SYNTHESIS OF 3-SUBSTITUTED PHENYL-1-(3-COUMARINYL) PROPAN-1-ONE DERIVATIVES USING SECONDARY AMINE CATALYSTS

NITIN KUMAR*

[1]Department of Pharmaceutical Technology, MIET, Meerut- 250005, UP, India.
*Corresponding Author: Email- nitinvermakr@gmail.com

Abstract- The present study was undertaken to study the effect of different secondary amines which are used as the dehydrating catalyst in the Knoevenagel synthetic mechanism for the synthesis of 3-substituted phenyl-1-(3-coumarinyl) propan-1-ones. Various studies have been done using piperidine as catalyst in the various condensation reactions. Here in this study differently arranged secondary amine compounds were used namely: piperidine, diethylamine and N-isopropylamine, to know their effects on the reaction pathway especially in the case of reaction time and the percentage yield of the final products. In the results it was evaluated that diethylamine has proven to be yielding larger amounts of final products while the reaction time of piperidine catalysed reaction was least. N-isopropylamine has proven to be least effective among two. These observations could further stimulate the research on the use of other amines apart from secondary amines as catalyst in condensation recations like Knoevenagels.
Keywords- Piperidine, diethylamine, N-isopropylamine, coumarin.

Introduction

In Organic Chemistry the frequently used Knoevenagel reaction is generally explained by condensation of an aldehyde or ketone with compounds possessing active methylene groups but not containing any α- hydrogen such as malonic esters, or malononitrile to yield an α,β-unsaturated carboxylate products [1] or ethylacetoacetate to yield acetyl coumarins [2]. Condensation reaction is in general a reaction that combines two molecules while removing a small molecule like water, ammonia or an alcohol. These reactions are usually catalysed by weak bases like amines (preferably secondary amines). In some reactions these amines may work as lewis acids, while many a times used as dehydrating catalysts. In the same type of condensation reaction if catalytic amounts amines in a basic organic solvent such as pyridine is used, it is called the "*Doebner modification of Knoevenagel reaction*" or the "*Knoevenagel-Doebner reaction* or *condensation*" [3,4]. The Knoevenagel reaction can be used to form different types of compounds, depending on the catalysts used, whether acidic or basic. The condensation of unprotected reducing sugars with 1, 3-dicarboxylic compounds under acidic conditions was reported in 1956 by Gonzalez [5]. The Knoevenagel condensation under basic conditions was first investigated with D-glucosamine chlorhydrate as the sugar [6].

Knoevenagel reaction mechanism has been used in synthesis of many medicinally important structural moieties like coumarins and pyrazolines. Till date catalytic amounts of piperidine a heterocyclic aliphatic secondary amine compound, is used in reaction which act as basic oxidizing catalyst, where it gives its lone pair of electron for completion of the reactions. Basic requirements of lone pair of electrons in the Knoevenagel could be fulfilled by such

other aliphatic secondary amines derivatives of varying numbers of carbon atoms attached to the lone pair containing nitrogen atom in amines. As mentioned in many literatures relating to the chemical natures of the secondary amines it is been discussed that aliphatic amines are more likeable of donating electrons than compared to the heterocyclic amines. The use of different amines as catalysts has paved way for the good yield of compounds which has their respective differences in purity and in reaction timings. In present research work piperidine, diethylamine and N-isopropylamine are used in synthesis of coumarin derivatives, to study their effect on yield, purity and reaction time. This study can give the idea of most economic way of synthesis of coumarins, which itself is medicinally important moiety.

Coumarins are naturally occurring benzopyrene derivatives. Coumarins are found in many families particularly *Fabiaceae*, *Umbelliferae*, and in some *Solanaceaeous* family plants. Coumarin is present either in free state or in glycosidal form, former being most common, coumarin nucleus corresponds to benzo-*a*-pyrone (2*H*-1 - benzopiran-2-one) whose systematic nomenclature was established by IUPAC, of which the simplest member of coumarin class is, coumarin itself [7]. They are widely occurring secondary metabolite that occurs naturally in several plant families, essential oils and has been used as a fragrance in food and cosmetic products. The fermentation product of coumarin is dicoumarol which is a potent anticoagulant. However natural coumarins are rendered inactive in the human gastrointestinal tract and on oral administration of therapeutic doses these herbs are not considered to be anticoagulant. But now, various derivatives of synthetic origin are developed which significantly increases characterstics of the coumarin structures with the great diversity in their biological activities and they are found to posses anti-oxidant [8-10], anti-inflammatory [10,11], anti-microbial [10,11], anti-hepatitis and hepatoprotective [12], anti-cancer [13], analgesic and anti-pyretic activities [11,13], cannabinoid receptor antagonists and inverse agonists [14], TNF-*a* inhibitors [15], inhibition of monoamine oxidases (MAO inhibitors) [16] and anticonvulsant activity [17].

Result and discussion
Chemistry

For the synthesis of targeted compounds, the reaction sequence outline in scheme 1, were followed. To the Cold solution of ethylacetoacetate, salicyladehyde was added dropwise with continuous stirring. Further different catalysts (piperidine, diethylamine, and N- isopropylamine) were added in the reaction mixture with vigrous shaking which gave 3-acetyl coumarin (1). This synthesized compound was refluxed with substituted aromatic aldehyde in the presence of *n*-butanol, then glacial acetic acid and catalysts (piperidine, diethylamine, and N- isopropylamine) were added in the reaction mixture yielded 3-substitutedphenyl-1-(3-coumarinyl)propan-1-ones (2). Then, this newly synthesized compound was dissolved in pyridine, hydrazine hydrate was added to the reaction mixture and on refluxing gave 3-(4, 5-dihydro-5-substituted phenyl-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one derivatives (3a-3j). The structures of the synthesized compounds were confirmed by their spectral analysis. The rates of reaction and percentage yield were calculated for studying the effect of catalyst (Table 1) and the physical data of these synthesized compounds are summarized in table 2 and table 3.
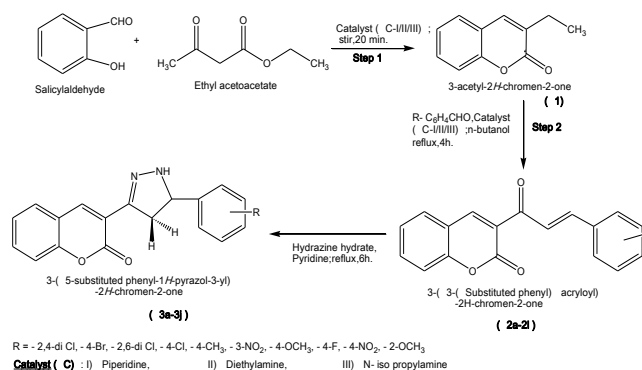
Scheme 1

Table 1- Data showing duration of reaction and percentage yield during step1 and step 2 of reaction using different catalysts.

Name of catalyst	% Yield		Duration of reaction	
	Step 1	Step 2	Step 1 (in min.)	Step 2 (in hrs)
Diethylamine	78	86	15-20	04-May
Piperidine	32	38	25-30	01-Feb
n-isopropylamine	46	52	40-45	3.5-4

Table 2- Physical data of the 3-(3-(Substituted phenyl) acryloyl)-2H-chromen-2-one (2a-2l)

Compound Code	Substitution (R)	Molecular Formula	Mol. Wt.	M. P. (°C)	Yield (%)	R$_f$
2a	-2,4- di methoxy	C$_{20}$H$_{16}$O$_5$	336.34	187-189	27.31	0.751
2b	-2,4- di chloro	C$_{18}$H$_{10}$Cl$_2$O$_3$	345.18	225-227	35.6	0.651
2c	-4- bromo	C$_{18}$H$_{11}$BrO$_3$	355.18	194-196	32.76	0.791
2d	-2,6- di chloro	C$_{18}$H$_{10}$Cl$_2$O$_3$	345.18	188-190	19.18	0.831
2e	-4- chloro	C$_{18}$H$_{11}$ClO$_3$	310.73	192-194	12.96	0.701
2f	-2- nitro	C$_{18}$H$_{11}$NO$_5$	321.28	196-198	35.8	0.531
2g	-4- methyl	C$_{19}$H$_{14}$O$_3$	290.31	95-97	38.96	0.811
2h	-3- nitro	C$_{18}$H$_{11}$NO$_5$	321.28	111-113	35.46	0.821
2i	-4- methoxy	C$_{19}$H$_{14}$O$_4$	306.31	150-152	45.73	0.751
2j	-4- floro	C$_{18}$H$_{11}$FO$_3$	294.28	125-127	40.35	0.801
2k	-4- nitro	C$_{18}$H$_{11}$NO$_5$	321.28	215-217	50.36	0.891
2l	-2- methoxy	C$_{19}$H$_{14}$O$_4$	306.31	130-132	19.86	0.682

Solvent Systems: [1]- Toluene: ethyl acetate: formic acid (4:2:1), [2]- Ethyl acetate: petroleum ether (2:1)

Table 3- Physical data of the 3-(5-(Substituted phenyl)-4, 5-dihydro-1H-pyrazol-3-yl)-2H-chromen-2-one (3a-3j)

Compound Code	Substitution (R)	Molecular Formula	Mol. Wt.	M. P. (°C)	Yield (%)	R$_f$
3a	-2,4- di chloro	C$_{18}$H$_{12}$Cl$_2$N$_2$O$_2$	359.21	105-107	77.09	0.551
3b	- 4- Bromo	C$_{18}$H$_{13}$BrN$_2$O$_2$	369.21	176-178	47	0.621
3c	-2,6- di chloro	C$_{18}$H$_{12}$Cl$_2$N$_2$O$_2$	359.21	158-160	66.09	0.742
3d	-4- chloro	C$_{18}$H$_{13}$ClN$_2$O$_2$	324.76	175-177	53.16	0.851
3e	-4- methyl	C$_{19}$H$_{16}$N$_2$O$_2$	304.34	165-167	40.09	0.651
3f	-3- nitro	C$_{18}$H$_{13}$N$_3$O$_4$	335.31	186-188	64.84	0.841
3g	-4- methoxy	C$_{19}$H$_{16}$N$_2$O$_3$	320.34	183-185	58.11	0.841
3h	-4- floro	C$_{18}$H$_{13}$FN$_2$O$_2$	308.31	174-176	24.85	0.792
3i	-4- nitro	C$_{18}$H$_{13}$N$_3$O$_4$	335.31	199-201	52.25	0.501
3j	-2- methoxy	C$_{19}$H$_{16}$N$_2$O$_3$	320.34	166-168	48.78	0.691

Solvent systems: [1]- Toluene: ethyl acetate: formic acid (4:2:1), [2]- Ethyl acetate: petroleum ether (2:1)

Role of Various Catalyst
Piperidine in Synthesis

Piperidine is an important amino compound in which nitrogen makes up part of ring. The nitrogen present in the piperidine has the tendency to share the pair of electrons which determines the entire chemical behavior of any amine (piperidine); their basicity and their action as nucleophiles. With this point they are extensively used in condensation processes as a base which catalysis the reaction in turn. The basic mechanism of coumarin synthesis (Fig. 1) in presence of the piperidine is discussed underneath :

STEP 1: Removal of acidic hydrogen from active methylene group

STEP 2: Nucleophilic attack

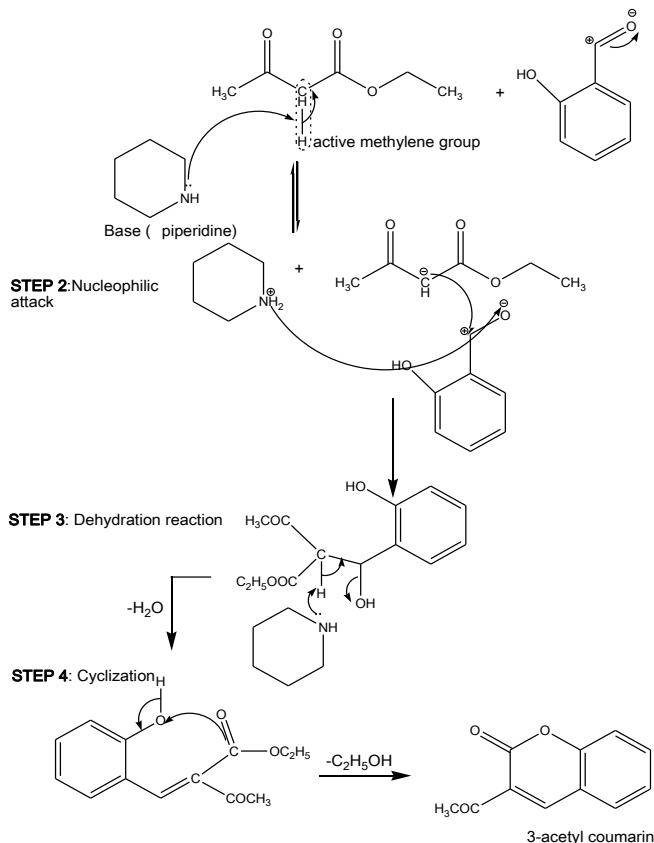**STEP 3**: Dehydration reaction

STEP 4: Cyclization

Fig.1- Catalyzing action of piperidine in reaction.

Thus piperidine acts as an effective base, as basicity of any amine is relative to the stability of its corresponding ions. Piperidine being aliphatic heterocyclic amine forms stable ion which relates to its use as basic catalyst in condensation reactions.

Diethylamine in Synthesis

Diethylamine is a simple aliphatic secondary amine type with two alkyl groups attached to the basic lone pair containing nitrogen atom. This amine compound is proposed for the reaction for synthesis of coumarin because this is simple amine compound where the study of effect of the alkyl group attached to the nitrogen atom could be done. The basicity of the compound could be studied same as that of the piperidine that is via stability of its ion. This study of basicity enables the diethylamine to be used as oxidizing catalyst in the Knoevenagel condensation reactions (coumarin synthesis). The mechanism of action of the diethylamine (Fig. 2) is detailed as:

STEP 1: Removal of acidic hydrogen from active methylene group

STEP 2: Nucleophilic attack

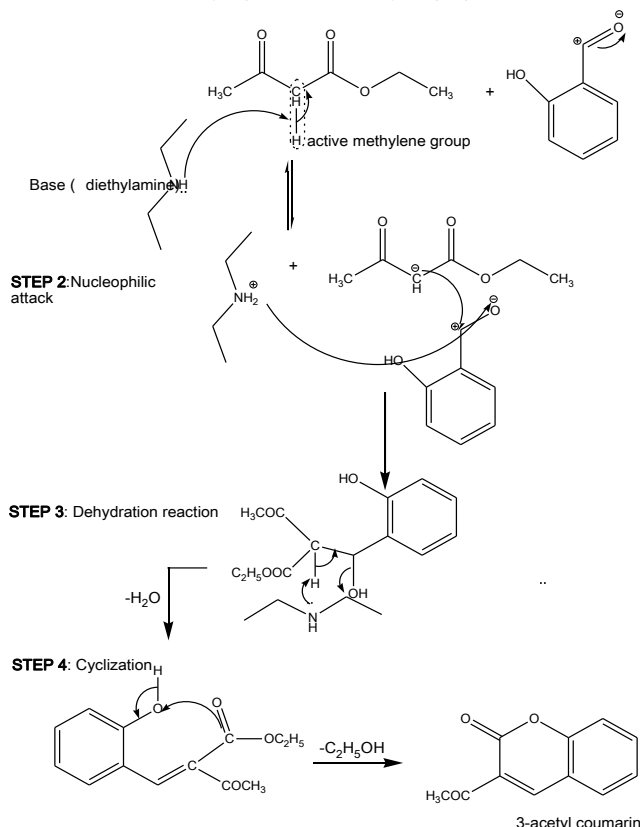**STEP 3**: Dehydration reaction

STEP 4: Cyclization

Fig. 2- Catalyzing action of diethylamine in reaction

Though the proposed mechanism of the diethylamine is same as that of piperidine difference comes in the basicity of the same due to more number of alkyl group attached to the nitrogen atom. This structural change improves the overall kinetics and efficiency of reaction as the fourth electron pair is more available for the catalytic action.

N- isopropylamine in synthesis

N- isopropylamine is another catalyst used which is again of aliphatic secondary amine class, but the variation in the structure is that the nitrogen atom is attached to only single carbon atom in the alkyl chain. This specification results in lesser availability of fourth pair of nitrogen atom for stabilization of its ion and showing of its basicity. Due to the formation of lesser stable ion of the N-isopropylamine results in weak base which shows poor result in the synthesis of the products of Knoevenagel condensation reactions.

Here structural relations are being put forward among the different catalysts used. Comparison between the heterocyclic structures is done with the aliphatic linear amines. Based on their structures it has been hypothesized that heterocyclic amine ring can be easily replaced by the aliphatic secondary amine derivatives in above discussed condensation reactions. Aliphatic amines are more basic relative to heterocyclic amines as explained by their stability of their ions formed. Diethylamine being aliphatic secondary amine has shown more effective results than compared to the piperidine which is a heterocyclic secondary amine compound. Thus from the results obtained it could be concluded that aliphatic

amines have more electronic cloud around them which make them more susceptible for being used as catalyst, while piperidine shows appreciable results but lesser than compared to the diethylamine. This effect could be explained as though both of them have same electronic cloud around them, but due to stearic hindrances the piperidine is less effective as dehydrating catalyst. To know the exact structure of compound which may shows effective results for the condensation, for this apart from comparing the cyclic structure with aliphatic one we have used two different aliphatic structural compounds- diethylamine and N- isopropylamine. Both the compounds have different arrangement of atoms around the nitrogen group. The effect of position of atoms has been demonstrated by the result thus obtained. It is being elucidated that when the nitrogen atom is surrounded by group of carbon atoms it shows an increased activity, while if nitrogen atom is terminally attached to carbon atoms shows weak activity even compared to the cyclic compounds. Thus on the basis of the structural studies the series of effect of their activity in decreasing order could be assumed as: diethylamine>piperidine>N- isopropylamine.

Conclusion

Coumarin derivatives could be synthesized by many mechanisms, but Knoevenagel synthesis mechanism has been used here. Till date piperidine has been used as dehydrating catalyst in this synthetic procedure. We have tried to study the effect of other secondary amine catalysts apart from piperidine. We have used diethylamine and N-isopropylamine (aliphatic secondary amines) to study their effect over cyclic secondary amines (piperidine). Result obtained showed that diethylamine has given the best yield of compounds among the three while the reaction time of the piperidine is least. Thus it could be concluded that in this synthesis diethylamine could be best substitution for the piperidine, while N-isopropylamine having irregular orientation of carbons around nitrogen group must be preferred least for synthesis of the coumarins by Knoevenagel condensation mechanism. Efforts are further being done to study other structural features which could be best alternatives for the above three catalysts studied in this research work.

Experimental
Chemistry

All the chemicals and reagents were obtained from Sigma (Germany) and CDH (India) and were recrystallized / redistilled as necessary. The melting points were determined by the open capillary tube method. The purity of the compounds was checked on thin layer chromatography (TLC) plates, which were precoated with silica gel G using solvent system toluene: ethyl acetate: formic acid (4:2:1) and ethyl acetate: petroleum ether (2:1). The spots were located under iodine vapors and ultraviolet (UV) light. *Infrared* (IR) spectra were recorded using KBr on Fourier transform infrared (FTIR) Shimadzu 8400S IR spectrophotometer (Japan). A JEOL AL300 FTNMR 300 MHz spectrometer was used to acquire High Resolution Nuclear Magnetic Resonance (^{1}HNMR) spectra with Acetone as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shift values are expressed in ppm. Mass spectra were obtained using a Kratos -AEI MS-902S instrument. Elemental analyses were carried out

with a Perkin Elmer Model 240-C apparatus (CDRI, Lucknow). The results of the elemental analysis (C, N, and S) were within ± 0.4% of the calculated amounts.

General Procedures for the Preparation of Compounds

Synthesis of 3-acetyl coumarin (1): General Procedure

Cold solution of ethylacetoacetate (0.2M, 5.13 ml) was taken in a beaker, salicyaldehyde (0.2M, 4.28 ml) was added in the solution dropwise with continuous stirring. 5-6 drops of catalyst (piperidine, diethylamine, and N- isopropylamine) was added in the reaction mixture with vigorous shaking. After few minutes yellow precipitate was separated out. The precipitate was filtered off, washed and recrystallized with ethanol. The purity of compounds was established on the basis of TLC. M.P. 111-113 ˚C, I.R. (KBr, cm^{-1}) 1677.95(C=O), 1454.23(Ar C=C), 757.97(Ar =C-H$_{def}$); ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm): δ 7.38-7.47 (m, 4H, Ar-H), 8.65 (s, 1H, H of coumarin), 2.5 (s, 3H, -CH$_3$); EIMS m/z: 189, 171, 135; Anal. Cal. C, 70.21; Found: C, 70.80.

Synthesis of 3-substituted phenyl-1-(3-coumarinyl) propan-1-ones (2a-2l): General Procedure

3-acetyl coumarin **(1)** (0.01M) was refluxed with substituted aromatic aldehyde (0.012 M) in the presence of *n*-butanol (10 ml) at a temperature of 40-50ºC, after 15-20 min 0.3 ml of glacial acetic acid and catalyst (piperidine, diethylamine, and N- isopropylamine) were added in the reaction mixture, refluxing was continued. After completion of reaction solvent was completely removed by evaporation. The precipitate obtained was washed with ethanol and recrystallized with appropriate solvent.

Synthesis of 3-(3-(2,4-dimethoxyphenyl)acryloyl)-2*H*-chromen -2-one (2a)

It was obtained from reaction of compound (1) with with 2, 4-dimethoxy benzaldehyde. IR (KBr, cm^{-1}): 1556.45 (Ar C=C), 1606.59 (- C= Cstr),1384.79 (Ar-C-OCH$_3$), 1172.64 (-OCH$_3$); ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm): δ 7.02-7.27 (m, 8H, Ar-H), 8.49 (s, 1H, H of coumarin), 4.25 (dd, 1H, H cis of ethylene), 3.50 (dd, ^{1}H, H trans of ethylene), 3.37 (s, 6H, -OCH$_3$); Anal. Cal. C, 71.42; Found: C, 71.50.

Synthesis of 3-(3-(2, 4-dichlorophenyl)acryloyl)-2*H*-chromen-2 -one (2b)

It was obtained from reaction of compound (1) with with 2, 4-dichloro benzaldehyde. IR (KBr,cm^{-1}): 1677.95(C=O), 1454.23(Ar C=C), 757.97(Ar =C-Hdef), 1080.06 (Ar C-Cl); ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ ppm): δ 7.22-7.38 (m, 8H, Ar-H), 8.40 (s, 1H, H of coumarin), 4.15 (dd, 1H, H cis of ethylene), 3.18 (dd, 1H, H trans of ethylene); Anal. Cal. C, 62.63; Found, C, 63.12%.

Synthesis of 3-(3-(4-bromophenyl)acryloyl)-2*H*-chromen-2-one (2c)

It was obtained from reaction of compound (1) with with 4-bromo benzaldehyde.IR (KBr, cm^{-1}): 1456.55(Ar-C=C),1676.36(-C=O), 1610.52 (- C= C$_{str}$), 658(C-Br) ; ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm):δ 7.02-7.38 (m, 8H, Ar-H), 8.48 (s, 1H, H of coumarin), 4.05 (dd, 1H, H $_{cis}$ of ethylene), 3.28 (dd, 1H, H$_{trans}$ of ethylene); Anal. Cal. C, 60.87; Found: C, 61.23.

Synthesis of 3-(3-(2, 6-dichlorophenyl)acryloyl)-2*H*-chromen-2-one (2d)

It was obtained from reaction of compound (1) with 2,6-dichloro benzaldehyde. IR (KBr, cm-1): 1527.52 (Ar-C=C),1660.60 (-C=O), 1608.52 (- C= C$_{str}$), 979.77 (Ar C-Cl) ; ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm):δ 7.02-7.27 (m, 8H, Ar-H), 8.45 (s, 1H, H of coumarin), 4.15 (dd, 1H, H$_{cis}$ of ethylene), 3.54 (dd, 1H, H$_{trans}$ of ethylene); Anal. Cal. C, 62.63; Found, C, 61.23.

Synthesis of 3-(3-(4-chlorophenyl)acryloyl)-2*H*-chromen-2-one (2e)

It was obtained from reaction of compound (1) with 4-chloro benzaldehyde. IR (KBr, cm-1): 1454.23 (Ar-C=C),1666.38 (-C=O), 1608.52 (- C= C$_{str}$), 1078.43 (Ar C-Cl) ; ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm):δ 7.32-7.46 (m, 8H, Ar-H), 8.5 (s, 1H, H of coumarin), 4.94 (dd, 1H, H$_{cis}$ of ethylene), 4.85 (dd, 1H, H$_{trans}$ of ethylene); ESI-ms m/z = 311,275,189; Anal. Cal. C, 69.58; Found, C, 68.89.

Synthesis of 3-(3-(2-nitrophenyl)acryloyl)-2*H*-chromen-2-one (2f)

It was obtained from reaction of compound (1) with 2-nitro benzaldehyde. IR (KBr, cm-1): 1480.90 (Ar-C=C),1622.02 (-C=O), 1525.59 (- C= C$_{str}$), 1488.94 (symmt N-O of NO$_2$), 1350.08 (asymmt N-O of NO$_2$) ; ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm):δ 7.02-8.14 (m, 8H, Ar-H), 8.49 (s, 1H, H of coumarin), 4.58 (dd, 1H, H$_{cis}$ of ethylene), 3.52 (dd, 1H, H$_{trans}$ of ethylene); Anal. Cal. C, 67.29; Found, C: 67.53.

Synthesis of 3-(3-(4-methylphenyl)acryloyl)-2*H*-chromen-2-one (2g)

It was obtained from reaction of compound (1) with 4-methyl benzaldehyde. IR (KBr, cm-1): 1484.35 (Ar-C=C),1620.98 (-C=O), 1524.05 (- C= C$_{str}$); ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm):δ 7.02-7.27 (m, 8H, Ar-H), 8.48 (s, 1H, H of coumarin), 4.05 (dd, 1H, H$_{cis}$ of ethylene), 3.50 (dd, 1H, H$_{trans}$ of ethylene), 2.35 (s, 3H of CH$_3$); Anal. Cal. C, 78.61; Found: C, 78.54.

Synthesis of 3-(3-(3-nitrophenyl)acryloyl)-2*H*-chromen-2-one (2h)

It was obtained from reaction of compound (1) with 3-nitro benzaldehyde. IR (KBr, cm-1)Vmax: 1452.30 (Ar-C=C),1606.59 (-C=O), 1552.59 (- C= C$_{str}$), 1527.52 (symmt N-O of NO$_2$), 1348.15 (assymt N-O of NO$_2$); ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm):δ 7.02-8.23 (m, 8H, Ar-H), 8.48 (s, 1H, H of coumarin), 4.15 (dd, 1H, H$_{cis}$ of ethylene), 3.54 (dd, 1H, H$_{trans}$ of ethylene), 2.35 (s, 3H of CH$_3$); ESI-ms m/z: 322, 275, 232, 209; Anal. Cal. C, 67.29, N, 4.36; Found: C, 66.99, N, 4.62.

Synthesis of 3-(3-(4-methoxyphenyl)acryloyl)-2*H*-chromen-2-one (2i)

It was obtained from reaction of compound (1) with 4-methoxy benzaldehyde. IR (KBr, cm-1): 1552.39 (Ar C=C), 1610.32 (- C= C$_{str}$),1380.55 (Ar-C-OCH$_3$), 1170.54 (-OCH$_3$); ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm): 6.72-7.27 (m, 8H, H of coumarin), 4.04 (dd, 1H, H$_{cis}$ of ethylene), 3.50 (dd, 1H, H$_{trans}$ of ethylene), 3.73 (s, 3H of -OCH$_3$); Anal. Cal. C, 74.50; Found, C, 74.00.

Synthesis of 3-(3-(4-florophenyl)acryloyl)-2*H*-chromen-2-one (2j)

It was obtained from reaction of compound (1) with 4-floro benzaldehyde. IR (KBr, cm-1): 1488.96 (Ar C=C), 1456.16 (-C= C$_{str}$),1072 (Ar-C-F) ; ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm): 6.92-7.28 (m, 8H, Ar-H), 8.47 (s, 1H, H of coumarin), 4.04 (dd, 1H, H$_{cis}$ of ethylene), 3.42 (dd, 1H, H$_{trans}$ of ethylene); Anal. Cal. C, 73.47; Found, C, 73.54.

Synthesis of 3-(3-(4-nitrophenyl)acryloyl)-2*H*-chromen-2-one (2k)

It was obtained from reaction of compound (1) with 4-nitro benzaldehyde. IR (KBr, cm-1): 1488.94 (Ar C=C), 1456.16 (- C= C$_{str}$),1515.94 (symmt N-O of NO$_2$), 1340.43(assymt N-O of NO$_2$) ; ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm): 7.02-8.14 (m, 8H, Ar-H), 8.48 (s, 1H, H of coumarin), 4.32 (dd, 1H, H$_{cis}$ of ethylene), 3.50 (dd, 1H, H$_{trans}$ of ethylene); Anal. Cal. C, 67.29, N, 4.36; Found: C, 67.14, N, 4.32.

Synthesis of 3-(3-(2-methoxyphenyl)acryloyl)-2*H*-chromen-2-one (2l)

It was obtained from reaction of compound (1) with 2-methoxy benzaldehyde. IR (KBr,cm-1): 1550.36 (Ar C=C), 1620.11 (- C= C$_{str}$),1382.54 (Ar-C-OCH$_3$), 1159.66 (-OCH$_3$); ^{1}H NMR (CDCl$_3$-d$_6$ 300MHz, δ, ppm): 6.72-7.27 (m, 8H, Ar-H), 8.48 (s, 1H, H of coumarin), 4.04 (dd, 1H, H$_{cis}$ of ethylene), 3.50 (dd, 1H, H$_{trans}$ of ethylene), 3.73 (s, 3H of -OCH$_3$); Anal. Cal. C, 74.50; Found: C, 73.99.

Synthesis of 3-(4, 5-dihydro-5-substituted phenyl-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3a-3j): general procedure

3-substitutedphenyl-1-(3-coumarinyl)propan-1-ones (2) (0.05M) were dissolved in pyridine (30 ml) with slight heating, hydrazine hydrate (0.2 M) was added to the reaction mixture and refluxed for 5-6 h. On completion of reaction, reaction mixture was neutralized by 2N hydrochloric acid, than rection mixture was poured onto the crushed ice; the precipitate obtained was filtered, dried and recrystallized with appropriate solvent.

Synthesis of 3-(5-(2,4-dichlorophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3a)

It was obtained from reaction of compound (2b) with hydrazine hydrate. IR (KBr, cm-1): 1454.35(Ar C=C), 1600.74(C=N), 1080.06 (Ar-Cl); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$, δ, ppm): δ 6.23-7.27 (m, 13H, aromatic proton), 7.46 (s, 1H, coumarin), 4.86 (d, 1H, 5-H of pyrazoline), 3.03(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.32 (d, 1H, 4-H$_{cis}$ of pyrazoline), 3.37(s, 3H, -OCH$_3$); Anal. Cal. C, 73.23; N, 6.57; Found: C, 73.26; N, 6.8.

Synthesis of 3-(5-(4-bromophenyl)-4, 5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3b)

It was obtained from reaction of compound (2c) with hydrazine hydrate. IR (KBr, cm-1) 1450.66(Ar C=C), 1623.53(C=N), 658(C-Br); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ, ppm): δ 7.01-7.38 (m, 13H, aromatic proton), 7.46 (s, 1H, coumarin), 4.89 (d, 1H, 5-H of pyrazoline), 3.28(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.33 (d, 1H, 4-H$_{trans}$ of pyrazoline); Anal. Cal. C, 58.56 N, 7.59; Found: C, 59.02; N, 7.11.

Synthesis of 3-(5-(2, 6-dichlorophenyl)-4, 5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3c)

It was obtained from reaction of compound (2d) with hydrazine hydrate.IR (KBr, cm^{-1}): 1455.73 (Ar C=C), 1619.33(C=N), 3285.59 (Ar N-H), 1082.35(Ar-Cl); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ, ppm): δ 6.96-7.27 (m, 13H, aromatic proton), 7.46 (s, 1H, coumarin), 4.56 (d, 1H, 5-H of pyrazoline), 3.29(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.33 (d, 1H, 4-H$_{cis}$ of pyrazoline); Anal. Cal. C, 60.19; N, 7.80; Found: C, 60.35; N, 8.00.

Synthesis of 3-(5-(4-chlorophenyl)-4, 5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3d)

It was obtained from reaction of compound (2e) with hydrazine hydrate. IR (KBr, cm^{-1}): 1488.94(Ar C=C), 1622.02(C=N), 3282.62 (Ar N-H), 1091.63(Ar-Cl); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ, ppm): δ 7.01-7.28 (m, 13H, aromatic proton), 7.40 (s, 1H, coumarin), 5.01 (d, 1H, 5-H of pyrazoline), 3.30(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.33 (d, 1H, 4-H$_{cis}$ of pyrazoline); ESI-ms m/z: 323, 279, 207; Anal. Cal. C, 66.57; N, 8.63; Found: C, 66.43; N, 8.27.

Synthesis of 3-(5-(4-methylphenyl)-4, 5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3e)

It was obtained from reaction of compound (2g) with hydrazine hydrate. IR (KBr, cm^{-1}): 1469.38(Ar C=C), 1620.58(C=N), 3284.89 (Ar N-H); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ, ppm): δ 7.00-7.27 (m, 13H, aromatic proton), 7.42 (s, 1H, coumarin), 4.55 (d, 1H, 5-H of pyrazoline), 3.29(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.31 (d, 1H, 4-H$_{cis}$ of pyrazoline), 2.35 (s, 3H, -CH$_3$); Anal. Cal. C, 74.98; N, 9.20; Found: C, 73.84; N, 8.56.

Synthesis of 3-(5-(3-nitrophenyl)-4, 5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one derivatives (3f)

It was obtained from reaction of compound (2h) with hydrazine hydrate. IR (KBr, cm^{-1}): 1458.08(Ar C=C), 1622.02(C=N), 3274.90 (Ar N-H), 1488.94(Symmt =N-O of NO$_2$), 1350.08(Asymmt =N-O of NO$_2$); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ ppm): δ 6.90-8.07 (m, 13H, aromatic proton), 7.49 (s, 1H, coumarin), 4.86 (d, 1H, 5-H of pyrazoline), 3.30(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.33 (d, 1H, 4-H$_{cis}$ of pyrazoline); ESI-ms m/z: 336, 219, 199; Anal. Cal. C, 64.47; N, 12.53; Found: C, 64.52; N, 11.98.

Synthesis of 3-(5-(4-methoxyphenyl)-4,5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3g)

It was obtained from reaction of compound (2i) with hydrazine hydrate. IR (KBr, cm^{-1}) 1454.69(Ar C=C), 1634.44(C=N), 3268.75 (Ar N-H), 1172.64(-OCH$_3$); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ ppm): δ 6.72-7.27 (m, 13H, aromatic proton), 7.46 (s, 1H, coumarin), 4.80 (d, 1H, 5-H of pyrazoline), 3.301(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.305 (d, 1H, 4-H$_{cis}$ of pyrazoline), 3.73 (s, 3H, -OCH$_3$); Anal. Cal. C, 71.24; N, 8.74; Found: C, 70.68; N, 8.55.

Synthesis of 3-(5-(4-florophenyl)-4, 5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3h)

It was obtained from reaction of compound (2j) with hydrazine hydrate. IR (KBr, cm^{-1}) 1454.69(Ar C=C), 1634.44(C=N), 3268.75 (Ar N-H), 1078.13 (Ar C-F); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ ppm): δ 6.813-7.5 (m, 13H, aromatic proton), 7.49 (s, 1H, coumarin), 4.86 (d, 1H, 5-H of pyrazoline), 3.25(d, 1H, 4-H$_{trans}$ of pyrazo-

line), 3.307 (d, 1H, 4-H$_{cis}$ of pyrazoline); ESI-ms m/z: 307, 280, 219, 198; Anal. Cal. C, 70.12; N, 9.09; Found, C, 69.86; N, 9.13.

Synthesis of 3-(5-(4-nitrophenyl)-4, 5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3i)

It was obtained from reaction of compound (2k) with hydrazine hydrate. IR (KBr, cm^{-1}): 1488.94(Ar C=C), 1558.38(C=N), 3234.40 (Ar N-H), 1519.80(symmt =N-O of NO$_2$), 1340.43(Asymmt =N-O of NO$_2$); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ, ppm): δ 7.02-8.14 (m, 13H, aromatic proton), 7.46 (s, 1H, coumarin), 4.86 (d, 1H, 5-H of pyrazoline), 3.301(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.305 (d, 1H, 4-H$_{cis}$ of pyrazoline); ESI-ms m/z: 323, 281, 232; Anal. Cal. C, 64.47; N, 12.53; Found, C, 64.30; N, 12.81.

Synthesis of 3-(5-(2-methoxyphenyl)-4, 5-dihydro-1*H*-pyrazol-3-yl)-2*H*-chromen-2-one (3j)

It was obtained from reaction of compound (2l) with hydrazine hydrate. IR (KBr, cm^{-1}): 1480.76(Ar C=C), 1554.28(C=N), 3245.12 (Ar N-H), 1177.12 (-OCH$_3$); ^{1}H-NMR (CDCl$_3$/DMSO-d$_6$ 300 MHz, δ ppm): δ 6.72-7.27 (m, 13H, aromatic proton), 7.65 (s, 1H, coumarin), 4.82 (d, 1H, 5-H of pyrazoline), 3.23(d, 1H, 4-H$_{trans}$ of pyrazoline), 3.30 (d, 1H, 4-H$_{cis}$ of pyrazoline), 3.73 (s, 3H, -OCH$_3$); Anal. Cal. C, 71.24, N, 8.74; Found, C, 70.85, N, 8.34.

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