; N, 50.1. $\text{C}_5\text{H}_6\text{N}_6\text{O}$ requires C, 36.1; H, 3.6; N, 50.6%), ν_{\max} 3350m (NH), 3050m, 2950m (NMe), 1650s (C=O str.), 1600m (NH), 1510m, 1350m, and 1285m cm^{-1} , $\tau(\text{CF}_3\cdot\text{CO}_2\text{H})$ 5.48 (s, NMe).

5,7-Dichloro-2-methyl-2H-v-triazolo[4,5-d]pyrimidine (2,6-Dichloro-8-methyl-8-azapurine).—2-Methyl-2H-*v*-triazolo[4,5-d]pyrimidine-5(4H),7(6H)-dione (8-methyl-8-azapurine-2,6-dione) (0.35 g), phosphoryl chloride (4.5 ml), and diethylaniline (1.5 ml) were heated under reflux for 8 h, then concentrated (to ca. 2 ml) and poured into ice-water (10 ml). The mixture was extracted with benzene, and the extract was washed with water and dried (Na_2SO_4). The benzene was distilled off and the residue was sublimed at 80° and 0.05 mmHg. Recrystallisation from light petroleum (b.p. 60–80°) (60 parts) gave the *dichloro-derivative* (55%), m.p. 116–117° (Found, for material dried at 65° and 0.05 mmHg: C, 29.3; H, 1.3; Cl, 34.95; N, 34.3. $\text{C}_5\text{H}_3\text{Cl}_2\text{N}_5$ requires C, 29.4; H, 1.5; Cl, 34.75; N, 34.3%), ν_{\max} 1545, 1450, 1385, 1165, and 1040 (all m) cm^{-1} , $\tau(\text{CDCl}_3)$ 5.28 (s, NMe).

Oxidation of 5,7-Bis(methylthio)-2-methyl-2H-v-triazolo[4,5-d]pyrimidine [2,6-Bis(methylthio)-8-methyl-8-azapurine].—To the bis(methylthio)-compound (0.10 g) in acetic acid (16N; 2 ml) at 20–25°, potassium permanganate (0.22 g) in water (4 ml) was added during 30 min, and stirring was continued for 15 min. The solution was decolourised by passing sulphur dioxide. The deposited crystals [recrystallised from ethanol (100 parts)] gave 2-methyl-5-methylsulphonyltriazolopyrimidin-7(6H)-one (54%), m.p. 222–223° (efferv.), identical with the material obtained by oxidation of 2-methyl-5-methylthiotriazolopyrimidin-7(6H)-one.

5,7-Diamino-2-methyl-2H-v-triazolo[4,5-d]pyrimidine (2,6-Diamino-8-methyl-8-azapurine) from the 5,7-Dichloro-analogue.—The dichloro-compound (0.070 g) and saturated ethanolic ammonia (7 ml) were heated at 170° for 12 h and evaporated to dryness under reduced pressure. The residue was mixed with *n*-acetic acid and impurities were filtered off. The filtrate was made alkaline with aqueous 2N-ammonia, and the deposited crystals [from water (250 parts)] gave the *diamine* (61.5%), m.p. 325° (decomp.), identical with the specimen obtained from 7-amino-2-methyl-5-methylsulphonyltriazolopyrimidine.

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