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"Synthesis and Characterization of Biologically active Schiff base"

Mr. S.S. Anjanikar[1], Dr. S.S. Chandole*[2]

[1] Department of Chemistry, Sharadchandra College, Naigaon.

*[2] Department of Chemistry, S.G.B. College, Purna Jn.

Abstract:

New Schiff bases were synthesized using substituted hydrazides as a source of amine and 3-acetyl 2-brom pyridine as a carbonyl source, 2-bromopyridin-3-yl ethylidene-benzohydrazide (L_1), 2-bromopyridin-3-ylethylidene 4-methylbenzohydrazide (L_2), 2-bromo pyridin-3-yl ethyli dene-4-methoxybenzohydrazide (L_3) & 2-bromopyridin 3-yl ethylidene-4-nitrobenzohydrazide (L_4) by condensation reaction. These newly synthesized Schiff bases wer characterized by IR, NMR spectroscopic method. Further they are screened for their antibacterial and antifunga activity and revealed good to moderate activity.

Keywords: Schiff base, Spectral Characterization, Biological activity

Introduction

Heterocyclic compounds are found in nature which are vital parts of amino acids, hormones, vitamins, an drugs that play an important role in the metabolism of all living cells.[1] A wide range of important drugs have bee synthesized from heterocyclic compounds. Heterocyclic compounds with nitrogen as a heteroatom are considered be a noteworthy and distinct class of organic molecule, with a significant amount of research devoted to th development of novel compounds. Nitrogen containing heterocyclic compounds like pyrrole, Pyridine, indol triazole, pyrimidines, quinoline, imidazole, pyrazole have a prominent place in medicinal chemistry.[2] Among thes pyridine are considered the most important hetero moieties because of their biological and pharmacological activitie such as antibacterial[3], antifungal[4], anti oxidant[5], anti cancer[6], anti inflammatory[7]. Enzyme inhibitor[8], antidepressan etc. Azomethines, imines, anils, or Schiff bases are useful intermediates in the synthesis of important pharmaceutic and biochemical substances due to multifunctional transformations via reductions, condensations, additions, etc.[10] A interest in the exploration of novel heteroaromatic azomethines has undoubtedly been growing due to their prove usefulness as attractive lead structures for the development of catalysts, intermediates in organic synthesis, dyes

textile industry[11]. In the present study, Schiff base compounds were synthesized and screened for their antibacteria and antifungal study.

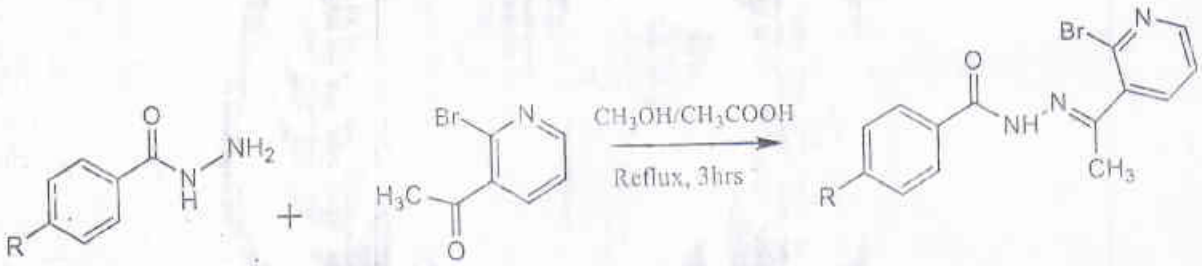
Materials and Methods

All the chemicals and solvents used in this work were AR grade. Melting point were recorded by ope capillary method. Elemental analysis was done on Eager 350 analyzer. H^1 -NMR spectra of metal complexes alon with Schiff base recorded on Bruker 300Hzs spectrometer in DMSO using TMS as internal Standard. IR spectra wer recorded on a Perkin-Elmer FTIR.

Experimental Procedure

Synthesis of 2-bromopyridin-3-yl ethylidene benzohydrazide

0.001M Substituted Benzohydrazide in10 ml glacial acetic acid was blended in with 0.001M 3-Acetyl bromoyridine in 10 ml methanol under steady mixing for 1 hr. The subsequent reaction mixture was then refluxe for 3hr in round bottom flask furnished with an air cooled condenser. The yellow precipitate was obtained. Tl precipitate was filtered under Buckner funnel. Washed with ethanol recrystallized and dried. The reaction is give below. Similar methods were used to synthesize other ligands.



R = -H, $-CH_3$, $-OCH_3$, $-NO_2$

Reaction Scheme

BIOLOGICAL ACTIVITY

Anti-Bacterial Activity:

The agar well diffusion method was used to test the antibacterial activity[12]. Mueller Hinton Agar for bacteria was used for all tests for antibacterial activity. For positive control of bacteriaAmpicillin was used. Thesolvent and positive control used was DMSO. Antibiotics and dehydrated media powder were brought from Hi-Media, India. Using sterile wire-loop, test organisms were aseptically added to sterile MH broth before being incubated at 37°C for 18 hours. This suspension was utilized as an inoculant. Wells in the media plates with a 10mm diameter were made using a sterile cork borer for the addition of compound solutions and controls. With the aid of a micropipette, [illegible] of the compound solution was aseptically added to the wellsto reach a final concentration of 10 g of compound in each well. As controls, the same quantity of DMSO

and ampicillin solution were introduced. The plates were cooled for 30 minutes to allow solutions to diffuse through the agar substrate. Plates were then incubated for 24 hours at 37°C.Bacillus subtilisandSalmonella typhi were gram positive bacteria that were utilized as test organisms, whereas Staphylococcus aureus and Escherichia coli were gram negative microorganisms. The zone margin should be regarded as the region that does not clearly display any expansion that the unaided eye can see. With a measuring scale in millimetres, the clean zone was measured.

Antifungal Activity

The poison plate approach was used to provide antifungal activity[13]. For the evaluation of antifungal activities, Aspergillus niger, Aspergillus flavus, Fusarium moneliforme, and Penicillium chrysogenum species were selected. Potato Dextrose Agar (PDA) media was utilized as a culture. To sterilize the medium, it was autoclaved at 121°C for 25 minutes under 15 psi of pressure. 20 ml of sterilized, melted PDA was added to sterilized petri plates with 2 ml of each component, and the mixture was then gently stirred in a circular motion to get homogenized. With positive Neomycin and negative DMSO controls, the identical process was followed. The fungal spores from the slant culture were transferred to a test tube containing sterile saline and thoroughly mixed with a sterile wire loop. As an inoculant, this spore solution was employed. The plates were incubated for four days at room temperature. After incubation, the growth of the infected fungi was monitored on the plates. The outcomes were noted.

Result and Discussion

All the reactions were carried out under conventional methods. The Schiff bases (L_1-L_4) were synthesized by condensation of substituted hydrazides with 3-acetyl 2-bromo pyridine. Assignment of significant peaks observed in IR, ^{1}HNMR, spectra of the compounds (L_1-L_4) is clarified in the analytical data.

The IR spectra of compound (L_1-L_4) showed high intensity band observed at 3236-3219 cm^{-1} is assigned to ν(N-H) vibration of hydrazide group. The band detected around 3065-3050 cm^{-1} notify presence of aromatic hydrogen. Azomethine group (C=N-) vibrations were identified around 1655-1640 cm^{-1} suggesting the formation of Schiff base. The band at 1540-1475 cm^{-1} is assigned to the combination of ν(C=C) of the aromatic ring.

Each one of the ^{1}H NMR spectra of (L_1-L_4) revealed singlet for 3H between 2.4-2.2 ppm assigned to imine methyl group. Peaks between 8.1-7.0 ppm are assigned to aromatic protons. All ^{1}HNMR spectra of compounds (L_1-L_4) showed multiplate for aryl moiety hydrogen. A singlet at 12.3-12.1 ppm confirms the presence of Hydrogen atom of hydrazide group. The hydrogen atom present on C-5 carbon of pyridine shows double doublet in the range of 7.2 ppm.

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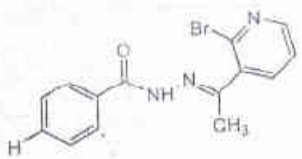
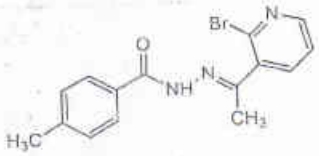
The Schiff's bases synthesized were evaluated for anti-bacterial and anti-fungal activity with different strain of bacteria and fungi. Results are shown in Table-3. All imines have shown lesser activity against *E. coli, S.aureu and B. subtilis* compared with penicillin taken as standard. The antibacterial activity of compound (L_4) was higher i comparison with other synthesized compounds. Antifungal activity observed against *P. Chrysogenum* wa encouraging in comparison with other fungal species. However, compounds (L_1-L_4) have reduced the growth of thes organisms. Therefore, it may be concluded from results that presence of Nitro group on bezohdrazide group of Schi base have enhanced the biological activity.

Table -1 Physical analysis of Synthesized Schiff Bases

Sr. No.	Synthesized Schiff bases	Mol. Formula	Colour	Melting Point in ^{0}C	Yield	Elemental Analysis			
						C	H	N	Br
L_1	2-bromopyridin-3-yl)ethylidene)benzohydrazide	$C_{14}H_{12}BrN_3O$	Yellowish White	165	82%	52.85	3.80	13.21	25.1
L_2	2-bromopyridin-3-yl)ethylidene)-4-methylbenzohydrazide	$C_{15}H_{14}BrN_3O$	Yellowish White	168	85%	54.23	4.25	12.65	24.0
L_3	2-bromopyridin-3-yl)ethylidene)-4-methoxybenzohydrazide	$C_{15}H_{14}BrN_3O_2$	Yellowish White	170	85%	51.74	4.05	12.07	22.9
L_4	2-bromopyridin-3-yl)ethylidene)-4-nitrobenzohydrazide	$C_{14}H_{11}BrN_4O_3$	Yellow	182	80%	46.30	3.05	15.45	22.(

Table No.2 Spectral Data of Synthesized Schiff Bases

Sr. No.	Structure of Synthesized Schiff bases	IR (ν in cm-1)	H^{1}NMRδ in ppm (300 MHz, DMSO
L_1		3219 (NH), 3057 (Ar CH), 1644 (C=O), 1575 (C=N) 1540, 1506, 1480 (C=C, Ar)	12.2(s, 1H, enolizable NH proton), 7.7 -7.5 (m, 5H, Ar-H), 7.5 & 7.9 (dd, 1H, Pyridine), 7.4 (d, 1H, Pyridine), 6.9 (d,1H, Pyridine), 2.4 (s, 3H, Azomethine)
L_2		3233 (NH), 3065 (Ar CH), 1650 (C=O), 1580 (C=N) 1520 C=C, Ar)	12.1(s, 1H, enolizable NH proton), 7.6 (m, 4H, Ar-H), 7.2 & 7.6 (dd, 1H, Pyridine), 7.2 (d, 1H, Pyridine), 6.8 (d,1H, Pyridine), 2.3 (s, 3H, Azomethine)

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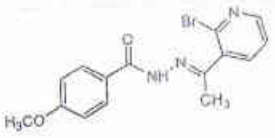
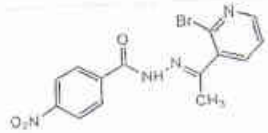
L_3		3225 (NH), 3050 (Ar CH), 1640 (C=O), 1580 (C=N), 1530, 1490, 1475 (C=C, Ar)	12.3(s, 1H, enolizable NH proton), 7.9 (m, 4H, Ar-H), 7. 3& 7.4 (dd, 1H, Pyridine), 7.3 (d, 1H, Pyridine), 7.0 (d,1H, Pyridine), 2.2 (s, 3H, Azomethine)
L_4		3236 (NH), 3064 (Ar CH), 1655(C=O), 1565 (C=N), 1520, 1490, 1480 (C=C, Ar)	12.3(s, 1H, enolizable NH proton), 8.1 (m, 4H, Ar-H), 7.4 & 7.6 (dd, 1H, Pyridine), 7.4 (d, 1H, Pyridine), 6.9 (d,1H, Pyridine), 2.3 (s, 3H, Azomethine)

Table No. - 3 Anti- Bacterial and Anti-Fungal Activity

Synthesized Schiffbase ligands	Antibacterial Study Zone of Inhibition (diameter in mm)				Antifungal Study Growth of Fungi			
	Gram Positive		Gram Negative		A. niger	A. flavus	F. monili forme	P. chryso genum
	S. typhi	B. subtilis	E. coli	S. aureus				
Ampicillin (Reference)	18	19	17	18	Neomycin (Reference)			
2-bromopyridin-3-yl)ethylidene)benzohydrazide	11	10	11	12	-	-	-	-
2-bromopyridin-3-yl)ethylidene)-4-methylbenzohydrazide	11	11	12	11	++	+	+	+
2-bromopyridin-3-yl)ethylidene)-4-methoxybenzohydrazide	12	11	12	12	++	+	+	-
2-bromopyridin-3-yl)ethylidene)-4-nitrobenzohydrazide	14	13	14	15	+	+	+	-
					-	+	+	-

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

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