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# Photo-oxidation of Thiouracil by Singlet Oxygen

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Photo-oxidation of thiouracil was carried out using eosin yellow, rose bengal and methylene blue as dye sensitizers. After completion of reaction two products were isolated and characterised as thiourea and acetyl thiourea by physical, chemical and spectral methods. A mechanism has been proposed for this reaction.

## INTRODUCTION

Simon and Vunakis[1] and later on Spikes and Livingston[2] have carried out systematic investigation of the photo-sensitized oxidation of uracil. They reported that uracil does not get photo-oxidised with methylene blue at neutrality but is slowly oxidised with eosin yellow and more rapidly with flavin mononucleotide (FMN). The rate of photo-oxidation increases with pH.

In the present work thiouracil has been taken for the study. Thiouracil and its propyl derivatives are mainly used in the treatment of hyperthyroidism, angina pectoris and congestive heart failure. The photo-oxidation of thiouracil has been carried out under various reaction conditions.

## EXPERIMENTAL

Photo-oxidation of thiouracil (I) has been carried out using eosin yellow, rose bengal and methylene blue as sensitizers. The photo-oxidation was also carried out in the presence of singlet oxygen scavengers such as β-carotene, nickel chloride and cobalt chloride.

Photochemical reactions were carried out by irradiating a solution of thiouracil (2 g) in 300 mL of distilled water in a reaction flask with a tungsten filament lamp (500 W, Sylvania) in the presence of different dyes: rose bengal, eosin yellow, methylene blue (2 mL/$4.5 \times 10^{-3}$ m). Oxygen was bubbled simultaneously. Progress of the reaction was followed by continuous and regular TLC analysis of the reaction mixture. After about 17 h the TLC indicated the formation of two spots (solvent system methanol, conc.HCl, water 7 : 2 : 1). The two products were separated by preparative TLC and purified.

Melting points were determined in sulphuric acid bath in open capillaries. IR, NMR and mass spectra were recorded. Photo-oxidation of thiouracil was also carried out in the presence of singlet oxygen scavengers β-carotene, nickel chloride and cobalt chloride ($1.0 \times 10^{-6}$ M) using the same procedure.

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## RESULTS AND DISCUSSION

Photo-oxidation of thiouracil gave two products (m.p. 180°C and 142°C) and their yields were determined in the presence of eosin yellow, methylene blue and rose bengal and reported in Table-1 below.

TABLE-1
EFFECT OF SENSITIZERS ON THE YIELD OF PHOTO PRODUCTS

| S. No. | Dye used | Time of reaction (h) | Approx. % of yield of two products | |
|---|---|---|---|---|
| | | | A | B |
| 1. | Eosin yellow | 20 | 15 | 17 |
| 2. | Methylene blue | 17 | 20 | 22 |
| 3. | Rose bengal | 17 | 18 | 20 |

Participation of singlet oxygen was confirmed by using different singlet oxygen scavengers in the reaction mixture. The yields of products were considerably reduced in the presence of these scavengers. The results are summarized in Table-2.

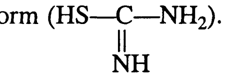
TABLE-2
EFFECTS OF SINGLET OXYGEN SCAVENGERS

| Scavengers[3-5] | Dye sensitizers | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Eosin yellow | | | Rose bengal | | | Methylene blue | | |
| | Time of reaction (h) | % yield of product | | Time of reaction (h) | % yield of product | | Time of reaction (h) | % yield of product | |
| | | A | B | | A | B | | A | B |
| β-carotene | 22.00 | 12 | 14 | 18.00 | 14 | 16 | 22.30 | 15 | 17 |
| Nickel chloride | 21.00 | 11 | 13 | 19.30 | 12 | 13 | 20.00 | 15 | 16 |
| Cobalt chloride | 21.30 | 11 | 13 | 19.00 | 12 | 12.5 | 20.00 | 15.5 | 15 |

The product A (white-coloured) has m.p. 180°C and on the basis of elemental analysis; molecular formula corresponds to $CH_4N_2S$.

The IR spectrum of product A showed bands at 1618 $cm^{-1}$, which is due to C═S group. Bands at 3381–3177 $cm^{-1}$ may be due to —$NH_2$ group attached to C═S group.

NMR peak at 5 ppm is due to solvent $CD_3OD$ as given in blank NMR of pure solvent. Peak at 5.8 ppm is due to —$NH_2$ group attached to C═S group. Peak at 7.2 ppm is due to enolic form (HS—C—$NH_2$).



$$(HS-\underset{\underset{NH}{\|}}{C}-NH_2)$$

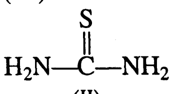
Thus in the light of above data the product A has been characterised as thiourea (II).

Product 'B' has m.p. 142°C. On the basis of elemental analysis molecular formula corresponds to $C_3H_6N_2OS$.

The IR spectrum showed bands at 1714 $cm^{-1}$ which may be due to (C═O) group, the band at 1690 $cm^{-1}$ is due to ν(C═S) group.

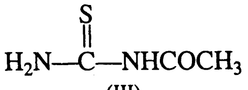
Strong peak at 2 ppm in NMR spectrum is due to —$CH_3$, —$NH_2$ and >NH groups.

On the basis of above spectral data analysis product 'B' has been characterised as acetyl thiourea (III).



$$H_2N-\overset{\overset{S}{\|}}{C}-NH_2$$

(II)



$$H_2N-\overset{\overset{S}{\|}}{C}-NHCOCH_3$$

(III)

The following scheme can be considered as describing the course of a singlet oxygen reaction.

$$D \xrightarrow{h\nu} {}^1D^* K_a$$

$${}^1D^* \longrightarrow {}^3D^* K_i$$

$${}^3D^* + {}^3O_2 \longrightarrow D + {}^1O_2 K_{O_2}$$

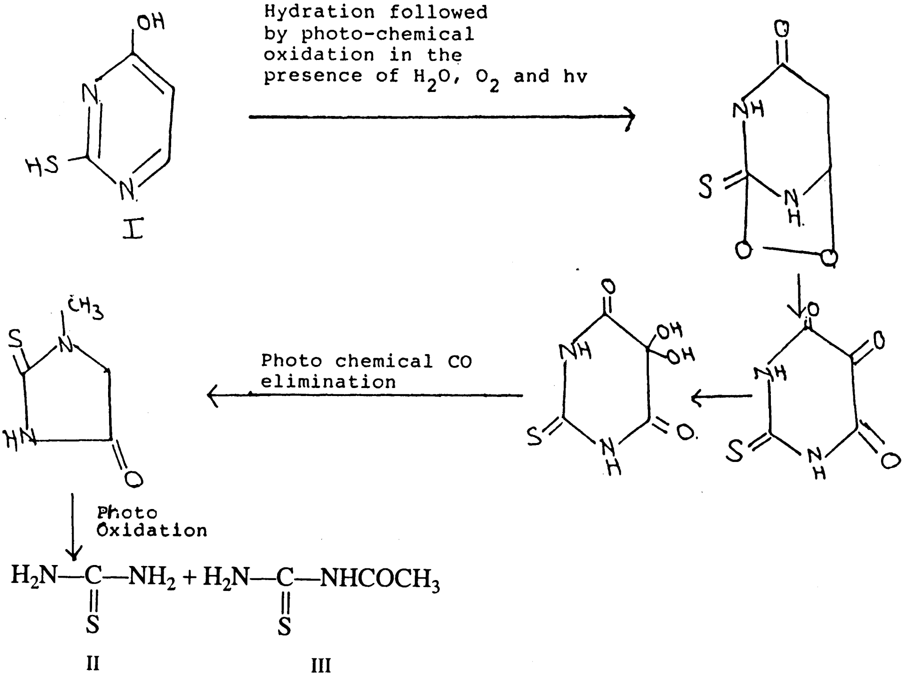
$${}^1O_2 + S \longrightarrow PK_r$$

$${}^1O_2 + Q \longrightarrow {}^3O_2 + QK_Q$$

$${}^1O_2 \longrightarrow {}^3O_2 K_d$$

where D = dye, S = substrate, Q = quencher and P = product.

The following tentative mechanism has been proposed for the dye sensitized photo-oxidation of thiouracil.



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