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# ANTIMICROBIAL EVALUATION OF SOME NEWLY SYNTHESIZED SCHIFF BASES DERIVED FROM 4, 4'-METHYLENE BIS (2, 5-DIMETHYL ANILINE)

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**Keywords:**

4,4'-methylene bis (2,5-dimethyl aniline), aromatic aldehydes, antimicrobial activity

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## ABSTRACT

A series of 4,4'-methylene bis (*N*-substituted benzylidene-2,5-dimethyl aniline) (4a–j) derived from the condensation of 4,4'-methylene bis (2,5-dichloro aniline) and various substituted aromatic aldehydes. All the synthesized compounds were characterized and screened for their vitro antibacterial activities against gram positive bacteria (*Staphylococcus aureus*, *Staphylococcus pyogenes)*, gram nagative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*) and antifungal activities against (*Candida albicans*, *S. cervecieaceae* and *Aspergillus clavatus)*. The structures of the compounds were elucidated by IR, $^{1}$H NMR spectra.

## INTRODUCTION

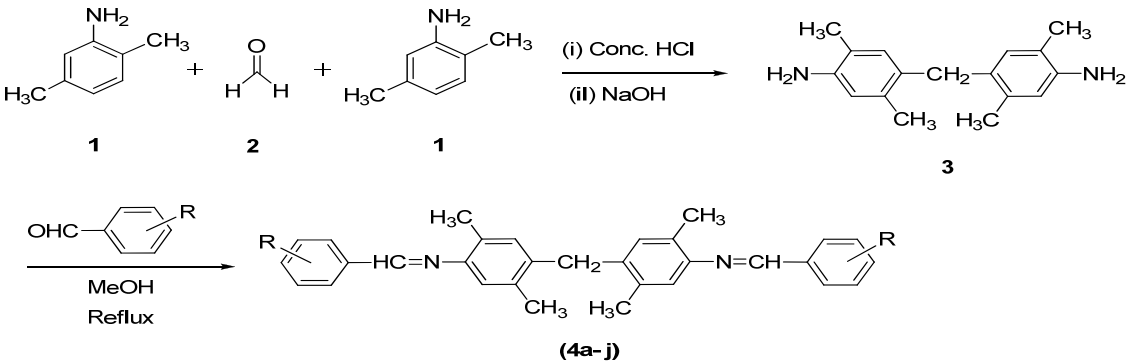
The Schiff bases play a significant role in the area of coordination chemistry. Synthesis of novel Schiff bases was opted for the research due to their commercial and medicinal importance. Schiff base have been synthesized from the condensation of amine and aldehyde in presence of acid as catalyst. Schiff base also possessed various biological activities like antibacterial[1-3], antifungal[4], antitumor[5], anti-inflammatory[6], antiviral[7], antioxidant[8-10] and anticancer[11]. Schiff bases are considered good bases for synthesis of several antibacterial compounds due to their easily preparing procedures and their ability to attach to several functional groups on their chemical skeleton. The Schiff bases were essentially appeared antibacterial influence against most of bacterial strain, and their resistance routes against different types of bacteria is based on using efficient biocides.

## RESULTS AND DISCUSSIONS

All the synthesized compounds were recrystallization and successive purified, by using structures of the newly synthesized compounds were determined on the basis of their FTIR and $^1$H NMR spectra data. Methylene C-H stretching vibrations observed near 2840 cm$^{-1}$ and 2940 cm$^{-1}$. Broad absorption bands observed in the region between 3080-3030 cm$^{-1}$ and 1520-1480 cm$^{-1}$ indicates the presence of C-H stretching and C=C stretching of Aromatic. Examination of IR spectra reveals that all the Schiff base derivatives exhibited a strong absorption band near 1640-1580 cm$^{-1}$ indicates the presence of –N=CH- group. The $^1$H NMR spectra of the synthesized compound showed chemical shifts, which are characteristics of the anticipated structure of compounds.

## EXPERIMENTAL

**Scheme-1:** Synthetic route for 4,4'-methylene bis (*N*-substituted benzylidene-2,5-dimethyl aniline) from 2,5-dimethyl aniline **(4a- j)**.




R = 2-F, 4-F, 2-OH, 2-OCH$_3$, 2,4-Cl, 4-Cl, 4-CH$_3$, 2-Cl, 4-OH, 2-NO$_2$

**Synthesis of 4,4'-methylene bis (2,5-dimethyl aniline) (3)**

4-4'-methylene bis (2,5-dimethyl aniline) (3) was synthesized by the procedure described in the literature[12].

**Synthesis of compounds (4a- j)**

The title compounds were synthesized by reaction between 4,4'-methylene bis 2,5-dimethyl aniline (2.54 g, 0.01 mol) and various substituted aromatic aldehydes (0.02 mol). Each reactant was dissolved in a minimum amount of methanol, then mixed together and followed by addition of few drops of glacial acetic acid as a catalyst. The solution was refluxed for 4 hrs. It was then poured into ice cold water to give solid product. It was filtered, washed with water, dried and recrystallized from ethanol[13].

***4,4'-Methylene bis-(N-(2-fluorobenzylidine)-2,5-dimethyl aniline) 4a***

Brown coloured solid powder, mp 198 $^0$C, yield 70%; IR (KBr, cm$^{-1}$): 3060 (C-H stretching, aromatic), 2935, 2825 (C-H stretching, -$CH_2$- group), 2920,2870 (C-H stretching, -$CH_3$ group), 1625 (C=N stretching, Schiff base), 1520 (C=C stretching, aromatic), 1455,1380 (C-H bending, -$CH_3$ group), 1435 (C-H bending, -$CH_2$- group); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.30 (s, 12H, -$CH_3$), 3.76 (s, 2H, -$CH_2$-), 6.97-7.72 (m, 12H, Ar-H), 8.60 (s, 2H, -HC=N-); Anal. Calcd for: $C_{31}H_{28}F_2N_2$ (466.56); found (C, 79.74), requires (C, 79.80); found (H, 6.00), requires (H, 6.05); found (N, 6.09), requires (N, 6.00).

***4,4'-Methylene bis-(N-(4-fluorobenzylidine)-2,5-dimethyl aniline) 4b***

Brown coloured solid powder, mp 139 $^0$C, yield 70%; IR (KBr, cm$^{-1}$): 3055 (C-H stretching, aromatic), 2940, 2825 (C-H stretching, -$CH_2$- group), 2925,2870 (C-H stretching, -$CH_3$ group), 1620 (C=N stretching, Schiff base), 1515 (C=C stretching, aromatic), 1450,1380 (C-H bending, -$CH_3$ group), 1435 (C-H bending, -$CH_2$- group); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.34 (s, 12H, -$CH_3$), 3.74 (s, 2H, -$CH_2$-), 6.88-7.72 (m, 12H, Ar-H), 8.70 (s, 2H, -HC=N-); Anal. Calcd for: $C_{31}H_{28}F_2N_2$ (466.56); found (C, 79.86), requires (C, 79.80); found (H, 6.01), requires (H, 6.05); found (N, 6.09), requires (N, 6.00).

***4,4'-Methylene bis-(N-2-hydroxybenzylidine)-2,5-dimethyl aniline) 4c***

Brown coloured solid powder, mp 178 $^0$C, yield 80%; IR (KBr, cm$^{-1}$): 3400 (O-H stretching, Ar-OH), 3030 (C-H stretching, aromatic), 2935, 2820 (C-H stretching, -$CH_2$- group), 2920, 2870 (C-H stretching, -$CH_3$ group), 1620 (C=N stretching, Schiff base), 1505 (C=C stretching, aromatic), 1455, 1380 (C-H bending, -$CH_3$ group) 1430 (C-H bending, -$CH_2$- group), 1330 (O-H bending, Ar-OH); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.27

(S, 12H, -$CH_3$), 3.79 (s, 2H, -$CH_2$-), 6.88-7.69 (m, 12H, Ar-H), 8.72 (s, 2H, -HC=N-), 12.86 (s, 2H, -OH); Anal. Calcd for: $C_{31}H_{30}N_2O_2$ (462.58); found (C, 80.45), requires (C, 80.49); found (H, 6.59), requires (H, 6.54); found (N, 6.09), requires (N, 6.06).

***4,4'-Methylene bis-(N-(2-methoxylbenzylidine)-2,5-dimethyl aniline) 4d***

Yellow coloured solid powder, mp 161 $^0$C, yield 75%; IR (KBr, $cm^{-1}$): 3050 (C-H stretching, aromatic), 2940, 2825 (C-H stretching, -$CH_2$- group), 2920, 2870 (C-H stretching, -$CH_3$), 1628 (C=N stretching, Schiff base), 1525 (C=C stretching, aromatic), 1470,1380 (C-H bending, -$CH_3$), 1435 (C-H bending, -$CH_2$- group); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.23 (s, 12H, -$CH_3$), 3.80 (s, 6H, -$OCH_3$), 3.92 (s, 2H, -$CH_2$-), 6.88-7.72 (m, 12H, Ar-H), 8.50 (s, 2H, -HC=N-); Anal. Calcd for: $C_{33}H_{34}N_2O_2$ (490.64); found (C, 80.70), requires (C, 80.78); found (H, 6.88), requires (H, 6.98); found (N, 5.79), requires (N, 5.71).

***4,4'-Methylene bis-(N-2,4-dichlorobenzylidine)-2,5-dimethyl aniline) 4e***

Yellow coloured solid powder, mp 184 $^0$C, yield 80%; IR (KBr, $cm^{-1}$): 3065 (C-H stretching, aromatic), 2945, 2825 (C-H stretching, -$CH_2$- group), 2925, 2875 (C-H stretching, -$CH_3$), 1630 (C=N stretching, Schiff base), 1510 (C=C stretching, aromatic), 1460,1385 (C-H bending, -$CH_3$), 1435 (C-H bending, -$CH_2$- group), 740 (C-Cl stretching, Chloro group); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.25 (s, 12H, -$CH_3$), 3.90 (s, 2H, -$CH_2$-), 6.77-7.72 (m, 10H, Ar-H), 8.70 (s, 2H, -HC=N-); Anal. Calcd for: $C_{31}H_{26}Cl_4N_2$ (568.36); found (C, 65.60), requires (C, 65.51); found (H, 4.52), requires (H, 4.61); found (N, 4.99), requires (N, 4.93).

***4,4'-Methylene bis-(N-(4-chlorobenzylidine)-2,5-dimethyl aniline) 4f***

Light yellow coloured solid powder, mp 160 $^0$C, yield 65%; IR (KBr, $cm^{-1}$): 3060 (C-H stretching, aromatic), 2940, 2850 (C-H stretching, -$CH_2$- group), 2920, 2870 (C-H stretching, -$CH_3$), 1635 (C=N stretching, Schiff base), 1505 (C=C stretching, aromatic), 1455,1380 (C-H bending, -$CH_3$), 1430 (C-H bending, -$CH_2$- group), 725 (C-Cl stretching, Chloro group); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.23 (s, 12H, -$CH_3$), 3.84 (s, 2H, -$CH_2$-), 6.76-7.95 (m, 12H, Ar-H), 8.53 (s, 2H, -HC=N-); Anal. Calcd for: $C_{31}H_{28}Cl_2N_2$ (499.47); found (C, 74.62), requires (C, 74.54); found (H, 5.57), requires (H, 5.65); found (N, 5.00), requires (N, 5.61).

***4,4'-Methylene bis-(N-(4-methylbenzylidine)-2,5-dimethyl aniline) 4g***

Light yellow coloured solid powder, mp 157 $^0$C, yield 75%; IR (KBr, $cm^{-1}$): 3050 (C-H stretching, aromatic), 2940, 2840 (C-H stretching, -$CH_2$- group), 2920, 2875 (C-H stretching, -$CH_3$), 1635 (C=N stretching, Schiff base), 1510 (C=C stretching, aromatic), 1450,1370 (C-H bending, -$CH_3$), 1440 (C-H bending, -$CH_2$- group); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.26

(s, 18H, -$CH_3$), 3.95 (s, 2H, -$CH_2$-), 6.85-7.60 (m, 12H, Ar-H), 8.60 (s, 2H, -HC=N-); Anal. Calcd for: $C_{33}H_{34}N_2$ (458.64); found (C, 86.51), requires (C, 86.42); found (H, 7.38), requires (H, 7.47); found (N, 6.04), requires (N, 6.11).

***4,4'-Methylene bis-(N-(2-chlorobenzylidine)-2,5-dimethyl aniline) 4h***

Light yellow coloured solid powder, mp 150 $^0$C, yield 68%; IR (KBr, cm$^{-1}$): 3065 (C-H stretching, aromatic), 2935, 2855 (C-H stretching, -$CH_2$- group), 2915, 2875 (C-H stretching, -$CH_3$), 1622 (C=N stretching, Schiff base), 1510 (C=C stretching, aromatic), 1450,1385 (C-H bending, -$CH_3$), 1435 (C-H bending, -$CH_2$- group), 735 (C-Cl stretching, Chloro group); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.25 (s, 12H, -$CH_3$), 3.86 (s, 2H, -$CH_2$-), 6.76-7.95 (m, 12H, Ar-H), 8.50 (S, 2H, -HC=N-); Anal. Calcd for: $C_{31}H_{28}Cl_2N_2$ (499.47); found (C, 74.49), requires (C, 74.54); found (H, 5.57), requires (H, 5.65); found (N, 5.67), requires (N, 5.61).

***4,4'-Methylene bis-(N-(4-hydroxybenzylidine)-2,5-dimethyl aniline) 4i***

Brown coloured solid powder, mp 147 $^0$C, yield 60%; IR (KBr, cm$^{-1}$): 3410 (O-H stretching, Ar-OH), 3030 (C-H stretching, aromatic), 2935, 2820 (C-H stretching, -$CH_2$- group), 2920, 2870 (C-H stretching, -$CH_3$ group), 1630 (C=N stretching, Schiff base), 1505 (C=C stretching, aromatic), 1455, 1380 (C-H bending, -$CH_3$ group), 1430 (C-H bending, -$CH_2$- group), 1330 (O-H bending, Ar-OH); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.29 (s, 12H, -$CH_3$), 3.79 (s, 2H, -$CH_2$-), 6.88-7.69 (m, 12H, Ar-H), 8.70 (s, 2H, -HC=N-), 12.86 (s, 2H, -OH); Anal. Calcd for: $C_{31}H_{30}N_2O_2$ (462.58); found (C, 80.42), requires (C, 80.49); found (H, 6.48), requires (H, 6.54); found (N, 6.12), requires (N, 6.06).

***4,4'-Methylene bis-(N-(2-nitrobenzylidine)-2,5-dimethyl aniline) 4j***

Light yellow coloured solid powder, mp 197 $^0$C, yield 75%; IR (KBr, cm$^{-1}$): 3020 (C-H stretching, aromatic), 2945, 2830 (C-H stretching, -$CH_2$- group), 2920, 2870 (C-H stretching, -$CH_3$ group),1618 (C=N stretching, Schiff base), 1580, 1350 (N=O stretching, Nitro group), 1530 (C=C stretching, aromatic), 1455, 1380 (C-H bending, -$CH_3$ group), 1445 (C-H bending, -$CH_2$- group); $^1$H NMR (400.1 MHz, DMSO): $\delta_H$ 2.27 (s, 12H, -$CH_3$), 3.94 (s, 2H, -$CH_2$-), 6.92-7.98 (m, 12H, Ar-H), 8.60 (s, 2H, -HC=N-); Anal. Calcd for: $C_{31}H_{28}N_4O_4$ (520.58); found (C, 71.57), requires (C, 71.52); found (H, 5.49), requires (H, 5.42); found (N, 10.82), requires (N, 10.76).

**Antimicrobial activity:**

**Antibacterial activity**

For the antibacterial activity, the newly synthesized compounds were screened for their antibacterial activity (Table-1) against gram positive bacteria *S. aureus* (MTCC-96) and

*Streptococcus pyogenes* (MTCC-443) and gram negative *E.Coli* (MTCC-442) and *Pseudomonas aeruginosa* (MTCC-2488)]. Antibacterial activity was carried out by serial broth dilution method[14-15]. The standard drug used in this study was 'Norfloxacin, Ciprofloxacin and Chloramphenicol' for evaluating antibacterial activity.

**TABLE-1 Antibacterial activity of compounds [4a to 4j]**

| Compound | Minimum Inhibitory Concentrations (µg/ml) | | | |
|---|---|---|---|---|
| | Gram negative bacteria | | Gram positive bacteria | |
| | *E. coli* | *P. aeruginosa* | *S. aureus* | *S. pyogenus* |
| **4a** | 250 | 250 | 125 | 250 |
| **4b** | 62.5 | 250 | 250 | 125 |
| **4c** | 500 | 250 | 250 | 250 |
| **4d** | 125 | 500 | 250 | 500 |
| **4e** | 250 | 500 | 125 | 500 |
| **4f** | 250 | 500 | 500 | 1000 |
| **4g** | 250 | 125 | 125 | 500 |
| **4h** | 125 | 250 | 250 | 250 |
| **4i** | 125 | 125 | 250 | 62.5 |
| **4j** | 125 | 250 | 250 | 250 |
| **Norfloxacin** | 50 | 50 | 50 | 50 |
| **Ciprofloxacin** | 50 | 50 | 50 | 50 |
| **Chloramphenicol** | 50 | 50 | 50 | 50 |

**Antifungal activity**

While for the antifungal activity, the synthesized compounds were screened (Table-2) for their antifungal activity against *C. albicans*, *S. cervecieaceae* and *A. clavatus.* "Nystatin-B" and "grisiofulvin" was used as a standard drug for antifungal activity.

**TABLE-2 Antifungal activity of compounds [4a to 4j]**

| Compound | Minimum Inhibitory Concentrations (µg/ml) | | |
|---|---|---|---|
| | Fungus | | |
| | *C. albicans* | *S. cervecieaceae* | *A. clavatus* |
| **4a** | 500 | 250 | 500 |
| **4b** | 500 | 500 | 500 |
| **4c** | 500 | 1000 | 1000 |
| **4d** | 1000 | 1000 | 1000 |
| **4e** | 500 | 1000 | 1000 |
| **4f** | 500 | 1000 | 1000 |
| **4g** | 500 | 1000 | 1000 |
| **4h** | 250 | 500 | 500 |
| **4i** | 500 | 500 | 500 |
| **4j** | 1000 | 500 | 500 |
| **Nystatin-B** | 100 | 100 | 100 |
| **Gresiofulvin** | 100 | 100 | 100 |

## CONCLUSIONS

A variety of Schiff base have been successfully synthesized in excellent appreciable yields and screened in vitro for their antimicrobial activities against both strains of Gram-positive, Gram-negative bacteria and fungal strains. Antibacterial activity results of compound 4b showed good active against *E. Coli* and compound 4i showed good active against *S. pyogenus.* Rest of compounds showed good to moderate activity. The antifungal results of compounds 4a and 4h showed more active against *S. cervecieaceae* and *C. albicans*. Rest of the compounds showed moderate to good activity.

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