A NOVEL SYNTHESIS OF SOME ANNELATED PYRIMIDINES : REACTION OF 6-HYDROXYLAMINO-1,3-DIMETHYLPYRIMIDINE-2,4-DIONE WITH IMINES AND α -CHLOROIMINES

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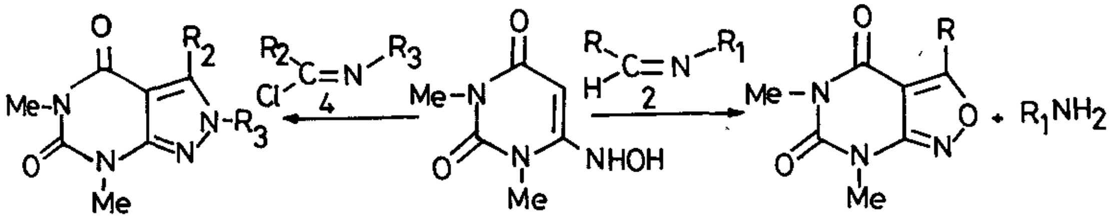
Abstract - Reaction of imines and α-chloroimines with 6-hydroxylamino-1,3-dimethylpyrimidine-2,4-dione gives isoxazolo[3,4-d]and pyrazolo[3,4-d]pyrimidines respectively in good yields.

The purine and pyrimidine nuclei are present in nucleic acids, nucleotides and several other naturally occurring biologically active substances. Because of this purine and pyrimidine derivatives occupy a unique position of significance and there has been tremendous effort to synthesize novel heterocycles having an annelated pyrimidine nucleus[1,2,3]. Several approaches have been reported to construct heterocycles on C-5, C-6 double bond of substituted uracils[4]. In this communication we describe a novel and facile method of synthesizing isoxazolo[3,4-d] and pyrazolo[3,4-d]pyrimidines.

6-Hydroxylamino-1,3-dimethylpyrimidine-2,4-dione 1[5] (1.71 g, 0.01 mol) and imine 2a (1.09 g, 0.01 mol) on stirring at room temperature for 3 h in absolute alcohol (15-20 ml), on concentration of the reaction mixture gave a solid 3a crystallizable from alcohol, mp 205°C in 63% yield. ^{1}H-NMR ($CDCl_3$) δ : 3.10 (3H,s), 3.25 (3H,s), 6.45 (1H,q,furan H_4), 7.50 (1H,d,furan H_3), 7.95 (2H,d, furan H_5). The mass spectrum of 3a showed molecular ion at m/e 247. When 2b was used the same compound 3a was obtained which clearly proved the elimination of amine part and was further confirmed by isolating the amine from the mother liquors (tlc). Use of 2c-d gave 3c in 70% yield[6].

In contrast when α -chloroimines were used the imine nitrogen was involved in the pyrazolo ring formation. When equimolar quantities of 1 and α -chloroimine 4a in the presence of dry triethylamine were refluxed in dry benzene for 2 h, a crystalline solid was obtained. This material on purification and crystallization gave 5a, mp 208°C, in 70% yield. ^{1}H-NMR (TFA) δ : 2.75 (3H,s), 2.98 (3H,s), 6.8-7.2 (10H,m). The mass spectrum of 5a showed molecular ion at m/e 332. Similarly were obtained 5b-d in good yields.



5 1 3

	R	R_1	R_2	R_3
(a)	2-furyl	Me	Ph	Ph
(b)	2-furyl	$C_6H_4OMe(p)$	Ph	$C_6H_4OEt(p)$
(c)	Ph	Me	Ph	$C_6H_4Me(p)$
(d)	Ph	$C_6H_5CH_2$	Ph	$C_6H_4Cl(m)$

Regarding the reaction mechanism involved in these transformations, the reaction appears to be triggered by the attack of electron rich C-5 position onto the imine carbon followed by cyclisation. However, further work is in progress to understand the mechanism as well as the scope of the reaction.

REFERENCES AND NOTES

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4. T. K. Bradshaw and D. W. Hutchison, Chem. Soc. Rev., 6, 43 (1977) and references cited therein.
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6. (a) We do not believe 2a-d can undergo simple hydrolytic cleavage because on stirring 2 alone in alcohol under identical conditions no such cleavage could be detected. (b) All the new compounds reported gave satisfactory spectral as well as analytical data.

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