New Convenient Syntheses of Oxadiazolo[3,4-*d*]pyrimidine 1-Oxides

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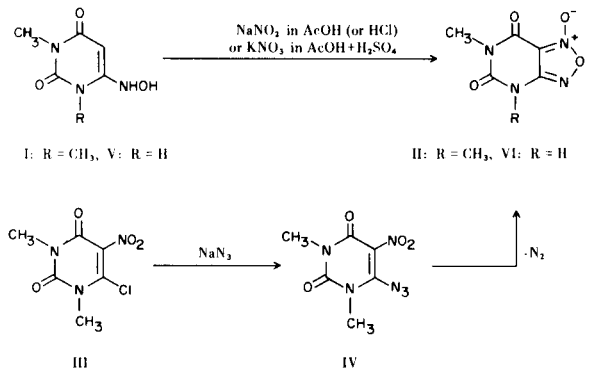
Sir:

We wish to report new convenient syntheses of oxadiazolo[3,4-*d*]pyrimidine 1-oxides from 6-hydroxylaminopyrimidines by means of nitrosative and nitrative cyclizations. The synthetic procedures known involve the reaction of 6-chloro-5-nitropyrimidines with sodium azide and the nitrosation of 6-hydrazino-5-nitropyrimines, both of which apparently proceed *via* both the intermediate 4-azido-5-nitropyrimidines and tetrazolo[1,5-*c*]-pyrimidines (1).

1,3-Dimethyl-6-hydroxylaminouracil (I) (2) in aqueous acetic acid or dilute hydrochloric acid was stirred with equimolar sodium nitrite under cooling at 3-5° for 1 hour, during which time yellow crystals gradually separated. The crystals were collected by filtration, washed with water and recrystallized from ethanol to give 4,6-dimethyl[1,2,5]oxadiazolo[3,4-*d*]pyrimidine-5,7(4*H*,6*H*)-dione 1-oxide (II) (3) as pale yellow prisms, m.p. about 210° with decomposition, in 60% yield.

The assignment of structure II is based on the satisfactory elemental analysis, and the presence of the parent ion (m/e 198) and a remarkable M+2 ion in its mass spectrum. It is known that powerful hydrogen acceptors such as *o*-benzoquinone-type compounds including benzofuroxan and pyridofuroxan exhibit intense M+2 peaks and water is the probable origin of the hydrogen molecule responsible for the M+2 peak (4); this also appears to be the case in the above M+2 peak of II.



I: R = CH_3, V: R = H

II: R = CH_3, VI: R = H

III

IV

SCHEME

Next, the nitrative cyclization of I was tried to obtain compound II. A mixture of I (1 mole) and potassium nitrate (1 mole) in acetic acid including a few drops of sulfuric acid was stirred at 90° for about 1 hour, followed by removal of the solvent by evaporation *in vacuo* and dilution with water to give II in 65% yield.

The structure of II was finally established by comparison with an authentic sample prepared by an unequivocal synthesis as follows. Reaction of 6-chloro-1,3-dimethyl-5-nitrouracil (III) with sodium azide in ether at room temperature gave 6-azido-1,3-dimethyl-5-nitrouracil (IV) (5), m.p. 148° with explosive decomposition, which was converted on heating at 160° into II, identical with the foregoing product prepared by nitrosative and nitrative cyclizations.

The above-mentioned nitrative cyclization (reflux, 1 hour) of 6-hydroxylamino-3-methyluracil (V), m.p. 190°, prepared by the condensation of 6-chloro-3-methyluracil and hydroxylamine, yielded likewise 6-methyl[1,2,5]-oxadiazolo[3,4-*d*]pyrimidine-5,7(4*H*,6*H*)dione 1-oxide (VI), m.p. > 300°, in 37% yield. Application of these procedures to the preparation of other oxadiazolo-[3,4-*d*]pyrimidine 1-oxides is in progress.

REFERENCES

(1) C. Temple, C. L. Kussner and J. A. Montgomery, *J. Org. Chem.*, 33, 2086 (1968).

(2) W. Pfleiderer and H. Ferch, *Ann.*, 615, 52 (1958).

(3) Satisfactory microanalytical and spectral data were obtained for all compounds.

(4) R. T. Aplin and W. T. Pike, *Chem. Ind.*, (London), 2009 (1966).

(5) Azido absorption is present at 2170 cm^{-1} in the infrared spectrum.