Photochemical Reactivity of 2,4-Dimethyl-1,2,4-triazine-3,5(2*H*)-dione (1,3-Dimethyl-6-azauracil)

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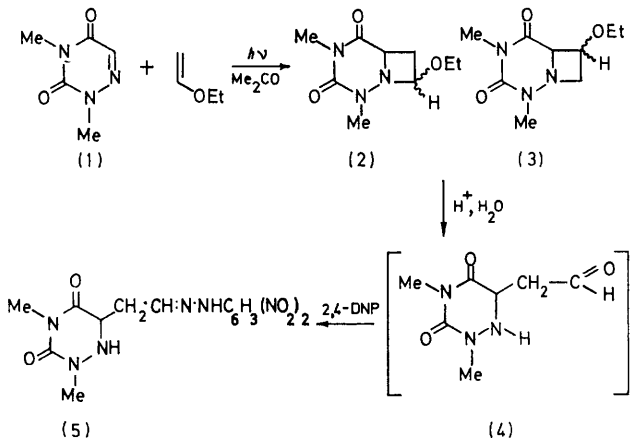
Summary In contrast to the general photochemical unreactivity of the 6-aza-analogues of uracils and thymines, 2,4-dimethyl-1,2,4-triazine-3,5(2*H*)-dione undergoes acetone-sensitized regioselective cycloaddition to ethyl vinyl ether yielding labile azetidine cycloadducts.

RECENTLY the photochemistry of nucleic acid nitrogen bases has been actively investigated,[1] and excited-state electron densities have been correlated successfully with the dimerization reactivity of uracil and thymine.[2,3] While calculations predict that the excited-state properties of the

6-aza-analogues of uracil and thymine should closely parallel those of the parent carbon systems, the apparent unreactivity of these aza-systems is anomalous.[2–5] We recently demonstrated that triplet 1,3-dimethyluracil undergoes ready regioselective addition to t-butyl vinyl ether, vinyl acetate, and keten diethyl acetal,[1] and we now report the high-yield regioselective cycloaddition of the 6-aza-analogue (**1**) [2,4-dimethyl-1,2,4-triazine-3,5(2*H*)-dione] to ethyl vinyl ether, demonstrating in this instance the similar photochemical reactivity of 1,3-dimethyluracil and (**1**).

Photolysis† of a 1% solution of (**1**) in acetonitrile containing acetone (0·5 M) and a 5–15 molar excess of ethyl vinyl ether led to rapid formation of four products in a ratio of 44 : 51 : 3 : 2 (>90% yield). Attempted preparative column- and vapour-phase-chromatographic separation led to decomposition of the adducts, but chromatography on Florosil allowed partial recovery of the major product in pure form; m.p. 58—61°; ν_{max} (KBr) 5·81, 5·94, 6·96, and 7·59 μm; τ ($CDCl_3$) 5·10 (1H, t, J 7 Hz), 5·80 (1H, q, J 4 and 8 Hz), 6·42 (2H, q, J 7 Hz), 6·79 (6H, s), 7·64 (2H, m), and 8·78 (3H, t, J 7 Hz); *m/e* (70 eV) 141 (100%), 72 (80%), and 213 (4%). Elemental analysis and the mass spectrum confirm that it is a 1 : 1 adduct of (**1**) and ethyl vinyl ether and the strong i.r. absorptions at 5·81 and 5·94 μm indicate it contains the urea fragment intact. Since it shows no vinylic n.m.r. absorptions, unsaturation is absent and the adduct is thus bicyclic. These data, together with the predominant reverse 2 + 2 cleavage in the mass spectrum, imply an azetidine adduct of type (**2**) or (**3**). Irradiation of the signal at τ 7·6 collapses both methine signals to singlets while irradiation at either τ 5·1 or 5·8 simplifies the methylene region but does not affect the other methine hydrogen. These decoupling results are only consistent with orientation (**2**).

The next most abundant adduct could not be purified in quantity, but its mass spectrum (g.l.c.–m.s.) was nearly identical to that of the crystalline product. An n.m.r. sample, enriched in this material,‡ gave a similar spectrum to that of the crystalline adduct except for small displacements in chemical shifts: τ ($CDCl_3$) 5·09 (1H, m), 5·71br (1H, d), 6·38 (2H, q), 7·01 (6H, s), 7·25 (2H, m), and 8·75 (3H, t). The signals at τ 5·09 and 5·71 collapsed to singlets upon irradiation of the multiplet at τ 7·25. Treatment of the crude mixture with 2,4-dinitrophenylhydrazine afforded a yellow crystalline derivative (**5**) (80%), m.p. 159—162°, which was also formed in 84% yield by treatment of the crystalline adduct with 2,4-dinitrophenylhydrazine. Formation of the same derivative from both major adducts can be accounted for in terms of acid-catalysed hydrolysis of the azetidine ring to a common amino-aldehyde intermediate (**4**) which subsequently yields (**5**).§ Thus, while the orientation and epimeric nature of the major adducts are established, the stereochemistry of the ethoxy-group cannot yet be assigned.



The similar regioselective photoadditions of 1,3-dimethyluracil and its 6-aza-analogue to vinyl ethers are in agreement with most theoretical reactivity considerations.[2,3] These results do not support speculation that the 6-aza-systems possess unreactive n–π^* transitions at lower energy than the 5–6 localized π–π^* level.[3] In view of these results, the suggestions that failure to isolate dimers of 6-aza-analogues of uracil[2,4] and similar compounds is related to lability of the dimeric diazetidines, are more significant. However, it is strange that the instability of these dimers results solely from dissociation into monomers and no other degradation products have been characterized.

The synthesis of azetidines by photoaddition of olefins to (**1**) followed by hydrolytic degradation of the urea fragment is currently under study.

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† Corex-filtered light from a 450-W Hanovia medium-pressure source was employed, with g.l.c. monitoring.

‡ The n.m.r. sample was contaminated with 25% of the crystalline adduct. The i.r. spectrum of this enriched sample was also similar to that of the crystalline adduct.

§ All n.m.r. spectra were determined for *ca.* 10% solutions in $CDCl_3$ at 100MHz. Satisfactory combustion analyses were obtained for (**2**) and (**5**).

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[2] B. Pullman, *Photochem. Photobiol.*, 1968, **7**, 525; M. J. Mentione and B. Pullman, *Biochem. Biophys. Acta*, 1964, **91**, 387.
[3] V. I. Danilov, Y. A. Kruglyak, V. A. Kuprievich, and V. V. Ogloblin, *Theor. Chim. Acta*, 1969, **14**, 242.
[4] R. Kloepfer and H. A. Morrison, *J. Amer. Chem. Soc.*, 1972, **94**, 255; A. Wacker, *Photochem. Photobiol.*, 1964, **3**, 369; W. H. Prusoff, *Biochem. Biophys. Acta*, 1962, **58**, 588; H. L. Gunther and W. H. Prusoff, *ibid.*, 1967, **149**, 361.
[5] The photohydration of 6-azauracil has been reported: L. Kittler and G. Loeber, *Monats. Ber. Deut. Akad. Wiss. Berlin*, 1971, **13**, 216; C.A., 1972, 85117k.