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A NOVEL SYNTHESIS OF 2,4-DIOXO-1,2,3,4-TETRAHYDRO-PYRROLO[2,3-d]PYRIMIDINE DERIVATIVES

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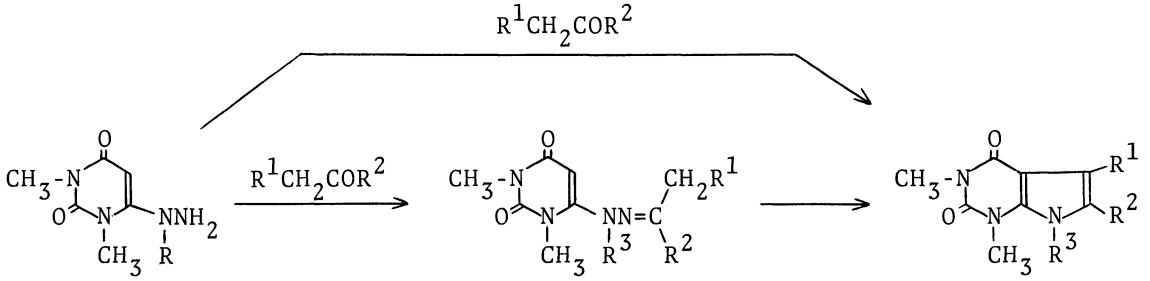
6-Hydrazinouracil derivatives were allowed to react with ketones or aldehydes to give 5,6-disubstituted 2,4-dioxo-1,2,3,4-tetrahydropyrrolo[2,3-d]pyrimidine derivatives. The mechanism for the formation of these compounds is presented.

Up to now, some 2,4-dioxo-1,2,3,4-tetrahydropyrrolo[2,3-d]pyrimidines or 7-deazaxanthines have been synthesized by J. Davoll[1], R. K. Robins[2], and E. C. Taylor[3].

The authors studied a new method for the synthesis of 5,6-disubstituted 2,4-dioxo-1,2,3,4-tetrahydropyrrolo[2,3-d]pyrimidine derivatives by heating 6-hydrazinouracil derivatives[4] with ketones or aldehydes. Thus 6-hydrazino-1,3-dimethyluracil (Ia) was refluxed in a mixture of methyl ethyl ketone and xylene and the resulting hydrazone (IIa) was refluxed in ethyleneglycol or tetraline for 2 to 3 hours to give 1,3,5,6-tetramethyl-2,4-dioxo-1,2,3,4-tetrahydropyrrolo-[2,3-d]pyrimidine (IIIa) with the evolution of ammonia (Method A). When Ia was refluxed in methyl ethyl ketone-ethyleneglycol or in methyl ethyl ketone-tetraline, IIIa could be directly obtained in a high yield without an isolation of the intermediate IIa (Method B). On heating Ia with a acidic catalyst such as $ZnCl_2$ or conc. H_2SO_4, a pyrrole ring closure was unsuccessful.

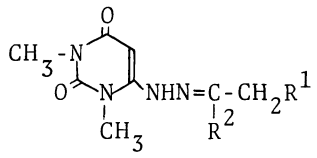


Ia: R = H [4a]
Ib: R = CH_3 [4b]

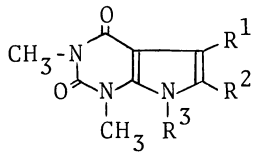
IIa — IId

IIIa — IIIg

In accordance with the above synthetic method, some hydrazone compounds (11b--d) and 5,6-disubstituted 2,4-dioxo-1,2,3,4-tetrahydropyrrlo[2,3-d]pyrimidines (111b--g) were also prepared.

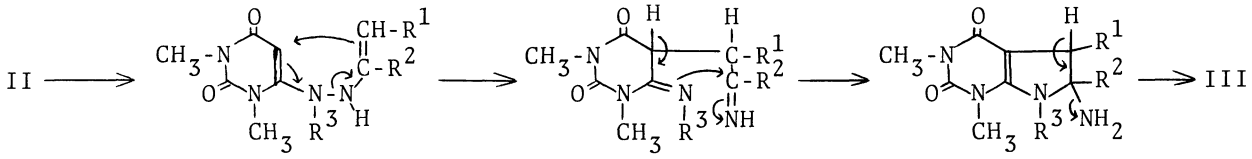


Compd. No.	R^1	R^2	mp (°C)
IIa	CH_3	CH_3	132-134
IIb	CH_3	H	203
IIc	C_6H_5	H	168
IId	H	CH_3	147-148



Compd. No.	R^1	R^2	R^3	mp (°C)	Method
IIIa	CH_3	CH_3	H	>300	A,B
IIIb	CH_3	H	H	>300	A
IIIc	C_6H_5	H	H	287	A
IIId	H	CH_3	H	>300	A
IIIe	CH_3	CH_3	CH_3	233-234	B
IIIf	CH_3	C_6H_5	H	285	B
IIIg	$(CH_2)_4$		H	>300	B

The mechanism for the formation of the 7-deazaxanthine derivatives can be considered that a pyrrole ring closure proceeds as in the case of Fischer's indole synthesis.



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