Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(5):267-270

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis, characterization and antimicrobial activity of some new schiff's bases of 3-acetyl-4-hydroxy-2*H*-chromen-2-one and amino pyridines

M. S. Mote, S. B. Patwari and S. P. Pachling*

P. G. Department of Chemistry and Research Centre; N. S. B. College, Nanded, India

---

ABSTRACT

Condensation of amino pyridines with 3-acetyl-4-hydroxy-2H-chromen-2-one gave 4-hydroxy-3-(1-(pyridinylimino)ethyl)-2H-chromen-2-oneand 4-hydroxy-3-(1-(methylpyridine-2-ylimino)ethyl)-2H-chromen-2-one. These are characterized by IR, ^{1}HNMR, ^{13}CNMR and mass spectral analysis. In vitro biological screening effects of the investigated compounds were tested against fungal species Aspergillusniger, Penicilliumchrysogenumand Aspergillusflavus by the poison plate method.

Key words: 3-acetyl-4-hydroxychromen-2-one, amino pyridine, Schiff base, Antifungal.

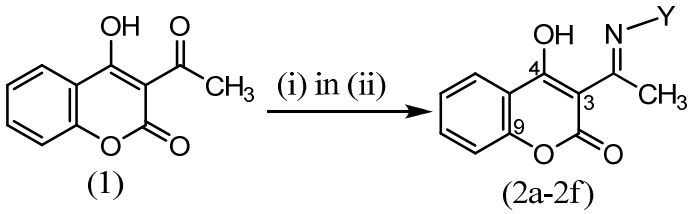
INTRODUCTION

Chromen-2-one moiety is a common fused heterocyclic nucleus found in many natural products of medicinal importance. Several of these exhibit exceptional biological and pharmacological activities such as antibacterial, antiviral, anti-HIV, anticoagulant and cytotoxic properties [1-6]. Further, chromen-2-one derivatives have been used as food additives, perfumes, cosmetics, dyes and herbicides [7,8]. In addition, schiff's bases perform important role in biological systems, where the >C=N- linkage is an essential structural requirement for biological activity.[9] Many Schiff bases exhibited remarkable antibacterial,[10,11] antifungal,[12,13] anticancer,[14] diuretic activities[15].

Literature survey reveals that work has been carried out on of Schiff bases derived from chromen-2-one having substitutions atbenzene nucleus.[16]Synthesis, characterization and Antimicrobial activity of Schiff bases derived from 3-acetyl-4-hydroxychroman-2-one and primary aromatic amine has been reported.[17] Acetylation of 4-hydroxy-2H-chromen-2-one yields 3-acetyl-4-hydroxy-2H-chromen-2-one. The later was condensed with amino pyridines such as 2-aminopyridine,3-aminopyridine,4-aminopyridine, 2-amino-3-methylpyridine,2-amino-4-methylpyridine and 2-amino-6-methylpyridineto synthesize 4-hydroxy-3-(1-(pyridinylimino)ethyl)chroman-2-one. These are characterized by IR, ^{1}HNMR, ^{13}CNMR and mass spectral analysis.

EXPERIMENTAL SECTION

All the chemical and solvents used were of A.R. grade. All chemicals used were of E-Merck and S.D. fine Ltd. Melting points were determined in an open capillary tube and are uncorrected. The purity of the compound has been checked by TLC. IR spectra were recorded in $CHCl_3$ on a Shimadzu FTIR-8300 spectrophotometer. The ^{1}H NMR (300 MHz) and ^{13}C NMR (70 MHz) were run on a BrukerAvance DPX-250 spectrometer in $CDCl_3$ using tetramethylsilane as an internal standard. Chemical shift values are given in δ scale. Mass spectra were recorded on Finnigan Mat LCQ Mass Spectrometer using methanol as mobile phase. The in vitro biological screenings of the investigated compounds were tested against fungal species by the poison plate method.



(i) Y and (ii) EtOH

Y = 2-aminopyridine (a), 3-aminopyridine (b), 4-aminopyridine (c), 2-amino-4-methylpyridine (d), 2-amino-5-methylpyridine (e), 2-amino-6-methylpyridine (f).

Fig. 1 : Schiff's base of 3-acetyl-4-hydroxy-2*H*-chromen-2-one

General procedure for the synthesis of 4-hydroxy-3-(1-(pyridinylimino)ethyl)chromen-2-ones: The Schiff bases(2a-2fFig.1) were prepared by adding 3-acetyl-4-hydroxy-chromen-2-one(0.01 mole) and the aminopyridines(0.01 mole) in ethanol (50 ml) and refluxing the mixture for 4 hrs. After cooling, the product was crystallized from ethanol. The purity of the ligands was checked by m.p. and TLC. These are characterized by IR, ^{1}HNMR ,^{13}CNMR and mass spectral studies.

CHARACTERIZATION OF SYNTHESIZED SCHIFF'S BASES (2a-2f)

Analytical data of*4-hydroxy-3-(1-(pyridin-2-ylimino)ethyl)-2H-chromen-2-one (2a)*

Colour: yellow; Yield: 88%; m.p. 142-144^{0}C ; **IR (KBr,cm^{-1}):**3500-2550 (broad phenolic ν_{OH}), 1720 ($\nu_{C=O}$) of lactone,1630 and 1610 ($\nu_{C=N}$) of imine, 1582 and 1503 aromatic ($\nu_{C=C}$), 1340 (ν_{C-O}) phenolic-OH);**^{1}HNMR:**δ2.02 (S, 3H, imine –CH_3), 7.5-7 (m, 4H, Py–H), and of (Ar-H of coumarin moiety), 15.88 (S,1H, O–H); **^{13}CNMR:**δ20.09 (imine-CH_3 carbon), 78.12 for C^3, 128-114 for aromatic carbons, 152 for C^9, 160.42 for lactone carbon, 165.9 for C^4, and 176.4 for imine carbon. Mass Spectra: [M^+]=281.22

Analytical data of*4-hydroxy-3-(1-(pyridin-3-ylimino)ethyl)-2H-chromen-2-one (2b)*

Colour: yellow; Yield: 84%; m.p. 170-172^{0}C; **IR (KBr,cm^{-1}):**3520-2550 (broad phenolic ν_{OH}), 1716 ($\nu_{C=O}$) of lactone ,1634 and1610 ($\nu_{C=N}$) of imine, 1587, 1503 aromatic ($\nu_{C=C}$), 1342 (ν_{C-O})phenolic-OH; **^{1}HNMR:**δ2.08 (S, 3H, imine –CH_3), 7.4-8.3 (m, 4H, Py–H), and of (Ar-H of coumarin moiety), 16.37 (S,1H, O–H); **^{13}CNMR:**δ19.78 (imine-CH_3 carbon), 78.33 for C^3, 128-114 for aromatic carbons, 152 for C^9, 160.88 for lactone carbon, 165 for C^4, and 175.5 for imine carbon. Mass Spectra: [M^+]=279.35

Analytical data of*4-hydroxy-3-(1-(pyridin-4-ylimino)ethyl)-2H-chromen-2-one (2c)*

Colour: pale yellow; Yield: 90%; m.p. 155-157^{0}C ; **IR (KBr,cm^{-1}):**3500-2560 (broad phenolic ν_{OH}), 1720 ($\nu_{C=O}$) of lactone ,1632 and 1612 ($\nu_{C=N}$) of imine, 1590, 1500 aromatic ($\nu_{C=C}$), 1340 (ν_{C-O})phenolic-OH; **^{1}HNMR:**δ2.12 (S, 3H, imine –CH_3), 8.5 and 7 (dd, 4H, Py–H), 7.8-7.4 (Ar-H of coumarin moiety), 16.7 (S,1H, O–H); **^{13}CNMR:**δ19.86 (imine-CH_3 carbon), 78.2 for C^3, 130-116 for aromatic carbons, 150 for C^9, 159.58 for lactone carbon, 166for C^4, and 176 for imine carbon. Mass Spectra: [M^+]=280.32

Analytical data of*4-hydroxy-3-(1-(4-methylpyridin-2-ylimino)ethyl)-2H-chromen-2-one (2d)*

Colour: yellowish Green; Yield: 92%; m.p. 192-194^{0}C ; **IR (KBr,cm^{-1}):**3500-2560(broad phenolic ν_{OH}),1720 ($\nu_{C=O}$) of lactone ,1636 and 1614 ($\nu_{C=N}$) of imine,1578 and 1492 aromatic ($\nu_{C=C}$), 1346 (ν_{C-O}) phenolic-OH; **^{1}HNMR:** δ2.09 (S, 3H, imine –CH_3), δ2.3 (S, 3H, py –CH_3), 7.16, 7.47 and 8.5(3H Py–H),7.8-7.4(Ar-H of coumarin moiety), 16.82 (S,1H, O–H); **^{13}CNMR:**δ20 and 21.8(two -CH_3 carbon), 79.05 for C^3, 129.4-115.4 for aromatic carbons, 155 for C^9, 168.34 for lactone carbon, 177.26 for C^4 and 184.14for imine carbon. Mass Spectra: [M^+]=294.8

Analytical data of*4-hydroxy-3-(1-(5-methylpyridin-2-ylimino)ethyl)-2H-chromen-2-one (2e)*

Colour: Green; Yield: 94%; m.p. 202-204^{0}C ; **IR (KBr,cm^{-1}):** 3500-2580 (broad phenolic ν_{OH}),1718 ($\nu_{C=O}$) of lactone ,1637 and 1610($\nu_{C=N}$) of imine, 1588 and 1492 aromatic ($\nu_{C=C}$), 1348 (ν_{C-O}) phenolic-OH; **^{1}HNMR**δ2.10 (S, 3H, imine –CH_3), δ2.32 (S, 3H, py –CH_3), 6.8,7.42and8.42 (3H Py–H),7.9-7.4 (Ar-H of coumarin moiety), 17.0 (S,1H, O–H); **^{13}CNMR:**17.58 and 20.06 (two -CH_3 carbon), 78.2 for C^3, 124.6-116.4 for aromatic carbons, 152.16 for C^9, 162.24 for lactone carbon, 166.38 for C^4 and 175.4for imine carbon. Mass Spectra: [M^+]=293.86

Analytical data of*4-hydroxy-3-(1-(6-methylpyridin-2-ylimino)ethyl)-2H-chromen-2-one (2f)*

Colour: Green; Yield: 75%; m.p. 198-201^{0}C ;**IR (KBr,cm^{-1}):** 3550-2580 (broad phenolic ν_{OH}),1716 ($\nu_{C=O}$) of lactone ,1635 and 1610 ($\nu_{C=N}$) of imine, 1590 and 1500 aromatic ($\nu_{C=C}$), 1342 (ν_{C-O}) phenolic-OH. **^{1}HNMR**δ2.15 (S, 3H, imine –CH_3), δ2.54 (S, 3H, py –CH_3), 6.88-7.4(3H Py–H), 7.9-7.5 (Ar-H of coumarin moiety), 16.0 (S,1H, O–

H); **^{13}CNMR:**17.58 and 20.06 (two -CH_3 carbon), 78.2 for C^3, 137.4-114.4 for aromatic carbons, 152 for C^9, 160.64 for lactone carbon, 166 for C^4 and 174.8for imine carbon. Mass Spectra: $[M^+]$=294.64

ANTIFUNGAL ACTIVITY

Procedure:

Antifungal activity was performed by Poison plate method.[18] The medium used was Potato Dextrose Agar (Himedia). The medium was prepared and sterilized at 10 Psi in autoclave for 15 minutes. Then the compound to be tested is added to the sterile medium in aseptic condition so as to get final concentration as 1%. A plate with ethanol was prepared as blank (negative control) similarly a plate with 1% Gresiofulvin was prepared as standard reference plate (positive control).

Aspergillusniger, *Penicilliumchrysogenum*, *Fusariummoneliforme*, *Aspergillusflavus*were selected as test fungal cultures. They were allowed to grow on slant for 48 hours so as to get profuse sporulation. 5ml of 1:100 aqueous solution of Tween 80 was added to the slant and spores were scraped with the help of nichrome wire loop to form suspension.

The fungal suspension was inoculated on the plates prepared using compound with the help of nicrome wire loop. The plates were incubated at room temperature for 48 hours.

After incubation plates were observed for the growth of inoculated fungi. Results were recorded (**Table-1**) as moderate growth of fungi (++), reduced growth of fungi (+) and no growth of inoculated fungi (-) antifungal activity.

Table-1Anti fungal activity

Compound	Growth of Fungi			
	A. niger	***P.chrysogenum***	***F.moneliforme***	***A. flavus***
Gresiofulvin	-	-	-	-
(2a)	+	++	++	+
(2b)	+	++	++	+
(2c)	+	++	++	+
(2d)	-	-	+	-
(2e)	-	+	+	-
(2f)	-	-	+	-

Moderate growth (++), Reduced growth (+) and No growth (-) of fungi

RESULTS AND DISCUSSION

All the reactions were carried out by conventional methods. Intermediate 3-acetyl-4-hydroxy-2H-chromen-2-one (**1**) was prepared from 4-hydroxy coumarin by action of POCl3in acetic acid.[19]Schiff bases 4-hydroxy-3-(1-(pyridinylimino)ethyl)-2H-chromen-2-one **(2a-2c)**and 4-hydroxy-3-(1-(methylpyridine-2-ylimino)ethyl)-2H-chromen-2-one **(2d-2f)**were prepared by action of amino pyridines with 3-acetyl-4-hydroxy-2H-chromen-2-one (**1**). The reactions were carried out in a protective hood. The intermediate product (**1**) formed was recrystallized in ethanol and purity was tested by TLC. 4-hydroxy-3-(1-(pyridinylimino)ethyl)-2H-chromen-2-one **(2a-2c)**and 4-hydroxy-3-(1-(methylpyridine-2-ylimino)ethyl)-2H-chromen-2-one **(2d-2f)**were obtained by refluxing in ethanol for 4 hrs. Increase in the time of refluxing did not improve the yield of product.

Assignment ofsignificant peaks observed in IR, ^{1}HNMR, ^{13}CNMR spectra of the compounds **2a-2f**isclarified in the analytical data. The IRspectra of compound **2a-2f** showed additional high intensity band observed at 1637-1630 cm^{-1} is assigned to ν(C=N) vibration suggesting the formation of Schiff base.[20] Broad weak band around 3550-2580 cm^{-1} is assigned to H bonded –OH in the Schiff bases. The band at 1567-1480 cm^{-1} is assigned to the combination of ν(C=C) of the aromatic ring. A high intensity band in the region 1348-1340 cm^{-1} is assigned to phenolic ν(C-O) vibration and 1720-1716 cm^{-1} for lactone carbonyl.[21]

Each one of the ^{1}H NMR spectraof 2a-2frevealed singlet for 3H between 2.02-2.15 ppm assigned to imino methyl group. Peaks between 8.2-7.0ppm are assigned to aromatic protons. All ^{1}HNMR spectra of 2-c and showed double doublet confirming 4- moiety bonded to imino nitrogen. A broad singlet at 15.63-15.92 ppm confirms the presence of 4-hydroxyl group. ^{13}CNMR showed peaks between 159.5-162.24 ppm for lactone carbon, between 174.8-177.78 ppm for imine carbon. Assignment given to other peaks observed in ^{1}HNMR, ^{13}CNMR spectra and also molecular ion peaks in mass spectra justifies the structures of compounds 2a-2f.

The Schiff's bases synthesized were evaluated for anti-fungal activity with different strains of fungi.Results are shown in Table-1. Antifungal activity observed against *Aspergillus*species was encouraging in comparison with *Penicilliumchrysogenum andFusariummoneliforme*. However, compounds 2d-2f has reduced the growth of these organisms.

Acknowledgements
The authors thank Principal, N.S.B. College, Nanded, Maharashtra for providing laboratory facility. Authors also wish to extend their gratitude to Head, Department of Microbiology for helping out in carrying out antimicrobial analysis. Authors also thankHOD, Department of Chemistry.

REFERENCES

[1] RDH Murray;J Mendez; SA Brown.The Natural Coumarins: Occurrence, Chemistry andBiochemistry; Wiley & Sons, New York, NY, USA, **1982**.
[2] B Naser-Hijazi; B Stolze; KS Zanker.2nd Proceedings of the International Society ofCoumarin Investigators; Springer, Berlin, Germany, **1994**.
[3] C Gnerre; M Catto; F Leonetti; P Weber; PA Carrupt; C Altomare; A Carotti; B Testa, *J. Med. Chem.*,**2000**, 43, 4747-4758.
[4] VK Gupta; V Arya. *J. Chem. Pharm. Res.*, **2011,** 3(1), 613-620..
[5] D Patel; P Kumari; N Patel. *J. Chem. Pharm. Res.*, **2010**, 2(5), 84-91.
[6] S Hesse; GA Kirsch, *Tetrahedron Lett.*,**2002**, 43, 1213-1215.
[7] LA Singer; NPKong.,*J. Am. Chem. Soc*. **1966**, 88, 5213-5219.
[8] S Carboni; V Malaguzzi; AMarzili,*Tetrahedron Lett.*,**1964**, 5, 2783-2785.
[9] CP Raptopoulou; AN Papadopoulos; DA Malamatari; E Loannidis; G Molsidis; AT erzis; DPKessissoglou, *Inorg. Chim. Acta*, **272**, 283 (1998).
[10] YK Vaghasiya; RS Nair; M Baluja; SS Chanda, *J. Serb. Chem. Soc*., **2004**, 69, 99.
[11] K Vashi; HB Naik, *Eur J. Chem.*, **1**, 272 (2004).
[12] HMSafwat; FARagab; NM Eid; GMAbdel,*Egyptian J.Pharm.Sci.*,**1988**, **29,**99
[13] R Mtrei; M Yadawe; SA Patil, *Orient J. Chem.*, **1996**, 12, 101.
[14] DR Shkawat; SS Sabnis; CV Deliwala, *Bull. Haffkine Inst.*, **1993**, 1, 35.
[15] CT Barboiu;MLuca; C Pop; E Brewster; ME Dinculescu, *Eur. J. Med. Chem.*, **1996**, 31, 597.
[16] N Singhal; PK Sharma; R Dudhe; N Kumar, *J. Chem. Pharm. Res.*,**2011**, 3(2), 126-133.
[17] JF Stephen; E Marcus, *J. Org. Chem.*,**1969**, 34(9), 2764-2766.
[18] RJ Cruickshank; PDuguid; RR Swain. Medical Microbiology, Churchill Livingstone, Vol. 1, **1998.**
[19] MV Girgaonkar; SG Shirodkar,, *J. Org. Chem.*,**2012,** 4(1), 260-264.
[20] V Mutalk; MA Phaniband. *J. Chem. Pharm. Res.*, **2011,** 3(2), 313.