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Photoelectron transfer catalysed reactions of amines with α,β-unsaturated esters and acrylonitrile using different sensitizers

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Abstract

A variety of sensitizers were screened for their ability to photocatalyse efficiently the carbon–carbon bond forming reactions between primary and secondary amines with electron-deficient olefinic substrates, such as α,β-unsaturated esters and acrylonitrile. The reactions with α,β-unsaturated esters led to the formation of lactams as the major products. Dicyanoanthracene and acridone were found to be inefficient, while anthraquinone, benzophenone, anthrone and xanthone photocatalyse these reactions with moderate efficiency. The anthraquinone-2-sodium sulphonate catalysed addition of tertiary amines to α,β-unsaturated esters in aqueous medium also yielded lactams as the major products. Reasonable mechanisms have been suggested for the formation of the different products.

Keywords: Photosensitization; α-Aminoalkyl radicals; Carbon–carbon bond formation

1. Introduction

Construction of carbon–carbon bonds adjacent to nitrogen is of significant importance, in view of the number of natural products containing this structural unit [1]. Recently there has been considerable interest in the development of methods for the generation of the highly reactive α-aminoalkyl radicals, which can be utilized for the construction of such bonds [2–7]. The mechanistic aspects as well as synthetic applications of α-aminoalkyl radical generation via photoinduced electron transfer reactions of α-silylamines have been extensively investigated [8–10]. Although there are several reports on the mechanistic aspects of photoelectron transfer catalysed generation of α-aminoalkyl radicals from underivatized amines using a variety of sensitizers such as ketones, flavins, porphyrins and semiconductors, there have been only few attempts to utilize these processes for carbon–carbon bond forming reactions [11,12].

We have reported earlier on the anthraquinone photocatalysed carbon–carbon bond forming reactions of various primary, secondary and tertiary amines with electron-deficient olefinic substrates [13,14]. The reactions of primary and secondary amines led to the formation of lactams and this method was utilized for the synthesis of indolizidone, pyrrolizidone and spirolactam derivatives. The synthetic utility of these reactions was, however, limited by their low conversion efficiency. Although during the initial stages of irradiation the conversion of the starting materials increases with increasing irradiation time, at longer times no further increase in conversion was observed, possibly as a result of an inner filter effect, caused by preferential absorption of light by the photoproducts.

The photosensitized addition of primary and secondary amines to α,β-unsaturated esters and acrylonitrile using sensitizers such as acridone, anthraquinone, anthrone, benzophenone, dicyanoanthracene and xanthone were studied in an effort to enhance the efficiency of these reactions. Here we report on these studies as well as on the anthraquinone-2-sulphonic acid (sodium salt) photocatalysed reactions of some tertiary amines to α,β-unsaturated esters in aqueous media, which also lead to lactam formation.

2. Results

2.1. Photoelectron transfer catalysed reactions of secondary amines

The photosensitized reaction of secondary amines with α,β-unsaturated esters and acrylonitrile led to the formation of 1:1 and 2:1 olefin–amine adducts. Most of the adducts formed between α,β-unsaturated esters and amines under-

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went further cyclization to yield the corresponding lactams. All products formed were isolated from the reaction mixture and characterized on the basis of spectral information.

Catalytic amounts of anthraquinone (10^{-4} M) were sufficient to photocatalyse these reactions and the corresponding lactams were the major products formed. Under identical conditions, benzophenone, anthrone and xanthone were unable to photocatalyse these reactions efficiently, whereas at higher concentrations (1–5 mM) efficient photocatalysis was observed. In these systems, together with the corresponding lactams, formation of substantial amounts of the 1:2 amine–olefin adducts was also observed. Anthraquinone could be recovered quantitatively from the reaction mixtures, whereas substantial loss of sensitizer (20%–30%) was observed for benzophenone, xanthone and anthrone. Gas chromatography–mass spectrometry (GC–MS) analysis indicated the formation of the corresponding pinacols in these cases. Under identical conditions dicyanoanthracene (DCA) and acridone were unable to sensitize these reactions.

2.1.1. Photocatalysed reaction of piperidine (1), pyrrolidine (5) and diisopropylamine (8) with methyl methacrylate (2)

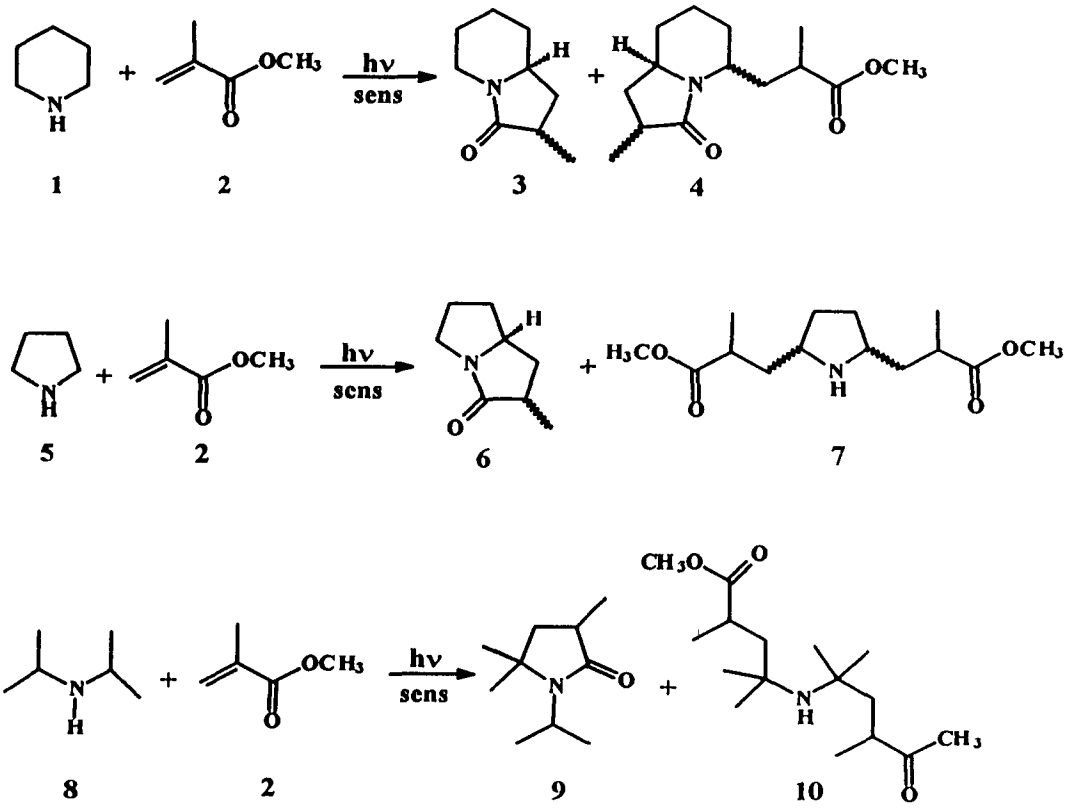
Irradiation of deareated solutions of piperidine containing methyl methacrylate and sensitizer led to the formation of 2-methyl-3-indolizidone (**3**) and indolizidone derivative (**4**) (Scheme 1). The yields, percentage conversion and distribution of products under a variety of irradiation conditions are shown in Table 1.

The photosensitized addition of pyrrolidine to methyl methacrylate led to the formation of a diastereomeric mixture of 2-methyl-3-pyrrolizidone (**6**) and the pyrrolidine derivative (**7**) (Scheme 1). The yields, percentage conversion and product distribution using different sensitizers were studied [15]. The best yield was obtained on using benzophenone as photosensitizer (Table 2).

Photosensitized addition of diisopropylamine to methyl methacrylate led to the formation of 1-isopropyl-3,5,5-trimethyl-2-pyrrolidone (**9**) and the 2:1 ester–amine adduct (**10**) (Scheme 1). The photoreactions were studied using different sensitizers and the best conversion efficiency in each case was obtained on using benzophenone as sensitizer (Table 2) [15].

2.1.2. Photosensitized addition of 2,6-dimethylpiperidine (11) to α,β-unsaturated esters and acrylonitrile

The photosensitized addition of 2,6-dimethylpiperidine (**11**) to methyl methacrylate (**2**), methyl acrylate (**12**), methyl crotonate (**15**) and acrylonitrile (**19**) led to the formation of the corresponding 1:1 and 2:1 olefin–amine adducts (Scheme 2). The yield, product distribution and percentage conversion obtained on using different sensitizers were determined [15]. The best conversion efficiency in each case was obtained on using benzophenone as sensitizer (Table 2).



Scheme 1.

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

Number	Sensitizer	[sensitizer] (M)	Solvent	Irradiation time (h)	Conversion of **2** (%)	Product distribution (%)	
						3	**4**
1	Anthraquinone	10^{-4}	CH_3CN	2	20	80	<5
2	Anthraquinone	10^{-4}	Benzene	2	10	–	–
3	Acridone	10^{-4}	CH_3CN	4	8	–	–
4	Dicyanoanthracene	10^{-4}	CH_3CN	8	<5	–	–
5	Benzophenone	10^{-4}	CH_3CN	4	5	40	20
6	Xanthone	10^{-4}	CH_3CN	4	5	40	20
7	Anthrone	10^{-4}	CH_3CN	4	5	40	40
8	Benzophenone	10^{-3}	CH_3CN	2	22	45	35
9	Benzophenone	10^{-3}	Benzene	2	25	60	30
10	Xanthone	10^{-3}	Benzene	2	20	30	40
11	Xanthone	10^{-3}	CH_3CN	2	24	50	30
12	Anthrone	10^{-3}	CH_3CN	2	20	40	15
13	Benzophenone	5×10^{-3}	CH_3CN	4	60	50	30
14	Benzophenone	5×10^{-3}	Benzene	2	55	60	30
15	Benzophenone	5×10^{-3}	Benzene	4	70	58	28

Table 2
Photosensitized addition of amine (15 mmol) to olefinic substrate (15 mmol) in 350 ml acetonitrile or benzene containing benzophenone (5×10^{-3} M) using a 450 W medium pressure Hanovia lamp (4 h)

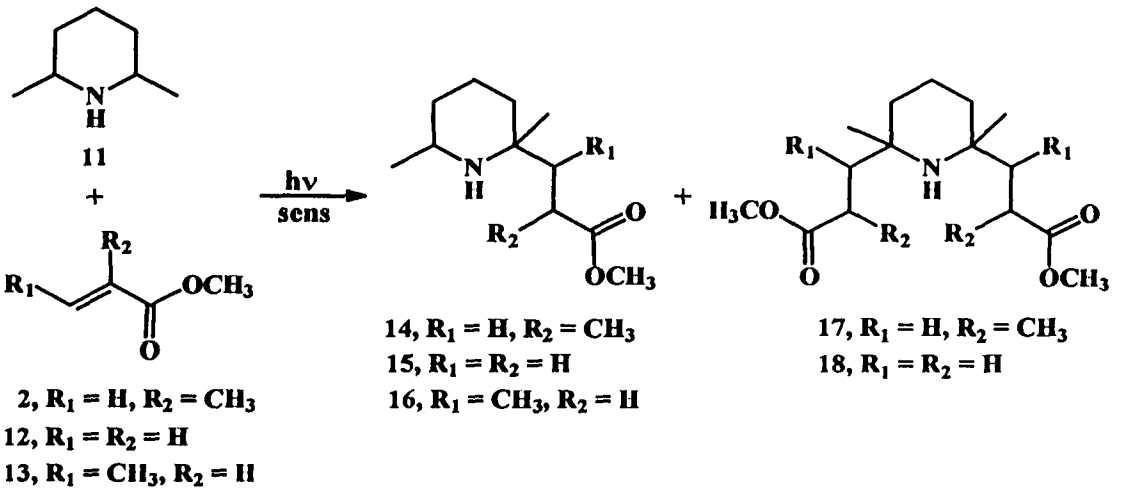
Number	Amine	Olefin	Solvent	Conversion of olefin (%)	Product distribution (%)
1	**5**	**2**	CH_3CN	50	**6** (30), **7** (25)
2	**5**	**2**	Benzene	60	**6** (30), **7** (20)
3	**8**	**2**	CH_3CN	55	**9** (35), **10** (40)
4	**8**	**2**	Benzene	65	**9** (30), **10** (35)
5	**11**	**2**	CH_3CN	70	**14** (45), **17** (30)
6	**11**	**12**	CH_3CN	75	**15** (40), **18** (30)
7	**11**	**12**	Benzene	80	**15** (40), **18** (30)
8	**11**	**13**	CH_3CN	35	**16** (50)
9	**11**	**19**	CH_3CN	70	**20** (30), **21** (50)
10	**22**	**12**	CH_3CN	70	**23** (65)
11	**22**	**12**	Benzene	80	**23** (60)

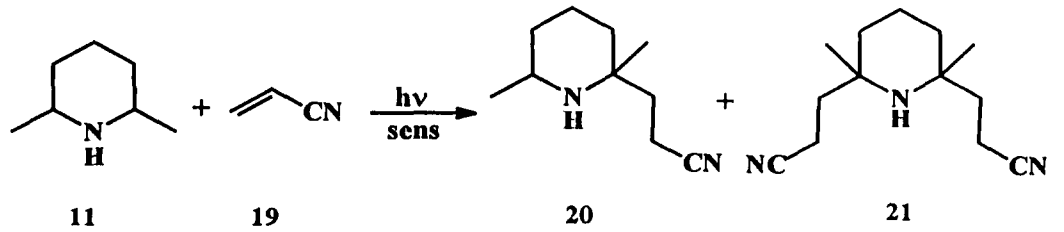
2.2. Photoelectron transfer catalysed reaction of cyclohexylamine (22) with methyl acrylate (12)

The photosensitized addition of cyclohexylamine to methyl acrylate in argon-bubbled solutions indicated the formation of the spirolactam (**23**). The structure of **23** was confirmed by comparing the gas chromatographic retention time and mass spectral data with those reported earlier for the same compound [13]. The photoreaction was carried out with different sensitizers [15] and best conversion was obtained when 5 mM of benzophenone was used to photocatalyse the reaction (Table 2). As in the reaction of secondary amines, anthraquinone was recovered quantitatively from the reaction mixtures, whereas approximately 20%–30% loss of sensitizers was observed when benzophenone, anthrone and xanthone were used. In these cases the formation of corresponding pinacols was observed. Under identical conditions, DCA and acridone did not sensitize these reactions.

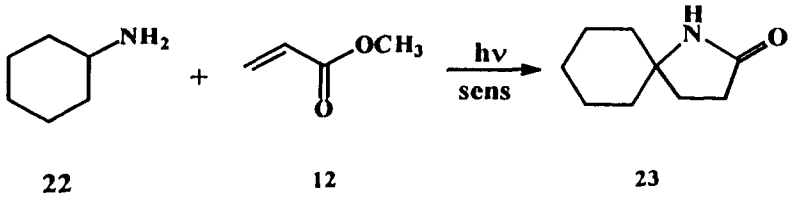
2.3. Anthraquinone-2-sodium sulphonate photocatalysed reaction of tertiary amines with α,β-unsaturated esters in aqueous media

The photosensitized reaction of triethylamine (**24**) with methyl methacrylate (**2**) in water was studied by irradiating an argon-purged solution of triethylamine and methyl methacrylate containing the sodium salt of anthraquinone-2-sulphonic acid, under Pyrex-filtered light ($\lambda > 290$ nm). One major product (**25**) was isolated from the reaction mixture (Scheme 4) and was characterized, on the basis of analytical results and spectral information, as 1-ethyl-3,5-dimethyl-2-pyrrolidone. Photosensitized reaction of triethylamine (**24**) with methyl acrylate (**12**) in water containing anthraquinone-2-sulphonic acid (sodium salt) gave 1-ethyl-5-methyl-2-pyrrolidone (**26**) (Scheme 4). Similarly, the photosensitized reactions of *N*-methylpiperidine (**27**) and *N*-ethylpiperidine (**28**) with methyl acrylate (**12**) gave 3-indolizidone (**29**) as





Scheme 2.



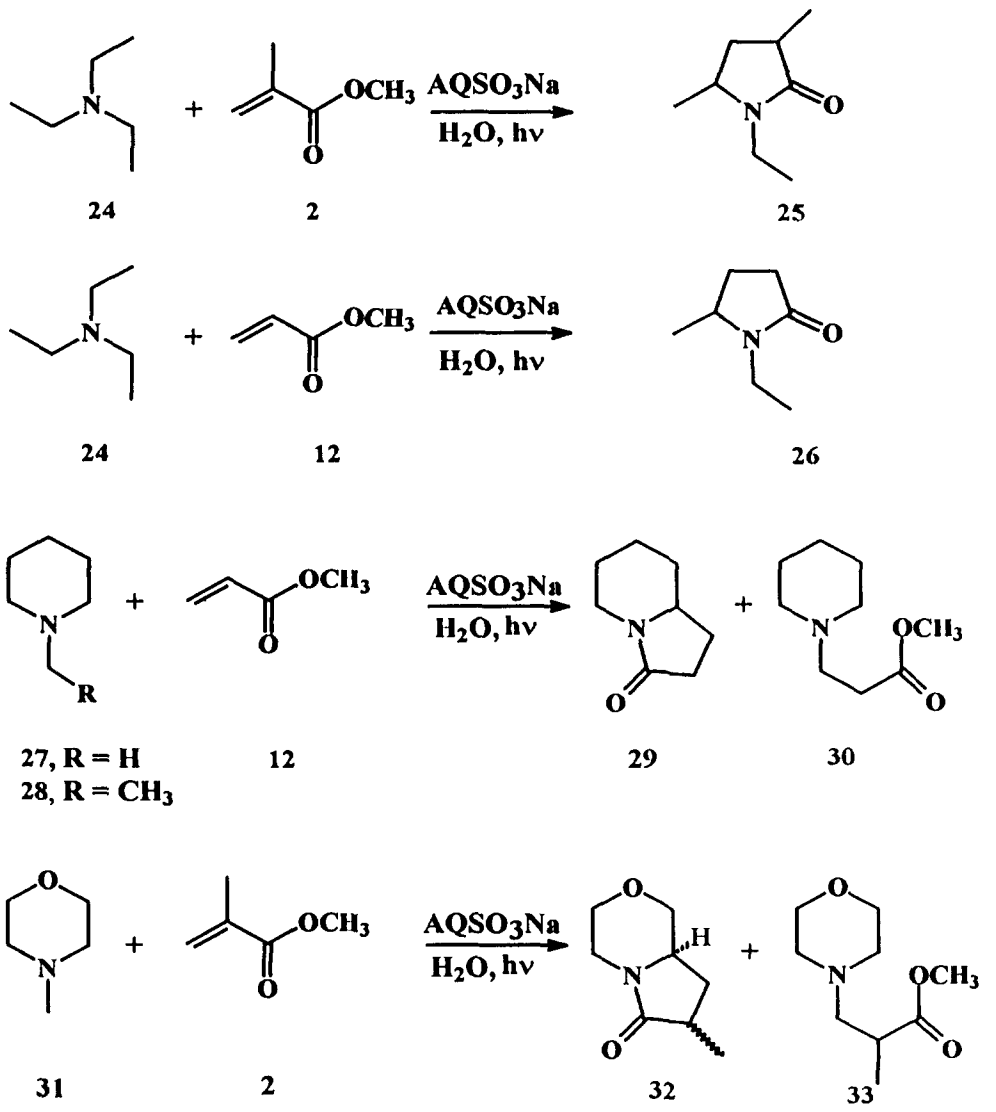
Scheme 3.

the major product together with small amounts of methyl 3-(1-piperidinyl)propionate (**30**) in each case (Scheme 4). The photosensitized reaction of *N*-methylmorpholine (**31**) with methyl methacrylate (**2**) in aqueous medium containing anthraquinone-2-sulphonic acid (sodium salt) gave a mixture of the bicyclic lactam **32** and the *N*-adduct **33** (Scheme 4).

3. Discussion

3.1. Photosensitized addition of piperidine (1), pyrrolidine (5) and diisopropylamine (8) to methyl methacrylate (2)

Irradiation of the different reaction mixtures would lead to the initial formation of the corresponding α-aminoalkyl radicals via 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, whereas benzophenone, anthrone and xanthone were relatively inefficient; however, when higher concentrations (10^{-3} M – 5×10^{-3} M) of these sensitizers were used, the conversion efficiency was much better. Because of 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 product formed was the corresponding lactam, whereas, in the benzophenone-, xanthone- and anthrone-sensitized reactions, together with the lactams, substantial amounts of lactam derivatives, containing another molecule of methyl methacrylate added on, were observed. 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 [15]. In order to explain these results, a mechanism based on the known reactions of α-aminoalkyl and ketyl radicals shown in Scheme 5 has been proposed. This mechanism describes the photosensitized reaction of piperi-

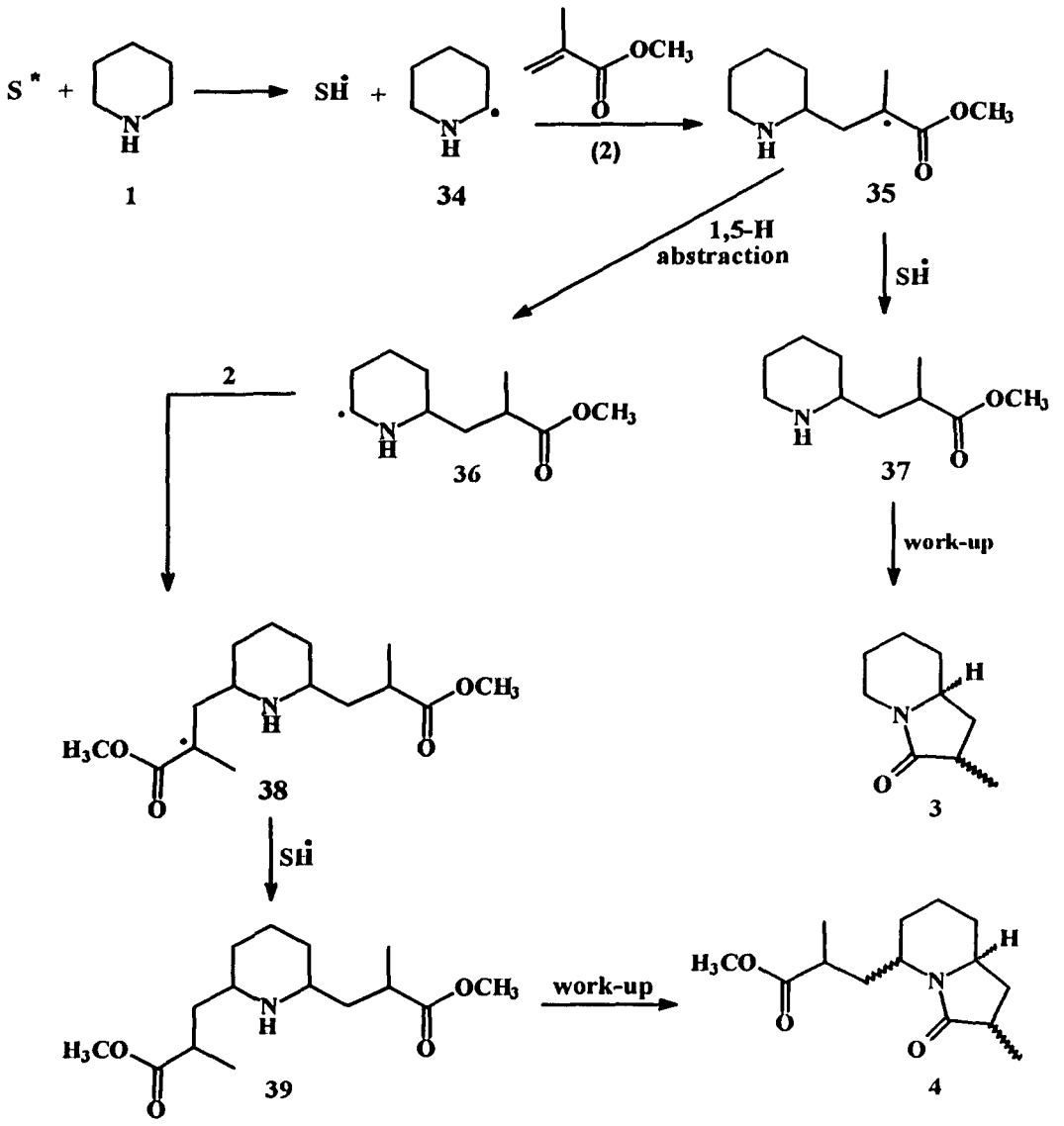


Scheme 4.

dine (**1**) with methyl methacrylate (**2**), as a representative example.

Electron transfer from the ground state of piperidine to the excited state of the sensitizer (S*) followed by proton exchange between the radical ions will lead to the formation of the α-aminoalkyl radical **34** and ketyl radical SH·. The role of the base strength of radical anions in bringing about deprotonation of the alkylamine radical cation has been well established [11]. Because of the low basicity of the radical anion of DCA in comparison with those of the other ketonic sensitizers, proton exchange between the solvent-caged radical ion pairs in the DCA-sensitized reactions will be inefficient. In addition, the singlet radical ion pairs formed in the DCA-sensitized reactions will have a strong tendency to undergo back electron transfer. These factors contribute to the low efficiency of α-aminoalkyl radical generation in the DCA-sensitized reactions.

The α-aminoalkyl radical **34** formed in these reactions can add on to methyl methacrylate (**2**) to give the 1:1 adduct radical **35**. Quenching of this radical by SH· can lead to **37** and regeneration of the sensitizer. The adduct **37** would yield the indolizidone derivative **3**, on work-up. Such intramolecular cyclizations are known to be very facile [16–18]. Alternatively, **35** can undergo a 1,5-hydrogen atom abstraction to yield the radical **36**, which can add to another molecule of methyl methacrylate (**2**) to give **38**. Subsequently it can be quenched by SH· to give the 2:1 olefin–amine adduct **39**. During work-up, the bis adduct **39** 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, indicating that in these cases intramolecular 1,5-hydrogen abstraction in **35** competes favourably with the quenching by SH·. In these cases, substantial losses of sensitizers were also observed as a result of the coupling reaction of sensitizer ketyl radicals (SH·), leading to the formation of the corresponding pinacol derivatives. It may be pointed out that we have not observed the formation of any of the coupling product arising through the combina-



Scheme 5.

tion of either **35** or **38** with SH' radical. This may be due to the ease with which both **35** and **38** can abstract hydrogen atom from either SH' or the starting amine (**1**). In addition, steric factors may also hinder the coupling of radicals such as **35** and **38** with SH' radical.

An alternative mechanism for the formation of **39** could be via the secondary photoreactions of **37**. However, this could be ruled out since the ratio of **3**:**4** was independent of irradiation time. For example, irradiation of a solution containing benzophenone (5×10^{-3} M), piperidine (**1**) (15 mmol) and methyl methacrylate (**2**) (15 mmol) in 350 ml benzene under an argon atmosphere for 2 h and 4 h led to 55% and 70% respectively conversion of **2**. The ratio of **3**:**4** remained unchanged within experimental error (Table 1). Earlier, time dependence studies on photocatalysed reactions of amines had clearly shown that such multiple olefin added products arise via a 1,5-hydrogen atom abstraction reaction of the adduct radicals and not via secondary photoreactions [13].

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

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 anthraquinone-sensitized reactions also. In these reactions, the 1,5-hydrogen abstraction of the initially formed adduct radical can 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 hydrogen attached to the α-carbon more labile.

These factors can lead to the formation of the bis adduct **10** in the anthraquinone-sensitized reactions.

3.2. Photosensitized addition of 2,6-dimethylpiperidine (11) to methyl methacrylate (2), methyl acrylate (12), methyl crotonate (13) and acrylonitrile (19)

The formation of the different photoproducts in these reactions can be rationalized in terms of the reaction mechanism shown in Scheme 5. The monoadducts formed from the reaction between the amine and esters (**14**, **15** and **16**), 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 the 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 susceptible 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 **11** and **13** may also be for steric reasons, which will make it difficult for the radical formed in this reaction to undergo the 1,5-hydrogen atom abstraction. The formation of the monoadduct **20** and the bis adduct **21** from the photosensitized reaction of 2,6-dimethylpiperidine with acrylonitrile can likewise be rationalized in terms of the pathways shown in Scheme 5. The best conversion efficiencies were obtained when high concentrations of benzophenone (5 mM) were used to photosensitize these reactions.

3.3. Photoelectron transfer catalysed reactions of cyclohexylamine (22) with methyl acrylate (12)

Only one product, namely the spirolactam **23**, is formed in the reaction of cyclohexylamine with methyl acrylate. The mechanism for the formation of **23** is similar to that mentioned earlier (Scheme 5). 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.

3.4. Photosensitized reactions of tertiary amines to α,β-unsaturated esters in water

For several years, study of organic reactions in aqueous media has 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 occurring in organic solvents [19–23]. The aqueous medium is both economical and environmentally compatible and the need for special handling of inflammable 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 has been extensively explored [24–26]. However, there are very few reports on the study of such reactions in aqueous media.

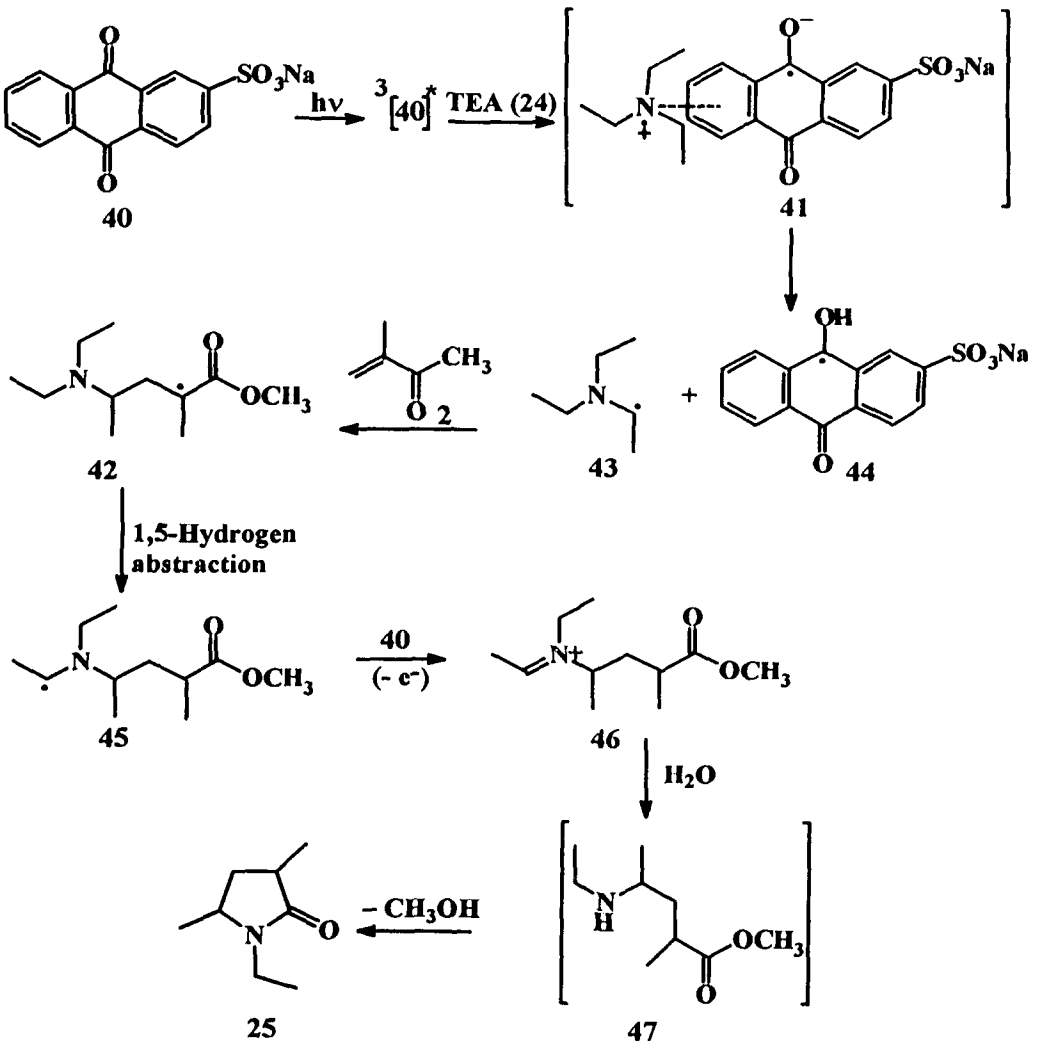
In the present study, the photosensitized reactions of tertiary amines with α,β-unsaturated esters in water (Scheme 4) were investigated. The formation of *N*-alkylpyrrolidones (**25** and **26**) and the bicyclic lactams (**29** and **32**) from the corresponding tertiary amines in these reactions is interesting. As reported previously, anthraquinone-sensitized photoreaction of tertiary amines with α,β-unsaturated esters in acetonitrile leads to multiple addition products [13]. Such products were not formed in aqueous media. A probable pathway for the formation of lactams in the reactions of tertiary amines with α,β-unsaturated esters is shown in Scheme 6. The α-aminoalkyl radical **43**, formed via the photosensitized reaction of anthraquinone-2-sulphonic acid (sodium salt) (**40**) with triethylamine (**24**), for example, could add to methyl methacrylate (**2**) to give the radical adduct **42**. Such adduct radicals have been shown to undergo 1,5-hydrogen atom abstraction to give radicals such as **45**, which in turn can lead to multiple addition products, as observed when the reaction is carried out in acetonitrile [13]. In aqueous medium, however, it appears that the radical **45** undergoes a further electron transfer, presumably through its interaction with the ground state anthraquinone-2-sulphonate anion (**40**), leading to the iminium ion **46**. Such electron transfer reactions between α-aminoalkyl radicals and ketones in the ground state are known to lead to the formation of iminium ions [27–29]. Subsequent hydrolysis of **46** under work-up would lead to the secondary amine derivative **47** and ultimately to the pyrrolidone **25** (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 **45** in these media. Water being highly polar compared with 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 the anthraquinone-2-sodium sulphonate 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 anthraquinone sulphonate.

4. Experimental section

All melting points are uncorrected and were determined on a Büchi-530 melting point apparatus. IR spectra were recorded on a Perkin Elmer 882 IR spectrometer. Electronic



Scheme 6.

spectra were recorded on a Shimadzu UV-2100 spectrophotometer. ^{1}H nuclear magnetic resonance (NMR) spectra were recorded on a JEOL EX 90 NMR spectrometer using tetramethylsilane as internal standard. ^{13}C NMR (22.5 MHz) spectra were recorded on a JEOL EX 90 NMR spectrometer. ^{13}C NMR resonances were assigned using QUART and DEPT programs to determine the nature of the carbon attachments. Mass spectra were recorded either on a Finnigan MAT model 8430 or JEOL JMS AX 505 HA mass spectrometer or 5890 series II Hewlett Packard gas chromatograph connected to a 5971 series mass selective detector. GC analyses were carried out on either a 5840 or a 5890 series II gas chromatograph. High performance liquid chromatography (HPLC) analyses were carried out employing a Shimadzu LC-8A liquid chromatograph (ODS column), using methanol as eluent. 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. Anthraquinone-2-sulphonic acid (sodium salt) was purified by recrystallization from water. Acridone (99%) was used as obtained from Aldrich. All other reagents and solvents were purified by distillation before use.

The general photolysis procedure in non-aqueous medium involves irradiation (2–8 h) of an argon- or nitrogen-purged solution, typically consisting of amine (15 mmol) and olefinic substrate (15 mmol) in acetonitrile or benzene (350 ml), containing sensitizer ($10^{-4}-5\times10^{-3}$ M). 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. 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 MS.

The general procedure of photolysis in aqueous medium 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 5×10^{-4} M of anthraquinone-2-sulphonic 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 (5×50 ml) and dried over anhydrous sodium sulphate. The product mixture was chromatographed over silica gel (flash column, 230–400 mesh, or Chromatotron).

4.1. Photosensitized addition 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 [13]. 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 (6H, m, $2CH_3$), 1.4–2.2 (10H, m, $5CH_2$), 2.3–2.6 (2H, m, 2CH) and 3.3–3.9 (5H, m, OCH_3 and 2CH). ^{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, FAB).

4.2. Photosensitized addition 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%). The GC retention time as well as the mass spectrum of **6** were found to be identical to those of 2-methyl-3-pyrrolizidone, reported previously [13].

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 (6H, m, $2CH_3$), 1.4–2.1 (8H, m, $4CH_2$), 2.2–2.8 (2H, m, 2CH) and 3.4–3.9 (8H, m, $2OCH_3$ and 2CH). ^{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, FAB).

4.3. 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 earlier for the same compounds [13]. The product distributions were based on **2** that reacted (25% conversion).

4.4. Photosensitized addition of 2,6-dimethylpiperidine (11) to methyl methacrylate (2)

Irradiation of a mixture of **11** (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 **14** and 170 mg (35%) of **17**. These yields were based on **2** that reacted (40%), as estimated by HPLC.

14: IR spectrum ν_{max} (neat): 3320 (broad, NH) and 1742 (C=O) cm^{-1}. ^1H NMR spectrum ($CDCl_3$): δ = 1.0–1.3 (9H, m, $3CH_3$), 1.5–2.2 (8H, m, $4CH_2$), 2.3–3.0 (2H, m, 2CH), 3.6–3.7 (3H, s, OCH_3) and 5.5–5.8 (1H, 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).

17: IR spectrum ν_{max} (neat): 3350 (broad, NH) and 1744 (C=O) cm^{-1}. ^1H NMR spectrum ($CDCl_3$): δ = 0.9–1.2 (12H, m, $4CH_3$), 1.4–2.2 (10H, m, $5CH_2$), 2.3–2.8 (2H, m, 2CH) and 3.6–3.7 (6H, s, $2OCH_3$). ^{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).

4.5. Photosensitized addition of 2,6-dimethylpiperidine (11) to methyl acrylate (12)

An argon-purged solution of a mixture of **11** (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 **15** and 170 mg

(45%) of **18**. These yields were based on **12** that reacted (40% conversion).

15: IR spectrum ν_{max} (neat): 3350 (broad, NH) and 1744 (C=O) cm^{-1}. ^1H NMR spectrum ($CDCl_3$): $\delta = 1.0–1.2$ (6H, m, $2CH_3$), 1.4–2.0 (8H, m, $4CH_2$), 2.2–2.8 (3H, m, CH_2 and CH) and 3.55–3.7 (3H, s, OCH_3). ^{13}C NMR spectrum ($CDCl_3$): $\delta = 27.11, 27.17$ (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 ($M-H^+$, 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, FAB).

18: IR spectrum ν_{max} (neat): 3300 (broad, NH) and 1744 (C=O) cm^{-1}. ^1H NMR spectrum ($CDCl_3$): $\delta = 1.0–1.2$ (6H, m, $2CH_3$), 1.3–2.0 (10H, m, $5CH_2$), 2.2–2.6 (4H, m, $2CH_2$) and 3.6–3.7 (6H, s, $2OCH_3$). ^{13}C NMR spectrum ($CDCl_3$): $\delta = 28.07$, 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, FAB).

4.6. Photosensitized addition of 2,6-dimethylpiperidine (11) to methyl crotonate (13)

Irradiation of an argon-purged solution of a mixture of **11** (1.7 g, 15 mmol), **13** (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 **16**. The yield of **16** was based on the percentage conversion of **13** (18%).

16: IR spectrum ν_{max} (neat): 3400 (broad, NH) and 1742 (C=O) cm^{-1}. ^1H NMR spectrum ($CDCl_3$): $\delta = 0.9–1.0$ (3H, d, CH_3), 1.05–1.15 (3H, d, CH_3), 1.15–1.25 (3H, s, CH_3), 1.4–1.95 (6H, m, $3CH_2$), 2.0–2.9 (4H, m, CH_2 and 2CH), 3.5–3.7 (3H, s, OCH_3) and 7.8–8.1 (1H, broad, NH). ^{13}C NMR spectrum ($CDCl_3$): $\delta = 14.37, 15.77, 25.32, 26.43$, 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).

4.7. Photosensitized addition of 2,6-dimethylpiperidine (11) to acrylonitrile (19)

Irradiation (4 h) of an argon-purged solution of a mixture of **11** (1.7 g, 15 mmol) and **19** (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 **20** and 140 mg (50%) of **21**. These yields were based on **19** that reacted (30%).

20: IR spectrum ν_{max} (neat): 3340 (broad, NH) and 2240 (nitrile) cm^{-1}. ^1H NMR spectrum ($CDCl_3$): $\delta = 1.0–1.2$ (6H, m, $2CH_3$), 1.4–2.0 (8H, m, $4CH_2$) and 2.1–2.6 (3H, m, CH_2 and CH). ^{13}C NMR spectrum ($CDCl_3$): $\delta = 11.84$, 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).

21: IR spectrum ν_{max} (neat): 3360 (broad, NH) and 2242 (nitrile) cm^{-1}. ^1H NMR spectrum ($CDCl_3$): $\delta = 1.0–1.2$ (6H, 2s, $2CH_3$), 1.2–1.4 (4H, m, $2CH_2$), 1.5–2.0 (6H, m, $3CH_2$) and 2.3–2.6 (4H, m, $2CH_2$). ^{13}C NMR spectrum ($CDCl_3$): $\delta = 11.36, 16.64, 16.82, 34.27, 36.72, 37.91, 40.24$ (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).

4.8. Photosensitized addition of cyclohexylamine (22) to methyl acrylate (12)

Irradiation of a mixture of **22** (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 **23**, which was previously characterized and the spectral features of which have been previously reported [13].

4.9. Photosensitized reaction of triethylamine (2) with methyl methacrylate (2) in water

Irradiation of a mixture of **24** (1.5 g, 15 mmol) and **2** (1.5 g, 15 mmol) in water (500 ml) containing 5×10^{-4} M of anthraquinone-2-sulphonic acid (sodium salt) 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 (**25**). The yield reported was based on **2** that reacted (10%), as estimated by HPLC. The photoreaction was repeated several times, the duration of irradiation being varied, and it was found that prolonged irradiation (8 h) did not bring about higher conversion of **2**.

25: 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 ($CDCl_3$): $\delta = 0.9–1.2$ (9H, m, $3CH_3$), 1.8–2.1 (2H, m, CH_2), 2.3–2.6 (2H, t, CH_2), 2.9–3.3 (1H, m, CH) and 3.5–3.8 (1H, m, CH). ^{13}C NMR spectrum ($CDCl_3$): $\delta = 12.61$, 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, FAB).

4.10. Photosensitized reaction of triethylamine (24) with methyl acrylate (12) in water

Irradiation (2 h) of an aqueous (500 ml) solution of a mixture of **24** (1.5 g, 15 mmol) and **12** (1.3 g, 15 mmol), containing 5×10^{-4} M of anthraquinone-2-sulphonic acid (sodium salt) 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 (**26**). The yield of **26** was based on percentage conversion of **12** (12%).

26: 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 ($CDCl_3$): $\delta=0.9$–1.2 (6H, m, $2CH_3$), 1.6–2.4 (4H, m, $2CH_2$), 3.0–3.8 (3H, m, CH_2 and CH). ^{13}C NMR spectrum ($CDCl_3$): $\delta=12.31$, 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, FAB).

4.11. Photosensitized reaction of N-methylpiperidine (27) with methyl acrylate (12) in water

Irradiation of a mixture of **27** (1.5 g, 15 mmol) and **12** (1.3 g, 15 mmol) in the presence of anthraquinone-2-sulphonic acid (sodium salt) in water for 2 h and product analysis by capillary GC–MS indicated the presence of 60% of **29** and 20% of **30**. The yields reported were based on the conversion of **12** (15%), as estimated by HPLC. The spectroscopic data of **29** and **30** were identical to those for the same compounds reported previously [14].

4.12. Photosensitized reaction of N-ethylpiperidine (28) with methyl acrylate (12) in water

Irradiation (2 h) of a mixture of **28** (1.7 g, 15 mmol) and **12** (1.3 g, 15 mmol) in water (500 ml), containing anthraquinone-2-sulphonic acid (sodium salt) (5×10^{-4} M) and analysis of the photoproduct mixture by GC–MS indicated the formation of 60% of **29** and 15% of **30**. These percentages are based on methyl acrylate conversion (17%). The photoproducts (**29** and **30**) were separated using column chromatography and they were characterized by comparison of their spectral data with those of identical compounds reported previously [14].

4.13. Photosensitized reaction of N-methylmorpholine (31) with methyl methacrylate (2) in water

Irradiation of a mixture of **31** (1.5 g, 15 mmol), **2** (1.5 g, 15 mmol) and anthraquinone-2-sulphonic acid (sodium salt) (5×10^{-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 **32** and 30% of **33**. The yields were based on the conversion of **2** (10%), as estimated by HPLC. The spectral data of **32** and **33** were in good agreement with those for the same compounds reported previously [14].

5. Conclusion

The photosensitized reactions discussed above suggest that these processes can be used as mild methods for carbon–carbon bond forming reactions. The one-step synthesis of indolizidone, pyrrolizidone and spirolactams from the parent amines promises the synthetic utility of these reactions and their potential applications in the synthesis of some biologically active compounds as well as natural products.

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