Synthesis and Mechanism of Formation of Novel 2,5-Dihydro-2,5-diimino-3,4-di[(*N,N*-dimethylamino)methylideneamino]pyrroles and 5-Amino-3,4-di[(*N,N*-dimethylamino)methylideneamino]-2*H*-2-iminopyrroles

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Formation of 5-amino-3,4-di[(*N,N*-dimethylamino)methylideneamino]-2*H*-2-iminopyrroles **3** from the reaction of (*Z*)-N^1-(2-amino-1,2-dicyanovinyl)-N^2-substituted-formamidines **1** with dimethylformamide diethyl acetal has been shown to occur by initial formation of (*Z*)-N^1-{1,2-dicyano-2-[(*N,N*-dimethylamino)methylideneamino]vinyl}formamidines **8** (isolated), followed by base catalysed cyclisation and imidazole ring opening by dimethylamine. The kinetic product of the ring opening reaction is the 2,5-diimino-2,5-dihydropyrrole derivatives **11**, which have been isolated and characterized spectroscopically and by a single crystal X-ray analysis on the R = Ph derivative. In solution at room temperature the *N*-aryl derivatives undergo a rapid Dimroth rearrangement to give the thermodynamically more stable isomer **3**, but compound **11** (R = Me) is much more stable in solution.

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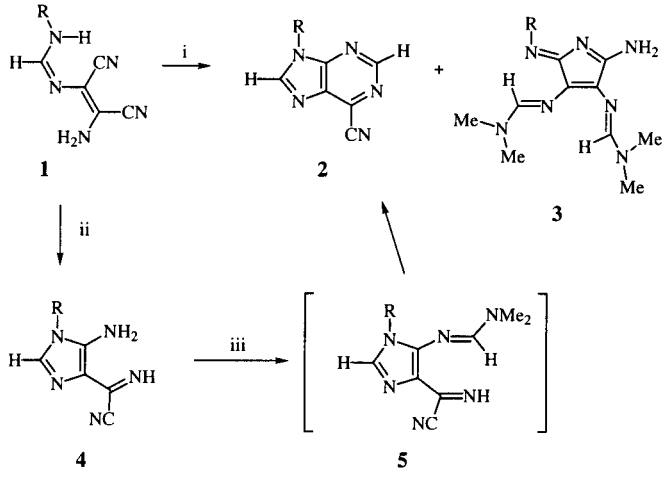
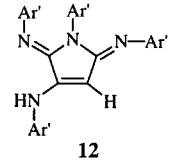
In a previous paper [1] we described a new synthesis of 6-cyanopurines **2** in medium to good yields by the reaction of (*Z*)-N^1-(2-amino-1,2-dicyanovinyl)-N^2-substitued-formamidines **1** (see Scheme 1) with *N,N*-dimethylformamide diethyl acetal at room temperature. Unexpected by-products of these reactions were novel 5-amino-3,4-di[(*N,N*-dimethylamino)methylideneamino]-2*H*-2-iminopyrroles with different substituents on the imino nitrogen (**3**) formed as crystalline red solids in low yields. We first considered that both of these compounds might arise from a common intermediate **5** formed by reaction of *N,N*-dimethylformamide diethyl acetal with a 5-amino-4-(cyanoformimidoyl)imidazole intermediate **4**. Compounds of type **4** have previously been isolated by our group from amidines of type **1** upon treatment with a base such as barium hydroxide or 1,8-diazabicyclo[5.4.0]undec-7-ene [2-5]. However, reaction of **4** with *N,N*-dimethylformamide diethyl acetal under similar conditions to those employed for the formation of the 6-cyanopurines failed to give any of the pyrroles **3**, but did result in high yields of 6-cyanopurines. This indicates that while the intermediates **4** and **5** may be responsible for the formation of **2** from **1** (see Scheme 1), a different mechanistic pathway must be responsible for the formation of the pyrroles **3.**

We reasoned that if the compounds **3** did not arise by initial base-catalysed cyclisation to **4** then they must be formed by reaction of *N,N*-dimethylformamide diethyl acetal with the amidines **1** before cyclisation, to give an intermediate such as **8**, which could then undergo cyclisation to **9** (see Scheme 2). Compounds of type **8** have not been described previously to our knowledge and in order to investigate this mechanistic pathway it was first necessary to devise a synthetic route to these compounds.

Scheme 1



[i] Dimethylformamide diethyl acetal 1-3 equivalents, acetonitrile, room temperature; [ii] Ethanol, 1,8-diazabicyclo[5.4.0]undec-7-ene; [iii] Dimethylformamide diethyl acetal 1.5 equivalents, acetonitrile.



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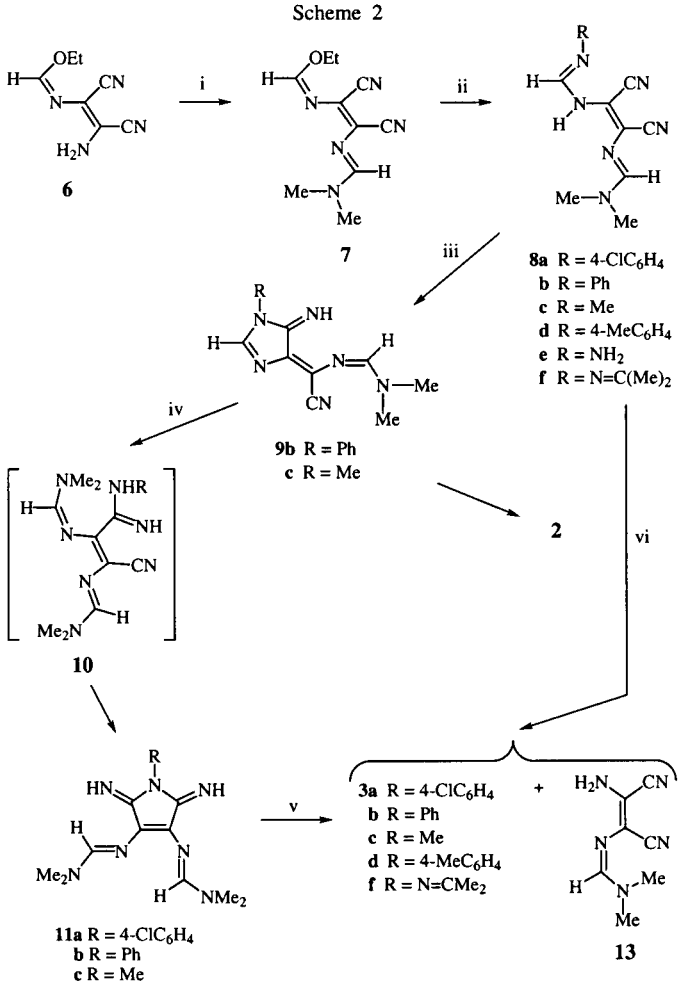
The reaction of the known imidate **6** [6] with *N,N*-dimethylformamide diethyl acetal led to compound **7** isolated in 82% yield after 15 minutes at room temperature using chloroform as solvent. The reaction of **7** with *p*-chloroaniline, methylamine, aniline, and *p*-toluidine led to the corresponding diamidines **8a-d** in good yields.

Scheme 2



[i] Dimethylformamide diethyl acetal 1.3 equivalents, chloroform, room temperature, 15 minutes; [ii] Amine 1 equivalent, ethanol, room temperature, 2 days; [iii] 1,8-Diazabicyclo[5.4.0]undec-7-ene, chloroform, 0°C; [iv] (1) Dimethylamine (large excess), chloroform, 0°C, 15 minutes approximately, (2) room temperature; [v] Ethanol, room temperature; [vi] Dimethylamine (large excess), chloroform, room temperature.

When *p*-phenylenediamine was used in this reaction the intermediate diamidine appears to be unstable and extensive decomposition occurred. The only product isolated from this reaction was the corresponding 6-cyanopurine **2** in only 24% yield. The amidrazone **8e** was isolated in quantitative yield by reaction of **7** with hydrazine monohydrate. The product always incorporates a variable amount of solvent (dioxane) and good elemental analysis results could not be obtained for this compound. Compound **8f** was isolated in 46% yield when a solution of **8e** in acetone was stirred at room temperature in the presence of silica.

The amidines **8a-f** show complex ^{1}H nmr spectra in deuterated dimethyl sulfoxide solution suggesting equilibration of tautomers in this solvent. In deuterated chloroform the signals are sharp indicative of a single species. The ir spectra usually show intense bands in the 3314-3338 cm^{-1} region (ν N-H). Only one band attributed to the CN stretching vibration can be observed in the 2201-2213 cm^{-1} region for all compounds except **8e** and **8c** where two close bands are present at 2206, 2198 cm^{-1} and 2200, 2212 cm^{-1} respectively. Elemental analysis and mass spectrometry both confirmed the empirical formulae (see Table 1). No ^{13}C nmr data could be recorded as the period of time required to accumulate a visible signal was too long compared with the stability of the compound in solution.

When a solution of compound **8d** in deuterated dimethyl sulfoxide was left at room temperature inside the nmr tube, deep red crystals gradually developed over a period of two months. The ^{1}H nmr data on the solution showed it to contain almost exclusively 9-(*p*-tolyl)-6-cyanopurine. The insoluble red solid was identified as the pyrrole **3d.** This observation suggests that **9** may be a common intermediate to pyrrole **3** and 6-cyanopurine **2**. The formation of 6-cyanopurine from either **5** or **9** requires the elimination of one equivalent of dimethylamine and this last compound could be implicated in the formation of pyrrole **3**.

Table 1

Analytical and Spectroscopic Data for the Compounds **8a-e** and **11a-c.**

Compound	Mp (°C)	Molecular Formula	Microanalytical Data (%)/Found (Calcd.) C	H	N	Cl	m/z (M+1)$^+$ [a]	M
8a	117 dec	$C_{14}H_{13}N_6Cl$	55.6 (55.9)	4.0 (4.3)	28.0 (28.0)	12.0 (11.8)	301	300
8b	125.9	$C_{14}H_{14}N_6$	63.4 (63.1)	5.1 (5.3)	31.4 (31.6)		267	266
8c	120	$C_9H_{12}N_6$	52.6 (52.9)	6.1 (5.9)	41.0 (41.2)		205	204
8d	142	$C_{15}H_{16}N_6$	64.6 (64.3)	5.4 (5.7)	29.8 (30.0)		281	280
8e [b]	101.4-102.0	$C_8H_{11}N_7$					206.1154	205.1078
8f	123.7-124.0	$C_{11}H_{15}N_7$	54.2 (53.9)	6.3 (6.1)	39.7 (40.0)		246	245
11a	110 dec	$C_{16}H_{20}N_7Cl$	55.6 (55.6)	5.9 (5.8)	28.2 (28.3)	10.6 (10.3)	346	345
11b	148.0-149.2	$C_{16}H_{21}N_7$	61.4 (61.7)	7.0 (6.8)	31.1 (31.5)		312	311
11c	118 dec	$C_{11}H_{19}N_7$	52.9 (53.0)	7.7 (7.6)	39.3 (39.4)		250	249

[a] Fast atom bombardment. [b] The product incorporates solvent (dioxane).

Confirmation of this comes from the observation that when an excess of dry dimethylamine is bubbled for *ca.* 15 minutes through a solution of diamidine **8a** in chloroform, kept in an ice bath and then the reaction mixture is stirred at room temperature for one hour, the deep red pyrrole **3a** is isolated in 75% yield and only traces of the 6-cyanopurine is detected in solution by tlc. If the same reaction is kept in an ice-bath at 0°, a deep yellow solution develops and a yellow solid **11a** precipitates. Other representative examples **11b** and **c** have been prepared using a similar experimental procedure. Elemental analysis and mass spectrometry (Table 1) indicate that **11a** and **b** are isomers of **3a** and **b** and a single crystal X-ray analysis on compound **11b** has established the structure shown in Figure 1. When dimethylamine was bubbled through a solution of **8c** in a mixture of ethanol and chloroform (1:4) at 0° there was no reaction after 1 hour. On allowing the solution to reach room temperature a yellow colour slowly developed and after 19 hours the solution was found to contain amidine **13** (8%), **11c** (24%), **3c** (1%) and 6-cyanopurine (38%).

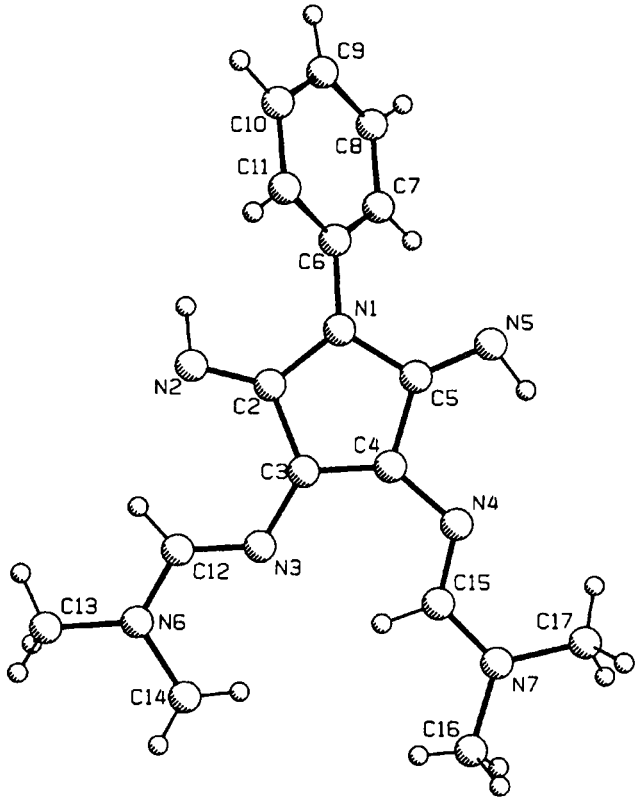


Figure 1. X-ray crystal structure of 2,5-dihydro-2,5-diimino-3,4-di[(*N,N*-dimethylamino)methylideneamino]-*N*-phenylpyrrole **11b**.

When a solution of **11b** in either chloroform or ethanol, at 0°, is allowed to warm to room temperature it is converted quantitatively to its isomer **3b**. It appears that when R is aromatic the yellow isomers **11** are the kinetic products of the reaction of **8** with dimethylamine and the isomers **3** are the thermodynamic products formed by a Dimroth rearrangement. All attempts to detect the rearrangement of the *N*-methyl derivative **11c** to **3c** were unsuccessful. When a solution of this compound in deuterated dimethyl sulfoxide was allowed to stand in the nmr tube, at room temperature, a complex mixture gradually developped. After 20 days, the starting material was completely absent in solution and there was no evidence for the presence of the red pyrrole **3c**.

The ir spectra of the new compounds **11a-c** all show two weak bands around 3270 and 3250 cm^{-1} for the =NH stretching vibrations. In the ^1H nmr spectra the four methyl groups appear as one singlet integrating for 12 protons (see Table 2). The high symmetry of compound **11b** is evidenced by its ^{13}C

Table 2

^1H NMR Spectroscopic Data for the Compounds **8a-f**, **11a-c** and **3c** and **3f**

Compound	δH (ppm) in deuteriochloroform
8a	3.04 (3H, br s, Me), 3.14 (3H, s, Me), 6.97 (2H, br s, ArH), 7.31 (2H, d, J = 7.2 Hz, ArH), 7.88 (1H, s, CH), 8.46 (1H, br s, CH), 8.65 (<1H, br s, NH)
8b	2.99 (3H, s, Me), 3.08 (3H, s, Me), 7.03 (2H, br s, ArH), 7.13 (1H, t, J = 7.2 Hz, ArH), 7.34 (2H, m, ArH), 7.84 (1H, s, CH), 8.56 (1H, s, CH), 9.08 (1H, br s, NH)
8c	3.08 (3H, d, J = 5.1 Hz, Me), 3.14 (6H, s, Me), 5.85 (<1H, br s, NH), 7.94 (1H, s, CH), 8.07 (1H, d, J = 4.4 Hz, CH)
8d	2.32 (3H, s, Me), 2.97 (3H, s, Me), 3.05 (3H, s, Me), 6.88 (2H, d, J = 8.1 Hz, ArH), 7.10 (2H, d, J = 8.1 Hz, ArH), 7.81 (1H, s, CH), 8.49 (1H, s, CH), 8.91 (1H, br s, NH)
8e [a]	2.94 (3H, s, Me), 3.07 (3H, s, Me), 7.77 (1H, br s, NH), 7.90 (1H, d, J = 8.3 Hz, CH), 8.03 (1H, s, CH)
8f [b]	**A:** 2.03 (3H, s, Me), 2.04 (3H, s, Me), 3.10 (3H, s, Me), 3.16 (3H, s, Me), 7.81 (1H, s, CH), 8.36 (1H, s, CH), 8.76 (1H, br s, NH) **B:** 2.04 (3H, s, Me), 2.07 (3H, s, Me), 3.09 (3H, s, Me), 3.16 (3H, s, Me), 7.48 (1H, br s, CH), 7.78(1H, s, CH), 8.76 (1H, br s, NH)
11a	3.06 (12H, s, Me), 7.20-8.40 (<2H,br s, NH), 7.29 (2H, d, J = 8.4 Hz, ArH), 7.46 (2H, d, J = 8.4 Hz, ArH), 8.84 (2H, s, CH)
11b	3.06 (12H, s, Me), 7.36 (3H, m, ArH), 7.50 (2H, m, ArH), 7.00-9.00 (<2H, br s, NH), 8.90 (2H, br s, CH)
11c	3.02 (12H, s, Me), 3.19 (3H, s, Me), 8.45 (2H, br s, CH)
3c [a]	2.91 (12H, br s, Me), 3.06 (3H, s, Me), 7.04 (<1H, br s, NH), 8.22 (<1H, br s, NH), 8.74 (1H, s, CH), 8.86 (1H, s, CH)
3f [a]	1.92 (3H, s, Me), 1.99 (3H, s, Me), 2.91 (3H, s, Me), 2.95 (3H, s, Me), 2.99 (6H, s, Me), 7.35-7.60 (<2H, br s, NH), 8.77 (1H, s, CH), 8.87 (1H, s, CH)

[a] Dimethyl-d_6 sulfoxide as solvent, [b] Mixture of two tautomers A and B in the ratio of 1:4.

Table 3

^{13}C NMR Spectroscopic Data for the Compounds **11a-c**

Compound	δC (ppm) in deuteriochloroform				
	C-2	C-3	C-H	NMe_2	R
11a	163.0	127.5	156.4	33.6 40.4	129.6 (CH), 129.7 (CH), 132.6 (C'or C*p*), 132.9 (C'or C*p*)
11b	163.0	127.6	156.4	33.6 40.3	127.3 (CH), 128.4 (CH), 129.0 (CH), 133.8 (C')
11c	164.3	127.2	155.9	33.7 40.3	24.7 (Me)

nmr spectrum which shows one signal for C(2) and C(5) (163 ppm), one signal for C(3) and C(4) (127.6 ppm) and one signal for both amidine C(H) (156.4 ppm) (see Table 3). From the crystal structure (Figure 1 and Tables 4 and 5) it can be seen that the bonds N(2)-C(2) [1.276(3) Å] and N(5)-C(5) [1.263(3) Å] have double bond character confirming that they are imino substituents. There appears to be little or no conjugation in the ring as the C(3)-C(4) bond is of normal C=C bond length and the C(2)-N(1) [1.402(3) Å] and C(5)-N(1) [1.399(3) Å] bond lengths are rather longer than expected for normal N-C_{sp}^2 bonds. The phenyl group on N(1) is twisted out of the plane of the pyrrole ring and it does not conjugate with the ring as evidenced by the N(1)-C(6) bond length of 1.425(3) Å. There have been very few reports on the synthesis of similar 2*H*-pyrroles and we are only aware of compounds of type **12** from perchlorobutenyne and primary aromatic amines [7]. No ^{13}C nmr data is reported for compound **12**, which was characterized by X-ray spectroscopy. The values reported for the bond lengths of the ring atoms are comparable to the values obtained for compound **11b**.

Although the formation of an intermediate such as **9** could not be proved directly in these reactions addition of 1,8-diazabicyclo[5.4.0]undec-7-ene to a chloroform solution of **8b** at 0° gave an unstable yellow solid believed to be **9** (R = Ph), which precipitated after 5 minutes. This compound appears to decompose rapidly even in moist air and it could not be fully characterised. However, its ir spectrum shows a weak band at 3322 cm^{-1} for an =NH stretching vibration and a band at 2194 cm^{-1} for the cyano groups. The ^1H nmr spectrum shows a singlet at δ 8.1 ppm typical of a formamidine, another singlet at δ 7.8 ppm for the proton of the imidazole ring, and NH singlet at δ 9.0 ppm. An NOE difference experiment has confirmed that one of the two *N*-methyl

Table 4

Crystallographic Data for **11b**

Formula	$C_{16}H_{21}N_7$
M_r	311.39
Crystal system	monoclinic
Space group	$P2_1/n$
T/ °C	23
λ/Å	0.71069
ß/(°)	93.38(2)
a/Å	6.979(2)
b/Å	15.828(5)
c/Å	14.599(5)
V/Å^3	1610(2)
Z	4
D_c/gcm^{-3}	1.285
F(000)	664
μ/cm^{-1}	0.78
reflections measured	2498
No. observations [I>2.00σ(I)]	1613
R	0.056
R_w	0.056

Table 5

Selected Bond Lengths [Å] and Angles [°] for Compound **11b**, with Estimated Standard Deviations in Parentheses

atom	atom	distance	atom	atom	atom	angle
N1	C2	1.402(3)	C2	N1	C5	109.9(2)
N1	C5	1.399(3)	C2	N1	C6	124.3(2)
N1	C6	1.425(3)	C5	N1	C6	124.8(2)
N2	C2	1.276(3)	C3	N3	C12	122.5(2)
N3	C3	1.380(3)	C4	N4	C15	119.0(2)
N3	C12	1.289(3)	C12	N6	C13	122.2(2)
N4	C4	1.378(3)	C12	N6	C14	121.1(2)
N4	C15	1.296(4)	C13	N6	C14	116.7(2)
N5	C5	1.263(3)	C15	N7	C16	120.2(2)
N6	C12	1.336(3)	C15	N7	C17	121.6(3)
N6	C13	1.443(4)	C16	N7	C17	118.0(3)
N6	C14	1.443(4)	N1	C2	N2	127.7(3)
N7	C15	1.323(4)	N1	C2	C3	106.8(2)
N7	C16	1.447(4)	N2	C2	C3	125.5(3)
N7	C17	1.429(4)	N3	C3	C2	128.4(2)
C2	C3	1.474(4)	N3	C3	C4	123.5(2)
C3	C4	1.361(4)	C2	C3	C4	108.0(2)
C4	C5	1.473(4)	N4	C4	C3	134.9(2)
C6	C7	1.390(4)	N4	C4	C5	116.0(2)
C6	C11	1.378(4)	C3	C4	C5	108.9(2)
C7	C8	1.377(4)	N1	C5	N5	124.4(3)
C8	C9	1.362(4)	N1	C5	C4	106.4(2)
C9	C10	1.386(4)	N5	C5	C4	129.2(3)
C10	C11	1.383(4)	N1	C6	C7	119.6(2)
			N1	C6	C11	120.2(2)
			C7	C6	C11	120.2(3)
			C6	C7	C8	119.1(3)
			C7	C8	C9	121.2(3)
			C8	C9	C10	119.8(3)
			C9	C10	C11	119.9(3)
			C6	C11	C10	119.8(3)
			N3	C12	N6	121.2(2)
			N4	C15	N7	123.6(3)

groups is close to the formamidine proton. When an excess of dimethylamine is bubbled through a chloroform solution of **9** (R = Ph) cooled at 0° an intense yellow colour develops and **11b** precipitates in 63% yield after only 10 minutes. When a solution of **9** (R = Ph) in deuterated chloroform was maintained at room temperature for 4 days, analysis by ^{1}H nmr spectroscopy showed no evidence for unchanged starting material and the only products were 6-cyano-9-phenylpurine and the pyrrole **3b** in a 1:1 ratio approximately. Under similar reaction conditions the diamidine **8b** gave a similar ratio of these two products. This suggests that in the absence of dimethylamine, intermediate **9** may lead to the cyanopurine and the dimethylamine eliminated in the process may give rise to the pyrrole by reaction with imidazole **9**. At room temperature, the reaction of a chloroform solution of **9** (R = Ph) with an excess of dimethylamine (bubbled at 0°) resulted only in the formation of **3b** and none of the cyanopurine could be detected by tlc. These experiments clearly support the suggestion that **9** is the initial intermediate formed upon treatment of **8** with dimethylamine, and that **9** then undergoes a facile ring opening reaction by attack of dimethylamine at the C(2) position of the imidazole ring. This type of ring opening reaction is not unknown, and a similar reaction has been observed for 6-azapurines [8] upon reaction with alcohols and water.

Complications may arise in the direct formation of **3** from **8** at room temperature when the rate of reaction is slow. In these cases a competing cleavage reaction may lead to compound **13**. This was the case when dimethylamine was bubbled through a solution of compounds **8c**, **8e** and **8f** in chloroform. When dimethylamine was bubbled through a solution of **8c** in chloroform kept at 0° and the solution was then stirred at room temperature for 18 hours, an oily mixture was obtained. The ^{1}H nmr showed the presence of **13** (50%), **3c** (24%) and **11c** (25%). When the reaction of **8c** with dimethylamine was carried out at room temperature for 18 hours, the products isolated by dry flash chromatography were **11c** (1%), **3c** (12%), **13** (8%) and the 6-cyanopurine **2** (R = Me, 37%). The reaction of **8e** with dimethylamine was very slow possibly due to its low solubility in the solvent. After 24 hours at 5° a complex mixture was obtained and **13** (23%) was the only product isolated after dry flash chromatography. In the presence of dimethylamine, diamidine **8f** evolved to the corresponding pyrrole **3f** (51% yield) after 3 hours at 15°. Compound **13** was also isolated in 16% yield by dry flash chromatography. This compound has been fully characterised and has been independently prepared by reaction of diaminomaleonitrile with *N,N*-dimethylformamide diethyl acetal. The reaction occurs immediately at 0° and the product was isolated in 46% yield after dry flash chromatography. The (*Z*)-N^2-{1,2-dicyano-2-[(*N,N*-dimethylamino)-methylideneamino]vinyl}-N^1,N^1-dimethylformamidine is always present as a contaminant in the reaction mixture. Compound **13** had been previously prepared [9] in 60% yield from the reaction of diaminomaleonitrile with *N,N*-dimethylformamide in the presence of phosphorus oxide trichloride.

EXPERIMENTAL

The ^{1}H nmr spectra were recorded on Varian Unity Plus 300 (300MHz) or Bruker XL300 (300MHz) instruments, the ^{13}C nmr spectra (with DEPT 135) on a Bruker WP80 or XL 300 instrument, and the ir spectra on a Perkin Elmer 1600 FT-IR spectrometer. Mass spectra were recorded on a Kratos Concept instrument. Melting points were measured on an Electrothermal digital melting point apparatus and are uncorrected.

Crystallography.

The crystal was mounted on glass fibre. All measurements were performed on a Siemens R3m/v diffractometer with graphite-monochromated Mo-Ka radiation. The data were collected at a temperature of -40°. The intensities were corrected for Lorentz and polarization effects, but absorption was ignored.

The structures were solved by SHELXS-86 [11] and refined by means of SHELXL-93 [12]. All non-hydrogen atoms were refined anisotropically. The methyl and phenyl hydrogens were constrained to chemically reasonable positions and the remainder subjected to isotopic refinement. Details are presented in Tables 4 and 5.

Tables of fractional coordinates, bond lengths and angles and thermal parameters are available on request from the Cambridge Crystallographic Data Centre.

Synthesis of Ethyl (*Z*)-*N*-{1,2-Dicyano-2-[(*N,N*-dimethylamino)methylideneamino]vinyl}formimidate **7**.

N,N-Dimethylformamide diethyl acetal (0.71 g, 4.84 mmoles) was added to a suspension of ethyl (*Z*)-*N*-(2-amino-1,2-dicyanovinyl)formimidate (0.66 g, 4.03 mmoles) in chloroform (2 ml) under magnetic stirring at room temperature. After 15 minutes all the starting material had been consumed (as evidenced by tlc) and the reaction mixture was concentrated in the rotary evaporator. Addition of diethyl ether gave the title compound **7** as an off-white solid (0.72 g, 3.3 mmoles, 82%), mp 119-120°; ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 1.20 (3 H, t, J = 7.2 Hz, Me), 2.88 (3 H, s, Me), 3.05 (3 H, s, Me), 4.15 (2 H, q, J = 7.2 Hz, CH_2), 7.91 (1 H, s, CH), 8.21 (1 H, s, CH); ^{13}C nmr (dimethyl-d_6 sulfoxide): δ 13.8 (Me), 34.7 (NMe), 40.3 (NMe), 63.1 (CH_2), 112.1 (C=C), 114.1 (CN), 116.4 (CN), 128.7 (C=C), 155.5 (CH), 160.9 (CH); ir (Nujol): ν 2214, 2203 cm^{-1} (CN); ms: (FAB) m/z 220 $(M+1)^+$.

Anal. Calcd. for $C_{10}H_{13}N_5O$: C, 54.8; H, 5.9; N, 32.0. Found: C, 54.5; H, 5.9; N, 32.1.

General Procedure for the Synthesis of N^2-Aryl-(*Z*)-N^1-{1,2-dicyano-[(*N,N*-dimethylamino)methylideneamino]vinyl}formamidines **8a-f**.

One equivalent of the amine was added to a suspension of ethyl (*Z*)-*N*-{1,2-dicyano-2-[(*N,N*-dimethylamino)methylideneamino]vinyl}formimidate in ethanol [a] in the presence of a catalytic amount of anilinium hydrochloride [b] with magnetic stirring at 5°. The reaction was monitored by tlc. If the reaction was too slow, the temperature was allowed to rise to room temperature. The product, present as a solid suspension, was filtered and washed with diethyl ether [c]. [a] In the reaction with hydrazine,

R = NH_2, dioxane was used instead. [b] No catalyst was used in the synthesis of **8** when R = *p*-$H_2NC_6H_4$ and R = NH_2. [c] Only 6-cyanopurine was isolated in reaction with *p*-phenylenediamine.

Synthesis of (*Z*)-N^2-{1,2-Dicyano-2-[(*N*,*N*-dimethylamino)methylideneamino]vinyl}-N^1-methylformamidine **8c**.

Methylamine (40% solution in water, 1.2 equivalents) was added with magnetic stirring to a suspension of **7** (0.54 g, 2.45 mmoles) in ethanol (5 ml) at room temperature. The suspension went into solution and a yellow solid precipitated. This was filtered, washed with diethyl ether to give **8c** (0.40 g, 1.95 mmoles, 79%).

Synthesis of (*Z*)-N^3-{1,2-Dicyano-2-[(*N*,*N*-dimethylamino)methylideneamino]vinyl}-N^1-(isopropylidene)formamidrazone **8f** from Amidrazone **8e**.

Kieselgel 60 (0.2 g) was added to a solution of amidrazone **8e** (0.41 g, 2.0 mmoles) in acetone (20 ml). The reaction mixture was stirred at room temperature for 1.5 hours. The suspension was filtered and the solution was concentrated in the rotary evaporator. The residue was dissolved in ethanol and concentration in a rotary evaporator gave a solid, which was filtered and washed with a mixture of ethanol:diethyl ether, 3:1. The product was identified as **8f** (0.3 g, 1.21 mmoles, 46%).

General Procedure for the Reaction of N^2-Aryl-(*Z*)-N^1-{1,2-dicyano-2-[(*N*,*N*-dimethylamino)methylideneamino]vinyl}-formamidine **8a** and **8d** with Dimethylamine.

A suspension of the amidine (1.37 mmoles) in chloroform (2 ml) was kept in a round bottom flask equipped with a magnetic stirrer and a serum cap. The flask was kept in an ice water bath and dimethylamine was bubbled for 15 minutes and the mixture was then kept at 0° for a further 90 minutes. The yellow solution formed was evaporated in a rotary evaporator to give a yellow oil. Addition of ethanol and cooling in an ice bath led to the formation of red crystals, which were filtered and washed with diethyl ether. The mother liquid was concentrated to dryness and addition of diethyl ether to the residue gave a second crop. The products were identified as compounds **3a** and **3d** respectively.

Reaction of (*Z*)-N^1-{1,2-Dicyano-2-[(*N*,*N*-dimethylamino)-methylideneamino]vinyl}-N^2-phenylformamidine **8b** with Dimethylamine.

A solution of the diamidine (0.46 g, 1.62 mmoles) in chloroform (3 ml) was kept in a round bottom flask equipped with a magnetic stirrer and a serum cap. The flask was kept in an ice bath and dimethylamine was bubbled through for 10 minutes, when all the starting material was consumed (as evidenced by tlc). The solution was removed from the ice bath and an orange colour developed as the temperature rose to room temperature. Flash chromatography on the reaction mixture using chloroform (200 ml) and acetone (100 ml) as solvents gave two crops of the same red crystals: 0.33 g from chloroform and 0.06 g from acetone. The product was identified as compound **3b**, total yield 0.39 g (1.19 mmoles, 73%).

Reaction of (*Z*)-N^3-{1,2-Dicyano-2-[(*N*,*N*-dimethylamino)-methylideneamino]vinyl}-N^1-(isopropylidene)formamidrazone **8f** with Dimethylamine.

A solution of the diamidine **8f** (0.20 g, 0.82 mmoles) in chloroform (2 ml) was kept in a round bottom flask equipped with a magnetic stirrer and a serum cap. The flask was kept in an ice bath and dimethylamine was bubbled through for 20 minutes. The reaction was followed by tlc and after 3 hours at 15° all the starting material had been consumed. The reaction mixture was concentrated in the rotary evaporator and addition of diethyl ether led to a red solid which was filtered and washed with diethyl ether. The product was identified as compound **3f** (0.12 g, 0.41 mmole, 51%). The mother liquid was flash chromatographed using chloroform (100 ml) as solvent. Partial removal of the solvent led to a cream solid identified as (*Z*)-N^2-(2-amino-1,2-dicyanovinyl)-N^1,N^1-dimethylformamidine **13** (0.02 g, 0.13 mmole, 16%) by comparison of its ir spectrum with that of an authentic sample.

Reaction of (*Z*)-N^3-{1,2-Dicyano-2-[(*N*,*N*-dimethylamino)methylideneamino]vinyl}formamidrazone **8e** with Dimethylamine.

A suspension of the diamidine **8e** (0.10 g, 0.50 mmoles) in chloroform (2 ml) was kept in a round bottom flask equipped with a magnetic stirrer and a serum cap. The flask was kept in an ice bath and dimethylamine was bubbled through for 5 minutes. The flask was introduced in an ultrasonic bath for 3 minutes to improve the solubility of the amidine. Dimethylamine was then bubbled for an additional 15 minutes keeping the flask in an ice bath. The reaction proceeded at 5° for 24 hours. The tlc indicated that the starting material was no longer present and a complex mixture had been formed. After flash chromatography using chloroform (50 ml) as solvent, a pale yellow solid was isolated and identified as (*Z*)-N^2-[2-amino-1,2-dicyanovinyl]-N^1,N^1-dimethylformamidine **13** (0.02 g, 0.11 mmole, 23%) by comparison of its ir spectrum with that of an authentic sample.

Synthesis of *N*-(*p*-Chlorophenyl)-2,5-dihydro-2,5-diimino-3,4-di[(*N*,*N*-dimethylamino)methylideneamino]pyrrole **11a**.

Dimethylamine was bubbled for 20 minutes through a suspension of the diamidine **8a** (0.26 g, 0.91 mmoles) in chloroform (2 ml) contained in a round bottom flask equipped with a magnetic stirrer and cooled in an ice-salt bath. The reaction mixture was kept at 0° for 90 minutes before allowing the excess of dimethylamine to evaporate and adding diethyl ether to precipitate a deep yellow solid (0,063 g). Filtration and concentration of the mother liquor followed by addition of ether gave a second crop (0.15 g) of the product, total yield of **11a** (0.21 g, 0.65 mmole, 71%).

Synthesis of 2,5-Dihydro-2,5-diimino-3,4-di[(*N*,*N*-dimethylamino)methylideneamino]-*N*-phenylpyrrole **11b**.

Following a similar procedure to that described above reaction of the diamidine **8b** (0,17 g, 0.65 mmoles) with dimethylamine in chloroform (1 ml) at 0° gave a yellow solution and after 5 minutes a yellow solid precipitated. This was filtered, washed with chloroform and diethyl ether to give a first crop of 0.078 g. Concentration of the mother liquor gave a further crop of 0.013 g, total yield of **11b** (0.09 g, 0.29 mmole, 45%).

Synthesis of 2,5-Dihydro-2,5-diimino-3,4-di[(*N*,*N*-dimethylamino)methylideneamino]-*N*-methylpyrrole **11c**.

Dimethylamine was bubbled for 30 minutes through a suspension of amidine **8c** (0.23 g, 1.10 mmoles) in a mixture of chloroform and ethanol (2 ml, 4:1). The mixture was then kept at room temperature for 18 hours when tlc showed that all the starting material had disappeared. The solvents were then removed under vacuum to give an oil, which was then chromatographed (kieselgel). Eluting with diethyl ether gave amidine **13** (0.01 g, 0.09 mmole, 8%), elution with chloroform gave 6-cyano-9-methylpurine (0.07 g, 0.41 mmole, 37%), and elution with ethanol gave

a first fraction containing pure **11c** (0.03 g, 0.13 mmole, 12%) and a second fraction containing **3c** (0.0024 g, 0.01 mmole, 1%).

Synthesis of 4-{Cyano-[(*N,N*-dimethylamino)methylideneamino]}-methylidene-4,5-dihydro-5-imino-1-phenylimidazole **9b**.

1,8-Diazabicyclo[5.4.0]undec-7-ene (15 µl) was added to a suspension of diamidine **8b** (0.17 g, 0.63 mmoles) in chloroform (1 ml) at 0° under magnetic stirring for 10 minutes. Removal of the solvent gave a yellow oil which slowly crystallised. The crystals were washed with dry diethyl ether to give **9b** (0.143 g, 0.31 mmole, 85%).

Synthesis of **11b** from **9b**.

When dimethylamine was bubbled for 10 minutes through a stirred solution of **9b** (0.1 g, 0.37 mmoles) in chloroform (1 ml) at 0° tlc showed that all the starting material had been consumed. Evaporation of the excess of dimethylamine and concentration of the solution gave a yellow oil, which on adding diethyl ether crystallised to give **11b** (0.07 g, 0.23 mmole, 63%) as a yellow solid.

Synthesis of (*Z*)-N^2-(2-Amino-1,2-dicyanovinyl)-N^1,N^1-dimethylformamidine **13**.

A solution of diaminomaleonitrile (0.4 g, 3.70 mmoles) in dry acetonitrile (7 ml) was kept in a round-bottom flask equipped with a magnetic stirrer bar and a serum cap, under a nitrogen atmosphere. *N,N*-Dimethylformamide diethyl acetal (0.54 g, 3.68 mmoles) was added dropwise over a period of 10 minutes, while the solution was kept in an ice bath with vigorous stirring. Stirring was continued for a further 15 minutes, when a tlc on the reaction mixture showed that the starting material was no longer present. Dry flash chromatography using diethyl ether as a solvent led to a cream solid identified as the title compound **13** (0.28 g, 1.70 mmoles, 46%), mp 162-163° (lit [9] 152-154°); ^{1}H nmr (dimethyl-d_6 sulfoxide): δ 2.96 (3 H, s, Me), 3.05 (3 H, s, Me), 6.08 (2 H, s, NH_2), 7.67 (1 H, s, CH); ^{13}C-nmr (dimethyl-d_6 sulfoxide): δ 34.4 (NMe), 40.2 (NMe), 105.8 (C=C), 115.1 (CN), 116.3 (CN), 116.4 (C=C); ir (Nujol): ν 3454, 3326 cm^{-1} (NH_2), 3139 cm^{-1} (CH), 2220, 2205 cm-^{1} (CN); ms: m/z 163 (M^+, 100%).

Anal. Calcd. for $C_7H_9N_5$: C, 51.5; H, 5.3; N, 42.7. Found: C, 51.8; H, 5.3; N, 42.7.

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