NITROSATIVE CYCLIZATION OF 1,3-DIMETHYL-6-(α-METHYLBENZYLIDENEHYDRAZINO)URACILS TO 6-ARYL-1,3-DIMETHYLLUMAZINES

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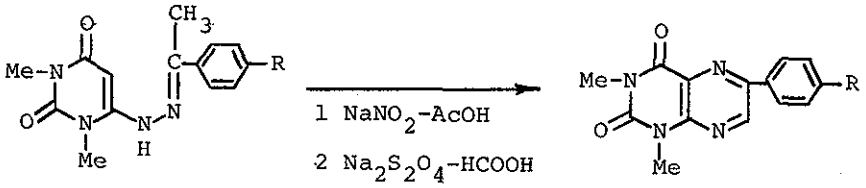
The reaction of 1,3-dimethyl-6-(α-methylbenzylidenehydrazino)uracils with sodium nitrite in acetic acid, followed by treatment with sodium dithionite in formic acid furnished the corresponding 6-aryl-1,3-dimethyllumazines.

We have recently described a new approach to the synthesis of v-triazolo[4,5-d]pyrimidines bearing vinyl substituents at position 2 by the nitrosative cyclization of 1,3-dimethyl-6-(α-methylalkylidene (or α-methylbenzylidene)hydrazino)uracils using N-nitrosodimethylamine-phosphorus oxychloride mixture.[1] We report here a different type of nitrosative cyclization of 1,3-dimethyl-6-(α-methylbenzylidenehydrazino)uracils (Ia-e) with sodium nitrite in acetic acid leading to 6-aryl-1,3-dimethyllumazines (IIa-e).

The key intermediates, (Ia-e), were prepared by the condensation of 1,3-dimethyl-6-hydrazinouracil[2] with the appropriate acetophenones according to the reported procedure.[1]

A mixture of (Ia) (0.002 mol) and sodium nitrite (0.006 mol) in acetic acid (5 ml) was stirred at room temperature for 30 min, and the mixture was brought to reflux for 3 hr. Evaporation of the reaction mixture, followed by addition of 50% aqueous ethanol caused the separation of crude product.[3] Treatment of the crude product with excess sodium dithionite in formic acid at 150° for 3 hr afforded 1,3-dimethyl-6-phenyllumazine (IIa), which was identical with the authentic sample reported by Angier.[4] Likewise, the reaction of other 1,3-dimethyl-6-(α-methylbenzylidenehydrazino)uracils (Ib-e) with sodium nitrite in acetic acid, followed by treatment with sodium dithionite in formic acid provided the corresponding 6-aryl-1,3-dimethyllumazines (IIb-e)(Table).



(I) (II)

This anomalous reaction involves without doubt the nitrosative cyclization, however, the definite mechanism for the formation of (II) is currently under investigation.

The yields of (IIa-e) have so far reached 10-15% but have not yet been optimized.

Table Formation of 6-Aryl-1,3-dimethyllumazines (II)

Starting Material[a] (Mp, °C; Yield, %)	R	Product[b] (Mp, °C; Yield, %)
Ia (203-205; 72)	H	IIa (273-275; 13)
Ib (209-210; 58)	Br	IIb (265-267; 10)
Ic (214-216; 70)	Cl	IIc (254-256; 10)
Id (166-168; 50)	Me	IId (234-236; 15)
Ie (178-180; 55)	OMe	IIe (237-238; 15)

a) All compounds were recrystallized from EtOH.

b) All compounds were recrystallized from DMF-EtOH and the yields were calculated on the basis of (I).

REFERENCES AND NOTE

1 K. Senga, Y. Kanamori, S. Nishigaki, and F. Yoneda, Chem. Pharm. Bull., 1976, 24, 1917.

2 W. Pfleiderer and K.H. Schündehütte, Ann., 1958, 612, 158.

3 The mass spectrum of the crude product revealed a strong parent ion (m/e 268) and a weak M+16 ion. The M+16 ion was disappeared when the crude product was treated with sodium dithionite in formic acid. These facts suggested that the crude product was a mixture of (IIa) and a small amount of its 5-oxide, however, we have no additional data at this time to prove this.

4 R.B. Angier, J. Org. Chem., 1963, 28, 1398.

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