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Design, prediction of bioactivity by physicochemical parameters and Synthesis of Schiff bases of 8-Amino chromone derivatives

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Abstract: *Drug-design and synthesis leading to the Drug discovery is the area of thirst today. The prediction of the bioassay of the drug before synthesis is treated as the novel approach in drug design. Chromones have drawn the attention of many pharmacologists because of their good biological activities like anti-cancer, antioxidant, antimicrobial, antibiotic, anti HIV, and as good vasodilators and were preferred due to their less mammalian toxicity. In this paper, the authors presented the synthesis and antimicrobial activities of Schiff bases of some chromones. The Schiff base is an important class of chemicals which acts as good intermediates for synthesis of many drugs. Schiff bases of* ***8-amino-7-hydroxy-2 methyl (or phenyl)-3-methyl chromones 4(a-d)*** *with a series of selected aldehydes* ***5(a-c)*** *were synthesized. The synthesized compounds* ***8-((phenylimino)methyl)-7-hydroxy-3-methyl-2-phenyl)-4H-Chromen-4-one, 6(a-l)*** *were formed. The newly synthesized compounds were characterized by spectral analysis like IR, NMR and Mass spectrometry.*

Key Words*: Prediction of bioassay, Physicochemical approach, Schiff base, Synthesis.*

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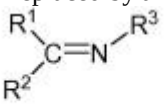
I. Introduction

Chromone derivatives are very versatile molecules in view of their biological importance. Apart from biological activities, many chromones show very well fluorescent activities and optical activities, which has to be extracted fully for biological or other industrial applications. Chromones and flavones were found ubiquitously in different parts of plants[1]. Many chromone derivatives were found to be potent biologically active molecules and were identified as lead molecules[2]. In recent history, vigorous work has been going on to modify these lead molecules suitable to increase the efficacy of the molecule and at the same time reduce the additional properties[3]. In this context, the amino chromones or nitro chromones (chromone moiety with functional groups containing nitrogen) were extensively studied and its derivatives were found to be used as anticancer, anti-HIV, anti-malarial [4-6] etc. The presence of nitrogen in the chromone moiety enhances its biological activity. Many patents have been obtained for such chromone derivatives[7].

Schiff bases, [8] are formed when any primary amine reacts with an aldehyde or a ketone under specific conditions. Structurally, a Schiff base (also known as imine or azomethine) is a nitrogen analog of an aldehyde or ketone in which the carbonyl group (C=O) has been replaced by an imine or azomethine.



R^1, R^2, and/or R^3 = alkyl or aryl

Schiff's bases are now gaining importance due to the ease of the synthesis and also the efficiency as an antagonist to microbial activities[9,10]. Also, Schiff bases have potential to form complexes with almost all biologically accepted metal ions and this enhances the antagonist properties of the ligands[11]. After studying the biological activities of the Schiff bases of 8-formyl chromones, we focused on flipping the functional groups i.e. we now synthesized the 8-amino-7-hydroxy-6-(substituted)-3-methyl- 2-phenyl chromones and then condensed the amines with series of aldehydes to obtain the 8-(amino methylene) substituted 7-hydroxy chromone derivatives.

II. Design and synthesis of the novel chromone derivatives

The First step before going for the synthesis of the8-(amino methylene) substituted 7-hydroxy chromone derivatives, the authors carried out a new designing approach to design and predict the biological activities of the molecules.

Prediction of bioassay of the Designed molecules:

This involves the designing of the schiff base derivatives of 8-Amino-7-hydroxy-2 methyl (or phenyl)-3-methyl chromones. The newly designed molecules were subjected to pre-synthetic physicochemical parameter study. This study helps us to predict the bio diffusivity and efficacy of the molecule as a biological important molecule.

Structure of the designed molecules: I (a-d), II (a-d) and III (a-d)

I (a-d) II (a-d) III (a-d)

Where for I, II, III (a-d): a: R = H, b: R = Cl, c: R= Br, d: R = CH3.

Figure 1.1 showing the structure of the designed compounds

Physicochemical parameters like partition coefficient i.e.(ClogP), is the measure of diffusivity of the molecule into the cell membrane[12], Molecular refractivity(MR) which is the measure of polarizability/solubility of the molecule[13] and the (tPSA) which accounts for the toxicity of the molecule[14] and the molecular weight(MW) which suggests the size of the molecule[15]. The quantitative physicochemical parameters for the above molecules were tabulated in the ***(Table1.1.)*** below:

Compound	C logP	MR	M.W.	tPSA
I a	4.186	107.44	355.39	58.89
I b	4.69	112.05	389.83	58.89
I c	4.89	115.13	434.28	58.89
I d	4.635	113.34	369.41	58.89
II a	3.36	99.96	345.35	68.12
II b	3.886	104.57	379.79	68.12
II c	4.067	107.65	424.24	68.12
II d	3.811	105.86	359.37	68.12
III a	4.685	113.34	369.41	58.89
III b	5.189	117.94	403.86	58.89
III c	5.38	121.03	448.31	58.89
III d	5.134	119.24	383.44	58.89

Table 1.1 showing the physicochemical parameters of the designed compounds

According to the quantitative physicochemical parameter study, by observing the Clog P values of the compounds, except for the last three molecules i.e.**(IIIb, IIIc,** and **IIId)**, all other compounds are having log P values less than **5**, which is optimum for the diffusivity according to Lipinski's rule of 5[16], then the Molecular refractivity lies within the limits of (90-140) [17] may be predicted to have good solubility. We consider the tPSA values within 90[17] **c**an predict that the molecules **Ia, Ib, IIa, IIb, IId, IIIa** may be having good oral bioavailability. However, we have synthesized all the twelve molecules and conducted an evaluation of bioactivity to check the validity of the same.

III. Synthesis of 8-(Benzylidene (substituted-methylene) amino)-7-hydroxy-6-(substituted)-3-methyl-2-phenyl-4H- chromen-4-ones.

Synthesis of schiff base of 8-Amino-7-hydroxy-3-methyl-2-phenyl chromone **1(a-d)** Involves four steps

1. Synthesis of 7-Hydroxy-3-methyl-2-phenyl-4*H*-chromen-4-one **4(a-d):**
2. Synthesis of 8-Nitro-7-hydroxy-3-methyl-2-phenyl-4*H*-chromen-4-one **6(a-d)**
3. Synthesis 8-Amino-7-hydroxy-3-methyl-2-phenyl-4*H*- chromen-4-one **7(a-d)**
4. Synthesis of 8-(Benzylidene (substituted-methylene) amino)-7-hydroxy-6-(substituted)-3-methyl-2-phenyl-4H- chromen-4-one)-4*H*-chromen-4-one **9(a-l)**

Step 1.: Synthesis of 7-hydroxy-3-methyl-2-phenyl-4H- chromen-4-one 4(a-d):
The compound 7-Hydroxy-3-methyl-2-phenyl chromen-4-one can be synthesized either by the modified Baker-Venkataraman transformations[18,19]

Step 2: Synthesis of 8-nitro-7-hydroxy-3-methyl-2-phenyl-4H- chromen-4-one*: 6(a-d)*
7-Hydroxy-3-methyl-2-phenyl chromones **(4a)** was treated with nitrating mixture maintained at 0-5^{o}C. The mixture was stirred well and allowed to stand for overnight. Then the contents were poured into crushed ice. The solid separated is filtered and dried. The solid was recrystallised using hot methanol to afford the title compound **(6a)** in 65-75%yield m.p. 301^{o}C, a (literature m.p. 300^{o} C) [20] ***(Scheme2)***

4a **6a**

Scheme2 showing the synthesis of 8-Nitro-7-hydroxy-3-methyl-2-phenyl-4*H*- chromen-4-one 17a

Similar method was adopted to synthesize 8-Nitro-7-hydroxy-6-chloro-3-methyl-2-phenyl chromone**(6b),** 8-Nitro-7-hydroxy-6-bromo-3-methyl-2-phenyl chromone **(6c),** 8-Nitro-7-hydroxy-3,6-dimethyl-2-phenyl chromone **(6d)** as in ***(Scheme2′)*** from 7-Hydroxy-6-chloro-3-methyl-2-phenyl chromone **(4b),** 7-Hydroxy-6-bromo-3-methyl-2-phenyl chromone and **(4c)** and 7-Hydroxy-6-chloro-3-methyl-2-phenyl chromone **(4d)** respectively.

4(b-d) **6(b-d)**
For 16 and 17: **b c d**
R_1 = Cl Br CH_3

***Scheme2′* showing the synthesis of 6(b-d) from 4(b-d)**

Step 3: Synthesis 8-Amino-7-hydroxy-3-methyl-2-phenyl-4H-chromen-4-one 7(a-d)
8-Nitro-7-hydroxy-3-methyl-2-phenyl chromone in ethanol was refluxed with stirring for half an hour. Then added the catalytic amount of tin solution (tin powder in conc. HCl) to the above solution and reflux was continued for an hour. The yellow coloured liquid obtained was neutralized with saturated Na_2CO_3 soln. A beige coloured precipitate was formed. It was cooled in ice bath, filtered and dried. The solid obtained was recrystallised from hot ethanol to afford **(7a)** in good yields ***(Scheme3).*** Yield 75-80%, sharp m.p.at 257^{o}C (lit. mp 258^{o}C)[21]
Similar procedure was adopted to synthesize 8-Amino-7-hydroxy-6-chloro-3-methyl-2-phenyl-chromone **(7b),** 8-Amino-7-hydroxy-6-bromo-3-methyl-2-phenyl-chromone **(7c)** and 8-Amino-7-hydroxy-3,6-dimethyl-2-phenyl-chromone **(7d)** correspondingly by taking the **(6b), (6c)** and **(6d)**.

6(a-d) **7(a-d)**
For 6 and 7: **a b c d**
R_1 = H Cl Br CH_3

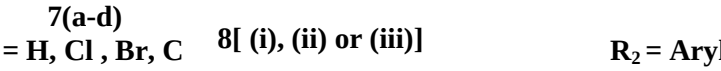
Scheme3 showing the synthesis of 8-Amino-7-hydroxy-3-methyl-2-phenyl chromen-4-one

Step 4: Synthesis of 8-(Benzylidene (substituted-methylene) amino)-7-hydroxy-6-(substituted)-3-methyl-2-phenyl-4H- chromen-4-ones: 9(a-l)
Selected aryl or heteroaryl aldehyde 8(i-iii) was taken in ethanol and stirred well. To this, a solution of 8-Amino-7-hydroxy-3-methyl-2-phenyl chromen-4-one in ethanol was added dropwise with stirring. A catalytic amount of glacial acetic acid was added and the contents were heated at reflux for about 3-4 h. After completion of the reaction, the solution was neutralized and poured into crushed ice. The solid separated was

filtered, dried and recrystallised from dichloromethane. The product **(9a)** was obtained ***(Scheme4)*** in good yields (76-84%).m.p.235-237^{o}C

Scheme4 showing the synthesis of 8-((Benzylidene methylene) amino)-7-hydroxy-3-methyl-2-phenyl-4H-chromen-4-one

By employing the similar procedure, **7(a-d)** were made to react with to form a series of Schiff's bases **9(a-l)** as shown by (Scheme4′)



Scheme 4 ′showing the synthesis 8-(Benzylidene (substituted-methylene) amino)-7-hydroxy-6-(substituted)-3-methyl-2-phenyl-4H- chromen-4-ones *9(a-l)*

Table 1.2 showing the structural details of the synthesized molecules:

Comp	R_1	R_2	Comp	R_1	R_2
9a	H	C_6H_5CHO	9g	Br	C_4H_3OCHO
9b	Cl	C_6H_5CHO	9h	CH_3	C_4H_3OCHO
9c	Br	C_6H_5CHO	9i	H	C_7H_7CHO
9d	CH_3	C_6H_5CHO	9j	Cl	C_7H_7CHO
9e	H	C_4H_3OCHO	9k	Br	C_7H_7CHO
9f	Cl	C_4H_3OCHO	9l	CH_3	C_7H_7CHO

Table 1.2 showing the structural details of the synthesized molecules

Structure of all the newly synthesized compounds were elucidated using IR, ^{1}H NMR, ^{13}C NMR and Mass spectra In IR spectrum (KBr)(cm^{-1}), 3450, 3219 (OH),1625(C=N),1580,disappearance of the peak at 1305 indicates the formation of imine Schiff base. In the ^{1}H NMR (400 MHz, DMSO-d_6), found at δ10.7 (OH), One methyl group C-3 appeared as a singlet at δ 2.5. Protons at C-5 and C-6, both appeared as doublets at 6.82 (J=8Hz) and 7.5(J=8.2Hz). δ 9.1(s, CH=N), δ6.9-8.1(m,Ar-protons); In the ^{13} C NMR(100MHz, DMSO-d_6) δ176.7(C=O),162.9(C-OH),159.9(C=N) appeared, confirming the formation of (–CH=N), 126.8-136.44(Aromatic carbons), 11.3(C-3) for CH_3. In the EIMS, the M^+ appeared at m/z355.02, corresponding the molecular weight of the above compound.

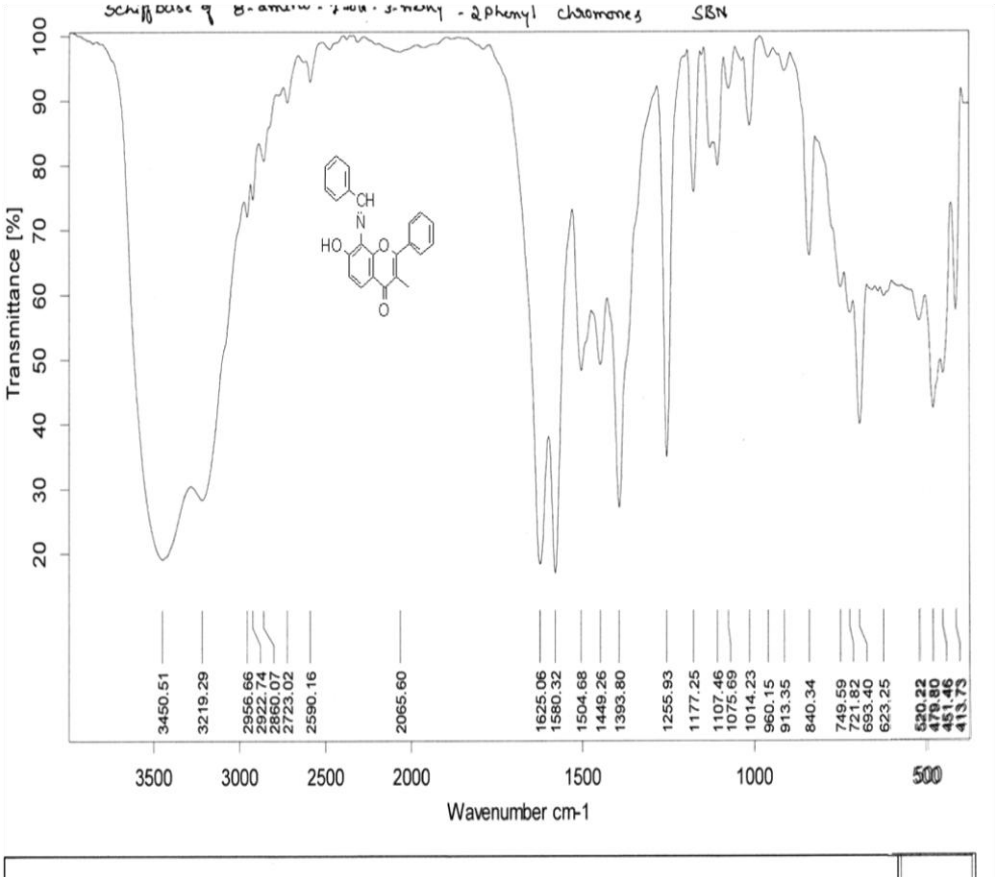


Fig. 3 showing FTIR of the compound 9a

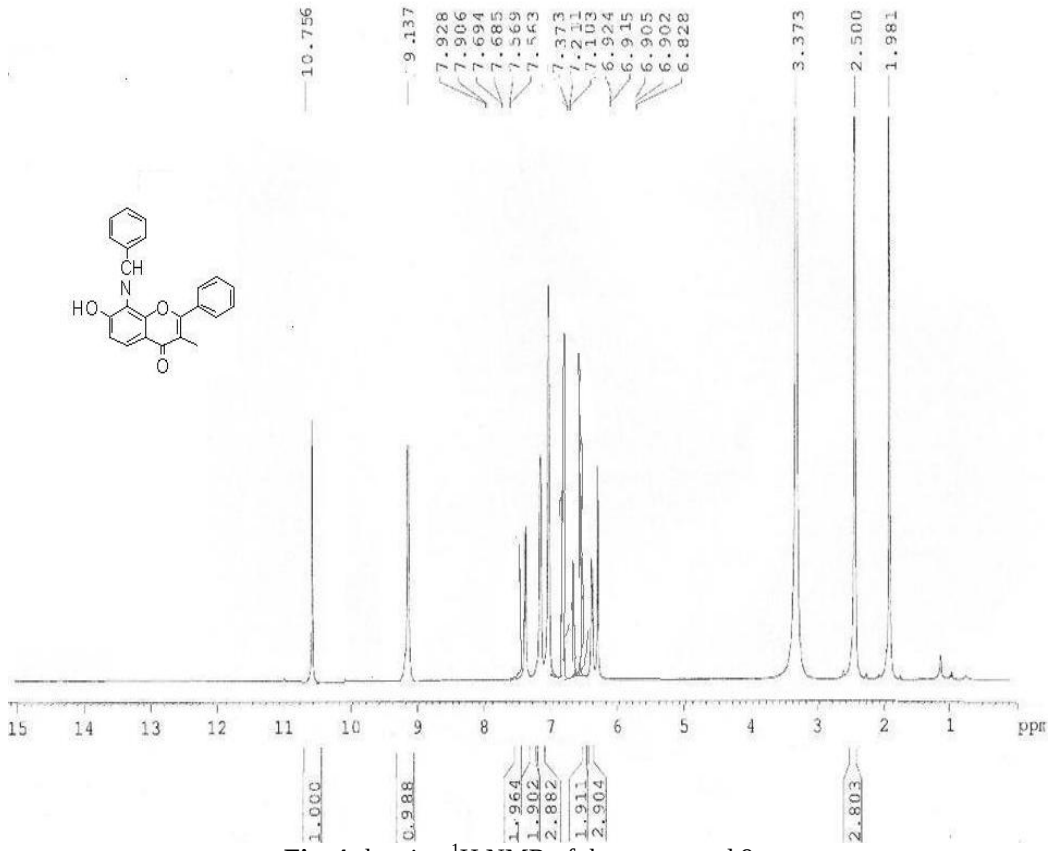


Fig. 4 showing ^{1}H NMR of the compound 9a

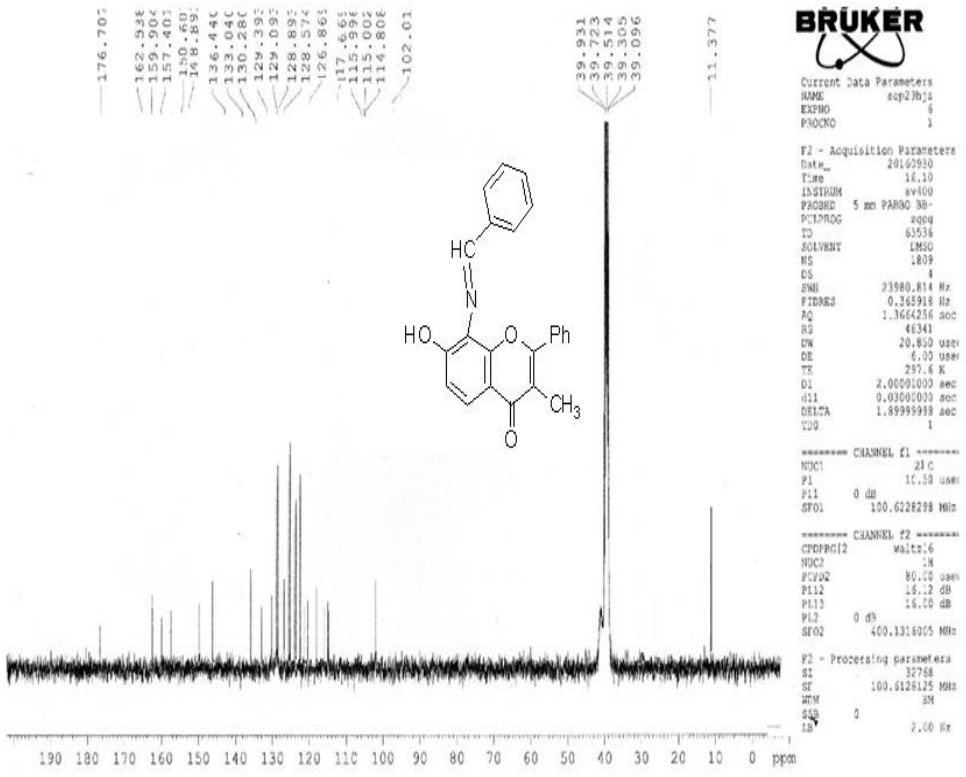


Fig. 5 showing ^{13}C NMR of the compound 9a

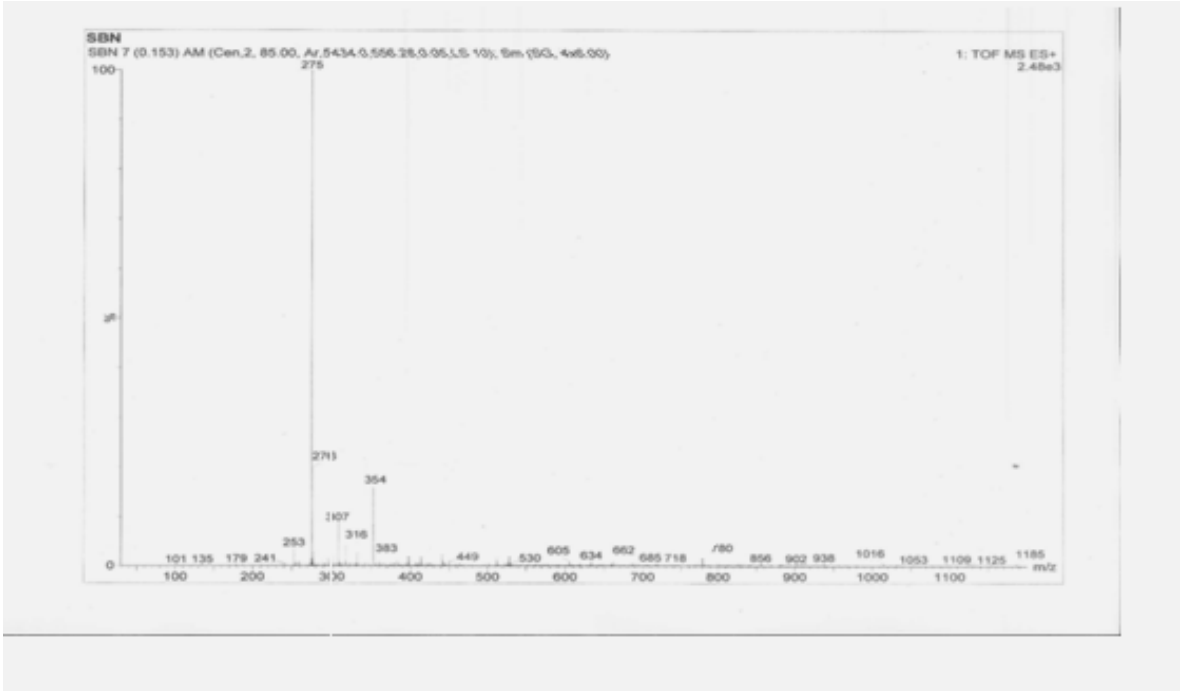


Fig 6 showing mass spectrum of the compound 9a

III. Experimental

Synthesis of 8-Nitro-7-hydroxy-3-methyl-2-phenyl-4H- chromen-4-one 6(a-d):

General procedure :

5mL of conc. H_2SO_4 in a 100mL beaker. Cool it in an ice bath (at 0^oC) then added 5mL of conc. HNO_3 to this and let it remain in that condition for 5-10 min. Then added 7-hydroxy-3-methyl-2-phenyl chromone **(4a)** (1g) slowly pinch by pinch (in small portions) with stirring. The reaction mixture was stirred for 10-15min. The beaker with contents was removed from the ice bath and kept at room temperature overnight. The contents of the beaker were transferred into a beaker containing crushed ice and stirred. The residue obtained was filtered and dried. The crude powder was then heated in alcohol(methanol) and boiled and filtered. The filtrate was collected in a teared dish and the methanol was evaporated to leave the white tiny crystals **(6a)** of the title compound. Yield obtained was 85%, mp 298-300^{o}C (lit mp 300^{o}C)

Synthesis of 8-Amino-7-hydroxy-3-methyl-2-phenyl-4H- chromones 7(a-d):

General procedure:

The 8-Nitro-7-hydroxy-3-methyl-2-phenyl chromone (**6a**) (1.67g) was taken in a dry 100mL round bottom flask. To this added 5mL of ethanol and stirred, then it is refluxed with stirring for half an hour. Then a 3mL solution of tin solution (0.5g of tin 10mL of con.HCl) was added dropwise into the flask and reflux was continued for one and half hour. The resulted soln (light yellow colored) was diluted with water (2mL) and then neutralized with Conc. Na_2CO_3 soln. dropwise. A white (beige) precipitate appeared. It is cooled in ice and filtered and dried. The compound obtained was boiled with ethanol (minimum) and filtered and recrystallised to afford the 8-Amino-7-hydroxy-3-methyl-2-phenyl chromones. m.p. 257^{o}C (Lite m.p.257 -258 ^{o}C). Adopting the similar procedure, compounds **7(b-d)** were prepared by taking the starting materials from **6(b-d).**

Synthesis of 8-(Benzylidene (substituted-methylene) amino)-7-hydroxy-6-(substituted)-3-methyl-2-phenyl-4H- chromen-4-one)-4*H*-chromen-4-one 9(a-l)

General procedure:

Benzaldehyde **(8 i)**, Furfural (**8 ii)**, 4-Methyl benzaldehyde **(8 iii)**) was dissolved in 2mL of ethanol and stirred for half an hour. To this ethanolic solution of the compound **(7a)** (0.5150g) was added dropwise with stirring. one drop of glacial acetic acid was added and the reaction mixture was further stirred for 1 hr. Then it was refluxed for 3-4hrs. After completion of the reaction, the contents were cooled to room temperature and were poured into a beaker containing crushed ice. The (light) white coloured precipitate formed was filtered to afford the title compound **(9a)** as white solid, yield 72%, m.p. 235-237^{o}C, IR(KBr)(cm^{-1}), 3450, 3219 (OH), 1625(C=N), 1580, ^{1}H NMR (400 MHz,DMSO-d_6), δ10.75 (s,OH), 2.5(s,3H), δ 6.9-8.1(m, due to aromatic protons) peak at δ9.1 (CH=N-) ^{13}C NMR(100MHz, DMSO-d_6) δ176.8(C=O), δ 162.9(C-OH), δ 159.9 (C=N) . δ 128-136(Ar-C), 11.3(C-3);EIMS, M^+ m/z 355.02, 307, 275. The molecular weight obtained from the mass spectrum confirms the title compound.

Similar procedure was employed to synthesize **9(b-l),** by employing different aldehydes **(8).** All the compounds **7(a-d)** were made to react with a series of aldehydes **8(i), 8 (ii)** and **8 (iii)** to form the compounds **9(a-l).**

8-((Benzylidene-methylene)amino)-7-hydroxy-6-chloro-3-methyl-2-phenyl-4H-chromen-4-one: (9b) White solid, yield 74%, m.p. (255-257^{o}C);IR KBr)(cm^{-1}): 3454 ,3198 (OH) , 1620(C=N), 1567,458; ^{1}H NMR (400 MHz,DMSO- d_6): δ11.0 (OH), 2.34(s,3H) , 6.74 (s,1H), 7.4(s,1H); ^{13} C NMR(100MHz, DMSO-d_6): δ177(C=O), 163(C-OH),161 (C=N) 128-135 (Ar-C), 11.3(C-3);EIMS, M^+ m/z 389.02.

8-((Benzylidene-methylene)amino)-7-hydroxy-6-bromo-3-methyl-2-phenyl-4H-chromen-4-one: **(9c)**

Whitish brown solid, yield 69%, m.p. (274-277^{o}C);IR (KBr)(cm^{-1}): 3550,321 (OH) , 1618(C=N), 1567,545; ^{1}H NMR (400 MHz,DMSO- d_6): δ10.57(OH), 2.24(s,3H) , 6.45 (s,1H), 7.4(s,1H); ^{13} C NMR(100MHz, DMSO-d_6): δ180(C=O), 170(C-OH),160 (C=N) 128-136 (Ar-C), 10.8(C-3);EIMS, M^+ m/z 355, 356(M+1).

8-((Benzylidene-methylene)amino)-7-hydroxy-3,6-dimethyl-2-phenyl-4H-chromen-4-one: **(9d)**

White solid, yield 72%, m.p. (244-245^{o}C);IR (KBr)(cm^{-1}): 3442, 3321 (OH) , 1621(C=N), 1267,784; ^{1}H NMR (400 MHz,DMSO- d_6): δ10.44(OH), 2.24(s,3H),2(s,3H), 6.48 (s,1H), 7.1(s,1H); ^{13} C NMR(100MHz, DMSO-d_6): δ178(C=O), 169(C-OH),159.9 (C=N) 126-135.5 (Ar-C), 10.8(C-3),11.2(C-6);EIMS, M^+ m/z 369.1. 370(M+1),371(M+2).

8-((Furan-2-yl-methylene)amino)-7-hydroxy-3-methyl-2-phenyl-4H-chromen-4-one :**(9e)**

Pale yellow solid, mp (215-218^{o}C);IR KBr)(cm^{-1}), 3350, 3197 (OH) , 1622(C=N), 1580; ^{1}H NMR (400 MHz,DMSO- d_6), δ10.5(OH), 2.4(s,3H),6.74 (d 1H,J=8Hz), 7.4(d,1H,J=8.2Hz), 6.6(dd,1H,J=4.8Hz, J=9.6Hz) , 6.9(dd,1H,J=3.6Hz,J=8.8Hz)7.2-7.9(m, 5H),8.98(s,1H), 7.9(dd,1H,J=4.8Hz,J=10 Hz); ^{13} C NMR(100MHz, DMSO-d_6) δ180(C=O), 169(C-OH),165, (C=N),145, 127-137(Ar-C),112,111.3(C-3);EIMS, M^+ m/z 345.2.

8-(Furan-2-ylmethyleneamino)-7-hydroxy-6-chloro-3-methyl-2-phenyl-4H-chromen-4-one (9f)

Beige color solid, mp (257-259^{o}C);IR KBr)(cm^{-1}), 3470, 3213(OH) , 1625(C=N), 1580,480; ^{1}H NMR (400 MHz,DMSO- d_6), δ10.49(OH), 2.38(s,3H), 7.8(s,1H,), 6.61(dd,1H,J=4.8Hz, J=9.6Hz) , 6.87(dd,1H,J=4.2Hz,J=8.4Hz)7.2-7.9(m, 5H),9.1(s,1H),7.9(dd,1H,J=3.8Hz,J=9.6 Hz); ^{13} C NMR(100MHz,

DMSO-d_6) δ181(C=O), 170(C-OH),163, (C=N),144, 126-139(Ar-C),111,11.3(C-3);EIMS, M^+ m/z 379, 380(M+1).

8-((Furan-2-ylmethylene)amino)-7-hydroxy-6-bromo-3-methyl-2-phenyl-4H-chromen-4-one : (9g)

Beige color solid, mp (287-289^{o}C);IR KBr)(cm^{-1}), 3450, 3219(OH) , 1624(C=N), 1587,580; ^{1}H NMR (400MHz,DMSO-d_6), δ10.49(OH), 2.3(s,3H), 7.84(s,1H,), 6.7(dd,1H,J=4.8Hz, J=9.6Hz) , 6.86(dd,1H,J=4.2Hz,J=8.4Hz)7.18-7.91(m, 5H),9.1(s,1H),7.88(dd,1H,J=3.8Hz,J=9.6 Hz); ^{13} C NMR(100MHz, DMSO-d_6) δ180(C=O), 172(C-OH),160, (C=N),144, 118-135(Ar-C),114,11.3(C-3);EIMS, M^+ m/z 423, 424(M+1),425(M+2).

8-((Furan-2-ylmethylene)amino)-7-hydroxy-3,6-dimethyl-2-phenyl-4H-chromen-4-one(9h):

Beige color solid, mp (232-233^{o}C);IR KBr)(cm^{-1}), 3380, 3081(OH) , 1624(C=N), 1587, ^{1}H NMR (400 MHz,DMSO- d_6), δ10.5(OH), 1.98(s,3H),2.4(s,3H), 7.6(s,1H,), 6.7(dd,1H,J=4.8Hz, J=9.6Hz), 6.86(dd,1H,J=4.2Hz,J=8.4Hz)7.18-7.91(m, 5H),9.1(s,1H),7.88(dd,1H,J=3.8Hz,J=9.6 Hz); ^{13} C NMR(100MHz, DMSO-d_6) δ181(C=O), 173(C-OH),160(C=N),144, 118-135(Ar-C),114,11.3(C-3);EIMS, M^+ m/z 359.

8-((4-methyl bezylidene)amino)-7hydroxy-3-methyl-2-phenyl-4H-chromen-4-one(9i):

Yield 74%, mp 235-238^{o}C;IR (KBr) (cm^{-1}) 3419(OH), 2165(C=O), 1625(C=N),1393(C-O-), 1255(-O-H),1177(C-CH_3),1075-840(Ar); ^{1}H NMR($CDCl_3$,400MHz,) δ=10.01 (1H,s,OH), 9.1(1H,s,HC=N), 6.64(1H,d,J=8,H-6), 7.012 -7.628 (10 Ar protons), 8.254(1H,d, J =9.2Hz,H-5),2.4(s,3H) 2.164 (s, 3H); ^{13}C NMR ($CDCl_3$,100MHz,) δ= 184.0(C=O, C-4), 117.4(C, C-10), 113.1(C, C-6), 104.9(C, C-3), 130.9(CH,C-5), 168.1(C-OH, C-7), 160.7(C, C-2), 128-131.4(Ar C), 6.2(CH_3) ; EIMS , M^+ m/z :359.

8-((4-methyl bezylidene)amino)-7hydroxy-6-chloro-3-methyl-2-phenyl-4H-chromen-4-one (9j):

White solid, yield 76%; mp 231-233^{o}C; IR(KBr) (cm^{-1}): 3066, 1703, 1621(C=N),1395, 1240, 690, 470; ^{1}H NMR: ($CDCl_3$,400MHz,) δ= 10.02(s,1H, OH), 9.10(s,1H, HC=N), 7.13-7.64(m, 10Ar-p), , 8.10(s,1H, H-5), 2.1(s,3H)2.45 (s,3H,CH_3); ^{13}C NMR ($CDCl_3$,100MHz) δ= 185.0 (C=O) , 117.4(C,C-10), 104.9(C, C-3), 121.0(C, C-6), 169.1(C-OH,C-7), 116-131(Ar-C), C135.1(CH,C-5), 10.2(C-CH_3), 6.2(C,CH_3) ; EIMS [M^+] m/z (%):403,404(M+1).

8-((4-methylbezylidene)amino)-7-hydroxy-6-bromo-3-methyl-2-phenyl-4H-chromen-4-one (9k):

Off white solid, yield 79%; mp 212-215^{o}C; IR (KBr) (cm^{-1}) 3120, 1715, 1622,1392, 1239,582,397; ^{1}H NMR: ($CDCl_3$,400MHz,): δ= 10.01(1H,s,OH), 9.11(1H,s, HC=N), 7.18-7.69(m, 10H-Ar),8.19(d,1H, *J* =8Hz,H-5),2.1(s,3H),2.43(s,3H,CH_3); ^{13}C NMR ($CDCl_3$,100MHz,): δ = 180.2, (C=O,), 117.6(C-10), 109.5(C, C-6), 105(C-CH_3,C-3), 174 (C-OH,C-7), 118-131.5(Ar-C),161.0(C,C=N), 139.1(CH,C-5),11.2(CH_3),6.3(C, CH_3) ; EIMS M^+ m/z% 447, 448(M+1),449(M+2).

8-((4-methylbezylidene)amino)-7-hydroxy-3,6-dimethyl-2-phenyl-4H-chromen-4-one: (9l):

Beige colour solid, yield 79%; mp 201-203^{o}C; IR (KBr) (cm^{-1}) 3258, 1715, 1622,1392, 1239, ^{1}H NMR: ($CDCl_3$,400MHz,): δ= 10.10(1H,s,OH), 9.11(1H,s, HC=N), 7.18-7.69(m, 10H-Ar),8.19(d,1H, *J* =8Hz,H-5),2.1(s,3H),2.43(s,6H,CH_3); ^{13}C NMR ($CDCl_3$,100MHz,): δ = 180.2, (C=O,), 117.6(C-10), 109.5(C, C-6), 15(C-CH_3,C-3), 174 (C-OH,C-7), 118-131.5(Ar-C),161.0(C,C=N), 127.1(CH,C-5),11.2(CH_3),6.3(C, CH_3) ; EIMS M^+ m/z% 383.

IV. Conclusion

A series of Schiff bases of 8-Amino chromones were designed, predicted for bioassay and synthesized. All the synthesized compounds were characterized and confirmed by IR, NMR and Mass spectral analysis.

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