Synthesis, Characterization and Biological Evaluation of Some Novel Schiff’s Bases Derived from Vanillin

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Abstract

Many drugs contain primary amino group can be utilized for synthesizing Schiff’s bases with different uses. A series of Schiff’s bases (Z1 - Z5) have been synthesized using (vanillin) and 3,4 diaminopyridine, procaine, Met form in, 2-arsanilic acid and Rhodamine Z1 and Z2 were synthesized using acid catalyst while basic catalyst has been used in the synthesis of Z3- Z5. The characterization was performed using elemental analysis, FT-IR and proton NMR spectroscopes. The prepared compounds were biologically evaluated against gram positive and gram negative bacteria. The results showed excellent to moderate anti-bacterial activity.

Keywords: Vanillin, Schiff’s bases, Met form in, Condensation reaction, Anti-bacterial activity, Disk diffusion method.

Introduction

The Schiff bases can be produced by the condensation reaction of a primary amines with a carbonyl compounds and they are contain an azomethine group (–CH=N–) (p6). Schiff bases have been widely used in many fields e.g. biological [1], inorganic [2], [3] drug synthesis [4] and as bidentate ligand in the field of coordination chemistry [5].

Schiff’s bases form a significant class of compounds in medicinal and pharmaceutical chemistry [6], [7] with several biological applications that include antibacterial [8], antifungal [9], anticancer [10], anti-inflammatory, antimicrobial[11], antiviral [12], and antitumor [13] activities. Schiff bases derived from vanillin have a potential biological activity against some of the gram positive and gram negative bacteria [14].

Vanillin (4-hydroxy-3-methoxybenzaldehyde) is a vanilla essential component. In old medicinal literature vanilla was considered as a cure for fevers[15]. In this work we are reported the synthesis, characterization and biological evaluation of five novel Schiff bases derived from vanillin.

Experimental and Instrumentation

Materials and Equipment

All chemicals that used are obtained from Merck, Fluka and Aldrich, further purification was not needed. Melting points were measured by using an (Electro thermal) melting point apparatus and they are uncorrected. FT-IR spectra were measured with SHIMADZU FTIR-4800S Infrared spectrophotometer by using KBr disk, Elemental analysis were recorded by using E.A.G.E.R.-100, Carlo Erba, Italy, in Babylon University. 1H-NMR spectra were recorded by using 300 MHz JNM ECP-600 spectrometer and DMSO-d6 was the solvent and tetramethylsilane, (TMS) was the internal standard.

Synthesis of Schiff’s Base

To a solution of vanillin (0.014 mol, 2.13g) 3,4-diaminopyridine (0.007 mol, 0.76 g) was added in 50 ml absolute ethanol (glacial acetic acid as a catalyst) , and the reaction mixture was refluxed for 6h with continuous stirring then the colored solution was allowed
to cool at room temperature, the formed precipitate was washed with dichloromethane and re-crystallization from dioxane. M.P 118-120 °C, Yield 73 %, Mol. Formula: C_{21}H_{16}N_{2}O_{4}; C, 66.83; H, 5.07; N, 11.13 %: found; C, 66.70; H, 5.09; N, 11.09.

Synthesis of Schiff's Base

An ethanol solution (50 ml) contains vanillin (0.01 mol, 1.52 gm) and procaine (0.01, 2.36 gm) was transferred into 250 ml round bottom flask, a few drops of glacial acetic acid was added and the reaction mixture was magnetically stirred for 48 h at room temperature. The colored solution was evaporated by a rotary vacuum and the obtained product was washed with acetone and diethyl ether, recrystallized from ethanol and dried over CaCl₂ desiccator. M.P: 115-117°C, yield 82 %, Mol. Formula: C_{21}H_{26}N_{2}O_{4}; C, 68.09; H, 7.07; N, 7.56 Found; C, 68.06; H, 7.09; N, 7.52.

Synthesis of Schiff's Base

A mixture of Met form in hydrochloride (0.008 mol, 0.448 gm) in 250 ml round bottom flask dissolved in 30 ml absolute ethanol was stirred for 15 min, vanillin solution (0.008 mol, 1.21 gm) in 20 ml absolute ethanol was drop-wise added and the reaction mixture was refluxed for 16 h, the volume of solution was reduced to half and allowed to cool, precipitate was formed, filtered off, washed with small portions of ethanol and diethyl ether, the product was air dried and recrystallized from methanol. M.P 105-107 °C, Yield 75 %, Mol. Formula: C_{12}H_{17}N_{3}O_{2}; C, 54.74; H, 6.51; N, 26.60 %: found; C, 54.78; H, 6.53; N, 26.57.

Synthesis of Schiff's Base

A mixture of 2-arsinilic acid (0.01 mol, 2.16 gm) and KOH (0.02 mol, 1.12 gm) dissolved in 30 ml absolute ethanol was stirred for 15 min, vanillin solution (0.01 mol, 1.52 gm) in 20 ml absolute ethanol was drop-wise added and the reaction mixture was refluxed for 24 h, the volume of solution was reduced to half and allowed to cool, precipitate was formed, filtered off, washed with small portions of ethanol and diethyl ether. The product was dried by CaCl₂ desiccator, re-crystallized from methanol. M.P: 179-181 °C, Yield 79 %, Mol. Formula: C_{13}H_{12}AsN_{3}O_{3}; C, 53.02; H, 3.81; N, 4.42 %: found; C, 53.05; H, 3.84; N, 4.38.

Synthesis of Schiff's Base

The same procedure in synthesis of compound Z3 and Z4 was used the product was washed with dichloromethane and diethyl ether, recrystallized from dioxane. M.P 310 – 312 °C, Yield 68 %, Mol. Formula: C_{28}H_{18}KN_{3}O_{5}; C, 66.92; H, 3.81; N, 5.57 %: found; C, 66.86; H, 3.84; N, 5.57.

Anti-Bacterial Activity

The disk diffusion method was used to screen the anti-bacterial activity for the synthesized Schiff's bases against gram positive (Staphylococcus aureus) and gram negative bacteria (Escherichia coli), the agar and Petri-dishes was sterilized by autoclave at 121°C for 15 min, then the agar was poured to the disks and allowed to solidify, then 4 holes (6 mm) are made, 0.1 ml solution of the synthesized compounds (500µg/ml DMSO) was added into each hole, These plates were incubated at (37°C) for (24 hours) [21]. The results are shown in Table 3.

Result and Discussion

Five novel Schiff bases were prepared by condensation reactions of equimolar amounts of vanillin and corresponding primary amines as shown in scheme 1:
The reaction was catalyzed by either acid or base[16], [17], in the case of amines that contain hydrochloric acid or acidic carboxyl group the acid cannot be used as a catalyst, instead base catalyst must be used to obtain a free amino group.

**FT-IR spectra**

The FT-IR spectra (KBr disk) for all of the prepared compounds show disappearance of the stretching vibration bands that belong to the primary amino group and aromatic carbonyl group of vanillin, the main characteristic FT-IR bands are listed in Table 1. A strong bands was appeared in the range of (1600 - 1675 cm\(^{-1}\)) which belong to the azomethine group, that conform the formation of the Schiff bases[18].

<table>
<thead>
<tr>
<th>Comp.NO.</th>
<th>ν OH</th>
<th>Aromatic ν C-H</th>
<th>Aliphatic ν C-H</th>
<th>νC=N</th>
<th>Aromatic ν C=C</th>
<th>νC-N</th>
<th>phenolic ν (c-o)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z1</td>
<td>3319</td>
<td>3068</td>
<td>2993</td>
<td>1645</td>
<td>1585</td>
<td>1278</td>
<td>1116</td>
</tr>
<tr>
<td>Z2</td>
<td>3352</td>
<td>3215</td>
<td>2960</td>
<td>1602</td>
<td>1518</td>
<td>1273</td>
<td>1172</td>
</tr>
<tr>
<td>Z3</td>
<td>3321</td>
<td>3155</td>
<td>2926</td>
<td>1651</td>
<td>1560</td>
<td>1369</td>
<td>1122</td>
</tr>
<tr>
<td>Z4</td>
<td>3388</td>
<td>3238</td>
<td>2841</td>
<td>1655</td>
<td>1579</td>
<td>1332</td>
<td>1111</td>
</tr>
<tr>
<td>Z5</td>
<td>3298</td>
<td>3122</td>
<td>2966</td>
<td>1676</td>
<td>1593</td>
<td>1327</td>
<td>1172</td>
</tr>
</tbody>
</table>

**1H-NMR data**

The 1H-NMR data for the Schiff bases were recorded by using DMSO-d6 as a solvent and the chemical shift in ppm. The signal of azomethine proton, (HC=N), was appeared in range of (δ 8 - 8.9) [19], phenolic OH (δ 9 - 9.8) [20], the aromatic protons was appeared in range of (6.5 - 7.5) while -OCH\(_3\) was appeared in range of (3.2 - 3.9) as shown in Table 2.

<table>
<thead>
<tr>
<th>Com.NO.</th>
<th>δ (OH) Phenolic</th>
<th>δ (HC=N)</th>
<th>δ (CH) Aromatic</th>
<th>δ (-OCH(_3))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z1</td>
<td>9.75</td>
<td>8.5</td>
<td>6.6-8</td>
<td>3.7</td>
</tr>
<tr>
<td>Z2</td>
<td>9.8</td>
<td>7.8</td>
<td>6.5-7</td>
<td>3.75</td>
</tr>
<tr>
<td>Z3</td>
<td>9.5</td>
<td>7.8</td>
<td>6.7-7</td>
<td>3.65</td>
</tr>
<tr>
<td>Z4</td>
<td>9.2</td>
<td>8.55</td>
<td>6.5-1.5</td>
<td>3.6</td>
</tr>
<tr>
<td>Z5</td>
<td>9.6</td>
<td>7.9</td>
<td>7.6-7.8</td>
<td>3.3</td>
</tr>
</tbody>
</table>

**Anti-bacterial Activity**

The anti-bacterial activity for the synthesized Schiff’s bases was screened against Staphylococcus aureus and Escherichia coli, the results was showed that all compounds have excellent biological activity against E. Coli except Z5 (moderate), in the case of Staphylococcus aureus Z1, Z2 and Z4 have excellent biological activity while Z3 and Z5 have moderate as shown below.

**Table 3: The inhibition zones of the synthesized Schiff’s bases (mm)**

<table>
<thead>
<tr>
<th>Com.NO.</th>
<th>Staphylococcus aureus</th>
<th>Escherichia coli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z1</td>
<td>27</td>
<td>25</td>
</tr>
<tr>
<td>Z2</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>Z3</td>
<td>13</td>
<td>20</td>
</tr>
<tr>
<td>Z4</td>
<td>20</td>
<td>28</td>
</tr>
<tr>
<td>Z5</td>
<td>12</td>
<td>14</td>
</tr>
</tbody>
</table>

**Conclusion**

From vanillin some of Schiff’s bases have been prepared, and the characterization by FT-IR and 1H-NMR confirm this preparation. The anti-bacterial study showed moderate to high anti-bacterial activity for all of prepared Compounds against both gram positive and gram negative bacteria.

**Acknowledgements**

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References


