PHOTOREACTIONS OF 6-(1'-TRIAZOLYL)URACILS. SYNTHESIS OF 7,8-DISUBSTITUTED PYRROLO[2,3d]PYRIMIDINES AND PYRIMIDO[4,5-c]ISOQUINOLINES

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Abstract: A series of 6-(1'-triazolyl)uracils 4a-f were subject to photolysis at 254 nm in acetonitrile. The C_4 , C_5 -disubstituted triazoles 4a-c afforded pyrrolo[2,3-d]pyrimidines 5a-c whereas mono-substituted triazoles gave rise to polymeric mixtures. C_5 -phenyl substituted adducts 4e,f generated pyrimido[4,5-c]isoquinolines 7 and 8 via a novel photorearrangement process.

Irradiation of 1-phenyl-benzotriazoles or 1-alkenyl-benzotriazoles 1 results in loss of nitrogen and has been shown to proceed via triplet diradical intermediates 2¹ which internally cyclize to afford either carbozoles²^a or substituted indoles 3²^b (eq 1). The azadiyl photocyclization of a 1-aryltriazole system has been applied as an effective strategy for the synthesis of 7-methoxymitosene.³ The extension of this process to triazoles which are connected to an electron deficient ring has not been reported. In the case where a pyrimidine ring is involved, an approach to the synthesis of pyrrolo[2,3-d]pyrimidines would be available (eq 2). A number of biologically interesting compounds contain the 7-deazapurine structural subunit.⁴ In this communication a series a 6-(1'-triazoly1)uracils 4⁵ were subject to photolytic conditions in anticipation of meeting this objective.



The substrates 4a-f were photolyzed in deoxygenated acetonitrile (0.003-0.01 M) using a Rayonet apparatus and 254 nm mercury lamps until the starting material was consumed as evidenced by TLC. Following solvent removal, the crude product was purified by either recrystallization or column chromatography over silica gel.⁶ The results are summarized in Table 1.



Table 1. Photolysis of 6-(1'-Triazolyl)uracils. 4a-f, at 254 nm in Acetonitrile.

a) All reported yields are for isolated and purified compounds. Analytical samples were obtained by recrystallization.
 b) This structure is consistent with the observed ¹H, ¹³C, IR, and mass spectral data.
 c) The remaining mass balance from this reaction was mainly uncharacterized polymeric materials and some starting material.

It is evident that the outcome of the photoreactions are highly dependant upon the substitution on the triazole ring. These results can be categorized into three groups. For substrates which have substituents in both the 4 and 5 positions of the triazole ring, i.e. 4a-c, respectable yields of the desired pyrrolo[2,3-d]pyrimidines 5a-c are observed except in the case for the fused pyridotriazole 4d where only the product of solvent trapping 6 was observed.⁷ A limitation was observed for both C₄ and C₅ mono-substituted triazoles (4, R₁ = Ph, CO₂Et, SO₂Ph, R₂ = H; R₁ = H, R₂ = CO₂Et) where mostly polymeric materials

were obtained. The presence of a radical stabilizing substituent in the C_4 position alone is not sufficient to promote efficient cyclization.⁸ However, in the two cases where a phenyl substituent is located in the 5-position of the triazole ring, i. e. **4e-f**, the rearranged photoproducts 7 and 8 were isolated.⁹ A mechanistic rational for the generation of these compounds in shown in Scheme 1.



Scheme 1

Following loss of nitrogen, the transient diyl 9 should be sufficiently long lived to populate resonance rotomer 10 which can then undergo internal radical insertion ortho to the phenyl ring.¹⁰ Hydrogen atom transfer would afford cycloadduct 11 which then tautomerizes to the observed product. This rearrangement apparently has no precedent in the area of triazole photochemistry.^{2,10,11}

The synthesis of certain 1,3-dimethyl-pyrrolo[2,3-d]pyrimidine-2,4-diones 5a-c bearing substituents at both C_7 and C_8 has been realized by photolysis of 6-(1'-triazolyl)uracils 4a-c. An unexpected triazole photorearrangement process has been discovered for C_5 phenyl substituted triazoles 4e-f and will be the subject of further explorations for generalized N-alkenyl-5aryltriazole systems.

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References and Notes

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- 5. The preparation of compounds **4a,b,e,f** was accomplished by heating 6-azido-1,3-dimethyluracil with the appropriate acetylene. Compounds **4c,d** were prepared by the combination of 6-chloro-1,3-dimethyluracil with benzenetriazole (NaOH, EtOH, H₂O) or triazolo[4,5-b]pyridine (NaH, DMF, RT). The details of this chemistry will be reported elsewhere.
- All new compounds were characterized spectroscopically using ¹H NMR, ¹³C NMR, and IR. Verification of the elemental composition for compounds 5a-c, 7, and 8 were obtained by combustion analysis and for compound 6 by high resolution mass spectroscopy.
- 7. Attempts to photolyze this compound in hexane or THF resulted in the formation of polymeric material.
- 8. Only in the case where $R_2 = SO_2Ph$ was a detectable amount (<10%) of the pyrrolo[2,3-d]pyrimidine observed.
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