Photochemical Synthesis of Cyclopenta[c]-Anellated Benzopyrans and Benzothiopyrans

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Abstract: On irradiation in the presence of 2,3-dimethylbut-2-ene the newly synthesized 2-oxo-2H-1-benzopyran- and 2-oxo-2H-1-benzothiopyran-4-carbonitriles are converted selectively to a cyclopenta[c]-benzopyran or -thiobenzopyran, respectively. The reaction proceeds via addition of the alkene to the nitrile- and olefinic C-atoms of the triplet excited coumarin derivatives.

Key words: photochemistry, heterocycles, cycloadditions, nitriles, imines

Aflatoxin B1 has become the paradigm mycotoxin.1 Recent preparative approaches have focused on the synthesis of its furofuran moiety,2,3 while the access to the cyclopenta[c]benzopyran substructure relies on earlier work by Büchi.4 We have recently communicated that α-cyano-α,β-unsaturated δ-lactones are (partially) converted to cyclopentapyrans on irradiation in the presence of 2,3-dimethylbut-2-ene.5 Here we report on the synthesis of 4-cyanocoumarin (1a) and 4-cyanothiocoumarin (1b) and on their selective conversion to cyclopenta[c]coumarins and -thiocoumarins, respectively. Carbonitriles 1 were obtained from aldehydes 2 via their oximes 3 by using acetic anhydride as dehydrating reagent.6 Irradiation (λ = 300 nm for 1a and 350 nm for 1b) of a solution containing nitrile 1 and a twenty-fold molar excess of 2,3-dimethylbut-2-ene in acetonitrile leads to the selective formation of imines 4a and 4b in yields >75%, respectively. Hydrolysis of imines 4 affords ketones 5 in yields around 80% (Scheme 1).

The structural assignment for both imines 4 and ketones 5 by 1H NMR is straightforward in view of the strong downfield shift observed for H-9 which is due to the anisotropy of the fixed imine-nitrogen or carbonyl-oxygen, respectively. A similar effect has already been described for cyclopentanaphthalen-1-ones.7 Regarding the multiplicity of the excited state of 1 involved in the formation of 4, both successful quenching experiments (irradiation with light of wavelength λ >340 nm) with naphthalene (Eτ = 61 kcal/mol) and sensitizing experiments (irradiation with light of wavelength λ >390 nm) with thioxanthone (Eτ = 65.5 kcal/mol) suggest a reactive excited triplet state with a triplet energy between these two values. The selective formation of 4 to the exclusion of any cyclobutane derivatives indicates that the rate of 1,5-cyclization of the triplet biradical 6 to the (triplet) vinyl nitrene 7 (Scheme 2) is much faster than its rate of intersystem crossing to the singlet biradical (i.e. the cyclobutane precursor).8,9 This chemoselectivity is remarkable, as both 3-cyanocoumarin and 2-cyanochromone afford mixtures of cyclopenta- and cyclobuta-derivatives on irradiation in the presence of alkenes.5,10

Scheme 1 Reagents and conditions: a) NH2OHHCl; b) Ac2O, Δ; c) H+, H2O

Scheme 2 Compounds 2,11 were prepared according to the literature procedure. Other reagents were obtained from commercial sources and used as received. Medium pressure column chromatography: Merck silica gel (0.063–0.200 mm) and Woelm alumina (neutral alumina, activity I). TLC: Merck silica gel 60 F254 analytical plates. GC: 30-m SE 30 capillary column. Photolyses: Rayonet RPR-100 photoreactor equipped with either 300 nm or 350 nm lamps. 1H and 13C NMR spectra: at 500 MHz and 125.8 MHz, respectively. MS: at 70 eV.
Oximes 3 and Nitriles 1; General Procedure

A solution of aldehyde 2 (5 mmol), hydroxylamine hydrochloride (0.52 g, 7.7 mmol) and oven-dried NaOAc (0.62 g, 7.5 mmol) in EtOH (40 mL) was refluxed for 1 h. After evaporation of roughly 50% of the solvent, H₂O (20 mL) was added, and the precipitate filtered and washed with cold Et₂O. Then a mixture of the oxime 3 (2 mmol) and Ac₂O (1.2 g, 12 mmol) was refluxed for 3 h. Ice-water was added to the cooled solution and the precipitate was filtered and purified by chromatography (silica gel, pentane-Et₂O, 2:1).

4-Oximino-2-oxo-2H-1-benzopyran (3a)

1H NMR (DMSO-d₆): δ = 12.39 (s, 1 H, OH), 8.48 (s, 1 H, CHOH), 8.45 (dd, 1 H, H-5, J = 1.5, 8.1 Hz), 7.66 (dd, 1 H, H-7, J = 1.5, 7.2, 8.1 Hz), 7.42 (dd, 1 H, H-8, J = 1.0, 8.1 Hz), 7.38 (dd, 1 H, H-6, J = 1.0, 7.2, 8.1 Hz), 6.70 (s, 1 H, H-3).

13C NMR (DMSO-d₆): δ = 159.7 (C-2), 153.5 (C-8a), 146.0 (CHNOH), 144.1 (C-4), 132.1 (C-7), 126.8 (C-5), 124.3 (C-6), 116.8 (C-8), 116.4 (C-4a), 115.2 (C-3).

4-Oximino-2-oxo-2H-1-benzothiopyran (3b)

1H NMR (CDCl₃): δ = 12.25 (s, 1 H, OH), 8.70 (s, 1 H, CHOH), 8.43 (dd, 1 H, H-5, J = 1.5, 8.1 Hz), 7.73 (dd, 1 H, H-8, J = 1.0, 8.1 Hz), 7.65 (dd, 1 H, H-7, J = 1.5, 7.2, 8.1 Hz), 7.53 (dd, 1 H, H-6, J = 1.0, 7.2, 8.1 Hz), 6.85 (s, 1 H, H-3).

13C NMR (DMSO-d₆): d = 183.3 (C-2), 147.1 (CHNOH), 144.4 (C-4), 136.4 (C-8a), 130.2 (C-7), 128.9 (C-5), 126.9 (C-6), 124.0 (C-8a), 124.0 (C-4a), 122.4 (C-3).

2-Oxoo-2H-benzopyran-4-carbonitrile (1a)

Yield: 62%; mp 185°C; Rr 0.73 (pentane-Et₂O, 2:1).

1H NMR (CDCl₃): δ = 7.82 (dd, 1 H, H-5, J = 1.5, 8.1 Hz), 7.69 (dd, 1 H, H-7, J = 1.5, 7.2, 8.1 Hz), 7.46–7.39 (m, 2 H, H-6,8), 6.87 (s, H-3).

13C NMR (CDCl₃): δ = 157.7 (C-2), 153.7 (C-8a), 143.0 (C-3), 127.2 (C-4), 126.1 (C-7), 125.5 (C-5), 123.8 (C-6), 117.6 (C-8a), 115.3 (C-4a), 112.9 (CN).

MS: mlz = 171 [M⁺] (61), 143 [M⁺ – CO] (100).

UV (MeCN): λmax = 294 nm (log ε = 3.94).


2-Oxoo-2H-benzothiopyran-4-carbonitrile (1b)

Yield: 52%; mp 183°C; Rr 0.36 (pentane-Et₂O, 2:1).

1H NMR (CDCl₃): δ = 8.13 (dd, 1 H, H-5, J = 1.5, 8.1 Hz), 7.64 (dd, 1 H, H-7, J = 1.5, 7.2, 8.1 Hz), 7.59–7.51 (m, 2 H, H-6,8), 6.98 (s, 1 H, H-3).

13C NMR (CDCl₃): δ = 182.4 (C-2), 149.4 (C-4), 137.2 (C-8a), 131.6 (C-7), 130.5 (C-3), 129.6 (C-5), 127.7 (C-6), 126.6 (C-8), 122.9 (C-4a), 115.2 (CN).


UV (MeCN): λmax = 375 nm (log ε = 3.48), 312 nm (log ε = 3.80).

Anal. Calcd for C₁₆H₁₆O₃ (256.3): C, 74.98; H 6.29. Found: C, 75.01; H 6.25.

2,3-Dihydro-2,3,3-tetramethyl-1H-4H-cyclopenta[c]benzothiopyran-2,4-dione (5b)

Yield: 41%; mp <5°C (light yellow oil at r.t.); Rr 0.62 (hexane-EtOAc, 3:1).

1H NMR (CDCl₃): δ = 9.01 (dd, 1 H, H-9, J = 1.5, 8.1 Hz), 7.61–7.51 (m, 3 H, H-6,7,8), 1.36 (s, 6 H), 1.13 (s, 6 H).

13C NMR (CDCl₃): δ = 211.8 (C-1), 183.4 (C-4), 154.1 (C-3a), 138.7 (C-5a), 138.0 (C-9b), 128.6 (C-8), 127.3 (C-9), 126.0 (C-7), 124.0 (C-9a), 123.9 (C-6), 128.4 (C-2,3), 22.0, 20.3 (CH₃).


Anal. Calcd for C₁₆H₁₆O₂S (272.4): C, 70.56; H 5.92. Found: C, 70.52; H 5.89.

References


