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# Review on 4-Hydroxycoumarin Chemistry: Synthesis, Acylation and Photochemical Properties

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**Abstract** Hydroxycoumarins are important compounds exhibiting several physical, chemical and biological properties. These compounds represent a part of secondary metabolites that are natural compounds and are studied for their importance in organic synthesis. Among the most well-known hydroxycoumarins are 7-hydroxycoumarin and 4-hydroxycoumarin. The objective of this review is to raise awareness of the reactivity of 4-hydroxycoumarin and its applications. In this study, we review the methods of synthesis and acylation of this compound as well as studies on the photochemical properties of its derivatives. Several methods for the synthesis of 4-hydroxycoumarin have been described in the literature, most of which use simple phenol and 1-(2-hydroxyphenyl)ethanone or 2'-hydroxyacetophenone as starting compounds. Other synthesis pathways exist, but they are based on intermediate synthesis compounds. About 4-hydroxycoumarin acylation, the literature reports two main types of acylation such as *C*-acylation and *O*-acylation. Several authors have synthesized and studied *C*-acylation in liquid medium and the solvent free. As for *O*-acylation, its compounds are more recent and less studied. Some studies have also been conducted on the photochemical properties of 4-hydroxycoumarin and its derivatives. Some compounds have proven to be excellent UV absorbers, others have fluorescent properties. With regard to the photo-acid properties generally sought in the hydroxycoumarins group, studies have shown that 4-hydroxycoumarin, unlike 7-hydroxycoumarin, cannot be considered as an active photo-acid.

***Keywords:*** *coumarin, 4-hydroxycoumarin, acylation, photochemical properties, fluorescence*

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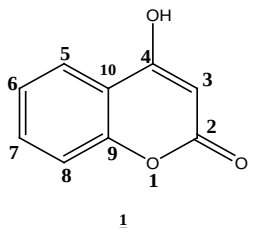
## 1. Introduction

Coumarins are one of the most significant families of natural product compounds and are also important in synthetic organic chemistry. They have been widely used as starting materials or precursor molecules in the pharmaceutical sciences [1-6]. They are used in perfumery [7,8,9], cosmetic [10] and agrochemical industries [11,12]. Coumarin derivatives are also used as fluorescent coumpounds due to their inherent photochemical characteristics. Many coumarin derivatives have been commercialized as blue-green lasers for fluorescent labels and fluorescent probes [13-19]. They exhibit intense fluorescence upon substitution with various functional groups at different positions [20].

This study focuses on hydroxycoumarins, specifically 4-hydroxycoumarin **1**, this compound (Figure 1) which known as 4-hydroxy-2H-chromen-2-one and 4-hydroxy-1-benzopyran-2-one or 2-Hydroxychromen-4-one in IUPAC system. It has other lesser-known names such as 4-coumarinol and benzotetronic acid. Its structure contains three tautomeric keto-enol forms [21,22] (Figure 2).




**1**

**Figure 1**. Numbered structure of 4-hydroxycoumarin

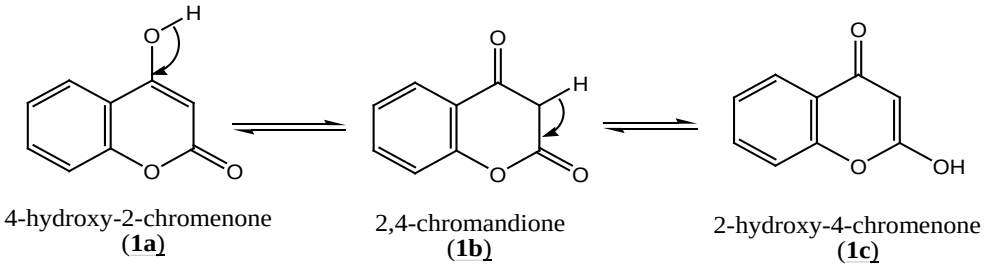



**Figure 2**. Tautomeric forms of 4-hydroxycoumarin

4-hydroxycoumarin represent nowadays, an important precursor in the realm of organic synthesis; its derivatives have shown a remarkably broad spectrum of biological activities [23-30]. They can be among others, anticoagulant [23,24], antibacterial [25,26], anti-inflammatory [27] and anti-tumoral [28] anti-pyretic [29] and anti-viral [30] properties. The acyl derivatives in particular have different biological activities for variable acyl groups. It has been reported by Crovatto et al. [31] that the activity evolves with the length of the carbon chain of the acyl group. With a short-chain acyl group, the compound has high ovicide rates, but the longer the chain, the lower the activity. The 3-acyl-4-hydroxycoumarins possessing long-chain (carbon number 10) with a terminal ethylene bond, have a high antibacterial activity. This review is not exhaustive, the objective of the study is to enhance the title compound, its reactivity, its acyl derivatives and its applications. Thus, in this review, we report the synthesis and acylation of 4-hydroxycoumarin. The photochemical properties of this compound and its derivatives will then be investigated. Herein, the discussion is supported by numerous lucid diagrams and reaction schemes, figures are supported by relevant and up-to-date references from the original literature.

# 2. Synthetic routes

## 2.1. Chemical reactions

Shah et al. [32] were among the first to be interested in the synthesis of 4-hydroxycoumarin and its derivatives. In their investigation, they noted the existence of three main methods for the synthesis of 4-hydroxycoumarins. Among these, a synthetic pathway first leads to the 3-substituted 4-hydroxycoumarin and this intermediate can then be converted to 4-hydroxycoumarin **1**. This is the condensation reaction of acetyl salicyloyl chlorides with acetoacetic, cyanoacetic or malonic ester. They subsequently discovered a new simple process in which phenol is treated with an equimolar proportion of malonic acid in the presence of a mixture of a double to triple molar amount of each anhydrous zinc chloride and phosphorus oxychloride as a condensation agent. In recent advances, there are many synthetic approaches to 4-hydroxycoumarin **1** [33], but the synthetic pathways using 2'-hydroxyacetophenone or phenol as starting marterials are still the most conventional (Figure 3).

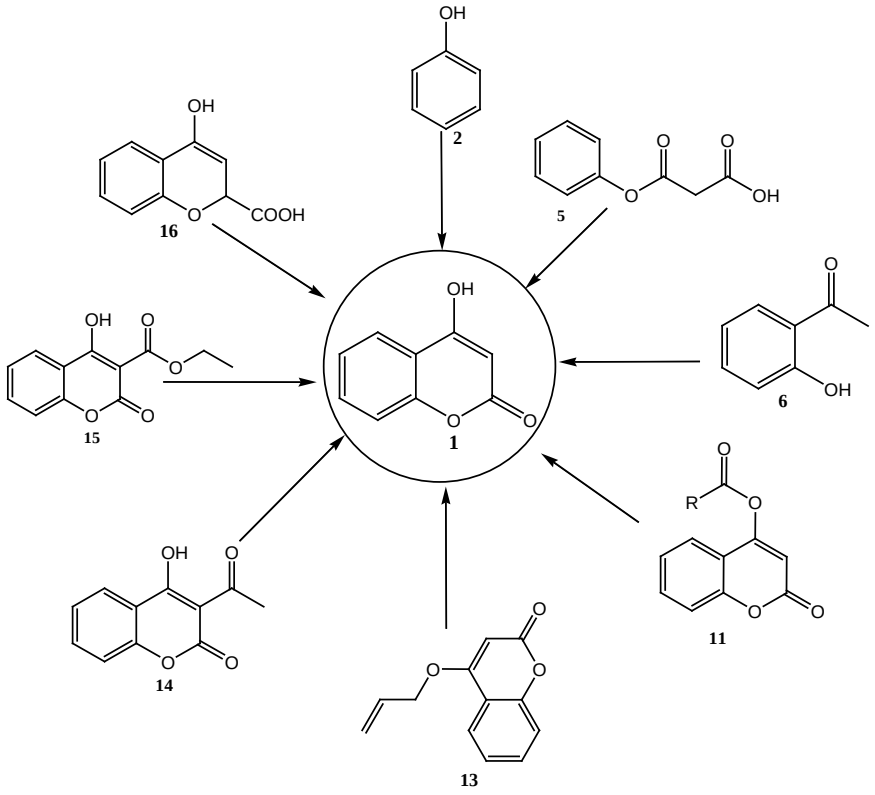



**Figure 3.** 4-hydroxycoumarin synthesis routes

## 2.2. Use of Phenol and 2'-hydroxyacetophenone as Starting Marterial

### 2.2.1. Phenol as Starting Material

The Pechman reaction is one of the methods widely applied in a practical sense, to synthesize coumarins, because it involves the condensation of phenols with β-ketoesters or carboxylic acids. To obtain 4-hydroxycoumarin **1** with a quantitative yield of 64%, Phenol **2** is treated with an equimolar proportion of a malonic acid **3** in phosphorus oxychloride ($POCl_3$) containing two equimolars of the amount of anhydrous zinc chloride ($ZnCl_2$) [34] (Figure 4).

The mixture of phenol **2** with Meldrum's acid or isopropylidene malonate **4** under solvent-free condition leads to an intermediate compound 3-oxo-3-phenoxypropanoic acid **5**. This compound is then converted into 4-hydroxycoumarin **1** by two routes with different yields. 3-oxo-3-phenoxypropanoic **5** is treated with the Eaton reagent (7.7 wt % phosphorus pentoxide solution in methane sulfonic acid) or polyphosphoric acid (PPA) to give 4-hydroxycoumarin **1** (Figure 5) [35,36,37].

### 2.2.2. 2'-hydroxyacetophenone as Starting Material

1-(2-hydroxyphenyl)ethanone or 2'-hydroxyacetophenone **6** reacts with an equimolar amount of acylating agents **7** such as phosgene **7a**, dimethyl carbonate **7b** or diethyl carbonate **7c**. The reaction is carried out in the presence of a suitable base in toluene or anhydrous xylene to give 4-hydroxycoumarin 1 with variable yield (Figure 6). When analysing the different yields, it is found that sodium hydride is the most effective base (Table 1) [38-41].

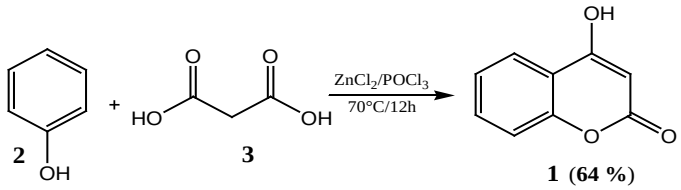



**Figure 4.** Compound 1: Synthesis by Pechman reaction

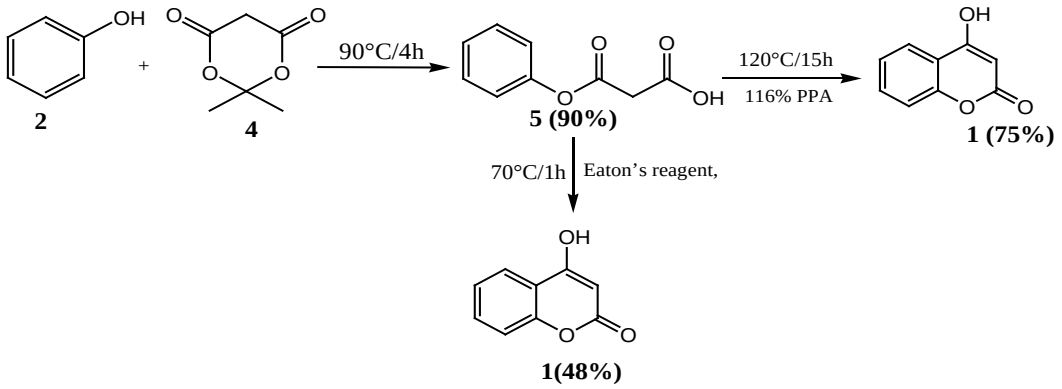



**Figure 5.** Compound 1: Synthesis using Meldrum's acid

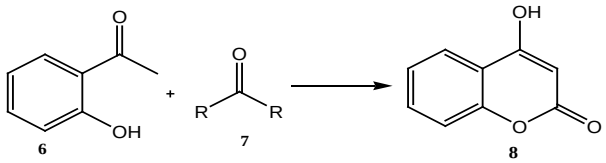



**Figure 6.** Compound **1:** synthesis using 2'-hydroxyacetophenone

**Table 1. Experimental conditions for obtaining compound 1**

| Solvents | R | Base | Yield (%) |
|---|---|---|---|
| Toluene | **7b**: Diethylcarbonate (R = OEt) | Sodium ethoxide | 80 |
| | | Sodium hydride | 85 |
| | | Sodium 3-aminopropylamide | 51 |
| | | Potassium 3-aminopropylamide | 63 |
| | | Sodium metal | 50 |
| | | Sodium 3-aminopropylamide | 85 |
| | **7a**: Phosgene (R = Cl) | Sodium hydride | 69 |
| | | Sodium ethoxide | 66. |
| | **7c** : Dimethylcarbonate (R = OMe) | Sodium 3-aminopropylamide | 60 |
| | | Sodium hydride | 84 |
| | | NaOEt | 71 |
| | | Potassium 3-aminopropylamide | 55 |
| Xylene | **7c**: Diethylcarbonate (R = OEt) | Sodium metal | 93 |

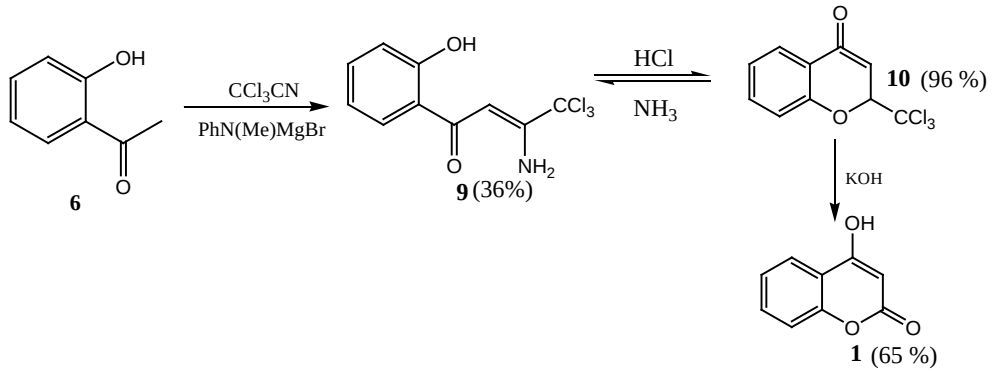



**Figure 7**. Compound **1:** formation by condensation of 1-(2-hydroxyphenyl)ethanone

The condensation of 2'-hydroxyacetophenone **6** with trichloroacetonitrile in the presence of N-methylanilinomagnesium bromide gives (Z)-3-amino-3,4,4-trichloro-1-(2-hydroxyphenyl)but-2-en-1-one **9**, which is transformed into 2-(trichloromethyl)chromones **10** during treatment with concentrated hydrochloric acid. Hydrolysis catalyzed by potassium hydroxide results in 4-hydroxycoumarin **1**[42] (Figure 7).

## 2.3. Use of Acyl Derivatives of 4-hydroxycoumarin

Liao et al. [43] reported a novel synthesis pathway to switch from *O*-acylation **11** compound to *C*-acylation **12** compound of 4-hydroxycoumarin **1**. The reaction first leads to a 4-coumarinyl carboxylate **11** corresponding to the *O*-acylation derivative. In the presence of potassium cyanide, this compound gives 3-acyl-4-hydroxycoumarin by the displacing of the acyl group (RCO). Using this method, 4-hydroxycoumarin can be obtained after acid hydrolysis (Figure 8).

## 2.4. Use of Cleavage Reaction

Ganguly et al. [44] described a method of synthesizing 4-hydroxycoumarin **1** from 4-allyl-coumarinyl ether. The cleavage reaction uses a catalytic amount of palladium on activated carbon in methanol, in combination with ammonium formate This reaction can also be catalyzed by other reagents such as molecular iodine [45] (Figure 9).

## 2.5. Use of Deacylation and Decarboxylation Reactions

Jung et al. [46] published a simple and facile method for obtaining 4-hydroxycoumarin. This synthesis pathway uses 3-acetyl-4-hydroxycoumarin **14** as the starting compound. By a deacylation reaction catalyzed by HCl acid, 4-hydroxycoumarin 1 is isolated in a 90% yield (Figure 10). Similarly, 3-carbethoxy-4-hydroxycoumarin **15** leads to 4-hydroxycoumarin-1 through acid-catalyzed hydrolysis and decarboxylation [46] (Figure 11).

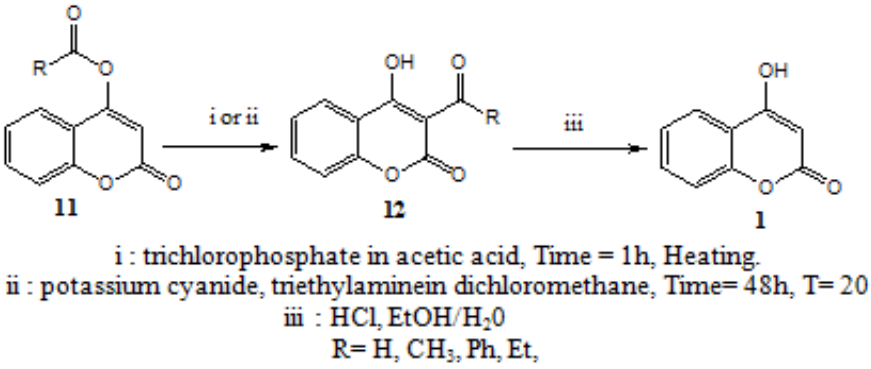



**Figure 8**. Compound **1 :** formation using 4-acyl-3-hydroxycoumarin and 4-coumarinyl carboxylate

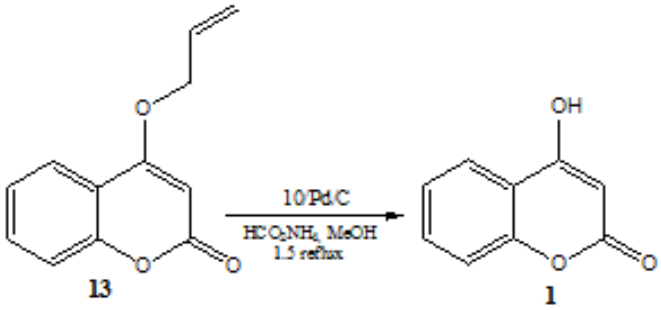



**Figure 9**. Compound **1:** formation by cleavage reaction

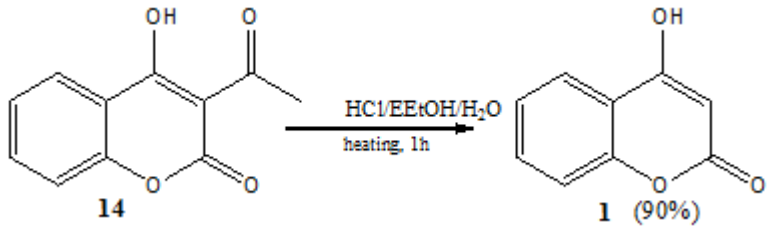



**Figure 10**. Compound **1:** formation by deacylation reaction

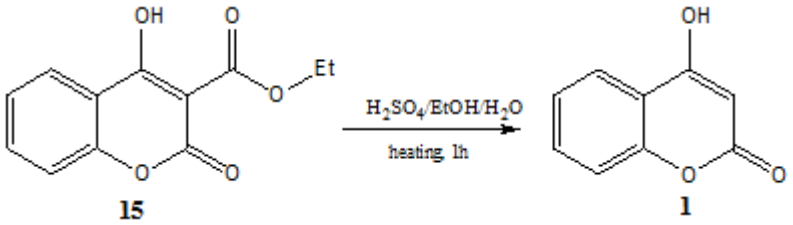



**Figure 11**. Compound **1** formation by decarboxylation reaction

## 2.6. Photooxygenation of Chromone-2-carboxylic Acid

Another approach was reported by Kawata et al. [47] via the photooxygenation of chromone-2-carboxylic acid **16** in ethanol solution. The reaction seems to proceed via the decarboxylation followed by the addition of the oxygen molecule (Figure 12).

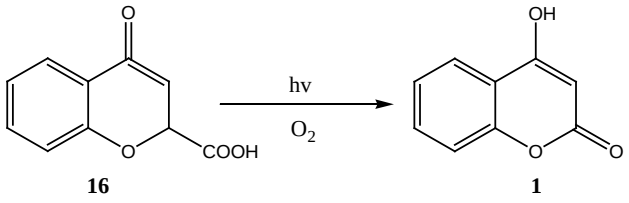



**Figure 12**. Compound **1:** formation by photooxygenation of chromone-2-carboxylic Acid

# 3. Acylation of 4-hydroxycoumarin

## 3.1. Acylation Reaction

Hydroxycoumarins react remarkably quickly with several acyl chlorides to give coumarin acyl derivatives [48-61]. Previous works has shown that phenols, particularly hydroxycoumarins and some similar compounds such as homophthalic anhydrides (isochroman-1,3-dione), are suitable for acylation reactions with different results. Indeed, in the case of homophthalic anhydride, in the case of homophthalic anhydride, there is only *C*-acylation, where as in the case of hydroxycoumarin derivatives, acylation could be either *O*-acylation or *C*-acylation [48,51]. In the literature, several processes for the acylation of 4-hydroxycoumarin have been described. According to the mechanism of this acylation in a basic medium, an alcoholate anion **1i** is formed at the hydroxyl function. This anion could be in equilibrium with mesomeric carbanion **1ii** as follows (Figure 13). In general, triethylamine ($Et_3N$), pyridine (Py), piperidine and potassium cyanide (KCN) are used as appropriate bases.

## 3.2. *C*-acylation of 4-hydroxycoumarin

### 3.2.1. Synthesis of 3-acyl-4-hydroxycoumarin

Cravotto et al. [51] studied the acylation of 4-hydroxycoumarin **1** using various long-chain acid chlorides **16** as acylating agents and piperidine as an appropriate base. The action of acid chlorides (RCOCl) with an aliphatic R group on 4-hydroxycoumarin **1** is carried out under the effect of 21 KHz ultrasound. The authors obtained a quantitative *C*-acylation in the presence of catalytic amount of piperidine (Figure 14). Similarly, 3-(10'-undecenoyl) chroman-2,4-dione **17a** (n = 8) was prepared by acetylation of 4-hydroxycoumarin 1 with 10-undecenoyl chloride **16a** in pyridine also containing a catalytic amount of piperidine [52,53].

The method proposed by Liao et al., for the acylation of 4-hydroxycoumarin **1** [43] is rather classical. The substrate reacts with acid chloride **18** in the presence of both triethylamine in methylene chloride to give the corresponding enol ester (*o*-acyl derivatives) which were further treated with potassium cyanide without purification at ambient temperature for two days to obtain a good yield of the 3-acyl-4-hydroxycoumarin (Figure 15).

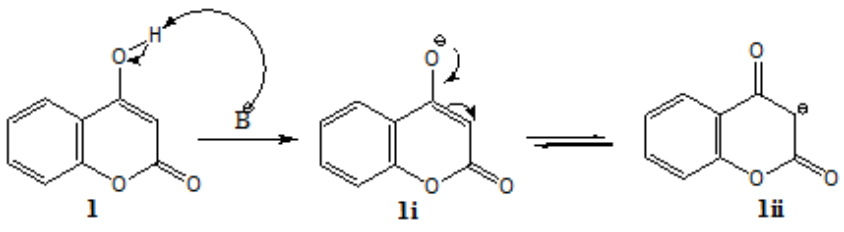
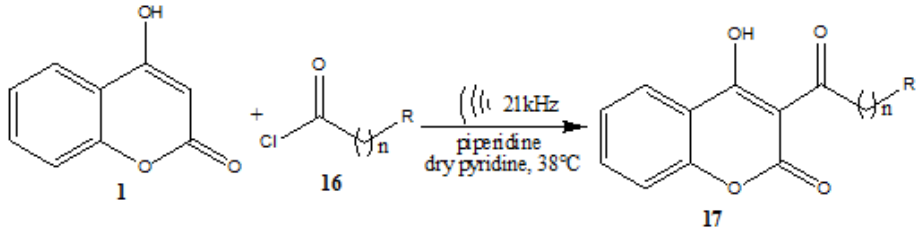



**Figure 13.** Mesomeric equilibrium between alcoholate anion and carbanion from 4-hydroxycoumarin

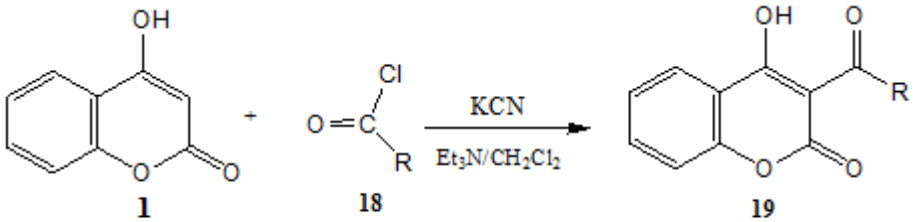



Solvent: Pyridine,

**17a** : (n = 8 ; R= -CH=$CH_2$) ; **17b** : (n= 7, R=CH=CH-$(CH_2)_7$-$CH_3$), **17c** : (n=14 ; R=$CH_3$)

**16a** : (n = 8 ; R= -CH=$CH_2$) ; **16b** : (n= 7, R=CH=CH-$(CH_2)_7$-$CH_3$), **16c** : (n=14 ; R=$CH_3$)

**Figure 14.** 3-acyl-4-hydroxycoumarin synthesis under ultrasound




**R**= $CH_3$ ; $C_2H_5$ ; $C_6H_5$

**Figure 15.** Formation of 3-acyl-4-hydroxycoumarin with R= Alkyl or aryl

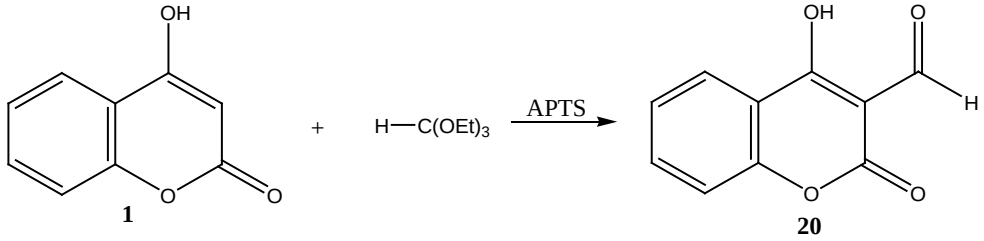



**Figure 16**. Formation of 3-formyl-4-hydroxycoumarin

Rad-Moghadam and Mohseni [60], in the absence of solvent, were able to obtained 3-formyl 4-hydroxy coumarin **20**. The reaction is performed under the effect of microwaves between 4-hydroxycoumarin and ethyl orthoformate H-C(OEt)3 in the presence of a catalytic amount of p-toluenesulfonic acid (APTS). The final compound is obtained with a quantitative yield (Figure 16).

### 3.2.2. Synthesis of 3-acetyl-4-hydroxycoumarin

Many synthetic approaches to 3-acetyl-4-hydroxycoumarin **22** have been reported using 4-hydroxycoumarin as starting material. Abdoullah S. AL-AYED et al. [50] prepared 3-acetyl-4-hydroxycoumarin **22** using the method described by Dholakia et al. [57]. This method involves reacting 4-hydroxycoumarin **1** with glacial acetic acid **21**, in the presence of phosphorus oxychloride (POCl3) as the catalyst (Figure 17).

The direct acetylation of 4-hydroxycoumarin **1** in the presence of triethylamine in methylene chloride **23** gave the corresponding enol esters (acetate of 4-coumarinyl) **24**, which were further treated with trichlorophosphate in acetic acid or potassium cyanide with triethylamine in dichloromethane. Using pyridine or piperidine as a catalyst to obtain 3-acetyl-4-hydroxycoumarin **22** [54,55,56] (Figure 18).

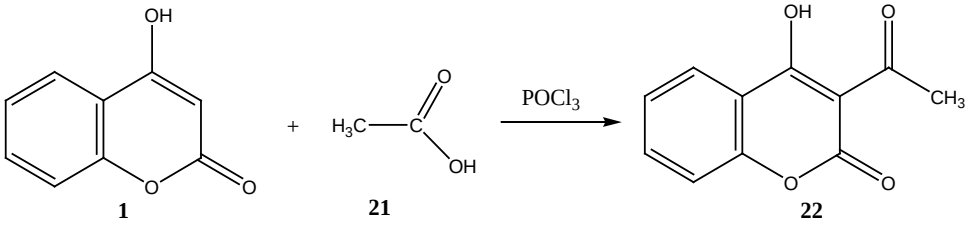



**Figure 17.** Formation of 3-acetyl-4-hydroxycoumarin

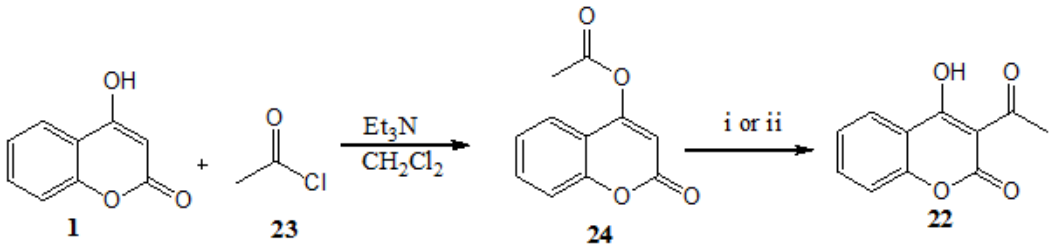



**Figure 18.** Formation of 3-acetyl-4-hydroxycoumarin via acetate of 4-coumarinyl

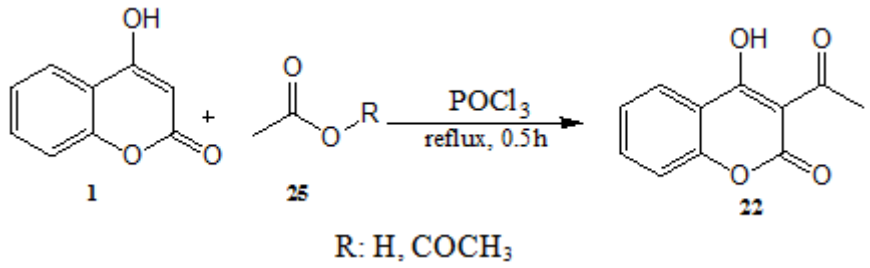



**Figure 19**. Formation of 3-acetyl-4-hydroxycoumarin using phosphorous oxychloride

Synthetic routes for 3-acetyl-4-hydroxycoumarin **22** have been published via the reaction using **1** with acetic acid or acetic anhydride **25** in the presence of phosphorous oxychloride as a catalyst [56] (Figure 19).

We note that the most recent studies mention *C*-acylation. To obtain *O*-acylation therefore seems rather difficult. However, the work of Tapase et al. and Saba et al. have recently led to the development of new *O*-acylation derivatives of 4-hydroxycoumarin, as indicated below.

## 3.3. *O*-acylation of 4-hydroxycoumarin

### 3.3.1. Solvent-free Synthesis under Microwave

The principle of preparation of coumarinyl carboxylates is an *O*-acylation of 4-hydroxycoumarin by the action of acyl chlorides or equivalent acid anhydrides in a basic medium [61]. Tapase et al. [48] prepared a series of *O*-acylated coumarins by the action of acid halides with 4-hydroxycoumarin, either in basic medium (NaOH) or in the presence of copper salts. The reactions were carried out in a microwave oven in the absence of solvent. The authors used 2.5 mmol of 4-hydroxycoumarin in an aqueous solution of sodium hydroxide. The mixture is then irradiated in 600 W for 60 seconds to obtain a solid coumarin salt. An organic halide (3.0 mmol) is then mixed with the resulting solid and a few drops of water have been added. The reaction mixture was irradiated at the specified power for the specified time. After cooling to room temperature, the final product was washed with water to remove unreacted salt and excess sodium hydroxide. Finally, it was purified by recrystallization (Figure 20).

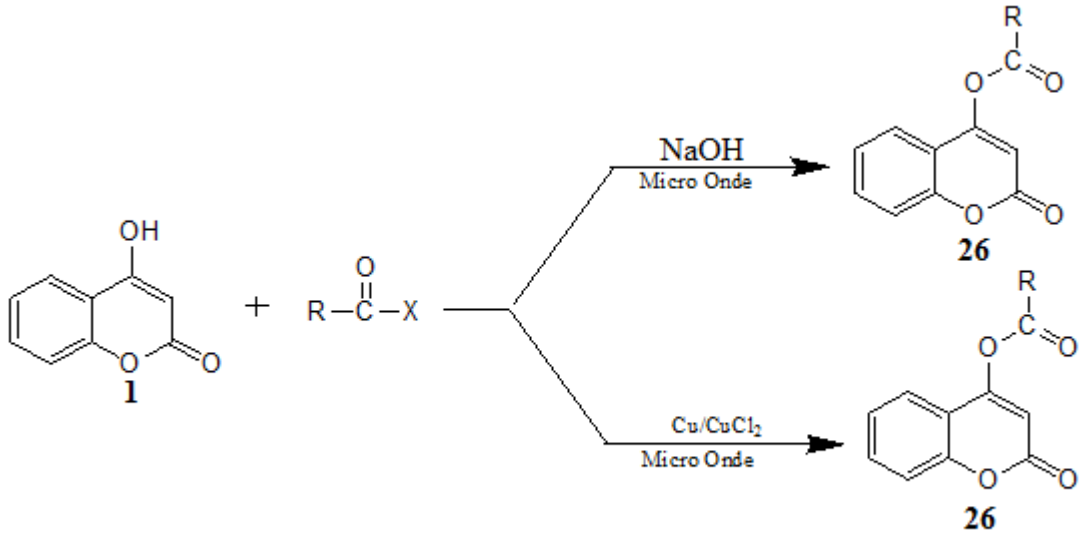



**Figure 20.** Microwave synthesis of *O*-acylated 4-hydroxycoumarin derivatives

It was observed that the presence of a few drops of water was very important for the NaOH method. The main effect was that the water could effectively couple to the microwaves or make the reaction mixture homogeneous. According to the authors, the absence of water would affect the efficiency of the reaction.

### 3.3.2. Synthesis Using HSAB Theory

Saba et al, [62,63] have developed an acylation method based on the "Hard and Soft Acid Base" (HSAB) theory developed by R. G. Pearson [64], in the choice of experimental conditions. It is indeed necessary to choose the base to be used taking into account the nature of the acylating agent. The research of Pearson has shown that hard bases react quickly and easily with hard acids while soft bases react well with soft acids. The choice of solvent is also an important factor that directly influences performance. This approach allowed isochromandione and hydroxycoumarins to be acylated [65,66,67,68,69]. Through this method, new *O*-acyl **27a-e** derivatives have been synthesized with good yield (Table 2), by an esterification reaction of 4-hydroxycoumarin with various benzoyl chlorides (Figure 21).

These new compounds **27** (27b-e) were analyzed by X-ray diffractometry to highlight the crystallographic data that justify their 3D structures [66,67,68,69]. A summary of the crystal data, experimental details and refinement results are given below in Table 4 (Figure 22 - Figure 25).

**Table 2. Microwave synthesis yields of compounds 26**

| Compound | R | Yield (%) NaOH method | Yield (%)Cu/CuCl2 method |
|---|---|---|---|
| **26a** | $CH_3$ | 66 | 64 |
| **26b** | $C_2H_5$ | 70 | 68 |
| **26c** | $C_4H_9$ | 62 | 60 |
| **26d** | $C_6H_5$ | 60 | 71 |
| **26e** | *p*-$ClC_6H_4$ | 49 | 73 |

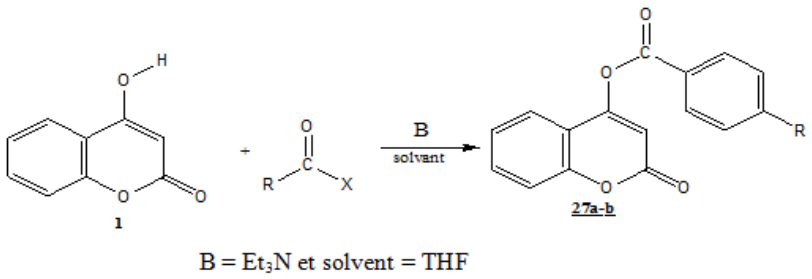



**Figure 21.** Carboxylate of 4-coumarinyl synthesis using HSAB theory

**Table 3. Preparation of 4-coumarinyl carboxylate by HSAB theory**

| Compound | R | Yield % | MP °C | Aspect |
|---|---|---|---|---|
| **27a** | H | 89 | 183-184 | White powder |
| **27b** | $CH_3$ | 76 | 120 | Colourless crystals |
| **27c** | *t*-Bu | 74 | 108-110 | Colourless crystals |
| **27d** | MeO | 84 | 148-149 | Colourless crystals |
| **27e** | $(CH_3)_2N$ | 83 | 172 | Colourless crystals |

**Table 4a. Crystallographic data of compounds 27b-e**

| Crystallographic data | **27b** R = $CH_3$ | **27c** R= *t*-Bu | **27d** R= *MeO* | **27e** R= $(CH_3)_2N$ |
|---|---|---|---|---|
| Cristal description | Colourless crystals | Colourless crystals | Colourless crystals | Colourless crystals |
| Recrystallization solvent | Chloroform-hexane | Chloroform-hexane | Chloroform-hexane | Chloroform-hexane |
| Chemical formula | $C_{17}H_{12}O_4$ | $C_{20}H_{18}O_4$ | $C_{17}H_{12}O_5$ | $C_{18}H_{15}NO_4$ |
| Formula Weight | 280.27 | 322.34 | 296.27 | 309.32 |
| Temperature (K) | 298 | 298 | 298 | 298 |
| Wavelength ( Å) | λ = 0.71073 | λ = 0.71073 | λ = 0.71073 | λ = 0.71073 |
| Radiation type | MoKα | Mo Kα | Mo Kα | Mo Kα |
| Crystal system | Triclinic | Triclinic | Triclinic | Triclinic |
| Espace group | P-1 | P-1 | P-1 | P-1 |
| Unit cell dimensions | a = 9.2790(5) Å | a = 6.4319(2) Å | a = 4.371 (1) Å | a = 7.4939 (2) Å |
| | b = 10.7696(5) Å | b = 9.3498(3) Å | b = 10.535 (1) Å | b = 10.2361(3) Å |
| | c = 14.5758(9) Å | c = 14.5505 (5) Å | c = 15.193 (10) Å | c = 10.6620 (3) Å |
| | α = 95.274(2)°; β = 97.875(2)°; γ = 81, 893(1)° | α = 98.481(1)°; β = 93.655 (1)°; γ = 102,359(2)° | α = 85.218(3)°; β = 90.751(2)°; γ = 81, 893(1)° | α = 92.307(3)°; β = 103.935(1)°; γ = 109.852(4)° |
| Volume (Å3) | 634.14 (6) | 841.27(5) | 686.08 (3) | 739.92(4) |
| Z | 2 | 2 | 2 | 2 |
| Density (Mg m−3) | 1.346 | 1.273 | 1.433 | 1.433 |
| Crystal size (mm) | 0.35 x 0.20 x 0.20 | 0.50 × 0.30 × 0.14 | 0.25 × 0.15 × 0.04 | 0.5x0.4x0.3 |
| Melting point (K) | 393 | 381-383 | 421-422 | 445 |

**Table 4b. Crystallographic data of compounds 27b-e**

| Crystallographic data | **27b** R = $CH_3$ | **27c** R = *t*-Bu | 27d R = MeO | **27e** R = $(CH_3)_2N$ |
|---|---|---|---|---|
| absorption Coefficient (mm−1) | 0.10 | 0.09 | 0.11 | 0.10 |
| F(000) | 584 | 340 | 308 | 324 |
| R [$F^2 > 2\sigma(F^2)$] | 0.071 | 0.057 | 0.066 | 0.048 |
| wR ($F^2$) | 0.193 | 0.157 | 0.163 | 0.120 |
| S | 1.02 | 1.05 | 1.11 | 0.98 |
| Rint | 0.055 | 0.031 | 0.055 | 0.024 |
| Reflections collected | 1645 | 11164 | 5683 | 8424 |
| Independent reflections | 6907 | 4198 | 2731 | 3590 |
| Reflections with [ I > 2σ(I)] | 3981 | 4198 | 2731 | 3595 |
| Parameters | 381 | 247 | 200 | 209 |
| Dihedral Angles | 69.82(9)° | 60.70(7) ° | 69.82(4) | 43,43 (6)° |

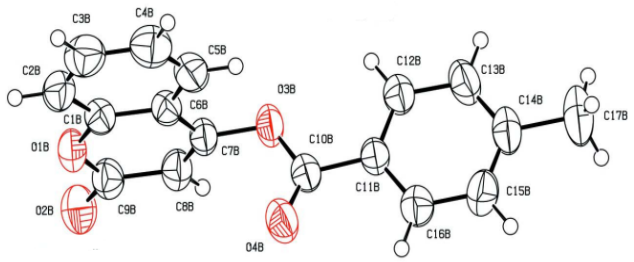



**Figure 22**. Ortep structure of compound of **27b**

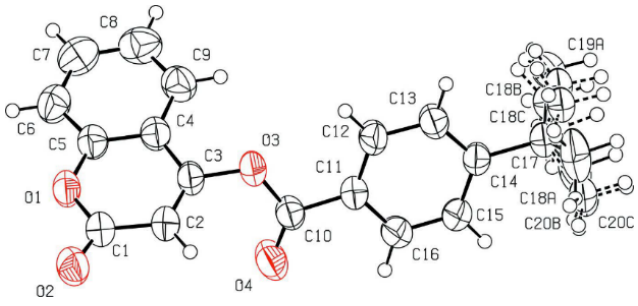



**Figure 23.** Ortep structure of compound **27c**

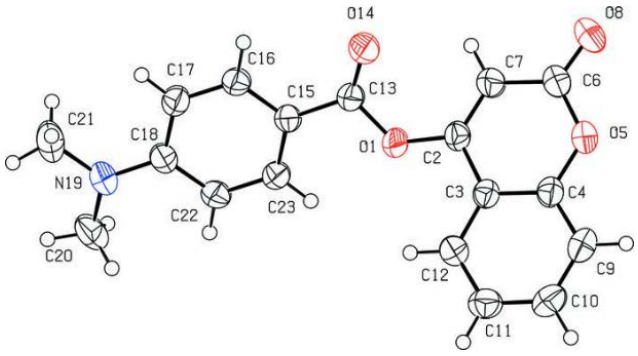



**Figure 24.** Ortep structure of compound of **27e**

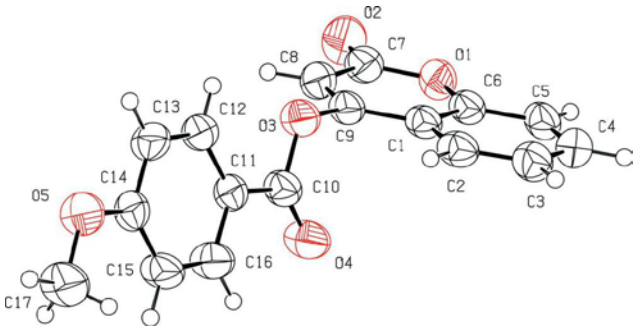
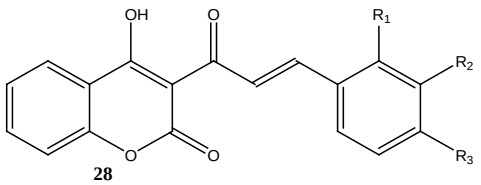



**Figure 25**. Ortep structure of compound of **27d**

# 4. Photochemical properties

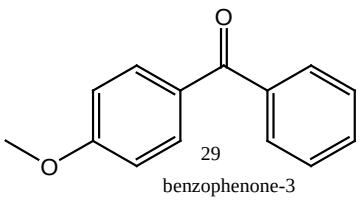
## 4.1. Absorption characteristics

2-Hydroxychromen-4-one **1**, trivially designated 4-hydroxycoumarin **1**, represents one of the most widespread and interesting classes of simple coumarins, which can play an important role related to their photochemical properties [61,70,71,72,73]. Recently, 4-hydroxycoumarin and its derivatives have attracted considerable attention for electronic and photonic applications. Ervina Becic et al. [70] studied the absorption characteristics of 4-hydroxycoumarin and its 3-substitute derivatives containing phenyl-prop-2-enoyl group at the 3-position **28** (Figure 26, Table 5), in solvents with different polarity (chloroform and acetonitrile) in regard to the influence of the substitution at the phenyl ring and influence of $H^+$ ion concentration. This study also provides a qualitative assessment of the new hydroxycoumarin derivatives as ultraviolet absorbers compared to specified organic UV absorbers such as benzophenone-3 **29** (Figure 27) and butylmethoxydibenzoylmethane **30** (Figure 28). Indeed, these compounds are organic UV absorbers that are often used for cosmetics and sun creams. They have wide bands in a wide range of UV spectrum [74]. These 4-hydroxycoumarin derivatives also showed high intensity broad-band UV spectra and good absorption over a wide region of 200-550 nm taking into account the property of substituents, polarity and pH of solvents. According to the results of their studies, these new compounds would be good candidates for UV absorbers.




**28**

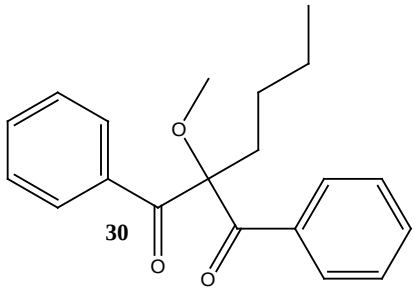
**Figure 26.** Structure of compound **28**




29

benzophenone-3

**Figure 27**. Structure of compound **29**




butylmethoxydibenzoylmethane

**Figure 28**. Structure of compound **30**

**Table 5. Chemical structure of synthesized molecules 28a-b**

| compounds | R1 | R2 | R3 |
|---|---|---|---|
| **28a** | H | H | H |
| **28b** | H | Cl | H |
| **28c** | H | H | $NHCOCH_3$ |
| **28d** | $OCH_3$ | H | H |
| **28e** | H | H | $N(CH_3)_2$ |
| **28f** | H | H | OH |
| **28g** | $NO_2$ | H | H |

## 4.2. Fluorescence Properties

Most coumarin derivatives possess good fluorescent properties, and as such are used as fluorescent markers and dyes for use in analyses, stains and clinical use [73,75]. A number of hydroxycoumarins have been synthesized and explored the possibility of their application to electro-optic materials, such as laser dyes, fluorescent probes or labels, solar collector systems, organic scintillators and photoelectronic sensitizers [75,76]. Specifically, 4-hydroxycoumarins are widely used due to their high emission yields, photo stability, extended spectral range and good solubility in various solvents [61,76]. Djandé et al.[61] studied the fluorescence of series of the new *O*-acyl derivatives of 4-hydroxycoumarin **27a-27e** in liquid medium with acetonitrile as solvent. From this investigation it appears that all the compounds **27** synthesized by considering the substitutes **R** with variable electron donation capacity, have a considerable fluorescence emission with a wavelength ranging from 372 to 394 nm (Table 6). (Coumarin-4-yl)-4-dimethylaminobenzoate (compound **27e**) showed the most intense fluorescence (Figure 29).

**Table 6. Excitation wavelengths (λex), emission wavelengths (λem) and fluorescence intensities ($I_F$)**

| Compounds | R | λex (nm) | λem (nm) | IF |
|---|---|---|---|---|
| **27a** | H | 317 | 372 | 45 |
| **27b** | Me | 291 | 378 | 95 |
| **27c** | *t*-Bu | 320 | 386 | 140 |
| **27d** | MeO | 305 | 392 | 225 |
| **27e** | $(Me)_2N$ | 312 | 394 | 450 |

## 4.3. Photoacid Properties

Photo-acids are generally hydroxyaryl compounds with low acidity in the basic state, while in their first electronic state they are much stronger acids. According to the pKa*, the pKa in the excited state, there are strong and weak photo-acids [77]. The photoacidity of hydroxycoumarins, particularly 7-hydroxycoumarin, is reportedly used for resistance to mould, fungal and bacterial infections by plants [78]. Luís Pinto da Silva et al. [77], in their research on photo-acids, studied 4-hydroxycoumarin using theoretical and experimental methods. Their theoretical studies were in agreement with the results of the experimental studies. It appears that, unlike the 7-hydroxycoumarins previously studied [78], 4-hydroxycoumarin cannot be considered as an active photoacid, and its non-radiative level is much higher than that of 7-hydroxycoumarins in the used solvents.

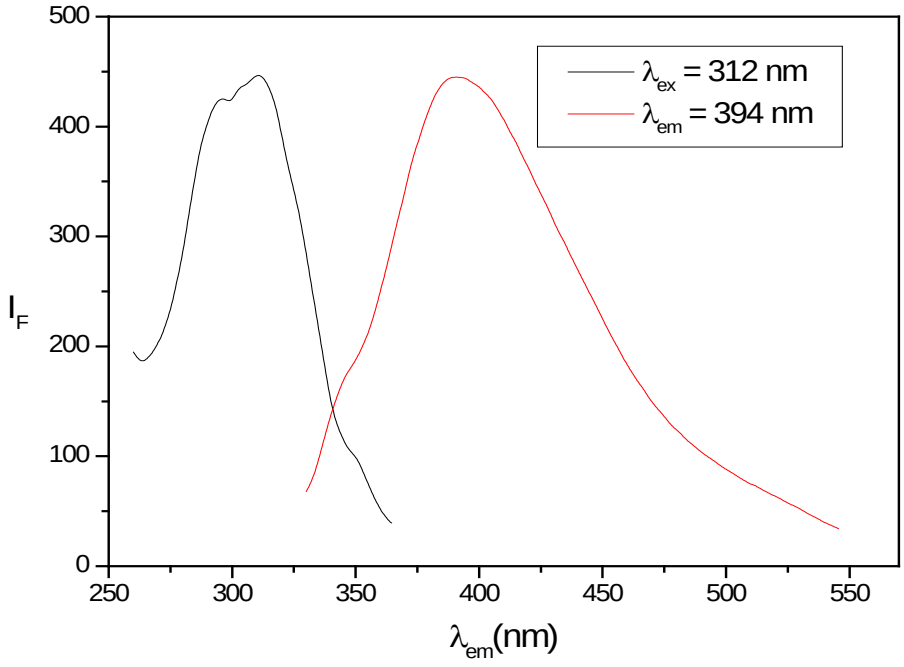



**Figure 29.** Fluorescence emission of compound **27e** in acetonitrile

## 5. Conclusion

In this review, we discussed the synthesis, acylation and photochemical properties of 4-hydroxycoumarin **1**. The aim of this review is to inform the readers of this review of the current interest of the scientific community in the chemical reactivity and photochemical properties of this compound. With regard to photochemical properties, we mentioned in particular the fact that the structure of the molecule positively influences the behaviour of derivatives, particularly with regard to fluorescence emission. It seems likely that this compound will remain a popular building block for synthetic chemists and that in the future, others innovative developments and applications will be discovered.

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