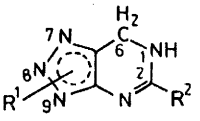
v-Triazolo[4,5-*d*]pyrimidines (8-Azapurines). Part 22.[1] Synthesis of 2-Amino- and 2-Oxo-derivatives of *N*-Alkyl-1,6-dihydro-8-azapurines from the Corresponding 4-Amino-5-aminomethyl-1,2,3-triazoles †

By **Adrien Albert**, Research School of Chemistry, Australian National University, P.O. Box 4, Canberra 2600, Australia

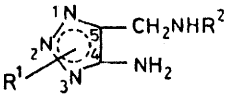
2-Amino-1,6-dihydro-8-azapurines (1c—e), alkylated on a ring-nitrogen atom, were synthesized from corresponding *N*-alkyl-4-amino-5-aminomethyl-1,2,3-triazoles, *e.g.* (2a), and cyanogen bromide. 1,6-Dihydro-8-azapurin-2-ones (3), similarly alkylated, were obtained by ring-closure of *N*-alkyl-4-amino-5-ethoxycarbonylaminomethyl-1,2,3-triazoles, *e.g.* (2e). Dehydrogenation of six dihydro-compounds with potassium permanganate gave 8-azapurines. These had strong covalent hydrating tendencies to form secondary alcohols of the type (5). Two of the 2-amino-compounds (4a and b) exhibited this property in the cations, and all the oxo-compounds (6) in the neutral species. Physical properties (^{1}H n.m.r., u.v., i.r.) of typical products were measured and discussed.

1,6-DIHYDRO-8-AZAPURINES, *e.g.* (1a and b), stable to atmospheric oxidation (unlike 1,6-dihydropurines), are candidate drugs in the chemotherapy of cancer. Of several 2-alkyl derivatives [made [2] by the action of amidines on *N*-alkyl-derivatives (2a—c) of 4-amino-5-aminomethyl-1,2,3-triazole, and tested in the Developmental Therapeutic Program of the National Cancer Institute (Bethesda, U.S.A.)], by far the most active was also the most polar, namely 9-benzyl-1,6-dihydro-2-trichloromethyl-8-azapurine (1b). Injection of this



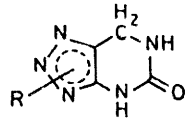
(1)

	R^1	R^2
a;	H	H
b;	9-CH_2Ph	CCl_3
c;	7-Me	NH_2
d;	8-Me	NH_2
e;	9-CH_2Ph	NH_2



(2)

	R^1	R^2
a;	1-Me	H
b;	2-Me	H
c;	3-CH_2Ph	H
d;	3-CH_2Ph	$-\overset{NH}{\overset{\|\|}{C}}-NH_2$
e;	1-Me	CO_2Et
f;	2-Me	CO_2Et
g;	3-CH_2Ph	CO_2Et



(3)

	R
a;	7-Me
b;	8-Me
c;	9-CH_2Ph

compound into mice, some implanted with the mammary tumour CD8F and the others with the colon-attacking tumour C8 (H38), led to a high survival rate, although few other drugs can control these malignancies without harm to the host. These results suggested the desirability of seeking *N*-alkyl-1,6-dihydro-8-azapurines with other polar groups in the 2-position. The present work reports new reactions that introduce the 2-amino- and 2-oxo-substituents. The properties of the new products (1c—e) and (3a—c), and of the 8-azapurines (4a—c) and (6a—c) into which dehydrogenation converts them, have been measured and are discussed.

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

RESULTS AND DISCUSSION

The choice, for synthesis, lay between suitably condensing 4-amino-5-aminomethyl-1,2,3-triazoles (2),[3] or reducing [4,5] 8-azapurines obtained either from 4,5-diaminopyrimidines [6] or from 4-amino-1,2,3-triazole-5-carbaldehydes.[7] The first of these methods proved to be the most convenient.

N-Alkyl derivatives of 2-amino-1,6-dihydro-8-azapurine (1c—e) were prepared from the corresponding 4-amino-5-aminomethyl-1,2,3-triazoles (2a—c) as was 2-aminobenzimidazole [8] from 1,2-diaminobenzene, and 2,8-diaminopurine [9] from 2,4,5-triaminopyrimidine, namely with cyanogen bromide. Methanol, as solvent, succeeded where water failed.

Because the 9-benzyl example (1e) was obtained in rather low yield, a different synthesis was attempted by condensing the diamine (2c) with *S*-methylisothiuronium acetate. Because the acetate of the product was hygroscopic, it was converted into the hydrochloride. The product was assigned the constitution 4-amino-3-benzyl-5-(guanidinomethyl)-1,2,3-triazole (2d), rather than the 4-guanidino-isomer, on the following grounds. In the ^{1}H n.m.r. spectrum of the hydrochloride, the signal assigned to CH_2NH (τ 5.65 is downfield from the corresponding one in the base (6.30) and cation (6.05) of the starting material (2c), which indicates that the deshielding guanidino-residue is attached to the methylene group. The u.v. spectra confirmed this assignment. Heating this guanidine (2d) under reflux with two equivalents of butanolic sodium butoxide furnished only a 10% yield of the required di-hydro-8-azapurine (1e).

The 2-amino-1,6-dihydro-8-azapurines (1c—e) remain unchanged on heating in CO_2-free air at 115 °C. The feeble solubility of the 7-methyl example (1c) in dimethyl sulphoxide and other common solvents used in n.m.r.

spectrometry was atypical, as was the ready solubility of the 8-methyl analogue (1d) in water. In a test of stability in this series, the 9-benzyl example (1e) was little affected by boiling for 1 h with 1N-sodium hydroxide or 1N-hydrochloric acid.

TABLE 1

^{1}H N.m.r. spectra (τ values) of 2-amino-1,6-dihydro-8-azapurines and 1,6-dihydro-8-azapurin-2-ones [a]

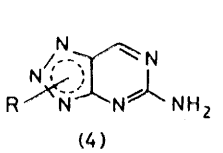
Compound	NH [b]	NH_2 [b]	Benzyl Ph	Benzyl CH_2	6-CH_2	Me
(1c) [c]						
(1d)	3.67	4.39			5.52	6.13
(1e)	3.51	4.09	2.76	4.76	5.46	
(3a)	0.65				5.53	6.15
	3.22					
(3b)	0.52				5.67	6.12
	3.20					
(3c)	−0.07		2.68	4.54	5.55	
	2.90					

[a] At 30 °C in solvent $(CD_3)_2SO$; all are singlet peaks; tetramethylsilane used as internal standard. [b] Peak vanished when D_2O was added. [c] Too poorly soluble in $(CD_3)_2SO$ to furnish clear signals, but cation in trifluoroacetic acid gave 2.38 (1 H, NH), 2.63 (2 H, NH_2), 4.98 (2 H, CH_2), and 5.81 (3 H, Me).

The required *N*-alkyl-derivatives (3a—c) of 1,6-dihydro-2-oxo-8-azapurine were prepared by the action of boiling butanolic sodium butoxide on the correspondingly alkylated derivatives (2e—g) of 4-amino-5-ethoxycarbonylaminomethyl-1,2,3-triazoles, which were on hand from earlier work.[3] The products were unchanged by heating in air at 115 °C or by boiling with 1N-sodium hydroxide (protection due to Coulombic repulsion of two anions). However 9-benzyl-1,6-dihydro-5*H*-8-azapurin-2(3*H*)-one (3c) was completely hydrolysed to 4-amino-5-(aminomethyl)-3-benzyl-1,2,3-triazole (2c) when heated under reflux for 10 min with 1N-hydrochloric acid.

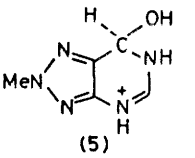
The ^{1}H n.m.r. spectra of these dihydro-8-azapurines are given in Table 1.

Oxidations of the 1,6-dihydro-8-azapurines to the corresponding 8-azapurines (4a—c) and (6a—c) were smoothly effected at room temperature with potassium permanganate. For the weak acids (3a—c), the dehydrogenation was easily performed in dilute alkali. The amines (1c—e) needed special solvents for dissolution: aqueous pyridine in two cases, and aqueous dimethylformamide in the other. No record could be found of the use of the latter solvent with a permanganate, but it performed well and consumed no oxidant



(4)

R
a; 7—Me
b; 8—Me
c; 9—CH_2Ph
d; H



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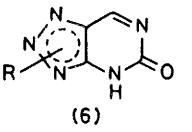


(6)

R
a; 7—Me
b; 8—Me
c; 9—CH_2Ph

TABLE 2

The covalent hydration of 2-amino-8-azapurine cations, as disclosed by their physical constants

Compound	Solvent [b]	^{1}H N.m.r. spectra [a] 6-CH	2-NH_2	Alkyl	Species [d]	U.v. spectroscopy [c] $\lambda_{max.}$/nm	log ε	pH
(4a)	A	0.84	3.14	5.70	AM	256, 338	3.57, 3.64	4.5
	B	0.84		5.71	AM			
	C	0.44		5.40	AC			
	D	3.37		5.77	HC	229, 328	4.96, 2.06	0
(4b)	A	0.75	3.02	5.62	AM	255, 332	3.58, 3.76	4.5
	B	0.74		5.61	AM			
	C	0.46		5.45	AC			
	D	3.60		5.82	HC	245, 322	4.09, 1.79	0
(4c)	A,B	0.84		2.70, 4.34	AM	*244*, 317	*3.66*, 3.89	E [f]
	C	0.40		2.59, 4.18	AC			
	D	0.48		2.56, 4.17	AC	228, 326	4.46, 3.58	0
(4d)	A	0.87	2.90		AM	*237*, 311 [e]	*3.68*, 3.84	4.5
	B	0.85			AM			
	C	0.35			AC			
	D	3.36			HC	*235*, *326* [e]	*3.98*, 2.53	0

[a] At 30 °C; all are singlet peaks, tetramethylsilane used as internal standard except sodium trimethylsilylpropane-1-sulphonate in solvent D. [b] A, $(CD_3)_2SO$; B, as A plus D_2O; C, trifluoroacetic acid; D, DCl-D_2O. [c] In water; inflections in italics; 1N-HCl (pH 0); acetate buffer (pH 4.5). [d] Anhydrous molecule (AM), anhydrous cation (AC), or hydrated cation (HC). [e] From A. Albert, *J. Chem. Soc.* (B), 1966, 427. [f] In 90% ethanol because it was insufficiently soluble in water [compound (4a) gave substantially the same spectrum in aqueous buffer, pH 4.5, and in 90% ethanol].

(this was also true for the use of the tosylate of one of the bases).

Covalent hydration, namely the addition of a molecule of water across a C=N double bond to give a secondary alcohol, as in (5), is becoming increasingly recognized among nitrogen heteroaromatic compounds, and has been broadly reviewed.[10] It can be seen from Table 2 that

the 7- and 8-*N*-methyl-derivatives of 2-amino-8-azapurine (4a, b) provide strong evidence of covalent hydration in the cation. The signal for the 6-CH group in the anhydrous cation, as recorded in trifluoroacetic acid, has a value (*ca.* τ 0.45) suitably downfield from that of the anhydrous neutral species (*ca.* τ 0.8). However, re-examination of the cation in deuterium oxide reveals a striking upfield shift to τ *ca.* 3.5, which indicates that the cation now contains the 6-CH(OH) group.

It is notable that the 9-benzyl-analogue (4c) does not hydrate in this way. This apparently reflects imposition by a 9-alkyl group of an electronic pattern unfavourable to hydration, because 9-benzyl-8-azapurine [11] and 9-methyl-8-azapurine [12,13] fail to give hydrated cations whereas 8-benzyl- [11] and 8-methyl-8-azapurine [13] have strongly hydrating cations.

Table 2 also provides u.v. evidence of hydration in the cations of amines (4a and b). The peak near 330 nm in each neutral species loses a large proportion of its intensity when the molecule is converted into the cation, an effect compensated by gain in intensity for a broad peak at shorter wavelength.

These results extend a purely spectroscopic study (both static [4] and with rapid-reaction apparatus [12]) of 2-amino-8-azapurine cation for which n.m.r. measurements, now presented, confirm the earlier indication of hydration (see Table 2).

Neither 2-aminopurines nor purin-2-ones undergo covalent hydration,[14] but it now turns out to be a characteristic feature of the 8-azapurin-2-ones and was already suspected for the parent 8-azapurin-2-one on

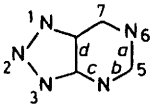
TABLE 3

The covalent hydration of 8-azapurin-2-ones (neutral species), as disclosed by their ^{1}H N.m.r. spectra [a]

Compound	Solvent [b]	6-CH	3-NH	1-NH	6-C*H*OH	alkyl
(6a)	A	0.25 (0.5 H)	2.46 (1 H)	3.67 [c]	4.20 [c]	6.20 (3 H)
	B				4.12 (1 H)	6.17 (3 H)
(6b)	A	0.09 (0.5 H)	2.45 (1 H)	3.74 [c]	4.26 [c]	6.04 (3 H)
	B				4.22 (1 H)	6.02 (3 H)
(6c)	A	0.60 (1 H)				2.61 (5 H); 4.34 (2 H)
	B				4.08 (1 H)	2.61 (5 H); 4.50 (2 H)

[a] At 30 °C, in solvent $(CD_3)_2SO$; all are singlet peaks when not marked otherwise; tetramethylsilane used as internal standard. [b] A, $(CD_3)_2SO$; B, as A plus D_2O. [c] 0.5 H, d, *J* 8 Hz.

u.v. spectroscopic grounds.[4] The ^{1}H n.m.r. results in Table 3 indicate that the neutral species of the 7- and 8-methyl derivatives (6a and b) reach a 1 : 1 equilibrium of the anhydrous and the hydrated species in the solvent used [$(CD_3)_2SO$] (these compounds, dried at 80 °C in air, had retained one molecule of water). The evidence for this equilibrium resides in the equal integration of the 6-CH (*ca.* τ 0.1—0.2) and the 6-CH(OH) (*ca.* τ 4.3) signals. It can be seen from Table 3 that addition of D_2O effects complete hydration, as in the parent type (5). The 9-benzyl-homologue (6c) is a borderline case. This compound is completely anhydrous when dried at 23 °C, and the n.m.r. reflects this state by furnishing no signal near τ 4.0. However, on the addition of a little D_2O, the signal indicates complete hydration. All undiscussed signals in Tables 2 and 3 had their usual values in this series. Most of the NH peaks were very sharp.



v—Triazolo[4,5—*d*]pyrimidine

(fusion numbering)

(7)

EXPERIMENTAL

^{1}H N.m.r. spectra were obtained with a 100-MHz JEOL Minimar-100 instrument at 30 °C, the i.r. spectra (Nujol mulls) with a Perkin-Elmer 257 grating instrument calibrated with polystyrene at 1 603 cm^{-1}, and the u.v. spectra with a Cary 219 spectrometer. Elemental analyses were performed by this University's Analytical Chemistry Service; the samples were dried in air at 110 °C except the amino-dihydro-compounds which were dried at 100 °C 0.01 mmHg. Substances stated to be identical were compared by mixed m.p., by i.r. spectrum, and on (ascending) chromatography papers developed separately in (*i*) aqueous 3% NH_4Cl and (*ii*) butanol–5N-acetic acid (7 : 3). Yields, microanalyses, and details of purification are given in Table 4.

2-*Amino*-1,6-*dihydro*-7-*methyl*-8-*azapurine* (5-*Amino*-6,7-*dihydro*-1-*methyl*-1H-v-*triazolo*[4,5-d]*pyrimidine*) * (1c).—A solution of cyanogen bromide (0.53 g, 2.5 equiv.) in methanol (4 ml) was added dropwise to a stirred solution of 4-amino-5-aminomethyl-1-methyl-1,2,3-triazole [3] (2a) (0.254 g, 0.002 mol) in methanol (20 ml). The solution was stirred at 20 °C for 15 min, then refluxed for 4 h. The methanol was distilled off and the residue dried at 50 °C and 25 mmHg. 1N-Sodium hydroxide (2.2 ml) was added, and the *title compound* was filtered off; $\nu_{max.}$ 3 330 and 3 280 (NH str), 1 660, 1 616, 1 535, 1 340, 1 240, 1 160, and 1 110 (all m) cm^{-1}.

2-*Amino*-1,6-*dihydro*-8-*methyl*-8-*azapurine* (1d).—A solution of cyanogen bromide (1.06 g) in methanol (8 ml) was added to a stirred suspension of the 1 : 1 phosphate [3] of 4-amino-5-aminomethyl-2-methyl-1,2,3-triazole (2b) (0.908 g, 0.004 mol) and sodium ethoxide (Fluka) (0.272 g, 0.004 mol) in methanol (40 ml). After 15 min at 20 °C, the suspension was refluxed for 4 h. Toluene-*p*-sulphonic acid monohydrate (0.76 g, 1 equiv.) was added to the hot mixture. The solution was set aside at −10° overnight, and crystals of the *tosylate* then filtered off. The *free base*, very soluble in cold water, was obtained by dissolving the tosylate in cold 1N-sodium hydroxide (enough to give pH 12). This solution was taken to dryness at 50° and 25 mmHg. The residue was ground with ethanol–benzene (2 : 1) and again taken to dryness, then extracted with boiling ethanol.

* See formula (7) for this type of *fusion* numbering.

2-Amino-9-benzyl-1,6-dihydro-8-azapurine (1e).—4-Amino-5-aminomethyl-3-benzyl-1,2,3-triazole [3] (2c) (1.6 g, 0.008 mol) in methanol (80 ml) was treated similarly to the 7-methyl-homologue. After distilling off the methanol, the residue was dissolved in boiling water (12 ml) and set aside at 20 °C overnight while a gum deposited. The decantate and rinsings of this gum, taken to pH 12 with 10N-sodium hydroxide, deposited the *title compound*. The *tosylate*, prepared in boiling ethanol, was used to purify the base which it re-furnished when suspended in cold 1N-sodium hydroxide (final pH 12).

4-Amino-3-benzyl-5-(guanidinomethyl)-1,2,3-triazole (2d).—The diamine (2c) (0.2 g, 0.001 mol), *S*-methylisothiuronium acetate (0.45 g, 3 equiv.), and ethanol (3 ml) were refluxed for 1 h (methanethiol evolved). The product was taken to dryness, and the residue dissolved in water (1 ml). Saturated aqueous NaCl (3 ml) was added and the whole refrigerated. The precipitate, well pressed and washed with ethanol, was recrystallized from 50 parts of ethanol, giving the *title compound hydrochloride* (in two crops), soluble in 20 parts of cold water; τ[$(CD_3)_2SO$] 2.71 (5 H, Ph), 4.06 (NH), 4.61 (2 H, CH_2PH), 5.65 (2 H, CH_2NH), and 6.67 (NH); $\lambda_{max.}$ (water) 245 nm (log ε 3.72) and $\lambda_{max.}$ (0.1N-NaOH) 246 nm (log ε 3.74).

1,6-Dihydro-7-methyl-8-azapurin-2-one {*6,7-Dihydro-1-methyl-1H-v-triazolo*[4,5-d]*pyrimidin-5(4H)-one*} (3a).—4-Amino-5-ethoxycarbonylaminomethyl-1-methyl-1,2,3-triazole [3] (2e) (0.20 g, 0.001 mol) and butanolic sodium butoxide (0.5M, 4.0 ml), freshly made from sodium hydride and butanol, were refluxed for 2 h (bath temperature 135 °C). The butanol was removed at 100 °C and 25 mmHg. The residue, dissolved in ice–water (2 g) and the solution adjusted to pH 5 with acetic acid, yielded the *title compound*. *1,6-Dihydro-8-methyl-8-azapurin-2-one* (3b) was obtained similarly but with heating limited to 1 h; $\nu_{max.}$ 3 220 and 3 150m (NH), 1 670s,br (Amide I), 1 585s,br (Amide II), 1 290ms, 1 235ms (Amide III), 1 115m and 990m cm^{-1}. *9-Benzyl-1,6-dihydro-8-azapurin-2-one* (3c) was made similarly, but with 2 h heating.

2-Amino-7-methyl-8-azapurine (*5-Amino-1-methyl-1H-v-triazolo*[4,5-d]*pyrimidine*) (4a).—The dihydro-analogue (1c) (0.304 g, 0.002 mol) was dissolved in pyridine trihydrate * (20 ml) at 40 °C, then cooled to 20 °C. 0.1M-Potassium permanganate (13.2 ml, 1 equiv.) was added dropwise. The mixture was stirred for a further 15 min. Kieselguhr (0.4 g) was added, and the mixture filtered. The insoluble part was dried at 20 °C at 25 mmHg, and then boiled with ethanol (4 ml). The combined filtrates were concentrated *in vacuo* to 4 ml, refrigerated, and the *title compound* filtered off; $\nu_{max.}$ 3 430, 3 355, 3 300, and 3 175 (NH str), 1 655, 1 605, 1 580, 1 505, 1 430, 1 310, and 1 180 (all m) cm^{-1}.

2-Amino-8-methyl-8-azapurine (4b).—0.1M-Potassium permanganate (13.2 ml) was added dropwise to a solution of 2-amino-1,6-dihydro-8-methyl-8-azapurine tosylate (0.648 g, 0.002 mol) in pyridine trihydrate (20 ml) at 20 °C. The whole was stirred for 15 min. When worked up as the 7-methyl isomer, the title compound was obtained.

2-Amino-9-benzyl-8-azapurine (4c).—0.1 M-Potassium permanganate (9.9 ml) was dropped into a solution of 2-amino-9-benzyl-1,6-dihydro-8-azapurine (1e) (0.342 g, 0.001 5 mol) in dimethylformamide–water (3 : 1) (9 ml), which was stirred for a further 20 min. Kieselguhr (0.3 g) was added, and the suspension filtered. The cake was dried at 20 °C and extracted with boiling ethanol (60 + 30 ml). The combined filtrates were concentrated to 6 ml, refrigerated, and the title compound filtered off.

7-Methyl-8-azapurin-2-one {*1-Methyl-1H-v-triazolo*[4,5-d]*pyrimidin-5(4H)-one*} (6a).—To the dihydro-analogue (3a) (0.153 g, 0.001 mol) in 0.5N-potassium hydroxide (4 ml, 2 equiv.) was added, dropwise, 0.1M-potassium permanganate (6.6 ml, 1 equiv.) at 20 °C, and stirring was continued for 15 min. Kieselguhr (0.1 g) was added and the suspension filtered. The cake was ground in a mortar with 1N-potassium hydroxide (1.5 ml). The combined filtrates were adjusted to pH 5 with acetic acid, which liberated the *title compound*. 1,6-Dihydro-8-methyl-8-azapurin-2-one (3b), which required twice as much 1N-potassium hydroxide for dissolution, similarly furnished *8-methyl-8-azapurin-2-one* (6b); $\nu_{max.}$ 3 310, 3 200, and 3 140s (NH str), 1 720s,br (Amide I), 1 590s (Amide II), 1 305s, 1 235s (Amide III), 1 105m, 1 030s, and 1 000m cm^{-1}.

9-Benzyl-8-azapurin-2-one.—Potassium permanganate (0.1M, 6.6 ml) was slowly added to a solution of the dihydro-

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

TABLE 4

Preparation and analysis of products

From	Product	Recrystallization solvent	Recrystallization parts	M.p.[b] (°C)	Yield (%)	Found C	Found H	Found N	Found S	Formula	Requires C	Requires H	Requires N	Requires S
(2a)	(1c)	Water	60	278	75	39.5	5.5	55.1		$C_5H_8N_6$	39.5	5.3	55.2	
(2b)	(1d)-Tos [a]	Water	22	267	55	44.7	5.0	26.2	9.9	$C_{22}H_{16}N_6O_3S$	44.4	5.0	25.9	9.9
	B	Ethanol	22	233d		39.7	5.5			$C_5H_8N_6$				
(2c)	(1e)-Tos	Ethanol	85	192	40	53.8	5.1	20.9	8.0	$C_{18}H_{20}N_6O_3S$	54.0	5.0	21.0	8.0
	B	Ethanol	60	238d		58.0	5.4	37.0		$C_{11}H_{12}N_6$	57.9	5.3	36.8	
(2c)	(2d)-HCl	Ethanol	50	195	75	47.3	5.9	34.9		$C_{11}H_{16}ClN_7$	46.9	5.7	34.8	
(2e)	(3a)	Water	28	297	51	39.1	4.6	45.6		$C_5H_7N_5O$	39.2	4.6	45.7	
(2f)	(3b)	Water	60	303	77	39.4	4.7	45.7		$C_5H_7N_5O$				
(2g)	(3c)	Ethanol	270	260	85	57.7	4.8	30.6		$C_{11}H_{11}N_5O$	57.6	4.8	30.6	
(1c)	(4a)	Water	20	245	75	40.0	4.0	56.0		$C_5H_6N_6$	40.0	4.0	56.0	
(1d)	(4b)	Ethanol	200	248 [e]	92	*d*								
(1e)	(4c)	Ethanol	140	200 [e]	87	*d*								
(3a)	(6a)	Water	200	230d	77	35.4	4.2	41.4		$C_5H_7N_5O_2$ [f]	35.5	4.2	41.4	
(3b)	(6b)	Water	120	240d	76	35.5	4.2	41.4		$C_5H_7N_5O_2$ [f]				
(3c)	(6c)	Water	400	251	92	58.0	4.2	30.7		$C_{11}H_9N_5O$	58.1	4.0	30.8	

[a] B, free base; Tos, tosylate. [b] d = Decomposes. [c] Also another crystalline form, m.p. 254 °C. [d] See Ref. 7. [e] Also another crystalline form, m.p. 206 °C. [f] Covalent hydrate.

analogue (3c) (0.23 g, 0.001 mol) in 0.25N-sodium hydroxide (4.8 ml) at 20 °C, and stirring was continued for 15 min. Kieselguhr (0.1 g) was added, and the whole was filtered. The solid portion was ground with 0.25N-sodium hydroxide (1.5 ml). The combined filtrates, acidified to pH 2.5 with 5N-sulphuric acid, deposited the *title compound* (6c); $\nu_{max.}$ 3 180w, 3 125m, 3 050s, 1 620s,br (Amide I), 1 585s (Amide II), 1 415m, 1 340m, and 955m cm^{-1}.

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