

A SYNTHESIS OF FLAVINS BY NITROSATIVE CYCLIZATION OF  
6-(N-ALKYLANILINO)URACILS WITH N-NITROSODIMETHYLAMINE-  
PHOSPHORUS OXYCHLORIDE MIXTURE

Fumio Yoneda,\* Kazuo Shinozuka, Yoshiharu Sakuma, and  
Keitaro Senga<sup>+</sup>

Faculty of Pharmaceutical Sciences, Kumamoto University,  
Oe-honmachi, Kumamoto, Japan and <sup>+</sup>Pharmaceutical  
Institute, Keio University, Shinjuku-ku, Tokyo, Japan

Treatment of 6-(N-alkylanilino)uracils with a mixture of N-nitrosodimethylamine (NDA) and phosphorus oxychloride gave directly the corresponding isoalloxazines (flavins).

A mixture of N-nitrosodimethylamine (NDA) and phosphorus oxychloride (referred to hereafter as NDA+POCl<sub>3</sub>) is a new type of nitrosating agent which has first been introduced by us.<sup>1,2</sup> For example, the nitrosation of 6-alkylamino-1,3-dimethyluracils,<sup>1</sup> 6-anilino-1,3-dimethyluracil,<sup>1</sup> 1,3-dimethyl-6-( $\alpha$ -methylalkylidenehydrazino)uracils<sup>3</sup> and 6-benzylidenehydrazino-1,3-dimethyluracil<sup>3</sup> with NDA+POCl<sub>3</sub> gave directly the corresponding theophyllines, alloxazine, 2-vinyl- $\gamma$ -triazolo[4,5-d]pyrimidines and fer-venulin. In this communication we describe the nitrosative cyclization of 6-(N-alkylanilino)uracils (I) to respective isoalloxazines (flavins) with this reagent.

Heating of a mixture of 6-(N-ethylanilino)-3-methyluracil (Ib) (1.23 g, 0.005 mole), NDA (0.74 g, 0.01 mole) and POCl<sub>3</sub> (1.54 g, 0.01 mole) in dioxane (30 ml) under reflux for 3 hr, followed by evaporation in vacuo to dryness and dilution with water, caused the separation of 10-ethyl-3-methylisoalloxazine

(IIb).<sup>4</sup> Similarly, several other 6-(N-alkylanilino)uracils (I) yielded the corresponding isoalloxazines (II) under the same conditions (see Table).

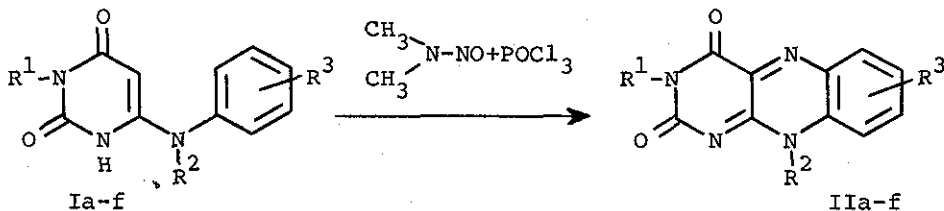


TABLE Isoalloxazines (Flavins)

Starting material	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Product	M.p./°C	Yield/%
Ia	CH <sub>3</sub>	CH <sub>3</sub>	H	IIa	334 <sup>4</sup>	68
Ib	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	H	IIb	299 <sup>4</sup>	65
Ic	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	7-CH <sub>3</sub>	IIc	276 <sup>5</sup>	70
Id	CH <sub>3</sub>	CH <sub>3</sub>	7-Br	IId	293	60
Ie	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	7-Br	IIe	275	67
If	H	C <sub>2</sub> H <sub>5</sub>	H	IIf	347 <sup>4</sup>	70

The usual nitrosation of (I) with sodium nitrite and acetic acid gives the corresponding isoalloxazine 5-oxides.<sup>4</sup> It should be noted that the nitrosative cyclization of (I) with NDA+POCl<sub>3</sub> gives directly isoalloxazines (flavins).

#### REFERENCES

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