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Synthesis and Charecterisation of Schiff Bases Derived From Acetyl Coumarin and Evaluated For Anti-Microbial Activity

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ABSTRACT

The Present research work is aimed to synthesize a serious of various substituted Schiff bases compounds of 7-hydroxy-4-methyl-8-[(1E)-N-phenylethanimidoyl]-2H-chromen-2-one form 8-acetyl-7-hydroxy-4-methyl Coumarin condenses with six different substituted aryl amines under conventional method. The structure for compounds has been determined by IR, ^{1}H-NMR and Mass spectroscopy. All the compounds are evaluated for its anti-microbial activity.

Keywords: 7-hydroxy-4-methyl-8-[(1E)-N-phenylethanimidoyl]-2H-chromen-2-one, Schiff bases, acetyl Coumarin and anti-microbial activity.

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INTRODUCTION

There are a number of reports that natural and synthetic Coumarin derivatives posses antimicrobial activity [1-4]. Novobiocin and Chlorobiocin are established antimicrobials containing a Coumarin (i.e.2H-1-benzopyran-2-ones) skeleton, there are many Coumarin derivatives which have been reported for anticoagulant, anti-inflammatory, anti-HIV, antioxidant, anti-allergic, anti-cancer, anti proliferative and antiviral activities[5-7]. It was found that when one biodynamic heterocyclic system was coupled with another heterocyclic system, enhanced biological activity was produced.

Compounds containing azomethine group (-CH=N-) is known as Schiff bases. Day by day Schiff bases are more frequently applied for the betterment of human welfare. The importance of the Schiff base is due its versatile nature. Literature survey shows that many Schiff bases exhibit biological activities such as antifungal, antibacterial, antitumor, anti-inflammatory, and Anticonvulsant[8-12]. From the above two discussion we have planned to synthesize the compounds which consist some heterocyclic compound with substituted Coumarin by Schiff base which will alter the activity of parent Coumarin to produce more useful products. The structure for synthesized compounds was characterized by physical and spectroscopic data's like M.P, TLC, IR, ^{1}H-NMR & FAB-Mass [13-14]. All the synthesized compounds are subjected to antimicrobial activity by the disc diffusion method by measuring diameter of zone of inhibition in mm [15-18]. This was carried over G+ve *Streptococci and Staphylococcus aureus* organism and for G-ve *Pseudomonas aeruginisa and Escherichia coli* organism for anti-bacterial activity. Antifungal activity was performed over *Candida albicans* and *Aspergillus Niger* the potency of activity was compared with know standard drugs.

MATERIALS AND METHODS

Experimental

All the chemicals are used in the synthesis are obtain from Merck & S.D. fine chemicals, melting point were determined by open capillary method which are uncorrected, the synthesized compounds are characterized and identified by elemental analysis, FT-IR by KBr method using Shimadzu 300 MHz FT-IR Spectrophotometer. Some selected compounds were subjected to ^{1}H-NMR spectra data were recorded on Bruker 400 MHZ in $CDCl_3$ using TMS as an internal standard and FAB-Mass for structural confirmation, all the compounds are screened for antimicrobial activity.

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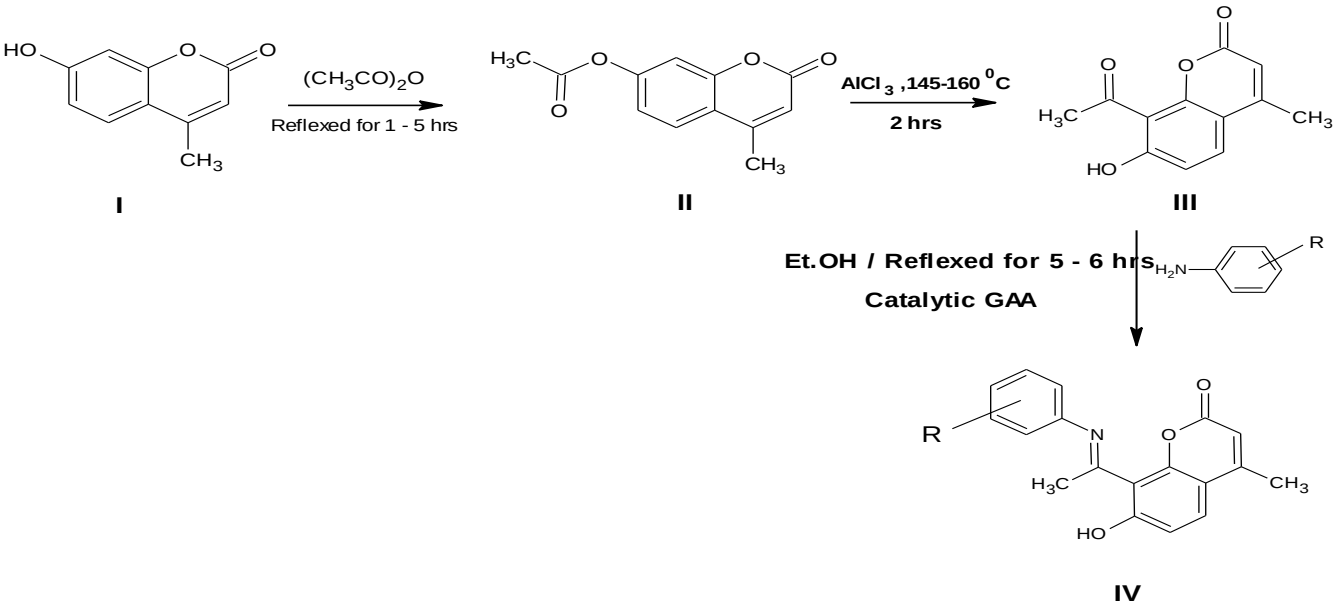
Synthetic Scheme



R = H , *ortho* - NH_2 , *para*- COOH , *para*- NO_2 , *para*- F, *para*- OH

Methadology

General method for synthesis of 7-hydroxy-4-methyl-8-[(1E)-N-phenylethanimidoyl]-2H-chromen-2-one (IV)

I. Synthesis of 7-hydroxy-4-methyl Coumarin (I)

The above product 7-hydroxy-4-methyl Coumarin was obtained by mixing (0.1mol, 11gm) of Resorcinol and (0.1mol, 13ml) of ethyl aceto acetate in 40ml of 85% sulfuric acid solution, heated for 1.30 hrs to get reddish brown solution cool and pour into crushed ice. The separated bright yellow colored solid was washed with excess cold water, dried and recrystallized from methanol to obtain pure product. **M.p - 176 ± 2^0C**

II. Synthesis of 7-acetoxy-4-methyl Coumarin (II)

A mixture of 7-hydroxy-4-methyl Coumarin (0.16 mol, 28.2 gm) and acetic anhydride (0.56 mol, 52.87 ml) was refluxed for 1-5hr under anhydrous conditions. While the solution was hot, it was poured into crushed ice and the product was separated out which was filtered and washed with cold water. The obtained product was recrystallized from ethanol. **M.p- 158 ± 2^0 C**

III. Fries rearrangement for 8-acetyl-7-hydroxy-4-methyl Coumarin (III)

The above obtained 7-acetoxy-4-methyl Coumarin (0.01 mol) and anhydrous $AlCl_3$ (0.03 mol) was heated under anhydrous conditions in an oil bath at 125^{0}C and the temperature was raised and maintained for 2 hr at 145-160^{0}C. To this mixture the crushed ice was added and

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acidified with dilute HCl. Stirring the mixture was left for 2-3 hr in order to decompose the complex. The separated product was filtered, washed with water and recrystallized from ethanol. **M.p – 186 ± 2^0 C**

IV. Synthesis of substituted Schiff Base of 7-hydroxy-4-methyl-8-[(1E)-N-phenylethanimidoyl] -2H -chromen-2-one (IV):

The Equimolar mixture of above obtain 8-acetyl-7-hydroxy-4-methyl Coumarin of (0.01mol) with substituted anilines of (0.01mol) are dissolved in 40 ml of redistilled ethanol this was condensed for 30min and later added with few drops of glacial acetic acid as catalyst and condensation was continued for 4-5 hrs. Later the mixture was poured in to crushed ice, stirred to obtained the product, this was filtered and dried and recrystallization was done by using ethanol.

The reaction is monitored by TLC and all the compounds are characterized by physical and spectral data as shown below table no 1.

Table 1 Physical data for the synthesized compounds BS (1-6)

Sl.No	C.C	MOLECULAR FORMULA	M. Wt	% YIELD	M.P ^{0}C	CALCULALED %				R_f value *
						C	H	N	O	
1	BS-1	$C_{18}H_{15}NO_3$	293.3	65	210	73.71	5.15	4.78	15.36	0.81
2	BS-2	$C_{18}H_{16}N_2O_3$	308.3	71	192	70.12	5.23	9.09	15.57	0.70
3	BS-3	$C_{19}H_{15}NO_5$	337.3	80	162	67.65	4.48	4.15	23.72	0.68
4	BS-4	$C_{18}H_{14}N_2O_5$	338.3	76	189	63.16	4.42	8.23	23.59	0.74
5	BS-5	$C_{18}H_{14}NO_3F$	311.4	69	178	69.87	4.50	4.29	15.65	0.65
6	BS-6	$C_{18}H_{15}NO_4$	309.3	62	217	69.81	4.90	4.53	21.19	0.63

* n-Hexane : Ethyl acetate (6:4)

Spectral data for the synthesized compounds BS (1-6)

BS-1: 7-hydroxy-4-methyl-8-[(1*E*)-*N*-phenyl ethanimidoyl]-2*H*-chromen-2-one
IR (KBr) cm-1: 1599 (C=C), 1697 (C=O), 1277 (C-O-C), 1595 (C=N), 1398(C-N). ^{1}H-NMR ($CDCl_3$, δ ppm) 2.44(s, 3H, -CH_3), 11.80(s,1H, -OH),7.15-7.96(m,8H,Ar-H). Mass m/z 292.

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BS-2: 8-[(1*E*)-*N*-(2-aminophenyl) ethanimidoyl]-7-hydroxy-4-methyl-2*H*-chromen-2-one
IR (KBr) cm-1: 1587 (C=C), 1690 (C=O), 1260 (C-O-C), 1610 (C=N), 1370(C-N).

BS-3: 4-{[(1*E*)-1-(7-hydroxy-4-methyl-2-oxo-2*H*-chromen-8-yl)ethylidene] amino} benzoic acid.
IR (KBr) cm-1: 1605 (C=C), 1670 (C=O), 1285 (C-O-C), 1602 (C=N), 1385(C-N).

BS-4: 7-hydroxy-4-methyl-8-[(1*E*)-*N*-(4-nitrophenyl) ethanimidoyl]-2*H*-chromen-2-one
IR (KBr) cm-1:1610(C=C),1660(C=O),1260(C-O-C),1598 (C=N),1372(C-N). ^{1}H-NMR ($CDCl_3$, δ ppm) 2.36 (s, 3H, -CH_3), 11.30(s, 1H, -OH), 6.90-7.86(m, 7H, Ar-H). Mass m/z 338.

BS-5: 8-[(1*E*)-*N*-(4-fluorophenyl) ethanimidoyl]-7-hydroxy-4-methyl-2*H*-chromen-2-one
IR (KBr) cm-1: 1596 (C=C), 1710 (C=O), 1276 (C-O-C), 1582 (C=N), 1370(C-N).

BS-6: 7-hydroxy-8-[(1*E*)-*N*-(4-hydroxyphenyl) ethanimidoyl]-4-methyl-2*H*-chromen-2-one
IR (KBr) cm-1: 1587 (C=C), 1697 (C=O), 1288 (C-O-C), 1603 (C=N), 1348(C-N). ^{1}H-NMR ($CDCl_3$, δ ppm)2.52(s, 3H, -CH_3),11.24(s,1H, -OH),7.21-8.16(m, 7H, Ar-H). Mass m/z 308.

Biological Activity

Antimicrobial Activity

All synthesized compounds were screened for antibacterial and antifungal activity by cup plate method from the standard procedure; the two concentrations are taken i.e. 50 & 100 µg/ml over a different bacterial strains and fungal strains as shown in table. The values obtained are compared with the values produced from the standard drugs like Ampicillin and Streptomycin for bacterial and Flucanazole for fungal, the dimethyl formamide (DMF) was used as control for all the strains. Some of the compounds show significant property compared with the standard and other shows moderate. This will be shown in the table no 2.

Table 2 Anti-Microbial activity of the synthesized compounds

Comp code.	Mean zone of inhibition in (mm)											
	Streptococci (G + ve)		Pseudomonas aeruginisa (G - ve)		Staphylococcus aureus (G + ve)		E.coli (G - ve)		Candida albicans		Aspergillus niger	
	50 µg	100µg	50µg	100µg	50 µg	100µg	50µg	100µg	50µg	100µg	50 µg	100µg
Ampicillin	18	21	-	-	19	22	-	-	-	-	-	-
Streptomycin	-	-	19	23	-	-	20	23	-	-	-	-
Flucanazole	-	-	-	-	-	-	-	-	19	21	20	23
BS-1	16	16	16	18	14	17	14	18	16	19	17	21
BS-2	17	20	16	19	17	20	16	19	15	18	16	19
BS-3	16	20	17	18	13	15	18	20	17	18	17	19
BS-4	14	18	14	16	14	18	13	17	15	17	14	16
BS-5	16	17	15	19	15	19	14	16	16	18	17	19
BS-6	15	19	16	18	16	19	15	18	17	19	16	18
Control	--	---	--	--	--	--	--	--	--	--	--	--

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RESULT AND DISCUSSION

The Synton 8-acetyl-7-hydroxy-4-methyl Coumarin were obtained by Fries rearrangement from 7-acetoxy-4-methyl Coumarin. The series of Schiff base was synthesized by reacting the Synton with substituted anilines in ethanol media and recrystallized. The reaction was monitored by TLC using silica gel 60 and final compounds melting point was determined by open capillary method and structure was determined by FT-IR by KBr method, selected compounds are subjected to ^{1}H-NMR and FAB-Mass spectroscopy. All the above compounds are subjected to antimicrobial activity among them the compound *BS-2, 3& 5* for antibacterial and BS-*1, 2 &6* for antifungal posse's significant activity and rest of the compounds showed moderate activity on both organism.

CONCLUSION

The Structure for synthesized compounds are identified by spectral analysis and compounds shows significant to moderate activity for antimicrobial (anti-bacterial & anti-fungal), based upon this the further studies will be done in future.

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