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ORIGINAL PAPER

Synthesis, X-ray Structure and Photo Chemistry of 2-(Methyl(1-Phenylvinyl)Carbamoyl)Phenyl Acetate

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Abstract 2-(Methyl(1-phenylvinyl)carbamoyl)phenyl acetate (**SM**), empirical formula $C_{18}H_{17}NO_3$, crystallizes in the triclinic space group, P−1, with unit cell parameters $a = 9.10870(10)$ Å, $b = 10.56940(10)$ Å, $c = 16.1340(2)$ Å, $\alpha = 78.0590(10)°$, $\beta = 89.5080(10)°$, $\gamma = 86.6830(10)°$, $Z = 4$. The 2-(methyl(1-phenylvinyl)carbamoyl)phenyl acetate (**SM**) molecule, upon irradiation of UV-light below 3,000 Å, releases acetate group to give six membered cyclic lactam **1** as the major product. The quantum yield for the lactam **1** was found to be 0.053. An alternate conrotatory 6-pi electron photochemically allowed electrocyclic ring closure reaction also occurs upon irradiation to give a six-membered cyclic zwitterionic intermediate which retains acetate as leaving group. A [1,5]-H shift would then give the isomerized product **2.** The quantum yield for the lactam **2** was found to be 0.026. A minor oxidation product lactam **3** that retains the leaving group also formed, likely from loss of a proton and tautomerization of enol. The loss of one hydrogen molecule is the driving force for revival of aromaticity in the minor product **3**. The quantum yield for the lactam **3** was found to be 0.012. The low value of total quantum yield (0.091) for photocyclization of **SM** can be explained as the photoproducts absorb light in competition with the photoreactant.

Keywords X-ray · 2-(Methyl(1-phenylvinyl) carbamoyl)phenyl acetate · Photochemistry · Enamide · Lactam · Quantum yield

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Introduction

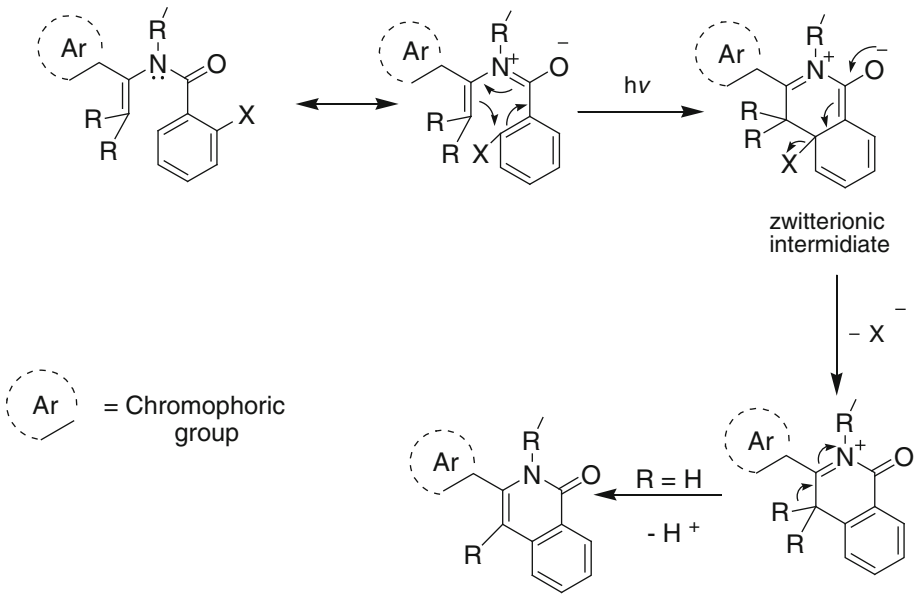
Aromatic enamides are an interesting class of conjugated systems possessing a marked degree of hexatrienic character. Therefore, photochemical electrocyclic ring closure reactions are possible which would potentially give zwitterionic intermediates [1–3] (Scheme 1). This research recognizes that the zwitterionic intermediates could eliminate leaving group anions. The goal is therefore to synthesize the suitable target molecules that can expel leaving group anions from zwitterions generated by a photochemical electrocyclization process.

The research has practical importance for solving problems in biological studies. Biological studies are confronted by the problem of instantly delivering biological reagents in order to trigger a specific biological process on a cellular level under physiological conditions. A protecting group is chosen that inactivates biological reagent or the bioeffector molecule until it is needed. The bioeffector is released by a short pulse of light within the cell to nearly instantaneously initiate the biological process to be studied [4–7]. The reagent or leaving group to be expelled should be a biologically important molecule.

Although a number of photo cleavable protecting groups are currently available for use in studies of biological processes, no single type meets all of the requirements needed for use in a given application. Therefore, there is still the need for the development of new photo removable leaving groups that can fulfill specific requirements for practical applications [8, 9]. The proposed research described herein focuses upon a new strategy for the elimination of acetate leaving group from photogenerated zwitterionic intermediates.

The zwitterionic intermediates would be generated photochemically via an electro cyclic ring closure reaction

Scheme 1 Zwitterionic intermediate that eliminate leaving group anions



of certain conjugated aromatic enamides. The electrocyclic ring closure can be considered to be a photochemically allowed 6-pi electron conrotatory process [10–12] in the excited state. The type of leaving group to be eliminated from the zwitterionic elimination would be the carboxylate group.

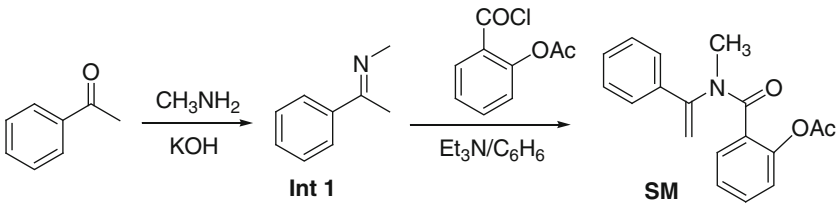
The chief advantage in the use of electrocyclic reactions to generate zwitterions is that chromophores (Ar) can be incorporated which would absorb at long wavelengths [13–15]. It should be possible to affect electrocyclization (and subsequent elimination of the leaving group) by use of long wavelengths of light. For example, visible light has long been used to achieve electrocyclic reaction in photochromic molecules.

In this article, we report the photochemistry of 2-(methyl(1-phenylvinyl)carbamoyl)phenyl acetate (**SM**) which bear acetate leaving group. Under aqueous conditions, the acetate leaving group is expelled upon irradiation of light (<300 nm) to give cyclic lactam as the major process.

Experimental

Synthesis of Photoreactant SM

The synthesis of **SM** involves the acylation of imine of acetophenone with o-acetylsalicyloyl chloride. The imine**Int1** was initially prepared from the reaction of methylamine in ethanol with acetophenone in presence of KOH as a dehydrating agent. KOH seems to provide the driving force for the reaction that leads to a net forward direction. The synthesis of title compound (**SM**) is represented in Eq. 1.



(1)

Synthesis of (E)-*N*-(1-phenylethylidene)methanamine (**Int1**)

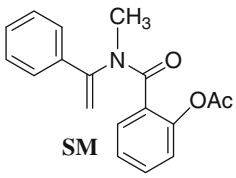
40 g (0.33 mol) of acetophenone was taken in a round bottom flask. Then 13.4 g (0.43 mol) of methylamine in ethanol was added dropwise via a syringe. 15 g KOH (0.26 mol) pellets were added and the mixture was stirred at room temperature for 4 h. The reaction mixture

was filtered and the filtrate was extracted with ether. The ether extract was washed 3 times. The organic layer was dried over sodium sulphate and concentrated in vacuum to give oil. The oil was distilled to give 24.5 g of acetophenone and imine mixture. One gram of mixture contains 1.17 mmol of imine (**Int1**) by ^{1}H NMR spectroscopy. The spectral data for imine (**Int1**) in the mixture: ^{1}H NMR ($CDCl_3$) δ 2.14 (s, 3H), 3.28 (s, 3H), 7.2–7.9 (m, 5H).

Synthesis of 2-(Methyl(1-Phenylvinyl)Carbamoyl)Phenyl Acetate (**SM**)

19 g of distilled mixture contains 3.0 g (22.3 mmol) of imine (**Int1**) was taken in a round bottom flask. 70 ml of triethyl amine was added to it. 8.8 g of o-acetylsalicyloyl chloride in 70 ml of benzene was added at 5–8 °C to the above mixture solution. The reaction mixture was warmed to room temperature and refluxed for 5 h. Upon cooling, triethylamine hydrochloride precipitate was filtered. The filtrate was concentrated in vacuo and the residue was dissolved in benzene. The benzene solution was washed with $NaHCO_3$, brine solution, dried over Na_2SO_4, and concentrated in vacuo to give 21.58 g crude oil. The residue was chromatographed on silica gel (76% yield), eluting with 33% ethyl acetate in hexane to obtain colorless, crystalline amide after crystallization from 25% ethyl acetate in hexane. The spectral data were as follows: ^{1}H NMR ($CDCl_3$) δ 2.23 (s, 3H), 3.15 (s, 3H), 5.04 (s, 1H), 5.23 (s, 1H), 6.8–7.5 (m, 9H); ^{13}C NMR (CDCl3) δ 21.64, 36.41, 112.74, 123.44, 125.54, 126.49, 128.05, 129.20, 129.26, 129.35, 129.66, 130.66, 136.61, 148.62, 168.55, 169.55 (Fig. 1).

Fig. 1 Molecular scheme of 2-(methyl(1-phenylvinyl) carbamoyl)phenyl acetate (**SM**)

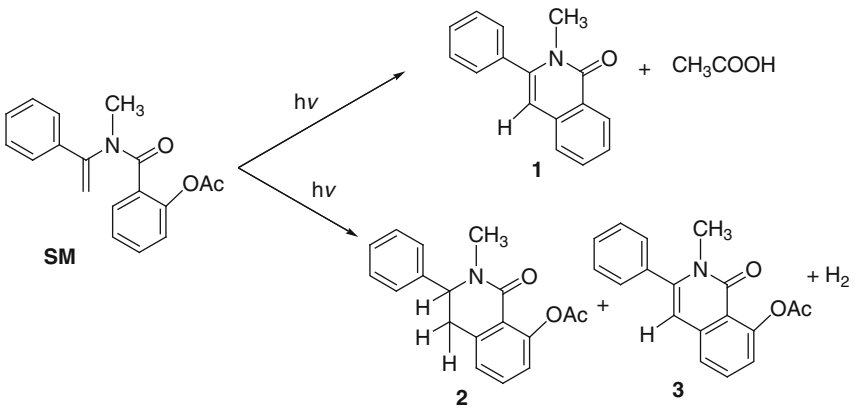


Crystal Structure of Title Compound (**SM**)

The crystal structure of compound (**SM**) was obtained from modern X-ray Diffractometer (Brucker-APEX2) with CCD camera and Cu-Kα (λ = 1.54178 Å) at 100(2) K. The data collection for structure **SM** was carried out by APEX2 v2.1-4 (Bruker 2007). The cell refinement and structure refinement was carried out by SAINT v7.23A (Bruker 2005) and SHELXL-97 v.97-2 (Sheldrick 1993–1997) respectively. In Fig. 2, the X-ray structure of enamide (**SM**) is shown with atomic labeling. The data completeness was found to be low (0.921) which may be due to imperfections present in the crystal during crystal growth. CheckCIF was carried out to identify the outliers as well as unusual parameters.

Photolysis Result

At lower concentrations, the compound **SM** has λ_{max} below 3,000 Å. The compound was thus photolysed without a Pyrex filter. From ^{1}H NMR spectroscopy, it was found that three photo-products were formed as a result of the photochemical reaction as shown in Eq. 2.



(2)

Photolysis of **SM** in 50% H_2O and CH_3CN gave lactam **1** as major product and lactam **3** as minor oxidation product. All three lactams were characterized by ^{1}H and ^{13}C NMR Spectroscopy. HPLC analyses were performed

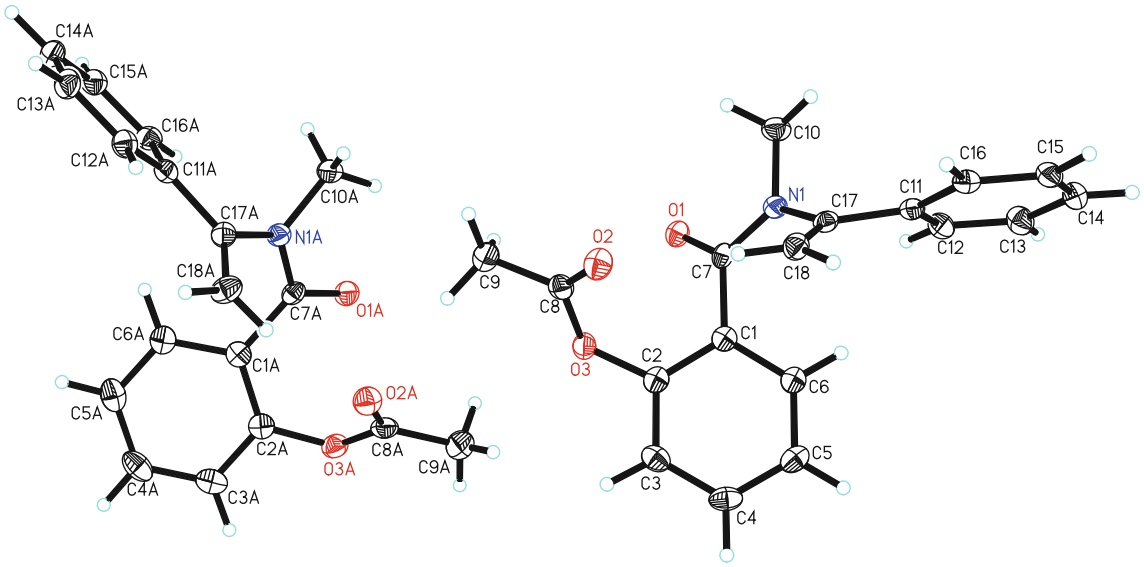


Fig. 2 X-ray strucrure of 2-(methyl(1-phenylvinyl)carbamoyl)phenyl acetate (**SM**)

Table 1 Crystal data and structure refinement for Compound (**SM**)

Empirical formula	C18 H17 N O3	
Formula weight	295.33	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Triclinic	
Space group	P−1	
Unit cell dimensions	$a = 9.10870(10)$ Å	$\alpha = 78.0590(10)°$
	$b = 10.56940(10)$ Å	$\beta = 89.5080(10)°$
	$c = 16.1340(2)$ Å	$\gamma = 86.6830(10)°$
Volume	1517.11(3) Å^3	
Z	4	
Density (calculated)	1.293 Mg/m^3	
Absorption coefficient	0.716 mm^{-1}	
F(000)	624	
Crystal size	0.55 × 0.45 × 0.40 mm^3	
Theta range for data collection	2.80–67.29°	
Index ranges	$-10 \leq h \leq 10$, $-12 \leq k \leq 12$, $0 \leq l \leq 19$	
Reflections collected	25399	
Independent reflections	5005 [R(int) = 0.0169]	
Completeness to theta = 67.29°	92.10%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7628 and 0.6943	
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	5005/0/534	
Goodness-of-fit on F^2	1.045	
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0311$, $wR_2 = 0.0793$	
R indices (all data)	$R_1 = 0.0318$, $wR_2 = 0.0798$	
Extinction coefficient	0.0083(4)	
Largest diff. peak and hole	0.262 and −0.166 e·Å^{-3}	

Table 2 Selected bond lengths (Å), Bond and Torsion angles (°) for compound (**SM**)

Bond lengths (Å)		Bond angles (°)		Torsion angles (°)	
O(1)–C(7)	1.2297(14)	C(8)–O(3)–C(2)	118.74(9)	C(6)–C(1)–C(2)–C(3)	3.06(17)
N(1)–C(10)	1.4686(15)	C(7)–N(1)–C(17)	126.08(10)	C(7)–C(1)–C(2)–C(3)	177.39(11)
N(1)–C(17)	1.4368(15)	C(7)–N(1)–C(10)	116.99(10)	C(6)–C(1)–C(2)–O(3)	−173.32(10)
C(1)–C(2)	1.3962(17)	C(17)–N(1)–C(10)	116.47(10)	C(7)–C(1)–C(2)–O(3)	1.01(17)
C(1)–C(6)	1.3974(17)	C(2)–C(1)–C(6)	117.20(11)	C(8)–O(3)–C(2)–C(3)	121.22(11)
C(1)–C(7)	1.5033(16)	C(2)–C(1)–C(7)	120.77(10)	C(8)–O(3)–C(2)–C(1)	−62.19(15)
C(17)–C(18)	1.3279(17)	C(6)–C(1)–C(7)	121.78(10)	C(17)–N(1)–C(7)–O(1)	168.08(10)
C(11)–C(17)	1.4878(16)	O(1)–C(7)–N(1)	121.11(11)	C(10)–N(1)–C(7)–O(1)	−3.81(16)
O(2)–C(8)	1.2001(15)	O(1)–C(7)–C(1)	120.07(10)	C(17)–N(1)–C(7)–C(1)	−14.37(16)
O(3)–C(8)	1.3618(14)	N(1)–C(7)–C(1)	118.77(10)	C(10)–N(1)–C(7)–C(1)	173.74(10)
O(3)–C(2)	1.4006(14)	O(2)–C(8)–O(3)	123.11(11)	C(2)–C(1)–C(7)–O(1)	−41.83(16)
N(1)–C(7)	1.3616(15)	C(18)–C(17)–N(1)	120.87(10)	C(6)–C(1)–C(7)–O(1)	132.24(12)
O(1A)–C(7A)	1.2283(14)	C(18)–C(17)–C(11)	123.78(11)	C(2)–C(1)–C(7)–N(1)	140.59(11)
O(2A)–C(8A)	1.1973(15)	N(1)–C(17)–C(11)	115.35(10)	C(6)–C(1)–C(7)–N(1)	−45.33(15)
O(3A)–C(8A)	1.3650(15)	C(7A)–N(1A)–C(17A)	125.08(10)	C(2)–O(3)–C(8)–C(9)	176.42(10)
O(3A)–C(2A)	1.3949(15)	C(7A)–N(1A)–C(10A)	118.13(10)	C(7)–N(1)–C(17)–C(18)	−52.47(16)
N(1A)–C(7A)	1.3650(15)	C(17A)–N(1A)–C(10A)	115.79(9)	C(10)–N(1)–C(17)–C(18)	119.46(13)
N(1A)–C(17A)	1.4415(15)	C(6A)–C(1A)–C(2A)	117.42(11)	C(7)–N(1)–C(17)–C(11)	126.90(12)
N(1A)–C(10A)	1.4676(15)	C(6A)–C(1A)–C(7A)	120.96(11)	C(10)–N(1)–C(17)–C(11)	−61.18(13)
C(1A)–C(6A)	1.3982(17)	O(1A)–C(7A)–C(1A)	119.58(10)	C(8A)–O(3A)–C(2A)–C(1A)	54.00(15)
C(1A)–C(2A)	1.3987(17)	N(1A)–C(7A)–C(1A)	118.58(10)	C(17A)–N(1A)–C(7A)–O(1A)	−166.30(11)
C(11A)–C(17A)	1.4873(16)	C(18A)–C(17A)–N(1A)	119.58(11)	C(10A)–N(1A)–C(7A)–O(1A)	1.72(16)
C(17A)–C(18A)	1.3257(18)	N(1A)–C(17A)–C(11A)	115.50(10)	C(10A)–N(1A)–C(17A)–C(11A)	64.03(13)

on a 14.6 × 250 mm Partisil ODS-2 column eluting with 75:25 (v/v) methanol and water as solvent for quantum yield determination.

Results and Discussion

The title compound, $C_{18}H_{17}NO_3$, consists of a phenylvinyl group in conjugation with *N*-methyl substituted benzamide moiety. The crystal data and structure refinement details are provided in Table 1. CheckCIF results tell us that diffractions were collected as low as theta value of 0.921. Absorption corrections were given as multi-scan process and reflection counts are less than 95% complete. The selected bond lengths, bond and torsion angles are reported in Table 2. The bond length of vinyl group C(17)–C(18) in compound (**SM**) is found to be 1.3279(17)Å which is very close to the theoretical value for a double bond.

It is found that compound **SM**, in solid state is dimeric in nature. **SM** can be cyclized at two ortho positions of the aromatic ring where one of ortho position is occupied by the acetate (OAc) leaving group and other ortho position by hydrogen atom itself. This compound thus can be cyclized photochemically at both the ortho-positions to give rise to six-membered cyclic lactams in solution. The bond distances from the alkene (phenyl vinyl group) to the two ortho positions for photocyclization are 3.39 and 3.99 Å for H and acetate ortho positions, respectively. It is found that the alkene for cyclization is closer to the ortho position where leaving group is not present. Hence, it can be concluded that the likely pathway for cyclization would be where no leaving group is present in solid state.

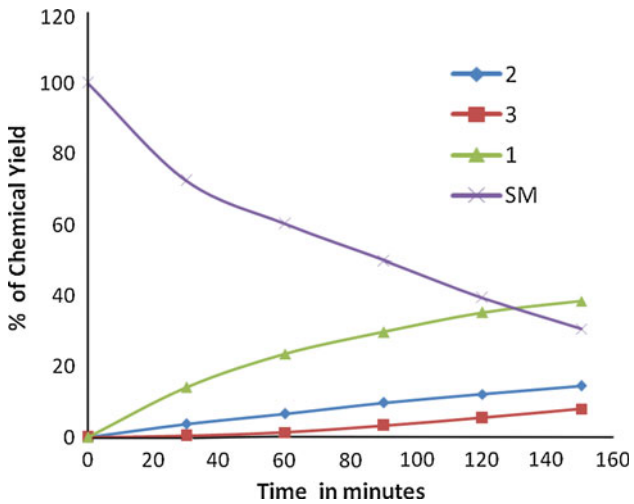


Fig. 3 Plot of % chemical yield versus time in minutes

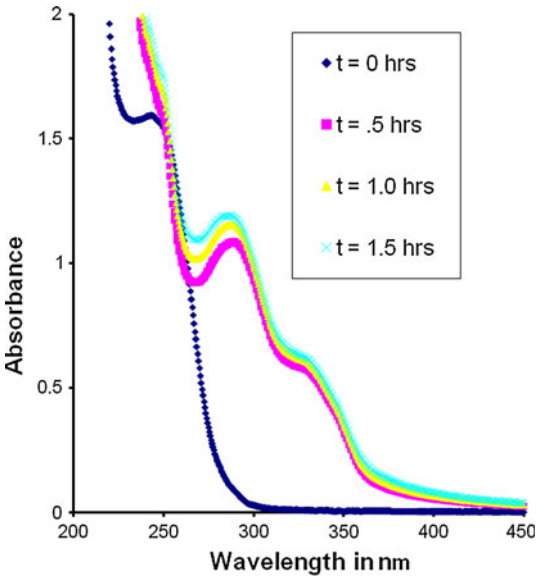


Fig. 4 UV-spectra of photolyzed reactant at different intervals of time

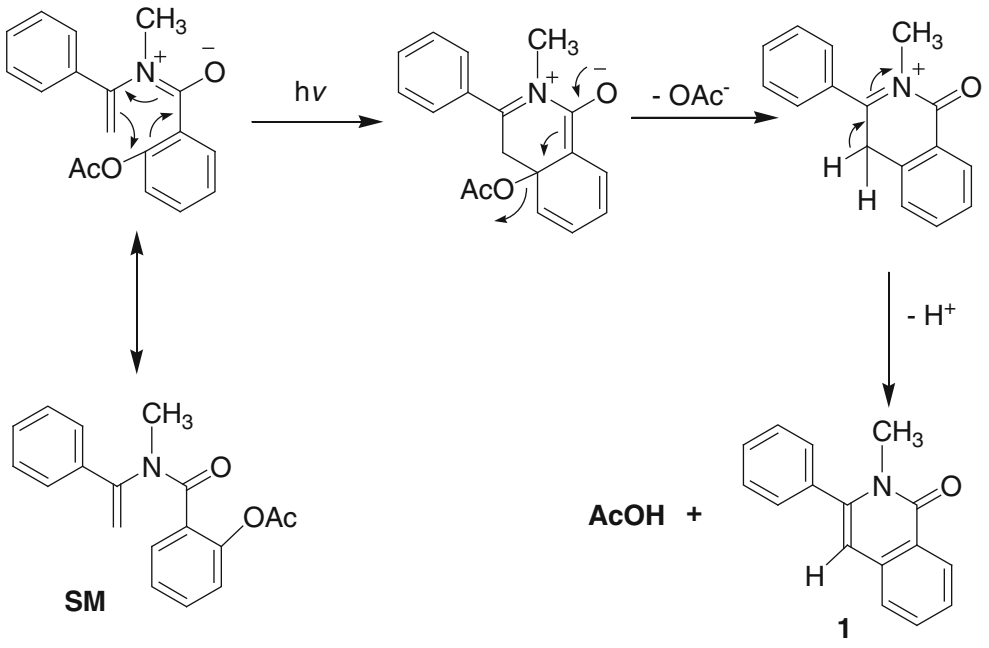
The Fig. 3 shows the plot of percentage of chemical yield vs time for the photolysis of **SM** as starting material. Within 30 min, 18% of starting material was converted into photoproducts. After 150 min, 38% of the major product was formed. It was found that the elimination of the ortho acetate leaving group is the major process in comparison to [1,5]-H shift, which forms lactam **1**. The other minor product was **3**, which would be formed by an oxidation that must occur at some stage of photolysis.

The quantum yield results were obtained for photolysis at 270 nm for 15 h. The electrocyclic reaction which would be required to form three products would have a total quantum yield of 0.091. The highest quantum yield for the process of formation of lactam **1** is found to be 0.053 where the release of acetic acid takes place. The minor oxidation product **3** has quantum yield value 0.012.

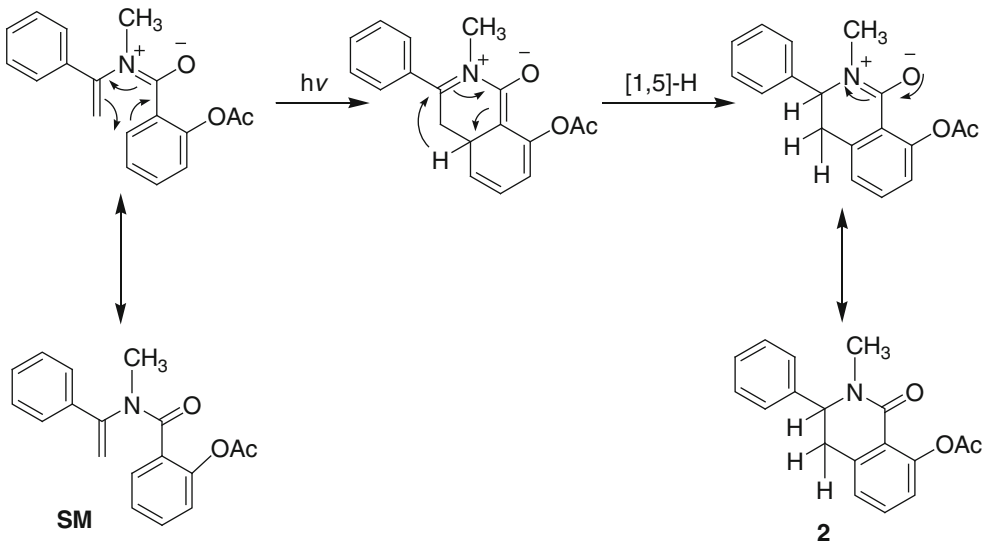
However, the overall low value of total quantum yield value for the photolysis of **SM** can be explained from the UV-spectra of the photolyzed starting material. Figure 4 shows that the photoproducts absorb light in competition with the starting material. Since, lactam **1** and **3** have stilbeneoid moiety present, they will definitely absorb light at higher wavelengths in comparison to the photoreactant. Hence, the absorption of light by co-products hinders the process of effective photolysis of **SM** which gives rise to a low total quantum yield value of 0.091.

The photoreactant **SM** undergoes cyclization to give rise to three products via different mechanistic pathways. Photo product **1** is formed via a zwitterionic intermediate where the elimination of acetic acid takes place (Scheme 2). The loss of proton from the molecule gives a neutral lactam containing stilbenoid moiety as stable product. An alternate electrocyclic ring closure reaction also occur upon irradiation to give a six-membered cyclic zwitterionic intermediate which retains acetate as leaving group (Scheme 3). A [1,5]-H shift would then give the isomerized product **2**.

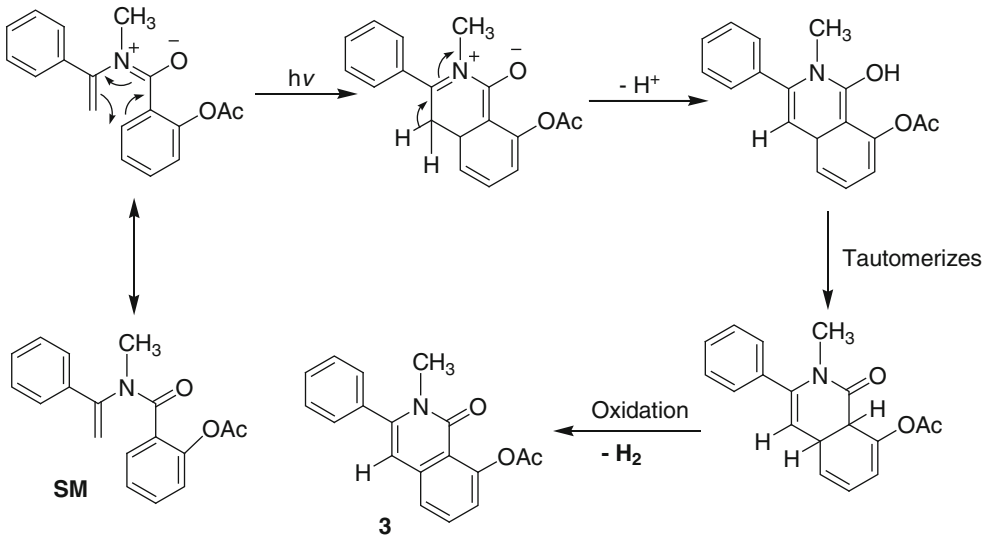
Interestingly, the product **3** is formed from the same photoreactant (**SM**) via a zwitterionic intermediate where the liberation of one molecule of hydrogen takes place due



Scheme 2 Mechanism for formation of lactam 1



Scheme 3 Mechanism for formation of lactam 2



Scheme 4 Mechanism for formation of lactam 3

to oxidation (Scheme 4). Loss of a proton can evidently compete with [1,5]-H shift to give the oxidized lactam **3** after tautomerization of the enol.

Supporting Information Available

X-ray crystallographic files, in Cif format, for the structure determinations of compound (**SM**) has been deposited with the Cambridge Crystallographic Data Center, (CCDC). Deposition number is CCDC 818894. Copies of this information may be obtained free of cost from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ (fax: +44-1223-336033; email: deposit@ccdc.cam.uk or at: http://www.ccdc.cam.ac.uk).

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