IJISET - International Journal of Innovative Science, Engineering & Technology, Vol. 3 Issue 6, June 2016
ISSN (Online) 2348 – 7968 | Impact Factor (2015) - 4.332
www.ijiset.com

Physico-Chemical Study Of Mixed Ligand Complexes Of Sulfamethoxazole And Imidazole

[2]Adewoyin, Samuel A., [1]Olanipekun, Oladapo T., [1]Odedokun, Omobola A. and [*1]Ishola, Kayode T.

[1]Federal College of Education (SPECIAL), Department of Chemistry, School of Science, P.M.B. 1089, Oyo, Oyo State, Nigeria.
[2]Ladoke Akintola University of Technology,Ogbomoso, Oyo State, Nigeria.

Abstract

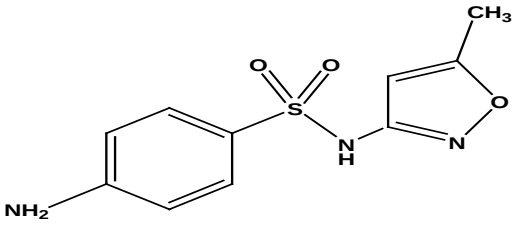
Mixed ligand metal (II) complexes of sulfamethoxazole and imidazole have been synthesized and physico-chemically characterized by solubility test, metal analysis, infrared and electronic spectra measurements. All the complexes were soluble in DMSO and THF and insoluble in H_2O, CH_2Cl_2 and $CHCl_3$. The expected and observed metal contents of metal complexes were in close agreement. From the infrared studies, sulfamethoxazole behaves as multidentate ligand coordinated to the metal ion via the aniline NH_2 group, sulphonyl group, and isoxazole nitrogen while imidazole acts as monodentate ligand coordinated through imine group.The electronic spectra revealed tentative octahedral geometry for all the complexes.

Keywords: Imidazole, Metal complexes, Mixed-ligand, Sulfamethoxazole

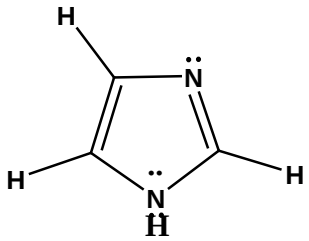
Introduction

The advances in inorganic chemistry provide better opportunities to use metal complexes as therapeutic agents. The mode of action of metal complexes on living organism is differing from non metals. These complexes show a great diversity in action[1]. Medicinal inorganic chemistry can exploit the unique properties of metal ions for the design of new drugs. Research has shown significant progress in utilization of transition metal complexes as drugs to treat several human diseases. The investigation of metal sulfonamide compounds has received much attention due to the fact that sulfonamides were the first effective chemotherapeutic agents to be employed for the prevention and cure of bacterial infections in humans[2]. The antibacterial activity of sulfonamides, on the one hand, and the antimicrobial activity of heavy metals, on the other, have

led to research on the combination of these chemical species. As a result, new metal complexes with higher antimicrobial activity than the free ligands or cationic metals were obtained[3,4]. Coordination compounds with sulfonamides and copper have also been used as reagents for the cleavage of nucleic acids[5-7]. Sulfamethoxazole, a well-known antibacterial sulfadrug, contains several groups with donor atoms that are able to interact with metal ions: Ar–NH2, NH sulfonamide, SO_2–R and N and O heterocyclic atoms. Sulfamethoxazole can act as a monodentate or a bidentate ligand. As part of a study dedicated to the investigation of the structural and physicochemical properties of metal complexes of chemoterapeutic agents, this paper reports interaction of sulfamethoxazole and imidazole with divalent metals in 1:1:1.



Sulfamethoxazole



Imidazole

Fig 1. Structures of the ligands

MATERIAL AND METHODS

The metals used are copper (II) acetate monohydrate, zinc(II) acetate dihydrate, cobalt(II) acetate tetrahydrate, manganese acetate tetrahydrate and zinc sulphate heptahydrate. All reagents and chemicals used are of analytical grade and used without further purification. The ligand (sulphametoxazole) was obtained from Drugfield Pharmaceutical Ltd, Sango ota, Ogun State, and used without further purification.

Solubility Test:

The solubility test of the complexes was determined in nine common organic solvents namely: methanol, ethanol, nitromethane, DMSO, THF, distilled water, dioxan, dichloromethane, chloroform.

Infrared Spectra:

The infrared spectra of the all complexes synthesized and those of ligands were recorded using Perkin Elmer FT−IR Spectrophotometer equipped with KBr disc. The infrared region is between 4000-400cm^{-1}.

Electronic spectra:

The electronic absorption spectra in the UV – Visible range was recorded on UVD- 2960 Double Beam PC Scanning spectrophotometer between 190- 400nm for the ligand and 400- 900nm for the complexes using DMSO and THF as the solvent.

Metal analysis:

Percentage copper composition in the complex was determined by complexometric titration using EDTA solution, murexide indicator and ammonia/ammonia chloride buffer.

Preparation of complexes

Preparation of CuSMXImi(OAc)$_2$

The complexes were prepared by the mixing of 1.226g (0.005mol) of sulfamethoxazole in 20 ml of hot ethanol, 0.999g (0.005mol) of copper acetate in 20ml of water and 0.340g (0.005mol) of imidazole in 10ml of water at ratio 1:1:1. A few drops of 0.002M NaOH was added to adjust the pH of the mixture to 5.5 and the reaction mixture was heated and continuously stirred for about 3-4 hours. The product was isolated after reduction of volume by evaporation. It was then filtered, washed with ethanol and dried in vacuum over silica gel.

The same procedure was used for the preparation of Mn(II), Zn(II) and Co(II) complexes.

$MOAc + SMX + Imi \rightarrow [MSMX\ Imi\ (OAc)_2]$ M= Cu(II), Mn(II), Zn(II), Co(II)

$ZnSO_4 + SMX + Imi \rightarrow [ZnSMX\ Imi\ (H_2O)_2]$

Table 1: Physical and analytical data for mixed ligand complexes of imidazole and Sulfamethoxazole.

Complexes	**Colour**	**Formular Weight (g)**	**Yield %**	**%M Observed**	**%M Expected**
$Cu(SMX)(Imi)(OAc)_2$	Light green	502.90	45.73	12.54	13.26
$Co(SMX)(Imi)(OAc)_2$	Pale pink	498.29	55.39	11.83	12.26
$Mn(SMX)(Imi))(OAc)_2$	White	412.27	47.43	13.32	13.58
$Zn(SMX)(Imi)(OAc)_2$	White	422.77	52.84	15.47	15.31
$Zn(SMX)(Imi)(SO_4)_2$	White	478.77	52.03	11.30	10.82

Table 2 Solubility data for mixed ligand complexes of imidazole and Sulfamethoxazole.

Compounds	**EtOH**	**MeOH**	**$CHCl_3$**	**CH_2Cl_2**	**DMSO**	**THF**	**H_2O**	**Dioxan**	**CH_3NO**
$Cu(SMX)(imidazole)(OAc)_2$	SH	S	I	I	S	S	I	S	SS
$Co(SMX)(imidazole)(OAc)_2$	SS	SH	I	I	S	S	I	SS	I
$Mn(SMX)(imidazole)(OAc)_2$	SS	SS	I	I	S	S	I	S	SS
$Zn(SMX)(imidazole)(OAc)_2$	S	SH	I	I	S	S	I	SS	S
$Zn(SMX)(imidazole)SO_4$	SH	S	I	I	S	S	I	SS	SH

Key: SH = Soluble when heated; SS = Slightly soluble; I = Insoluble; S = Soluble

Table 3: Infrared spectra for mixed ligand complexes of imidazole and Sulfamethoxazole.

Complexes/ Ligands	υNH_{2n}, asym, sym	$\upsilon C = N$	υSO_2 asym, sym	$\upsilon C{-}N$	$\upsilon S - N$	$\upsilon C{=}C$	$\upsilon N{-}H$	$\upsilon M{-}N$	$\upsilon M{-}O$
Sulpamethoxazole	3462_w 3383_w	1615_s	1370_m 1310_m	–	928_w	1475_m	3297_w	–	–
Imidazole	-	1646_m	-	1150_w	-	1535_w	3222_m	–	–
$Cu(SMX)(Imi)(OAc)_2$	3453_s 3365_s	1608_s	1406_s 1316_s	1152_s	942_m	1509_w	3251_w	686_m	567_m
$Co(SMX)(Imi)(OAc)_2$	– 3371m	1606s	1352s 1315s	1145s	939s	1461m	3240w	682w	560s
$Mn(SMX)(Imi)(OAc)_2$	3451_w 3360_w	1598_m	1395_w 1307_m	1145_w	931_w	–	3234	677_w	555_m
$Zn(SMX)(Imi)(OAc)_2$	3457w 3369m	1609s	1401w 1315s	1147s	934_m	1497w	3302w	685s	561s
$Zn(SMX)(Imi)SO_4$	3457_w 3369_m	1609_s	1401_w 1315_s	147_s	934_m	1497_w	3302_w	685_s	561_s

Table 4: Electronic spectra data for the mixed ligand complexes of imidazole and Sulfamethoxazole

.

Complex/ Ligand	**$\lambda(cm^{-1})$**	**Tentative Assignment**	**Probable Geometry**
Sulpamethoxazole	42194 32680	$\pi \longrightarrow \pi^*$ $n \longrightarrow \pi^*$	
Imidazole	32895	$n \longrightarrow \pi^*$	
$Cu(SMX)(Imi)(OAc)_2$	24752	CT $^2E_g \rightarrow {}^2T_{2g}$	Octahedral

	18050		
$Co(SMX)(Imi)(OAc)_2$	23923 18248 14471	$^4T_{1g} \rightarrow {}^4T_{1g}(P)$ $^4T_{1g} \rightarrow {}^4A_{2g}$ $^4T_{1g} \rightarrow {}^4T_{2g}$	Octahedral
$Mn(SMX)(Imi)(OAc)_2$	24449	$^6A_{1g} \rightarrow {}^4T_{2g}$	Octahedral
$Zn(SMX)(Imi)\ (OAc)_2$	24213	CT	Octahedral
$Zn(SMX)(Imi)SO_4$	23148	CT	Octahedral

Discussion:

All the prepared complexes were characterized on the basis of solubility test, metal content, infrared and electronic spectra.

From Table 2, the mixed-ligand complexes of imidazole and Sulfamethoxazole are all soluble in DMSO, THF and insoluble in H_2O, CH_2Cl_2,$CHCl_3$.

The relevant infrared spectra data in the mixed-ligand complexes are given in Table 3. In the infrared spectrum of free Sulfamethoxazole, the absorption bands at ($3462_{w,}$ 3383_w) and (1370_m,1310_m) are attributed to υNH_2 (asymmetric and symmetric) and υSO_2 (asymmetric and symmetric) vibrations respectively[8,9] . While bands at 1615_s, 928_w and 3297_w are assigned to $\upsilon C = N$, $\upsilon S - N$ and $\upsilon N{-}H$ stretching vibrations respectively. And in the free imidazole, bands at 1646_m, 1150_w and 3222_m are assigned to $\upsilon C = N$, $\upsilon C{-}N$ and $\upsilon N{-}H$ stretching vibrations respectively. All the bands experienced lower shifts in the spectra of the metal complexes suggesting coordination through the groups to the metal ions. The appearances of bands between 550-700 cm^{-1} which are attributed to $\upsilon M{-}N$ and $\upsilon M{-}O$ vibrations confirmed the coordination of the ligands to the metals[10].

The electronic spectra of the ligands and their complexes are shown in Table4. The electronic spectra of free Sulfamethoxazole showed bands at 32680cm^{-1} and 42194 cm^{-1} which are

assigned to n⟶π* and π⟶π* transitions, respectively. In the free imidazole ligand, the band which appeared at 32895cm^{-1}is assigned n⟶π*transition. In the spectrum of Cu(SMX)(Imi) $(OAc)_2$ complex, band at 24752cm^{-1} and 18050 cm^{-1} that observed at visible region are assigned to Charge transfer and $^2E_g \rightarrow {}^2T_{2g}$ transitions, respectively. In the Co(SMX)(Imi)$(OAc)_2$ complex, the bands which appeared at 23923cm^{-1} , 18248cm^{-1} and 14471cm^{-1} are attributed to $^4T_{1g} \rightarrow {}^4T_{1g}(P)$, $^4T_{1g} \rightarrow {}^4A_{2g}$ and $^4T_{1g} \rightarrow {}^4T_{2g}$ transitions, respectively[11]. The band that appeared at 24449cm^{-1} in the Mn(SMX)(Imi)$(OAc)_2$ complex is attributed to $^6A_{1g} \rightarrow {}^4T_{2g}$. The two bands which appeared at 24213cm^{-1} and 23148 cm^{-1} in the spectra of Zn(SMX)(Imi)$(OAc)_2$ and ZnSMX Imi $(H_2O)_2$ complexes respectively, are assigned to Charge transfer transitions.

Conclusion

A mixed ligand metal complexes of sulpamethoxazole and imidazole were synthesized and characterized using physico-chemical method. The complexes exhibited different degree of solubility in different solvents. Based on the data obtained from Infrared spectra of the ligands and the mixed-ligand complexes, Sulfamethoxazole acted as a tridentate ligand coordinating through the aniline N, sulponyl O, isoxazole N, and imidazole acted as a monodentate ligand coordinated via the imine N group. Electronic spectra showed a six coordinate octahedral geometry for all the complexes.

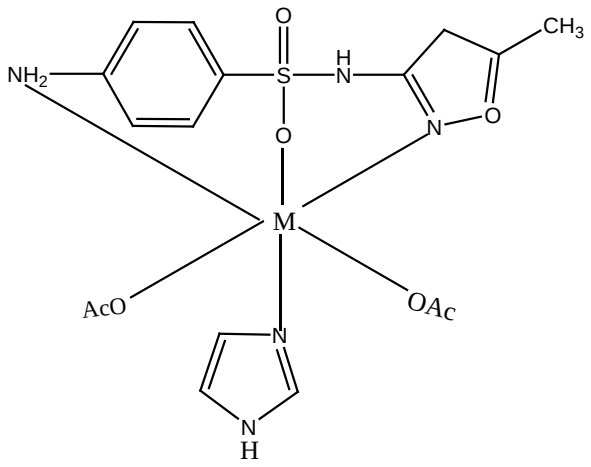


Fig2. Proposed structure for metal complexes of M(SMX)(Imi) $(OAc)_2$. M= Co(II), Cu(II) & Zn

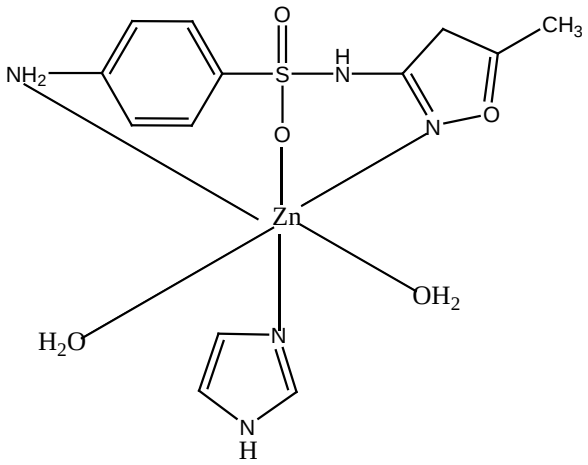


Fig3. Proposed structure of ZnSMX Imi $(H_2O)_2$

ACKNOWLEDGEMENT

The authors acknowledge Drugfield Pharmaceutical Ltd, Sango ota, Ogun State , Nigeria, for the supply of unprocessed sulfamethoxazole powder for this work.

References

1. Hariprasath K., Deepthi, B., Sudheer I.,Babu, P., Venkatesh, S. ,Sharfudeen, V. (2010). Metal Complexes in Drug Research. *J.chem Pharm. Res*, 2(4): 496-499

2. Bellú, S. Hure, E. Trapé E. and Rizzotto, M. (2003).'The interaction between mercury (II) and sulfathizole. *Quim. Nova*,26 (2):188-192,

3. Reynolds J.E.F. (Ed.) (1996). *Martindale, The Extra Pharmacopoeia*, Royal Pharmaceutical Society, London.

4. Blasco F., Perello L., Latorre J., Borra´ s J., and Garcia-Granda S. (1996). Nickel II and copper II complexes of sulfanilamide derivatives. *J. Inorg. Biochem*., 61, 143 .

5. Macı´as B., Garcı´a I., Villa M.V., Borra´ s J., Gonza´ lez-A´ lvarez M., Castin eiras A. (2003).Structural characterization and nuclease activity of mixed copper II complexes with sulfonamides and bipyridil *Inorg. Chim. Acta*, 353, 139

6. Gonza´ lez-A´ lvarez M., Alzuet G., Borra´ s J., Pitie´ v , Meunier. B. (2003). Selective DNA Strand Scission with Binuclear copper complexes. *J. Biol. Inorg. Chem*., 8, 644

7. Macı´as B., Villa M.V., E. Fiz E., Garcı´a I., Castineiras A., Gonza´ lez-A´ lvarez M., J. Borra´ s J. (2002).Synthesis,Structure and Physicochemical properties of Zinc and Copper complexes based on sulfonamides containing 8-Aminoquinoline ligands. *J. Inorg. Biochem*., 88, 101

8. Torre M. H., Calvo S., Pardo V. and Mombru A.W. (2005). Synthesis, Spectroscopic characterization and crystal structure of disulfamethoxazole diaquo Ni(II) monohydrate. *Journal of Coordination Chemistry*, 58:513–520

9.Kesimli B., and Topacli A. (2001) Infrared studies on Co and Cd complexes of Sulfamethoxazole. *Spectrochimica Acta Part A* 57:1031–1036

10. Adedibu C. Tella and Joshua A. Obaleye (2010), Metal complexes as antibacterial agents: Synthesis, characterization and antibacterial activity of some 3d metal complexes of sulphadimidine . *The electronic Journal of Chemistrty*, 2(1): 10-20

11. Catherine, E.H. and G.S. Alan, 2005. Inorganic Chemistry 3rd ed, Pearson NJ., pp: 620-650.