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4-AMINOPYRAZOLO[3,4-d]PYRIMIDINES

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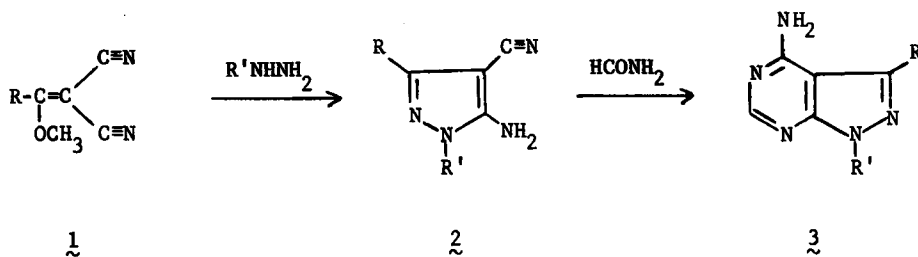
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4-AMINOPYRAZOLO[3,4-d]PYRIMIDINES

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Interest in the derivatives of 4-aminopyrazolo[3,4-d]pyrimidine (3) has continued because of the activity of the parent compound (3, R = R' = H) against a wide spectrum of tumors.¹ More recently, several new derivatives of 4-aminopyrazolo[3,4-d]pyrimidine have been prepared and found to possess antitumor^{2,3} and antimicrobial⁴ activities. We recently described the preparation of several 4,6-diamino- and 4-aminopyrazolo[3,4-d] pyrimidine derivatives with variations in substitution at the 1- and 3- positions.⁵ In this paper, we report the preparation of seven new 4-aminopyrazolo[3,4-d]pyrimidine derivatives (3) which were obtained by the reaction of 5-amino-4-cyanopyrazoles (2) with formamide. The intermediate 5-amino-4-cyanopyrazoles (2) were obtained by the reaction of methoxymethylenemalononitrile derivatives (1) with hydrazine, methylhydrazine or arylhydrazines (Scheme I). Results are recorded in Tables I and II.



SCHEME I

TABLE I. 5-Amino-4-cyanopyrazoles (2)

2		mp. (°C)	Yield ^a (%)	2 Formula	Analysis ^d Calcd. (Found)		
R	R'				C	H	N
4-CH ₃ O-C ₆ H ₄	H	180-181	62(A)	C ₁₁ H ₁₀ N ₄ O ^b	61.67 (61.49)	4.71 (4.55)	26.16 (26.03)
4-CH ₃ -C ₆ H ₄	CH ₃	161-162	78(C)	C ₁₂ H ₁₂ N ₄	67.90 (67.97)	5.70 (5.50)	26.40 (26.17)
4-CH ₃ -C ₆ H ₄	4-Cl-C ₆ H ₄	174-175	45(B)	C ₁₇ H ₁₃ ClN ₄ ^c	66.13 (66.35)	4.21 (4.37)	18.15 (18.15)
4-Cl-C ₆ H ₄	2,4-Cl ₂ C ₆ H ₃	210-211	36.5(C)	C ₁₆ H ₉ Cl ₃ N ₄ ·1.5 H ₂ O	49.16 (49.80)	3.07 (2.96)	14.34 (14.50)

- a) A indicates crystallization from water; B from ethanol; C from aqueous ethanol.
- b) Ir (Nujol): 2.96, 3.00, 3.12 (NH), 4.46 (C≡N), 6.08, 6.18, 6.30, 6.50, 6.60, 6.69, 7.75, 7.98, 8.50, 9.30, 9.74, 10.40, 12.05, 13.00, 13.56 μm; NMR (CDCl₃-trifluoroacetic acid (TFA)); δ 3.98 (s, 3, OCH₃); 7.10-7.93 (q, J = 9Hz, 4, aromatic).
- c) Ir (Nujol): 2.82, 2.95 (NH), 4.48 (C≡N), 6.16, 6.42, 9.26, 10.00, 10.24, 12.14, 13.3, 12.28, 13.78 μm. NMR (CDCl₃-TFA); δ 2.47 (s, 3, CH₃); 7.20-7.87 (m, 8, aromatic).
- d) Microanalyses by M-H-W Laboratories, Phoenix, Arizona.

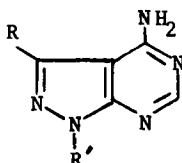
EXPERIMENTAL

5-Amino-4-cyanopyrazoles (2). - Compounds in which R'=H or CH₃ were obtained essentially by the methods described⁵ for similar compounds. 1,3-Diaryl-5-amino-4-cyanopyrazoles were obtained as follows.

An arylhydrazine hydrochloride was added to an equimolar quantity of 0.5 molar ethanolic sodium ethoxide. An equimolar amount of arylmethoxymethylenemalononitrile⁵ was then added in small portions and the mixture was refluxed for 60-90 minutes on a steam bath. The mixture was then cooled and the product was collected by filtration. In the case of 5-amino-3-(p-chlorophenyl)-1-(2,4-dichlorophenyl)pyrazole-4-carbonitrile

the product did not separate on cooling. The solution in this case was evaporated to dryness and water was added to the residual paste to obtain a reddish solid. The crude samples were washed with petroleum ether (bp 30-60°C) to remove a red color and purified by crystallization from the solvents indicated in Table I.

TABLE II. 4-Aminopyrazolo[3,4-d]pyrimidines (3)



R	R'	mp. (°C)	Yield ^a (%)	Formula	Analysis ^d		
					Calcd. C	Calcd. H	(Found) N
4-CH ₃ OC ₆ H ₄	H	304-305	40.4 (A)	C ₁₂ H ₁₁ N ₅ O	59.74 (59.75)	4.60 (4.36)	29.03 (29.23)
4-CH ₃ OC ₆ H ₄ CH ₂	H	266	65 (B)	C ₁₃ H ₁₃ N ₅ O ^b	61.16 (60.90)	5.13 (4.88)	27.44 (27.49)
CH ₃	3-Cl-4-CH ₃ C ₆ H ₃	218-219	66 (A)	C ₁₃ H ₁₂ ClN ₅	57.04 (56.86)	4.39 (4.20)	25.59 (25.57)
CH ₃	4-Cl-2-CH ₃ C ₆ H ₃	256-257	66 (B)	C ₁₃ H ₁₂ ClN ₅	57.04 (56.99)	4.39 (4.19)	25.59 (25.70)
4-CH ₃ C ₆ H ₄	CH ₃	183-184	61 (A)	C ₁₃ H ₁₃ N ₅	65.25 (65.22)	5.48 (5.50)	29.27 (29.28)
4-CH ₃ C ₆ H ₄	4-ClC ₆ H ₄	288-289	64 (B)	C ₁₈ H ₁₄ ClN ₅ ^c	64.38 (64.21)	4.17 (4.22)	20.86 (20.84)
4-ClC ₆ H ₄	2,4-Cl ₂ C ₆ H ₃	237-238	67 (B)	C ₁₇ H ₁₀ Cl ₃ N ₅	52.24 (52.48)	2.56 (2.47)	17.92 (17.80)

a) A indicates crystallization from aqueous ethanol; B, from absolute ethanol.

b) Ir (Nujol): 2.86, 2.98, 6.00, 6.28, 6.60, 7.60, 7.80, 8.00, 9.70, 12.45, 12.70, 13.20 μm. NMR (CDCl₃-TFA): δ 3.95 (s, 3, OCH₃); 4.50 (s, 3, CH₂); 6.97-7.37 (q, J = 9Hz, 4, aromatic); 8.63 (s, 1, H at 6-position).

c) Ir (Nujol): 2.86, 3.02 (NH), 6.02, 6.30, 6.40, 6.65, 7.64, 9.18, 10.10, 11.90, 12.52 μm. NMR (CDCl₃-TFA): δ 2.50 (s, 3, CH₃); 7.40-7.80 (m, 8, aromatic); 8.54 (s, 1, H at 6-position).

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4-Aminopyrazolo[3,4-d]pyrimidines (3). - The 5-amino-4-cyanopyrazole (1.0 g) was added to 10 ml of formamide. The mixture was refluxed for 2 or 3 hours then poured into water. The solid that precipitated was collected by filtration and purified by crystallization from ethanol or aqueous ethanol. Results are recorded in Table II.

REFERENCES

1. R. K. Robins, *J. Med. Chem.*, 7, 186 (1964) and references therein.
2. C. I. Hong, N. C. De, G. L. Tritsch and G. B. Chheda, *J. Med. Chem.*, 19, 555 (1976).
3. E. Hayashi, T. Higashino, S. Suzuki, T. Kato, M. Kohno, H. Shinoda and D. Mizuno, *Yakugaku Zasshi* (1977), 97, 1328; *Chem. Abstr.* 88, 121096m, (1978).
4. G. A. Howarth and J. Gainer, U.S. Patent 4,044,130; *Chem. Abstr.* 87, 189471q, (1976). See also H. Friedman, German Patent 2,521,046; *Chem. Abstr.* 84, 59476x, (1976).
5. P. L. Southwick and B. Dhawan, *J. Heterocyclic Chem.*, 12, 1199 (1975).