

Synthesis of 5-Amino-4-(cyanoformimidoyl)-1*H*-imidazole: a Reactive Intermediate for the Synthesis of 6-Carbamoyl-1,2-dihydropurines and 6-Carbamoylpurines

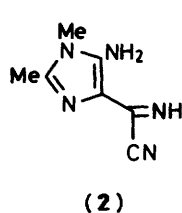
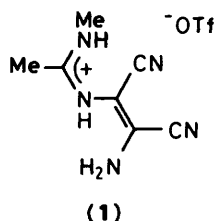
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5-Amino-4-(cyanoformimidoyl)-1*H*-imidazole (**3**) has been prepared in good yield by the base-catalysed cyclisation of (*Z*)-*N*-(2-amino-1,2-dicyanovinyl)formamidinium. Compound (**3**) reacts with ketones, R¹COR² [R¹ = R² = Et, Me, Bu, -(CH₂)₅-, PhCH₂; R¹ = Me, R² = Ph] to give 2,2-disubstituted-6-carbamoyl-1,2-dihydropurines as the major products, together with minor amounts of compounds believed to be novel 7-amino-1-carbamoyl-3,3-disubstituted 3*H*-imidazo[1,5-*c*]imidazole derivatives, which have been isolated when R¹ = R² = Et, Bu, and PhCH₂; when R¹ = R² = Ph the only product isolated is tentatively assigned the imidazo[1,5-*c*]imidazole structure. In the reaction with acetylacetone the 1,2-dihydropurine intermediate is unstable and loses acetone to give 2-methyl-6-carbamoylpurine. The aldehydes RCHO [R = Me, Et, (*E*)-MeCH=CH-, *c*-C₄H₄O] also react readily with (**3**) at room temperature to give the corresponding 6-carbamoyl-1,2-dihydropurine derivatives, which can be isolated when R = Me or Et; these oxidise in solution to afford the corresponding 6-carbamoylpurines.

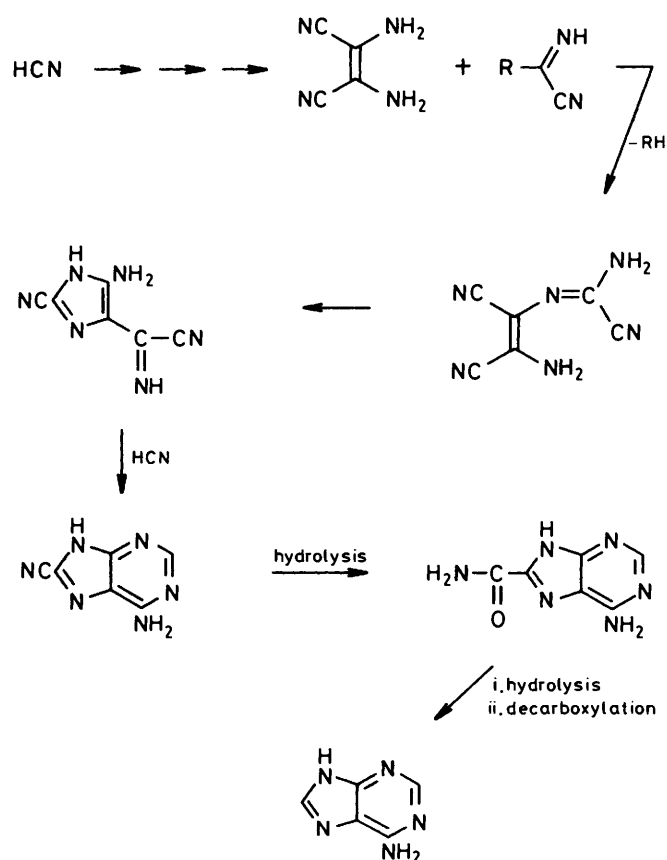
We have reported previously¹ that the amidinium salt (**1**), obtained from reaction between *N*-methylacetoneitrilium triflate and diaminomaleonitrile (DAMN), cyclises on treatment with aqueous NaHCO₃ to 5-amino-4-(cyanoformimidoyl)-1,2-dimethylimidazole (**2**) in high yield. Compound (**2**) has proved to be a useful precursor to 9-methyl-2,8-substituted 6-carbamoyl-1,2-dihydropurines, 6-carbamoylpurines, and 6-cyano-



purines.^{1,2} For some time we have been particularly interested in developing a route to the hitherto unknown compound, 5-amino-4-(cyanoformimidoyl)-1*H*-imidazole (**3**), as a precursor of potential value for the synthesis of a range of new 1,2-dihydropurine and purine derivatives, which could be coupled to carbohydrate and pseudo-carbohydrate systems through the N-9 position using available synthetic methodology as a route to new *N*-nucleosides. Additional interest in this compound stems from the fact that (**3**),³ and the 2-cyano derivative of (**3**),⁴ have been implicated as key intermediates in the prebiotic synthesis of adenine from hydrogen cyanide (Scheme 1). We now report the successful synthesis of (**3**), and its use as an intermediate for the preparation of new 1,2-dihydropurines and 6-carbamoylpurines.

Results and Discussion

Clearly, a nitrilium salt route to (**3**) was not feasible since NH nitrilium salts are not stable, and, with one exception,⁵ have not been isolated. However, it has been reported in the patent literature⁶ that diaminomaleonitrile (DAMN) reacts with



Scheme 1.

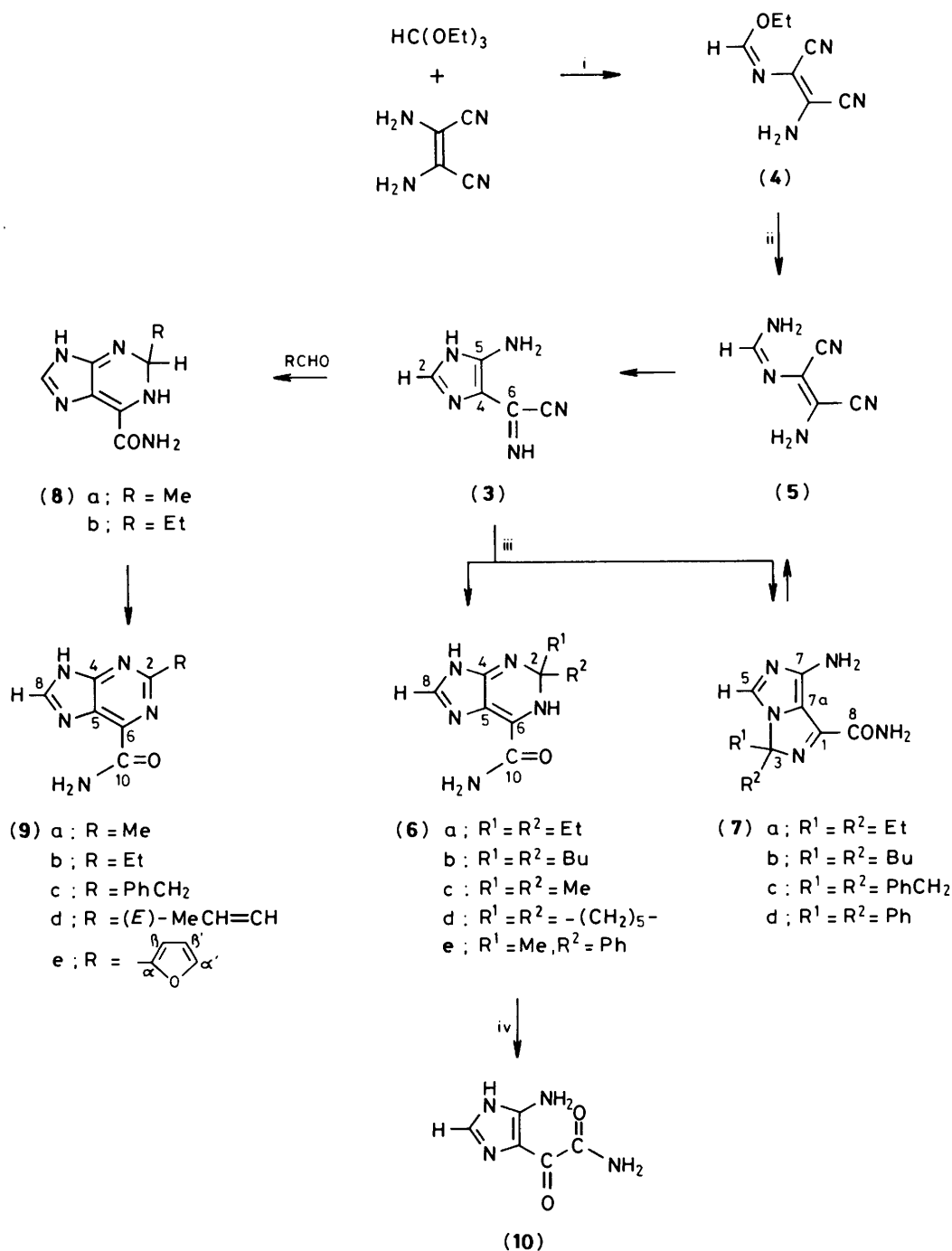
triethyl orthoformate in refluxing dry dioxane to give the imidate (**4**) in high yield. We have confirmed this result and have

used this reaction routinely to obtain (4) in 80–85% yields. Compound (4) reacts cleanly with ammonia gas at room temperature in the presence of a catalytic amount of anilinium hydrochloride to give (*Z*)-*N*-(2-amino-1,2-dicyanovinyl)-formamidine (5) in 95% isolated yield. The addition of anilinium hydrochloride is important as it appears to act as a general acid catalyst, and significantly improves the rate of reaction resulting in little or no decomposition of (5). Compound (5) has been isolated previously in 2% yield from the reaction between DAMN and formamidine acetate in refluxing ethanol, but its chemistry has not been explored in detail.³ As noted previously,³ (5) is unstable on heating for prolonged periods, but is quite stable if stored under nitrogen at room temperature in the dark. In solution, it reacts rapidly with a base at room temperature to form initially the desired imidazole (3) as shown by TLC. However, in order to isolate (3) in good yield the choice of base is critical. If a relatively weak base is used, such as Et₃N, pyridine or 4-diethylaminopyridine, cyclisation is quite slow and appreciable decomposition of (3) to an intractable black oil occurs before all the starting material is converted. Saturated aqueous Na₂CO₃ and NaHCO₃, and 1M aqueous NaOH, cause rapid cyclisation with disappearance of all the starting material at room temperature, but the base reacts further with (3) causing elimination of HCN and formation of 5-amino-4-cyanoimidazole. The most satisfactory method we have found for the isolation of pure (3) in up to 72% yield is treatment of an ethanolic solution of (5) with solid Ba(OH)₂, following the reaction closely by TLC. When all the starting material has been consumed diethyl ether is added, and any base remaining in solution is precipitated as BaCO₃ by bubbling carbon dioxide through the solution. Filtration and concentration gives (3) as a pale, yellow-green solid, which can be stored in the solid state at room temperature for several months without appreciable decomposition. In solution in air it darkens rapidly and decomposes to a black oil.

Compound (3) reacts with ketones at room temperature either as neat liquids or in dry methanol solution with the formation of a characteristic red-orange spot on TLC for the 6-carbamoyl-1,2-dihydropurine derivatives. These can be isolated as air stable, red-orange solids (6a–e) (see Scheme 2) after chromatographic separation. In the majority of the reactions with ketones a yellow spot was also observed, and it was clear from TLC that this spot was being produced at a different rate from that due to the corresponding dihydropurine (6). In some of the reactions the yellow products were formed in such small amounts that they could not be isolated in sufficient quantity for characterisation, but chromatographic separation and isolation was possible from the reactions with pentan-3-one, nonan-3-one, and dibenzyl ketone to give the compounds (7a–c) (Scheme 2). In the reaction with dibenzyl ketone the other product isolated after work-up was not the expected 1,2-dihydropurine derivative, but 2-benzyl-6-carbamoylpurine (9c) in 13% yield; this may arise from the dihydropurine by loss of toluene. Microanalysis and mass spectrometry established that the minor yellow products (7a) and (7b) were isomers of the 1,2-dihydropurine derivatives (6a) and (6b) respectively. A comparison of the spectroscopic data for compounds of type (6) with those for compounds of type (7) suggested that the structures were closely related. So, for example, the mass spectrum of (6a) [*m/z* 221 (*M*⁺) 33.8%, 204 (*M* – NH₃) 5.1%, 192 (*M* – C₂H₅) 100%, 177 (*M* – CONH₂) 6.5%, 176 (*M* – CONH₃) 6.2%, 165 (*M* – C₂H₅ – HCN) 10.6%] is virtually identical to that of (7a) [*m/z* 221 (*M*⁺) 76.2%, 204 (*M* – NH₃) 10.8%, 192 (*M* – C₂H₅) 100%, 177 (*M* – CONH₂) 9.3%, 176 (*M* – CONH₃) 17.3%, and 165 (*M* – C₂H₅ – HCN) 35.2%]. The IR spectra of (6a) and (7a) are similar in the ν(NH) region, and both show bands for an amide group. The UV spectrum of (6a) has three bands at 211.2, 307.3,

and 417.2 nm, and this is typical of all the dihydropurine derivatives. In contrast, the UV spectrum of (7a) has only two bands at 207.3 and 365.5 nm, and this pattern is seen for compounds (7b) and (7c). In the ¹H NMR spectra there are characteristic bands for two ethyl groups, and in both cases the CH₂ protons are diastereotopic; in addition, the spectrum of (6a) shows four NH resonances at δ 6.0, 7.5–8.0 (br), 9.0 and 11.8 ppm, as does that of (7a) [δ 5.35 (2 H) and 7.98 (2 H) ppm]. One diagnostic difference between the two types of compounds is that the dihydropurines all show a sharp singlet for the C-8 proton in the range of δ 7.3–7.4 ppm, while the compounds (7a–c) show a sharp singlet in the range 7.7–7.9 ppm. There are also significant differences in the ¹³C NMR spectra. Those of the dihydropurine derivatives (6a–e) show sharp bands for the substituents in the 2-position of the ring, but the resonances for the ring carbon atoms are broadened, and, in some cases give two distinct sets of bands. This broadening of the ring carbon resonances is attributed to a slow equilibration of two possible tautomers of the dihydropurines, in which the hydrogen on N-9 migrates to the N-7 position. Characteristically, the C-8 carbon atom of these dihydropurines appears at 141–145 ppm. In contrast, the resonances due to the C-H ring carbon atom in the spectra of compounds (7a–c) is in the range of 136–137 ppm, and all the ring carbon atoms appear as sharp bands indicating that tautomerism either does not, or can not, occur. Only one product was isolated from the reaction between (3) and benzophenone. The ¹³C NMR spectrum has sharp signals suggesting structure (7d), and the chemical shift values, particularly of the Ph₂C atom, agree with those expected for this structure. However, in the ¹H NMR spectrum both the presence of an NH band at δ 12.1 ppm and a band for the C-8 proton at δ 7.5 ppm are more consistent with a structure of type (6). The UV spectrum is not conclusive as it shows only two distinct bands at 202.4 and 382.4 nm expected for structure (7d), but there is evidence of another weak absorption at ca. 295 nm. From a consideration of all the spectroscopic data it seems most likely that the compounds (7a–c), and possibly (7d), have the novel 7-amino-1-carbamoyl-3,3-dialkyl-3*H*-imidazo[1,5-*c*]-imidazole structure shown in Scheme 2. Unfortunately, we have been unable to obtain crystals of sufficiently high quality for X-ray analysis. A plausible mechanism for the formation of (7a–c) is shown in Scheme 3. From this it can be seen that both compounds (6) and (7) can be obtained from the common precursor (3) depending on whether reaction with the ketone occurs at the 5-amino group or at the N-3 position. A similar intramolecular reaction of benzimidazole with ketones has been reported.⁷ When the N-1 position is blocked by an aryl or alkyl substituent compounds of type (7) are never observed in the TLC.⁸ Interestingly, there is also no evidence of their formation in the reactions between (3) and aldehydes (see below). There is some evidence that the formation of compounds of type (7) may be reversible in methanol solution. So, for example, a solution of (7a) in a dry methanol was monitored by TLC and it was seen that a new spot for (6a) appeared slowly over a period of 20 days, and grew at the expense of that for (7a). A possible mechanism for this reaction in methanol is shown in Scheme 4.

The initial product formed on reaction between (3) and an aldehyde is the corresponding 6-carbamoyl-1,2-dihydropurine derivative (8). These have been isolated from the reactions with acetaldehyde (8a) and propionaldehyde (8b) (see Scheme 2). They oxidise slowly in solution to form the 2-substituted 6-carbamoylpurines (9a) and (9b), as noted previously¹ for the products from reactions of 5-amino-4-(cyanoformidoyl)-1,2-dimethylimidazole and aldehydes. In the reactions with crotonaldehyde and 2-furfuraldehyde it was impossible to isolate compounds of type (8), and only the purine derivatives (9d) and (9e) were obtained. The reaction between (3) and



Scheme 2. Reagents and conditions: i, dioxane; ii, NH₃, -78 °C, PhNH₃⁺ Cl⁻; iii, R¹R²CO; iv, SiO₂ or MeOH aq.

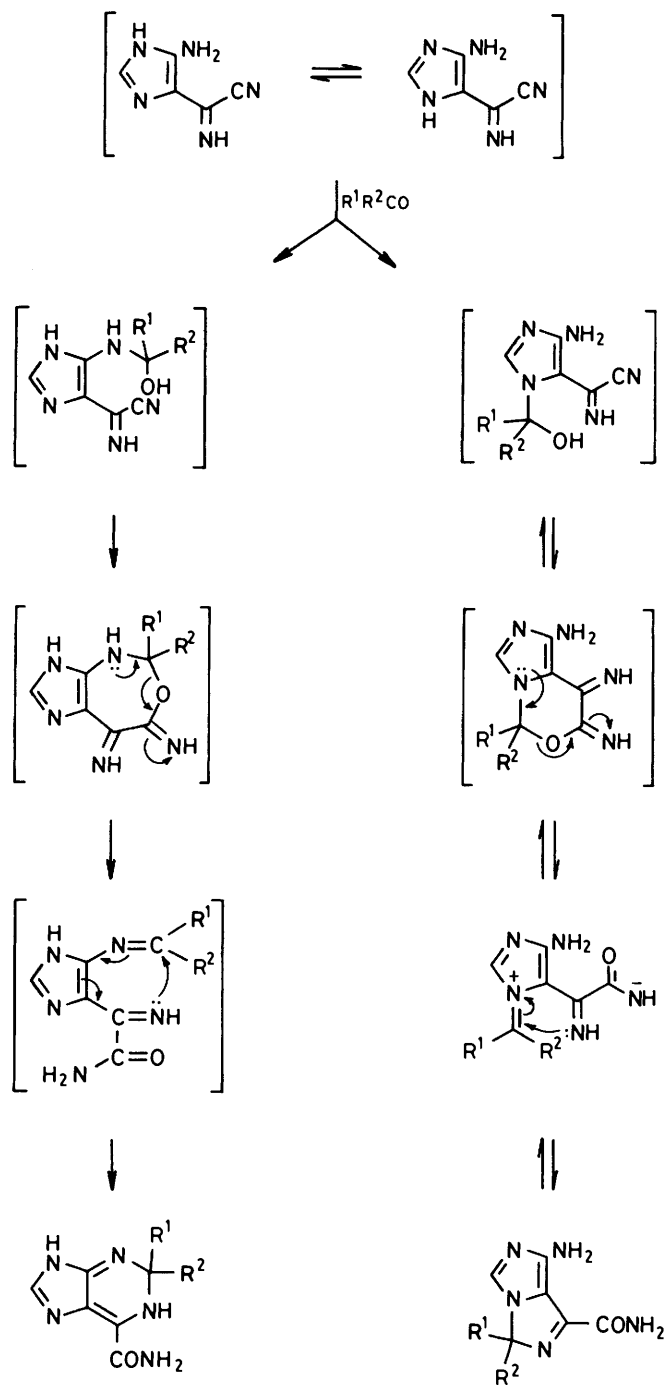
acetylacetone was also atypical in that the initial 1,2-dihydropurine product rapidly loses a molecule of acetone in solution and only 2-methyl-6-carbamoylpurine (**9a**) could be isolated after work-up.

Although the compounds (**6a–e**) are quite stable when in the solid state, they slowly decompose in solution over several hours at room temperature, and more rapidly when in aqueous ethanol or when passed down a silica gel chromatography column. This instability explains the poor microanalysis figures for compound (**6a**), which had to be chromatographed repeatedly to separate it from (**7a**). The major decomposition product is a white solid, which, on the basis of microanalysis and spectroscopic data, has been tentatively identified as

5-amino-4-oxoacetamidoimidazole (**10**). This shows three ν(NH) bands at 3 403, 3 370, and 3 310 cm⁻¹ in the IR spectrum, and strong bands at 1 698 and 1 681 cm⁻¹ for two carbonyl groups. The high resolution mass spectrum shows a molecular ion at *m/z* 154, with loss of CONH₂, and COCONH₂, as expected for this structure. Both the ¹H and ¹³C NMR spectra indicate that this compound exists in solution as a mixture of two tautomers.

Experimental

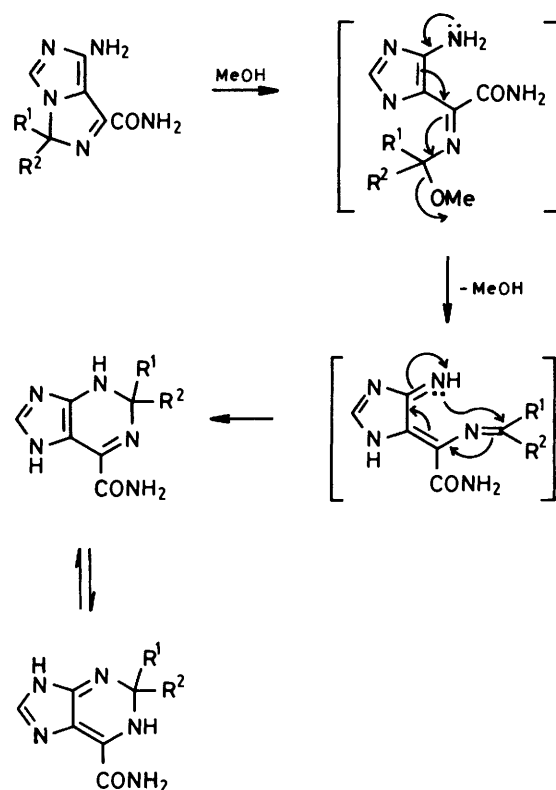
¹H NMR spectra were recorded on Hitachi-Perkin-Elmer R24B (60 MHz) or Bruker XL300 (300 MHz) instruments, ¹³C NMR



Scheme 3.

spectra either on a Bruker WP80 or XL300 instrument, and IR spectra on a Shimadzu IR-435. Mass spectra were recorded either on a Kratos MS45 or on a Kratos Concept instrument, and UV spectra on a Perkin-Elmer Lambda 15 UV/VIS spectrometer. The melting points are uncorrected.

Preparation of Ethyl (Z)-N-(2-Amino-1,2-dicyanovinyl)formimidate (4).—A mixture of diaminomaleonitrile (2.0 g, 18.5 mmol), and triethyl orthoformate (2.74 g, 18.5 mmol, 3.07 cm³) in dioxane (31.5 cm³) was heated in a flask fitted with a short Vigreux column, distillation head, condenser, and receiver. Ethanol mixed with dioxane (17 cm³) was removed continuously until the temperature in the distillation head reached



Scheme 4.

99 °C (approximately 10 min). The clear, brown solution in the distillation pot was allowed to cool overnight, then hexane (16 cm³) was added producing dark brown crystals; further hexane can be added if necessary to ensure complete precipitation. The solid was filtered off and dissolved in the minimum amount of hot diethyl ether to remove a dark-brown solid impurity, and then left to cool overnight to give (4), as white needles, (2.55 g, 15.5 mmol, 84%), m.p. 132.5 °C (dec.) [lit.,⁶ 135–137 °C] [Found: C, 50.9; H, 4.9; N, 34.4%; (M + 1)⁺ Cl(NH₃) 165 (39.2%). Calc. for C₇H₈N₄O: C, 51.2; H, 4.9; N, 34.1%; M 165]; δ_H(300 MHz, CDCl₃, Me₄Si) 1.38 (t, 3 H, CH₃, J 7 Hz), 4.28 (q, 2 H, CH₂), 4.73, (s, 2 H, NH₂), and 7.93 (s, 1 H, CH); δ_C([²H₆]acetone) 13.6 (CH₃), 63.6 (CH₂), 110.2 (C=N), 113.7 (CN), 114.1 (CN), 122.6 (C=), and 156.8 (C=N); ν_{max}(Nujol) 3 400m, 3 300s, 3 160m (NH), 2 250m, 2 200m (C≡N), 1 635s, and 1 605s cm⁻¹; λ_{max}(EtOH) 204 (ε 13 319) and 310 (ε 19 662) nm.

Preparation of (Z)-N-(2-Amino-1,2-dicyanovinyl)formimidate (5).—Ammonia was bubbled for 30 min through a cold (−78 to −20 °C), stirred, suspension of ethyl (Z)-N-(2-amino-1,2-dicyanovinyl)formimidate (4.0 g, 24.36 mmol) in dry chloroform (90 cm³) containing a catalytic amount (0.01 g) of anilinium hydrochloride. When all the imidate had dissolved the solution was allowed to warm up to room temperature and was then stirred at this temperature for 19 h during which time the product precipitated out of solution as an off-white solid. The product was filtered off, washed with diethyl ether–dry chloroform (1:1), and dried under vacuum to give (5) (3.11 g, 23.07 mmol, 95%), m.p. > 300 °C (lit.,³ m.p. > 300 °C). [Found: C, 44.7; H, 3.70; N, 51.9%; M⁺ 135 (26.2%). Calc. for C₅H₅N₅: C, 44.44; H, 3.75; N, 51.83%; M 135]; δ_H[CDCl₃: [²H₆]DMSO (1:1), 60 MHz, Me₄Si] 5.57 (s, 2 H, NH₂), 7.02 (br s, 2 H, NH₂), and 7.73 (t, 1 H, CH, J 9.8 Hz); δ_C[²H₆]DMSO) 111.0, 119.2, 120.2, 120.8, and 156.7; ν_{max}(Nujol mull) 3 433s,

3 404s, 3 345s, 3 186s (NH), 2 214s, 1 995s (C≡N), and 1 686s (C=N), cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 221.5 (ϵ 11 301) and 323.2 (ϵ 25 427) nm.

Preparation of 5-Amino-4-(cyanoformimidoyl)imidazole (3).—Solid $\text{Ba}(\text{OH})_2 \cdot 2\text{H}_2\text{O}$ (8.0 g) was added to a suspension of the amidine (3.0 g, 22.2 mmol) in 95% ethanol (270 cm^3), and the mixture was stirred vigorously for approximately 50 min until TLC showed that all the amidine had been consumed, and the solution had turned deep yellow. Diethyl ether (300 cm^3) was then added and carbon dioxide was bubbled through the solution for 10 min. The precipitate of BaCO_3 and unchanged $\text{Ba}(\text{OH})_2 \cdot 2\text{H}_2\text{O}$ was removed by filtration, and the solid was washed with ether. The filtrate and washings were combined, and the solvent removed on a rotary evaporator with a bath temperature $< 30^\circ\text{C}$ to give crystals of the product (1.75 g). Further concentration of the filtrate gave a second crop of the product (0.42 g) to give a total yield of (3) of 2.17 g (16.05 mmol, 72%) as a pale green solid, m.p. $> 300^\circ\text{C}$ (decomp.) [Found: C, 44.2; H, 3.6; N, 52.1%; M^+ (EI) 135 (65.3%). $\text{C}_5\text{H}_5\text{N}_5$ requires C, 44.4; H, 3.7; N, 51.8%; M 135]; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]} \text{DMSO}, 60 \text{ MHz}, \text{Me}_4\text{Si})$ 7.21 (s, 1 H, CH) (NH protons are not observed); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]} \text{DMSO})$ 118.1 (4-C), 119.3 (C≡N), 135.7 (2-C), 146.2 (5-C), and 149.9 (6-C); $\nu_{\text{max}}(\text{Nujol mull})$ 3 407s, 3 304m, 3 265s, 3 115w, 3 045w (NH), 1 621s (C=N)?, 1 560s, and 1 520m (imidazole ring) cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 220.9 (ϵ 8 940) and 351.9 (ϵ 7 839) nm.

Reaction of 5-Amino-4-(cyanoformimidoyl)imidazole with Ketones.—(a) **Pentan-3-one.** A suspension of the imidazole (0.5 g, 3.7 mmol) in pentan-3-one (5 cm^3) was stirred at room temperature for 30 min. When the typical orange colour had developed methanol (5 cm^3) was added to solubilize the solids, and after 1 h at room temperature TLC indicated that the imidazole starting material had been consumed with the formation of two products. Removal of the methanol on a rotary evaporator followed by washing with diethyl ether gave a first crop of crystals (0.61 g). Further evaporation of the mother liquor and washings gave a second crop of solid (0.10 g) (combined yield 0.71 g, 3.21 mmol, 87%), which was a mixture of the two components by TLC.

A solution of 0.2 g of the mixture in methanol was separated by preparative TLC (silica 60 H; CHCl_3 -EtOH, 9:1) to give a yellow solid (0.025 g) and an orange solid (0.1 g). The yellow solid was identified as 7-amino-1-carbamoyl-3,3-diethyl-3H-imidazo[1,5-c]imidazole (7a) (estimated yield by ^1H NMR spectroscopy: 0.237 g, 1.07 mmol, 29%), m.p. 165°C (decomp.) [Found: C, 54.1; H, 7.1; N, 32.0%; M^+ (CI) 221 (79.16%). $\text{C}_{10}\text{H}_{15}\text{N}_5\text{O}$ requires C, 54.29; H, 6.78; N, 31.67%; M 221]; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]} \text{DMSO}, 300 \text{ MHz})$ 0.62 (t, 6 H, $2 \times \text{CH}_3$, J 7 Hz), 2.01 (overlapping ABX₃ pattern, 4 H, $2 \times \text{CH}_2$, J_{AB} 14 Hz, J_{AX} 7 Hz), 5.35 (s, 2 H, NH), 7.73 (s, 1 H, HCN₂), 7.98 (s, 1 H, NH), and 8.12 (s, 1 H, NH); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]} \text{DMSO})$ 10.7 (CH₃), 35.5 (CH₂), 94.6 (3-C), 123.0 (7a-C), 136.7 (5-C), DEPT 135), 143.9 (7-C), 158.9 (1-C), and 166.9 (8-C); $\nu_{\text{max}}(\text{CHBr}_3 \text{ mull})$ 3 407m, 3 350m, 3 281s, 3 178s, 3 109m (NH), 1 684s (C=O), 1 636s (C=N)?, 1 561m, and 1 527s (imidazole ring) cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 207.31 (ϵ 10 566) and 365.5 (ϵ 5 490) nm.

The orange compound was identified as 2,2-diethyl-6-carbamoyl-1,2-dihydropurine (6a) (estimated yield by ^1H NMR spectroscopy: 0.47 g, 2.14 mmol, 58%), m.p. 130°C (decomp.) [Found: C, 52.7; H, 6.6; N, 29.2%; M^+ (CI) 221.1270 (31.18%). $\text{C}_{10}\text{H}_{15}\text{N}_5\text{O}$ requires C, 54.29; H, 6.78; N, 31.67%; M 221]; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]} \text{DMSO}, 300 \text{ MHz})$ 0.93 (t, 6 H, $2 \times \text{CH}_3$, J 7 Hz), 1.63 (br m, 2 H, CH₂), 1.83 (br m, 2 H, CH₂), 6.0 (br s, 1 H, NH), 7.39 (s, 1 H, HCN₂), 7.5–8.0 (br, 1 H, NH), 9.0 (br s, 1 H, NH), and 11.8 (br s, 1 H, NH); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]} \text{DMSO})$ 11.9 (CH₃), 33.7 (CH₂), 79.3 (2-C)*, 80.8 (2'-C)*, 125.8 (5-C)*, 141.5* (8-C by DEPT

135), 144.9 (8'-C by DEPT 135)*, 151.2 (6-C)*, 158.1 (6'-C)*, 163.1 (4-C)*, 166.0 (4'-C*), 168.2 (10-C)*, and 170.4 (10'-C)* (* broad signals due to slow exchange); $\nu_{\text{max}}(\text{CHBr}_3 \text{ mull})$ 3 348s, 3 286s, 3 157s (NH), 1 684s (C=O), 1 636s (C=N)?, 1 584s, and 1 528m (imidazole ring) cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 211.2 (ϵ 10 268), 307.3 (ϵ 2 651), and 417.2 (ϵ 2 735) nm.

(b) **Nonan-5-one.** A solution of imidazole (0.5 g, 3.7 mmol) and nonan-5-one (0.54 g, 3.78 mmol) in methanol was stirred at room temperature for 19 h. The solvent was then removed under reduced pressure and the residual black oil was dissolved in ethyl acetate, and purified by flash chromatography (silica 60 H, EtOAc eluant) to remove the dark impurity. The solvent was removed from the resultant orange solution to give an orange oil. Addition of ether to the oil gave 2,2-dibutyl-6-carbamoyl-1,2-dihydropurine (6b) (0.41 g, 1.47 mmol, 40%) as a red solid, m.p. 128 – 129°C [Found: C, 60.6; H, 8.4; N, 25.5%; M^+ 277 (12.5%). $\text{C}_{14}\text{H}_{23}\text{N}_5\text{O}$ requires C, 60.65; H, 8.3; N, 25.27%; M 277]; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]} \text{DMSO}, 300 \text{ MHz})$ 0.95 (t, 6 H, $2 \times \text{CH}_3$, J 7 Hz), 1.35 (m, 8 H, $4 \times \text{CH}_2$), 1.65 (m, 2 H, CH₂), 1.83 (m, 2 H, CH₂), 6.0 (br s, 1 H, NH), 7.30 (s, 1 H, HCN₂), 7.7 (br s, 2 H, NH), and 11.8 (br s, 1 H, NH); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]} \text{DMSO})$ 18.1 (CH₃), 26.5 (CH₂), 29.4 (CH₂), 41.6 (CH₂), 79.7 (2-C)*, 109 (5-C)*, 125.5 (5'-C)*, 141.6 (8-C, by DEPT 135)*, 149–151 (8'-C by DEPT 135)*, 154 (6-C)*, 158.5 (6'-C)*, 162–163 (4-C and 4'-C)*, 166.5 (10-C)*, and 170 (10'-C) (* broad signals due to slow exchange); $\nu_{\text{max}}(\text{CHBr}_3 \text{ mull})$ 3 270s, 3 160m (NH), 1 685s (C=O), 1 640s (C=N)?, 1 595m, and 1 525w (imidazole ring) cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 211.6 (ϵ 9 922), 306.6 (ϵ 2 470), and 419.2 (ϵ 2 547) nm.

Removal of the solvent from the filtrate gave 7-amin-1-carbamoyl-3,3-dibutyl-3H-imidazo[1,5-c]imidazole (7b) (0.046 g, 0.166 mmol, 45%), m.p. 127 – 128°C [Found: C, 60.3; H, 8.3; N, 25.0%; M^+ 277 (14.1%). $\text{C}_{14}\text{H}_{23}\text{N}_5\text{O}$ requires C, 60.65; H, 8.3; N, 25.27%; M 277]; $\delta_{\text{H}}(60 \text{ MHz}, [\text{}^2\text{H}_6\text{]} \text{DMSO}, \text{Me}_4\text{Si})$ 0.5–1.4 (m, 14 H, $2 \times \text{Bu}$), 1.7–2.1 (m, 4 H, $2 \times \text{CH}_2$), 5.0–5.3 (br, 2 H, NH₂), 7.6 (s, 1 H, CHN₂), and 7.7–8.1 (br, 2 H, NH₂); $\nu_{\text{max}}(\text{Nujol mull})$ 3 460m, 3 425m, 3 340m, 3 150m (NH), 1 690s $\nu(\text{C=O})$, 1 630s (C=N)?, 1 570m, and 1 520m (imidazole ring) cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 209.1 (ϵ 10 430) and 365.8 (ϵ 4 893) nm.

(c) **Dibenzyl ketone.** A mixture of the imidazole (0.5 g, 3.7 mmol) and dibenzyl ketone (0.8 g, 3.8 mmol) in freshly distilled methanol (5 cm^3) was stirred at room temperature for 23 h to give two compounds by TLC. The methanol was removed to give a dark, oily residue, which was dissolved in ethyl acetate before chromatography (silica 60 H; ethyl acetate eluant). On partial removal of the ethyl acetate from the dark solution shiny, pale yellow crystals of 7-amino-1-carbamoyl-3,3-dibenzyl-3H-imidazo[1,5-c]imidazole (7c) (0.134 g, 0.39 mmol, 10.5%) were obtained, m.p. 161 – 162°C [Found: C, 68.2; H, 5.2; N, 19.7%; M^+ (EI) 345 (2.9%). $\text{C}_{20}\text{H}_{19}\text{N}_5\text{O}$ requires C, 69.56; H, 5.5; N, 20.28%; M 345]; $\delta_{\text{H}}([\text{}^2\text{H}_6\text{]} \text{DMSO}, 300 \text{ MHz})$ 3.50 (AB quartet, 4 H, $2 \times \text{CH}_2$, J_{AB} 13.5 Hz), 4.96 (s, 2 H, NH), 7.15 (m, 4 H, ArH), 7.24 (m, 6 H, ArH), 7.80 (s, 1 H, NH), 7.85 (s, 1 H, HCN₂), and 8.00 (s, 1 H, NH); $\delta_{\text{C}}([\text{}^2\text{H}_6\text{]} \text{DMSO})$ 48.7 (CH₂), 93.5 (3-C), 122.8 (7a-C), 130.7 (*p*-C), 131.6 (*o*-C), 134.3 (*m*-C), 136.8 (HCN₂, (5-C, by DEPT 135), 138.2 (C'), 143.1 (7-C), 158.9 (1-C), and 166.5 (8-C); $\nu_{\text{max}}(\text{CHBr}_3 \text{ mull})$ 3 460m, 3 365s, 3 250m, 3 180m, 3 110m (NH), 1 695s, 1 665s (C=O) and (C=N)? 1 630s, 1 585w, and 1 530s (imidazole ring?) cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 205.8 (ϵ 25 724) and 371.4 (ϵ 4 836) nm.

The mother liquor from the filtration was evaporated to dryness and the residue was redissolved in chloroform. This solution was chromatographed (silica 60 H, EtOAc eluant) and slow evaporation of the solvent over 3 days followed by addition of chloroform gave cream crystals of 2-benzyl-6-carbamoylpurine (9c) (0.12 g, 0.48 mmol, 13%) which were recrystallised from ethanol to give the pure product, m.p. 252 – 252.5°C (decomp.) [Found: C, 61.3; H, 4.2; N, 27.5%; M^+ 253 (43.3%). $\text{C}_{13}\text{H}_{11}\text{N}_5\text{O}$ requires C, 61.66; H, 4.35; N, 27.67%; M

253]; $\delta_{\text{H}}([^2\text{H}_6]\text{DMSO}, 300 \text{ MHz})$ 4.42 (s, 2 H, CH_2), 7.25–7.5 (m, 5 H, Ph), 8.25 (s, 1 H, NH), 8.50 (s, 1 H, NH), 8.78 (s, 1 H, CHN_2), and 13.45 (br s, <1 H, NH); $\delta_{\text{C}}([^2\text{H}_6]\text{DMSO})$ 48.9 (CH_2), 124.0 (5-C), 130.2 (*m*-C), 132.3 (*o*-C), 133.1 (*p*-C), 143.1 (C'), 145.0 (6-C), 154.1 (8-C), 165.8 (4-C or 2-C?), 168.0 (2-C or 4-C?), and 169.5 (10-C); $\nu_{\text{max}}(\text{Nujol mull})$ 3490m, 3380m, 3140m, 3070m (NH), 1695s (C=O), 1570s, and 1565s cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 204.5 (ϵ 27 253) and 292.5 (ϵ 7 394) nm.

(d) *Acetone*. A suspension of the imidazole (0.5 g, 3.7 mmol) in acetone (10 cm^3) was stirred at room temperature for 3 h when all the starting material had been converted into the orange dihydropurine (pure by TLC). The solid was filtered, washed with diethyl ether and dried to give 2,2-dimethyl-6-carbamoyl-1,2-dihydropurine (**6c**) (0.62 g, 3.21 mmol, 87%), m.p. 135 °C (decomp.) [Found: C, 49.6; H, 5.9; N, 36.6%; M^+ (CI) 193.0952 (58.7%). $\text{C}_8\text{H}_{11}\text{N}_5\text{O}$ requires C, 49.74; H, 5.7; N, 36.27%; M 193.3041]; $\delta_{\text{H}}([^2\text{H}_6]\text{DMSO}, 60 \text{ MHz})$ 1.41 (s, 6 H, 2 \times CH_3), 6.1 (s, 1 H, NH), 7.3 (s, 1 H, HCN_2), and 7.8 (br s, 2 H, NH); $\delta_{\text{C}}([^2\text{H}_6]\text{DMSO})$ 31.3 (CH_3), 73.0 (2-C)*, 75.65 (2'-C)*, 110.2 (5-C)*, 126.8 (5'-C)*, 142.4 (CHN_2 , 8-C, by DEPT 135)*, 151.0 (6-C)*, 158.1 (6'-C)*, 166.4 (4-C)*, 164.4 (4'-C)*, 167.8 (10-C)*, and 170.8 (10'-C)*; $\nu_{\text{max}}(\text{CHBr}_3 \text{ mull})$ 3310m, 3155m, 3070m (NH), 1690m (C=O), 1588s, and 1523w (imidazole ring) cm^{-1} ; λ_{max} 654.1 (ϵ 945.3), 400.1 (ϵ 3 259), 305.7 (ϵ 2 662), and 209.3 (ϵ 11 094) nm.

(e) *Cyclohexanone*. The imidazole (0.5 g, 3.7 mmol) and cyclohexanone (5 cm^3) were stirred together at room temperature for 15 min. The mixture was then flash chromatographed (silica 60 mesh, CHCl_3 eluant) to remove any excess of cyclohexanone, and the product was then eluted with propanone. Removal of the solvent from the propanone fraction gave an orange solid (0.53 g, 2.27 mmol, 75%), which was recrystallised from propanone–light petroleum (b.p. 40–60 °C) to give 6-carbamoyl-1,2-dihydropurine-2-spirocyclohexane (**6d**) (0.3 g, 1.29 mmol, 35%), which decomposed on heating (the temperature of decomposition depended upon the rate of heating and was not reproducible). [Found: C, 56.3; H, 6.3; N, 30.1%; ($M + 1$)⁺ (CI) 234 (83.4%). $\text{C}_{11}\text{H}_{15}\text{N}_5\text{O}$ requires C, 56.65; H, 6.43; N, 30.0%; M 233]; $\delta_{\text{H}}([^2\text{H}_6]\text{DMSO}, 300 \text{ MHz})$ 1.2–2.0 (m, 10 H, 5 \times CH_2), 5.90 (s, 1 H, NH), 7.40 (s, 1 H, HCN_2), 7.60 (s, 1 H, NH), 7.62 (s, 1 H, NH), and 12.0 (s, 0.5 H, NH?); $\delta_{\text{C}}([^2\text{H}_6]\text{DMSO})$ 25.1 (CH_2), 29.6 (CH_2), 39.6 (CH_2), 76.7 (2-C)*, 110.2 (5-C)*, 141.7 (HCN_2 , 8-C by DEPT 135)*, 150.4 (6-C)*, 157.6 (4-C)*, and 170.3 (10-C)* (* broad bands due to slow exchange); $\nu_{\text{max}}(\text{CHBr}_3 \text{ mull})$ 3382m, 3321s, 3235s, 3147s, 3105m (NH), 1679s (C=O), 1616s, 1569s, and 1512m cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 211.3 (ϵ 10 697), 305.5 (ϵ 2 463), and 403.2 (ϵ 2 858) nm.

Partial evaporation of the mother liquor from the recrystallisation gave a small amount of the decomposition product, 5-amino-4-(α -oxoacetamido)imidazole (0.06 g, 0.39 mmol; 10.5%), which had an IR spectrum identical to that of an authentic sample.

(f) *Acetophenone*. A mixture of imidazole (0.5 g, 3.7 mmol) and acetophenone (0.45 g, 3.7 mmol) in dry, de-oxygenated methanol (5 cm^3) was stirred at room temperature for 72 h, when TLC showed that all the starting material had been consumed. The solvent was removed to give a black oil, which was dissolved in the minimum amount of acetone and was flash chromatographed (silica 60 H; acetone eluant) to give a deep yellow solution. Most of the acetone was removed under vacuum and addition of light petroleum (b.p. 40–60 °C) gave a yellow powder, which was washed with light petroleum and dried to give 2-methyl-2-phenyl-6-carbamoyl-1,2-dihydropurine (**6e**) (0.59 g, 2.31 mmol, 62.5%), m.p. >160 °C with decomposition. [Found: C, 60.9; H, 5.1; N, 27.1. M^+ (EI) 255 (55.1%). $\text{C}_{13}\text{H}_{13}\text{N}_5\text{O}$ requires C, 61.2; H, 5.1; N, 27.5%. M 255]; $\delta_{\text{H}}([^2\text{H}_6]\text{DMSO}, 60 \text{ MHz})$ 1.74 (s, 3 H, CH_3), 6.86 (s, 1 H, NH),

7.1–7.7 (m, 6 H, CH + PhH), 8.0–8.6 (br, <1 H, NH), and 9.0–9.5 (br s, <1 H, NH); $\delta_{\text{C}}([^2\text{H}_6]\text{DMSO})$ 42.7 (CH_3), 78.6 (2-C)*, 111.6 (5-C)*, 129.3 (*o*-C), 130.7 (*p*-C), 131.4 (*m*-C), 142.4 (CHN_2 , 8-C, by DEPT 135)*, 151.4 (6-C or 1-C)*, 151.8 (1-C or 6-C)*, 158.5 (4-C)*, and 170.2 (10-C)* (* broad bands due to slow exchange); $\nu_{\text{max}}(\text{CHBr}_3)$ 3460w, 3415w, 3271s, 3240s, 3175m, 3055w (NH), 1680s (C=O), 1625s, 1600m, 1590m, 1577m, 1558w, and 1520w cm^{-1} λ_{max} 205.7 (ϵ 18 633), 226.4 (ϵ 8 533), 304.0 (ϵ 2 304), and 390.1 (ϵ 3 187) nm.

(g) *Benzophenone*. A mixture of imidazole (0.5 g, 3.7 mmol), and benzophenone (0.67 g, 3.7 mmol) in de-oxygenated methanol (5 cm^3) was stirred for 72 h at room temperature. Removal of the solvent gave a black oil which was dissolved in acetone and purified by flash chromatography (silica; acetone eluant) to give a yellow solution. TLC showed that this was a mixture of compounds including a small quantity of 2,2-dimethyl-6-carbamoyl-1,2-dihydropurine, presumably obtained by reaction of the acetone eluant with a trace of imidazole remaining after reaction. The yellow solution was re-chromatographed (silica 60 H; 15 $\text{cm} \times 2.5 \text{ cm}$ column) first eluting with chloroform to give several impurities which were not examined further. Then elution with a mixture of ethanol (2%) and chloroform gave a yellow solution. Slow evaporation of the solvent gave shiny yellow crystals of a compound believed to be 7-amino-1-carbamoyl-3,3-diphenyl-3H-imidazo-[1,5-c]imidazole (**7d**). A further crop of crystals was obtained by removal of the solvent and recrystallisation from acetone–light petroleum (b.p. 40–60 °C), and the total yield of (**7d**) was 0.14 g (0.44 mmol, 12%), m.p. 170–171 °C (decomp.) [Found: C, 61.0; H, 4.4; N, 19.4%; M^+ (EI) 317 (64.4%). $\text{C}_{18}\text{H}_{15}\text{N}_5\text{O}$ requires C, 68.14; H, 4.7; N, 22.0%; M 317]; $\delta_{\text{H}}([^2\text{H}_6]\text{DMSO}, 300 \text{ MHz})$ 7.1 (s, 1 H, NH), 7.25 (t d, 2 H, 2 \times *p*-Ar H, *J* 7, 1.5 Hz), 7.35 (t d, 4 H, 4 \times *m*-Ar H, *J* 7, 1.5 Hz), 7.5 (s, 1 H, HCN_2), 7.75 (dd, 5 H, 4 \times *o*-Ar H + NH), 8.2 (s, 1 H, NH), and 12.1 (s, 1 H, NH); $\delta_{\text{C}}([^2\text{H}_6]\text{DMSO})$ 112.7 (3-C + 7a-C), 130.6 (*o*-C), 130.7 (*p*-C), 131.6 (*m*-C), 142.8 (5-C), CHN_2 by DEPT 135), 150.7 (C'), 151.2 (7-C), 158.7 (1-C), and 170.3 (8-C); $\nu_{\text{max}}(\text{CHBr}_3)$ 3460s, 3404m, 3315m, 3111m (NH), 1710s (C=O), 1702m, 1625m, 1593m, 1566m, and 1500s cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 202.4 (ϵ 36 158), *ca.* 295 (ϵ *ca.* 1 500), and 382.4 (ϵ 3 112) nm.

(h) *Acetylacetone*. A suspension of the imidazole (0.5 g, 3.7 mmol) in acetylacetone (3.9 g, 0.39 mmol) was stirred at room temperature for 30 min. There was very little colour change after this period and TLC showed an appreciable amount of starting material. Six portions of methanol (5 cm^3) were added at 30 min intervals and the solution was stirred for 2 h; TLC after this period still showed an appreciable amount of starting material present. The mixture was transferred to a larger flask and more acetylacetone (2.5 cm^3) in methanol (150 cm^3) was added. A suspension persisted and after 2 h TLC showed no starting material remained. Most of the solvent was then removed on a rotary evaporator to give 2-methyl-6-carbamoylpurine (**9a**) (0.25 g, 1.4 mmol, 38%) as a white solid, m.p. 250 °C with (decomp.) [Found: C, 47.2; H, 4.0; N, 39.8%; ($M + 1$)⁺ (CI) 178 (100%). $\text{C}_7\text{H}_7\text{N}_5\text{O}$ requires C, 47.5; H, 3.95; N, 39.6%; M 177], (recrystallised from acetonitrile); $\delta_{\text{H}}([^2\text{H}_6]\text{DMSO}, 60 \text{ MHz})$ 2.80 (s, 3 H, CH_3), 8.35 (br s, 1 H, NH), 8.45 (br s, 1 H, NH), and 8.75 (sh s, 1 H, CHN_2); $\delta_{\text{C}}([^2\text{H}_6]\text{DMSO})$ 29.4 (CH_3), 124.8 (5-C), 145.3 (6-C), 153.6 (HCN_2 , 8-C, by DEPT 135), 163.9 (4-C or 2-C), 167.1 (2-C or 4-C), and 169.6 (10-C); ν_{max} 3435s, 3274s (NH), 1777s (C=O), 1573m, and 1558m cm^{-1} ; $\lambda_{\text{max}}(\text{EtOH})$ 203.4 (ϵ 21 079) and 296.7 (ϵ 8 409) nm.

Evaporation to dryness of the mother liquor gave a yellow solid having the same R_{F} value on TLC as 2,2-dimethyl-6-carbamoyl-1,2-dihydropurine, together with other impurities. Flash chromatography (silica) with chloroform as eluant removed the impurities, and elution with acetone gave the 2,2-dimethyl-6-

carbamoyl-1,2-dihydropurine (0.03 g, 0.156 mmol, 4.2%) as an orange solid, having identical IR and ^1H NMR spectra to those of an authentic sample.

Reaction of 5-Amino-4-(cyanoformimidoyl)imidazole with Aldehydes.—(a) *Acetaldehyde*. A mixture of imidazole (0.5 g, 3.7 mmol), acetaldehyde (0.18 g, 4.0 mmol) and methanol (20 cm^3) was stirred at room temperature for 10 min. The solvent was then evaporated and the resultant oil crystallised. The crystals (0.09 g) were washed with a small amount of methanol and filtered. The mother liquor was evaporated to give a black oil, which was dissolved in chloroform and passed through a flash chromatography column (silica, 60 mesh) to give a yellow fraction, which contained no dihydropurine and was rejected. Elution with acetone gave a second fraction, which, on evaporation and then addition of a minimum amount of acetone, gave orange crystals of 2-methyl-6-carbamoyl-1,2-dihydropurine (**8a**) (0.27 g). The total yield of (**8a**) was 0.36 g (2.01 mmol, 54%), m.p. > 125 °C (decomp.) [Found: C, 46.6; H, 4.8; N, 39.1%; M^+ (CI) 179 (18.0%). $\text{C}_7\text{H}_9\text{N}_5\text{O}$ requires C, 46.9; H, 5.03; N, 39.1%; M 179]; δ_{H} ($[\text{}^2\text{H}_6\text{]} \text{DMSO}$, 60 MHz) 1.48 (d, 3 H, CH_3 , J 6.6 Hz), 4.78 (q, 1 H, CH, J 6.6 Hz), 7.43 (s, 1 H, CHN_2), and 7.3–8.8 (br, 2 H, NH); δ_{C} ($[\text{}^2\text{H}_6\text{]} \text{DMSO}$) 24 (CH_3), 70 (2-C)*, 113 (5-C)*, 143 (6-C)*, 154 (8-C, HCN_2 , by DEPT 135)*, 160 (4-C)*, and 170 (10-C)* (* broad signals); ν_{max} (CHBr_3) 3 370m, 3 252s, 3 135m, 3 062m (NH), 1 683s ($\text{C}=\text{O}$), 1 609s, 1 569s, and 1 517m cm^{-1} ; λ_{max} (EtOH) 205.3 (ϵ 11 714), 298.7 (ϵ 3 049), and 385.8 (ϵ 2 413) nm.

The mother liquor was allowed to stand at room temperature for 11 days and a small amount of a white solid precipitated. This was found to be 2-methyl-6-carbamoylpurine on comparison of its IR and NMR spectra with those of an authentic sample.

(b) *Propionaldehyde*. A small excess of propionaldehyde (0.23 g, 4.02 mmol) was added to a suspension of the imidazole (0.5 g, 3.7 mmol) in methanol (5 cm^3). As the solid dissolved slowly a deep yellow colour developed. Further methanol (20 cm^3) and propionaldehyde (0.113 g, 1.94 mmol) was added, and on stirring for 5 min TLC showed that all the starting material had reacted. The solvent was removed and the deep yellow crystals precipitated from the concentrated solution; a second crop was obtained on further concentration of the mother liquor to give 2-ethyl-6-carbamoyl-1,2-dihydropurine (**8b**) (0.4 g, 2.1 mmol, 57%), m.p. > 125 °C (decomp.) [Found: C, 49.6; H, 5.7; N, 36.2%; M^+ (CI) 193 (70.0%). $\text{C}_9\text{H}_{11}\text{N}_5\text{O}$ requires C, 49.74; H, 5.7; N, 36.27%; M 193]; δ_{H} ($[\text{}^2\text{H}_6\text{]} \text{DMSO}$) 1.12 (t, 3 H, CH_3 , J 7.5 Hz), 1.85 (complex m, 2 H, CH_2), 4.6 (m, 1 H, CHEt), 5.6–6.5 (br s, 1 H, NH), 7.5 (s, 1 H, CHN_2), 7.8 (br, 1 H, NH), and 12.00 (br s, 1 H, NH); δ_{C} ($[\text{}^2\text{H}_6\text{]} \text{DMSO}$) 13.4 (CH_3), 30.4 (CH_2), 75 (2-C)*, 113 (5-C)*, 143 (6-C)*, 153 (8-C, CHN_2 , by DEPT 135)*, 160 (4-C)* and 169 (10-C)* (* broad signals); ν_{max} (CHBr_3) 3 397s, 3 341s, 3 183s (NH), 1 686s ($\text{C}=\text{O}$), 1 660s, 1 603s, and 1 541m cm^{-1} .

(c) *Crotonaldehyde*. Crotonaldehyde (0.26 g, 3.7 mmol) was added to a suspension of the imidazole (0.5 g, 3.7 mmol) in methanol (5.5 cm^3). On stirring at room temperature the solution gradually turned yellow-orange, but after 1 h TLC still showed the presence of starting materials. A further quantity of crotonaldehyde (0.0085 g, 0.12 mmol) was added and after 15 min. the solvent was evaporated to give a black oil. This was dissolved in acetone (ca. 75 cm^3) and passed through a flash chromatography column (silica). The solvent was removed from the resulting orange solution to give pale yellow crystals, which were filtered and washed with ether to give 2-[(*E*)-prop-1-enyl]-6-carbamoylpurine (**9d**) (0.37 g, 1.82 mmol, 49%), m.p. > 250 °C (decomp.) [Found: C, 52.9; H, 4.4; N, 34.5%; M^+ 203 (42.5%). $\text{C}_9\text{H}_9\text{N}_5\text{O}$ requires C, 53.2; H, 4.4; N, 34.5%; M 203]; δ_{H} ($[\text{}^2\text{H}_6\text{]} \text{DMSO}$, 300 MHz) 2.02 (dd, 3 H, CH_3 , J 7.0, 1.5 Hz),

6.7 (d, 1 H, =CH, J 15.5, 1.5 Hz), 7.4 (dq, 1 H, =CH, J 7, 15.5 Hz), 8.2 (br s, 1 H, NH) 8.6 (br s, 1 H, NH), 8.7 (s, 1 H, HCN_2), and 13.4 (br s, < 1 H, NH); ν_{max} (CHBr_3) 3 450m, 3 430s, 3 198s (NH), 1 684s ($\text{C}=\text{O}$), 1 578s, 1 559s, and 1 553s cm^{-1} ; λ_{max} (EtOH) 201.7 (ϵ 16 929), 238.1 (ϵ 25 355), and 321.4 (ϵ 5 812) nm.

(d) *2-Furfuraldehyde*. The aldehyde (0.36 g, 3.8 mmol) was added to a suspension of the imidazole (0.5 g, 3.7 mmol) in methanol (5 cm^3) and the mixture was stirred for 30 min, when TLC showed that all the starting material had disappeared. The solvent was removed on a rotary evaporator to give a dark yellow oil, which could not be crystallised using methanol–ether or acetone–ether. An acetone solution of the oil was purified by flash chromatography (silica 60 H; acetone eluant), and partial evaporation of the solvent from the first fraction gave an off-white solid (0.3 g). The mother liquor was evaporated further and left for 19 h to give a white precipitate (0.24 g). Finally, evaporation to dryness gave a dark solid (0.113 g). The first two fractions were combined, suspended in acetonitrile (250 cm^3), and heated at reflux temperature for 4 h, whereupon a white solid (0.35 g) which precipitated was filtered off and dried. The third fraction was heated in acetonitrile (250 cm^3) containing animal charcoal, and, after hot filtration and evaporation of the solvent, gave a white solid (0.06 g) identical to that isolated from the first two fractions. The combined yield of 2-(2'-furyl)-6-carbamoylpurine (**9e**) was 0.4 g (1.75 mmol, 47%), m.p. > 250 °C (decomp.) [Found: C, 52.3; H, 2.9; N, 30.3%; M^+ (EI) 229 (100%). $\text{C}_{10}\text{H}_7\text{N}_5\text{O}_2$ requires C, 52.4; H, 3.05; N, 30.6%; M 229]; δ_{H} ($[\text{}^2\text{H}_6\text{]} \text{DMSO}$, 60 MHz) 6.72 (dd, 1 H, J 4, 2 Hz), 7.61 (dd, 1 H, J 4 Hz), 7.95 (br s, 1 H), 8.05–8.35 (br s, 1 H, NH), 8.4–8.7 (br s, 1 H, NH), and 8.79 (s, 1 H, HCN_2); δ_{C} ($[\text{}^2\text{H}_6\text{]} \text{DMSO}$) 116.3 (C_β), 116.8 ($\text{C}_\beta + 5\text{-C}$), 148.9 (6-C + C_α), 154.3 (C_α), 154.5 (8-C), 156.1 (4-C), and 169.2 (2-C + CONH_2); ν_{max} (CHBr_3) 3 421s, 3 313s, 3 157m, 3 140m, 3 110m, 3 067m (NH), 1 690s ($\text{C}=\text{O}$), 1 663s, 1 586s, 1 560s, and 1 540m cm^{-1} ; λ_{max} (EtOH) 202.4 (ϵ 14 492), 278.7 (ϵ 19 348), and 338.6 (ϵ 5 291) nm.

Decomposition of 2,2-Dimethyl-6-carbamoyl-1,2-dihydropurine.—When a solution of the title compound (0.64 g, 3.3 mmol) in aqueous methanol (10 cm^3) was left at room temperature for 19 h shiny, transparent needles were formed. These were filtered and dried, and were tentatively identified as 5-amino-4-oxoacetamidoimidazole (0.29 g, 1.9 mmol, 57.6%), m.p. > 210 °C (decomp.) [Found: C, 39.1; H, 4.0; N, 36.4. $\text{C}_5\text{H}_7\text{N}_5\text{O}$ requires C, 38.9; H, 3.9; N, 36.2%; m/z (EI) 154.0497 (M^+) 100%, 110.0352 ($M - \text{CONH}_2$) 41.6%, 82.0404 ($M - \text{COCONH}_2$) 8.6%; δ_{H} (60 MHz, $[\text{}^2\text{H}_6\text{]} \text{DMSO}$) 7.0 (s, 1 H, NH), 7.5 (s, 1 H, CHN_2), 7.75 (s, < 1 H, NH), 7.95 (s, < 1 H, NH), 8.05 (s, < 1 H, NH), 8.20 (s, < 1 H, NH), 8.26 (s, < 1 H, NH), and 12.0 (br s, < 1 NH); δ_{C} ($[\text{}^2\text{H}_6\text{]} \text{DMSO}$) 113.9, 116.5, 114.8, 146.9, 160.7, 164.5, 169.8, 170.4, 174.3, and 175.0; ν_{max} (CHBr_3) 3 403s, 3 370s, 3 310s, 3 188s, 3 104s (NH), 1 698m, 1 681m, 1 600s, and 1 529s cm^{-1} ; λ_{max} (EtOH) 359.2 (ϵ 9 595) and 224.3 (ϵ 7 495) nm.

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