AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Synthesis and Antibacterial Property of Schiff Bases Derived from Toluidine and Benzaldehydes

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ABSTRACT

Schiff bases and their complexes are playing very important role in medicinal chemistry from ancient period because of their broad range of biological activities such as antibacterial, antifungal, antimalarial and antiviral etc. In this research project several Schiff bases have been synthesized from *p*-toluidine and derivatives of benzaldehyde to investigate the antibacterial activity. The synthesized Schiff bases have been characterized by IR and ^{1}H-NMR spectral analysis. All the synthesized compounds have been screened for their *in vitro* antibacterial activity against gram (+) and gram (–) bacterial strains by disc diffusion method. Among the synthesized compounds, the compound 5 showed strong efficacy against *E. coli* and the others showed moderate activity against bacterial strains.

Keywords: Schiff base, *p*-Toluidine, Benzaldehyde, Antibacterial activity

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Received 14 November 2017, Accepted 16 December 2017

Please cite this article as: Ali IM *et al*., Synthesis and Antibacterial Property of Schiff Bases Derived from Toluidine and Benzaldehydes. American Journal of PharmTech Research 2018.

INTRODUCTION

Schiff base reactions are valuable in making carbon-nitrogen (–CH=N–) bonds in organic syntheses. This class of compounds has versatile synthetic applications viz., preparative use, identification, detection and determination of aldehydes or ketones, purification of carbonyl or amino compounds, or protection of these groups during complex or sensitive reactions. Moreover, Schiff bases are very important class of organic compounds in many biological aspects [1].

In the recent years, chemists have been paid much attention to the chemistry of the metal complexes of Schiff bases containing nitrogen and other donor atoms [2-5]. Most of the Schiff bases and their complexes have been found to possess important biological and catalytic activity [6, 7]. Furthermore, Biochemists are now paying their active attention to the chemotherapeutic Schiff bases [8, 9]. It has been observed that several Schiff bases have potential biological activities like antifungal [10], antiinflammatory [11], antibacterial [12], antiviral [13], antioxidant [14] and anticancer [15]. The imine group present in such compounds has been shown to be critical to their biological activities [10-12].

Although many works have been done on Schiff bases from *p*-toluidine and benzaldehydes but it has been observed that the biological activities of some Schiff bases derived from *p*-toluidine and benzaldehydes are yet to establish. Inspired from the biological activity of many Schiff bases, our aim was to synthesize Schiff bases from *p*-toluidine and benzaldehydes to investigate their antibacterial activities.

MATERIALS AND METHOD

General Procedure for the Preparation of Schiff bases

A mixture of equimolar amounts (0.01 mol) of *p*-toluidine and an aromatic aldehydes (*p*-chlorobenzaldehyde, *p*-hydroxybenzaldehyde, 3-nitrobenzaldehyde, *p*-tolualdehyde, *p*-nitrobenzaldehyde, salicylaldehyde and benzil*) were dissolved in ethanol (≈25 mL) and the mixture was refluxed for 6-8 hrs. The completion of the reaction was checked by thin layer chromatography (TLC) and then the reaction mixture was allowed to cool to room temperature. At room temperature the Schiff bases was settled as crystalline solid. After filtration the product was further recrystallized from ethanol and afforded the Schiff bases crystals in good yields.

(*twice mol of *p*-toluidine was taken with benzil)

In vitro antibacterial assays

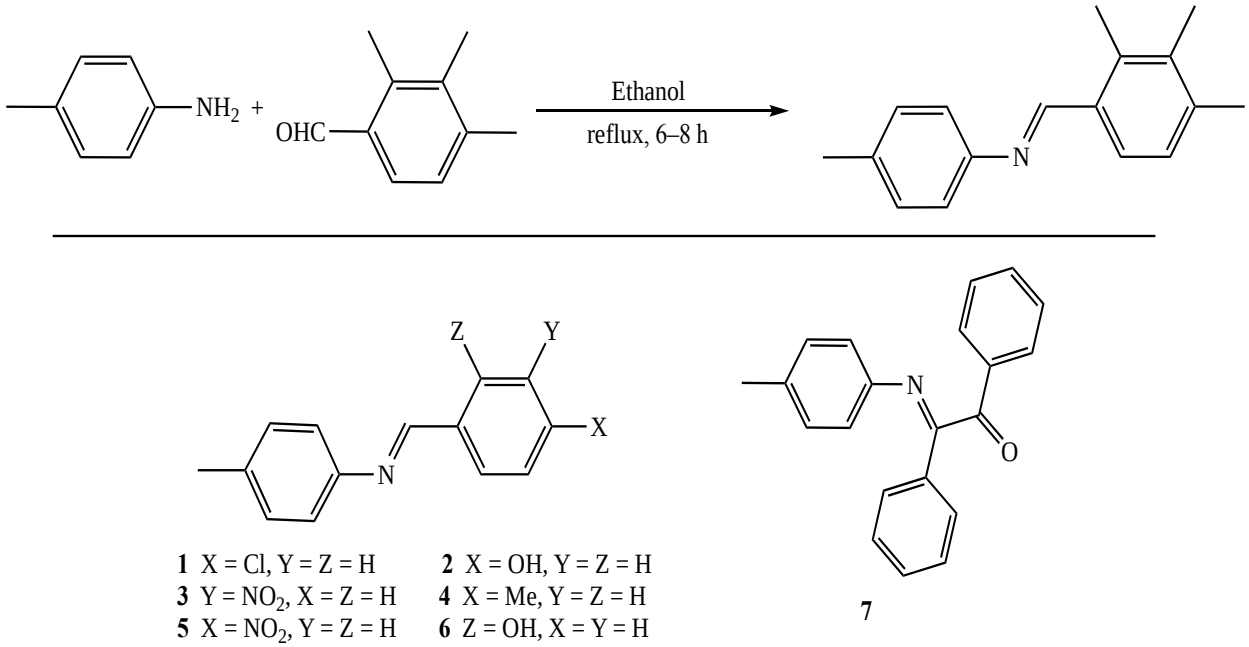
The synthesized Schiff bases were screened for antibacterial activity against the gram-positive and gram-negative pathogens namely, *Streptococcus agalactiae, Staphylococcus aureus, Escherichia*

coli, Shigella sonnei by the reported method [16]. The stock solution (1 $mgmL^{-1}$) of the test chemical was prepared in DMF solvent. The stock solution was further diluted with sterilized distilled water to different dilutions in μgmL^{-1}. The test chemicals of different dilutions were added to sterile blank antimicrobial susceptibility discs. The bacteria were sub cultured in nutrient agar (NA) medium and the discs were kept onto the same. The petri dishes were incubated for 24 hr at 37 ˚C. The standard antibacterial drug (streptomycin) was also screened under similar conditions for comparison. Activity was determined by measuring the zones of growth inhibition surrounding the discs and inhibition was compared with the standard drug. In order to clarify the effect of solvent (DMF) on the biological screening, DMF alone was added to separate discs and used as control, and it showed no activity against bacterial strains.

RESULTS AND DISCUSSION

Synthesis of desired Schiff bases

The Schiff bases (**1-7**) have been synthesized by the condensation of *p*-toluidine and benzaldehyde derivatives according to the following reaction (**Scheme 1**). All the products are solid at room temperature and stable under air. The products (**1-7**) were characterized by IR and ^{1}H-NMR spectral analysis.



1 X = Cl, Y = Z = H **2** X = OH, Y = Z = H
3 Y = NO_2, X = Z = H **4** X = Me, Y = Z = H
5 X = NO_2, Y = Z = H **6** Z = OH, X = Y = H

7

Scheme 1: Synthesis of desired Schiff bases

Biological Investigation

The Schiff bases reported here were evaluated for antibacterial activity against gram-positive (*Streptococcus agalactiae*, *Staphylococcus aureus)* and gram-negative *(Escherichia coli* and

Shigella sonnei). The inhibition details at maximum concentration (100 µg mL^{-1}) are tabulated in **Table 1**. The synthesized Schiff bases have shown moderate antibacterial activity and the compound **5** has shown maximum activity against *E. coli* amongst all the tested compounds. The activity of control dimethyl formamide (DMF) was also checked for its toxicity and observed no effect on the growth of any microorganisms taken.

Table 1: Antibacterial activity for maximum concentration (100 µgmL^{-1})

Compound	Zone of inhibition diameter in mm			
	S. aureus	***S. agalactiae***	***E. coli***	***Shigella sonnei***
1	00	12	10	11
2	7	10	00	13
3	9	00	12	00
4	12	8	14	13
5	13	7	20	11
6	9	4	11	10
7	00	13	14	00
DMF	-	-	-	-
Streptomycin	22	30	23	25

CONCLUSION

p-Toluidine is an excellent amine precursor for preparing Schiff bases with high yield and some of them exhibit strong to moderate antibacterial activity. Although our research on this subject is incipient, the present investigations may serve the basis towards development of a new class of effective antibacterial agents from *p*-toluidine. However, the biological activity of this class of compounds deserves further investigation.

Analytical and Spectral Data

All the chemicals used in this work were purchased from Sigma Aldrich, which were used without further purification. Ethanol was distilled before using. Stuart melting point apparatus (Model-SMP-10) was used for recording the melting point of the products by open glass capillary and are uncorrected. Infrared spectra were recorded on a Perkin Elmer FT-IR spectrometer (Model-Spectrum Two) using KBr pellets in the range of 4000-400 cm^{-1}. ^{1}H-NMR spectra were recorded on BRUKER 400 MHz spectrometer with $CDCl_3$ as solvent.

Compound 1

Yield 74%, bright white crystal, m.p. 132–135 ˚C**.** FT-IR (KBr): 3083, 3024, 2922, 1623, 1592, 1564, 1500, 1450, 1403, 1356, 1100, 1084, 1000, 850 and 700 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.43 (s, 1H, –CH=N–), 7.84 (d, *J* = 8.8 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H) and 2.38 (s, 3H).

Compound 2

Yield 75%, off white powder, m.p. 225–227 ˚C**.** FT-IR (KBr): 3449, 3060, 3028, 2922, 1608, 1573, 1517, 1500, 1443, 1289, 1191, 1150, 980, 850 and 800 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 9.87 (s, 1H), 8.45 (s, 1H, –CH=N–), 7.80 (d, *J* = 8.4 Hz, 2H), 6.99 (d, *J* = 4.8 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 2H) and 2.40 (s, 3H).

Compound 3

Yield 80%, off white powder, m.p. 97–99 ˚C. FT-IR (KBr): 3091, 3024, 2926, 1624, 1600, 1576, 1525, 1500, 1443, 1352, 1163, 1050, 850 and 790 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.73 (s, 1H, –CH=N–), 8.56 (s, 1H), 8.32 (d, *J* = 7.4 Hz, 1H), 8.25 (d, *J* = 7.6 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H) and 2.39 (s, 3H).

Compound 4

Yield 80%, off white crystal, m.p. 88–90 ˚C. FT-IR (KBr): 3056, 3030, 2879, 1626, 1603, 1564, 1500, 1449, 1367, 1150, 1100, 900 and 750 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.44 (s, 1H, –CH=N–), 7.80 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 2.42 (s, 3H) and 2.38 (s, 3H).

Compound 5

Yield 87%, bright yellow crystal, m.p. 130–133 ˚C. FT-IR (KBr): 3103, 3087, 2926, 1620, 1600, 1510, 1502, 1340, 1325, 1108, 900, 800 and 750 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.57 (s, 1H, –CH=N–), 8.32 (d, *J* = 8.8 Hz, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H) and 2.39 (s, 3H).

Compound 6

Yield 71%, orange crystal, m.p. 98–100 ˚C. FT-IR (KBr): 3457, 3052, 3016, 2918, 1620, 1596, 1565, 1498, 1415, 1368, 1285, 1100, 900, 800 and 750 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 13.38 (s, 1H), 8.63 (s, 1H, –CH=N–), 7.39–7.35 (m, 2H), 7.25–7.19 (m, 4H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.94 (t, *J* = 7.6 Hz, 1H) and 2.39 (s, 3H).

Compound 7

Yield 80%, bright yellow crystal, m.p. 124–126 ˚C. FT-IR (KBr): 3075, 3020, 2922, 1671, 1616, 1596, 1576, 1500, 1454, 1250, 1195, 908, 800 and 730 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.87 (d, *J* = 7.6 Hz, 2H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.51–7.41 (m, 4H), 7.35 (t, *J* = 7.6 Hz, 2H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.4 Hz, 2H) and 2.18 (s, 3H).

ACKNOWLEDGEMENTS

We are grateful to Wazed Miah Science Research Centre (WMSRC), Jahangirnagar University,

Bangladesh for ^{1}H-NMR data. We also express heartiest gratitude to the department of Biotechnology and Genetic Engineering, MBSTU for antibacterial property study.

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