Journal of

The Chemical Society,

Chemical Communications

NUMBER 16/1975 20 AUGUST

Photoaddition of Tetrahydrofuran to 1,3-Dimethyluracil

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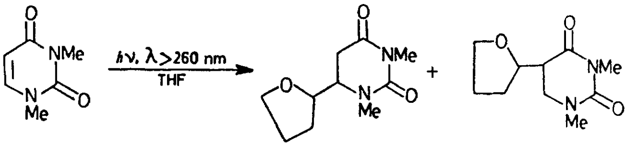
Summary Photoexcited 1,3-dimethyluracil (I) adds tetrahydrofuran to form 1,3-dimethyl-6-(tetrahydrofuran-2-yl)-5,6-dihydrouracil (II) and 1,3-dimethyl-5-(tetrahydrofuran-2-yl)5,6-dihydrouracil (III) as the predominant products.

Recent studies on the photochemistry of the nucleic acid component uracil, and its analogues, show that it is reactive towards addition of such species as water,[1a] alcohols,[1b] amines,[1c] and amino acids.[1d,1e] We have found that the water-soluble uracil derivative (I) reacts with the cyclic ether, tetrahydrofuran (THF), to form (II) (see below) and (III) in a combined yield of *ca.* 80% based on (I). This is evidently the first example of photoaddition of an ether to a chemical species closely related to the biologically important pyrimidine bases.[2] Interestingly, THF has the same basic ring structure as the ribose and deoxyribose units which occur in the nucleic acids. Thus the present system may be viewed as a model for a possible type of photoinduced crosslinking between RNA and DNA.

Irradiations of 7×10^{-3} M solutions of (I) in freshly distilled, deoxygenated, THF were carried out for 48 h (*ca.* 90% conversion) using a Corex shielded ($\lambda > 260$ nm) medium pressure Hg lamp as the light source. Compounds (II) and (III) were isolated from the crude mixture by high pressure liquid chromatography on Bio-sil A with 200:10:1 heptane–propan-2-ol–methanol as the eluent. The ratio of the yield of (III) to (II), measured by g.l.c. after separation, was about 1:1; (II) and (III) had identical retention times on gas chromatography on SE-30 and OV-3 columns. G.l.c. indicated that a small amount of 5,6-dihydro-1,3-dimethyluracil and *ca.* 15% of the cyclobutane dimers[3] of (I) were also formed. Compounds (II) and (III) were characterized by their mass spectra (*M*; 212 $C_{10}H_{16}N_2O_3$), and i.r. [ν (C–H) 2850—3000, ν(C=O, amide) 1665 and 1710 cm^{-1}] and u.v. spectra [no absorption maxima >240 nm, indicating saturation of the 5,6 double bond of (I)]. The 60 MHz n.m.r. spectrum of (II) in $CDCl_3$, with Me_4Si as internal standard, showed two singlets [δ 3·11 and 3·14, (each 3H, NMe)], complex multiplets [δ *ca.* 3·78 (3H) and 1·93 (4H)] from the THF ring, the AB part of an ABX multiplet [δ 2·71 (sharp) and 2·74 (2H, br.)], and a complex group of peaks [δ 3·42 (1H)] corresponding to the X part of the ABX multiplet. The n.m.r. spectrum of (III) in the same solvent showed a singlet [δ 3·16 (6H, s, NMe)] overlapping what is probably the AB part of an ABX multiplet [unobscured slightly doubled peaks: δ 3·33 and 3·42 (2H)], complex multiplets [δ *ca.* 3·83 (3H) and δ *ca.* 1·88 (4H)] from the THF ring, and a complex group of 4 peaks [δ 2·75 (1H)] corresponding to the X part of the ABX multiplet. The above assignments of the site of attachment of the THF ring to the 6-position in (II) and the 5-position in (III) were confirmed by studying the n.m.r. spectra of the reaction products obtained by irradiating 1,3-dimethyl[5-^{2}H]uracil[4] in THF. The AB part of the ABX multiplet became a broadened one-proton doublet in the case of (II); the absorption in the region of the X part of the ABX multiplet



(I) (II) (III)

of (III) disappeared, accompanied by sharpening of the peaks in the AB region.

The reaction to form (II) and (III) can also be induced by photolytic decomposition of di-t-butyl peroxide ($\lambda > 290$ nm) in a 7×10^{-3} M solution of (I) in THF. The resultant t-butoxyl radicals react with THF to form tetrahydrofuran-2-yl radicals which evidently add to (I) to form (II) and (III) in approximately equal amounts. The similarity between the end products from the direct photolysis and the radical initiator-induced reaction indicates that radicals derived through hydrogen abstraction from THF by excited (I) are likely to be involved in the directly induced photoreaction.

Preliminary results indicate that (I) also forms high yields of products, analogous to (II) and (III), when irradiated in tetrahydropyran. Other preliminary results obtained from photolysis of 1,3-dimethylthymine–THF systems shows that the predominant adduct formed is 1,3-dimethyl-6-(tetrahydrofuran-2-yl)-5,6-dihydrothymine; cyclobutane dimer formation, however, is the main reaction in these systems at concentrations of 1,3-dimethylthymine of 7×10^{-3}M.

Support from an N.I.H. Grant and the Academic Senate of the University of California is gratefully acknowledged.

(*Received*, 3*rd April* 1975; *Com.* 377.)

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