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SYNTHESIS OF 2- AND 4-IMINO(1,2-*a*)PYRIDOPYRIMIDINES FROM ALLENIC NITRILES AND 2-AMINOPYRIDINES

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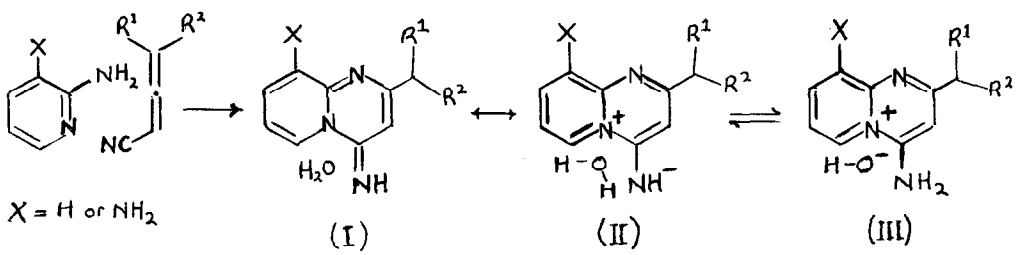
4,4-Dialkylallenyl nitriles and 2-aminopyridines give 2-alkyl-4-iminopyrido(1,2-*a*)pyrimidines as monohydrates in about 90% yield and 4-monoalkylallenyl nitriles similarly give 4-alkyl-2-imino(1,2-*a*)pyrimidines.

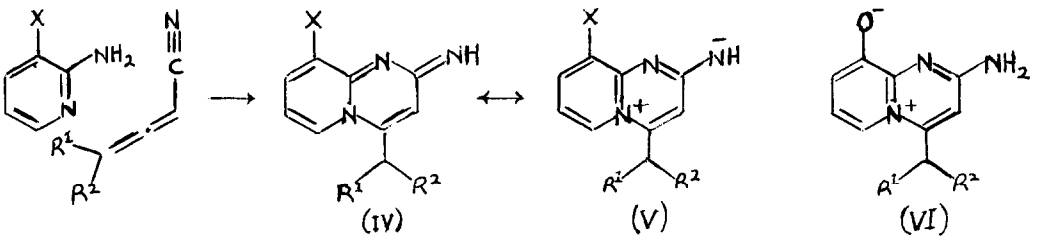
Pyrido(1,2-*a*)pyrimid-4-ones have recently been shown to possess antiatherosclerotic, antipyretic, analgesic and analgetic properties and some are now in clinical use[1]. We now report the synthesis of the closely related 4-iminopyrido-(1,2-*a*)pyrimidines and some 2-iminopyrido(1,2-*a*)pyrimidines from readily available allenic nitriles[2].

When 4,4-dialkylallenyl nitriles are heated under reflux with 2-amino- or 2,3-diaminopyridine in alcoholic solution for 48 hours 2-alkyl-4-iminopyrido(1,2-*a*)-pyrimidines are formed in excellent yield (see Table). 4-Iminopyrido)1,2-*a*)-pyrimidines, which are isolated as monohdrates, show a typical absorption pattern in the u.v. region (neutral conditions) with λ_{max} near 242, 250, and 323 nm. (cf. u.v. of 2-alkyl-4-oxopyrido(1,2-*a*)pyrimidines[3]), strongly hydrogen-bonded hydroxyl in the i.r. and a deshielded OH proton in the n.m.r. spectrum. The spectroscopic data and elemental and mass spectral analyses are rationalised by structures (I), (II) and (III).



However, when 4-monoalkylallenyl nitriles are similarly heated with 2-aminopyridine, 4-alkyl-2-iminopyrido(1,2-*a*)pyrimidines are formed. 2-Iminopyrido(1,2-*a*)-pyrimidines do not form hydrates and show a typical u.v. absorption pattern with λ_{max}

near 231, 281, 290, and 326 (cf. u.v. of 4-alky-2-oxopyrido(1,2-α)pyrimidines[3]) and comparatively high melting points (275-285°). 3,3-Dimethylallene-1-carbonitrile can give both 4-imino- and 2-iminopyridopyrimidines under slightly different conditions. 3-hydroxy-2-aminopyridine gives only anhydrous 2-imino compounds with mono or dialkylallene nitriles.



Apparently steric interference by the 4-alkyl groups on the allenyl nitrile to the approach of the less accessible ring nitrogen tips the balance in favour of prior nucleophilic attack by the side chain amino group at the Michael position for 4,4-disubstituted allenyl nitriles to yield 4-iminopyridopyrimidines. Furthermore, modification of the nucleophilic properties of the 2-amino groups by substituents in the 3-position of the 2-aminopyridine may lead to 2-iminopyridopyrimidines (as in the case of the hydrogen bonded 3-OH) or 4-imino compounds (as with 3-NH_2).

TABLE. 4-Imino and 2-Iminopyrido(1,2-α)pyrimidines*

	R^1	R^2	X	Yield	m.p.°	λ_{max} (ε) [neutral conditions]
4-imino-compounds	Me	Et	H	90%	124	242(8,900),250(8,700),323(36,600)
(I,II and III)	Me	Pr	H	87	156	241(11,000),251(10,600),323(43,800)
	Et	Et	H	90	162	241(8,700),250(8,400),324(34,000)
	Me	Et	NH_2	88	120	244(24,400),298(18,100),339(41,000)
	Me	Pr	NH_2	92	126	244(27,900),299(20,200),338(45,100)
	Et	Et	NH_2	94	139	244(26,500),299(19,400),338(43,600)
2-imino-compounds	Me	Me	H	90	275	231(19,300),281(8,300),290(8,400),326(2100)
(IV)&(V)	Pr	H	H	92	286	231(18,200),282(7,800),290(7,800),326(2100)
(VI)	Me	Et	OH	90	142	204(15,400),246(14,000),370(7,200)
"	Et	Et	OH	92	155	204(15,200),246(13,000),370(7,200)

References and Notes

1. Z. Meszaros, Kem. Kozl., 1978, 50, 173.
2. P.M. Greaves, S.R. Landor and D.R.J. Laws, J.Chem.Soc.(C), 1968,291.
3. R. Adams and I.J. Pachter, J.Amer.Chem.Soc., 1952, 74, 5491.

* All new compounds gave satisfactory elemental analyses and spectroscopic properties in accord with these structures.

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