PHOTOELECTRON TRANSFER CATALYZED REACTIONS OF SOME AMINES: SYNTHETIC APPLICATIONS AND MECHANISTIC STUDIES

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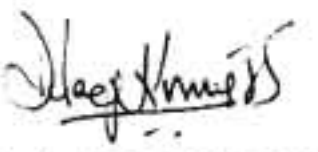
STATEMENT

I hereby declare that the matter embodied in this thesis is the result of the investigations carried out by me at the Photochemistry Research Unit of the Regional Research Laboratory, Trivandrum, under the guidance of Dr. Suresh Das and the same has not been submitted elsewhere for a degree.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.



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CERTIFICATE

Certified that the work embodied in this thesis entitled: **"Photoelectron Transfer Catalyzed Reactions of Some Amines: Synthetic Applications and Mechanistic Studies"** has been carried out by Mr. J. S. Dileep Kumar, under my supervision and the same has not been submitted elsewhere for a degree.

SURESH DAS
(THESIS SUPERVISOR)

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CONTENTS

Preface

The thesis entitled : "Photoelectron Transfer Catalyzed Reactions of Some Amines: Synthetic Applications and Mechanistic Studies" consists of six chapters.

The first Chapter of the thesis consists of a brief review on the photoinduced electron transfer reactions of amines and a description of the objectives of the present investigation.

Chapter 2 deals with the mechanistic studies of photoelectron transfer catalyzed addition of a tertiary amine (triethylamine) and a secondary amine (diisopropylamine) to electron deficient olefinic substrates such as methyl methacrylate and acrylonitrile. Anthraquinone, acridone, and dicyanoanthracene were used as photosensitizers in these reactions. Anthraquinone and acridone were found to catalyze the addition reactions with greater efficiency than dicyano-anthracene. These studies reveal that the α-aminoalkyl radicals generated by photosensitized electron transfer undergo multiple addition reactions with olefinic substrates. For example, irradiation of an argon-saturated solution of triethyl-amine (**2**) (1.5 g, 15 mmol) and methyl methacrylate (**5**) (1.5 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M anthraquinone (**1**) for 1 h using Pyrex filtered light of a medium pressure mercury lamp (Hanovia 450 W) and separation of the photoproducts by column chromatography gave amine adducts, containing one (**8**), two (**11**), three (**12**) and four (**17**) methyl methacrylate molecules added on to one molecule of triethylamine.# The reported yields of products are based on the amount of **5** that has reacted (20 %).

A mechanism involving the addition of α-aminoalkyl radicals to olefinic substrates, followed by a 1,5-hydrogen abstraction of the adduct radicals has been

proposed to rationalise the formation of the multiple addition products. In the photosensitized addition of diisopropylamine (**23**) with methyl methacrylate (**5**), along with the multiple addition product (**28**), the formation of a pyrrolidone derivative (**26**) was also observed. These results suggest that the addition of α,β-unsaturated esters to primary and secondary amines could be developed as a simple procedure for the synthesis of the corresponding lactams.

The use of photoelectron transfer sensitized addition of primary and secondary amines to α,β-unsaturated esters as a method for synthesising lactams was explored and these results are presented in Chapter 3 of the thesis. Anthraquinone photocatalyzed reaction of secondary amines such as pyrrolidine, piperidine and morpholine, as well as a primary amine such as cyclohexylamine with different α,β-unsaturated esters has been investigated. For example, irradiation of an argon-purged solution of a mixture of piperidine (**2**) (1.3 g, 15 mmol), methyl methacrylate (**3**) (1.5 g, 15 mmol) and 10^{-4} M anthraquinone (**1**) for 2 h, using Pyrex filtered light gave a diastereomeric mixture of 2-methyl-3-indolizidone (**4**) (70%) as the major product. The yield of **4** was based on the amount of **3**, that reacted (20%). Similarly, the anthraquinone photosensitized reactions of cyclohexylamine (**7**) with methyl acrylate (**8**) gave rise to the spirolactam **9** in a 75 % yield (based on the conversion of **8** (32%)). A major problem that was encountered in these reactions was that unlike methyl methacrylate, α,β-unsaturated esters such as methyl acrylate and methyl crotonate undergo facile thermal Michael-type addition to give the N-adducts, quantitatively. By carrying out these reactions at low temperatures (~0°C), the thermal reactions could, however be effectively controlled, without adversely affecting the photo-chemical free radical reactions. Using this procedure, indolizidone, pyrrolizidone and a diastereomeric mixture of heliotridone and pseudoheliotridone could be

synthesized from the parent amines. Although the yields of the products were modest, the simple one step procedure for the synthesis of such products from the parent amines could give it some advantage as a synthetic tool.

Our studies on the anthraquinone photosensitized reactions of some aliphatic allylamines with α,β-unsaturated esters form the subject matter of Chapter 4. The major photoproducts formed in these reactions were the corresponding lactams. These results are very different from those obtained in the photosensitized addition reactions of tertiary amines to α,β-unsaturated esters, described in Chapter 2. In some cases, an additional minor product arising out of the addition of the α-aminoalkyl radical of allylamine to α,β-unsaturated ester, followed by a tandem cyclization of the adduct radical, was observed. Thus, for example irradiation of an argon-bubbled acetonitrile solution of N-allyldiethyl-amine (**2**) with methyl crotonate (**6**), containing catalytic amounts of anthra-quinone under Pyrex filtered light gave a diastereomeric mixture of N-ethyl-4,5-dimethyl-2-pyrrolidone (**8**) as the major product, along with minor amounts of the piperidine derivative **9**, arising out of the tandem radical addition. Probable mechanisms have been suggested for the formation of the various photoproducts, in these reactions.

Chapter 5 of the thesis deals with our studies on the photoinduced electron transfer reactions of a variety of aliphatic amines in aqueous media using the sodium salt of anthraquinone-2-sulfonic acid (**1**) as sensitizer. These studies revealed an interesting difference between the photosensitized addition reactions of tertiary amines to α,β-unsaturated esters in organic and aqueous media. Whereas in non-aqueous media, the major process observed was the formation of multiple olefin-amine adducts, in aqueous media, the major products were the

corresponding lactams. These results suggest that in aqueous medium, dealkylation of the starting amine is much more facile than in non-aqueous media. Thus, the sodium salt of anthraquinone-2-sulfonic acid sensitized photoreaction of triethylamine (**2**) with methyl methacrylate (**3**) gave a 60 % yield of N-ethyl-3,5-dimethyl-2-pyrrolidone (**4**), based on the conversion of methyl methacrylate (10 %). A probable mechanism has been suggested for the formation of the different products in these reactions. The photosensitized addition of both secondary and primary amines with α,β-unsaturated esters in aqueous medium, however, were similar to those observed in non-aqueous media.

Chapter 6 of the thesis deals with some comparative studies of the efficiency and selectivity of different sensitizers in the addition reactions of amines to α,β-unsaturated olefinic substrates. The sensitizers that we have used include anthraquinone, acridone, anthrone, benzophenone, dicyanoanthracene and xanthone. The main objective of this study was to optimize the reaction conditions with respect to the percentage conversion, as well as product selectivity. These studies reveal that maximum efficiency with respect to percentage conversion could be obtained by using higher concentrations of benzophenone as sensitizer. Thus, for example, $5x10^{-3}$ M of benzophenone sensitized photoreactions of cyclohexylamine (**11**) with methyl acrylate (**12**) under pyrex filtered light for 4 h gave the lactam **13** (65%) with 80% conversion of methyl acrylate. In the benzophenone ($5x10^{-3}$ M) sensitized photoreaction of piperidine (**1**) with methyl methacrylate (**2**), besides the expected product namely, 2-methyl-3-indolizidone (**3**), an adduct of **3** with methyl methacrylate, (**4**) was also observed. A probable route to the formation of these products has been suggested.

The compound numbers listed in this preface refer to those given in the different Chapters of this thesis.

Chapter 1. A Brief Review on Photoinduced Electron Transfer Reactions of Amines and Objectives of the Present Investigation

1.1. Introduction

The fundamental aspects of photoinduced electron transfer processes have received considerable attention in recent years in view of their relevance to a number of important areas such as photosynthesis, solar energy conversion and storage and imaging processes.[1-6] Most of these studies deal with theoretical and mechanistic aspects of photoinduced electron transfer. More recently, there has also been a growing interest in the development of organic synthetic procedures, based on photoinduced electron transfer processes.[7-12]

1.2. Photoinduced Electron Transfer

Photochemical excitation of an electron acceptor (A) or an electron donor (D) leads to changes in their redox properties and Figure 1 illustrates the reason for these changes. When a sensitizer (Sens) molecule is excited, an electron is transferred from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO). The electron from the LUMO can be transferred to the vacuum continuum with less energy than an electron in the HOMO. The excited state of the sensitizer therefore is a far better reducing agent than its ground state. Similarly, the excitation of the sensitizer also leads to an increase in the electron affinity of the excited state relative to that of the ground state, due to a vacancy in the HOMO as shown in Figure 1. Thus, the excited state of the sensitizer is a better electron donor as well as a better electron acceptor, relative to its ground state. The magnitude of this enhancement is given by the HOMO-LUMO gap of the molecule. When the excited state molecule

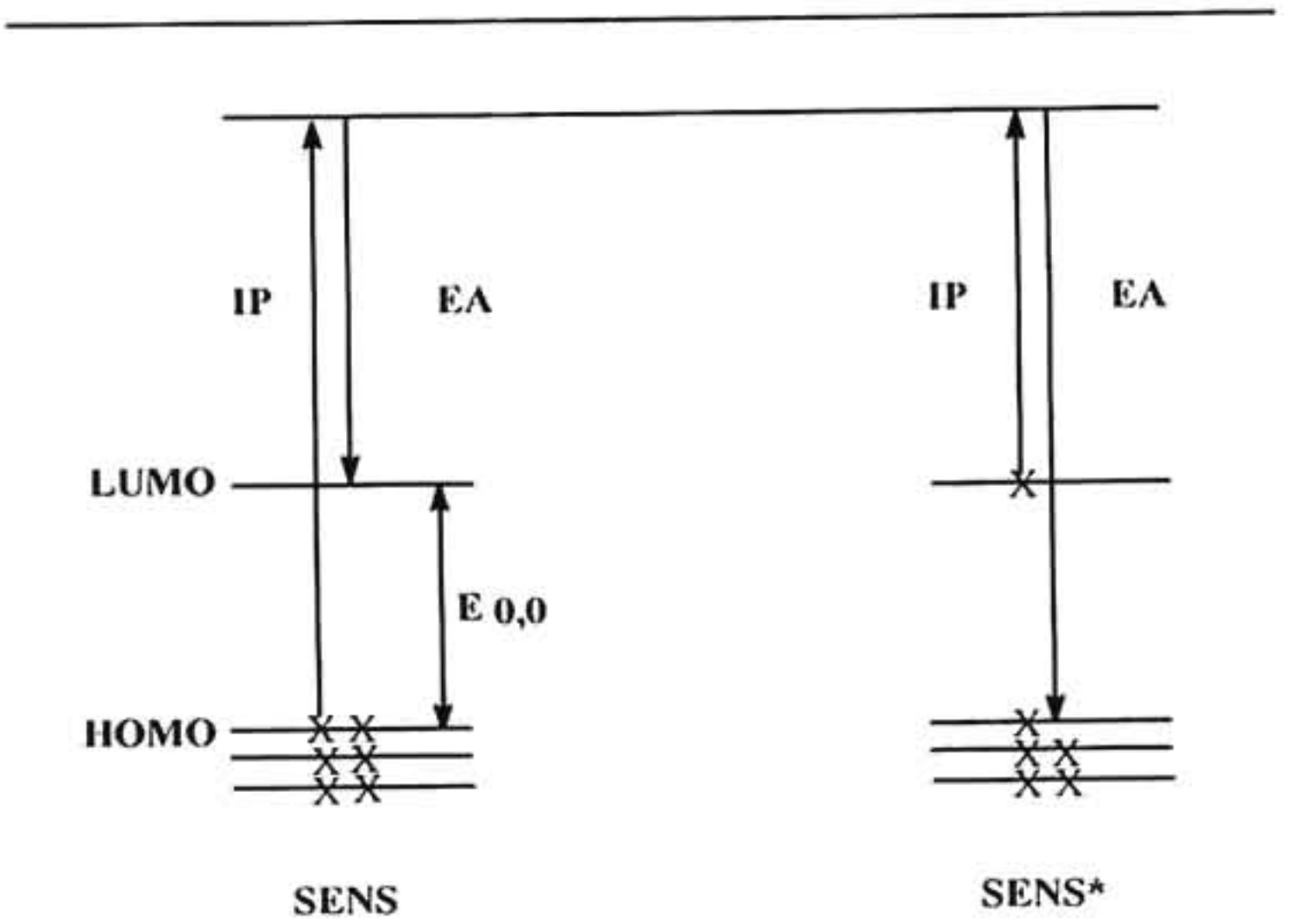


Figure 1. Redox properties of a sensitizer in the ground and excited states

comes in contact with a ground state electron donor or acceptor within the excited state lifetime, then electron transfer can occur. The feasibility of producing radical ions via these processes can be predicted by the well known Weller equation (Eqn. 1).[13]

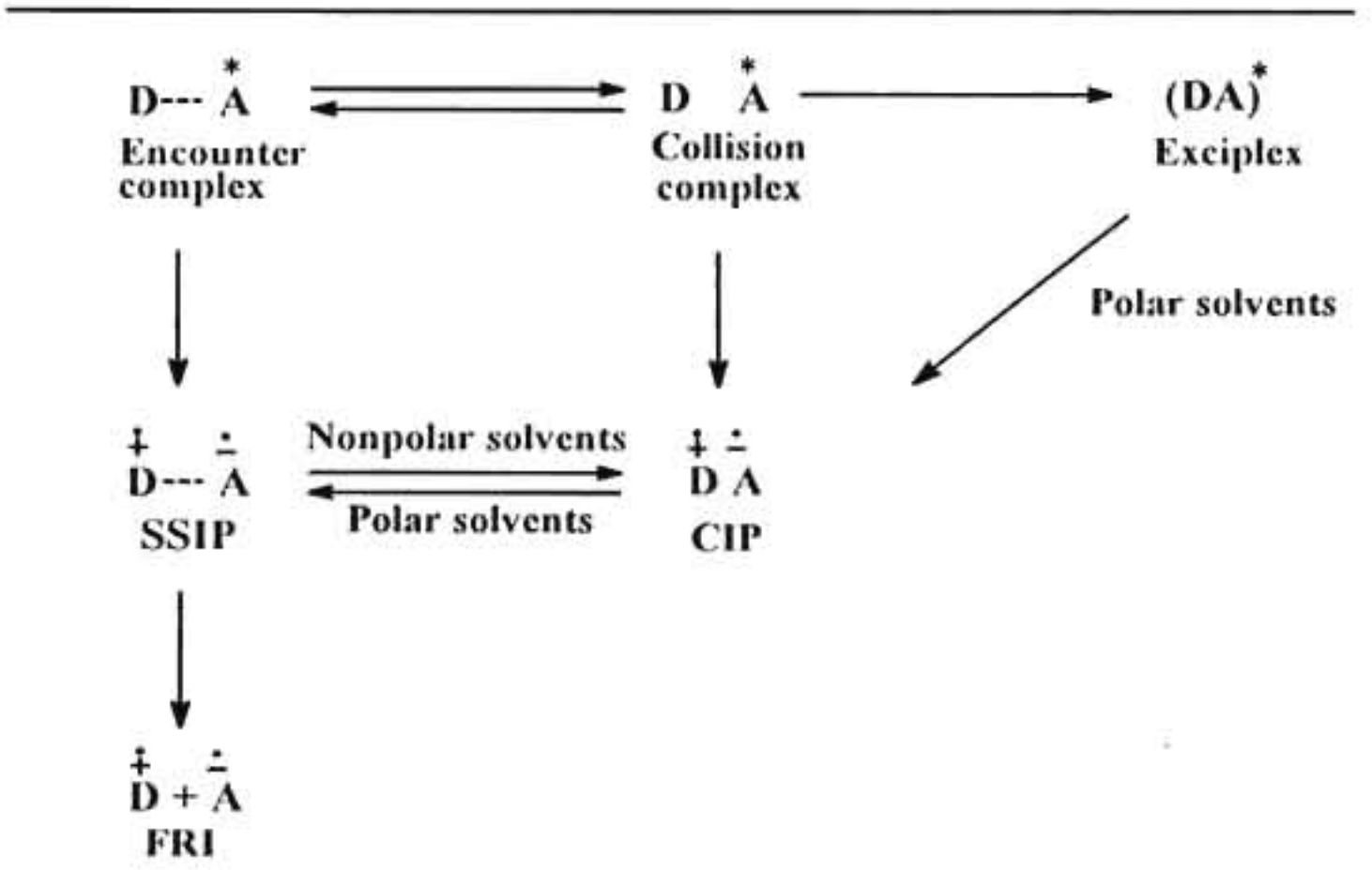
$$\Delta G = E^{ox}_{1/2}(D) - E^{red}_{1/2}(A) - \Delta E_{exit} + \Delta E_{coul} \qquad \text{Eqn. 1}$$

where, $E_{1/2}^{ox}(D)$ is the oxidation potential of the donor, $E_{1/2}^{red}(A)$, is the reduction potential of the acceptor, ΔE_{exit} is the excitation energy of the electronically excited species, ΔE_{coul} is the coulombic repulsion associated with solvent and ΔG is the free energy change associated with the electron transfer reaction.

The above equation can be used to estimate the degree and direction of the electron transfer reactions. Based on this equation, it can be assumed that, in general, electron transfer from D to A may proceed relatively rapidly, whenever ΔE is more positive than -0.4 V ($\Delta G < 9.23$ kcal/ mol) and that the electron transfer will be complete whenever ΔE is more positive than 0.4 V.[14]

The overall mechanism involving the electron transfer process in a fluid medium is illustrated in Scheme 1. The dynamics of the electron transfer process in a fluid medium involves the formation of an encounter complex between the excited state and the ground state molecule.[3,15,16] The encounter complex can be described as an intermolecular ensemble of excited and ground state molecules separated by a small distance (~7 Å) and surrounded by solvent molecules. During the lifetime of the encounter complex, the reactants undergo mutual collisions inside the solvent cage and as a result of these collisions a stage is reached where the reactants are in contact to form what is called the collision complex. If the interaction between the reactants is strong enough (~5-20 kcal/ mol), the collision complex can rapidly change to a new intermediate called exciplex, having partial charge transfer character and large dipole moment. Electron transfer may occur at any one of these stages.[3] Electron transfer from the collision complex or from the exciplex leads to the charge-transfer species called contact ion pair (CIP). The contact ion pair can undergo slight separation in the solvent cage to generate a

solvent separated ion pair (SSIP). Alternatively, electron transfer from the encounter complex can directly lead to the SSIP. The solvent saperated ion pairs can then diffuse apart from the solvent cage and become separated to form the free solvated radical ion (FRI), which are analogous to free radicals and can undergo chemical reactions to yield products.



Scheme 1. Schematic representation of the electron transfer reaction of Donor and Acceptor molecules in solution

All these processes, i.e., the formation of the encounter complex, collision complex, contact ion pairs, solvent separated ion pairs and free radical ion pairs, are reversible. For the generation of free radicals in good yields, forward electron transfer processes have to compete efficiently with the energy wasting back electron transfer processes. Over the years, considerable amount of work has been carried out in devising methods to circumvent the back electron transfer process.

As a result of these studies, some of the factors listed below have been identified as those that control the back electron transfer (BET).[17, 18]

1.2.1. Control of Back Electron Transfer Processes

a) Solvent polarity. One of the most important factors that control the efficiency of radical ion formation via photoinduced electron transfer processes is the polarity of the reaction medium (solvent polarity). The effect of solvent in electron transfer processes is depicted in Figure 2.

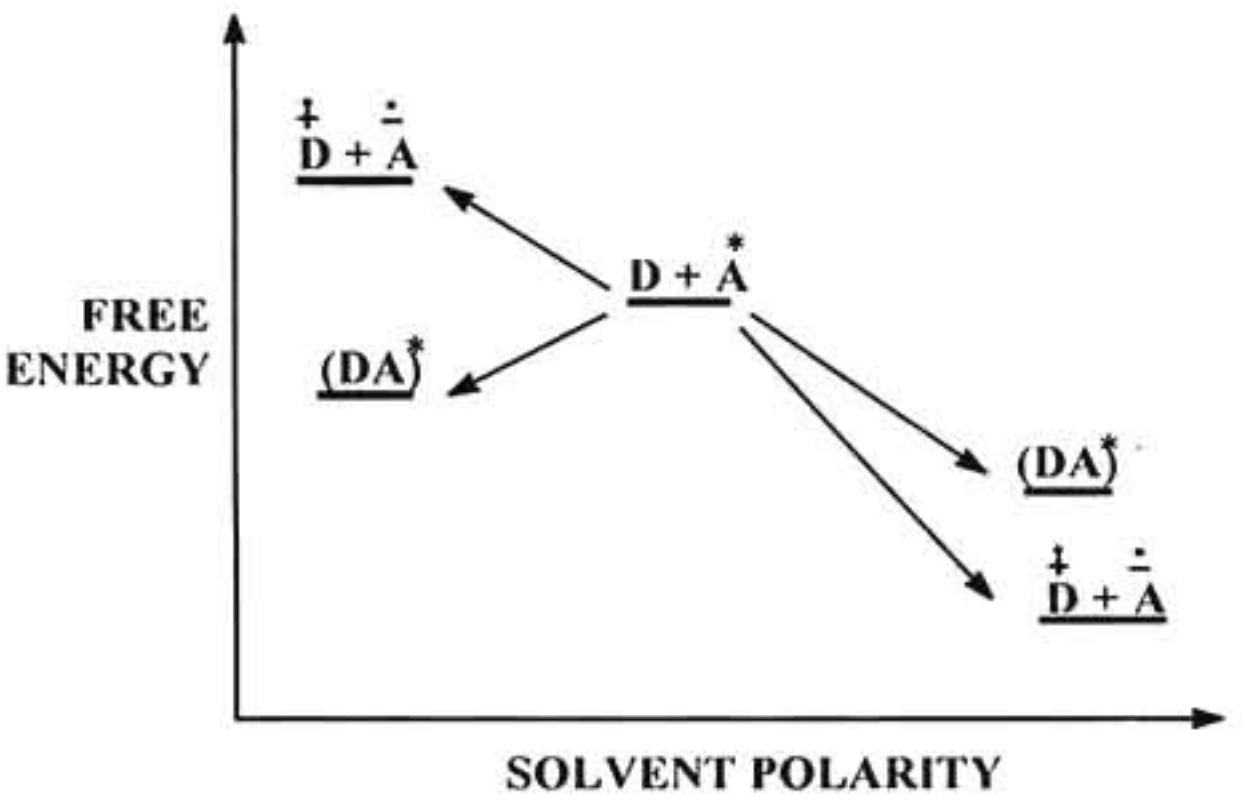


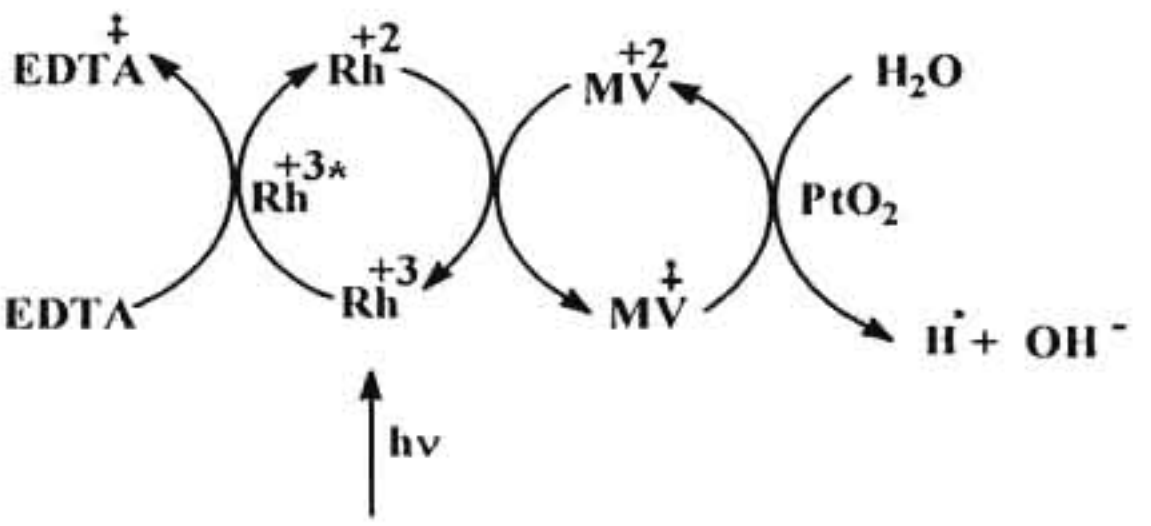
Figure 2. Effect of solvent polarity on the energetics of electron transfer

In polar solvents, the contact ion pair (CIP) rapidly dissociates to the more stabilized solvent separated ion pair (SSIP), which in turn separates to form free radical ions (FRI). In polar solvents, exciplexes are stabilized to a lesser extent

than the free radicals, whereas in non-polar solvents, formation of free radicals is energetically unfavourable. Thus, in non-polar solvents, exciplex emission is the most favoured route of deactivation.[18]

b) Use of triplet sensitizers. The spins of the electrons are conserved during electron transfer. Thus, electron transfer from singlet excited state yields singlet radical ion pairs, which can easily undergo BET. Electron transfer from the triplet excited state, however, leads to the triplet radical ion pairs and for back electron transfer to occur the radical ion pairs have to undergo a spin flip. Before the spin flip occurs however, the radicals can diffuse apart (10-20 Å) and thereby reduce BET.

c) Use of sacrificial electron donors and mediators (relays). Sacrificial electron donors which are irreversibly oxidised can be utilized for preventing back electron transfer, whereas certain molecules which can generate stable free radicals can act as electron relay molecules which can also prevent the back electron transfer.



Scheme 2

An example in which ethylenediaminetetraacetic acid (EDTA) is used as a sacrificial electron donor and methyl viologen cation (MV^{+2}) is used as the relay in the sensitized generation of hydrogen from water is depicted in Scheme 2. [4,19]

d) Use of ionic species. A very efficient way to inhibit the BET is the use of an ionic species as one of the reactants. After electron transfer, the product will consist of a neutral and an ionic species which are not electrostatically attracted, thereby reducing the tendency for back electron transfer.

e) Formation of reactive intermediates. Reactive intermediates produced after the electron transfer process can undergo further transformation. The product thus formed can be energetically more stable, making BET thermodynamically unfavourable. An example of the reactive intermediate formation is shown in Scheme 3. Carboxylate anions can undergo electron transfer with excited state of acceptors (A*). The radical cation, produced after the electron transfer process is highly reactive and undergoes facile decarboxylation to give an alkyl radical. Since one of the partners involved in the BET decays rapidly, charge saperation becomes efficient in such processes.

$$R_2N\text{-}CH_2\text{-}COO^- + A^* \longrightarrow R_2\overset{+}{\dot{N}}\text{-}CH_2\text{-}COO^- + \bar{A}^{\cdot} \longrightarrow R_2N\text{-}\dot{C}H_2 + CO_2 + \bar{A}$$

Scheme 3

f) Electron transfer at interfaces. The separation of the donor and acceptor, after the electron transfer process can be achieved by partitioning the reactants in different phases by using microheterogeneous systems such as micelles, bilayers, polyelectrolytes, semiconductors and polymer bound sensitizers.[6,20-23] Among these microheterogeneous systems, the use of

semiconductors have several advantages over other molecular assemblies. Thus, for example, in a semiconductor such as TiO_2, the diffusion constant of electron is 10^{-4} times larger than that of molecular charge carriers in micelles or vesicles. The use of semiconductors for photoinduced charge separation has however been investigated more from the point of view of solar energy harvesting than for the photocatalysis of organic reactions.[5,6]

1.2.2. Comparison of Photoelectron Transfer Processes and Electrochemistry

The redox processes induced by photoexcitation are very similar to electrochemical processes, in which radical ions are eventually generated. However there are a few significant differences. [24]

a) In excited state electron transfer, generally single electron transfer processes are observed. This is due to the relatively short lifetimes of the redox-active excited states. In conventional electrochemistry, the initial electron transfer process can be followed by a second electron transfer from the intermediate ion to the electrode if the oxidation potential of the intermediate is lower than that of the starting material. For example, the oxidation potentials of α-aminoalkyl radicals are much lower than those of the parent amines and subsequent electron transfer from α-aminoalkyl radicals prevent the possibility of using such radicals in synthetically useful reactions, involving electrochemical and thermal electron transfer processes.

b) In electrode reactions, the effective reaction volume is limited, thereby creating a high local concentration of reactive intermediates, which can lead to dimerization and disproportionation reactions.

c) The electrode is not capable of becoming chemically involved. For example, the radical anion formed in the photoinduced electron transfer is capable of removing or accepting a proton, radical coupling, disproportionation and a variety of other chemical transformations.

1.3. Photoinduced Electron Transfer Reactions of Amines

Photoinduced electron transfer reactions of amines have been reviewed extensively in the literature[1-6] and only those aspects relevant to the present work are discussed here.

1.3.1. Mechanistic Aspects

Amines are one of the most easily oxidizable class of organic substrates because of their low oxidation potential (0.8-0.5 V).[25,26] Electron transfer oxidation of amines leads to the removal of a single electron, resulting in the formation of aminium radicals (cation radical of amines). Aminium radicals are highly reactive intermediates and can react via four different modes, namely i) deprotonation at nitrogen, ii) deprotonation at an α-carbon, iii) intra- or intermolecular hydrogen abstraction and iv) coupling reactions. Nitrogen deprotonation usually requires an added base, in addition to the parent amine especially in aprotic solvents such as acetonitrile. The resulting nitrogen centered radicals can couple to form dimers or can undergo further oxidation to yield nitrenium ions. The subsequent oxidation of nitrogen centered radicals form a minor process in photoinduced electron transfer reactions (PIET), whereas in thermal electron transfer reactions of amines, the second electron removal is very efficient. Hydrogen atom abstraction and coupling reactions of aminium radicals are found to be less important processes. The best known examples in the case of

intramolecular hydrogen abstraction reactions of the aminium radicals is the Hoffman-Löffler-Freytag reaction in which the aliphatic aminium radicals derived from N-haloamines undergo hydrogen abstraction with high stereo-selectivity from the 'δ' or 'ω' carbon of the amine.

Intermolecular hydrogen abstraction by aminium radicals have been reported to occur from a carbon 'α' to a heteroatom. For example, it has been observed that the rate of hydrogen abstraction from the α-carbon of alcohols increases in the order MeOH > EtOH > i-PrOH.

The most common reaction of aminium radicals is however the α-CH deprotonation to produce α-aminoalkyl radicals (Scheme 4). [27]

Scheme 4

The mechanistic aspects of these deprotonation reactions have been studied extensively. The overall mechanism of deprotonation involves partial overlap of the half vacant nitrogen 'p' orbital and the α-carbon 'σ' orbital which is controlled by a stereoelectronic effect or the ability of the α-CH bond to align itself with the half vacant 'p' orbital. As a result of this interaction, the α-CH bond gets weakened and this facilitates the deprotonation, giving rise to α-amino-alkyl radicals. α-Aminoalkyl radicals are known to undergo a number of reactions such as disproportionation, dimerization, oxidation, hydrogen abstraction, as well as carbon-carbon bond formation with olefinic substrates.

There are a number of reports on the α-CH kinetic acidity of tertiary amine radical cations.[9,10,28-30] The rate of deprotonation of the α-carbon depends on the relative kinetic acidity of the eliminating protons. The relative acidities of some protonated amines and their corresponding radical cations are listed in Table 1.

Table 1. Acidities of radical cations and protonated parent amines

Radical cation precursor	pKa values	
	$N^{+\cdot}$	NH^+
Ammonia	6.7	9.2
Diethylamine	7.0	10.7
Hydroxylamine	4.2	6.1
Methoxylamine	7.0	4.6
Trimethylamine	8.0	9.8

The differences in the acidities of the protonated amines and their corresponding radical cations have been justified in terms of the differences expected in the deprotonation of an 'sp^3' center in the parent amine and an 'sp^2' center in the oxidized form. Hydrogen attached to an atom with more 's' character is expected to be more acidic. The ease with which protons can be removed depends on the type of carbon to which they are attached. As discussed earlier, this deprotonation is governed by the stereoelectronic effects or ability of a C-H bond to align itself with the half vacant 'p' orbital. The most important finding of these studies is that a relationship exists between the thermodynamic and kinetic acidities of the cation radicals. These studies show that electron withdrawing substituents, adjacent to the α-C of amines decrease the oxidation potentials,

thereby lowering the pK_a values of the aminium radicals and enhancing the rate constant for α-CH deprotonation. [31]

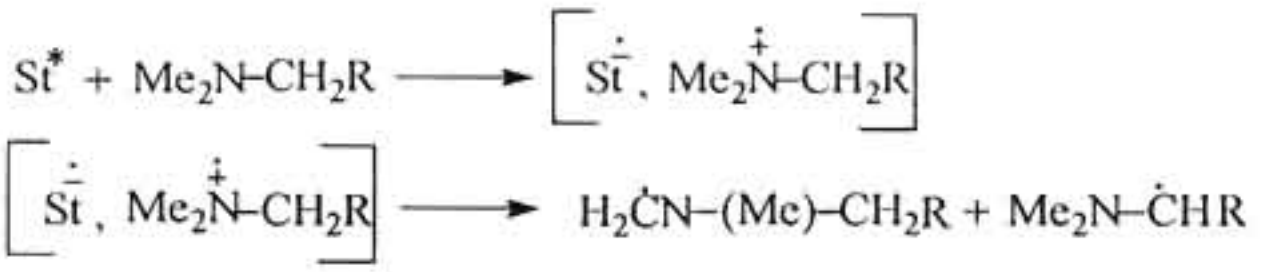
Equation 2 shows the relation of the pK_a values of the aminium radicals to the oxidation potential of the neutral precursor (E^0) and the bond dissociation energy (BDE) of the C-H bond, undergoing cleavage.[30]

$$pK_a = \frac{-E^0}{0.059} + \frac{BDE - 37.5}{1.36} \qquad \text{Eqn. 2}$$

Thus, substituents which can decrease E^0 can reduce the pK_a values and thereby increase the rates of deprotonation. Likewise, α-substitution should govern the α-CH pK_a values of tertiary amine cation radicals, principally through a control of α-CH bond dissociation energies. Thus, substituents which stabilize the resulting α-aminoalkyl radical (lower BDE) should enhance the thermodynamic acidity of the charged radical intermediate (decreasing pK_a). Stabilization of the transition state for the α-CH deprotonation by radical stabilizing groups are found to enhance the kinetic acidity of the concerned protons.[32]

An extensive investigation on the various aspects of deprotonation of tertiary amine cation radicals and the influence of the substituents on the kinetic aciditiy of α-CH protons has been conducted by Lewis and co-workers.[10,33] They have studied the photoinduced electron transfer reactions of a variety of stilbene-amine systems. In nonpolar solvents, the singlet excited state of *trans*-stilbenes form nonreactive but fluorescent exciplexes with tertiary amines. Increasing polarity brings about a decrease in the fluorescence yield along with a concomitant

increase in the amount of 1:1 adduct formation. The reaction sequence is indicated in Scheme 5.



St = stilbene

Scheme 5

Studies on the quenching rate constants of the excited singlet states of stilbenes by amines as well as the product composition, reveal that the reactivity for methyl vs alkyl oxidation by the excited singlet state of stilbene increases in favour of the methyl groups. Thus, with isopropylamines, highly selective oxidation of the methyl group could be observed. This is because the conformation necessary for the methyl deprotonation is of lower energy than that for the isopropyl deprotonation. Thus, the stereoelectronic effect serves to counterbalance the greater product stability of the more substituted free radical. However, it has been shown that more substituted α-aminoalkyl radicals are formed selectively from several tertiary amines of the type Me_2NCH_2G where G is the radical stabilizing group with minimal steric requirements (e.g.,G = CH_2=$CHCH_2$, $PhCH_2$, HC≡CCH_2 and CH_2CO_2Et).

Mariano and co-workers have studied the relative rates of α-CH de-protonation of various α-substituted tertiary amine cation radicals by product distribution studies of the amine-enone SET systems and by following the rate constants for *n*-butyl acetate promoted deprotonation of N-alkyl-N,N-diphenyl-

aminium radicals using laser spectroscopic techniques, in an effort to understand how the substituents govern the kinetic α-CH acidities of tertiary amine cation radicals. They have compared these results with stilbene-amine SET photosystems reported by Lewis and co-workers.[34] Table 2 shows the relative rates of α-CH deprotonation of α-substituted tertiary aminium radicals from the product distribution studies of the stilbene-amine and enone-amine as well as from the laser spectroscopy studies of the acetate promoted deprotonation of N-alkyl-N,N-diphenylaminium radicals. For the stilbene-amine system (Column 4) it is observed that increasing alkyl substitution leads to a decrease in the rate of deprotonation. A decrease in the deprotonation was also observed for the ethylene substituents, whereas, for the acetylene moiety large increase in the rate of deprotonation was observed. As discussed earlier, for stilbene-amine systems, these results indicate that α-CH kinetic acidity is largely determined by steric factors and not by electronic effects, with the exception of acetylene, which has minimal steric requirements.

Different conclusions about the effect of α-substituents on tertiary aminium radicals on α-CH kinetic acidity have been made from product distribution studies with tethered amino-enones. The SET promoted photoreactions of these systems follow pathways in which α-CH proton transfer occurs via an intermediate zwitterionic diradical. The results of this work (Column 5, Table 2) suggest that steric factors are less pronounced in governing the kinetic acidity. A regular increase in the relative rate of deprotonation is observed for compounds 'a' to 'f' in Table 2. Radical stabilizing groups enhance the relative rates of deprotonation of the tethered enone-amine photoreactions, indicating thereby that in these systems the electronic effect of α-substituent groups play a predominant role in describing α-CH kinetic acidity.

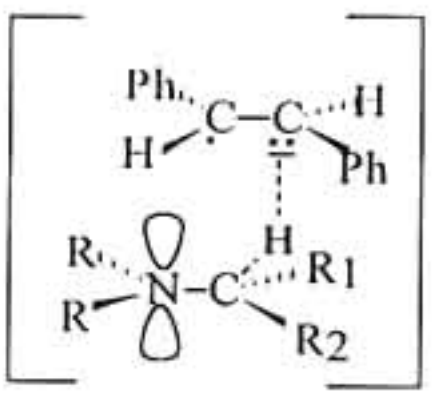
Table 2. Relative rates of deprotonation of α-substituted tertiary amine cation radicals from product distribution and laser spectroscopy studies

Entry	X	Y	Relative rate of deprotonation: From stilbene-amine SET system	From enone-amine SET system	From rate constant for acetate promoted deprotonation of diphenylaminium radical (laser spectroscopy)
a)	H	H	1.1	0.1	0.3
b)	H	CH_3	0.5	0.2	0.1
c)	CH_3	CH_3	0.05	–	0.05
d)	H	Ph	1.0	1.0	1.0
e)	H	$CH{=}CH_2$	0.5	1.9	0.8
f)	H	C≡CH	111	3.9	22

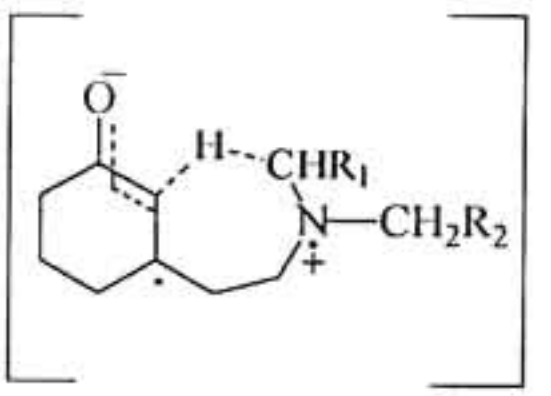
Proton transfer in the stilbene-amine photoreaction occurs from a contact ion radical pair whose rigid structure (i.e. relative orientation of negative and positive radical partners) may be governed by the need for maximum charge neutralization.[35,36] This effect could cause kinetic acidities to become greatly influenced by steric factors, whereas, the intramolecular nature of proton transfer in the amine-enone zwitterionic diradical disfavours coplanar alignment of 'σ' CH and the nitrogen 'p' orbitals at the carbon radical center. This could very well result in the minimization of the influence of both steric and stereoelectronic

factors on kinetic acidity and greater importance of electronic effects of α-substituents.

The results of the acetate base promoted intermolecular deprotonation of aminium radicals obtained from laser spectroscopic studies are shown in column 6 of the Table 2. Here the relative rates of deprotonation values were found to be in good agreement with those of stilbene-amine systems. The slight differences seen in the stilbene-amine and the laser spectroscopic studies may be due to the differences in the pKa of the bases (ketyl anion versus acetate) involved in these reactions.



Stilbene- Amine



Enone- Amine

The mechanism of photoreduction of various quinones, dyes and metal complexes via electron transfer or hydrogen atom transfer from amines, alcohols and aminoalcohols have been extensively studied by Whitten and co-workers.[27,37] These studies show that the overall reactions involve two electron oxidation of the corresponding donors and studies on quantum efficiency show the role of a secondary dark reaction, involving quinones and the primary photolysis products. The second electron oxidation of the donor species can occur via a thermal oxidation of the initially formed radical (after the deprotonation of the cation radical)

by the ground state acceptor or via a disproportionation reaction between the products formed in the initial electron transfer process.

The mechanism of photoinduced electron transfer between aromatic carbonyl compounds and amines has been studied in detail using nanosecond and picosecond laser flash photolyses techniques.[38] Using these techniques, the various stages of the photoinduced electron transfer processes such as the formation of the collision complex, contact ion pair, free radical ions and free radicals have been monitored.

The transient absorption spectra of free radicals and radical ions of several amines and aromatic carbonyl compounds have been well characterized by pulse radiolysis. The optical absorption spectra of the ion pairs that are produced by photoelectron transfer will be similar to the sum of the donor and acceptor radical ions. The electrostatic interaction between the donor and acceptor radical ions in the collision complex and contact ion pair can however lead to minor differences in the absorption spectrum of the ketyl and aminoalkyl radical ions. Since the amine radicals absorb in the ultraviolet region, where the aromatic carbonyl compounds have a very strong ground-state absorption, the formation and decay of the ketyl radicals are generally monitored in ketone-amine systems.

Cohen and co-workers have studied the photochemical reactions of benzophenone with aliphatic amines (Scheme 6) by product analysis, as well as by using nanosecond laser flash photolysis technique.[39] In nanosecond laser flash photolysis studies, there was no evidence for the participation of the intermediate charge-transfer complex (^{3}CTC*); however, it has been assumed that the interaction between the amine molecule and triplet benzophenone results in the formation of ^{3}CTC*. The laser flash photolysis studies of benzophenone in the

presence of a variety of aliphatic amines indicate the formation of ketyl radicals (λ_{max}, 555 nm) with a quantum yield of almost unity. Ketyl radicals could be generated via hydrogen abstraction processes rather than via the electron transfer mechanism. However, the extremely fast (diffusion controlled) quenching of the benzophenone triplet by amines support the view that electron transfer reactions are involved. In order to prove that electron transfer reactions are involved in these reactions, Cohen and co-workers have examined the flash photolysis of the benzophenone-DABCO (1,4-diazabicyclo[2.2.2]octane) system.[40] The benzophenone-DABCO system indicated the formation of the ketyl radical anion as a transient species (λ_{max}, 660 nm). The formation of the ketyl radical anion in this system is due to the increased stability of the radical cation of the DABCO, as compared to other aliphatic amines. Deprotonation of the α-CH protons of DABCO is not facile due to the low overlap of the half vacant 'p' orbital of nitrogen with the α-CH bond of this constrained amine.

$$\Phi_2 CO^{*3} + \dot{N}R_1R_2R_3 \longrightarrow {}^3\left[\Phi_2\dot{C}{-}O^{-}\text{-----}\dot{+}NR_1R_2R_3\right]^{*} \text{ or } ({}^3CTC^{*})$$

$$^3CTC^{*} \longrightarrow \Phi_2\dot{C}{-}OH + \text{Amine radicals}$$

Scheme 6

In order to study the formation of radical anions in benzophenone-amine systems, Shizuka and co-workers have carried out the nanosecond flash photolysis studies of benzophenone in neat amines such as secondary butylamine and triethylamine at various temperatures (300-77 K).[41] At higher temperatures, they observed the formation of the ketyl radical (λ_{max}, 555 nm), whereas on decreasing the temperature, the transient absorption spectrum showed a decrease in intensity

around 555 nm which was accompanied by an increase in absorption at 660 nm. This can be attributed to the slowing down of the proton transfer between the radical ion pairs at low temperatures, thus making it possible to measure the ketyl radical anion absorption at 660 nm.[42] At very low temperatures, however (~120 K) only the triplet state of benzophenone was observed (λ_{max}, 525 nm) indicating thereby that under these conditions, the triplets do not undergo electron transfer with the amines.

Direct evidence for the formation of radical anion intermediates in the benzophenone-amine system was also obtained by Peters et al.[43] Picosecond laser flash photolysis studies have indicated the formation of the ketyl radical anions within 10 ps of irradiation. The transient absorption decays with a lifetime of 15±5 ps to give ketyl radical via an intracomplex proton transfer. Based on their studies, they have proposed a mechanism in which the solvent separated ion pair (SSIP) is formed first, which collapses into a contact ion pair (CIP) and proton transfer to form the ketyl radical takes place in the CIP. This mechanism was based on the observation that the ketyl radical ion undergoes a time dependent blue shift. The SSIP being more solvated than the CIP is expected to have its absorption spectrum red shifted as compared to that of the CIP. Recent studies by Devadoss and Fessenden on benzophenone-DABCO system however indicate that the spectrum of initial transient has an absorption maximum at 700 nm, which shifts to the red (720 nm) in the picosecond time domain.[44] These results seem to suggest that it is the CIP which is initially formed, which eventually leads to the SSIP and proton transfer occurs at this stage.

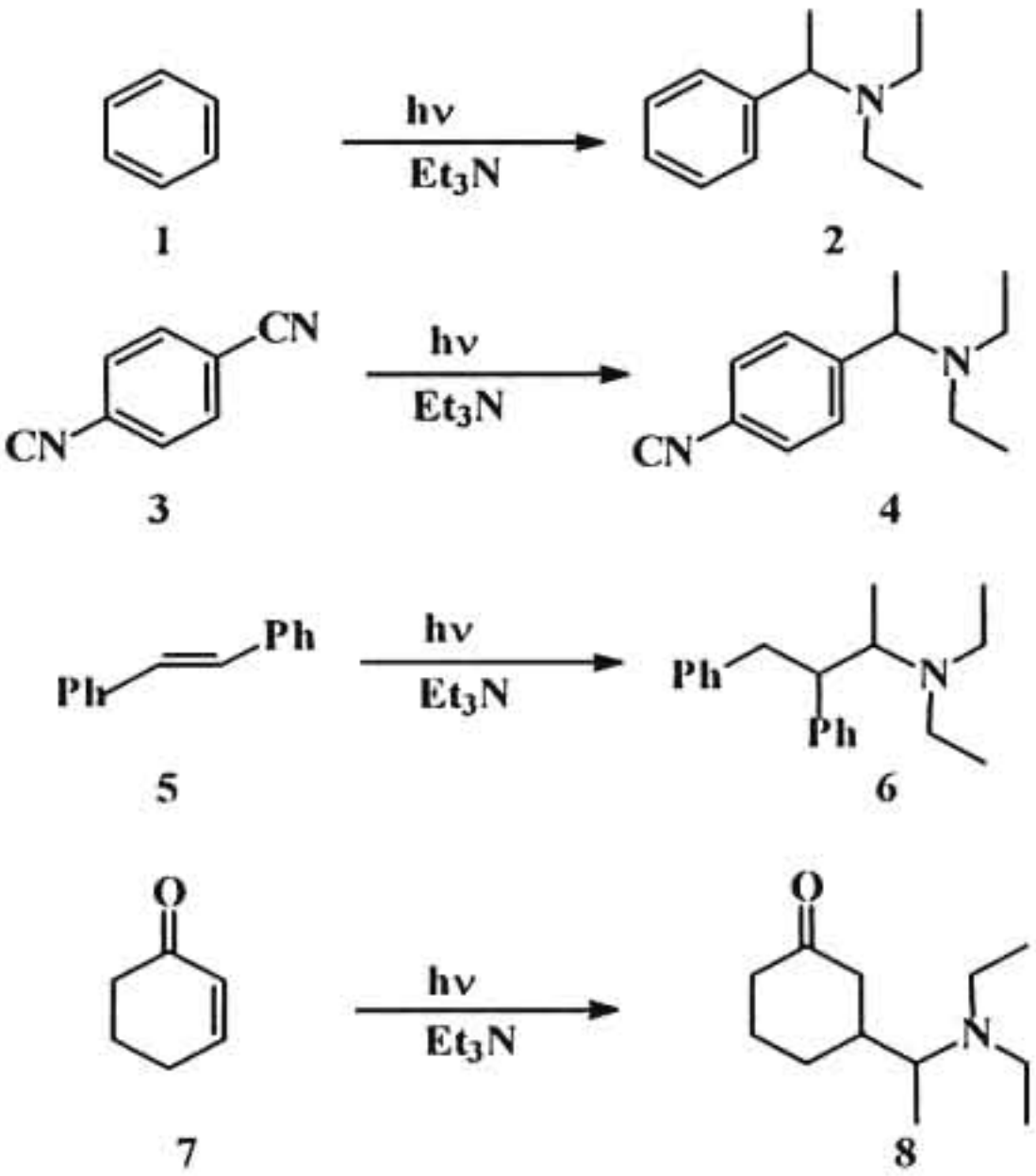
Hamanoue et al. have investigated the electron transfer reactions of several amines with the triplet state of anthraquinones.[45] The photochemistry of anthra-

quinones is expected to vary depending on the nature of the lowest excited state. It has been observed that the lowest n-π^* state abstracts a hydrogen atom, while the lowest π–π^* state reacts via electron transfer. By introducing substituents on the anthraquinone chromophore, the nature of the lowest triplet state can be changed from n-π^* to π–π^*. Picosecond laser flash photolysis studies of the mixtures of anthraquinone and 1-chloroanthraquinone with amines reveal that the anthraquinone triplet forms a triplet exciplex with triethylamine. This exciplex changes to a contact ion pair in polar protic solvents such as ethanol and polar aprotic solvents such as acetonitrile. The contact ion pair disappears by proton transfer from the triethylamine cation radical to the anion radical of anthraquinone, to generate the α-aminoalkyl radical and the ketyl radical of anthraquinone. In acetonitrile, two transients due to the SSIP and the triplet exciplex were observed. Among these transients, the SSIP is assumed to be produced by electron transfer from triethylamine to a higher triplet (T_2) of anthraquinone upon laser excitation, whereas the exciplex is produced by the reaction of the lowest triplet (T_1) of anthraquinone with triethylamine. Deprotonation of the aminium cation, produced after the electron transfer reaction with anthraquinone, was proposed to occur in the contact ion pair. Recent CIDNP studies of the deprotonation of the aminium cation, generated from the anthraquinone sensitized electron transfer reaction reveal that the relative group reactivity or substituent effect plays a key role in determining the site of proton elimination.[46] These studies show that deprotonation of the methyl, ethyl and isopropyl substituents occurs exclusively in the solvent separated ion pair whereas the deprotonation of the allyl substituents occurs in contact ion pair. The different behaviour of the deprotonation can be explained on the basis of an increase of the rate of incage proton transfer relative to the cage life with increasing ΔG of the reaction.

1.3.2. Synthetic Applications

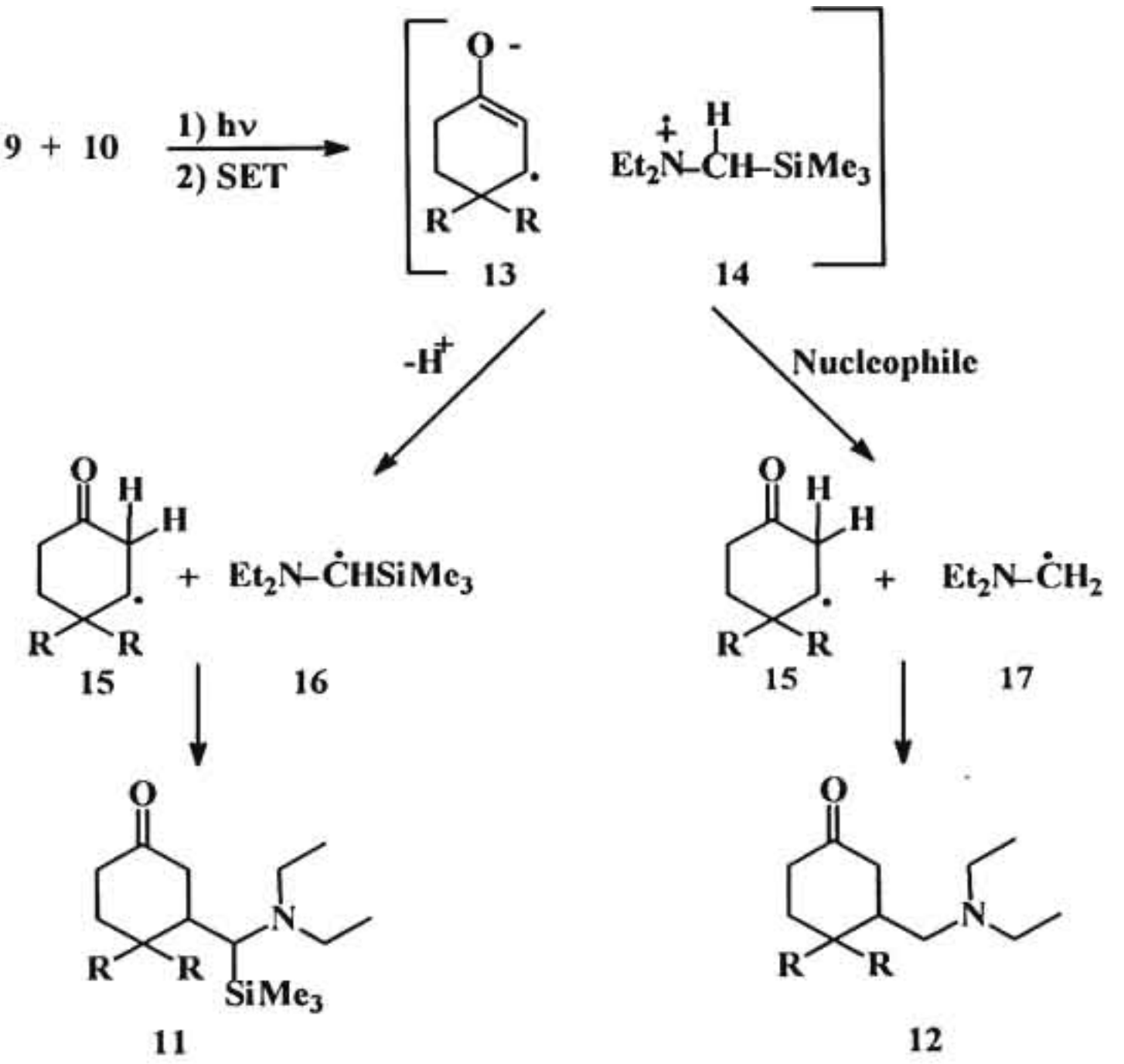
Although the mechanism of the photoinduced electron transfer reactions of amines, leading to α-aminoalkyl radicals, using a variety of sensitizers have been extensively investigated, the use of these reactions in organic synthesis has been limited. According to frontier molecular theory (FMO), it has been suggested that α–aminoalkyl radicals are nucleophilic in nature and can react very fast with olefinic substrates, substituted with electron withdrawing groups (nitrile, ketone or esters etc.) with rate constants of $k \sim 10^5$-10^6 $m^{-1}s^{-1}$.[47] The increase in the rate of addition to electron deficient olefins with respect to neutral and electron rich olefins is due to the lower LUMO energy of the electron deficient olefinic substrates, which reduces the SOMO-LUMO difference.

There have been numerous studies on the mechanistic and synthetic aspects of the addition of amines to alkenes via the sequential SET deprotonation route. Direct excitation of arenes, cyanoarenes, alkenes, α,β–unsaturated esters and ketones in the presence of triethylamine leads to the corresponding α-aminoalkyl derived products (Scheme 7).[48] In earlier reports, Mariano and co-workers have shown that the photoreactions of silylated tertiaryamines, such as **10** with cyclo-hexenone, **9** gave two types of adducts, the trimethylsilyl (TMS) containing adduct **11** and non-TMS adduct **12** (Scheme 8). The distribution of **11** and **12** varied, depending on the nature of the solvent.[49] The TMS adduct was found to predominate in less polar aprotic solvents such as acetonitrile, whereas the non-TMS adduct was formed in higher yields in polar protic solvents such as methanol. These results can be explained on the basis of the mechanism shown in Scheme 9, where the relative rates of amine cation radical deprotonation and desilylation are controlled by the basicity of the enone-radical anion **13**. Thus,



MeCN,	R = H	30 %	0 %
	R = CH_3	70 %	8 %
MeOH,	R = H	4 %	30 %
	R = CH_3	30 %	60 %

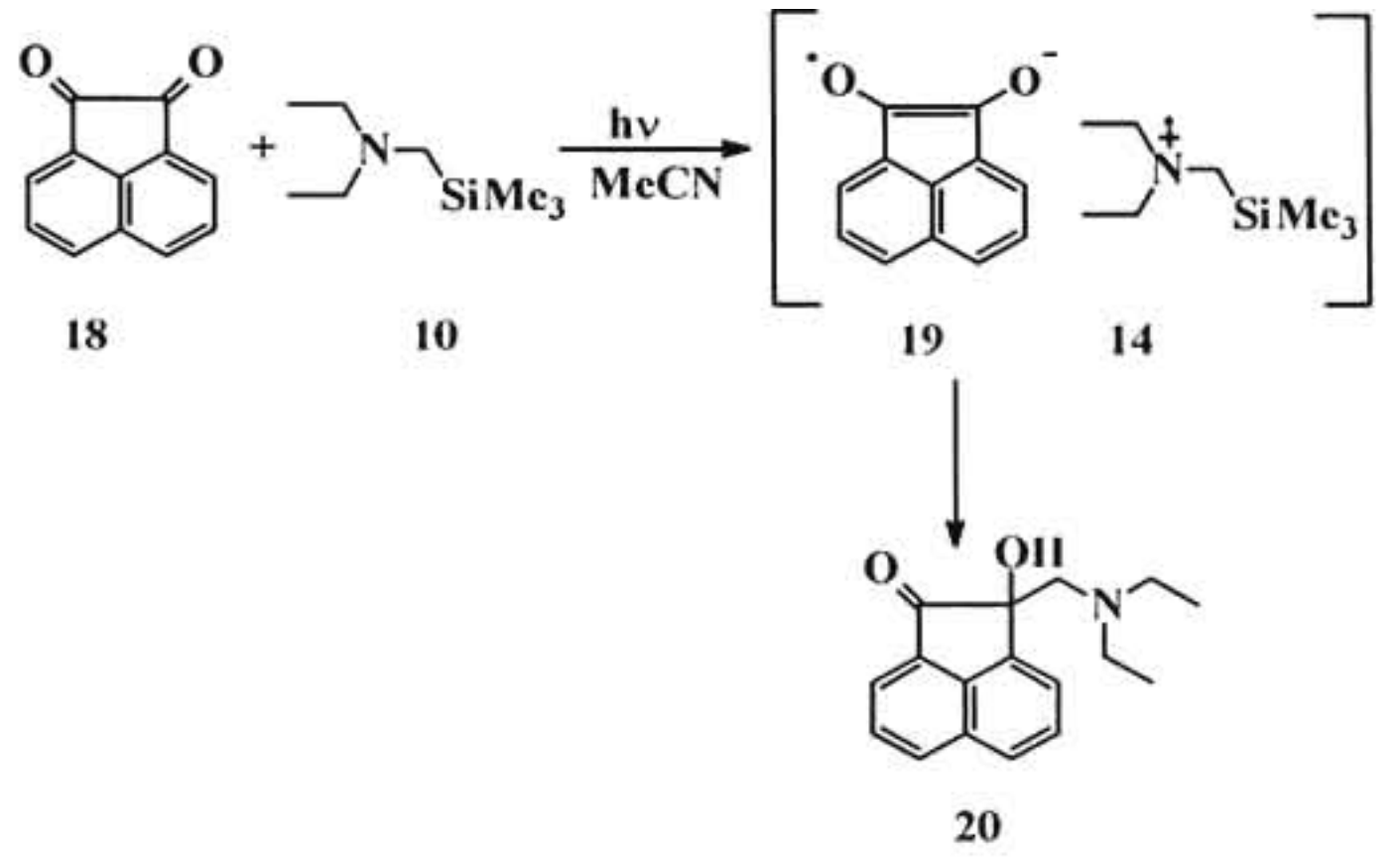
Scheme 8


9 + 10
1) hν
2) SET
13
14
-H+
Nucleophile
+ Et2N–ĊHSiMe3
+ Et2N–ĊH2
15
16
17
11
12

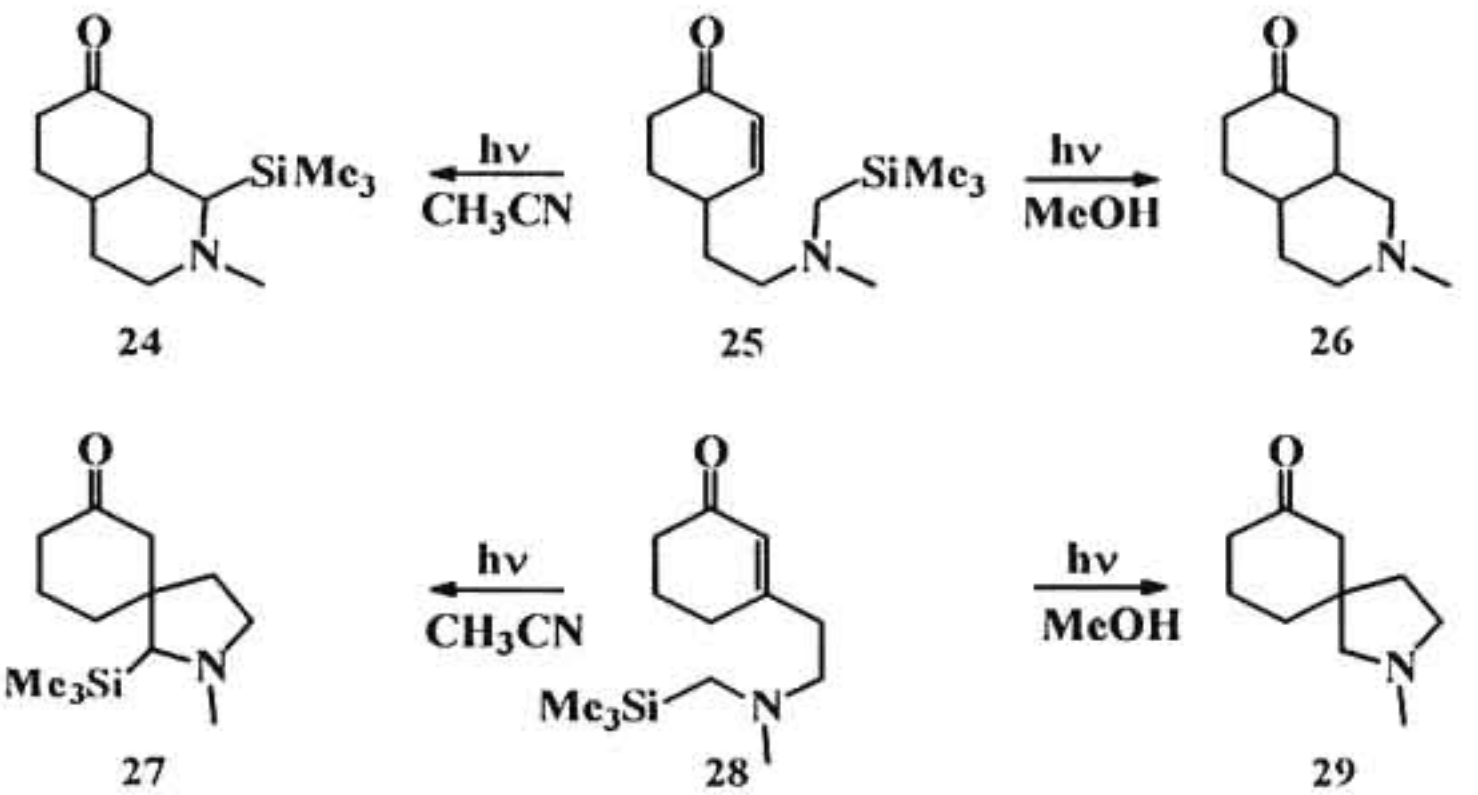
Scheme 9

the proton transfer from **14** to **13** in a contact ion pair (CIP) can lead to the TMS adduct **11**, in an aprotic solvent (CH_3CN). In protic solvents, however the enone radical anion can pick up a proton from the solvent, permitting the amine radical cation to undergo desilylation to yield the radical pair **15** and **17**, which can subsequently couple to yield the observed product (**12**). In the presence of oxophilic metal cations also the major product formed is the adduct **12** and this can be attributed to the coordination of the radical anion by metal cations leading to a decrease in the anion strength. The exclusive formation of the non-TMS adducts (**20, 23**) from the photoreactions of the silylamine **10** with acenaphthene-quinone (**18**) and N-methylphthalimide (**21**) in acetonitrile (Scheme 10) supports the view that the base strength of the anion radical plays a key role in determining the chemoselectivity of the α-silylamine cation radical reactions.[9]

A higher chemoselectivity was observed in the photoreactions of silylamines **25** and **28** (Scheme 11). Irradiation of **25** and **28** in methanol leads to the cyclized non-TMS products **26** and **29**, respectively, whereas the TMS containing products **24** and **27** were formed when the irradiations were carried out in acetonitrile.[50] Similar silylamine-enone photocyclization reactions were promoted by single electron transfer (SET) sensitization process as shown in Scheme 12. Thus, the irradiation of dicyanoanthracene (DCA) in an acetonitrile-methanol solution containing **25** resulted in the efficient production of the diastereomeric mixture (6:1) of perhydroisoquinolinones (**30, 31**) and <2 % of perhydroindolinone **32**.[9] Likewise, the DCA sensitized photoreaction of **33** and **34** in acetonitrile-methanol gave the substituted piperidines **35** and **36**, respectively in high yields, along with the pyrrolidine ester **37** in the case of **34**. The formation of the pyrrolidine **37** in the DCA sensitized reaction of **34** is due to the dealkylation of the initially formed radical cation containing the silyl group (Scheme 12).


O
O
+
N
SiMe3
hν
MeCN
O
O
N
SiMe3
18
10
19
14
O
OH
N
20
O
N
+
10
hν
MeCN
O
N
14
OH
N
N
O
O
21
22
23

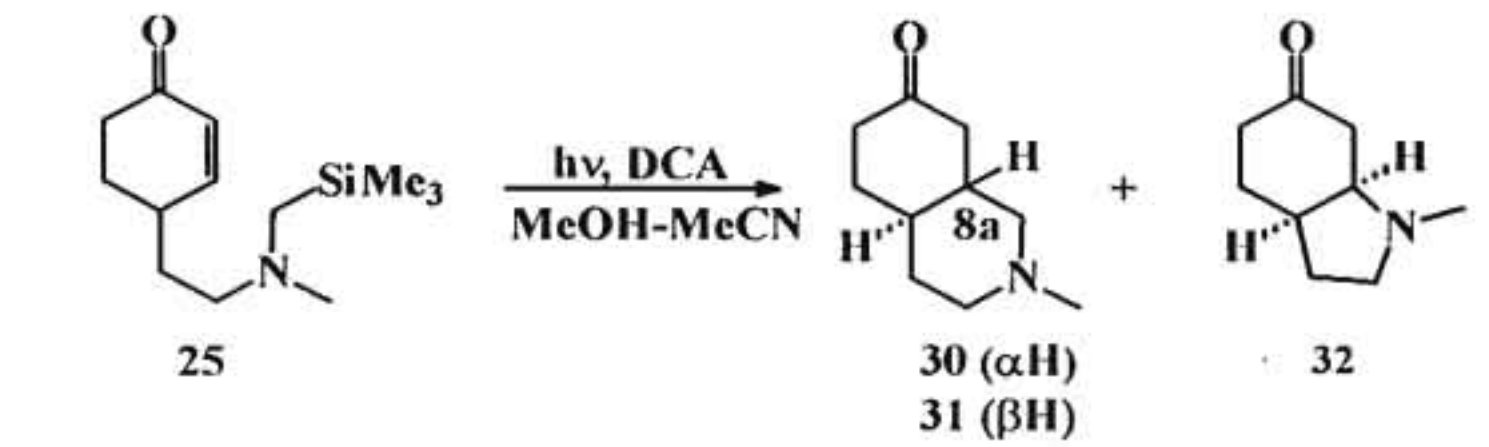
Scheme 10



24 25 26

27 28 29

Scheme 11



25

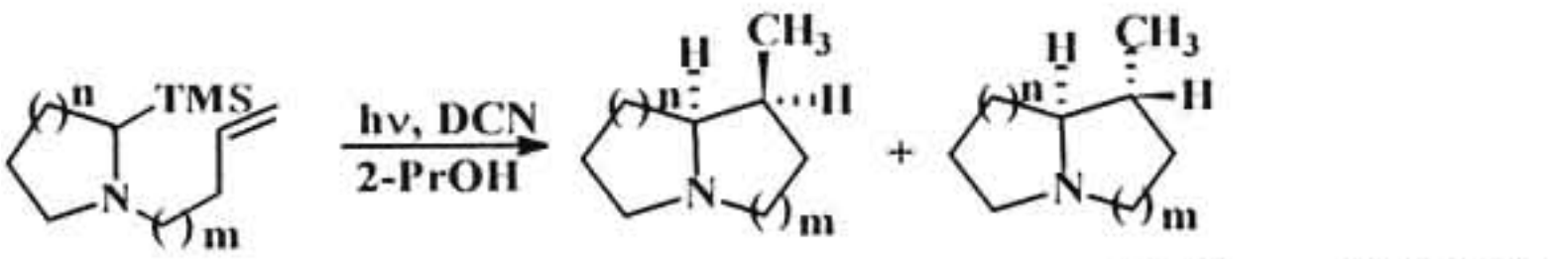
30 (αH)
31 (βH)
32

33 (Y = CH_3)
34 (Y = OCH_3)

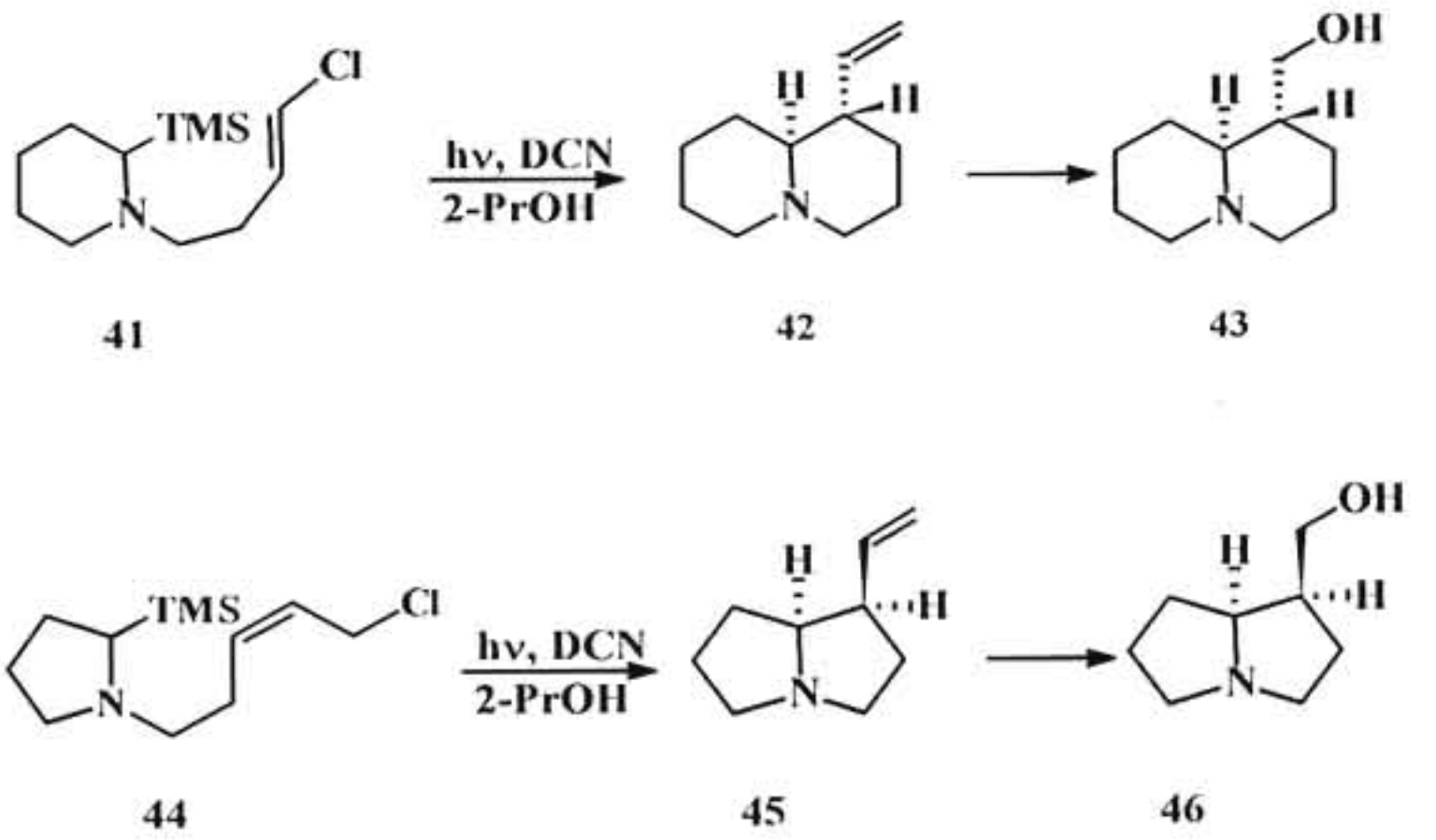
35
36

37

Scheme 12



			39 : 40	Yield (%)
38a	n = m = 1	**39a**	**40a** 97 : 3	90
b	n = m = 2	**39b**	**40b** 0 : 100	88
c	n = 1, m = 2	**39c**	**40c** 2 : 98	85
d	n = 2, m = 1	**39d**	**40d** 95 : 5	87



41 **42** **43**

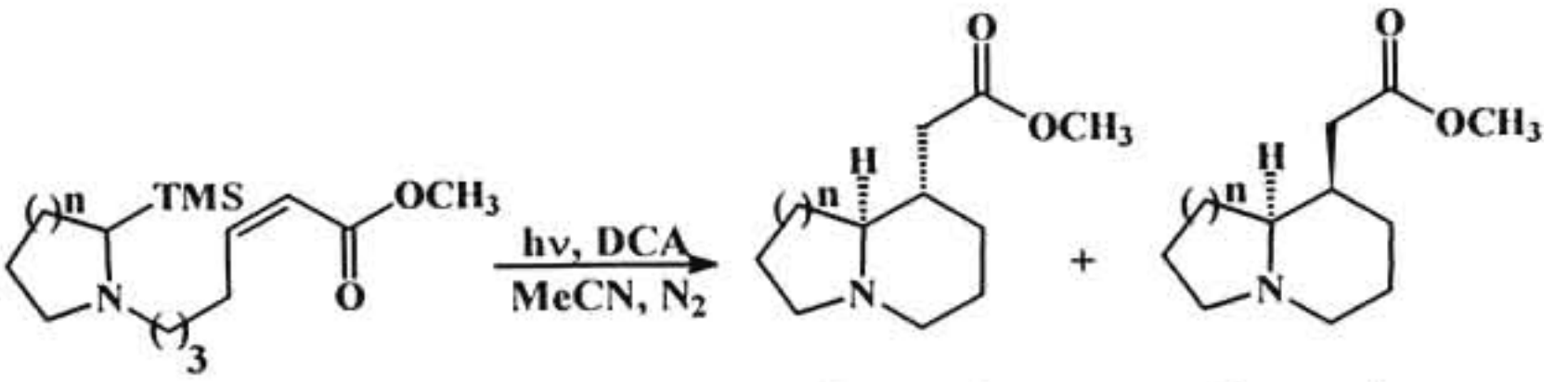
44 **45** **46**

Scheme 13

This dealkylation pathway is analogous to the two electron oxidation of amines observed in thermal reactions and this was proved by synthesising the same pyrrolidine derivative via metal cation oxidation of the silylamine **34** in acetonitrile.[51]

Pandey and co-workers had observed that the DCA-sensitized intramolecular photoreaction of the silylamines **38a-d** proceed in a regio and stereoselective manner yielding the cyclized products **39a-d** and **40a-d** (Scheme 13).[52] Similarly, the synthesis of the biologically active natural product (±) epilupine (**43**) and (±) isoretronecanol (**46**) were achieved using the DCA sensitized photoreactions of the silylamines **41** and **44**, respectively (Scheme 13).[52]

In a recent reinvestigation, Mariano and coworkers have shown that the DCA sensitized photoreaction of **38b** in presence of oxygen leads to the corresponding pyrrolidones and not the azabicyclic products.[53] They have demonstrated that activated olefins (electron withdrawing substitution) are necessary for the formation of azabicyclic ring system as shown in Scheme 14.



47a, n = 1
47b, n = 2

48a, n = 1
48b, n = 2

49a, n = 1
49b, n = 2

Scheme 14

These results are in agreement with the earlier studies by Padwa et.al. in which it was shown that α-aminoalkyl radicals, unlike their α-amido analogues, do not efficiently add intramolecularly to unactivated olefins.[54] It may be pointed out that the photocyclized products such as **48a** could be the precursors of several natural products. Thus, the synthesis of (±) epilupine was achieved by a two step chemical transformation of **48a**.

1.2.3. Objectives of the Present Investigation

Although the mechanistic aspects of the generation of α-aminoalkyl radicals from amines, using a variety of photosensitizers such as quinones, porphyrins, flavins and semiconductors have been well studied, the synthetic applications, such as carbon-carbon bond forming reactions of the α-aminoalkyl radicals thus generated, have not been well investigated. Studies on the synthetic applications have mainly been concerned with the use of dicyanoanthracene (DCA) and dicyanonaphthalene (DCN) as photosensitizers in the generation of α-aminoalkyl radicals from α-silylamine derivatives.

In this thesis, we describe the results of our studies on the photosensitized generation of α-aminoalkyl radicals from primary, secondary and tertiary amines in the presence of electron deficient olefinic substrates, using sensitizers such as anthraquinone, benzophenone, anthrone and xanthone. The mechanistic aspects, as well as the synthetic applications of these reactions have been looked into.

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Chapter 2. Photoelectron Transfer Catalyzed Reactions of Triethylamine and Diisopropylamine with Methyl Methacrylate and Acrylonitrile[1]

2.1. Abstract

The result of an investigation of single electron transfer (SET) promoted photoreaction of triethylamine and diisopropylamine with methyl methacrylate and acrylonitrile, using various sensitizers such as anthraquinone, acridone and dicyanoanthracene are presented. Photoexcitation of the sensitizers leads to the generation of α-aminoalkyl radicals from the amines in good yields, which add on to methyl methacrylate and acrylonitrile, leading to amine-olefin addition products. The sensitized photoreaction of triethylamine (**2**) with methyl methacrylate (**5**), for example gave a mixture of products **8, 11, 12** and **17**, formed through the addition of one, two, three and four methyl methacrylate moieties, respectively. A mechanism involvng the addition of the α-aminoalkyl radicals of triethylamine, generated via the photoelectron transfer process, to methyl methacrylate and the subsequent 1,5-hydrogen atom abstraction reactions of the amine-olefin adduct radicals have been proposed to explain the formation of the multiple-olefin added products. A similar mechanism has also been proposed for the formation of multiple-olefin added products in the photosensitized reaction between triethylamine (**2**) and acrylonitrile (**18**), which led to a mixture of products **19, 20, 21** and **22**. The sensitized photoreaction of diisopropylamine (**23**) with acrylonitrile (**18**) gave multiple-olefin addition products **24** and **25**. Similarly, the sensitized photoreaction of diisopropylamine (**23**) with methyl methacrylate (**5**) gave rise to a multiple-olefin added product **28** and a pyrrolidone derivative **26**. A resonable mechanism has been suggested for the formation of **26**. Anthraquinone and acridone were found to sensitize these photoreactions with greater efficiency than dicyanoanthracene.

2.2. Introduction

The generation and subsequent reactions of α-aminoalkyl radicals have been topics of extensive studies in recent years.[2-10] These radicals can be utilized for the construction of carbon-carbon bonds adjacent to nitrogen, which is of significant importance in alkaloid chemistry.[11-13] α-Aminoalkyl radicals can be generated via single electron transfer oxidation of amines. Removal of a single electron from an amine results in the formation of the aminium radical cation, which can decay via the following modes, i) deprotonation at nitrogen, ii) deprotonation at an α-carbon, iii) intra and intermolecular hydrogen atom abstraction and iv) coupling reactions. Of these possible modes, deprotonation at α-carbon, adjacent to nitrogen is a major pathway and this leads to the formation of the α-aminoalkyl radicals.[9] There have been several studies on the mechanistic aspects of α-CH deprotonation. Pulse radiolysis investigations have shown that the pKa (water, 25°C) of $Me_3N^{+\cdot}$ is about eight and that the rate of CH deprotonation of this radical cation is relatively fast.[14,15] Proton transfer from $Me_3N^{+\cdot}$ to Me_3N in water is found to have a bimolecular rate constant of $7 \times 10^8\ M^{-1}s^{-1}$.

Amine radical cations having electrofugal groups other than protons at the α-C positions can undergo heterolytic fragmentation. Decarboxylation of the aminium radicals, derived from α-aminoacids and the more recently reported studies on the fragmentation of the α-silylamine radical cations, generated via photosensitization, are examples of this type of fragmentation.[10-16] The intra and intermolecular carbon-carbon bond forming reactions of α-aminoalkyl radicals, generated via photoelectron transfer mediated reactions of α–silylamines, using sensitizers such as dicyanoanthracene (DCA) and dicyanonapthalene (DCN) have been investigated in detail.[2] An interesting observation in the direct excitation

studies of α-silylamine-enone systems is that in protic solvents, the major product is the one formed by addition of the α-aminoalkyl radical, generated via desilylation of the aminium radical cation, to the ketyl radical. However, in aprotic solvents, the major product formed is the one obtained via the addition of α-aminoalkyl radical, formed via deprotonation of the aminium radical cation, to the ketyl radical.[17] These differences can be explained on the basis of the acid-base properties of the aminium radical cation and the ketyl radical anion formed in the electron transfer process as discussed below.

Picosecond laser flash photolysis studies of tertiary amine-ketone systems have shown that photoelectron transfer from amines to the triplet state of ketones occurs at diffusion controlled rates to produce the aminium radical cation and the ketyl radical anion as a solvent separated-ion radical pair (SSIRP). This collapses in the picosecond time scale to a contact ion radical pair (CIRP), where proton transfer takes place very fast ($k \sim 10^9\ s^{-1}$) to produce the ketyl and α-amino-radicals.[18] This proton transfer is facilitated by the acid-base properties of the radical ion-pairs. Pulse radiolysis studies have shown that the aminium radical could be relatively less basic (pKa~8), when compared to the parent amine; ketyl radical anions are known to be more basic (pKa~10).[14] In aprotic solvents, rapid proton exchange can take place, whereas in protic solvents the ketyl radical anion can rapidly pick up a proton from the solvent leaving the aminium radical to do its own chemistry. Thus, in the case of α-silylamines, the aminium radical cations undergo preferential deprotonation in aprotic solvents and preferential desilylation in protic solvents. The aminoalkyl radical that is formed via these processes is much easier to oxidize than the parent amine. Thus, the rapid proton exchange converts the highly oxidising aminium radical cation to highly reducing

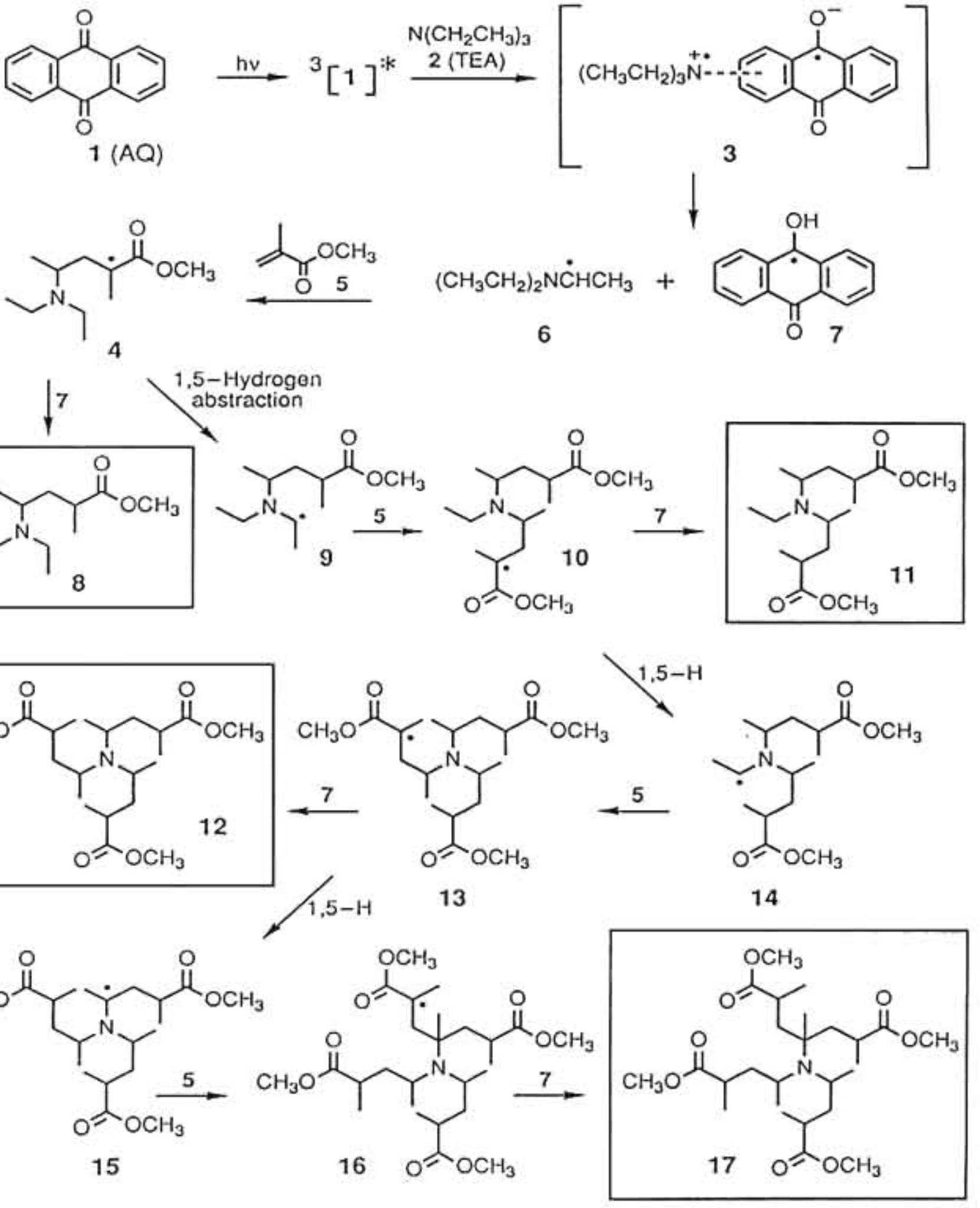
aminoalkyl radicals. This process effectively controls the energy wasting back electron transfer between the radical ion-pairs.[9]

Although, the mechanistic aspects of the α–aminoalkyl radical generation via ketone sensitized reactions of amines, have been studied extensively, there have been very few attempts to utilize these processes for carbon-carbon bond forming reactions. In the present study, the photosensitized generation of α–aminoalkyl radicals from triethylamine and diisopropylamine, using anthraquinone and acridone as sensitizers and the subsequent intermolecular reactions of these radicals with methyl methacrylate and acrylonitrile have been examined. These processes have been compared to the reactions, sensitized by dicyanoanthracene.

2.3. Results

2.3.1. Photosensitized Addition of Triethylamine (2) to Methyl Methacrylate (5)

The photosensitized addition of triethylamine (**2**) to methyl methacrylate (**5**) was effected by irradiating argon-purged acetonitrile solutions of triethylamine and methyl methacrylate, containing catalytic amounts of (10^{-4} M) anthraquinone (**1**), under Pyrex filtered light ($\lambda >$ 290 nm). Four products were isolated from the reaction mixture (**8, 11, 12** and **17**, Scheme 1) and they were characterized on the basis of analytical results and spectral information. The IR spectrum of **8**, for example showed an absorption band at 1736 cm^{-1}, due to the ester carbonyl group. The ^1H NMR spectrum of **8** showed a multiplet at δ 0.85-1.3 (12 H), which was assigned to the CH_3 protons. The methoxy protons (3 H) appeared as a singlet at δ 3.6-3.7. The ^1H NMR spectral features indicate that **8** is a 1:1 adduct of methyl


hν
3[1]*
N(CH2CH3)3
2 (TEA)
1 (AQ)
3
OCH3
5
4
(CH3CH2)2NCHCH3
+
6
OH
7
1,5–Hydrogen
abstraction
8
9
10
11
12
13
14
1,5–H
15
16
17

Scheme 1

methacrylate and triethylamine. The ^{13}C NMR spectrum of **8** showed several signals and the one at δ 174.0 has been assigned to the ester carbonyl carbon. The mass spectrum of **8** showed the molecular ion peak at m/z 201, which is in agreement with the assigned structure.

The IR spectrum of **11** showed an absorption band at 1738 cm^{-1}, characteristic of ester carbonyl groups. The ^{1}H NMR spectrum of **11** showed a multiplet at δ 0.9-1.2 (15 H), which was assigned to the CH_3 protons. The protons of the two methoxy groups appeared as a singlet at δ 3.6-3.7. The spectral features indicate that **11** is a 2:1 adduct between methyl methacrylate and triethylamine. The ^{13}C NMR spectrum of **11** showed several signals and the one at δ 177.54 has been assigned to the ester carbonyl carbon. The mass spectrum of **11** showed the molecular ion peak at m/z 301, which is in agreement with the assigned structure.

The IR spectrum of **12**, showed an ester carbonyl absorption at 1730 cm^{-1}. The ^{1}H NMR spectrum of **12** showed multiplets at δ 0.93-1.0 (9 H), assigned to the three sets of CH_3 protons of triethylamine and at δ 1.1-1.26 (9 H), assigned to the three sets of CH_3 protons of the added methyl methacrylate. The protons due to the three methoxy groups appeared as a singlet at δ 3.6-3.75. This indicates that **12** is a 3:1 adduct between methyl methacrylate and triethylamine. The ^{13}C NMR spectrum of **12** showed two peaks at δ 17.7 and 20.7, corresponding to CH_3 carbons, one peak at δ 41.2 due to CH_2 carbons, two peaks at δ 36.8 and 47.1 due to CH carbons, one peak at δ 51.4 due to the OCH_3 carbons and one peak at δ 177.4, attributable to the C=O carbon. The ^{1}H NMR spectrum of **12** is indicative of the symmetrical nature of the structure. The mass spectrum of **12**

showed the molecular ion peak at m/z 401, which is in agreement with the assigned structure.

The IR spectrum of **17**, showed an ester carbonyl absorption at 1741 cm^{-1}. The ^{1}H NMR spectrum of **17** showed a multiplet at δ 0.9-1.25 (21 H), assigned to the CH_3 protons. The methoxy protons (12 H) appeared as a multiplet at δ 3.65-3.75. This indicates that **17** has a complex structure, consisting of a 4:1 adduct between methyl methacrylate and triethylamine. The ^{13}C NMR spectrum of **17** showed several signals due to different chiral centres associated with the structure. The signals at δ 176.80-177.48, for example, have been assigned to the ester carbonyl carbons. The mass spectrum of **17** showed the molecular ion peak at m/z 501, which is in agreement with the assigned structure.

Table 1 lists the percentage conversion of the starting material (**5**) and product distribution under a variety of conditions in the reaction of triethylamine with methyl methacrylate.

It has been observed that the changes in the irradiation time and substrate concentrations brought about only minor changes in the product distribution. However, on using a large excess of triethylamine (1 mol), there was some increase in the yield of **8** at the expense of **17**. When acridone was used as the sensitiser, instead of anthraquinone, the percentage conversion and product yields were found to be similar to those observed in the case of anthraquinone. Dicyanoanthracene (DCA), however, was found to be much less efficient as a sensitiser, when compared to either anthraquinone or acridone (Table 1). Also, the percentage distribution of products indicated that more of the lower molecular weight products such as **8** and **11** were formed at the expense of the higher molecular weight products **12** and **17** in the case of DCA sensitized reactions.

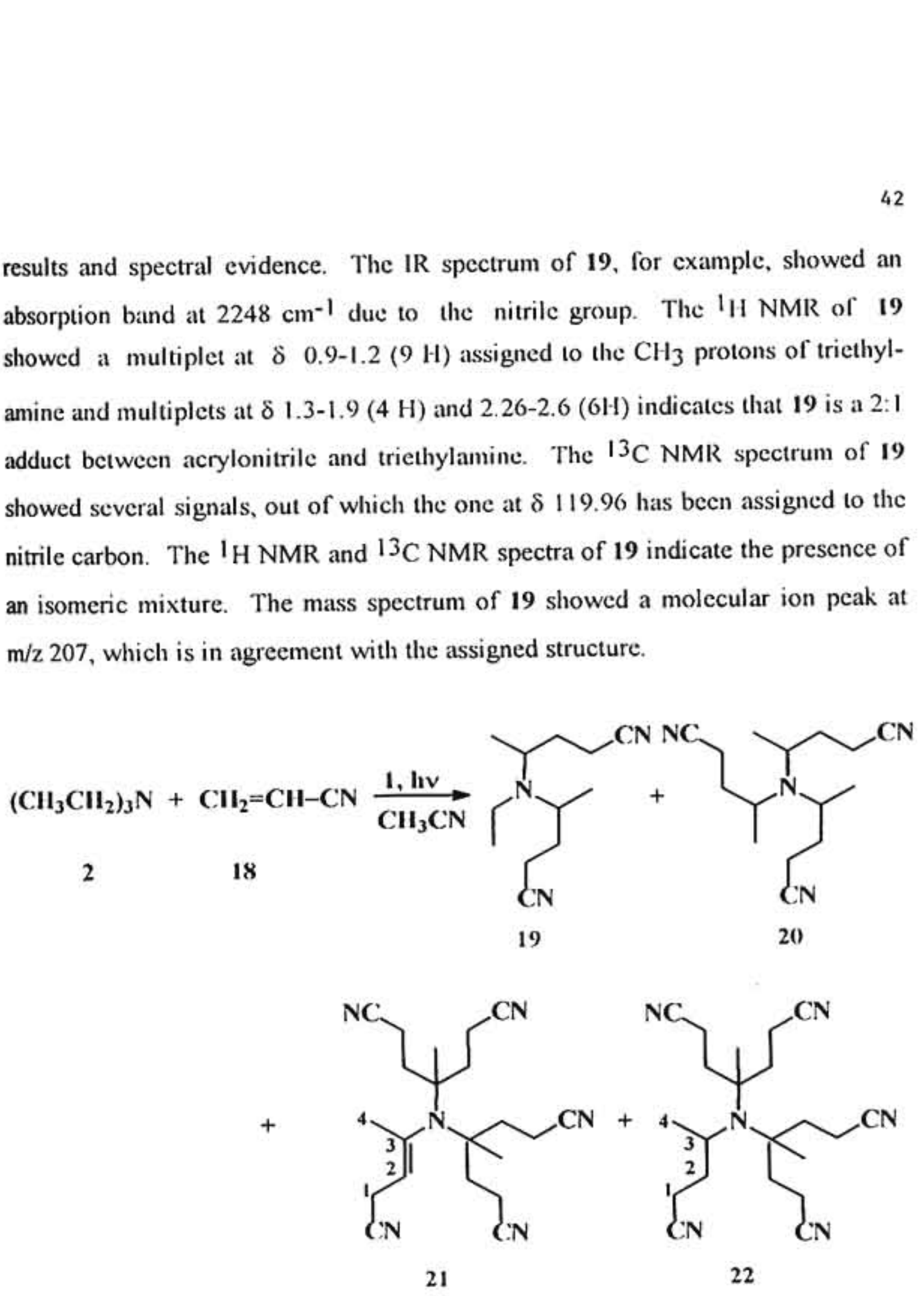
Table 1. Photosensitized addition of triethylamine (**2**) to methyl methacrylate (**5**) in acetonitrile (350 mL) at 298 K using 450 W medium pressure Hanovia lamp (Pyrex filter)

Sensitizer 10^{-4} (M)	**2** mmol	**5** mmol	Duration of irradiation (h)	% Conversion of **5**	Product distribution (%)			
					8	**11**	**12**	**17**
Anthraquinone	15	15	1	20	10	11	28	12
"	15	15	2	26	10	18	28	16
"	15	15	3	30	10	15	28	18
"	15	15	4	35	10	14	24	22
"	15	2	1	40	8	18	26	8
"	15	45	1	17	10	14	24	8
"	1000	15	1	20	20	25	30	10
Acridone	15	15	1	28	10	20	32	18
"	15	15	4	38	10	18	30	20
Dicyanoanthracene	15	15	4	8	35	20	18	5
"	15	15	8	12	30	24	20	8

2.3.2. Photosensitized Addition Reactions of Triethylamine (2) to Acrylonitrile (18)

The photosensitized addition of triethylamine (**2**) to acrylonitrile (**18**) was carried out by irradiating argon-purged acetonitrile solutions of triethylamine and acrylonitrile containing catalytic amounts of (10^{-4} M) anthraquinone (**1**), under Pyrex filtered light. Four products were isolated from the reaction mixture (**19, 20, 21** and **22**, Scheme 2) and they were characterized on the basis of analytical

results and spectral evidence. The IR spectrum of **19**, for example, showed an absorption band at 2248 cm^{-1} due to the nitrile group. The ^1H NMR of **19** showed a multiplet at δ 0.9-1.2 (9 H) assigned to the CH_3 protons of triethylamine and multiplets at δ 1.3-1.9 (4 H) and 2.26-2.6 (6H) indicates that **19** is a 2:1 adduct between acrylonitrile and triethylamine. The ^{13}C NMR spectrum of **19** showed several signals, out of which the one at δ 119.96 has been assigned to the nitrile carbon. The ^1H NMR and ^{13}C NMR spectra of **19** indicate the presence of an isomeric mixture. The mass spectrum of **19** showed a molecular ion peak at m/z 207, which is in agreement with the assigned structure.



Scheme 2

The IR spectrum of **20** showed an absorption band at 2248 cm^{-1} due to the nitrile group. The ^1H NMR spectrum of **20** showed two doublets at δ 0.9-1.2 (9 H) assigned to the three sets of CH_3 protons of triethylamine. The multiplet at

δ 1.4-1.9 (6 H) has been assigned to the three sets of CH_2 protons from the acrylonitrile component in the adduct. The multiplet at δ 2.8-3.2 (3 H) has been assigned to the three CH protons. The ^{13}C NMR spectrum of **20** showed several signals out of which those at δ 120.10, 120.54 and 120.61 have been assigned to the nitrile carbons. The ^{1}H NMR and ^{13}C NMR spectra of **20** indicate the presence of an isomeric mixture. The mass spectrum of **20** showed a molecular ion peak at m/z 260, which is in agreement with the assigned structure.

Products **21** and **22** have nearly identical physical properties and could not be separated using chromatographic techniques including preparative HPLC. Evidence for the two components in the product mixture was obtained by the presence of two distinct spots on silver nitrate-doped silica gel TLC plates. High resolution ^{1}H NMR spectrum of **21** and **22** (500 MHz) clearly showed that two compounds were present in the purified mixture in approximately equal ratio. The IR spectrum of **21** and **22** showed a band at 2248 cm^{-1} due to the nitrile group. In the ^{1}H NMR spectrum of the mixture of **21** and **22**, the group of signals centered around δ 1.2 (15 H) has been assigned to the three sets of methyl protons of **22** and two sets of methyl protons of **21.** The C-4 methyl protons adjacent to the olefinic carbon of **21** appeared as a singlet centered at δ 1.85 (3 H). Nine sets of methylene protons of **21** and **22** have appeared around δ 1.7-2.0 (18 H), whereas another set of eighteen methylene protons of (**21** and **22**) appeared at δ 2.25-2.5 (18 H). The methine protons at C-3 position of **22** appeared as a broad multiplet centered at δ 3.25. The ^{1}H NMR spectrum of this mixture showed a doublet at δ 3.1 (2 H, J=7 Hz) which was assigned to the methylene protons at the C-1 positions and the triplet at δ 5.3 (1 H, J=7 Hz) to the olefinic proton at the C-2 position of **21**. The ^{13}C NMR spectrum of the mixture of **21** and **22** showed several signals out of which those at δ 117.36 and 142.16 were characteristic of

the olefinic carbon of **21**. The signals at δ 119.24 and 119.57 have been assigned to the nitrile carbons. The mass spectrum of **21** and **22** showed two molecular ion peaks at m/z 365 (MH^+, **21**) and 367 (MH^+, **22**), which is in agreement with the assigned structure.

The percentage conversion of the starting material (**18**) and product distributions under varying conditions are shown in Table 2. As in the case of the addition of methyl methacrylate to triethylamine, here also it has been observed that the product distribution is fairly independent of the substrate concentration and irradiation time.

Table 2. Photosensitized addition of triethylamine (**2**) to acrylonitrile (**18**) in acetonitrile (350 mL) at 298 K using a Pyrex-filtererd light of a 450 W medium pressure Hanovia lamp

Sensitizer 10^{-4} M	**2** mmol	**18** mmol	Duration of irradiation (h)	% Conversion of **18**	Product distribution (%) **19**	**20**	**21+22**
Anthra-quinone	15	15	1	17	8	10	60
"	15	45	1	11	8	12	50
"	150	15	1	21	10	15	40
Acridone	15	15	1	30	18	42	28
"	15	15	1	20	15	33	32
"	150	15	1	40	12	40	18
Dicyano-anthracene	15	15	4	< 2	–	–	–

On using acridone as the sensitiser, the percentage conversion and product yields were found to be slightly higher than in the case of anthraquinone sensitized

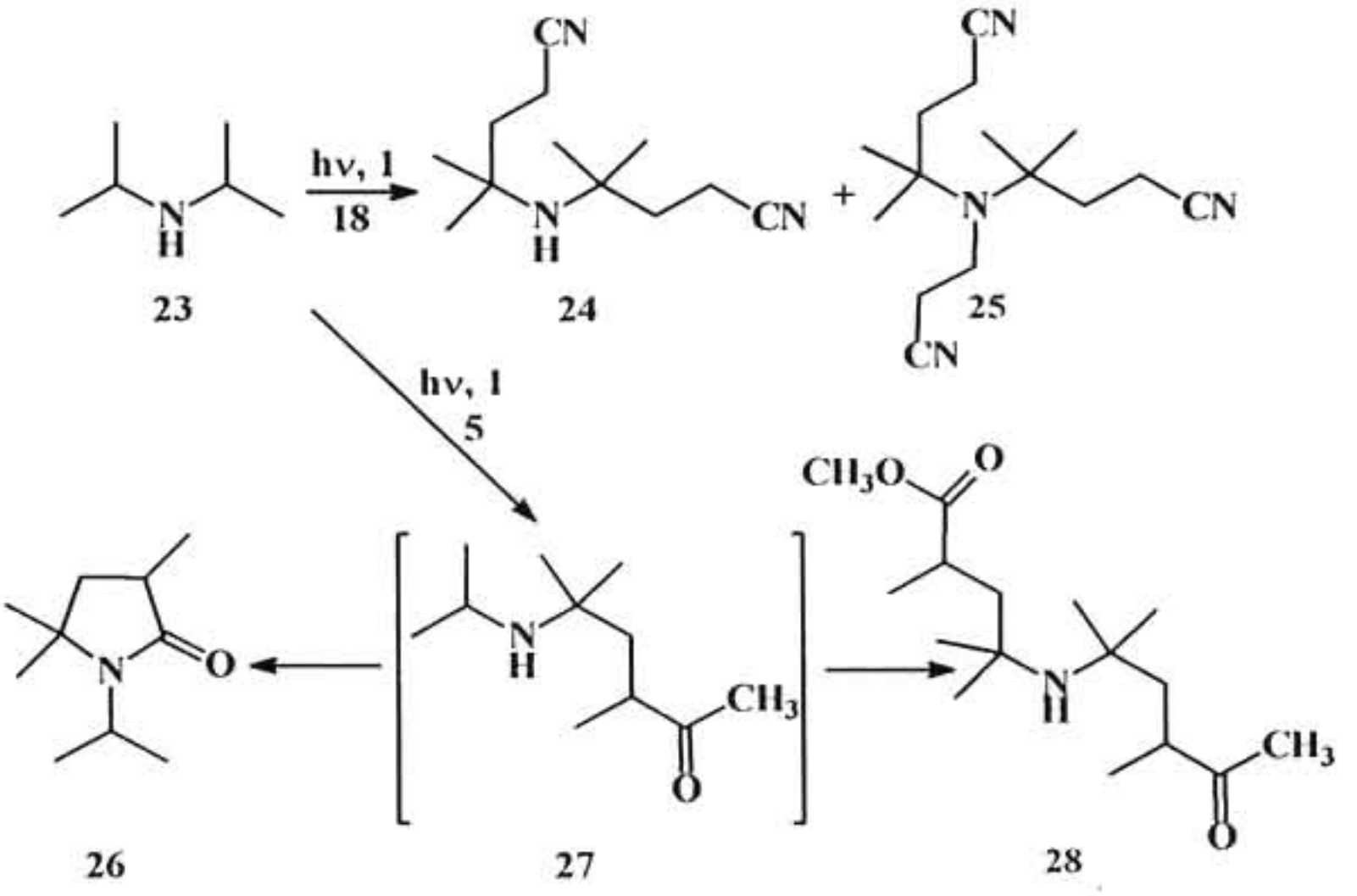
reactions. In the acridone sensitized reactions of **2** and **18**, the percentage yield of **20** was found to increase at the expense of **21** and **22**, as compared to the anthraquinone-sensitized reactions. Under identical conditions, DCA was found to be inefficient as a sensitiser. These results are summarised in Table 2.

2.3.3. Photosensitized Addition of Diisopropylamine (23) to Acrylonitrile (18)

The photosensitized addition of diisopropylamine (**23**) to acrylonitrile (**18**) was carried out by irradiating an argon-purged acetonitrile solution of diisopropylamine and acrylonitrile, containing catalytic amounts (10^{-4} M) of anthraquinone (**1**), under Pyrex filtered light. Two products, **24** and **25**, were isolated from the reaction mixture (Scheme 3) and they were characterized on the basis of analytical results and spectral information.

The IR spectrum of **24** and **25** showed absorption bands at 2248 cm^{-1}, due to the nitrile groups. The ^1H NMR spectrum of **24** showed a singlet at δ 1.1-1.3 (12 H) indicating the presence of CH_3 groups. The multiplet centered around δ 1.60-1.85 (4 H) and δ 2.35-2.60 (4 H) have been assigned to the CH_2 protons. The ^{13}C NMR spectrum of **24** showed several signals, out of which the one at δ 120.61 has been assigned to the nitrile carbon. The mass spectrm of **24** showed the molecular ion peak at m/z 208, which is in agreement with the assigned structure. The ^1H NMR spectrum of **25** showed a singlet at δ 1.1-1.3 (12 H) which has been assigned to the CH_3 protons. The multiplet at δ 1.6-2.1 (6 H) has been assigned to the three sets of CH_2 protons, whereas the one at δ 2.4-2.7 (6 H) has been assigned to the three additional sets of CH_2 protons. The ^{13}C NMR spectrum of **25** showed several signals, out of which, those at δ 120.50 and 120.61 have been assigned to the nitrile carbons. The mass spectrum of **25**

showed the molecular ion peak at m/z 261, which is in agreement with the assigned structure.



Scheme 3

Table 3 lists the percentage conversion of the starting material (**18**) and product distribution under varying conditions. It has been observed that the product distributions of **24** and **25** are independent of substrate concentrations and irradiation time (Table 3).

On using acridone as the sensitizer, the percentage conversion was found to be greater than that of anthraquinone under similar conditions. DCA, on the other hand was found to be quite ineffective, under analogous conditions.

Table 3. Photosensitized addition of diisopropylamine (**23**) to acrylonitrile (**18**) in acetonitrile (350 mL) at 298 K using Pyrex filtered light of a 450 W medium pressure Hanovia lamp

Sensitizer 10^{-4} M	**23** mmol	**18** mmol	Duration of irradiation (h)	%Conversion of **18**	Product distribution (%) **24**	**25**
Anthraquinone	15	15	1	12	40	20
"	15	45	1	14	50	20
"	15	45	6	8	45	25
Acridone	15	45	1	20	45	25
Dicyanoanthracene	15	45	8	< 2	–	–

2.3.4. Photosensitized Addition of Diisopropylamine (23) to Methyl Methacrylate (5)

The photosensitized addition of diisopropylamine (**23**) to methyl methacrylate (**5**) was effected by irradiating an argon-purged acetonitrile solution of diisopropylamine and methyl methacrylate containing catalytic amounts of (10^{-4} M) anthraquinone (**1**), under Pyrex filtered light (λ >290 nm). Two products were isolated from the reaction mixture (**26** and **28**, Scheme 3) and they were characterized on the basis of analytical results and spectral information. The IR spectrum of **28** showed a broad absorption band at 3400 cm^{-1}, due to the N-H group and a band at 1740 cm^{-1} due to the ester C=O group. The ^1H NMR spectrum of **28** showed a multiplet at δ 1.0-1.2 (18 H), assigned to six sets of CH_3 protons and a second multiplet at δ 1.8-2.2 (4 H), assigned to two sets of CH_2 protons. In addition, the spectrum showed a multiplet at δ 2.4-2.8 (2 H)

due to the two CH protons and singlets at δ 3.5-3.7 (6 H) due to two methoxy protons. The ^{13}C NMR spectrum of **28** showed several signals out of which the one at δ 179.60 has been assigned to the ester carbonyl carbon. The NMR data suggests that **28** is a 2:1 adduct of methyl methacrylate and diisopropylamine. The mass spectrum of **28** showed the molecular ion peak at 301, which is in agreement with the assigned structure.

The IR spectrum of **26** showed an absorption band at 1685 cm^{-1}, due to the amide carbonyl group. The ^1H NMR spectrum of **26** showed several multiplets at δ 1.1-1.6 (15 H) due to five sets of CH_3 protons. The multiplet centered around δ 2.0-2.3 (3 H) is due to CH_2 and CH protons and the multiplet at δ 3.2-3.6 (1 H) has been assigned to the CH proton of the isopropyl group. The ^{13}C NMR spectrum of **26** showed five CH_3 signals at δ 15.94, 19.61, 20.66, 25.04 and 28.18, one CH_2 signal at δ 43.33, two CH signals at δ 35.01 and 44.05, one quarternary carbon signal at δ 58.62 and a carbonyl carbon signal at δ 175.87. The structure of **26** on the basis of spectral evidence has been assigned as N-isopropyl-3,5,5-trimethyl-2-pyrrolidone. The mass spectrum of **26** showed a molecular ion peak at m/z 169, which is in agreement with the assigned structure.

The product distribution and percentage conversion of the starting material (**5**) were found to be independent of the substrate concentration and irradiation time (Table 4). Acridone was found to be marginally more efficient in terms of the percentage conversion of methyl methacrylate. Under analogous conditions, DCA was found to be quite inefficient.

Table 4. Photosensitized reactions of diisopropylamine (**23**) with methyl methacrylate (**5**) in acetonitrile (350 mL) at 298° K using a Pyrex filtered light of a 450 W medium pressure Hanovia lamp

Sensitizer 10^{-4} M	**23** mmol	**5** mmol	Duration of irradiation (h)	% Conversion of **5**	Product distribution (%) **26**	**28**
Anthraquinone	15	15	1	10	26	30
	15	45	1	5	55	30
"	15	45	6	10	50	30
"	15	45	8	15	50	30
Acridone	15	15	1	13	15	40
Dicyanoanthracene	15	15	4	< 2	–	–

2.4. Discussion

2.4.1. Photosensitized Addition of Triethylamine (2) to Methyl Methacrylate (5) and Acrylonitrile (18)

Irradiation of the reaction mixtures with Pyrex-filtered light would lead to the selective excitation of the sensitizers since triethylamine as well as methyl methacrylate and acrylonitrile, do not have significant absorbance above 290 nm. Excitation of anthraquinone (**1**) would lead to the formation of anthraquinone triplets via rapid intersystem crossing from the excited singlet state (ϕ_T ~0.93).[19] Quenching of the anthraquinone triplet by triethylamine (**2**) would result in the formation of the contact ion pair (CIP) (**3**), involving the aminium radical cation and the anthraquinone radical anion. The basic nature of the anthraquinone ketyl radical anion can facilitate abstraction of a proton from the relatively acidic

aminium radical cation to yield the α-aminoalkyl radical. The subsequent thermal reactions of the α-aminoalkyl radical with methyl methacrylate and those of the adduct radicals depicted in Scheme 1, is proposed as the mechanism for the formation of products, **8, 11, 12** and **17.** Addition of the aminoalkyl radical **6** to methyl methacrylate would give rise to the adduct radical **4**, which can be quenched by the ketyl radical **7** to yield **8** and anthraquinone. The adduct radical **4,** can also undergo 1,5-hydrogen abstraction to bring about a translocation of the radical centre to give **9**. Intramolecular 1,5-hydrogen atom abstractions are well documented in free radical chemistry.[20-22] Radical adducts of α-aminoalkyl radicals are also known to undergo 1,5 hydrogen atom abstraction reactions.[23,24] A sequence of addition of the adduct radical to the olefinic ester and subsequent quenching by anthraquinone ketyl radical and 1,5-hydrogen atom abstraction reactions as shown in Scheme 1 could subsequently lead to rest of the observed products, **11, 12** and **17**. The formation of these products may be attributed to the inefficiency of the anthraquinone ketyl radical to terminate the initially formed 1:1 adduct radical. The ketyl radical anion of anthraquinone is known to be relatively stable in argon-purged solutions and is only quenched very slowly by electron acceptors. [9]

An alternative reaction mechanism would involve the formation of the 1:1 adduct **8** and its subsequent secondary electron transfer reaction with the excited state of anthraquinone. This can, however, be ruled out since the product distribution is fairly independent of the reaction conditions. For irradiation periods of 1, 2, 3 and 4 h, where the conversion of methyl methacrylate varies from 20 to 40% (Table 1), the product distribution remains unchanged within experimental error, indicating that secondary photoprocesses are not important. Also, under these conditions, substantial amounts of unreacted amine present would prevent

secondary photoreactions by effectively quenching the excited state of the sensitizers.

The mechanism was further confirmed by carrying out these reactions in the presence of large excess of triethylamine. Under these conditions the probability of the excited state of the sensitizer being quenched by the photoproducts would be very low. The results indicate (Table 1) that even under these conditions, the formation of the multiple olefin added products predominate (**12** (30 %) and **11** (25 %)). There is a slight variation in the percentage distribution in the products with greater amounts of the lower molecular weight products being formed at the expense of the higher molecular weight products. This may be attributed to the increase in intermolecular hydrogen transfer between the adduct radicals and the free amine in the presence of excess amine.

Acridone-sensitized reactions of triethylamine and methyl methacrylate are comparable (Table 1). Dicyanoanthracene, however was found to be highly inefficient in sensitizing these reactions. This clearly supports the role of the anion radical base strength in bringing about the deprotonation of the alkylamine radical cation. Unlike the ketyl radical anion, the DCA radical anion is more acidic. Also, the product distribution for the DCA sensitized reactions clearly indicates the ability of the DCA radical anion to quench the amine-alkene adduct more efficiently than the ketyl radicals. Thus, the lower molecular weight products are formed in better yields than the higher molecular weight products, unlike in the anthraquinone and acridone-sensitized reactions.

Triethylamine possesses six abstractable methylene atoms, and six olefinic moieties can, in principle, add to the amine moiety. However, the formation of the

five and six addition products is probably inhibited by steric factors due to the bulkiness of methyl methacrylate.

Studies with acrylonitrile, where the steric factor would be considerably less important, indicated the formation of the 5-added product also. The mechanism for the formation of the products, **19**, **20** and **22** can be similar to that proposed for the methyl methacrylate addition in Scheme 1. The formation of **21** can occur via a hydrogen atom abstraction from the precursor radical adduct consisting of five acrylonitrile moieties added to the amine or via a disproportionation reaction of the same radical which would eventually yield equal amounts of both **21** and **22.** The formation of enamine derivatives in the sensitized reactions of tertiary amines has been reported before.[25-27]

Acridone-sensitized reactions were slightly more efficient with regard to the percentage conversion of acrylonitrile. The product distribution, however indicated that the lower molecular weight products were formed in preference to the higher molecular weight products. With DCA as sensitizer the radical anion generated in the electron transfer process is not sufficiently basic to abstract a proton from the aminium radical anion. The α-aminoalkyl radicals are therefore not generated efficiently and DCA was found to be least efficient in sensitizing these reactions.

2.4.2. Photosensitized Addition of Diisopropylamine (23) to Acrylonitrile (18) and Methyl Methacrylate (5)

Single electron transfer (SET), followed by deprotonation or hydrogen atom abstraction from primary and secondary amines can lead to either aminyl or α-aminoalkyl radicals.[28] Since α-aminoalkyl radicals are known to be thermodynamically more stable, aminyl radicals can readily be converted to α-aminoalkyl

radicals via hydrogen abstracton from the parent amines. These processes lead predominantly to the formation of α-aminoalkyl radicals.[3] In the present study, the photosensitized reactions of diisopropylamine led specifically to products derived from reactions of α-aminoalkyl radicals.

Anthraquinone-sensitized reactions of diisopropylamine (**23**) with acrylonitrile (**18**) led to two major products, **24** and **25.** Anthraquinone sensitization would generate the α-aminoalkyl radicals of diisopropylamine as discussed above, which could add to acrylonitrile to yield an adduct radical. Radical translocation by 1,5-hydrogen abstraction, addition to another molecule of acrylonitrile at the new radical site and subsequent quenching of the adduct radical by the ketyl radical of anthraquinone can lead to **24**. The mechanism proposed for this reaction is analogous to the one depicted in Scheme 1. The product **25** could arise through a thermal Michael type addition of **24** with acrylonitrile. The percentage conversion was better when acridone was used as the sensitizer (Table 3). Dicyanoanthracene did not sensitize the photoreaction of diisopropylamine with acrylonitrile to any noticeable extent.

The anthraquinone-photosensitized reaction of diisopropylamine (**23**) with methyl methacrylate (**5**) leads to a 1:2 amine-olefin addition product (**28**). However, the major fraction of the product mixture consists of N-isopropyl-3,5,5-trimethyl-2-pyrrolidone (**26**), which could arise through **27**. The adduct **27** was not isolated from the reaction mixture. However there are several reports of such intramolecular cyclization reactions being very facile.[29,30] The photoreactions of diisopropylamine with methyl methacrylate offers a mild and convenient one step route to synthesize substituted pyrrolidone rings. Acridone was found to sensitize this reaction with nearly the same efficiency in comparison to that of

anthraquinone with respect to the percentage distribution of **28** at the expense of **26**. Dicyanoanthracene was found to be ineffective in sensitizing these reactions. These studies indicate that the photosensitized reactions of α,β-unsaturated esters with amines can be utilized to develop a simple one-step procedure for the synthesis of lactams. Such reactions have been investigated and these results are outlined in Chapter 3.

2.5. Experimental Section

The IR spectra were recorded on a Perkin Elmer model 882 Infrared Spectrometer. The electronic spectra were recorded on a Shimadzu UV-2100 Spectrophotometer. The ^{1}H NMR spectra were recorded on JEOL EX 90, Bruker WH 270 or Varian VXR 500 S NMR spectrometers, using tetramethylsilane (TMS) as internal standard. The ^{13}C NMR (22.5 MHz) resonances were assigned using QUART and DEPT programmes to determine the type of carbon attachments. The mass spectra were recorded either on a Finnigan MAT model 8430 or JEOL JMS AX 505 HA mass spectrometer or 5890 series II Hewlet Packard GC-MS. GC data were obtained on OV 101 (25 m length, 0.2 mm ID) or on HP-FFAP (25 m length, 0.2 mm ID) capillary column, using a FID detector. HPLC analyses were carried out using a Shimadzu HPLC with either shim-pack preparative ODS column (20.0 mm ID, 25 cm length) or shim-pack CLC-ODS analytical column (5 mm ID, 25 cm length) and using methanol as eluent.

Preparative photochemical reactions were carried out using a 450 W medium pressure mercury vapour lamp in Pyrex-jacketed water cooled immersion well. Anthraquinone was purified by vacuum sublimation and dicyanoanthracene was purified either by column chromatography or by recrystallization from

benzene. Acridone (99%) from Aldrich was used as obtained. All other reagents and solvents were purified by distillation before use.

The photolysis mixture, typically consisting of the amine (15 mmol) and olefinic substrate (2-45 mmol) in acetonitrile (350 mL), containing the sensitizer (10^{-4} M) was purged with argon or nitrogen before irradiation (1-8 h). The solvent and unchanged reactants were removed under reduced pressure and the product mixture was chromatographed (flash column) over silica gel (250-400 mesh) or by using a Harrison Chromatotron. All the photoproducts were finally purified using a semipreparative HPLC. The yield reported are based on the olefinic substrate consumed, which was estimated by HPLC before removal of the solvent from the irradiation mixture. The reported product distributions are based on GC-analysis of the product mixtures. The sensitizers were recovered quantitatively (> 90%) under all irradiation conditions. All the photoproducts were characterized on the basis of their spectral data and analytical results, including high resolution mass spectrometry data.

2.5.1. Photosensitized Addition of Triethylamine (2) to Methyl Methacrylate (5)

Irradiation of an argon purged solution of **5** (1.5 g, 15 mmol) and **2** (1.5 g, 15 mmol) in acetonitrile (350 mL), containing anthraquinone (10^{-4} M) for 1 h and separation of products by column chromatography using a mixture (1:9) of ethyl acetate and pertroleum ether gave 40 mg (10%) of **8**, 80 mg (20%) of **11**, 150 mg (28%) of **12** and 48 mg (12%) of **17**. These yields are based on methyl methacrylate reacted (22%), as estimated by HPLC. These reactions were repeated under various reaction conditions and also using acridone and dicyanoanthracene

as sensitizers, instead of anthraquinone. The percentage conversion and product distribution in these reactions are given in Table 1.

8 : IR spectrum ν_{max} (neat) : 2975, 2870 (CH) and 1736 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 2500) and 254 (408, sh).

^1H NMR spectrum ($CDCl_3$) : δ 0.85-1.3 (12 H, m, 4 CH_3), 1.5-1.8 (2 H, m, CH_2), 1.8-2.9 (6 H, m, 2 CH_2, 2 CH) and 3.6-3.7 (3 H, s, OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 13.50, 14.25, 17.50 (CH_3), 37.10 (CH), 38.20, 42.60 (CH_2), 51.15 (OCH_3), 52.5 (CH) and 174.40 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 201 (M^+, 4), 186 (11), 170 (7), 154 (4), 143 (6), 126 (8), 100 (100), 83 (10), 68 (7) and 55 (10). Molecular weight calculated for $C_{11}H_{23}NO_2$: 201.1728. Found : 201.1714 (high-resolution mass spectrometry).

11 : IR spectrum ν_{max} (neat) : 2972, 2875 (CH) and 1738 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 3400) and 254 (418, sh).

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.2 (15 H, m, 5 CH_3), 1.7-2.1 (4 H, m, 2 CH_2), 2.2-2.9 (6 H, m, CH_2, 4CH) and 3.6-3.7 (6 H, s, 2 OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 15.35, 15.58, 17.05,17.55,17.80 (CH_3), 36.20, 36.80 (CH), 38.00, 39.50, 40.20 (CH_2), 49.50, 50.20 (CH), 51.20 (OCH_3) and 177.54 (C=O, ester).

Mass spectrum, m/z (relative intensity): 301 (M^+, 6), 286 (12), 270 (4), 200 (100), 170 (30), 142 (28), 129 (40), 97 (32), 83 (15), 69 (16) and 55 (10). Molecular weight calculated for $C_{16}H_{31}O_4N$: 301.2253. Found : 301.2245 (high-resolution mass spectrometry).

12 : IR spectrum ν_{max} (neat) : 2975, 2875 (CH) and 1730 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 3400) and 254 (460, sh).

^1H NMR spectrum ($CDCl_3$): δ 0.93-1.1 (9 H, m, 3 CH_3), 1.1-1.26 (9H, m, 3 CH_3), 1.26-1.5 (6 H, m, 3 CH_2), 2.3-2.56 (3H, m, 3CH), 2.66-2.93 (3 H, m, 3 CH) and 3.6-3.75 (9 h, s, 3 OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 17.7, 20.7 (CH_3), 36.8 (CH), 41.2 (CH_2), 47.1 (CH), 51.4 (OCH_3) and 177.4 (C=O, ester).

Mass spectrum, m/z (relative intensity): 401 (M^+, 6), 386 (12), 370 (8), 300 (100), 271 (20), 243 (34), 211 (20), 183 (54), 151 (30), 129(54),123 (36), 109 (20), 95 (15), 81 (18), 69 (40) and 55 (16). Molecular weight calculated for $C_{21}H_{39}O_6N$: 401.2777. Found : 401.2773 (high-resolution mass spectrometry).

17 : IR spectrum ν_{max} (neat) 2975, 2875 (CH) and 1741 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 2600) and 254 (415, sh).

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.25 (21 H, m, 7 CH_3), 1.25-1.8 (8 H, m, 4 CH_2), 2.35-2.75 (4 H, m, 4 CH), 2.75-3.0 (2 H, m, 2 CH) and 3.65-3.75 (12 H, m, 4 OCH_3).

^{13}C NMR[31] spectrum ($CDCl_3$) : δ 16.95,-18.4, 19.25-20.85 (CH_3), 35.45-37.57, 39.99-41.2, 44.32-44.46, 45.60-46.18, 47.55-47.90, 48.30, 51.33-51.63 (OCH_3) and 176.80-177.48 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 502 (MH^+, 65), 486 (16), 400 (70), 300 (100), 229 (30), 169 (48), 154 (30), 129 (100), 110 (25), 69 (50) and 55 (10). Molecular weight calculated for $C_{26}H_{47}O_8N$: 501.3301. Found : 501.3290 (high-resolution mass spectrometry).

2.5.2. Photosensitized Addition of Triethylamine (2) to Acrylonitrile (18)

Irradiation of an argon-purged solution of **2** (1.5 g, 15 mmol) and **18** (2.4 g, 45 mmol) in acetonitrile (350 mL) containing 10^{-4} M of anthraquinone (**1**) for 2 h and separation of products by column chromatography using a solvent mixture (4:1) of petroleum ether and ethyl acetate gave 40 mg (8%) of **19**, 60 mg (12%) of **20** and 250 mg (50%) of **21** and **22** (unseparated mixture). The reactions were repeated under various conditions and also using acridone and dicyanoanthracene as sensitizers, instead of anthraquinone. The percentage conversion of **18** and product distribution are tabulated in Table 2.

19 : IR spectrum ν_{max} (neat) : 2972, 2897 (CH) and 2248 (CN) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 210 nm (ε, 2800) and 254 (420, sh).

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.2 (9 H, m, 3 CH_3), 1.3-1.9 (4 H, m, 2 CH_2), 2.2-2.6 (6 H, m, 3 CH_2) and 2.8-3.2 (1 H, m, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 14.67, 14.(CH_2),15.36,16.30,17.06, 17.89 (CH_3), 30.93, 31.38, 36.93, 38.30 (CH_2) 50.85, 53.28 (CH) and 119.96 (CN, nitrile).

Mass spectrum, m/z (relative intensity) : 208 (MH^+, 4), 171 (30), 143 (92), 127 (8), 115 (58), 102 (72), 83 (100), 69 (20), 55 (30) and 41 (25). Molecular weight calculated for $C_{12}H_{21}N_3$: 207.1813. Found : 207.1815 (high-resolution mass spectrometry).

20 : IR spectrum ν_{max} (neat) : 2969, 2886 (CH) and 2248 (nitrile) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 210 nm (ε, 2400) and 254 (400, sh).

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.2 (9 H, 2 d, 3 CH_3), 1.4-1.9 (6 H, m, 3 CH_2), 2.2-2.6 (6 H, m, 3 CH_2) and 2.8-3.2 (1 H, m, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 15.06 , 15.27, 16.14, 19.98, 20.19, 24.22, 31.26, 48.41, 48.65, 120.10, 120.54 and 120.61 (CN, nitrile).

Mass spectrum, m/z (relative intensity) : 260 (M^+, 7), 245 (12), 206 (100), 164 (9), 125 (32), 82 (12) 68 (18) and 55 (20). Molecular weight calculated for $C_{15}H_{24}N_4$: 260.2001. Found : 260.2004 (high-resolution mass spectrometry).

21 and **22**[32] : IR spectrum ν_{max} (neat) : 2977, 2886 (CH) and 2248 (CN, nitrile) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 213 nm (ε, 1400) and 254 (1300).

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.36 (15 H, m, 5 CH_3), 1.7-2.0 (18 H, m, 9 CH_2 and 3H, s, CH_3), 2.25-2.50 (18 H, m, 9 CH_2), 3.05-3.15 (2 H, d, CH_2), 3.2-3.3 (1 H, m, CH) and 5.25-5.35 (1 H, t, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 12.16, 12.25, 14.67, 15.83 (CH_2), 20.22, 21.53, 21.98 (CH_3), 33.08, 34.49 (CH_2), 49.34 (CH), 59.33 (C), 117.36 (C, olefinic), 119.24, 119.57 (CN, nitrile) and 142.16 (C, olefinic).

Mass spectrum, m/z (relative intensity) : 366 (M^+, 2), 351 (9), 312 (60), 257 (50), 231 (8), 206 (40), 176 (58), 137 (100), 123 (56),108 (16), 96 (20), 82 (50), 67(10) and 55 (30). Molecular weight calculated for $C_{21}H_{29}N_6$ (MH^+, **21**): 365.2454. Found : 365.2439 and for $C_{21}H_{31}N_6$ (MH^+, **22**) : 367.2610, found : 367.2598 (high -resolution mass spectrometry).

2.5.3. Photosensitized Addition of Diisopropylamine (23) to Acrylonitrile (18)

Irradiation of an argon-purged solution of **23** (1.5 g, 15 mmol) and **18** (0.8 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** for 1 h and separation of products by column chromatography using a mixture (20:1) of petroleum ether and ethyl acetate yielded 100 mg (50%) of **24** and 40 mg (20%) of **25** .The yields are based on **18** reacted (12%). On using acridone as sensitizer, instead of anthraquinone, the percentage conversion of **18** after 1 h of irradiation was 20%, while there was no significant change in the product distribution (Table 3). Dicyanoanthracene-sensitized reactions did not indicate measurable conversion of **18** even after 8 h of irradiation.

24 : IR spectrum ν_{max} (neat) : 3400 (broad, NH), 2975, 2912 (CH) and 2248 (CN, nitrile) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 210 nm (ε, 2000) and 254 (800).

^1H NMR spectrum ($CDCl_3$) : δ 1.1-1.3 (12 H, s, 4 CH_3), 1.60-1.85 (4 H, t, 2 CH_2) and 2.35-2.60 (4 H, t, 2 CH_2).

^{13}C NMR spectrum ($CDCl_3$) : δ 12.07 (CH_2), 29.51 (CH_3), 40.48 (CH_2), 53.07 (C) and 120.61 (CN, nitrile) .

Mass spectrum, m/z (relative intensity) : 208 (M^+, 32), 192 (35), 153 (100), 113 (65), 97 (25), 89 (15), 75 (10) and 58 (30). Molecular weight calculated for $C_{15}H_{25}N_3$ (MH^+) : 208.1814. Found : 208.1813 (high resolution mass spectrometry).

25 : IR spectrum ν_{max} (neat) : 2970, 2905 (CH) and 2248 (nitrile) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 210 nm (ε, 2100) and 254 (400).

^1H NMR spectrum ($CDCl_3$) : δ 1.1-1.3 (12 H, s, 4 CH_3), 1.6-2.1 (6 H, m, 3 CH_2) and 2.4-2.7 (6H, m, 3 CH_2).

^{13}C NMR spectrum ($CDCl_3$) : δ 10.80, 13.50, 25.38 (CH_2), 28.51, 29.10, 29.25, 29.50, 29.60 (CH_3), 39.50, 46.80 (CH_2), 52.50,52.68 (C) and 120.50, 120.61 (CN, nitrile).

Mass spectrum m/z (relative intensity) : 261 (MH^+, 40), 245 (55), 206 (82), 160 (60), 153 (100), 113 (68), 97 (30), 82 (10) and 58 (45). Molecular weight calculated for $C_{15}H_{25}N_4$ (MH^+) : 261.2059. Found : 261.2079 (high-resolution mass spectrometry).

2.5.4. Photosensitized Addition of Diisopropylamine (23) to Methyl Methacrylate (5)

An argon-purged solution of **23** (1.5 g, 15 mmol) and **5** (4.5 g, 45 mmol) in acetonitrile (350 mL) containing 10^{-4} M of anthraquinone was irradiated for 3 h and separation of the products by column chromatography using a mixture (20:1) of petroleum ether and ethyl acetate gave 150 mg (30%) of **28** and 300 mg (50%) of **26**. These yields are based on percentage conversion of **5** (10%). Under the same conditions of irradiation, the acridone-sensitized photoreaction yielded 100 mg (40%) of **28** and 25 mg (15 %) of **26** (Table 4). Dicyanoanthracene did not sensitize these addition reactions.

28 : IR spectrum ν_{max} (neat) : 3400 (broad, NH), 2977, 2880 (CH) and 1740 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 203 nm (ε, 2500) and 254 (500).

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.2 (18 H, m, 6 CH_3), 1.8-2.2 (4 H, m, 2 CH_2), 2.4-2.8 (2 H, m, 2 CH) and 3.6-3.7 (6 H, s, 2 OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 19.85, 29.52, 29.85, 30.85, 30.95 (CH_3), 35.85 (CH), 49.55, 49.95 (C), 51.50 (CH_2), 53.85 (OCH_3) and 179.60 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 302 (MH^+, 55), 286 (18), 200 (100), 143 (100), 111 (30), 83 (65), 69 (10) and 55 (20). Molecular weight calculated for $C_{16}H_{31}O_4$: 301.2253. Found : 301.2249 (high-resolution mass spectrometry).

26 : IR spectrum ν_{max} (neat) : 2980, 2868 (CH) and 1684 (C=O)cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 203 nm (ε, 2500) and 254 (460).

^1H NMR spectrum ($CDCl_3$) : δ 1.1-1.6 (15 H, m, 5 CH_3), 2.0-2.3 (3 H, m, CH_2, CH) and 3.2-3.6 (1 H, m, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 15.94, 19.61, 20.66, 25.04, 28.18 (CH_3), 35.01 (CH), 43.33 (CH_2), 44.05 (CH), 58.62 (C) and 176.87 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 169 (M^+, 30), 154 (100), 112 (72), 84 (13), 69 (13) and 55 (10). Molecular weight calculated for $C_{10}H_{19}NO$: 169.1466. Found : 169.1495 (high-resolution mass spectrometry).

2.6. References

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(31) The poor resolution of signals may be due to the possibility of isomeric mixtures, arising due to the presence of several chiral centers in the molecule.

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Chapter 3. Anthraquinone Photosensitized Addition of Primary and Secondary Amines to α,β-Unsaturated Esters

3. 1. Abstract

Anthraquinone (**1**) photosensitized electron transfer reactions between several primary and secondary amines such as cyclohexylamine, piperidine, pyrrolidine and morpholine with α,β-unsaturated esters have been investigated. Anthraqui- none (**1**) sensitized photoreaction of piperidine (**2**) with methyl methacrylate (**3**) gave a diastereomeric mixture of 2-methyl-3-indolizidone (**4**) as the major product. Similarly, the photosensitized addition of pyrrolidine (**5**) to methyl methacrylate yielded a diastereomeric mixture of 2-methyl-3-pyrrolizidone (**6**). The photosensitized addition of cyclohexylamine (7) to methyl acrylate (**8**), methyl methacrylate (**3**) and methyl crotonate (**10**) led to the formation of the spirolactams **9**, **11** and **12**, respectively. Apart from methyl methacrylate, most α,β-unsaturated esters undergo facile Michael type addition reaction with amines such as piperidine, pyrrolidine and morpholine to yield the N-addition products. In order to control the thermal Michael type addition reactions, the photosensitized reactions were carried out at low temperatures. Thus, the anthraquinone photosensitized addition of piperidine (**2**) to methyl acrylate (**8**) at low temperature gave a mixture of 3-indolizidone (**13**) and the N-addition product **14**. Similarly, addition of pyrrolidine (**5**) to methyl acrylate (**8**) yielded 3-pyrrolizidone (**15**) and the N-adduct (**16**). A diastereomeric mixture of heliotridone and pseudoheliotridone (**17a** and **17b**) and the corresponding N-adduct (**18**) were isolated from the anthraquinone photocatalyzed reaction between pyrrolidine (**5**) and methyl crotonate (**10**). The photosensitized reaction of morpholine (**19**) with methyl methacrylate (**3**) led to a mixture of the bicyclic lactam **21** and the N-adduct **20**. It was

observed that the Michael type N-adduct formation could be reduced to a considerable extent by lowering the temperature of the reaction, whereas the free radical reaction remained unaffected, under these conditions.

3. 2. Introduction

The development of routes for the synthesis of indolizidone and pyrrolizidone ring systems continues to attract attention due to the wide variety of natural products containing these structural units.[1] This can be achieved under thermal conditions through electrophilic addition of the appropriate reagents to α-carbanion centres derived from amines or via reactions of iminium derivatives.[2,3] More recently, there have been efforts to utilize α-aminoalkyl radicals for assembling carbon-carbon bonds.[4-6] Photoelectron transfer catalyzed reactions of α-silylamines using sensitizers such as dicyanoanthracene (DCA) and dicyano-naphthalene (DCN), for the generation and subsequent carbon-carbon bond forming reactions of α-aminoalkyl radicals, for these purposes have been extensively explored.[7-12]

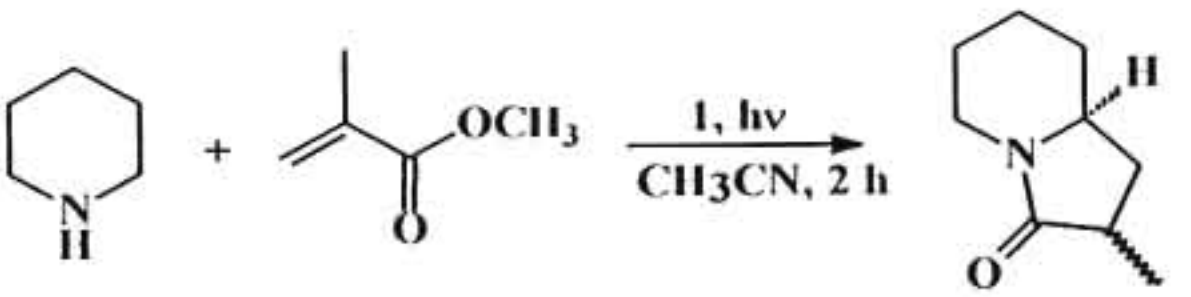
In the course of our studies on the anthraquinone photosensitized reactions of amines with α,β–unsaturated esters, described in Chapter 2 of this thesis, we had observed in the case of diisopropylamine, apart from the multiple olefin added products, the formation of a pyrrolidone derivative. As mentioned in the earlier chapter, this reaction can be developed as a potential method for synthesizing lactams from primary and secondary amines. Thus, this method could provide a route for the synthesis of indolizidone and pyrrolizidone ring systems from the corresponding secondary amines.

In this chapter, we describe our studies on the anthraquinone photosensitized generation of α-aminoalkyl radicals from secondary amines such as piperidine, pyrrolidine and morpholine and a primary amine such as cyclohexylamine and the subsequent reactions of these radicals with α,β-unsaturated esters such as methyl acrylate, methyl methacrylate and methyl crotonate.

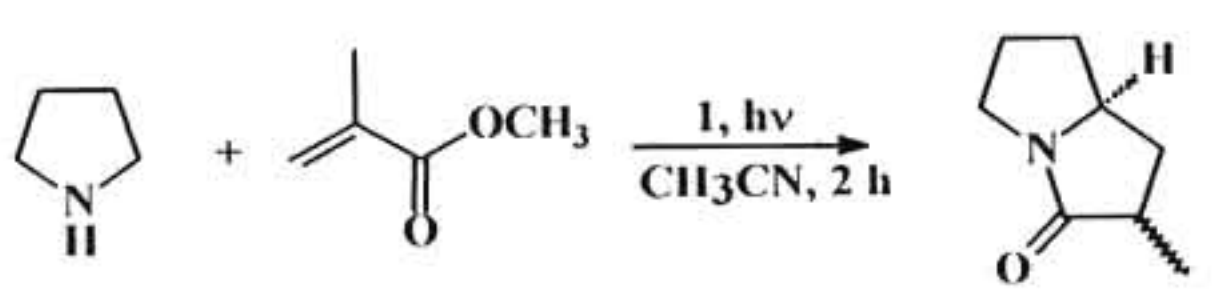
3.3. Results

3.3.1. Photosensitized Addition of Piperidine (2) to Methyl Methacrylate (3)

The photosensitized addition of piperidine (**2**) to methyl methacrylate (**3**) was effected by irradiating a nitrogen-purged solution of piperidine and methyl methacrylate in acetonitrile, containing catalytic amounts of anthraquinone (**1**), using Pyrex filtered light ($\lambda_{max} > 290$ nm). The major product isolated from this reaction was a diastereomeric mixture of 2-methyl-3-indolizidone (**4**), characterized through spectral data (Scheme 1). The IR spectrum of **4** showed an absorption band at 1692 cm^{-1} due to the amide carbonyl group. The ^1H NMR spectrum of **4** showed two doublets at δ 1.1-1.3 (3 H), which were assigned to the CH_3 protons of the diastereomers, whereas, the methylene protons (10 H) appeared as multiplets centered around δ 1.5-2.2 and 2.3-2.9, respectively. The methine protons (2 H) appeared as two multiplets centered around δ 3.1-3.6 and 3.4-4.2. The ^{13}C NMR spectrum of **4** showed several signals, out of which, the one at δ 175.68 has been assigned to the lactam carbonyl carbon. The mass spectrum of **4** showed a molecular ion peak at m/z 153, which is in agreement with the proposed structure.



2 3 4



5 3 6

Scheme 1

Table 1. Anthraquinone (**1**) photosensitized addition of piperidine (**2**) to methyl methacrylate (**3**) in acetonitrile (350 mL) at 298 K using 450 W medium pressure mercury lamp (Pyrex filter)

No	Sensitizer anthraquinone (M)	**2** mmol	**3** mmol	Time of irradiation (h)	% conversion of **3**	Product distribution(%) **4**
1	10^{-4}	15	15	1	15	80
2	10^{-4}	15	15	2	20	75
3	10^{-4}	15	15	3	22	70
4	10^{-4}	15	15	4	25	68
5	10^{-4}	15	2	2	40	78
6	$5x10^{-4}$	15	15	2	20	70
7	$5x10^{-4}$	15	15	8	30	50

Table 1 lists the percentage conversion of the starting material (**3**) and the product distribution under a variety of conditions for the photosensitized reactions between piperidine and methyl methacrylate.

3.3.2. Photosensitized Addition of Pyrrolidine (5) to Methyl Methacrylate (3)

The photosensitized addition of pyrrolidine (**5**) to methyl methacrylate (**3**) was carried out by irradiating a nitrogen-purged acetonitrile solution of pyrrolidine and methyl methacrylate, containing catalytic amounts of anthraquinone (**1**) under Pyrex filtered light. The product isolated was a diastereomeric mixture of the bicyclic lactam **6**, which was characterized on the basis of analytical results and spectral information (Scheme 1). The IR spectrum of **6** showed an absorption band at 1684 cm^{-1} due to the amide carbonyl group. The ^{1}H NMR spectrum of **6** showed two doublets at δ 1.1-1.35 (3 H), assigned to the methyl protons of the diastereomers, whereas, the methylene protons appeared as two multiplets at δ 1.8-2.2 (4 H) and 2.2-3.2 (4 H). In addition, the spectrum showed a multiplet at δ 3.3-4.0 (2 H), which has been assigned to the methine protons. The ^{13}C NMR spectrum of **6** showed several signals, out of which the signals at δ 175.89 and 178.50 were assigned to the carbonyl carbons (lactam). Based on spectral evidence, the structure of **6** has been assigned as 2-methyl-3-pyrrolizidone. The mass spectrum of **6** showed a molecular ion peak at m/z 139, which is in agreement with the assigned structure.

Table 2 lists the percentage conversion of the starting material (**3**) and product distribution under a variety of conditions in the photosensitized reaction between pyrrolidine and methyl methacrylate.

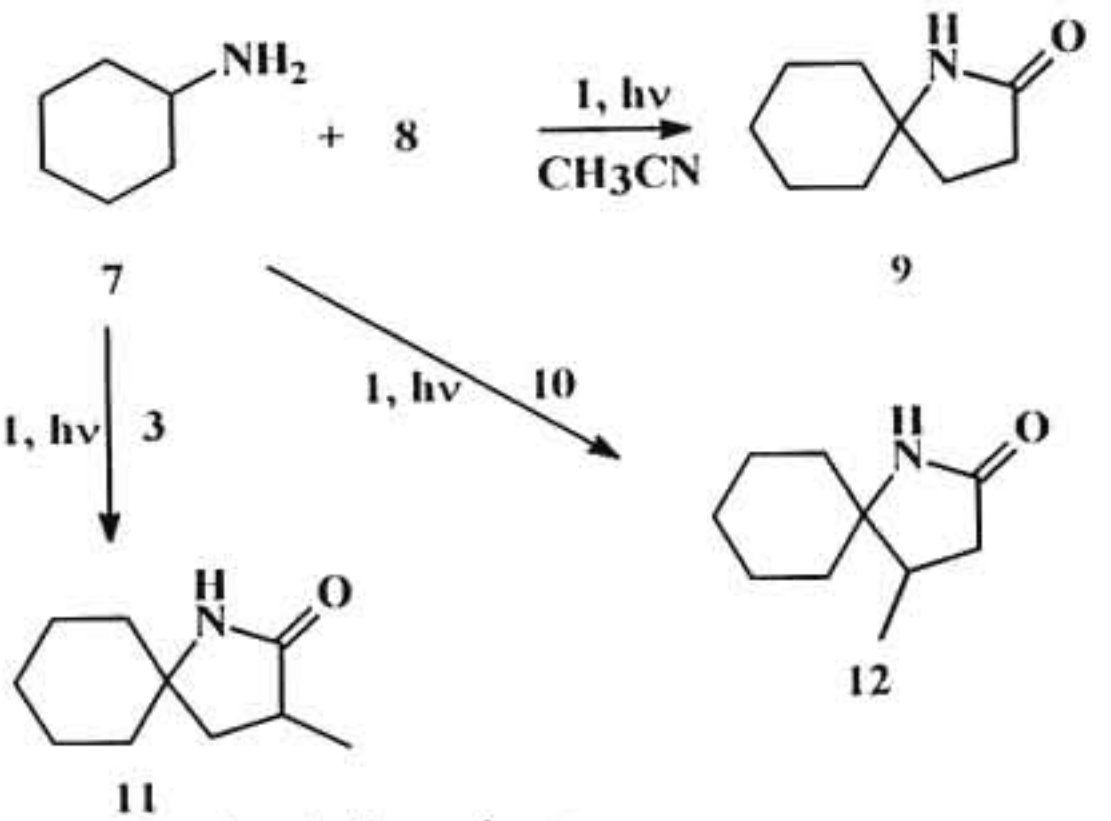
Table 2. Anthraquinone (1) photosensitized addition of pyrrolidine (**5**) to methyl methacrylate (**3**) in acetonitrile (350 mL) at 298 K using 450 W medium pressure mercury lamp (Pyrex filter)

No	Sensitizer anthraquinone (M)	**5** mmol	**3** mmol	Time of irradiation (h)	% conversion of **3**	Product distribution (%) **6**
1	10^{-4}	15	15	1	12	70
2	10^{-4}	15	15	2	18	65
3	10^{-4}	15	15	4	20	60
4	10^{-4}	15	2	2	45	65
5	10^{-4}	15	15	8	25	45
6	$5x10^{-4}$	15	15	2	20	60

3.3.3. Photosensitized Addition of Cyclohexylamine (7) to Methyl Acrylate (8)

The photosensitized addition of cyclohexylamine (7) to methyl acrylate (**8**) was effected by irradiating an argon-saturated acetonitrile solution of cyclohexylamine and methyl acrylate, containing catalytic amounts of anthraquinone (**1**), under Pyrex filtered light. The spirolactam **9** was isolated as the major product from the reaction mixture (Scheme 2) and was characterized on the basis of analytical results and spectral information. The IR spectrum of **9** showed a broad absorption band at 3361 cm^{-1} due to the NH group and a band at 1696 cm^{-1}, due to the amide carbonyl group. The ^1H NMR spectrum of **9** showed a multiplet centered around δ 1.2-1.7 (10 H), assigned to the cyclohexyl protons and two triplets centered around δ 1.8-2.0 and δ 2.2-2.5 due to the two methylene protons of the lactam ring. The broad signal centered around δ 7.4-7.7 (1 H, D_2O exchangeable) has been assigned to the NH proton. The ^{13}C NMR spectrum of **9**

showed five CH_2 carbon signals at δ 22.70, 24.90, 29.86, 32.42 and 38.09, one quarternary carbon at δ 59.24 and a carbonyl carbon at δ 177.36. The mass spectrum of **9**, showed the molecular ion peak at m/z 153, which is in good agreement with the proposed structure.



Scheme 2

3.3.4. Photosensitized Addition of Cyclohexylamine (7) to Methyl Methacrylate (3)

The photosensitized addition of cyclohexylamine (7) to methyl methacrylate (**3**) was carried out by irradiating an argon-purged solution of cyclohexylamine and methyl methacrylate containing catalytic amounts of anthraquinone (**1**), under Pyrex filtered light. One major product was isolated,

which was characterized on the basis of analytical results and spectral information as the spirolactam **11** (Scheme 2). The IR spectrum of **11** showed a broad absorption band at 3220 cm^{-1}, due to the NH group and a band at 1698 cm^{-1}, due to the amide carbonyl group. The ^1H NMR spectrum of **11** showed a doublet at δ 1.0-1.1 (3 H), assigned to the methyl protons and the cyclohexyl protons (10 H) appeared as a multiplet centered around δ 1.2-1.6. The multiplet centered around δ 1.9-2.6 (3 H) has been assigned to the lactam methylene and methine protons. The NH proton appeared as a broad singlet centered around δ 7.5-7.8 (1 H, D_2O exchangeable). The ^{13}C NMR spectrum of **11** showed one CH_3 carbon signal at δ 16.40, six CH_2 carbon signals at δ 22.64, 22.76, 24.87, 37.49, 39.40 and 41.28, one CH carbon signal at δ 35.26, one quarternary carbon signal at δ 56.83 and a carbonyl carbon signal at δ 179.33. The mass spectrum of **11**, showed the molecular ion peak at m/z 167, which is in good agreement with the assigned structure.

3.3.5. Photosensitized Addition of Cyclohexylamine (7) to Methyl Crotonate (10)

The photosensitized addition of cyclohexylamine (7) to methyl crotonate (**10**) in the presence of catalytic amounts of anthraquione in acetonitrile gave the spirolactam **12** as the major product (Scheme 2). The structure of 12 was arrived at on the basis of spectral data. The IR spectrum of **12** for example, showed a broad band at 3200 cm^{-1} due to the NH group and a band at 1698 cm^{-1}, due to the amide carbonyl group. The ^1H NMR spectrum of **12** showed a doublet centered around δ 0.9-1.1 (3 H), assigned to the CH_3 protons, whereas the cyclohexyl protons appeared as a multiplet centered around δ 1.2-1.6 (10 H). The multiplet around δ 1.8-2.6 (3 H), was assigned to the methylene protons and a methine

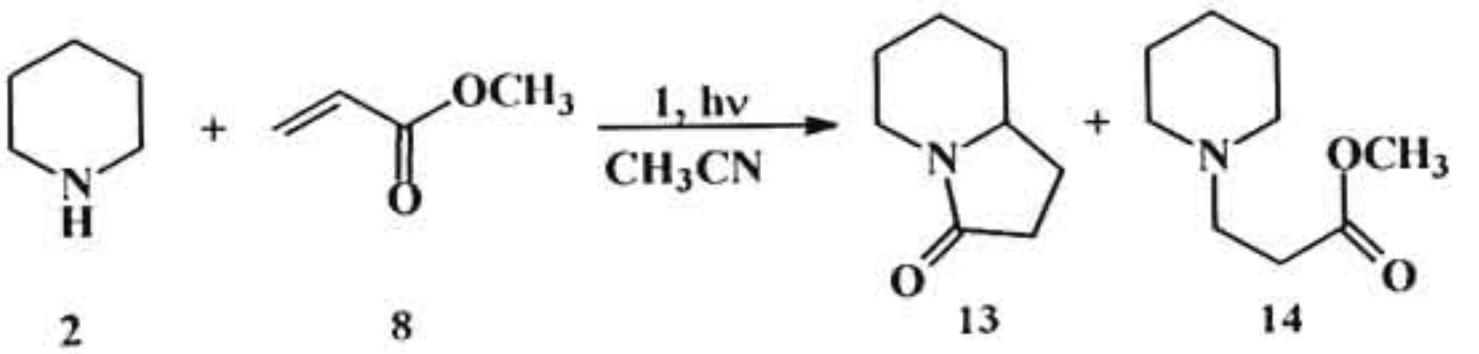
proton of the lactam ring in **12**. The NH proton (1 H) appeared as a broad singlet centered around δ 7.5-7.8 (1 H, D_2O exchangeable). The ^{13}C NMR spectrum of **12** showed one CH_3 signal at δ 14.37, six CH_2 signals at δ 22.22, 23.32, 25.41, 31.77, 38.12 and 39.70, one CH signal at δ 39.96, one quarternary carbon at δ 60.97 and a carbonyl carbon at δ 178.83. The mass spectrum of **12** showed the molecular ion peak at m/z 168, which is in agreement with the assigned structure.

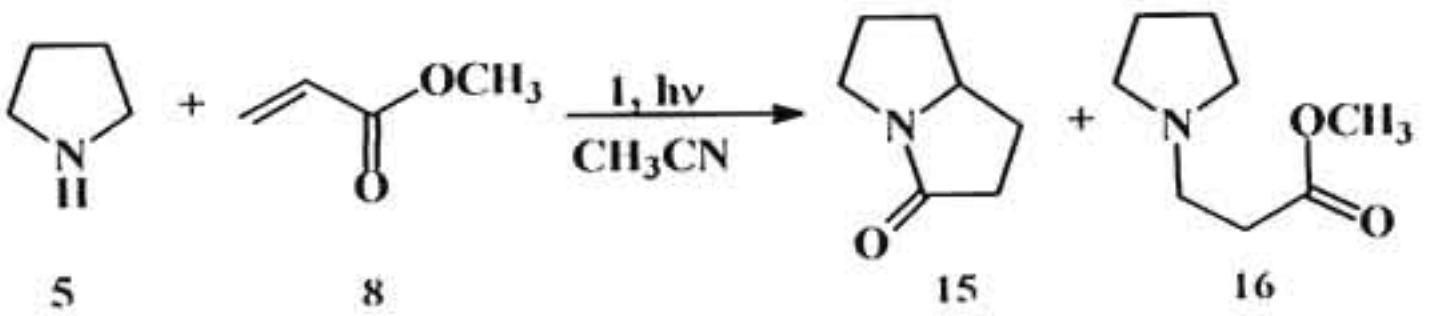
3.3.6. Photosensitized Addition of Piperidine (2) to Methyl Acrylate (5)

Irradiation of a mixture of piperidine (**2**) and methyl acrylate (**5**) in the presence of catalytic amounts of anthraquinone (**1**) in acetonitrile gave a mixture of **13** and **14** (Scheme 3). The structures of both **13** and **14** were arrived at on the basis of spectral evidence. The IR spectrum of **13**, for example, showed an absorption band at 1680 cm^{-1} due to the amide carbonyl group. The ^1H NMR spectrum of **13** showed three multiplets due to the methylene protons centered around δ 1.4-2.1 (6 H), δ 2.15-2.9 (4 H) and δ 3.3-3.9 (2 H), respectively. The multiplet centered around δ 4.1-4.4 has been assigned to the methine proton in **13**. The ^{13}C NMR spectrum of **13** showed six CH_2 signals at δ 23.38, 24.16, 25.12, 29.98, 33.29 and 39.91, one CH signal at δ 56.98 and a carbonyl carbon at δ 173.24. The structure of **13**, on the basis of spectral evidence, has been assigned as 3-indolizidone. The mass spectrum of **13** showed the molecular ion peak at m/z 139, which is in agreement with the assigned structure.

The IR spectrum of **14**, showed an absorption band at 1744 cm^{-1} due to the ester C=O group. The ^1H NMR spectrum of **14** showed two multiplets at δ 1.3-1.7 (6 H) and δ 2.2-2.8 (8 H), assigned to the fourteen methylene protons. The methoxy protons appeared as a singlet at δ 3.5-3.7 (3 H). The ^{13}C NMR spectrum of **14** showed four CH_2 signals at δ 23.93, 25.60, 31.72 and 50.90, one methoxy

carbon signal at δ 53.88 and an ester carbonyl carbon at δ 172.45. The mass spectrum of **14** showed the molecular ion peak at m/z 171, which is in agreement with the assigned structure.





Scheme 3

Table 3. Temperature dependence of the anthraquinone (10^{-4} M) photosensitized addition of piperidine (**2**) to methyl acrylate (**8**) in degassed acetonitrile (300 mL) using a 450 W medium pressure mercury lamp (Pyrex filter)

No	**2** mmol	**8** mmol	Temp °C	Time of irradiation (h)	% Conversion of **8**	Product distribution (%) **14**	**13**
1	15	15	30	2	95	98	1
2	15	15	15	2	50	80	10
3	15	15	5	2	40	75	20
4	15	15	0	1	22	60	20
5	15	15	0	2	25	60	20
6	15	15	0	3	30	60	25

Table 3 lists the percentage conversion of the starting material (**8**) and the product distribution under different temperatures and irradiation times. It has been observed that lowering of temperature and increasing the irradiation time brings about substantial changes in the product distribution. The percentage distribution of products indicates that at lower temperatures the yield of the Michael adduct (N-adduct) **14** is significantly reduced, whereas the yield of **13** increases, indicating thereby that the photochemically induced free radical reactions are not significantly affected by lowering the temperature.

3.3.7. Photosensitized Addition of Pyrrolidine (5) to Methyl Acrylate (8)

Photosensitized reaction of pyrrolidine (**5**) with methyl acrylate (**8**) in the presence of catalytic amounts of anthraquinone (**1**) gave a mixture of two products, **15** and **16** (Scheme 3). The structures of these products were arrived at on the basis of spectral evidence. The IR spectrum of **15**, for example, showed an absorption band at 1682 cm^{-1} due to the amide carbonyl group. The ^1H NMR spectrum of **15** showed multiplets centered around δ 1.8-2.1 (4 H), 2.15-2.6 (4 H) and 3.2-3.6 (2 H) due to the methylene protons, whereas the methine proton appeared as a multiplet centered around δ 4.2-4.6. The ^{13}C NMR spectrum of **15** showed five CH_2 signals at δ 26.75, 26.93, 31.94, 35.11 and 40.70, one CH signal at δ 61.87 and a carbonyl carbon signal at δ 174.62. The structure of **15**, on the basis of spectral evidence has been assigned as 3-pyrrolizidone. The mass spectrum of **15** showed the molecular ion peak at m/z 125, which is in good agreement with the assigned structure.

The IR spectrum of **16** showed an absorption band at 1742 cm^{-1} due to the ester carbonyl group. The ^1H NMR spectrum of **16** showed multiplets at δ 1.65-1.85 (4 H) and 2.4-2.9 (8 H) due to the methylene protons, whereas the methoxy

protons (3 H) appeared as a singlet centered around δ 3.6-3.75. The ^{13}C NMR spectrum of **16** showed four CH_2 signals at δ 22.93, 30.62, 33.38 and 50.83, one methoxy carbon signal at δ 53.34 and a carbonyl carbon signal at δ 171.93. The mass spectrum of **16** showed the molecular ion peak at m/z 157, which is in agreement with the assigned structure.

The product distribution and percentage conversion of **8** under different temperatures are shown in Table 4. Lowering the temperature of the reaction medium led to a reduction in the yield of **16** (thermal product) and an increase in the yield of **15**.

Table 4. Temperature dependence of the anthraquinone (10^{-4} M) photosensitized addition of pyrrolidine (**5**) to methy acrylate (**8**) in acetonitrile (350 mL) using 450 W medium pressure mercury lamp (Pyrex filter)

No	**5** mmol	**8** mmol	Temp °C	Time of irradiation (h)	% Conversion of **8**	Product distribution (%) **16**	**15**
1	15	15	30	2	98	98	<1
2	15	15	15	2	75	88	5
3	15	15	5	2	60	82	14
4	15	15	0	1	35	70	15
5	15	15	0	2	40	70	18

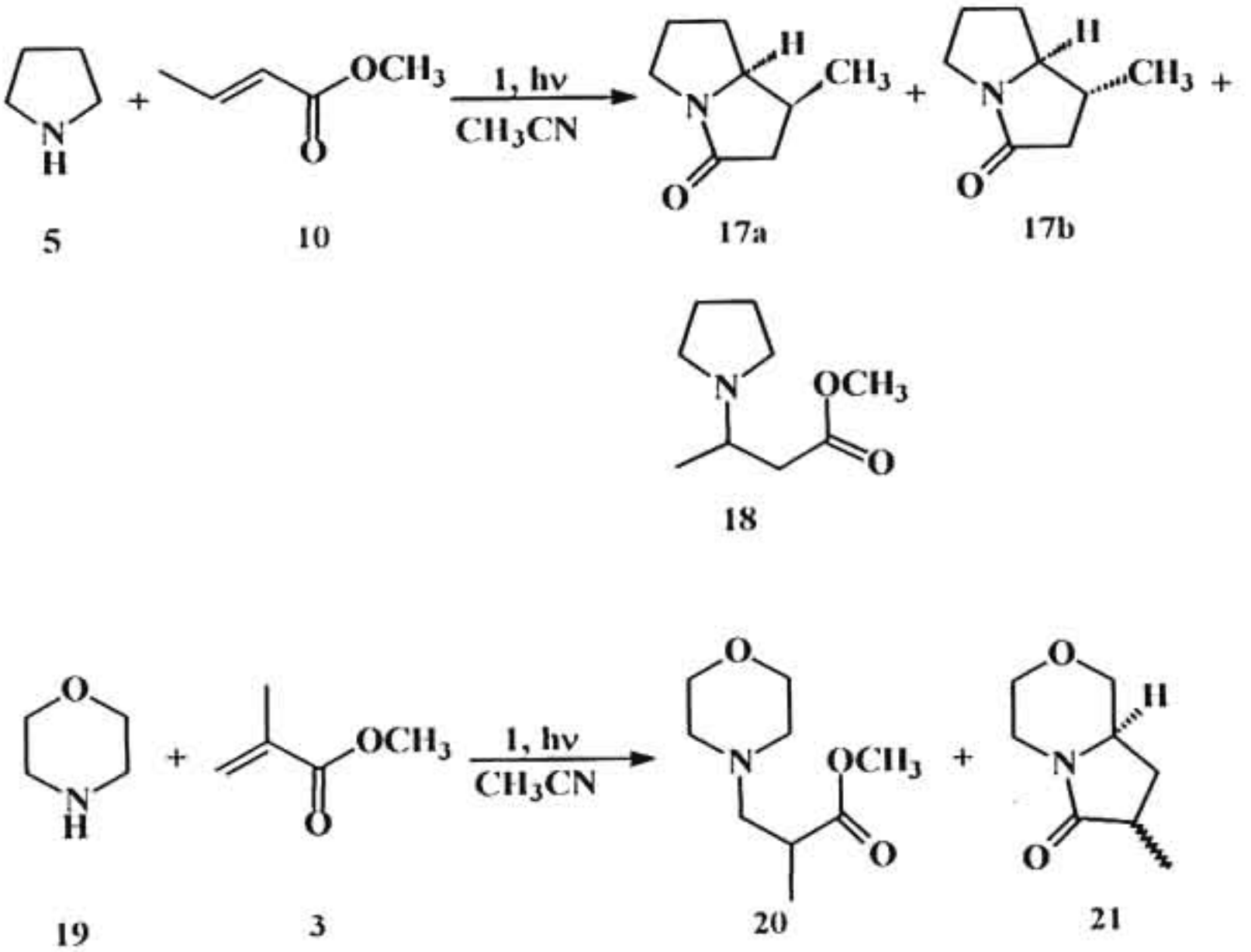
3.3.8. Photosensitized Addition of Pyrrolidine (5) to Methyl Crotonate (10)

The photosensitized addition of pyrrolidine (**5**) to methyl crotonate (**10**) in the presence of catalytic amounts of anthraquinone (**1**) gave a diastereomeric mixture of products consisting of **17a** and **17b** and the N-adduct **18** (Scheme 4).

The structures of **17a** and **17b** were arrived at on the basis of spectral data. The structure of **18** was confirmed by comparing the spectral data and gas chromatographic retention time with those of the N-adduct, formed from the thermal reaction of **5** with **10**. The IR spectrum of the mixture of **17a** and **17b** showed an absorption band at 1686 cm^{-1} due to the amide carbonyl group. The ^1H NMR spectrum of **17a** and **17b** showed two doublets at δ 0.9-1.2 (3 H), assigned to the methyl protons of the diastereomers. The multiplets at δ 1.2-2.2 (4 H) and 2.25-2.6 (2 H) are assigned to the methylene protons, whereas the multiplet centered around δ 3.25-3.8 (3 H) is assigned to two methylene and one methine protons. The spectrum showed another multiplet at δ 2.8-3.2 (1 H), which is assigned to a methine proton. The ^{13}C NMR spectrum of **17a** and **17b** showed two CH_3 signals, eight CH_2 signals, four CH signals and two carbonyl carbon signals at δ 174.25 and 175.05. The structures of **17a** and **17b**, on the basis of spectral evidence, has been assigned as 1,8-*trans*-1-methyl-3-pyrrolizidone or heliotridone (**17a**) and 1,8-*cis*-1-methyl-3-pyrrolizidone or pseudoheliotridone (**17b**). The diastereomeric ratio of **17a:17b** was estimated as 3:7 by gas chromatography using a pure sample of **17b**, as reference. The mass spectrum of the mixture of **17a** and **17b** showed the molecular ion peak m/z 139, which is in good agreement with the assigned structure.

The IR spectrum of **18** showed an absorption band at 1744 cm^{-1} due to an ester carbonyl group. The ^1H NMR spectrum of **18** showed a doublet at δ 1.1-1.3 (3 H), assigned to the methyl protons. The multiplet at δ 1.7-1.9 (4 H) has been assigned to four methylene protons, whereas the one centered around δ 2.1-3.2 (7 H) has been assigned to six methylene and one methine protons. The singlet at δ 3.6-3.8 (3 H) has been assigned to the methoxy protons. The ^{13}C NMR spectrum of **18** showed several signals due to one CH_3, three CH_2, one CH and

one methoxy carbons. The carbonyl carbon signal was observed at δ 172.11. The mass spectrum of **18** showed the molecular ion peak at m/z 171, which is in agreement with the assigned structure.



Scheme 4

The percentage conversion of the starting material (**10**) and product distributions of (**17a, 17b** and **18**) under varying conditions are shown in Table 5. As in the cases of the sensitized photoreactions of piperidine and pyrrolidine with methyl acrylate, here also it was observed that the product distribution varies with temperature. It has been observed that at low temperatures the yield of the thermal product **18** decreases, whereas the yield of **17a** and **17b** increases.

Table 5. Temperature dependence of the anthraquinone (10^{-4} M) photosensitized addition of pyrrolidine (**5**) to methyl crotonate (**10**) in degassed acetonitrile (300 mL) using a 450 W medium pressure mercury lamp (Pyrex filter)

No	**5** mmol	**10** mmol	Temp °C	Time of irradiation (h)	% Conversion of **10**	Product distribution (%) **18**	**17a+17b**
1	15	15	30	2	40	40	25
2	15	15	15	2	35	35	30
3	15	15	5	2	30	25	40
4	15	15	0	2	20	15	45

3.3.9. Photosensitized Addition of Morpholine (19) to Methyl Methacrylate (3)

The photosensitized addition of morpholine (**19**) to methyl methacrylate (**3**) under anthraquinone sensitization gave a mixture of products consisting of the diastereomeric mixture of the bicyclic lactam **21** and the N-adduct **20** (Scheme 4). The IR spectrum of **21** showed an absorption band at 1692 cm^{-1} due to the amide carbonyl group. The ^{1}H NMR spectrum of **21** showed a doublet at δ 1.0-1.2 (3 H), assigned to the methyl protons. The spectrum showed several multiplets centered around δ 1.6-2.0 (2 H) (methylene protons), δ 2.1-2.6 (1 H) (methine proton), δ 2.8-3.2 (2 H) (methylene protons) and δ 3.2-4.1 (5 H) (four methylene and one methine protons). The ^{13}NMR spectrum of **21** showed two CH_3 carbon signals, seven CH_2 carbon signals, three CH carbon signals and two carbonyl carbon signals at δ 175.06 and 175.63. The ^{13}C NMR spectrum of **21** suggests the presence of a diastereomeric mixture of products. The mass spectrum of **21**

showed a molecular ion peak at m/z 155, which is in agreement with the assigned structure.

The IR spectrum of **20** showed an absorption band at 1740 cm^{-1} due to the ester carbonyl group. The ^1H NMR spectrum of **20** showed a doublet at δ 0.9-1.0 (3 H), assigned to the methyl protons and two multiplets centered around δ 2.4-3.2 (7 H) (six methylene and one methine protons) and δ 3.4-3.8 (7 H) (four methylene and three methoxy protons). The ^{13}C NMR spectrum of **20** showed one CH_3 signal, one CH signal, one methoxy carbon signal and a carbonyl carbon signal at δ 172.45. The mass spectrum of **20** showed a molecular ion peak at m/z 187, which is in agreement with the assigned structure. The structure of **20** was further confirmed by comparing the gas chromatographic retention time with that of the compound obtained in the thermal reaction between **19** and **3**.

Table 6. Temperature dependence of the anthraquinone (10^{-4} M) photosensitized addition of morpholine (**19**) to methyl methacrylate (**3**) in argon-purged acetonitrile (300 mL) using 450 W medium pressure mercury lamp (Pyrex filter)

No	**19** mmol	**3** mmol	Temp °C	Time of irradiation (h)	% Conversion of **3**	Product distribution (%) **20**	**21**
1	15	15	30	2	35	30	35
2	15	15	5	2	25	10	40
3	15	15	0	2	20	<5	45

The percentage conversion of **3** and product distribution of **20** and **21** at different temperatures are shown in Table 6. The percentage distribution shows

that at lower temperatures the yield of **20** decreases, whereas the yield of **21** increases substantially.

3.4. Discussion

3.4.1. Photosensitized Addition of Piperidine (2), Pyrrolidine (5) and Cyclohexylamine (7) to Methyl Methacrylate (3), Methyl Acrylate (8) and Methyl Crotonate (10)

As discussed in Chapter 2, excitation of a mixture of the amine and α,β-unsaturated ester in presence of anthraquinone (**1**) with Pyrex filtered light would lead to the selective excitation of anthraquinone. The excited triplet state of anthraquinone will be quenched by the amine leading to the formation of the anion radical of anthraquinone and the cation radical of the amine.[7,13,15] The basic ketyl radical anion can abstract a proton from the relatively acidic alkylamine radical cation. The amine radical cation generated from primary and secondary amines can deprotonate via two possible modes, namely, deprotonation at the N-site, leading to aminyl radicals and deprotonation at the α-carbon, leading to the formation of α-aminoalkyl radicals.[16] Since α-aminoalkyl radicals are thermodynamically more stable than the aminyl radicals, aminyl radicals would be readily converted to α-aminoalkyl radicals via hydrogen abstraction from the parent amines.[12,17] Thus, in the photoelectron transfer catalyzed reactions of primary and secondary amines, the main radicals formed eventually are the α-aminoalkyl radicals.

The formation of 2-methyl-3-indolizidone (**4**) from the anthraquinone sensitized photoreaction of piperidine (**2**) with methyl methacrylate (**3**) may be understood in terms of the pathways shown in Scheme 5. Addition of the

α-aminoalkyl radical (**24**), generated from the radical cation of piperidine, to methyl methacrylate (**3**) would give rise to the adduct radical **23**, which can be quenched by the ketyl radical of anthraquinone (**25**) to give the adduct **26**. The quantitative recovery of anthraquinone used in these reactions strongly supports this mechanism. The lactam **4**, could arise through the thermal intramolecular cyclization of **26** during work up.

Scheme 5

Attempts to isolate **26** were not successful. However, there are several reports in the literature in support of such intramolecular reactions being highly efficient.[5,14] Similarly, the formation of the pyrrolizidone derivative **6** in the reaction of pyrrolidine (**5**) with methyl methacrylate (**3**) can be rationalized in terms of the pathway shown in Scheme 5. Secondary amines are known to undergo thermal reactions (Michael type) with electron deficient olefinic substrates. However, it was observed that piperidine does not add thermaly to methyl methacrylate at room temperature or even on refluxing.

In the course of the present studies, the anthraquinone photosensitized addition of a primary amine such as cyclohexylamine to olefinic substrates was also investigated. It was observed that cyclohexylamine (7) does not add thermaly to the α,β-unsaturated esters such as methyl methacrylate (**3**), methyl acrylate (**8**) and methyl crotonate (**10**) under our experimental conditions. Anthraquinone sensitized photoreactions of cyclohexylamine with these olefinic substrates (**3**, **8** and **10**), however gave the spirolactams **11**, **9** and **12**, respectively. Cyclohexylamine radical cation, generated via photoinduced electron transfer can undergo deprotanation as in the case of secondary amines, to yield the α-amino-alkyl radical. The aminoalkyl radical, thus formed, can add to α,β-unsaturated esters to yield the corresponding adduct radicals. Since the catalytic amounts of anthraquinone used in these reactions were recovered quantitatively, it is assumed that the adduct radicals are quenched by anthraquinone ketyl radicals. The adducts formed in these reactions can subsequently undergo thermal cyclization during work-up to yield the observed products. The formation of the spirolactams in better yields in non polar solvents such as benzene would suggest that these reactions can also proceed via hydrogen abstraction by the excited state anthra-quinone. In polar solvents, such as acetonitrile, the reactions are known to

proceed predominantly via the photoinduced electron transfer route, whereas in non-polar solvents such as benzene, hydrogen abstraction predominates.

3.4.2. Photosensitized Addition of Piperidine (2), Pyrrolidine (5) and Morpholine (19) to Methyl Acrylate (8), Methyl Crotonate (10) and Methyl Methacrylate (3)

Photoinduced free radical fomation and subsequent carbon-carbon bond forming reactions of piperidine, pyrrolidine and morpholine with α,β-unsaturated esters, other than methyl methacrylate could not be studied at room temperature because of the facile thermal Michael type addition between amines and the α,β-unsaturated esters, to give the N-adducts. This difficulty could however be overcome by carrying out the photoreactions at low temperatures, where the Michael type addition was minimized.

The photosensitized addition of piperidine (**2**) to methyl acrylate (**8**) resulted in the formation of a mixture of the 3-indolizidone (**13**) and the N-adduct **14**. As mentioned earlier the N-adduct **14** could arise through the thermal Michael type addition of piperidine to methyl acrylate or via the addition of aminyl radicals to methyl acrylate. In a blank run, it was observed that piperidine undergoes efficient thermal addition to methyl acrylate to give the N-adduct **14**. Table 3 shows the effect of temperature on these reactions. At normal temperatures (30 °C), nearly quantitative formation of **14** was observed along with trace amounts of **13**. At lower temperatures, however, the yield of the Michael adduct **14** is significantly reduced, whereas the yield of **13** increases. This clearly indicates that the formation of **14** in the photosensitised reaction can be attributed to the thermal reactions between **2** and **8** and not due to the reaction between the aminyl radical and methyl acrylate. Furthermore, as discussed earlier aminyl

radicals have short lifetimes since they can rapidly be converted to the thermodynamically more stable α-aminoalkyl radicals. The mechanism for the formation of **13** is analogous to that of **4**, depicted in Scheme 5. In a similar manner, the anthraquinone sensitized reactions of pyrrolidine (**5**) with methyl acrylate (**8**) yielded 3-pyrrolizidone (**15**) and the thermal adduct **16** (Scheme 3). Here also it was observed that at 30 °C, 98% of **16** was obtained along with a trace amount of **15**. As indicated in Table 4, lowering of reaction temperature led to a reduction in the yield of **16** and an increase in the yield of 3-pyrrolizidone (**15**).

The formation of the diastereomeric mixture of heliotridone (**17a**), pseudoheliotridone (**17b**) and the N-addition product **18** in the photosensitized addition reaction of pyrrolidine (**5**) with methyl crotonate (**10**) could also be understood in terms of pathways similar to those presented in Scheme 5. Table 5 shows that the lowering of the reaction temperature leads to an increase in the yield of **17a** and **17b**, whereas the yield of the N-addition product (**18**) is significantly reduced. The stereochemistry of **17a** and **17b** was established by comparing the ^{13}C NMR and ^{1}H NMR chemical shifts of the diastereomers. In the ^{13}C NMR, signals due to **17a** appear upfield in comparison to **17b**. Similarly, ^{1}H NMR signals, due to **17a** appear upfield in comparison to that of **17b**. For example, the ^{13}C NMR signal of the CH_3 carbon of **17a** appeared at δ 15.77, whereas the CH_3 protons of **17b** appeared at δ 17.89. Similarly, in the ^{1}H NMR spectrum of **17a**, the CH_3 proton signal appeared at δ 0.98 (J =7 Hz), whereas in **17b**, it appeared at δ 1.15 (J=6 Hz). It has been well documented that the chemical shifts of diastereomers having axial substitution always appear upfield.[10,18] The assignments were further supported by comparing the ^{1}H NMR values of **17a** and **17b** with those reported in the literature.[19]

The formation of the N-adduct **20** and the bicyclic lactam **21** in the reaction of morpholine (**!9**) with methyl methacrylate (**3**) could likewise be understood in terms of pathways similar to those of the reactions of piperidine and pyrrolidine with the appropriate α,β-unsaturated esters.

These studies indicate that the anthraquinone photosensitized addition of secondary and primary amines to α,β-unsaturated olefinic substrates can form a convenient route to the synthesis of bicyclic lactams and spirolactams. Although, the yields of the lactams in these reactions are modest, the simple one-step process for obtaining such products from underivatized amines could make this method one of the preferred routes for their synthesis. Natural products such as δ-conicene, heliotridane and pseudoheliotridane can be easily obtained by the reduction of substrates such as **13**, **17a** and **17b**, respectively.[20]

3.5. Experimental Section

All melting points are uncorrected and were determined on a Büchi-530 melting point apparatus. The IR spectra were recorded on a Perkin Elmer 882 Infrared Spectrometer. The electronic spectra were recorded on a Shimadzu UV-2100 spectrophotometer. The ^{1}H NMR spectra were recorded on a JEOL EX 90 NMR spectrometer using tetramethylsilane (TMS) as internal standard. The ^{13}C NMR (22.5 MHz) spectra were recorded on a JEOL EX 90 NMR spectrometer. The ^{13}C NMR resonances were assigned using QUART and DEPT programmes to determine the nature of the carbon attachments. The mass spectra were recorded either on a Finnigan MAT model 8430 or JEOL JMS AX 505 HA mass spectrometer or 5890 series II Hewlet Packard GC connected to a 5971 series mass selective detector. Gas chromatographic analyses were carried out either on

a 5840 or 5890 series II gas chromatograph. HPLC analyses were carried out employing a Shimadzu HPLC (ODS column), using methanol as eluent.

Preparative photochemical reactions were carried out using a 450W medium pressure mercury vapour lamp in Pyrex jacketed, water cooled immersion wells. The reaction vessel was immersed in a temperature controlled bath and the temperature of the reaction vessel was monitored continuously. Anthraquinone (mp 278 °C) was purified by sublimation. All other reagents and solvents were purified by distillation, prior to use.

The photolysis mixture, typically consisting of the amine (15 mmol) and olefinic substrate (2-15 mmol) in acetonitrile (350 mL) containing anthraquinone (10^{-4} M) was saturated with argon or nitrogen before irradiation (1-8 h). On completion of the reaction, the solvent and unchanged starting materials were removed under reduced pressure and the product mixture was chromatographed on a flash column or on a Harrison Chromatotron. All the photoproducts were finally purified by preparative HPLC. The yields reported are based on GC analysis of the product mixture using N,N-diethylbenzamide as internal standard. Anthraquinone was recovered quantitatively (~90 %) in all cases.

All the photoproducts were characterized on the basis of their spectral data. The Michael type (N-addition) products formed in the reaction mixtures (**14**, **16**, **18**, and **20**) were characterized by comparing their spectral data with those of the compounds obtained in the thermal reaction between the corresponding amines and α,β-unsaturated esters. The indolizidone (**13**) and pyrrolizidone derivatives (**15**, **17a** and **17b**) were characterized by comparing their spectral data with those reported in the literature.[19,20]

3.5.1. Photosensitized Addition of Piperidine (2) to Methyl Methacrylate (3)

Irradiation of an argon-saturated solution of **3** (1.5 g, 15 mmol) and **2** (1.3 g, 15 mmol) in acetonitrile (350 mL) containing anthraquinone (**1**) (10^{-4} M) for 2 h and seperation of the product mixture over a Chromatotron using a mixture of (3:7) ethyl acetate and petroleum ether gave 200 mg (75 %) of **4**. The yield of **4** is based on the amount of **3** reacted (20%), as estimated by HPLC. The reactions were repeated under a variety of conditions and the percentage conversion of **3** and product distribution are shown in Table 1.

4 : IR spectrum ν_{max} (neat) : 2967, 2862 (CH) and 1692 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 3080) and 254 (580 sh).

^1H NMR spectrum ($CDCl_3$) : δ 1.1-1.3 (3 H, 2 d, CH_3), 1.5-2.2 (6 H, m, 3 CH_2), 2.3-2.9 (4 H, m, 2 CH_2), 3.1-3.6 (1 H, m, CH) and 3.9-4.2 (1 H, m, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 16.03, 16.60 (CH_3), 22.22, 23.40, 23.94, 24.09, 32.59, 33.07, 33.40, 35.01, 39.75, 39.96 (CH_2), 35.39, 35.90, 55.06, 55.67 (CH) and 175.68 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 153 (M^+, 72), 152 (100), 138 (29), 124 (20), 112 (12), 97 (12) and 83 (32). Molecular weight calculated for $C_9H_{15}NO$: 153.1153. Found : 153.1153 (high resolution mass spectrometry).

3.5.2. Photosensitized Addition of Pyrrolidine (5) to Methyl Methacrylate (3)

Irradiation of an argon-purged solution of **5** (1.05 g, 15mmol) and **3** (1.5 g, 15 mmol) in acetonitrile (350 mL) containing (10^{-4}) M anthraquinone (**1**) for 2 h and separation of the product mixture Chromatotron using a solvent mixture of

(4:1) petroleum ether and ethyl acetate gave 170 mg (68 %) of **6**. The yield reported was based on **3** reacted (18 %). The reaction was repeated under various conditions and the percentage conversion of **3** and the product distribution of **6** are listed in Table 2.

6 : IR spectrum ν_{max} (neat) : 2970, 2880 (CH) and 1684 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 3080) and 254 (540 sh).

^1H NMR spectrum ($CDCl_3$) : δ 1.1-1.35 (3 H, 2 d, CH_3), 1.8-2.2 (4 H, m, 2 CH_2), 2.3-3.2 (4 H, m, 2 CH_2) and 3.3-4.0 (2 H, m, 2 CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 15.29, 16.93 (CH_3), 26.24, 26.30, 31.49, 31.84, 37.24, 40.50, 40.62 (CH_2), 40.79, 41.15, 58.81, 59.62 (CH) and 175.89, 178.50 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 139 (M^+, 83), 124 (15), 111 (100), 96 (15) and 83 (28). Molecular weight calculated for $C_8H_{13}NO$: 139.0997. Found : 139.0990 (high resolution mass spectrometry).

3.5.3. Photosensitized Addition of Cyclohexylamine (7) to Methyl acrylate (8)

Argon-purged solution of **7** (1.5 g, 15 mmol) and **8** (1.3 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** was irradiated for 4 h and separation of the products by column chromatography using a mixture of (4:1) petroleum ether and ethyl acetate gave 450 mg of **9** (80 %). The percentage yield is based on the amount of **8** that reacted (35 % conversion). In benzene solution, under the same conditions of irradiation, the reaction between **7** and **8** yielded 500 mg (80 %) of **9** with 38 % conversion of **8**.

9: mp. 106-108 °C.

IR spectrum ν_{max} (KBr) : 3361 (broad, NH), 2964, 2860 (CH) and 1698 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 2530) and 254 (520).

^1H NMR spectrum ($CDCl_3$) : δ 1.2-1.7 (10 H, m, cyclohexyl), 1.8-2.0 (2 H, t, CH_2), 2.2-2.5 (2 H, t, CH_2) and 7.4-7.7 (1 H, broad, NH, D_2O-exchangeable).

^{13}C NMR spectrum ($CDCl_3$) : δ 22.70, 24.90, 29.86, 32.42, 38.09 (CH_2), 59.24 (C) and 177.36 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 153 (M^+,32), 110 (100), 97 (22), 82 (20) and 69 (15). Molecular weight calculated for C9H15NO : 153.1153. Found : 153.1154 (high resolution mass spectrometry).

3.5.4. Photosensitized Addition of Cyclohexylamine (7) to Methyl Methacrylate (3)

Argon-saturated solution of 7 (1.5 g, 15 mmol) and **3** (1.5 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M anthraquinone was irradiated for 4 h and separation of the product mixture by column chromatography using a mixture of (4:1) petroleum ether and ethyl acetate gave 350 mg (70 %) of **11**. The yield is based on **3**, that reacted (30 % conversion). In benzene solution, photosensitized addition of 7 to **3** yielded 400 mg (70 %) of **11** with 35 % conversion of **3**.

11 : mp. 95-97 °C.

IR spectrum ν_{max} (KBr) : 3220 (broad, NH), 2987, 2836 (CH) and 1698 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 2890) and 254 (520).

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.1 (3 H, d, CH_3), 1.2-1.6 (10 H, m, cyclohexyl), 1.9-2.6 (3 H, m, CH_2 and CH) and 7.5-7.8 (1 H, broad, NH, D_2O-exchangeable).

^{13}C NMR spectrum ($CDCl_3$) : δ 16.40 (CH_3), 22.64, 22.76, 24.87, 37.49, 39.40, 41.28 (CH_2), 35.26 (CH), 56.83 (C) and 179.33 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 167 (M^+, 27), 138 (8), 124 (100), 111 (23), 96 (12), 78 (60) and 55 (10). Molecular weight calculated for $C_{10}H_{17}NO$: 167.1310. Found : 167.1301 (high resolution mass spectrometry).

3.5.5. Photosensitized Addition of Cyclohexylamine (7) to Methyl Crotonate (10)

Irradiation of an argon-purged solution of a mixture of **7** (1.5 g, 15 mmol), **10** (1.5 g, 15 mmol) and **1** (10^{-4} M) in acetonitrile (350 mL) for 4 h and separation of the reaction mixture by column chromatography using a mixture (3:1) of petroleum ether and ethyl acetate gave 150 mg (50 %) of **12**. The yield reported is based on methyl crotonate reacted (18 %), as estimated by HPLC.

12 : mp. 92-94 °C.

IR spectrum ν_{max} (KBr) : 3220 (broad, NH), 2987, 2836 (CH) and 1698 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 2680) and 254 (510).

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.1 (3 H, d, CH_3), 1.1-1.7 (10 H, m, cyclohexyl), 1.8-2.6 (3 H, m, CH, CH_2) and 6.3-6.7 (1 H, broad, D_2O- exchangeable).

^{13}C NMR spectrum ($CDCl_3$) : δ 14.37 (CH_3), 22.22, 23.32, 25.41, 31.77, 38.12, 39.70 (CH_2), 36.96 (CH), 60.97 (C) and 178.93 (C=O, lactam).

Mass spectrum , m/z (relative intensity) : 167 (M^+, 32, 124 (100), 111 (20), 86 (8), 81 (15) and 55 (6). Molecular weight calculated for $C_{10}H_{17}NO$: 167.1310. Found : 167.1315 (high resolution mass spectrometry).

3.5.6. Photosensitized Addition of Piperidine (2) to Methyl Acrylate (8)

Irradiation of a nitrogen-purged solution of **2** (1.3 g, 15 mmol) and **8** (1.3 g, 15 mmol) in acetonitrile (300 mL) containing anthraquinone (10^{-4} M) for 2 h at 0 °C and separation of the reaction mixture by column chromatography gave 120 mg (25 %) of **13** and 400 mg (60 %) of **14**. These yields are based on **8**, that reacted (25 %), as estimated by HPLC. The reaction was repeated at different temperatures and the percentage conversion and product yields are shown in Table 3.

13 : IR spectrum ν_{max} (neat) : 2987, 2880 (CH) and 1680 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.4-2.1 (6 H, m, 3 CH_2), 2.15-2.9 (4 H, m, 2 CH_2), 3.3-3.9 (2 H, m, CH_2) and 4.1-4.4 (1 H, m, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 23.38, 24.16, 25.02, 29.90, 33.29, 39.91 (CH_2), 56.98 (CH) and 173.24 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 139 (M^+, 82), 138 (100), 124 (20), 115 (15), 98 (25), 83 (60), 68 (25) and 55 (50).

14 : IR spectrum ν_{max} (neat) : 2980, 2870 (CH) and 1744 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.3-1.7 (6 H, m, 3 CH_2), 2.2-2.8 (4 H, m, 4 CH_2) and 3.5-3.7 (3 H, s, OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 23.93, 25.60, 31.72, 50.90 (CH_2), 53.88 (OCH_3), 172.45 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 171 (M^+, 10), 143 (20), 114 (30), 98 (100), 88 (16), 73 (10) and 55 (30).

3.5.7. Photosensitized Addition of Pyrrolidine (5) to Methyl Acrylate (8)

Nitrogen-purged solution of **5** (1.06 g, 15 mmol) and **8** (1.3 g, 15 mmol) in acetonitrile (300 mL) containing 10^{-4} M anthraquinone was irradiated for 2 h at 0 °C and separation of the products by column chromatography using a mixture of (4:1) petroleum ether and ethyl acetate gave 100 mg (15 %) of **15** and 950 mg (70 %) of **16**. These yields are based on methyl acrylate reacted (40 %). The percentage conversion of **8** and product yields at different temperatures are shown in Table 4.

15 : IR spectrum ν_{max} (neat) : 2980, 2880 (CH) and 1682 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.8-2.1 (4 H, m, 2 CH_2), 2.15-2.6 (4 H, m, 2 CH_2). 3.2-3.6 (2 H, m, CH_2) and 4.2-4.6 (1 H, m, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 26.75, 26.93, 31.94, 35.11, 40.78 (CH_2), 61.87 (CH) and 174.62 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 125 (M^+, 80), 110 (10), 97 (100), 80 (40, 69 (44) and 55 (18).

16 : IR spectrum ν_{max} (neat) : 2975, 2868 (CH) and 1742 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.65-1.85 (4 H, m, 2 CH_2), 2.4-2.9 (8 H, m, 4 CH_2) and 3.6-3.75 (3 H, s, OCH_3).

13C NMR spectrum (CDCl3) : δ 22.93, 33.38, 50.62, 50.83, (CH_2) 53.34, (OCH_3) and 171.93 (C=O, ester)

Mass spectrum, m/z (relative intensity) : 157 (M^+, 5), 129 (15), 98 (25), 83 (100), 68 (10) and 55 (20).

3.5.8. Photosensitized Addition of Pyrrolidine (5) to Methyl Crotonate (10)

Irradiation of an argon-purged solution of **5** (1.06 g, 15 mmol) and **10** (1.5 g, 15 mmol) in 300 mL acetonitrile containing anthraquinone (10^{-4} M) for 2 h at 0 °C and chromatographic separation of the products using a mixture of (3:1) petroleum ether and ethyl acetate gave 120 mg (40 %) of a diastereomeric mixture (3:7) of **17a** and **17b** and 70 mg (15 %) of **18**. The yields reported are based on methyl crotonate reacted (20%). The percentage conversion and product yields at different temperatures are shown in Table 5.

17a and **17b** : IR spectrum ν_{max} (neat) : 2970, 2876 (CH) and 1688 (C=O) cm^{-1}.

^{1}H NMR spectrum ($CDCl_3$) : δ 0.9-0.98 (3 H, d, CH_3, J= 7 Hz, **17a**), 1.0-1.15 (3 H, d, CH_3, J= 6 Hz, **17b**), 1.8-2.2 (8 H, m, 4 CH_2), 2.25-2.6 (4 H, m. 2 CH_2), 2.8-3.2 (2 H, m, 2 CH) and 3.25-4.0 (6 H, m, 2 CH_2 and 2 CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 15.77, 17.89 (CH_3), 24.96, 26.94, 29.50, 30.60, 41.07, 41.28, 42.95, 43.70 (CH_2), 35.05, 37.85, 65.05, 68.85 (CH) and 174.05, 174.25 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 139 (M^+, 23), 124 (4), 111 (18), 96 (6), 85 (6), 70 (80) and 56 (4).

18 : IR spectrum ν_{max} (neat) : 2980, 2872 (CH) and 1744 (C=O) cm^{-1}.

^{1}H NMR spectrum ($CDCl_3$) : δ 1.1-1.3 (3 H, d, CH_3), 1.7-1.9 (4 H, m, 2 CH_2), 2.1-3.2 (7 H, m, 3 CH_2, CH), 3.6-3.8 (3 H, S, OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 17.92, 22.96, 39.58, 49.99, 50.77, 54.83, 172.11 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 171 (M^+, 5), 156 (15), 124 (5), 98 (100), 70 (5), 56 (10).

3.5.9. Photosensitized Addition of Morpholine (19) to Methyl Methacrylate (3)

Irradiation of a nitrogen-purged solution of **19** (1.3 g, 15 mmol) and **3** (1.5 g, 15 mmol) in acetonitrile (300 mL) containing 10^{-4} M anthraquinone for 2 h at 0 °C and separation of the product mixture by column chromatography using a mixture of (4:1) petroleum ether and ethyl acetate gave 150 mg (45 %) of **21** and 40 mg (5%) of **20**. The yields reported are based on **3** reacted (20%). The percentage conversion and product distribution are shown in Table 6.

21: IR spectrum ν_{max} (neat) : 2976, 2878 (CH), 1692 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε 3620), 254 nm (510 sh).

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.2 (3 H, d, CH_3), 1.6-2.0 (2 H, m, CH_2), 2.1-2.6 (1 H, m, CH), 2.8-3.2 (2 H, m, CH_2), 3.2-4.1 (5 H, m, 2 CH_2, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 15.80, 16.79 (CH_3), 28.19, 29.95 (CH_2), 35.44 (CH), 39.58, 39.97 (CH_2), 52.41, 52.98 (CH), 65.48, 71.83, 72.67 (CH_2), 175.06, 175.63 (C=O, lactam).

Mass spectrum m/z (relative intensity) : 155 (M^+, 80), 125 (65), 110 (7), 97 (100), 82 (86), 69 (42), 54 (84). Molecular weight calculated for $C_8H_{13}NO_2$: 155.0868. Found : 155.0866 (high resolution mass spectrometry).

20 : IR spectrum ν_{max} (neat) : 2985, 2870 (CH), 1740 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$): δ 0.9-1.0 (3H, d, CH_3), 2.4-3.2 (7 H, 3 CH_2, CH), 3.4-3.8 (7 H, m, 2 CH_2, OCH_3).

^{13}C NMR spectrum ($CDCl_3$): δ 18.02 (CH_3), 41.28, 43.54, 70.80 (CH_2), 45.76 (CH), 52.80 (OCH_3) and 172.45 (C=O, ester).

Mass spectrum, m/z (relative intensity): 187 (M^+, 2), 156 (5), 142 (5), 114 (5), 100 (100), 86 (5), 76 (10), 56 (15).

3.6. References

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Chapter 4. Anthraquinone Photosensitized Reactions of N-Allylamines with α,β-Unsaturated Esters

4.1. Abstract

Anthraquinone (**1**) photosensitized reactions of a few N-allylamines with α,β-unsaturated esters were investigated. The α-aminoalkyl radicals, generated via anthraquinone sensitized photoreactions of N-allylamines add to α,β-unsaturated esters and the adduct radicals formed in these cases undergo hydrogen abstraction to give the corresponding α-substituted products, which in turn undergo further transformations to give lactams as end products. In some cases, the formation of trace amounts of tandem radical addition products were also observed. Thus, the photosensitized reaction of N-allyldiethylamine (**2**) with methyl methacrylate (**3**) gave 1-ethyl-3,5-dimethyl-2-pyrrolidone (**4**), whereas the photosensitized reaction of **2** with methyl acrylate (**5**) gave 1-ethyl-5-methyl-2-pyrrolidone (**7**). Similarly, the sensitized photoreaction of **2** with methyl crotonate (**6**) gave a diastereomeric mixture of 1-ethyl-4,5-dimethyl-2-pyrrolidone (**8**), along with minor amounts of the piperidine derivative **9**. The photosensitized reactions of N-allylpiperidine (**10**) with methyl methacrylate (**3**) and methyl acrylate (**5**) gave the corresponding indolizidone derivatives **11** and **12**, respectively. The photosensitized reaction of **10** with methyl crotonate (**6**) gave a diastereomeric mixture of 1-methyl-3-indolizidone (**13**) and an isomeric mixture of a quinolizidine derivative **14**. Similarly, the photosensitized addition of N-allylpyrrolidine (**15**) to **3** and **5** gave the pyrrolizidone derivatives **16** and **17**, respectively, whereas, the sensitized photoreaction between **15** and **6** yielded a mixture of heliotridone (**18a**) and pseudoheliotridone (**18b**) along with minor amounts of an isomeric mixture of indolizidine derivative **19**. The photosensitized reactions of

N-allylcyclohexylamine (**20**) with methyl acrylate (**5**) gave minor amounts of the spirolactam **21**, whereas the photosensitized reaction of N-allyl-2,6-dimethylpiperidine (**22**) with methyl acrylate (**5**) gave a 1:2 amine-olefin addition product **23**. Reasonable mechanisms have been suggested for the formation of the various products in these reactions.

4.2. Introduction

Electron transfer between excited state sensitizers and amines leads to the formation of the radical ion-pairs.[1-3] Among the various reaction pathways available to the radical ion-pairs, proton exchange between the radical ion and the aminium radical is the prominent one.[4-6] The regioselectivity for α-CH deprotonation in such processes, has been extensively studied by Lewis and co-workers for the stilbene-amine systems and by Mariano and co-workers for the enone-amine systems.[7-10] The results of these studies show that both steric and electronic effects, associated with the α-substituent govern the rate as well as the regioselectivity of the deprotonation of the aminium radicals. For example, alkyl substituents slow down the rate of deprotonation, indicating the importance of steric factors. Substitution at the α-carbon by radical stabilizing groups with minimal steric requirements such as CH=CH- or -C≡C- groups, however bring about highly selective deprotonation at the substituted carbon. Recent CIDNP studies on allylamine cation radicals show highly selective deprotonation leading to the formation of α–allylamine radicals.[11]

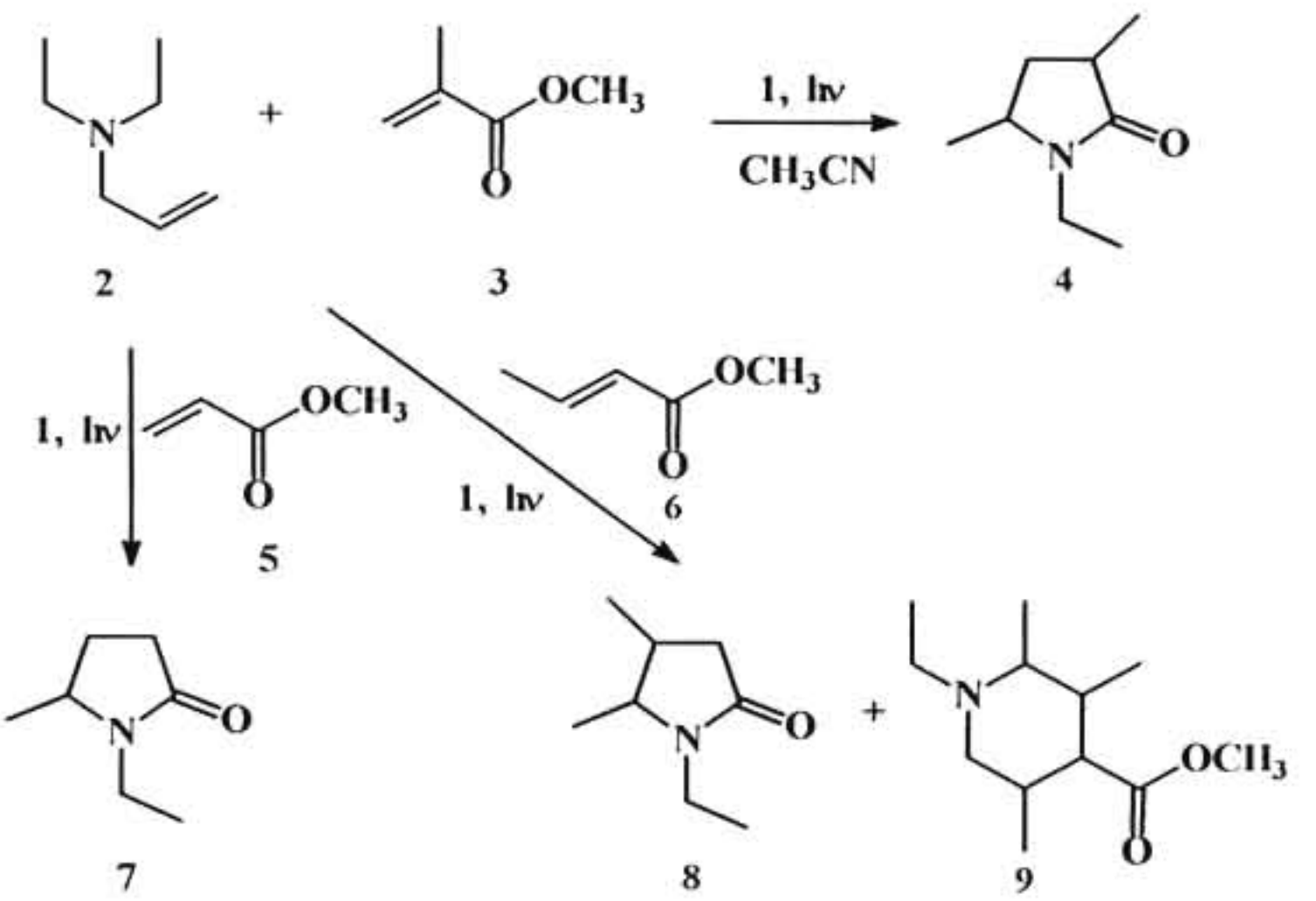
In the present studies, we have examined the anthraquinone photosensitized electron transfer reactions of a variety of allylamines. The carbon-carbon bond forming reactions between the α-aminoalkyl radicals, generated from these amines and a few α,β-unsaturated esters were studied.

4.3. Results

4.3.1. Photoelectron Transfer Catalyzed Reactions of N-Allyldiethylamine (2) with Methyl Methacrylate (3), Methyl Acrylate (5) and Methyl Crotonate (6)

The anthraquinone (**1**) sensitized photoreaction of N-allyldiethylamine (**2**) with methyl methacrylate (**3**), using Pyrex filtered output of a 450 W medium pressure mercury lamp gave 1-ethyl-3,5-dimethyl-2-pyrrolidone (**4**) as the major product (Scheme 1). The IR spectrum of **4** showed an absorption band at 1685 cm^{-1} due to a carbonyl group. The ^1H NMR spectrum of **4** showed a multiplet at δ 0.9-1.2 (9 H) due to the methyl protons, whereas, the multiplets around δ 2.3-2.6 and δ 2.9-3.2 were assigned to the CH_2 protons. The two CH protons appeared as multiplets around δ 2.9-3.2 and 3.5-3.8. The ^{13}C NMR spectrum of **4** showed three CH_3, two CH_2 and two CH carbon signals and a carbonyl carbon at δ 172.42. The mass spectrum of **4** showed the molecular ion peak at m/z 141, which is in agreement with the assigned structure.

Similarly, the sensitized photoreaction of **2** with methyl acrylate (**5**) gave 1-ethyl-5-methyl-2-pyrrolidone (**7**, Scheme 1). The IR spectrum of **7** showed an absorption band at 1688 cm^{-1} due to a carbonyl group. The ^1H NMR spectrum of **7** showed a multiplet centered around δ 0.9-1.2 (6 H), assigned to the CH_3 protons. The multiplets at δ 1.6-2.4 (4 H) and δ 3.0-3.8 (3 H) have been assigned to the methylene and methine protons. The ^{13}C NMR spectrum of **7** showed two CH_3 signals, three CH_2 signals, one CH signal and a carbonyl carbon signal at δ 174.44. The mass spectrum of **7** showed the molecular ion peak at m/z 127, which is in agreement with the assigned structure.



Scheme 1

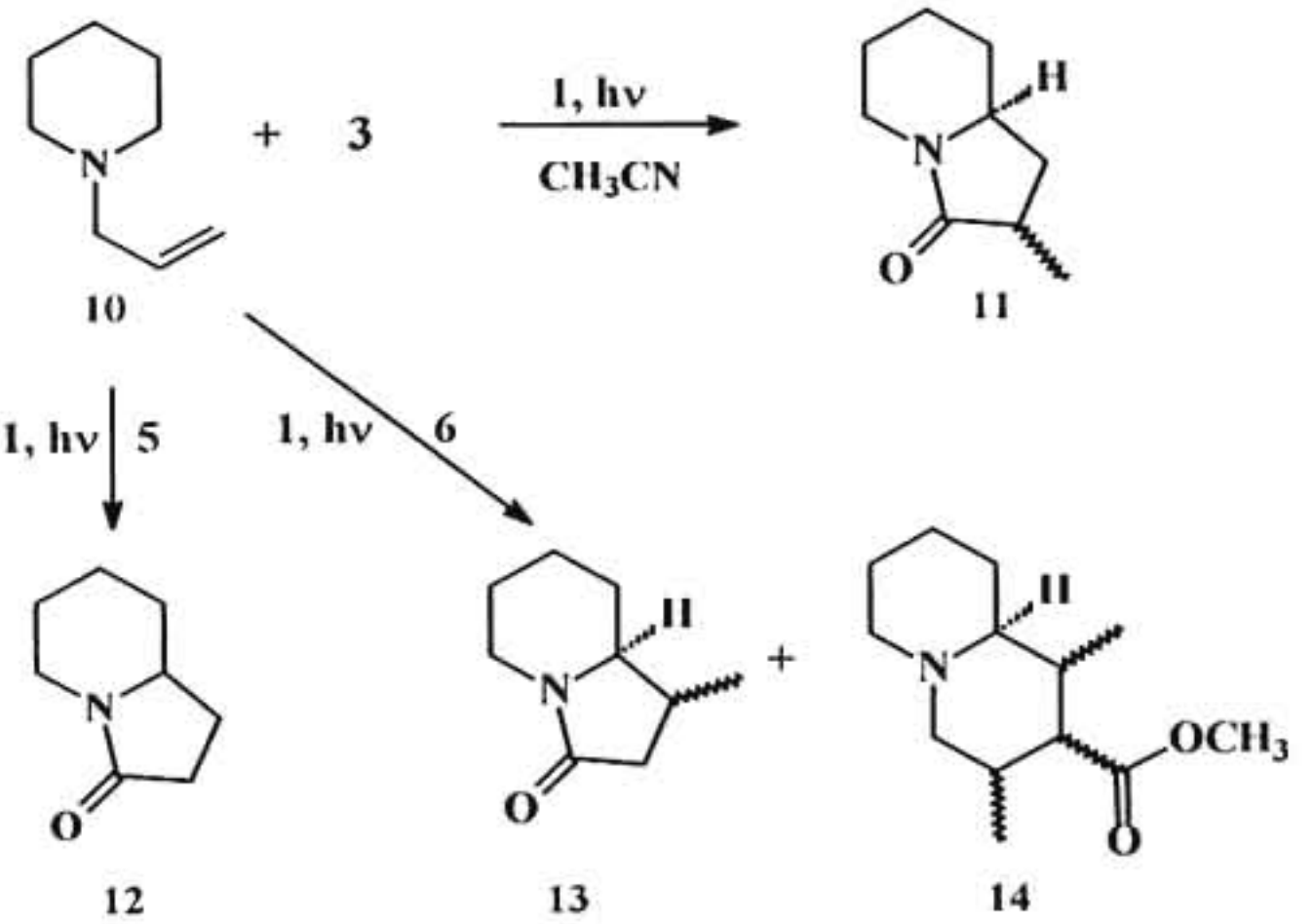
The photosensitized addition of **2** to methyl crotonate (**6**) was effected by irradiation of an argon saturated acetonitrile solution of **2** and **6** containing catalytic amounts of **1**, using Pyrex filtered light. Two products were isolated from the reaction mixture (**8** and **9**, Scheme 1) and they were characterized on the basis of analytical results and spectral data. The IR spectrum of **8** showed an absorption band at 1688 cm^{-1} due to a carbonyl group. The ^{1}H NMR spectrum of **8** showed a multiplet around δ 0.9-1.2 (9 H) which was assigned to the methyl protons. Other multiplets centered around δ 1.8-2.7 (3 H) and δ 2.8-3.9 (3 H) have been assigned to methylene and methine protons. The ^{13}C NMR spectrum of **8** showed six methyl, four methylene and four methine carbon signals and two carbonyl carbon signals at δ 174.26 and 175.50. The ^{13}C NMR spectral features indicate that **8** is present as an isomeric mixture and the structure of **8** has been

assigned as 1-ethyl-4,5-dimethyl-2-pyrrolidone. The mass spectrum of **8** showed a molecular ion peak at m/z 141, which is in agreement with the assigned structure.

The IR spectrum of **9** showed an absorption band at 1740 cm^{-1} due to an ester carbonyl group. The ^1H NMR spectrum of **9** showed a multiplet centered around δ 0.85-1.2 (12 H) which was assigned to the methyl group protons and a second multiplet centered around δ 1.9-3.2 (8 H) which was assigned to four CH_2 and four CH protons. The methoxy protons (3 H) appeared as a singlet at δ 3.6-3.8. The ^{13}C NMR spectrum of **9** showed several signals, out of which the ones around δ 172-175 have been assigned as ester carbonyl carbons. Based on the spectral data, the structure of **9** has been assigned as 4-carbomethoxy-1-ethyl-3,5,6-trimethylpiperidine and the ^{13}C NMR spectral features indicate that it is present as an isomeric mixture. The molecular ion peak at m/z 213, is in good agreement with the proposed structure.

4.3.2. Photoelectron Transfer Catalyzed Reactions of N-Allylpiperidine (10) with Methyl Methacrylate (3), Methyl Acrylate (5) and Methyl Crotonate (6)

Anthraquinone (10^{-4} M) sensitized photoreaction between **10** and **3** in acetonitrile using Pyrex filtered light gave a diastereomeric mixture of 2-methyl-3-indolizidone (**11**, Scheme 2). The structure of **11** was arrived at on the basis of spectral data and also by comparison of its gas chromatographic retention time and mass spectra with those reported in Chapter 3 for 2-methyl-3-indolizidone (Section **3.5.1**). Similarly, the anthraquinone phtosensitized reaction of **10** with methyl acrylate (**5**) gave **12** (Scheme 2), as the major product. The structure of **12** identified as 3-indolizidone on the basis of spectral data and comparison of its gas chromatographic retention time and mass spectral data with those of 3-indolizidone reported in Chapter 3 (Section **3.5.6**).



Scheme 2

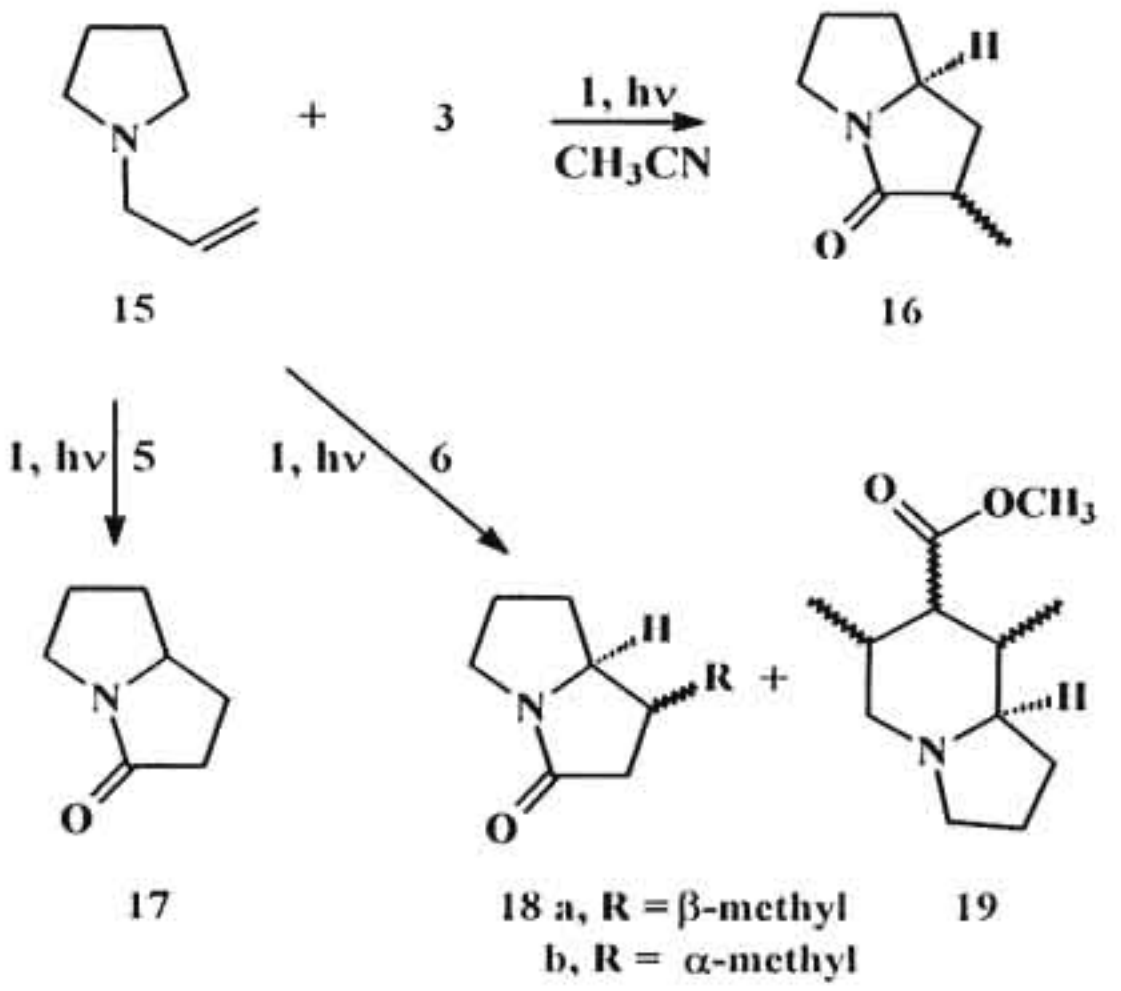
The photosensitized reaction of **10** with methyl crotonate (**6**) gave a mixture of **13** and **14** (Scheme 2). The structures of **13** and **14** were arrived at on the basis of analytical results and spectral data. The IR spectrum of **13**, for example, showed an absorption band at 1690 cm^{-1} due to a carbonyl group. The ^{1}H NMR spectrum of **13** showed a doublet at δ 1.0-1.2 (3 H), assigned to the methyl protons. The methylene protons appeared as multiplets centered around δ 1.4-2.2 (6 H) and 2.3-2.8 (2 H). The multiplets centered around δ 3.2-3.8 (1 H) and δ 3.9-4.2 (1 H) have been assigned to the CH protons. The ^{13}C NMR spectrum of **13** showed two CH_3, ten CH_2, four CH carbon and two carbonyl carbon signals at δ 173.09 and

173.27. The structure of **13**, on the basis of spectral evidence, has been assigned as 1-methyl-3-indolizidone. The mass spectrum of **13** showed a molecular ion peak at m/z 153, which is in agreement with the assigned structure.

Similarly, the IR spectrum of **14** showed an absorption band at 1738 cm^{-1} due to an ester carbonyl group. The ^1H NMR spectrum of **14** showed two doublets at δ 0.9-1.15 (6 H), assigned to the two CH_3 protons. The multiplet centered around δ 1.4-2.0 (6 H) has been assigned to the CH_2 protons, whereas the multiplet centered around δ 2.4-3.3 (7 H) has been assigned to the four CH_2 protons and three CH protons. The methoxy protons appeared as a singlet around δ 3.6-3.8 (3 H). The ^{13}C NMR spectrum of **14** showed several signals due to different chiral centers associated with the structure, out of which the signals at δ 174-175 have been assigned to ester carbonyl carbons. The structure of **14** on the basis of spectral evidence has been assigned as 2-carbomethoxy-1,3-dimethyl-quinolizidine. The mass spectrum of **14** showed a molecular ion peak at m/z 225, which is in good agreement with the assigned structure.

4.3.3. Phtoelectron Transfer Catalyzed Reactions of N-Allylpyrrolidine (15) with α,β-Unsaturated Esters

Anthraquinone (**1**) sensitized photoreaction of N-allylpyrrolidine (**15**) with methyl methacrylate (**3**) gave 2-methyl-3-pyrrolizidone (**16**) which was identified on the basis of spectral data and comparison of its gas chromatographic retention time and mass spectral data with those of the same compound reported in Chapter 3 (Section **3.5.2**) (Scheme 3). Similarly, the sensitized photoreaction of **15** with methyl acrylate (**5**) gave 3-pyrrolizidone (**17**) (Scheme 3). The structure of **17** was arrived at by comparing its gas chromatographic retention time and mass spectral data with those of 3-pyrrolizidone reported in Chapter 3 (Section **3.5.7**).



Scheme 3

Photosensitized reaction of **15** with methyl crotonate (**6**) gave a diastereomeric mixture of heliotridone (**18a**) and pseudoheliotridone (**18b**), along with a minor amount of **19**. The structures of **18a** and **18b** were assigned by comparing the spectral and analytical data with those of 1-methyl-3-pyrrolizidones reported in Chapter 3 (Section **3.5.8**). The structure of **19** was characterized on the basis of analytical results and spectral data. The IR spectrum of **19**, for example, showed an absorption band at 1738 cm^{-1} due to an ester carbonyl group. The ^{1}H NMR spectrum of **19** showed two doublets centered around δ 0.9-1.25 (6 H), assigned to two methyl protons. The multiplet centered around δ 1.5-2.2 (4 H) was assigned to four CH_2 protons, the one at δ 2.4-3.2 (6 H) to the four CH_2 protons and two CH protons and the one δ 3.2-3.5 (2 H) to two CH protons. The methoxy protons appeared as a multiplet centered around δ 3.6-3.8 (3 H). The ^{13}C NMR spectrum

of **19** showed several signals due to the different chiral centres associated with the molecule, out of which those at δ 175.54-176.60 have been assigned to the ester carbonyl carbons. The structure of **19**, on the basis of spectral evidence, has been assigned as 7-carbomethoxy-6,8-dimethyl-indolizidine. The mass spectrum of **19** showed a molecular ion peak at m/z 197, which is in good agreement with the assigned structure.

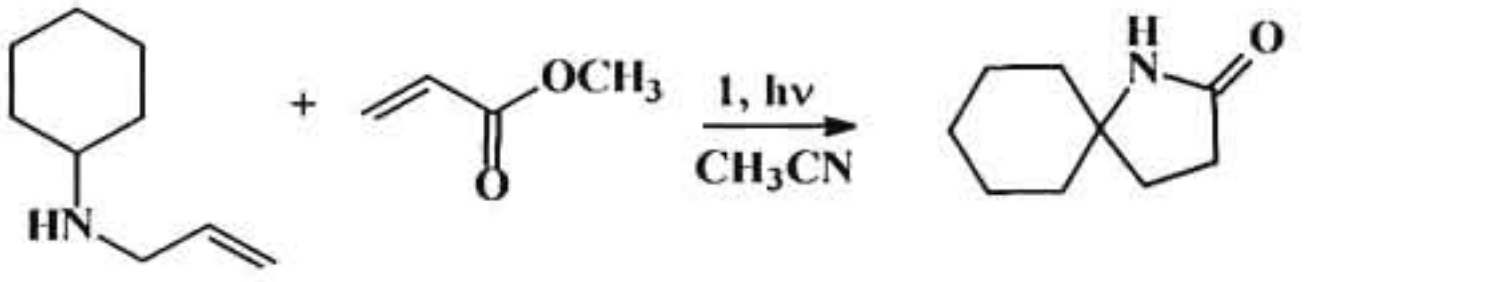
4.3.4. Photoelectron Transfer Catalyzed Reactions of N-Allylcyclohexylamine (20) with Methyl Acrylate (5)

Photosensitized reaction of N-allylcyclohexylamine (**20**) with methyl acrylate (**5**) gave the spirolactam **21** (Scheme 4) which was characterized by comparing its spectral data with the same spirolactam, obtained in the anthraquinone sensitized photoreaction of cyclohexylamine with methyl acrylate reported in Chapter 3 of this thesis (Section **3.5.3**).

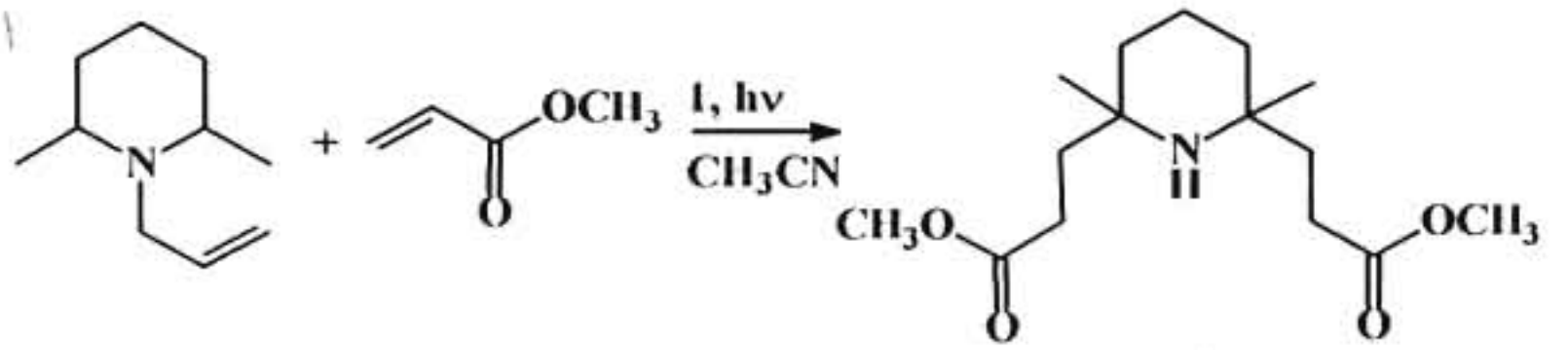
4.3.5. Photoelectron Transfer Catalyzed Reactions of N-Allyl-2,6-dimethylpiperidine (22) with Methyl Acrylate (5)

Anthraquinone sensitized photoreaction of N-allyl-2,6-dimethylpiperidine (**22**) and methyl acrylate (**5**), under conditions similar to those employed in the earlier cases gave the piperidine derivative **23** as the major product (Scheme 4). The IR spectrum of **23** showed an absorption band at 3300 cm^{-1} due to an NH group and one at 1744 cm^{-1} due to an ester carbonyl group. The ^{1}H NMR spectrum of **23** showed two singlets at δ 1.0-1.15 (6 H) which was assigned to the CH_3 protons, and three multiplets centered around δ 1.2-1.4 (4 H), δ 1.5-2.0 (6 H) and δ 2.2-2.6 (4 H), assigned to the CH_2 protons. The methoxy protons (6 H) appeared as a singlet at δ 3.6-3.75. The ^{13}C NMR spectrum of **23** showed

one CH_3, four CH_2, one methoxy and one quarternary carbon signals and one carbonyl carbon signal at δ 174.73. The mass spectrum of **23** showed a molecular ion peak at m/z 286, which is in good agreement with the assigned structure.



20 **5** **21**



22 **5** **23**

Scheme 4

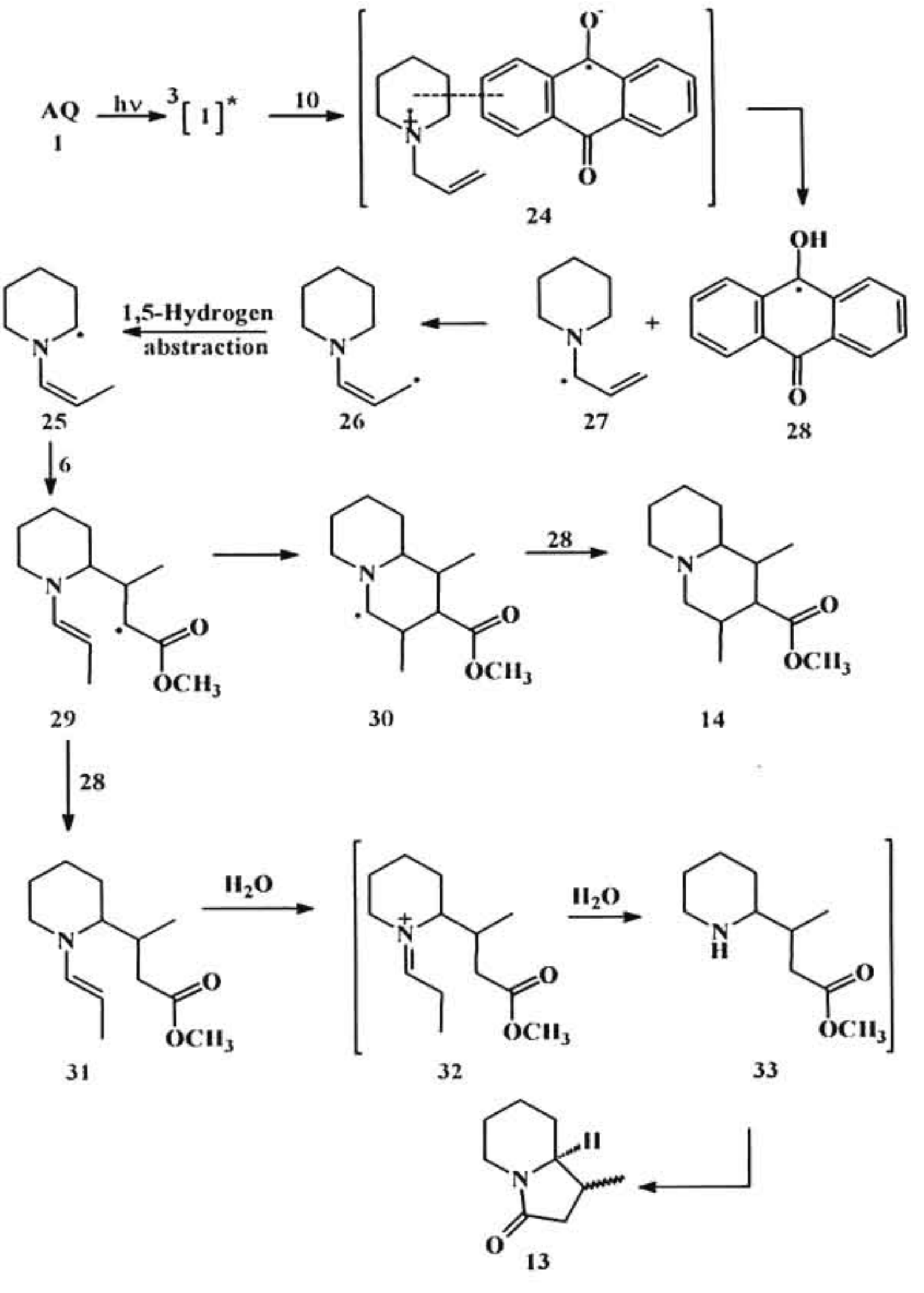
4.4. Discussion

As discussed earlier, irradiation of amines in presence of anthraquinone using Pyrex filtered light leads to selective excitation of anthraquinone. The excited singlet state of anthraquinone rapidly undergoes intersystem crossing to form triplets with a quantum efficiency of nearly one. Quenching of the anthraquinone triplets by allylamine will lead to the formation of aminium and ketyl radical ions. The radical ions, thus formed can undergo a rapid proton exchange within the solvent cage. Goez and Frisch have recently studied the anthraquinone photocatalyzed reactions of several amines including allylamine derivatives using the chemically induced dynamic nuclear polarization (CIDNP)

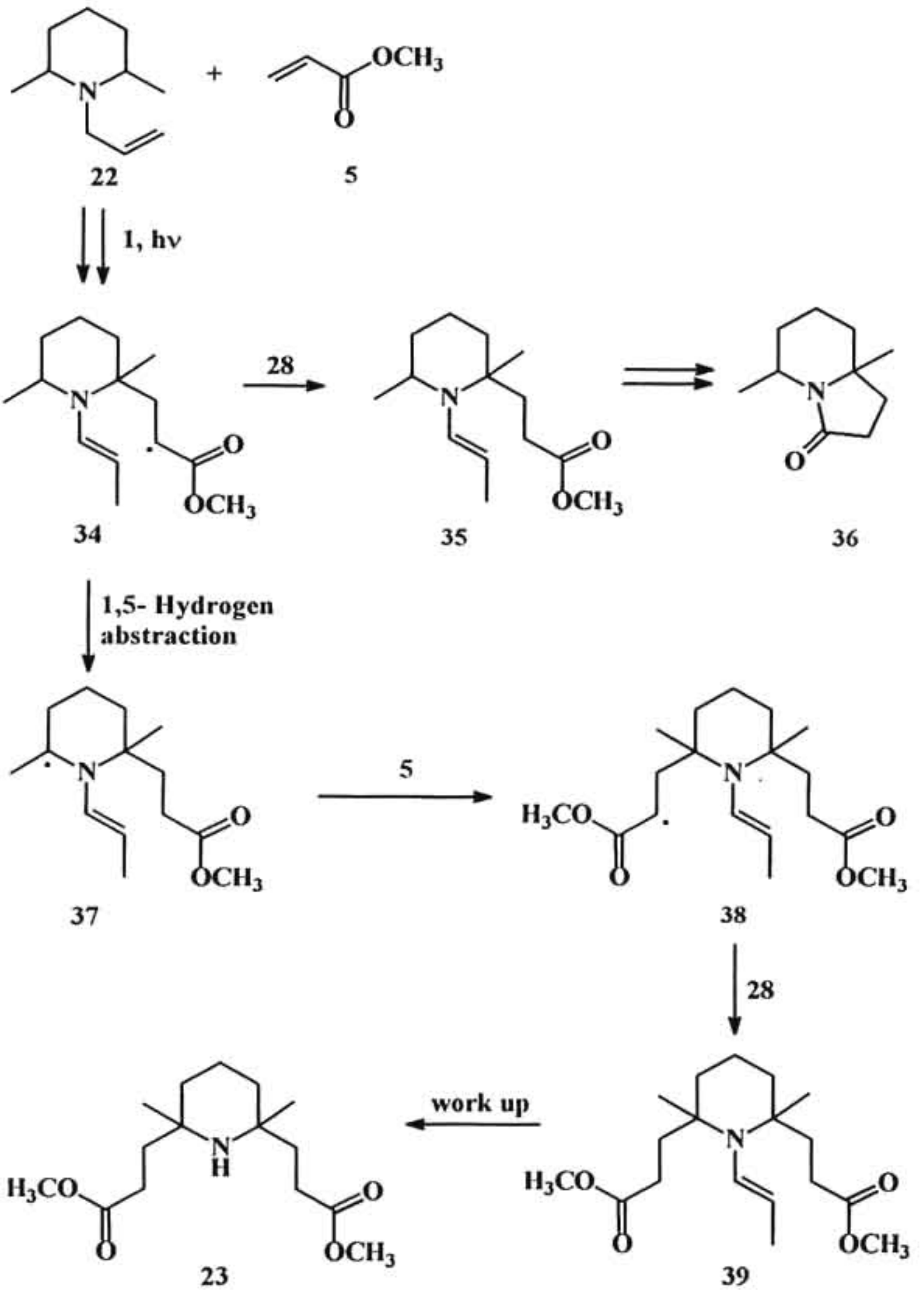
technique.[11] Their study reveals that the aminium cation intermediates that are formed can be deprotonated either within the cage by the sensitizer radical anion or outside the cage by surplus amines. With methyl, ethyl and isopropyl substituents, they observed that the deprotonation occurs exclusively outside the solvent cage, whereas deprotonation within the cage dominated in the case of allyl substituents. The difference in behaviour can be explained in terms of an increase in the rate of in-cage proton transfer, relative to the cage life with increasing driving force of this reaction. Thus, in the case of anthraquinone sensitized photoreaction of triallylamine, there is a clear manifestation of a dominant in-cage proton transfer from the aminium radical to the ketyl radical anion. For comparing the reactivities of allyl and ethyl groups they have studied the photo-CIDNP spectrum of the N-diallylethylamine-anthraquinone system. Their studies have indicated that the deprotonation of the allyl group occurs predominantly inside the cage, whereas the deprotonation at the ethyl group occurs outside the cage. Similar results were obtained for N-allyldimethylamine, where deprotonation of the allyl groups occurs within the cage and deprotonaton of the methyl group occurs outside the cage. These studies clearly indicate that in-cage proton transfer from the allyl groups of the aminium radical is able to compete with escape of the radical ions from the cage, whereas these reactions are obviously slow in the case of ethyl and methyl protons. The rate of ethyl and allyl deprotonation outside the solvent cage is more or less of the same order of magnitude. From these studies and those by Lewis etal. and Mariano et al., it is evident that in anthraquinone photoelectron transfer catalyzed reactions of N-allylamines, α-aminoallyl radical formation will predominate over α-aminoalkyl radical formation.[8-10] However, the formation of the different products in the anthraquinone sensitized photoreactions of N-allylamines with α,β-unsaturated esters, in the present study, indicates that the initial carbon-carbon bond forming reations occur through α-aminoalkyl

radicals. It is quite likely that the initially formed α-aminoallyl radicals, undergo transformation to α-aminoalkyl radicals, which then participate in the addition reactions. A reasonable pathway for the formation of different products in the reaction of N-allylpiperidine (**10**) with methyl crotonate (**6**) is shown in Scheme 5. The α-aminoallyl radical **27**, formed initially can isomerise to give the radical **26**, which can undergo a 1,5-hydrogen abstraction to yield the α-aminoalkyl radical **25**. Addition of **25** to methyl crotonate (**6**) would give the adduct radical **29**. The formation of the quinolizidine derivative **14** is attributed to the tandem intramolecular addition of the adduct radical **29** to give **30** and subsequent quenching of the radical **30** by the anthraquinone ketyl radical (**28**). Alternatively, the adduct radical **29** can be quenched by **28** to yield an enamine derivative **31**. This enamine can undergo dealkylation under work-up to give **33**, presumably through the iminium intermediate **32**. Lactonization of of **33** will result in the formation of the indolizidone **13** (Scheme 5). Pathways similar to those shown in Scheme 5 may be operating in the formation of the piperidine derivative **9** in the reaction of N-allyldiethylamine (**2**) with methyl crotonate (**6**) (Scheme 1) and the indolizidine derivative **19** in the reaction of N-allylpyrrolidine (**15**) with methyl crotonate (**6**) (Scheme 3).

The major product isolated from the reaction of N-allyl-2,6-dimethylpiperidine (**22**) with methyl acrylate (**5**) was the 2:1 ester-amine adduct **23**. The formation of **23** in this reaction can be rationalized in terms of the pathways shown in Scheme 6. The photosensitized addition of **22** to **5** in presence of anthraquinone can lead to the adduct radical **34**, following the initial pathways similar to those indicated in Scheme 5. One of the possible modes of transformation of **34** is to undergo hydrogen atom abstraction from anthraquinone ketyl radical (**28**) to give **35**, which ultimately can lead to the indolizidone **36**. We have not been able to


AQ
1
hν
3[1]*
10
24
OH
1,5-Hydrogen
abstraction
25
26
27
28
6
29
30
28
14
28
H2O
H2O
31
32
33
H
13

Scheme 5


22
5
1, hν
34
28
35
36
1,5- Hydrogen abstraction
37
5
38
28
work up
23
39

Scheme 6

isolate **36** from the product mixture. However, the GC-MS data showed a peak at m/z 167, which could be due to **36** (M^+). An intramolecular hydrogen abstraction in **34** could result in the formation of a new radical **37**, which could then add on another methyl acrylate molecule to give the bis-adduct radical **38**. Subsequent hydrogen abstraction of **38** from **28** would give the bis-adduct **39**, which under work-up conditions could give **23**, by pathways similar to those shown in Scheme 5.

4.5. Experimental Section

The IR spectra were recorded on a Perkin-Elmer model 882 Infrared Spectrophotometer. The ^1H and ^{13}C NMR spectra were recorded on a JEOL EX-90 FT NMR Spectrometer, using tetramethylsilane (TMS) as internal standard and the ^{13}C signals were assigned by using QUART and DEPT programmes. The mass spectra were recorded either on a Finnigan MAT model 8430 or JEOL JMS AX 505 HA mass spectrometer or 5890 Series 2 Hewlett-Packard GC-MS. The GC analysis were obtained on a Hewlett-Packard 5890 Series II gas chromatograph and the HPLC analyses were carried out using a Shimadzu HPLC. All steady state photoreactions were carried out using a 450 W medium pressure mercury lamp with a Pyrex filter (λ >290 nm) under argon or nitrogen atmosphere. The allylamines were prepared by known procedures. Anthraquinone was purified by sublimation. All other solvents and reagents were purified and distilled before use.

In a typical run, the photolysis mixture, consisting of 15 mmol (or 10 mmol) of allylamine and 15 mmol of α,β-unsaturated ester in acetonitrile (350 mL) containing (10^{-4} M) anthraquinone was purged with argon or nitrogen before irradiation. The solvent and the unchanged reactants were removed under reduced

pressure and the product mixture was chromatographed using either a flash column or Chromatotron. The yields reported are based on the olefinic substrate consumed, which was estimated by HPLC. The reported product distribution was based on GC and GC-MS analyses of the product mixtures.

4.5.1. Anthraquinone Sensitized Photoaddition of N-Allyldiethylamine (2) to α,β-Unsaturated Esters

a) Photosensitized addition of N-allyldiethylamine (2) to methyl methacrylate (3). Irradiation of an argon-purged solution of **2** (1.8 g, 15 mmol) and **3** (1.5 g, 15 mmol) in acetonitrile (350 mL), containing 10^{-4} M of **1** for 4 h and separation of the photolysate by column chromatography using a mixture (3:1) of petroleum ether and ethyl acetate gave 140 mg (65 %) of 1-ethyl-3,5-dimethyl-2-pyrrolidone (**4**). The yield was based on **3** that reacted (22 %), as estimated by HPLC.

4: IR spectrum ν_{max} (neat) : 2980, 2875 (CH) and 1685 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 2880) and 255 (450).

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.2 (9 H, m, 3 CH_3), 1.8-2.1 (2 H, m, CH_2), 2.3-2.6 (2 H, t, CH_2), 2.9-3.3 (1 H, m, CH) and 3.5-3.8 (1 H, m, CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 12.61, 16.52, 20.28 (CH_3), 34.72, 36.54 (CH_2), 36.69, 51.07 (CH) and 172.42 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 141 (M^+, 10), 126 (40), 112 (100), 98 (6), 84 (30), 76 (6) and 56 (15). Molecular weight calculated for $C_8H_{15}NO$: 141.1154. Found : 141.1153 (high resolution mass spectrometry).

b) Photosensitized addition of N-allyldiethylamine (2) to methyl acrylate (5). Irradiation of an argon-purged solution of a mixture of **2** (1.8 g, 15 mmol) and **5** (1.3 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** for 4 h, and separation of the product mixture by column chromatography using a solvent mixture (3:1) of petroleum ether and ethyl acetate gave 130 mg (55 %) of 1-ethyl-5-methyl-2-pyrrolidone (7). The yield reported was based on **5** that reacted (20 % conversion), as estimated by HPLC.

5: IR spectrum ν_{max} (neat) : 2980, 2875 (CH) and 1685 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 2880) and 255 (450).

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.2 (6 H, m, 2 CH_3), 1.6-2.4 (4 H, m, 2 CH_2), 3.0-3.8 (3 H, m, CH_2 and CH),

^{13}C NMR spectrum ($CDCl_3$) : δ 12.31, 19.44 (CH_3), 26.37, 29.92, 34.42 (CH_2), 52.83 (CH) and 174.44 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 127 (M^+, 30), 112 (100), 84 (40), 70 (6) and 56 (15). Molecular weight calculated for $C_7H_{13}NO$: 127.0997. Found : 127.0098. (high resolution mass spectrometry).

c) Photosensitized addition of N-allyldiethylamine (2) to methyl crotonate (6). An argon-purged solution of a mixture of **2** (1.8 g, 15 mmol) and **6** (1.5 g, 15 mmol) in acetonitrile (350 mL), containing 10^{-4} M of **1** was irradiated for 4 h and separation of the photoproducts by column chromatography using a mixture (2:3) of petroleum ether and ethyl acetate gave 90 mg (40 %) of 1-ethyl-4,5-dimethyl-2-pyrrolidone (**8**) and 30 mg (10 %) of a 4-carbomethoxy-1-ethyl-2,3,5-trimethyl-piperidine (**9**), based on **6** that reacted (15 % conversion).

8: IR spectrum ν_{max} (neat) : 2970, 2882 (CH) and 1688 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.2 (9 H, m, 3 CH_3), 1.8-2.7 (3 H, m, CH_2 and CH) and 2.8-3.9 (3 H, m, CH_2 and CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 12.58, 12.79, 13.33, 14.58, 18.31, 18.46 (CH_3), 29.64, 30.96, 38.12, 39.69 (CH_2), 34.69, 34.93, 56.11, 60.41 (CH) and 174.26, 175.50 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 141 (M^+, 35), 126 (100), 98 (10), 78 (20) and 55 (18). Molecular weight calculated for $C_8H_{15}NO$: 141.1232. Found : 141.1238 (high resolution mass spectrometry)

9 : IR spectrum ν_{max} (neat) : 2976, 2860 (CH) and 1740 (ester) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 0.85-1.2 (12 H, m, 4 CH_3), 1.9-3.2 (8 H, m, 2 CH_2 and 4 CH) and 3.6-3.8 (3 H, s, OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 14.00-20.00 (CH_3), 32-36, 44.32-46.82, 50.85-55.28 and 172-175 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 213 (M^+, 15), 198 (100), 180 (12), 152 (10), 138 (25), 126 (30), 112 (28), 98 (20), 78 (50) and 56 (30). Molecular weight calculated for $C_{12}H_{23}NO_2$: 213.1728. Found : 213.1725 (high resolution mass spectrometry).

4.5.2. Photoelectron Transfer Catalyzed Reactions of N-Allylpiperidine (10) with α,β-Unsaturated Esters

a) Photosensitized addition of N-allylpiperidine (10) to methyl methacrylate (3). Irradiation of an argon-purged solution of a mixture of **10** (1.85 g, 15 mmol), **3** (1.5 g, 15 mmol) and **1** (10^{-4} M) in acetonitrile (350 mL) for 2 h and analysis of the product mixture on a GC-MS indicated 65 % yield of a diastereomeric mixture of **11**. The yield of **11** was based on **3**, that reacted (22 % conversion). The photoproduct **11** was isolated by column chromatography and its analytical results and spectral data were in good agreement with those of 2-methyl-3-indolizidone reported in Chapter 3 (Section **3.5.1**).[12]

b) Photosensitized addition of N-allylpiperidine (10) to methyl acrylate (5). An argon-bubbled solution of a mixture of **10** (1.85 g, 15 mmol) and **5** (1.3 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** was irradiated for 2 h and separation of the photoproduct mixture by column chromatography using a mixture (3:1) of petroleum ether and ethyl acetate gave 150 mg (55 %) of 3-indolizidone (**12**). The spectral data and analytical results were found to be identical to those of 3-indolizidone reported in Chapter 3 (Section **3.5.6**). The reported yield of **12** was based on 25% conversion of **5**, as estimated by HPLC.

c) Photosensitized addition of N-allylpiperidine (10) to methyl crotonate (6). Irradiation of an argon-bubbled solution of a mixture of **10** (1.85 g, 15 mmol) and **6** (1.5 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** for 2 h and separation of the reaction mixture by column chromatography using a solvent mixture (3:2) of petroleum ether and ethyl acetate gave 110 mg (40 %) of 1-methyl-3-indolizidone (**13**) and 20 mg (15 %) of the quinolizidine **14**. The yield of the products were based on 15 % conversion of **6**.

13: IR spectrum ν_{max} (neat) : 2980, 2865 (CH) and 1690 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.2 (3 H, d, CH_3), 1.4-2.2 (6 H, m, 3 CH_2), 2.3-2.8 (2 H, m, CH_2) and 3.2-3.8 (3 H, CH_2 and CH).

^{13}C NMR spectrum ($CDCl_3$): δ 14.73, 17.89 (CH_3), 23.20, 24.01, 24.37, 24.75, 26.25, 28.54, 31.50, 34.18, 38.39, 39.76 (CH_2), 41.33, 46.53, 60.38, 63.96 (CH) and 173.09, 173.27 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 153 (M^+, 69), 152 (100), 138 (20), 124 (15), 112 (18), 96 (10), 83 (35) and 55 (10). Molecular weight calculated for $C_9H_{15}NO$: 153.1188. Found : 153.1233 (high resolution mass spectrum).

14: IR spectrum ν_{max} (neat): 2970, 2860 (CH) and 1738 (ester) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.15 (6 H, 2 d, m, 2 CH_3), 1.4-2.0 (6 H, m, 3 CH_2), 2.4-3.3 (7 H, m, 2 CH_2 and 3 CH) and 3.6-3.8 (3 H, s, OCH_3).

^{13}C NMR spectrum ($CDCl_3$): δ 15.03, 16.82, 24.40, 24.69, 24.93, 25.38, 25.89, 29.65, 30.01, 47.10, 50.17, 54.53, 56.92, 59.18 and 174.12, 175.68 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 225 (M^+, 30), 210 (30), 196 (20), 166 (25), 150 (15), 124 (40), 98 (100), 83 (35) and 55 (15). Molecular weight calculated for $C_{13}H_{23}NO_2$:225.1788. Found : 225.1728 (high resolution mass spectrometry).

4.5.3. Photosensitized Addition of N-Allylpyrrolidine (15) to α,β-Unsaturated Esters

a) Photosensitized addition of N-allylpyrrolidine (15) to methyl methacrylate (3). An argon-purged solution of a mixture of **15** (1.65 g, 15 mmol) and **3** (1.5 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** was irradiated for 2 h and the product mixture on GC-MS analysis indicated a 50 % yield of **16**. The photoproduct was isolated using column chromatography and its spectral data were found to be identical to those of the previously characterized 2-methyl-3-pyrrolizidone, reported in Chapter 3 (Section **3.5.2**).[12] The yield of **16** was based on **3**, that reacted (15 % conversion).

b) Photosensitized addition of N-allylpyrrolidine (15) to methyl acrylate (5). Irradiation of an argon-bubbled solution of a mixture of **15** (1.65 g, 15 mmol) and **5** (1.3 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** for 2 h and separation of the product mixture by column chromatography using a solvent mixture (3:1) of petroleum ether and ethyl acetate gave 80 mg (50 %) of 3-pyrrolizidone (**17**). The spectral and analytical data of **17** were found to be identical to those of 3-pyrrolizidone reported in Chapter 3 (Section **3.5.7**). The yield of **17** was based on **5**, reacted (18 % conversion).

c) Photosensitized addition of N-allylpyrrolidine (15) to methyl crotonate (6). An argon-bubbled solution of a mixture of **15** (1.65 g, 15 mmol) and **6** (1.5 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** was irradiated for 2 h and separation of the product mixture by column chromatography using a mixture (3:2) of petroleum ether and ethyl acetate gave 80 mg (40 %) of a diastereomeric mixture of 1-methyl-3-pyrrolizidone (**18a,b**) and 30 mg (15 %) of the indolizidine **19**. These yields were based on percentage conversion of **6** (12 %). The sperctral

data of **18a,b** were found to be identical to those of 1-methyl-3-pyrrolizidones, reported in Chapter 3 (Section **3.5.8**).

19: IR spectrum ν_{max} (neat): 2980, 2860 (CH) and 1738 (ester) cm^{-1}.

^1H NMR spectrum ($CDCl_3$): δ 0.9-1.25 (6 H, m, 2 CH_3), 1.5-2.2 (4 H, m, 2 CH_2), 2.4-3.2 (6 H, m, 2 CH_2 and 2 CH), 3.2-3.5 (2 H, m, 2 CH) and 3.6-3.8 (3 H, m, OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 16.50, 16.80, 17.50, 21.56, 24.52, 25.08, 25.62, 26.86, 28.80, 29.72, 34.50, 38.15, 38.86, 43.22, 43.88, 55.10, 51.66, 53.78, 57.50, 58.62, 59.40 and 175.54-176.60 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 211 (M^+, 15), 196 (25), 180 (10), 152 (28), 110 (100), 96 (30), 83 (90), 70 (50) and 55 (40). Molecular weight calculated for $C_{12}H_{21}NO_2$: 211.1831. Found : 211.1928 (high resolution mass spectrum).

4.5.4. Photosensitized Addition of N-Allylcyclohexylamine (20) to Methyl Acrylate (5)

Irradiation of an agron-purged solution of a mixture of **20** (1.4 g, 10 mmol), **5** (1.3 g, 15 mmol) and **1** (10^{-4} M) in acetonitrile (350 mL) for 2 h and the product mixture upon GC-MS analysis indicated a 20 % yield of the spirolactam **21** and 75 % of unchanged **20**. The GC and GC-MS data of **21** were found to be identical to those of the spirolactam reported earlier in Chapter 3 (Section **3.5.3**).[12]

4.5.5. Photosensitized Addition of 1-Allyl-2,6-dimethylpiperidine (22) to Methyl Acrylate (5)

An argon-purged solution of a mixture of **22** (1.53 g, 10 mmol) and **5** (1.3 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of **1** was irradiated for 2 h and separation of the product mixture by column chromatography using a mixture (3:1) of petroleum ether and ethyl acetate gave 70 mg (30 %) of the bis- adduct **23**. The yield of **23** was based on **5**, that reacted (18 % conversion).

23: IR spectrum ν_{max} (neat) : 3300 (NH), 2985, 2860 (CH) and 1744 (ester) cm^{-1}.

^1H NMR spectrum $CDCl_3$) : δ 1.0-1.15 (6 H, 2 s, 2 CH_3), 1.2-1.4 (4 H, m, 2 CH_2), 1.5-2.0 (6 H, m, 3 CH2), 2.2-2.6 (4 H, m, 2 CH_2) and 3.6-3.75 (6 H, s, 2 OCH_3)

13C NMR spectrum ($CDCl_3$) : δ 28.07, 28.63 (CH_3), 37.32, 37.61, 39.94 (CH_2), 50.77 (C), 51.22 (OCH_3) and 174.73 (C=O, ester).

Mass spectrum, m/z (relative intensity): 286 (MH^+, 70), 270 (20), 254 (10), 198 (100), 154 (25), 130 (10), 115 (!5), 85 (30), 70 (38) and 55 (15). Molecular weight calculated for $C_{15}H_{27}NO_4$: 286.2018 (MH^+). Found (MH^+) : 286.2011 (high resolution mass spectrometry).

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Chapter 5. Anthraquinone-2-sulfonic Acid (Sodium Salt) Photosensitized Reactions of Primary, Secondary and Tertiary Amines with α,β-Unsaturated Esters in Water

5.1. Abstract

The anthraquinone-2-sulfonic acid (sodium salt) (**1**) sensitized photoaddition of some primary, secondary and tertiary amines with α,β-unsaturated esters in water have been investigated. The products obtained from the photosensitized reactions of tertiary amines in aqueous medium are very different from those obtained in acetonitrile. Whereas in acetonitrile multiple addition of the amines to olefinic substrates were observed, in aqueous solutions, the major products formed were the lactams. Thus, for example, the sensitized reaction of triethylamine (**2**) with methyl methacrylate (**3**) in water gave 1-ethyl-3,5-dimethyl-2-pyrrolidone (**4**) as the major product. Likewise, the reaction of **2** with methyl acrylate (**5**) gave 1-ethyl-5-methyl-2-pyrrolidione (**6**). In the case of primary and secondary amines, the products formed in aqueous media were similar to those observed in non-aqueous media. The reasons for the difference in reactivity of tertiary amines in aqueous media are discussed and a mechanism has been suggested for the formation of the lactams in the sensitized photoreaction of tertiary amines with α,β-unsaturated esters in water.

5.2. Introduction

For several years, study of organic raections in aqueous media have been limited mainly to electrochemical processes and aldol condensation reactions, whereas in nature several complex organic reactions are carried out in the aqueous environment. More recently, there has been a renewed interest in the study of

organic reactions in aqueous media, as this may offer several advantages over those occuring in organic solvents.[1-8] The aqueous medium is both economical and environmentally compatible and the need for special handling of inflamable and toxic organic solvent residues can also be avoided. Product isolation and catalyst recyclization may also be simplified in aqueous media. Carbon-carbon bond forming reactions are important in organic chemistry and the use of organic radicals for such reactions have been extensively explored.[9-11] However, there are very few reports on the study of such reactions in aqueous media, although a large amount of information on the reactive properties of the radicals in aqueous media have been documented from pulse radiolysis studies.[12]

The photoinduced electron transfer reactions of aminoketones in wet benzene was reported by Whitten and co-workers.[13] They have shown that aminoketones react with photoexcited electron acceptors such as anthraquinone and dicyanoanthracene via single electron quenching, ultimately leading to two electron redox products. The overall mechanism of this process involves the initial electron transfer from the aminoketones to the excited state of the sensitizer, followed by deprotonation to yield the α-aminoalkyl radical. This radical can be oxidised, presumably by dark (ground state) electron transfer to yield the iminium cation. The iminium cations are then rapidly hydrolysed to give secondary amines and the corresoponding carbonyl compound with the required stoichiometry.[14-16] The second oxidization step does not occur in some photochemical reactions owing to the absence of a suitable oxidant.[17] The mechanism proposed for the two electron oxidation is similar to that of the electrochemical oxidation of tertiary amines.[18]

The sensitizer selected for the present study is anthraquinone-2-sulfonic acid (sodium salt) (**1**). Using this sensitizer, the photoelectron transfer catalyzed reactions of several primary, secondary and tertiary amines with α,β-unsaturated esters in water, have been studied.

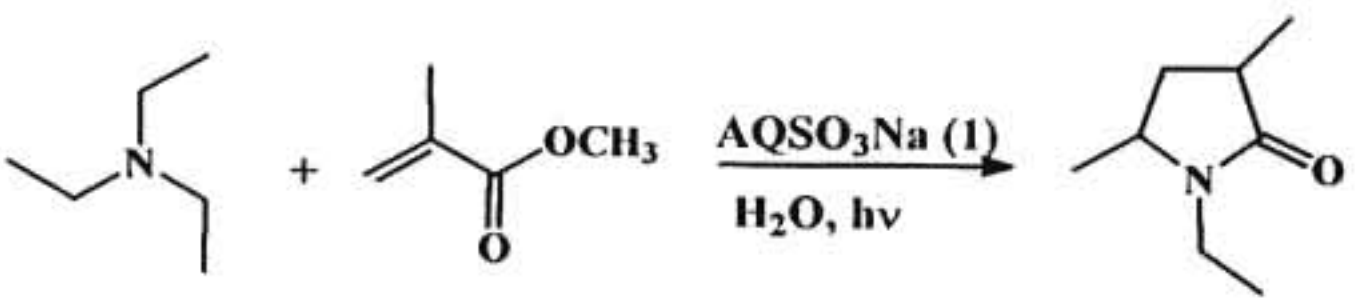
5.3. Results

5.3.1. Photosensitized Addition of Tertiary Amines to α,β-Unsaturated Esters

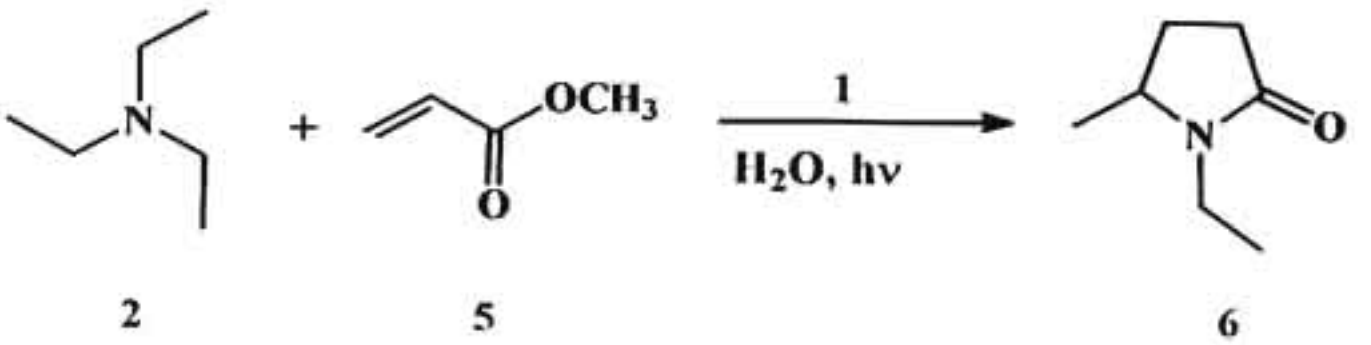
The photosensitized reaction of triethylamine (**2**) with methyl methacrylate (**3**) was studied by irradiating an argon-purged aqueous solution of triethylamine and methyl methacrylate containing anthraquinone-2-sulfonic acid (sodium salt) (**1**), under Pyrex filtered light ($\lambda > 290$ nm). One major product was isolated from the reaction mixture (**4**, Scheme 1) and was characterized on the basis of analytical results and spectral information as 1-ethyl-3,5-dimethyl-2-pyrrolidone. The spectral data of **4** were found to be identical to those of 1-ethyl-3,5-dimethyl-2-pyrrolidone reported in Chapter 4 (Section **4.5.1a**).

Photosensitized reaction of triethylamine (**2**) with methyl acrylate (**5**) was carried out by irradiating an argon saturated aqueous solution of a mixture of **2** and **5**, containing anthraquinone-2-sulfonic acid (sodium salt), under Pyrex filtered light. The major product isolated from the reaction mixture was 1-ethyl-5-methyl-2-pyrrolidone (Scheme 1), identified through spectral evidence and comparison with an authentic sample, obtained from the reaction of N-allyldiethylamine and methyl acrylate, reported in Chapter 4 (Section **4.5.1b**).

Similarly, the photosensitized reactions of N-methylpiperidine (**7**) and N-ethylpiperidine (**8**) with methyl acrylate (**5**) gave 3-indolizidone (**9**) as the major

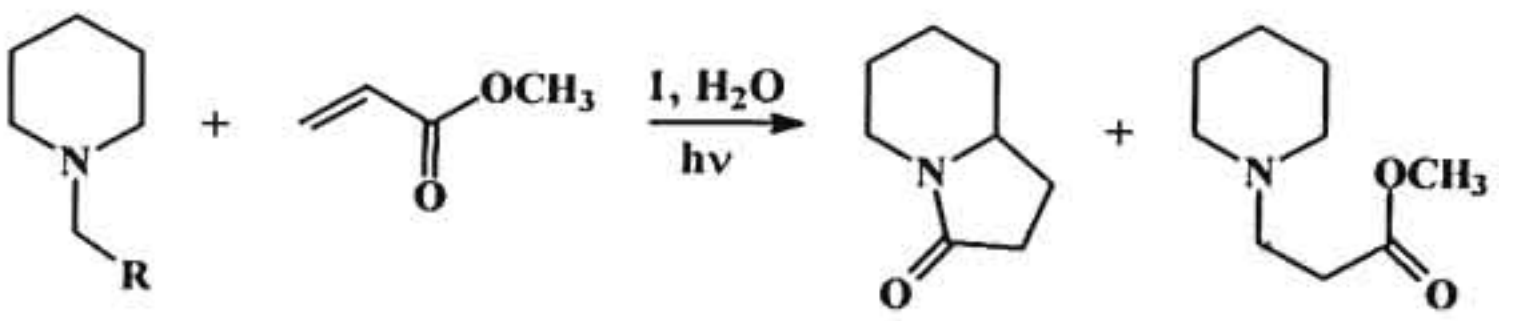


2 3 4



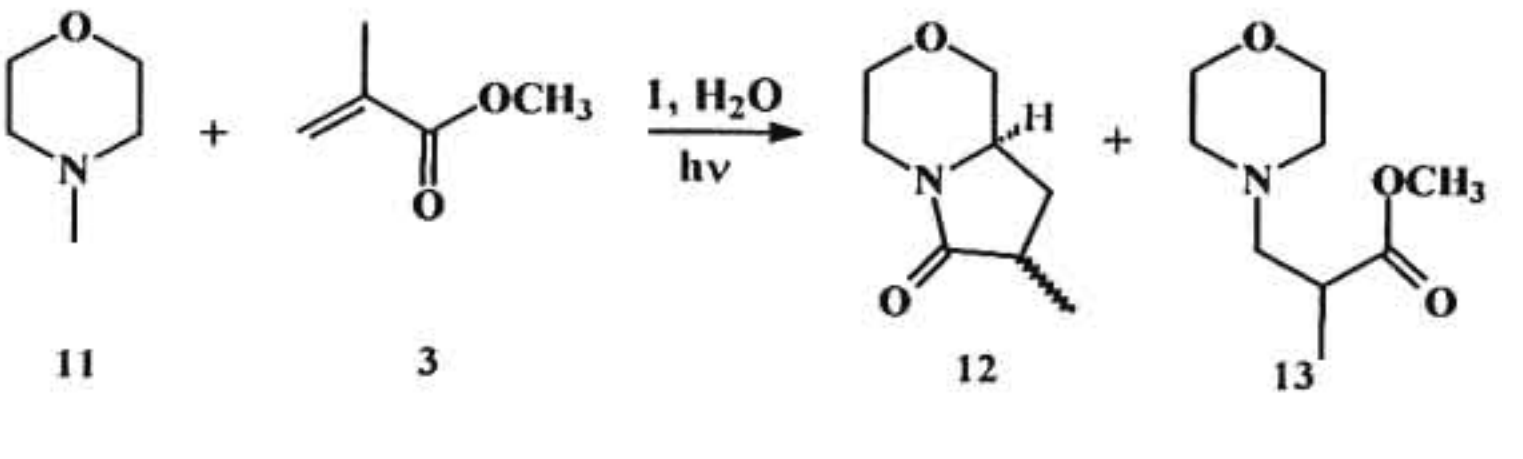
2 5 6

Scheme 1



7, R = H
8, R = CH_3

5 9 10



11 3 12 13

Scheme 2

product along with small amounts of methyl 3-(1-piperidinyl)propionate **10**, in each case (Scheme 2).

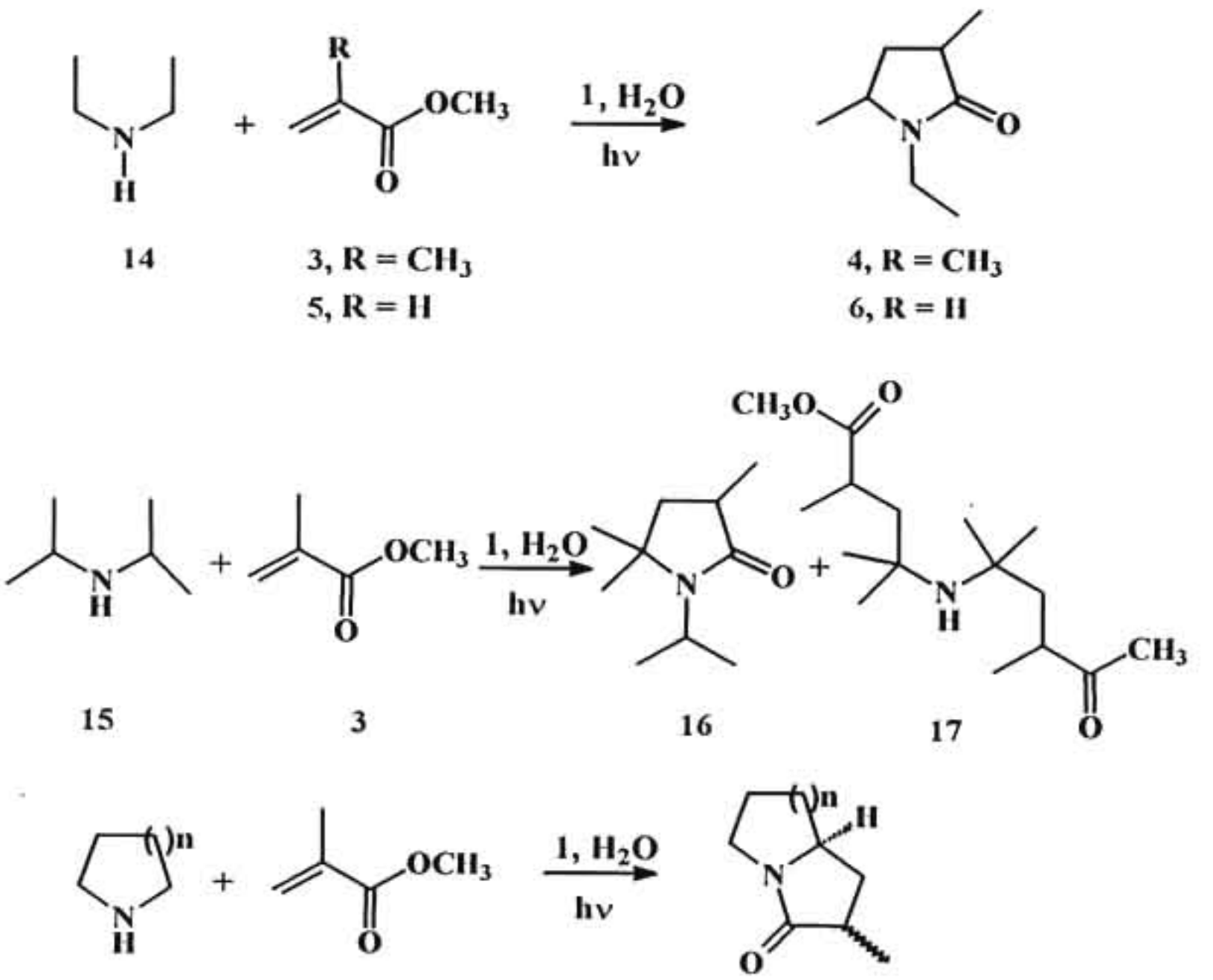
The photosensitized reaction of N-methylmorpholine (**11**) with methyl methacrylate (**3**) in aqueous medium gave a mixture of the bicyclic lactam **12** and the N-adduct, **13** (Scheme 2). The same mixture of products was formed in the anthraquinone-sensitized photoaddition of morpholine to methyl methacrylate (Section **3.5.9**).

5.3.2. Photosensitized Reactions of Secondary Amines with α,β-Unsaturated Esters

Photosensitized addition of diethylamine (**14**) with methyl methacrylate (**3**) in presence of the sodium salt of anthraquione-2-sulfonic acid in water gave 1-ethyl-3,5-dimethyl-2-pyrrolidone (**4**), whereas the reaction of **14** with methyl acrylate (**5**), under analogous conditions gave N-ethtyl-5-methyl-2-pyrrolidone (**6**) (Scheme 3). The same products **5** and **6** were obtained in the anthraquinone sensitized reactions of allyldiethylamine with methyl methacrylate and methyl acrylate, respectively (Section **4.5.1**). The photosensitized reactions of diisopropylamine (**15**) with methyl methacrylate (**3**), using anthraquinone-2-sulfonic acid (sodium salt) in water gave a mixture of the pyrrolidone derivative **16** and the bis-adduct **17** (Scheme 3). The same products were obtained in the anthraquinone sensitized photoreaction of diisopropylamine with methyl methacrylate (Section **2.5.4**).

In a similar manner, the sensitized photoreaction of piperidine (**18**) with **3** in aqueous medium gave a diastereomeric mixture (2:3) of the indolizidone **19** as the major product (Scheme 3). The same product (**19**) was obtained in anthraquinone

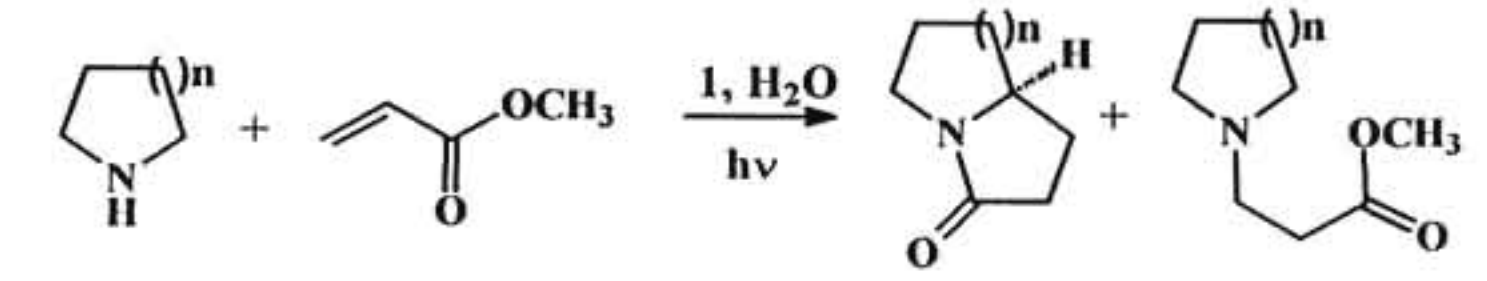
sensitized reaction between piperidine and methyl methacrylate, reported in Chapter 3 (Section **3.5.1**). The photosensitized reaction of pyrrolidine (**20**) with methyl methacrylate in water yielded a diastereomeric mixture (3:2) of the pyrrolizidone **21**. The structure of **21** was assigned as 2-methyl-3-pyrrolizidone by comparison of its spectral and analytical data with those of 2-methyl-3-pyrrolizidone reported in Chapter 3 (Section **3.5.2**) (Scheme 3).



Scheme 3

The photosensitized reaction between piperidine (**18**) and methyl acrylate (**5**) in water gave a mixture of the 3-indolizidone **9** and the N-adduct **10** (Scheme 4), identified through comparison of the spectral data with those obtained in the anthraquinone-sensitized photoreaction between piperidine and methyl methacrylate in acetonitrile (Section **3.5.6**). Similarly, the photosensitized reactions of pyrrolidine (**20**) with methyl acrylate (**5**) gave a mixture of the 3-pyrrolizidone (**22**) and the thermal N-addition product, methyl 3-(1-pyrrolidynyl)propionate (**23**) (Scheme 4). The anthraquinone-2-sulfonic acid (sodium salt) sensitized photoreaction of **20** with methyl crotonate (**24**) in aqueous medium gave a diastereomeric mixture (97:3) of **25a** (heliotridone) and **25b** (pseudoheliotridone), along with the N-adduct 26 (Scheme 4). The diastereomeric ratio of **25a** and **25b** was determined by GC analysis and the stereochemical assignment was made by comparing the ^{1}H NMR data with those reported for the same compounds in the literature.[19] The structure of **26** was assigned as the N-addition product, by comparing the spectral data and gas chromatographic retention time with those of the same product reported in Chapter 3 (Section **3.5.8**).

Anthraquinone-2-sulfonic acid (sodium salt) catalyzed photoreaction of morpholine (**27**) with methyl methacrylate (**3**) gave a diastereomeric mixture of the bicyclic lactam **12** along with the N-adduct **13** (Scheme 4). The structures of both **12** and **13** were established by comparison with the products obtained in the anthraquinone sensitized photoreaction between morpholine and methyl methacrylate (Section **3.5.9**).

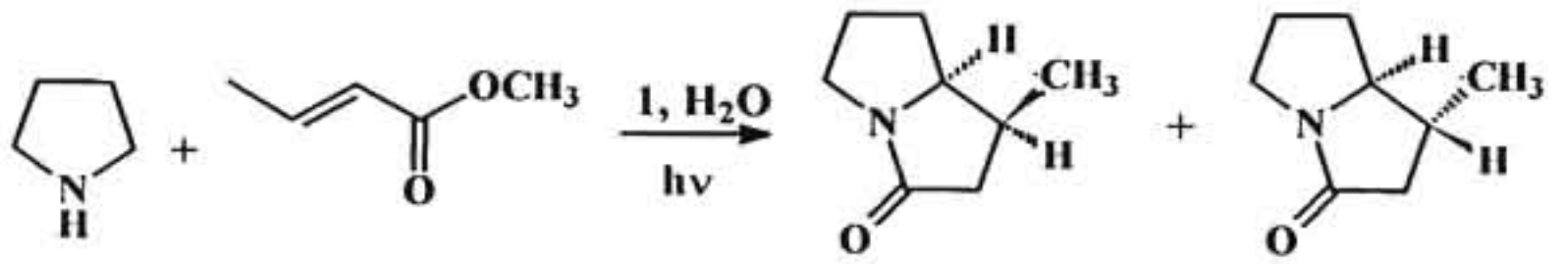


18, n = 2
20, n = 1

5

9, n = 2
22, n = 1

10, n = 2
23, n = 1

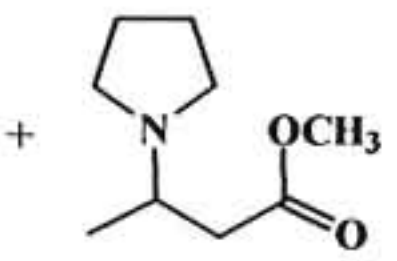


20

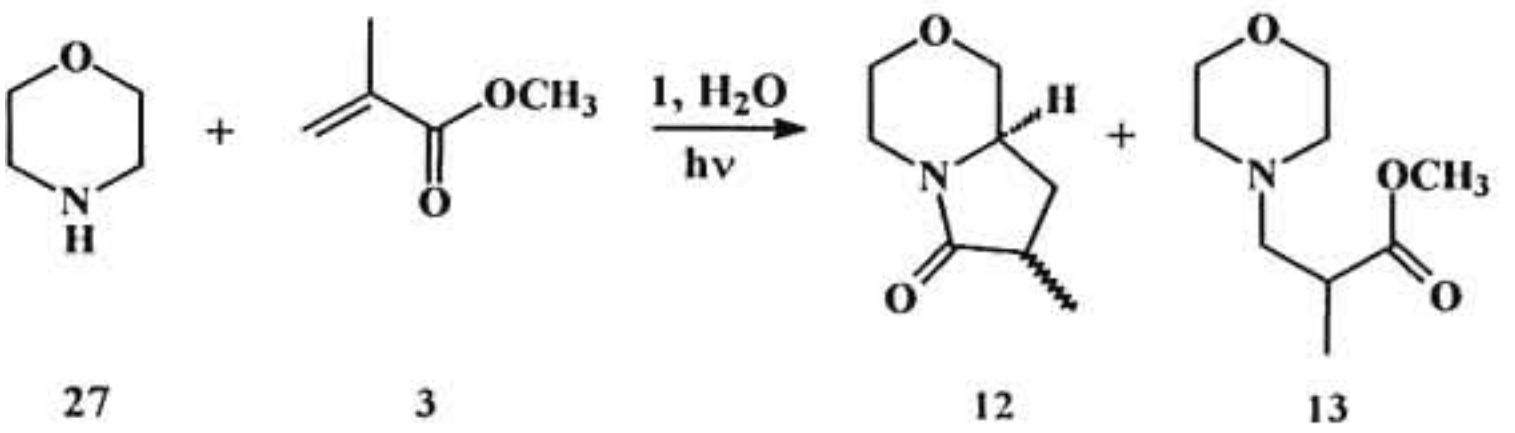
24

25a

25b



26



27

3

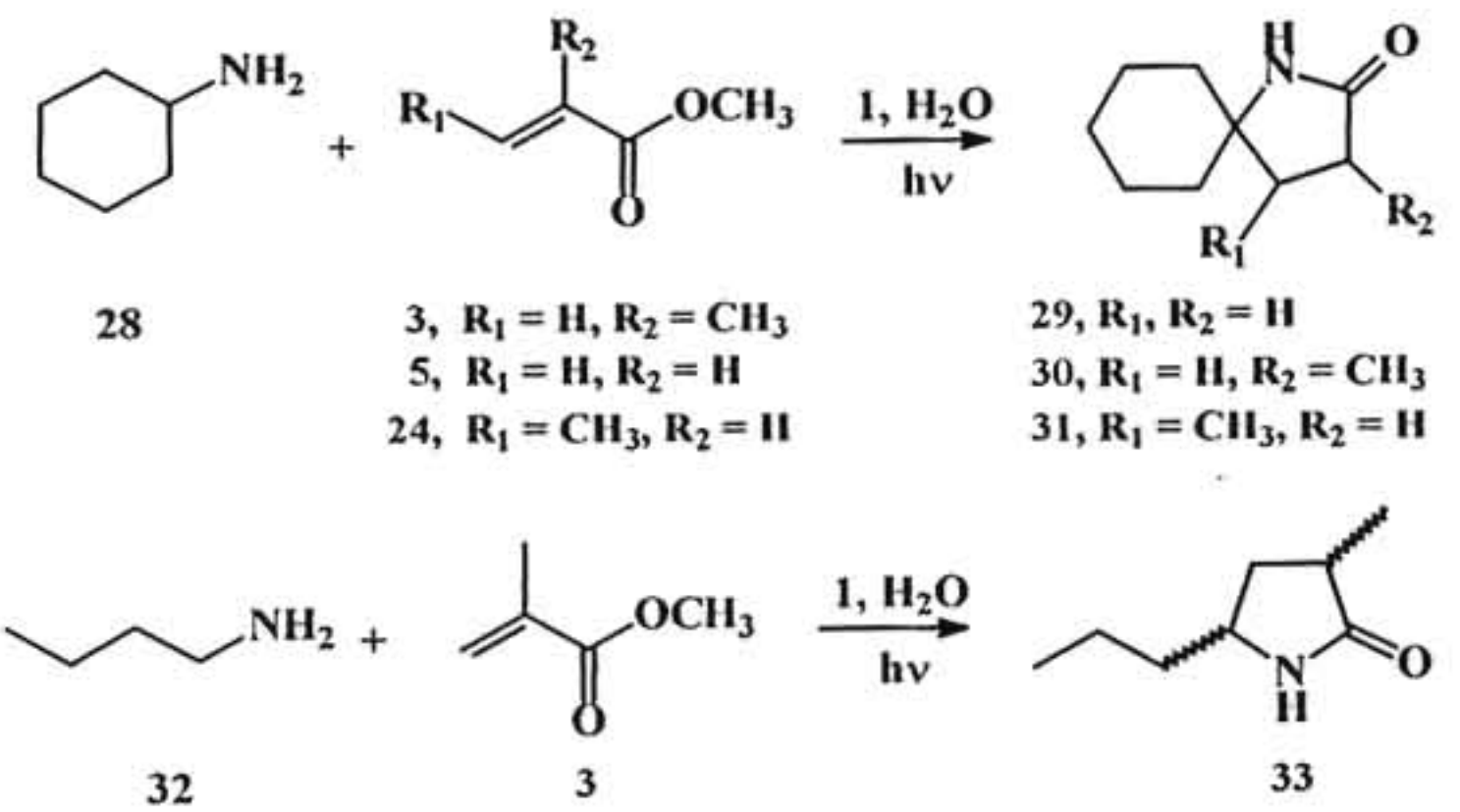
12

13

Scheme 4

5.3.3. Photosensitized Reactions of Primary Amines with α,β–Unsaturated Esters

The photosensitized addition of cyclohexylamine (**28**) to methyl methacrylate (**3**), methyl acrylate (**5**) and methyl crotonate (**24**) in aqueous media under Pyrex filtered light gave rise to the spirolactams **29**, **30** and **31**, respectively. The products were characterized on the basis of their spectral data and comparison with the same products obtained in the anthraquinone-sensitized photoreaction of cyclohexylamine with the appropriate α,β-unsaturated esters (Scheme **3.5.3-5**).



Scheme 5

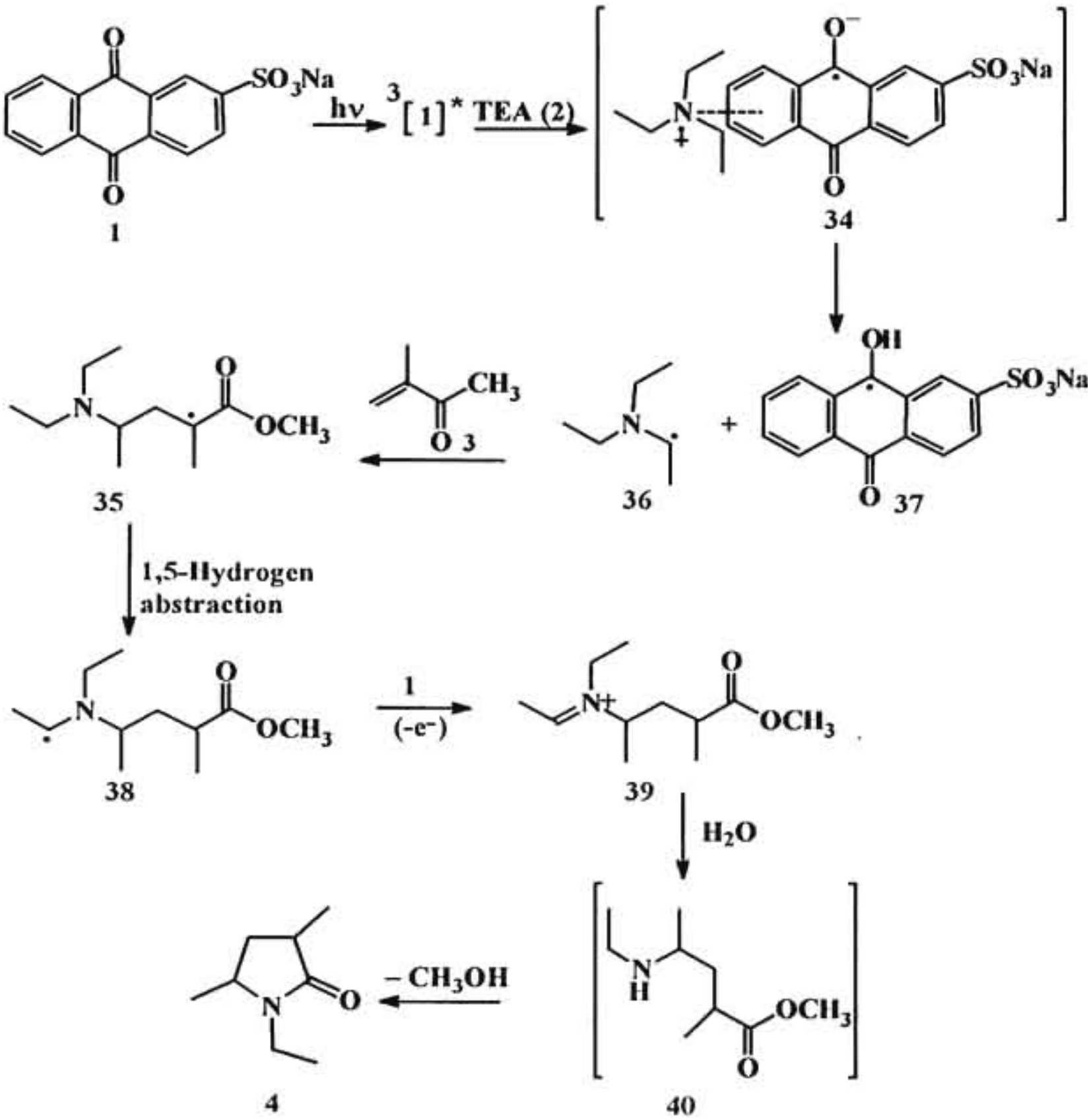
Similarly, the photosensitized addition of *n*-butylamine (**32**) to methyl methacrylate (**3**) in aqueous medium gave a diastereomeric mixture (2:3) of the pyrrolidone **33**. The structure of **33** was characterized on the basis of spectral information and analytical data. The IR spectrum of **33** showed an absorption

band at 1688 cm^{-1} due to a carbonyl group. The ^1H NMR spectrum of **33** showed multiplets at δ 0.85-1.0 (3 H) and δ 1.05-1.2 (3 H), assigned to the CH_3 protons. The methylene protons appeared as multiplets centered around δ 1.25-1.55 (4 H) and δ 1.75-1.95 (2 H), whereas the methine protons appeared as multiplets centered around δ 2.2-2.6 (1 H) and 3.2-3.7 (1 H). The broad peak around δ 7.5-7.8 (1 H, D_2O-exchangable) was assigned to the NH proton. The ^{13}C NMR spectrum of **33** showed three CH_3, six CH_2, four CH carbon signals, and two carbonyl carbon signals at δ 180.37 and 180.79. The mass spectrum of **33** showed a molecular ion peak at m/z 141, which is in good agreement with the assigned structure.

5.4. Discussion

5.4.1. Photosensitized Reactions of Tertiary Amines to α,β-Unsaturated Esters in Water

The formation of N-alkylpyrrolidones (**4** and **6**) and the bicyclic lactams (**9** and **12**) in the photosensitized reactions of tertiary amines with α,β-unsaturated esters in water (Schemes 1 and 2) is intriguing. As reported in Chapter 2, the reaction of tertiary amines with α,β-unsaturated esters in acetonitrile on the otherhand leads to multiple addition products (Section **2.4.1-4**). A probable pathway for the formation of the bicyclic lactams in the reactions of tertiary amines with α,β-unsaturated esters is shown in Scheme 6. The α-aminoalkyl radical **36**, that would be expected to be present in the photosensitized reaction of anthraquinone-2-sulfonic acid (sodium salt) (**1**) with triethylamine (**2**), for example, could add to methyl methacrylate (**3**) to give the radical adduct **35**. Such adduct radicals have been shown to undergo 1,5-hydrogen atom abstraction to give radicals such as **38**, which in turn can lead to multiple addition products, as


SO3Na
hν
3[1]*
TEA (2)
O⁻
SO3Na
1
34
OH
SO3Na
CH3
O 3
OCH3
35
36
+
O 37
1,5-Hydrogen
abstraction
OCH3
38
1
(-e⁻)
OCH3
39
H2O
– CH3OH
OCH3
4
40

Scheme 6

observed when the reaction is carried out in acetonitrile. In aqueous media, however, it appears that the radical **38** undergoes a further electron transfer, presumably through its interaction with the anthraquinone-2-sulfonate anion (**1**), leading to the iminium ion **39**. Subsequent hydrolysis of **39**, under work-up would lead to the secondary amine derivative **40** and ultimately to the pyrrolidone **4** (Scheme 6).

The difference in the reaction pathways in an organic solvent such as acetonitrile and in water may be due to the difference in the rates of reactions of the α-aminoalkyl radical **38** in these media. Water being highly polar compared to acetonitrile would favour electron transfer reactions over radical addition or radical quenching reactions. The relative enhancement in the rate of electron transfer in water may facilitate the dealkylation process.

It is interesting to note that in the anthraquinone-2-sodium sulfonate sensitized reactions of tertiary amines with α,β-unsaturated esters in acetonitrile yielded the multiple olefin added products. Thus, the difference in the reaction modes of tertiary amines in water and acetonitrile in the present case cannot be attributed to differences in the redox properties of anthraquinone and the sodium salt of anthraquinone sulfonate.

5.4.2. Photosensitized Addition of Primary and Secondary Amines to α,β-Unsaturated Esters

The products isolated from the sensitized photoreaction between primary and secondary amines with α,β-unsaturated esters in water were very similar to those formed in acetonitrile. Dealkylation, which appeared to be an important process in the corresponding reaction of the tertiary amines was not observed with

the primary and secondary amines. The dealkylation was assumed to occur via a mechanism involving an intramolecular 1,5-hydrogen atom abstraction of the adduct radical, followed by oxidation of the translocated radical to an iminium cation and subsequent hydrolysis of this cation during work-up (Scheme 6). The α-CH of primary and secondary amines are less labile than that of tertiary amines. Therefore the 1,5-hydrogen atom abstraction may not be facile in secondary amines (for primary amines this reaction cannot take place). In the case of diisopropylamine, the multiple olefin addition product was indeed observed and this may be attributed to the increased lability of α-CH brought about by alkyl substitution. The formation of the 2:1 ester-amine adduct, instead of dealkylation in the case of diisopropylamine suggests that the oxidation does not occur as easily as with secondary α-aminoalkyl radicals.

An interesting observation in the reaction of pyrrolidine with methyl crotonate in water was that a diastereoselectivity of 97:3 for the formation of pseudoheliotridone (**25b**) to heliotridone (**25a**) was observed (Scheme 4). The corresponding ratio in acetonitrile was 70:30 (see Section **3.3.8**). The reason for the changes in diastereoselectivity in water and acetonitrile are not quite clear.

5.5. Experimental Section

The instruments and methods adopted for the spectral recording and analytical data are same as those described in earlier Chapters (Chapters 2-4 of this thesis). Photochemical reactions were carried out under Pyrex filtered light using a 450 W medium pressure mercury lamp. Anthraquinone-2-sulfonic acid (sodium salt) from Aldrich was used after recrystallization from water. All other reagents and solvents were purified by distillation before use.

The general procedure of photolysis consisted of irradiation (2 h) of an argon or nitrogen-bubbled solution of the amine (15 mmol) and α,β-unsaturated ester (15 mmol) in water (500 mL) containing $5x10^{-4}$ M of anthraquinone-2-sulfonic acid (sodium salt) (**1**), using a 450 W medium pressure mercury lamp, kept in a Pyrex jacketed immersion well. The products were extracted with dichloromethane (5 x 50 mL) and dried over anhydrous sodium sulfate. The product mixture was chromatographed over silica gel (flash column, 230-400 mesh or Chromatotron). The photoproducts were finally purified using preparative HPLC. The yields reported are based on the α,β-unsaturated ester consumed, which was estimated in each case by HPLC. All new products were characterized on the basis of their spectral and high resolution mass data.

5.5.1. Photosensitized Reaction of Tertiary Amines with α,β-Unsaturated Esters

a) Photosensitized addition of triethylamine (2) to methyl methacrylate (3). Irradiation of a mixture of **2** (1.5 g,15 mmol) and **3** (1.5 g, 15 mmol) in water (500 mL) containing $5x10^{-4}$ M of anthraquinone-2-sulfonic acid (sodium salt) (**1**) for 2 h and separation of the product mixture by column chromatography using a mixture (3:1) of petroleum ether and ethyl acetate gave 80 mg (50 %) of 1-ethyl-3,5-dimethyl-2-pyrrolidone (**4**). The yield reported was based on **3**, that reacted (10%), as estimated by HPLC. The photoreaction was repeated several times, varying the duration of irradiation and it was found that prolonged irradiation (8 h), did not bring about greater conversion of **3**. The spectral and analytical data of **4** were similar to those reported for the same compound in Chapter 4 (Section **4.5.2a**).

b) Photosensitized reaction of triethylamine (2) with methyl acrylate (5). Irradiation (2 h) of an aqueous (500 mL) solution of a mixture of **2** (1.5 g, 15 mmol) and **5** (1.3 g, 15 mmol), containing $5x10^{-4}$ M of **1** and separation by column chromatography using a mixture (7:3) of petroleum ether and ethyl acetate gave 90 mg (70 %) of 1-ethyl-5-methyl-2-pyrrolidone (**6**). The yield of **6** was based on percentage conversion of **5** (12 %). The spectral and other analytical data of **6** were found to be similar to those reported for the same compound in Chapter 4 (Section **4.5.2b**).

c) Photosensitized addition of N-methylpiperidine (7) to methyl acrylate (5). Irradiation of a mixture of 7 (1.5 g, 15 mmol) and **5** (1.3 g, 15 mmol) in the presence of **1** in water for 2 h and product analysis by capillary GC-MS indicated the presence of 60 % of **9** and 20 % of **10**. The yields reported were based on the conversion of **5** (15 %),as estimated by HPLC. The spectroscopic data of **9** and **10** were identical to those reported for the same compounds in Chapter 3 (Section **3.5.6**).

d) Photosensitized addition of N-ethylpiperidine (8) to methyl acrylate (5). Irradiation (2 h) of a mixture of **8** (1.7 g, 15 mmol) and **5** (1.3 g, 15 mmol) in water (500 mL), containing **1** ($5x10^{-4}$ M) and analysis of the photoproduct mixture by GC-MS indicated the formation of 60 % of **9** and 15 % of **10**. These percentages are based on methyl acrylate conversion (17 %). The photoproducts (**9** and **10**) were separated using column chromatography and they were characterized by comparison of their spectral data with those of identical compounds reported in Chapter 3 (Section **3.5.6**).

e) Photosensitized addition of N-methylmorpholine (11) to methyl methacrylate (3). Irradiation of a mixture of **11** (1.5 g, 15 mmol), **3** (1.5 g, 15 mmol) and **1** ($5x\ 10^{-4}$ M) in water (500 mL) for 2 h and product analysis by capillary GC-MS indicated the formation of 30 % of a diastereomeric mixture of **12** and 30 % of **13**. The yields were based on the conversion of **3** (10%), as estimated by HPLC. The spectral data of **12** and **13** were in good agreement with those reported for the same compounds in Chapter 3 (Section **3.5.9**).

5.5.2. Photosensitized Addition of Secondary Amines to α,β-Unsaturated Esters

a) Photosensitized addition of diethylamine (14) to methyl methacrylate (3). An argon-purged solution of **14** (1.05 g, 15 mmol) and **3** (1.5 g, 15 mmol) in water (500 mL) containing $5x10^{-4}$ M of **1** was irradiated for 2 h. Product analysis by GC-MS indicated the formation of 50 % of **4**. The yield was based on **3**, that reacted (15 % conversion).

b) Photosensitized addition of diethylamine (14) to methyl acrylate (5). An argon-purged solution of **14** (1.05 g, 15 mmol) and **5** (1.3 g, 15 mmol) in water (500 mL) containing $5x10^{-4}$ M of **1** was irradiated for 2 h and product analysis through gas chromatography indicated the formation of 60 % of **6** (yield based on 12 % conversion of **5**).

c) Photosensitized addition of diisopropylamine (15) to methyl methacrylate (3). Irradiation of an argon-purged solution of **15** (1.5 g, 15 mmol), **3** (1.5 g, 15 mmol) and $5x10^{-4}$ M of **1** in water (500 mL) for 2 h and separation of the product mixture by column chromatography gave 90 mg (40 %) of **16** and 80 mg (35 %) of **17**. The yields were based on the amount of **3**, that reacted

(10 % conversion). The structures of **16** and **17** were confirmed through comparison of their gas chromatographic retention times and mass spctral data with those reported for identical compounds in Chapter 2 (Section **2.5.4**).

d) Photosensitized addition of piperidine (18) to methyl methacrylate (3). Irradiation of a mixture of **18** (1.3 g, 15 mmol), **3** (1.5 g, 15 mmol) and **1** ($5x10^{-4}$ M) in water (500 mL) for 2 h and separation of the product mixture by column chromatography gave 80 mg (60 %) of a diastereomeric mixture (2:3) of **19**. The yield was based on **3** that reacted (10 %). The spectroscopic and analytical data of **19** were in good agreement with those reported for the same compound in Chapter 3 (Section **3.5.1**).

e) Photosensitized addition of piperidine (18) to methyl acrylate (5). Irradiation of a mixture of **18** (1.3 g, 15 mmol), **5** (1.3 g, 15 mmol) and **1** ($5x10^{-4}$ M) in water (500 mL) for 2 h and separation of the product mixture by column chromatography gave 60 mg (40 %) of **9** and 50 mg (35 %) of **10**. These yields were based on **5**, that reacted (12 %), as estimated by HPLC. The spectroscopic and GC-MS data of **9** and **10** were in good agreement with those reported for the same compounds in Chapter 3 (Section **3.5.6**).

f) Photosensitized addition of pyrrolidine (20) to methyl methacrylate (3). Irradiation of an argon purged water solution (500 mL) of **20** (1.05 g, 15 mmol) and **3** (1.5 g, 15 mmol) containing $5x10^{-4}$ M of **1** for 2 h and product analysis by GC-MS indicated the formation of 70 % of a diastereomeric mixture (3:2) of **21**. The yield was based on **3**, that reacted (12 %). The spectral data of **21** were identical to those reported for the same compound in Chapter 3 (Section **3.5.2**).

g) Photosensitized addition of pyrrolidine (20) to methyl acrylate (5). Irradiation of a solution of **20** (1.05 g, 15 mmol) and **5** (1.3 g, 15 mmol) in water (500 mL) containing $5x10^{-4}$ M of **1** for 2 h and separation of the photoproducts by column chromatography gave 40 mg (30 %) of **22** and 60 mg (35 %) of **23**. The yields were based on **3** that reacted (10 %). The spectroscopic data of **22** and **23** were in good agreement with those reported in the Chapter 3 for the same compounds (Section **3.5.7**).

h) Photosensitized addition of pyrrolidine (20) to methyl crotonate (24). Irradiation of an argon-purged solution of **20** (1.05 g, 15 mmol) and **24** (1.5 g, 15 mmol) containing $5x10^{-4}$ M of **1** in water (500 mL) for 2 h and separation of the reaction mixture by column chromatography using a mixture (3:2) of petroleum ether and ethyl acetate gave 40 mg (45 %) of **25a,b** (diastereomeric mixture, 97:3) and 30 mg (30 %) of **26**. The yields are based on the percentage conversion of **24** (8 %). The spectroscopic data of **26** was in good agreement with those reported in Chapter 3 for the same compound (Section **3.5.8**).

25b: IR spectrum ν_{max} (neat) : 2972, 2880 (CH) and 1690 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.1-1.25 (3 H, d, CH_3), 1.8-2.3 (4 H, m, 2 CH_2), 2.4-2.7 (2 H, m, CH_2), 2.9-3.3 (1 H, m, CH) and 3.4-3.8 (3 H, m, CH_2 and CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 17.56 (CH_3), 26.57, 30.27, 40.98, 43.40 (CH_2), 37.55, 68.64 (CH) and 174.05 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 139 (M^+, 80), 124 (12), 115 (85), 96 (15), 83 (12), 70 (100) and 55 (10). Molecular weight calculated for $C_8H_{13}NO$: 139.0997. Found: 139.0990 (high resolution mass spectrometry).

i) Photosensitized addition of morpholine (27) to methyl methacrylate (3). Irradiation of an argon-purged solution of a mixture of **27** (1.3 g, 15 mmol), **3** (1.5 g, 15 mmol) and **1** ($5x10^{-4}$ M) in water (500 mL) for 2 h and product analysis by GC-MS indicated the formation of 30 % of a diastereomeric mixture (3:2) of **12** and 50 % of **13**. The percentage yields were based on the conversion of **3** (12 %), as estimated by HPLC. The spectral and analytical data of **12** and **13** were similar to those reported for the same compounds in Chapter 3 (Section **3.5.9**).

5.5.3. Photosensitized Addition of Primary Amines to α,β-Unsaturated Esters

a) Photosensitized addition of cyclohexylamine (28) to methyl methacrylate (3). Irradiation of a solution of **28** (1.5g, 15 mmol) and **3** (1.5 g, 15 mmol) in water (500 mL), containing $5x10^{-4}$ M of **1** for 2 h and separation of the photoproducts by column chromatography gave 120 mg (60 %) of **30** (m.p. 95-97 °C). The yield reported was based on **3**, that reacted (15%). The spectroscopic and analytical data of **30** were in good agreement with those reported for the same compound in Chapter 3 (Section **3.5.4**).

b) Photosensitized addition of cyclohexylamine (28) to methyl acrylate (5). Irradiation of an argon-purged solution of a mixture of **28** (1.5 g, 15 mmol), **5** (1.3 g, 15 mmol) and **1** ($5x10^{-4}$ M) in water (500 mL) for 2 h and separation of the reaction mixture by column chromatography gave 140 mg (70 %) of **29** (m.p. 106-108 °C). The yield was based on **5**, that reacted (18 %). The

spectroscopic data of **29** were identical to those reported for the same compound in Chapter 3 (Scheme **3.5.3**).

c) Photosensitized addition of cyclohexylamine (28) to methyl crotonate (24). Irradiation of an argon-purged water solution (500 mL) of a mixture of **28** (1.5 g, 15 mmol), **24** (1.5 g, 15 mmol) and **1** ($5x\ 10^{-4}$ M) for 2 h and separation of the reaction mixture gave 50 mg (40 %) of **31** (m.p. 92-94 °C). The yield of **31** was based on the conversion of **24** (10 %). The analytical and spectroscopic data of **31** were found to be identical to those reported for the same compound in Chapter 3 (Section **3.5.5**).

d) Photosensitized addition of *n*-butylamine (32) to methyl methacrylate (3). An argon-purged solution of a mixture of **32** (1.1 g, 15 mmol) and **3** (1.5 g, 15 mmol) in water (500 mL) containing $5x10^{-4}$ M of **1** was irradiated for 2 h and separation of the product mixture by column chromatography using a mixture (3:2) of petroleum ether and ethyl acetate gave 120 mg (60 %) of a diastereomeric mixture (3:2) of **33**. The yield was based on percentage conversion of **3** (15 %), as estimated by HPLC.

33: IR spectrum ν_{max} (neat) : 3340 (broad, NH), 2982, 2875 (CH) and 1688 (C=O) cm^{-1}.

UV spectrum λ_{max} (CH_3CN) : 205 nm (ε, 3100) and 254 (480)

^1H NMR spectrum ($CDCl_3$) : δ 0.8-1.0 (3 H, m, CH_3), 1.05-1.2 (3 H, m, CH_3), 1.25-1.55 (4 H, m, 2 CH_2), 1.7-1.95 (2 H, m, CH_2), 2.2-2.6 (1 H, m, CH), 3.2-2.7 (1 H, m, CH) and 7.5-7.8 (1 H, broad, NH, D_2O-exchangeable).

^{13}C NMR spectrum ($CDCl_3$) : δ 13.63, 15.74, 15.98 (CH_3), 18.70, 18.79, 35.08, 36.60, 38.39, 38.75 (CH_2), 34.99, 36.51, 51.84, 52.20 (CH) and 180.37, 180.79 (C=O, lactam).

Mass spectrum, m/z (relative intensity) : 141 (M^+, 15), 124 (10), 98 (100), 72 (20) and 55 (10). Molecular weight calculated for $C_8H_{15}NO$: 141.1153. Found : 141.1153 (high resolution mass spectroscopy).

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Chapter 6. Evaluation of Sensitizer Efficiency in the Photoelectron Transfer Catalyzed Reactions of Some Primary and Secondary Amines with α,β-Unsaturated Esters and Acrylonitrile

6.1. Abstract

A variety of sensitizers such as dicyanoanthracene, acridone, anthraquinone, benzophenone, anthrone and xanthone were screened for their ability to efficiently photocatalyze the reactions of primary and secondary amines with some α,β–unsaturated esters and acrylonitrile. Dicyanoanthracene and acridone were found to be inefficient, whereas, anthraquinone, benzophenone, anthrone and xanthone were found to be moderately efficient in photocatalyzing these reactions. There were some differences in the nature of the photoproducts formed in the anthraquinone-sensitized reactions as compared to those catalyzed by the other sensitizers. For example, the anthraquinone photosensitized reaction between piperidine (**1**) and methyl methacrylate (**2**) led predominantly to the formation of 2-methyl-3-indolizidone (**3**), whereas, with sensitizers such as benzophenone, anthrone or xanthone, along with **3**, substantial amounts of the indolizidone derivative **4** was obtained. Similarly, the anthraquinone photosensitized reaction of pyrrolidine (**5**) with methyl methacrylate (**2**) led predominantly to the formation of 2-methyl-3-pyrrolizidone (**6**) as the major product, whereas with benzophenone, xanthone or anthrone as sensitizers, along with **6**, the pyrrolidine derivative **7** was also formed. The difference in the product composition in the anthraquinone sensitized reactions as compared to those catalyzed by other sensitizers, could arise, due to the difference in the reactivities of the sensitizer ketyl radicals and a reasonable mechanism has been proposed to explain the observed results. The ability of these sensitizers to catalyze the reaction between amines such as

diisopropylamine and 2,6-dimethylpiperidine with olefinic substrates has also been investigated.

The best conversion efficiencies were observed when benzophenone was used as the sensitizer in high concentrations. Thus, for example, 4 h irradiation of cyclohexylamine (**11**) and methyl acrylate (**12**) in benzene containing $5x10^{-3}$ M of benzophenone led to 80 % conversion of 12. The yield of the spirolactam (**13**), based on conversion of **12** was 60 %.

6.2. Introduction

The anthraquinone-photocatalyzed reaction of amines with electron deficient olefinic substrates, described in the earlier chapters, appears to be a convenient method for constructing carbon-carbon bonds adjacent to nitrogen.[1] The reactions of some of the amines with α,β-unsaturated esters afford a simple one step procedure for constructing lactams including bicyclic lactams such as indolizidones, pyrrolizidones and spirolactams. The synthetic utility of this procedure however, is limited by its low conversion efficiency. Although during the initial stages of irradiation, the percentage conversion increases with increasing irradition time, after about 4 h, no further increase in conversion was observed. A possible contributing factor may be the inner filter effect, i.e., the products formed during irradiation may themselves absorb the incident light thereby preventing efficient excitation of the sensitizer.

Several known sensitizers such as acridone,[2] anthraquinone,[3] anthrone,[4,5] benzophenone[3,6], dicyanoanthracene[7,8] and xanthone[9-11] were screened for their ability to efficiently photosensitize the reactions of some primary and secondary

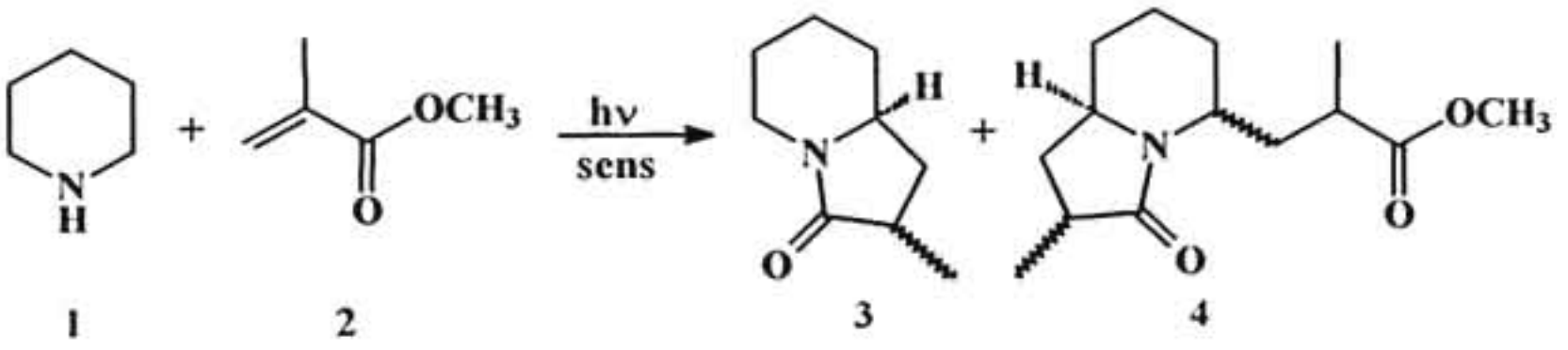
amines with electron deficient olefinic substrates in order to optimize the reaction conditions.

6.3. Results

6.3.1. Photoelectron Transfer Catalyzed Reactions of Piperidine (1) with Methyl Methacrylate (2)

The photosensitized reaction of piperidine (**1**) with methyl methacrylate (**2**) in presence of catalytic amounts of anthraquinone (10^{-4} M) led predominantly to the formation of 2-methyl-3-indolizidone (**3**). GC-MS analysis indicated the formation of also trace amounts (<5%) of the indolizidone derivative **4** (Scheme 1). Under similar conditions, with benzophenone, xanthone and anthrone as sensitizers, along with **3**, substantial amounts of **4** were also formed in each case. The structure of **3** was confirmed by comparing its gas chromatographic retention time and mass spectral data with those of 2-methyl-3-indolizidone, reported in Chapter 3 of this thesis (Section **3.3.1**). Compound **4** was isolated as a diastereomeric mixture, and was characterized on the basis of analytical results and spectral data. The IR spectrum of **4** showed an absorption band at 1744 cm^{-1} due to an ester carbonyl group and 1680 cm^{-1} due to an amide carbonyl group. The ^{1}H NMR spectrum of **4** showed a multiplet at δ 1.1-1.3 (6 H), which was assigned to the CH_3 protons of the diastereomers. The methylene protons (10 H) appeared as a multiplet at δ 1.4-2.2, whereas the multiplet at δ 2.3-2.6 was assigned to the two CH protons. The multiplet at δ 3.3-3.9 (5 H) has been assigned to three methoxy protons and two methine protons. The ^{13}C NMR spectrum of **4** showed several signals due to the isomeric mixture, out of which the signals at δ 177.81 and 178.05 have been assigned to two carbonyl carbons.

The mass spectrum of **4** showed the molecular ion peak at m/z 253, which is in agreement with the proposed structure.



1 2 3 4

Scheme 1

Table 1 lists the percentage conversion and product distribution under a variety of irradiation conditions. Anthraquinone did not sensitize this reaction in benzene whereas, with other sensitizers, the reactions were slightly more efficient in benzene than in acetonitrile. After work-up of the irradiated solution, anthraquinone could be recovered quantitatively, whereas substantial losses (20-30 %) were observed in the case of sensitizers such as benzophenone, anthrone and xanthone. In these cases, the formation of sensitizer dimers was observed. It was found that the best conversion efficiency was obtained when a substantially higher concentration of benzophenone (5 mM) was used to photo-catalyze these reactions (Table 1).

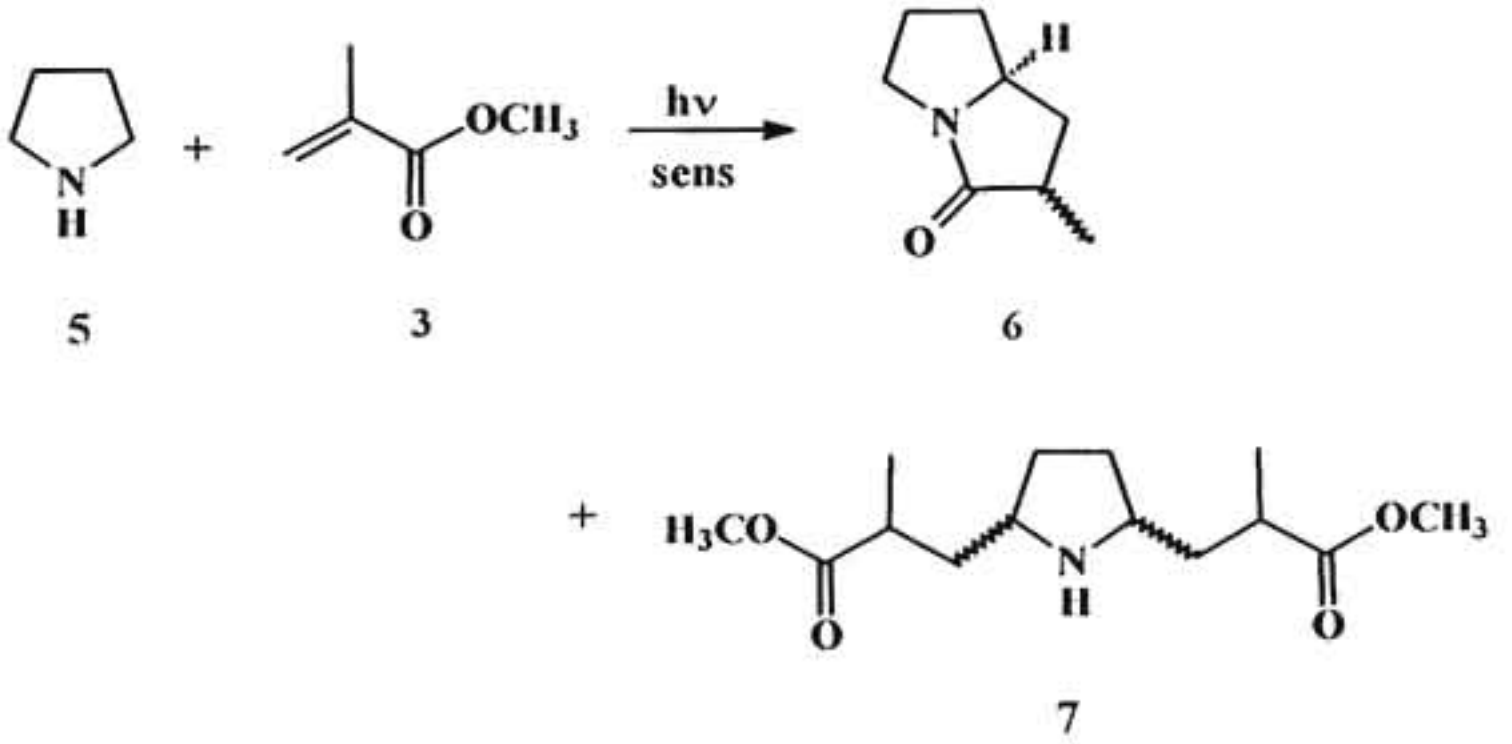
6.3.2. Photoelectron Transfer Catalyzed Reactions of Pyrrolidine (5) with Methyl Methacrylate (2)

The photosensitized addition of pyrrolidine (**5**) to methyl methacrylate (**2**) in the presence of catalytic amounts of anthraquinone (10^{-4} M) led to a diastereomeric mixture of 2-methyl-3-pyrrolizidone (**6**), as the major product. GC-MS analysis of the product mixture indicated the formation of trace amounts of

Table 1. Photosensitized addition of 15 mmol piperidine (**1**) to 15 mmol methyl methacrylate (**2**) in 350 mL of acetronitrile or benzene using a 450 W medium pressure Hanovia lamp (Pyrex filter)

No	Sensitizer	[Sensitizer] (M)	Solvent	Duration of irradiation h	% Conversion of **2**	Product distribution (%) **3**	**4**
1	Anthraquinone	10^{-4}	CH_3CN	2	20	80	<5
2	"	"	Benzene	2	10	–	–
3	Acridone	"	CH_3CN	4	8	–	–
4	Dicyanoanthracene	"	"	6	<5	–	–
5	Benzophenone	"	"	4	5	50	20
6	Xanthone	"	"	4	5	40	20
7	Benzophenone	10^{-3}	"	2	22	45	35
8	"	"	Benzene	2	25	60	30
9	"	$5x\ 10^{-3}$	"	4	70	58	28
10	"	"	CH_3CN	4	60	50	30
11	Anthrone	10^{-4}	CH_3CN	4	5	40	10
12	"	10^{-3}	"	2	20	40	15
13	"	"	Benzene	2	30	40	30
14	Xanthone	10^{-3}	"	2	20	30	40
15	"	"	CH_3CN	2	24	50	30

(<3%) of the pyrrolidine derivative 7 (Scheme 2). Under similar conditions, with benzophenone, anthrone or xanthone as sensitizer, formation of **6** and 7 as major products was observed. The structure of **6** was confirmed by comparing its gas chromatographic retention time and mass spectral data with those of 2-methyl-3-pyrrolizidone which was previously characterized as described in Chapter 3 (Section **3.3.2**).



5 3 6 7

Scheme 2

The photoproduct 7 was isolated as a diastereomeric mixture and was characterized on the basis of anlytical results and spectral data. The IR spectrum of 7 showed an absorption band at 3340 cm^{-1} due to an NH group and one at 1744 cm^{-1}, due to the ester carbonyl group. The ^1H NMR spectrum of 7 showed multiplets at δ 1.0-1.2 (6 H), assigned to the CH_3 protons and at δ 1.4-2.1 (8 H), assigned to the CH_2 protons. The two methine protons appeared as a multiplet centered around δ 2.2-2.8 and the multiplet at δ 3.4-3.9 (8 H) was assigned to two OCH_3 group protons and two CH protons. The ^1H NMR spectral data indicates that 7 is a 2:1 adduct of methyl methacrylate and pyrrolidine. The ^{13}C NMR

spectrum of 7 showed several signals due to the isomeric mixture, out of which the signals at δ 174.50 and 176.70 have been assigned to the ester carbonyl carbons. The mass spectrum of 7 showed the molecular ion peak at m/z 271, which is in good agreement with the assigned structure.

The percentage conversion of methyl methacrylate (**2**) and product distribution using different sensitizers are shown in Table 2. As in the case of the photosensitized addition of piperidine to methyl methacrylate, here also it has been observed that better conversion of methyl methacrylate is obtained on using benzophenone as the sensitizer and at higher concentrations (5 mM) in benzene. In the case of anthraquinone sensitized reactions, the sensitizer was recovererd quantitatively whereas, substantial losses were observed (~20-30 %) for benzophenone, anthrone and xanthone. In these cases, the formation of the sensitizer dimers was observed. Under identical conditions DCA and acridone were unable to sensitize this reaction.

6.3.3. Photoelectron Transfer Catalyzed Reactions of Diisopropylamine (8) with Methyl Methacrylate (2)

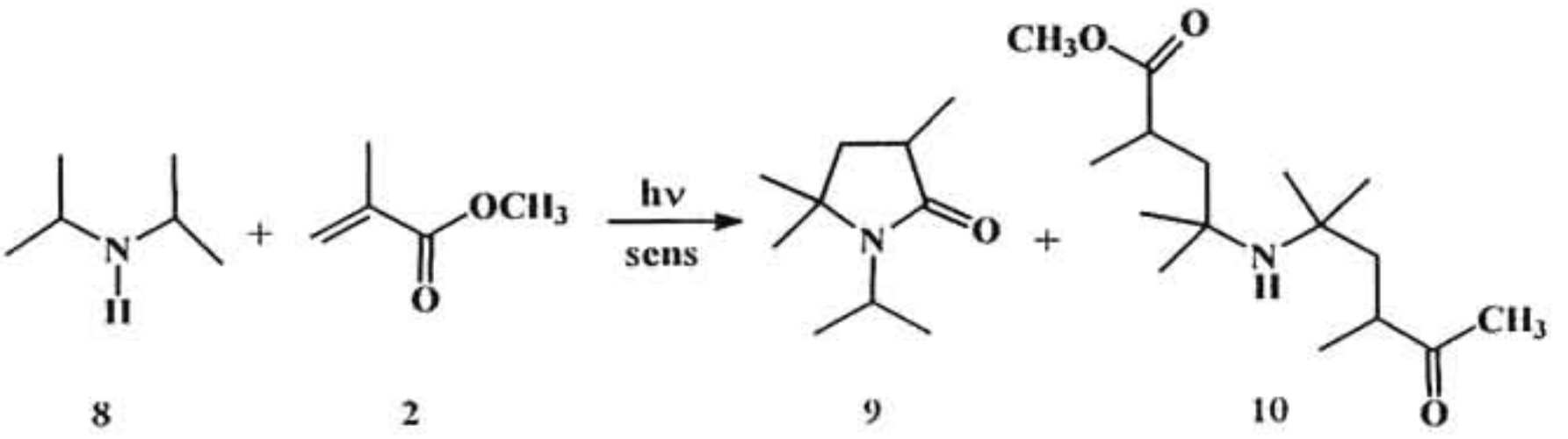
In order to examine the efficiency with which the various sensitizers photocatalyze the addition of diisopropylamine (**8**) to methyl methacrylate (**2**), argon bubbled solutions of **8** and **2**, containing sensitizers were irradiated by Pyrex filtered light of a medium pressure mercury lamp. The products formed in these reactions were 1-isopropyl-3,5,5-trimethyl-2-pyrrolidone (**9**) and the 2:1 ester-amine adduct **10** (Scheme 3). Their structures were established by comparing the gas chromatographic retention times and mass spectral data with those of the same compounds reported in Chapter 2 of this thesis (Section 2.3.4). The percentage conversion and the product distribution on using different sensitizers are shown in

Table 2. Photosensitized addition reactions of 15 mmol pyrrolidine (**5**) to 15 mmol methyl methacrylate (**2**) in 350 mL of acetonitrile or benzene using a 450 W medium pressure Hanovia lamp (Pyrex filter)

No	Sensitizer	[Sensitizer] (M)	Solvent	Duration of irradiation h	% Conversion of **2**	Product distribution (%)	
						6	**7**
1	Anthraquinone	10^{-4}	CH_3CN	2	18	80	<3
2	"	"	Benzene	2	5	–	–
3	Acridone	"	CH_3CN	4	<5	–	–
4	Dicyanoanthracene	"	"	6	<5	–	–
5	Benzophenone	"	"	4	5	40	20
6	Xanthone	"	"	4	5	30	20
7	Benzophenone	10^{-3}	"	2	20	35	25
8	"	"	Benzene	2	22	30	25
9	"	$5x\ 10^{-3}$	"	4	60	30	20
10	"	"	CH_3CN	4	50	30	25
11	Anthrone	10^{-3}	"	2	25	35	20
12	"	"	Benzene	2	28	40	25
13	Xanthone	"	"	2	22	35	25
14	"	"	CH_3CN	2	25	40	20

Table 3. The best conversion efficiency was obtained when benzophenone was used as the photosensitizer at higher concentrations (5 mM). DCA was found to be inefficient as a sensitizer for this reaction.

As in the earlier cases, anthraquinone could be recovered quantitatively from the reaction mixture, whereas substantial losses of sensitizers (~20-30 %), were observed with benzophenone, xanthone and anthrone. In these cases, the formation of the sensitizer dimers was observed.



8 2 9 10

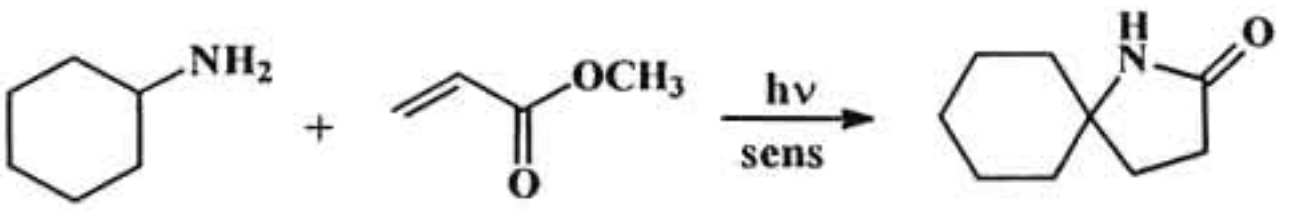
Scheme 3

6.3.4. Photoelectron Transfer Catalyzed Reactions of Cyclohexylamine (11) to Methyl Acrylate (12)

The photosensitized addition of cyclohexylamine (**11**) to methyl acrylate (**12**) in argon bubbled solutions in the presence of sensitizers was studied in acetonitrile and benzene. The product formed in these cases was the spirolactam **13** and its structure was confirmed by comparison of its gas chromatographic retention time and mass spectral data with those of an identical compound reported in Chapter 3 (Section **3.3.3**).

Table 3. Photosensitized addition of 15 mmol diisopropylamine (**8**) to 15 mmol methyl methacytlate (**2**) in 350 mL of acetonitrile or benzene using a 450 W medium pressure Hnovia lamp (Pyrex filter)

No	Sensitizer	[Sensitizer] (M)	Solvent	Duration of irradiation h	% Conversion of **2**	Product distribution (%) **9**	**10**
1	Anthraquinone	10^{-4}	CH_3CN	2	12	50	30
2	Acridone	"	"	2	20	8	35
3	Dicyanoanthracene	"	"	6	–	–	–
4	Benzophenone	"	"	2	5	30	20
5	"	10^{-3}	"	2	25	40	30
6	"	"	Benzene	2	22	40	30
7	"	$5x10^{-3}$	"	4	65	30	35
8	"	"	CH_3CN	4	55	35	40
9	Anthrone	10^{-3}	CH_3CN	2	25	30	60
10	"	"	Benzene	2	30	30	50
11	Xanthone	"	CH_3CN	2	22	35	30
12	"	"	Benzene	2	25	40	30



11 **12** **13**

Scheme 4

The percentage conversion of methyl acrylate (**12**) and product distribution, on using the various sensitizers are shown in Table 4. When benzophenone was used at higher concentrations (5 mM), better conversion of **12** was obtained. Under identical conditions, DCA and acridone were found to be inefficient. As in the earlier cases, anthraquinone could be recovered quantitatively from the reaction mixture, whereas substantial losses of sensitizers (~20-30 %) were observed for benzophenone, xanthone and anthrone. In these cases the formation of the sensitizer dimers was observed.

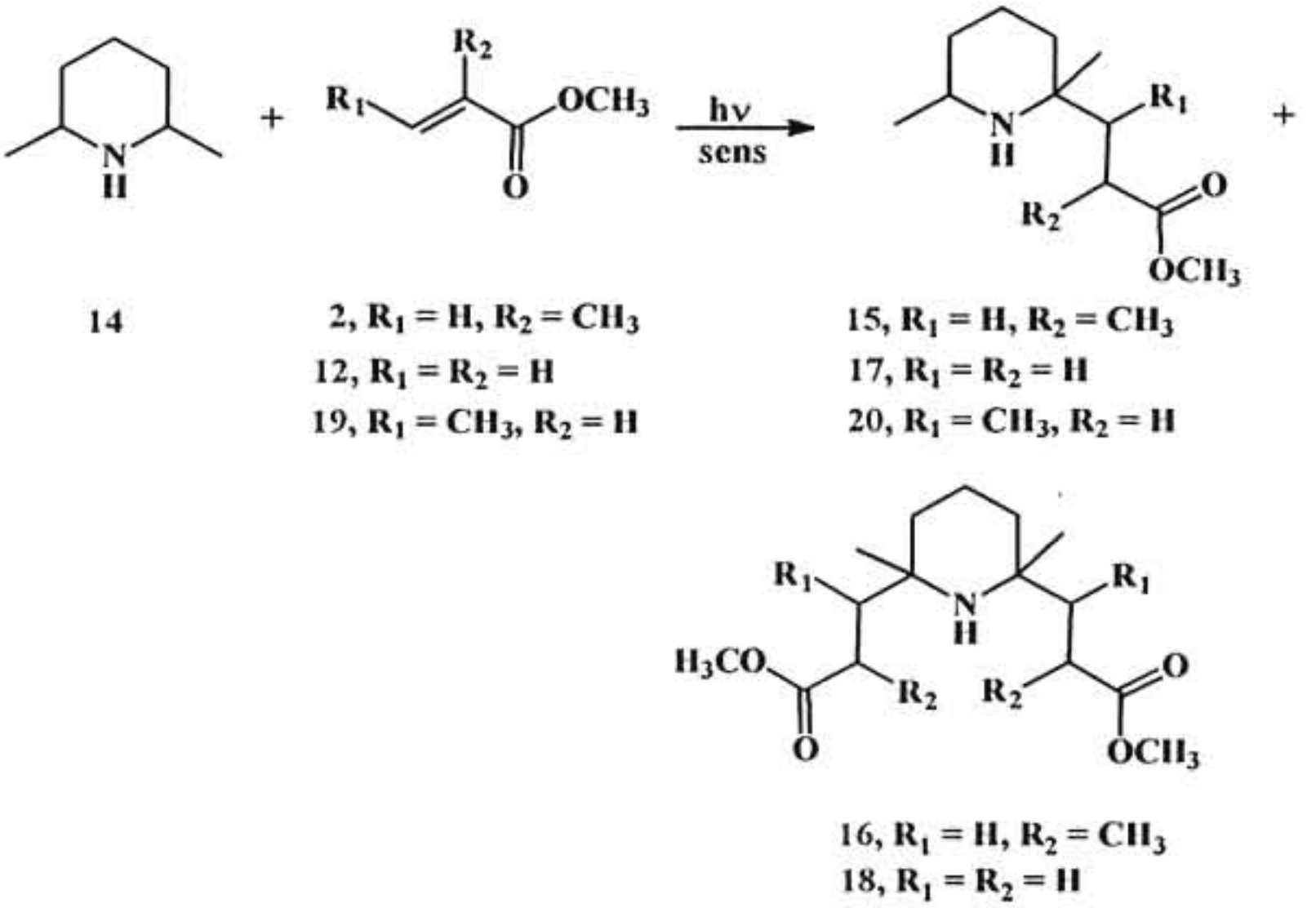
6.3.5. Photoelectron Transfer Catalyzed Reactions of 2,6-Dimethylpiperidine (14) with α,β-Unsaturated Esters and Nitriles

a) Photosensitized reaction of 2,6-dimethylpiperidine (14) with methyl methacrylate (2). Photosensitized reaction of 2,6-dimethylpiperidine (**14**) with methyl methacrylate (**2**) was studied by irrradiating argon-purged acetonitrile solutions of a mixture of **14** and **2**, containing the different sensitizers. Two products, **15** and **16** were isolated in each case and they were characterized on the basis of analytical data and spectral information (Scheme 5). The IR spectrum of **15**, for example, showed absorption bands at 3320 cm^{-1} due to an NH group and 1742 cm^{-1} due to an ester carbonyl group. The ^1H NMR spectrum of **15** showed multiplets at δ 1.0-1.3 (9 H), assigned to CH_3 protons and at δ 1.5-2.2 (8 H),

Table 4. Photosensitized addition reaction of 15 mmol cyclohexylamine (**11**) to 15 mmol methyl acrylate (**12**) in 350 mL of acetonitrile or benzene using Pyrex filtered light using a 450 W medium pressure Hanovia lamp

No	Sensitizer	[Sensitizer] (M)	Solvent	Duration of irradiation (h)	%Conversion of **12**	Product distribution (%) **13**
1	Anthraquinone	10^{-4}	CH_3CN	4	32	80
2	"	"	Benzene	4	38	80
3	Benzophenone	"	CH_3CN	4	10	60
4	"	10^{-3}	"	4	40	55
5	"	"	Benzene	4	44	60
6	"	$5x\ 10^{-3}$	"	4	80	60
7	"	"	CH_3CN	4	70	65
8	Xanthone	10^{-4}	CH_3CN	4	8	62
8	Xanthone	10^{-3}	Benzene	4	45	65
9	Anthrone	10^{-4}	"	4	12	60
10	"	10^{-3}	"	4	40	50

assigned to CH_2 protons. The multiplet centered around δ 2.3-3.0 (2 H) was assigned to two CH protons, whereas the singlet centered around δ 3.6-3.7 (3 H) was assigned to the methoxy protons. The NH proton (1 H) appeared as a broad signal centered around δ 5.5-5.8. The ^{13}C NMR spectrum of **15** showed several signals, out of which the one at δ 177.57 was assigned to the ester carbonyl carbon. The mass spectrum of **15** showed a molecular ion peak at m/z 213, which is in good agreement with the assigned structure.



14

2, R_1 = H, R_2 = CH_3
12, R_1 = R_2 = H
19, R_1 = CH_3, R_2 = H

15, R_1 = H, R_2 = CH_3
17, R_1 = R_2 = H
20, R_1 = CH_3, R_2 = H

16, R_1 = H, R_2 = CH_3
18, R_1 = R_2 = H

Scheme 5

The IR spectrum of **16** showed absorption bands at 3320 cm^{-1} due to an NH group and at 1740 cm^{-1} due to an ester carbonyl group. The ^1H NMR spectrum of **16** showed multiplets at δ 0.9-1.2 (12 H), assigned to CH_3 protons,

and at δ 1.4-2.2 (10 H), assigned to five CH_2 protons. The multiplet around δ 2.3-2.8 (2 H) has been assigned to CH protons, whereas the methoxy protons (6 H) appeared as a singlet at δ 3.6-3.7. The ^{13}C NMR spectrum of **16** showed four CH_3, four CH_2, two CH, one quarternary carbon and two methoxy carbon signals, and two ester carbonyl carbon signals at δ 178.31 and 178.56. The mass spectrum of **16** showed a molecular ion peak at m/z 313, which is in good agreement with the assigned structure. The product distribution and percentage conversion of **2** under different irradiation conditions are shown in Table 5. Anthraquinone was recovered quantitatively after the reaction, whereas, in the case of sensitizers such as benzophenone, xanthone and anthrone, substantial losses (~20-30 %) were observed. In these cases, the formation of the sensitizer dimers was observed.

Table 5. Photosensitized addition of 2,6-dimethylpiperidine (**14**) (15 mmol) to methyl methacrylate (**2**) (15 mmol) in 350 mL acetonitrile solution at 298 K for 4 h using a 450 W medium pressure Hanovia lamp (Pyrex filter)

No.	Sensitizer	[Sensitizer] (M)	% Conversion of **2**	Product distribution (%)	
				15	**16**
1	Anthraquinone	10^{-4}	40	45	35
2	Benzophenone	"	10	40	30
3	Xanthone	"	12	40	30
4	Benzophenone	10^{-3}	42	40	30
5	Xanthone	"	38	50	30
6	Benzophenone	$5x10^{-3}$	70	45	30

Photosensitized addition of 2,6-dimethylpiperidine (14) to methyl acrylate (12). The photosensitized addition of **14** to methyl acrylate (**12**) yielded two products (**17** and **18**, Scheme 5), which were characterized on the basis of

analytical data and spectral evidence. The IR spectrum of **17** showed an absorption band at 3350 cm^{-1} due to an NH group and a band at 1744 cm^{-1} due to an ester carbonyl group. The ^{1}H NMR spectrum of **17** showed multiplets at δ 1.0-1.2 (6 H), assigned to CH_3 protons and at δ 1.4-2.0 (8 H), assigned to CH_2 protons. The multiplet centered around δ 2.2-2.8 (3 H) has been assigned to the CH_2 protons and one CH proton, whereas the methoxy protons (3 H) appeared as a singlet at δ 3.5-3.7. The ^{13}C NMR spectrum of **17** showed two CH_3, five CH_2, two CH, one quarternary carbon and one methoxy carbon signals, and a carbonyl carbon signal at δ 174.73. The mass spectrum of **17** showed a molecular ion peak at m/z 199, which is in agreement with the assigned structure.

The IR spectrum of **18** showed an absorption band at 3350 cm^{-1} due to an NH group and at 1742 cm^{-1} due to an ester carbonyl group. The ^{1}H NMR spectrum of **18** showed two singlets at δ 1.0-1.2 (6 H), assigned to the CH_3 protons and multiplets at δ 1.3-2.0 (10 H) and δ 2.2-2.6 (4 H), assigned to the CH_2 protons. The singlet at δ 3.6-3.7 (6 H) has been assigned to the methoxy protons. The ^{13}C NMR spectrum of **18** showed one CH_3, four CH_2, one CH and one quarternary carbon signals, and a carbonyl carbon signal at δ 174.73. The mass spectrum of **18** showed a molecular ion peak m/z at 285, which is in good agreement with the assigned structure.

The percentage conversion of the starting material (**12**) and product distribution under different irradiation conditions are shown in Table 6. Anthraquinone was recovered quantitatively after the reaction whereas, substantial losses of sensitizers (20-30 %) were observed in the case of benzophenone, anthrone and xanthone. In these cases the formation of the sensitizer dimers was observed.

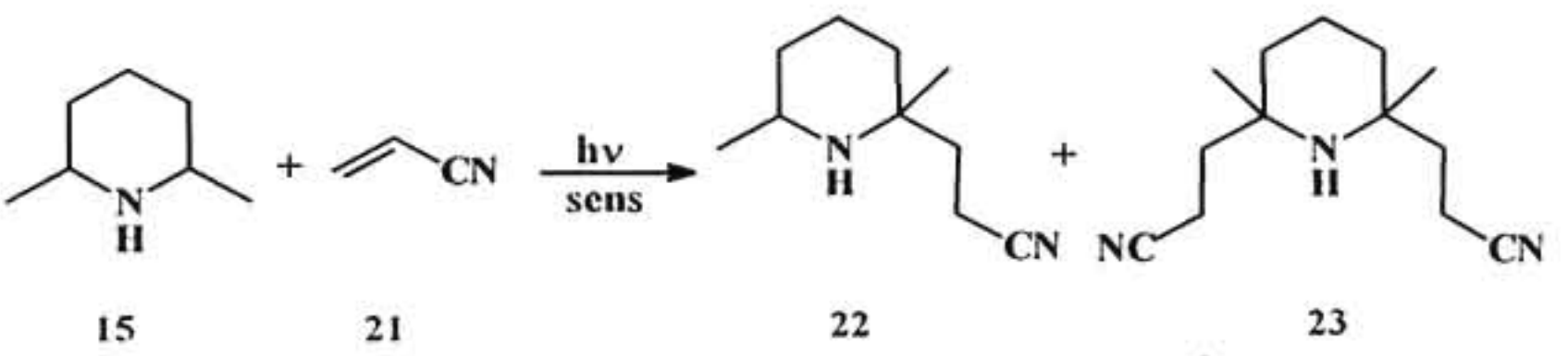
Table 6. Photosensitized addition reaction of 2,6-dimethylpiperidine (**14**) (15 mmol) to methyl acrylate (**12**) (15 mmol) in acetonitrile (350 mL) at 298 K for 4 h using Pyrex filtered light of a medium pressure Hanovia lamp

No	Sensitizer	[Sensitizer] (M)	% Conversion of **12**	Product distribution (%) **17**	**18**
1	Anthraquinone	10-4	45	40	40
2	Benzophenone	"	15	35	30
3	Xanthone	"	12	35	30
4	Benzophenone	10-3	45	30	30
5	Xanthone	"	40	35	30
6	Benzophenone	5x10-3	75	40	30

Photosensitized addition reactions of 2,6-dimethylpiperidine (14) to methyl crotonate (19). Photosensitized addition of 2,6-dimethylpiperidine (**14**) to methyl crotonate (**19**) was effected by irradiating argon-purged acetonitrile solutions of **14** and **19**, containing sensitizers such as anthraquinone, benzophenone or xanthone. One major product **20** (Scheme 5) was isolated in each case and it was characterized on the basis of analytical results and spectral data. The IR spectrum of **20**, for example, showed absorption bands at 3360 cm^{-1} due to an NH group and at 1738 cm^{-1} due to an ester carbonyl group. The ^{1}H NMR spectrum of **20** showed two doublets at δ 0.9-1.05 (3 H) and 1.05-1.15 (3 H), and a singlet at δ 1.25 (3 H), assigned to the methyl protons. The multiplet at δ 2.0-2.8 (4 H) was assigned to two CH_2 protons and two CH protons. The methoxy protons (3 H) appeared as a singlet centered around δ 3.5-3.7 and the NH proton (1 H) appeared as a broad singlet at δ 7.8-8.1. The ^{13}C NMR spectrum of **20** showed three CH_3, four CH_2, two CH, one quarternary carbon and one methoxy carbon signals, and an ester carbonyl carbon signal at δ 173.96. The mass spectrum of **20** showed a

molecular ion peak at m/z 214, which is in good agreement with the assigned structure. On using anthraquinone (10^{-4} M) as sensitizer, a 18 % conversion of **19** was observed, whereas under similar conditions, xanthone and benzophenone were found to be inefficient sensitizers. However, on using higher concentrations (5 mM) of benzophenone or xanthone, the conversion efficiencies of methyl crotonate (**19**) were found to be 35% and 28%, respectively.

Photoelecron transfer catalyzed reaction of 2,6-dimethylpiperidine (14) with acrylonitrile (21). The photosensitized addition of **14** to **21**, under argon atmosphere, led to the formation of a mixture of **22** and **23** (Scheme 6).



15 21 22 23

Scheme 6

The photoproducts (**22** and **23**)were characterized on the basis of spectral evidence and analytical results. The IR spectrum of **22**, for example, showed a broad absorption band at 3340 cm^{-1} due to an NH group and one at 2240 cm^{-1} due to a nitrile group. The ^1H NMR spectrum of **22** showed a multiplet at δ 1.0-1.2 (6 H), assigned to the two sets of CH_3 protons. The multiplet centered around δ 1.4-2.0 (8 H) has been assigned to the CH_2 protons, whereas the multiplet at δ 2.1-2.6 (3 H) has been assigned to two methylene and one methine protons. The ^{13}C NMR spectrum of **22** showed two CH_3 carbon, five CH_2 carbon, one CH carbon and one quarternary carbon signals besides a nitrile

carbon signal at δ 120.38. The ^{1}H and ^{13}C NMR spectral data suggest that **22** is a 1:1 adduct of acrylonitrile and 2,6-dimethylpiperidine. The mass spectrum of **22** showed a molecular ion peak at m/z 156, which is in agreement with the proposed structure.

The IR spectrum of **23**, showed a broad absorption band at 3360 cm^{-1} due to an NH group and one at 2242 cm^{-1} due to a nitrile group. The ^{1}H NMR spectrum of **23** showed two singlets at δ 1.0-1.2 (6 H), which were assigned to the CH_3 prorons. The multiplets centered around δ 1.2-1.4 (4 H), at δ 1.5-2.0 (6 H), and at δ 2.3-2.6 (4 H) were assigned to the CH_2 protons. The ^{13}C NMR spectrum of **23** showed two CH_3 carbon, seven CH_2 carbon and two quarternary carbon signals, besides two nitrile carbon signals at δ 120.49 and 120.76, respectively. The ^{1}H and ^{13}C NMR spectral data suggest that **23** is an isomeric mixture of a 2:1 adduct of acrylonitrile and 2,6-dimethylpiperidine. The mass spectrum of **23** showed the molecular ion peak at m/z 219 which is in good agreement with the assigned structure.

Table 7. Photosensitized addition of 15 mmol 2,6-dimethylpiperidine (**14**) to 15 mmol acrylonitrile (**21**) in 350 mL of acetonitrile for 4 h using Pyrex filtered light of a medium pressure Hanovia lamp

No.	Sensitizer	[Sensitizer] (M)	% Conversion of **21**	Product distribution (%) **22**	**23**
1	Anthraquinone	10^{-4}	30	30	50
2	Benzophenone	"	10	40	45
3	Xanthone	"	8	40	40
4	Benzophenone	10^{-3}	35	25	40
5	Xanthone	"	40	30	45
6	Benzophenone	$5x10^{-3}$	70	25	50

Table 7 lists the percentage conversion of the starting material (**21**) and product distributions of **22** and **23**, under varying conditions. On using xanthone and benzophenone as sensitizers, the percentage conversions were found to be better. Anthraquinone used in this reaction was recovered quantitatively and substantial losses of sensitizers were observed (~20-30 %) in the case of benzophenone, xanthone and anthrone. In these cases, the sensitizer dimers were formed in appreciable amounts.

6.4. Discussion

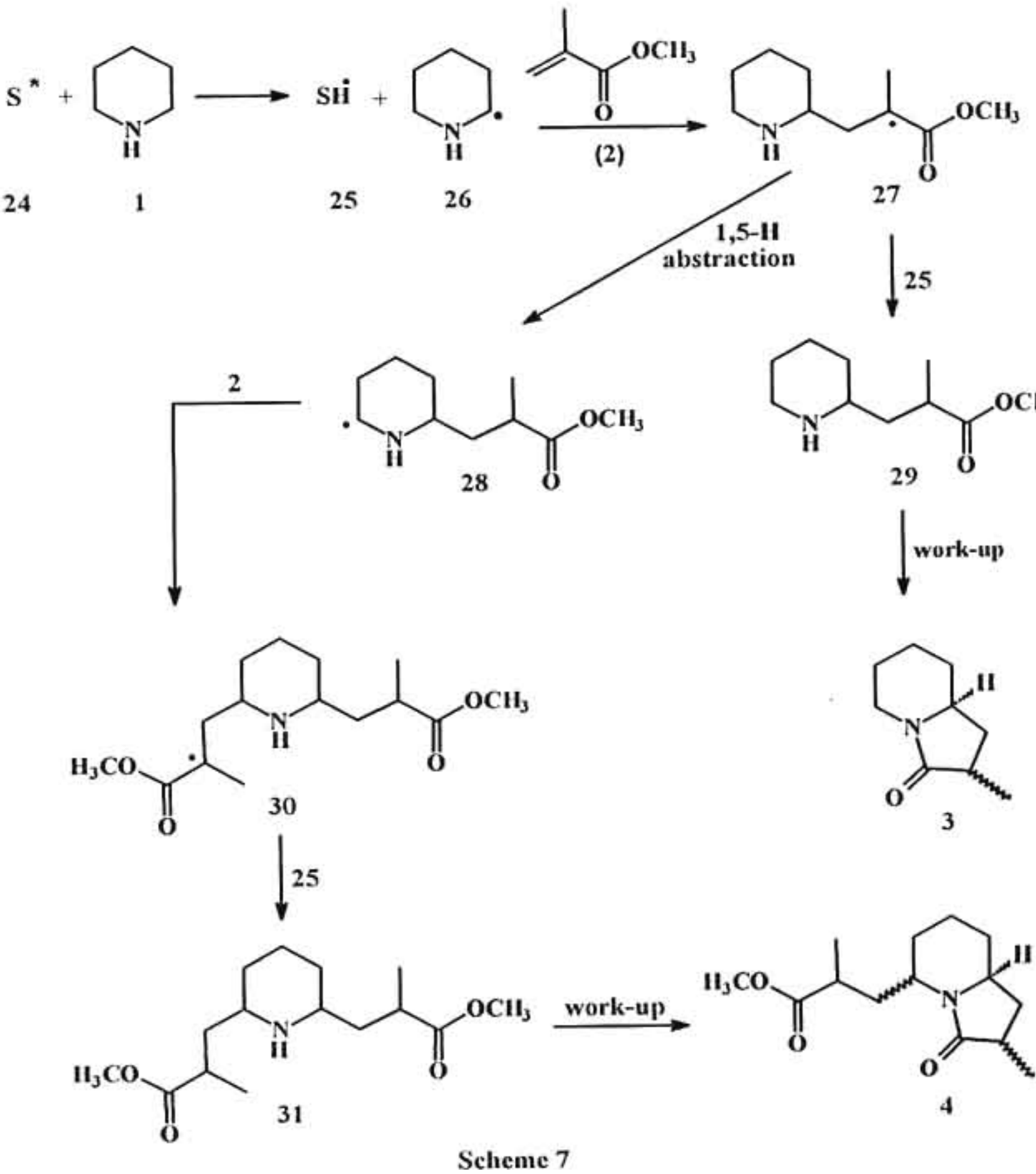
6.4.1. Photosensitized Addition of Piperidine (1), Pyrrolidine (5) and Diisopropylamine (8) to Methyl Methacrylate (2)

Irradiation of the different reaction mixtures mentioned in this Chapter would lead to the initial formation of the corresponding α-aminoalkyl radicals via a mechanism similar to those indicated in the earlier Chapters, i.e. electron transfer from the ground state amine to the excited state of the sensitizer, followed by the deprotonation of the aminium radical cation. Dicyanoanthracene was found to be inefficient as a photosensitizer for these reactions. At low concentrations of the sensitizer (10^{-4} M), it was observed that anthraquinone was most efficient in photocatalysing these reactions. At low concentrations, benzophenone and xanthone were relatively inefficient; however, when higher concentrations (10^{-3} M - $5x10^{-3}$ M) of these sensitizers were used, the conversion efficiency was much better. Due to the limited solubility of anthraquinone, the effect of higher concentrations of anthraquinone in these photosensitized reactions could not be studied. Another interesting observation was that, in the anthraquinone sensitized reactions, the major products formed were the corresponding lactams, whereas, in the benzophenone, xanthone and anthrone sensitized reactions, along with the

lactams, substantial amounts of products containing lactams with an additional molecule of the olefinic substrates were observed. Moreover, anthraquinone could be recovered quantitatively from the reaction mixtures, whereas with benzophenone, anthrone and xanthone about 20-30 % loss of the sensitizer was observed in each case. In order to explain these results a mechanism shown in Scheme 7 has been proposed. This mechanism describes the photosensitized reaction of piperidine (**1**) with methyl methacrylate (**2**), as a representative example.

Electron transfer from the ground state of piperidine to the excited state of the sensitizer (**24**), followed by proton transfer will lead to the formation of the α-aminoalkyl radical **26** and ketyl radical **25** (**SH·**). The radical **26** can add on to methyl methacrylate (**2**) to give the 1:1 adduct radical **27** and the sensitizer will be regenerated. The adduct **29** would yield the indolizidone **3**, on work-up. If the quenching reaction between **27** and **SH·** is however not efficient, **27** can undergo a 1,5-hydrogen atom abstraction to yield the radical **28**, which can add to another molecule of methyl methacrylate (**2**) to give the methyl methacrylate-amine radical adduct **30** and subsequently the bis-adduct **31**. During work-up, the bis-adduct **31** would lead to the indolizidone derivative **4**. The formation of **4** in substantial amounts was only observed when benzophenone, anthrone and xanthone were used as sensitizers. In these cases, substantial losses of sensitizers were also observed due to the coupling reaction of sensitizer ketyl radicals (**SH·**), leading to dimeric products.

The photosensitized addition of pyrrolidine (**5**) to methyl methacrylate (**2**) can also be understood in terms of a mechanism similar to the one shown in Scheme 7.


S*
SH
OCH3
(2)
24
1
25
26
27
1,5-H
abstraction
25
2
28
29
work-up
30
25
3
31
work-up
4

Scheme 7

The product distribution in the case of the photosensitized reaction of diisopropylamine (**8**) with methyl methacrylate (**2**) shows that the 2:1 ester-amine moiety (**10**) is formed in substantial amounts in the case of anthraquinone sensitized reactions also. In these reactions, the 1,5-hydrogen abstraction of the initially formed adduct radical compete favourably with the quenching by the ketyl radical (**SH·**), for two reasons. Unlike piperidine and pyrrolidine, the alkyl substituents of diisopropylamine are more flexible which will make the 1,5-hydrogen abstraction more facile. Also, the presence of an additional alkyl group will stabilize the radical generated, making the α-carbon hydrogen more labile. These factors can lead to the formation of the bis-adduct **10** in the anthraquinone sensitized reactions.

6.4.2. Photoelectron Transfer Catalyzed Reactions of Cyclohexylamine (11) with Methyl Acrylate (12)

Only one product namely, the spirolactam **13** is formed in the reaction of cyclohexylamine with methyl acrylate. The mechanism for the formation of **13** is similar to the one mentioned earlier. At low concentrations (10^{-4} M), anthraquinone is able to photosensitize these reactions with a conversion efficiency (with respect to methyl acrylate) of 32 % and 38 % in acetonitrile and benzene, respectively. Anthraquinone is not able to photosensitize the reaction between secondary amines and α,β-unsaturated esters in benzene. These results indicate that for primary amines, the formation of α-aminoalkyl radical may involve both electron transfer as well as hydrogen atom abstraction processes. In polar solvents such as acetonitrile, electron transfer mechanism will predominate, whereas in benzene the hydrogen atom abstraction mechanism will predominate.[3,6,12-15]

6.4.3. Photosensitized Addition Reactions of 2,6-Dimethylpiperidine (14) to Methyl Methacrylate (2), Methyl Acrylate (12), Methyl Crotonate (19) and Acrylonitrile (21)

The formation of the different photoproducts in these reactions can be rationalized in terms of the reaction mechanism shown in Scheme 7. The monoadducts formed from the reaction between the amine and esters (**15**, **17** and **20**) however, do not undergo lactonization during work-up and this may be due to the steric strain associated with the cyclization of these molecules. As in the case of photosensitized reaction of diisopropylamine, the formation of a 2:1 adduct, in substantial amounts, is observed in the anthraquinone sensitized reaction also. The presence of the alkyl group at the α-carbon will make the hydrogen attached to the α-carbon more labile, making it succeptable to 1,5-hydrogen atom abstraction. Thus, this route will be able to compete effectively with the quenching of the monoadduct radical by the ketyl radical. The absence of any 2:1 adduct in the reaction between **14** and **19** may also be due to steric reasons. The monoadduct radical formed in this reaction may not be able to undergo the 1,5-hydrogen atom abstraction reaction. The formation of the monoadduct **22** and the bis-adduct **23** from the photosensitized reaction of 2,6-dimethylpiperidine with acrylonitrile may likewise be rationalized in terms of the pathways shown in Scheme 7.

The best conversion efficiencies were obtained when higher concentrations of benzophenone (5 mM) were used to photosensitize these reactions (see Tables 5, 6, and 7).

6.5. Experimental Section

The instruments and methods adopted for the spectral recording and analytical data were the same as those described in earlier Chapters (Chapters 2-4). All the photochemical experiments were carried out using a 450 W medium pressure mercury lamp under Pyrex filtered light. Anthraquinone was purified by vacuum sublimation. Dicyanoanthracene, anthrone, xanthone and benzophenone were purified by recrystallization from benzene. Acridone (99 %) was used as obtained from Aldrich. All other reagents and solvents were purified by distillation before use.

The photolysis mixture, typically consisting of the amine (15 mmol) and the olefinic substrate (15 mmol) in acetonitrile or benzene (350 mL), containing the sensitizer (10^{-4} to $5x10^{-3}$ M) was purged with argon or nitrogen before irradiation (2-8 h). The solvents and unchanged starting materials were removed under reduced pressure and the product mixture was chromatographed over silica gel using a flash column or Harrison Chromatotron. The yields reported are based on the consumption of the olefinic substrate, as estimated by HPLC before removal of the solvent from the irradiation mixture. All new photoproducts were characterized on the basis of spectral and analytical data including high resolution mass spectrometry.

6.5.1. Photosensitized Addition Reaction of Piperidine (1) to Methyl Methacrylate (2)

Irradiation of a mixture of **1** (1.3 g, 15 mmol) and **2** (1.5 g, 15 mmol) containing benzophenone (10^{-3} M) in acetonitrile (350 mL) for 2 h and separation of the product mixture by column chromatography using a mixture (3:1) of

petroleum ether and ethyl acetate gave 160 mg (45 %) of **3** and 150 mg (35 %) of **4**. The spectral data and GC retention times of **3** were identical to those reported earlier for 2-methyl-3-indolizidone[1] (Chapter 3, Section **3.5.1**). These yields are based on **2** that reacted (22 %), as estimated by HPLC. The photoreaction was repeated under a variety of conditions using different sensitizers and the results are summarized in Table 1.

4: IR spectrum ν_{max} (neat) : 1744 (C=O, ester) and 1680 (C=O, ketone) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.1-1.3 (6 H, m, 2 CH_3), 1.4-2.2 (10 H, m, 5 CH_2), 2.3-2.6 (2 H, m, 2 CH) and 3.3-3.9 (5 H, m, OCH_3 and 2 CH).

^{13}C NMR spectrum ($CDCl_3$): δ 19.26, 19.80, 20.52, 21.53, 25.55, 36.15, 36.39, 36.60, 39.02, 41.55, 43.17, 51.64, 65.30 and 177.18, 178.05 (C=O, lactam and ester).

Mass spectrum, m/z (relative intensity) : 252 ($M-H^+$, 20), 236 (10), 220 (15), 204 (15), 176 (10), 150 (100), 136 (25), 122 (10), 77 (10) and 55 (15). Molecular weight calculated for $C_{14}H_{23}NO_3$: 253.1678. Found : 253.1642 (high resolution mass spectrometry).

6.5.2. Photosensitized Addition Reaction of Pyrrolidine (5) to Methyl Methacrylate (2)

An argon-purged solution of a mixture of **5** (1.1 g, 15 mmol) and **2** (1.5 g,15 mmol) in acetonitrile (350 mL) containing 10^{-3} M of benzophenone was irradiated for 4 h and separation of the product mixture by column chromatography using a mixture (4:1) of petroleum ether and ethyl acetate gave

120 mg (35 %) of **6** and 100 mg (25 %) of **7**. These yields were based on the percentage conversion of **2** (20 %). This reaction was repeated with a variety of sensitizers and the results are summarized in Table 2. The gas chromatographic retention time as well as the mass spectrum of **6** were found to be identical to that of 2-methyl-3-pyrrolizidone, reported in Chapter 3 (Section **3.5.2**).[1]

7: IR spectrum ν_{max} (neat) : 3340 broad (NH), and 1744 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.2 (6 H, m, 2 CH_3), 1.4-2.1 (8 H, m, 4 CH_2), 2.2-2.8 (2 H, m, 2 CH) and 3.4-3.9 (8 H, m, 2 OCH_3 and 2 CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 19.15, 19.50, 21.38, 22.31, 26.57, 35.44, 37.58, 38.15, 40.87, 42.57, 43.28, 51.34, 51.61, 59.21, 60.53 and 174.56, 176.70 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 271 (M^+, 20), 270 (100), 238 (20), 210 (10), 178 (12), 138 (10), 110 (10), 83 (100) and 55 (10). Molecular weight calculated for $C_{14}H_{23}NO_4$: 271.1705. Found : 271.1707 (high resolution mass spectrometry).

6.5.3. Photosensitized Addition of Diisopropylamine (8) to Methyl Methacrylate (2)

Irradiation of a mixture of **8** (1.5 g, 15 mmol) and **2** (1.5 g, 15 mmol) containing 10^{-3} M of benzophenone in acetonitrile (350 mL) for 2 h and analysis of the product mixture by GC-MS indicated the formation of 40% of **9** and 30% of **10**. The GC-MS data of **9** and **10** were in good agreement with those reported for the same compounds in Chapter 2 of this thesis (Section **2.5.4**).[1] The product distributions were based on **2**, that reacted (25 % conversion). The photoreaction

was repeated using various sensitizers and the product distributions of **9** and **10** and the percentage conversion of **2** are shown in Table 3.

6.5.4. Photosensitized Addition Reactions of Cyclohexylamine (11) to Methyl Acrylate (12)

Irradiation of a mixture of **11** (1.45 g, 15 mmol), **12** (1.3 g, 15 mmol) and benzophenone (5 mmol) in benzene (350 mL) for 4 h and analysis of the product mixture by GC-MS indicated the formation of 60 % of the spirolactam **13**, which was previously characterized and the spectral features are reported in Chapter 3 (Section **3.5.3**).[1] The photoreaction was repeated with a variety of sensitizers and Table 4 lists the product distribution of **13** with respect to the percentage conversion of **12**.

6.5.5. Photosensitized Addition Reactions of 2,6-Dimethylpiperidine (14) to Methyl Methacrylate (2)

Irradiation of a mixture of **14** (1.7 g, 15 mmol) and **2** (1.5 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of anthraquinone for 4 h and separation of the product mixture (400 mg) by flash column using a mixture (3:1) of petroleum ether and ethyl acetate gave 160 mg (45 %) of **15** and 170 mg (35 %) of **16**. These yields were based on **2**, that reacted (40 %), as estimated by HPLC. The photoreaction was repeated using different sensitizers and the percentage conversion of **2** and product yields are tabulated in Table 5.

15: IR spectrum ν_{max} (neat): 3320 (broad, NH) and 1742 (C=O) cm^{-1}.

^{1}H NMR spectrum ($CDCl_3$) : δ 1.0-1.3 (9 H, m, 3 CH_3), 1.5-2.2 (8 H, m, 4 CH_2), 2.3-3.0 (2 H, m, 2 CH), 3.6-3.7 (3 H, s, OCH_3) and 5.5-5.8 (1 H, broad, NH).

^{13}C NMR spectrum ($CDCl_3$) : δ 19.83, 26.40, 27.41 (CH_3), 29.74, 30.87, 35.41, 31.56 (CH_2), 35.58, 43.52, 46.09 (CH), 51.34 (OCH_3), 56.12 (C) and 177.57 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 212 ($M-H^+$, 5), 196 (10), 180 (15), 169 (5), 152 (18), 124 (100), 111 (80), 96 (40), 83 (35), 69 (25) and 55 (20).

16: IR spectrum ν_{max} (neat): 3350 (broad, NH) and 1744 (C=O) cm^{-1}.

^{1}H NMR spectrum ($CDCl_3$) : δ 0.9-1.2 (12 H, m, 4 CH_3), 1.4-2.2 (10 H, m, 5 CH_2), 2.3-2.8 (2 H, m, 2 CH) and 3.6-3.7 (6 H, s, 2 OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 17.21, 19.86, 27.71, 29.35 (CH_3), 35.41, 35.91, 35.20, 44.74 (CH_2), 46.74, 49.85 (CH), 51.31, 51.73 (OCH_3), 51.99 (C) and 178.31, 178.56 (C=O, ester).

Mass spectrum, m/z (relative intensity) : 312 (M^+, 5), 298 (20), 282 (4), 250 (8), 212 (100), 180 (15), 156 (8), 124 (10), 110 (20), 95 (24), 70 (28) and 55 (10).

6.5.6. Photosensitized Addition Reactions of 2,6-Dimethylpiperidine (14) to Methyl Acrylate (12)

An argon-purged solution of a mixture of **14** (1.7 g, 15 mmol) and **12** (1.3 g, 15 mmol) in acetonitrile (350 mL), containing 10^{-4} M of anthraquinone was irradiated for 4 h and separation of the product mixture (400 mg) by column

chromatography using a mixture (3:1) of petroleum ether and ethyl acetate gave 160 mg (40 %) of **17** and 170 mg (45 %) of **18**. These yields were based on **12**, that reacted (40 % conversion). The reaction was repeated with different sensitizers and the results are summarized in Table 6.

17: IR spectrum ν_{max} (neat): 3350 (broad, NH) and 1744 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.2 (6 H, m, 2 CH_3), 1.4-2.0 (8 H, m, 4 CH_2), 2.2-2.8 (3 H, m, CH_2 and CH) and 3.55-3.7 (3 H, s, OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 27.11, 27.17 (CH_3), 28.93, 29.50, 31.04, 37.67, 41.07 (CH_2), 41.04 (CH), 51.46 (OCH_3), 54.83 (C) and 174.73 (C=O, ester).

Mass spectrum, m/z (relative intensity): 198 ($M\text{-}H^+$, 10), 182 (5), 166 (20), 138 (10), 124 (100), 110 (70), 96 (50), 82 (55), 69 (30) and 55 (15). Molecular weight calculated for $C_{11}H_{24}NO_2$: 200.1494 (MH^+). Found: 200.1501 (MH^+) (high resolution mass spectrometry).

18: IR spectrum ν_{max} (neat): 3300 (broad, NH) and 1744 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.2 (6 H, m, 2 CH_3), 1.3-2.0 (10 H, m, 5 CH_2), 2.2-2.6 (4 H, m, 2 CH_2) and 3.6-3.7 (6 H, s, 2 OCH_3).

^{13}C NMR spectrum ($CDCl_3$) : δ 28.07, 28.63 (CH_3), 37.32, 37.61, 39.94 (CH_2), 50.77 (OCH_3), 51.22 (C) and 174.73 (C=O, ester).

Mass spectrum, m/z (relative intensity): 286 (MH^+, 70), 270 (30), 254 (10), 222 (8), 198 (100), 166 (15). 110 (15), 70 (30) and 55 (15). Molecular

weight calculated for $C_{15}H_{27}NO_4$: 285.2018. Found: 285.2011(high resolution mass spectrometry).

6.5.7. Photosensitized Addition Reactions of 2,6-Dimethylpiperidine (14) to Methyl Crotonate (19)

Irradiation of an argon-purged solution of a mixture of **14** (1.7 g, 15 mmol), **19** (1.5 g, 15 mmol) and anthraquinone (10^{-4} M) in acetonitrile (350 mL) for 4 h and separation of the product mixture by column chromatography using a mixture (3:2) of petroleum ether and ethyl acetate gave 150 mg (50 %) of **20**. The yield of **20** was based on the percentage conversion of **19** (18 %). The reaction when repeated under similar conditions of irradiation, but using 5 mM of benzophenone, gave **20** with 35 % percentage conversion of **19**, whereas xanthone (5 mM) yielded **20** with 28 % conversion of **19**. Catalytic amounts of these sensitizers were found to be inefficient for the photosensitized reaction of **14** with **19**.

20: IR spectrum ν_{max} (neat): 3400 (broad, NH) and 1742 (C=O) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 0.9-1.0 (3 H, d, CH_3), 1.05-1.15 (3 H, d, CH_3), 1.15-1.25 (3 H, s, CH_3), 1.4-1.95 (6 H, m, 3 CH_2), 2.0-2.9 (4 H, m, CH_2 and 2 CH), 3.5-3.7 (3 H, s, OCH_3) and 7.8-8.1 (1 H, broad, NH).

^{13}C NMR spectrum ($CDCl_3$) : δ 14.37, 15.77, 25.32, 26.43, 26.66, 26.81 (CH_3), 29.05, 29.65, 29.86, 36.33, 36.63 (CH_2), 39.79, 40.45 (CH), 51.13 (OCH_3), 57.60, 58.67 (C) and 173.96 (C=O, ester).

Mass spectrum, m/z (relative intensity): 211 (M^+, 10), 196 (12), 180 (15), 164 (18), 138 (70), 110(100), 82 (60), 69 (35) and 55 (15).

6.5.8. Photosensitized Adddition Reactions of 2,6-Dimethylpiperidine (14) to Acrylonitrile (21)

Irradiation (4 h) of an argon-purged solution of a mixture of **14** (1.7 g, 15 mmol) and **21** (0.8 g, 15 mmol) in acetonitrile (350 mL) containing 10^{-4} M of anthraquinone and separation of the product mixture by column chromatography using a mixture (3:1) of petroleum ether and ethyl acetate gave 90 mg (30%) of **22** and 140 mg (50 %) of **23**. These yields were based on **21**, that reacted (30 %). The reaction was repeated under various conditions and the percentage conversion of **21** and product distributions of **22** and **23** are listed in Table 7.

22: IR spectrum ν_{max}(neat): 3340 (broad, NH) and 2240 (nitrile) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.2 (6 H, m, 2 CH_3), 1.4-2.0 (8 H, m, 4 CH_2) and 2.1-2.6 (3 H, m, CH_2 and CH).

^{13}C NMR spectrum ($CDCl_3$) : δ 11.84, 15.65, 17.59, 29.86, 30.84 (CH_2), 26.37, 26.54 (CH_3), 33.08 (CH), 55.22 (C) and 120.38 (nitrile).

Mass spectrum, m/z (relative intensity): 165 ($M-H^+$, 5), 163 (60), 149 (10), 135 (15), 125 (100), 110 (20), 96 (25), 82 (50), 68 (15) and 55 (25).

23: IR spectrum ν_{max} (neat): 3360 (broad, NH) and 2242 (nitrile) cm^{-1}.

^1H NMR spectrum ($CDCl_3$) : δ 1.0-1.2 (6 H, 2 s, 2 CH_3), 1.2-1.4 (4 H, m, 2 CH_2), 1.5-2.0 (6 H, m, 3 CH_2) and 2.3-2.6 (4 H, m, 2 CH_2).

^{13}C NMR spectrum ($CDCl_3$) : δ 11.36, 16.64, 16.82, 34.27, 36.72, 37.91, 40.24 (CH_2), 27.38, 28.01 (CH_3), 50.56, 51.04 (C) and 120.49, 120.76 (nitrile).

Mass spectrum, m/z (relative intensity): 218 ($M-H^+$, 5), 204 (20), 179 (5), 165 (100), 124 (5), 109 (10), 97 (15), 70 (25) and 55 (8).

6.6. References

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