International Journal of Scientific Research in Science and Technology
Available online at : www.ijsrst.com
Print ISSN: 2395-6011 | Online ISSN: 2395-602X
doi : https://doi.org/10.32628/IJSRST52411174

The Synthesis, Characterization, and Biological Activities of Some Novel Schiff Bases Derived From 3-Acetyl-4-Hydroxy-2H-Chromen-2-One And 2-Aminooxadiazole Derivatives Have Been Investigated

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ARTICLEINFO

Article History:

Accepted: 15 Jan 2024

Published: 30 Jan 2024

Publication Issue :

Volume 11, Issue 1

January-February-2024

Page Number :

479-488

ABSTRACT

A set of five novel Schiff's bases (5a-e) incorporating coumarin-1, 3, 4-oxadiazole derivative were synthesized through condensation reaction of 3-acetyl-4-hydroxy-2H-chromen-2-one with 2-aminooxadiazole derivatives as heterocyclic aromatic amines. The novel structures of these compounds were confirmed based on their elemental analysis and spectral data. All these investigated derivatives were tested against bacterial species *S. aurous*, *E. coli*, *S. typhi*, *B. substilis* using the Agar cup method, and against fungal species *A. niger, P. chrysogenum, F. moneliforme* and *A. flavus* using poison plate method. Schiff bases incorporating coumarin and 1,3,4-oxadiazole moieties have shown notable efficacy against both bacterial and fungal strains.

Keywords: Coumarin, 3-acetyl-4-hydroy chromen-2-one, 2-aminooxadiazole, 3, 4-oxadiazole, Schiff's bases and anti-microbial activity.

I. INTRODUCTION

A huge number of natural products contain the fused heterocyclic nucleus known as coumarin. Its derivatives form a significant category of compounds with a broad range of biological activities, particularly in the medicinal applications. Many researchers have reported the antibacterial, antiviral, anti-HIV, anticoagulant and cytotoxic nature of coumarin derivatives [1-9]. In addition, they are used in perfumes, dyes, cosmetics, food additives, and herbicides [10, 11]. Coumarin-based Schiff bases, characterized by the azomethine >C=N- linkage, are responsible for their biological activities [12]. Numerous Schiff bases have demonstrated outstanding antibacterial [13, 14], antifungal [15, 16], anti-cancer [17], diuretic activities [18], and enzyme model mimetic properties [19]. Furthermore a few Schiff bases can also exhibit as anti-HIV activity [20].

Likewise, oxadiazole is a five-membered heterocyclic compound containing two nitrogen and one oxygen atom in an aromatic ring [21, 22]. It exhibits a variety of useful biological activity [23]. It is considered to result from furan by replacing two methine (-CH=) groups with two pyridine-type nitrogen (-N=) [22]. There are four probable isomers of oxadiazole, namely, 1,3,4-oxadiazole, 1,2,4-oxadiazole, 1,2,3-oxadiazole and 1,2,5-oxadiazole. Among these isomers 1,3,4-Oxadiazole serves as a versatile pilot nucleus for designing potential bioactive agents [24]. The extensive application of 1,3,4-oxadiazoles as a scaffold in pharmaceutical chemistry has found that this template is a member of the privileged structure due to its outstanding biological and pharmacological properties. These properties include anticancer [25-28], anti-tubercular [29, 30], antibacterial [30], antifungal [31], anti-HIV [32], anti-inflammatory [33], and insecticidal [34] activities.

Because of the increased hydrolytic and metabolic stability of the oxadiazole ring, which has been experimentally to enhance pharmacokinetic properties, this skeleton emerges as a significant structural moiety in the pharmaceutical manufacturing [35]. Consequently, of this, the 1,3,4-oxadiazole moiety has become the focus drug discovery programs encompassing analgesic, antibacterial, anti-inflammatory, anti-malarial, antidepressant, hyperglycemic, fungicidal and other therapeutic agents [36,37]. Notably, several presently employed therapeutically dynamic compounds, designated as medical incorporate the 1,3,4-oxadiazole moiety. These include the HIV integrase inhibitor Raltegravir® (**5**), an antiretroviral drug [2] Zibotentan® (**6**) an anticancer agent [3]; the nitrofuran antibacterial furamizole; and antihypertensive agents such as tiodazosin and nesapidil (6a), all of which are based on 1,3,4-oxadiazole moiety. Subsequently, the synthesis and transformations of several of 1,3,4-oxadiazoles have garnered significant attention due to their remarkable biological activity over an extended period.

"Hence, the derivatives of coumarin and oxadiazole have garnered increasing attention due to their broad biological and pharmacological activities. In recent decades, many researchers have focused on importance of designing and developing coumarin and oxadiazole-based derivatives as novel guide drugs molecules for disease therapy."

Review of literature has shown that sufficient work has been carried out on Schiff bases derived from 3-acetyl-4-hydroxy-2H-chromen-2-one and substituted anilines and hydrazones [38-40]. However, little work has been reported on Schiff Bases derived from 3-acetyl-4-hydroxychromen-2-one and heterocyclic amines [41-43]. In this paper, we report the preparation of new compound, 3-acetyl-4-hydroxy-2H-chromen-2-one, from 4-hydroxy-2H-chromane-2-one using a previously described method [38-44] with few modifications. Furthermore, 3-acetyl-4-hydroxy-2H-chromen-2-one was condensed with (4-substituted phenyl) 2-amino-1-3-4-oxadiazole as aromatic amines to synthesize some novel Schiff bases that constitute coumarin-incorporated 1-3-4-oxadiazole nucleus, such as 4-hydroxy-3-(1-((5-p-substitutedphenyl-1,3,4-oxadiazol-2-yl) imino) ethyl)-2H-chromen-2-one**(5a-5e).** The synthesized novel Schiff bases were characterized by IR, ^{1}HNMR, ^{13}CNMR and mass spectral analysis, and their purity was checked by TLC, M.P, and elemental analysis. In this study, the synthesized novel Schiff bases have been intended for potential use in biological applications.

II. METHODS AND MATERIAL

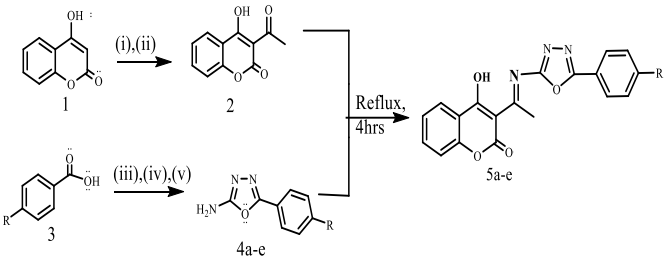
All the reagents, starting materials, and solvent used were of AR Grade and were purchased from SD fine chemicals and E Merk. The purity of these compounds was checked by TLC, and melting points were recorded in an open capillary tube and

uncorrected. Shimadzu FTIR-8300 spectrophotometer was used to record the IR spectra using $CHCl_3$ solvent. The ^{1}HNMR (300 MHz) and ^{13}CNMR (300 MHz) spectra were obtained on a Brucker Avance DPX-250 spectrometer in $CDCl_3$, with TMS used as an internal standard. Chemical shift values are reported on the δ scale. Mass spectra were recorded on Finnigan Mat LCQ mass spectrometer using methanol as the mobile phase. The synthesized Schiff bases were screened against different bacterial species by using Agar cup method and fungal species using the poison plate method.

Procedure for the synthesis of 3-acetyl-4-hydroxychromen-2-one (2): The reaction mixture containing 4-hydroxy-chromen-2-one (4g, 24.7 m moles) in acetic acid (16 ml) and phosphorous oxychloride (7.5 ml) was refluxed for 30 minutes. Upon cooling, the precipitate was obtained and subsequently recrystallized from ethanol. The product, 3-acetyl-4-hydroxy-chromen-2-one (2), was collected as white needles with yield of 4.64g (92%) and a melting point of 134-136^{0}C. The melting point was found to be consistent with the literature values [38-44].

General method of synthesis of 2-aminooxadiazole derivatives i.e., 5-(aryl)-1, 3, 4-oxadiazol-2-amine (4a-e): These aromatic primary amines are synthesized according to the reported procedure with relevant modification [45-47]. The mixture of p-substituted benzoic acid (1 mol) and semi-carbazide (0.455g, 1 mole) was dissolved in 5 mL of phosphorous oxychloride and refluxed for 50 minutes. The reaction was cooled to room temperature, and 5 mL water was added carefully, followed by refluxing for 4-5 hours.

General procedure for the synthesis of (novel Schiff bases) 4-hydroxy-3-(1-((5-p-substitutedphenyl-1,3,4-oxadiazol-2-yl) imino) ethyl)-2H-chromen-2-one **(5a-5e):** The novel Schiff bases were prepared by mixing equimolar solutions of 3-acetyl-4-hydroxy-chromen-2-one and 2-aminooxadiazole derivatives or 5-(4-substituted phenyl)-1,3,4-oxadiazol-2-amine in ethanol and refluxing the mixture for 4 hours (scheme 1). After cooling, the product was crystallized from suitable solvents. The purity of the Schiff bases was checked by TLC, melting point (m. p.), and elemental analysis. These compounds were also characterized by IR, ^{1}HNMR, ^{13}CNMR and mass spectral studies.



(i) Ac-OH, (ii) $POCl_3$, (iii) Semicarbazide, (iv) $POCl_3$, (v) KOH
R=(a)-H, (b)-CH_3, (c) -OH, (d) -OCH_3,(e)-NO_2

Fig.1: Reaction Scheme for Synthesis of Novel Schiff's Bases (5a-5e)

III.RESULTS AND DISCUSSION

Analytical data of compound:

(5a): 4-hydroxy-3-(1-((5-phenyl-1,3,4-oxadiazol-2-yl) imino) ethyl)-2H-chromen-2-one: MF: $C_{19}H_{13}N_3O_4$; Colour: Pink white, Yield: 65%; m. p. 253-255 ^{O}C; Elemental Analysis: C: 65.70(Theoretical:65.73); H: 3.77(3.75); N: 12.10(12.12); O: 18.43(18.40); IR (KBr,cm^{-1}): 3595-2592(νOH phenolic), 3012(νC-H aromatic), 2873(νC-H aliphatic), 1716(νC=O lactone), 1657(νC=N imine), 1598 (νC=N of 1,3,4-oxadiazole nucleus), 1590,1450 and 1422 (νC=C aromatic), 1269,1067(C–O-C of 1,3,4-oxadiazole nucleus), 1361 and 1238 (>C—O) and (enolic —O—H), 825 (C–N); 850 (νN-N) stretching frequency, 722 aromatic ring C-H in plane deformation (Wagging) and 567 aromatic ring C-H out of plane deformation. ^{1}HNMR ($CDCl_3$): δ2.14 (S, 3H, –CH_3 imine), 7.96-7.18 (m, 5H, Ph–H), 7.84 and 7.39-7.78 (Ar-H of coumarin moiety), 14.72 (S,1H, O–H); ^{13}CNMR ($CDCl_3$) (300 MHz) δ(ppm): [81.12 for C_3 ,125.50-116.54 for aromatic carbons,154.43 for C_9, 163.40 for lactone carbon, 170.0 for C_4] of coumarin nucleus. The value at 20.13 for (imine-CH_3 carbon), 175.99 due to imine carbon and 181.70 for 1,3,4-oxadiazol ring carbon. The peaks at about 126.33-138.42 for aromatic carbons of phenyl

ring bonded to C^2 of 1,3,4-oxadiazol ring. Mass Spectra $[M+1]^+$: 348.18

(5b): 4-hydroxy-3-(1-((5-(p-tolyl)-1,3,4-oxadiazol-2-yl) imino) ethyl)-2H-chromen-2-one: MF: $C_{20}H_{15}N_3O_4$; Colour: white solid, Yield: 72%; m.p. 265-267^{O}C; Elemental Analysis: C: 66.48(66.45); H: 4.18 (4.20); N: 11.63(11.61); O: 17.71 (17.74); IR (KBr,cm^{-1}): 3595-2592 (broad phenolic νOH), 3014 (νC-H aromatic), 2876(νC-H aliphatic), 1714 (νC=O) of lactone, 1615 for (νC=N) of imine, 1595 for (ν-C=N) in oxadiazole moiety, 1574 -1476 for aromatic (νC=C), 1366 and 1226 (νC-O) and enolic-OH); 1259(νC-O-C assymm), 1166(C-H bend), 1085(C–O of 1,3,4-oxadiazole nucleus), 823.2 (C–N); 854 for ($_\delta$N-N) stretching frequency, 801 Aromatic ring C-H out of plane deformation (para disubstituted benzene). ^{1}HNMR ($CDCl_3$) (300 MHz): δ2.08 (S, 3H, –CH_3 imine), 2.38 (S, 3H, for p-CH3); 7.48 and 7.24 (dd of p-methylphenyl), 7.84 and 7.39 (Ar-H of coumarin moiety), 14.72 (S,1H, O–H);^{13}CNMR (CDCl3) (300 MHz): [82.48 for C^3, 125.49-116.64 for aromatic carbons, 154.04 for C^9 carbon, 162.38 for C_2 lactone carbon, 169.86 for C^4 carbon] of coumarin moiety. The δ value at 20.47 (imine-CH_3 carbon),178.29 for imine carbon and 181.78 for 1,3,4-oxadiazol ring carbon, 126.39-138.91 for aromatic carbons of tolyl ring bonded to C^2 of 1,3,4-oxadiazol ring and 23.02 for -CH_3 carbon of p-tolyl. Mass Spectra $[M+1]^+$: 362.52

(5c): 4-hydroxy-3-(1-((5-(4-hydroxyphenyl)-1,3,4-oxadiazol-2-yl)imino)ethyl)-2H-chromen-2-one: MF:$C_{19}H_{13}N_3O_5$; Color: Buff solid, Yield: 64%; m.p.205-210^{O}C; Elemental Analysis: C:62.81(62.78); H:3.61(3.63); N:11.57(11.56); O:22.02 (22.03); IR (KBr,cm^{-1}): 3595-2595 (broad phenolic ν-OH), 3023 (νC-H aromatic), 2887(νC-H aliphatic), 1715 (ν>C=O) of lactone, 1646 for (νC=N) of imine, 1602 for (ν-C=N) in oxadiazole moiety, 1591-1483 for aromatic (ν>C=C<), 1238 (νC-O-C assymm), 1386 and 1228 for (ν>C-O) and for enolic-OH); 1163(C-H bend), 1075 (C–O of 1,3,4-oxadiazole nucleus), 819 (C–N); 853 for ($_\delta$N-N) stretching frequency, 802 Aromatic ring C-H out of plane deformation (para disubstituted benzene). ^{1}HNMR ($CDCl_3$) (300 MHz): δ2.10 (S,3H, –CH_3 imine), 9.70(S, -OH), 6.9 and 7.59 (dd of p-hydroxyphenyl), 7.82 and 7.38-7.69 (Ar-H of coumarin moiety), 14.98 (S,1H, O–H); ^{13}CNMR (CDCl3) (300 MHz): [78.59 for C_3, 125.49-116.64 for aromatic carbons, 152.07 for C_9 carbon, 159.77 for C_2 lactone carbon, 164.86 for C_4 carbon] of coumarin moiety. The δ value at 21.68 (imine-CH_3 carbon),177.5 for imine carbon, 181.76 for 1,3,4-oxadiazol ring carbon and for 115.58-127.88 for aromatic carbons of p-hydroxyphenyl ring bonded to C^2 of 1,3,4-oxadiazol ring and 157.8 for carbon at -OH substituted. Mass Spectra$[M+1]^+$: 364.02.

(5d): 4-hydroxy-3-(1-((5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-yl) imino) ethyl)-2H-chromen-2-one: MF:$C_{20}H_{15}N_3O_5$; Colour: pale yellow; Yield: 75%; m.p.244-246^{O}C; Elemental Analysis: C:63.66(63.63); H:4.01(4.05); N:11.14(11.12); O:21.20 (21.20); IR (KBr,cm^{-1}): 3589-2598 (broad phenolic νOH), 3018 (νC-H aromatic), 2821 for aliphatic (νCH);1708 (νC=O) of lactone, 1611 for (νC=N) of imine, 1599 for (ν-C=N) in oxadiazole moiety, 1566 and 1507 for aromatic (ν >C=C<), 1388 and 1226 for (ν>C-O) and for enolic-OH); 1083 (C–O of 1,3,4-oxadiazole nucleus), 822 (C–N); 848 for ($_\delta$N-N) stretching frequency, 801 aromatic ring C-H out of plane deformation (para disubstituted benzene).^{1}HNMR ($CDCl_3$) (300 MHz):δ2.16 (S,3H,–CH_3 imine), 4.08(S,-OCH_3); 6.96-7.57 (Ar-H of coumarin moiety), 8.06 and 7.18 (dd of p-methoxyphenyl),14.80 (S,1H, O–H); ^{13}CNMR ($CDCl_3$) (300 MHz): [85.59 for C^3, 120.73-114.98 for aromatic carbons, 156.07 for C_9 carbon, 159.77 for C_2 lactone carbon, 169.86 for C_4 carbon] of coumarin moiety. The δ value at 21.73 (imine-CH_3 carbon), and 176.44 for imine carbon. Peak at about 181.55 for 1,3,4-oxadiazol ring carbon, 123.61-133.86 for aromatic carbons of p-methoxyphenyl ring bonded to C_2 of 1,3,4-oxadiazol ring, 156.2 for p-substituted -carbon; and 56.55 for carbon of -OCH_3 group. Mass Spectra: $[M+1]^+$: 378.59

(5e) : 4-hydroxy-3-(1-((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)imino)ethyl)-2H-chromen-2-one: MF: $C_{19}H_{12}N_4O_6$; Colour: yellow solid, Yield:72%; m.p.234-236^{O}C; Elemental Analysis: C: 58.17 (58.11); H:3.08(3.07); N:14.28(14.30); O:24.47 (24.48); IR (KBr,cm^{-1}): 3597-2595 (broad phenolic ν-OH), 3018 (ν>C-H aromatic), 2827 for aliphatic (νCH);1714 (νC=O) of lactone, 1608 for (ν>C=N) of imine, 1592 for (ν-C=N) in oxadiazole moiety, 1575 and1478 for aromatic (ν>C=C<), 1372 and 1222 (ν>C-O) and enolic (-OH); 1078 (C–O of 1,3,4-oxadiazole nucleus), 799 aromatic ring C-H out of plane deformation (p-disubstituted phenyl ring), 825 (C–N); 845 for ($_{\delta}$N-N) stretching frequency. ^{1}HNMR ($CDCl_3$) (300 MHz): δ2.18 (S,3H, –CH_3 imine), 8.08 and 7.54 (dd, 4H, p-NO_2 Phenyl), 7.94-7.42 and 7.38-7.40 (Ar-H of coumarin moiety), 14.78 (S,1H, O–H);^{13}CNMR ($CDCl_3$) (300 MHz): [80.18 for C^3, 136.19-116.06 for aromatic carbons, 156.06 for C_9 carbon, 162.62 for lactone carbon(C_2), 170.96 for C^4 carbon] of coumarin moiety. The δ value at 20.22 (imine-CH_3 carbon), and 177.77 for imine carbon. 180.81 for 1,3,4-oxadiazol ring carbon, 125.93-138.19 for aromatic carbons of 4-nitrophenyl ring bonded to C_2 of 1,3,4-oxadiazol ring and 147.6 for –NO_2 substituted phenyl carbon. Mass Spectra$[M+1]^+$: 393.12

Biological Activity: Generally, **a**ntimicrobial testing can be applied to new drug development, epidemiology and therapeutic conclusions. Therefore, novel Schiff bases have been screened for biological testing for *in vitro* examine of extracts and compare them with pure drugs as potential antimicrobial agents.

Antibacterial Evaluation:

The assessment of antibacterial activity was conducted using the agar cup-plate method [48-49]. Nutrient agar (Himedia) was meticulously prepared and subsequently sterilized in an autoclave at 15 Psi for 15 minutes. Following sterilization, it was allowed to cooled below 45^{0}C and inoculated with a turbid suspension of testing bacteria, individually, cultured from slant cultures prepared 24 hour earlier, with a consistent 3% inoculation ratio. The bacterial strains chosen included gram-negative *Escherichia coli, Salemonella typhi,* while the gram-positive species encompassed *Staphylococcus aureus* and *Bacillus subtilis.* Each bacteria seed was individually dispensed onto a sterilized Petri dish under septic conditions and left to solidify. To create wells for the experiment, cups with a 10mm diameter were carefully arranged on the agar plate using a sterilized cork borer. Subsequently, 1% ethanolic solution of Schiff base were introduced into each cup under aseptic conditions, utilizing a 100µl micropipette. Separate cups containing 100µl of ethanol were designated for the blank reading (negative control). In addition, for the positive control, a 100µl solution of penicillin in 0.1% ethanol was placed on the seeded nutrient agar surface. To facilitate the diffusion of the compound from agar cup into the medium, the Petri plates were placed in a refrigerator for 15 minutes. Following this, the plates were incubated at 37^{0}C for 24 hours. After the incubation period, the plates were carefully examined for zones of inhibition, indicating a reduction in bacterial growth around the agar cup. Finally, a zone reader was employed to measure and record the zone of inhibition in millimetres (mm). The results regarding the antibacterial compounds zones of inhibition are summarized in Table 1.

Table-1: Anti-Bacterial activity

Compound	Bacterial strain zone of inhibition (Diameter in mm)			
	Escherichia coli	*Salmonella typhi*	*Staphylococcus aureus*	*Bacillus subtilis*
Penicillin	25	19	20	15
5(a)	15	14	16	13
5(b)	17	12	13	14
5(c)	15	15	17	12
5(d)	19	14	18	14
5(e)	22	18	20	18

Antifungal Evaluation:

The evaluation of antifungal activity was carried out using the Poison plate method [48-49]. The Potato Dextrose Agar (Himedia) was meticulously prepared and subsequently sterilized at 10 Psi in an autoclave for 15 minutes. Following sterilization, the Schiff base was introduced into the sterile medium under aseptic conditions, achieving a concentration 1%. For the negative control, a plate with containing ethanol was prepared, and similarly, a plate containing 1% Griseofulvin was established as the standard reference plate (positive control). The fungal cultures selected for investigation comprised *Aspergillus niger, Penicillium chrysogenum, Fusarium moniliform,* and *Aspergillus flavus.* These cultures were allowed to grow on a slant for a time period of 48 hours to facilitate abundant sporulation. Subsequently, a 5 mL aqueous solution of Tween 80 (at a ratio 1:100) was added to the slant, and spores were carefully collected using a Nichrome wire loop to create suspension. The fungal suspension was then inoculated onto the prepared plates using the compound, with the assistance of a Nichrome wire loop. Following the incubation, the plates were scrutinized for the presence of growth of the inoculated fungi. The results were recorded in (Table-2), denoting reduced growth of fungi (+), moderate growth of fungi (++) and the absence of growth of inoculated fungi (-) as indicators of antifungal activity.

Table-2: Anti-fungal activity

Compound	Fungi strain zone of inhibition (Diameter in mm)			
	A. niger	*P. chrysogenum*	*F. moniliform*	*A. flavus*
Griseofulvin	--	--	--	--
5(a)	+	++	+	+
5(b)	++	+	++	++
5(c)	+	++	++	+
5(d)	++	-	+	-
5(e)	-	+	-	+

Discussion:

In the realm of chemistry, the synthesis of novel Schiff bases entailed a series of reactions conducted through conventional methods, as illustrated in Scheme 1. In the initial stage, the intermediate compounds (2 and 4a-e) were meticulously synthesized, followed by re-crystallized in ethanol to ensure purity, which was subsequently verified using TLC. The progression of the reaction was continuously monitored using TLC. Interestingly, prolonging the reflux time did not yield any improvement in the product yield. Subsequent characterization procedures confirmed that these intermediates exhibited characteristics consistent with literature values. The Schiff bases, denoted as 4-hydroxy-3-(1-((5aryl)-1,3,4-oxadiazol-2-yl) imino) ethyl)-2H-chromen-2-one (5a-5e) were then synthesized, and their purity was ascertained through standard laboratory techniques, including p.m., and elemental analysis. Further characterization involved the application of analytical tools such as IR, ^{1}HNMR, ^{13}CNMR and mass spectral studies.

IR: In FT-IR spectra of the compounds 5a-5e prominent peaks are observed, characterized by a high intensity band ranging from 1657-1608 cm^{-1}, which is attributed to the ν(C=N) vibration and for the group of C=N in oxadiazole ring ~1600 for cm^{-1}. This observation strongly implies the formation of Schiff bases. Furthermore, the assignment of hydrogen-bonded –OH groups in the Schiff bases revels a distinct but broad, weak band spanning from 3598-2598 cm^{-1}. Another noteworthy feature in the spectra is the appearance of a band within the range of 1592-1507 cm^{-1}, signifying the presence of ν(C=C) vibrations in the aromatic ring. Additionally, 1372 and 1222 (ν>C-O) and enolic (-OH); while a band in the range of 1716-1708 cm^{-1} is associated with lactone carbonyl [29]. Furthermore, specific bands are observed around 1388-1361 for (ν>C-O) and 1238-1228 for enolic (-OH); ~1078 for (C–O of 1,3,4-oxadiazole nucleus). 848-853 cm^{-1} for ν(N-N)

stretching frequency. These findings provide valuable insights into the molecular structure and vibrations of compounds 5a-e.

^{1}H-NMR: In the context of the Schiff bases, ^{1}H-NMR spectra were observed in DMSO. The signals ranging from δ2.18-2.04 ppm can be attributed to the (S, 3H, imine –CH_3) moiety. Additionally, peaks at 6.9-7.59 and 7.2-8.30 (doublets, 4H) confirm para substitution. Notably, the phenolic –OH group exhibits a singlet at δ14.72-14.98 ppm. Furthermore, singular peaks manifest at δ 2.38, 9.70 and 4.08, which corresponds to –CH_3 in 5b, -OH in 5c and for –OCH_3 in 5d respectively. The aromatic protons manifest as a multiplate within the 6.95-8.3 ppm, depending on the aromatic substituent.

^{13}CNMR and Mass spectra: The ^{13}CNMR peak between 159.77-163.40 ppm confirms the presence of lactone carbon, and the peak between 175.99-178.29 ppm corresponds to the imine carbon. The peaks at about 123.61-138.91 for aromatic carbons of phenyl ring bonded to C^2 of 1,3,4-oxadiazol ring and 23.02 for -CH_3 carbon of p-tolyl, 56.55 for carbon of -OCH_3 group. The peaks at about 180.81-181.78 ppm due to presence of the carbon atom of oxadiazole ring. Assigning the other peaks observed in ^{1}HNMR, ^{13}CNMR spectra, and the molecular ion peaks in mass spectra justifies the structures of compounds 5a-5e.

Biological Activity: The effects of the investigated compounds (5a-e) on in vitro biological screening were tested against bacterial species *S. aurous*, *E. coli*, *S. typhi*, and B. *substilis* using the Agar cup method. Additionally, they were tested against fungal species *A. niger, P. chrysogenum, F. moniliform,* and *A. flavus* using the poison plate method. The results of these testes presented in Table-3 and Table-4. All imines exhibited lower activity against *E. coli, S. aureus* and *B. subtilis* when compared to penicillin, which was used as standard. Conversely, compounds 5d-5f demonstrated higher activity and exhibited antimicrobial effects against both bacteria and fungi. Notably, in compounds 5d displayed antifungal activity against *A. niger* and *F. moniliform*, while compound 5d were effective against *P. chrysogenum* and *A. flavus*. However, compounds 5a did inhibit the growth of these organisms to some extent but 5c reduced the growth. In conclusion, it can be inferred that the antimicrobial activity may be attributed to the presence of the of oxa-diazole moiety in the molecule.

IV. CONCLUSION

Schiff bases incorporating coumarin and 1,3,4-oxadiazole moieties have shown notable efficacy against both bacterial and fungal strains. These synthesized compounds display inhibitory effects on microbial cell wall formation, thereby impeding further growth. The presence of a phenolic hydroxyl group in the molecule facilitates enhanced penetration through specialized channels in gram-negative bacteria. Consequently, both electron-withdrawing and electron-donating groups play crucial roles in the activity of these compounds. Notably, compounds containing electron-withdrawing groups on the aromatic ring exhibit considerable antifungal activity. These findings underscore the potential of coumarin-incorporated 1,3,4-oxadiazole Schiff bases as promising agents against microbial infections.

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Cite this article as :

Jadhav Rajpal L., Ubale Sanjay B., "The Synthesis, Characterization, and Biological Activities of Some Novel Schiff Bases Derived From 3-Acetyl-4-Hydroxy-2H-Chromen-2-One And 2-Aminooxadiazole Derivatives Have Been Investigated", International Journal of Scientific Research in Science and Technology (IJSRST), Online ISSN : 2395-602X, Print ISSN : 2395-6011, Volume 11 Issue 1, pp. 479-488, January-February 2024. Available at doi :

https://doi.org/10.32628/IJSRST52411174

Journal URL : https://ijsrst.com/IJSRST52411174