

Synthesis of 6-Cyano- and 6-Carbamoyl-purines and 6-Carbamoyl-1,2-dihydropurines from $[\text{MeC}\equiv\text{NMe}]^+\text{O}_3\text{SCF}_3$ and Diaminomaleonitrile

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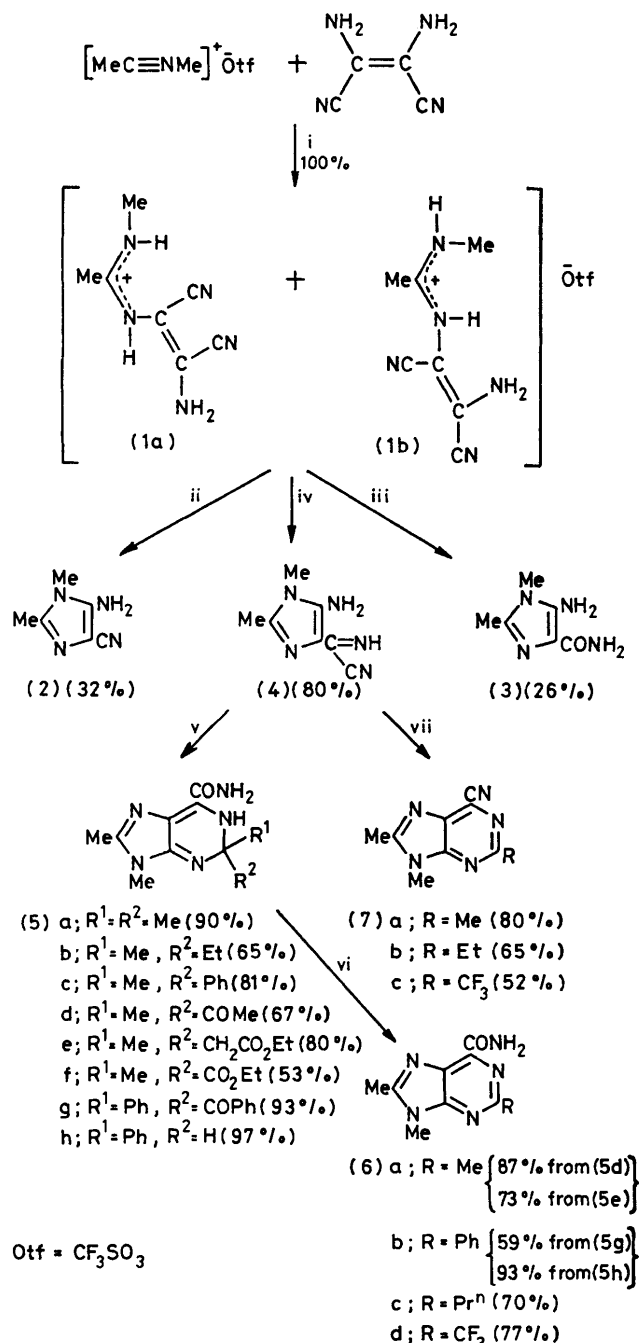
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Summary Diaminomaleonitrile reacts with *N*-methylacetoneitrilium trifluoromethanesulphonate to give, after base treatment, the 5-amino-4-(cyanoformimidoyl)imidazole (4) which forms 6-cyanopurines with carboxylic acid anhydrides, and with aldehydes, ketones, 1,2- and 1,3-diketones, and keto-esters gives 6-carbamoyl-1,2-dihydropurine derivatives from which 6-carbamoyl-purines can be obtained.

DIAMINOMALEONITRILE (DAMN), a tetramer of hydrogen cyanide,¹ has been implicated as an intermediate in the prebiotic synthesis of adenine,² and has also proved to be a useful reagent for the synthesis of a variety of heterocyclic compounds, such as 4,5-dicyanoimidazoles,³ 5,6-dicyanopyrazines,^{4,5} 2,3-dicyanodiazepines, and 2,3-dicyanodihydrodiazepines.⁶ We now report that addition of DAMN to a solution of $[\text{MeC}\equiv\text{NMe}]^+\text{O}_3\text{SCF}_3$ in dry nitromethane at room temperature affords a quantitative yield of the yellow amidinium salt (1), isolated as a mixture of the *cis*-(1a) and *trans*-(1b) isomers [¹H n.m.r., (CD₃)₂CO, Me₄Si internal reference, 60 MHz: (1a) δ 2.54 (s, CMe) and 3.23 (s, NMe); (1b) δ 2.43 (s, CMe) and 3.18 (s, NMe)] in the approximate ratio of 1.4:1 (Scheme). Basification of (1) with aqueous NaOH solution at room temperature gave (2), ν(C≡N) 2200 cm⁻¹, in 32% yield. When the salt (1) was boiled in NaOH solution for 30 min the product was the imidazole (3) isolated in 26% yield. Controlled basification of (1) to pH 8–9 with 1 M sodium carbonate solution gave an 80% yield of compound (4) as a pale yellow, crystalline solid. The i.r. spectrum of this compound showed no absorption in the ν(C≡N) region, but the spectrum of its hydrochloride derivative had a band of medium intensity at 2245 cm⁻¹.

Addition of an excess of acetone to (4) at room temperature resulted in a rapid, exothermic reaction with precipitation of the 6-carbamoyl-1,2-dihydropurine (5a) as orange-red crystals; the structure of this compound has been fully confirmed by a single-crystal X-ray structure analysis, details of which will appear elsewhere.⁷ Similar reactions occur with butan-2-one, acetophenone, butane-2,3-dione, ethyl acetoacetate, ethyl pyruvate, benzil, and benzaldehyde to give compounds (5b–h), respectively. The compounds (5a–c) can be recovered unchanged from solutions in chloroform or ethanol after several weeks, but solutions of (5d–f) in these solvents are slowly converted into the 6-carbamoyl-2-methylpurine (6a), which is insoluble and precipitates as white needles. In an analogous manner compounds (5g) and (5h) can be converted into the 6-carbamoyl-2-phenylpurine (6b). In the reactions between pentane-2,4-dione, butanal, and 1,1,1,5,5,5-hexafluoropentane-2,3-dione and compound (4) the intermediate dihydropurine derivatives were not isolated but the solution was kept at room temperature for several days to give the corresponding purines (6a), (6c), and (6d) in 65, 70, and 77% yield, respectively.

An immediate reaction occurs when an excess of a carboxylic acid anhydride is added to (4) at room temperature to give the 6-cyanopurines (7a–c) isolated as white crystal-



SCHEME. Reagents: i, dry MeNO₂, 20 °C, 18 h; ii, 2 M NaOH, pH 10–11, 20 °C; iii, 2 M NaOH, pH 10–11, reflux, 30 min; iv, 1 M Na₂CO₃, pH 8–9, 20 °C; v, R¹CO-R², neat or in ethanol, 20 °C, 5 min to 2 days; vi, solution in ethanol or CHCl₃, 20 °C, 1–2 days; vii, (RCO)₂O, 20 °C, 10 min.

All new compounds were fully characterised by microanalysis (C, H, and N), i.r., u.v., and ¹H n.m.r. spectroscopic data, and high resolution mass spectrometry. ¹³C N.m.r. spectra were also obtained for compounds (5a) and (7a).

line solids after addition of water and extraction with chloroform. These compounds showed either no absorption or only a very weak $\nu(\text{C}\equiv\text{N})$ absorption in the i.r. spectrum, as reported previously for other 6-cyanopurines.⁸ The structure of (7a) was confirmed by its hydrolysis with aqueous Na_2CO_3 solution to give the previously isolated 6-carbamoylpurine (6a) obtained in 71% yield; hydrolysis of (7a) with NaOH solution gave a 70% yield of the corresponding 6-carboxylic acid derivative.

The sequence of reactions described above and shown in the Scheme represents a new regioselective synthesis of

purines in which substituents in the 2-, 6-, 8-, and 9-positions of the purine nucleus can be introduced by a suitable choice of nitrilium salt and either carbonyl compound or acid anhydride.

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