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Synthesis and Investigation of Photophysical Behaviour and Antioxidant Activities of Sulfamic acid Catalyzed dimethyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2,3-dicarboxylate Series

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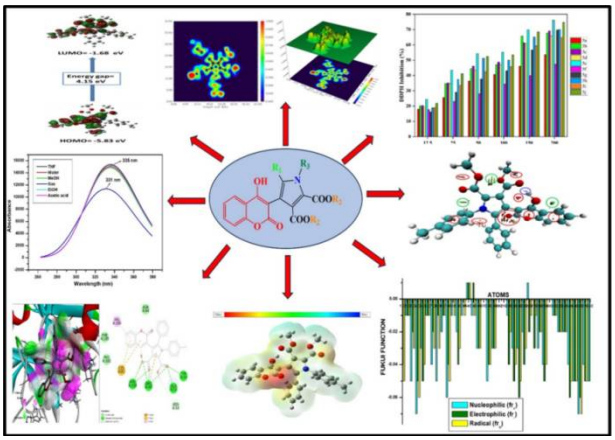
ABSTRACT

This study reports the synthesis of dimethyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2,3-dicarboxylate derivatives. The structural aspects of the newly synthesized compounds were accomplished by several physio-chemical techniques like ^{1}H-NMR, ^{13}C-NMR, and HRMS. The synthesized compound was photo-physically characterized by UV-Vis studies. The spectroscopic characteristics of the synthesized substances were studied using time-dependent density functional theory (TD-DFT). The integral equation formalism polarisable continuum model (IEFPCM) was used to simulate different solvent environments, such as the gas phase, ethanol, tetrahydrofuran (THF), methanol, water, and acetic acid. To validate the computational model, theoretical UV-Visible spectra for each solvent condition were created and compared to experimental spectroscopic data. Antioxidant activity was evaluated at different concentrations. In-silico ADMET predictions were performed, confirming adherence to Lipinski's rule of five.

Graphical abstract:



Keywords: Sulfamic acid, NBO, Docking, Population analysis, ELF, UV-Vis spectra, Biological evaluation and RDG.

INTRODUCTION

Coumarins (2H-1-benzopyran-2-one) are a subclass of lactones chemically [1] *Nikhil et al.*, Other names for coumarin include 1, 2-benzopyrone and o-hydroxycinnamic acid-8-lactone [2]. Natural coumarins are categorized into various structural categories: simple coumarins, furanocoumarins, pyranocoumarins (both linear and angular), dihydrofuranocoumarins, and phenylcoumarins (Figure 1) [3]. In 1820, Vogel discovered coumarin, the primary component of this class, from the tonka bean (*Dipteryx odorata*)[4, 5]. The term "coumarin" comes from the French word "coumarou," which means tonka bean [6, 7].

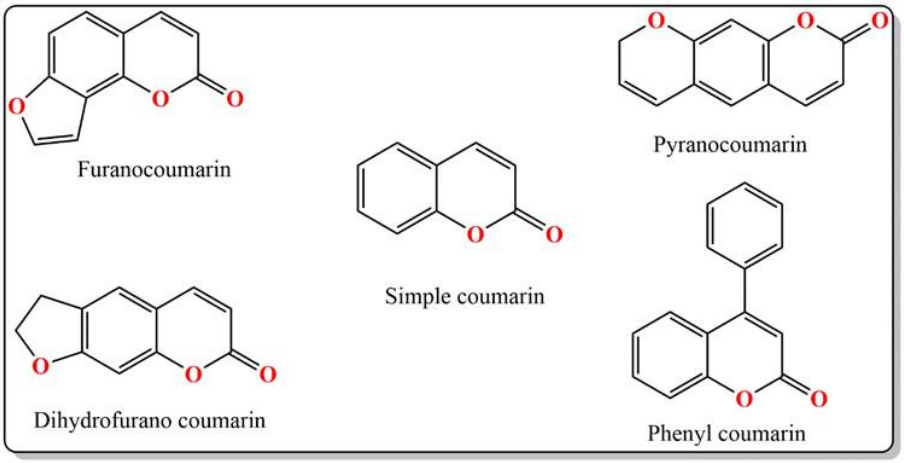


Figure 1. Structure of natural coumarin.

Significant biological effects are displayed by a number of heterocyclic compounds with coumarin rings, including antibacterial, anticoagulant, anticancer [8], antioxidant, anti-inflammatory [9] and HIV protease inhibition [10]. Furthermore, coumarin-based compounds are widely employed as fluorescence sensors [11], insecticides, perfumes, and scents. The anticoagulant and rodenticide properties of the coumarin derivatives warfarin [12], flocoumafen [13], and bromadiolone [14] are known (Figure 2). Additionally, aminocoumarin novobiocin functions as an efficient DNA-binding antibiotic [15] and benzimidazole-coumarin nucleosides [16] have anti-hepatitis C virus properties (Figure 2). Due to the wide range of activities that coumarins and their derivatives have demonstrated, coumarin synthesis and pharmacological research are still ongoing [17].

Coumarin derivatives exhibit a wide range of spectroscopic properties, which are mostly determined by their molecular structure. Many fluorescent coumarin compounds absorb light in the UV spectrum and emit blue light. However, coumarin derivatives with donor-acceptor substituents or extra ring systems are often yellow dyes with green fluorescence emission. The most commonly used commercial coumarin-based fluorescent dyes contain a heterocyclic electron-acceptor moiety at the 3-position and an electron-donating group, such as N,N-diethylamino,at the 7-position of the coumarin scaffold [18].

Recent research has focused on changing the spectral characteristics of coumarin dyes in order to shift their absorption and emission maxima from the ultraviolet to the near-infrared range. This has been accomplished by strategically introducing various electron-accepting groups at the 3- or 4-position, such as cyano groups, dicyanomethine moieties, dicyanomethine vinyl groups, carbonylvinyl units, or heterocyclic systems like benzoxazole, benzothiazole, or benzimidazole. Simultaneously, the 7-position was functionalised with stiff or freely rotating alkylamino substituents [19]. These modifications to the structures enable fine-tuning of the photophysical properties of coumarin-based

fluorophores, hence broadening their potential applications in a variety of domains. These coumarin compounds have several applications, including chemosensor, NLO, biolabeling, and others.

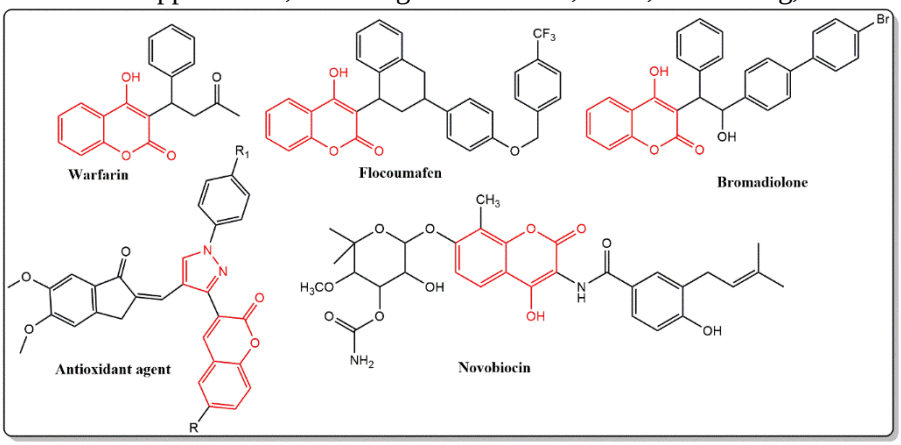


Figure 2. Examples of pharmacologically useful coumarin derivative molecular scaffolds.

The therapeutic and luminous potential of coumarins, both their natural and synthetic analogs, has been assessed for a wide range of disease manifestations, including oxidative stress [**20**], blood coagulation [**21**], cancerous symptoms [**22**], tuberculosis [**23**], inflammations [**24**], AIDS [**25**], Alzheimer's disease [**26**], biolabeling, high quantum yield and large stokes shift [**27**]. In addition, because of their potential uses and presence in numerous natural products, pyrrole-fused coumarins, a promising class of N-heterocycles, have caught the interest of chemists and pharmacologists.

Pyrrole's derivatives can now be created using a variety of synthetic techniques that have been developed. While these techniques have been in use over the past century, they have a number of severe limitations that have led to the desire for alternative methods, including MCRs [**28**], cycloaddition reactions [**29**], and transition-metal-catalyzed cyclization. Some of these novel methods do, however, have important drawbacks, such as arduous preparatory steps, stringent reaction conditions, poor yields, prolonged reaction periods, or the need for an inert atmosphere. Thus, the pursuit of a straightforward, effective pyrrole synthesis process continues to be alluring.

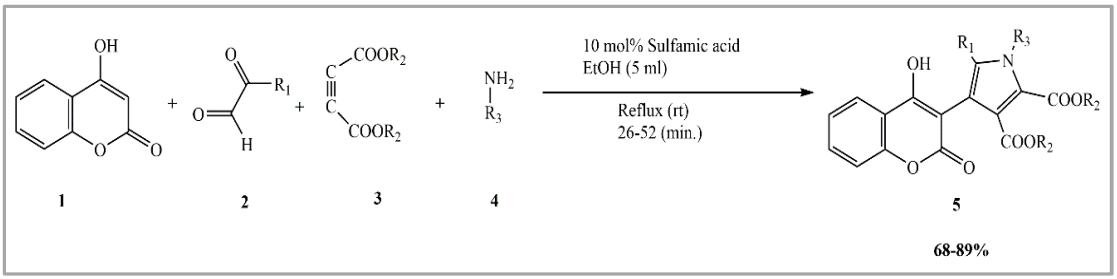
MATERIALS AND METHODS

Chemicals and Reagents: All solvents were purchased from Sigma-Aldrich and utilised without additional purification. 4-Hydroxycoumarin and di-alkyl but-2-ynedioate chemical were purchased from SPECTROCHEM Pvt. Ltd. Mumbai, glyoxal were purchased from TCI Chemicals (India) Co., Ltd, and amine were purchased from Sigma-Aldrich. Ethanol was purchased from Loba Chemie Pvt. Ltd. Mumbai, India. Sulfamic acid GR was purchased from E. MERCK Ltd. Mumbai. 1,1-Diphenyl-2-picrylhydrazyl (DPPH*) was obtained from Hi Media Pvt. Ltd. (Mumbai, India).

Instrumentation and Analytical Methods: Thin-layer chromatography (TLC) was used on precoated silica gel 60 F_{254} plates to evaluate the reaction's development. A Buchi Rotary Evaporator was used to concentrate organic solutions. A UV-Visible spectrophotometer (Systronic, Model No. 118) was used to take quantitative molecule absorption measurements. Melting points were calculated and presented uncorrected. Nuclear Magnetic Resonance (NMR) spectroscopy was carried out using a Bruker Av III HD DRX 300 spectrometer (^{1}H NMR: 300 MHz, ^{13}C NMR: 75 MHz), with DMSO-d_6 as the solvent. Chemical changes (δ) are reported in parts per million (ppm) compared to tetramethylsilane (TMS) as an internal standard. The coupling constants (J) are expressed in hertz (Hz). Signal multiplicities are denoted by the following abbreviations: s (singlet), d (doublet), dd (doublet of doublets), dt (doublet of triplets), t (triplet), and m (multiplet). Compound **5c** was synthesized and used as a reference compound for all in silico studies.

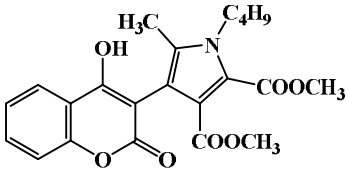
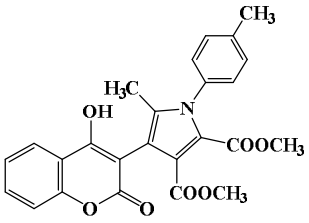
Chemical Synthesis: The reaction involved the condensation of 1,3-dicarbonyl compounds (1), substituted glyoxal monohydrate (2), di-alkyl acetylene dicarboxylate (3), and amines (4) in ethanol, which was catalysed by sulfamic acid (Scheme 1). The reaction mixture was refluxed at room temperature, and the progress was monitored by thin-layer chromatography (TLC) until completion. This procedure proved effective, yield the expected products with high efficiencysummarized in (Table 1). This methodology has various advantages over earlier methods, including enhanced reaction profiles and a greater synthetic scope, while aligning with green chemistry principles.

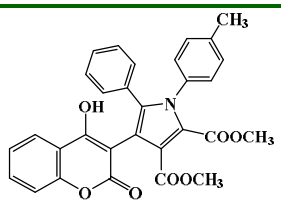
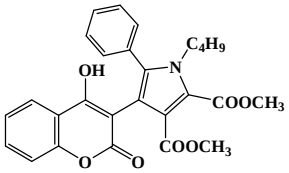
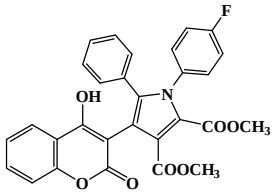
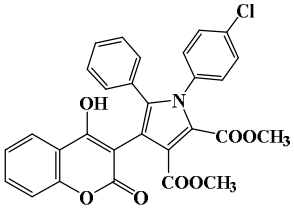
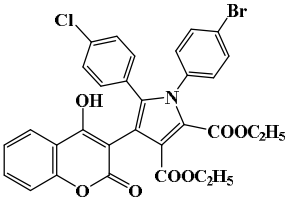
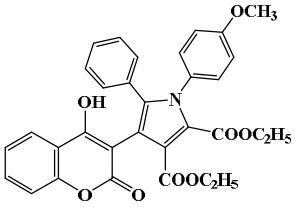
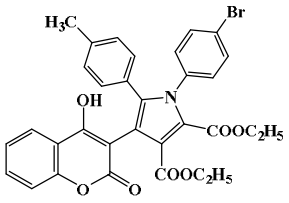
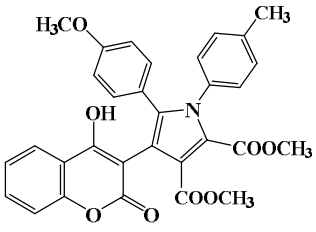
Compared to previously described techniques [30], the sulfamic acid-catalyzed protocol offers considerable advantages that significantly boost synthesis efficiency. The use of sulfamic acid (H_3NSO_3) as a heterogeneous catalyst provides numerous advantages, including a broader substrate scope that includes both electron-rich and electron-deficient compounds, shorter reaction times, and increased operational simplicity at room temperature. The protocol's use of the ecologically friendly EtOH as a solvent, combined with a recyclable reaction media, considerably increases sustainability. The technology ensures consistent yields in large-scale applications, while the catalyst's heterogeneous nature allows for easy separation and recycling across several cycles without activity loss. The mild reaction conditions, low catalyst loading (5-10 mol%), and simple workup procedures all contribute to economic feasibility. These enhancements, together with excellent yields and selectivity, distinguish this technology as a preferable alternative to existing protocols.



Scheme 1. Synthesis of dimethyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2,3-dicarboxylate from 4-hydroxycoumarin.

Table 1. Sulfamic acid catalyzed synthesis of dimethyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2,3-dicarboxylate scaffolds.

Entry	Product	Nomenclature	Time (min.)	Yield (%)
5a		Dimethyl 1-butyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-methyl-1H-pyrrole-2,3-dicarboxylate	48	68
5b		dimethyl 4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-methyl-1-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate	36	77

5c		dimethyl 4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-phenyl-1-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate	52	84
5d		Dimethyl 1-butyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-phenyl-1H-pyrrole-2,3-dicarboxylate	26	78
5e		Dimethyl 1-(4-fluoro phenyl)-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-phenyl-1H-pyrrole-2,3-dicarboxylate	32	80
5f		dimethyl 1-(4-chloro phenyl)-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-phenyl-1H-pyrrole-2,3-dicarboxylate	45	76
5g		diethyl 1-(4-bromo phenyl)-5-(4-chlorophenyl)-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2,3-dicarboxylate	35	83
5h		diethyl 4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1-(4-methoxyphenyl)-5-phenyl-1H-pyrrole-2,3-dicarboxylate	39	81
5i		diethyl 1-(4-bromo phenyl)-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate	42	**89**
5j		dimethyl 4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-(4-methoxyphenyl)-1-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate	47	85

In the optimization of pyrrole coumarin synthesis we assessed variables like time and solvent to determine the ideal reaction conditions. The target product was initially created using a range of solvents, including water, THF, Ethanol (EtOH), acetic acid, methanol, and N, N-dimethylformamide (DMF). With the exception of acetic acid, all reactions produced moderate to outstanding yields of the intended product in (Table 2). However, the reaction proceeded particularly well when EtOH was used as a solvent at reflux temperature, yielding the desired product with 89% yield in 42 min. As a result, EtOH was selected as the solvent for every subsequent process.

Table 2. Optimization of reaction conditions for the synthesis of compound

Entry	Solvent	Time (min.)	Yield (%)
1	CH_3COOH	42	38
2	EtOH	42	89
3	MeOH	42	78
4	H_2O	42	54
5	DMF	42	49
6	THF	42	69

Reaction condition: **1**(3.08 mmol), **2** (3.08 mmol), **3** (3.08 mmol), and **4** (3.08 mmol) in presence of sulfamic acid (10 mol%) catalyst in 5 ml of ethanol at room temperature.

A systematic solvent screening was conducted to optimize the reaction conditions. Ethanol (EtOH) emerged as the most effective solvent, and it was used without additional purification. Tetrahydrofuran (THF) and methanol (MeOH) also showed promising results, giving 49% and 52% of the target product, respectively. The impact of catalyst loading on product yield was also investigated (Table 3). At 5 mol% catalyst concentration, the isolated yield was just 20%. Incremental improvements were found with catalyst loadings of 10 mol%. Using 10 mol% of the catalyst in ethanol produced optimal results, with an isolated product yield of 89%. Further increases in catalyst concentration beyond this point did not result in substantial yield improvements. These findings emphasise the importance of both solvent selection and catalyst concentration in optimising reaction efficiency. The use of ethanol as a solvent is consistent with green chemistry principles, and determining an optimal catalyst loading allows for effective resource utilisation without sacrificing yield.

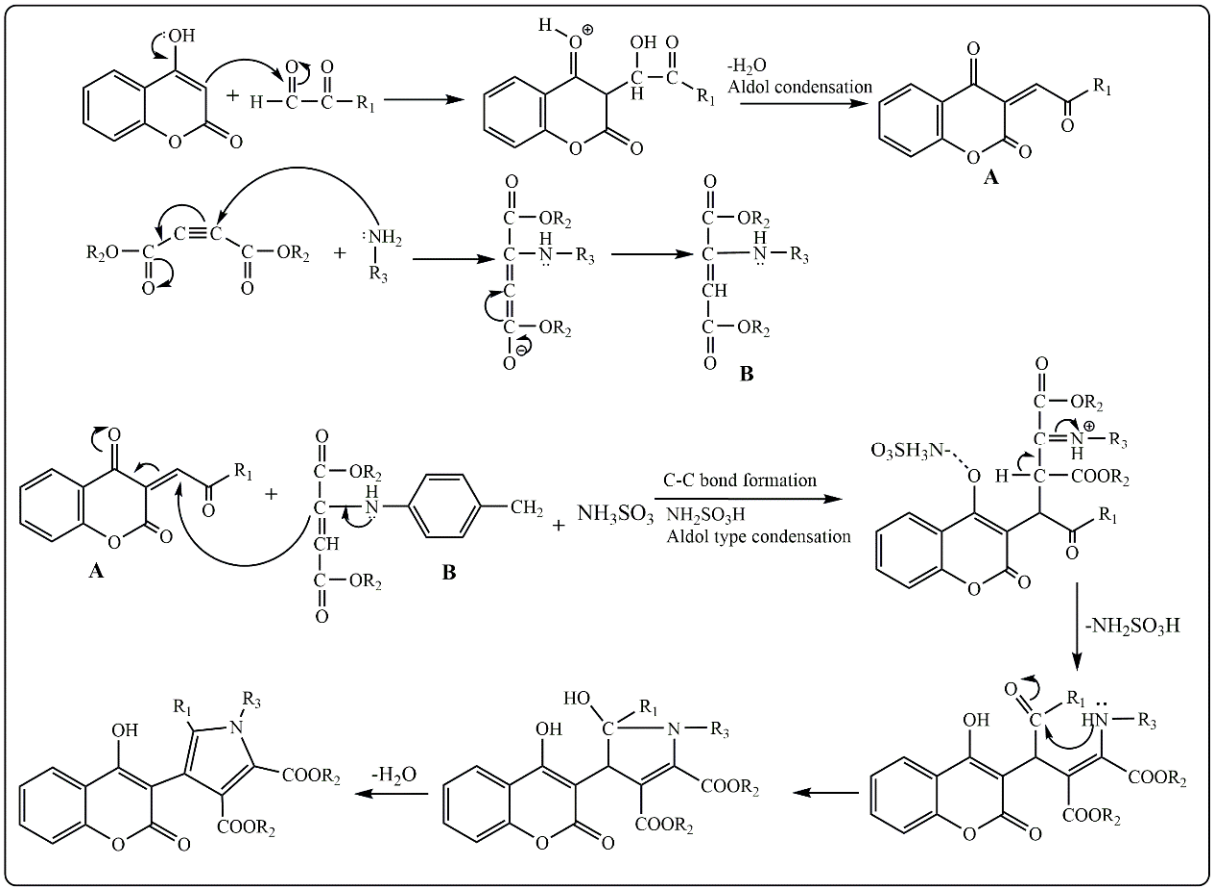
Table 3. Investigation of the amounts of catalyst and solvent effects on the model reaction[a]

Entry	Catalyst loading (mol%)	solvent	Yield (%)[b]
1	10	THF	49
2	5	H_2O	20
3	10	DMF	28
4	10	MeOH	52
5	**10**	**EtOH**	**89**
6	5	EtOH	73
7	20	Neat	Nil

[a]Reaction condition: **1**(3 mmol), **2** (3 mmol), **3** (3 mmol), and **4** (3 mmol) in presence of sulfamic acid (10 mol%) in 5 mL of ethanol as solvent at room temperature. [b]Isolated yield.

Typical Procedure for Synthesis of Compounds (5a-5j): In an oven-dried round bottom flask, a mixture of 1,3-dicarbonyl (**1**; 3.08 mmol), substituted glyoxal monohydrate (**2**; 3.08 mmol), di-alkyl but-2-ynedioate (**3**; 3.08 mmol), and amine (**4**; 3.08 mmol) was added sequentially in the presence of sulfamic acid (10 mol%) catalyst illustrated in (Scheme 2). The mixture was stirred in ethanol (5 ml) and reflux at room temperature (rt) for 26-52 min. The progress of the reaction was monitored by TLC. After the completion of product, the reaction mixture was cooled at room temperature. The crystalline product was isolated by filtration to give the product, and the crude crystal thus obtained was recrystallized from EtOH to give pure product illustrated in (Scheme 2). The model procedure

yielded 89% when completed with 10 mol% sulfamic acid as the catalyst and ethanol as the solvent over 42 min. reaction time. The product was investigated by its antioxidant, photophysical, spectral (^{1}H NMR, ^{13}C NMR and HRMS), *in-silico* studies and kinetic analysis. All the compounds are known and only compound **5c** and **5g** were characterized for comparison of their spectral data with those reported in the literature [**30**].



Scheme 2. Proposed mechanism for the formation of compound (5a-5j).

RESULTS AND DISCUSSION

NMR Analysis

Dimethyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-5-phenyl-1-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate(5c)[**30**]: Yield: 84%; mp.: 143-144 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.29 (s, 1H, OH), 7.82 (d, J = 7.6 Hz, 1H, ArH), 7.52 (t, J = 7.6 Hz, 1H, ArH), 7.39-7.24 (m, 2H, ArH), 7.14-6.89 (m, 9H, ArH), 3.92 (s, 3H, CH_3O), 3.84 (s, 3H, CH_3O), 2.43 (s, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, DMSO-d_6): δ 166.17, 163.11,161.83, 152.44, 138.92, 136.97, 133.07, 127.51, 125.43, 117.49, 114.38, 111.79, 51.56, 21.32 ppm; HRMS m/z calculated for [$C_{30}H_{23}NO_7$]: 509.5141; found: 509.5130; Anal. Calcd. for $C_{30}H_{23}NO_7$: C 70.73, H 4.55, N 2.94; Found: C 69.74, H 3.81, N 2.68.

Diethyl-1-(4-bromophenyl)-5-(4-chlorophenyl)-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2,3-dicarboxylate(5g)[30]; Yield: 83%; mp.:>140 °C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 12.26 (s, 1H, OH), 7.97 (d, J = 7.6 Hz, 1H, ArH), 7.83 (t, J = 7.6 Hz, 1H, ArH), 7.67-7.63 (m, 2H, ArH), 4.28 (s, 3H, C_2H_5O), 4.26 (s, 3H, C_2H_5O) ppm; 13C NMR (75 MHz, DMSO-d6): 161.62, 151.15, 136.64, 121.36, 129.34, 123.54, 103.81, 60.88, 14.20 ppm; HRMS m/z calculated for [$C_{31}H_{23}BrClNO_7$]: 636.8791; found: 636.8783; Anal. Calcd. for $C_{31}H_{23}BrClNO_7$: C 58.47, H 3.65, Br 12.56, Cl 5.58, N 2.21; Found: C 58.36, H 3.57, Br 12.43, Cl 5.41, N 2.14.

Photophysical Evaluation: The absorption spectra of 5a and its derivatives (5b to 5j) in EtOH as a solvent were shown in (Figure S2; see the Supporting Information). Compound and its derivatives are employed at room temperature (293 K). Spectroscopic assessment of the compounds displayed an interaction between absorbance values and aromatic ring substituents. The absorption spectra (Figure S2) showed two different bands. A shorter wavelength band (260-305 nm) was detected, attributed mostly to the aromatic/heteroaromatic ring systems' π-π* transitions. Additionally, a longer wavelength band (320-360 nm) was also found, which presumably corresponds to n-π* transitions, indicating charge transfer from donor to acceptor moieties [**31**]. The values of extinction coefficients, transmittance, absorption coefficient and band gap were estimated from absorption data and given in the (Table S1; see the Supporting Information). The bandgap value (eV) of titled compound in ethanol solvent was taken for comparison with the TD-B3LYP method and 6-31G basis set in different solvents.

UV-Vis spectrophotometry was used at room temperature to further examine optical properties, including transmittance percentage (T%) and extinction coefficient. The generated spectra have two main interpretations. The first region, defined by high photon energies (250-450 nm), includes the absorption edges and has a decreased transmittance (Figure S3, Supporting Information). The second zone, located in the visible spectrum (350-700 nm), is highly transparent, with transmittance values ranging from 84-98% to 79-98%, depending on the compound. The spectra of pyrrole-coumarin derivative (5g) were recorded in four different concentrations (0.25 mL, 0.5 mL, 0.75 mL, 1 mL) in the range of 250-640 nm to study the concentration effect on electronic spectra of compound (5g). The spectra of compound 5g recorded in different concentrations are given in (Figure S4; see the Supporting Information). The spectral result displayed that the pyrrole-coumarin derivative 5g exhibit a characteristic absorption band in the range of 308-357 nm, which is probably due to π-π* and/or n-π* transition. It is evident that as the concentration of the solution increases, the intensity of the absorption band also increases and exhibits a red-shift, which means that the absorption peaks are shifting towards longer wavelengths (or lower energies).

To analyze the UV-Vis spectra of the target titled compound, TD-DFT has been employed along with the appropriate solvent model integral equation formalismpolarizable continuum model (IEFPCM) and a specified basis set B3LYP/6-31G. The calculated UV-Visible spectra of titled compound were analyzed in the gas as well as in the solvent phase, specifically THF, H_2O, MeOH, EtOH and Acetic acid, as presented in (Table S6; see the Supporting Information). The combined graph of these spectra across different environments was illustrated in (Figure S5; see the Supporting Information). The maximum wavelength absorption was observed to be 331 nm in the gas phase and approximately 335 nm in all the corresponding solvents, whereas it was experimentally recorded as 276 nm in ethanol solvent, mentioned above and shown in (Figure S5). These findings indicate that the solvent has minimal impact on the spectral properties of **5c**, as the wavelength absorption values are nearly identical across different conditions.

Arrhenius plot and calculation of energy of activation (E_a): The lowest kinetic energy required by reactants to generate products is known as the activation energy. As a result, procedures with low activation energy are faster, whereas processes with high activation energy are slower. The rate at which a certain reaction will proceed is determined by the energy of activation (E_a) of that process. When the value of E_a is high, the chemical reaction will proceed at a slower rate. Kinetic studies have been performed to study the effect of temperature in the synthesis of dimethyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2,3-dicarboxylatederivatives,andenergy of activation (E_a) is calculated with the help of Arrhenius equation.

$$ln\,k = ln\,A - \left(\frac{E_a}{R}\right)\left(\frac{1}{T}\right)$$

Where: k is rate constant (min^{-1}); A is the pre-exponential component; E_a is activation energy (cal mol^{-1}); R is the gas constant (1.987 cal mol^{-1} K^{-1}) and T is the temperature measured in (K).

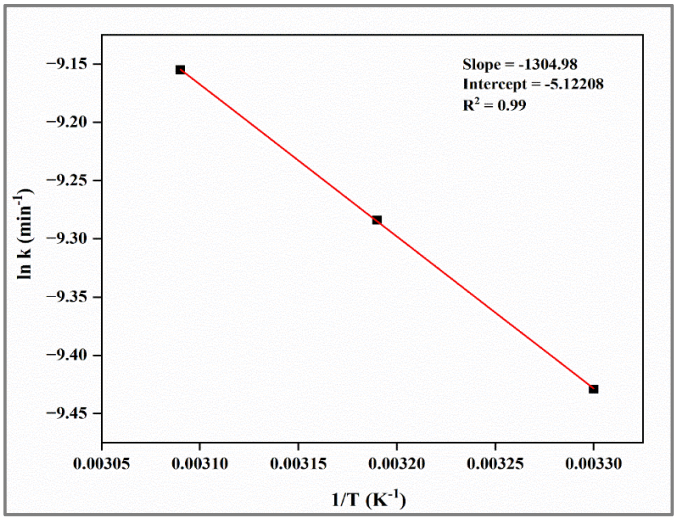


Figure 4. Arrhenius plot of titled derivative.

Table 4. Rate constant at different temperature

T (K)	1/T (K^{-1})	k (min^{-1})	ln k
303	0.00330	0.0000803	-9.429
313	0.00319	0.0000929	-9.284
323	0.00309	0.0001057	-9.155

Different rate constants (k) were calculated at different temperatures (K) and a plot was made between ln k and (1/T), where a straight line is attained. The Slope of straight line gives the value of energy of activation (E_a) and found as 6.01 kcal mol^{-1} represented in (Table 4) and (Figure 4).

APPLICATION

Drug likeness/Analysis of pharmacokinetic properties: In drug development, ligand structural features are crucial in steering the process towards effective and efficient outcomes, a concept known as drug-likeness[32]. The analysis of major ADME (Absorption, Distribution, Metabolism, and Excretion) parameters for the molecule and its derivatives resulted in significant insights (Table S7, Supporting Information). The factors studied included the quantity of hydrogen bond donors (HBD) and acceptors (HBA), molar refractivity (MR), topological polar surface area (TPSA), blood-brain barrier penetration (BBB), log kp, and bioavailability ratings. The findings show that all derivatives in this study have HBD and HBA values ranging from 1 to 8, which is consistent with the established endorsement of less than 10 for both parameters. The highest TPSA value observed among all derivatives is 117.20 $Å^2$, which is within the allowed range for drug-like substances.

Similarly, the molar refractivity must have a value between 111.14and 159.59. The (Table S7) shows that skin permeability (log K_p) falls within -6.50 to -5.17, GI absorption was on the low side, BBB penetration was achievable for all derivatives, and bioavailability values measured were equal to 0.55 for most of the derivatives. The analogy presented in the (Table S7, Supporting Information) illustrates how compound possess sufficient biological characteristics.

Biological Evaluation

In-vitro Antioxidant Activity*:* 1,1-Diphenyl-2-picrylhydrazyl (DPPH) Radical Scavenging Assay

The antioxidant capacity of compounds (5a-5j) was assessed using a DPPH radical scavenging test. This approach determines the ability of compounds to quench the stable free radical DPPH in methanolic solution. The assay was carried out at various doses of the test substances to determine

their dose-dependent effects. The majority of the investigated compounds have considerable DPPH radical scavenging activity. The presence of hydroxyl (-OH) groups in their molecular structures may explain their high antioxidant capacity. These groups can donate hydrogen atoms to the DPPH radical in a stoichiometric way, resulting in the reduced and stable DPPH-H molecule [**33**].

DPPH* was used as a radical scavenger and had an odd electron, due to which it gives maximum absorption at 517 nm, and the procedure follows the decrease in absorption and shows the antioxidant activity of that compound.

The formula used for the calculation is: -

$$\% \text{ Inhibition of DPPH* activity} = \frac{A_C - A_S}{A_C} \times 100$$

Where: A_c represents the absorbance of the control sample and A_s denotes the absorbance of the tested sample.

The antioxidant activity of dimethyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2, 3-dicarboxylate derivatives (5a-j) was determined using the DPPH radical-scavenging test. This approach relied on previously established methods*Blois et al.*, [**34**] and *Joyeux et al.*, [**35**]. Stock solutions of the test substances were produced in methanol at a concentration of 0.1 mg mL^{-1}. Similarly, a DPPH stock solution was produced in methanol at a concentration of 0.02 mg mL^{-1}. Different concentrations such as 2 mL, 1.5 mL, 1 mL, 0.5 mL, 0.25 mL, 0.125 mL of compounds were taken out in the test tube separately and made up the volume up to 2 mL by adding methanol respectively. Now add 2 mL DPPH* solution in each test tube and make the volume up to 4 mL and kept the solutions for 30 minutes in dark at rt for incubation. After the incubation, the absorbance of all the samples were recorded at λ = 517 nm by UV-spectrophotometer. By either hydrogen or electron donation, antioxidant compounds scavenge DPPH radicals. The DPPH radical scavenging activity is identified by a colour change from purple to yellow, which is measured by a decline in absorbance at 517 nm. The synthesized compounds exhibited a variety of antioxidant properties, from moderate to high, with radical scavenging percentages ranging from 47.38% to 76.08% (Figure.S9; see the Supporting Information). The data in (Table S8; see the Supporting Information) show that the type of the substituents on the aromatic ring has a considerable influence on antioxidant activity. Electron-withdrawing and electron-donating groups appear to play critical roles in modifying the compound's ability to neutralise free radicals *Kadhum et al.*, [**36**]. This finding is consistent with earlier research on structure-activity relationships in antioxidant chemicals.

CONCLUSION

To summarise, we successfully synthesised a series of dimethyl-4-(4-hydroxy-2-oxo-2H-chromen-3-yl)-1H-pyrrole-2,3-dicarboxylate derivatives employing an efficient and ecologically friendly synthetic approach. This one-pot multi-component reaction included 4-hydroxycoumarin **(1)**, substituted glyoxal monohydrate **(2)**, di-alkyl acetylene dicarboxylate **(3)**, and substituted amines **(4)**, with sulfamic acid serving as an environmentally benign solid acid-catalyst in aqueous ethanol. The protocol has several advantages, including the use of commercially available and cost-effective starting materials, metal-free synthesis, good to excellent yields, short reaction times, energy efficiency, reusability of reaction media, and the elimination of column chromatography for product separation. The green metrics research proved the process's environmental sustainability. Antioxidant activity was found to be moderate to good, indicating that these compounds have promise for further development as antioxidants. Photophysical investigations on the target molecule and its derivatives revealed consistent absorbance across diverse solvent conditions, indicating stable optical characteristics. Temperature variation experiments were used to calculate activation energy (6.01 kcal mol^{-1}) and drug-likeness assessments were carried out. These findings lay the groundwork for future

research into these coumarin-pyrrole compounds and their prospective applications in antioxidant and medicinal research.

Conflict of Interest: Author declares no conflict of interest.

Supplementary Information: Photophysical data of compound (5a-5j); Absorption spectra of compound (5a-5j); Transmittance Spectra of compound (5a-5j); UV-Visible absorption spectra of compound 5g showing different concentration; Combined UV-Visible plot of compound **5c** in gas and solvent phase; The experimental and calculated spectral (TD-B3LYP/6–311G) data for **5c** in various solvents; ADME properties of compound and its derivatives; DPPH* scavenging activities of compound 5a and its derivatives (5b-5j); DPPH* scavenging antioxidant activities of compound (5a-5j) at different concentration.

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