Synthesis, Analytical and Antibacterial Studies of *N*-[4-(phenyliminomethyl)phenyl]acetamide 0.67-hydrate and its Complexes with Manganese (II), Cobalt (II) and Nickel (II)

[1]TARIQ MAHMUD*, [1]RABIA REHMAN, [2]AADIL ABBAS AND [1]JAMIL ANWAR
[1]*Institute of Chemistry, University of the Punjab, Lahore, Pakistan.*
[2]*Department of Chemistry, University of the Gujrat, Gujrat, Pakistan.*
tariqm06@yahoo.co.uk*

(Received on 7th December 2010, accepted in revised form 29th June 2011)

Summary: The Schiff base (*N*-[4-(Phenyliminomethyl)phenyl]acetamide 0.67-hydrate) was prepared from 4-acetoamino benzaldehyde and aniline by refluxing the two in ethanolic solution. The metal complexes of Mn (II), Co (II) and Ni (II), were prepared by mixing and refluxing methanolic solutions of $MnCl_2$, $CoCl_2$ and $NiCl_2$ with *N*-[4-(Phenyliminomethyl)phenyl]acetamide 0.67-hydrate. Metal Schiff base complexes were prepared and characterized by using different techniques, such as; infrared and atomic absorption spectroscopy. Octahedral geometry was proposed for synthesized metal complexes by comparing theoretical and estimated metal ligand ratio. All the synthesized compounds were tested for their antibacterial activity against S*taphylococcus epidermidis*, *Escherichia coli* and *Staphylococcus aureus* bacteria. Schiff base itself was inactive against these bacteria whereas its complexes with Mn (II), Co (II) and Ni (II) have remarkable action against these bacteria, indicating that they can be used as bactericidal agents.

Key Words: Schiff base, Azomethine group, Metal Schiff base complexes.

Introduction

There has been a significant exploitation in recent years towards the formulation of new materials containing polyfunctional units (ligands) able to coordinate with metallic ions. Schiff base macroligands are synthesized from the reaction of aldehydes and amino compounds. In recent years, the chemistry of transition metal complexes, mainly of those derived from N-donor ligands, remained focalized by several researchers, due to their significant applications in organic synthesis, new materials, catalysis and medicinal science (e.g. antitumor drugs). The synthesis of metal complexes of these ligands also gaining importance in growing area of research of applied inorganic chemistry [1-5]. Metal complexes of Schiff bases are extensively studied due to synthetic flexibility, selectivity and sensitivity towards a variety of metal atoms. They are found useful in catalysis, in medicine as antibiotics, anti-inflammatory agents and in the industry as anti-corrosion.

Schiff bases are the compounds containing azomethine group (-HC=N-). Schiff base ligands are able to coordinate metals through imine's nitrogen and another group, usually linked to the aldehyde. Formation of Schiff base generally takes place under acid or base catalysis or with heat. The common Schiff bases are crystalline, slightly basic but at least some form insoluble salts with strong acids. Schiff bases also act as a ligand. These ligands have significant importance in chemistry; especially in the development of Schiff base metal complexes, because these ligands are potentially capable of forming stable complexes with metal ions [3, 4]. Schiff bases are able to stabilize many different metals in various oxidation states, controlling the performance of metals in a large variety of useful catalytic transformations. The mechanism of Schiff base metal complex formation is important in bio-chemical reaction. In addition, a number of Schiff bases have attracted considerable attention, mainly in connection with investigation of the chelating abilities and analytical applications.

Many Schiff base complexes show excellent catalytic activity in various reactions at high temperature (>100 °C) and in the presence of moisture. Over past few years, there have been many reports on their applications in homogeneous and heterogeneous catalysis [6, 7]. In aprotic solvents, at atmospheric pressure and room temperature, cobalt chelated with Schiff bases, catalyzes the oxygenation of indols, phenols, flavones, nitroalkanes, hydrazones, olefins, etc [8]. Polydentate Schiff bases, assisted by metal ions, provide highly organized supramolecular metal complexes. Such complexes possess binding sites and cavities for various cations, anions and organic molecules [9].

Schiff base macrocycles have been of remarkable versatility in macrocyclic and supramolecular chemistry and therefore they have played an important role in the development of

*To whom all correspondence should be addressed.

coordination chemistry as they readily form stable complexes with most of the transition metals [10, 11]. The research field dealing with transition metal complexes with macrocyclic Schiff bases has been expanded enormously and diversified subjects comprising vast areas of organometallic compounds [12]. In the area of bioinorganic chemistry, the interest in the Schiff base complexes lies in that, they provide synthetic models for the metal-containing sites in metalloproteins / enzymes and also contribute enormously to the development of medicinal chemistry, radio immunotherapy, cancer diagnosis and treatment of tumor [13, 14]. In addition, some of the complexes containing N and O as donor atoms are effective as stereospecific catalysts for oxidation reduction, hydrolysis, biocidal activity and other transformations of organic and inorganic chemistry [15-18].

Schiff bases have appeared to be an important intermediate in a number of enzymatic reactions involving interaction of enzyme with amino or carbonyl groups of the substrate. In the lysine class, represented by fructose diphosphate aldolase, an intermediate Schiff base is formed between amino group of lysine, constituent of enzyme and a carbonyl group of the substrate [19]. Another important role of Schiff base structure is a transamination. Transaminases are found in mitochondria and cytosole of eukaryotic cells [20]. All the transaminases appear to have the same prosthetic group. New Schiff base ligands have been synthesized to study their selectivity towards complexation of different metallic ions. These newly synthesized compounds are also used as precursors for the formation of other acyclic and cyclic ligands.

In the present study, *N*-[4-(Phenylimino-methyl)phenyl]acetamide 0.67-hydrate, Schiff base was prepared by refluxing the ethanolic solutions of 4-acetoaminobenzaldehyde and aniline [21]. Then metal -Schiff base complexes were prepared by using $MnCl_2$, $CoCl_2$ and $NiCl_2$. These were prepared by refluxing methanolic solutions of the Schiff base and that of the respective metal chlorides.

Results and Discussion

The Schiff base (*N*-[4-(Phenylimino-methyl)phenyl]acetamide) 0.67-hydrate, was prepared and characterized in our previous research work [21]. In the following study, its metal complexes were synthesized and analyzed. Fig. 1 is showing the proposed scheme of the chemical reaction involving in synthesis of Schiff base (*N*-[4-(Phenyliminomethyl)phenyl]acetamide).

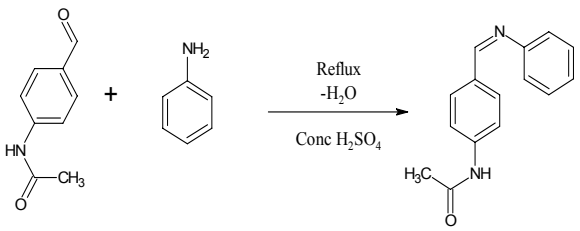

Fig. 1: Synthesis of Schiff base (*N*-[4-(Phenylimi-nomethyl)phenyl]acetamide) 0.67 Hydrate.

The color, melting point and yield of the Schiff base and its metal complexes were determined. They are presented in Table-1. The solubility of Schiff base and its metal complexes in different solvents were shown in Table-2. The complexes were not completely soluble in organic solvents but soluble in DMSO. Infrared spectroscopic technique was used to confirm the presence of –HC=N- which is the characteristic group of Schiff base. Their results were depicted in Table-3. In FTIR spectrum of Schiff base, a very strong peak at 1670 cm^{-1} confirmed the presence of –C=N- group which is the characteristic of Schiff base. The bands at 903(w), 830(s) cm^{-1} are due to the aromaticity of the compound. The band at 1310(s) cm^{-1} corresponds to C–N stretching (aromatic amines). The band in the range of 2900-2950 confirmed the presence of N-H stretching vibrations. The band in the range of 3415-3380 confirmed the presence of N-H stretching vibrations which is characteristic of aromatic amines. These peaks were shifted to lower wave numbers in case of almost all the synthesized metal complexes. This confirms the formation of metal complexes.

Table-1: Physical properties and yield of the Schiff base and its metal complexes.

Sr. No	Compound	Colour	Melting Point	Yield
1	*N*-[4-(Phenyliminomethyl)phe-nyl]acetamide (Schiff base)	Light brown	Decomposed above 125 ºC	22%
2	Schiff base complex with Mn (II)	Dark Brown	Decomposed above 198 ºC	13%
3	Schiff base complex with Co (II)	Chocolate Brown	Decomposed above 220 ºC	20%
4	Schiff base complex with Ni (II)	Green	Decomposed above 180 ºC	15%

M-L ratio was calculated after finding the concentration of respective metal ion in the synthesized metal complexes by atomic absorption spectrophotometer. By comparing these experimental M-L ratio values with theoretical values of different geometries of these metal complexes like square planar and octahedral, appropriate geometries was proposed. The experimental ligand to Mn (II) ratio matches with theoretical ratio corresponding to 2:1. Similarly, the experimental ligand to metal ratio matches with theoretical ratio corresponding to 2:1 in case of Co (II) and Ni (II) [22]. The synthesized complexes were proposed to exhibit octahedral

geometry as shown in Fig.2. The two vacant sites around metal ion may be occupied by the chloro groups.

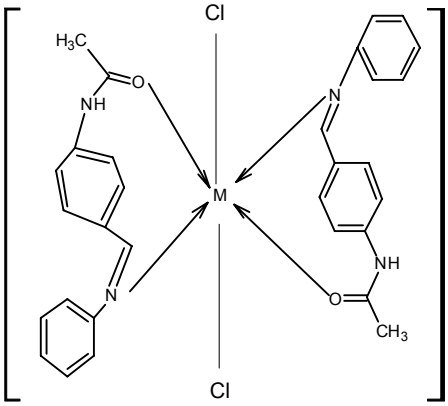

Fig. 2: Proposed octahedral geometry of the complexes of M with Schiff base (*N*-[4-(Phenyliminomethyl)phenyl]acetamide). Where M= Co (II), Mn (II) and Ni (II).

Antibacterial Studies

The antibacterial activities of the synthesized Schiff base and its metal complexes were determined against three strains of bacteria i.e. *Staphylococcus aureus, Escherichia coli* and *Staphylococcus epidermidis,* using Disc-diffusion method [23]. The Schiff base itself was found to be inactive against all these different strains of bacteria. All of the metal complexes were found to be active against these three bacterial strains. In general, Mn (II) and Ni (II) complexes with Schiff base were found to have highest activity against the *Staphylococcus epidermidis* and *Staphylococcus aureus* bacteria studied under the test conditions, showing that it has a good activity against these bacteria. The Co (II) complexes with Schiff base showed a little activity against *Staphylococcus* a*ureus* and *Escherichia coli.* This is shown in Table-4.

Experimental

Reagents Required

4-acetoaminebenzaldehyde, aniline, ethanol, methanol, acetonitrile, nickel(II) chloride, potassium hydroxide, manganese(II) chloride, cobalt(II) chloride, were of reagent grade (Sigma-Aldrich) and were used without any further purification.

Materials and Methods

Gallen-Kamp melting point apparatus was used for the determination of melting points. FTIR spectra of Schiff base and its metal complexes were recorded on FTIR spectrophotometer (Model Perkin-Elmer spectrum-RX-I) using Nujol mull with a full scan wavelength range of 4000-500 cm^{-1}. The amounts of metal ions in the complexes were estimated by atomic absorption spectrophotometery (Perkin Elmer AAnalyst 100) using air-acetylene flame.

Synthesis of Schiff Base

4-acetoaminebenzaldehyde (0.0163 g = 1.02 mmol) and aniline (0.0911 ml = 1.0 mmol) were dissolved in 10 ml 95% ethanol separately. Both solutions were mixed in 100 ml round bottom flask. It was refluxed for three hours with continuous stirring. Resultant precipitates were of light brown colour which were then filtered off and dried at 105°C in an oven. They were then recrystallized by using a mixture of acetonitrile, methanol and water in the ratio 1: 3: 4 respectively [10, 21].

Synthesis of Metal Complexes

Complex with Manganese (II) Chloride

1.0 mmol solution of $MnCl_2.4H_2O$ and 2.0 mmol solution of Schiff base (*N*-[4-(Phenylimino-methyl)phenyl]acetamide) were prepared by dissolving their 0.0198 g and 0.0474 g in 10 ml methanol separately. Both solutions were mixed in the presence of 2-3 ml 1% KOH. The mixture was refluxed at 70 ^{o}C and stirred for 2-3 hours on a hot plate with magnetic stirrer. Dark brown precipitates of complex were formed. They were filtered off and dried in an oven at 105°C. These were then recrystallized by using a mixture of acetonitrile, methanol and water in the ratio 1: 3: 4 respectively.

Table-2: Solubility of Schiff base and its metal complexes.

Solvent	Compound			
	N-[4-(Phenyliminomethyl) phenyl]acetamide (Schiff base)	Schiff base complex with Mn (ll)	Schiff base complex with Co (ll)	Schiff base complex with Ni (ll)
Chloroform	Soluble	Insoluble	Insoluble	Sparingly Soluble
n-Hexane	Insoluble	Insoluble	Insoluble	Insoluble
Diethyl ether	Sparingly Soluble	Sparingly Soluble	Sparingly Soluble	Insoluble
Carbon tetra chloride	Sparingly Soluble	Insoluble	Sparingly Soluble	Sparingly Soluble
DMSO	Soluble	Soluble	Soluble	Soluble

Table-3: Characteristic IR band absorption frequencies of Ligand and their metal complexes.

Sr. No.	Compound	Main IR frequencies (cm^{-1})
1	*N*-[4-(Phenyliminomethyl)-phenyl]acetamide (Schiff base)	1670(s),1463(s) , 1362(m), 1310(s), 903(w), 830 (s)
2	Schiff base complex with Mn (II)	1650 (w), 2926 (s) 3410 (s), 1532(w), 1463 (s), 978 (w)
3	Schiff base complex with Co (II)	1611 (w), 2920 (s) 2556 (s) 1462(s),1376(s), 842(s)
4	Schiff base complex with Cr (III)	1630(s), 2917(s) 3403(w), 1463(s) ,1376(s), 920(w)

* 's' = strong, 'm' = medium and 'w' = weak signal in IR spectrum.

Table-4: Antibacterial activity of Schiff base and its metal complexes.

Sr. No.	Compound	Bacterial Species		
		Staphylococcus aureus	*Escherichia coli*	*Staphylococcus epidermidis*
1.	*N*-[4-(Phenyliminomethyl)-phenyl]acetamide (Schiff base)	-	-	-
2.	Schiff base complex with Mn (II)	++	-	++
3.	Schiff base complex with Co (II)	+	+	-
4.	Schiff base complex with Ni (II)	++	+	+

* + Active, ++ Very active, - Inactive.

Complex with Cobalt (II) Chloride

1.0 mmol methanolic solution of $CoCl_2.6H_2O$ and 2.0 mmol metahnolic solution of Schiff base (*N*-[4-(Phenyliminomethyl)phenyl]acetamide) were prepared separately. These two solutions were mixed in the presence of 2-3 ml 1% KOH. The mixture was refluxed at 70 ^oC and stirred for 2-3 hours on a hot plate with magnetic stirrer. Chocolate brown precipitates of complex were formed. They were filtered off and dried in an oven at 105^oC. These were then recrystallized by using a mixture of acetonitrile, methanol and water in the ratio 1: 3: 4 respectively.

Complex with Nickel(II) Chloride

1.0 mmol methanolic solution of $NiCl_2.6H_2O$ (0.0237 g) and 2.0 mmol methanolic solution of Schiff base (*N*-[4-(Phenyliminomethyl)phenyl]acetamide) were prepared separately. These two solutions were mixed in the presence of 2-3 ml 1% KOH. The mixture was refluxed at 70 ^oC and stirred for 2-3 hours on a hot plate with magnetic stirrer. Dark green precipitates of complex were formed. They were filtered off and dried in an oven at 105^oC. These were then recrystallized by using a mixture of acetonitrile, methanol and water in the ratio 1: 3: 4 respectively.

Antibacterial Studies

The Schiff base and its metal complexes were evaluated for antibacterial activity against the following bacterial species, using Disc-diffusion method.

- *Escherichia coli*
- *Staphylococcus aureus*
- *Staphylococcus epidermidis*

The Discs were prepared by adopting the standard method [24, 25]. Every compound solution (prepared by dissolving 30 µg in DMF 0.01mL) was applied to a separate paper disc with the help of micropipette. The discs were placed in an incubator for 48 hours at 37 ^oC and then applied to the bacteria grown on agar plates. Inoculation was performed with the help of a platinum wire loop which was made red hot in flame, cooled and then used for the application of bacterial strains. Sterilized forceps were used for the application of the paper disc on the inoculated agar plates. When the discs were applied, they were incubated at 37 ^oC for 24 hours. The zone of inhibition (diameter in mm) was then measured around the disc to evaluate the antibacterial activity.

References

1. J. Iqbal, S. A. Tirmizi and T. M. Butt, *Journal of Pure and Applied Sciences*, **16**, 55 (1997).
2. T. Mahmud, M. H. R. Mahmood, A. Haq, A. Amin and H. M. Farooq, *Acta Scienticia*, **11**, 9 (2001).
3. P. Souza, J. A. Garcia-Vazquez and J. R. Masaguer, *Transition Metal Chemistry,* **10**, 410 (1985).
4. A. A. Osowole, *E-Journal of Chemistry,* **5**, 130 (2008).
5. T. Mahmud, J. Iqbal, M. Irshad, M. R. J. Elsegood and V. McKee, *Acta Crystallographica Section* ***E61***, 1789 (2005).
6. H. Naeimi, J. Safari and A. Heidarnezhad, *Dyes Pigments*, **73**, 251 (2007).
7. S. J. Lippard and J. M. Berg, *Principles of bioinorganic chemistry,* University Science Books, California, 411 (1994).
8. A. Pui, I. Berdan, I. Morgenstern-Badarau, A. Gref and M. Perree-Fauvet, *Inorganica Chimica Acta,* **320**, 167 (2001).
9. N. Dixit, L. Mishra, S. M. Mustafi, K. V. R. Chary and H. Houjou, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **73**, 29 (2009).
10. N. E. Borisova, M. D. Reshetova and Y. A. Ustynyuk, *Chemical Reviews,* **107**, 46 **(**2007).
11. W.R. Paryzek, V. Patroniak and J. Lisowski, *Coordination Chemistry Reviews,* **249**, 2156 (2005).

12. S.A.S. Sunaga, T. Taniguchi, H. Miyazaki and T. Nabeshima, *Inorganic Chemistry,* **46**, 2959 (2007).
13. A. G. Quiroga and C. N. Ranninger, *Coordination Chemistry Reviews,* **248**, 119 (2004).
14. L. Yet, *Chemical Reviews,* **103**, 4283 (2003).
15. R.I. Kureshy, N.H. Khan, S.H.R. Abdi, S.T. Patel and P. Iyer, *Journal of Molecular Catalysis A: Chemical,* **150**, 175 (1999).
16. Y. Aoyama, J. T. Kujisawa, T. Walanawe, A. Toi and H. Ogashi, *Journal of the American Chemical Society,* **108**, 943 (1986).
17. R. S. Sdrawn, M. Zamakani and J.L. Coho, *Journal of the American Chemical Society,* **108**, 3510 (1986).
18. P. Sengupta, S. Ghosh and T.C.W. Mak, *Polyhedron*, **20**, 975 (2001).
19. A. L. Lehlinger, *Principles of biochemistry*, Worth, New York, p.84, 85, 220-224, 563-564 (1975).
20. C. Spınu, M**.** Pleniceanu**,** M**.** Isvoranu and L. Spınu, *Asian Journal of Chemistry*, **14**, 2122 **(**2005).
21. T. Mahmud, K. H. Thebo, R. Rehman, M. A. Malik and M. Helliwell, *Acta Crystallographica, Section **E*66**, 2781 (2010).
22. T. Mahmud, R. Rehman, A. Gulzar, A. Khalid, J. Anwar, U. Shafique, W-u. Zaman, M. Salman, *Arabian Journal of Chemistry*, **3**, 219 (2010).
23. P. Mishra, H. Rajak and A. Mehta, *Journal of General and Applied Microbiology*, **51**, 133 (2005).
24. R. J. Singh, *Journal of the Chemical Society of Pakistan*, **33**, 485 (2011).
25. A. Sharif, E. Ahmed, M. A. Munawar, S. Jabeen, M. U. K. Khan, R. Begum, A. Farrukh, M. Ashraf, S. Arshad and N. Afza, *Journal of the Chemical Society of Pakistan*, **33**, 578 (2011).