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RESEARCH ORGANISATION

Volume 1, Issue 1
May 1, 2015

Journal of Progressive Research in Chemistry
www.scitecresearch.com

# Design and Synthesis of New Series of One Pot Schiff Bases of 4-Aminobenzenesulfon-Amideas Potent Antibacterial and Anti-Fungal Agents

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## Abstract

Schiff bases are imines formed by the condensation of a primary amine and a carbonyl compound. These classes of compounds are very important due to their wide range of biological activities and industrial applications. In this study, some Schiff bases (coded GAS1-5) were synthesized by condensation of 4–Aminobenzenesulfonamide and some selected carbonyl molecules via MW irradiation for 1 minute at 385 watt power; and were characterized by FT-IR and elemental analyses. These Schiff bases were then evaluated for their bactericidal effects against two Gram positive and two Gram negative bacteria (*Staphylococcus aureus, Bacillus subtilis* and *Escherichia coli, Pseudomonas aeruginosa respectively*) and for their fungicidal activities against one fungus (*Candida albicans*). Their biocidal activities were also evaluated against one standard antibacterial drug, Zyprox (Ciprofloxacin), and one standard antifungal drug , Nizoral (ketoconazole), in the market. All the synthesized bases, except one, exhibited interesting antimicrobial activities against the selected microbes; some even exhibited better biocidal effects at the chosen concentration for this work (5µM) than the standard commercial reference drugs used in this study.

**Keywords:** Schiff bases; 4–Aminobenzenesulfonamide; Zyprox; Nizoral; MW irradiation; biocidal activities .

## 1. Introduction

Schiff bases are typically formed by the condensation of a primary amine and an aldehyde. Schiff bases are important intermediates for the synthesis of various bioactive compounds [1]. Furthermore, they are reported to show a variety of biological activities including antibacterial, antifungal, anti-cancer and herbicidal activities [1]. Some of their synthetic methods have not been entirely satisfactory owing to a number of drawbacks such as low yields and tedious workup procedures [2, 3] Over the past few decades, significant research has been directed towards the development of new technologies for environmentally benign processes (green chemistry [2-6].

## 2. Review of Literature

Schiff bases are very important class of compounds due to their wide range of biological activities and even industrial applications [7- 11]. Schiff bases contain the azomethine functional group, (-HC=N-) ,formed by the condensation of a primary amine with an active carbonyl compound [12. 13].These classes of compounds have varied structures and exhibit a great variety of biological activities. These activities are reported to include pharmacological applications such as antimicrobial [14 - 16], antibacterial [17 - 20] , antifungal [21 - 25] , antimalarial [26], antifeedant [27], anti-inflammatory [29- 30], anticancer[17, 31] , antitubercular [32, 33] , antiviral [34] , anticonvulsant [35 - 38] and analgesic properties[39 - 42].

Among the many different families of organic–inorganic compounds that are currently being investigated are sulfonamides and their N-derivatives because of their applications in various biological and pharmacological fields

[7 - 42]. Sulfonamides were the first effective chemotherapeutic agents employed systematically for the prevention and cure of bacterial infections in humans. Sulfa drugs are still today among the drugs of first election (together with ampicillin and gentamycin) as chemotherapeutic agents in bacterial infections [42, 43].

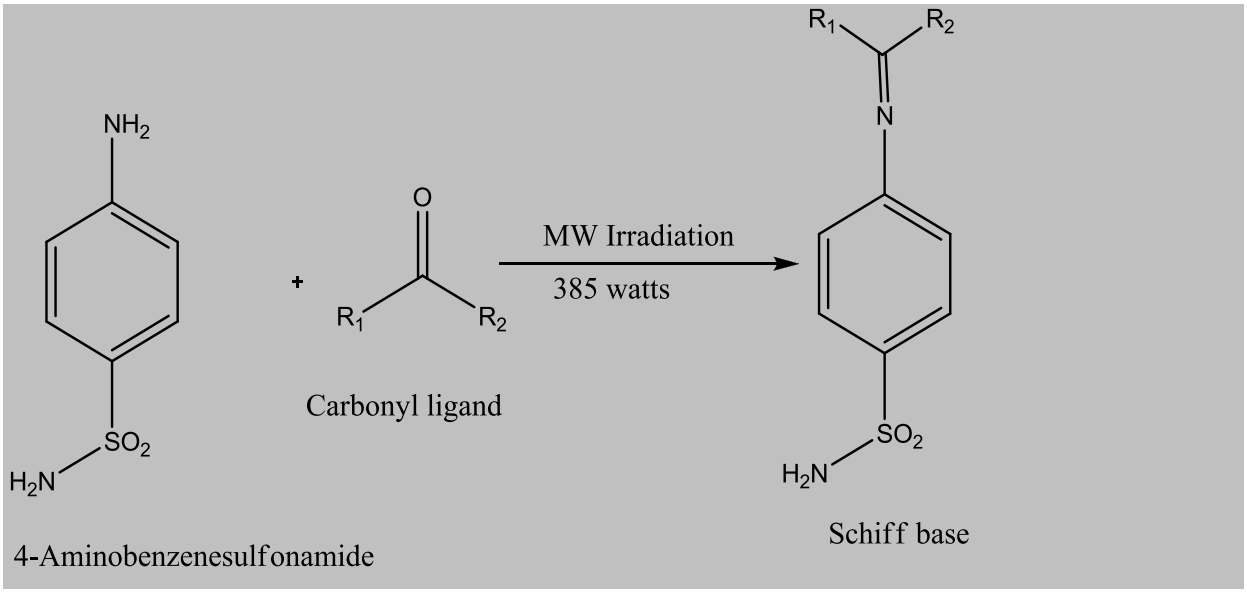
## 3. Materials and Methodology

### 3.1 Chemicals and drugs

All chemicals, solvents and reagents used in the present study were of analytical grade purchased from Sigma, BDH, May & Baker or Fluka. The reference drugs, Zyprox (Ciprofloxacin) and Nizoral (ketoconazole), were obtained from De-Fryo, a local patent medicine store in Samaru, Zaria.

### 3.2 Synthesis of Schiff bases

The respective reaction mixtures were prepared by taking equimolar solutions (0.02 M) of sulfanilamide and the appropriate carbonyl ligand dissolve in anhydrous ethanol, into a chromic acid scrubbed, cleaned and dried crucibles. The reaction mixtures were swirled vigorously to get uniform mixing before the mixtures were transferred to a Continent MW800G microwave oven. These mixtures were subjected to MW irradiation for 1 minute at 385 watt power. After cooling, the formed crystals were filtered off, washed with several portions of anhydrous ethanol. The general synthetic route is demonstrated in scheme 1. The appropriate carbonyl ligands used for the synthesis of the various Schiff bases (GAS 1-5) are shown in table 1.




**Scheme 1: Synthetic route of the Schiff bases**

### 3.3 Physical measurements

The melting points were determined by open capillary method. The purities of the synthesized compounds were confirmed by thin layer chromatography using Silica coated aluminum sheets. The IR spectra of the Schiff bases were recorded on an AVATAR 330 FT-IR, Thermo Nicolet instrument. The Elemental analyses were performed with Thermo scientific Flash 2000, CHNS-O Elemental analyzer.

### 3.4 Biological studies

The biocidal activities of the synthesized compounds were determined using agar well diffusion method [43 - 45]. The test microorganisms employed for these studies include two Gram positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*), two Gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) and one fungus (*Candida albicans*). The clinical isolates were all obtained from the Department of Medical Microbiology, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria; and transported in slants of nutrient agar and MacConkey agar. ME CURE Zyprox (Ciprofloxacin) and Nizoral (ketoconazole), obtained from De-Fryo, a local medicine store in Samaru, Zaria, were used as reference drugs for antibacterial and antifungal activities respectively.

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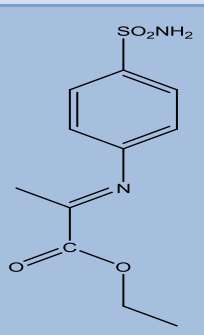
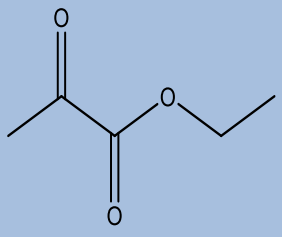
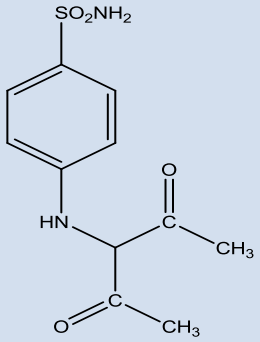
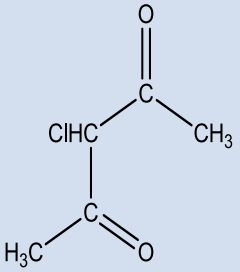
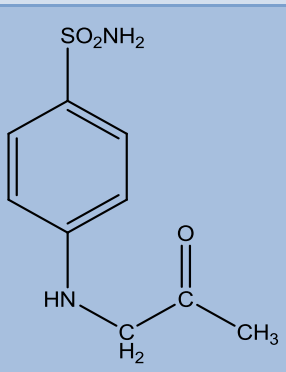
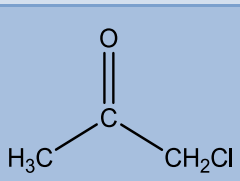
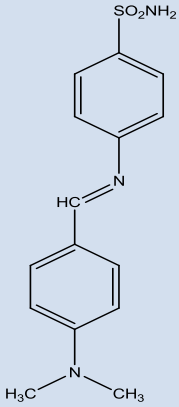
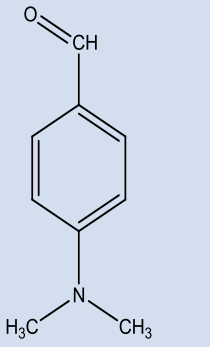
## 4. Results.

**Table1:The Synthesized Bases (GAS 1-5), their Percentage Yields and the Carbonyl Ligands Used.**

| Code | Schiff base | Carbonyl ligand | Yeild (%) |
|---|---|---|---|
| **GAS 1** |  (*E*)-ethyl 2-(4-sulfamoylphenylimino)propanoate |  ethyl-2-oxopropanoate | 73 |
| **GAS 2** |  4-(2,4-dioxopentan-3-ylamino)benzenesulfonamide |  3-chloropentane-2,4-dione | 71 |
| **GAS 3** |  4-(2-oxopropylamino)benzenesulfonamide |  1-chloropropan-2-one | 76 |
| **GAS 4** |  (*E*)-4-(4-(dimethylamino)benzylideneamino)benzenesulfonamide |  4-(dimethylamino)benzaldehyde | 92 |

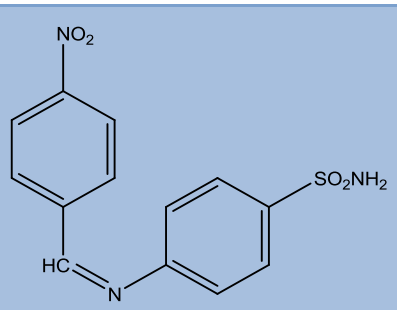
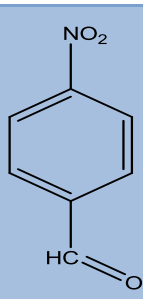
| | | | |
|---|---|---|---|
| **GAS 5** |  (*Z*)-4-(4-nitrobenzylideneamino)benzenesulfonamide |  4-nitrobenzaldehyde | 92 |

**Table 2: Physico-chemical data of synthesized Schiff bases (GAS 1-5)**

| Code | Mol Wt | Molecular Formula | M.P. ($^0$C) | FT-IR (cm-1) | Elemental analysis (% ) ( Experimental / Calculated) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | C | H | N | S | O |
| **GAS 1** | 270.30 | $C_{11}H_{14}N_2O_4S$ | 142-144 | 3463, 3374 (NH2); 1738 (ester CO); 1629 (C=N); 1311, 1151 (-$SO_2NH_2$); 829, 722 (S-O) | 48.82 | 5.22 | 10.52 | 11.81 | 23.63 |
| | | | | | 48.88 | 5.22 | 10.36 | 11.86 | 23.68 |
| **GAS 2** | 270.30 | $C_{11}H_{14}N_2O_4S$ | >250 | 3476, 3373, 3272 ($NH_2$& NH); 1698 (CO); 1295, 1145 (-$SO_2NH_2$); 801, 704 (S-O) | 49.00 | 5.13 | 10.34 | 12.00 | 23.53 |
| | | | | | 48.88 | 5.22 | 10.36 | 11.86 | 23.68 |
| **GAS 3** | 228.27 | $C_9H_{12}N_2O_3S$ | 183-185 | 3477, 3382 ($NH_2$); 3318 (NH); 1723 (CO); 1310, 1150 (-$SO_2NH_2$); 825, 741 (S-O) | 47.34 | 5.30 | 12.30 | 21.07 | 13.99 |
| | | | | | 47.35 | 5.30 | 12.27 | 21.03 | 14.05 |
| **GAS 4** | 303.38 | $C_{15}H_{17}N_3O_2S$ | 192-193 | 3278(N-H str), 1569(HC=N), 1518(C=C aromatic), 1143, 1329 (-$SO_2NH_2$)). | 59.39 | 5.65 | 13.85 | 10.56 | 10,55 |
| | | | | | 59.38 | 5.65 | 13.85 | 10.57 | 10.55 |
| **GAS 5** | 305.31 | $C_{13}H_{11}N_3O_4S$ | 200-202 | 3265(N-H str), 3105(C-H aromatic), 1591(C=C aromatic), 1628(HC=N), 1598($NO_2$), 1145, 1341(-$SO_2NH_2$), 1277(OH). | 51.15 | 3.63 | 13.75 | 10.55 | 20.99 |
| | | | | | 51.14 | 3.63 | 13.76 | 10.50 | 20.96 |

**Table 3:The Antimicrobial Activity of the Schiff Bases Showing Zones of Inhibitions (Mm)**

| Code | Staphylococcus aureus | Bacillus subtilis | Pseudomonas aeruginosa | Escherichia coli | Candida albicans |
|---|---|---|---|---|---|
| **GAS 1** | 28 | 24 | 25 | 19 | 22 |
| **GAS 2** | No effect | No effect | No effect | No effect | No effect |
| **GAS 3** | 17 | 34 | 33 | 28 | 25 |
| **GAS 4** | 19 | 29 | 30 | No effect | 30 |
| **GAS 5** | 26 | 23 | 24 | 17 | 25 |
| **Zyprox** | 28 | 34 | 32 | 33 | -- |
| **Nizoral** | -- | -- | -- | -- | 24 |

## 5. Discussion

The Schiff bases (GAS1-5) were prepared by condensation of sulfanilamide with carbonyl ligands (ketones or aldehydes) in the ratio of 1:1 via MW irradiation method. Table 1showed that GAS 5 and 4 had yields of 92% each, followed by GAS 3 with 76% yield, then GAS 1and GAS 2 with 73% and 71%, respectively. The purities of the new synthesized compounds were checked by TLC and the structures of the synthesized compounds were determined on the basis of their FT-IR coupled with the result of the elemental analysis as shown in table 2.

The FT-IR spectra of the synthesized compounds as shown in table 2 showed the presence of C=N stretching bands at 1500-1690 $cm^{-1}$ ; and those for C=O, usually at 1700 $cm^{-1}$ had shifted to lower frequencies due to asymmetric and symmetric $SO_2$ group. The absorption at 1738$cm^{1}$ for Gas1 was attributed to ester carbonyl (C=O).

All the synthesized compounds were screened for antimicrobial activities at the concentration of 5µM against two Gram (+) bacterial strain (*Staphylococcus aureus* and *Bacillus subtilis*), two Gram (-) bacterial strain (*Escherichia coli* and *Pseudomonas aeruginosa*) and fungi strain *Candida albicans*) by agar diffusion methods.

The results of the bioassay indicated that GAS 1 exhibited very good bactericidal activity against *S. aureus, B. subtilis* and *P, aeruginosa* while it showed moderate activity against *E. coli* when compared to the standard drug, Zyprox, as indicated by table 3. The same compound also performed excellently against *C. Albicans* compared with Nizoral, a standard fungicidal drug. GAS 2 has no bactericidal or fungicidal effect at all. GAS 3 showed excellent bactericidal activity against *B. subtilis* and *P, aeruginosa*, good effect against *E. coli* and moderate activity against *S. aureus* when compared with the activity of the standard drug, Zyprox. In a similar trend GAS 4 exhibited good biocidal effect against *B. subtilis* and *P. aeruginosa* and moderate activity against *S. aureus*; while GAS 5 was excellently biocidal against *S. aureus*, good against *B. subtilis* and *P, aeruginosa* and moderate against *E. coli* in comparison to the standard bactericidal drug used. On the other hand, all the synthesized compounds, with the exception of GAS 2, showed excellent fungicidal activities against *C. Albicans* in comparison to Nizoral, the standard fungicide drug used for this study as indicated in table 3.

## 6. Conclusion

All the synthesized Schiff bases were characterized by FT-IR and elemental analyses. These Schiff bases were also evaluated for their antibacterial and antifungal activities. All, except one, were found to be active against all the selected microbes used in this study; some even have comparable or better biocidal effects than the commercial standard reference drugs, Zyprox and Nizoral, used in this work.

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