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NOVEL PHOTOCYCLIZATIONS OF 1,3-DIMETHYL-5-NITRO-6-BENZYLIDENEMETHYLHYDRAZINOURACIL

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A recent article[1] from our laboratory described a convenient and widely applicable synthetic route to pyrazolo(3,4-d)pyrimidines by the reaction of 1,3-dimethyl-5-nitro-6-chlorouracil with hydrazones of a wide variety of aldehydes and ketones. This reaction apparently involves a thermal cyclization of the initially formed 1,3-dimethyl-5-nitro-6-benzylidene(or alkylidene) hydrazinouracils.

In a continuation of the study of this system, we have observed that 1,3-dimethyl-5-nitro-6-benzylidenemethylhydrazinouracil(I) undergoes photocyclization to afford 3-phenyl-1,5,7-trimethyl-4,6(5H,7H)-pyrazolo(3,4-d)pyrimidine-dione(II) and 3,4,6-trimethyl-5,7(4H,6H)-triazolo(4,5-d)pyrimidine-dione-1-oxide(III). The present results provide new examples of photocyclizations which involve novel, nonoxidative photocyclization with elimination of a nitro group, and photochemical interaction between a nitro group and a hydrazone C=N bond.

A solution of (I) in degassed benzene(4 mg/ml) was irradiated under nitrogen with a 100 W high-pressure mercury arc lamp surrounded by a water-cooled Pyrex filter for 10 hr. After being allowed to stand at room temperature for several hours, the reaction mixture deposited a product, mp 293°, which was recrystallized from acetone, in 35% yield. The mother liquor was concentrated and the solid residue was recrystallized from ethanol to give an additional product, mp 188°, in 40% yield. The latter compound[2] was identical in every respect with (II) obtained by the thermal cyclization of (I) as previously reported.[1,3] The mass spectrum of the former compound revealed a strong M-16 peak indicating the presence of a labile oxygen, most probably an N-oxide group. This conclusion was confirmed by its deoxygenation to the known 3,4,6-trimethyl-5,7(4H,6H)-triazolo(4,5-d)pyrimidine-dione.[4] Thus, the former product must be one of the two possible 1- and 2-oxides. That the N-oxide function is located at position 1 can be deduced from the unequivocal synthesis of 3-methyl-6-chlorobenzotriazole-1-oxide(V) obtained by photocyclization of 2-benzylidenemethylhydrazino-5-chloronitrobenzene(IV).

When (IV) in benzene was irradiated for 20 hr, an N-oxide(V), mp 197°, and its deoxygenated product, mp 88°, were isolated in 10% and 17% yields respectively. The synthesis of (V) was accomplished as follows: 2,5-dichloronitrobenzene was heated in excess hydrazine hydrate and the resulting hydrazine salt of 6-chlorobenzotriazole-1-oxide(VI) was treated with hydrochloric acid to liberate (VI), mp 194°, in 60% yield. N-methylation of (VI) was achieved unambiguously according to the procedure[5] previously reported in the N-methylation of benzotriazole-1-oxide(reflux in dimethy sulphate). (V) thus prepared was identical in every respect with the sample obtained by irradiation of (IV).(see Chart 1)

It is worthwhile noting that while (I) gave (II) as the major product, (IV) did not cyclize to 1-methylbenzopyrazole. This marked difference can be ascribed in part to the facility of a 5-nitro group on the uracil ring of (I) to act as a leaving group.[1,6]

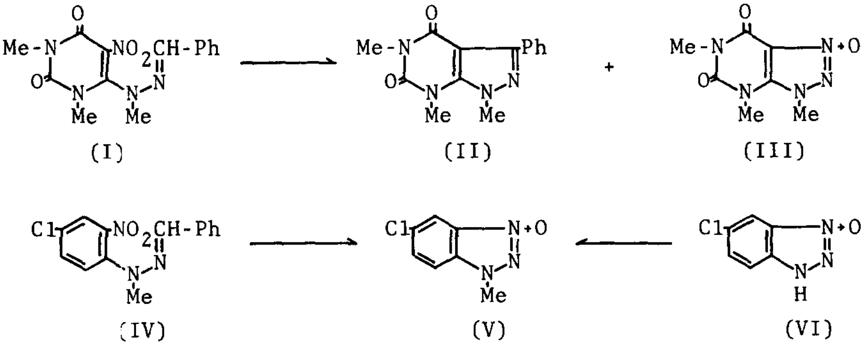

Chart 1

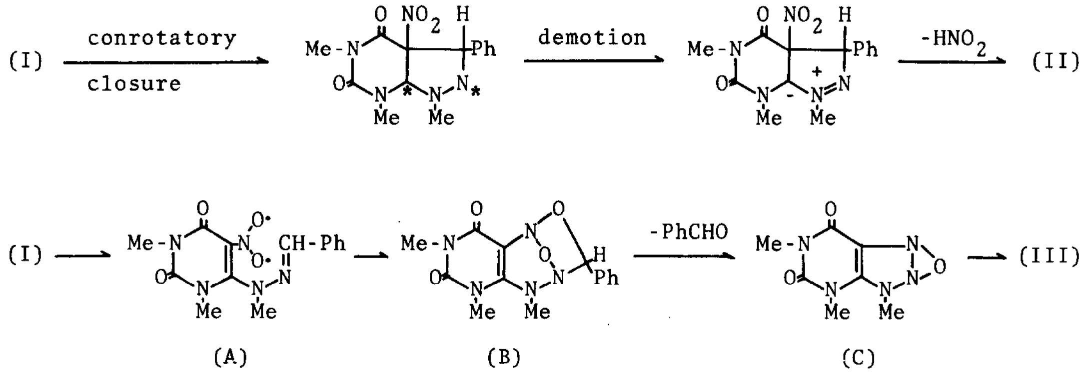

Chart 2

The photochemical cyclization of (I) to (II) seems to be best explained in terms of a photochemical electrocyclic reaction as outlined in Chart 2. It has been predicted that the photocyclization of the arylated enamines proceeds via the electrocyclic process.[7]

The formation of N-oxide(III)(see Chart 2) appears to be initiated by photocycloaddition of an excited nitro group(A) to the hydrazone C=N bond to form a cyclic intermediate(B). An analogous addition of the nitro group to the C=N bond of a Schiff base has been proposed previously[8], and recently it has been shown that the photochemical addition of aromatic nitro compounds to alkenes gives 1,3,2-dioxazolidines.[9] In the present case, subsequent collapse of the intermediate(B) with loss of benzaldehyde could lead to an oxadiaziridine intermediate(or its equivalent biradical intermediate), which affords (III) by isomerization. Postulation of an oxadiaziridine intermediate has precedent in the photochemical isomerization of azoxy compounds.[10,11]

Footnotes and References

1. Y. Maki, K. Izuta and M. Suzuki, Chem. Comm., 1422 (1971).
2. All compounds described herein gave satisfactory microanalytical results and spectral data consistent with their structures.
3. (I) is so stable that its thermal cyclization to (II) requires drastic conditions(reflux in dimethyl sulphoxide).

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11. For isolation of an oxadiaziridine intermediate, see J. Swigert and K.G. Taylor, J. Am. Chem. Soc., 93, 7337 (1971).