Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(11):501-505

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Biological important Co(II) ternary complexes of 2-substituted benzazoles and amino acids

Chandni Jain, Meena Nagar and Gita Seth*

Department of Chemistry, University of Rajasthan, Jaipur, India

---

ABSTRACT

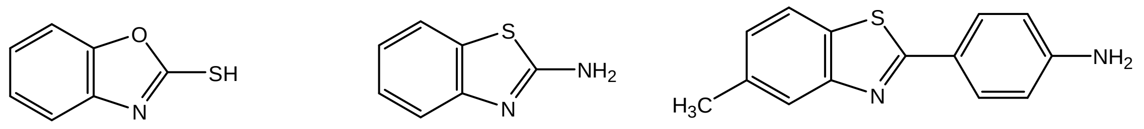
Some new ternary complexes of Co(II) with 2-mercapto benzoxazole, 2-amino benzothiazole and 2-(4´-aminophenyl)-6-methyl benzothiazole and with some amino acids (Leucine, Isoleucine) were synthesized and characterized by elemental analysis, IR, ^{1}H NMR spectral studies. The antibacterial activity of these metal complexes has been evaluated against pathogenic bacteria Staphylococcus aureus (+ve) and Escherichia coli (-ve). The antifungal activity of these metal complexes has been evaluated against pathogenic fungi Aspergillus niger and Fusariumoxy sporium. The results indicate that the metal complexes are found more active than the parent ligands.

Keywords: Benzoxazole, Benzothiazole, Amino acids, Antibacterial activity, Antifungal activity.

INTRODUCTION

It is well known that mixed ligand ternary complexes of some metal plays an important role in the activation of enzymes. [1] It is studied that mixed ligand complexes are biologically active against pathogenic microorganisms [2-3]. The studies transition metal complexes of benzoxazole and benzothiazole have gained importance because of their biological significance [4-10]. It was observed that biological activities of these ligand increased on complexation with metal ion [11-12]. The ligation behaviour of benzoxazole, benzimidazole and benzothiazole and their derivatives have been reported by Seth et al. [13-16].

We described here the synthesis, characterization and biological activity of Co(II) ternary complexes derived from 2-mercapto benzoxazole, 2-amino benzothiazole and 2-(4´-aminophenyl)-6-methyl benzothiazole and amino acids Leucine and isoleucine ligands. The resulting mixed ligand complexes may be of potential biological importance. The structure of ligands used to synthesize the metal complexes and chemical structure of Co(II) ternary complexes are shown in Fig. 1,2 and 3.



2-Mercapto Benzoxazole (MBO)
2-Aminobenzothiazole (ABT)
2-(4´-aminophenyl)-6-methyl benzothiazole (APMBT)

Fig.-1 : Structure of Ligands

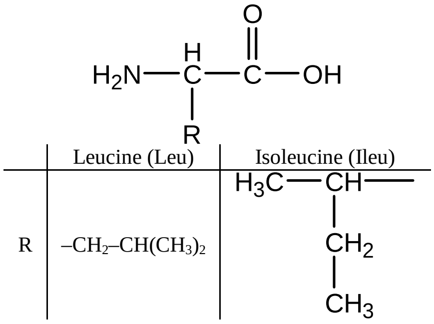


Fig. 2 Structure of amino acid

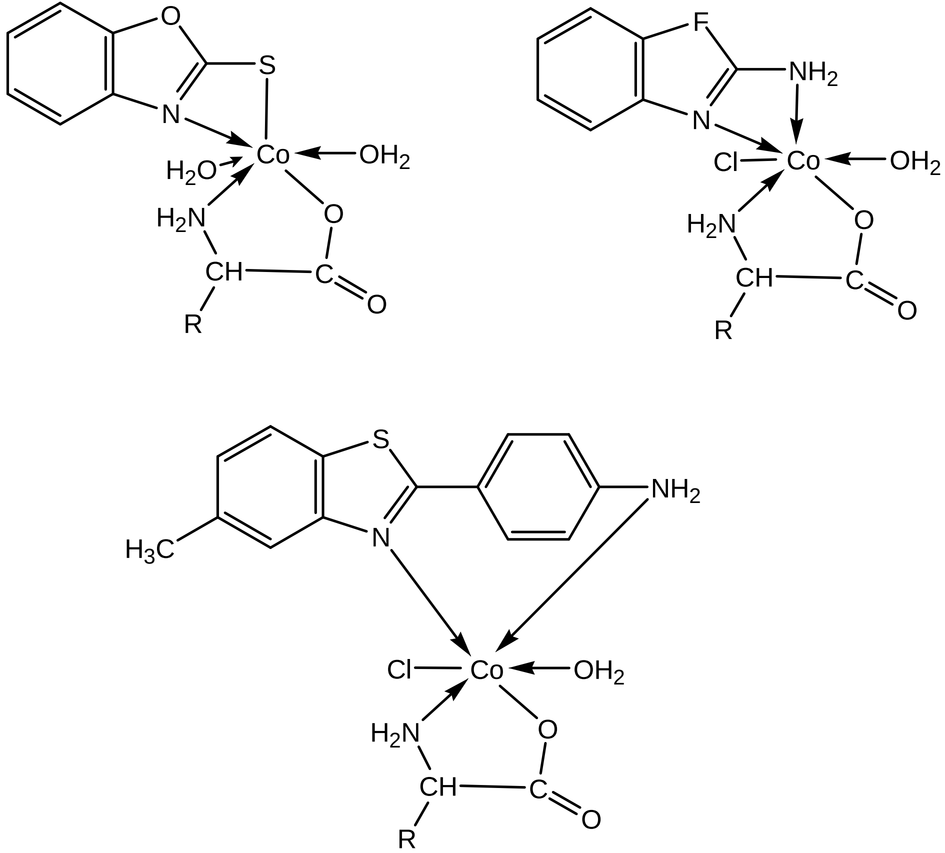


Fig.-3 The Suggested Chemical Structure of Co(II) Ternary Complexes

EXPERIMENTAL SECTION

All the chemicals used were of reagent grade. $CoCl_2.6H_2O$, MBO, ABT and APMBT were purchased from sigma-Aldrich. All the solvents were distilled before use. Infrared spectra was recorded (with KBr pellets) on SHIMADZU 8400 FT-IR spectrophotometer. ^1H NMR spectra were recorded on a JEOL AL 300 MHz FT-NMR spectrometer in $CDCl_3$ using TMS as an internal reference. Melting points were determined on a capillary melting point apparatus and are uncorrected. Molecular weight were determined by the Rast camphor method. Nitrogen was determined by the Kjeldahl's method and sulphur was estimated by messenger's method. Chlorine was estimated volumetrically by using volhard method. Cobalt was estimated by gravimetrically.

Preparation of Cobalt(II) ternary complexes

Solution of $CoCl_2.6H_2O$ (0.1 mol) in dry MeOH (10 ml) was added to MBO (0.1 mol)/ABT (0.1 mol)/APMBT (0.1 mol) and leucine (0.1mol)/Iso-leucine (0.1 mol) in dry methanol MeOH (10 ml). Then the reaction mixture was refluxed with continuous stirring for 4 hours and allowed to stand at room temperature overnight. These were filtered, recrystallized from EtOH and dried in vaco.

RESULTS AND DISCUSSION

The Co(II) ternary complexes were synthesized by $CoCl_2.6H_2O$ with 2-substituted benzazoles (MBO, ABT, APMBT) or amino acids (Leu, Ileu) in 1:1:1 molar ratio according to the following equation.

$$CoCl_2.6H_2O + (L\text{-}L) + (A\text{-}A) \xrightarrow[\text{Reflux}]{\text{Methanol}} [Co(L\text{-}L)(A\text{-}A)(H_2O)_2]$$

$$CoCl_2.6H_2O + (L\text{-}L') + (A\text{-}A) \xrightarrow[\text{Reflux}]{\text{Methanol}} [CoCl(L\text{-}L')(A\text{-}A)(H_2O)]$$

L-L = MBO

L-L´ = ABT, APMBT

A–A = Leu, Ileu

These reactions processed easily and lead to the formation of coloured solid which are stable to air and moisture. The resulting Co(II) ternary complexes are soluble in methanol, ethanol, DMSO and DMF.

The analytical data and physical properties of Co(II) ternary complexes of 2-substituted benzazoles are given in Table-1.

Table-1 Analytical data and physical properties of Co(II) ternary complexes of 2-substituted benzazoles with leucine & isoleucine

	Compound	Colour	Yield (%)	M.P. (°C)	Elemental analysis (%) Found (Calcd.)						Mol. Wt. Found (Calcd)
					C	H	N	S	Cl	Co	
1.	$Co(MBO)(leu)(H_2O)_2$ $CoC_{13}H_{20}N_2O_5S$	Purple blue	56	195	41.37 (41.60)	5.24 (5.37)	7.22 (7.46)	8.21 (8.54)	-	15.50 (15.70)	374.00 (375.31)
2.	$Co(MBO)(Ileu)(H_2O)_2$ $CoC_{13}H_{20}N_2O_5S$	Purple blue	59	197	41.47 (41.60)	5.25 (5.37)	7.34 (7.46)	8.25 (8.54)	-	15.55 (15.70)	374.00 (375.31)
3.	$CoCl(ABT)(leu)(H_2O)$ $CoClC_{13}H_{20}N_3O_3S$	Pinkish blue	54	132	39.61 (39.75)	5.00 (5.13)	10.59 (10.70)	8.02 (8.16)	9.00 (9.02)	14.81 (15.00)	391.50 (392.77)
4.	$CoCl(ABT)(Ileu)(H_2O)$ $CoClC_{13}H_{20}N_3O_3S$	Pinkish blue	65	130	39.64 (39.75)	5.03 (5.13)	10.55 (10.70)	8.05 (8.16)	9.00 (9.02)	14.90 (15.00)	391.50 (392.77)
5.	$CoCl(APMBT)(leu)(H_2O)$ $CoClC_{20}H_{26}N_3O_3S$	Pale violet	51	190	49.44 (49.75)	5.19 (5.43)	8.49 (8.70)	6.31 (6.64)	7.12 (7.34)	12.00 (12.20)	481.50 (482.90)
6.	$CoCl(APMBT)(Ileu)(H_2O)$ $CoClC_{20}H_{26}N_3O_3S$	Blue	60	193	49.57 (49.75)	5.30 (5.43)	8.49 (8.70)	6.33 (6.64)	7.13 (7.34)	12.10 (12.20)	481.50 (482.90)

IR SPECTRA

The important IR spectral bands and their tentative assignments are summarized in Table 2. The ligand MBO, ABT and APMBT, Leu and Ileu act as bidentate ligands in their Co(II) ternary complexes. The absorption band at ~ 3350 and ~ 3250 cm^{-1} are assigned to ν_{as} (N–H) and ν_s (N-H) vibrations of $-NH_2$ group of amino acid & ABT & APMBT, indicating the coordination of nitrogen atom to the metal atom without any deprotonation. This gets further supported by the appearance of non ligand bands of medium intensity in the region ~ 450-430 cm^{-1} due to ν(Co←N) vibration. This is further supported by the presence of non ligand band in the region ~ 320-300 cm^{-1} due to ν(S–H) vibration of the free ligand MBO, disappears in the spectra of respective ternary metal complexes indicating the deprotonation of the –SH group and simultaneous formation of Co-S band. This is further supported by the appearance of new band of medium intensity in the region ~ 385-330 cm^{-1} due to ν(Co-S) vibration. In the IR spectra of metal complexes the absorption bands observed in the region ~ 1615-1600 cm^{-1} are assigned to ν(C=N) vibration.

Table-2 IR Spectral data (cm^{-1}) of ternary complexes of Co(II)

Compound	$\nu(NH_2)$		ν(C=N)	ν(C=O)	ν(C=C)	Co-N	Co-O	Co-S	Co-Cl
	Asy.	Symm.							
1. $Co(MBO)(Leu)(H_2O)_2$	-	-	1600	1620	1577	425	435	325	-
2. $Co(MBO)(ILeu)(H_2O)_2$	-	-	1605	1640	1565	430	432	330	-
3. $CoCl(ABT)(Leu)(H_2O)$	3320	3210	1600	1620	1575	428	440	-	300
4. $CoCl(ABT)(ILeu)(H_2O)$	3340	3200	1608	1670	1570	440	438	-	290
5. $CoCl(APMBT)(Leu)(H_2O)$	3325	3180	1612	1630	1572	435	445	-	308
6. $CoCl(APMBT)(ILeu)(H_2O)$	3335	3185	1615	1625	1580	430	430	-	320

^{1}H NMR SPECTRA

The ^{1}H NMR spectra of the ligands (MBO, ABT, APMBT) and their Co(II) ternary complexes were recorded in $CDCl_3$. (Table-3). The ^{1}H NMR spectrum of ligand MBO exhibit broad singlet at δ 3.80 ppm due to -SH proton but it disappears in the spectra of metal complexes, thereby suggesting the deprotonation of the -SH group on complexation with the metal ion.

The ligand ABT and APMBT exhibit singlet at δ 3.68 ppm and δ3.80 ppm due to $–NH_2$ proton respectively but it shifted slightly downfield in the metal complexes, suggesting the coordination of nitrogen of the $-NH_2$ group with the metal. The aromatic protons of the ligand (MBO, ABT and APMBT) were observed as multiplets atδ 7.02-8.45 ppm shifted downfield in their respective Co(II) ternary complexes which may be possible due to deshielding on coordination of ligands with metal.

Table-3 ^{1}H NMR spectral data (ppm) of the ligands (MBO, ABT, APMBT) and their Co(II) complexes

Compound	-SH	$-NH_2$	$-CH_3$	$-CH_2$	-CH	Aromatic proton
1. MBO	3.80 (bs)	-	-	-	-	7.25-8.20
2. ABT	-	3.68	-	-	-	7.35-8.25
3. APMBT	-	3.80	-	-	-	7.10-8.28
4. $Co(MBO)(Leu)(H_2O)_2$	-	2.14	1.31	3.63	3.62	7.04-8.20
5. $Co(MBO)(ILeu)(H_2O)_2$		2.18	1.30	3.60	3.62	7.02-8.01
6. $CoCl(ABT)(Leu)(H_2O)$	-	3.60	1.28	3.61	3.67	7.00-8.15
7. $CoCl(ABT)(Ileu)(H_2O)$	-	3.62	1.28	3.63	3.66	7.02-8.07
8. $CoCl(APMBT)(Leu)(H_2O)$	-	3.75	1.30	3.60	3.66	7.16-8.22
9. $CoCl(APMBT)(ILeu)(H_2O)$ (bs = broad singlet)	-	3.75	1.31	3.60	3.68	7.15-8.25

ANTIBACTERIAL ACTIVITY

The results of antibacterial activity of 2-substituted benzazole ligands and their Co(II) ternary complexes are summarized in Table-4. The organism selected for the studies are *Staphylococcus aureus* (+ve) and *Escherichia coli*(-ve). The antibacterial activity was evaluated by Inhibition zone technique.

Table-4 Antibacterial Screening data of the ligands (MBO, ABT, APMBT) and their Co(II) ternary complexes

Compounds	Diameter inhibition zone (mm)			
	Staphylococcus aureus		***Escherichia coli***	
	500	**1000**	**500**	**1000**
1. MBO	10	15	12	14
2. ABT	12	18	15	20
3. APMBT	18	22	17	25
4. $Co(MBO)(Leu)(H_2O)_2$	14	17	22	24
5. $Co(MBO)(ILeu)(H_2O)_2$	18	20	27	30
6. $CoCl(ABT)(Leu)(H_2O)$	20	23	25	31
7. $CoCl(ABT)(Ileu)(H_2O)$	22	28	30	32
8. $CoCl(APMBT)(Leu)(H_2O)$	25	30	28	34
9. $CoCl(APMBT)(ILeu)(H_2O)$	28	35	31	37
Streptomycin (Standard)	45	60	52	64

Table-5 Fungcidal Screening Data for the ligands(MBO, ABT & APMBT) and their Co(II) ternary complexes

Compound	Average % inhibitor concentration (in ppm) after 72 hours					
	Aspergillus niger			***Fusarium oxysporium***		
	50	**100**	**200**	**50**	**100**	**200**
1. MBO	35	45	55	38	45	60
2. ABT	38	50	58	42	55	65
3. APMBT	40	55	60	45	60	67
4. $Co(MBO)(Leu)(H_2O)_2$	46	68	78	51	72	82
5. $Co(MBO)(ILeu)(H_2O)_2$	50	75	80	53	73	83
6. $CoCl(ABT)(Leu)(H_2O)$	50	70	82	55	69	78
7. $CoCl(ABT)(Ileu)(H_2O)$	52	78	87	62	78	84
8. $CoCl(APMBT)(Leu)(H_2O)$	55	67	85	57	72	90
9. $CoCl(APMBT)(ILeu)(H_2O)$	61	72	90	65	88	92
Dithane M-45 (Standard)	77	94	100	75	95	100

Antifungal activity

The results of antifungal activity of 2-substituted benzazole ligands and their Co(II) ternary complexes were summarized in Table-5. 2-substituted benzazole derivatives and their Co(II) ternary complexes have been screened for fungicidal properties against *Aspergillus niger*and *Fusarium oxysporium* at concentration 50, 100 and 200 ppm.The radial growth method was used to check an activity against fungi by taking Dithane M-45 as a standard. The antifungal screening data reveals that Co(II) ternary complexes are more fungitoxic than the parent ligand (MBO, ABT & APMBT). The enhanced activity of the Co(II) ternary complexes may be described to the increased liophilic nature of these complexes arising due to the chelation. The toxicity increased with increasing concentration.

Acknowledgements
The authors are thankful to the Head, Department of Chemistry, University of Rajasthan, Jaipur, India for providing necessary facilities to carry out this research work. Chandni Jain is grateful to university grant commission, New Delhi, India for the financial support in the form of CSIR-JRF wide grant number 09/149(0591)/2011 EMR-I.

REFERENCES

[1] MNHughes Coordination Compounds in Biology In :G Wilkinson, RD Gillard, JAMcCleverty, Editors. *Comprehensive Coordination Chemistry*, Vol. 6, Oxford, U.K. : Pergamon Press; **1987**, P. 541.
[2] JRThakkar; NVThakkar.*Synthesis and Reactivity in Inorganic and Metal Organic Chemistry*, **2000**, 30(10), 1871-1887.
[3] VSShivankar; NVThakkar.*ActaPoloniaePharmaceutica*,**2003**, 60(1), 45-50.
[4] PPattanayak; JLPratihar; DPatra; C Lin; S Paul; KChakraborty. *Polyhedron*, **2013**, 51, 275-282.
[5] ZQu; J Su; Z Mao; X Le.*Synthesis and Reactivity in Inorganic, Metal-Organic and Nano-metal Chemistry*, **2013**, 43(6), 728-733.
[6] Z Qu; S Huang; X Le. *Wuji Huaxue Xuebao*, **2012**, 28(8), 1580-1586.
[7] Premlata; G Seth, *J. Chem. Pharm. Res.*,**2012**, 4(5), 2771-2774.
[8] RKDubey; UKDubey; SKMishra, *J. Coord. Chem.*,**2011**, 64(13), 2292-2301.
[9] H Gu; Z Wang; W Chen*Asian J. Chem.*,**2012**, 24(2), 915-919.
[10] H Gu;Z Wang; W Chen, *WujiHuaxueXuebao*, **2012**, 28(3), 591-600.
[11] NMShivakumaraiah; NGowda.*Indian J. Chem.*,**2003**, 42A, 1856.
[12] N Bharti; MRMaurya; L Naqui; AAzam.*Bioorg. Med. Chem.Lett.*, **2000**, 10, 2243.
[13] J Kaur; MKSamota;SOjha;VKabra. Seth, G. *Phosphorus Sulfur Silicon Relat. Elem.*,**2006**, 181, 1925.
[14] MKSamota; GSeth.*Heteroatom Chem.*,**2010**, 21(1), 44-50.
[15] Verma S;GSeth.*J. Indian Chem. Soc.*, **2011**, 88(9), 1435-1438.
[16] NPal; M Kumar; G ESeth.*J. Chem.*, **2011**, 8(3), 1174-1179.