RJC

RASĀYAN *J. Chem.*
Vol. 6 | No.4 | 284 - 287 | October- December| 2013
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

SYNTHESIS OF AMINO ACID BASED SCHIFF BASE AND ITS COMPLEXES AS MICROBIAL GROWTH INHIBITORS

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ABSTRACT

The amino acid ligand [(1-(5-chloro-2-hydroxyphenyl)ethanone-(S)-alpha-amino-4-hydroxybenzenepropanoic acid] was prepared by the reaction of [(1-(5-chloro-2-hydroxyphenyl)ethanone] with (S)-alpha-amino-4-hydroxybenzenepropanoic acid under reflux in methanol. The complexes of this ligand have been prepared using metal acetates of Mn(II), Co(II), Ni(II), Cr(III), Cu(II), Zn(II) and Cd(II) under reflux in methanol. The products were found to be crystalline solid. The ligand is characterized by analytical, FT-IR, thermogravimetric analysis, proton NMR spectral data while complexes have been characterized by analytical, FT-IR, thermogravimetric analysis, diffused reflectance and magnetic susceptibility measurements. The compounds were screened for antibacterial activity against some clinically important bacteria, such as *E. coli, S. typhy, S. aureus, P. aeruginosa* and *K. pneumonie* by using nutrient agar medium and antifungal activity against *C. albicans* and *A. niger* species by using potato dextrose agar medium.

Keywords: Amino acid, CHPEAHP, antibacterial, antifungal.

INTRODUCTION

Complexes of transition metal ions with multidentate organic ligands have been the subject of intensive research because they not only have interesting spectral and magnetic properties, but they also possess a diverse spectrum of biological activities[1-3]. The unique ability of transition metal ions and their complexes to control the chemistry of environmental, industrial, and biological processes has increased the importance of clarifying their mechanistic behavior in simple and complex chemical processes[4-6]. Amino acids and their derivatives are extensively studied as typical N, O-donor ligands. The coordination compounds of amino acids also show good antimicrobial activities towards various micro organisms. N-protected amino acids are of special interest, in that they not only possess many potential donor sites but there is also possibility of keto-enol toutomerism which may lead to varied bonding and stereochemical behavior in the complexes in which they act as neutral or mononegative or even as dianionic ligands depending on the aroyl substituents and the reaction conditions[7,8].

EXPERIMENTAL

Manganese(II), cobalt(II), nickel(II), chromium(III), copper(II), zinc(II), and cadmium(II) acetate salts used were of Merck and BDH mark. Organic solvents such as absolute ethanol, methanol, petroleum ether, dimethylformamide (DMF) and dimethylsulfoxide (DMSO) were of AR grade. The antibacterial activities of the compounds were assessed by using nutrient agar medium and antifungal activity by using potato dextrose agar medium.

Preparation of Schiff base ligand [CHPEAHP]

The Schiff base was synthesized by adding a methanolic solution of 1-(5-chloro-2-hydroxyphenyl)ethanone (0.1mole) to a methanolic solution of (S)-Alpha-amino-4-hydroxybenzenepropanoic acid. The reaction mixture was then refluxed on a water bath for about 4 hours. The condensation product was filtered, washed thoroughly with ethanol and petroleum ether,

recrystallized and dried under vacuum. The purity of the synthesized compounds was monitored by TLC using silica gel (Yield = 79.5 %).

Preparation of metal complexes

All the complexes were synthesized by mixing a methanolic solution of $M(CH_3CO)_n$ nH_2O with the methanolic solution of Schiff base CHPEAHP in a 2:1 molar ratio. The resulting mixture was refluxed on a water bath for 5–9 hours. A colored product appeared on standing and cooling the solution. The complexes were filtered, washed with petroleum ether and dried under reduced pressure over anhydrous $CaCl_2$ in desiccators. They were further dried in an electric oven at 60–70 °C.

Table-1: Important IR spectral bands (cm^{-1}) of CHPEAHP and its metal complexes

S.N.	Compounds	*v*(O-H)	*v*(C-O)	*v*(C=N)	*v*(M-O)	*v*(M-N)	*v*(H_2O)
1.	CHPEAHP	3323	1210	1642	--	--	--
2.	Mn-CHPEAHP	--	1230	1610	583	422	3412,1581,822
3.	Co- CHPEAHP	--	1275	1612	669	470	3425
4.	Ni- CHPEAHP	--	1228	1616	667	418	3441,1560,813
5.	Cr- CHPEAHP	--	1219	1635	669	424	3402,1561,810
6.	Cu -CHPEAHP	--	1277	1612	615	421	--
7.	Zn -CHPEAHP	--	1265	1614	621	419	--
8.	Cd –CHPEAHP	--	1252	1633	617	418	--

Table-2: Antimicrobial activity ligand CHPEAHP and its complexes (diameter in mm)

Compound	Antibacterial					Antifungal	
	E. coli	*S. typhi*	*S. aureus*	*P. auruginosa*	*K. pneumonie*	*A. niger*	*C. albicans*
CHPEAHP	10	14	12	14	20	16	17
Mn-CHPEAHP	18	17	13	13	12	22	24
Co-CHPEAHP	-	12	14	15	20	16	17
Ni- CHPEAHP	-	-	-	08	12	20	19
Cr- CHPEAHP	18	10	-	20	18	19	22
Cu-CHPEAHP	15	12	10	12	08	22	20
Zn- CHPEAHP	-	17	17	08	20	16	22
Cd-CHPEAHP	-	20	18	22	18	18	23
Amikacin	28	28	23	25	22	--	--
Fluconazole	-	-	-	-	-	25	24

Including the well diameter of 6 mm. Zone of inhibition in mm (15 or less) resistant, (16-20 mm) moderate and (more than 20 mm) sensitive.

RESULTS AND DISCUSSION

Microanalysis

The obtained elemental analysis data were in a good a agreement with the calculated values and display the formation of 1:2 [M:L] ratio.

Spectral Study

^{1}H NMR (300MHz, $CDCl_3$, δ in ppm): 7.46-6.75 (7H, m, Ar-H), 2.1(3H, s, -CH_3), 2.68-2.54(2H, d, -CH_2), 3.76-3.65(1H, t, -CH), 5.2-6.4(1H, s, Ar–OH).

IR (KBr, cm^{-1})

In order to get bonding mode of ligand to metal in the complex, IR spectrum of the free ligand was compared with the spectra of metal complexes[9]. The structurally important vibration bands of the free

ligands and their metal complexes which are useful for determining the mode of coordination of the ligand are given in Table 1.

Antibacterial activity

To access the antibacterial activity of obtained compound Agar Well Diffusion method[10] was used. This activity was determined by using Mullar Hinton Agar[11]. A loop full culture of each test organism were inoculated in sterilized nutrient agar and incubated overnight to obtain the broth culture. All the culture were inoculated on Mullar Hinton Agar plate by using sterile cotton swab after swabbing well was punched on media and the different dilutions of the compounds were added in to the well with the help of dropper. After addition of sample the plate were incubated at 37^0C for 24 hours. After incubation period plates were examined and zone of inhibition were measured (Figure 1).

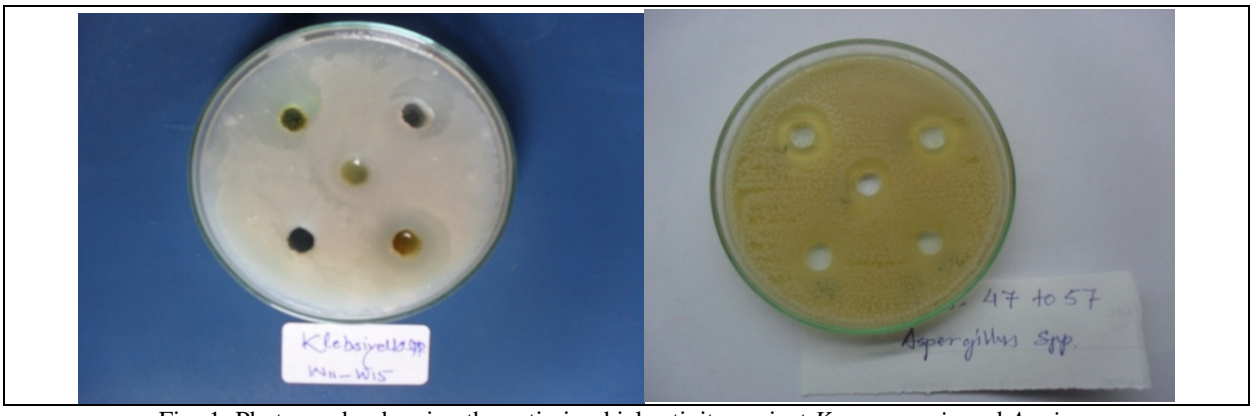

Fig.-1: Photographs showing the antimicrobial activity against *K. pneumonia* and *A. niger*

Antifungal activity

The *in vitro* antifungal assay was performed by the disc diffusion method[12-13]. The complexes and ligand were tested against the fungi *Aspergillus niger*, and *Candida albicans*, cultured on potato dextrose agar as the medium. In a typical procedure, a well was created on the agar medium and nystatin as the control was inoculated with the fungi. The well was filled with the test solution, which diffuses and the growth of the inoculated fungi is affected. The inhibition zone which developed on the plate was measured. The *MIC* values of the complexes were determined by the serial dilution technique and are shown in Table 2.

ACKNOWLEDGMENTS

The authors are greatly thankful to SAIF, CDRI Lucknow and SAIF Cochin (Kerala) for providing spectral data, Head, Department of Microbiology for microbial activity and the Principal, Shri Shivaji college of Arts, Commerce and Science, Akola for providing necessary facilities.

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[RJC-1082/2013]