Synthesis of 4-Substituted 8-Amino-4,5-dihydro-3*H*-pyrrolo[3,4-*f*]-1,3,5-triazepin-6-ones and 5-Amino-2-aryl-4-(1-aryl-5-alkylideneaminoimidazol-4-yl)-1,3-oxazoles[1]

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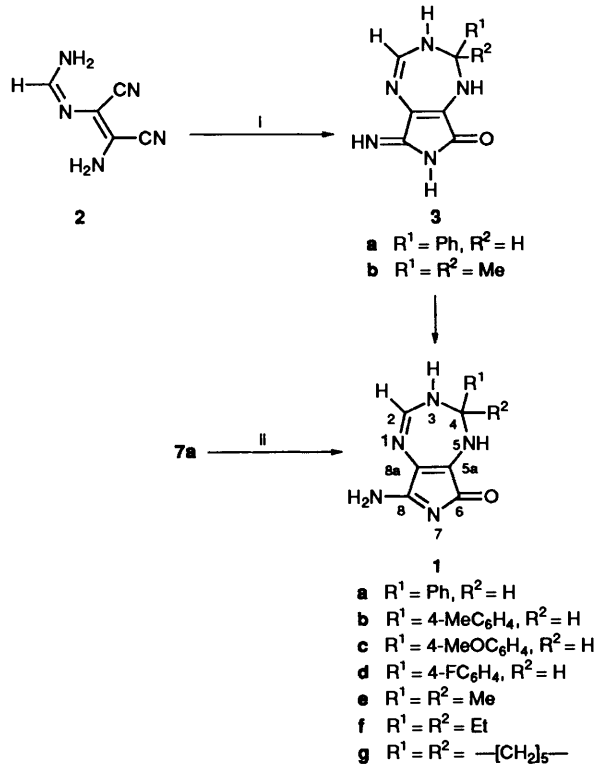
The title compounds have been prepared from (*Z*)-*N*^{2}-(2-amino-1,2-dicyanovinyl)formimidamide by reaction of an excess of an aldehyde or ketone in the presence of a base. The triazepine **1e** can also be obtained by the reaction of ethyl (*Z*)-*N*-(2-carbamoyl-1-cyano-2-isopropylideneaminovinyl)-formimidate **7a** with ammonia and a catalytic amount of anilinium hydrochloride. Under similar conditions the 2-benzylideneamino derivative **7b** affords the corresponding amidine **6**, and only a low yield of the triazepine. In this last reaction aminolysis of the alkylideneamino bond competes with amidine formation to give compound **8**, and reaction between the formimidate **7c** and *p*-anisidine resulted only in the formation of ethyl (*Z*)-*N*-(2-amino-2-carbamoyl-1-cyanovinyl)-formimidate **8**. Reactions between *N*^{2}-aryl-(*Z*)-*N*^{1}-(2-amino-1,2-dicyanovinyl)formimidamides and aldehydes in the presence of a base do not give 1,3,5-triazepines, but instead afford novel 5-amino-2-aryl-4-(1-aryl-5-alkylideneaminoimidazol-4-yl)-1,3-oxazoles **11** together with the known 9-aryl-6-carbamoyl-1,2-dihydropurines, the corresponding purines and other products.

As a class of compounds the 1,3,5-triazepines have been little explored. Fully unsaturated monocyclic 1,3,5-triazepines have been synthesised by photolysis of 2-azidopyrazines and 4-azidopyrimidines in the presence of methoxide ion or diethylamine.[2] A similar procedure has also been used to prepare 1,3,5-triazepine-2,7-diones from 6-azidouracil derivatives,[3] and 1,3,5-triazepines have been proposed as intermediates in the thermal rearrangement of 1,3,5-triazahepta-1,3-dien-7-ones to 1,4,6-triazahepta-3,5-dien-7-ones.[4] Several examples of condensed 1,3,5-triazepines, such as imidazo[1,2-*a*][1,3,5]benzotriazepines,[5] imidazo[2,3-*b*][1,3,5]triazepines,[6] and 7,8,9,10-tetrahydro-2*H*,6*H*-triazino[2,3-*c*][1,3,5]triazepines[7] have been described, and, recently, compounds having the novel ring system 1,2,4-triazolo[3,4-*b*]-1,3,5-triazepine-5(9*H*)-thione have been synthesised.[8,9]

For some time now we have been interested in the chemistry of diaminomaleonitrile (DAMN) derivatives,[10-13] and in a recent communication [1] we have described the synthesis of some derivatives of 8-amino-4,5-dihydro-3*H*-pyrrolo[3,4-*f*]-1,3,5-triazepin-6-ones **1** from (*Z*)-*N*^{2}-(2-amino-1,2-dicyanovinyl)-formimidamide **2**. We have now carried out a more detailed investigation of this reaction and have devised an alternative procedure for the synthesis of compounds of type **1** as well as some new derivatives of DAMN.

Results and Discussion

Addition of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to a suspension or solution of the amidine **2** in a large excess of an aldehyde or ketone at room temperature gave an immediate exothermic reaction with dissolution of compound **2** and the precipitation of a solid. In the case of aldehydes these products **3** are yellow–orange, while with acetone it is off-white. Upon dissolution in alcohol solvents or recrystallisation from methanol–light petroleum these compounds were rapidly converted into the red compounds **1a–g** (Scheme 1). Initially it was considered that these red compounds may be 6-carbamoyl-1,2-dihydropurine derivatives **4** as it was known from earlier



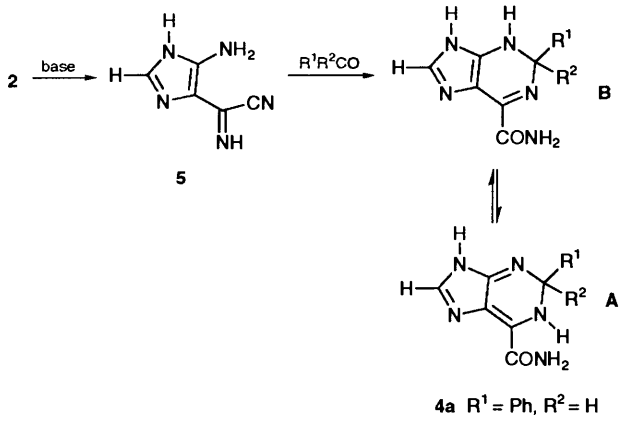
Scheme 1 *Reagents:* i, R^1R^2CO, DBU; ii, NH_3, $CHCl_3$

work [10] that the amidine **2** cyclises in the presence of a base to form 5-amino-4-(cyanoformimidoyl)-1*H*-imidazole **5** in good yield, and that **5** reacts with aldehydes and ketones to form the dihydropurine **4**, which exist in solution mainly as the orange tautomer **A** (Scheme 2). Microanalysis and FAB mass spectrometry (Table 1) do not distinguish between the structures **1** and **4**, and it was necessary to prepare a sample of compound **4a** by

Table 1 Microanalytical, m.p. and mass spectroscopic data for the compounds **1a–g**, **3a**, **b** and **4a**

	Yield (%)	M.p. (°C)[a]	Molecular formula	Microanalytical data (%)/ found (calc.) C	H	N	*m/z* $(M + 1)^{+}$[b]	*M*
1a	92	> 130	$C_{12}H_{11}N_5O$	59.6 (59.8)	4.3 (4.6)	28.7 (29.0)	242	241
1b	69	> 175	$C_{13}H_{13}N_5O$	60.9 (61.2)	5.4 (5.1)	27.2 (27.5)	256	255
1c	66	> 170	$C_{13}H_{13}N_5O_2$	57.3 (57.6)	4.5 (4.8)	25.5 (25.8)	272	271
1d	70	> 165	$C_{12}H_{10}FN_5O$	55.5 (55.6)	3.7 (3.9)	26.7 (27.0)	260	259
1e	76	> 200	$C_8H_{11}N_5O$	49.5 (49.7)	5.8 (5.7)	36.8 (36.3)	194[c]	193
1f	61	> 190	$C_{10}H_{15}N_5O$	54.5 (54.3)	6.7 (6.8)	31.8 (31.7)	222	221
1g	72	> 187	$C_{11}H_{15}N_5O$	56.7 (56.6)	6.3 (6.4)	30.1 (30.0)	234	233
3a	92	> 167	$C_{12}H_{11}N_5O$	59.6 (59.8)	4.3 (4.6)	28.7 (29.0)	242	241
3b	53	> 188	$C_8H_{11}N_5O$	49.5 (49.7)	5.4 (5.7)	36.0 (36.3)	194	193
4a	72	> 130	$C_{12}H_{11}N_5O$	60.0 (59.8)	4.5 (4.6)		242	241

[a] All decomposed. [b] Fast atom bombardment. [c] Chemical ionisation.



Scheme 2

treatment of the imidazole **5** with benzaldehyde in methanol at room temperature. This gave **4a** as an orange solid in 72% yield. A comparison of the IR, ^1H and ^{13}C NMR spectra of compounds **4a** and **1a** (see Tables 2 and 3) quickly established that these compounds had different structures. Both compounds show a strong carbonyl stretching vibration in the 1670–1680 cm^{-1} region of the IR spectra and the ^1H NMR spectra were similar except that the spectrum of **4a** showed four NH signals (integration 1:1:1:1), while that of **1a** showed only three (integration 1:1:2). The major difference was in the ^{13}C NMR spectra (Table 3), where the spectrum of **4a** showed a signal for C-5 at 114.2 ppm, which is typical for a dihydropurine.[10] This signal was absent in the spectrum of **1a** and instead there was one at 170.6 ppm attributable to a N–C=N group. A single crystal X-ray structure determination[1] on **1a** has established that the compounds **1a–g** have the structure shown in Scheme 1. The crystal structure shows that the lone pair electrons of the exocyclic amino group are declocalised into the pyrrole ring and that the structure is more accurately described by the contributing resonance form **1B**.

Examination of the initially formed products **3a** and **b** by microanalysis and FAB mass spectrometry (Table 1) indicates that they have the same molecular formulae as the triazepines, but their IR spectra are quite different. It is not possible to obtain ^1H and ^{13}C NMR spectra of these compounds as in solution they change to the triazepines too rapidly. However, determination of the solid-state ^{13}C NMR spectrum of **3b** shows signals at 26.9 (Me), 31.4 (Me), 68.9, 117.6, 129.6, 148.7, 165.7 and 169.1 ppm. As a comparison, the solid-state spectrum of compound **1e** determined under similar conditions shows signals at 28.2, 28.5 (Me), 32.4, 33.2 (Me), 67.6 (C-4), 118.3 (C-8a), 130.8 (C-5a), 148.7 (C-2), 178.8 (C-8) and 179.6 (C-6) ppm. Not surprisingly, the chemical-shift values for the solid-state spectrum are slightly different from those obtained in solution (see Table 3), and the signals for the methyl carbon atoms are split. This is not an uncommon phenomenon and is believed to be due to a packing effect in the unit cell. From a comparison of the spectra of **3b** and **1e** it is apparent that these two compounds have very similar structures and the only significant differences are in the chemical shift values for C-6 and C-8 in the pyrrole ring. On this basis we assume that the solids **3a** and **b** are tautomers of **1a** and **e**, respectively (see Scheme 1).

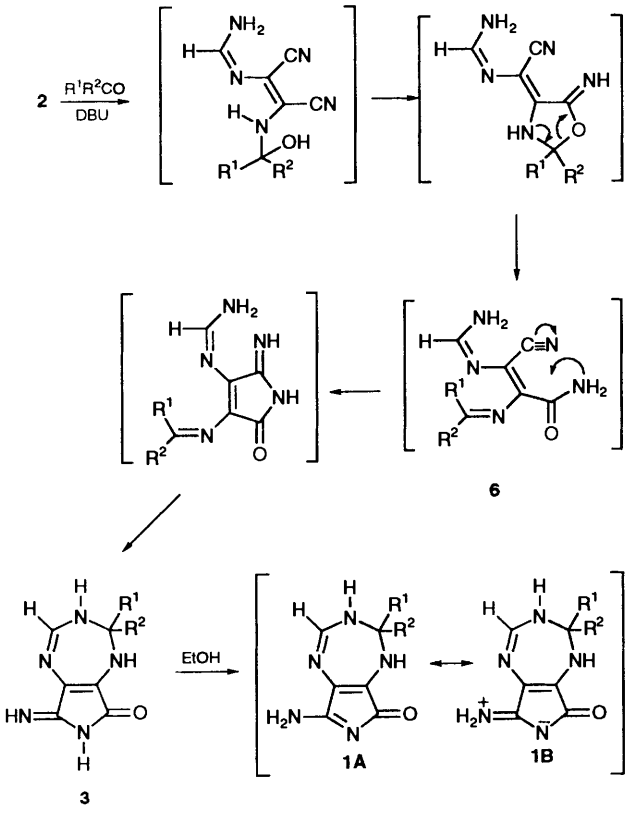
Table 2 ^1H NMR spectroscopic data for the compounds **1a–g** and **4a**

Compound	δ_H (ppm) in [$^2H_6$]DMSO
1a	5.50 (1 H, s, 4-H), 7.05 (1 H, s, NH), 7.30–7.50 (6 H, m, ArH + 2-H), 8.5 (2 H, br s, NH_2), 9.70–10.00 (< 1 H, br s, NH)
1b	2.35 (3 H, s, Me), 5.5 (1 H, s, 4-H), 7.00 (1 H, s, NH), 7.20–7.35 (5 H, m, ArH + 2-H), 8.5 (2 H, br s, NH_2), 9.80–10.10 (< 1 H, br s, NH)
1c	3.87 (3 H, s, OMe), 5.45 (1 H, m, 4-H), 6.90 (1 H, s, NH), 7.05 (2 H, d, *J* 8.5, ArH), 7.30 (3 H, d, *J* 8.5, ArH + 2-H), 8.45 (2 H, br s, NH_2), 9.70–10.10 (< 1 H, br s, NH)
1d	5.50 (1 H, m, 4-H), 7.05 (1 H, s, NH), 7.20–7.50 (5 H, m, ArH + 2-H), 8.50 (2 H, br s, NH_2), 9.70–10.00 (< 1 H, br s, NH)
1e	1.40 (6 H, s, Me), 6.60 (1 H, s, NH), 7.10–7.22 (1 H, d, *J* 4, 2-H), 7.95 (1 H, d, *J* 4, NH), 8.25–8.75 (< 1 H, br s, NH), 9.50–10.00 (< 1 H, br s, NH)
1f	0.84 (6 H, t, *J* 7, Me) 1.61 (2 H, dq, CH_2), 1.67 (2 H, dq, CH_2), 6.58 (1 H, s, NH), 7.16 (1 H, d, *J* 7, 2-H), 7.67 (1 H, d, *J* 7, NH), 8.37 (1 H, d, NH), 9.86 (1 H, s, NH)
1g	1.56 [10 H, m, $(CH_2)_5$], 6.23 (1 H, s, NH), 7.10 (1 H, d, *J* 7.5, CH), 7.72 (1 H, d, *J* 7.5, NH), 8.32 (< 1 H, br s, NH_2), 9.79 (< 1 H, br s, NH_2)
4a	5.8 (1 H, d, *J* 4.5, 2-H), 6.50 (1 H, d, *J* 4.5, NH), 7.4 (3 H, m, ArH), 7.55 (1 H, s, 8-H), 7.65 (1 H, s, NH), 7.70 (2 H, m, ArH), 7.90 (1 H, s, NH) 12.2 (1 H, s, NH)

A plausible mechanism for the formation of **3** and its tautomer **1** is shown in Scheme 3. Initial reaction is believed to occur between the 2-amino group of the amidine **2** and the carbonyl compound to form an amino alcohol intermediate, followed by intramolecular attack on the 2-cyano group to give the amide **6**. Diaminomaleonitrile is known to undergo a similar reaction with various aromatic aldehydes in the presence of triethylamine to give the corresponding 1-amino-2-methyl-ideneamino-2-carbamoylacrylonitrile.[14,15] Triazepine ring formation can result from nucleophilic attack of the amidine on the alkylideneamino (imino) group, but this may be prior to or subsequent to formation of the pyrrole ring and not necessarily

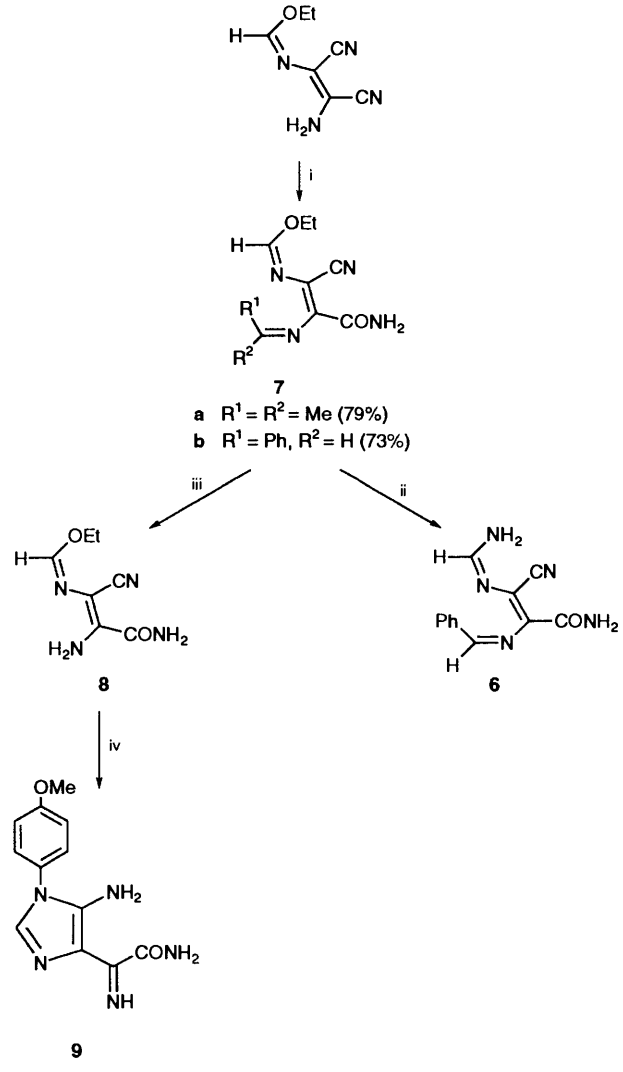
Table 3 ^{13}C NMR spectroscopic data for the compounds **1a–g** and **4a**

	δ_C (ppm) in [$^2H_6$]DMSO						
	C-2	C-4	C-5a	C-6	C-8	C-8a	Other signals
1a	153.1	72.5	134.6	174.2	170.6	121.9	146.2 (C-1'), 131.0 (C_o), 133.0 (C_m), 132.4 (C_p)
1b	152.8	72.0	134.4	174.0	170.4	122.0	24.8 (Me), 142.9 (C-1'), 130.6 (C_o), 133.2 (C_m), 141.4 (C_p)
1c	152.9	72.1	134.3	173.9	170.3	122.1	59.3 (OMe), 137.6 (C-1'), 132.1 (C_o), 116.0 (C_m), 165.9 (C_p)
1d	152.8	71.4	134.4	173.9	170.3	122.0	141.8 (*J* 2.2), 133.0 (*J* 8.4), 119.5 (*J* 21.5), 165.9 (*J* 242.5)
1e	151.4	71.8	133.2	174.3	170.5	120.6	21.3 (Me)
1f	151.7	77.4	133.3	174.3	170.5	119.9	11.6 (Me), 36.2 (CH_2)
1g	151.6	73.6	132.7	174.1	170.1	120.9	25.5, 28.5, 40.5
4a	77.5	160.6	114.2 (C-5)	147.5	154.8		144.5 (C-1'), 133.4 (C_o), 132.6 (C_m), 133.1 (C_p), 171.7 (C=O)



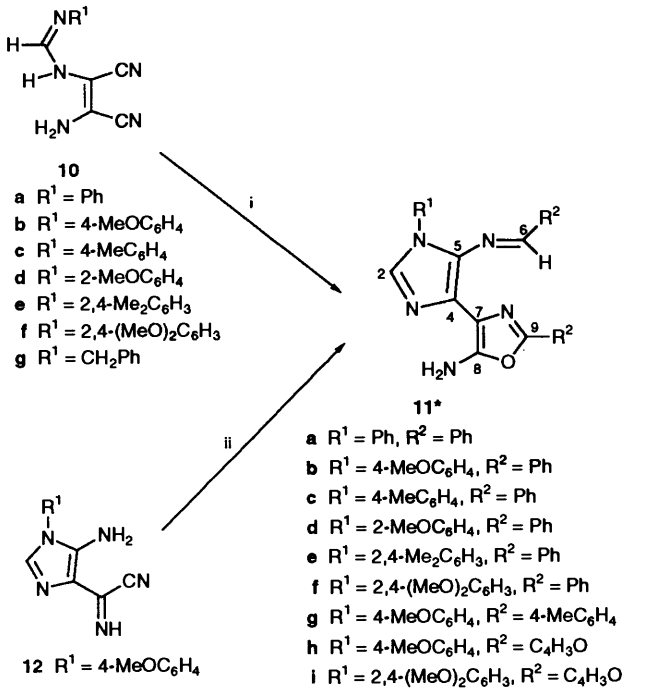
Scheme 3

as shown in the scheme. In an effort to substantiate this mechanism attempts have been made to synthesise intermediates with structure **6**. One obvious route to these compounds is shown in Scheme 4 and starts from ethyl (*Z*)-*N*-(2-amino-1,2-dicyanovinyl)formimidate, which is available from the reaction between DAMN and triethyl orthoformate.[16] The imidate reacts readily at room temperature with acetone and benzaldehyde in the presence of triethylamine to give the compounds **7a** and **b**, respectively, in high yields. In the IR spectra these compounds show a weak cyano stretching vibration at 2200 cm^{-1} in addition to a strong amide carbonyl absorption at 1660 cm^{-1}. In the ^{13}C NMR spectrum the carbon atom of the amide carbonyl appears at δ 164 and the imino carbon at δ 167. The presence of the nitrile group was confirmed by a signal at δ 113. These compounds are insoluble in most common organic solvents, but when ammonia was bubbled through a suspension of compound **7a** in chloroform containing a catalytic amount of anilinium hydrochloride the 1,3,5-triazepine **1e** was formed in 65% yield (see Scheme 1). This indicates that intermediates of structure **6** are not stable in basic solution, and supports the mechanism outlined in Scheme 3. When ammonia was bubbled



Scheme 4 *Reagents:* i, R^1R^2CO Et_3N; ii, NH_3, $CHCl_3$, $PhNH_3^+Cl^-$ (cat.), for **7b**; iii, 4-$MeOC_6H_4NH_2$, $CHCl_3$, $PhNH_3^+Cl^-$ (cat.), for **7b**; iv, 4-$MeOC_6H_4NH_2$, MeOH

through a solution of compound **7b** under similar conditions compound **6** (R^1 = H, R^2 = Ph) precipitated as a pale green solid in 42% yield. The residual solution, when stirred at room temperature for several hours, turned orange and an orange solid precipitated. This was shown by ^1H and ^{13}C NMR spectroscopy to be a mixture of the imidate **8** and the desired triazepine **1a** (ratio *ca.* 2.3:1). It is clear that under these conditions aminolysis of the imino bond competes with formation of the amidine **6**, and hence the triazepine **1a**. Attempts to promote formation of **1a** from **6** under several basic

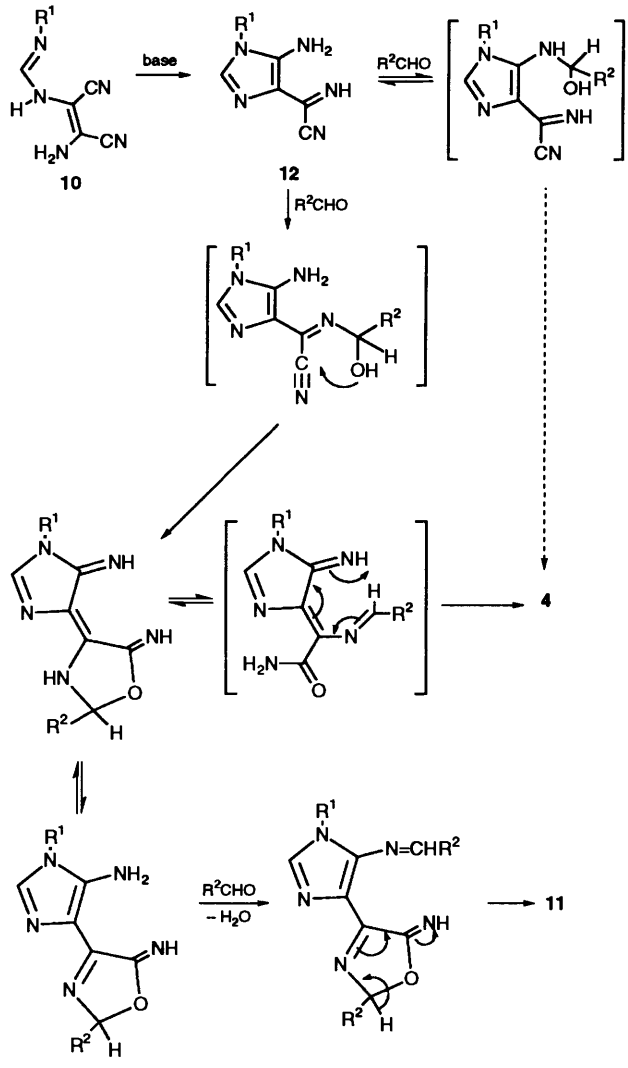


Scheme 5 *Reagents:* i, R^2CHO, DBU; ii, PhCHO or furan, DBU, **11b** (56%), **11i** (24%); * numbering scheme used in Tables 5 and 6

and neutral conditions [NH_3, $CHCl_3$, room temp. (RT); NH_3 (aq.); DBU, EtOH; EtOH, 60 °C] resulted in extensive decomposition and only traces of the desired triazepine could be detected among the products by TLC. The reaction of the imidate **7b** with aromatic amines at room temperature also caused aminolysis of the imino bond to occur. Thus, addition of *p*-anisidine to a suspension of compound **7b** in chloroform with a catalytic amount of anilinium hydrochloride did not give the N^1-arylformimidamide hoped for, but instead gave an 83% yield of the imidate **8** after only 1 h at room temperature. This last reaction represents the most convenient synthesis of compound **8** found so far. Reaction of the imidate **8** with an excess of anisidine in methanol resulted in cyclisation to the new imidazole derivative **9**, isolated in 36% yield.

It is apparent from the work described above that the route to the 1,3,5-triazepines described in Scheme 4 is of limited synthetic value for aldehydes as aminolysis of the imino group can compete with formation of the desired amidines of type **6**. We have recently described the synthesis of a number of N^2-substituted (*Z*)-N^1-(2-amino-1,2-dicyanovinyl)formimidamides, where the substituent can be alkyl,[11] amino,[12] benzyl,[17] and aryl,[13] and it was of interest, therefore, to examine whether the route from the amidine **2** could be extended to some of these other amidines.

When DBU was added to (*Z*)-N^1-(2-amino-1,2-dicyanovinyl)-N^2-arylformimidamides **10a–g** in benzaldehyde new orange–red solids could be isolated from these reactions in low to medium yields. The reactions were not clean and the product mixture always contained variable amounts of the known dihydropurines[13] and the corresponding purines as well as decomposition products as evidenced by TLC. After flash chromatography using silica gel the red products could be isolated pure since the decomposition products were retained and the dihydropurines decompose on silica. It was clear from microanalysis and mass spectrometry that reaction had occurred with the incorporation of two molecules of benzaldehyde with loss of a molecule of water. The ^1H NMR spectra also show two phenyl rings in addition to the aryl substituent present in the amidine starting material, and the two



Scheme 6

phenyl rings are not equivalent. From a detailed analysis of the spectroscopic data these compounds have been assigned the novel structures **11a–i** (see Scheme 5). Evidence that these compounds do have the basic imidazole skeleton was obtained by treating 5-amino-4-cyanoformimidoyl-1-(4-methoxyphenyl)imidazole **12** with an excess of benzaldehyde in the presence of DBU to give compound **11b**. This suggests that the first step in the reactions with the formimidamides is the rapid cyclisation to the 5-amino-4-cyanoformimidoyl-1-arylimidazole followed by the reactions shown in Scheme 6. The main evidence leading to the assignment of the structures **11a–i** is two NH stretching vibrations in the IR spectra and a strong band at 1580 cm^{-1} which has been attributed to the N=C–O stretching vibration of the oxazole ring.[18] The ^1H NMR spectra show a singlet around δ 8.55 ppm for the proton of the imino group, a singlet at *ca.* 7.3 ppm for the imidazole proton and a signal at 5.5 ppm for the NH_2 group. In the ^{13}C NMR spectrum the signals due to the oxazole ring are seen at δ 158 (C-2), 144 (C-5) and 113 (C-4) ppm in agreement with reported values for oxazoles.[18] Other important features of the ^{13}C NMR spectra are the signals at 150 ppm for the imino carbon and bands at *ca.* 132, 127 and 129 ppm for the imidazole ring. These reactions appear to be quite general for aromatic aldehydes. So, for example, the amidine **10b** reacts with toluene-4-carbaldehyde to give the imidazole **11g**, and the compounds **11h** and **11i** have been isolated in low yields from the reactions of **10b** and **10f** with 2-furaldehyde;

Table 4 Microanalytical, m.p. and mass spectroscopic data for the compounds **11a–i**

	Yield (%)	M.p. (°C)[a]	Molecular formula	Microanalytical data (%)/found (calc.) C	H	N	*m/z* $(M + 1)^+$	*M*
11a	32[b]	199–201	$C_{25}H_{19}N_5O$	74.7 (74.1)	4.7 (4.7)	17.1 (17.3)	406	405
11b	29[b], 56[c]	174–176	$C_{26}H_{21}N_5O_2$	71.4 (71.7)	4.6 (4.8)	15.8 (16.1)	436	435
11c	25[b]	208–209	$C_{26}H_{21}N_5O$	74.2 (74.5)	4.7 (5.0)	16.4 (16.7)	420	419
11d	14[b]	165–170	$C_{26}H_{21}N_5O_2$				436.1766	436.1774
11e	38[b]	> 150	$C_{27}H_{23}N_5O$	74.5 (74.8)	5.2 (5.3)	15.9 (16.2)	434	433
11f	16[b]	196–197	$C_{27}H_{24}N_5O_3$				466.1884	466.1879
11g	38[b]	208–210	$C_{28}H_{25}N_5O_2 \cdot H_2O$	70.5 (69.9)	5.7 (5.6)	14.6 (14.6)	464	465
11h	10[b], 24[c]	148–149	$C_{22}H_{17}N_5O_4$				416.1332	416.1280
11i	35[b]	171–172	$C_{22}H_{19}N_5O_4$	62.3 (62.0)	4.3 (4.3)	15.4 (15.7)	446	445

[a] All decomposed. [b] Method A. [c] Method B. [d] Fast atom bombardment.

Table 5 ^1H NMR spectroscopic data for the compounds **11a–i**[a]

Compound	δ_H (ppm) in $CDCl_3$
11a	6.32 (< 2 H, s, NH_2), 7.48–7.63 (12 H, m, ArH + 2-H), 7.90 (2 H, m, ArH), 8.2 (2 H, m, ArH), 8.75 (1 H, s, =CH)
11b	3.9 (3 H, s, OMe), 5.6 (2 H, br s, NH_2), 7.05 (2 H, d, *J* 9, ArH), 7.35–7.45 (9 H, m, ArH + 2-H), 7.8 (2 H, m, ArH), 8.2 (2 H, m, ArH), 8.55 (1 H, s, =CH)
11c	2.45 (3 H, s, Me), 5.65 (2 H, s, NH_2), 7.5 (10 H, m, 2 × ArH), 7.77 (2 H, m, ArH), 8.24 (2 H, m, ArH), 8.55 (1 H, s, =CH)
11d	3.9 (3 H, s, OMe), 5.6 (2 H, br s, NH_2), 7.1 (2 H, m, ArH), 7.3–7.5 (9 H, m, ArH + 2-H), 7.8 (2 H, m, ArH), 8.3 (2 H, m, ArH), 8.55 (1 H, s, =CH)
11e	2.2 (3 H, s, Me), 2.4 (3 H, s, Me), 5.5 (2 H, br s, NH_2), 7.2–7.3 (4 H, m, ArH + 2-H), 7.4 (3 H, m, ArH), 7.5 (3 H, m, ArH), 7.8 (2 H, m, ArH), 8.25 (2 H, m, ArH), 8.55 (1 H, s, =CH)
11f	3.8 (3 H, s, OMe), 3.9 (3 H, s, OMe), 5.5 (2 H, br s, NH_2), 6.6 (2 H, m, ArH), 7.2–7.3 (2 H, m, ArH + 2-H), 7.45 (6 H, m, ArH), 7.8 (2 H, m, ArH), 8.25 (2 H, m, ArH), 8.55 (1 H, s, =CH)
11g[b]	2.45 (3 H, s, CH_3), 2.50 (3 H, s, CH_3), 3.90 (3 H, s, OCH_3), 6.30 (2 H, br s, NH_2), 7.15 (2 H, d, *J* 8.5, ArH), 7.30 (2 H, d, *J* 8, ArH), 7.4 (3 H, m, 2-H and ArH), 7.50 (2 H, d, *J* 8.5, ArH), 7.80 (2 H, d, *J* 8, ArH), 8.10 (2 H, d, *J* 7.5, ArH), 8.65 (1 H, s, 6-H)
11h	3.88 (3 H, s, OMe), 5.78 (2 H, br s, NH_2), 6.53 (1 H, dd, *J* 5 and 3.5, furan), 6.58 (1 H, dd, *J* 5 and 3.5, furan), 6.82 (1 H, d, furan), 7.08 (2 H, d, *J* 9, ArH), 7.28 (1 H, d, furan), 7.3 (1 H, s, 2-H), 7.38 (2 H, d, ArH), 7.73 (1 H, d, furan), 7.79 (1 H, d, furan), 8.2 (1 H, s, =CH)
11i	3.80 (3 H, s, OMe), 3.85 (3 H, s, OMe), 5.7 (2 H, br s, NH_2), 6.5 (1 H, dd, *J* 5 and 3.5, furan), 6.58 (1 H, dd, *J* 5 and 3.5, furan), 6.6 (1 H, d, furan), 6.65 (1 H, d, furan), 6.8 (2 H, d, *J* 9, ArH), 7.2 (1 H, s, 2-H), 7.25 (2 H, d, ArH), 7.5 (1 H, d, furan), 7.55 (1 H, d, furan), 8.2 (1 H, s, =CH)

[a] For numbering scheme see structure **11** in Scheme 5. [b] $[^2H_6]$DMSO–$CDCl_3$ (1:1) as solvent.

compound **11i** has also been obtained from the reaction between **12** and 2-furaldehyde. When these reactions starting from either **10** or **12** are monitored by TLC the 9-aryl-6-carbamoyl-1,2-dihydropurines are seen as by-products as well as several other unidentified impurities and it would appear that dihydropurine formation is always a competing process and this would explain, in part, the variable yields obtained.

In summary, the reactions described above demonstrate that 2-amino-1,2-dicyanoformimidamide, which cyclises only slowly to the corresponding 5-amino-4-cyanoformimidoylimidazole in the presence of base, reacts with aromatic aldehydes and aliphatic ketones to afford the 4-substituted 8-amino-4,5-dihydro-3*H*-pyrrolo[3,4-*f*]-1,3,5-triazepin-6-ones by an initial reaction at the 2-amino position. With aliphatic ketones the choice of base can be critical. So, for example, reaction between the amidine **2** and acetone in the presence of a saturated solution of $NaHCO_3$ in aqueous methanol takes 8 days at room temperature to give the triazepine **1e** (65%) together with a trace of the 6-carbamoyl-2,2-dimethyl-1,2-dihydropurine. In acetone with DBU reaction takes 19 h to give **1e** in 76% yield. With N^2-aryl-N^1-2-amino-1,2-dicyanovinylformimidamides **10**, under similar conditions, cyclisation to the 5-amino-4-cyanoformimidoylimidazole **12** occurs rapidly before reaction with the aldehyde can occur resulting in the formation of 5-amino-2-aryl-4-(1-aryl-5-alkylideneaminoimidazol-4-yl)-1,3-oxazole **11** mixed with the corresponding 1,2-dihydropurines and other products (see Scheme 6).

Experimental

The (*Z*)-N^2-(2-amino-1,2-dicyanovinyl)formimidamide **2**[10] and the compounds **10a–g** and **12** used in this work were prepared by previously reported procedures.[13] All solvents were purified and dried using established procedures.[19]

IR spectra were recorded either on a Perkin-Elmer model 298 or Shimadzu IR-435 spectrometer. ^1H and ^{13}C NMR spectra on a Bruker XL300 spectrometer and mass spectra on a Kratos Concept instrument. Solid-state ^{13}C NMR spectra were obtained using a Brucker MSL 400 instrument.

Typical Procedures for the Synthesis of the 8-*Amino*-4,5-*dihydro*-3H-*pyrrolo*[3,4-f]-1,3,5-*triazepin*-6-*ones* **1a–g** *from the Amidine* **2**.—(a) *With benzaldehyde.* DBU (0.05 cm^3, 0.33 mmol) was added to a stirred suspension of the amidine **2** (180 mg, 1.3 mmol) in a large excess of benzaldehyde (2.0 cm^3, 2.08 g, 19.6 mmol). An immediate exothermic reaction occurred and the amidine dissolved. After a few minutes a precipitate appeared and this was filtered off, washed with diethyl ether and then with acetone to give a pale orange solid, which, upon recrystallisation from methanol–light petroleum (b.p. 30–40 °C, 1:1) gave red needles.

(b) *With acetone.* The amidine **2** (0.27 g, 2.04 mmol) was dissolved in a large excess (9 cm^3) of acetone and DBU (50–70 cm^3, 0.3–0.4 mmol) was added dropwise *via* a microsyringe with efficient stirring. The product precipitated as an orange–red solid after approximately 15 min and stirring was continued

Table 6 ^{13}C NMR spectroscopic data for the compounds **11a–j**[a]

	δ_C (ppm) in $CDCl_3$							
	C-2	C-4	C-5	C-6	C-7	C-8	C-9	Other signals
11a	131.6	127.1	137.1	150.2	113.6	143.9	158.0	125.2, 126.8, 127.9, 128.4, 128.7, 128.8, 130.0, 130.7, 130.9, 131.9, 134.1, 135.2
11b	132.0	127.2	137.2	150.0	113.2	143.9	158.1	55.6 (OMe), 115.0, 126.8, 126.9, 127.8, 128.6, 128.9, 130.6, 130.8, 136.3, 159.7
11c	132.1	127.1	137.5	154.9	116.5	142.5	161.5	24.9 (Me), 126.0, 127.0, 128.5, 130.0, 130.5, 133.3, 133.4, 134.4, 135.2, 135.9, 147.8
11d	132.1	127.2	137.9	149.9	113.6	144.0	158.0	56.0 (OMe), 112.5, 121.4, 126.9, 127.8, 128.2, 128.6, 128.8, 129.7, 130.4, 130.5, 130.7, 132.1, 136.3, 138.0, 154.2
11e	132.1	127.2	137.5	149.6	112.6	143.8	158.1	17.5 (Me), 21.1 (Me), 126.9, 127.7, 128.5, 128.8, 130.6, 130.7, 131.8, 136.1, 136.4, 139.9
11f	132.2	127.2	138.1	149.7	113.2	143.9	158.0	55.6, 55.9 (OMe), 99.9, 104.9, 116.7, 126.8, 127.8, 128.6, 128.8, 128.9, 130.5, 130.6, 133.0, 136.4, 155.4, 161.3
11g[b]	131.9	128.0	137.7	154.4	116.0	142.3	160.9	25.1 (Me), 25.2 (Me), 59.5 (OMe), 118.2, 118.9, 130.2, 130.6, 131.8, 133.7, 134.9, 135.7, 144.9, 145.1, 147.2, 162.9
11h	132.1	127.4	137.7	150.9	112.6	144.5	158.7	55.6 (OMe), 112.2, 112.6, 113.0, 115.0, 114.6, 127.0, 131.8, 135.4, 142.8, 145.3, 158.7
11i	133.3	127.4	136.5	150.0	114.4	143.7	159.6	59.6, 59.7 (OMe), 103.6, 109.2, 116.7, 116.9, 117.1, 119.9, 133.3, 135.5, 140.1, 145.9, 146.2, 150.3, 156.3

[a] For numbering scheme see structure **11** in Scheme 5. [b] $[^2H_6]$DMSO–$CDCl_3$ (1 : 1) as solvent.

at room temperature for a further 16 h. The product was filtered off and washed with ether. Concentration of the filtrate gave a second crop of solid.

(c) *From ethyl* (Z)-N-(2-*carbamoyl*-1-*cyano*-2-*isopropylideneaminovinyl*)*formimidate* **7a**. The imidate **7a** (0.33 g, 1.5 mol) was suspended in chloroform (5 cm^3) and a catalytic amount of anilinium chloride (0.01 g) was added. The mixture was cooled in an ice–salt bath, ammonia gas was bubbled through the cooled suspension for 15 min and the mixture was then stirred at room temp. for 3 days. The orange solid which precipitated was filtered off, and washed with chloroform–diethyl ether (1:1) to give the corresponding 1,3,5-triazepine **1e** (65%). This compound was identical in all respects to the compound prepared by the procedure described above.

6-*Carbamoyl*-2-*phenyl*-1,2-*dihydropurine* **4a**.—To a stirred suspension of 5-amino-4-(cyanoformimidoyl)imidazole[10] (0.20 g, 1.48 mmol) in methanol (2 cm^3) was added benzaldehyde (0.2 cm^3, 1.97 mmol). After a short period a homogeneous orange solution was obtained and an orange solid precipitated. This was filtered off and washed with methanol to give the title compound **4a** (0.225 g, 1.06 mmol, 72%).

Reaction of Ethyl (Z)-N-(2-*Amino*-1,2-*dicyanovinyl*)*formimidate with Carbonyl Compounds*.—(a) *With acetone*. The imidate (1.5 g, 7.8 mmol) was partially solubilised in acetone (3 cm^3) and triethylamine (1.5 cm^3) was added. The reaction mixture was stirred at room temp. for 2 days and ethyl (*Z*)-*N*-(2-carbamoyl-1-cyano-2-isopropylideneaminovinyl)formimidate **7a** precipitated as a pale yellow solid (1.13 g). This was filtered off and washed with chloroform–diethyl ether (1:1). Slow evaporation of the filtrate gave a second crop of the product (0.27 g); total yield 1.4 g, (6.2 mmol, 79%) [Found: (M + 1) (FAB) 207 (100%). $C_{10}H_{14}N_4O$ requires *M*, 206]. A satisfactory elemental analysis could not be obtained on this compound as it decomposes after a few hours; ν_{max}(Nujol)/cm^{-1} 3430m, 3357w, 3281m, 3146m (NH str), 2207m (CN), 1691s (C=O), 1667s, 1622s, 1565s and 1461s; δ_H($CDCl_3$) 1.32 (3 H, t, *J* 7, CH_3), 1.83 (3 H, s, CH_3), 2.18 (3 H, s, CH_3), 4.15 (2 H, q, *J* 7, CH_2), 6.13 (1 H, br s, NH), 6.35 (1 H, br s, NH) and 8.2 (1 H, s, CH); δ_C($CDCl_3$) 13.9 (CH_3), 23.5 (CH_3), 27.8 (CH_3), 63.5 (OCH_2), 105.8 (C=C), 113.9 (CN), 143.9 (C=C), 160.1 (CH), 164.5 (C=O) and 174.4 (C=N).

(b) *With benzaldehyde*. Dry triethylamine (2 cm^3) and the imidate (2.00 g, 12.2 mmol) in benzaldehyde (4 cm^3) were stirred for 25 min. at room temp. under argon. Filtration, followed by washing with dry diethyl ether gave ethyl (*Z*)-*N*-(2-benzylideneamino-2-carbamoyl-1-cyanovinyl)formimidate **7b** (2.40 g, 8.9 mmol, 73%) as a yellow solid, m.p. 129–132 °C (decomp.) [Found: C, 61.9; H, 5.5; N, 21.0%; (M + 1) (FAB), 271 (100%). $C_{14}H_{14}N_4O_2$ requires C, 62.2; H, 5.2; N, 20.7%; *M*, 270]; ν_{max}(Nujol)/cm^{-1} 3400s, 3340s, 3020s, (NH str), 2200w (CN), 1660s (C=O) and 1630s (C=N); δ_H($CDCl_3$) 1.20 (3 H, t, *J* 7, CH_3), 4.10 (2 H, q, *J* 7, CH_2), 5.75 (1 H, br s, NH), 6.80 (1 H, br s, NH), 7.50 (3 H, m, ArH), 8.30 (2 H, m, ArH) and 8.45 (1 H, s, CH); δ_C($CDCl_3$) 14.1 (CH_3), 63.7 (OCH_2), 109.6 (C=C), 113.7 (CN), 129.0 (Ph), 129.1 (Ph), 132.9, 134.7, 144.6 (C=C), 161.7 (CH), 164.6 (C=O) and 167.0 (C=N).

Ethyl (Z)-N-(2-*Amino*-2-*carbamoyl*-1-*cyanovinyl*)*formimidate* **8**.—A catalytic amount of anilinium chloride (0.001 g) was added to a solution of the imidate **7b** (2.32 g, 8.6 mmol) and freshly sublimed *p*-anisidine (1.06 g, 8.6 mmol) in dry chloroform (50 cm^3). The mixture was stirred for 1 h after which the product was filtered off and washed with chloroform and diethyl ether to give the title compound **8** as an off-white solid (1.30 g, 7.1 mmol, 83%), m.p. 120–124 °C (decomp.) [Found: C, 46.5; H, 5.6; N, 30.5%; (M + 1) (CI), 183 (100%). $C_7H_{10}N_4O_2$ requires C, 46.2; H, 5.5; N, 30.8%; *M*, 182]; ν_{max}(Nujol)/cm^{-1} 3480m, 3380s, 3340s, 3200 (NH str), 2200s (CN), 1675s (C=O) and 1650s (C=N); δ_H($CDCl_3$) 1.35 (3 H, t, *J* 7, CH_3), 4.30 (2 H, q, *J* 7, CH_2), 6.4 (2 H, br s, NH_2), 7.80 (1 H, br s, CONH), 7.90 (1 H, s, CH) and 8.0 (1 H, br s, CONH); δ_C($[^2H_6]$DMSO) 18.2 (CH_3), 66.6 (OCH_2), 92.1 (C=C), 120.5 (CN), 151.3 (C=C), 157.3 (CH) and 168.5 (C=O).

5-*Amino*-4-(*carbamoylformimidoyl*)-1-(4-*methoxyphenyl*)-*imidazole* **9**.—To a stirred solution of *p*-anisidine (170 mg, 1.4 mmol) and a catalytic amount of anilinium hydrochloride in methanol (5 cm^3) was added the imidate **8** (420 mg, 2.5 mmol) and the mixture was stirred for 2 days, whereupon the product **9** precipiated as a yellow solid (130 mg, 0.5 mmol, 36%), m.p. 169–172 °C (decomp.) [Found: C, 55.5; H, 5.0; N, 26.9%; $(M + H)^+$ FAB, 260 (100%). $C_{12}H_{13}O_2N_5$ requires C,

55.6; H, 5.0; N, 27.0%; *M*, 259]; ν_{max}(Nujol)/cm^{-1} 3430s, 3300s, 3220s, 3140s (N–H str), 1690s (C=O str) and 1630s (C=N str); δ_H([$^2H_6$]DMSO) 3.90 (3 H, s, OCH_3), 6.90 (2 H, br s, NH_2), 7.20 (2 H, d, *J* 8, ArH), 7.55 (2 H, d, *J* 8, ArH), 7.60 (1 H, s, 2-H), 8.30 (1 H, br s, CONH), 9.85 (1 H, br s, CONH) and 10.20 (1 H, br s, NH); δ_C([$^2H_6$]DMSO) 59.7 (OCH_3), 118.4 (C-4), 119.1 (Ar), 130.8 (Ar), 130.9 (Ar), 134.6 (C-2), 149.1 (C-5), 163.4 (C-6 or Ar) and 166.0 (CO).

Reaction between Ethyl (Z)-N-(2-*Benzylideneamino*-2-*carbamoyl*-1-*cyanovinyl*)*formimidamide and Ammonia.*—Ammonia gas was bubbled for 15 min through a stirred, cold solution of the imidate **7b** (0.330 g, 1.2 mmol) in dry chloroform (5 cm^3) cooled at 0 °C and containing a catalytic amount (2 mg) of anilinium hydrochloride. The mixture was then warmed to room temperature over 90 min when TLC indicated that no imidate starting material remained. The resultant pale-green precipitate of the amidine **6** (0.121 g, 0.5 mmol, 42%) was filtered off and recrystallised from acetone [Found: C, 59.5; H, 4.6; N, 28.7%; (M + 1) (FAB), 242 (100%). $C_{12}H_{11}N_5O$ requires C, 59.8; H, 4.6; N, 29.0%; *M*, 241]; ν_{max}(Nujol)/cm^{-1} 3424s, 3345s, 3174s, (NH str), 2208m (C≡N), 1664s (C=O) and 1649s (C=N); δ_H([$^2H_6$]DMSO) 7.58 (3 H, m, Ph), 7.75 (1 H, br s, NH), 7.80 (1 H, br s, CONH), 7.90 (2 H, m, Ph), 8.02 (1 H, s, CH), 8.15 (1 H, br s, NH), 8.55 (1 H, br s, CONH) and 8.70 (1 H, s, CH); δ_C([$^2H_6$]DMSO) 117.8 (CN), 128.3 (Ph), 132.4 (Ph), 133.0 (Ph), 135.5 (Ph), 140.5 (C=C), 144.8 (C=C), 159.6 (C=N), 163.2 (C=N) and 168.8 (C=O).

General Procedure for the Reactions of (Z)-N^1-(2-*Amino*-1,2-*dicyanovinyl*)-N^2-*arylformimidamides* **10** *with Benzaldehyde, Toluene*-4-*carbaldehyde and* 2-*Furaldehyde.*—To a stirred suspension of the amidine (500 mg, 1.9 mmol) in freshly distilled aldehyde (4 cm^3) was added DBU (72 cm^3, 0.4 mmol). An immediate bright red colour developed and in some cases an orange solid precipitated after 10–50 min. In these cases the solid was filtered off, washed with diethyl ether and a little acetone and purified by dry flash chromatography eluting with $CHCl_3$. In cases where a solid did not precipitate diethyl ether (30 cm^3) was added to give a sticky red solid. This was triturated with diethyl ether until it solidified. It was then filtered off, washed with diethyl ether, and purified by dry flash chromatography to give the analytically pure compounds **11a–i**.

Reaction of 5-*Amino*-4-*cyanoformimidoyl*-1-(4-*methoxyphenyl*)*imidazole* **12** *with Aldehydes.*—(a) *With benzaldehyde.* The imidazole (145 mg, 0.61 mmol) was added to a stirred solution of DBU (30 cm^3, 0.015 mmol) in benzaldehyde (1.5 cm^3) and after 10 min the product **11a** precipitated (150 mg, 0.34 mmol, 56%). The product was identical with that isolated by the procedure described above.

(b) *With* 2-*furaldehyde.* To a stirred suspension of the imidazole (0.20 g, 0.83 mmol) in DBU (15 cm^3) was added 2-furaldehyde (0.5 cm^3). The mixture was stirred at room temp. for 30 min then diethyl ether (5 cm^3) was added. The resulting solid was filtered off, washed with diethyl ether and purified by flash chromatography to give compound **11h** (0.083 g, 0.20 mmol, 24%).

Acknowledgements

Thanks are due to the SERC for a studentship award (P. R. E.), the Junta Nacional de Investigação Científica e Tecnológica, Portugal for financial support and the Treaty of Windsor Programme for travel grants. Thanks are also due to Dr. João Rocha, University of Aveiro, for the solid-state NMR spectra.

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Paper 4/04503C
Received 22*nd July* 1994
Accepted 24*th August* 1994