

THIOCARBONYL PHOTOCHEMISTRY. III. THIETANES OBTENTION
FROM 4-THIOURACIL DERIVATIVES

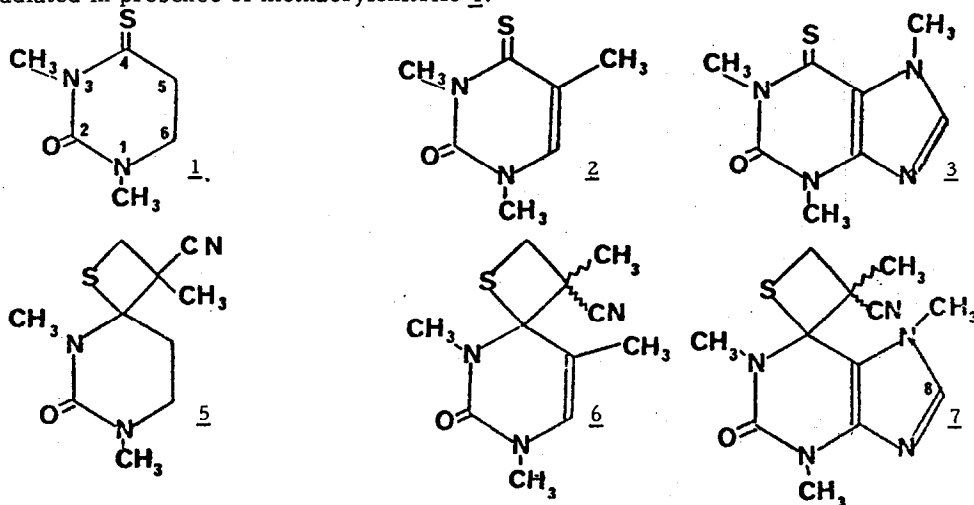
J. L. FOURREY P. JOUIN and J. MORON

Institut de Chimie des Substances Naturelles, C.N.R.S., 91190 Gif-sur-Yvette, France

(Received in UK 2 July 1974; accepted for publication 11 July 1974)

Recently we have reported some of our results dealing with light induced interaction between 4-thiouracil derivatives and electron deficient olefins (1). Our investigation was devised to obtain some insight towards the mechanism of 4-thiouridine photochemical cross-linking with cytidine in several *E. coli* tRNAs (2). The latter photoreaction has been assumed by LEONARD to involve an unstable thietane intermediate (3). Since this result could be relevant in tRNA structure elucidation studies (4) it was important to demonstrate that thietanes can be obtained photochemically starting from 4-thiouracil derivatives.

We have now established that thietanes can be isolated when compounds 1, 2 and 3 are irradiated in presence of methacrylonitrile 4.



Thietane 5 (5) [m. p. 103°C] is prepared from 1 in 75 % yield. The mass spectrum of compound 5 shows a molecular ion peak at m/e 225 and displays two characteristic fragments at m/e 179 ($M^+ - CH_2S$) and m/e 158 ($M^+ - C_4H_5N$).

Methyl signals in the NMR spectrum of 5 appear at : 1.6 ppm (C-CH₃) ; 2.90 and 3.30 ppm (2N-CH₃). The AB system centered at 2.95 and 3.35 ppm ($J_{AB} = 10$ Hz) is attributed to the CH₂S methylene protons in agreement with literature.

When compounds 2 and 3 were irradiated in presence of 4 a significant yield (80 %) of

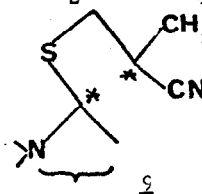
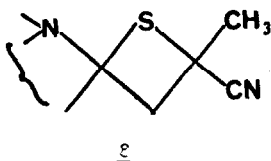
mixtures of thietane isomers, respectively (6a + 6b) (60 : 20) and (7a + 7b) (40 : 40), were obtained. Complete separation of the isomers could not be achieved.

Spectral data which support the structural assignement (7 and 8) are given below :

δ (ppm)	<u>6a</u>		<u>6b</u>		<u>7a</u>		<u>7b</u>			
N(CH ₃)	3.05	3.40	3.05	3.60	3.34	3.60	4.20	3.34	3.70	4.10
S-CH ₂	2.85	3.33	2.75	*	3.12		3.35	2.85		*
	(d)	(d)	(d)		(d)		(d)	(d)		

(d) doublet * attribution of the signal due to this proton is not certain.

Since in the mass spectra 5 compounds 6 and 7 the main fragmentations derived from the molecular ion lead to peaks at masses corresponding to M-CH₂S and M-C₄H₅N, Alternate structure 8 must be ruled out.



The obtention of compounds 5, 6 and 7 is a good indication that the photochemical interaction of a 4-thiouracil derivative with an electron deficient olefin can yield a thietane. A necessary but not sufficient requirement to stabilize the latter is N-3 substitution, a condition which cannot be met with 4-thiouracil in tRNA.

Since unreacted thiocarbonyl compound could not be detected after low temperature experiment (8) and usual work up we suggest that, in contrast to aromatic thioketones (9), thietanes 5, 6 and 7 arise after ring closure of a hitherto uncharacterised intermediate such as 9 and not after a dark reaction of the latter with ground state thiocarbonyl derivative. Evidence to confirm that thietanes are directly formed by the photoreaction of thionamides with electron deficient olefins is currently being sought in this laboratory.

Acknowledgement : We are grateful to Dr J. POLONSKY for her encouragements.

REFERENCES

- 1 - J. L. Fourrey, P. Jouin and J. Moron, (1973) Tetrahedron Letters, 3239.
- 2 - A. Favre, M. Yaniv and A. M. Michelson, (1969) Biochem. Biophys. Res. Comm., 37, 266.
- 3 - D. E. Berstrom and N. J. Leonard, (1972) Biochemistry, 11, 1
- 4 - A. A. Lamola, (1973) Pure and Applied Chemistry, 34, 281.
- 5 - A $5 \cdot 10^{-3}$ M solution of the 4-thiouracil derivative in CH₂Cl₂ : methacrylonitrile (9:1) was irradiated under nitrogen in a pyrex apparatus using a Hanau QF 81 lamp.
- 6 - A. Ohno, Y. Ohnishi, G. Tsuchimashi, (1969) J. Amer. Chem. Soc. 91, 5038.
- 7 - Dr Guilhem has confirmed structure 5 by X-ray analysis.
- 8 - Thiocarbonyl compound is irradiated at -50° C until its complete disappearance.
- 9 - P. de Mayo and A. A. Nicholson, (1972) Israel J. Chem., 10, 341.