Arylidenemalononitriles in Heterocyclic Syntheses: a Novel Synthesis of Pyrido[2,3-*d*]pyrimidines

Mukti Gogoi, Pulakjyoti Bhuyan, Jagir S. Sandhu,* and Jogendra N. Baruah

Regional Research Laboratory, Jorhat 785006, India

Arylidenemalononitriles react with 6-amino and 6-hydroxyamino-1,3-dimethyl- and 3-methyl-pyrimidine-2,4(1*H*, 3*H*)-dione to give pyrido[2,3-*d*]pyrimidines in good yields.

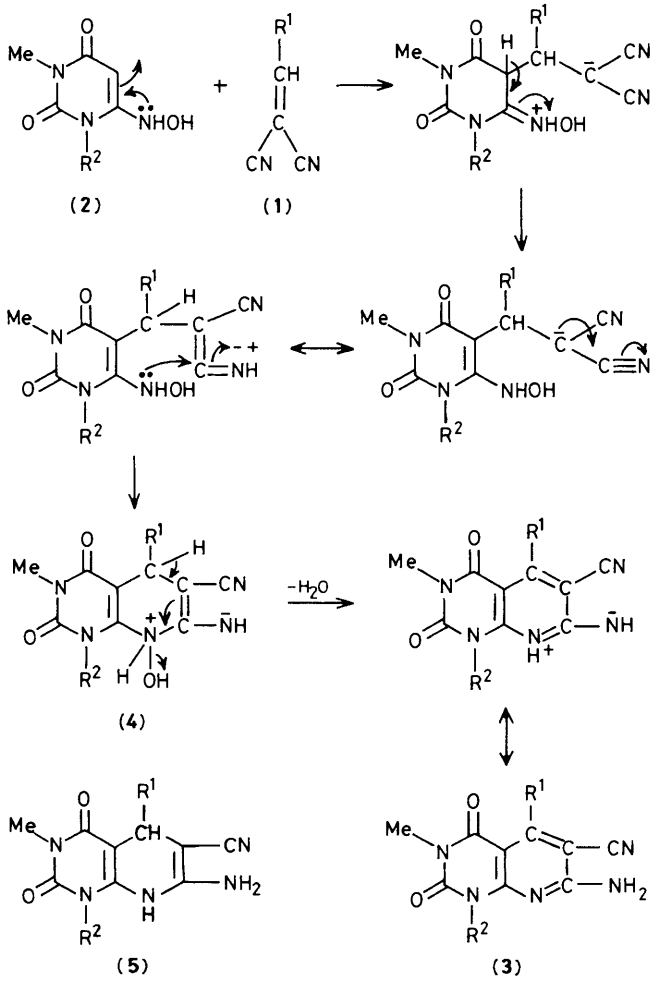
Ylidene nitriles are versatile tools for the construction of a variety of novel complex heterocycles.[1—3] We have developed a very simple and novel method which affords pyrido[2,3-*d*]pyrimidines in good yields.

The reaction of equimolar quantities of (**1a**) (0.01 mol) and (**2a**) (X = NH_2; 0.01 mol) in refluxing alcohol for 6 h, gave (**3a**) which could be crystallised from ethanol, m.p. 308—312 °C, in 80% yield on removal of solvent. The structure of (**3a**) is fully supported by spectral and microanalytical data [^{1}H n.m.r. (CF_3CO_2H)δ 2.90 (s, 3H), 3.42 (s, 3H), and 6.78—7.25 (m, 5H); i.r. $\nu_{max.}$ (KBr) 2195, 3300, and 3435 cm^{-1}; chemical ionisation mass spectrometry *m/z* M^+ 307]. Under identical conditions the 6-hydroxyamino analogue (X = NHOH) of (**2a**) gave the same product (**3a**) in 85% yield. In this case,

Table 1

Product (3)	M.p./°C	Yield %[a]	ν_{max}(KBr)/cm^{-1}	δ_H (60 MHz, CF_3CO_2H)	M^+
b	315—316	60 (65)	2190, 3300, 3440	2.87 (s, 3H), 3.26 (s, 3H), 3.50 (s, 3H), 6.57 (d, 2H), 6.8 (d, 2H)	337
c	305—307	85 (90)	2190, 3295, 3435	2.83 (s, 3H), 3.25 (s, 3H), 7.03 (d, 2H), 8.02 (d, 2H)	352
d	308—310	70 (75)	2195, 3295, 3440	2.35 (s, 3H), 2.87 (s, 3H), 3.29 (s, 3H), 6.92—7.32 (m, 4H)	321
e	320—321	80 (85)	2200, 3200, 3300, 3435	2.98 (s, 3H), 6.88—7.25 (m, 5H)	293
f	319—320	75 (80)	2195, 3195, 3305, 3430	2.85 (s, 3H), 3.10 (s, 3H), 6.65—6.92 (m, 4H)	323
g	319—320	82 (85)	2200, 3200, 3305, 3435	2.96 (s, 3H), 7.45 (d, 2H), 8.05 (d, 2H)	330

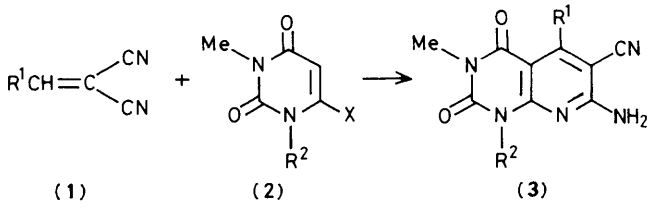
[a] Yields shown in brackets are those obtained from (**2**) when X = NHOH.



Scheme 1

although there was the possibility of the formation of the corresponding N(8)→O isomer of (**3**), we did not find any such product.†

† *Added in proof:* In 6-aminouracils the C(5)–C(6) double bond displays considerable enamine type character and electrophiles normally attack the C(5) position only (ref. 5).



X = NH_2, NHOH

	R^1	R^2
a	Ph	Me
b	*p*$MeOC_6H_4$	Me
c	*p*-$NO_2C_6H_4$	Me
d	*p*-MeC_6H_4	Me
e	Ph	H
f	*p*-$MeOC_6H_4$	H
g	*p*-$NO_2C_6H_4$	H

The versatility of this new heterocyclisation is demonstrated using the arylidenemalononitriles (**1b—g**) and the characteristics of the products (**3b—g**) thus obtained are given in Table 1.

A plausible mechanism for the formation of (**3**) is outlined in Scheme 1. In the case of X = NH_2 the proposed intermediate (**5**) can arise from a similar sequence to that which gives (**4**), to provide (**3**) by loss of H_2. This type of loss is well precedented.[4]

We thank CSIR New Delhi for the award of research fellowships to two of us (M. G. and P.B.)

Received, 25th June 1984; Com. 894

References

1 For recent reviews see: E. Campaigne and S. W. Schneller, *Synthesis*, 1976, 705; F. Freeman, *Chem. Rev.*, 1980, **80**, 329; *Synthesis*, 1981, 925.
2 B. R. Baker, 'Design of Site-directed Irreversible Enzyme Inhibitors,' Wiley, New York, 1967; R. K. Robins, 'Heterocyclic Compounds,' ed. R. C. Elderfield, New York, 1967, vol. 8; T. Sasaki, K. Minamato, T. Suzuki, and S. Yamashita, *Tetrahedron*, 1980, **36**, 865.
3 T. K. Bradshaw and D. W. Hutchison, *Chem. Soc. Rev.*, 1977, **6**, 43, and references cited therein.
4 F. Yoneda, T. Yano, and M. Higuchi, *Chem. Lett.*, 1979, 155.
5 J. S. Kim, R. Niess, and A. D Broom, *J. Org. Chem.*, 1972, 578 and references cited therein.