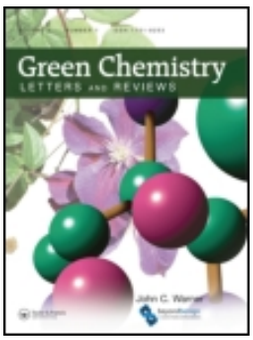

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A green synthesis of thieno[2,3-*c*]xanthen-6-ones through the tandem photochemical sigmatropic shift and cyclization

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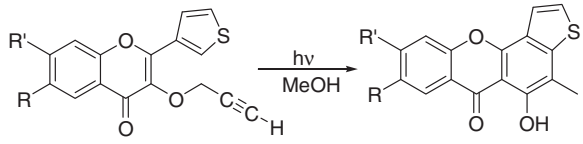
A green and clean route for the synthesis of 5-hydroxy-4-methyl-6*H*-thieno[2,3-*c*]xanthen-6-ones (**2**) has been developed by the photoirradiation of 3-(prop-2-ynyloxy)-2-(thiophen-3-yl)-4*H*-chromen-4-ones (**1**). This photoreaction of the 3-propynyloxychromenones being observed for the first time is very interesting and appears to be the result of a tandem sigmatropic shift and cyclization. The structure of **2** has been determined by the spectroscopic (Fourier transform infrared [FTIR], nuclear magnetic resonance [NMR], and mass) and single crystal X-ray crystallographic studies.



1 **2**

Keywords: thieno[2,3-*c*]xanthen-6-one; 3-propynyloxychromenone; photoirradiation; sigmatropic shift

1. Introduction

Photochemical processes like isomerization (*1*), cyclizations (*2*), sigmatropic shifts (*3*), C–C bond cleavages (*4*), H-abstractions (*5*), etc., in a variety of organic molecules afforded, of course, in eco-friendly approach, an enormous range of simple to complex organic compounds which are otherwise difficult to obtain through thermal means. Chromones (*6*) constitute one of the leading modules of oxygenated heterocyclic compounds occurring in the vegetal kingdom (*7*) and have attracted the major attention of the organic chemists because of their diverse biological activities such as anti-inflammatory (*8*), antitumor (*9*), antioxidant (*10*), antiulcer (*11*), and biocidal (*12*).

The photochemistry of acetylene and its derivatives, such as acetylene dicarboxylate (*13*), diaryl acetylenes (*14*), conjugated acetylenes (*15*), ethoxy acetylenes (*16*), acyclic acetylenic di-p-methane systems (*17*), etc., has been of great interest. Recently, gold-catalyzed reactions of heteroarene-yne systems have been used for obtaining many interesting molecules (*18*). In the recent past, the studies in our laboratory on the photochemical transformation of chromones (*19*) tethered with propynyloxy group at 3-position demonstrated that the photoproducts were obtained mainly through the H-abstraction followed by cyclization. In our continued effort in the photochemistry of these molecules, herein we report their unusual behavior of being transformed to the thienoxanthenones through the involvement of heteroarene-yne reaction. Xanthenones derivatives have gained the enormous attention due to their antibilharzial, antitumor, and antischistosomal activities (*20*).

2. Experimental procedures

Solvents were dried and purified by conventional methods prior to use. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectroscopic data were recorded on Bruker 400 MHz spectrometer in $CDCl_3$ solution using trimethylsilane as an internal standard. The infrared (IR) spectra were scanned in KBr pellets on a MB3000 FTIR with Horizon MB^{TM} FTIR software from ABB Bomen. The mass spectral data were obtained on Waters, Q-TOF Micromass (LC-MS) spectrometer.

The substrates, 2-(thiophen-3-yl)-4*H*-chromen-4-ones **1**, were synthesized by the condensation of 2′-hydroxyacetophenones with thiophene-3-carbaldehyde in the presence of NaOH/EtOH, followed by reacting the resulting chalcones with 50% H_2O_2/OH^- under Algar–Flynn–Oyamada conditions (*21*) and

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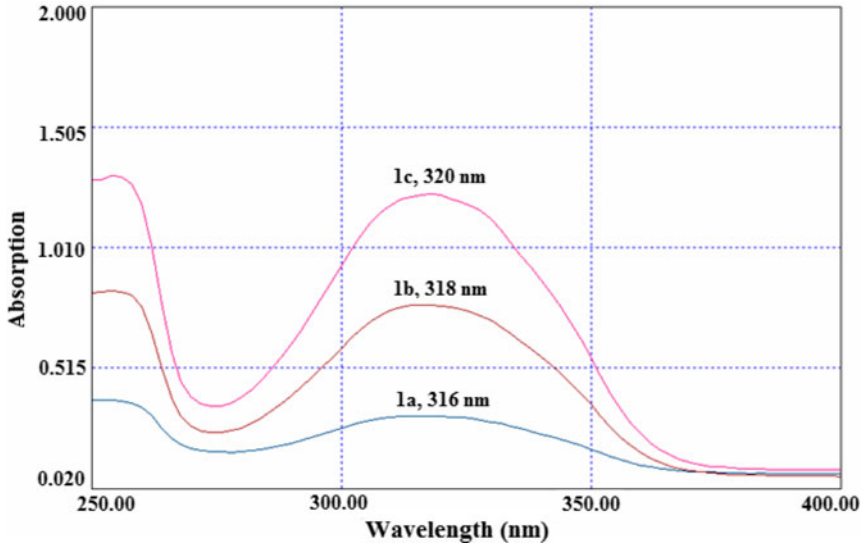


Figure 1. Electronic spectra of the substrates **1**.

subsequent alkylation of the 3-hydroxychromenones with propargyl bromide in the presence of dry acetone, freshly dried K_2CO_3, and tetra-*n*-butyl ammonium iodide. These chromenones showed λ_{max} in the range of 316–320 nm (Figure 1).

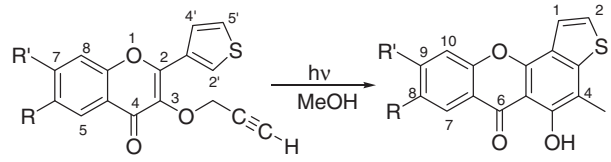
6-Methyl-3-(prop-2-ynyloxy)-2-(thiophen-3-yl)-4*H*-chromen-4-one, **1a** White solid; mp 112–114°C; Yield 77.8%; ν_{max} (cm^{-1}): 2129 (C≡C), 1612 (C=O); ^1H NMR (400 MHz, $CDCl_3$): δ = 8.41 (1H, dd, $J_{2',4'}$ = 3.0 Hz, $J_{2',5'}$ = 1.2 Hz, H-2′), 8.03 (1H, d, J_m = 2.4 Hz, H-5), 7.90 (1H, dd, $J_{5',4'}$ = 5.1 Hz, $J_{5',2'}$ = 1.2 Hz, H-5′), 7.50 (1H, dd, J_o = 9.0 Hz, J_m = 2.4 Hz, H-7), 7.44 (2H, m, H-8, H-4′), 5.09 (2H, d, $J_{1'',3''}$ = 2.4 Hz, H-1″), 2.48 (3H, s, C_6-CH_3), 2.41 (1H, t, $J_{3'',1''}$ = 2.4 Hz, H-3″); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.6 (C-4), 153.2, 152.8, 137.5, 134.8, 134.7, 132.1, 129.5, 127.4, 125.6, 124.9, 123.7, 117.6, 78.7, 76.1, 59.1, 20.9 (C_6-CH_3); Mass (m/z, +Q1): 297.1 (M^+, 100%).

3. Results and discussion

The deoxygenated 1.0 mM methanolic solution of **1** taken in a Pyrex glass vessel was purged with nitrogen for 30 min and then irradiated under nitrogen with light from a 125W Hg vapor lamp for 45 min (Scheme 1). The removal of solvent under reduced pressure yielded a gummy mass that was chromatographed over a column of silica gel. The columns were eluted with increasing proportion of benzene in benzene–petroleum ether mixture to obtain **2** (yield and mp: **2a** = 34%, 210°C; **2b** = 32%, 162°C; **2c** = 29%, 185°C) as one of the products.

A deoxygenated 1.0 mM methanolic solution of **1a** taken in a Pyrex glass vessel was purged with nitrogen for 30 min and then irradiated under nitrogen with light from a 125W Hg vapor lamp for 45 min. The removal of solvent under reduced pressure yielded a gummy mass that was chromatographed over a column of silica gel. The column was eluted with increasing proportion of benzene in benzene–petroleum ether mixture to obtain **2a** as yellowish white solid in 34% yield. mp 210°C; ν_{max} (cm^{-1}): 1682 (C=O); ^1H NMR (400 MHz, $CDCl_3$): δ = 12.78 (1H, s, –OH), 8.1 (1H, d, J_m = 2.2 Hz, H-7), 7.59 (1H, dd, J_o = 8.4 Hz, J_m = 2.2 Hz, H-9), 7.49 (1H, d, J_o = 8.4 Hz, H-10), 7.72 (1H, J = 5.6 Hz, H-2), 7.31 (1H, J = 5.6 Hz, H-1), 2.49 (3H, s, 4-CH_3), 2.45 (3H, s, 8-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.1, 154.0, 153.6, 150.1, 136.5, 134.3, 125.3, 123.3, 120.9, 120.7, 120.3, 117.6, 111.5, 106.4, 98.6, 20.9, 12.8; Mass (m/z, +Q1): 297 (M^+, 100%).

The Fourier transform infrared (FTIR) spectrum of **2a** shows a strong absorption band at 1682 cm^{-1} due to the C=O group of the pyrone moiety. In the NMR spectrum (Table 1) of the product **2a** was seen a doublet at δ 8.1 (J_m = 2.2 Hz) for H-7. The other two benzenoid protons showed the resonances between δ 7.59 (dd, J_o = 8.4 Hz and J_m = 2.2 Hz,



1 **2**

1a, 2a; R = CH_3, R' = H
1b, 2b; R = Cl, R' = CH_3
1c, 2c; R = Cl, R' = H

Scheme 1. Conversion of **1** to **2** *via* the photoirradiation process.

Table 1. ^{1}H NMR shifts of photoproducts.

H's	2a	2b	2c
C_1–H	7.31 (d)	7.35 (d)	7.37 (d)
C_2–H	7.72 (d)	7.72 (d)	7.75 (d)
C_4–CH_3	2.49 (s)	2.54 (s)	2.59 (s)
C_5–OH	12.78 (s)	12.67 (s)	12.55 (s)
C_7–H	8.13 (d)	8.31 (s)	8.33 (d)
C_8–CH_3	2.45 (s)	–	–
C_9–H	7.59 (dd)	–	7.60 (dd)
C_9–CH_3	–	2.48 (s)	–
C_{10}–H	7.49 (d)	7.37 (s)	7.35 (d)

H-9) and between δ 7.49 (d, J_o = 8.4 Hz, H-10). The two thienyl protons gave the signals between δ 7.72 (H-2) and 7.31 (H-1) with the usual characteristic thienyl coupling of J = 5.6 Hz. The –OH protons absorption disappearing on D_2O shake appeared as singlet at δ 12.78. The two methyl groups' protons showed their signal as singlets at δ 2.49 (4-CH_3) and δ 2.45 (8-CH_3). These assignments in the NMR spectrum are in consistent with the structure of **2a**.

For corroborating these protons' assignments in ^{1}H NMR spectrum, the 2D-COSY spectrum of photoproduct **2a** was recorded which shows H-2 directly interacting with H-1. The H-7 is correlated to H-9 which is also correlated to H-10. The structure of **2a** was further ascertained by its single crystal X-ray analysis. Compound **2a** crystallizes in the Monoclinic *C2/c* space group. An ORTEP diagram is shown in Figure 2. The C–O distance of the carbonyl group is 1.249(11) Å whereas the C–OH distance is 1.355(12) Å.

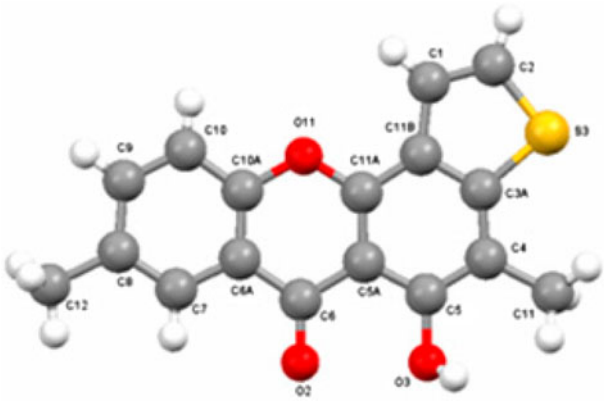
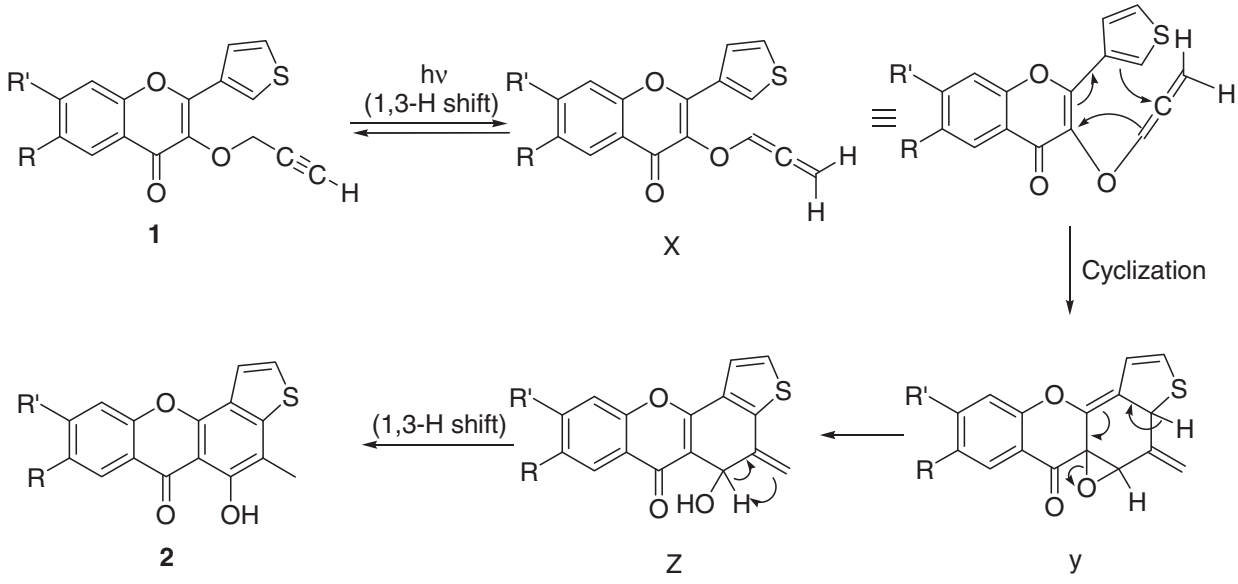


Figure 2. Structure of **2a** determined by single crystal X-ray analysis.

Crystal data for **2a**: $C_{17}H_{12}O_3S$, M = 296.33, Monoclinic, space group *C2/c*, a = 35.275(14) Å, b = 4.6660(17) Å, c = 16.136(7) Å, α = 90°, β = 101.03 (3)°, γ = 90°, V = 2606.8(18) Å^3, Z = 8, Dc = 1.51 mg/cm^3, μ(Mo-Kα) = 0.255 mm^{-1}, T = 100 K, 1682 reflections collected. Refinement of 734 reflections (108 parameters) with $I > 2\sigma(I)$ converged at a final R_1 = 0.0976, wR_2 = 0.2169, gof = 1.081. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary material (publication no. CCDC 959007).[1]

The product formation may be rationalized (Scheme 2) through the initial photochemical



Scheme 2. A proposed mechanism of the formation of **2** from **1**.

sigmatropic 1,3-H shift in **1** to furnish the allenyloxy chromenone **X** that undergoes cyclization to furnish **Y**. The support for the formation of allenyloxy chromenone intermediate **X** can be derived from the earlier observations made in conjugated acetylenic carbonyl compounds (*22*) where the acetylenic compounds have been rearranged to the allenes photochemically. The intermediate **Y** upon sigmatropic 1,5-H shift yields the another intermediate **Z**, which is converted to **2** again by the 1,3-H sigmatropic shift.

4. Conclusions

The photoreaction of 3-(prop-2-ynyloxy)-2-(thiophen-3-yl)-4*H*-chromen-4-ones (**1**) yielded 5-hydroxy-4-methyl-6*H*-thieno[2,3-*c*]xanthen-6-ones (**2**), the tetracyclic compounds in one shot, in appreciable high yield. This can become a useful method for synthesizing the thienoxanthenones in a cleaner environment. Expansion of the scope of this reaction, further elucidation of the reaction mechanism, and the application to other aromatic systems are ongoing in our laboratory which will be presented in due course.

Acknowledgments

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Note

1. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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