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STUDY ON THE SYNTHESIS AND CHARACTERIZATION OF HETEROCYCLIC COMPOUNDS CONTAINING 4 - HYROXY COUMARIN

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ABSTRACT
This paper presents the synthesis of a series of heterocyclic azo dyes containing 4-hydroxy coumarin via diazo-coupling reaction. Various physico-chemical techniques, including UV-Visible, FT-IR, NMR, and mass spectrometry, were used to characterize the newly synthesized compounds. Computational calculations and geometrical optimization of the azo dyes were performed using Gaussian software with the DFT/B3LYP method and 6-31G(d,p) basis set at gaseous phase. Additionally, quantum chemical parameters were evaluated to understand the structural activity relationship of the dyes.The in silico molecular docking results indicated effective binding properties of the compounds against RpsA target receptor.
Keywords: Receptor, physico-chemical, FT-IR.

1. INTRODUCTION

The derivatives of coumarin are known to possess numerous pharmacological properties and have a wide range of biochemical and therapeutic applications. Among them, 4-hydroxy coumarin has been extensively studied for its various biological activities such as anticoagulant, insecticidal, anthelminthic, hypnotic, antifungal, phytoalexin, and HIV protease inhibition activities, which has generated considerable interest in this class of compounds among researchers worldwide.
Recent advances in the synthesis of heterocyclic compounds containing azo chromophore have made them more attractive due to their unique properties based on effective conjugation and substituent's electronic effect. Coumarin, with its excellent physical, thermal, optical, and biological properties, can be utilized as dyes for coloring fabrics, fluorophores, and optical brightening agents. Incorporating an azo group in the mesogenic core of coumarin has increased the dipole moments and stability of coumarin azo-ester series as compared to coumarin esters. A molecule with an azo linkage exhibits reversible isomerization transformations upon irradiation with ultraviolet and visible light. The presence of extended conjugation and electron-releasing substituents on the diazo group enhances the electron density of the molecule, resulting in intense optical absorption and related optical properties. The azo benzene derivatives have found numerous applications in liquid crystal studies due to their rod-like shape, photosensitive ability, and photo-induced alignment with reversible cis-trans transformation, dimerization in cross-linking material, and irreversible photo degradation. Azo dyes containing coumarin nucleus possess potential biological, optical, and electrochemical properties and have therefore been extensively studied by many researchers.

Based on the extensive findings on coumarin analogues, this study reports the synthesis of coumarin-based azo dyes and their structural characterization. Quantum chemical techniques were employed to optimize the molecular geometry of the newly synthesized compounds, and biological activities were also carried out to assess their inhibitory effect against organisms.

2. OBJECTIVES OF THE STUDY

The objectives of the study are as follows:

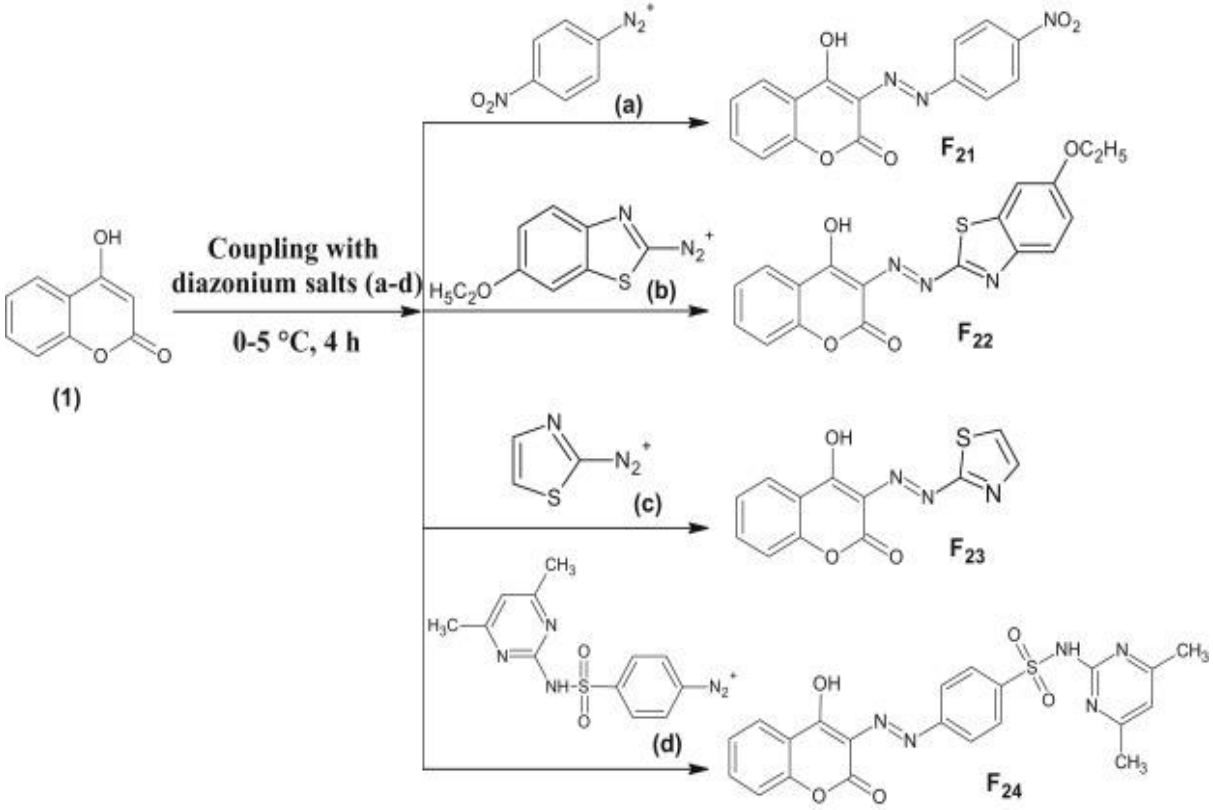
1. To investigate the binding properties of newly synthesized heterocyclic azo dyes containing 4-hydroxy coumarin against RpsA target receptor.
2. To evaluate the inhibitory activity of newly synthesized heterocyclic azo dyes containing 4-hydroxy.

3. EXPERIMENTAL METHODOLOGY

The research utilized analytical grade chemicals and reagents bought from Chemical Company. The compounds' melting points were recorded without corrections using an electrothermal apparatus. Electronic absorption spectra, meanwhile, were obtained from UV-1800 Shimadzu spectrophotometer with a 10^-6 M solution of DMSO, DMF, THF, and DCM in the range of 200-800 nm. KBr pellets were used to obtain FT-IR spectra through Perkin Elmer-RX-FTIR spectrophotometer. Bruker spectrometer 400 MHz and 100 MHz was used for 1H and 13C-NMR spectra, respectively, with tetramethylsilane as a reference. Meanwhile, LC-MS 2010, Shimadzu mass spectrometer was utilized for mass spectra. For computational studies, the researchers used the DFT/B3LYP method with Gaussian 09W software, while Density functional theory was analyzed at the same basis set level. To synthesize coumarin-based azo dyes (F21-F24), the researchers used a general procedure involving hydrochloric acid, sodium nitrite in sulphuric acid, and aqueous KOH solution. F21 was a yellow solid with a melting point of 182-184 °C and a yield of 80%. Meanwhile, F22 was a reddish-colored solid with a yield of 75% and a melting point of 224-226°C. The research characterized the synthesized compounds using different techniques, including FT-IR, 1H and 13C-NMR spectra, and mass spectra.

4. RESULTS AND DISCUSSIONS

The aim of this investigation is to examine the structural and biological characteristics of newly synthesized coumarin-based azo dyes. The conventional diazo-coupling reaction method was employed to synthesize these dyes, which include the 4-hydroxy coumarin nucleus. Scheme 1 illustrates the reaction pathway used to obtain the desired compounds.



Scheme 1 Synthetic route adopted for the preparation of coumarin based azo dyes (F_{21}–F_{24}).

Table 1The comparative analysis of experimental and calculated vibrational frequencies for the coumarin based azo dyes (F_{21}–F_{24}).

Compounds	Assignments	FT-IR absorption frequencies (cm−1)	
		Experimental	Theoretical
F21	υOH	3421	3686
	υAr-CH	3072	3185
	υC=O	1660	1672
	υN=N	1461	1458
	υC-N	1421	1409
F22	υOH	3449	3569
	υAr-CH	3055	3047
	υC=O	1663	1821
	υN=N	1491	1515
	υC-N	1447	1496

F23	υOH	3442	3642
	υAr-CH	2925	3154
	υC=O	1728	1814
	υN=N	1512	1531
	υC-N	1488	1473
F24	υOH	3420	3598
	υNH	3073	3229
	υAr-CH	2928	3052
	υC=O	1724	1672
	υN=N	1515	1502
	υC-N	1444	1458

KBr pellets were used to record FTIR spectra of synthesized compounds F21-F24 in the 4000-400 cm^{-1} region, with important IR bands displayed in Table 1. The absorption frequencies of the compounds were compared with theoretical values obtained using the DFT/B3LYP method and 6-31G(d,p) bases set at gaseous state, also summarized in Table 1. A medium intensity broad peak in the 3449-3420 cm^{-1} region was attributed to the O–H group attached to the coumarin ring, with a corresponding theoretical value of 3686-3569 cm^{-1}. An absorption band at 3073 cm−1 was attributed to the N–H functionality of the sulfamethazine moiety in compound F24, with a corresponding theoretical N–H stretching value of 3229 cm^{-1}. Aromatic C–H stretching vibrations for all compounds were observed in the 3100-2925 cm^{-1} region, with their respective theoretical values observed at 3185-3052 cm^{-1}. Medium intensity carbonyl (C=O) and –N=N- functionalities were observed in the 1728-1660 cm^{-1} and 1515-1461 cm^{-1} regions, respectively, with corresponding theoretical values in the 1821-1672 cm^{-1} and 1531-1458 cm^{-1} regions, respectively. Lastly, a low intensity absorption band in the 1488-1421 cm^{-1} region was attributed to the C–N stretching vibrations in all dyes, with corresponding theoretical values in the 1496-1409 cm^{-1} region.

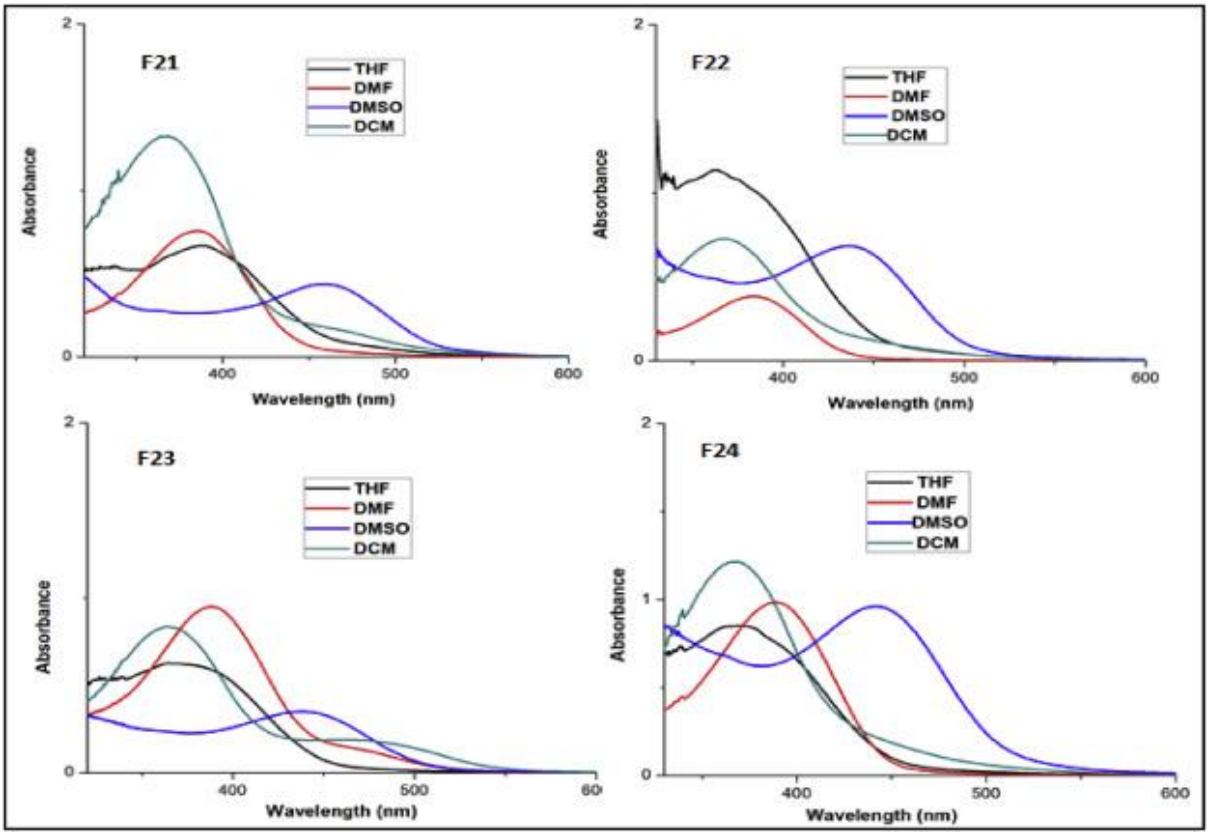


Fig 1 The electronoic spectra of the compounds (F_{21}–F_{24}) in various solvents recorded at room temperature at 10^{-6} M concentration.

The study investigated the impact of solvent polarity and electronic substitution on four compounds (F21–F24) in different solvents (DMSO, DMF, THF, and DCM) at a concentration of 10^{-6} M and ambient temperature. Figure 1 displayed the typical absorption spectra, while Table 2 summarized the absorption maxima (λmax) and logarithmic molar extinction coefficient for all the compounds in the studied solvents.

The electronic spectra of the synthesized compounds exhibited broad peaks in the 461–436, 389–382, 389–362, and 365–369 nm range in DMSO, DMF, THF, and DCM solvents, respectively, due to π→π∗ or n→π∗ transitions. Analysis of the spectral data (Table 2) revealed a bathochromic shift in all compounds as the polarity of the solvent increased, with the absorption maxima shifting towards longer wavelengths. This shift could be attributed to the effective interaction between the solvent molecules and the diazo component's lone pair of electrons. Furthermore, the presence of electron-releasing substituents on the aromatic ring bearing the azo group also contributed to the bathochromic shift. In conclusion, the study underscores the significant role of solvent polarity and electronic substitution in the shift of λmax for all the studied azo dyes.

Table 2 The electronic spectral data of the compounds (F_{21}–F_{24}) obtained indifferent solvents.

Compounds	λmax(nm)				Logε			
	DMSO	DMF	THF	DCM	DMSO	DMF	THF	DCM
F21	436	382	362	369	5.84	5.57	6.05	5.87
F22	461	386	389	366	5.64	5.88	5.81	6.12
F23	443	389	371	367	5.98	5.99	5.93	6.09
F24	441	388	376	365	5.53	5.99	5.8	5.93

5. CONCLUSION

This study has successfully synthesized a series of heterocyclic azo dyes containing 4-hydroxy coumarin and characterized them using various physico-chemical techniques. The study has also employed computational calculations to optimize the molecular geometry of the synthesized compounds and evaluate their quantum chemical parameters. Furthermore, the pharmacological efficacy of the synthesized compounds has been investigated by antimicrobial, antitubercular, DNA cleavage, and in silico molecular docking studies. The results indicate that the synthesized compounds exhibit significant inhibitory activity against tested microbes, with effective binding properties against the RpsA target receptor. This study's findings demonstrate the potential applications of coumarin-based azo dyes in various fields, including dyeing, fluorescence, and optical brightening agents, and provide insights for future studies in this area.

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