Syntheses, spectral and antibacterial activity of Schiff bases derivatives from Benzidine and aromatic aldehydes

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Abstract

A new series of Schiff bases derived from benzidine and various aromatic aldehydes. Molecular Structures were obtain from their elemental analyses, I.R, H¹-NMR, and evaluated for their potential as antibacterial active against some Gram positive and Gram negative bacterial strains. The biological activity was studied against P. pseudoalcaligenes, P. vulgaris, C. freundii, E. areogenes, S. subfava and B. megaterium. The determination of the biological activity was done by using Agar dish method. The Schiff bases derived from benzidine as the central molecule with various aromatic aldehydes as the side chains in DMSO effectively inhibited the investigated bacteria and appear to be promising antibacterial agents.

Introduction

Schiff bases of benzidine and its derivatives have a variety of applications in biological, clinical, analytical and pharmaceutical areas (1-3). Due to the great flexibility and drives structural aspects, a wide range of Schiff bases have been synthesized behavior studied (4). They have been synthesized from a variety of compounds, such as amino thiazole, 2-hydroxy-1-naphthaline, amino sugars, aromatic aldehydes, isatin, the thiazole ring, thiosemicarbazides, amino acids, pyrazolone etc. (5-9). Schiff bases are characterized by the –N=CH- (imine) group which is formed by condensation of an aldehyde and amine (10). The antibacterial activity was evaluated in two solvents, dimethyl sulfoxide and N, N-dimethyl formamide.

Dimethyl sulfoxide (DMSO) is a versatile non-aqueous dipolar aprotic solvent having a dielectric constant 46.6(25°C) and a dipolar moment of 3.9D (25°C). It's a highly polar and aprotic solvent, which can mix very well with any liquid. Its also called a super solvent and exhibit quite interesting properties.

N,N-Dimethylformamide (DMF) is a very good aprotic protophilic medium for organic and inorganic substances (11). It is one of the most important solvent in analytical chemistry and for practical purposes. It's dielectric constant and dipolar moment are 36.71 (25°C) and 3.86D (25°C), respectively.
Experimental
The following Schiff bases were synthesized:
1- 4,4′-Bis-(benzylidine amino)biphenyl [A]
2- 4,4′-Bis-(4-hydroxyl benzylidine amino)biphenyl [B]
3- 4,4′-Bis-(3-hydroxyl benzylidine amino)biphenyl [C]
4- 4,4′-Bis-(3,4-dihydroxyl benzylidine amino)biphenyl [D]
5- 4,4′-Bis-(4-nitro benzylidine amino)biphenyl [E]
6- 4,4′-Bis-(3-Bromo benzylidine amino)biphenyl [F]

Synthesis of Schiff bases derived from benzidine:
To the required of aldehyde dissolved in (100ml) of absolute ethanol was add (0.01 mole) of a known amine and few drops of glacial acetic acid as a catalyst.
The mixture was stirred for approximately (1 h) and a solid crystalline product was formed. The formed product was filtrated off and washed with sodium sulfate solution to remove the excess aldehyd and recrystalized from ethanol.
In this reaction $R_1$-$NH_2$ is benzidine and $R$ is a given constituent.
Test microorganisms

The investigated microorganisms were *P. Psudoalcaligenes*, *P. Vulgaris*, *C. Freundii*, *E. areogenes*, *S. Subfava* and *B. Megaterium*.

Preparation of the test compounds

The compounds were dissolved at a ratio concentration of 10mg/ml in either of the two solvents (DMSO or DMF) in order to obtain a final concentration of 1mg/0.1ml, 0.01mg. The synthesized Schiff bases are soluble only in DMF, 1,4-dioxane and only DMSO and DMF selected for the present study.

Preparation of the planets and microorganism assays

A pool full of the given test strain was inoculated into (25ml) of N-broth (nutrient agar) and inoculated for (24hrs) in an incubator at (37°C) in order to activate the bacterial strain. A Petri-dish of 100ml diameter was filled with (28-30ml) of Mueller Hinton Agar No.2 media. Inoculation was performed by the pour-plate technique, and a (0.2ml) of the activated strain was inoculated into the media when it had reached a temperature of (40-45°C). The complete procedure of the dish preparation was done in a laminar airflow to maintain strict sterile and aseptic condition. The media was allowed to solidify. After solidification of the media, a well was made in the media with the help of a cup-borer (0.85cm) and then (0.1ml) of the synthetic compound dissolved in (DMSO/DMF) was inoculated in the well. Controls were performed (for each bacterial strain and each solvent), where (0.1ml) of the pure solvent was inoculated into the well. The plats were incubated for (24hrs) at (37°C). The inhibition zone formed by the compounds against the particular test bacterial strain determined the antibacterial activities of the synthetic compounds. The mean value obtained for three individual replicates was used to calculate the zone of the growth inhibition of each sample.

Discussion

A total 6 compounds (Schiff bases) were synthesized, and their FTIR and NMR structural data confirmed their molecular structure which are given below:-

A: FTIR (KBr , cm⁻¹) –C=N : 1628, C=C :1580 , C-H(aromatic):3100

B: FTIR (KBr, cm⁻¹)–C=N:1618 , -OH(str.):3412,C=C:1589
   C-H(aromatic):3050.
   H¹-NMR(δ,ppm): 9.76(2H, OH) , 9.6(2H, N=CH) , 6,927.33(16H,Ar–H).

C: FTIR (KBr, cm⁻¹): OH(str):3422, -C=N :1640, C=C: 1591, C-H(aromatic):
   3080
   H¹-NMR(δ,ppm): 9.72(2H, -OH), 9.6(2H, N=CH) , 6,88-7.21(16H,Ar-H).

D: FTIR(KBr,cm⁻¹):OH(str):3450, -C=N :1648, C=C: 1595,C-H(aromatic): 3060

E: FTIR (KBr, cm⁻¹): OH(str):-C=N :1622, C=C: 1590,C-H(aromatic): 3075.
   z(δ,ppm):  9.58(2H, N=CH) , 6,82-7.54(16H,Ar-H).

F: FTIR (KBr, cm⁻¹):-C=N :1644, C=C: 1610 ,C-H(aromatic): 3130, -Br: 425.
   H¹-NMR (δ,ppm): 9.5(2H, N=CH) , 6,44-7.35(16H,Ar-H).

The molecular formulas , molecular weight , melting points , % yields, Rf value with the solvent system of the 6 Schiff bases , color and found (cald) CHN are given in table I.
### Table I: Investigated analytical and physical data of the synthesized compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molecular formula</th>
<th>Molecular weight /gmmole-1</th>
<th>m.p °C</th>
<th>Yield %</th>
<th>R_f solvent value systm.</th>
<th>Found (cal)</th>
<th>Color</th>
</tr>
</thead>
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<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>C</td>
<td>H</td>
</tr>
<tr>
<td>A</td>
<td>C_{26}H_{20}N_{2}</td>
<td>408</td>
<td>142</td>
<td>64</td>
<td>0.50 EA : H 4 : 6</td>
<td>86.66</td>
<td>7.77</td>
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<td>B</td>
<td>C_{26}H_{20}N_{2}O_{2}</td>
<td>392</td>
<td>138</td>
<td>58</td>
<td>0.61 EA : H 4 : 6</td>
<td>79.59</td>
<td>7.14</td>
</tr>
<tr>
<td>C</td>
<td>C_{26}H_{20}N_{2}O_{2}</td>
<td>392</td>
<td>151</td>
<td>61</td>
<td>0.59 EA : H 4 : 6</td>
<td>79.59</td>
<td>7.14</td>
</tr>
<tr>
<td>D</td>
<td>C_{26}H_{20}N_{2}O_{4}</td>
<td>424</td>
<td>155</td>
<td>66</td>
<td>0.59 EA : H 4 : 6</td>
<td>73.58</td>
<td>6.60</td>
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<tr>
<td>E</td>
<td>C_{26}H_{20}N_{4}O_{4}</td>
<td>452</td>
<td>166</td>
<td>72</td>
<td>0.59 EA : H 3 : 7</td>
<td>73.58</td>
<td>6.60</td>
</tr>
<tr>
<td>F</td>
<td>C_{26}H_{20}N_{2}Br_{2}</td>
<td>597</td>
<td>167</td>
<td>78</td>
<td>0.59 EA : H 4 : 6</td>
<td>60.23</td>
<td>5.46</td>
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</table>

EA: ethylacetate; H:Hexane
Figure (1) $^1$H NMR spectrum of compound
All compounds have different antibacterial activity in vitro against the tested bacterial strain in different solvents. The controls were detected from the tested compounds; their effect was noticeably different depending on the type of the solvent used. The antibacterial activity of the Schiff bases synthesized from benzidine against the Gram positive bacteria *S. Sudfva* and *B. meqaterium* and show in fig. (1). The inhibitory activity was greater in DMSO than DMF. Of these Gram positive bacteria: a *S. Sudfva* was more resistant to the synthesized compounds than *B. meqaterium.*

Considering the Gram positive *B. meqaterium*, DMF was ineffective while almost all the compounds in DMSO produced inhibitory zones. The most active compounds were A, B, C, D and E; the compound F completely failed to inhibit this microorganism. The differences in the inhibitory activity are due to molecular diversity. All 6 compounds have different side chains via in A benzaldehyde , in B it was 4-OH benzaldehyde in C it was 3-OH benzaldehyde , in D it was 3,4-diOH benzaldehyde , in E it was 4-NO₂ benzaldehyde and in F it was 3-Br benzaldehyde.

The interaction between the solvent and the Schiff bases play an important role in inhibiting the studied bacterial strains. *In vitro* antibacterial elucidation of the six synthesized compounds against *P. Pseudoalcaligenes* and *P. Vulgaris* are shown in fig. 2. All the compounds dissolved in DMF showed considerable inhibitory zones against *P. Pseudoalcaligenes.*

The compounds (D,E,F) were more active than the compounds (A,B,C). The compound F was the only compound in DMSO which show high inhibition zone, while all the other 5 compounds were ineffective in DMSO. An entirely different trend was observed with *P. Vulgaris.*

The compounds extracted in DMF did not inhibit these Gram negative bacteria. Also when dissolved in DMSO only F showed a great inhibitory activity.

**fig(1):** Antibacterial activity of some synthetic compounds against: a) *S. subfava,*  
 b) *B. megaterium*  

**fig(2):** Antibacterial activity of some synthetic compounds against: a) *P. Pseudoalcaligenes*  
 b) *P. Vulgaris*
The differences in the bacterial activity of the compounds dissolved in the employed polar solvents towards the Gram negative bacteria *C. freundii* are shown in fig. 3. The compound (A,B,C,D,E) irrespective of whether they were dissolved in DMF or DMSO did not produce any inhibitory zones against either of the bacteria.

(F) in DMF was only Schiff base showed inhibitory activity against *C. freundii* while compounds D-F showed inhibitory activity against *E.aerogenes* when dissolved in DMSO. The other compounds did not inhibit either of the studied bacteria.

Fig(3) :Antibacterial activity of some synthetic compounds against a) *C. freundii*  b) *E.aerogenes*

**References**