



2-oxo-2H-chromen-3-yl Propionate and 2-oxo-2H-chromen-3-yl Acetate: Short-step Synthesis, Characterization and Fluorescence Properties

Jules Yoda^{1,2,*}, Salfo Ouédraogo¹, Adama Saba²

¹Department of Medicine, Traditional Pharmacopeia and Pharmacy / Research Institute for Health Sciences, Ouagadougou, Burkina Faso

²Laboratory of Molecular Chemistry and Materials, University Joseph KI-Zerbo, Ouagadougou, Burkina Faso

Email address:

jules_yoda@yahoo.fr (J. Yoda), ouedraogosolfo35@yahoo.fr (S. Ouédraogo), asaba@univ-ouaga.bf (A. Saba)

*Corresponding author

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Abstract: Natural or synthetic coumarins are of great interest, since many of them show prominent biological activity and photochemical characteristics. In particular, hydroxycoumarins and their derivatives have been extensively studied in various fields such as biology, medicine, physics and chemistry. Among the well-known compounds is 7-hydroxycoumarin, also known as umbelliferone and 4-hydroxycoumarin. Against 3-hydroxycoumarin and its derivatives are less known and studied. In this study, new acyl derivatives were synthesized from 3-hydroxycoumarin or chromen-2,3-dione its tautomeric form and chloride acid in the presence of an appropriated base. The structures of the newly obtained compounds were confirmed by elemental analysis, mass spectrometry (MS), IR and NMR spectrometry and X-ray diffractometry. In addition, the fluorescence properties of the titre compounds were also studied in both liquid and solid state. In liquid media, the study concerned their behaviour in fluorescence emission spectrometry in 6 solvents of different polarities. The new heterocyclic compounds have been successfully synthesized. Fluorescence spectrum analyses show that these compounds are all fluorescent in both solid and liquid state with varying fluorescence intensities (I_f). On solvatochromic analyses, it appears that the behaviour of the spectrum depends strongly on the solvent. The fluorescence intensity and wavelength (λ_{em}) vary depending on the nature of the substituent (R) and especially that of the solvent. It should also be noted that chloroform is the solvent that most enhances the fluorescence of the compounds.

Keywords: Coumarins, 3-Hydroxycoumarin, Chromen-2, 3-Dione, Fluorescence Properties

1. Introduction

Hydroxycoumarins and their derivatives are heterocycles prevalent in family of naturally and synthetics compounds. They are used in the fields of biology, photochemistry and polymer sciences [1-5]. They have been identified as anticoagulant [6-7], antibacterial [8], anticancer [9-10], anti-inflammatory [11, 12] and anti-viral properties [13-14]. Hydroxycoumarins are also used as fluorescent compounds due to their inherent photochemical characteristics [2, 15].

As part of the current research on new coumarin derivatives, we study the acylation of 3-hydroxycoumarin 1 tautomeric form of chromen-2,3-dione 2 (figure 1). In

this study, we described synthesis and characterization of 2-oxo-2H-chromen-3-yl propionate and 2-oxo-2H-chromen-3-yl acetate, 3-substituted coumarin derivatives. Fluorescence properties of these compounds were then reported. So, the titre compounds were synthesized according to a described convenient method, in satisfactory yields, from 3-hydroxycoumarin or chromen-2,3-dione and acid chloride or acid anhydrides in the presence of pyridine. The structures were characterized by the means of FT-IR, ^1H and ^{13}C -NMR, ESI-MS and EIMS spectrometry and were additionally determined by X-ray

diffraction. The fluorescence spectra were recorded in liquid and solid-state.

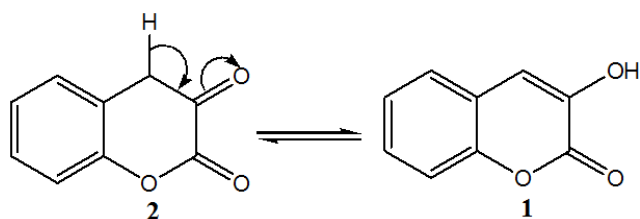


Figure 1. Tautomeric form of 3-hydroxycoumarin.

2. Materials and Methods

2.1. Synthesis Route

The method used for the synthesis of compounds 4 have been early described for (Coumarin-3-yl)-benzoates [2]. Thus, 3-hydroxycoumarin 1 or chroman-2,3-dione 2 is reacted with acid chloride or acid anhydrides 3 in the presence of an appropriated base and solvent according to the following reaction (figure 2).

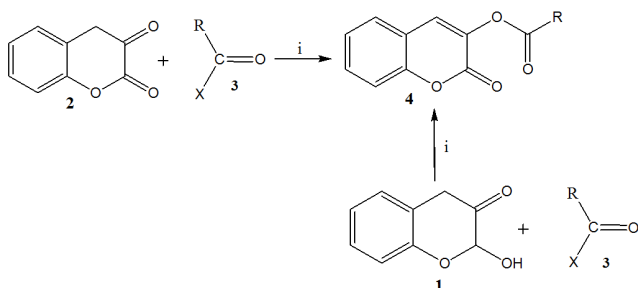


Figure 2. Formation of compounds 4.

i: Solvent=Diethylether, Base=Pyridine

4a: (R=CH₃; X=OCOCH₃); 4b: R=C₂H₅; X=Cl

Synthesis and crystallization (compound 4a): A solution of acetic anhydride (6.17 mmol) in dried diethyl ether (25 mL) was added dried pyridine (2.35 mL; 4.7molar equivalents) and chroman-2,3-dione or 3-hydroxycoumarin (1 g; 6.17 mmol) by small portions over 30 min, under strong stirring. The reaction mixture was left under agitation at room temperature for 3 h. The obtained solution was poured in a separating funnel containing 40 mL of chloroform and washed with diluted hydrochloric acid solution until the pH was 2-3. The organic phase was extracted, washed with water to neutrality, dried using MgSO₄ and the solvent removed. The crude product was filtered off with suction, washed with petroleum ether and recrystallized from a solvent mixture of chloroform–hexane (1/3, V/V) to obtain Yellow-laminar crystals 4a.

Synthesis and crystallization (compound 4b): A solution of propionyl chloride (6.17 mmol) in dried diethyl ether (25 mL) was added dried pyridine (2.35 mL; 4.7molar equivalents) and chroman-2,3-dione or 3-hydroxycoumarin (1g; 6.17 mmol) by small portions over 30 min, under strong stirring. The reaction mixture was left under agitation at room temperature for 3 h. The obtained solution was poured

in a separating funnel containing 40 mL of chloroform and washed with diluted hydrochloric acid solution until the pH was 2-3. The organic phase was extracted, washed with water to neutrality, dried using MgSO₄ and the solvent removed. The crude product was filtered off with suction, washed with petroleum ether and recrystallized from a solvent mixture of chloroform–hexane (1/3, V/V) to offer yellow crystals 4b.

2.2. Materials and Measurement

Melting points were determined in capillary tubes on a Stuart SMP 11 apparatus and are uncorrected. IR spectra were recorded on a Bruker IFS 66 / S Fourier Transform Infra red spectrometer (FT-IR), driven by the OPUS 6.5 software and using the ATR (Attenuated Total Reflection) technique. NMR spectra: ¹H and ¹³C (+ DEPT 135) NMR spectra were recorded on a BRUKER AMX spectrometer at 500 MHz, 300 MHz and 100 MHz, using TMS as internal standard (chemical shifts in values, J in Hz). The EIMS spectra were obtained with a PERKIN-ELMER spectrometer. The ESI-MS spectra were obtained on a 3200 QTRAP (Applied Biosystems SCIEX) spectrometer equipped with pneumatically assisted air pressure ionization (API) source. The compound 4b has been analyzed by X-ray diffraction. Data were collected by the X scan technique at 293 K on an Agilent Super Nova Dual diffractometer with an Atlas S2 detector, using Cu K α radiation (λ = 1.54184 Å). The structure was solved by direct methods which revealed the positions of all non-hydrogen atoms, and were refined on F2 by a full-matrix least-squares procedure using anisotropic displacement parameters. The fluorescence spectra of the compounds were recorded in solid-state on a SAFAS Xenius fluorimeter. All compounds were excited at their maximum excitation wavelength. In liquid state, the spectra were recorded on a spectrometer KONTRON SFM-25 (Zurich, Switzerland) at temperature ambient, the concentration is 3.10⁻⁵ molL⁻¹ for all samples.

2.3. Characterization

2.3.1. 2-oxo-2H-chromen-3-yl Acetate

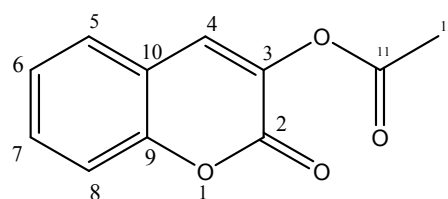


Figure 3. Structure of the numbered compound 4a.

Yield: 72%; Mp: 98-100°C, IR (cm⁻¹): 1776 (C=O ester), 1731 (C=O, lactone), 1607 (C=C), 3064 (C-H Aromatic), 2960 (C-H aliphatic), 1189 (CO, ester), 1081,7 (CO, lactone); ESI-MS (m/z; %): 205 [MH]⁺ (100), 163 (53,33); EIMS (m/z; %): 204 (M) (15), 164 (2), 163 (20), 162 (100), 135 (2), 134 (20), 133 (5), 107 (2), 106 (30), 105 (20). ¹H-RMN (CD₃OD; 400MHz): 2,35 (s, 3H, CH₃); 7,52 (d, 1H, J = 8 H-6); 7,47 (d, 1H, J = 7,87Hz, H-5), 7,32 (d, 1H, J = 8;

2,1 Hz, H-7); 7,35 (d, 1H, $J = 8$, H-8), 7,49 (s, 1H, H-4); ^{13}C -RMN: 20,12 (CH₃); 116,16 (C-8), 118,27 (C-10); 125,04 (C-4), 128,44 (C-6); 131,47 (C-5), 131,68 (C-7), 135,33 (C-3); 151,52 (C-9), 156,08 (C-2), 168,19 (C-11); DEPT 135°: 20,12 (CH₃); 116,16 (C-8); 125,04 (C-4); 128,44 (C-6); 131,47 (C-5); 131,68 (C-7).

2.3.2. Crystal Structure Determination (4a)

The structure of compound 4a has not been established. compound 4a is a lamellar crystals, X-ray diffractometry analysis has given a high reliability coefficient, greater than 0,07.

2.3.3. 2-oxo-2H-chromen-3-yl Propionate

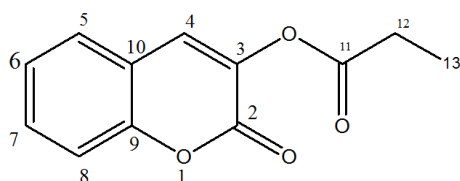


Figure 4. Structure of the numbered compound 4b.

Yield: 65%; Mp: 78-80°C, IR (cm⁻¹): 1759 (C=O ester), 1728 (C=O, lactone), 1607 (C=C), 3330 (C-H Aromatic), 2960 (CH Aliphatic), 1121 (CO, ester), 1099 (CO, lactone). ESI-MS (m/z; %): 219 [MH]⁺ (89,33), 163 (100), 57 (53,33); EIMS (m/z; %): 218 (M) (11), 164 (1.5), 163 (11), 162 (100), 135 (1), 134 (9), 133 (5), 107 (1.5), 106 (15), 105 (10). ^1H -RMN (CD₃OD; 500 MHz): 1,25 (t, 3H, $J = 8,19$ Hz, CH₃); 2,65 (q, 2H, $J = 8,19$ Hz, CH₂); 7,52 (t (d), 1H, $J_1 = 8$ Hz, 1,42 Hz, H-6); 7,36 (d, 1H, $J = 8,57$ Hz, H-8); 7,30 (d, 1H, $J_1 = 8,21$ Hz, $J_2 = 1,07$ Hz H-7); 7,46 (d (d), 1H, $J_1 = 7,87$ Hz, $J_2 = 1,57$ Hz, H-5); 7,48 (s, 1H, H-4). ^{13}C -RMN (CD₃OD, 100 MHz): C-2 (156,67); C-3 (136,36); C-4 (131,13); C-5 (127,82); C-6 (124,91); C-7 (130,73); C-8 (116,72) C-9 (152,15) C-10 (118,53); C-11 (171,83); C-12 (27,27); C-13 (8,83). DEPT 135°: C-4 (131,13); C-5 (127,82); C-6 (124,91); C-7 (130,73); C-8 (116,72); C-12 (27,27); C-13 (8,83).

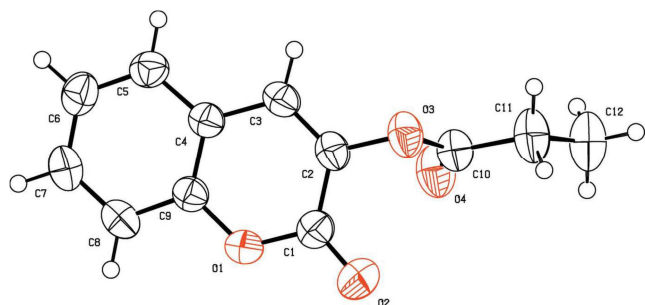


Figure 5. Molecular structure of compound (1), with displacement ellipsoids drawn at the 50% probability level.

2.3.4. Crystal Structure Determination (4b)

Chemical formula: C₁₂H₁₀O₄; Formula weight: 218.20; Crystal description: prism, colourless; Melting point (K): 351; Crystal system: Monoclinic; space group: *P*2₁/*c*; Temperature (K): 293; Wavelength (Å): 1.54184; Unitcell dimensions: *a* = 12.1179 (4) Å, *b* = 5.7243 (2) Å, *c* = 15.3275 (5) Å, β = 94.881

(3)°; Volume (Å³): 1059.36 (6); *Z* = 4; Radiation type: Cu *K*α; Absorption coefficient (mm⁻¹): 0.87; Density (Mgm⁻³): 1.368; *F* (000): 456; Crystal size (mm): 0.46 × 0.16 × 0.08; 6028 measured reflections; 1930 independent reflections; *R*_{int} = 0.020; *R* [*F*² > 2σ (*F*²)] = 0.038; *wR* (*F*²) = 0.117; *S* = 1.06; 1930 reflections; 145 parameters.

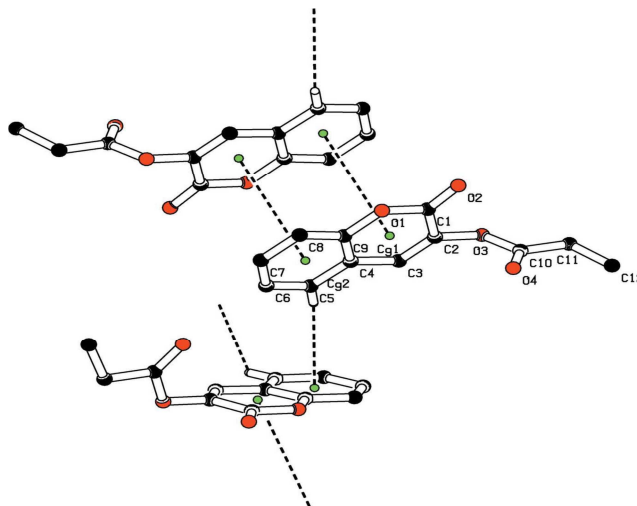


Figure 6. A view of the crystal packing, showing the π - π stacking and C—H π interactions (dashed lines). The green dots are ring centroids. H atoms not involved in the C—H... π interactions have been omitted for clarity.

3. Resultats and Discussion

3.1. Characterization

The method used seems reliable, almost simple and accessible. It allowed us to prepare compounds 4 with quantitative yields. This study complements and confirms previous work on the EIMS and ESI-MS mass spectra of its two compounds [16-17]. It also complements by the analysis of IR spectra, ^1H -NMR, ^{13}C -NMR, DEPT-135°, Characterization in the solid state by X-ray diffraction of the compound 4b [18].

3.2. Fluorescence Properties

3.2.1. Solvatochromic Behavior on the Fluorescence Spectra

In a previous paper, we have investigated the solvatochromic behaviour of these types of compounds in variable solvents including dichloromethane (DCM), chloroform, 1,4-dioxane, methanol, acetonitrile and dimethylsulfoxide (DMSO). From these studies, it appears that these compounds 4 are all liquid fluorescent with a fluorescence intensity (*I_F*) that varies according to the nature of the substituent and the solvent [19]. There was also an important solvent effect on the behaviour of the different fluorescence emission spectra. Among the solvents used, chloroform is the one that most enhances the fluorescence intensity of compounds 4 in liquid medium [20].

3.2.2. Fluorescence Properties in Solide State

In order to study the influence of substituent and minimize

the effects of the solvent on fluorescence, we subjected our 3-substituted coumarin derivatives to the solid state fluorescence study. The different bands are characterized by the position of the emission maxima. All emission bands have a single maximum. The bands are analyzed through wavelength (λ_F) and fluorescence intensity (I_F). The results are reported in the table below (Table 1). Analysis of the figures shows that the compounds 4 are fluorescent with a variation in fluorescence intensity related to the substituent R. We found the same results with the study of (coumarin-3-yl)-benzoates (R= aryl substituents) [2].

Table 1. Longueurs d'ondes d'excitation (λ_{Ex}); Longueurs d'onde (λ_F) et intensités (I_F) des maxima des bandes d'émission de fluorescence.

Comp	R	λ_{Ex} (nm)	λ_F (nm)	I_F (u. a)
4a	CH ₃	460	508	99,05
4b	C ₂ H ₅	460	508	100,06

Analysis of the table shows that the compounds absorb at the same wavelength ($\lambda_{Ex} = 460$ nm) and fluoresce at the same wavelength ($\lambda_{Em} = 508$ nm). In addition, we observe different behaviours at the level of fluorescence intensity. It can be seen that the intensity fluorescence I_F is higher for compound 4b (R = C₂H₅) than for compound 4a (R = CH₃). The substituent R being aliphatic (R = alkyl), the elongation of the hydrocarbon chain could explain this slight hyperchromatic effect (figures 7 and 8).

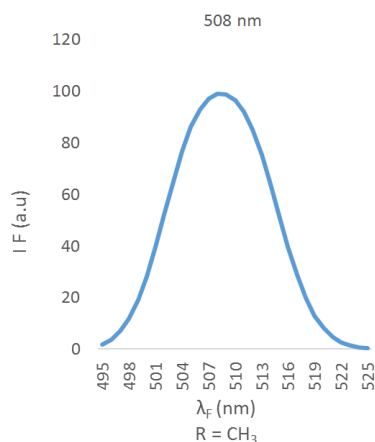


Figure 7. Fluorescence emission of compound 4a.

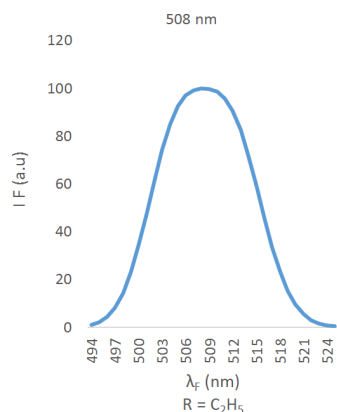


Figure 8. Fluorescence emission of compound 4b.

4. Conclusion

Compounds 4 were successfully synthesized and the proposed structures were determined by spectral analysis performed by IR, NMR, EIMS, ESI-MS. Compound 4b has been confirmed by X-ray diffractometry. The fluorescence properties of these 3-substituted coumarin derivatives were studied in both the solid and liquid state. The compounds exhibit relatively high fluorescence in both medium. In the solid state, the fluorescence emission was influenced by molecular structure and electronic nature of the substitution group R. In the liquid state, the behaviour of the spectra is strongly influenced by the nature of the solvent. Among the solvents used, chloroform is the solvent that the most increases the fluorescence intensity.

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