Synthesis of 6-Cyano- and 6-Carbamoyl-purines and 6-Carbamoyl-1,2-dihydropurines from $[MeC{\equiv}NMe]O_3SCF_3$ and Diaminomaleonitrile

By BRIAN L. BOOTH,* and M. FERNANDA PROENÇA

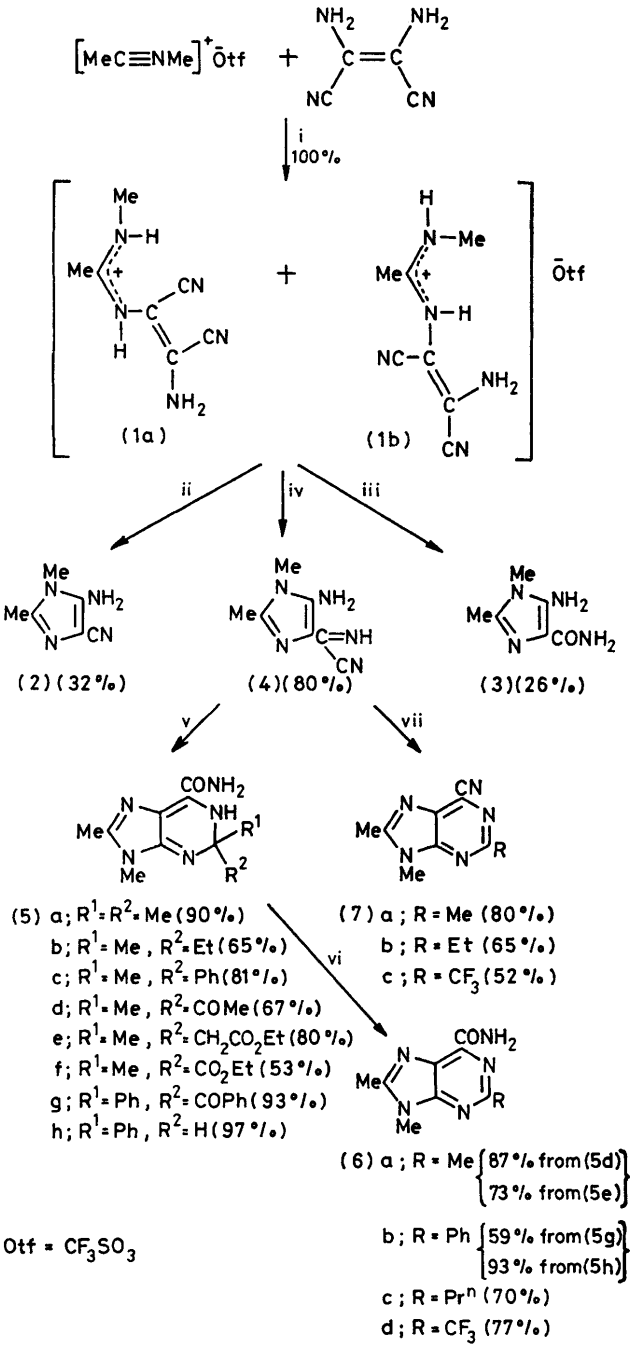
(*Department of Chemistry, University of Manchester Institute of Science and Technology, Manchester* M60 1QD)

Summary Diaminomaleonitrile reacts with *N*-methylacetonitrilium 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-carbamoylpurines 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.[5] We now report that addition of DAMN to a solution of $[MeC{\equiv}NMe]O_3SCF_3$[6] 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 [^{1}H n.m.r., $(CD_3)_2CO$, Me_4Si 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 $MeNO_2$, 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 Na_2CO_3, pH 8—9, 20 °C; v, R^1COR^2, neat or in ethanol, 20 °C, 5 min to 2 days; vi, solution in ethanol or $CHCl_3$, 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 ^{1}H n.m.r. spectroscopic data, and high resolution mass spectrometry. ^{13}C 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 ν(C≡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.

Thanks are due to Dr. B. Beagley and Dr. R. G. Pritchard of this Department for the *X*-ray crystal-structure determination, and to the Instituto Nacional de Investigação Cientifica, Portugal, for a maintenance grant (M. F. P.).

(*Received, 27th May* 1981; *Com.* 625.)

[1] H. Bredereck, G. Schmotzer, and E. Oehler, *Liebigs Ann. Chem.*, 1956, **600**, 81.
[2] R. A. Sanchez, J. P. Ferris, and L. E. Orgel, *J. Mol. Biol.*, 1967, **30**, 223; J. Oro and A. P. Kimball, *Arch. Biochem. Biophys.*, 1962, **96**, 293; R. F. Shuman, W. E. Shearin, and R. J. Tull, *J. Org. Chem.*, 1979, **44**, 4532.
[3] H. Wakamatsu, Y. Yamada, T. Saito, I. Kumashiro, and T. Takenishi, *J. Org. Chem.*, 1966, **31**, 2035; Y. Yamada, I. Kumashiro, and T. Takenishi, *ibid.*, 1968, **33**, 642; W. A. Sheppard and O. W. Webster, *J. Am. Chem. Soc.*, 1973, **95**, 2695.
[4] L. E. Hinckel, G. O. Richards, and O. J. Thomas, *J. Chem. Soc.*, 1937, 1432; W. Rasshofer and F. Vögtle, *J. Chem. Res.* (*S*), 1977, 265; Y. Ohtsuka, E. Tohma, S. Kojima, and N. Tomita, *J. Org. Chem.*, 1979, **44**, 4871.
[5] R. W. Begland, D. R. Hartter, F. N. Jones, D. J. Sam, W. A. Sheppard, O. W. Webster, and F. J. Weigert, *J. Org. Chem.*, 1974, **39**, 2341.
[6] B. L. Booth, K. O. Jibodu, and M. F. Proença, *J. Chem. Soc., Chem. Commun.*, 1980, 1151.
[7] B. Beagley, B. L. Booth, R. G. Pritchard, and M. F. Proença, *Acta Crystallogr.*, submitted for publication.
[8] A. Yamane, A. Matsuda, and T. Ueda, *Chem. Pharm. Bull.*, 1980, **28**, 150.