HETEROCYCLES, Vol. 6, No. 11, 1977

A NEW SYNTHESIS OF 6-HYDROXYPTERIDINE DERIVATIVES

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Treatment of 6-amino-1,3-dimethyl-5-nitrosouracil with phenacylpyridinium halides in pyridine containing aqueous sodium hydroxide gave the corresponding 7-aryl-6-hydroxy-1,3-dimethyllumazines.

We wish to report a new synthetic route to 6-hydroxypteridine derivatives (i.e., 7-aryl-6-hydroxy-1,3-dimethyllumazines; IIIa-g) by the reaction of 6-amino-1,3-dimethyl-5-nitrosouracil (I) with phenacylpyridinium halides (IIa-g) in pyridine containing aqueous sodium hydroxide.

Refluxing (I)(0.001 mol) with phenacylpyridinium bromide (IIa) (0.001 mol) in pyridine (3 ml) containing 1N sodium hydroxide (1 ml) for 1 hr afforded a good yield of 6-hydroxy-1,3-dimethyl-7-phenyllumazine (IIIa), which was isolated by evaporation of the reaction mixture and addition of ethanol. The structure of (IIIa) was confirmed by its conversion to the known 1,3-dimethyl-7-phenyllumazine (V)[1,2] *via* 6-chloro-1,3-dimethyl-7-phenyllumazine (IV).[3]

This reaction was equally applicable to other phenacylpyridinium halides (IIb-g) to give the corresponding 7-aryl-6-hydroxy-1,3-dimethyllumazines (IIIb-g)(Scheme I)(Table).[4]

Scheme I

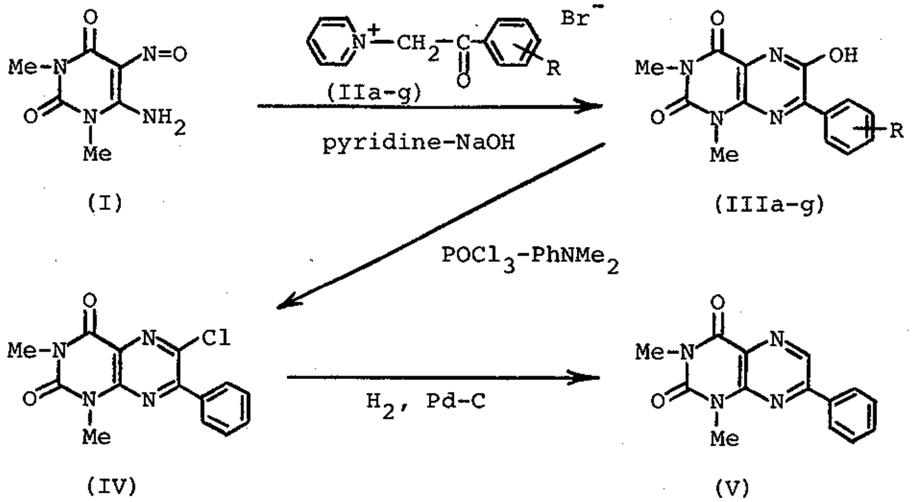


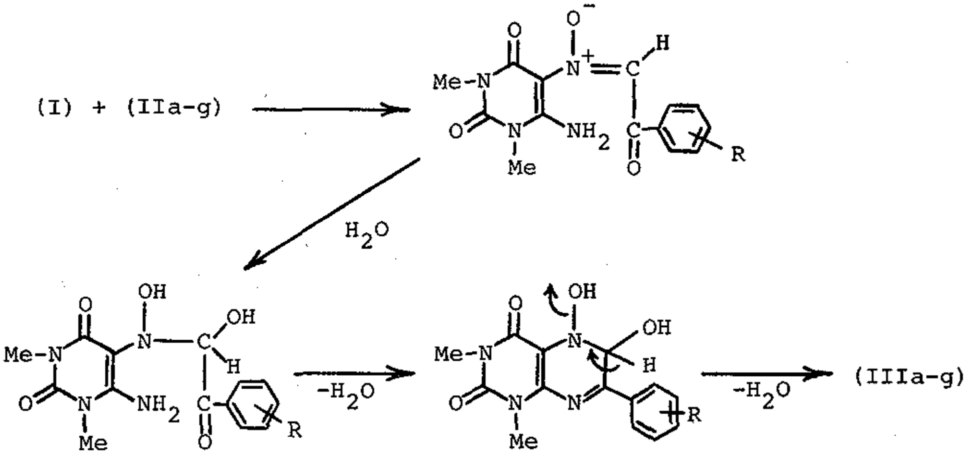
Table Formation of 7-Aryl-6-hydroxy-1,3-dimethyllumazines (III)

Phenacyl-pyridinium halide	R	Product[a)]	Mp(°C)	Yield(%)
IIa	H	IIIa	>300	71
IIb	4-Br	IIIb	>300	68
IIc	4-Cl	IIIc	>300	55
IId	4-Me	IIId	291-292	64
IIe	4-OMe	IIIe	299.5-300	68
IIf	2,5-OMe$_2$	IIIf	261-262	67
IIg	4-Ph	IIIg	284	69

a) All products were recrystallized from DMF.

As depicted in the Scheme II, this new 6-hydroxypteridine synthesis probably involves the initial formation of the pyrimidine nitrone, followed by nucleophilic addition of water,[5] and subsequent cyclization and aromatization by the elimination of water.[6]

Scheme II



REFERENCES AND NOTES

1 K. Senga, H. Kanazawa, and S. Nishigaki, J.C.S. Chem. Comm., 1976, 588.

2 In the reaction of (I) with (IIa), a trace amount of (V) was also obtained from the filtrate which removed (IIIa).

3 Refluxing (IIIa)(0.002 mol) in phosphorus oxychloride (4 ml) containing N,N-dimethylaniline (0.004 mol) for 4.5 hr gave (IV) (94%, mp 203-205° from ethanol), which was then converted to (V) (47%, mp >300° from ethanol) by the catalytic dechlorination

over palladium-carbon in ethanol.

4 Satisfactory analytical and spectral data were obtained for all products.

5 Refluxing (I)(0.001 mol) with (IIa)(0.001 mol) in pyridine (3 ml) containing water (1 ml) for 1 hr provided (IIIa) in 46% yield.

6 An analogous mechanism has been reported in the synthesis of 6-thiopteridines: W.W. Parish and H.S. Broadbent, J. Heterocycl. Chem., 1971, **8**, 527.

Received, 26th July, 1977