

Photo-oxygenation of Amithiazone by Singlet Oxygen

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The thiosemicarbazone amithiazone has been known to be quite effective in the treatment of pulmonary tuberculosis¹. Since no attention has been given to the photo-oxygenation of this drug, the same was carried out with singlet oxygen, an effective oxidant for biomolecules².

Results and Discussion

The effect of the nature of solvent on photo-oxygenation of amithiazone has been studied using different solvents. However, because of differences in solubilities, the amount of substrates could not be kept the same throughout. The results are presented in Table 1.

TABLE 1—EFFECT OF SOLVENTS

[Methylene blue] = $1.0 \times 10^{-5} M$, Time of irradiation = 100 min

Solvent	Life time* μs	Yield of product %	Time of initiation min
Water	2	11.0	90.0
Acetone	42	44.0	30.0
Dioxane	32	40.0	32.0
Pyridine	17	30.0	45.0
Ethanol	19	35.0	40.0
Methanol	11	28.0	50.0

*Ref. 3

Dye-sensitised photo-oxygenation of amithiazone has been carried out in the presence of various photosensitisers keeping all other factors identical. The yield of the product was found to depend on the triplet energies of the sensitisers (Table 2).

TABLE 2—EFFECT OF TRIPLET ENERGIES

[Dye] = $1.0 \times 10^{-5} M$, Time of irradiation = 100 min

Sensitiser	Triplet energy* kcal mol ⁻¹	Yield of product %	Time of initiation min
Methylene blue	23.0	28.0	50.0
Eosin-Y	43.2–46.0	18.0	65.0
Rose Bengal	37.5–42.2	20.0	60.0
Thionine	48.0	11.0	70.0
Riboflavin	57.8	8.0	82.0

*Ref. 4.

The effect of various singlet oxygen scavengers on the yield of photoproduct has also been studied and the results are shown in Table 3.

The crystallised product has been characterised on the basis of analytical, physical, chemical and

spectral evidence: m. p. 177–78° (Found: C, 54.26; H, 5.40; N, 25.12. Calcd.: C, 54.54; H, 5.45; N, 25.45); λ_{max} (MeOH) 261, 228 and 216 nm (the bands due to C=S at 235 and 197 nm of the reactant were absent in the product, indicating that C=S band affected during oxidation); ν_{max} (KBr) 3430m, 3390m, 3342m, 1730s, 1681s, 1674m, 1651s, 1625s, 1610s, 1605w, 1600m, 1580m, 1530s, 1500m, 972m, 830w and 790w cm⁻¹; ¹H nmr τ (CDCl₃) 7.63 (3H, s), 5.94 (1H, s), 5.02 (1H, s), 3.31 (2H, s), 3.20 (1H, s), 3.01 (2H, d), 2.95 (2H, d), the values for the last two doublets are very small; *m/z* 220 (*M*⁺12), 177(15), 176(9), 161(7), 134(4), 118(22) and 43(100).

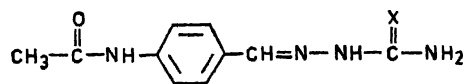
TABLE 3—EFFECT OF SINGLET OXYGEN SCAVENGERS

[Methylene blue] = $1.0 \times 10^{-5} M$, Time of irradiation = 100 min, [Scavenger] = $1.0 \times 10^{-5} M$

Scavenger*	Yield of product %
—	28.0
Nickel chloride	Nil
Cobalt chloride	0.2
β -Carotene	Nil
DABCO	Nil
α -Tocopherol	0.4

*Ref. 5.

On the basis of the results, the product of photo-oxygenation of amithiazone (1) by singlet oxygen has been identified as the corresponding semicarbazone (2).

1; X = S
2; X = O

In the first step, singlet molecular oxygen attacks the C=S bond of amithiazone (1) to produce as expected a dioxetane derivative which then dissociates into the product (2) and a molecule of sulphur monoxide which, in turn, rapidly disproportionates into SO₂ and sulphur⁶.

It was observed that the yield of the product was higher in non-polar solvents as compared to water. This may be attributed to the longer life-time of singlet oxygen in organic solvents³. Also, the yield was highest in case of methylene blue and lowest with riboflavin. This may be due to the fact that methylene blue has lower triplet energy

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whereas riboflavin has higher triplet energy and all the dyes having higher triplet energies generate more $^1\Sigma_g$ oxygen and less $^1\Delta_g$ oxygen and vice versa.

Further, the drastic reduction in the yield of the product in the presence of scavengers confirms that the singlet oxygen is the active oxidising species in the photo-oxygenation of amithiazone.

Experimental

Amithiazone (0.5 g) dissolved in methanol (40 ml) containing methylene blue ($1.0 \times 10^{-5} M$) was exposed to a tungsten lamp kept at a distance of 20 cm from the lower surface of the reaction flask. Oxygen gas was continuously bubbled through the solution. The progress of the reaction was monitored by tlc using the solvent system n-butanol-acetic acid-water (4 : 1 : 5, v/v). The

resulting, solid, m.p. 118° (identified as sulphur) was filtered out. The filtrate was decolourised with active charcoal and evaporated to yield a residue which was crystallised from alcohol.

References

1. J. P. JOWIN and BUN-HOI, *Ann. Inst. Pasteur (Paris)*, 1946, 76, 580.
2. J. J. WORMAN, M. SHEN and P. C. NICHOLS, *Can. J. Chem.*, 1972, 50, 3923; C. C. WAMSER and J. W. HERRING, *J. Org. Chem.*, 1976, 41, 1476; R. DUBBY, P. GANDHI, S. JAIN and M. M. BOKADIA, *Curr. Sci.*, 1985, 54, 340.
3. R. H. YOUNG, D. BREWER and R. A. KELLER, *J. Am. Chem. Soc.*, 1973, 95, 375.
4. D. R. KEARNS, *Photochem. Photobiol.*, 1969, 10, 215; K. ESKINS, *Photochem. Photobiol.*, 1979, 29, 609.
5. D. J. CARLSSON, T. SPRUNCHUK and D. M. WILES, *Can. J. Chem.*, 1974, 52, 3728.
6. P. B. PUNJABI, S. C. AMETA, T. C. SHARMA and M. M. BOKADIA, *J. Indian Chem. Soc.*, 1988, 65, 130.