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Research Article

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A Studies about synthesis, characterization and antibacterial activities of newly synthesized coumarin derivatives

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ABSTRACT

Five new coumarin derivatives were synthesized by well known condensation chemistry comprising with azo functional group. The structures of compounds were confirmed with help of Melting point, TLC, Uv-Vis, IR, NMR spectra and evaluated their antibacterial activity by using disc diffusion method.

Keywords: 4-Methylaniline, Coupling reaction, Claisen-schmidt reaction, Piperidine

INTRODUCTION

Benzopyrones are a group of compounds whose members include Coumarins and flavonoides hugely distributed in plants. Till now, more than 1300 coumarins were identified from natural sources [1]. These natural compounds serve as important models for advanced design and synthesis of more active coumarins analogous and were shown various pharmacological activities. They have been widely used as starting materials and intermediates in the synthetic organic chemistry. Mostly, the coumarin derivatives are used in pharmaceutical, perfumery and agrochemical industries for various purposes [2-9]. Furthermore, these compounds also used as fluorescent brighteners, efficient laser dyes, additives in food and cosmetics [10-13]. In view of versatile application of coumarin analogs and continuation of our previous studies towards heterocyclic compounds [14-15], herein we focus on the design of some novel coumarin derivatives in order to examine their biological activities.

EXPERIMENTAL SECTION

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Paragon 1000 FTIR spectrophotometer as potassium bromide discs unless otherwise indicated. ^{1}H NMR spectra were obtained on a Brucker (400 MHz) instrument in $CDCl_3$ solutions using tetramethylsilane as an internal standard. *J* Values are given in Hz. All the basic chemicals were purchased from Merck (India), *s.d* fine chemicals (India).

General procedure for preparation of aromatic diazonium chloride solution:
A suspension of 4-methylaniline (5.52 g, 40 mmol) in hydrochloric acid (36 mL) and water (16 mL) was heated to 70 °C until complete dissolution. The clear solution was cooled in ice cold condition and was diazotized below 5 °C with sodium nitrite solution (2.8 g, 40 mmol) for 20-30 min.

General procedure for preparation of diazocoupled product:
The cold diazonium solution obtained from above step was added over the course of 30 min to the ice cold solution of salicylaldehyde (4.26 mL, 40 mmol) in water (75 mL) containing sodium hydroxide (1.6 g). During the addition process solid was formed, the solution was vigorously stirred to complete the reaction. After complete addition, small amount of urea was added to decompose the unreacted nitrous acid. The product was collected by vacuum filtration and pure product obtained by recrystalization of crude sample in ethanol.

Yield; 85%, Mp; 138-140^{o}C, Rf; 0.85, IR (KBr,cm^{-1}); 3187.35, 3030.53, 2919.07, 1657.70,1480.15, 762.98;^{1}H-NMR ($CDCl_3$, δppm); 2.20 (s, 3H, CH_3), 7.13-7.16(d,1H, Ar-H), 7.94-8.26 (m,6Ar-H), 10.05 (s,1H,OH),11.41(s,1H,CHO),^{13}HNMR($CDCl_3$,δppm),21.20($COCH_3$),113.38,114.73,116.66,118.00,119.72,123.10,123.58,123.74,124.57,124.72, 125.44,126.39.

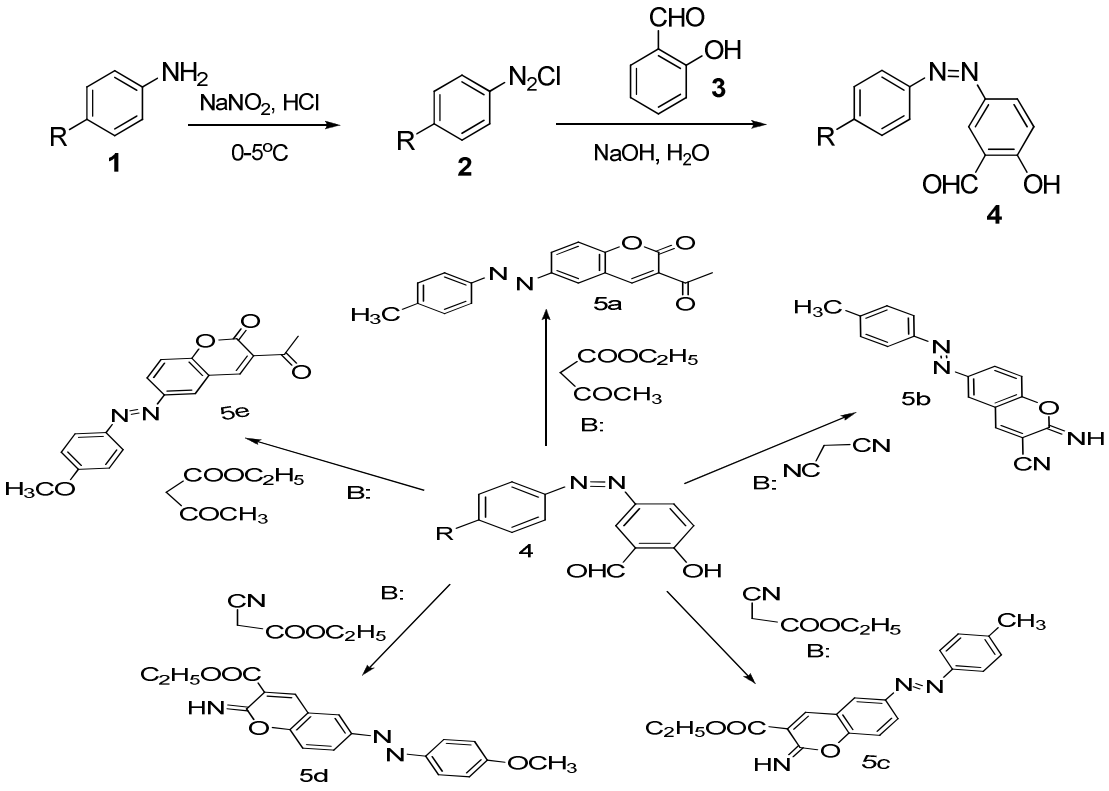
General procedure for synthesis of novel coumarin derivatives:
A mixture of diazocoupled product and ethylacetoacetate/ethylcyanoacetate /malanonitrile in 1:1 ratio was taken in pestle and mortar. This mixture was grinded up to 40 min in presence of few drops of piperidine at room temperature. During the reaction progress heat is generated, the solid material turn into liquid and finally solid formed. The mixture was cooled and poured into ice cold water and stirred vigorously. The compounds were precipitated, filtered, dried and recrystallized from ethanol.

(E)-3-acetyl-6-(p-tolyldiazenyl)-2H-chromen-2-one (5a): Yield; 90%, Mp; 196-198^{o}C, Rf; 0.50, IR (KBr,cm^{-1}); 3048.68, 2923.56, 1742.11, 1680.51, 1235.32, 969.77; ^{1}H-NMR ($CDCl_3$, δppm); 2.68 (s, 3H, COCH3), 2.76 (s, 3H, CH3), 7.51-7.54 (d,1H, Ar-H), 7.92-8.02 (m,6H, Ar-H), 8.12-8.15 (d,2H, Ar-H) 8.62 (s, 1H, CH=C),^{13}C-NMR (CDCl3, δppm), 29.38 (COCH3), 29.64 (COCH3),113.43 (CH=C),114.04,115.74, 120.338,127.66, 128.92, 129.97, 130.75,131.68, 131.93, 132.18, 145.73, 153.04 (12Ar-C), 186.64(COO), 196.48 (CO).

(E)-2-imino-6-(p-tolyldiazenyl)-2H-chromene-3-carbonitrile (5b): Yield; 86%, Mp; 150-152^{o}C, Rf; 0.15, IR(KBr,cm^{-1}); 3340.81, 3203.12, 2193.28, 1645.99. 1604.39, 1576.22, 1241.32; ^{1}H-NMR ($CDCl_3$, δppm); 2.70 (s, 3H, COCH3), 7.71(s,1H, Ar-H), 7.88-8.40 (m,6H, Ar-H), 8.41(s, 1H, CH=C),^{13}C-NMR ($CDCl_3$, δppm), 26.6 ($COCH_3$), 117.91(CH=C) 120.09 (C-CN), 122.17, 122.48, 127.42, 128.76, 129.37, 131.22, 140.69, 144.63, 145.09, 153.81, 163.49, 194.76.

RESULTS AND DISCUSSION

This work explains about synthesis of some novel coumarin derivatives by using following synthetic steps. The product **4** obtained by diazotization of *4*-methylaniline **1** into diazoniumchloride **2** which further coupled with salicylaldehyde **3**. The compound **4** involved condensation reactions with various active methelene compounds (Ethylacetoacetate, Ethylcyanoacetate and malanonitrile) produced corresponding coumarin derivatives **5a-e.** The synthetic routes, detailed structure of 5a-e are given in scheme-1.



Scheme-1, R=CH_3,OCH_3,B:=Piperidine

The physical data as well as UV-Vis, FT-IR, ^{1}H-NMR and ^{13}C-NMR spectral data confirmed formation of the desired products. All the synthesized compounds showed very good activity against selective bacteria.

Table-1: Physical properties of coumarin derivatives 5a-e:

Code	R	Active methelene	Yield (%)	Mp (^{o}C)	R_f value
5a	CH_3	Ethylacetoacetate	90	196-198	0.50
5b	CH_3	Malononitrile	86	150-152	0.15
5c	CH_3	Ethylcyanoacetate	91	118-120	0.56
5d	OCH_3	Ethylcyanoacetate	88	140-142	0.42
5e	OCH_3	Ethylacetoacetate	76	176-178	0.46

Table-2: Antibacterial activity data of novel coumarin derivatives 5a-e:

S. No.	Sample	Zone of inhibition in mm in diameter (30mg) standard=Gentamicin			
		Bacillus subtilis	*Staphylococcus aureus*	*Escherichia coli*	*Pseudomonas aeruginosa*
1	PC*	25	18	24	18
2	C	–	–	–	–
3	**5a**	27	15	26	—
4	**5b**	24	14	20	—
5	**5c**	26	20	26	—
6	**5d**	22	17	30	—
7	**5e**	20	19	33	14

CONCLUSION

A new series of coumarin derivatives were successfully synthesized and structure of these compounds proposed with help of various spectroscopic techniques such as UV-Vis, FT-IR, ^{1}H-NMR, and ^{13}C-NMR. The in vitro antibacterial activities of these compounds examined and most of the compounds were showed very good activities against selective bacteria except *Pseudomonas aeruginosa.*

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