PHOTOCHEMISTRY OF IMIDAZOLINONES

P.A. Mohamed Basheer “Synthesis of some imidazole derivatives and the study of their chemical and photochemical reactions ” Thesis. Department of Chemistry, University of Calicut, 2001
CHAPTER VI

PHOTOCHEMISTRY OF IMIDAZOLINONES

Introduction and Scope

In the last 50 years photochemistry has seen a tremendous upsurage of interest and activity. In recent years the growth of photochemistry has been stimulated anew by the keen interest of not only the physical chemists but also the physical organic, organic and inorganic chemists, molecular spectroscopists, kineticists and photobiologists.

Rapidly increasing number of investigations since 1960 have shown that many novel and synthetically useful reactions including oxidation, reduction, dimerisation, cycloaddition, rearrangement substitution and elimination may be consequent upon the absorption of light by organic molecules. Many chemical transformations can be effected photochemically which would otherwise require a large number of steps by standard chemical procedures. Now a days the study of organic photochemical reactions has become an inevitable tool for the understanding of a number of biological transformations. Heterocyclic ring systems which are the constituents of almost all of the biological systems, play an important role in the interaction of light with biological materials.
The study of photochemistry deals with a unique type of chemical reaction. It is concerned with the "bimolecular" interaction of light quantum and a molecule and subsequent chemical and physical changes which result from the interactions. Light is always one of the reactants in photochemical reactions.

The current interest in organic photochemistry is reflected in the increase in the number of publications\textsuperscript{140-143} concerned with the photochemistry of heterocyclic systems. Photo-oxidation of heterocyclic compounds is important in a number of photobiological and photomedical phenomena.\textsuperscript{144} Photo oxygenation reactions of nitrogen heterocyclics have been the subject of recent review\textsuperscript{145}.

Many heterocyclics including drugs are responsible for phototoxic or photo allergic behaviour due to photo oxidation\textsuperscript{146}. Formation of heterocyclics both by photo addition and photo cyclisation has become a preferable method for their synthesis in a number of cases\textsuperscript{147}.

The relevance of photochemistry also lies in its varied applications in science and technology. Synthetic organic photochemistry has provided methods for the manufacture of many chemicals which could not be produced by dark reactions. Some industrially viable photo chemical syntheses are the synthesis of vitamin $D_2$ from ergosterol isolated from certain yeasts, synthesis of
cubanes which are antiviral agents, industrial synthesis of caprolactam the monomer of Nylon-6, and synthesis of antioxidants by photo sulphonation. Photo initiated polymerisation is used in photography, lithoprinting and manufacture of printed circuits for the electronic industry. The destructive effects of sunlight on coloured cotton fabrics is of everyday experience, the worst sufferer being window curtains. The light absorbed by dyes used for colouring fabrics initiates oxidative chain reaction to cellulose fibres. This causes the tendering of cotton. The photo physical phenomenon of fluorescence and phosphorescence have found varied applications in fluorescent tube lights, X-ray and T.V screens as luminescent dials, as optical brighteners in white dress materials, as paints in advertisement boardings which show enhanced brilliance by utilizing fluorescence.

Photo oxidation reactions play a significant role in the chemistry and biology of a number of naturally occurring system containing the imidazole ring.

The photo reactions of substituted imidazoles are also important in the study of chemiluminescence. Great interest has centered on the involvement of 2,4,5-triphenyl imidazole (lophine) and similar compounds in the phenomenon of chemiluminescence.

The work presented in this thesis deals with the photochemical reactions of some 2,4-disubstituted imidazolin-5-ones of the type.
As a background to these investigations a survey of the literature of photochemical reactions of imidazoles is presented below.

**Photochemistry of imidazoles - A Review**

In 1877 Radziszewski\textsuperscript{151} observed the emission of light when 2,4,5-triphenyl imidazole (lophine) was decomposed with alcoholic potash in presence of light. In presence of potassium ferricyanide lophine give rise to a piezochromic dimer (1) which gives an intensely violet solution of the radical (2) in organic solvents. Other dimeric species (3), (4) have also been reported\textsuperscript{152-155}.
In 1953 Weil, James Buchert noticed the loss of biological activity during photolysis of the enzyme Ribonuclease is due to the disappearance of histidine residues and accordingly with the oxidative destruction of the imidazole fragment. The oxidative degradation was also found to be responsible for the loss of biological activity of insulin on photolysis.

Wasserman and coworkers observed that irradiation of imidazole with UV-visible light in methanol in presence of methylene blue as sensitizer results in the formation of dimethoxy hydantoin.

In a study of photosensitized oxygenation of imidazoles, Wasserman found that 2,4,5-triphenyl imidazole reacts with singlet oxygen to yield an N,N'-diaryl benzamidine probably through hydroperoxide.
They also found that 4,5-diphenylimidazole on photooxygenation under similar conditions yields 5-methoxy-4,5-diphenylimidazolin-2-one and 4,5-dimethoxy-4,5-diphenylimidazolidin-2-one.

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{C}_6\text{H}_5 & \quad \text{NH} \\
\text{O}_2 & \quad \text{MB, CH}_3\text{OH} \\
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{C}_6\text{H}_5 & \quad \text{NH} \\
\text{OCH}_3 & \quad \text{CH}_3\text{O} \\
\end{align*}
\]

Photo-oxidation of alkyl imidazoles under similar conditions gave degraded products like acetamidines and oxamide.\textsuperscript{164}

\[
\begin{align*}
\text{N} & \quad \text{CH}_3 \\
\text{N} & \quad \text{CH}_3 \\
\text{NH} & \quad \text{CH}_3 \\
\text{NH} & \quad \text{CH}_3 \\
\text{O} & \quad \text{NH}_2 \\
\end{align*}
\]

Wasserman and coworkers\textsuperscript{158-160} reported the formation of N-phenyl N,N\textsuperscript{1}-dibenzoyl benzamidine by the photooxygenation of tetraphenyl imidazole.

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5 & \quad \text{NH} \\
\text{O}_2 & \quad \text{MB, CH}_3\text{OH} \\
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{C}_6\text{H}_5 & \quad \text{C}_6\text{H}_5 \\
\end{align*}
\]

2,5 substituted imidazoles undergo cleavage at the enamine double bond yielding products similar to that of dioxetane intermediates. The
photooxidation of fused ring imidazole gave corresponding diamide in good yield.

The photosensitized reactions of imidazolones and imidazoline derivatives are less available. Phenyl substituted imidazolones were found to undergo thermal singlet oxygenation to give \( N,N^1 \)-diacyl ureas.

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{R} \\
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{N} & \quad \text{CO} \\
\end{align*}
\]

\[ \xrightarrow{h\nu} \]

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{R} \\
\text{O} & \quad \text{N} \\
\text{O} & \quad \text{N} \\
\text{CO} & \quad \text{C}_6\text{H}_5 \\
\end{align*}
\]

\( a: \text{R} = \text{CH}_3 \)
\( b: \text{R} = \text{C}_6\text{H}_5 \)

Irradiation 1,3,4,5-tetraphenyl imidazolin-2-one in benzene under nitrogen atmosphere gave \( N \)-substituted phenanthrimidazolone.
1,3 diphenyl imidazolin-2-one undergoes photodimerisation
giving cyclobutane system.

\[
\begin{align*}
\text{N} & \quad \text{N} \\
C_6H_5 & \quad C_6H_5 \\
\text{h\textgamma} & \\
\text{N} & \quad \text{N} \\
O & \quad O \\
C_6H_5 & \quad C_6H_5
\end{align*}
\]

Synthesis of (±) biotin is based on photochemical cycloaddition\textsuperscript{168} reaction of 1,3 diacetyl-imidazolin-2-one.

Imidazolines were found to undergo photosensitized cis-trans
isomerisation between amarine and isoamarine\textsuperscript{169}.

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{C}_6\text{H}_5 & \quad \text{N} \\
\text{CH}_3\text{OH} & \\
\text{CH}_2\text{CHOH} & \quad \text{C}_6\text{H}_5 \\
\text{Acetone} &
\end{align*}
\]

The rose bengal sensitized photo-oxygenation of cis-2,4,5-
triphenyl imidazoline has been found to give a mixture of products\textsuperscript{170}. The products are 2,5,5-triphenyl imidazolin-4-one, dibenzamide and benzamide.
1,2-disubstituted imidazoline in presence of acetone or benzophenone undergoes photodehydrogenation to form imidazole. \(^{171}\)

The photoaddition of acetone to 1,2-dimethyl imidazole gives \(\alpha\)-hydroxy alkyl imidazoles\(^ {172}\) which results from selective attack of excited carbonyl oxygen at C-5.

Benzophenone forms oxetanes across the 4,5 bond in its photoaddition\(^ {173}\) to 1-acyl imidazoles.
1,2-dimethyl imidazole adds benzophenone at the 2-methyl group but with 1-benzylimidazole, the methylene group is also involved.\textsuperscript{173}

Photoaddition of 1-methyl-2,4,5-triphenylimidazole with acrylonitrile forms an addition product across 4,5 bond. \textsuperscript{168-170}
Imidazole 3-oxides when photolyzed gives unsymmetrical benzil diimines. Photooxidation of diaminoimidazole gives a mixture of triazine and triazole.\textsuperscript{172-173}

4,5-diaryl imidazoles undergo singlet oxygenation\textsuperscript{174} and cleavage to give N,N\textsuperscript{1} diaroyl ureas. On irradiation with alcoholic solution in presence of methylene blue as sensitizer.
1,3-dihydro-4,5-diphenyl-2H-imidazole-2-one undergoes conversion to 2,2-dialkoxy-4,5-diaryl-2H-imidazolines by a characteristic solvent interaction of the carbonyl group on irradiation in alcoholic solvents.

UV induced trifluoromethylation of 1-methyl-2-(methylthio) imidazole using CF₃I give 1.5% 1-methyl-2-methylthio-4-(trifluoromethyl) imidazole and 25% 1-methyl-2-(methylthio)-5-(trifluoromethyl) imidazole.

Photolysis of imidazole (R=Ph,ClC₆H₄, CH₃C₆H₄) in ethanol in presence of methylene blue and oxygen give photo oxidation product N,N¹-dibenzoyl-S-benzyl isothio ureas in 35-65% yield.
4,5-Diaryl imidazolin-2-thiones have been converted to bis-(4,5-diarylimidazol-2-yl) sulphides by photolysis in ethanolic solution\textsuperscript{178}.

\[
\begin{array}{c}
\text{Ar} \quad \text{N} \quad \text{S} \\
\text{Ar} \\
\end{array}
\xrightarrow{h_{\nu}}
\begin{array}{c}
\text{Ar} \quad \text{N} \quad \text{S} \\
\text{Ar} \quad \text{N} \quad \text{S} \\
\text{Ar}
\end{array}
\]

PRESENT WORK

Photoirradiation of 4-Cyclohexylidene-2-(p-methylphenyl)-2-imidazolin-5-one

A solution of 4-Cyclohexylidene-2-(p-methylphenyl)-2-imidazolin-5-one (1.25g) in benzene (300 mL) was irradiated with 125 W Philips mercury quartz lamp in a water cooled photochemical reactor of 500 mL capacity. The lamp was surrounded by a jacket containing the solution to be irradiated. The reaction was monitored by TLC. On completion of the reaction (34 hours) the brown coloured product formed at the sides of the reactor was removed, washed with benzene and dried. The melting point was 144-48°C. TLC of this product showed a number of spots and it was subjected to column chromatography using benzene-ethylacetate mixture. The silica gel used was BDH sample.
(60 - 120 mesh). But the compound was not obtained in the pure form even after repeated chromatography.

The solvent in the photochemical reactor was distilled out. The concentrated solution showed a number of spots in the TLC and therefore subjected to column chromatography. But any single compound in the pure form could not be separated. So spectral study was not done and thereby the structure elucidation of photoirradiated product was not possible.

The photoirradiation was repeated using 4-Cyclohexylidene-2-(m-methylphenyl)-2-imidazolin-5-one and 4-Cyclohexylidene-2-phenyl-2-imidazolin-5-one. In these cases also the result was same and could not separate any single compound in pure form.

4-Cyclohexylidene-2-aryl-2-imidazolin-5-one was prepared by refluxing benzimidic ester, glycine ester and cyclohexanone for 5 hours.

**Photoirradiation of 4-Benzylidene-2-phenyl-2-imidazolin-5-one**

A solution of 4-Benzylidene-2-phenyl-2-imidazolin-5-one (100 mg) in benzene (300 mL) was irradiated with 125 W philips mercury quartz lamp in a water cooled photochemical reactor of 500 mL capacity. The lamp was surrounded by a jacket containing the solution to
be irradiated. But even after irradiation of 50 hours the TLC examination of the reaction mixture showed that no reaction had taken place. The experiment was further repeated in isopropanol as the solvent. After irradiation of 50 hours no change in the reaction mixture was noted by TLC examination.