INTRODUCTION

Schiff bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that include antibacterial, antifungal and antivirus activity. They also serve as a backbone for the synthesis of various heterocyclic compounds. Schiff bases are the condensation products of ketones or aldehydes with primary amines and were first reported by Hugo Schiff in 1864. Now a day, Schiff bases are used as intermediates for the synthesis of amino acids or as ligands for preparation of metal complexes having a series of different structures.

A large number of Schiff bases and their complexes have been studied for their interesting and important properties, e.g., their ability to reversibly bind oxygen, catalytic activity in hydrogenation of olefins and transfer of an amino group, photochromic properties, and complexing ability towards some toxic metals.

There are wide applications of Schiff bases and their metal chelates in biological systems, catalysis, dying processes and analytical applications, the spectral studies of the Schiff bases containing a heterocyclic ring are comparatively minor. An interesting application of Schiff bases is their use as an effective corrosion inhibitor, which is based on their ability to spontaneously form a monolayer on the surface to be protected. Many commercial inhibitors include aldehydes or amines, but presumably due to the C=N bond the Schiff bases function more efficiently in many cases.

A Schiff base behaves as a flexidentate ligand and commonly coordinates through the O atom of the deprotonated phenolic group and the N atom of azomethine group. Schiff base ligands have significant importance in chemistry; especially in the development of Schiff base complexes, because Schiff base ligands are potentially capable of forming stable complexes with metal ions. Many Schiff base complexes show excellent catalytic activity in various reactions at high temperature (>100 °C) and in the presence of moisture. Over the past few years, there have been many reports on their applications in homogeneous and heterogeneous catalysis, hence the need for a review article highlighting the catalytic activity of Schiff base complexes realized.

Today, Schiff bases are used as intermediates for the synthesis of amino acids or as ligands for preparation of metal complexes having a series of different structures. This paper presents a series of new Schiff bases with a potential biological activities.

MATERIALS AND METHODS

Experimental section

Melting points were taken in open capillaries and are uncorrected. Purity of compounds was monitored on silica gel ‘G’ coated TLC plates. IR spectra were recorded on Schimadzu FTIR-8400S Spectrometer in KBr, 1H NMR spectra were taken in CDCl3+DMSOδ on Bruker AVANCE II 400 NMR Spectrometer using TMS as an internal standard and Mass spectra were recorded on a Joel SX-102 (EI/CI/FAB) mass spectrometer.

Preparation of new Schiff bases (1-8)

Synthesis of 2-(3-hydroxy-4-methoxybenzilideneamino) benzoic acid (1):

Isovanillin (1.52g, 10 mmol), Anthranilic acid (1.37g, 10 mmol) and triethylamine (1ml, 10 mmol) were mixed in 50 ml ethanol in a round flask. The mixture was refluxed on a water bath for 3 h at 323 K to give yellow precipitate. After filtration and washing the precipitate with ethanol, a pure Schiff base ligand, 2-(3-hydroxy-4-methoxybenzilideneamino) benzoic acid (yield: 0.25 g, 66%) was obtained.
The mixture was refluxed with agitation for 4 h at 323 K to give a yellow precipitate. After filtration and washing the precipitate with ethanol, a pure Schiff base ligand, (E)-2-(3-hydroxy-4-methylbenzylideneamino) benzoic acid (yield: 0.90 g, 68%) was obtained.

IR (KBr, cm⁻¹): 1483 (C=N str), 1592 (C≡C str), 3206 (COOH str), 1273 (C-N str), 1424 (C=N str); ¹H-NMR: 11.0 (s, OH), 7.87 -7.89 (m, 4H, Ar-H), 8.40 (s, CH); m/z: 357.04 (100.0%), 270.09 (16.5%), 273.09 (2.1%).

Synthesis of (E)-1-(5-chloro-2-(3-hydroxy-4-methoxybenzylideneamino) phenyl)-2, 2, 2-trifluorourethanone (6):

Vanillin (1.52g,10mmol), 1-(2-amino-5-chlorophenyl)-2,2,2-trifluoroethane-1,1-diol hydrochloride (1.01gr, 10 mmol) and triethylamine (1 ml, 10 mmol) were mixed in 50 ml ethanol in a round flask. The mixture was refluxed with agitation for 4 h at 323 K to give a yellow precipitate. After filtration and washing the precipitate with ethanol, a pure Schiff base ligand, (E)-1-(5-chloro-2-(3-hydroxy-4-methoxybenzylideneamino) phenyl)-2, 2, 2-trifluorourethanone (yield: 1.10 g, 79%) was obtained.

IR (KBr, cm⁻¹): 1444 (C=N str), 1649 (C=O str), 3131 (OH str), 1584 (C=C str), 2700 (OCH₃ str), 1142 (C-N str); ¹H-NMR: 5.35 (s, OH), 6.89 -7.40 (m, 4H, Ar-H), 7.38 -7.86 (m, 3H, Ar-H), 8.66 (s, CH); m/z: 357.04 (100.0%), 359.04 (34.0%), 358.04 (17.5%), 360.04 (5.6%).

Synthesis of (E)-1-(5-chloro-2-(pyridin-2-ylmethyl eneamino) phenyl)-2, 2, 2-trifluorourethanone -e (7):

Pyridine 2-carboxylicaldehyde (1.07g, 10 mmol), 1-(2-amino-5-chlorophenyl) 2, 2, 2-trifluoroethane-1,1-diol hydrochloride, triethylamine (1 ml, 10 mmol) were mixed in 50 ml ethanol in a round flask. The mixture was refluxed with agitation for 4 h at 323 K to give a yellow precipitate. After filtration and washing the precipitate with ethanol, a pure Schiff base ligand, (E)-1-(5-chloro-2-(pyridin-2-ylmethyl eneamino) phenyl)-2, 2, 2-trifluorourethanone (yield: 0.25 g, 69%) was obtained.

IR (KBr, cm⁻¹): 1387 (C=N str), 1615 (C=O str), 1560 (C=C str), 1178 (C-CHO), 1273 (C-N str); ¹H-NMR: 7.38 -7.86 (m, 3H, Ar-H), 7.65 -7.85 (m, 4H, Ar-H), 8.40 (s, CH); m/z: 312.03 (100.0%), 314.02 (32.0%), 313.03 (15.3%), 315.03 (4.9%), 314.03 (1.4%).

Synthesis of (E)-6-(4-chloro-1-(2, 5-dihydrothiazol-2-yl)-3-oxazetidin-2-ylidene) cyclohexa-1,3-dienecarboxylic acid (8):

A mixture of Schiff base (3.10gr, 0.01mol) in benzene was taken in a 50ml round bottom flask. It was added to bromoaetyl bromide (2.02g, 0.01mol), triethylamine hydrochloride (1.01gr, 0.01mol) were added slowly. It was refluxed for 15-16hrs. The triethylamine hydrochloride was formed during the reaction, was removed and the benzene was distilled off to get the product. The crude product obtained was recrystallised from ethanol a pure Schiff base ligand (yield: 3.50 g, 72%) was obtained.
IR (KBr, cm⁻¹): 1483 (C=N str), 1796 (C=O str), 1592 (C=C str), 3206 (COOH str), 1273 (C-N str), 1326 (s, C-S); 1690 (s, Azetidinone ring); ¹H-NMR: 11.0 (s, OH), 8.30 (s, H), 7.50 (s, CH), 5.47 (s, CH); m/z: 310.02 (100.0%), 312.01 (36.5%), 311.02 (15.1%), 313.02 (5.2%), 312.02 (1.7%), 314.01 (1.5%).

Synthesis of new Schiff bases (1-8):

**Scheme-1**

**Scheme-2**

**Scheme-3**

**Scheme-4**

**Scheme-5**

**Scheme-6**

**Scheme-7**
Table 1: Physical and analytical data of Schiff bases (1-8)

<table>
<thead>
<tr>
<th>Molecular Formula</th>
<th>M.W.</th>
<th>Yield (%)</th>
<th>M.P.(°C)</th>
<th>Elemental Analysis Cal/exp.</th>
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<td>138-142</td>
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<td>62</td>
<td>222-225</td>
<td>50.24/49.98</td>
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Table 2: Results of Screening antibacterial activity of products 1-9 of 1,5-Benzodiazepene in mg/ml.

<table>
<thead>
<tr>
<th>New Schiff bases</th>
<th>Tested Bacteria</th>
<th>Zone of inhibition Diameter (mm) [1mg/2ml]</th>
<th>Zone of inhibition Diameter (mm) [1mg/4ml]</th>
<th>Zone of inhibition Diameter (mm) 1mg/6ml</th>
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<tr>
<td>1</td>
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<td>15</td>
<td>13</td>
<td>11</td>
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<tr>
<td>10</td>
<td>Control</td>
<td>-</td>
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</tr>
</tbody>
</table>

Graph 1: Anti-bacterial Activities
Biological Activity

The synthesized Schiff bases were screened for antibacterial activity.

Antibacterial Studies

The synthesized Schiff bases, their derivatives and their metal complexes were screened for their antibacterial activity against the bacterial species, E. coli.

The paper disc diffusion method was used for the determination of the antibacterial activity.

Preparation of Discs

The ligand complex (20 mg to 80 mg) in DMF (0.01 ml) was applied on a paper disc, [prepared from blotting paper (3 mm diameter)] with the help of a micropipette.

The discs were left in an incubator for 48 h at 37° C and then applied on the bacteria grown agar plates.

Preparation of Agar Plates

Minimal agar was used for the growth of specific bacterial species. For the preparation of agar plates for E.coli, MacConkey agar (50g), obtained from Merck Chemical Company, was suspended in freshly distilled water (l l). It was allowed to soak for 15 minutes and then boiled on a water bath until the agar was completely dissolved. The mixture was autoclaved for 15 minutes at 120’ C and then poured into previously washed and sterilized Petri dishes and stored at 40 °C for inoculation.

Procedure of Inoculation

Inoculation was done with the help of a platinum wire loop which was made red hot in a flame, cooled and then used for the application of bacterial strains.

Inoculation of Discs

A sterilized forceps was used for the application of paper disc on then already inoculated agar plates. When the discs were applied, they were incubated at 37°C for 24 h. The zone of inhibition was then measured (diameter in mm) around the disc.

Figure 1: Showing zone of inhabitation against, Streptomycin and E. coli

[S - Standard (Streptomycin); C - Control (Solvent); E - 20 mg of sample (A) -Soluble in DMF, Ca - 40 mg of sample (A), M - 60 mg of sample (A).]

RESULTS AND DISCUSSION

Various Schiff bases are synthesized by 2-amino benzoic acid with the help of catalyst and solvent Et3N /MeOH. These Schiff bases have reversible nature of synthesized Schiff bases reaction. All the synthesized compounds (1-8) were purified by successive recrystallization using ethanol. The purity of the synthesized compounds was checked by performing TLC. The structures of the synthesized compounds were determined on the basis of their FTIR and 1HNMR data.

All the synthesized Schiff bases (1-8) show the antibacterial activities. The antibacterial activity was evaluated against pathogenic strain E.coli. The zone of inhibition and activity index were determined by comparison with the standard drug streptomycin. The outcome of this study is presented in table-2. The antibacterial screening against E.coli showed that amongst the compounds (1-8), the compound (5) displayed highest activity in (mg/2ml, mg/4ml, mg/6ml) and compound (8) displayed lowest activity. The remaining compounds showed moderate activity.

CONCLUSION

Various Schiff bases were synthesized by the analytical and spectral techniques. These compounds exhibited significant activity against all the tested microorganisms.

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REFERENCES


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