A NEW, FACILE SYNTHESIS OF 10-ARYLISOALLOXAZINES

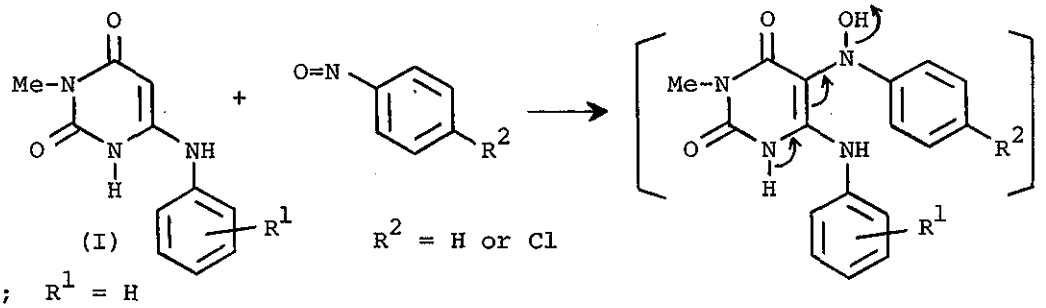
Fumio Yoneda,* Kazuo Shinozuka, and Yoshiharu Sakuma
Faculty of Pharmaceutical Sciences, Kumamoto University,
Oe-honmachi, Kumamoto 862, Japan
Yoshihiro Nitta
Shizuoka College of Pharmacy, Oshika, Shizuoka 422, Japan

The condensation of 6-arylaminouracils with nitrosobenzenes in acetic anhydride gave the corresponding 10-arylisoalloxazines.

Hydrolysis of simple 3,10-dialkylisoalloxazines provides the corresponding spirohydantoins *via* nucleophilic addition of hydroxide ion to the 10a-position.[1] By contrast, 3-alkyl-10-arylisoalloxazines, which are sterically hindered at the 10a-position, undergo the initial hydrolytic scission at the 4-position to lead the quinoxalone derivatives;[2] thus, 10-arylisoalloxazines are useful in determining the importance of the availability of the 10a-position to nucleophilic addition. Furthermore, 10-arylisoalloxazines have been found to undergo photocyclization giving benzimidazo[1,2,3-*ij*]benzo[*g*]pteridine-6(5*H*),8(7*H*)-diones.[3]

The only known synthetic method for the preparation of 10-arylisoalloxazines has involved the condensation of alloxans with

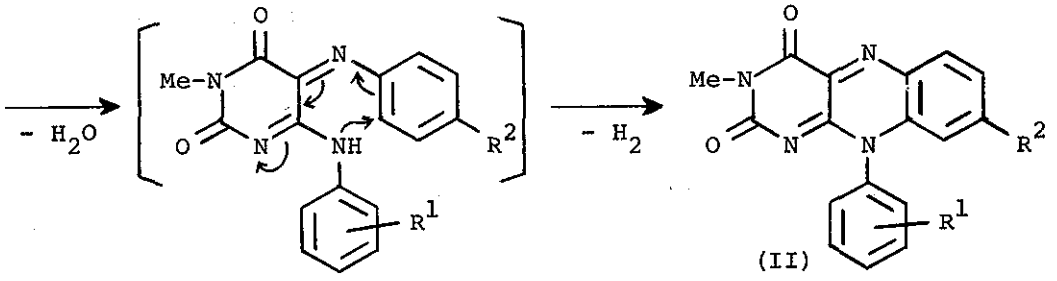
2-aminodiphenylamines.[2-5] We now report a new, facile synthesis of 10-arylisoalloxazines involving treatment of 6-arylaminouracils (Ia-f) with nitrosobenzenes in acetic anhydride.



(I) R^2 = H or Cl

a; R^1 = H
b; R^1 = 3-Me
c; R^1 = 3,4-Me_2
d; R^1 = 4-Cl
e; R^1 = 3,4-Cl_2
f; R^1 = 4-CN

(III)



(IV)

(II)

a; R^1 = R^2 = H
b; R^1 = 3-Me, R^2 = H
c; R^1 = 3,4-Me_2, R^2 = H
d; R^1 = 4-Cl, R^2 = H
e; R^1 = 3,4-Cl_2, R^2 = H
f; R^1 = 4-CN, R^2 = H
g; R^1 = H, R^2 = Cl
h; R^1 = 4-Cl, R^2 = Cl

The starting materials (Ia-f) were prepared by fusion of 6-chloro-3-methyluracil with the respective anilines according to the reported procedure.[6]

Refluxing of Ia (0.003 mole) with excess nitrosobenzene (0.009 mole) in acetic anhydride (70 ml) for 20 min afforded 3-methyl-10-phenylisoalloxazine (IIa),[2] which is isolated by concentration of the reaction mixture and addition of ethanol. Other 10-aryl-isoalloxazines (IIb-h) were similarly prepared by refluxing I with a nitrosobenzene in acetic anhydride.

TABLE 10-Arylisoalloxazine formation by the reaction of 6-arylamino-3-methyluracils with nitrosobenzenes

Starting materials			10-Arylisoalloxazines	M.p./°C[a]	Yield/%
Ia[6]	+	Nitrosobenzene	IIa[2]	>360	51
Ib[7]	+	Nitrosobenzene	IIb	326	56
Ic[8]	+	Nitrosobenzene	IIc	347	46
Id[7]	+	Nitrosobenzene	IId	>360	36
Ie	+	Nitrosobenzene	IIe	>360	48
If	+	Nitrosobenzene	IIf	>360	42
Ia[6]	+	p-Chloronitrosobenzene	IIg[9]	>360	75
Id[7]	+	p-Chloronitrosobenzene	IIh	>360	70

[a] Recrystallized from acetic acid.

This synthesis apparently involves the initial formation of a 5-hydroxylamine intermediate (III), whose dehydration to the diimine (IV) is facilitated by the presence of acidic hydrogen at the 1-position of the uracil. Cyclization and hydrogen transfer would then give the 1,5-dihydroisoalloxazine, which is dehydrogenated

with excess nitrosobenzene to lead the isoalloxazine.

It is noted that the known nitrosative cyclization[10] of 6-N-alkylanilinouracils to 10-alkylisoalloxazines could not be applied to the synthesis of 10-arylisoalloxazines, because the intermediary 6-N-arylanilinouracils were not available by the usual condensation of 6-chlorouracils with diphenylamines.

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