(Z)-N^3-(2-Amino-1,2-dicyanovinyl)formamidrazone: a Precursor in the Synthesis of 1,5-Diaminoimidazoles and 6-Carbamoyl-1,2-dihydropurines

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The reaction of ethyl (Z)-*N*-(2-amino-1,2-dicyanovinyl)formimidate with hydrazine monohydrate leads to (Z)-N^3-(2-amino-1,2-dicyanovinyl)formamidrazone in almost quantitative yield. This compound proved to be an important starting material for the synthesis of the corresponding N^1-isopropylidene- and N^1-acetyl-formamidrazones.

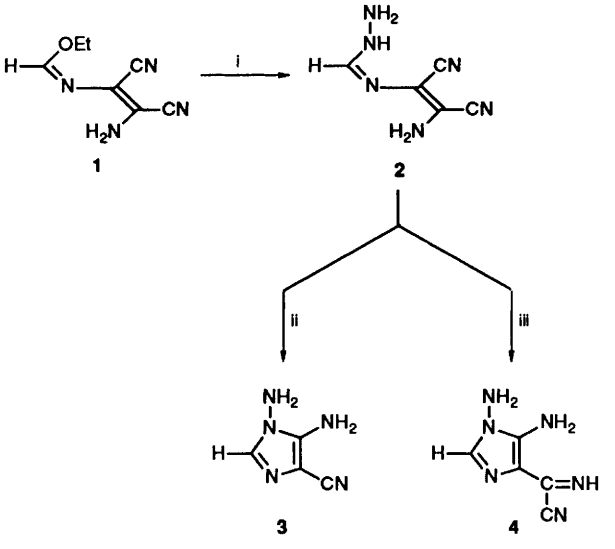
The amidrazones prepared promptly cyclize in the presence of base to give a 1,5-diamino-4-cyanoimidazole or a 1,5-diamino-4-(cyanoformimidoyl)imidazole, depending on the reaction conditions and mainly on the nature of the base used to induce cyclization.

1,5-Diamino-4-(cyanoformimidoyl)imidazole was treated with carbonyl compounds and the 1,2-dihydropurines thus isolated indicated that the amino group in position 5 is more reactive than that in position 1.

5-Amino-4-(cyanoformimidoyl)imidazoles and 5-amino-4-cyanoimidazoles are useful intermediates for purine synthesis.[1] There are relatively few reports of 9-aminopurine derivatives [2–8] and most of the routes described are from 5-amino-4-hydrazinopyrimidine precursors, substituted in the 2- and 6-position.[2,3,7] The synthesis of these precursors are not trivial and there is a need for a more simple and general procedure. The synthesis of 9-aminoguanines using this method has been recently reported and the 9-(hydroxyalkylamino)guanines, obtained after imine formation and subsequent reduction, have been claimed as novel antiviral agents.[7]

The other routes reported include direct amination [5,8] and the use of 1,5-diamino-4-carbamoylimidazole precursors.[4,6]

We now report the synthesis of (Z)-N^3-(2-amino-1,2-dicyanovinyl)formamidrazone **2** and its conversion into new 1-aminoimidazole and 9-amino-1,2-dihydropurine derivatives.



Scheme 1 *Reagents and conditions:* i, $NH_2NH_2 \cdot H_2O$, dioxane, room temp.; ii, 1 mol dm^{-3} KOH, aq. room temp.; iii, $Ba(OH)_2$, EtOH, 15 °C.

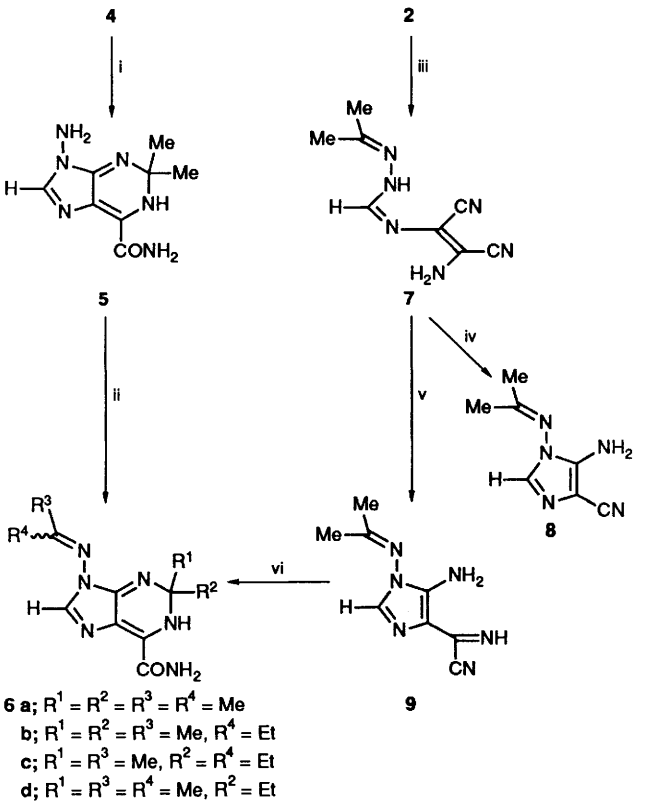
Results and Discussion

Imidate **1** was prepared in high yield from diaminomaleonitrile and triethyl orthoformate, according to a previously described procedure.[1] Its reaction with hydrazine hydrate occurs readily in 1,4-dioxane at room temperature, leading to the amidrazone **2** in almost quantitative yield. In the presence of base, amidrazone **2** cyclizes either to 1,5-diamino-4-cyanoimidazole **3** or to the novel 1,5-diamino-4-(cyanoformimidoyl)imidazole **4** depending on the experimental conditions (Scheme 1). In 1 mol dm^{-3} aq. KOH solution, the imidazole **3** precipitates out in 82% yield. For the isolation of the imidazole **4**, milder basic conditions and a carefully controlled reaction time are essential. The most satisfactory method involves treatment of a suspension of amidrazone **2** in ethanol with a catalytic amount of $Ba(OH)_2$ for *ca.* 20 min. The imidazole **4** was isolated in up to 75% yield and was used without further purification in the synthesis of the novel 6-carbamoyl-1,2-dihydropurines **5** and **6** (Scheme 2).

The amino groups in positions 1 and 5 of the imidazole ring show different reactivity towards carbonyl compounds. In the reaction with acetone, at room temperature, it is possible to isolate the dihydropurine **5** in 80% yield, and the 1-amino group of the imidazole remains unaffected. Treatment of compound **5** with further acetone or butan-2-one provides the corresponding Schiff's base **6a** or **6b**, respectively.

When the imidazole **4** is combined with butan-2-one or with acetone in the presence of silica gel 60, the initially formed *N*-amino-1,2-dihydropurine reacts rapidly to give the corresponding Schiff's base **6c** or **6a**, respectively, directly and it is not possible to isolate the intermediate dihydropurines.

Compound **6a** can also be obtained by reaction of 5-amino-4-(cyanoformimidoyl)-1-isopropylidenaminoimidazole **9** with acetone. The imidazole **9** can be prepared only from N^3-(2-amino-1,2-dicyanovinyl)-N^1-(isopropylidene) formamidrazone **7**, which in turn is readily obtained from amidrazone **2** in the presence of acetone. Once again, the isolation of the imidazole **9** required carefully controlled reaction conditions in terms of base, temperature, and reaction time. A catalytic amount of $Ba(OH)_2$ was added to a suspension of amidrazone **7** in cold water and after 8 min the mixture was extracted with chloroform. In this reaction, it is particularly difficult to avoid contamination of the product with 5-amino-4-cyano-1-(isopropylidenamino)imidazole **8**, and careful control of the temperature seems to be critical to minimize this by-product. In a separate experiment, the imidazole **8** was prepared in 48% yield from a similar reaction mixture [amidrazone **7** in aq.



Scheme 2 *Reagents and conditions:* i, Me_2CO, room temp.; ii, R^3COR^4, room temp.; iii, Me_2CO, SiO_2, room temp.; iv, $Ba(OH)_2$, water, 30–35 °C; v, $Ba(OH)_2$, H_2O, 10–15 °C; vi, R^1COR^2, room temp.

$Ba(OH)_2$], the only difference being the temperature, which in this case was kept at 30–35 °C.

The imidazole **9** was also treated with butan-2-one, to give the dihydropurine **6d** in 65% yield.

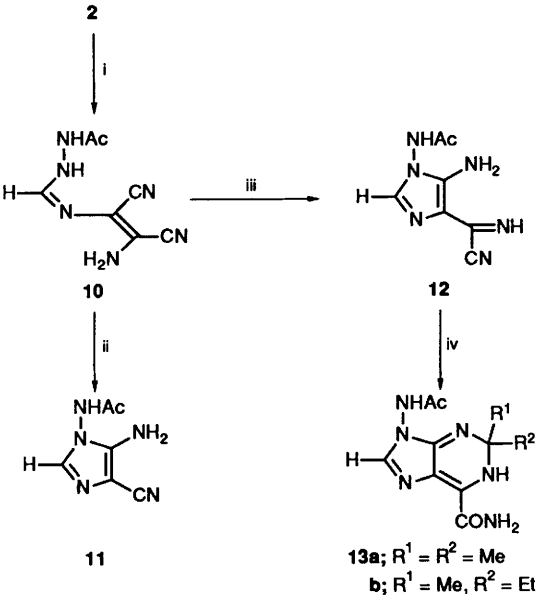
Compound **4** also reacts readily with benzaldehyde at 0 °C (during 3 min) to give a mixture of products which appear to be mainly the Schiff base derivatives of 9-amino-6-carbamoyl-2-phenyl-1,2-dihydropurine and 9-amino-6-carbamoyl-2-phenylpurine. So far, we have been unable to separate these two compounds efficiently since dry flash chromatography on silica results in some decomposition of the dihydropurine. Attempts to oxidize the mixture to give only the purine derivative have, so far, proved unsuccessful.

Treatment of amidrazone **2** with acetic anhydride led to the *N*-acetylamidrazone **10**, and from this compound, the *N*-acetylimidazoles **11** and **12** were prepared, depending on whether 1 mol dm^{-3} aq. KOH or aq. Na_2CO_3 was used as the base. The intermediate amidrazone **10** decomposed upon attempted recrystallization and was used without purification. Similar difficulties were experienced in the synthesis of the imidazole **12**, which cannot stand further purification. In the presence of base, the imidazole **12** readily undergoes elimination of HCN, giving compound **11**.

Reaction of 1-acetamido-5-amino-4-(cyanoformimidoyl)-imidazole **12** with acetone and butan-2-one led to the corresponding 6-carbamoyl-1,2-dihydropurines **13a** and **13b** (Scheme 3).

An attempt to prepare N^1-*tert*-butyloxycarbonyl derivatives of formamidrazone **2** by direct reaction of imidate **1** with *tert*-butyl carbazate in 1,4-dioxane,[9] resulted in formation of diaminomaleonitrile as the only isolable product (46% yield).

The structures of the compounds were established on the basis of microanalysis and spectroscopic data. In the ^1H NMR spectra of the amidrazones the proton on C-2 (or C-8 for purine



Scheme 3 *Reagents and conditions:* i, Ac_2O, MeCN, room temp.; ii, 1 mol dm^{-3} aq. KOH, room temp.; iii, aq. Na_2CO_3, room temp.; iv, R^1COR^2, room temp.

derivatives) appears as a sharp singlet in the region δ 7.4–7.9, and in the region δ 7.1–7.3 for the imidazoles and dihydropurines prepared.

The ^{13}C NMR spectra of the dihydropurines show very broad bands for the carbon atoms participating in the π system (C-4, -5, -6, -8, and, in some cases, $CONH_2$ and $N{=}CR_2$). This broadening has been attributed to tautomerism of the mobile proton between positions N^1 and N^3. Only for compound **13a** can all the carbon atoms be identified in the ^{13}C NMR spectrum. For the other dihydropurines the broadening is so extensive that no signal is registered for C-4, -6, -8, and, in some cases, C-5. In the spectrum of compound **6c** only the sp^3-hybridized carbon atoms can be identified.

In the IR spectrum of the amidrazones two medium ν(CN) bands in the 2220 and 2200 cm^{-1} region are always present, while in the 5-amino-4-cyanoimidazoles a strong ν(CN) band in the 2200 cm^{-1} region is a characteristic feature of these compounds. In IR spectra of the 5-amino-4-(cyanoformimidoyl)imidazoles, the ν(CN) band either shows up as a very weak absorption in the 2200 cm^{-1} region, or is completely absent (compound **12**). The 6-carbamoyl-1,2-dihydropurines, besides the similar ν(NH) region, all show strong ν(C=O) absorptions between 1680 and 1700 cm^{-1}.

Experimental

^1H NMR spectra were recorded on Hitachi–Perkin-Elmer R24B (60 MHz) or Bruker XL300 (300 MHz) instruments (with *J* values given in Hz), ^{13}C NMR spectra (with DEPT 135) either on a Bruker WP80 or XL300 instrument, and IR spectra on a Shimadzu IR-435 spectrophotometer. Mass spectra were recorded on a Kratos Concept instrument, and UV spectra on a Perkin-Elmer Lamda 15 UV–VIS spectrometer. M.p.s were measured on an Electrothermal digital melting point apparatus and are uncorrected.

Preparation of (Z)-N^3-(2-*Amino*-1,2-*dicyanovinyl*)*formamidrazone* **2**.—Hydrazine monohydrate (0.39 g, 0.38 cm^3, 7.72 mmol) was added, at room temperature, to a suspension of ethyl (*Z*)-*N*-(2-amino-1,2-dicyanovinyl)formimidate **1** (1.27 g, 7.72 mmol) in dry 1,4-dioxane (8 cm^3). An immediate and slightly

exothermic reaction occurred, leading to a homogeneous yellow solution. The product precipitated out of solution as pale-yellow needles which were filtered off, washed with diethyl ether, and dried *in vacuo* to give compound **2** (1.14 g, 98%). A small amount of the product was recrystallized from cold methanol to give pale-yellow crystals, m.p. >300 °C (decomp.). A satisfactory elemental analysis could not be obtained due to the presence of bound solvent; ν_{max}(Nujol)/cm^{-1} 3437m, 3420m, 3341s, 3270s, 3138m, 2216m (CN), 2180m (CN), 1640sh, 1625s, 1599s and 1578s; δ_H(60 MHz; [$^2H_6$]acetone; Me_4Si) 4.2–4.8 (<2 H, br s, NH_2), 5.2–5.8 (2 H, br s, NH_2) and 7.8 (1 H, s, CHN_2); δ_C[$(CD_3)_2SO$] 110.0 (C=), 119.2 (C=), 120.4 (CN), 120.5 (CN) and 152.4 (CH); *m/z* (CI, NH_3) 168 [$(M + NH_4)^+$, 7.4%], 151 [$(M + 1)^+$, 100], 136 (38.1), 124 (55.5) and 109 (8.6).

Preparation of 1,5-*Diamino*-4-*cyanoimidazole* **3**.—Compound **2** (1.01 g, 6.73 mmol) was solubilized in 1 mol dm^{-3} aq. KOH (10 cm^3). Shortly after, a yellow solid precipitated out and was filtered off, and washed with diethyl ether to give *compound* **3** (0.68 g, 82%), m.p. 214–215.5 °C (decomp.) (Found: C, 38.8; H, 4.1; N, 57.0. $C_4H_5N_5$ requires C, 39.0; H, 4.1; N, 56.9%); λ_{max}(EtOH)/nm 324.0 (ε/dm^3 mol^{-1} cm^{-1} 25) and 245.4 (12 340); ν_{max}(Nujol)/cm^{-1} 3380s, 3350s, 3320s, 3280s, 3100s, 2200s (CN), 1665s, 1610s and 1515w; δ_H[60 MHz; $(CD_3)_2SO$; Me_4Si] 5.65 (2 H, s, NH_2) 6.0 (2 H, s, NH_2) and 7.1 (1 H, s, 2-H); δ_C[$(CD_3)_2SO$] 91.4 (C-4), 121.7 (CN), 137.4 (C-2) and 152.2 (C-5); *m/z* (CI, NH_3) 141 [$(M + NH_4)^+$, 5.2%], 124 [$(M + 1)^+$, 100], 109 (17.4), 94 (6.8) and 78 (6.7).

Preparation of 1,5-*Diamino*-4-(*cyanoformimidoyl*)*imidazole* **4**.—Solid $Ba(OH)_2 \cdot H_2O$ (catalytic amount) was added to a suspension of the amidrazone **2** (1.00 g, 6.67 mmol) in 95% ethanol (100 cm^3), and the mixture was stirred at room temperature for *ca.* 20 min, until TLC showed that all the amidrazone had been consumed. A fine, dark suspension had developed, and this was filtered off, together with the $Ba(OH)_2$ crystals, through glass-fibre filter paper. The filtrate was concentrated on a rotary evaporator, with the bath temperature kept below 30 °C, to give title compound **4** as yellow brownish crystals (0.76 g, 75.7%), m.p. 135.6–136.2 °C (decomp.); λ_{max}(EtOH)/nm 346.3 (6810), 227.4 (8590) and 202.6 (6430); ν_{max}(Nujol)/cm^{-1} 3381s, 3329s, 3300m, 3236s, 3178m, 3150m, 2200w (CN), 1650sh, 1639s, 1570sh, 1560sh and 1550s; δ_H[60 MHz; $(CD_3)_2SO$; Me_4Si] 5.7 (2 H, s, NH_2) and 7.1 (1 H, s, 2-H); δ_C[$(CD_3)_2SO$] 117.4 (C-4)?, 117.8 (CN)?, 136.9 (C-2), 147.0 (C-5)? and 148.5 (C=NH)?; *m/z* (CI, NH_3) 151 [$(M + 1)^+$, 1.4%], 125 (12.4), 124 (100) and 109 (6.4).

Reaction of 1,5-*Diamino*-4-(*cyanoformimidoyl*)*imidazole* **4** *with Ketones*.—(a) *Acetone*. A suspension of the imidazole **4** (0.34 g, 2.25 mmol) in acetone (15 cm^3) was stirred at room temperature for 42 h, when all the starting material had been converted into the orange dihydropurine. The solvent was removed on a rotary evaporator to give orange crystals, which were filtered off, and washed with diethyl ether to give *compound* **5** (0.37 g, 79.6%). A small amount was purified by dry-column flash chromatography (silica gel 60, 0.5 × 2 cm; 1,4-dioxane eluent), m.p. 146.8–147.3 °C (decomp.) (Found: C, 46.1; H, 5.7; N, 40.1. $C_8H_{12}N_6O$ requires C, 46.1; H, 5.8; N, 40.4%); λ_{max}(EtOH)/nm 423.4 (2425) and 217.0 (9110); ν_{max}(Nujol)/cm^{-1} 3350s, 3297s, 3186s, 3113s, 1690s (C=O), 1653s, 1640sh, 1613m, 1583s and 1518m; δ_H[60 MHz; $(CD_3)_2SO$; Me_4Si] 1.4 (6 H, s, 2-Me_2), 5.5 (2 H, s, NH_2), 6.1 (1 H, br s, NH), 7.2 (1 H, s, 8-H), 7.7 (1 H, br s, CONH) and 8.15 (1 H, br s, CONH); δ_C[$(CD_3)_2SO$] 32.5 (Me), 76.2 (C-2), 118.3 (C-5)? and 168.2 (C=O); *m/z* (CI, NH_3) 209 [$(M + 1)^+$, 100], 194 (77.2), 193 (58.3), 192 (26.0), 179 (14.2), 178 (56.2), 177 (10.4), 164 (31.9), 150 (10.1), 149 (19.5), 148 (10.4), 135 (18.2), 124 (14.8), 109 (32.5), 58 (73.0) and 32 (34.5).

(b) *Acetone in the presence of silica gel*. A suspension of the imidazole **4** (0.06 g, 0.31 mmol) in acetone (3 cm^3) with a small amount of silica gel 60 was stirred at room temperature for 2–3 h. The silica was removed by filtration and washed with acetone. The filtrate and washings were combined and the solvent was removed on a rotary evaporator to give orange crystals, which were filtered off, and washed with diethyl ether to give *compound* **6a** (0.05 g, 64.5%), m.p. 179.5–180.4 °C (decomp.) (Found: C, 53.0; H, 6.6; N, 34.2. $C_{11}H_{16}N_6O$ requires C, 53.2; H, 6.5; N, 33.9%); ν_{max}(Nujol)/cm^{-1} 3326s, 3259s, 3098m, 3060m, 1680s (C=O), 1654sh, 1648s, 1591s and 1518s; δ_H[300 MHz; $(CD_3)_2SO$; Me_4Si] 1.45 (6 H, s, 2-Me_2), 2.05 (3 H, s, Me), 2.2 (3 H, s, Me), 6.3–6.6 (<1 H, s br, 1-H), 7.5 (1 H, s, 8-H), 7.9 (1 H, br s, CONH) and 8.2 (1 H, s, CONH); δ_C[$(CD_3)_2SO$] 24.3 (Me), 28.9 (Me), 32.6 (2-Me_2), 76.2 (C-2), 119.0 (C-5)?, 167.7 (C=O) and 181.4 (C=N); *m/z* (CI, NH_3) 249 [$(M + 1)^+$, 100%], 233 (12.4), 194 (4.7), 178 (5.9) and 58 (15.7).

(c) *Acetone followed by butan-2-one*. A suspension of the 1,2-dihydropurine **5** (0.38 g, 1.81 mmol) in butan-2-one (10 cm^3) was stirred at room temperature for 3 days. The resulting suspension was concentrated on a rotary evaporator to give an orange solid, which was filtered off, and washed with diethyl ether to give *compound* **6b** (0.45 g, 96%). An analytical sample was obtained after dry-column flash chromatography (silica gel 60, 0.5 × 2 cm; 1,4-dioxane eluent) to give orange crystals, m.p. 155.0–156.4 °C (decomp.) (Found: C, 54.7; H, 7.2; N, 31.9. $C_{12}H_{18}N_6O$ requires C, 55.0; H, 6.9; N, 32.1%); λ_{max}(EtOH)/nm 429.5 (2880) and 218.3 (11 260); ν_{max}(Nujol)/cm^{-1} 3349s, 3240s, 3098s, 3050s, 1680s (C=O), 1655sh, 1648s, 1628sh, 1589s and 1516s; δ_H[300 MHz; $(CD_3)_2SO$; Me_4Si) 1.0 (3 H, t, *J* 7, CH_2Me)*, 1.1 (3 H, t, *J* 7, CH_2Me), 1.35 (6 H, s, 2-Me_2)*, 1.4 (6 H, s, 2-Me_2), 1.9 (3 H, s, Me), 2.1 (3 H, s, Me)*, 2.3 (2 H, q, *J* 7, CH_2Me)*, 2.5 (2 H, q, *J* 7, CH_2Me), 6.4 (1 H, br s, 1-H), 7.4 (1 H, br s, CONH), 7.85 (1 H, br s, CONH) and 8.15 (1 H, s, 8-H) (* *Z* isomer, *E*/*Z* in a 10:1 ratio); δ_C[$(CD_3)_2SO$] 14.2 (CH_2Me), 23.0 (Me), 32.6 (2-Me_2), 35.6 (CH_2Me), 76.2 (C-2), 119.0 (C-5)?, 167.7 (C=O) and 184.5 (N=C); *m/z* (CI, NH_3) 263 [$(M + 1)^+$, 81.5%], 247 (32.0), 218 (6.1), 194 (16.7), 178 (23.0), 135 (14.7), 72 (100), 58 (62.2), 45 (20.8) and 30 (34.0).

(d) *Butan-2-one*. A suspension of the imidazole **4** (0.32 g, 2.15 mmol) in butan-2-one (5 cm^3) was stirred at room temperature and the reaction was followed by TLC. From the beginning two different products were present, corresponding to two orange spots on TLC [R_f 0.2 and 0.6, $CHCl_3$–EtOH (1:1)]. One of these compounds (R_f 0.2) changed to the other one (R_f 0.63) with time. After *ca.* 5 days the reaction was complete and only one product was present (TLC evidence). The ketone was filtered off to give an orange solid, which was dissolved in 1,4-dioxane, and purified by dry-column flash chromatography (silica gel 60, 0.5 × 2 cm; 1,4-dioxane eluent). On partial removal of the 1,4-dioxane orange crystals of *compound* **6c** were obtained (0.44 g, 75%), m.p. 151.9–153.0 °C (decomp.) (Found: C, 56.2; H, 7.3; N, 30.7. $C_{13}H_{20}N_6O$ requires C, 56.7; H, 7.2; N, 30.4%); ν_{max}(Nujol)/cm^{-1} 3349m, 3240s, 3096m, 1685sh, 1680s (C=O), 1655sh, 1647s, 1635sh, 1586s, 1559w and 1516s; δ_H[300 MHz; $(CD_3)_2SO$; Me_4Si] 0.94 (3 H, t, *J* 7, 2-CH_2Me)*, 0.95 (3 H, t, *J* 7, 2-CH_2Me), 1.15 (3 H, t, *J* 7, CH_2Me)*, 1.2 (3 H, t, *J* 7, CH_2Me), 1.3 (3 H, s, 2-Me)*, 1.35 (3 H, s, 2-Me), 1.75 and 1.8 (each 1 H, dq, *J* 7 and 14, 2-CH_2Me), 2.05 (3 H, s, Me), 2.24 (3 H, s, Me)*, 2.4 (2 H, q, *J* 7, CH_2Me)*, 2.6 (2 H, q, *J* 7, CH_2Me), 6.4 (1 H, br s, 1-H), 7.4 (1 H, br s, 8-H), 7.9 (1 H, br s, CONH) and 8.2 (1 H, s, CONH) (* *Z* isomer, *E*/*Z* in a 5:1 ratio); δ_C[$(CD_3)_2SO$] 12.7 (Me), 14.2 (Me), 35.5 (CH_2), 37.8 (CH_2) and 79.1 (C-2); *m/z* (CI, NH_3) 277 [$(M + 1)^+$, 67.9%], 247 (33.1), 208 (7.9), 178 (18.8), 135 (3.7) and 72 (100).

Preparation of (Z)-N^3-(2-*Amino*-1,2-*dicyanovinyl*)-N^1-(*isopropylidene*)*formamidrazone* **7**.—A solution of (*Z*)-*N*^{3}-(2-amino-1,2-dicyanovinyl)formamidrazone (1.60 g, 10.67 mmol) in dry acetone (80 cm^3) containing a small amount of silica gel 60 was stirred at room temperature for *ca.* 1 h. The silica gel suspension was filtered off, and the filtrate was concentrated on a rotary evaporator, with the bath temperature kept below 30 °C, to give pale yellow crystals, which were filtered off, and washed with diethyl ether to give *title compound* **7** (1.79 g, 88%). When this reaction was carried out in the absence of silica gel, compound **7** was isolated in 81% yield after 2 days at room temperature. A small amount of the product was recrystallized from hot ethanol to give off-white crystals, m.p. 153.5–154.5 °C (decomp.) (Found: C, 50.4; H, 5.1; N, 44.0. $C_8H_{10}N_6$ requires C, 50.5; H, 5.3; N, 44.2%); λ_{max}(EtOH)/nm 343.7 (32 330) and 247.8 (12 725); ν_{max}(Nujol)/cm^{-1} 3373m, 3310s, 3255s, 3137s, 2222m (CN), 2200s (CN), 1665sh, 1655s, 1609s, 1590sh and 1533s; δ_H[60 MHz; $(CD_3)_2SO$; Me_4Si] 1.9 (3 H, s, Me), 1.92 (3 H, s, Me), 6.3 (2 H, br s, NH_2) and 7.9 (1 H, s, CHN_2); δ_C[$(CD_3)_2SO$] 21.6 (Me), 28.8 (Me), 109.2 (C=), 119.0 (CN), 119.6 (CN), 122.7 (C=) and 156.7 (CH); *m*/*z* (CI, NH_3) 191 [(M + 1)$^+$, 86.9%], 164 (54.3), 136 (67.5), 109 (15.9), 73 (16.6) and 58 (100).

Preparation of 5-*Amino*-4-*cyano*-1-(*isopropylidenamino*)*imidazole* **8**.—Solid $Ba(OH)_2 \cdot H_2O$ (catalytic amount) was added to a suspension of the amidrazone **7** (0.15 g, 0.78 mmol) in warm water (30–35 °C) (12 cm^3) in a separatory funnel. A homogeneous solution was obtained after 10 min of efficient stirring in a warm water-bath (30–35 °C), and was extracted with chloroform (7 × 12 cm^3). The extracts were combined, and dried with anhydrous magnesium sulfate. The solvent was partly removed on a rotary evaporator to give *title compound* **8** as needles (0.06 g, 48%), m.p. 147.2–147.9 °C (Found: C, 51.2; H, 5.5; N, 42.9. $C_7H_9N_5$ requires C, 51.5; H, 5.5; N, 42.9%); ν_{max}(Nujol)/cm^{-1} 3200s, 3100s, 2200s (CN), 1655s, 1635s, 1580s and 1505m; δ_H[300 MHz; $(CD_3)_2SO$; Me_4Si] 2.0 (3 H, s, Me), 2.3 (3 H, s, Me), 6.2 (2 H, s, NH_2) and 7.3 (1 H, s, 2-H); δ_C[$(CD_3)_2SO$] 23.7 (Me), 29.1 (Me), 92.0 (C-4), 121.4 (CN), 131.9 (C-2), 148.7 (C-5) and 184.2 (C=N); *m*/*z* (CI, NH_3) 164 [(M + 1)$^+$, 100%], 126 (2.6), 109 (18.4) and 58 (25.6).

Preparation of 5-*Amino*-4-*cyanoformimidoyl*-1-(*isopropylidenamino*)*imidazole* **9**.—Solid $Ba(OH)_2 \cdot H_2O$ (catalytic amount) was added to a suspension of *N*^{3}-(2-amino-1,2-dicyanovinyl)-*N*^{1}-(isopropylidenamino)formamidrazone **7** (0.15 g, 0.79 mmol) in cold water (10–15 °C) (12 cm^3) in a separatory funnel. The mixture was stirred for 8 min in an ice-bath, and extracted rapidly with chloroform (7 × 10 cm^3). The extracts were combined, and dried with anhydrous magnesium sulfate, and the solvent was removed on a rotary evaporator with the bath temperature kept below 30 °C to give *title compound* **9** as a yellow-greenish solid (0.07 g, 48%), m.p. 117.3–118.4 °C (decomp.) (Found: C, 50.4; H, 5.3; N, 44.4. $C_8H_{10}N_6$ requires C, 50.5; H, 5.3; N, 44.2%); ν_{max}(Nujol)/cm^{-1} 3404m, 3306m, 3275s, 3139m, 2198w (CN), 1647m, 1619s, 1573s and 1535m; δ_H[300 MHz; $(CD_3)_2SO$; Me_4Si] 2.1 (3 H, s, Me), 2.3 (3 H, s, Me), 6.6 (2 H, s br, NH_2), 7.4 (1 H, s, 2-H) and 11.0 (1 H, s br, NH); δ_C[$(CD_3)_2SO$] 23.8 (Me), 29.1 (Me), 117.4 (C-4), 118.2 (CN), 131.8 (C-2), 145.1 (C-5), 147.1 (C=NH) and 183.5 (C=N); *m*/*z* (CI, NH_3) 191 [(M + 1)$^+$, 59.0%], 164 (100), 136 (4.7), 109 (12.1) and 58 (19.3).

Reaction of 5-*Amino*-4-*cyanoformimidoyl*-1-(*isopropylidenamino*)*imidazole* **9** *with Ketones*.—(a) *Acetone*. A small amount of silica gel 60 was added to a suspension of the imidazole **9** (0.06 g, 0.31 mmol) in acetone (3 cm^3) and the mixture was stirred at room temperature for 3 h. The silica was removed by filtration and washed with acetone. The filtrate and washings were combined and the solvent was partly removed on a rotary evaporator to give orange crystals, which were filtered off, and washed with diethyl ether to give compound **6a** (0.05 g, 64.5%).

(b) *Butan*-2-*one*. A small amount of silica gel 60 was added to a solution of imidazole **9** (0.19 g, 0.99 mmol) in butan-2-one (10 cm^3) and the mixture was stirred for 3 h. The silica gel was removed by filtration and washed with 1,4-dioxane. The filtrate and washings were combined, and the solvent was partly removed on a rotary evaporator to give orange crystals, which were filtered off, and washed with light petroleum (boiling range 40–60 °C) to give *compound* **6d** (0.17 g, 65%), m.p. 186.6–187.3 °C (decomp.) (Found: C, 54.7; H, 6.6; N, 31.8. $C_{12}H_{18}N_6O$ requires C, 55.0; H, 6.9; N, 32.1%); λ_{max}(EtOH)/nm 435.6 (3000) and 218.4 (11 270); ν_{max}(Nujol)/cm^{-1} 3324s, 3268s, 1682s (C=O), 1650s, 1592s and 1518s; δ_H[300 MHz; $(CD_3)_2SO$; Me_4Si] 0.9 (3 H, t, *J* 7, 2-CH_2*Me*), 1.4 (3 H, s, 2-Me), 1.7 and 1.8 (each 1 H, dq, *J* 7 and 13.5, 2-C*H*$_2$Me), 2.1 (3 H, s, Me), 2.25 (3 H, s, Me), 6.4 (1 H, br s, 1-H), 7.5 (1 H, br s, 8-H) and 8.2 (1 H, br s, CONH); δ_C[$(CD_3)_2SO$] 12.6 (2-CH_2*Me*), 28.9 (Me), 37.8 (2-*C*H$_2$Me) and 79.1 (C-2); *m*/*z* (CI, NH_3) 263 [(M + 1)$^+$, 11.3%], 233 (24.9), 208 (2.5), 178 (3.8), 135 (9.1), 120 (13.9), 72 (47.2), 58 (100) and 45 (15.2).

Preparation of (Z)-N^1-*Acetyl*-N^3-(2-*amino*-1,2-*dicyanovinyl*)-*formamidrazone* **10**.—Acetic anhydride (0.19 g, 0.18 cm^3, 1.91 mmol) was added to a suspension of (*Z*)-*N*^{3}-(2-amino-1,2-dicyanovinyl)formamidrazone **2** (0.27 g, 1.80 mmol) in acetonitrile (5 cm^3) at room temperature. The reaction was immediate, and a homogeneous solution was formed. The product precipitated out of solution as pale green crystals, which were filtered off, and washed with diethyl ether to give *compound* **10** (0.29 g, 83%), m.p. > 200 °C (decomp.) [Found: M$^+$ (EI), 192.0755. $C_7H_8N_6O$ requires M, 192.0760]; λ_{max}(EtOH)/nm 328.0 (19 950) and 225.6 (8275); ν_{max}(Nujol)/cm^{-1} 3443w, 3425m, 3377m, 3350s, 3307s, 3246m, 3096m, 2227m (CN), 2200m (CN), 1668s (C=O), 1622s, 1600s, 1560sh and 1540sh; δ_H[60 MHz; $(CD_3)_2SO$; Me_4Si] 1.9 (3 H, s, Me), 6.35 (2 H, br s, NH_2) and 7.45 (1 H, s, CHN_2); *m*/*z* (CI, NH_3) 193 [(M + 1)$^+$, 4.9%], 175 (69.8), 166 (21.1), 126 (12.8), 109 (59.4), 94 (15.8), 84 (65.7), 77 (53.0), 75 (56.0), 60 (100) and 45 (23.4).

Preparation of 1-*Acetamido*-5-*amino*-4-*cyanoimidazole* **11**.—Aq. 1 mol dm^{-3} KOH (6 cm^3) was added to the amidrazone **10** (0.48 g, 2.48 mmol). TLC of the resulting solution after 5 min revealed that all the amidrazone had been consumed. A small amount of silica gel 60 was added to the solution and, after evaporation to dryness on a rotary evaporator, the remanent solid was placed on top of a silica flash chromatography column (1.5 × 2 cm) and was eluted with acetone. The solvent was removed on a rotary evaporator to give *title compound* **11** as crystals (0.32 g, 79%), m.p. 202.2–202.8 °C (Found: C, 43.5; H, 4.3; N, 42.7. $C_6H_7N_5O$ requires C, 43.6; H, 4.2; N, 42.4%); ν_{max}(Nujol)/cm^{-1} 3439s, 3325s, 3238m, 3163m, 3110m, 2200s (CN), 1715s (C=O), 1639s, 1582w, 1536m and 1504m; δ_H[300 MHz; $(CD_3)_2SO$; Me_4Si] 2.1 (3 H, s, Me), 6.6 (2 H, s, NH_2), 7.3 (1 H, s, 2-H) and 11.5 (1 H, s, NH); δ_C[$(CD_3)_2SO$] 24.8 (Me), 91.1 (C-4), 121.3 (CN), 136.4 (C-2), 152.0 (C-5) and 173.1 (C=O); *m*/*z* (CI, NH_3) 183 [(M + NH_4)$^+$, 9.2%], 166 [(M + 1)$^+$, 100], 151 (4.6), 126 (8.6), 109 (42.3), 77 (13.7) and 60 (10.4).

Preparation of 1-*Acetamido*-5-*amino*-4-(*cyanoformimidoyl*)-*imidazole* **12**.—Saturated aq. sodium carbonate (13 drops) was added dropwise to the amidrazone **10** (0.10 g, 0.52 mmol) kept in a round-bottom flask equipped with a magnetic bar. A homogeneous solution was obtained, and after 4 min under efficient stirring at room temperature, the imidazole **12** precipitated out, giving a very thick mixture. Ethanol (~ 10 cm^3) was added to solubilize the imidazole and to precipitate the

sodium carbonate, which was removed by filtration. A small amount of silica gel 60 was added to the filtrate, and the mixture was evaporated to dryness on a rotary evaporator. The resulting solid was placed on top of a silica flash chromatography column (1.5 × 2 cm) and was eluted with 1,4-dioxane. On partial removal of the solvent green crystals were obtained, which were filtered off, and washed with diethyl ether to give *title compound* **12** (0.08 g, 79%), m.p. >200 °C (decomp.) [Found: C, 45.7; H, 4.7; N, 35.6%; M^+ (EI), 192.0760. $C_7H_8N_6O$·0.5 dioxane requires C, 45.8; H, 5.1; N, 35.3%; M, 192.0760]; λ_{max}(EtOH)/nm 345.1 (7110) and 222.9 (8080); ν_{max}(Nujol)/cm^{-1} 3438m, 3285s, 3250sh, 3150sh, 3116m, 1699s (C=O), 1633s, 1576s and 1544s; δ_H[60 MHz; $(CD_3)_2SO$; Me_4Si] 2.0 (3 H, s, COMe) and 7.2 (1 H, s, 2-H); δ_C[$(CD_3)_2SO$] 24.8 (Me), 117.4 (CN and/or C-4), 136.0 (C-2), 147.0 (C-5)?, 148.3 (C-6)? and 173.1 (C=O); *m/z* (CI, NH_3) 193 [$(M + 1)^+$, 5.3%], 175 (13.7), 166 (52.3), 136 (10.5), 124 (16.0), 109 (88.8), 94 (22.3), 77 (39.5), 60 (100) and 45 (27.5).

Reaction of 1-*Acetamido*-5-*amino*-4-(*cyanoformimidoyl*)*imidazole* **12** *with Ketones*.—(a) *Acetone*. A small amount of silica gel 60 was added to a suspension of the imidazole **12** (0.38 g, 1.98 mmol) in acetone (5 cm^3) and the mixture was stirred at room temperature for 2 h. The silica was removed by filtration and washed with acetone. The filtrate and washings were combined and the solvent was partly removed on a rotary evaporator to give orange crystals, which were filtered off, and washed with diethyl ether to give *compound* **13a** (0.33 g, 66%), m.p. 173.8–174.6 °C (decomp.). When this reaction was carried out in the absence of silica gel, compound **13a** was isolated in 70% yield after 24 h at room temperature [Found: C, 45.7; H, 5.8; N, 31.5%; M^+ (EI), 250.1177. $C_{10}H_{14}N_6O_2$·0.78H_2O requires C, 45.5; H, 5.9; N, 31.8%; M, 250.1178]; λ_{max}(EtOH)/nm 424.8 (3920) and 215.6 (10 680); ν_{max}(Nujol)/cm^{-1} 3420m, 3380s, 3287s, 3167s, 1690s (C=O), 1664s, 1602s, 1578m, 1559sh and 1526s; δ_H[60 MHz; $(CD_3)_2SO$; Me_4Si] 1.5 (6 H, s, 2-Me_2), 2.05 (3 H, s, COMe) and 7.25 (1 H, s, 8-H); δ_C[$(CD_3)_2SO$] 24.6 (CO*Me*), 32.7 (2-Me_2), 76.3 (C-2), 118.9 (C-5)?, 135.6 (C-8), 150.0 (C-4)?, 153.0 (C-6)?, 167.2 ($CONH_2$) and 173.1 (*C*OMe); *m/z* (CI, NH_3) 251 [$(M + 1)^+$, 1.3%], 192 (1.2), 178 (1.5), 135 (9.1), 77 (35.7), 60 (100), 58 (87.5) and 45 (47.5).

(b) *Butan*-2-*one*. A suspension of the imidazole **12** (0.21 g, 1.09 mmol) in butan-2-one (8 cm^3) was stirred for 2.5 h at room temperature, when TLC showed that all the starting material had been consumed. A homogeneous solution with a fine dark suspension was obtained and the mixture was filtered through a very short flash chromatography column (silica gel 60, 0.5 × 2 cm) and washed with 1,4-dioxane. The filtrate and washings were combined and concentrated on a rotary evaporator to give orange crystals, which were filtered off, and washed with diethyl ether to give *compound* **13b** (0.17 g, 59%), m.p. 149.8–151.5 °C (decomp.) [Found: C, 45.9; H, 6.1; N, 28.5%; $(M + 1)^+$ (CI), 265.1405. $C_{11}H_{16}N_6O_2$·1.5H_2O requires C, 45.4; H, 6.5; N, 28.9%; M + 1, 265.1413]; λ_{max}(EtOH)/nm 431.0 (3290) and 214.9 (10 720); ν_{max}(Nujol)/cm^{-1} 3475w, 3388m, 3292s, 3180m, 1692s (C=O), 1664s (C=O), 1606m, 1572w, 1532m and 1496m; δ_H[300 MHz; $(CD_3)_2SO$; Me_4Si] 0.9 (3 H, t, *J* 7, 2-CH_2*Me*), 1.4 (3 H, s, 2-Me), 1.7 and 1.8 (each 1 H, dq, *J* 7 and 14, 2-CH_2Me), 2.1 (3 H, s, COMe) and 8.1 (1 H, s, 8-H); δ_C[$(CD_3)_2SO$] 12.3 (2-CH_2*Me*), 24.5 (CO*Me*), 31.5 (2-Me), 37.9 (2-*C*H_2Me), 79.2 (C-2), 152.8 (C-6)?, 167.4 ($CONH_2$) and 172.8 (*C*OMe); *m/z* (CI, NH_3) 265 [$(M + 1)^+$, 12.8%], 239 (30.3), 235 (5.9), 192 (8.9), 178 (22.5), 135 (25.5), 120 (15.7), 77 (61.8), 72 (80.3), 60 (100) and 45 (38.5).

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