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Synthesis, Characterization and antibacterial activity of 2-aminopyridine based Schiff`s Bases

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ABSTRACT

Schiff`s bases play a vital role in the field of pharmaceutics. They are important class of molecules for the synthesis of novel drugs as intermediates. The present work involves condensation of 2-aminopyridine derivatives and salicylaldehyde to yield 2-{(Z)-[(3-methylpyridin-2-yl)imino]methyl}phenol and 2-{(Z)-[(3-methoxypyridin-2-yl)imino]methyl}phenol. This method is experimentally simple, clean, high yielding with reduced time period. The compounds are characterised by IR, 1HNMR, and elemental analysis. The final products are purified in ethanol and screened for biological activities by using broth dilution method.

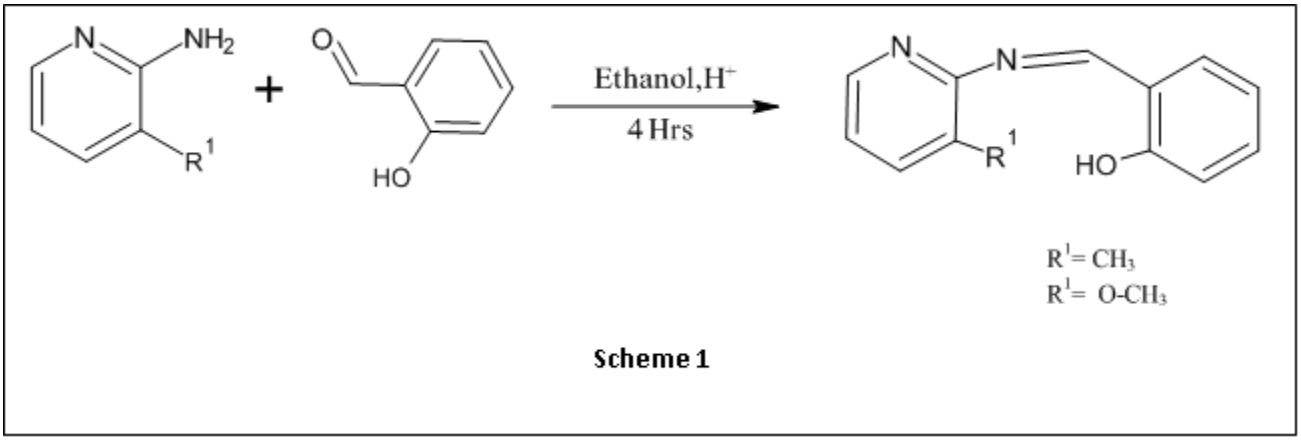
Keywords: Schiffs base, 2-aminopyridine, SalicylaldehydeAntibacterial activity.

I. INTRODUCTION

During the past decade, life-threatening infectious diseases caused by gram positive and gram negative pathogenic bacteria have increased to an alarming level around the world. This increase coupled with emergence of bacteria resistant to commonly used antibiotics has resulted in the need to evolve new classes of antibacterial agents to combat infections. Understanding the chemistry of molecular biology has created a significant class of compounds that are now employed as antibacterial agents[1]. A class of compounds that has shown great promise in this area are the Schiff bases. A Schiff base is the nitrogen analogue of aldehyde in which the C=O group is replaced by a C=N group. Schiff bases are reported to exhibit antibacterial, antifungal and antitumor activity[2,3]. In addition, the compounds and their metal complexes exhibit interesting photophysical properties[4]. Salicylidimines show important photochromism where light absorption causes interconversion between enol-imine and keto-amine tautomers through intramolecular hydrogen transfer[5]. They have also been shown to exhibit a variety of biological activities with substituted salicylaldehyde compounds possessing higher activities[6,7]. Aromatic aldehydes especially with an effective conjugation system, form stable Schiff bases, where as those aliphatic aldehydes are unstable and readily polymerize. Schiff base ligands with aldehydes are formed more readily than with ketone (carbonyl carbon).Schiff bases have very flexible and different structures[8]. A wide range of Schiff base compounds and their behaviour studied because these compounds have very flexible and diverse structureSchiff bases are generally are bi ,tri, or tetra-dentate chelate ligands and from very stable complexes with metal ions.

II. MATERIALS AND METHODS

The reagent grade chemicals were obtained from commercial sources and purified by either distillation or recrystallization before use. The purity of synthesized compounds was checked by thin layer chromatography (TLC) on silica gel plate using ethyl acetate:CycloHexene (7:3). Melting points were determined by open capillary method and are uncorrected. Elemental analyses were performed with a Perkin-Elmer 2400 CHNS/O analyzer. IR spectra are recorded on FT-IR Perkin-Elmer spectrophotometer using KBr disc. 1H-NMR spectra are recorded in CDCl3 on a Bruker -400 MHz using TMS as internal standard.



Scheme 1

General procedure for preparation of Schiff bases

[A] 2-{(*Z*)-[(3-methylpyridin-2-yl)imino]methyl}phenol

A mixture of 3-methylpyridin-2-amine (1.08gm, 0.01M) and Salicylaldehyde (1.22gm, 0.01M) in absolute ethanol was refluxed in waterbath for 4 hrs. in presence of 1ml glacial acetic acid.Yellow orange coloured Solid Product obtained after crystallization from absolute ethanol.

IR (cm -1): 3434,2920, 1613, 1589, 1278, 1256, 1148, 993, 915, 845, 790, 732,695, 578. 1HNMR (CDCl3, 400mHz): 6.91-8.49(m, 8H), 9.41(s,1H), 13.40(s,1H),(s,3H). Yield, 2.05gm (89.13%), M.P: 63°C ($C_{13}H_{12}N_2O$); Calculated: C, 73.58; H, 5.66; N, 13.20; O,7.6 Found: C, 72.92; H, 5.64; N, 13.34; O,7.54%).

[B] 2-{(*Z*)-[(3-methoxypyridin-2-yl)imino]methyl}phenol

A mixture of 3-methoxypyridin-2-amine (1.24gm, 0.01M) and Salicylaldehyde (1.22gm, 0.01M) in absolute ethanol was refluxed in waterbath for 4 hrs. in presence of 1ml glacial acetic acid. Orange coloured Solid Product obtained after crystallization from absolute ethanol.

IR (cm -1): 1609, 1575, 1549, 1484, 1325, 1271, 1143, 1027, 991,890, 830, 770, 623. 1HNMR (CDCl3, 400 MHZ): 3.77(s, 3H), 6.92 to 8.48(m,7H), 9.37(s, 1H), 12.93(s, 1H). Yield, 2.1gm (92.10%), M.P: 65°C ($C_{13}H_{12}N_2O_2$); Calculated: C, 68.42; H, 5.26; N, 12.28; O,14.03 Found: C, 67.90; H, 5.10; N, 12.30; O,14.1%).

III. RESULTS AND DISCUSSION

Synthesis Condensation of the 3-methylpyridin-2-amineand 3-methoxypyridin-2-amine with the corresponding aldehyde readily gave rise to the corresponding Schiff bases 2-{(*Z*)-[(3-methylpyridin-2-yl)imino]methyl}phenoland 2-{(*Z*)-[(3-methoxypyridin-2-yl)imino]methyl}phenol. All the compounds are air stable with sharp melting points indicating the purity of the compounds. The elemental analysis of the compounds is in agreement with the composition suggested for the compounds. The IR of each compound

confirms the formation of imine bond (–C=N-) and absence of the original aldehydic bond (-C=O)[9]. A band at 1607-1615 cm -1 is assigned to the stretching vibration of the imine group v (C=N)[10,11]. All the compounds displayed a band at 1271-1289 cm -1 which is assigned to v(C-O) stretching vibration of the Phenolic – OH, respectively. The v(OH) band at 3434-3438 cm -1 was observed only in compounds I and II. Proton NMR showed sharp singlet at 9.34-9.53 ppm which further confirmed the formation of –C=N- bonds[12-14].

IV. ANTIBACTERIAL ACTIVITY

Antibacterial Activities of the compounds in DMF and dioxane are reported in Table 1 and 2[12]. The morphology of the cell wall is a key factor that influences the activity of antibacterial agents. The cell wall of the bacteria is composed of peptidoglycan which is thicker in gram positive bacteria and this usually possess a barrier to the degree of diffusion of antibacterial agents in to the enzyme. Four standard bacteria strains screened were gram positive S.aureus(ATCC 25923), and E. feacalis (ATCC 29212) and gram negative E.coli(ATCC 25922) and P.aeroginosa (ATCC 27853)[15-18].All compounds were active against S. aureusand E.coli and inactive against E. feacalis and P.aeroginosa. . The unsubstitutedsalicylaldehyde Schiff base I had minimal activity against bacteria studied in both solvents. The change of solvent to less polar dioxane I was active at lower concentrations of 5 m g/ml respectively. The higher activity reported in less polar solvent may be due to easier diffusion across the cell wall[19-21].

Table1.

Compounds	S. aureus E. feacalisE.coliP.aeroginosa
	Concentrations (mg/ml) 40 20 10 5 40-5 40 20 10 5 40-5
I	3+ 2+ 0 0 0-0 3+ 2+ 2+ 0 0-0
II	3+ 3+ 3+ 2+ 0-0 3+ 3+ 2+ 0 0-0

Table 2.

Compounds	S. aureus E. feacalisE.coliP.aeroginosa
	Concentrations (mg/ml) 40 20 10 5 40-5 40 20 10 5 40-5
I	3+ 3+ 1+ 0 0-0 1+ 0 0 0 0-0
II	3+ 2+ 3+ 1+ 0-0 3+ 3+ 2+ 0 0-0

V. CONCLUSION

The 2-aminopyridine based Schiff bases are synthesized by condensing 3-methylpyridin-2-amine and 3-methoxypyridin-2-amine with Salicylaldehyde. The obtained products are characterized by IR, ^{1}HNMR spectral data and elemental analysis. The compounds have the capacity of inhibiting metabolic growth of S. aureus and E. coli to different extent. The antibacterial activity of the compounds depends on the nature of substituent present on the pyridine ring. The importance of this lies in the potential use of the compounds as narrow spectrum antibiotics in treatment of some common diseases.

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