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Synthesis Characterization and Biological evaluation of Schiff base Containing Coumarine Moiety

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Abstracts: Schiff bases are versatile organic compounds commonly synthesized through the condensation reaction between a primary amine and an aldehyde or ketone. In the present work first coumarine was syntheses then the alkylation takes place and the Schiff base was synthesized. The physical measurement and structural elucidation by spectrum like FT-IR and 1H-NMR, used in this work.

Keywords: Coumarine, aromatic aldehyde, Ethyl acetoacetate.

Introduction:

Schiff bases containing coumarin represent a fascinating class of organic compounds with diverse applications in medicinal chemistry, materials science, and other fields. Coumarin, characterized by its unique aromatic structure fused with a lactone moiety, is widely known for its various biological activities, including antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. Schiff bases incorporating coumarin moieties have attracted significant attention due to their enhanced pharmacological properties and structural versatility. The synthesis of Schiff bases containing coumarin typically involves the condensation reaction between a coumarin-derived aldehyde or ketone and a primary amine. This reaction yields a Schiff base with a coumarin scaffold, offering a platform for the design and development of compounds with tailored properties for specific applications.The incorporation of the coumarin moiety into Schiff bases imparts several advantages. Firstly, coumarin derivatives are known to exhibit fluorescence properties, making Schiff bases containing coumarin useful probes for fluorescence-based detection methods in biological and chemical sensing applications. Additionally, the presence of the coumarin scaffold can modulate the physicochemical properties and biological activities of Schiff bases, potentially enhancing their efficacy as therapeutic agents.

In medicinal chemistry, Schiff bases containing coumarin have shown promise as multifunctional agents with diverse biological activities. For instance, they have been explored as potential anticancer agents due to their ability to inhibit tumor cell proliferation and induce apoptosis. Moreover, their antioxidant and anti-inflammatory properties make them attractive candidates for the treatment of various diseases associated with oxidative stress and inflammation.

Overall, Schiff bases containing coumarin represent a versatile class of compounds with promising applications in various fields. Their unique combination of structural features, fluorescence properties, and biological activities makes them valuable tools for research and potential candidates for the development of novel therapeutics, diagnostic tools, and functional materials. Continued exploration of their chemical properties and biological functions is likely to uncover new opportunities for innovation and application in diverse areas of science and technology.Their structural versatility and potential therapeutic benefits continue to drive interest in exploring their biological activities and therapeutic potential.

EXPERIMENTAL

Solvents were employed as commercial anhydrous grade. The column chromatography was done over the silica gel (100-120 mesh). Melting points were determined in open capillary tube and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker advance II-400 MHz spectrometer. The molar conductivity measurements of complexes in (1 × 10−3 M) DMSO solution were measured at 25 ^{0}C with a Bibby conduct meter.

Material and Methods:

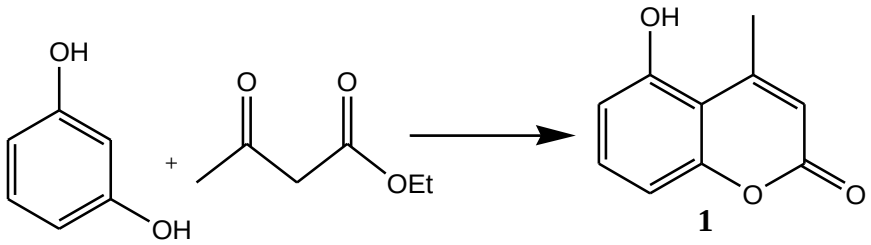
All solvents were labouring as commercial anhydrous mark without further Refining. The column chromatography was carried out over silica gel (100120esh). Melting points determined by open capillary tube. ^{1}H NMR spectra were recorded on a Bruker 400 MHz spectrometer in DCl3 solvent TMS as internal standard. The crude product was recrystallizing from 80 percentage ethanol.

Present Work:

In the present work, the aromatic substituted Schiff bases were synthesized by condensing substituted amine containing coumarine moiety.

Step I: General Procedure for the synthesis of Schiff base:

The resorcinol (0.01 mole) and ethyl acetoacetate (0.01 mole) in round bottom flask containing 15ml ethanol and 3 ml of conc. Sulphuric acid was reflux for 1.5 hour a solid were obtain which is further cool and recrystallize from ethanol.



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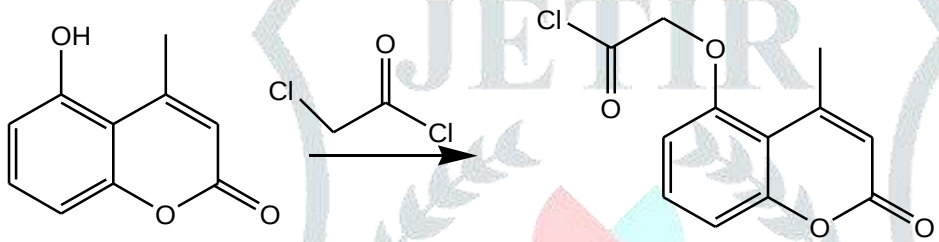
Scheme I

Step II :

The mixture of Coumarine (0.01 mole) and Chloroacethyl chloride (0.01 mole) in round bottom flask containing 10 ml potassium carbonate was stirred at room temperature for 1.5 hour. After completion of reaction (by TLC) the mixture was poured on ice cold water and dried at room temperature.



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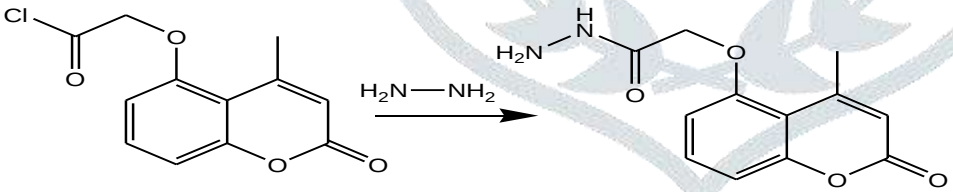
Scheme II

Step III:

The compound 2 was heated with hydrazine hydrate in ethanol on a water bath for 1 hour to obtain 2-[4-Methyl-2-oxo-2H-Croman-7-yl)oxy] acetohydrazide compound 3.



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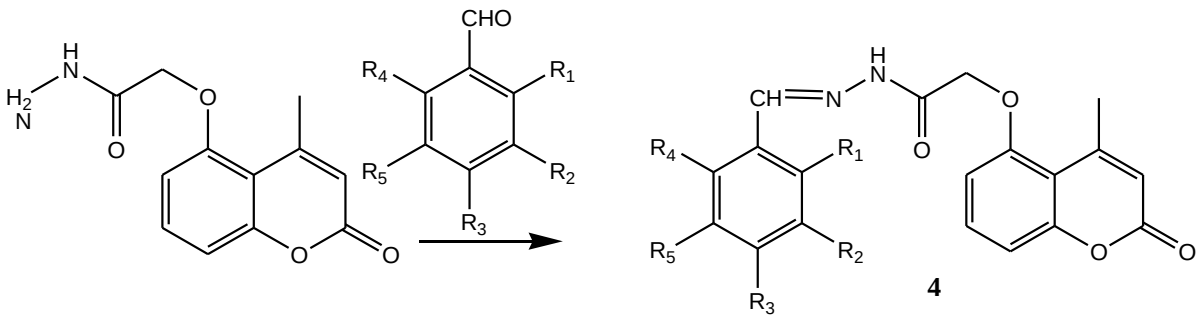
Scheme III

Step IV:

A mixture of alcohol (20 ml) and aromatic aldehyde (0.02 mol) was taken into a 100 ml round bottom flask. The mixture was stirred until a homogeneous solution was obtained; comarine Contain primary amine group (0.02 mol) was added with stirring. (As the reaction is exothermic it should be carried out by placing flask in a freezing mixture). Reaction mass is stirred for another 45 min. the Schiff base was precipitated out. The reaction mixture was cool with stirring. The isolated crude product is purified by the washing in acetone.



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Scheme IV

Compound also purify by silica gel column chromatography eluent ethyl acetate hexane reaction was. Monitored by TLC & spot were visualized in iodine.

Table 1. Synthesis of M_1, M_2 M_3 & M_4 in terms of Yield and melting point

S.N.	Compound	R_1	R_2	R_3	R_4	R5	M.P.(^{0}C)	% Yield
1	M_1	H	H	H	Br	H	276	80.58
2	M_2	H	H	H	H	I	280	82.05
3	M_3	I	H	Cl	H	H	296	81.20
4	M_3	H	I	H	H	OCH_3	258	70.25
5	M_5	NO_2	I	H	H	OCH_3	270	60.25

1)**M_1**

FT-IR 660 cm^{-1} for aromatic C-C stretching, 770 cm^{-1} for aromatic C-I stretching, 1130 cm^{-1} for C-O stretching , 1620 cm^{-1} for C=N stretching , 1690 cm^{-1} for C=O stretching 1350 for C=C stretching, 1190 cm-1 for C-N stretching, 3110 for N-H stretching.

NMR :

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.5 (s, 3H), δ 5.5 (s, 2H,), δ 6.6-7.6 (m, 9H), δ 8.0 (s, 1H NH), δ 8.4(s, 1H).

2) **M_2**

FT-IR, 670 cm^{-1} 1for C-I stretching, 750 cm^{-1} for aromatic C-C stretching, 1150 cm^{-1} for C-O stretching , 1070 cm-1 for C-N stretching, 1560 cm^{-1} for Ar C=C stretching, 1620 cm^{-1} for C=O stretching, 2960 cm^{-1} Ar C-H stretching 3190 for N-H stretching.

^{1}H NMR (400 MHz, $CDCl_3$): δ 2.1 (s, 3H), δ 5.5 (s, 2H,), δ 7.00-7.98 (m, 9H), δ 8.53 (s, 1H NH), δ 8.12(s, 1H).

3) **M_3**

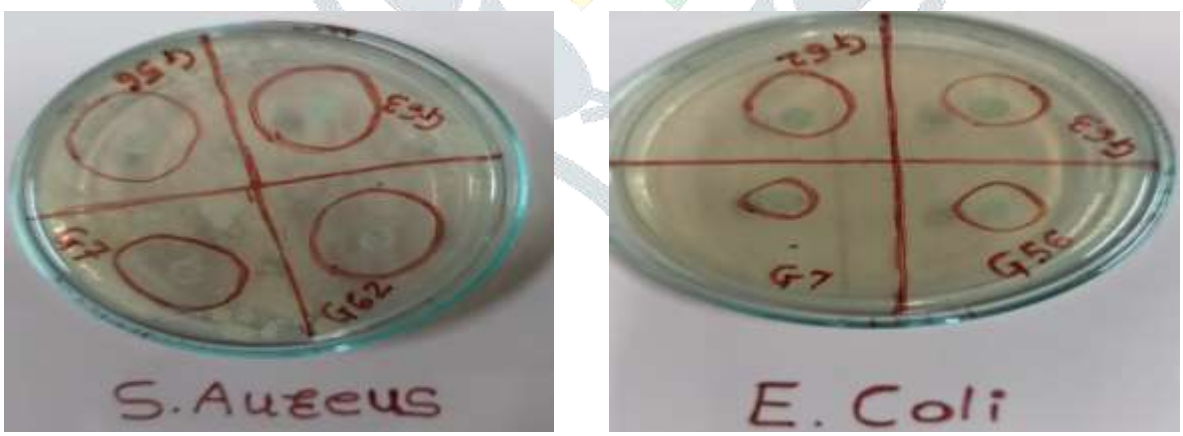
FT-IR: 550 cm^{-1} for C-Cl stretching, 790 cm^{-1} for aromatic C-C stretching, 1060 cm-1 for C-O stretching, 1190 cm^{-1} for C-N stretching , 1440 cm^{-1} for Ar C=C stretching, 1670 cm^{-1} for C=O stretching,28100cm^{-1} Ar C-H stretching, 3120 for N-H stretching.

^{1}H NMR (400 MHz, $CDCl_3$): δ2.6 (S, 3H), δ 5.0 (S, 2H,), δ 6.20-7.98 (m, 9H), δ 8.55 (s, 1H NH), δ 8.20(s, 1H).

Antibacterial properties of the synthesized Schiff base metal complex [Zone of inhibition (mm)]

The in vitro antimicrobial activity of the investigated compounds was tested against the bacteria such as E. coli, S. aureus, by the serial dilution method. The minimum inhibitory concentration (MIC) values of the compounds against the growth of microorganisms are summarized in graph.

Antibacterial properties of the synthesized Schiff base metal complex



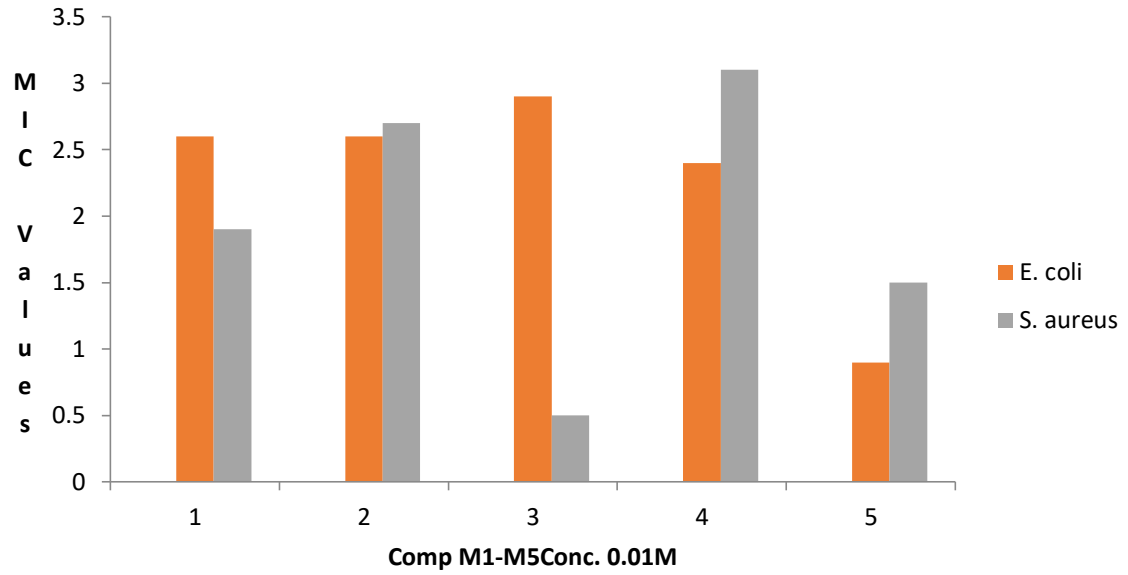


Fig : Zone of inhibition of comp. G_7, G_{56}, G_{63}, and G_{65} against S. Aureus and E. Coli.

Result and Discussion

All the six Schiff base Congaing coumarine moiety i.e. compounds M_1, M_2, M_3, M_4& M_5 were successfully synthesized in excellent yield and their structures are elucidated using elemental analysis, FTIR, & ^{1}HNMR spectroscopy. All the Synthesised Compound will screed for their biological activity.

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