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A NEW SYNTHESIS OF ALLOXAZINE 5-OXIDES

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The condensation reaction of 4,6-dimethyloxadiazolo[3,4-d]pyrimidine-5,7(4H,6H)dione 1-oxide with anilines offers a new synthetic method for 1,3-dimethylalloxazine 5-oxides

It is known that 5- and 6-substituted benzofuroxans can equilibrate with each other, presumably through the intermediary of the dinitroso structure.[1] Oxadiazolo[3,4-d]pyrimidine 1-oxides also could be anticipated to be in equilibration with their 3-oxides. We now wish to describe the reaction in which 4,6-dimethyl[1,2,5]-oxadiazolo[3,4-d]pyrimidine-5,7(4H,6H)dione 1-oxide (I)[2] in its 3-oxide tautomeric form (II) apparently reacts with anilines offering a new synthetic method of 1,3-dimethylalloxazine 5-oxides.

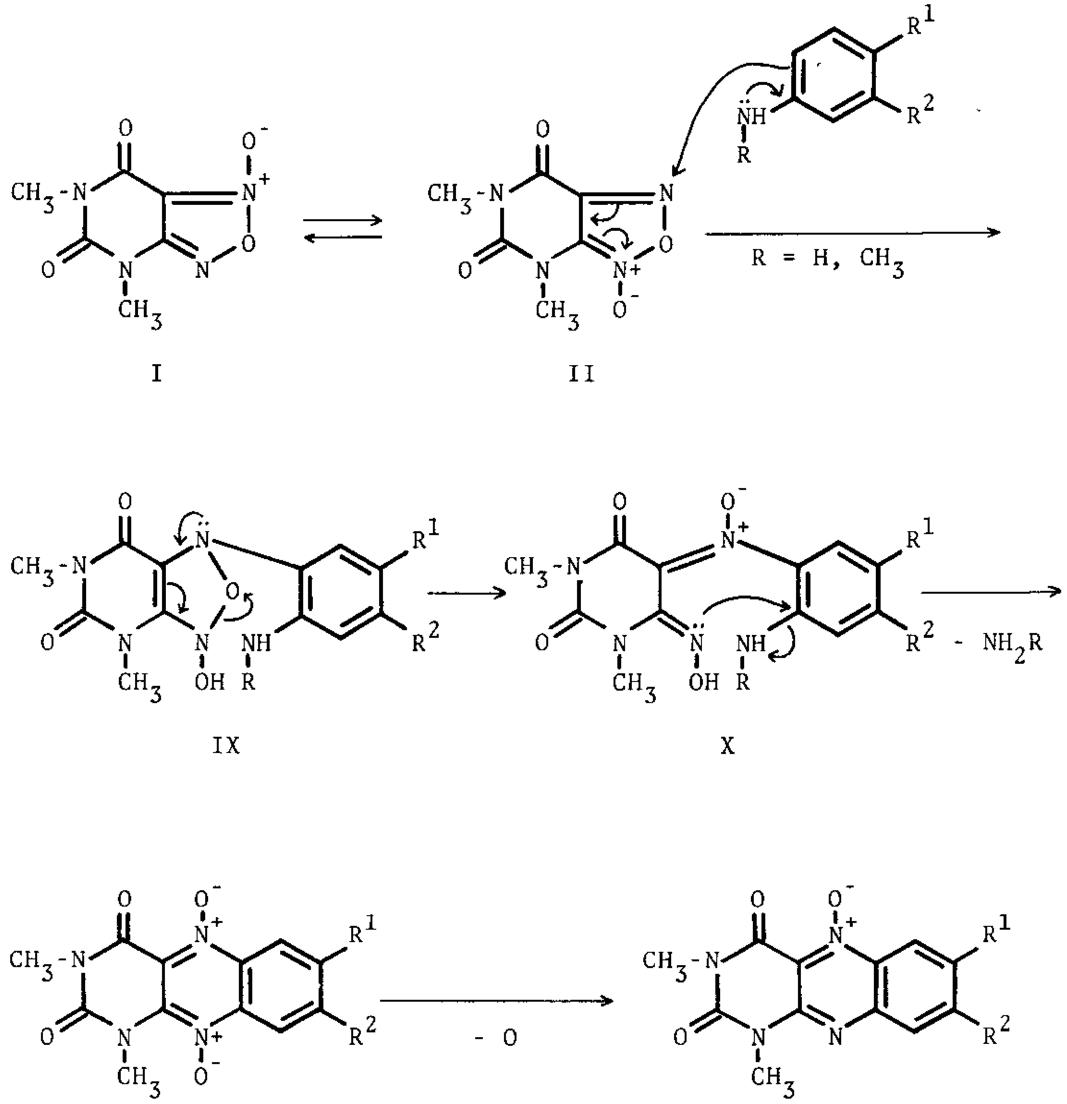
A mixture of 1 part of I and 3 parts of xylidine was heated at 95° for 8 hr under stirring. The resulting mixture was diluted with a mixture of ethanol and ether and allowed to stand overnight at room temperature to precipitate 1,3-dimethyllumichrome 5-oxide (VI). This reaction is equally applicable to other aniline derivatives to give the corresponding alloxazine 5-oxides; in this reaction the nitrogen atom of 3-position of II becomes the 10-N of the final 1,3-dimethylalloxazine 5-oxides. This is supported by the fact that the reaction of I with N-methylaniline derivatives under the same conditions also yielded the same alloxazine 5-oxides.

Table 1,3-Dimethylalloxazine 5-Oxides Formation by Reaction of Oxadiazolo[3,4-d]pyrimidine 1-Oxide and Anilines

Anilines	Product	Mp(°C)	Recrystn. solvent	Yield(%)
Aniline	III	237[3]	Acetone	55
p-Toluidine	IV	242[3]	Ethanol	68
m-Toluidine	V	236	Ethanol	65
3,4-Xylidine	VI	235	Ethanol	75
p-Anisidine	VII	214	Ethanol	59
m-Anisidine	VIII	248	Ethanol	69

This new alloxazine 5-oxide synthesis is best rationalized by assuming the initial nucleophilic attack of the aniline derivatives as enamines at 1-position of II to form hydroxylamine intermediates (IX), followed by nitrogen-oxygen bond cleavage giving the 6-oximes (X), which are suited for intramolecular cyclization to XI. Subsequent elimination of one oxygen could lead to the alloxazine 5-oxides.

It is noted that 4,6-dimethyl[1,2,5]oxadiazolo[3,4-d]pyrimi-



I

II

IX

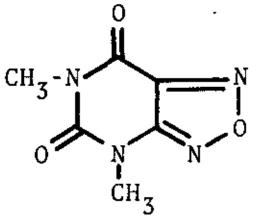
X

XI

III $R^1=R^2=H$
IV $R^1=CH_3$, $R^2=H$
V $R^1=H$, $R^2=CH_3$

VI $R^1=R^2=CH_3$
VII $R^1=OCH_3$, $R^2=H$
VIII $R^1=H$, $R^2=OCH_3$

dine-5,7(4*H*,6*H*)dione [4,6-dimethylfurazano[3,4-*d*]pyrimidine-5,7(4*H*,6*H*)dione] (XII)[4] did not react with anilines under similar conditions, with the starting material being recovered.



XII

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