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REACTION OF NITRILES UNDER ACIDIC CONDITIONS: A NOVEL, DIRECT FORMATION OF CONDENSED 4-CHLOROPYRIMIDINES

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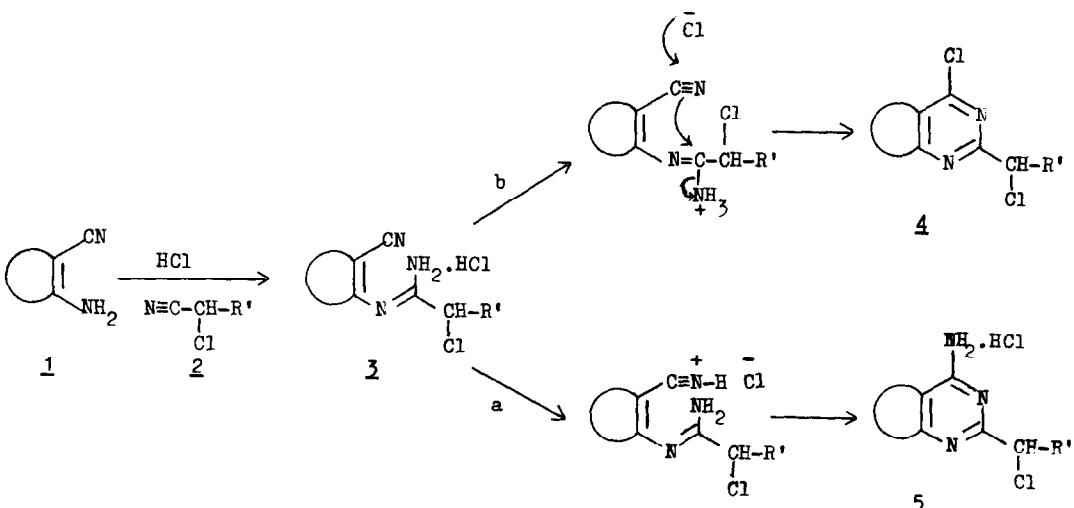
Summary: An unusual formation of condensed 4-chloropyrimidines in the reaction of o-aminonitriles with halogenoacetonitriles in the presence of dry hydrogen chloride gas is described.

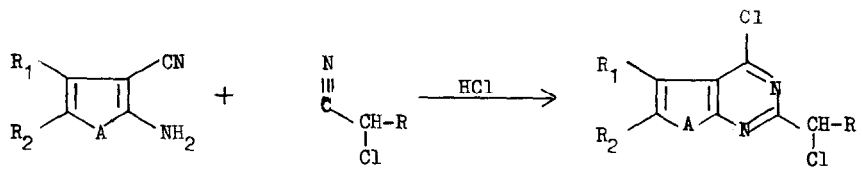
We have earlier described[1,2] a facile one-pot synthesis of fused pyrimidines by the reaction of nitriles with o-aminocarbonyl compounds in the presence of dry hydrogen chloride gas. We have now observed the unusual direct formation of condensed 4-chloropyrimidines 4 instead of the normally expected 4-aminopyrimidines 5 in the condensation of o-aminonitriles 1 with certain halogenoacetonitriles 2. Thus, passing a stream of dry hydrogen chloride gas through a mixture of the reactants in dioxane at 5-10°C for 8 hours and the usual work-up of the reaction mixture yielded the condensed 4-chloropyrimidines presented in Table I.

The exclusive formation of 4-chloropyrimidines 4 over that of 4-aminopyrimidines 5 can be rationalized as occurring through the preferential cyclization of the initially formed amidine intermediate 3 by the pathway 'b' which may be attributed to the increased electrophilicity of the amidine carbon and the decreased nucleophilicity of the amidine nitrogen in the intermediate 3, as a consequence of the electron withdrawing effect of the chlorine atom (Scheme I).



Scheme I

Table I



R_1	R_2	A	R	Mol. Formula[a]	Mass[b] M^+	M.P. °C	Yield %
H	H	CH=CH	H	$C_9H_6N_2Cl_2$	212	100-102[c]	85
H	H	CH=CH	Cl	$C_9H_5N_2Cl_3$	246	135-137	87
$-(CH_2)_4-$		S	H	$C_{11}H_{10}N_2SCl_2$	272	98-100	69
$-(CH_2)_4-$		S	Cl	$C_{11}H_9N_2SCl_3$	306	118-120	78
CH_3	CH_3	S	H	$C_9H_8N_2SCl_2$	246	141-143	73
C_6H_5	C_6H_5	O	H	$C_{19}H_{12}N_2OCl_2$	354	120-122	58

a) All the compounds were recrystallized from hexane. All the compounds gave correct analysis. b) Mass spectra were recorded on a Varian-Atlas CH-7 mass spectrometer at 70 ev ionizing beam using direct insertion probe. c) Ref. No. 3; Reported M.P. 95-96°C.

This novel cyclization bears a formal resemblance to the cyclization of α,ω-dinitriles and analogues to halogenoazines[4] and of o-cyanophenyl isocyanates to 4-halogenoquinazolin-2-ones[5], catalyzed by halogen acids. A detailed paper on the mechanism and the scope of this reaction, as well as, the factors influencing the formation of 4-chloro- and 4-amino- condensed pyrimidines in the condensation of electronegatively substituted nitrile derivatives with o-aminonitriles will be published shortly.

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