Regioselective Photocyclization Reactions of 3-Allyloxy-6-chloro-2-(thiophen-3-yl)-4H-chromen-4-one: Solvent Effect

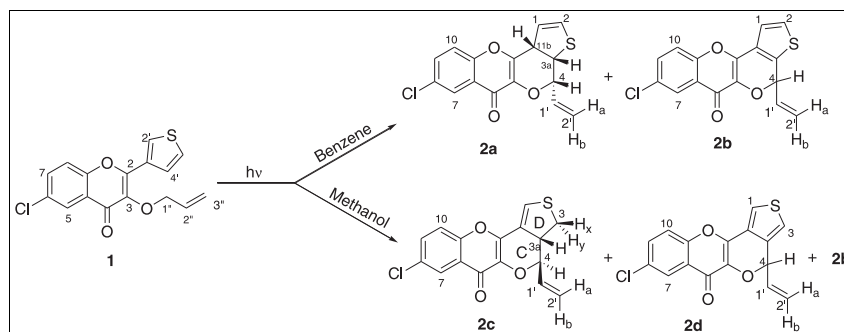Ramesh C. Kamboj,* Dinesh Kumar, Rita Arora, Surinder Berar, and Geeta Sharma

Department of Chemistry, Kurukshetra University, Kurukshetra 136119, India
*E-mail: rckamboj@rediffmail.com

The photo-irradiation of thienylchromenone resulted in the regioselective cyclization which is exclusively controlled by the nature of solvent used as reaction medium. Compared to nonpolar medium, polar solvent furnished a diverse array of novel angular tetracyclic photoproducts with gem-dihydro functionality and exocyclic double bonds on the fused pyran ring, which is unprecedented to best of our knowledge.

J. Heterocyclic Chem., **50**, E200 (2013).

INTRODUCTION

Regioselective photochemical reactions have become key topics in organic photochemistry. Many research efforts have been directed to obtain regioselective photocyclized products [1]. In most cases, because several types of photoproducts were produced, controlling the selectivity of the product is very hard. In our earlier study, an attempt was made to study the regioselective photocyclization of 3-alkoxy-chromones bearing a 3-furyl [2] group at C-2, possessing two sites for clipping of 1,4-biradical. In that case, the photoproducts were furnished only by clipping at C-2′ position of furyl moiety and no photoproduct formation by clipping at C-4′ (Fig. 1) was observed in methanolic media. And also, no isomeric product was realized through the photo-activation of furan moiety [3,4], which itself is a good chromophore (Scheme 1).

We irradiated the chromenone having 3-thienyl group at 2-position (in place of 3-furyl) and also studied the effect of reaction media (benzene/methanol) to further explore the possibility of regioselective photocyclization in such type of molecules. Here, the interesting results were obtained. The photolysis of 3-allyloxy-6-chloro-2-(thiophen-3-yl)-4H-chromen-4-one **1** in a nonpolar solvent, that is, benzene, effectively afforded the cyclized and cyclodehydrogenated photoproducts by the clipping of initially formed 1,4-biradical (**A**) with the C-2′ position of the thiophene ring (Scheme 2). The photolysis of same in a polar solvent, that is, methanol, selectively produced entirely different type of cyclized and cyclodehydrogenated photoproducts enclosed the *gem*-dihydro functionality and exocyclic double bonds onto the

fused pyran ring, respectively, by clipping of 1,4-biradical (**B**) to the C-4′ position of the thienyl group that is unforeseen in the studied chromenone (Scheme 3); furthermore, this indicated that the product selectivity in thienylchromenone **1** is perfectly controlled by the reaction media.

RESULTS AND DISCUSSIONS

The required substrate for photolysis, 3-allyloxy-6-chloro-2-(thiophen-3-yl)-4H-chromen-4-one **1** was synthesized by the literature procedure [2] and examined toward photolysis in both polar (methanol) and nonpolar (benzene) solvents (Scheme 1).

The photo-irradiations of **1** in benzene, a nonpolar solvent, with pyrex filtered UV-light from 125 W high-pressure mercury lamp under nitrogen atmosphere produced the photoproducts **2a** and **2b** (Scheme 1). The formation of products **2a** and **2b**, in benzene, plausibly occurs through the clipping of 1,4-biradical (**A**) with C-2′ position (Scheme 2). The structure of compounds **2a** and **2b** was unequivocally establish by their spectral data when compared with our earlier studies [4,5].

To study the photochemical behavior of **1** in a polar media, it was photolysed under identical conditions in its methanolic solution (1.0 mM) that furnished the exclusive diverse photoproducts **2c**, **2d** as major and a minor product **2b**. The structure and stereochemistry were suggested by the spectral data. The compound **2c** in its IR spectrum exhibited a strong absorption band at $1628 \, \text{cm}^{-1}$ that may be assigned to the C=O of the pyrone moiety. The
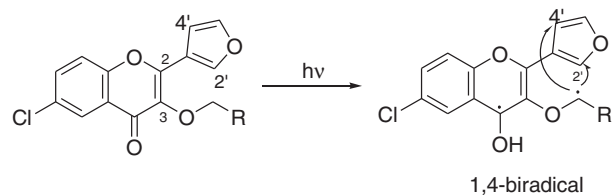
Figure 1. Possible sites for clipping at furyl group with 1,4-biradical.

distinguishing feature in the ^{1}H NMR spectra of **2c** is the diastereotopic protons (H_x and H_y) at C-3 that resonated at different δ values. The 2D HSQC spectra also confirmed the presence of the C-3 bearing two hydrogens in the structure of **2c** as the spots aroused below H_x-3 and H_y-3 corresponds to the negative signal at δ 39.03 that became available due to C-3. The proton H_x-3 appeared downfield as it falls in deshielding zone of allyl group and showed a resonance at δ 4.04 (1H, ddd, $J_{gem} = 16.5$ Hz, $J_{3Hx,3a} = 4.7$ Hz, $J_{3Hx,1} = 2.4$ Hz) with *gauche* conformation giving it approximately a *cis*-disposition with respect to the H-3a. The proton H_y-3 resonated at δ 3.86 (ddd, $J_{gem} = 16.5$ Hz, $J_{3Hy,3a} = 5.0$ Hz, $J_{3Hy,1} = 3.7$ Hz). The coupling constant $J_{3Hy,3a} = 5.0$ Hz indicated H_y-3 to have a near *trans*-disposition to C-3a. The proton H-1 was located at δ 6.62 (ddd, $J_{1,3Hy} = 3.6$ Hz, $J_{1,3Hx} = 2.4$ Hz, $J_{1,3a} = 2.4$

Hz). The ring junction proton H-3a was seen at δ 4.49 (dddd, $J_{3a,4} = 10.8$ Hz, $J_{3a,3y} = 5.0$ Hz, $J_{3a,3x} = 4.7$ Hz, $J_{3a,1} = 2.2$ Hz). The pyran proton H-4 gave a dd at δ 4.37 ($J_{4,3a} = 10.8$ Hz, $J_{vic} = 6.9$ Hz). The 2D spectral (COSY and NOESY) studies further confirmed the existence of the respective couplings between these protons.

The dehydrogenated photoproduct **2d**, in its mass spectrum, showed the *m/z* 317 as the base peak as that of **2b** but in the ^{1}H NMR spectrum, the two thienyl protons H-1 and H-3 resonated as a singlet at δ 7.44 that distinguished it from the **2d**. The pyran proton H-4 appeared as doublet at δ 6.05 ($J_{vic} = 6.3$ Hz) that again illustrates the absence of proton at C-3a in **2d**.

The formation of photoproducts **2c** and **2d** cannot be explained simply by the aforementioned route (Scheme 2) and there is no other favorable path except the one given in the succeeding text (Scheme 3):

According to this path, the initially formed 1,4-biradical (**B**) clipped with C-4′ position of the *in situ* generated Dewar thiophene type intermediate to give the photoproducts consequently. A number of reports are available on the valence bond isomerization of thiophene to Dewar thiophene on photo-irradiation [6]. The minor photoproduct **2b** in methanol is formed simply by the interaction of 1,4-biradical [7,8] with C-2′ of activated and/or unactivated thiophene ring.

Scheme 1. Photocyclization of thienylchromenone **1**.
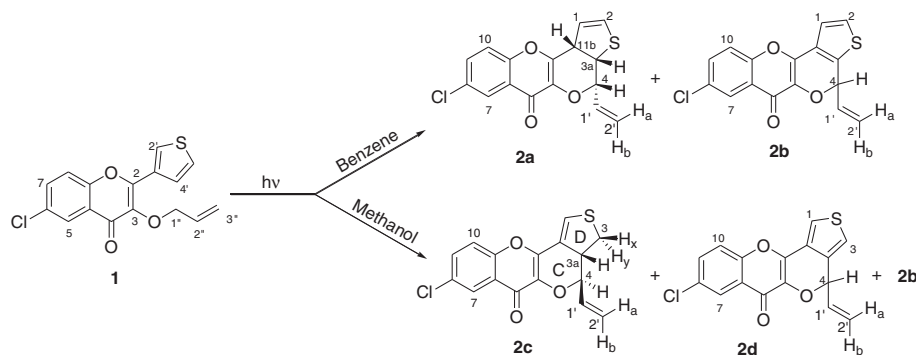
Scheme 2. Photocyclization of thienylchromenone **1** in benzene.
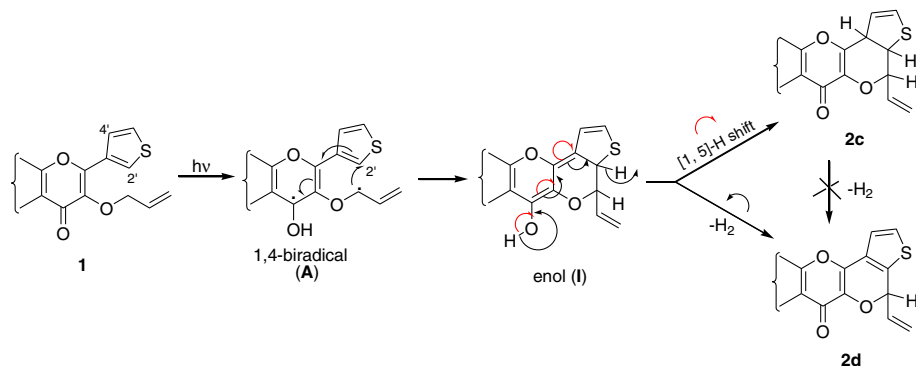
Scheme 3. Photocyclization of thienylchromenone **1** in methanol.
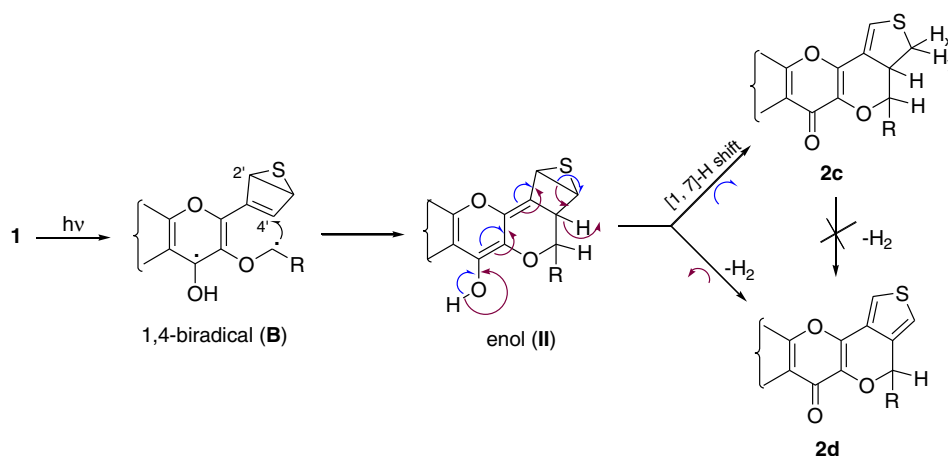
Even though we have not isolated any Dewar thiophene type intermediate, but one of the possible reasons for the formation of different photoproducts in different solvents (i.e., methanol and benzene) is solvatochromism [9]. This is supported by the absorption spectra of the target chromenone **1** in these solvents (Fig. 2).

In methanol, the chromenone **1** showed strong $\pi \to \pi^*$ absorption in the range of 250–310 nm ($\lambda_{max} = 302$ nm) and $n \to \pi^*$ absorption at 348 nm. But in benzene, the same chromenone **1** showed a strong absorption band due to $n \to \pi^*$ ($\lambda_{max} = 354$ nm) with no/or very weak $\pi \to \pi^*$ absorption (250–310 nm). Thus, a polar solvent, that is, methanol lowers the $\pi \to \pi^*$ excitation energy ($\lambda_{max} = 302$ nm) of the conjugated thienyl group in chromenone **1** and probably leads to the photoisomerisation of thienyl group into Dewar thiophene type moiety that is responsible for the formation of the diverse photoproducts **2c** and **2d** (Scheme 3). However, in benzene, a nonpolar solvent, the $\pi \to \pi^*$ excitation is less favorable and the photoproducts **2a** and **2b** were formed simply by the interaction of 1, 4-biradical (**A**) with C-2′ position of the thienyl group (Scheme 2) as analogously reported in earlier cases [4,5].

In conclusion, the photo-irradiation of thienylchromenone **1** resulted in the regioselective formation of a diverse array of novel angular tetracyclic photoproducts and their formation is exclusively controlled by the nature of solvent used as reaction media.

EXPERIMENTAL

The photo-irradiation was carried out with a 125-W Hg lamp using a pyrex filter. The ¹H NMR spectra were recorded on 400-MHz Bruker spectrometer and 300-MHz (75.4 MHz for ¹³C NMR) Bruker spectrometer using TMS as internal standard. The electronic absorption spectra were recorded on a double beam spectrophotometer: 2203 SMART. Mass spectra were recorded at 3500 eV as (ESI + Q1 mode). The columns for purification were packed with Silica gel 100–200 mesh in pet.ether. The elution was carried out with increasing proportion of benzene in petroleum ether–benzene mixture.

Synthesis of 3-Allyloxy-6-chloro-2-(thiophen-3-yl)-4H-chromen-4-one (1). To a suspension of respective 3-hydroxychromenone (0.556 g, 0.002 mol) and freshly ignited K₂CO₃ (1.38 g, 0.01 mol) in dry acetone, allyl bromide (0.242 g, 0.002 mol) and tetra-n-butylammonium iodide (0.050 g) was added. The reaction mixture was refluxed for 4 h and the color of
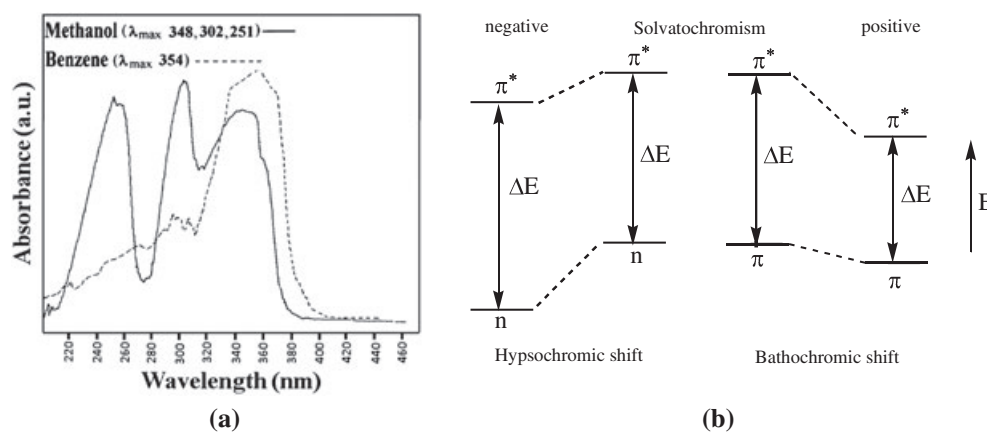
Figure 2. (a) Absorption spectrum of chromenone **1** in methanol and benzene. (b) Solvatochromism by changing the polarity of solvent.

reaction mixture change from orange-red to white. Filtration, evaporation of solvent, and crystallization of the residue gave **1** (81%), white solid; mp 102–104°C; IR: 1636 (C=O), 1605 (C=C) cm^{-1}; UV: λ_{max} (methanol) 348, 302, 251 nm; λ_{max} (benzene) 354 nm; ^{1}H NMR (CDCl$_3$/300 MHZ): δ 8.37 (1H, dd, $J_{2',4'}=3.0$ Hz, $J_{2',5'}=1.2$ Hz, H-2'), 8.23 (1H, d, $J_m=2.4$ Hz, H-5), 7.86 (1H, dd, $J_{5',4'}=5.1$ Hz, $J_{5',2'}=1.2$ Hz, H-5'), 7.63 (1H, dd, $J_o=9.0$ Hz, $J_m=2.4$ Hz, H-7), 7.51 (1H, d, $J_o=9.0$ Hz, H-8), 7.47 (1H, dd, $J_{4',5'}=5.1$ Hz, $J_{4',2'}=3.0$ Hz, H-4'), 6.08 (1H, ddt, $J_{trans}=17.1$ Hz, $J_{cis}=10.5$ Hz, $J_{vic}=6.0$ Hz, H-2''), 5.39 (1H, dt, $J_{trans}=17.1$ Hz, $J_{allyl}=1.2$ Hz, H$_a$-3''), 5.26 (1H, d, $J_{cis}=10.5$ Hz, H$_b$-3''), 4.78 (2H, dd, $J_{vic}=6.0$ Hz, $J_{allyl}=1.2$ Hz, H-1''); ^{13}C NMR (CDCl$_3$/75.4MHz): δ 173.66 (C-4), 153.21, 152.71, 140.15, 138.62, 133.57, 133.35, 131.83, 130.63, 129.44, 127.09, 125.97, 125.10, 119.59, 119.10 (C-3''), 72.92 (C-1''); MS (m/z, +Q1): 318.96 (M$^+$, 100%).

Photolysis in benzene. A 1.0mM solution of chromone **1** in dry benzene contained in a pyrex glass vessel was purged with nitrogen for 30 min and then irradiated under nitrogen with light from a 125-W Hg vapor lamp for 50 min at 20–30°C. The removal of solvent under reduced pressure left a gummy mass, which was chromatographed to yield **2a** and **2b**.

Compound (2a). Yield 26%, yellow solid; mp 192–194°C; IR: 1636(C=O) cm^{-1}; ^{1}H NMR (CDCl$_3$/300 MHz): δ 8.26 (1H, d, $J_m=2.4$ Hz, H-7), 7.63 (1H, dd, $J_o=9.0$ Hz, $J_m=2.4$ Hz, H-9), 7.50 (1H, d, $J_o=9.0$ Hz, H-10), 6.58 (1H, dd, $J_{2,1}=2.7$ Hz, $J_{2,11b}=1.2$ Hz, H-2), 6.00 (1H, ddd, $J_{trans}=17.4$ Hz, $J_{cis}=10.8$ Hz, $J_{vic}=6.9$ Hz, H-1') 5.49 (1H, dd, $J_{trans}=17.4$ Hz, $J_{2'Ha,4}=1.2$ Hz, H$_a$-2'), 5.41 (1H, d, $J_{cis}=10.8$ Hz, $J_{2'Hb,4}=0.9$ Hz, H$_b$-2'), 5.21 (1H, dd, $J_{1,11b}=8.4$ Hz, $J_{1,2}=2.7$ Hz, H-1), 5.13 (1H, dd, $J_{4,1'}=6.9$ Hz, $J_{4,3a}=6.6$ Hz, H-4), 3.92 (1H, dd, $J_{3a,11b}=10.5$ Hz, $J_{3a,4}=6.6$ Hz, H-3a), 3.05 (1H, ddd, $J_{11b,3a}=10.5$ Hz, $J_{11b,1}=8.4$ Hz, $J_{11b,2}=1.2$ Hz, H-11b); MS (m/z, +Q1): 319 (M$^+$, 100%); Anal. Calcd. for C$_{16}$H$_{11}$ClO$_3$S: C, 60.28; H, 3.48. Found: C, 60.42; H, 3.61.

Compound (2b). Yield 21%, white solid; mp 178–180°C; IR: 1637(C=O) cm^{-1}; ^{1}H NMR (CDCl$_3$/300 MHZ): δ 8.26 (1H, d, $J_m=2.4$ Hz, H-7), 7.63 (1H, dd, $J_o=9.0$ Hz, $J_m=2.4$ Hz, H-9), 7.47 (1H, d, $J_o=9.0$ Hz, H-10), 7.44 (1H, d, $J_{2,1}=5.1$ Hz, H-2), 7.35 (1H, d, $J_{1,2}=5.1$ Hz, H-1), 6.60 (1H, ddd, $J_{trans}=17.1$ Hz, $J_{cis}=10.5$ Hz, $J_{vic}=6.3$ Hz, H-1'), 6.03 (1H, d, $J_{vic}=6.3$ Hz, H-4), 5.15–5.03 (2H, m, H-2'a, H-2'b); ^{13}C NMR (CDCl$_3$/75.4MHz): δ 171.21 (C-6), 153.65, 143.74, 138.78, 133.78 (C-9), 133.01, 130.86, 129.34, 127.13, 126.94, 125.67, 125.51 (C-7), 125.04, 123.87, 119.85 (C-10), 74.30 (C-4); MS (m/z, +Q1): 317 (M$^+$, 100%); Anal. Calcd. for C$_{16}$H$_9$ClO$_3$S: C, 60.67; H, 2.86. Found: C, 60.67; H, 2.78.

Photolysis in methanol. A 1.0mM methanolic solution of chromone **1** under similar conditions for 50 min yielded **2c**, **2d**, and **2b**.

Compound (2c). Yield 29%, white solid; mp 210–212°C; IR: 1628 (C=O) cm^{-1}; ^{1}H NMR (CDCl$_3$/400 MHZ): δ 8.23 (1H, d, $J_m=2.6$ Hz, H-7), 7.59 (1H, dd, $J_o=9.0$ Hz, $J_m=2.6$ Hz, H-9), 7.41 (1H, d, $J_o=9.0$ Hz, H-10), 6.62 (1H, ddd, $J_{1,3Hy}=3.6$ Hz, $J_{1,3Hx}=2.4$ Hz, $J_{1,3a}=2.4$ Hz, H-1), 5.99 (1H, ddd, $J_{trans}=17.2$ Hz, $J_{cis}=10.6$ Hz, $J_{vic}=6.9$ Hz, H-1'), 5.58 (1H, dd, $J_{trans}=17.2$ Hz, $J_{2'a,4}=0.9$ Hz, H-2'a), 5.44 (1H, dd, $J_{cis}=10.6$ Hz, $J_{2'b,4}=0.9$ Hz, H-2'b), 4.49 (1H, dddd, $J_{3a,4}=10.8$ Hz, $J_{3a,3Hy}=5.0$ Hz, $J_{3a,3Hx}=4.8$ Hz, $J_{3a,1}=2.2$ Hz, H-3a), 4.37 (1H, dd, $J_{4,3a}=10.8$ Hz,

$J_{4,1'}=6.9$ Hz, H-4), 4.04 (1H, ddd, $J_{gem}=16.5$ Hz, $J_{3x,3a}=4.8$ Hz, $J_{3x,1}=2.4$ Hz, H$_x$-3), 3.86 (1H, ddd, $J_{gem}=16.5$ Hz, $J_{3Hy,3a}=5.0$ Hz, $J_{3Hy,1}=3.7$ Hz, H$_y$-3); ^{13}C NMR (CDCl$_3$/75.4 MHz): δ 170.66 (C-6), 152.96, 142.92, 138.33, 133.80 (C-9), 133.00(C-1'), 132.03, 130.48, 128.90 (C-1), 125.48 (C-7), 124.81, 120.75 (C-2'), 119.50 (C-10), 83.02 (C-4), 53.44 (C-3a), 39.02 (C-3); MS (m/z, +Q1): 319 (M$^+$, 100%); Anal. Calcd. for C$_{16}$H$_{11}$ClO$_3$S: C, 60.28; H, 3.48. Found: C, 60.46; H, 3.60.

Compound (2d). Yield 36%, light yellow solid; mp 198–200°C; IR: 1643 (C=O) cm^{-1}; ^{1}H NMR (CDCl$_3$/400 MHZ): δ 8.30 (1H, d, $J_m=2.4$ Hz, H-7), 7.61 (1H, dd, $J_o=9.0$ Hz, $J_m=2.4$ Hz, H-9), 7.50 (1H, d, $J_o=9.0$ Hz, H-10), 7.44 (2H, s, H-1, H-3), 6.18 (1H, ddd, $J_{trans}=17.1$ Hz, $J_{cis}=10.5$ Hz, $J_{vic}=6.3$ Hz, H-1'), 6.05 (1H, d, $J_{vic}=6.3$ Hz, H-4), 5.45–5.39 (2H, m, H-2'a, H-2'b); ^{13}C NMR (CDCl$_3$/75.4 MHz): δ 170.01 (C-6), 152.56, 146.74, 138.81, 134.02, 133.21 (C-9), 130.75, 128.34, 127.13, 126.89, 125.59, 125.45 (C-7), 121.96, 119.92, 119.58 (C-10), 76.30 (C-4); MS (m/z, +Q1): 317 (M$^+$, 100%); Anal. Calcd. for C$_{16}$H$_9$ClO$_3$S: C, 60.67; H, 2.86. Found: C, 61.06; H, 2.72.

Compound (2b). Yield 10%.

REFERENCES AND NOTES

[1] (a) Cho, D. W.; Choi, J. H.; Oh, S. W.; Quan, C.; Yoon, U. C.; Wang, R.; Yang, S.; Mariano, P. S. J Am Chem Soc 2008, 130, 2276 (b) Itou, T.; Yoshimi, Y.; Kamiya, K.; Takedani, H.; Morita, T.; Hatanaka, M. J Photochem Photobiol Chem 2009, 202, 235 (c) Coskun, N.; Cetin, M. Tetrahedron 2007, 63, 2966 (d) Zimmerman, H. E.; Shorunov, S. J Org Chem 2009, 74, 5411 (e) Kamijo, S.; Hoshikawa, T.; Inoue M. Tetrahedron Lett 2010, 51, 872 (f) Takechi, H.; Takahashi, H.; Machida, M. J Heterocycl Chem 2005, 42, 201.

[2] Kamboj, R. C.; Berar, U.; Berar, S.; Thakur, M.; Arora, R.; Gupta, S. C. Canadian J Chemistry 2009, 87, 422.

[3] (a) Van Tamelen, E. E.; Whitesides, T. H. J Am Chem Soc 1968, 90, 3894 (b) Van Tamelen, E. E.; Whitesides, T. H. J Am Chem Soc 1971, 93, 6129.

[4] Gupta, S. C.; Saini, A.; Kumar, D.; Yadav, N. S.; Chand, K.; Mor, S.; Dhawan, S. N. J Chem Soc Perkin Trans 1 1995, 177.

[5] Gupta, S. C.; Sharma, S.; Saini, A.; Dhawan, S. N. J Chem Soc Perkin Trans 1 1999, 2391.

[6] (a) Rendall, W. A.; Torres, M.; Strausz, O. P. J Am Chem Soc 1985, 107, 724 (b) D'Auria, M. J Photochem Photobiol Chem 2002, 149, 31.

[7] (a) Gupta, S. C.; Saini, A.; Sharma, S.; Kapoor, M.; Dhawan, S. N. Tetrahedron Lett 1996, 37, 8913 (b) Kamboj, R. C.; Arora, R.; Berar, S.; Thakur, M.; Berar, U.; Gupta, S. C. Indian J Heterocyclic Chem 2009, 18, 271 (c) Gupta, S. C.; Yusuf, M.; Sharma, S.; Arora, S. Tetrahedron Lett 2002, 43, 6875 (d) Yusuf, M.; Kumar, R.; Gupta, S. C. J Heterocycl Chem 2008, 45, 963.

[8] (a) Waiss, A. C.; Lundin, R. E.; Lee, A.; Corse, J. J Am Chem Soc 1967, 89, 6213 (b) Matsuura, T.; Matsushima, H. Tetrahedron 1968, 24, 6615 (c) Gupta, S. C.; Mukerjee, S. K. Ind J Chem 1973, 11, 1263 (d) Gupta, S. C.; Yadav, N. S.; Dhawan, S. N. J Ind Chem Soc 1990, 67, 770.

[9] Cowan, D. O.; Drisko, R. L. Elements of Organic Photochemistry; Plenum Press: New York, 1976; pp 15–16.