

THIOCARBONYL PHOTOCHEMISTRY VI. LIGHT INDUCED ADDITION
OF A PRIMARY AMINE TO 4-THIOURACIL DERIVATIVES

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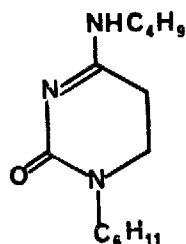
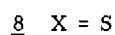
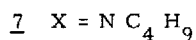
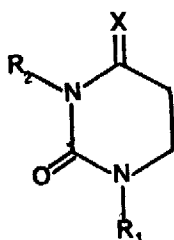
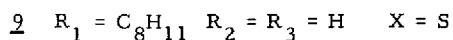
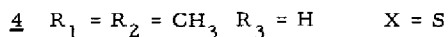
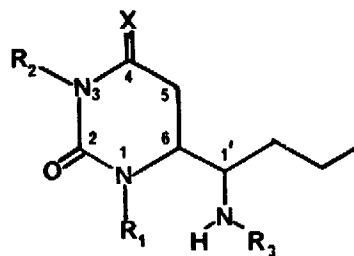
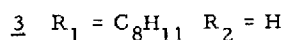
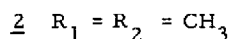
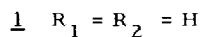
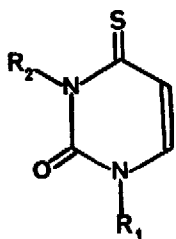
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The photochemistry of the minor nucleic acid constituent 4-thiouracil 1 which possesses an $\alpha\beta$ unsaturated thiocarbonyl function is of special interest. So far, it has been reported that 4-thiouracil derivatives are photoreactive towards oxygen (1), olefins (2, 3), alcohols (4) and sodium borohydride (5). We have now observed that a primary amine, 1-aminobutane, interacts photochemically with 4-thiouracil derivatives 2 and 3.

When a solution (water, methanol, methylene chloride) of 1, 3-dimethyl 4-thiouracil 2 is irradiated (6) in presence of 1-aminobutane the former disappears rapidly. Mass spectrometry ($M^+ 229 = 156 + 73$) and analytical data of the two major photoproducts A (mp 193-194°) and B (mp 162-163°) (isolated in 60 % yield from a CH_2Cl_2 solution irradiated at -40°) indicate that they result from the addition of 1-aminobutane to 1, 3-dimethyl 4-thiouracil 2. Adducts A and B display very similar spectral data suggesting that they are diastereoisomers.

Acetic anhydride treatment of compounds A and B yields monoacetyl derivatives which have been assigned structures 5a (mp 148-149°) and 5b (mp 120-123°). They manifest in their proton NMR spectra a characteristic $COCH_3$ signal at 2.00 and 1.90 ppm respectively. Other data, such as UV absorption maxima and the position of the two N-methyl signals for each compound (Table), indicate that both are 5, 6-dihydro 4-thiouracil derivatives. Inspection of the ^{13}C NMR spectra of acetates 5a and 5b shows that they have two trisubstituted carbon atoms which appear at 50.89 and 57.00 ppm for 5a and at 49.59 and 58.30 ppm for 5b. This demonstrates that a carbon-carbon bond has been formed in this photoaddition process.

Irradiation of acetates 5a and 5b in presence of oxygen (4) yields the 5, 6-dihydro-uracil derivatives 6a (mp 145-146°) and 6b (mp 56°). The site of attachment of the aminobutyl moiety to the C-6 position in 6a and 6b is in agreement with the following NMR data. In the proton NMR spectra of 6a and 6b the H-5 signals (2H) appear as an AB system centered at 2.80 ppm ($J_{AB} = 16$ Hz) in both compounds while the H-6 signal (1H) is observed at 3.70 ppm (6a) and 3.50 ppm (6b). The observed diamagnetic shift ($\Delta\delta = 0.5$ ppm) for the H-5 signal induced by the replacement of sulfur by oxygen at C-4 is in accordance with previous observations made on 5, 6-dihydrouracil derivatives (4, 7).



These results lead us to attribute tentatively structure 4 to the diastereoisomers A and B. The discrepancy between the spectral data of compounds A (4a) and B (4b) and other 5, 6-dihydro 4-thiouracil derivatives (Table) (position of the NMR N-3 methyl signal and wavelength of the UV λ_{max}) results from the interaction between the amino group at C-1' and the thiocarbonyl at C-4. Because of this interaction the thiocarbonyl is masked to thermal addition of excess 1-aminobutane (see below)

A third and minor product has also been isolated in this photoreaction. It has been found identical to the dihydrocytosine derivative 7 which we have prepared by treatment of 5, 6 dihydro 1, 3-dimethyl 4-thiouracil 8 with 1-aminobutane at room temperature (8)

TABLE

m. s.	I. R.	U. V.	N. M. R.*						
			M ⁺	ν (cm ⁻¹)	$\epsilon_{\lambda \text{ max}}$	N ₁ -CH ₃	N ₃ CH ₃	H ₅	H ₆
<u>4a</u>	229	3510, 3420 1650	$\epsilon_{271}=13800$	2.80	2.80	2.80	3.00	4.00	4.60 5.4
<u>4b</u>	229	3510, 3430 1650	$\epsilon_{269}=13800$	2.80	2.80	2.85	3.10	3.60	4.70 5.0
<u>5a</u>	271	3470, 3360 1700	$\epsilon_{283}=12600$	3.20	3.60	3.30	3.50	4.20	6.00
<u>5b</u>	271	3470, 3360 1700	$\epsilon_{285}=12500$	3.20	3.60	3.30	3.30	4.40	5.40
<u>6a</u>	255	3470, 3380 1730, 1670	—	3.30	3.30	2.80	3.70	4.30	6.40
<u>6b</u>	255	3460, 3370 1730, 1680	—	3.20	3.20	2.80	3.70	4.30	6.00

* Solvent = CDCl₃ δ are given in ppm

Accordingly, 7 could arise from 8 through this mode of formation suggesting that the latter is produced in the photoreaction.

We have irradiated (9) 1-cyclohexyl 4-thiouracil 3 in presence of 1-aminobutane. In this case also we have observed very similar results since diastereoisomeric compounds 9 as well as the 5,6-dihydrocytosine 10 (mp 174-177°) are the main photoproducts. The proposed structures for these compounds are in agreement with their analytical and spectral data.

In conclusion, 6-aminoalkyl 5,6-dihydropyrimidine derivatives can be readily available by irradiation of mono- and disubstituted 4-thiouracils in presence of primary amines. It has been previously reported that, unlike its 4-thio analogue, light induced interaction of 1,3-dimethyl uracil with primary amines is much less specific and leads to several types of photoproducts (10)

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REFERENCES

- 1 M.G. Pleiss and P.A. Cerutti (1971) *Biochemistry*, 10, 3093.
- 2 D E Berstrom and N.J. Leonard (1972) *Ibid.*, 11, 1
- 3 J.L. Fourrey, P Jouin and J Moron (1973) *Tetrahedron Letters*, 3229.
J.L. Fourrey, P. Jouin and J. Moron (1974) *Ibid* , 3005.
C. Fombert, J.L. Fourrey, P. Jouin and J. Moron (1974) *Ibid* , 3007
P. Jouin and J.L. Fourrey (1975) *Ibid.*, 1329
- 4 J.L. Fourrey and P. Jouin (1973) *Ibid.*, 3225
- 5 E. Sato and Y Kanaoka (1974) *Chem.Pharm Bull.*, 22, 799
- 6 A solution containing 1 % of 1-aminobutane is made 1.10^{-2} M in 1,3-dimethyl 4-thio-uracil 2 and irradiated through Pyrex under N_2 atmosphere with a Hanau TQ 150 lamp until complete disappearance of the starting material
- 7 P Jouin, Thesis Université Paris-Sud (Orsay) (1973)
- 8 D M Brown and M.J E Hewling (1968) *J Chem Soc (C)* 2050
V. Skaric, B. Gaspert, M. Hohnjec and G. Lacan (1974) *J. Chem Soc.(P. T 1)* 267.
- 9 A 5.10^{-3} M solution 3 in CH_2Cl_2 (or CH_3OH) containing 1 % 1-aminobutane is irradiated as above (6) at 0°C.
- 10 L.S. Gorelic, P Lisagor and N C. Yang (1972) *Photochem and Photobiol.*, 16, 465.