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

M. Idrish Ali¹*, Sonia Akter Nupur¹, Md. Ashrafuzzaman¹, Md. Mahbubul Hoque²
1. Department of Chemistry, Mawlana Bhashani Science and Technology University, Tangail-1902, Bangladesh
2. Department of Environmental Science and Resource Management, Mawlana Bhashani Science and Technology University, Tangail-1902, Bangladesh

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 ¹H-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

*Corresponding Author Email: idrish@mbstu.ac.bd
Received 14 November 2017, Accepted 16 December 2017
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 mg mL$^{-1}$) of the test chemical was prepared in DMF solvent. The stock solution was further diluted with sterilized distilled water to different dilutions in µg mL$^{-1}$. 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.

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 µg/mL\(^{-1}\))**

| 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) \(\delta\) 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 (CDCl₃, 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 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 (CDCl₃, 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 (CDCl₃, 400 MHz) δ 8.44 (s, 1H, –CH=N–), 7.80 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.4 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 (CDCl₃, 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 (CDCl₃, 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 (CDCl₃, 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.

REFERENCES

1. Tovrog BS, Kitko DJ, Drago RS. Nature of the bound oxygen in a series of cobalt dioxygen adducts. J Am Chem Soc 1976; 98: 5144-53.

2. Djebbar-Sid S, Benali-Baitich O, Deloume JP. Synthesis, characterization and electrochemical behavior of some copper(II) complexes with linear and tripodal tetradentate ligand derived from Schiff bases. Polyhedron 1997; 16: 2175-82.

3. Bhattacharyya P, Parr J, Ross AT, Slawin AMZ. First synthesis of a unique dilead Schiff base complex. J Chem Soc Dalton Trans 1998; 0; 3149-50.

4. He L, Gou S, Shi Q, Qian M. The formation of a Schiff base intermediate: a nickel(II) complex of an asymmetric tripodal ligand. J Chem Crystallogr 1999; 29: 207-10.

5. Shirodkar SG, Mane PS, Chondhekar TK. Synthesis and fungitoxic studies of Mn(II), Co(II), Ni(II) and Cu(II) with some heterocyclic Schiff base ligands. Indian J Chem 2001, 40A, 1114-7.

6. Henri LKW, Tagenine J, Minu B. Synthetic and antibacterial studies of Schiff base complexes derived from 2,3-diaminopyridine and o-vanillin. Indian J Chem 2001; 40: 999-1003.

7. Soliman AA, Mohammed GG. Study of the ternary complexes of copper with salicylidene-2-aminothiophenol and some amino acids in the solid state. Thermochim Acta 2004; 421: 151-9.

8. Choi YK, Chjo KH, Park SM, Doddapaneni N. Oxygen reduction at Co(II)$_2$-disalophen modified carbon electrodes. J Electrochem Soc 1995; 142(12): 4107-12.

9. Bernardo K, Leppard S, Robert A, Commenges G, Dahan F, Meunier B. Synthesis and Characterization of new chiral Schiff base complexes with diiminobinaphthyl or diiminocyclohexyl moieties as potential enantioselective epoxidation catalysts. Inorg Chem 1996; 35(2): 387-96.

10. Pandey VK, Yadav S, Chandra K, Joshi MN. Antiviral activity of 7-arylamido/imido-alkyl-2,3-dihydro-2,3-diphenyl-1,3-benzoazaine-4-ones. Indian Drugs 1999; 36(8): 532-4.

11. Vazzanaa I, Terranovaa E, Mattiolib F, Sparatorea F. Synthesis and antimicrobial activity of 2-phenyl-3-{1-cyclopropyl-6-fluoro-7-[4-methylpiperazin-1-yl]-4-quinolone}-carboxamido-3-thiazolidin-4-ones. ARKIVOC 2004; 5: 364-74.
12. Nair VR, Soni M, Baluja S. Synthesis, structural determination and antibacterial activity of compounds derived from vanillin and 4-aminoantipyrine. J Serb Chem Soc 2004; 69: 991-998.

13. Garg HG, Kaur N. Synthesis of N-substituted arylsulfonylpyrazoles, their anthelmintic activity, and the cytotoxicity of some hydrazides. J Med Chem 1972; 15(5): 554-5.

14. Ambroziak K, Rozwadowski Z, Dziembowska T, Bieg B. Synthesis and spectroscopic study of Schiff bases derived from trans-1,2-diaminocyclohexane. Deuterium isotope effect on $^{13}$C chemical shift. J Mol Struct 2002; 615: 109-20.

15. Desai SB, Desai PB, Desai KR. Synthesis of some Schiff bases, thiazolidones, and azetidinones derived from 2,6-diaminobenzol[1,2-d:4,5-d] bithiazole and their anticancer activities. Heterocycl Commun 2001; 7(1): 83-90.

16. Sadana AK, Mirza Y, Aneja KR, Prakash O. Hypervalent iodine mediated synthesis of 1-aryl/hetryl-1,2,4-triazolo[4,3-a] pyridines and 1-aryl/hetryl 5-methyl-1,2,4-triazolo[4,3-a] quinolines as antibacterial agents. Eur J Med Chem 2003; 38: 533-6.