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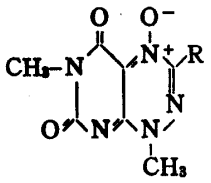
The Novel Use of Diethyl Azodicarboxylate in a New Synthesis of 7-Azapteridine-N-oxides

The nitrosation of the hydrazones of 3-methyl-6-(1'-methylhydrazino)uracil (I) undergoes simultaneous cyclization to give in general the respective 3-substituted toxoflavins.[1] The process may involve the key intermediates hydroxylamines (II), which give the toxoflavins by intramolecular dehydration. The dehydrogenation of the intermediates (II) may lead to the formation of the toxoflavin-4-oxides (III). From these considerations, we have examined the utility of diethyl azodicarboxylate (IV), which is a strong hydrogen-abstracting agent,[2-4] as an effective dehydrogenating agent for the formation of toxoflavin-4-oxides. Thus, stirring of the hydrazones I in acetic acid with an equimolar amount of saturated aqueous sodium nitrite solution in the presence of 2 equivalents of IV at 5—20° for 20 min, followed by dilution with ether to give exclusively the corresponding toxoflavin-4-oxides. Compound IV was converted into diethyl hydrazodiacarboxylate, which was isolated from the mother solution.

Table I. Preparation of Toxoflavin-4-oxides[a]



3-Substituent (R)	Reaction temp. (°C)	mp (°C)	Yield (%)
Hydrogen	5	187—189 (decomp.)	35
Phenyl	20	203—204 (decomp.)	56
3,4-Dimethoxyphenyl	20	189—191 (decomp.)	63
Styryl	20	207—209 (decomp.)	75
3-Pyridyl	20	198—200 (decomp.)	61
4-Pyridyl	20	213—215 (decomp.)	40

a) All compounds were recrystallized from MeOH.

The structures of III were ascertained by satisfactory elemental analyses, the presence of the strong parent ions and remarkable M-16 ions in their mass spectra and the formation of the corresponding toxoflavins (V)[1] by their reduction using sodium dithionite or benzenethiol in methanol.

IV is also effective for the formation of unknown fervenulin-4-oxides (VI). For example, treatment of benzaldehyde hydrazone of 1,3-dimethyl-6-hydrazinouracil[5] in acetic acid with sodium nitrite in the presence of IV under similar conditions (25°, 10 hr), followed by dilution with water to precipitate 3-phenylfervenulin-4-oxide, mp 129—131°, in 30% yield. This product is not very stable and partially converted into 3-phenylfervenulin[6] even on recrystallization from ethanol.

1) F. Yoneda, K. Shinomura and S. Nishigaki, *Tetrahedron Letters*, **1971**, 851.
2) F. Yoneda, K. Suzuki and Y. Nitta, *J. Am. Chem. Soc.*, **88**, 2328 (1966).
3) F. Yoneda, K. Suzuki and Y. Nitta, *J. Org. Chem.*, **32**, 727 (1967).
4) E.C. Taylor and F. Yoneda, *Chem. Commun.*, **1967**, 199.
5) W. Pfleiderer and G. Blankenhorn, *Tetrahedron Letters*, **1969**, 4699.
6) F. Yoneda, M. Kanahori, K. Ogiwara and S. Nishigaki, *J. Hetrocyclic Chem.*, **7**, 1443 (1970).

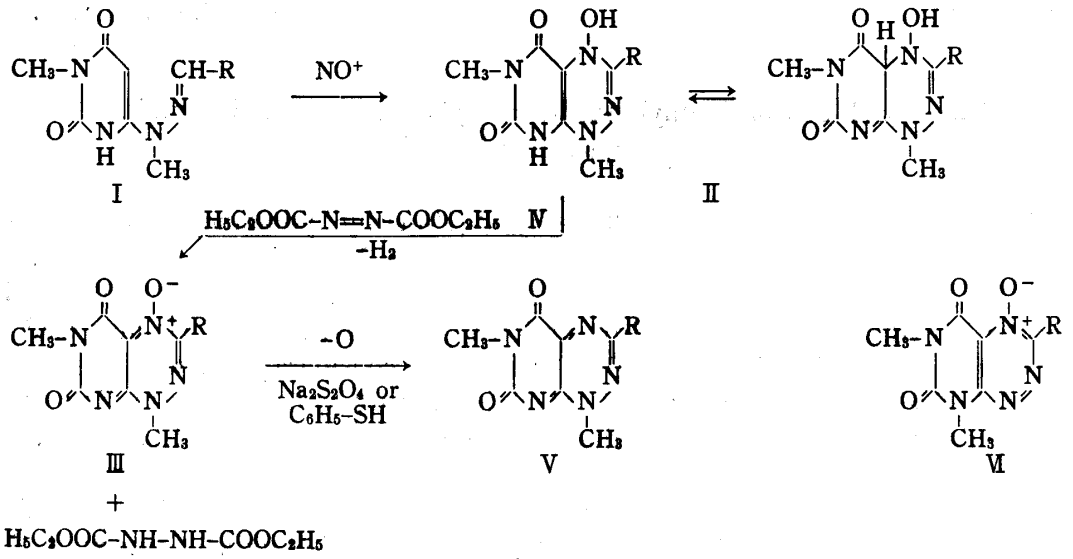


Chart 1

We consider this oxidative cyclization involving hydrogen abstraction as possessing considerable potential utility for the synthesis of other heterocycle-N-oxides. Moreover, it should be noted that the azapteridine-4-oxides mentoned above can not be obtained by the conventional peracid oxidation of the respective azapteridines. This would be connected with the π-electron distributions of the azapteridine system, and in fact the 4-positions are not sufficiently high in the π-electron densities.[7]

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7) Details will be published in the full paper.

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A Wittig Reaction of N-Sulfonyl Lactam

We wish to report here the successful Wittig reaction on substances having an N-sulfonyl lactam grouping,[1] and by utilizing this knowledge, we propose the reaction sequence of Chart 1 with a new synthetic pathway for the purpose of functionalization of the amide-carbonyl group.

1) The Wittig reaction of succinimide and phthalimide has been described. W. Flitsch and H. Peters, *Chem. Ber.*, **103**, 805 (1970).