Synthesis, characterization and fluorescence properties of newly synthesized chalcones derivatives from coumarin

J. V. Chavhan [1] Dr. P. D. Polytechnic Amravati.
Dr. S.S. Patil[2] Director and Head Lifelong learning and extension department Sant Gadgebaba Amravati University, Amravati.

ABSTRACT

In this work, substituted coumarin based chalcones have been synthesized from resorcinol. The study was conducted with two primary objectives. The first objective was to synthesize coumarin based chalcones and second objective was to study fluorescence activity of synthesized compounds. The structures of the compounds were elucidated by elemental and spectral (IR, ^{1}HNMR, and MS) analysis. The reactions are easy to conduct, under mild conditions, and form coumarine substituted flavones in moderate to excellent yields.

Keywords: Chalcone, Coumarine, fluorescence activity.

Introduction

Coumarins exist in an important place in the kingdom of natural products and synthetic organic chemistry[1-5]. Coumarins act as antioxidant, enzyme inhibitors as well as precursors of toxic substances and thus exhibit important effects in plant biochemistry and physiology. Coumarins as benzopyrene derivatives found in a group of natural products. In addition, these compounds regulate respiration, photosynthesis, plant growth and activate growth regulators etc[6-10]. Further coumarins have long been known to possess anti carcinogenic, antiviral, anti-inflammatory, anti-oxidant, anti-allergic, Hepatoprotective, anti-thrombotic, anti-viral and anti-carcinogenic activities[11-13]. In addition to biological activities they are used as additives to food and cosmetics[14, 15] and optical brightening agents[16].

2. MATERIAL AND METHOD

Melting points were determined on a Veego Melting Point Apparatus Mod. VMP-DS ± 0.5˚C accuracy and are uncorrected. The ^{1}H NMR spectra were recorded on a BRUKER Spectrometer (400 MHz) in DMSO

solvent. Chemical shifts were reported in parts per million using tetramethylsilane as an internal standard and were given in δ units. The solvent for NMR spectra was DMSO. Infrared spectra were taken on SHIMADZU-FTIR-8400 Spectrophotometer instrument in the frequency range of 4000-400 cm^{-1} by KBr powder method. The Mass spectra were recorded by MS-SHIMADZU-QP2010. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60F254 (Merk) plates using UV light for detection. Common reagent grade chemicals are either commercially available and were used without further purification.

Preparation of 7-hydroxy-4-methyl-2H-chromen-2-one (3):

Compound **3 (**7-hydroxy-4-methyl-2H-chromen-2-one) was synthesized using the Pechmann reaction, In a 100 ml round bottom flask resorcinol (9.1 mmol, 1.0 g, 1.0 eq.) was added with ethyl acetoacetate (9.1 mmol, 1.15 mL, 1.0 eq.) and this mixture was cooled. 7 ml conc. H_2SO_4 was added with constant stirring for 8hr. Reaction mixture was poured in crushed ice. The solid product obtained was dissolve in ethanol and crystallized in hot ethyl alcohol. The progress and completion of reaction was monitored by thin layer chromatography (TLC) to obtained yellowish solid 7-hydroxy-4-methyl-2H-chromen-2-one **(3)** with yield 94%. Melting point 185^{o}C.

IR spectrum (KBr), υ (cm^{-1}): 3124 cm^{-1} (O-H str.); 2980 cm^{-1} (Ar C-H str.); 2808cm^{-1} (Al C-H str.); 1584 cm^{-1} (Ar C=C str.); 1672 cm^{-1} (C=O ketone str.); 1066-1132 cm^{-1}(C-O-C str.); ^{1}H-NMR (300 MHz, DMSO-d6): δ [ppm] = 2.24 (d, *J* = 1.1 Hz, 3H), 6.06 (d, *J* = 1.1 Hz, 1H), 6.70 (d, *J* = 2.4 Hz, 1H), 7.42 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.28 (d, *J* = 8.7 Hz, 1H), 9.64 (s, 1H). ^{13}C-NMR (75 MHz, DMSO-d6): δ [ppm] = 18.0, 102.1, 110.1, 111.9, 112.7, 126.5, 153.4, 154.7, 160.2, 161.0.

MS (ESI): *m/z* (%) = 176.1 (100) [M·+], 148.1 (85) [M·+-CO].

Preparation of 4-methyl-2-oxo-2H-chromen-7-yl acetate (4):

Compound **4 (**4-methyl-2-oxo-2H-chromen-7-yl acetate) was synthesized by common method of acylation reaction. In a 100 ml round bottom flask compound **3** coumarin (1.0 g, 1.0 eq.) taken followed by

the addition of acetic anhydride (5ml) and heated in the presence of pyridine as base for 2.5 hr. The progress and completion of reaction was monitored by thin layer chromatography (TLC). After the completion, reaction mixture was poured in crushed ice. The solid product filtered off and treated with brine solution and dried over anhydrous sodium sulphate (10gms). The solid product obtained was dissolve in ethanol and crystallized in hot ethyl alcohol. The progress and completion of reaction was monitored by thin layer chromatography (TLC) to obtained brownish solid **4-methyl-2-oxo-2H-chromen-7-yl acetate (4)** with the yield 89%. Melting point 195^0 C

IR spectrum (KBr), υ (cm^{-1}): 3121 cm^{-1} (Ar C-H str.); 2809cm^{-1} (Al C-H str.); 1450 cm^{-1} (Ar C=C str.); 1671 cm^{-1} (C=O ketone str.); 1272 cm^{-1}(C-O-C str.);

^{1}H-NMR (300 MHz, DMSO-d6): δ [ppm] = 2.35 (d, *J* = 1.1 Hz, 3H), 2.2 (s, 3H), 6.11 (d, *J* = 1.1 Hz, 1H), 6.9 (d, *J* = 2.4 Hz, 1H), 7.01 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.01 (d, *J* = 8.7 Hz, 1H), ^{13}C-NMR (75 MHz, DMSO-d6): δ [ppm] = 18.0, 22.12, 102.1, 110.1, 111.9, 112.7, 126.5, 153.4, 154.7, 160.2, 161.

Preparation of 8-acetyl-7-hydroxy-4-methyl-2H-chromen-2-one (5):

Compound **5** **(**8-acetyl-7-hydroxy-4-methyl-2H-chromen-2-one) was synthesized by fries rearrangment reaction. In a 100 ml round bottom flask compound **4** (1.0 g, 1.0 eq.) taken followed by the addition of anhydrous aluminium chloride ($AlCl_3$) a catalyst and refluxed at 160^0C for 3 hour in water condenser. The progress and completion of reaction was monitored by thin layer chromatography (TLC). After the completion, reaction mixture was poured in crushed ice. The solid product filtered off and treated with brine solution and dried over anhydrous sodium sulphate (10gms). The solid product obtained was dissolve in ethanol and crystallized in hot ethyl alcohol. The yield of product was 84%. Melting point 225^0C.

IR spectrum (KBr), υ (cm^{-1}): 3094 cm^{-1} (Ar C-H str.); 2952cm^{-1} (Al C-H str.); 1440 cm^{-1} (Ar C=C str.); 1664 cm^{-1} (C=O ketone str.); 1228 cm^{-1}(C-O-C str.); 3486 cm^{-1} (O-H Str.)

^{1}H-NMR (300 MHz, DMSO-d6): δ [ppm] = 2.4 (s, *J* = 1.1 Hz, 3H), 2.48 (s, *J* = 1.1 Hz, 3H), 6.0 (d, *J* = 1.1 Hz, 1H), 6.8 (d, *J* = 2.4 Hz, 1H), 7.6 (dd, *J* = 8.7, 2.4 Hz, 1H), 10.33 (s, *J* = 8.7 Hz, 1H, OH),

Preparation of 8-((E)-3-(4-chlorophenyl)acryloyl)-7-hydroxy-4-methyl-2H-chromen-2-one (7a):

Compound (**5**) and Chlorobenzaldehyde (**6a**) was taken in 1:1 proportion, to this 50 ml of ethanol as a solvent, and 9ml of 40 % KOH was added, the reaction mixture was refluxed for 2 hrs to get the compound (**7a**). The product obtained was washed with water and crystallized from ethanol.

8-((E)-3-(4-chlorophenyl)acryloyl)-7-hydroxy-4-methyl-2H-chromen-2-one (7a):

It is brownish amorphous solid; yield 84%; mp. 180-183℃; IR spectrum (KBr), υ (cm^{-1}) : 1517 cm^{-1} (Ar C=C str.); 1275 cm^{-1} (C-O-C str.); 1665 cm^{-1} (C=O ketone str.); 3487 cm^{-1} (O-H str.); 749 cm^{-1} (C-Cl str.); ^{1}HNMR spectrum (δ ppm): 2.27 (3H, s, CH_3); 9.64 (1H, s, OH); 6.71 (2H, d, CH); 6.8 (2H, d, CH); 7.2 (1H, d, CH); 7.4 (1H, d, CH); 7.84 (1H, d, C-H adj to benzene); 7.79 (1H, d, C-H adj to benzene) 6.06 (1H, s, CH).

MS (ESI): *m/z* (%) = 340.05 [M·+],

7-hydroxy-8-((E)-3-(4-hydroxyphenyl)acryloyl)-4-methyl-2H-chromen-2-one (7b)

It is amorphous solid; yield 74%; mp. 186-188℃; IR spectrum (KBr), υ (cm^{-1}) : 1451 cm^{-1} (Ar C=C str.); 1253 cm^{-1} (C-O-C str.); 1687 cm^{-1} (C=O ketone str.); 3389 cm^{-1} (O-H str.); ^{1}HNMR spectrum (δ ppm): 2.21 (3H, s, CH_3); 10.48 (1H, s, OH); 5.89 (1H, d, CH); 6.68 (1H, d, CH); 6.82 (1H, d, CH); 7.51 (1H, d, CH); 7.31-7.42(4Ar-H); 10.28 (1H, s, OH).

MS (ESI): *m/z* (%) = 322 [M·+],

7-hydroxy-4-methyl-8-((E)-3-(4-nitrophenyl)acryloyl)-2H-chromen-2-one (7c)

It is brownish crystalline solid; yield 78%; mp. 163-16 7℃; IR spectrum (KBr), υ (cm^{-1}): 1474.23 cm^{-1} (Ar C=C str.); 1700.97 cm^{-1} (C=O ketone str.); 1267.08 cm^{-1}(C-O-C str.); cm^{-1} 1345/1568cm^{-1} (NO_2

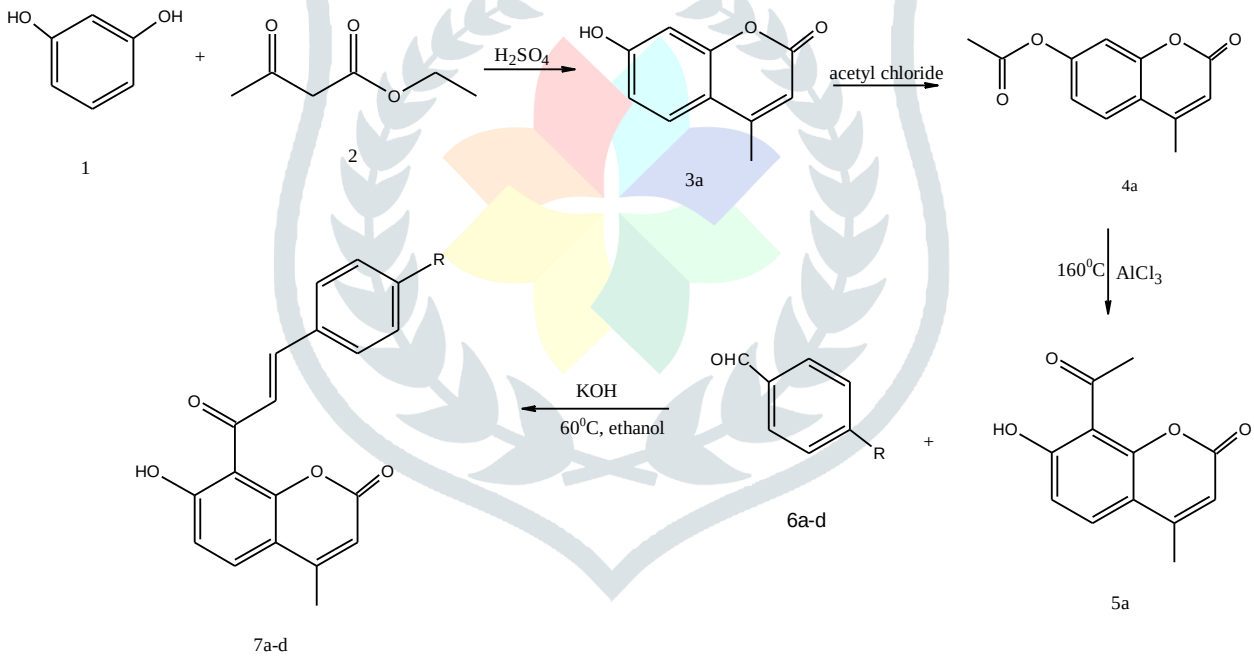
str.); ^{1}HNMR spectrum (δ ppm): 2. 67 (3H, s, CH_3); 7.02 (1H, d, CH); 7.28 (1H, d, CH); 7.58-7.72 (4Ar-H); 6.72(1H, d, CH); 6.76(1H, d, CH); 5.98(1H, d, CH); 10.46(1H,s,OH).MS (ESI): *m/z* (%) = 351[M·+].

7-hydroxy-8-((E)-3-(4-methoxyphenyl)acryloyl)-4-methyl-2H-chromen-2-one (7d)

It is brownish crystalline solid; yield 69%; mp.186℃; IR spectrum (KBr), υ (cm^{-1}): 1473.52 cm^{-1} (Ar C=C str.); cm^{-1} 1700.39 cm^{-1} (C=O ketone str.); 1263.93 cm^{-1}(C-O-C str.); ^{1}HNMR spectrum (δ ppm): 2. 23 (3H, s, CH_3); 2.55 (3H, s, CH_3); 6.01 (1H, d, CH); 6.6 (1H, d, CH); 6.8 (1H, d, CH); 7.4-7.5 (4Ar-H); 7.18 (1H, d, CH); 7.2 (1H, d, CH); 10.04 (1H, s, OH).

MS (ESI): *m/z* (%) = 336 [M·+]

Reaction scheme



R=[-Cl, -OH,-NO_2,-OCH_3]

RESULT AND DISCUSSION:

1) **FLUROSCENCE PROPERTIES**:

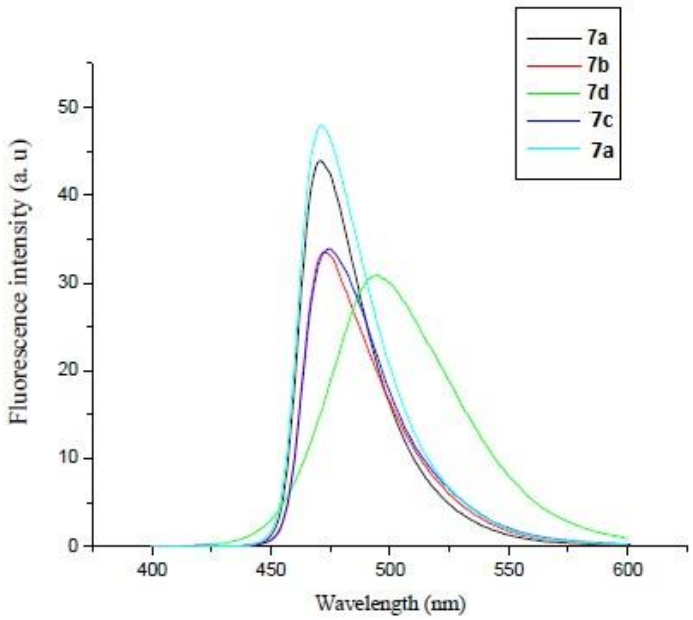
The fluorescence properties of unfamiliar chalcones linked coumarins 7**a-d** were investigated. The effect of different substituent's on coumarin moiety with various solvents with respect to polarity has been studied. The molecules were

designed with distinctive combination of electron donor at the 7th position like benzene substituted with chloro, hydroxy, nitro, methoxy , etc coumarin moiety.

The fluorescence spectral data of all the compounds 7a-d are summarized in Table 1. These compounds exhibited varying trend of fluorescent property with 21 to 88 nm strokes shift in chloroform, Acetonitrile, methanol and DMSO respectively when compared with Rhodamine B.

Table 1. Spectral property of compound **7a-d** in four solvent viz. MeOH, Acetonitrile ,Chloroform dimethylsulphoide.

Compounds	Solvent	λabs (nm)	λem (nm)	Strokes shift
7a	Chloroform	437	470	33
	Acetonitrile	425	466	41
	Methanol	427	477	50
	DMSO	415	460	45
7b	Chloroform	422	455	33
	Acetonitrile	398	445	47
	Methanol	401	489	88
	DMSO	410	440	30
7c	Chloroform	--	--	--
	Acetonitrile	435	456	21
	Methanol	455	499	44
	DMSO	445	474	29
7d	Chloroform	475	505	30
	Acetonitrile	466	501	35
	Methanol	455	494	39
	DMSO	450	490	40



The absorption, emission and strokes shift are also given in Table 1. Chalcones linked coumarin emits light due to electron donating (EDG) groups and (EWG) groups. Solubility has been remaining the

main hurdle for the chalcone compounds to investigate their fluorescence property. Hence in order to increase properties of these compounds conjugation is increased. Hence the synthesized compounds showed high fluorescent properties. However; no specific structure–activity relationship could be established.

1. CONCLUSION

The successful synthesis of chalcone and flavone compounds follows a mild, efficient route with a good to moderate yield. In present work we synthesized chalcone from easily available resorcinol and ethylacetoacetate. The synthesized compounds manifest good fluorescence activity.

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