v-Triazolo[4,5-*d*]pyrimidines (8-Azapurines). Part XII.[1] Cleavage of the Pyrimidine Ring in 8-Azapurines by Some Active Methylene Reagents and Eventual Closure to give *v*-Triazolo[4,5-*b*]pyridines

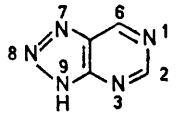
By **Adrien Albert** * and **William Pendergast**, Department of Medical Chemistry, John Curtin School of Medical Research, Australian National University, Canberra 2600, Australia

8-Azapurine (1) and its 2-amino-, 2-thioxo-, and 2-oxo-derivatives reacted with ethyl cyanoacetate to form 4-aminomethyleneamino-, 4-diaminomethyleneamino-, 4-thioureido-, and 4-ureido-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazoles † [(4a), (4b), (5a), and (5b), respectively], and with malononitrile to form the corresponding derivatives of 5-(2,2-dicyanovinyl)-1,2,3-triazole [(4c), (4d), (5c), and (5d), respectively]. The triazoles underwent cyclisation either to regenerate the starting azapurine or to form 5-amino-6-cyano-*v*-triazolo[4,5-*b*]-pyridine (7a). 8-Azapurine and its 2-oxo-derivative reacted with cyanoacetamide to give 5-amino-6-carbamoyl-*v*-triazolo[4,5-*b*]pyridine (7b), and with dimedone to give 5,6-dihydro-6,6-dimethyl-*v*-triazolo[4,5-*b*]quinolin-8(7*H*)-one (10). 8-Azapurine formed 6-acetyl- and 6-ethoxycarbonyl-5-methyl-*v*-triazolo[4,5-*b*]pyridine (11a and b) in reactions with acetylacetone and ethyl acetoacetate, respectively.

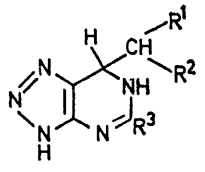
U.v. and ^{1}H n.m.r. spectra are reported and discussed.

We have shown recently [2] how derivatives of 8-azapurine (1) with a free 6-position form (in neutral or mildly alkaline solution) stable 1,6-adducts [types (2) and (3) where R^1 and R^2 are electron-withdrawing] with the following activated methylene compounds: diethyl malonate, malonamide, ethyl acetoacetate, acetylacetone, barbituric acid, and 2-thiobarbituric acid. We now find that when one (or both) of the activating groups is cyano, as in ethyl cyanoacetate, a ring opening reaction occurs which involves scission of the 1,6-bond.

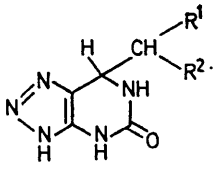
Thus ethyl cyanoacetate reacted with 8-azapurine and with its 2-amino-, 2-thioxo-, and 2-oxo-derivatives [3] yielding, respectively, 4-aminomethyleneamino-, 4-diaminomethyleneamino-, 4-thioureido-, and 4-ureido-5-



(1)

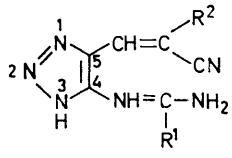


(2)



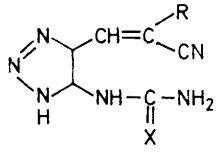
(3)

(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazoles [(4a), (4b), (5a), and (5b)]. Similarly malononitrile gave 4-aminomethyleneamino-, 4-diaminomethyleneamino-, 4-thioureido-, and 4-ureido-5-(2,2-dicyanovinyl)-1,2,3-triazoles [(4c), (4d), (5c), and (5d), respectively]. The structures of these eight scission products were established as follows. Elemental analysis showed that the



(4)

a; R^1 = H, R^2 = CO_2Et
b; R^1 = NH_2, R^2 = CO_2Et
c; R^1 = H, R^2 = CN
d; R^1 = NH_2, R^2 = CN
e; R^1 = H, R^2 = $CO{\cdot}NH_2$



(5)

a; X = S, R = CO_2Et
b; X = O, R = CO_2Et
c; X = S, R = CN
d; X = O, R = CN

azapurine had combined with the Michael reagent in a 1 : 1 ratio, and i.r. spectroscopy confirmed the presence of a C≡N group ($\nu_{max.}$ 2240—2260 cm^{-1}) in each product. U.v. and n.m.r. spectroscopy revealed that these were not the usual 1,6-adducts of types (2) and (3) which must show, like their stable analogues,[2] a large hypsochromic shift (25—90 nm relative to the starting azapurines) in the u.v. absorption maxima, commensurate with the decrease in conjugation. By contrast, the nitrile-containing products had absorption maxima in the region 340—360 nm, a bathochromic shift of 40—60 nm (see Table 1). This pointed to an extension of conjugation provided by ring-opening as in formulae (4) and (5). N.m.r. spectroscopy of normal adducts,[2,4] types (2) and (3), showed that the C-6 proton signals occurred between τ 3·7 and 4·8, values compatible with saturation of the 1,6-double bond.[5] However in the present compounds the CH signals lie between τ 1·5 and 2·2 (see Table 2). For example, whereas the n.m.r. spectrum in $(CD_3)_2SO$ of the product from 8-azapurin-2(3*H*)-one and diethyl malonate (3; $R^1 = R^2 = CO_2Et$) showed [2] the C-6 proton signal at τ 4·62, the product obtained with ethyl

† To facilitate comparisons, the amino-group in 1,2,3-triazoles is numbered 4 throughout this series.

[1] Part XI, A. Albert and D. Thacker, *J.C.S. Perkin I*, 1972, 468.
[2] A. Albert and W. Pendergast, *J.C.S. Perkin I*, 1972, 457.
[3] A. Albert, *J. Chem. Soc.* (*B*), 1966, 427.
[4] A. Albert and W. L. F. Armarego, *Adv. Heterocyclic Chem.*, 1965, **4**, 1.
[5] J. W. Bunting and D. D. Perrin, *J. Chem. Soc.* (*B*), 1966, 433.

cyanoacetate gave a signal at τ 1·53 (1H), indicative of structure (5b) [*cf.* the chemical shift (τ 1·87) of the vinyl proton in methyl α-cyanocinnamate [6] (6)].

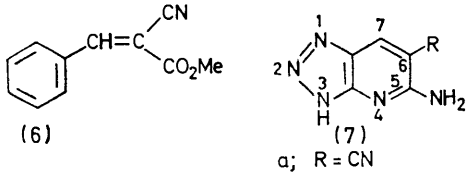
The structures assigned to these nitriles are supported by the products which they gave by either (i) elimination of the substituent on the 4-amino-group with cyclisation to form the triazolopyridine (7a), or (ii) cyclisation with elimination of a molecule of Michael reagent to regenerate the original azapurine. Thus, upon treatment with alkali, 4-aminomethyleneamino-5-(2,2-dicyanovinyl)-1,2,3-triazole (4c), obtained from 8-azapurine and malononitrile, gave 5-amino-6-cyano-*v*-triazolo[4,5-*b*]pyridine (7a) in moderate yield. The structure of the triazolopyridine was determined by elemental analysis and by i.r. [$\nu_{max.}$ 2250 cm^{-1} (CN)], u.v. [$\lambda_{max.}$ (MeOH) 340 nm], n.m.r. {τ [$(CD_3)_2SO$] 1·19 (H-7)}, and mass spectroscopy (M^+ 160). The n.m.r. spectrum obtained when the triazole (4c) was dissolved in $(CD_3)_2SO$ contained signals for an equilibrium mixture of the triazole (4c) (*ca.* 33%), 8-azapurine (45%), and the triazolopyridine (7a) (22%). The equilibrium in this solvent was established too rapidly for the reaction course to be followed by n.m.r. spectroscopy, but the u.v. spectrum in methanol showed strong absorption at 354 nm due to the ring-opened compound (4c). This peak changed to 340 nm over 30 min, due to cyclisation of the triazole (4c) to the triazolopyridine (7a). An inflection in the region 260—265 nm indicated the presence of 8-azapurine. Comparison of the triazole (4c) with authentic specimens, by paper chromatography in butan-1-ol–5N-acetic acid (7 : 3) (henceforth called butanol–acetic acid), confirmed the presence of 8-azapurine and compound (7a).

TABLE 1

U.v. spectroscopy [a]

	$\lambda_{max.}$/nm	log ε	Solvent [b]
4-Aminomethyleneamino-5-(2,2-dicyanovinyl)-1,2,3-triazole (4c)	239, 260, 354	3·80, 3·66, 3·86	M
	239, *260*, 340	3·87, *3·60*, 3·49	M [c]
5-Amino-6-cyano-1,2,3-triazolo[4,5-*b*]pyridine (7a)	238, 340	4·29, 3·99	M
4-Aminomethyleneamino-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazole (4a)	264, 356	3·86, 3·86	M
	264	3·77	M [c]
	247	3·86	M [d]
8-Azapurine (for comparison) [e]	263	3·87	3·4
1,6-Dihydro-6-methoxy-8-azapurine hydrochloride (8a) (for comparison) [f]	247	3·87	M
4-Diaminomethyleneamino-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazole (4b)	356	4·16	M
	219, *237*, 313	4·22, *3·61*, 3·74	M [c]
	234	3·97	M [d]
2-Amino-8-azapurine (for comparison) [e]	217, *237*, 311	4·38, *3·68*, 3·84	4·5
2-Amino-1,6-dihydro-6-methoxy-8-azapurine hydrochloride (8b) (for comparison)	234	4·07	M
4-Diaminomethyleneamino-5-(2,2-dicyanovinyl)-1,2,3-triazole (4d)	349	3·48	M
	218, 238, 330	3·94, 3·78, 3·55	M
	234, 344	3·83, 3·34	M
5-(2-Cyano-2-ethoxycarbonylvinyl)-4-thioureido-1,2,3-triazole (5a) (potassium salt)	267, 360	4·17, 4·32	7·0
	235, 267, 364	4·06, 4·40, 3·56	7·0 [c]
5-(2,2-Dicyanovinyl)-4-thioureido-1,2,3-triazole (5c) (potassium salt)	237, 263, 347	4·12, 3·74, 4·02	7·0
	236, 267, 340	4·13, 3·94, 3·76	7·0 [c]
5-(2-Cyano-2-ethoxycarbonylvinyl)-4-ureido-1,2,3-triazole (5b)	348	3·89	4·5
5-(2,2-Dicyanovinyl)-4-ureido-1,2,3-triazole (5d)	212, 238, 340	4·16, 4·29, 3·99	M
5-Amino-6-cyano-1,2,3-triazolo[4,5-*b*]pyridine (7a), cation [g]	231, 269, 337	4·02, 3·45, 4·01	−2·0
neutral species	236, 337	3·94, 3·60	4·0
anion	237, 293, 337	4·11, 3·63, 3·81	8·5
5-Amino-6-carbamoyl-1,2,3-triazolo[4,5-*b*]pyridine (7b), neutral species [h]	235, 330	4·04, 3·91	3·5
anion	237, *285*, 331	4·07, *3·46*, 3·88	7·5

[a] Inflections in italics. [b] M = methanol; numerals refer to the pH or H_0 values of aqueous solutions. [c] Equilibrium spectrum. [d] Equilibrium spectrum after treatment with gaseous hydrogen chloride. [e] All values from ref. 3. [f] All values from ref. 2. [g] Basic $pK_a = -0·06 \pm 0·04$; acidic $pK_a = 6·53 \pm 0·02$ determined spectrophotometrically [8] (concn. $5·5 \times 10^{-5}$M). [h] Acidic $pK_a = 5·35 \pm 0·05$, determined spectrophotometrically (concn. $2·5 \times 10^{-4}$M).



(6)

(7)

a; R = CN

b; R = CO·NH$_2$

4-Aminomethyleneamino-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazole (4a) was quantitatively converted into 8-azapurine on vacuum sublimation. A 10% solution in $(CD_3)_2SO$ underwent 50% cyclisation to the azapurine (Table 2); complete cyclisation occurred in dilute methanolic solution. That the final u.v. spectrum was of 8-azapurine was demonstrated by passage of dry HCl gas through the solution, which converted the azapurine into the methanol 1,6-adduct [2] of its cation (8a) (Table 1), and by paper chromatography in 2·7% phosphate buffer [7] (pH 7).

4-Diaminomethyleneamino-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazole (4b) underwent a similar but more rapid retrogression to ethyl cyanoacetate and 2-amino-8-azapurine (Tables 1 and 2), confirmed as before by conversion of the azapurine into the methanol 1,6-adduct of its cation (8b). Aqueous alkali also converted the triazole (4b) into 2-amino-8-azapurine,

[6] H. Kasiwagi, N. Nakagawa, and J. Niwa, *Bull. Chem. Soc., Japan*, 1963, **36**, 410.

[7] A. Albert and H. Mizuno, *J. Chem. Soc.* (*B*), 1971, 2423.

identical with an authentic specimen,[3] whereas 4-diaminomethyleneamino-5-(2,2-dicyanovinyl)-1,2,3-triazole (4d) gave the triazolopyridine (7a). In $(CD_3)_2SO$, however, the latter triazole gave solely 2-amino-8-azapurine (Table 2) while in methanol (Table 1) both the triazolopyridine and the azapurine were formed.

(5c) in water to give the triazolopyridine (7a) in good yield.

5-(2-Cyano-2-ethoxycarbonylvinyl)-4-ureido-1,2,3-triazole (5b) was stable in $(CD_3)_2SO$ and methanol. The corresponding dicyano-compound (5d) was immediately converted by $(CD_3)_2SO$ (Table 2) and by methanol

TABLE 2

^1H N.m.r. data (33·3°)

Vinyltriazoles (4a—d) and (5a—d) and their cyclisation products

Compound	τ Values: Vinyl proton	Azapurine proton(s)	Ester group(s): CH_2 [a]	Ester group(s): CH_3 [b]	Others	Solvent [c]
4-Aminomethyleneamino-5-(2,2-dicyanovinyl)-1,2,3-triazole (4c) [d]	1·82	0·30, 0·80			1·22,[e] 2·07 [f]	$(CD_3)_2SO$–D_2O
8-Azapurine (for comparison)		0·30, 0·80				$(CD_3)_2SO$
4-Aminomethyleneamino-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazole (4a) [g] A	1·97(1) [h]		5·71(2), 8·70(3)		1·97(1) [h]	$(CD_3)_2SO$
B [i]	1·97	0·27, 0·80	5·71, 8·70 5·79,[j] 8·76 [j]		1·97, 6·01 [j,k]	$(CD_3)_2SO$
Ethyl cyanoacetate (for comparison)			5·79(2), 8·76(3)		5·97 [k]	$(CD_3)_2SO$
4-Diaminomethyleneamino-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazole (4b) [l]		0·73(1)	5·78(2),[j] 8·76(3) [j]		2·85(2),[k] 5·96(2) [j,k]	$(CD_3)_2SO$
4-Diaminomethyleneamino-5-(2,2-dicyanovinyl)-1,2,3-triazole(4d) [l]		0·70(1)			2·80(2),[k] 5·25(5) [k,m]	$(CD_3)_2SO$
2-Amino-8-azapurine (for comparison)		0·70(1)			2·80(2) [k]	$(CD_3)_2SO$
5-(2-Cyano-2-ethoxycarbonylvinyl)-4-thioureido-1,2,3-triazole (5a)	1·81		5·72, 8·66 5·77 [j] 8·72 [j]		0·93 [n]	D_2O
5-(2,2-Dicyanovinyl)-4-thioureido-1,2,3-triazole (5c)	2·13					D_2O
5-(2-Cyano-2-ethoxycarbonylvinyl)-4-ureido-1,2,3-triazole (5b)	1·53(1)		5·63(2), 8·69(3)		3·34(2) [k]	$(CD_3)_2SO$
5-(2,2-Dicyanovinyl)-4-ureido-1,2,3-triazole (5d) [o]					1·15 [o]	$(CD_3)_2SO$–D_2O

Triazolopyridines

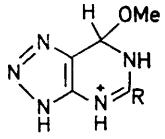
Compound	Signal	Assignment	Solvent
5-Amino-6-cyano-1,2,3-triazolo[4,5-*b*]pyridine (7a)	1·19(1)	7-H	$(CD_3)_2SO$
	2·76(2) [k]	NH_2	
5-Amino-6-carbamoyl-1,2,3-triazolo[4,5-*b*]pyridine (7b)	1·35(1)	7-H	$(CD_3)_2SO$
	2·40(4) [k]	NH_2	
5,6-Dihydro-6,6-dimethyl-1,2,3-triazolo[4,5-*b*]quinolin-8(7*H*)-one (10)	1·01(1)	9-H	$(CD_3)_2SO$
	6·77(2)	7-CH_2	
	7·28(2)	5-CH_2	
	8·90(6)	6-CH_3	
6-Acetyl-5-methyl-1,2,3-triazolo[4,5-*b*]pyridine (11a)	0·80(1)	7-H	$(CD_3)_2SO$
	7·21(3), 7·24(3)	CH_3	
6-Ethoxycarbonyl-5-methyl-1,2,3-triazolo[4,5-*b*]pyridine (11b)	1·00(1)	7-H	$(CD_3)_2SO$
	5·55(2) [a]	CH_2 (ethyl)	
	7·11(3)	5-CH_3	
	8·61(3) [b]	CH_3 (ethyl)	

[a] Quartet, J 7·2 Hz. [b] Triplet, J 7·2 Hz. [c] For spectra in $(CD_3)_2SO$ tetramethylsilane was used as internal standard; $(CD_3)_2SO$–D_2O indicates that the spectrum was obtained after addition of 1 drop of D_2O to remove exchangeable protons. For measurements in D_2O, sodium 3-trimethylsilylpropane-1-sulphonate was the internal standard. [d] Spectrum of equilibrium mixture. Signal ratios indicate presence of (4c), 8-azapurine, and the triazolopyridine (7a) (33, 45, and 22 mol %, respectively). [e] 7-Proton (7a). [f] Amidine proton (4c). [g] Spectrum obtained as soon as possible after dissolution. [h] Vinyl and amidine protons of (4a) represented by a 2-proton singlet at τ 1·97. [i] Spectrum of equilibrium mixture, indicating presence of (4a), 8-azapurine, and ethyl cyanoacetate (50, 25, and 25 mol %, respectively). [j] Protons of ethyl cyanoacetate. [k] Signal removed by addition of 1 drop of D_2O. [l] Spectrum indicates complete cyclisation to 2-amino-8-azapurine. [m] Protons of malononitrile and HOD. [n] Unknown decomposition product (<10% at equilibrium). [o] Spectrum indicates complete cyclisation to the triazolopyridine (7a).

5-(2-Cyano-2-ethoxycarbonylvinyl)-4-thioureido-1,2,3-triazole (5a) decomposed slowly in neutral aqueous solution into an unknown compound which could not be isolated. Changes in the u.v. and n.m.r. spectra of the corresponding dicyano-compound (5c) (Tables 1 and 2) indicated formation of the triazolopyridine (7a), confirmed preparatively by heating the potassium salt of (Table 1) into the triazolopyridine (7a). It was also converted in good yield into this triazolopyridine by 4N-sodium hydroxide.

Thus the triazolopyridine (7a) was isolated from all four azapurines studied *via* ring-opened derivatives of types (4) and (5). This provided additional evidence for the structures of this triazolopyridine and of the

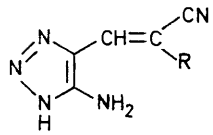
triazoles (4) and (5) in that the triazole ring remained intact, and the azapurine N-3 and C-2 atoms and any substituent on C-2 were lost in each case. Similarly, both 8-azapurine and its 2-oxo-derivative reacted with



(8)

a; R = H

b; R = NH_2



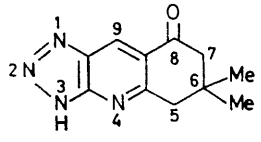
(9)

a; R = $CO{\cdot}NH_2$

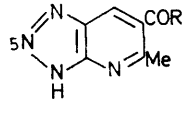
b; R = CN

cyanoacetamide to form 5-amino-6-carbamoyl-*v*-triazolo-[4,5-*b*]pyridine (7b). 8-Azapurin-2(3*H*)-one and cyanoacetamide gave the triazolopyridine (7b) directly on heating the reactants together in mildly alkaline solution; 8-azapurine gave an unstable intermediate, probably the triazole (4e), which was converted into the triazolopyridine (7b) by heating with 4N-NaOH. The structure of the compound (7b) was determined by elemental analysis, u.v. ($\lambda_{max.}$ 235 and 330 nm), n.m.r. {τ [$(CD_3)_2SO$] 1·35 (H-7)}, and mass spectroscopy (M^+ 178). The absence of a C≡N absorbtion in the i.r. spectrum confirmed that the compound was not the open-chain isomer (9a) but had cyclised *via* the CN group to give the 2-aminopyridine structure (7b). The similarity in n.m.r. and u.v. spectra (see Tables 1 and 2) between the triazolopyridine (7b) and the corresponding product from malononitrile provided final confirmation of the cyclic structure (7a) for the latter, in preference to the ring-opened isomer (9b).

8-Azapurine reacted with dimedone in neutral methanolic solution to give the triazoloquinoline (10), obtained also by reaction of 8-azapurin-2(3*H*)-one with dimedone in mildly alkaline aqueous solution. 8-Aza-



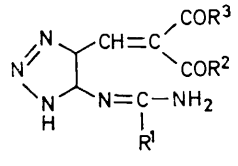
(10)



(11)

a; R = Me

b; R = OEt



(12)

purine reacted with ethyl acetoacetate and with acetylacetone in aqueous acidic solution to give the triazolopyridine derivatives (11a and b), respectively. These compounds are probably formed *via* addition of the Michael reagent and ring-opening across the azapurine 1,6-bond, and subsequent cyclisation involving loss of the azapurine N-3 and C-2 atoms, but the likely intermediates such as (12) were not isolated.

EXPERIMENTAL

Samples for microanalysis were dried at 56—60° and 20 mmHg unless otherwise stated. Ionisation constants, in water at 20°, were determined by methods previously described.[8] U.v. spectra were measured on Perkin-Elmer 450 and Unicam SP 800 recording spectrophotometers, and the wavelengths and intensities of maxima were confirmed with a Unicam SP 500 or an Optical CF4 manual instrument. Initial spectra of unstable species were obtained by recording the optical densities of solutions at intervals, and extrapolating back to the moment of dissolution. I.r. spectra (Nujol mulls) were obtained with a Unicam SP 200 spectrophotometer, and ^1H n.m.r. spectra with a Perkin-Elmer R10 instrument operating at 33·3° and 60 MHz.

Reactions of 8-Azapurines (v-Triazolo[4,5-d]pyrimidines) with Ethyl Cyanoacetate and with Malononitrile.—To a solution of the azapurine (0·0005 mol) and potassium hydrogen carbonate (0·1 g) in water (0·5 ml), clarified by centrifugation, was added ethyl cyanoacetate (0·0005—0·003 mol) or malononitrile (0·0005—0·003 mol). The suspension was shaken vigorously for the stated period, and the deposited solid washed by centrifugation with ice-cold water. The results are summarised in Table 3. All compounds had $\nu_{max.}$ 2240—2260 cm^{-1} (CN).

Cyclisation of 4-Aminomethyleneamino-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazole (4a).—Sublimation of the triazole (4a) at 0·05 mmHg, while the bath temperature was raised from 20 to 150° during 2 h, resulted in quantitative conversion of the triazole (4a) into 8-azapurine (*v*-triazolo[4,5-*d*]pyrimidine), identical with an authentic specimen [3] (i.r. spectroscopy and mixed m.p.).

Cyclisation of 4-Diaminomethyleneamino-5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazole (4b).—The triazole (4b) (0·025 g, 0·0001 mol) was dissolved in 0·5N-NaOH (0·25 ml) at 20° and set aside for 2 min. Acidification of the solution with glacial acetic acid yielded 2-amino-8-azapurine (5-amino-*v*-triazolo[4,5-*d*]pyrimidine) (72%) identical with an authentic specimen.[3]

5-Amino-6-cyano-v-triazolo[4,5-b]pyridine (7a).—(*a*) The potassium salt of 5-(2,2-dicyanovinyl)-4-thioureido-1,2,3-triazole (5c) (0·05 g, 0·00019 mol) was dissolved in water (0·5 ml), set aside for 5 min at 20°, then heated to 90° for 5 min. The deposited crystals of the *triazolopyridine* (7a) (washed well with cold water) (65%) darkened above 250° and finally decomposed at 325° [Found (material dried at 100° and 20 mmHg): C, 44·9; H, 2·3; N, 52·4%; M^+, 160. $C_6H_4N_6$ requires C, 45·0; H, 2·5; N, 52·5%; *M*, 160], $\nu_{max.}$ 2250m cm^{-1} (CN).

(*b*) 4-Aminomethyleneamino-5-(2,2-dicyanovinyl)-1,2,3-triazole (4c) (0·05 g, 0·00027 mol) was heated with 4N-NaOH (0·5 ml) at 90° for 1 min. The solution was cooled and adjusted to pH 4 with glacial acetic acid. The deposited crystals of the triazolopyridine (7a) (32%) (washed well with water) were identical with those obtained in (*a*) (i.r. spectroscopy).

(*c*) Similar treatment of 4-diaminomethyleneamino-5-(2,2-dicyanovinyl)-1,2,3-triazole (4d) (0·05 g, 0·00025 mol)

[8] A. Albert and E. P. Serjeant, ' The Determination of Ionisation Constants,' 2nd edn., Chapman and Hall, London, 1971.

gave the triazolopyridine (7a) (41%), identical with that already obtained.

(*d*) 5-(2,2-Dicyanovinyl)-4-ureido-1,2,3-triazole (0·05 g, 0·00025 mol), stirred for 30 min with 4N-NaOH (1 ml), also gave the triazolopyridine (7a) (58%) (after acidifying the solution and washing the precipitate as before).

*5-Amino-6-carbamoyl-*v*-triazolo*[4,5-b]*pyridine* (7b).—(*a*) A solution of 8-azapurin-2(3*H*)-one {*v*-triazolo[4,5-*d*]pyrimidin-5(4*H*)-one} monohydrate (0·075 g, 0·0005 mol) and potassium hydrogen carbonate (0·1 g) in water (1 ml) was heated with cyanoacetamide (0·17 g, 0·002 mol) at 90° for 3 h. The mixture was cooled and adjusted to pH 4 with glacial acetic acid to deposit fine needles of the *amide* (7b) (58%) (after washing with water), which decomposed slowly above 320° [Found (material dried at 100° and 0·1 mmHg): C, 37·2; H, 4·1; N, 43·2%; M^+, 178. $C_6H_6N_6O,H_2O$ requires C, 36·8; H, 4·1; N, 42·8%; $C_6H_6N_6O$ requires *M*, 178].

(*b*) A solution of 8-azapurine (*v*-triazolo[4,5-*d*]pyrimidine) (0·06 g, 0·0005 mol) in water (0·5 ml) was shaken with cyanoacetamide (0·05 g, 0·0006 mol) for 30 min, and the deposited yellow precipitate was washed with water and dissolved in 4N-NaOH. The solution was heated to 90° and acidified while still hot with glacial acetic acid to yield the amide (7b), identical with that obtained in (*a*) (i.r. spectroscopy).

*5,6-Dihydro-6,6-dimethyl-*v*-triazolo*[4,5-b]*quinolin*-8(7H)-*one* (10).—(*a*) A solution of 8-azapurine (*v*-triazolo[4,5-*d*]-pyrimidine) (0·06 g, 0·0005 mol) and dimedone (0·07 g, 0·0005 mol) in methanol (2 ml) was set aside overnight. Platelets of the *triazoloquinoline* (10) (37% after washing with methanol) had m.p. 281° (decomp.) (Found: C, 61·1; H, 5·7; N, 26·0. $C_{11}H_{12}N_4O$ requires C, 61·1; H, 5·6; N, 25·9%).

(*b*) A solution of 8-azapurin-2(3*H*)-one {*v*-triazolo[4,5-*d*]-pyrimidin-5(4*H*)-one monohydrate} (0·075 g, 0·0005 mol), dimedone (0·07 g, 0·0005 mol), and potassium hydrogen carbonate (0·1 g) in water (1 ml) was set aside at 20° for 6 days, then diluted to 10 ml, and adjusted to pH 4 with acetic acid. The solution was stored for 6 days, then reduced in volume to *ca.* 2 ml; the triazolopyridine (10) (65%), identical with that obtained in (*a*), was deposited.

*6-Acetyl-5-methyl-*v*-triazolo*[4,5-*b*]*pyridine* (11a).—8-Azapurine (*v*-triazolo[4,5-*d*]pyrimidine) (0·06 g, 0·0005 mol) was dissolved in water (0·25 ml), and sulphuric acid (0·05 g) was added. Acetylacetone (0·05 g, 0·0005 mol) was then added and the solution was set aside for 16 h. The deposited fine needles of the *triazolopyridine* (11a) (39%) (after washing with water) had m.p. 172° (Found: C, 54·5; H, 4·8; N, 31·7. $C_8H_8N_4O$ requires C, 54·6; H, 4·6; N, 31·8%). Similarly ethyl acetoacetate (0·065 g, 0·0005 mol) gave *6-ethoxycarbonyl-5-methyl-*v*-triazolo*[4,5-b]*pyridine* (11b) (38·5%), m.p. 189° (Found: C, 52·4; H, 4·6; N, 27·5. $C_9H_{10}N_4O_2$ requires C, 52·4; H, 4·9; N, 27·2%).

TABLE 3

Reaction of 8-azapurines (*v*-triazolo[4,5-*d*]pyrimidines) with ethyl cyanoacetate and malononitrile

8-Azapurine	Reagent $CH_2(CN)CO_2Et$ (mol)	Reaction time (min)	Product	Yield (%)	M.p. (°C)	Analyses: Found (%) C	H	N	Formula	Required (%) C	H	N
			4-Substituted 5-(2-cyano-2-ethoxycarbonylvinyl)-1,2,3-triazoles									
2-H	0·001	30	4-Aminomethyleneamino (4a) [a]	71	119	45·5	4·0	35·6	$C_9H_{10}N_6O_2$	46·1	4·3	35·9
2-NH_2	0·003 [b]	60	4-Diaminomethyleneamino (4b)	77	>320 [d]	43·5	4·6	39·2	$C_9H_{11}N_7O_2$	43·4	4·45	39·3
2(3*H*)-thione	0·0005	180	4-Thioureido (5a),[e] K salt	62	175 [f]	32·9	3·7	24·9	$C_9H_9KN_6O_2S,1·5H_2O$	32·65	3·6	25·4
2(3*H*)-one	0·0015	180	4-Ureido (5b), K salt	56	>300	33·7	3·5	25·8	$C_9H_9KN_6O_3,2H_2O$	33·3	4·0	25·9
			4-Ureido (5b) [g]	94	199	43·2	3·9	33·2	$C_9H_{10}N_6O_3$	43·2	4·0	33·6
	$CH_2(CN)_2$ (mol)		4-Substituted 5-(2,2-dicyanovinyl)-1,2,3-triazoles									
2-H	0·0005	60	4-Aminomethyleneamino (4c) [a,h]	96	decomp. >200	44·9	2·5	52·1	$C_7H_5N_7$	44·9	2·7	52·4
2-NH_2	0·003	5	4-Diaminomethyleneamino (4d)	66	322 (decomp.)	41·3	3·1	55·6	$C_7H_6N_8$	41·6	3·0	55·4
2(3*H*)-thione	0·0005	30	4-Thioureido (5c), K salt	73	242 (decomp.)	31·7	1·5	37·3	$C_7H_4KN_7S,0·5H_2O$	31·6	1·9	36·9
2(3*H*)-one	0·0006	10	4-Ureido (5d) [i]	75	315	39·6	3·0	46·25	$C_7H_5N_7O$	39·6	2·9	46·25

[a] Potassium hydrogen carbonate omitted from reaction mixture. [b] 3 Portions of 0·001 mol; solid removed after each addition. [c] Dried at 56° in air overnight, then at 56° and 20 mmHg for 1 h. [d] Gradually darkened above 210°. [e] Crystallised from water with a minimum of heating. [f] Decomposed sharply with effervescence. [g] Isolated from the foregoing potassium salt by acidification of an aqueous solution with acetic acid. [h] Dried at 60° and 20 mmHg, then ground with ether, filtered, and redried at 56° and 0·01 mmHg. [i] Solution acidified with acetic acid to yield the triazole.

We thank Drs. W. L. F. Armarego, T. J. Batterham, D. J. Brown, and H. Mizuno for discussions. Microanalyses were performed by Dr. J. E. Fildes and her staff; ionisation constants were determined by Mr. D. T. Light and Mr. I. Hawkins (under the supervision of Dr. D. D. Perrin), u.v. spectra of stable species by Mr. Light (under Dr. E. Spinner), and n.m.r. spectra by Mr. S. E. Brown (under Dr. Batterham), all of whom we thank.

[1/2038 *Received*, 2*nd November*, 1971]