International Journal of Innovative Research and Advanced Studies (IJIRAS)
Volume 4 Issue 2, February 2017

ISSN: 2394-4404

# Synthesis, Spectroscopic And Inhibitory Study Of Some Substituted Schiff Bases

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***Abstract:*** ***A series of Schiff bases namely (E)-4-methoxy-2-((phenylimino)methyl)phenol [I], (E)-2-(((4-chlorophenyl)imino)methyl)-4-methoxyphenol [II], (E)-2-(((2-hydroxyphenyl)imino)methyl)-4-methoxyphenol [III], (E)-2-(((5-chloro-2-methylphenyl)imino)methyl)-4-methoxyphenol [IV] derived from substituted aniline and 5-methoxysalicylaldehyde were synthesized and characterized by elemental analysis, IR, UV, and $^1$H NMR. The results revealed that the compounds are capable to prevent the growth Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Streptococcus agalactiae, Staphylococcus aureus and Salmonella typhimurium in diverse concentrations. The growth prevention capability was affected by the substituent on the aniline.***

***Keywords: Schiff base, antimicrobial activity, substituent, aniline.***

## I. INTRODUCTION

Schiff bases are aldehyde or ketone like compounds in which the carbonyl group is replaced by an imine or azomethine (C=N−) group. They are formed via the condensation of primary amines with carbonyl compounds (Aziz, Salaem, Sayed, & Aboaly, 2015; Dueke-Eze, Fasina, & Idika, 2011; Fasina, Ejiah, Dueke-Eze, & N, 2013; Vinita, Sanchita, & Y.K, 2013). They are generally represented by the formula $R_1HC=NR_2$ where $R_1$ and $R_2$ are alkyl or aryl groups (Dueke-Eze et al., 2011).

Salicylaldimine Schiff bases exhibit significant photochromism where light absorption causes interconversion between enol-imine and keto-imine tautomers through intramolecular hydrogen transfer. They play important role in coordination chemistry, so also in biological system (Ikram et al., 2015; Khan et al., 2013; Muhammad et al., 2013; Oloyede-Akinsulere, Salihu, Babajide, & Auta, 2016; Yiheyis, Nithyakalyani, & Ananda, 2014). Schiff bases show a wide range of biological activities such as antifungal, antibacterial, antiviral, antipyretic, antimalarial, anti-inflammatory properties etc. (Abo-Aly, Salem, Sayed, & Aziz, 2015; Aziz et al., 2015; Belal, El-Deen, Farid, Rosan, & Moamen, 2015; Saha, Jana, Gupta, Ghosh, & Nayek, 2016; Yiheyis et al., 2014). The imine group is important in elucidating the mechanism of transamination and racemization reaction in biological system (Ndosiri et al., 2013; Subbaraj, Ramu, Raman, & Dharmaraja, 2013).

This study presents the antimicrobial activity of Schiff bases derived from substituted aniline and 5-methoxysalicylaldehyde.

ISSN: 2394-4404

## II. MATERIALS AND METHOD

### REAGENTS

Aniline, 2-aminophenol, 4-chloroaniline, 5-chloro-2-methylaniline and 5-methoxysalicylaldehyde were purchased from Merck (Germany) and used as supplied. The solvent DMSO (dimethyl sulfoxide) and absolute ethanol were of analytical grade and were used without further purification. Elemental analysis was carried out on Finnigan Flash EA 1112 series. The electronic spectra were recorded on Shimadzu UV-2600 series (Japan), in DMSO. The infrared spectra were recorded on a Perkin-Elmer 400 FT-IR/FT-FIR while the NMR spectra were obtained using a Bruker Avance 111 600 in DMSO-$D_6$ solution with tetramethylsilane (TMS) as internal standard.

### SYNTHESIS OF SCHIFF BASES

0.015 mole amine in 15 ml of absolute ethanol was added to a stirring solution of 0.015 mole of 5-methoxysalicylaldehyde in 10 ml absolute ethanol. Three drops of formic acid were added and the resulting mixture was stirred for 2 hrs. The precipitates were filtered and washed with cold ethanol, recrystallized from ethanol and dried in a desiccator over silica gel for two days.

I=(E)-4-methoxy-2-((phenylimino)methyl)phenol. Yield 74%, IR ($cm^{-1}$): 3630, 3035, 2937, 2830, 1616, 1565, 1491, 1447, 1395, 1360, 1272, 1209, 1183, 1045, 973, 941, 870, 794, 750, 679, 554, 517. UV: 308 ($n-\pi^*$), 367 ($\pi-\pi^*$). $^1H$ NMR (ppm): 12.36 (s, 1H, OH), 8.90 (s, 1H, C=N), 7.40-6.80 (m, 6H, C−$H_{Ar}$), 3.70 (s, 3H, C−$H_{methoxy}$). Elemental analysis in % for $C_{14}H_{13}NO_2$ (Calculated): 73.99, 5.77, 6.16. Found: 74.01, 5.79, 6.15.

II=(E)-2-(((4-chlorophenyl)imino)-4-methoxyphenol. Yield 80%, IR ($cm^{-1}$): 3640, 2937, 2831, 1617, 1591, 1566, 1488, 1397, 1360, 1271, 1207, 1179, 1156, 1092, 1046, 973, 944, 871, 826, 786, 758, 699, 515. UV: 313 ($n-\pi^*$), 371 ($\pi-\pi^*$). $^1H$ NMR (ppm): 13.00 (s, 1H, OH), 8.90 (s, 1H, C=N), 7.40-6.70 (m, 5H, C−$H_{Ar}$), 3.37 (s, 3H, C−$H_{methoxy}$). Elemental analysis in % for $C_{14}H_{12}ClNO_2$ (Calculated): 64.25, 4.62, 5.35. Found: 64.23, 4.58, 5.38.

III=(E)-2-(((2-hydroxyphenyl)imino)methyl)-4-methoxyphenol. Yield 88%, IR ($cm^{-1}$): 3747, 3046, 2987, 2896, 2560, 1626, 1591, 1494, 1456, 1300, 1246, 1163, 1143, 1039, 941, 869, 810, 786, 738, 662, 589, 566, 471. UV: 270 ($n-\pi^*$), 370 ($\pi-\pi^*$). $^1H$ NMR (ppm): 13.07 (s, 1H, OH), 9.68 (s, 1H, OH), 8.89 (s, 1H, C=N), 7.29-6.82 (m, 7H, C−$H_{Ar}$), 3.39 (s, 3H, C−$H_{methoxy}$). Elemental analysis in % for $C_{14}H_{13}NO_3$ (Calculated): 69.12, 5.39, 5.76. Found: 69.10, 5.40, 5.80.

IV=(E)-2-(((5-chloro-2-methylphenyl)imino-4-methoxyphenol. Yield 84%, IR ($cm^{-1}$): 3640, 2973, 2820, 1614, 1564, 1487, 1387, 1331, 1270, 1200, 1160, 1093, 1035, 995, 914, 877, 815, 787,747,651, 602, 470. UV: 320 ($n-\pi^*$), 372 (*P.mirabilis*). 1H NMR (ppm): 12.33 (s, 1H, OH), 8.84 (s, 1H, C=N), 7.37-6.86 (m, 6H, C−$H_{Ar}$), 3.71 (s, 3H, C−$H_{methoxy}$), 2.25 (s, 3H, C−$H_{methyl}$). Elemental analysis in % for $C_{15}H_{14}ClNO_2$ (Calculated): 65.34, 5.12, 5.08. Found: 65.35, 5.15, 5.10.

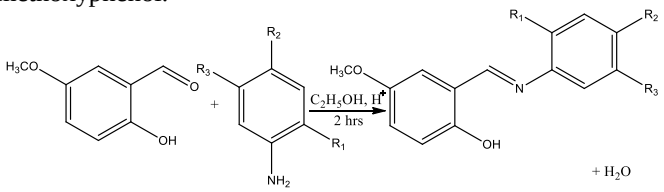
### ANTIMICROBIAL

The antibacterial potentials of the samples were evaluated by agar-well diffusion method against multi-drug resistance Gram-positive (*Streptococcus agalactiae and Staphylococcus aureus),* and Gram-negative *(Escherichia coli, Klebsiella pneumonia, Proteus mirabilis, Pseudomonas aeruginosa and Salmonella typhimurium*) organisms. The bacteria isolates were sub-cultured in Nutrient agar and incubated at 37 $^oC$ for 24 hours. All the bacteria cultures were adjusted to 0.5 McFarland standards, 20 ml of sterilized Nutrient agar medium was dispensed into each Petri dish aseptically and allowed to gel and the plates were swabbed with inocula of the test organisms, and kept for 15 minutes for adsorption unto the gel. Using sterile cork borer of 6 mm diameter, wells were bored into the seeded agar plates, and these were loaded with different concentrations of the samples. The plates were allowed to stand in the refrigerator for 1 hour to allow proper diffusion of the sample into the medium and incubated at 37 $^oC$ for 24 hours before visual assessment of the inhibition zones. Antimicrobial activities were expressed as inhibition diameter zones in millimeter (mm). Gentamicin (GEN) and Cloxicillin (CXC) were used as control.

## III. RESULT AND DISCUSSION

### SYNTHESIS

The condensation of 5-methoxysalicyladehyde and corresponding substituted aniline give the corresponding Schiff bases: [I] (E)-4-methoxy-2-((phenylimino)methyl) phenol, [II] (E)-2-(((4-chlorophenyl)imino)-4-methoxyphenol, [III] (E)-2-(((2-hydroxyphenyl)imino)methyl)-4-methoxy phenol, [IV] (E)-2-(((5-chloro-2-methylphenyl)imino-4-methoxyphenol.




[I] $R_1$= H, $R_2$= H, $R_3$= H
[II] $R_1$= H, $R_2$= Cl, $R_3$= H
[III] $R_1$= OH, $R_2$= H, $R_3$= H
[IV] $R_1$= $CH_3$, $R_2$= H, $R_3$= Cl

*Scheme 1: Synthesis of Schiff bases [I-IV]*

The IR of each compound confirms the formation of azomethine bond ν(HC=N−) and the absence of the original aldehydic bond (−C=O). A band at 1626-1614 $cm^{-1}$ is assigned to the stretching vibration of the azomethine group ν(HC=N−). All the compounds displayed a band at 1270-1246 $cm^{-1}$ which is assigned to the phenolic stretching vibration. The ν(−OH) band appeared between 3630-3747 $cm^{-1}$. The $^1H$ NMR (Fig. 1-4) showed sharp singlet at 8.84-9.90 ppm which further confirmed the formation of the ν(HC=N−) bonds. The UV spectra of the Schiff bases showed two absorption peaks at 270-320 nm assigned to $n-\pi^*$ of the azomethine and 367-372 nm assigned to $\pi-\pi^*$ of the aromatic ring in the Schiff bases.

ISSN: 2394-4404

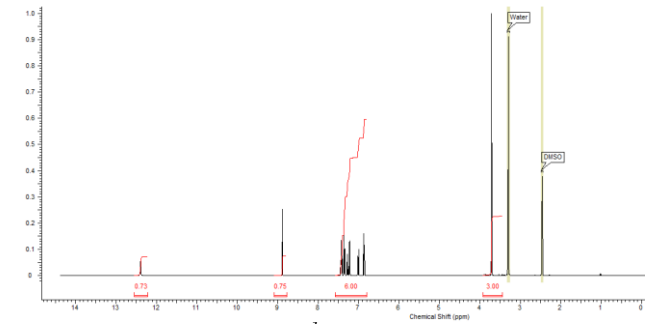



*Figure 1: $^{1}H$ NMR of [I]*

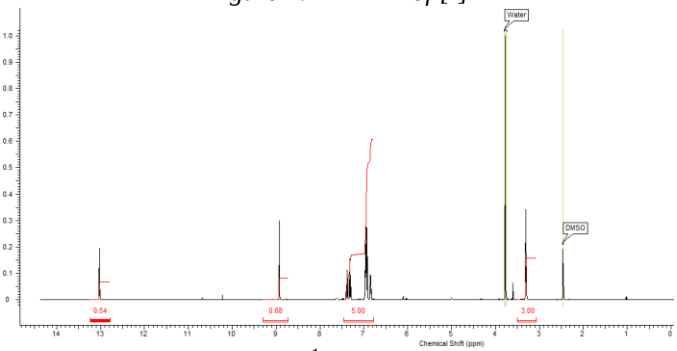



*Figure 2: $^{1}H$ NMR of [II]*

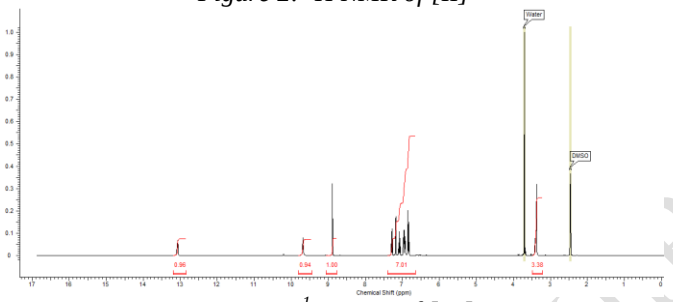



*Figure 3: $^{1}H$ NMR of [III]*

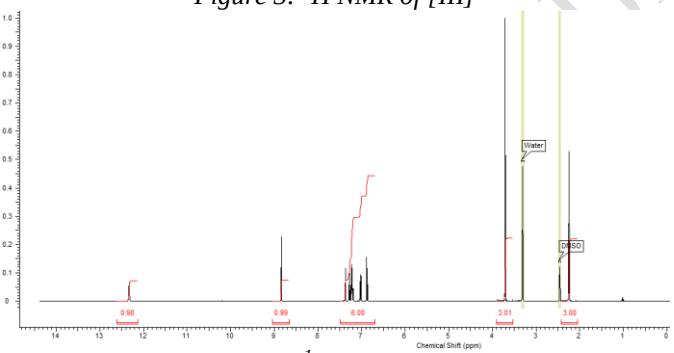



*Figure 4: $^{1}H$ NMR of [IV]*

| Bacteria | Concentration of compounds / Zones of inhibition | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | I | | | II | | | III | | | IV | | |
| | 40 (mg/ml) | 20 (mg/ml) | 10 (mg/ml) | 40 (mg/ml) | 20 (mg/ml) | 10 (mg/ml) | 40 (mg/ml) | 20 (mg/ml) | 10 (mg/ml) | 40 (mg/ml) | 20 (mg/ml) | 10 (mg/ml) |
| *E. coli* | 15 | 13 | 13 | 12 | 12 | 12 | 25 | 22 | 22 | 10 | 10 | 10 |
| *K. pneumonia* | 25 | 20 | 20 | 12 | 12 | 12 | 20 | 20 | 20 | 18 | 15 | 15 |
| *P. aeruginosa* | 18 | 18 | 18 | 14 | 14 | 14 | 30 | 30 | 30 | 18 | 16 | 15 |
| *S. agalactiae* | 15 | 15 | 15 | 10 | 10 | 10 | 22 | 22 | 22 | 10 | 10 | 10 |
| *S. aureus* | 13 | 13 | 13 | 10 | 10 | 10 | 30 | 30 | 30 | 10 | 10 | 10 |
| *S. typhimurium* | 16 | 12 | 12 | 20 | 12 | 12 | 18 | 18 | 18 | 15 | 15 | 15 |
| *P.mirabilis* | 22 | 14 | 14 | 0 | 0 | 0 | 25 | 25 | 25 | 0 | 0 | 0 |

*Table 1: Zone of inhibition showing the antimicrobial potentials of compounds (I-IV)*

## IV. ANTIMICROBIAL ACTIVITY

Table 1 shows the antimicrobial activity of the different compounds [I-IV]. The Table revealed that compounds [I] and [III] are active against all the bacteria strains. Compounds [II] and [IV] exhibited activity against all the bacteria except *P.mirabilis*.

Compounds [III] exhibited the highest activity against all the bacteria strains because of the OH which is an electron donating group on the aniline. The methyl substituent (electron releasing group) on [IV] contributed to its higher activity than [II].

The resistance of the pathogens towards the tested compounds can be attributed to the existence of cell wall in gram positive bacteria which reduces the permeability of the tested compounds, while the activity against them can be attributed to the greater lipophilicity of the compounds.

## V. CONCLUSION

All the compounds have the ability to prevent the metabolic growth of *Escherichia coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Streptococcus agalactiae, Staphylococcus aureus and Salmonella typhimurium* at different extent. The antimicrobial activity of the compounds depends on the nature of the substituent on the amine.

## ACKNOWLEDGEMENT

The authors appreciate the Organization of Women in Science in Developing World for the research fellowship granted to Demehin, A.I. to study in the Department of Chemistry, University of Malaya, Kuala Lumpur, Malaysia. They are grateful to Prof. Dr. Hapipah, M. A. Department Of Chemistry, University of Malaya for providing for the NMR analyses and allowing the use of her laboratory for the research. They express their profound gratitude to Dr. Ololade, Z.S. of Department of Chemical Sciences, Bells University, Ota, Nigeria who helped with the antimicrobial analyses. Also, the authors acknowledge the management of Adeyemi College of Education, Ondo, Nigeria for granting Demehin, A.I. a study leave.

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ISSN: 2394-4404

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