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THIOCARBONYL PHOTOCHEMISTRY. V. LIGHT INDUCED REACTIONS OF 3-METHYL 4-THIOURACIL WITH METHACRYLONITRILE

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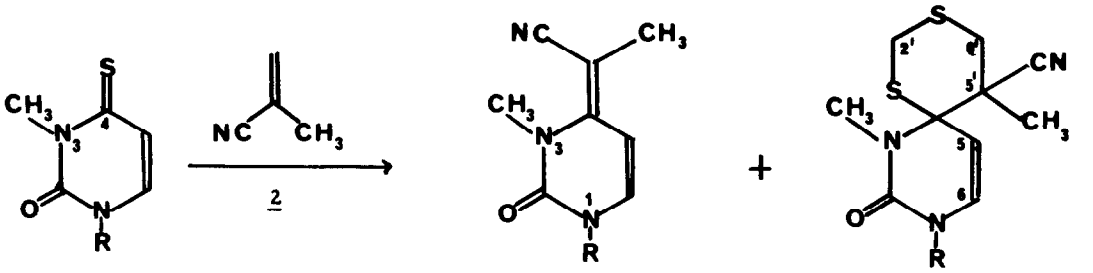
Previously we have shown that 1,3-dimethyl 4-thiouracil 1 interacts photochemically with methacrylonitrile 2 yielding two products, namely 3 and the rather unexpected 4 (1). As the mechanistic study of this photoreaction could help understand 4-thiouridine photochemistry in E.coli tRNA (2-5), we have tried to characterise the intermediates involved in the reaction steps between the excited 4-thiouracil derivative and the isolated products 3 and 4.



1 R = CH_3 3 R = CH_3 4 R = CH_3

5 R = H 6 R = H 7 R = H

For this investigation which is reported in this communication 3-methyl 4-thiouracil 5 has been found very suitable.

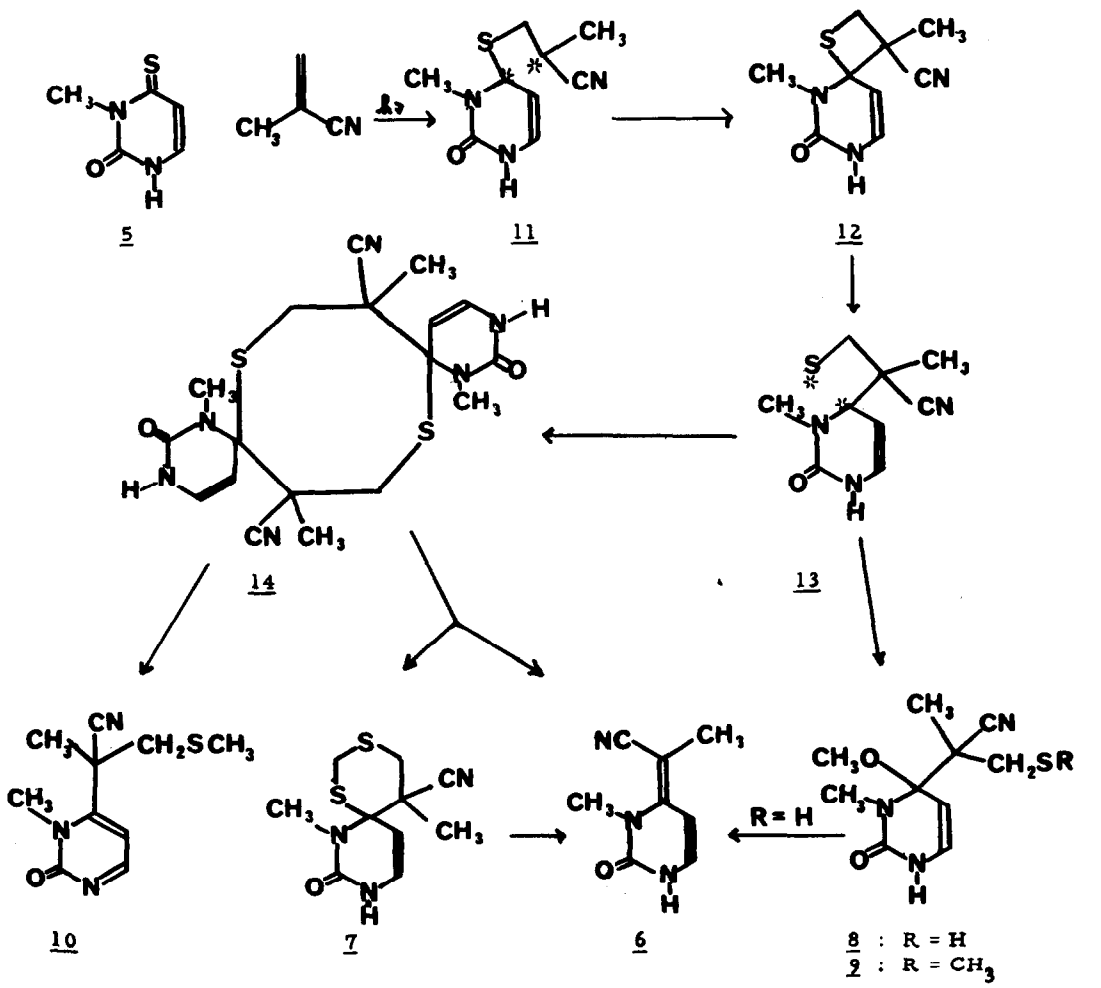
Photochemisal interaction of 3-methyl 4-thiouracil 5 with methacrylonitrile 2

When a solution of 3-methyl 4-thiouracil 5 in a non hydroxylic solvent (CH_2Cl_2) is irradiated (6) at 0° in presence of methacrylonitrile 2 an equimolecular mixture of compounds 6 m.p. 184-186° and 7 m.p. 176-178° is isolated; thus, compounds 1 and 5 react in the same manner.

Structural assignement for 6 and 7 is in complete agreement with spectral data :

Compound 6 $C_8H_9N_3O$ is an unsaturated nitrile (IR ν_{CN} 2,200 cm^{-1} ; UV ϵ_{262} = 13,000 and ϵ_{321} = 16,000) whose NMR spectrum displays an olefinic methyl signal at 1.85 ppm.

Compound 7 $C_{10}H_{13}N_3OS_2$ is both a dihydropyrimidine and a 1,3-dithiane. This follows from UV (ϵ_{251} = 4,000) and NMR data ; chemical shifts and geminal coupling constants for the protons of the methine groups (C-2' and C-6') are in agreement with literature (7) (Table). Since decomposition of 7 in refluxing pyridine yields 6, it is established that C-4 is bonded to the carbon C-5' bearing the cyano group.



When the photoreaction between 2 and 5 is effected in methanol (instead of CH_2Cl_2) the formation of products is temperature dependant. Irradiation below -10° followed by room temperature work up yields compound 6 exclusively. On the other hand, room temperature irradiation gives rise to compound 8, $C_{10}H_{15}N_3O_2S$ m.p. 136-138°. This is a dihydropyrimidine ($UV\varepsilon_{242} = 4,800$) and its structure can be deduced from the NMR data (Table). Futhermore the latter decomposes in refluxing toluene yielding compound 6 ; treatment of 8 with diazomethane gives the oily compound 9. In refluxing toluene compound 9 is unstable and produces 3-methyl uracil.

Mechanism of the reaction : Evidence for thietane formation :

Clearly compound 8 arises through methanol addition to a so far uncharacterised intermediate, tentatively represented as 13, which must result from the ring opening of thietane 12. On the other hand, either at low temperature in methanol or at 0° in CH_2Cl_2 intermediate 13 dimerises and produces 14. Indeed, work up of the reaction product at -20° yields a compound whose electron impact mass spectrum displays a peak at m/e 362 ($M-CH_2S$) while the chemical ionization spectrum (8) exhibits the M+1 peak at m/e 419 thus favouring the attribution of structure 14. In non hydroxylic solvent (CH_2Cl_2, pyridine) 14 decomposes at room temperature yielding an equimolecular amount of 6 and 7 ; however,

TABLE

	Molecular ion	N.M.R.							
	$M^{+\cdot}$	H_5	H_6	$N\text{-}CH_3$	$\overset{CN}{\underset{}{C}}\text{-}CH_3$	CH_2S	$CH_2\begin{smallmatrix}S\\S\end{smallmatrix}$	SCH_3	OCH_3
6	163	5.6 J=8	6.8	3.7	1.85	-	-	-	-
7	255	5.4 J=8	6.6	3.7	1.55	(a) 3.3 ; (e) 2.7 J=15	(e) 3.6 ; (a) 4.4. J=15 ^4J=2.5	-	-
8	241	4.6 J=8	6.6	3.1	1.45	*	-		3.3
9	255	4.55 J=8	6.5	3.1	1.45	2.4 ; 2.8	-	2.3	3.2
10	223	6.6	8.7	3.8	2.05	3.3 ; 3.6	-	2.35	

* not attributed

δ are given in ppm and coupling constant in Hz, Solvent : $CDCl_3$, compounds 8, 9 and 10
C_5D_5N compounds 6 and 7

in methanol 6 is the only product. In presence of diazomethane 14 is split to produce 10 (oil) whose structure can be deduced from analytical and spectral data (UV λ_{max} 318)(Table).

These findings rule out alternative pathway : 5 → 11 → 14 → (13) → 8 for the formation of compound 8 and confirm that a thietane is indeed an intermediate in the reaction of photoexcited 4-thiouracil with methacrylonitrile as it has already been shown in a few cases (9). At this stage we cannot ascertain that thietane is formed directly after photon absorption or through cyclisation of a species such as 11.

In conclusion, it can be inferred from the above results that thietane is produced in the photoreactions of 4-thiouracil with olefins. We think that this finding is valid for such reactions which occur in polynucleotides (10). Accordingly, structural requirement for E.coli tRNA tertiary structure is that the C=S group of the eighth residue (4-thio-uridine). must be parallel, at a bonding distance, to the C-5 ; C-6 bond of the cytidine residue in position 13 (11).

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