v-Triazolo[4,5-*d*]pyrimidines (8-Azapurines). Part 23.[1] Synthesis and Properties of *N*-Alkyl-1,6-dihydro-8-azapurin-2-thiones. Migration (N → N′) of Acyl Group in 5-Aminomethyl-4-oxamoylamino-1,2,3-triazoles †

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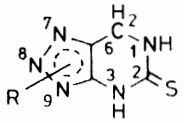
1,6-Dihydro-7-(and 8-)methyl-8-azapurine-2-thione (1a and b) were made by the action of carbon disulphide on 4-amino-5-aminomethyl-1-(and 2)-methyl-1(and 2)*H*-1,2,3-triazole (2c and d) respectively. These thiones were methylated to the corresponding 2-methylthio-derivatives (5a and b), which were oxidized by manganese dioxide to 7-(and 8-)methyl-2-methylthio-8-azapurine (6a and b), and the latter was further oxidized to the sulphoxide (6c).

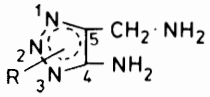
During attempts to prepare some 1,6-dihydro-8-azapurine-2-carboxamides, hydrogenation of 3-benzyl-(and 1-methyl-)4-oxamoylamino-3(and 1)*H*-1,2,3-triazole-5-carbonitrile gave the 5-aminomethyl analogues (10b and d) which underwent an unusual acid-catalysed migration of the acyl group to give 4-amino-3-benzyl-(and 1-methyl-)(5-oxamoylaminomethyl-3(and 1)*H*-1,2,3-triazole. Direct syntheses of these products (10a and e), and also of four related ethoxalylaminotriazoles (9a and c; 10c and f) are described. ^{1}H N.m.r. and i.r. spectra were recorded and are discussed.

1,6-Dihydro-8-azapurines, substituted in the 2-position, are proving useful in the treatment of experimentally induced cancers in mice.[1] The present work seeks to extend the range of substituents to sulphur- and carbonyl-containing types. It was hoped to produce 1,6-dihydro-8-azapurine-2-thiones (1) from 4-amino-5-aminomethyl-1,2,3-triazoles (2) by the combined action of carbon disulphide and a base according to a general reaction which converts, for example, 2-aminobenzylamine into 1,4-dihydroquinazoline-2-thione (3).[2] However, it was



(1)

R
a; 7-Me
b; 8-Me

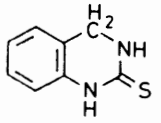


(2)

R
a; 3-Me
b; 3-CH_2Ph
c; 1-Me
d; 2-Me

recently found[3] that 3-methyl- (2a) and 3-benzyl- (2b) derivatives of 4-amino-5-aminomethyl-1,2,3-triazole gave, not the expected 8-azapurines, but analogously substituted 3-alkyl-3,7-dihydro-3*H*-1,2,3-triazolo[4,5-*d*]thiazine-5(4*H*)-thiones (4a and b) in high yields. Fortunately a more favourable[3] distribution of electrons in the 1- and 2-methyltriazoles (2c and d) permitted the normal reaction which furnished 1,6-dihydro-7-methyl-(and 8-methyl-)8-azapurine-2-thione (1a and b) respectively.

These two thiones were readily methylated, by iodomethane in aqueous alkali, to 1,6-dihydro-7-methyl-(and 8-methyl-)2-methylthio-8-azapurine (5a and b) respectively. The ^{1}H n.m.r. spectra of these four dihydro-8-azapurines (Table 1) were consonant with those of other 1,6-dihydro-8-azapurines.[1,4,5]



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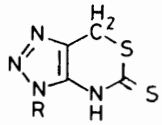
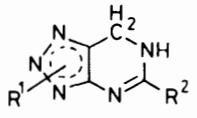


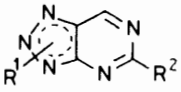
(4)

R
a; 3-Me
b; 3-CH_2Ph



(5)

R^1	R^2
a; 7-Me	SMe
b; 8-Me	SMe
c; 9-CH_2Ph	$CONH_2$
d; 9-CH_2Ph	CO_2Et



(6)

R^1	R^2
a; 7-Me	SMe
b; 8-Me	SMe
c; 8-Me	S(:O)Me

The two methylthio-compounds were oxidized by manganese dioxide to 7-(and 8-)methyl-2-methylthio-8-azapurine (6a and b) respectively. The n.m.r. spectra (Table 1) provided no indication of covalent hydration in the neutral species, consistent with the result of an u.v. spectral examination[5,6] of the parent (2-methylthio-8-azapurine).

8-Methyl-2-methylthio-8-azapurine (6b) was oxidized, by 3-chloroperbenzoic acid, to 8-methyl-2-methyl-

† In this series, the amino-group attached to the triazole ring is consistently numbered 4 to facilitate comparisons.

sulphinyl-8-azapurine (6c). Although it was expected that this sulphoxide would exchange, metathetically, with nucleophilic reagents such as potassium cyanide, the compound proved too unstable.

A possible route to 2-carboxy-derivatives of 1,6-dihydro-8-azapurine was suggested by the conversion of

TABLE 1

^{1}H N.m.r. spectra of 8-azapurines and 1,2,3-triazoles

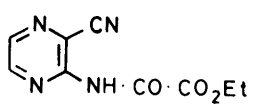
Compound	τ values [a]
(1a)	−0.88 * (1 H, 3-NH), 1.45 * (1 H, 1-NH), 5.40 (2 H, CH_2), 6.11 (3 H, Me)
(1b)	−1.29 * (1 H, 3-NH), 1.31 * (1 H, 1-NH), 5.48 (2 H, CH_2), 5.99 (3 H, Me)
(5a)	2.37 * (1 H, NH), 5.28 (2 H, CH_2), 6.21 (3 H, NMe), 7.63 (3 H, SMe)
(5b)	2.19 * (1 H, NH), 5.38 (2 H, CH_2), 6.03 (3 H, NMe), 7.62 (3 H, SMe)
(6a)	0.58 (1 H, 6-CH), 5.63 (3 H, NMe), 7.40 (3 H, SMe)
(6b)	0.41 (1 H, CH), 5.45 (3 H, NMe), 7.40 (3 H, SMe)
(6c)	0.08 (1 H, CH), 5.29 (3 H, NMe), 7.03 (3 H, SMe)
(9a)	2.62 (5 H, Ph), 4.28 (2 H, PhCH_2), [5.65 (q, 2 H) + 8.67 (t, 3 H), Et]
(9b)	1.61 * (1 H, NH), 1.91 * (2 H, NH_2), 2.75 (5 H, Ph), 4.34 (2 H, CH_2)
(10a)	1.11 * (2 H, $CONH_2$), 2.11 * (1 H, d, NH), 2.77 (5 H, Ph), 4.22 * (2 H, 4-NH_2), 4.69 (2 H, PhCH_2), 5.80 † (2 H, d, J 5 Hz)
(10c)	0.6 *br (1 H, NH), 2.70 (5 H, Ph), 4.46 * (2 H, 4-NH_2), 4.66 (2 H, CH_2Ph), 5.75 (centre of complex signal from CH_2 of Et and CH_2NH, slightly simplified by D_2O), 8.74 (3 H, t, Me of Et)
(11)	0.9 *br, (NH), 2.72 (10 H, 2 × Ph), 4.44 * (4 H, 2 × NH_2), 4.68 (4 H, 2 × PhCH_2), 5.76 † (4 H, d, J 6 Hz, 2 × CH_2NH)
(9c)	5.70 (centre) (2 H, q, CH_2 of Et), 5.82 (3 H, Me), 8.72 (3 H, t, Me of Et)
(9d)	1.60 *br (NH), 1.97 *br (NH), 5.82 (3 H, Me)
(10e) [b]	0.80 * (1 H, NH), 2.14 * (2 H, d, NH_2), 2.74 * (2 H, NH_2), 5.58 † (2 H, d, J 6 Hz, CH_2), 5.89 (3 H, 1-Me)
(10e) [c]	[2.55 (2 H, d, J 8 Hz) + 2.93 (2 H, d), 4 × CH] 7.71 (3 H, Me)
(10e) [d]	0.7 *br (NH), 2.06 * (1 H, d, NH), 5.28 * (2 H, NH_2), 5.76 † (2 H, d, J 6 Hz), 6.09 (3 H, Me)
(10d) [e]	2.00 * (NH), 5.35 * (2 H, NH_2), 5.83 (2 H, CH_2), 6.14 (3 H, Me)
(10f)	0.65 *br (NH), 5.33 *br (2 H, NH_2), 5.75 (4 H, centre of complex signal of CH_2NH and CH_2Me), 6.14 (3 H, 1-Me), and 8.74 (3 H, t, Me of Et)
(10g)	0.9 * (NH), 1.99 * (1 H, NH), 2.23 * (1 H, NH), 5.58 † (2 H, d, J 6 Hz), 5.95 (3 H, Me)
(2b) [f,g]	6.04 (2 H, s, CH_2NH)
(2b) [f,h]	6.06 (2 H, s, CH_2NH)
(2b) [f,i]	6.30 (2 H, s, CH_2NH)

* Peak vanished when D_2O was added. † Doublet (due to 5-CH_2 coupling to NH·CO) collapsed to a singlet when D_2O was added.

[a] At 30 °C in solvent $(CD_3)_2SO$; tetramethylsilane used as internal standard. [b] As tosylate, peaks due to triazole cation. [c] Peaks due to tosylate anion (checked with sodium tosylate). [d] Neutral species. [e] As basic carbonate, see text. [f] For comparison. [g] As hydrochloride (ref. 4). [h] As acetate. [i] As neutral species (ref. 9).

3-ethoxalylaminopyrazine-2-carbonitrile (7) into ethyl 3,4-dihydropteridine-2-carboxylate (8) during catalytic hydrogenation.[7] A suitable starting material, 3-benzyl-4-ethoxalylamino-3*H*-1,2,3-triazole-5-carbonitrile (9a), was made from 4-amino-3-benzyl-3*H*-1,2,3-triazole-5-carbonitrile [8] and ethoxalyl chloride. However, the ester was severely decomposed during hydrogenation over Raney nickel and hence a more stable substrate was sought in the corresponding amide (9b), obtained from the ester (9a) by the action of cold ethanolic ammonia.

This amide, hydrogenated in ethanolic ammonia over Raney nickel, furnished a mixture, separated by cold 1N-hydrochloric acid into a non-basic compound and a basic product [presumably 5-aminomethyl-3-benzyl-4-oxamoylamino-3*H*-1,2,3-triazole (10b)] the cold, acidic solution of which continued to deposit the non-basic compound. The latter gave microanalytical figures



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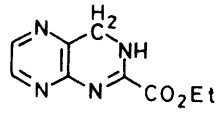

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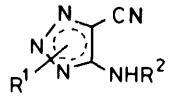
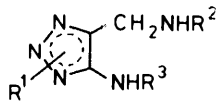


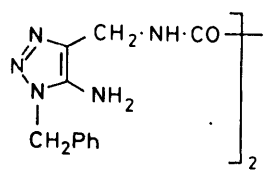
(9)

	R^1	R^2
a;	3-CH_2Ph	CO·CO_2Et
b;	3-CH_2Ph	CO·$CONH_2$
c;	1-Me	CO·CO_2Et
d;	1-Me	CO·$CONH_2$



(10)

	R^1	R^2	R^3
a;	3-CH_2Ph	CO·$CONH_2$	H
b;	3-CH_2Ph	H	CO·$CONH_2$
c	3-CH_2Ph	CO·CO_2Et	H
d;	1-Me	H	CO·$CONH_2$
e;	1-Me	CO·$CONH_2$	H
f;	1-Me	CO·CO_2Et	H
g;	1-Me	CO·$CONH_2$	CO·CF_3



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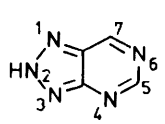

(12)

compatible with its being a monohydrate of 9-benzyl-1,6-dihydro-8-azapurine-2-carboxamide (5c). However, unlike all known 1,6-dihydro-8-azapurines, it did not reduce cold, aqueous potassium permanganate.

The n.m.r. spectrum (Table 1) suggested a 5-acylaminomethyltriazole because of (*a*) the characteristic downfield shift of the signal for CH_2NH, from *ca.* τ 6.30, as in the diamine (2b), to. 5.75, and (*b*) the coupling of the CH_2NH protons. Such displacement and coupling following acylation of a 5-aminomethyl-group is well established,[9] and further examples are in Table 1. Hence the new compound was assigned the constitution 4-amino-3-benzyl-5-oxamoylaminomethyl-3*H*-1,2,3-triazole (10a), presumably formed by acid-catalysed isomerism of the base (10b). This assignment was confirmed by comparison with an authentic specimen (10a) prepared by the action of cold ethanolic ammonia on 4-amino-3-benzyl-5-ethoxalylaminomethyl-3*H*-1,2,3-triazole (10c). This ester was made[9] by treating 4-amino-5-aminomethyl-3-benzyl-3*H*-1,2,3-triazole (2b) with diethyl oxalate, and its position of acylation established by the loss of basic properties [the starting material (2b) has pK_a 8.85].

In a related study, the diamine (2b), when condensed with ethyl triethoxyacetate, furnished a mixture of the ester (10c) and a product of higher molecular weight (M^+ 460), namely *NN'*-bis-(4-amino-3-benzyl-3*H*-1,2,3-triazol-5-ylmethyl)oxamide (11).

Hydrogenation of 1-methyl-4-oxamoylamino-1*H*-1,2,3-triazole-5-carbonitrile (9d) went a little differently. This nitrile was prepared by condensing 4-amino-1-methyl-1*H*-1,2,3-triazole-5-carbonitrile[9] with ethoxalyl chloride, followed by ethanolic ammonia, to give in turn the 4-ethoxalylamino- (9c) and 4-oxamoylamino- (9d) derivatives. Hydrogenation of the latter (9d) gave only basic material which rapidly absorbed carbon dioxide from the air. Microanalysis indicated a product in which three molecules of 5-aminomethyl-4-oxamoylamino-1-methyl-1*H*-1,2,3-triazole (10d) were combined with one molecule of carbonic acid. The mass spectrum, scanned to *m/e* 900, showed no peak above M^+ 198, which corresponds to the base (10d), indicating that carbonic acid was loosely bound and lost in the ion furnace. Thus this compound is not, as at first seemed likely, a hydrated carbamate or a urea, but simply a highly basic carbonate. A similar $B_3{\cdot}H_2CO_3$ complex, formed by the action of carbon dioxide on the diamine (2b) has been reported, but not discussed.[9]

The carbonate of the base (10d), dissolved in cold, aqueous toluene-4-sulphonic acid, gave a tosylate of which the n.m.r. signal for CH_2NH was shifted downfield and the singlet became a doublet, indicative of acylation of the aminomethyl group. Evidently isomerism had occurred to give (the tosylate of) 4-amino-5-oxamoylaminomethyl-1-methyl-1*H*-1,2,3-triazole (10e). This easily hydrolysed salt yielded a free base identical with the product from the action of cold ethanolic ammonia on 4-amino-5-ethoxalylaminomethyl-1-methyl-1*H*-1,2,3-triazole (10f), made from the diamine (2c) and diethyl oxalate.

No precedent could be found for these examples of migration of an acyl group from an aromatic to an aliphatic amino-group [producing (10a and e)]. It was unexpected that an electrophilic group (acyl) should attack a cation ($-CH_2NH_3^+$), but crowding is relieved, and anchimeric assistance likely. The closest precedent lies in an old observation[10] that cold, dilute hydrochloric acid catalyses the isomerism of *N*-(2-aminobenzyl)-acetanilide to *N*-(2-acetamidobenzyl)aniline, but both of these amines were aromatic.

TABLE 2

Preparation and analysis of products

From	Product	Recrystallization: Solvent[b]	Recrystallization: Parts	M.p.[a] (°C)	Yield (%)	Found (%): C	Found (%): H	Found (%): N	Found (%): S	Formula	Requires (%): C	Requires (%): H	Requires (%): N	Requires (%): S
(2c)	(1a)	D	35	255d	95	35.6	4.2	41.0	19.1	$C_5H_7N_5S$	35.5	4.2	41.4	19.0
(2d)	(1b)	D	45	284d	94	35.7	4.2	41.4	19.1	$C_5H_7N_5S$				
(1a)	(5a)	N	27	218d	47	39.3	5.3	38.4	17.3	$C_6H_9N_5S$	39.3	5.0	38.2	17.5
(1b)	(5b)	E	35	207	93	39.3	4.7	38.0	17.6	$C_6H_9N_5S$				
(5a)	(6a)	E	85	203	87	40.0	3.8	38.6	17.9	$C_6H_7N_5S$	40.0	3.9	38.6	17.7
(5b)	(6b)	E	16	134	96	40.0	4.0	38.7	17.7	$C_6H_7N_5S$				
(6b)	(6c)	B	32	125	60	36.8	3.9	35.7	16.1	$C_6H_7N_5OS$	36.5	3.6	35.5	16.3
	(9a)	F	3	111	90	56.4	4.3	23.6		$C_{14}H_{13}N_5O_3$	56.2	4.4	23.4	
(9a)	(9b)	E	75	220	90	53.3	3.7	31.1		$C_{12}H_{10}N_6O_2$	53.3	3.7	31.1	
	(9c)	E	17	142	94	43.1	4.0	31.2		$C_8H_9N_5O_3$	43.1	4.1	31.4	
(9c)	(9d)	D		236	92	37.3	3.2	43.1		$C_6H_6N_6O_2$	37.1	3.1	43.3	
(10c)	(10a)	A	9	232	93	52.2	5.1	30.3		$C_{12}H_{14}N_6O_2$	52.5	5.1	30.6	
(9d)	(10d)[c]	E	70	163	51	34.6	4.8	38.7		$C_{19}H_{32}N_{18}O_9$	34.7	4.9	38.4	
(10f)	(10e)	E	110	186	55	36.5	5.1	42.5		$C_6H_{10}N_6O_2$	36.4	5.1	42.4	
(9d)	(10e)[d]	E	40	171	72	42.1	5.0	22.5	8.5	$C_{13}H_{18}N_6O_5S$	42.2	4.9	22.7	8.7
(2c)	(10f)	E	35	167	93	42.1	5.8	31.1		$C_8H_{13}N_5O_3$	42.3	5.8	30.8	
(10e)	(10g)	E	265	253d	83	32.9	3.3	28.4 (F, 19.2)		$C_8H_9F_3N_6O_3$	32.7	3.1	28.6 (F, 19.4)	

[a] d means decomposes. [b] A, acetic acid; D, dimethylformamide–water (3 : 1 v/v); E, ethanol; F, ethanol–water (1 : 1 v/v); N, nitromethane. [c] Basic carbonate. [d] Tosylate.

The ^1H n.m.r. measurements (Table 1) show that all CH_2Ph values lie near to τ 4.5, and hence no Dimroth rearrangement of the benzyl group (which would shift the signal to near τ 5.6) has taken place.[8] Four i.r. spectra of oxamoyl derivatives (see Experimental section) have carbonyl absorptions in the 1 660 and 1 960 cm^{-1} regions, as found for substituted oxamides.[11] The i.r. spectrum of an ethoxalyl derivative (9c) shows

carbonyl absorption in the 1 710 and 1 760 cm^{-1} regions, comparable to ethyl oxalate.[12]

Attempts to cyclize the oxalyl derivatives (10a, c, e, and f) were unsuccessful with boiling decanol (240 °C), stannic chloride, phosphoryl chloride in pyridine, thionyl chloride, and boiling butanolic sodium butoxide. The oxamide (10e) gave, in boiling trifluoroacetic acid, 1-methyl-5-oxamoylaminomethyl-4-trifluoroacetamido-1*H*-1,2,3-triazole (10g).

EXPERIMENTAL

I.r. spectra (Nujol mulls) were obtained with a Perkin-Elmer 257 (grating) spectrometer calibrated with polystyrene at 1 603 cm^{-1}, and ^1H n.m.r. spectra with a 100 MHz Minimar-100 instrument at 30 °C with tetramethylsilane as internal standard. Elemental analyses were carried out by the Analytical Chemistry Service of this University. All substances were examined by ascending paper chromatography, after application in aqueous pyridine * and development severally in (i) aqueous 3% NH_4Cl and (ii) butanol–5N-acetic acid (7 : 3 v/v). Yields, microanalyses, and details of purification are given in Table 2.

1,6-*Dihydro*-8-*methyl*-8-*azapurine*-2-*thione* (1b) {6,7-*Dihydro*-2-*methyl*-2H-v-*triazolo*[4,5-d]*pyrimidine*-5(4H)-*thione* †}.—4-Amino-5-aminomethyl-2-methyl-1,2,3-triazole (2d) [9] (0.127 g, 0.001 mol), pyridine (4 ml), triethylamine (0.202 g, 2 mol equiv.), and carbon disulphide (0.76 g, 10 mol. equiv.) were heated under reflux for 6 h (bath at 115 °C). Volatile materials were then removed at 90 °C at 25 mmHg and the residue was stirred with water (2.5 ml). The suspension (pH 2.5) was refrigerated, then filtered to give the *title compound*, which was poorly soluble in boiling alcohols or chlorinated solvents. The 7-*methyl isomer* (1a) was made similarly and had similar solubilities.

1,6-*Dihydro*-8-*methyl*-2-*methylthio*-8-*azapurine* (5b) {6,7-*Dihydro*-2-*methyl*-5-*methylthio*-2H-v-*triazolo*[4,5-d]*pyrimidine* †}.—8-Methyl-1,6-dihydro-8-azapurine-2-thione (0.169 g, 0.001 mol) was stirred with cold 1N-potassium hydroxide (1.2 ml). To the suspension of potassium salt, iodomethane (0.17 g, 1.2 mol equiv.) was added, and the whole stirred for 12 h, chilled, and filtered to give the *title compound* which was soluble in hot benzene and cold chloroform, $\nu_{max.}$ 3 240 (NH), 1 555, 1 500, 1 405, 1 300, and 1 270 (all m) cm^{-1}. The 7-*methyl isomer* (5a) was made similarly, but the alkaline stirring had to be limited to 2 h because of decomposition; almost insoluble in boiling benzene.

8-*Methyl*-2-*methylthio*-8-*azapurine* (6b).—The dihydro-analogue (5b) (0.366 g, 0.002 mol) was suspended in cold chloroform (10 ml). Manganese dioxide (1.85 g, 5 mol equiv.) was added, and the whole stirred at 20 °C overnight. The suspension was filtered, and the cake triturated with cold chloroform (5 ml). The combined filtrates were taken to dryness, giving the *title compound*. The 7-*methyl isomer* (6a) was made similarly, but more chloroform (100 ml) was required during the oxidation.

8-*Methyl*-2-*methylsulphinyl*-8-*azapurine* (6c).—8-Methyl-2-methylthio-8-azapurine (0.364 g, 0.002 mol), in chloroform (16 ml), was stirred at 0 °C while 3-chloroperbenzoic acid (90%, 0.384 g, 1 mol equiv.) in chloroform (8 ml) was added slowly. The mixture was set aside at 20 °C overnight, washed with 1N-sodium hydrogen carbonate (3 ml), then with water (2 ml). The chloroform layer was dried (K_2CO_3) and taken to dryness, giving the *title compound*, which was very soluble in water and moderately so in ethanol, $\nu_{max.}$ 1 580, 1 545, 1 320, 1 290, 1 255, 940, and 805 (all m), and 1 070s (Me$\overset{\cdot\cdot}{S}$O) cm^{-1}.

3-*Benzyl*-4-*ethoxalylamino*-3H-1,2,3-*triazole*-5-*carbonitrile* (9a).—Ethoxalyl chloride (5.48 g, 2 mol equiv.) was added to a stirred solution of 4-amino-3-benzyl-3*H*-1,2,3-triazole-5-carbonitrile [8] (4.00 g, 0.02 mol) in pyridine (30 ml) at 1 °C, and stirred for a further 1 h at 1 °C. Ethanol (5 ml) was added to destroy the excess of reagent, and the mixture was stirred at 20 °C for 5 min. The volatile components were removed at 50 °C and 25 mmHg, and the residue was mixed with water (30 ml). The suspension was set aside at room temperature for 6 h, and the *title compound* filtered off as two crystalline forms, m.p. 97 and 111 °C, which both crystallized well from a little ethanol or benzene.

3-*Benzyl*-4-*oxamoylamino*-3H-1,2,3-*triazole*-5-*carbonitrile* (9b).—The ethoxalyl compound (9a) (15 g, 0.05 mol) and 3N-ethanolic ammonia (150 ml) were stirred at 20 °C overnight. The volatile components were removed at 50 °C and 25 mmHg and the residue was stirred with water (80 ml) and enough acetic acid to give pH 5. The *title compound* was filtered off and dried in air at 110 °C. It was soluble in 2N-aqueous ammonia, $\nu_{max.}$ 3 435, 3 400, 3 330, 3 220m (NH str), 2 250m (CN), 1 680br s (CO), 1 580br s (CO), 1 520br s, 1 485m, 1 325m, and 1 250 cm^{-1}.

4-*Ethoxalylamino*-1-*methyl*-1H-1,2,3-*triazole*-5-*carbonitrile* (9c).—This triazole was prepared like the 3-benzyl analogue (9a) except that refrigeration preceded filtration of the *title compound* which was more soluble in water, $\nu_{max.}$ 3 210, 3 070 (NH str), 2 250 (CN), 1 760 (CO), 1 710 (CO), 1 565br, 1 345, 1 300, 1 235, 1 215, and 1 165 (all m) cm^{-1}.

1-*Methyl*-4-*oxamoylamino*-1H-1,2,3-*triazole*-5-*carbonitrile* (9d).—This triazole was prepared like the 3-benzyl analogue (9b). The *title compound*, which was feebly soluble in boiling ethanol, was dried in air at 110 °C, $\nu_{max.}$ 3 410m, 3 270m (NH), 2 240 (CN), 1 680br s (CO), 1 575s (CO), 1 540br s, 1 350m, and 940m cm^{-1}.

4-*Amino*-3-*benzyl*-5-*oxamoylaminomethyl*-3H-1,2,3-*triazole* (10a).—(a) *Preferred method.* 4-Amino-3-benzyl-5-ethoxalylaminomethyl-3*H*-1,2,3-triazole [9] (10c) (1.0 g, 0.0033 mol) and 3N-ethanolic ammonia (18 ml) were stirred at 25 °C for 8 h, then taken to dryness at 60 °C and 25 mmHg. The residue was mixed with water (8 ml), the pH lowered to 4.5 with acetic acid, and the *title compound* filtered off. It was insoluble in cold 1N-sodium hydroxide and soluble in *ca.* 300 parts of boiling ethanol, $\nu_{max.}$ 3 370, 3 300, 3 180m (NH), 1 695m (CO), 1 650br s (CO), 1 600m, 1 535m, 1 410m, 1 245m, and 1 215m cm^{-1}.

(b) 3-Benzyl-4-oxamoylamino-3*H*-1,2,3-triazole-5-carbonitrile (9b) (2.7 g, 0.01 mol) in 3N-ethanolic ammonia (250 ml) was hydrogenated over Raney nickel (5.5 g, weighed wet) for 18 h at 70 °C and 4 atm. The mixture was filtered and the cake boiled with ethanol (150 ml). The combined filtrates were taken to dryness and the residue was stirred with 1N-hydrochloric acid (10 ml). The undissolved material consisted of the title compound (60%), and the filtrate at once began to deposit more of it (total yield 85%).

5-*Aminomethyl*-1-*methyl*-4-*oxamoylamino*-1H-1,2,3-*triazole* (10d).—1-Methyl-4-oxamoylamino-1*H*-1,2,3-triazole-5-carbonitrile (9d) (1.94 g, 0.01 mol) was ground under 3N-ethanolic ammonia (300 ml) and hydrogenated over Raney nickel (4 g) for 7 h at 70 °C and 4 atm. The mixture was filtered and the cake was boiled with ethanol (100 ml) and

* The azeotrope (b.p. 92 °C) from pyridine (40 ml) and water (27 ml).

† See formula (12) for this type of fusion numbering.

the mixture filtered. The combined filtrates were concentrated to 140 ml, refrigerated, and filtered, giving the *title compound* as its highly basic carbonate. The filtrate, on further manipulation, deposited more of this salt, very soluble in cold water to give a solution of pH 9, M^+ 198 (other prominent signals at *m/e* 100, 88, 82, and 60).

*4-Amino-1-methyl-5-oxamoylaminomethyl-*1H*-1,2,3-triazole* (10e).—(a) *Preferred method.* 4-Amino-5-ethoxalylaminomethyl-1-methyl-1*H*-1,2,3-triazole (10f) (0.692 g, 0.0035 mol) was stirred with 3N-ethanolic ammonia (14 ml) for a day. The volatile components were removed at 60 °C and 25 mmHg. The residue was suspended in water (2 ml) and the pH adjusted to 4 with acetic acid. The *title compound* was filtered off and dried at 80 °C in air.

(b) The basic carbonate of the amine (10d) (0.642 g) and toluene-4-sulphonic acid monohydrate (0.608 g, 1 mol equiv.) in ethanol (45 ml) deposited, at −6 °C, the tosylate of the title compound, very soluble in cold water to yield a solution of pH 1, from which 1N-sodium hydroxide (1 mol equiv.) deposited the title compound.

*4-Amino-5-ethoxalylaminomethyl-1-methyl-*1H*-1,2,3-triazole* (10f).—4-Amino-5-aminomethyl-1-methyl-1*H*-1,2,3-triazole (2c) (0.508 g, 0.004 mol), diethyl oxalate (3.0 g, 5 mol equiv.), and ethanol (40 ml) were heated under reflux for 1 h. The ethanol was distilled off, and the residue mixed with light petroleum (b.p. 60—80 °C) (15 ml) to remove unchanged ester. The *title compound* was insoluble in boiling chloroform.

*1-Methyl-5-oxamoylaminomethyl-4-trifluoroacetamido-*1H*-1,2,3-triazole.*—The tosylate of 4-amino-1-methyl-5-oxamoylaminomethyl-1*H*-1,2,3-triazole (10e) (0.370 g, 0.001 mol) and trifluoroacetic acid (20 ml) were heated under reflux for 1 day, then taken to dryness at 50 °C and 25 mmHg. Aqueous sodium acetate was added to the residue to give pH 4, and the *title compound* filtered off.

*Action of Ethyl Triethoxyacetate on 4-Amino-5-aminomethyl-3-benzyl-*3H*-1,2,3-triazole* (2b).—The acetate [4] of the diamine (2b) (0.26 g, 0.001 mol), ethyl triethoxyacetate,[13] (1.0 ml, 9 mol equiv.) and ethanol (1 ml) were heated under reflux (bath at 100 °C) for 1 h. The volatile components were removed at 50 °C and 25 mmHg. The residue was stirred with light petroleum (b.p. 60—80 °C) (1 ml), and the mixture was refrigerated and then filtered. The solid was boiled with ethanol (10 ml) and filtered hot. The filtrate deposited 4-amino-3-benzyl-5-ethoxalylaminomethyl-3*H*-1,2,3-triazole (10c) (25%), m.p. 150 °C (from ethanol), identical with authentic material.[9] The ethanol-insoluble portion was *NN'-bis(4-amino-3-benzyl-*3H*-1,2,3-triazole-5-ylmethyl)oxamide* (11) (27%), m.p. 262 °C (from pyridine trihydrate * (Found: C, 57.7; H, 5.75; N, 30.5. $C_{22}H_{24}N_{10}O_2$ requires C, 57.4; H, 5.25; N, 30.4%), $\nu_{max.}$ 3 360, 3 240m (NH), 1 645s (CO), 1 520m, and 1 210w cm^{-1}.

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* The azeotrope (b.p. 92 °C) from pyridine (40 ml) and water (27 ml).

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