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One-shot photochemical synthesis of 5-(thiophen-3-yl)pyrano[2,3-c]chromen-2(3H)ones from 3-propynyloxy-chromenones: a case of an intramolecular Paterno–Buchi reaction[†]

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5-(Thiophen-3-yl)pyrano[2,3-c]chromen-2(3*H*)-ones (2), angular tricyclic compounds, were synthesized in significantly high yields through the photoinduced intramolecular coupling of the acetylenic group with the carbonyl centre in 3-(prop-2-ynyloxy)-2-(thiophen-3-yl)-4*H*-chromen-4-ones (1). This photoreaction is a case of an intramolecular Paterno–Buchi reaction and is unprecedented in 3-propynyloxy-chromenones. The structure of 2 has been determined by spectroscopic (FTIR, NMR and mass) and single crystal X-ray crystallographic studies.

The photoinduced [2 + 2] cycloaddition of an olefin to a carbonyl center - the Paterno-Buchi reaction¹ - is a facile and versatile access for oxetane² preparation with high regio- and stereoselectivity.3,4 The ring opening of oxetanes followed by bond-formation has been found to be very useful in synthetic chemistry.^{4,5} Insect pheromones, asteltoxin⁶ (a potent inhibitor of ATP synthesis) and (+)-Preussin⁶ (an antifungal agent) can also be synthesized by Paterno-Buchi reactions followed by ring opening. The photoinduced [2 + 2] cycloaddition of acetylene with carbonyl compounds leads to the formation of a 1,4-biradical which on cyclization gives labile oxetenes.^{7,8} There are many reports⁹ on the photoproduction of enones on irradiation of carbonyl compounds in the presence of acetylenes. In most of these, an unstable oxetene intermediate was believed to be formed which easily fragmented to give enone products. In the framework of our research program on the determination of the photolytic behavior of 3-alkoxychromones¹⁰ bearing a propynyloxy group at the 3-position and its extension, herein, we report our investigations on the photocoupling through the intramolecular Paterno-Buchi reaction¹¹ of the acetylenic moiety with the carbonyl center in

3-propynyloxy-chromenones which led to the expedient synthesis of 5-(thiophen-3-yl)pyrano[2,3-*c*]chromen-2(3*H*)-ones (2), the angular pyranochromenones. These synthesized pyranochromenones may mimic the activities (antineoplastic,¹² antimicrobial,¹³ anti-cancer,¹⁴ anti-HIV,¹⁵ antiproliferative,¹⁶ *etc.*) elicited by many pyranochromenone analogs.

The substrates, 3-(prop-2-ynyloxy)-2-(thiophen-3-yl)-4*H*chromen-4-ones (1),¹⁷ were synthesized by (a) the condensation of 2-hydroxyacetophenones with thiophene-3-carboxaldehyde in the presence of NaOH/EtOH, (b) reacting the resulting chalcones with 50% H_2O_2/OH^- under Algar–Flynn– Oyamada¹⁸ reaction conditions, and (c) subsequent alkylation of the 3-hydroxychromenones with propargyl bromide in the presence of dry acetone, freshly dried K₂CO₃ and tetra-*n*-butyl ammonium iodide. These chromenones **1(a-c)** showed λ_{max} in the range of 316–320 nm (Fig. 1).

The chromatographic separation of the photolysate obtained by the photo-irradiation (Scheme 1) of a methanolic solution of **1** with pyrex filtered UV-light using a 125 W Hg lamp under a nitrogen atmosphere yielded the 5-(thiophen-3-yl)pyrano[2,3-c]chromen-2(3H)-ones **2**¹⁹ (yield, mp: **2a**, 32%, 76 °C; **2b**, 29%, 65 °C and **2c**, 31%, 94 °C) as one of the



Fig. 1 Electronic spectra of 1.

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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	6.33(s)	6.26(s)	6.69(s)
C ₃ -H	4.68(s)	4.73(s)	4.67(s)
C ₇ -H	7.39-7.37(d)	7.32-7.30(d)	7.47-7.45(d)
C_8 -H	7.45-7.42(dd)	_	7.52-7.49(dd)
C8-CH3	_ ``	2.54(s)	_ ``
C ₉ -CH ₃	2.46(s)	_ ``	_
C ₁₀ -H	7.71(d)	7.77(d)	7.78(d)
$C_{2'}$ -H	8.22-8.21(dd)	8.24-8.18(dd)	8.12-8.05(dd)
$C_{4'}$ -H	7.54–7.52(dd)	7.49–7.45(dd)	7.66-7.62(dd)
С _{5′} -Н	7.78–7.77(dd)	8.05–7.97(dd)	8.20-8.19(dd)

products. The formation of these pyranochromenones (yield: 2a, 31%; 2b, 29% and 2c, 30%) from 1 also occurs in benzene. Moreover, no chromenone-sensitized addition of methanol to the acetylenic moiety in 3-(prop-2-ynyloxy)-4*H*-chromen-4-ones was observed.

The FTIR spectrum of 2a showed a strong absorption band at 1643 cm^{-1} that may be assigned to the C=O of the pyrone moiety. In the NMR spectrum (Table 1) of 2a, a doublet at δ 7.71 (I = 1.64 Hz) for H-10 was observed. For the other two benzenoid protons, resonances between δ 7.45 and 7.42 (dd, $J_{\rm o}$ = 8.4 Hz and $J_{\rm m}$ = 1.64 Hz, H-8) and between δ 7.39 and 7.37 $(d, J_o = 8.4 \text{ Hz}, \text{H-7})$ were observed. The three thienyl protons gave one signal as dd between δ 8.22 and 8.21 ($J_{2',5'}$ = 3.0 Hz and $J_{2',4'}$ = 1.2 Hz, H-2'), another between δ 7.78 and 7.77 ($J_{5',4'}$ = 5.2 Hz and $J_{5',2'}$ = 1.2 Hz, H-5') and third one between δ 7.54 and 7.52 ($J_{4',5'}$ = 5.2 Hz and $J_{4',2'}$ = 1.2 Hz, H-4'). This shows that during photo-irradiation the thienyl ring remained intact. The H-1 proton absorption appeared as a singlet at δ 6.33. The -O-CH₂-protons (C₃-H's) exhibited a singlet at δ 4.68 and the methyl group (9-CH₃) protons showed their signal as a singlet at δ 2.46. These assignments in the NMR spectrum of 2a are consistent with the structure of the pyranochromenone 2a obtained as a photoproduct from 1a.

In order to provide further confirmation of these ¹H NMR assignments to the different protons in **2a**, its 2D-COSY (Fig. 2) was recorded. As can be seen in Fig. 2, H-1 is directly interacting with H-10 and the latter is also correlating to H-8. The H-7 and H-8 as expected are close and thus showing their interaction with each other. In the case of thienyl protons, the interactions of H-2' with H-4' and H-5' and between H-5' and H-4' are observed.



Fig. 2 2D-COSY spectrum of 2a.



Fig. 3 Structure of 2a determined by single crystal X-ray analysis.

The structure of **2a** was further corroborated (Fig. 3) by its single X-ray structure analysis.²⁰ The compound crystallizes in the monoclinic $P2_1/n$ space group. In addition to FTIR spectroscopy, the presence of the carbonyl group is also confirmed by the C=O distance of 1.230(4) Å in **2a**. The O6–C4 and O6–C5 bonds (1.371(4) Å and 1.369(4) Å, respectively) are shorter than the O4–C3 bond (1.422(4) Å) but are similar to the O4–C13 bond (1.366(4) Å). This indicates that C3 is a sp³ hybridized carbon whereas C5 and C4 are sp² hybridized.

The formation of **2** from **1** can be envisioned (Scheme 2) to occur through the intramolecular Paterno–Buchi reaction, involving the initial C–O bond formation to give a 1,4-biradical **A** which cyclizes to an oxetene **B**. This oxetene thus formed seems to be highly strained and thus easily opens up to furnish **2**. Earlier also, the formation of such oxetenes^{7–9,21} has been demonstrated, which on subsequent cleavage gave enones as observed here.



Scheme 2 Mechanistic rationale of formation of 2 from 1.

Conclusions

We have developed a highly efficient synthesis of 5-(thiophen-3-yl)pyrano[2,3-c]chromen-2(3H)-ones (2), the angular tricyclic compounds in one shot, in appreciable yield from the photoreaction of 3-(prop-2-ynyloxy)-2-(thiophen-3-yl)-4H-chromen-4ones (1). We believe this method should provide a practical entry for synthesizing these types of angular pyranochromenones in environment-benign conditions. Further details of this reaction, the application to other aromatic systems and the exploration of biological activities of these angular pyranochromenones are ongoing in our laboratory and will be presented in due course.

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- 17 Solvents were dried and purified by conventional methods prior to use. ¹H and ¹³C NMR spectroscopic data were recorded on a Bruker 400 MHz spectrometer in CDCl₃ solution using trimethylsilane as an internal standard. The infrared (IR) spectra were scanned in KBr pellets on a MB3000 FT-IR with HORIZON MBTM FTIR software from ABB Bomen. The mass spectral data were obtained on WATERS, Q-TOF MICROMASS (LC-MS) spectrometer. The X-ray structure of **2a** was collected on a Bruker Kappa APEX II diffractometer equipped with CCDC detector and sealedtube monochromated MoKα radiation using the program

APEX2. 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: CDCl₃): 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), 7.46–7.43 (2H, m, H-8, H-4'), 5.09 (2H, d, $J_{1'',3''}$ = 2.4 Hz, H-1''), 2.48 (3H, s, C6-CH₃), 2.41 (1H, t, $J_{3'',1''}$ = 2.4 Hz, H-3''); ¹³C NMR (100 MHz, CDCl₃): δ = 174.59 (C-4), 153.22, 152.81, 137.45, 134.79, 134.71, 132.06, 129.46, 127.37, 125.57, 124.95, 123.70, 117.64, 78.74, 76.08, 59.09, 20.90 (C₆-CH₃); mass (m/z, +Q1): 297.1 (M⁺, 100%).

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- 20 Crystal data for **2a**: $C_{17}H_{12}O_3S$, M = 296.33, monoclinic, space group $P2_1/c$, a = 5.0173(5) Å, b = 14.9931(14) Å, c =18.012(2) Å, $\beta = 93.897(7)^\circ$, V = 1351.8(2) Å³, Z = 4, $D_c =$ 1.456 Mg cm⁻³, μ (Mo-K α) = 0.246 mm⁻¹, T = 296 K, 8163 reflections collected. Refinement of 1461 reflections (191 parameters) with $I > 2\sigma(I)$ converged at a final $R_1 = 0.0526$, $wR_2 = 0.1390$, gof = 1.055. Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 956397.
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