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THIOCARBONYL PHOTOCHEMISTRY. VIII. PHOTOCYCLIZATION OF 5-HYDROXYPROPYL 4-THIOURACIL DERIVATIVES

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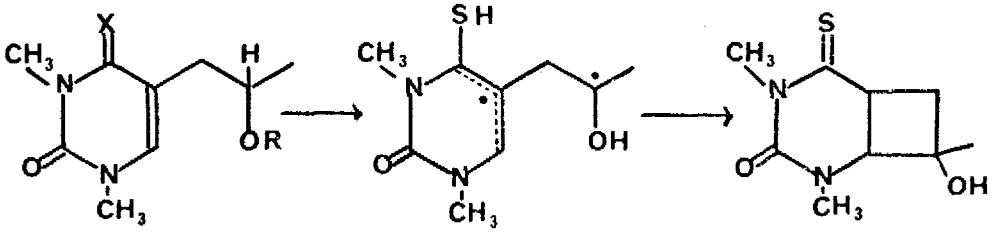
Intramolecular photocylization and photoelimination reactions of carbonyl compounds involve biradical intermediates resulting from a hydrogen abstraction process (1). In general, these intermediates are 1, 4-biradicals which derive from a lower $n\pi^*$ excited state. Similar type II reactions are also encountered with several thiocarbonyl compounds provided the C-H bond (γ-hydrogen abstraction) be weakened by substitution or insaturation (2-5). In contrast, short wavelength irradiation of phenyl thioketones induces specific photoreactivity which arises from an upper excited state (4) (presumably $\pi\pi^*$). In this case δ-H abstraction is preferred over γ-H abstraction indicating 1, 5-biradical formation.

Photoaddition of alcohols (ethanol, isopropanol) to 4-thiouracil derivatives, which possess an α,β-unsaturated thiocarbonyl system, has been reported (6). Assuming that the latter reaction was initiated by an intermolecular hydrogen abstraction process (followed by radicals recombination) it was of interest to compare the photochemistry (intramolecular process) of compounds 1 and 4 after excitation of the $\pi\pi^*$ transition.

Compounds 1 (mp 140-143°) and 4 (mp 88-89°) were prepared from the corresponding 5-substituted uracil (7) by using standard methylation and thiation procedures. When compound 1 was irradiated (8) up to 60 % conversion (9) one major photoproduct was isolated (yield 50 %) for which structure 3 (mp 152-154°) was assigned on the basis of analytical and spectral data. Compound 3, an isomer of the starting material (1), has a UV spectrum (λ_{max} 291 nm) typical of a 5, 6-dihydro 4-thiouracil derivative. Its NMR spectrum is characterized by the presence of a methyl group singlet, (3H) at δ 1.25 ppm ; an expected position for a methyl on a tetrasubstituted carbon bearing a hydroxyl (IR ν_{OH} 3625 cm^{-1}).

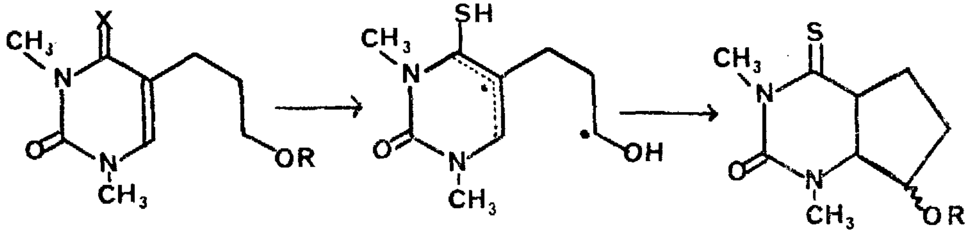
Under the same irradiation (8) conditions compound 4 was found twenty times less reactive than its isomer 1. After 30 % conversion of the starting material, three photoproduct could be detected. The two major ones were isolated as a mixture of alcohols (6, oil, yield : 30 %, IR ν_{OH} 3640 cm^{-1}). Compounds 6 are 5, 6-dihydro 4-thiouracil derivatives (UV λ_{max} 287 nm) which have the same molecular weight ($M^{\cdot +}$ m/e 214) as 4. They could be separated as acetates 7a (oil) and 7b (mp 85-87°) (IR ν_{CO} : 1755 and 1705 cm^{-1}) whose NMR spectra



	X	R
1	S	H
10	S	COCH$_3$
12	O	H

2

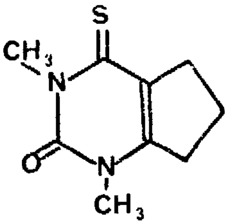
3



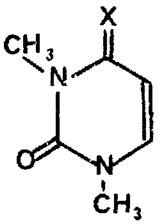
	X	R
4	S	H
11	S	COCH$_3$
14	O	H

5

	R
6	H
7	COCH$_3$



8



9 X = S

13 O

exhibit a multiplet (1 H) found at δ 5.18 ppm (7a) and δ 5.37 ppm (7b). In agreement with the paramagnetic shift observed after acetylation, this signal was attributed to the secondary acetate proton ($\Delta\delta \simeq 0.9$ ppm).

The third, minor, photoproduct mp 145-147° ($M^{\cdot +}$ m/e 196) is a 4-thiouracil derivative (λ_{max} 334 nm) which has been tentatively represented as 8 since its NMR spectrum is devoid of olefinic proton signal.

Alcohols 3 and 6 formed by irradiation of compounds 1 and 4, clearly arise through cyclization of the initially formed biradicals 2 and 5 respectively. The observed difference of reactivity between 1 and 4 is exceedingly larger than expected for a secondary and a primary alcohol. Indeed, isopropanol and ethanol display similar reactivity towards excited 1,3-dimethyl 4-thiouracil 9. Assuming that the cyclization ability of both radicals 2 and 5 is comparable, 1,4-biradical formation seems to be the preferred process in the case of 5-substituted 4-thiouracils. This behaviour, typical of the $n\pi^*$ excited state (1-3), makes us suggest that excitation of the $\pi\pi^*$ transition of 4-thiouracil leads to a photoreactive state which has $n\pi^*$ character. This finding should be relevant for the elucidation of the nature of the excited state(s) responsible for emission (10-11) and photoreactivity of 4-thiouracil in solution (12).

In the case of compound 4 the absence of photoproduct resulting from γ-hydrogen abstraction reflects the inability of excited 4-thiouracil to abstract non activated methylenic hydrogen. This conclusion is supported by the fact that acetylated derivatives 10 and 11 were both found photostable.

In phenyl ketone photochemistry 1,5-biradical formation has been reported to compete with γ-hydrogen abstraction when δ position is activated (13). However, when the C-H bond strength at γ and δ position is similar the δ process is not detectable. The above comparison of the reactivity of the 4-thiouracil derivatives 1 and 4 indicates that the thiocarbonyl of compounds of this class is not as selective towards γ and δ photoprocesses as the carbonyl of phenyl ketones ($n\pi^*$ excited state).

It is also noteworthy that compounds 1 and 4 differ photochemically from their uracil analogues 12 and 14. The only photoproduct obtained after irradiation of 12 was 1,3-dimethyl uracil 13 (14) while compound 14 suffered mostly photodegradation. In both cases we did not detect the formation of cyclobutyl derivatives (15) ; this could mean that cyclization of an initially formed 1,4-biradical is not a favoured process with this particular type of molecule.

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8 - A 2.5 10^{-4} M methanolic solution of the 4-thiouracil derivative was irradiated through Pyrex at -10°C under nitrogen atmosphere with a Hanau TQ 150 lamp.

9 - Higher conversion of 1 resulted in photolysis of photoproduct 3 leading to 1,3-dimethyl 4-thiouracil 9.

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14 - 1,3-dimethyl uracil 13 was produced in 15% yield when 12 was irradiated in water with light of wavelength greater than 280 nm.

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