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# Microwave induced synthesis of bis-Schiff bases from propane-1, 3-diamine as promising antimicrobial analogs

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**Abstract:** Propane-1,3-diamine **1** on condensation with different halogeno substituted benzaldehydes **2a-p** under microwave irradiation affords novel series of bis-schiff bases **3a-p**. Structures of the newly synthesized bis-Schiff bases established on the basis of spectroscopic data. Further, all compounds screened for antimicrobial activity against *Staphylococus aureus*, *Escherchia coli*, *Aspergillus niger* and *Aspergillus flavus*. Most of the titles compounds show potent activity.

**Keywords:** 1,3-Diamine; bis-schiff bases; microwave irradiation; microbial activity.



## 1. Introduction

Schiff bases have been playing vital roles in pharmaceuticals,rubber additives,[1] as amino protective groups in the synthetic organic chemistry and several biologically active organic compounds.[2-4] They are also useful in analytical[5],medicinal[6,7] and polymer chemistry.[8,9] Besides their utility in phosphorus chemistry, Schiff's bases have been used for the preparation of α-aminophosphonate esters and *H*-phosphonate esters with repeatable Pudovik reaction[10-13] which possess bioactivity such as inhibitor of cancers and viruses and as antibiotics. Particular attention has recently been paid to the synthesis and study of imino, diimino Schiff's bases and their complexes. This is due to various reasons, such as the biological function of bacteriorhodopsin[14]. Schiff's base complexes of small organic molecules with metal cations have found broad applications in the field of interactions with biogenic macromolecules such as DNA, RNA and peptides.[15, 16]

The microwave induced enhancement of organic reactions is currently a focus of attention for chemists due to the decreased reaction time, improved yields and easier work up as compared to conventional methods.[17, 18] In microwave synthesis, to avoid accidents low boiling, toxic and poisonous solvents are often avoided. The use of microwave for the synthesis of organic compounds has proved to be efficient, safe and environmentally benign techniques with shorter reaction time.[19] In view of above findings, we have identified the new bis-Schiff bases that may be of value in development of new, potent, selective and less toxic antimicrobial agents. In the present paper, we have successfully to explore the possibility of a greater route with the help of microwave assisted technique for the synthesis of bis-Schiff bases as possible antimicrobial agents. Therefore, this paper describes, for the first time, microwave synthesis, characterization and in vitro antimicrobial activity

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of the bis-schiff bases **3a-p**. A comparison of the results obtained from the two synthetic approaches indicate that the effect of microwave irradiation is not purely thermal, besides giving decreased reaction times and improved yields (Table-**1**).

## 2. Results and discussion

### 2.1 Chemistry

In view of the application of bis-Schiff bases and in continuation of our earlier investigations, reported on green synthetic strategy towards synthesis of biologically active compounds including Schiff bases.[20-25] Therefore in present paper, we synthesized a new class of bis-Schiff bases by the reaction between propane-1,3-diamine (**1**) with halogeno substituted benzaldehydes (**2a-p**) by conventional as well as microwave irradiation technique.

The use of non-conventional energy over conventional energy for the enhancement of organic reactions that is Microwave Organic Reactions Enhancement provides greater reaction conditions coupled with clean products, increased yield and better time economy.[26-29] Thus MW technique has advantage including easy work-up procedure, short reaction time, and does not need effort for isolation of products giving high percentage yield. The structures of products (**3a-p**) are well confirmed on the basis of spectral data.

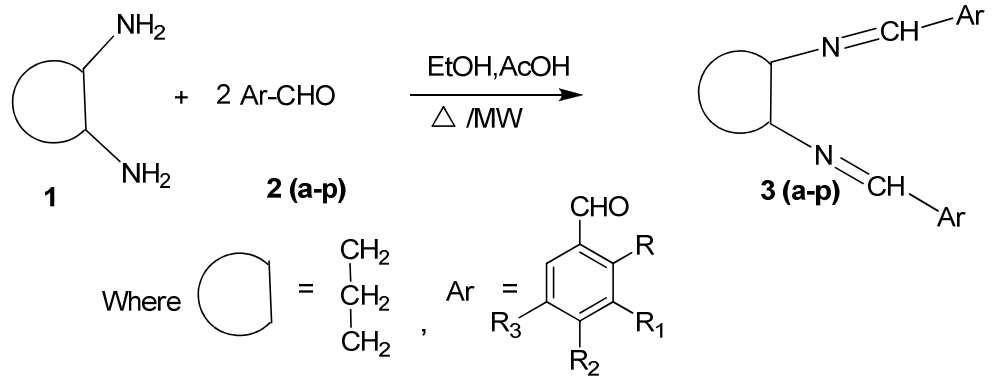


**Figure 1.** Microwave induced synthesis of bis-Schiff bases

IR spectra of corresponding condensed product display the characteristic absorption band within 1613-1636 $cm^{-1}$ due to C=N stretch. Absence of carbonyl absorption C=O stretch indicate the formation bis-Schiff. In the $^{1}H$ NMR spectra the azomethine (-CH=N) protons appear within δ 8.00 to 9.00 ppm, further the –OH proton resonates between δ13-15 ppm. The aromatic protons are observed at the expected chemical shift and integral values. In the $^{13}C$ NMR spectra, the imine carbon appears within δ 160.00 to 165.00 ppm. Progress of the reaction can be easily monitored by Thin Layer Chromatography (TLC).

**Table 1.** Physical data for bis-Schiff bases (**3a-3p)**.

| Entry | R | $R_1$ | $R_2$ | $R_3$ | M. P.$^0$C | Yield % | |
|---|---|---|---|---|---|---|---|
| | | | | | | A | B |
| 3a | OH | H | H | H | 62 | 70 | 80 |
| 3b | OH | Br | H | Br | 95 | 72 | 82 |
| 3c | OH | H | H | Cl | 100 | 75 | 85 |
| 3d | OH | H | I | I | 160 | 75 | 88 |
| 3e | OH | H | OH | H | 102 | 60 | 80 |
| 3f | H | OEt | OH | H | 70 | 65 | 85 |
| 3g | H | OEt | OH | Br | 130 | 72 | 83 |
| 3h | H | OEt | OH | I | 190 | 70 | 80 |
| 3i | H | OMe | OH | H | 55 | 72 | 85 |
| 3j | H | OMe | OH | Br | 85 | 70 | 82 |
| 3k | H | OMe | OH | Cl | 90 | 75 | 88 |
| 3l | H | OMe | OH | I | 80 | 70 | 84 |
| 3m | H | H | OMe | OMe | 110 | 75 | 88 |
| 3n | H | OMe | OMe | OMe | 123 | 70 | 82 |
| 3o | H | H | Cl | H | 115 | 65 | 80 |
| 3p | H | H | F | H | 120 | 60 | 75 |

**A:** Yield obtained by conventional technique
**B:** Yield obtained by microwave technique

## 2.2 Antimicrobial activity:

The investigation of antibacterial and antifungal screening data revealed that all tested compounds (**3a-p)** showed good to moderate inhibition at 12.5-200μg/mL in DMSO. The compounds **3c**, **3d**, **3h**, **3k**, and **3n** showed comparatively good activity against all the bacterial strains. The good activity is attributed to the presence of pharmacologically active –Cl (3c, 3k), I (3d, 3h), -OH (3c, 3d, 3h, 3k), –OEt (3h), and –OMe (3k,3n) groups attached to phenyl group at 2,3 and 4$^{th}$ position in bis-Schiff bases. When the substitution of these groups is replaced by hydrogen or another group, a sharp decrease in activity against most of strains was observed. Compounds **3a**, **3g**, **3l**, **3m**, **3o** exhibited moderate activity compared to that of standard ofloxacin against all the bacterial strain. Further the result showed that Gram-negative exhibited better activity than Gram-positive organism.

Compounds **3c**, **3d**, **3h**, **3i**, **3o** showed comparatively good activity against all the fungal strains, while compound **3f**, **3p** showed moderate activity against the fungal strains. The structures of these compounds contain biologically active, chloro, iodo, bromo substituted vanilines.

**Table 2.** Antibacterial and Antifungal activity of title compounds **3a-3p**

| Entry | Zone of inhibition in mm and MIC (minimum inhibitory concentration) in µg/mL | | | |
|---|---|---|---|---|
| | S. *aureus* | E.*coli* | A.*niger* | A.*flavus* |
| 3a | 13(100) | 17(50) | 7(<200) | 9(<200) |
| 3b | 5(<200) | 8(<200) | 14(100) | 20(50) |
| 3c | 22(25) | 25(25) | 25(25) | 24(25) |
| 3d | 22(25) | 30(12.5) | 28(12.5) | 27(12.5) |
| 3e | 3(<200) | 8(<200) | 12(100) | 14(100) |
| 3f | 8(<200) | 7(<200) | 20(50) | 19(50) |
| 3g | 14(100) | 19(50) | 19(50) | 19(50) |
| 3h | 27(12.5) | 30(12.5) | 28(12.5) | 29(12.5) |
| 3i | 5(<200) | 9(<200) | 30(12.5) | 29(12.5) |
| 3j | 4(<200) | 8(<200) | 6(<200) | 9(<200) |
| 3k | 22(25) | 29(12.5) | 13(100) | 15(100) |
| 3l | 14(100) | 19(50) | 15(100) | 13(100) |
| 3m | 13(100) | 20(50) | 12(100) | 14(100) |
| 3n | 24(28) | 27(12.5) | 9(<200) | 8(<200) |
| 3o | 12(100) | 17(50) | 28(12.5) | 30(12.5) |
| 3p | 8(<200) | 6(<200) | 20(50) | 15(100) |
| Ofloxacin | 22(25) | 30(12.5) | ------- | ------- |
| Ketoconazole | ------- | ------- | 28(12.5) | 25(25) |

The figures in the table show zone of inhibition (mm) and the corresponding MIC (µg/mL) values in brackets

## 4. Experimental Section:

### *4.1 Instrumentation:*

Melting points were determined in an open capillary tube and are uncorrected. The chemicals and solvents used were of laboratory grade and were purified. Completion of the reaction was monitored by thin layer chromatography using hexane/ethyl acetate as the mobile phase on precoated sheets of silica gel-G (Merck, Germeny) using iodine vapour for detection. IR spectra were recorded in KBr on a Perkin-Elmer spectrometer. $^{1}$H NMR and $^{13}$C NMR (70MHz)spectra were recorded in DMSO-$d_6$ with an Avance spectrometer (Bruker, Germany)at 400-MHz frequency using TMS as an internal standard. The mass spectra were recorded on EISHIMADZU-GC/MS spectrometer. Elemental analyses were performed on a Perkin-Elmer 240 CHN elemental analyzer.Synthos-3000, Anton Paar reaction system was used for microwave synthesis.

### *4.2. General procedure for the preparation of compounds 3 (a-p)*

#### *4.2.1 Conventional technique*

A solution of Propane-1,3-diamine (**1**) (0.01mol, 0.74mg) in ethanol (95%) (15mL) was heated under reflux with halogeno substituted benzaldehyde (**2a-p**) (0.02 mol) for 2-3hrs. The progress and completion of reaction was monitored on TLC. The reaction mixture was kept at room temperature and the deposited solid was filtered, washed, dried and recrystalized by ethanol (95%) to give the bis-Schiff bases (**3a-p**).

#### *4.2.2 Microwave technique*

A homogeneous mixture of Propane-1,3-diamine (**1**) (0.01mol, 0.74mg), halogeno substituted benzaldehyde (**2a-p**) (0.02 mol), acetic acid (0.2 ml) in ethanol (10 ml), was introduced into a microwave reaction vessel equipped with a magnetic stirrer (Synthos-3000). The vessel was sealed and the reaction was irradiated by 50 W intermittently at 30 sec. interval for 3 min. The solid formed was washed with water and crystallized from ethanol (95%) to give bis-Schiff bases (**3a-p**).

*4.2.3. N, N' Bis (2-hydroxybenzylidene)-propane-1,3-diamine (3a):*Colour (white); purity by TLC > 90%; IR (KBr) 3420cm$^{-1}$, 3047cm$^{-1}$, 1627cm$^{-1}$; $^{1}$H NMR (DMSO $d_6$); δ 2.10 (m,2H, -$CH_2$), δ3.71 (t, 4H, 2N-$CH_2$), δ7.30-7.52 (m, 8H, Ar proton), δ8.46 (s,2H, 2N=CH), δ14.0 (s, 2H, 2Ar-OH); $^{13}$C NMR; δ 32.1 ($CH_2$), δ56.3 ($CH_2$x2), δ120.2 (CHx2), δ122.5 (CHx2), δ131.1 (CHx2) δ133 (CHx2) δ160 (CHx2) δ165.2 (CH=Nx2)
EIMS=282 (M+).

*4.2.4.N,N'Bis(3,5-dibromo-2-hydroxybenzylidene)-propane-1,3-diamine(3b):*Colour (brown);purity by TLC > 95%; IR (KBr) 3390cm$^{-1}$, 3040cm$^{-1}$, 1620cm$^{-1}$; $^{1}$H NMR (DMSO $d_6$); δ 2.16 (m,2H, -$CH_2$), δ3.69 (t, 4H, 2N-$CH_2$), δ6.90-7.42 (m, 4H, Ar proton), δ8.35 (s,2H, 2N=CH), δ14.10 (s, 2H, 2Ar-OH); $^{13}$C NMR; δ 32.0 ($CH_2$), δ55.2 ($CH_2$x2), δ120.1 (CHx2), δ135.3 (CHx2),δ138.2 (CHx4), δ143.6 (CHx2) δ159.1 (CHx2), δ163.4 (CH=Nx2)
EIMS=437 (M+).

*4.2.5.N,N'Bis(5-chloro-2-hydroxybenzylidene)-propane-1,3-diamine(3c)*:Colour(yellow); purity by TLC > 95%; IR (KBr) 3410cm$^{-1}$, 2947cm$^{-1}$, 1635cm$^{-1}$; $^{1}$H NMR (DMSO $d_6$); δ 2.10 (m,2H, -$CH_2$), δ3.60 (t, 4H, 2N-$CH_2$), δ6.90-7.52 (m, 6H, Ar proton), δ8.52 (s,2H, 2N=CH), δ13.50 (s, 2H, 2Ar-OH); $^{13}$C NMR; δ 32.0 ($CH_2$), δ56.1 ($CH_2$x2), δ118.4 (CHx2), δ120.2 (CHx2),δ122.3 (CHx2), δ130.4 (CHx2),δ135.7 (CHx2) δ155.3 (CHx2), δ164.6 (CH=Nx2)
EIMS=351 (M+).

*4.2.6.N, N' Bis (2-hydroxy 3,5-diiodobenzylidene)-propane-1,3-diamine (3d):*Colour (orange);purity by TLC > 95%; IR (KBr) 3435cm$^{-1}$, 3060cm$^{-1}$, 1627cm$^{-1}$; $^{1}$H NMR (DMSO $d_6$); δ 2.19 (m,2H, -$CH_2$), δ3.73 (t, 4H, 2N-$CH_2$), δ6.90-7.00 (m, 4H, Ar proton), δ8.40 (s,2H, 2N=CH), δ14.60 (s, 2H, 2Ar-OH); $^{13}$C NMR; δ 33.0 ($CH_2$), δ55.1 ($CH_2$x2), δ121.1 (CHx2), δ123.5 (CHx2),δ128.3 (CHx2), δ135.2 (CHx4) δ158.5 (CHx2), δ164.2 (CH=Nx2)
EIMS=786 (M+).

*4.2.7.N, N' Bis (2,4-hydroxybenzylidene)-propane-1,3-diamine (3e):*Colour (brown);purity by TLC > 90%; IR (KBr) 3450cm$^{-1}$, 2960cm$^{-1}$, 1625cm$^{-1}$; $^{1}$H NMR (DMSO $d_6$); δ 2.15 (m,2H, -$CH_2$), δ3.60 (t, 4H, 2N-$CH_2$), δ6.80-7.35 (m, 6H, Ar proton), δ8.25 (s,2H, 2N=CH), δ9.37 (s, 2H, Ar-OH(*Para*)) δ13.21 (s, 2H, 2Ar-OH(*ortho*)); $^{13}$C NMR; δ 31.9 ($CH_2$), δ54.3 ($CH_2$x2), δ119.1 (CHx2), δ122.6 (CHx2),δ134.2 (CHx2), δ139.6 (CHx2) δ159.0 (CHx4), δ163.2 (CH=Nx2)
EIMS=314 (M+).

*4.2.8.N, N' Bis (5-ethoxy,4-hydroxybenzylidene)-propane-1,3-diamine (3f):*Colour (white);purity by TLC > 90%; IR (KBr) 3438cm$^{-1}$, 3117cm$^{-1}$, 1618cm$^{-1}$; $^{1}$H NMR (DMSO $d_6$); δ1.35 (t,3H, $CH_3$), δ 2.12 (m,2H, -$CH_2$), δ3.52 (t, 4H, 2N-$CH_2$), δ 4.15 (q, 2H, $OCH_2$)δ7.10-7.90 (m, 6H, Ar proton), δ8.45 (s,2H, 2N=CH), δ9.60 (s, 2H, Ar-OH); $^{13}$C NMR; δ 18.0 ($CH_3$) δ 32.3 ($CH_2$), δ54.5 ($CH_2$x2), δ 65.1($OCH_2$), δ116.8 (CHx4), δ130.3 (CHx2),δ150.2 (CHx2), δ160.1 (CHx2), δ164.7(CH=Nx2)
EIMS=360 (M+).

*4.2.9.N, N' Bis (3-bromo,5-ethoxy,4-hydroxybenzylidene)-propane-1,3-diamine (3g):*Colour (pale yellow);purity by TLC > 90%; IR (KBr) 3430cm$^{-1}$, 3090cm$^{-1}$, 1622cm$^{-1}$; $^{1}$H NMR (DMSO $d_6$); δ1.38 (t,3H, $CH_3$), δ 2.15 (m,2H, -$CH_2$), δ3.55 (t, 4H, 2N-$CH_2$), δ 4.18 (q, 2H, $OCH_2$) δ7.15-7.65 (m, 4H, Ar proton), δ8.35 (s,2H, 2N=CH), δ9.85 (s, 2H, Ar-OH); $^{13}$C NMR; δ18.2 ($CH_3$) δ 32.1 ($CH_2$), δ54.6 ($CH_2$x2),δ65.8($OCH_2$), δ116.4 (CHx2), δ117.5 (CHx4),δ135.5 (CHx2), δ152.2 (CHx2), δ163.8(CH=Nx2) EIMS=528 (M+).

*4.2.10.N, N' Bis (5-ethoxy,4-hydroxy,3-iodobenzylidene)-propane-1,3-diamine (3h):*Colour (yellow);purity by TLC > 90%; IR (KBr) 3445cm$^{-1}$, 3110cm$^{-1}$, 1620cm$^{-1}$; $^{1}$H NMR (DMSO $d_6$); δ1.38 (t,3H, $CH_3$), δ 2.16 (m,2H, -$CH_2$), δ3.58 (t, 4H, 2N-$CH_2$), δ 4.13(q, 2H, $OCH_2$) δ7.20-7.69 (m,

6H, Ar proton), δ8.39 (s,2H, 2N=CH), δ9.53 (s, 2H, Ar-OH); $^{13}$C NMR; δ 18.6 ($CH_3$) δ 33.3 ($CH_2$), δ55.2 ($CH_2$x2), δ 66.4($OCH_2$), δ118.4 (CHx4), δ132.2(CHx2),δ149.1 (CHx2), δ158.6(CHx2), δ163.8(CH=Nx2) EIMS=622 (M+).

*4.2.11.N, N' Bis (4-hydroxy,5-methoxybenzylidene)-propane-1,3-diamine (3i):*Colour (faint brown);purity by TLC > 90%; IR (KBr) 3380cm$^{-1}$, 3066cm$^{-1}$, 1620cm$^{-1}$; $^1$H NMR (DMSO $d_6$); δ 2.20 (m,2H, -$CH_2$), δ3.55 (t, 4H, 2N-$CH_2$), δ 3.73(s, 3H, $OCH_3$) δ7.05-7.60 (m, 6H, Ar proton), δ8.13 (s,2H, 2N=CH), δ9.80 (s, 2H, Ar-OH); $^{13}$C NMR; δ 32.3 ($CH_2$), δ55.0 ($CH_2$x2), δ 65.1($OCH_2$), δ115.6 (CHx2), δ117.2(CHx2),δ131.1 (CHx2), δ145.6(CHx2), δ158.0(CHx2), δ162.2(CH=Nx2) EIMS=342 (M+).

*4.2.12.N,N'Bis (3-bromo,4-hydroxy,5-methoxybenzylidene)-propane-1,3-diamine (3j):*Colour (paleyellow);purity by TLC > 90%; IR (KBr) 3420cm$^{-1}$, 3040cm$^{-1}$, 1627cm$^{-1}$; $^1$H NMR (DMSO $d_6$); δ 2.15 (m,2H, -$CH_2$), δ3.58 (t, 4H, 2N-$CH_2$), δ 3.72(s, 3H, $OCH_3$) δ7.15-7.60 (m, 4H, Ar proton), δ8.13 (s,2H, 2N=CH), δ9.65 (s, 2H, Ar-OH); $^{13}$C NMR; δ 31.8 ($CH_2$), δ55.4 ($CH_2$x2), δ 65.4($OCH_2$), δ122.6 (CHx2), δ133.2(CHx2),δ135.1 (CHx2), δ138.6(CHx2), δ152.0(CHx2), δ159.0(CHx2),δ163.2(CH=Nx2) EIMS=500 (M+).

*4.2.13.N, N' Bis (3-chloro,4-hydroxy,5-methoxybenzylidene)-propane-1,3-diamine (3k):*Colour (white);purity by TLC > 90%; IR (KBr) 3410cm$^{-1}$, 3040cm$^{-1}$, 1625cm$^{-1}$; $^1$H NMR (DMSO $d_6$); δ 2.18 (m,2H, -$CH_2$), δ3.55 (t, 4H, 2N-$CH_2$), δ 3.74(s, 3H, $OCH_3$) δ7.20-7.80 (m, 4H, Ar proton), δ8.32 (s,2H, 2N=CH), δ9.79 (s, 2H, Ar-OH); $^{13}$C NMR; δ 32.3 ($CH_2$), δ54.6 ($CH_2$x2), δ 65.2($OCH_2$), δ123.1 (CHx2), δ134.1(CHx2),δ137.1 (CHx2), δ139.6(CHx2), δ154.0(CHx2), δ160.0(CHx2),δ164.3(CH=Nx2) EIMS=413 (M+).

*4.2.14.N, N' Bis (4-hydroxy,5-methoxy,3-iodobenzylidene)-propane-1,3-diamine (3l):*Colour (yellow);purity by TLC > 90%; IR (KBr) 3425cm$^{-1}$, 3065cm$^{-1}$, 1622cm$^{-1}$; $^1$H NMR (DMSO $d_6$); δ 2.13 (m,2H, -$CH_2$), δ3.50 (t, 4H, 2N-$CH_2$), δ 3.79(s, 3H, $OCH_3$) δ7.35-7.85 (m, 4H, Ar proton), δ8.52 (s,2H, 2N=CH), δ9.85(s, 2H, Ar-OH); $^{13}$C NMR; δ 32.0 ($CH_2$), δ55.6 ($CH_2$x2), δ 65.0($OCH_2$), δ122.7 (CHx2), δ135.0(CHx2),δ136.3 (CHx2), δ138.6(CHx2), δ153.8(CHx2), δ159.2(CHx2),δ163.1(CH=Nx2) EIMS=596 (M+).

*4.2.15.N, N' Bis (3,4-dimethoxybenzylidene)-propane-1,3-diamine (3m):*Colour (white);purity by TLC > 90%; IR (KBr) 3066cm$^{-1}$, 1620cm$^{-1}$; $^1$H NMR (DMSO $d_6$); δ 2.14 (m,2H, -$CH_2$), δ3.56 (t, 4H, 2N-$CH_2$), δ 3.85(s, 6H, $OCH_3$) δ7.05-7.60 (m, 6H, Ar proton), δ8.55 (s,2H, 2N=CH), δ9.85(s, 2H, Ar-OH); $^{13}$C NMR; δ 32.3 ($CH_2$), δ55.4 ($CH_2$x2), δ 64.0($OCH_3$x2), δ116.7 (CHx2), δ128.0(CHx2),δ130.3 (CHx2), δ136.6(OCHx4), δ162.9(CH=Nx2) EIMS=370 (M+).

*4.2.16.N,N'Bis(3,4,5-trimethoxybenzylidene)-propane-1,3-diamine (3n):*Colour (white);purity by TLC > 90%; IR (KBr) 2947cm$^{-1}$, 1622cm$^{-1}$; $^1$H NMR (DMSO $d_6$); δ 2.13 (m,2H, -$CH_2$), δ3.49 (t, 4H, 2N-$CH_2$), δ 3.95(s, 9H, $OCH_3$) δ7.13-7.65 (m, 4H, Ar proton), δ8.20 (s,2H, 2N=CH), δ9.85(s, 2H, Ar-OH); $^{13}$C NMR; δ 32.5 ($CH_2$), δ55.5 ($CH_2$x2), δ 61.9($OCH_3$x3), δ119.7 (CHx4), δ131.4(CHx2), δ138.2(OCHx6), δ162.5(CH=Nx2) EIMS=402 (M+).

*4.2.17.N, N' Bis (4-chlorobenzylidene)-propane-1,3-diamine (30):*Colour (brown);purity by TLC > 90%; IR (KBr) 3117cm$^{-1}$, 1618cm$^{-1}$; $^1$H NMR (DMSO $d_6$); δ 2.16 (m,2H, -$CH_2$), δ3.53 (t, 4H, 2N-$CH_2$),δ6.69-7.45 (m, 8H, Ar proton), δ8.25 (s,2H, 2N=CH); $^{13}$C NMR; δ 32.0 ($CH_2$), δ55.1 ($CH_2$x2),δ118.3 (CHx4), δ123.1(CHx4), δ131.4(CHx2), δ139.4(CHx2) δ162.8(CH=Nx2) EIMS=319 (M+).

*4.2.18.N, N' Bis (4-fluorobenzylidene)-propane-1,3-diamine (3p):*Colour (brown);purity by TLC > 90%; IR (KBr) 3133cm$^{-1}$, 1620cm$^{-1}$; $^1$H NMR (DMSO $d_6$); δ 2.12 (m,2H, -$CH_2$), δ3.54 (t, 4H, 2N-$CH_2$),δ6.70-7.90 (m, 8H, Ar proton), δ8.32 (s,2H, 2N=CH); $^{13}$C NMR; δ 33.4 ($CH_2$), δ56.4

($CH_2$x2), δ120.3 (CHx4), δ125.2(CHx4), δ134.3(CHx2), δ140.5(CHx2) δ163.7(CH=Nx2) EIMS=286 (M+).

### *4.3. Antimicrobial activity*

Newly synthesized compounds (**3a-p**) were screened for antimicrobial activity against Gram-positive bacteria *Stephylo cocusaureus* (MTCC-96), the Gram-negative bacteria *Escherichia coli* (MTCC-443) in the nutrient agar media, and fungi *Aspergillus niger* (MTCC-281) and *Aspergillus flavus* (MTCC-1323) in sabouraud dextrose medium at 200, 100, 50, 25, and 12.5μg/mL concentrations by using borth dilution method.[30] The minimum inhibitory concentrations (MIC's) values were determined by comparison to ofloxacin and ketoconazole as the reference drugs for bacterial and fungal activity respectively, as shown in table-2. Standard antibiotics ofloxacin and ketoconazole were used as reference drugs at 50, 25, 12.5μg/mL concentrations. The minimum inhibitory concentration (MIC) was defined as the lowest concentration of the compound that inhibits the visible growth of microorganism on the plate.

## 5. Conclusion

In conclusion, salient feature of our approach is coupling microwave with keeping modernization and simplification over classical procedure for avoiding the generation of valuable toxic organic solvents, which are corrosive, and an efficient and cheap technology to synthesize bis-Schiff bases. In continuation of our previously published results[22] and as a part of our research work, focus has been given on the development of new bis-Schiff bases as bioactive agents.Synthesis and preliminary antimicrobial screening of new bis-Schiff bases have been demonstrated. The presence halogeno substituted vaniline in bis-Schiff bases provides a positive influence on antimicrobial activity. Owing to encouraging results, it was found that synthesized compounds have broader value of activity than standard drug used for screening of bacterial and fungal strains. The electronic effect also played a role in activity, as can be seen for the compounds having electron donor character such as –OEt, -OMe and –OH. Thus in future, this class of bis-Schiff bases may be used as templates for generatings better lead molecules to fight against bacterial and fungal strains.

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