

## **Photolytic Irradiation of Pharmaceutical Compound 2 (-4 thiazolyl) benzimidazole**

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**Abstract :** Photolytic irradiation of 2(-4 thiazolyl) benzimidazole in acidic and neutral medium using benzophenone (methyl orange) as sensitizer. Photochemical reactions depend on the source of the reaction. for example Sunlight, UV light and visible light. 2-(-4 thiazolyl) benzimidazole(2gm powder) was dissolved in dried and distilled ethyl alcohol (C<sub>2</sub>H<sub>5</sub>OH) 200 ml and add 0.01gm sensitizer. The solution mixture was irradiated in presence of 125w and 250 w mercury vapor lamp for around 40 to50 hrs. The progress of the reaction mixture was observed at regular intervals from Thin layer chromatography method every10 hrs. After 41 and 55 hrs two new spots appeared on the plate of TLC. At the end of the reaction two products were found. This products show many pharmaceutical properties like primarily in treatment to control the stomach warm mold and fungal diseases infection, also widely used in (thiabendazole medicine), anti parasitic medicine for treatment of roundworm, hookworm and helminthes.

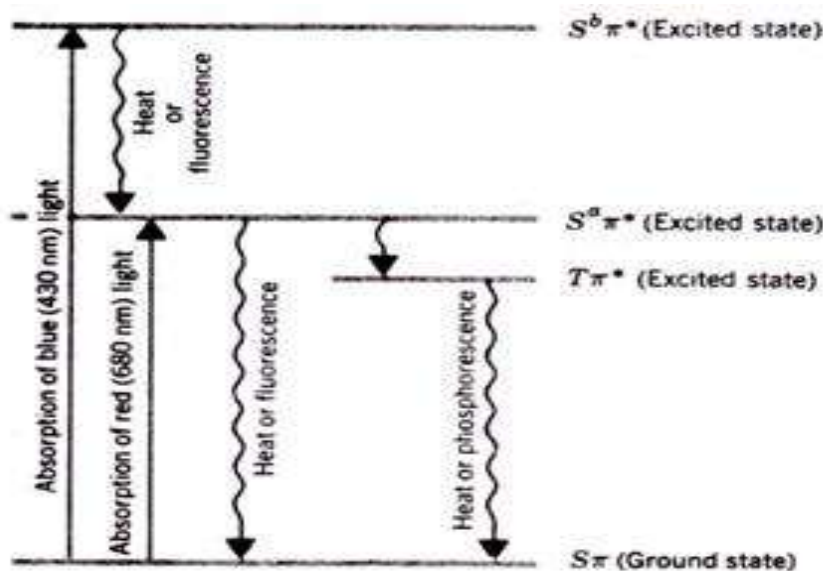
**Keywords :** Photolytic Irradiation, 2(-4 thiazolyl) benzimidazole.

### **I. Introduction**

Organic photochemistry gives us the way for the new chemical reaction. Some of these reaction are unique, that is, they are only known by photochemical means. Heterocyclic constitutes a major segment of Medicinal organic chemistry and manifests significant pharmacological activity. The photochemistry of heterocyclic pharmaceutical is intriguing because of the wide array of new chemical reactions. The electromagnetic radiation consists in the direction of propagation of the beam, when these radiation are absorbed by the molecules, they increase the potential energy. The relevance of photochemistry also lined in its varied application in science and technology. Synthetic organic photochemistry has provided methods for manufacture of many chemicals which could not be produced by dark reaction. Efficiency and selectivity of these methods have an added advantage. Some example of industrially viable photochemical syntheses are available<sup>2</sup>. The most interesting type of electronic excitation in organic molecules are pi and pi to pi star transition. These transitions have low energy requirement and occur at longer wavelength. These transition are

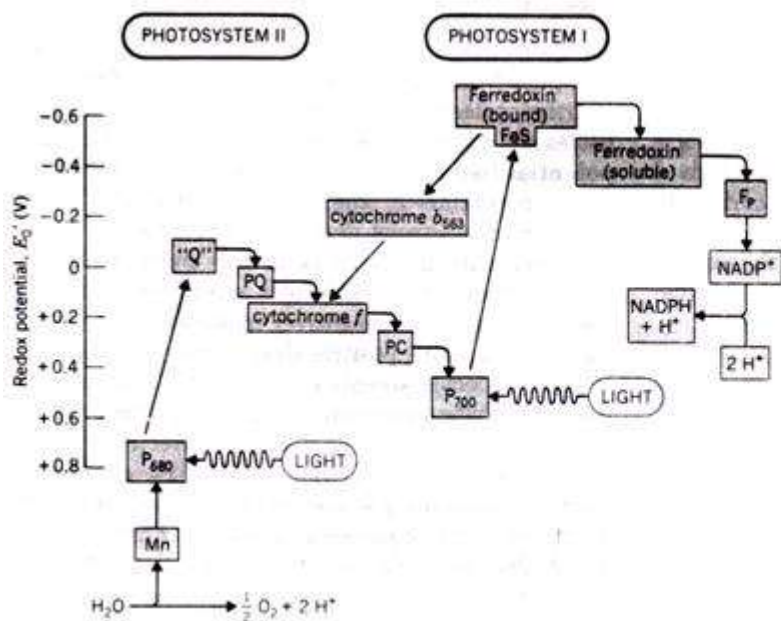
associated only with unsaturated centers, though the energy of n-pi\* transition. There are even number of electrons in a typical organic molecule and these electrons are usually paired in the ground state. On promotion of an electron from any of occupied orbital, the energy state of the molecule changes, these states may have singlet or triplet character.

According to Wyhe<sup>2</sup>, Photochemistry is a natural meeting point of spectroscopic energy transfer and reaction kinetics. According to Chapman<sup>3</sup>, High pressure mercury lamps are the most intense source of uv radiation. These lamps are excellent for qualitative and semiquantitative photochemical work. Medium pressure mercury lamps are also used as UV source. Low pressure hydrogen discharge and high intensity noble discharge using Krypton and Xenon are found to rich in short wavelength UV radiations<sup>4,5</sup>. The rediscovery of singlet oxygen was made in 1964 by Foot and Wexler<sup>6</sup> and Corey and Taylor<sup>7</sup>. Fluorescein are example of sensitizer which are used for photo oxidation of proteins amino acids, alkaloids and many other organic compounds<sup>8</sup>. Photolysis or photo irradiation of organic compounds has been a vast field of research since last forty years.<sup>9-31</sup>



**FIGURE 17-11** Main electronic states in the excitement of chlorophyll by red and blue light.

During electron transfer, the molecules accept electrons from less positive (more negative) molecules and donate electrons to more positive (less negative) molecules. When a molecule accepts electrons, it is said to be reduced, and when electrons are given up, the molecule is said to be oxidized. The transfer of electrons following the absorption of light energy by chlorophyll therefore involves a sequence of oxidation-reduction reactions. This sequence is shown in Figure 17-14, which also identifies the intermediate electron acceptors and their redox potentials.

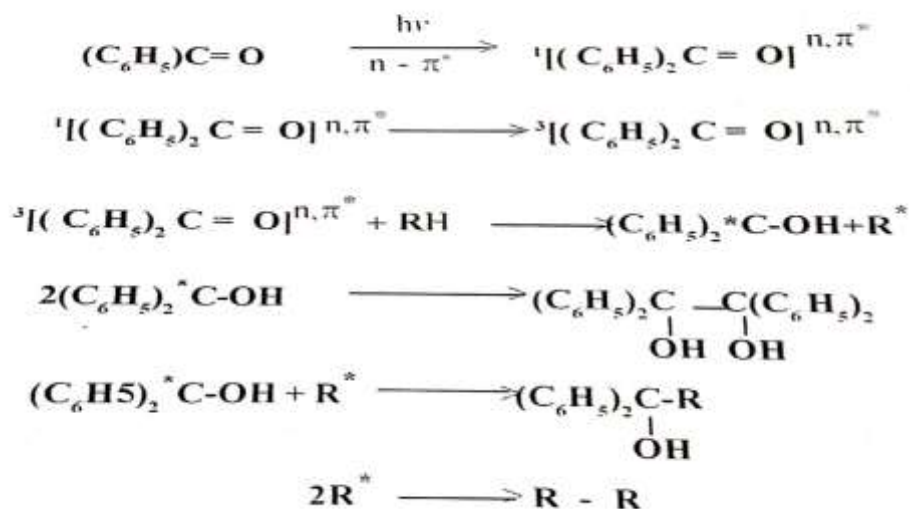


**FIGURE 17-14** Movements of electrons during the light reactions of photosynthesis.

Standard free energy change that takes place when ATP is formed from ADP and  $P_i$  is about 30.5 kJ/mole (7.3 kcal/mole); this is equivalent to a redox potential of about 0.45 to 0.61V. Most of the measurements that have been made indicate that one molecule of ATP is produced for each pair of electrons moved from photosystem II to photosystem I (i.e., non-cyclic photophosphorylation). Several recent studies strongly suggest that more than one molecule of ATP is produced by the reactions that begin with the splitting of water (i.e., photolysis) and end with the reduction of  $NADP^+$ . The second phosphorylation is believed to be coupled to the photochemical reaction. If the number of molecules produced during the light reactions is to balance the number consumed by the dark reactions, then three ATP must be produced for each pair of electrons transported from  $H_2O$  to may be generated by cyclic photophosphorylation. Therapy is the treatment of disease by the use of visible or near infrared light together with an administered photosensitizer and in the presence of molecular oxygen at ambient levels. Light is absorbed by the photosensitizer, which then serves to activate oxygen in some way. The activated oxygen (principally singlet oxygen) then causes damage to the living systems, e.g. PDT of cancer; photodynamic destruction of microbes.

In recent years, naturally occurring plant furocoumarins have been actively investigated with respect to their photosensitizing ability to induce skin erythema. Psoralens have also been found to possess carcinogenic and mutagenic properties when applied in conjunction with near ultraviolet light exposure. Psoralen plus near UV light treatment (PUVA therapy) has also been shown to induce various other adverse biological changes.

Photo reduction it has been known for many years that photo excited alkyl and aryl ketone and aldehyde can act as photo oxidizing agent by abstracting hydrogen from suitable donor molecules. The most extensively studied reaction of this type is formation of benzpinacol from the irradiation of benzo-phenone in the presence of hydrogen donors.



## II .Experimental

Photolytic Irradiation of 2 (-4 thiazolyl) benzimidazole in acidic and neutral medium using benzophenone as sensitizer. Substrate (2g) was dissolved in 200ml distilled ethyl alcohol . The medium was made acidic by adding 2-3 drops of dil. HCL in a beaker and benzophenone (0.01g) was added as sensitizer. The solution was then transferred in the photo reactor and irradiation was started. The temperature of the reaction mixture was kept constant by continuous water circulation. The progress of the reaction was observed at regular intervals. After about 70 hrs no change was reaction mixture so after 72 hrs irradiation was stopped. procedure was followed as in the previous experiment. Photolytic irradiation of same substrate in neutral medium. The 2gm substrate was dissolved in 200ml distilled ethyl alcohol. Add 0.01 gm of benzophenon as sensitizer. This solution was then transferred in the photo reactor and irradiation was started in 125 w lamp. The progress of the reaction mixture was observed at regular intervals. After 41 hrs. tow new spots appeared on Thin Layer Chromatography plate and the substrate disappeared. At the end of the reaction, the reaction mixture was concentrated and the product IV and V were separated by preparative TLC.

### PRODUCT -IV

Yield	0.8 gm
Melting point	170 0c
Test of nitrogen	Positive
Test of Sulpher	Negative

### PRODUCT -V

Yield	0.7gm
Melting point	2230c
Test of nitrogen	Positive
Test of Sulpher	Positive

## III. Results and Discussion -IV

The photolytic Irradiation of the compounds has been carried out benzophenon as sensitizer under the uv lamp(125w),when 2(-4 thialyl)benzimidazole was irradiated by UV light in neutral medium .It give product IV &V in the structure of the product has been confirmed by the IR,1HNMR,13CNMR.

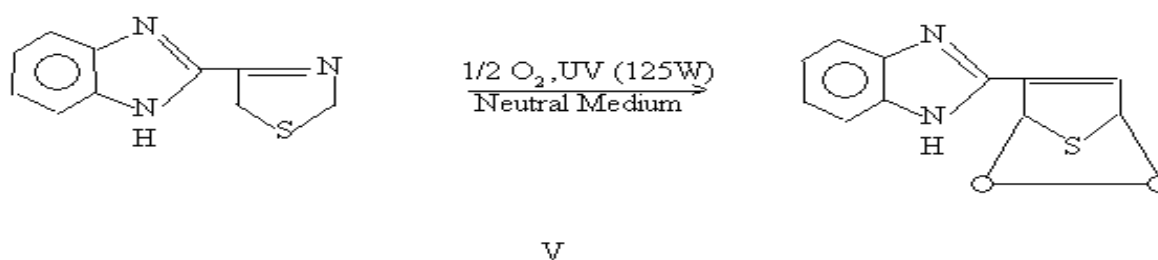
1. The IR spectrum of the product show peaks at 3369.3(NH stretching),1596.4(CN stretching),1274.9 (C-N bending) 1086.5( C-O & C-N stretching), 933.5(O-O stretching) 831.8Cm-1(aromatic CH bending).

2. The <sup>1</sup>H NMR spectrum of product show peaks at 7.5-7.5(aromatic protons)6.2.(NH protons).4.7-4.5( CH<sub>2</sub> proton of 5 member ring).

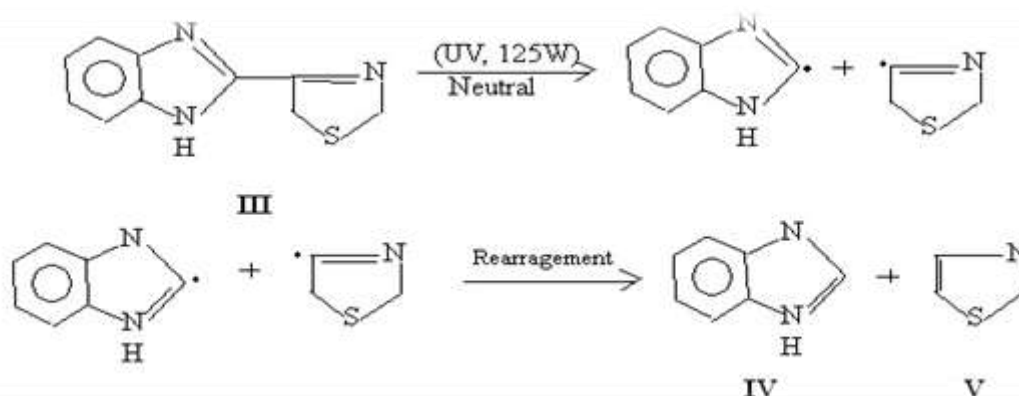
3. The <sup>13</sup>C NMR spectrum of the product show peaks at 155.0(C1 & C2) 141(C3 carbon), 138(C4 carbon atom),124-131(aromatic carbon atoms).

#### IV.NOTE- STRUCTURE ANALYSIS

Formation of new compound in presence of UV(125w).



#### V-MECHANISM OF COMPOUND



#### IV. Results and Discussion -VI

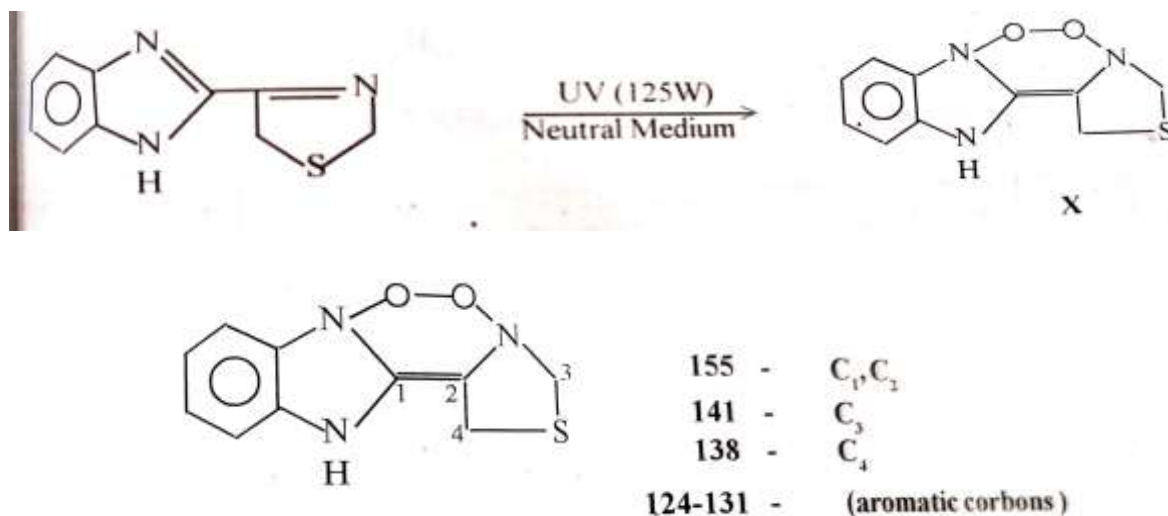
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4. The Mass Sppectrum of the product at m/z 233 which correspond to the to the molecular weight of the product.Other important peak are as follows;217,201,199,117,102,91,83,76 etc.



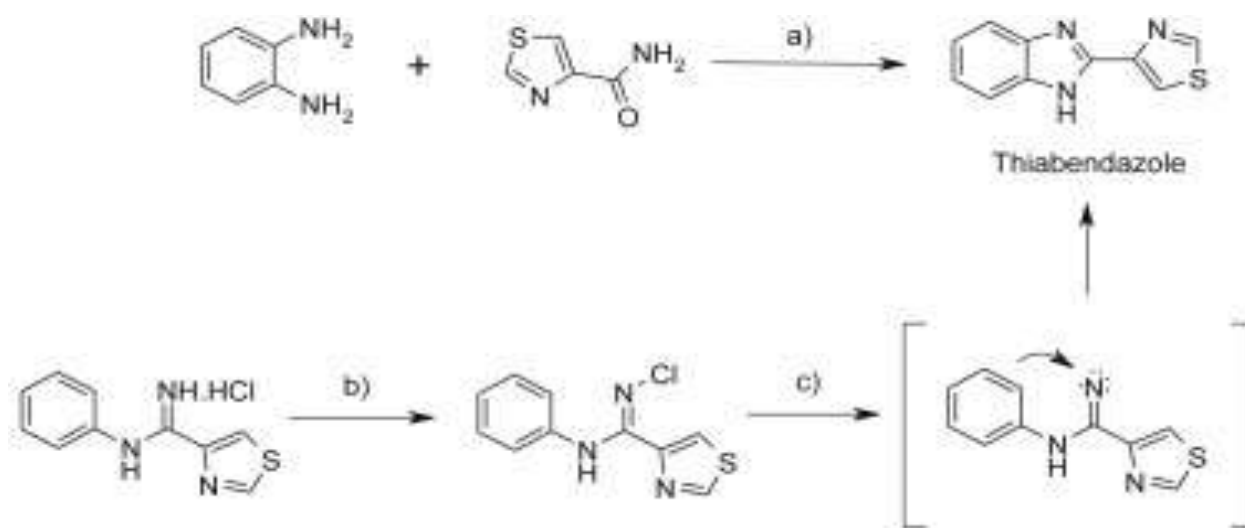
#### IV. Medicinal Properties:

It is antifungal, antipyretic and ant parasitic. Photolysis of benzimidazole and its 2- alkyl derivatives has been studied by Edward and George<sup>32</sup>. Photolysis of various 2- substitute benzimidazole has been studied by Crank and Ahmad<sup>33</sup>. Its derivatives have wide range of pharmaceutical applications, like Anticancer properties, antipertensives properties, antiviral properties, antifungal properties, anti HIV properties, anti-convulsions properties and anti-diabetics properties. Riboflavin and rose Bengal sensitized photo oxidation of this type of compound, its kinetic study and microbiological implication has been studied by Posadz<sup>11</sup>.

2-(4-thiazolyl) benzimidazole in approved by oral use as an anti-fungal and anti-helminthic drug since 1967, has recently been repurposed as a vascular disrupting agent. The structure of the compound showing moderate inhibitory cell proliferation reactivity. It is confirmed as anti-angiogenesis and vascular. Substituted Benzimidazole first introduced in 1962. It is active against a variety of nematodes and is the drug of choice for strongyloidiasis. It has CNS side effects and hepatotoxic potential. (From Smith and Reynard, Textbook of Pharmacology, 1992), thiabendazole is a fungicide and parasiticide. This drug is also a chelating agent, which means that it is used medicinally to bind metals in cases of metal poisoning, such as lead and mercury poisoning or antimony poisoning. It is vermin-fugal against *Ascaris lumbricoides*, *Strongyloides stercoralis*, *Ancylostoma duodenale*, *Trichuris trichiura* and *Ancylostoma Brazilians* (dog and cat hookworm), *Toxocara* and pinworm.

Substituted: They are the potent inhibitors of Parietal cell proton pump, the Na and K. The substituted benzimidazoles are capable of blocking gastric acid secretion in response to some stimuli. For the activity sulfoxide group, methylene group with heterocyclic compound is important for reactive activity.

## Structure of Drug



**Reagents and Conditions:** a) Polyphosphoric acid, heat. b) NaOCl. c) NaOH

## V. Acknowledgement

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