Ligating Behavior Of Some Sulphur Containing Benzotriazole Derivatives Towards Some Transition Metal Ions And Their Biological Effect

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Abstract: New Cu^{2+} and Ni^{2+} complexes of N[1]-phenyl-2-[1H-1,2,3-bezotriazol-1-yl] 3-phenyl-3-oxopropane thioamide, HL, has been synthesized and characterized by different spectral and magnetic measurements and elemental analysis. The spectral studies indicated that HL exist in the thion form in the solid state and the IR spectra of the complexes indicated that the ligand act as monobasic bidentate ligand giving distorted tetragonal structure in case of $Cu^{2+}$and square planar structure in case of Ni^{2+}, which was the reason of their different antimicrobial activity. Thermal decomposition of both complexes showed similar steps.

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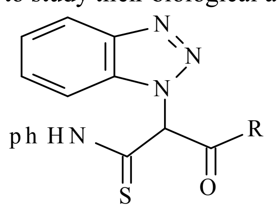
1.Introdction

Compounds containing triazole derivatives have attracted much interest because of their biological applications [1-9]. Furthermore, triazole appears frequently in the structures of various natural products [10]. Triazole containing compounds appear in many metabolic products of fungi and primitive marine animals. Many triazole derivatives having different functionalities are used as dyes and as photographic chemicals [11]. The coordination chemistry of benzotriazole derivatives was studied due to their importance in industry, agriculture, synthesis of supramolecular complexes which are useful in the functional materials with controlled non-linear optical, magnetic and photo luminescent properties [11 - 22] as well as their biological activity. The mercapto group often coordinates to metal ions in many biological molecules [22- 26] and information about the relative reactivity of the coordinated mercapto group might give insight into the specific reactivity of active sites in some metalloproteins. On the other hand, some of the transition metals such as vanadium, copper, iron and magnesium present in trace quantities are essential elements for biological systems. In view of the above facts and in continuation of our interest in studying the ligating behavior of such compounds [12 - 27], we aim to (i) synthesize and characterize the solid complexes of the ligands containing both the triazole and thioamide moieties,, **I**, with, some transition metal ions, (ii) to characterize both organic ligands and their complexes, (iii) to study of their thermal decomposition characteristics and (iv) to study their biological activity



(I)

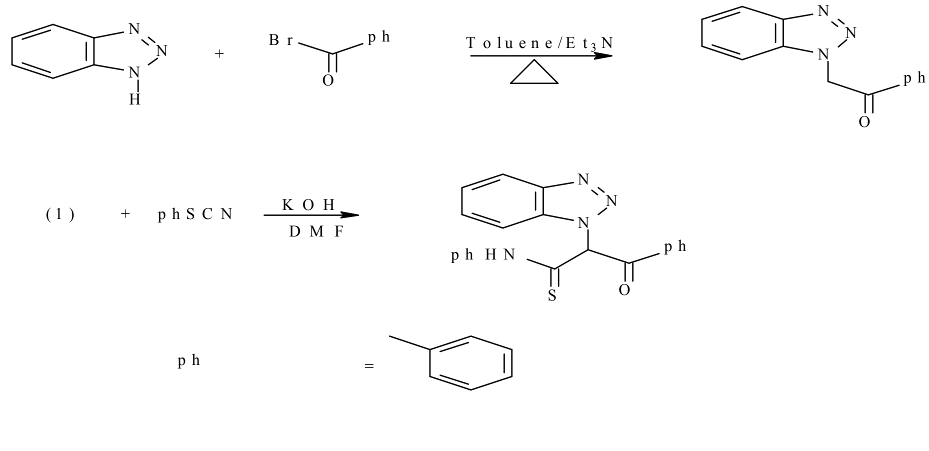
2. Material and Methods:

Materials: All chemicals were reagent grade quality obtained from Fluka and Aldrich Chemical Companies, and used as received. All solvents used were of high analytical reagent grade and used without further purification.

Instruments: CHNS analysis was obtained using LECO-CHNS 932 analyser, FT-IR spectra was recorded as KBr discs with Schimadzu 2000 FT-IR spectrophotometer. Electronic spectra Beckman DB.G spectrophotometer or 160A u.v. visible recording spectrophotometer, Schimadzu in matched quartz cells at room temperature, the room temperature magnetic susceptibility measurement for complexes were determined by Gouy balance using $Hg[Co(NCS)_4]$ as a calibrant. Thermal analysis measurement was performed by using a dynamic nitrogen atmosphere with a TGA-50 Schimadzu thermogravimetric analyzer at a flow rate of 50 $mL.min^{-1}$. The heating rate was $10^{\circ}C.min^{-1}$ and the sample sizes ranged in mass (6-8) mg.

[1]HNMR was determined on a Bruker DPX 400 MHz superconducting spectrometer in $CDCl_3$ and DMSO-d_6 as solvents and using TMS as internal standard.

Synthesis of the organic ligands: The organic ligands were synthesized according to the previously reported method [29] as shown in scheme 1.



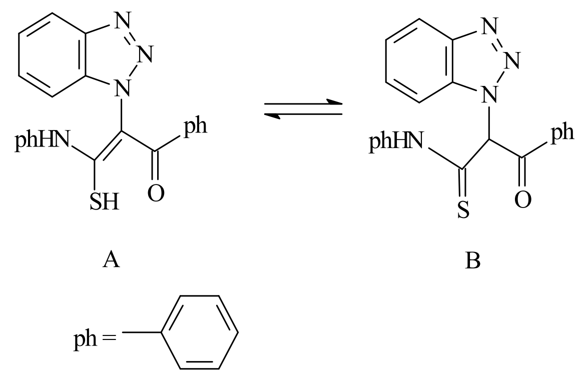
Scheme 1

Synthesis of the Cu(II) complexes: The complexes were synthesized according to general procedure: A stoichiometric amount of Cu $(OAc)_2.H_2O$ (0.001mol) was dissolved in methyl alcohol followed by the addition of 3-5 mL triethylamine (TEA) and added to ethanolic solution of the ligand (0.0022mol) and the reaction mixture was refluxed for 2-3 hours on a water bath and cooled at room temperature, the solid products was filtered and washed with ethanol and diethyl ether.

Synthesis of the Ni(II) complexes: The complexes are synthesized according to general procedure: A stoichiometric amount of Ni $(OAc)_2.4H_2O$ (0.001mol) was dissolved in ethyl alcohol followed by the addition of 3-5 mL triethylamine (TEA) and added to ethanolic solution of the ligand (0.0022mol) and the reaction mixture was refluxed for 2-3 hours on a water bath and cooled at room temperature, the solid products was filtered and washed with ethanol and diethyl ether.

Biological activity : The antimicrobial activity of synthesized HL, copper(II), and nickel(II) complexes against *staphylococcus aurous, salmonella sp*[1], *Salmonella sp*[2] and *Bacillus,* using the gel diffusion and respirometric method as previously described [30]

3. Results and Discussion:



Characterization of the ligands and their solid complexes:

The reaction of HL with $Cu(OAc)_2$. H_2O and $Ni(OAc)_2$. $4H_2O$ gave the complexes presented in table 1

Table 1: Elemental analysis, color, and room temperature effective magnetic moments of HL(1 and 2) and their complexes

Compound	Color	μ_{eff}	Calc. (found) %			
			C	H	N	S
HL, $C_{21}H_{16}N_4SO$	Buff	—	67.72 (67.70)	4.32 (4.52)	15.04 (15.16)	8.6 (8.4)
$[L_2Cu]$ $C_{42}H_{30}N_8S_2O_2$ Cu	Light blue	1.82	62.56 (62.54)	3.75 (3.77)	13.89 (13.9)	7.96 (7.87)
$[L_2Ni]$ $C_{42}H_{30}N_8S_2O_2$ Ni	Dark blue	Dia	62.94 (63.00)	3.77 (3.6)	13.98 (14.0)	7.99 (8.0)

NMR and IR spectra: The ^{13}C NMR spectra of HL(1and 2) in d_6-DMSO was recorded [29], showing a signal at *ca.* 190 ppm which is assigned to the presence of conjugated carbonyl carbon and the signal of CH_2 group was not observed, The infrared of ligands and their complexes are collected in table 2, the spectra of the ligands do not show bands at 2600-2500 cm^{-1}correspond to ν(SH). The spectra of the ligands showed four bands at *ca.* 1493, 1360,1073 and 836 cm^{-1}which are assigned to the thioamide (HNC=S) bands [31,32]. The thioamide bands at ν;1073 and 836 cm^{-1} are strongly shifted to lower wave numbers in the complexes supporting sulphur donation and deprotonation of the ligand as well, while the bands at 1493 and 1360 $cm^{-1}$are not greatly affected indicating that nitrogen is not bonded to the metal ion. The HL posses weak band at ν1607cm^{-1}corresponds to C=O and medium to strong band at ν 3163cm^{-1}corresponds to NH, the shifting of the NH band and weakness of CO band may be attributed to hydrogen bond formation. A band appeared at 3045 cm^{-1} which is attributed to CH stretching for sp^2carbon.

These data indicated that the ligand is found in the form B in the solid state. Upon complexation red shift by (18-44) cm^{-1}indicating the M-O bonding, the ligand act as monobasic bidentate ligand coordinating the metal through the thiolo-sulphure and keto-oxygen atoms [33,34].

Table 2: Main IR bands for HL and its metal complexes.

Compound	ν (NH)	ν (C=O)	ν (thioamide)			
			I	II	III	IV
HL, $C_{21}H_{16}N_4SO$	3163 S	1607 w	1493 Vs	1360 s	1073m	841m
$[L_2Cu]$ $C_{42}H_{30}N_8S_2O_2$ Cu	3230 S	1578 w	1495 S	1380s	1026m	735m
$[L_2Ni]$ $C_{42}H_{30}N_8S_2O_2$ Ni	3280 s	1578 w	1499 M	1389s	1034m	723m

(w= weak, m= medium, s= strong)

Electronic spectra and magnetic studies: The electronic spectra (Table 3) showed intense bands at 375- 350 and 340- 335 nm suggesting O-M(II) bond. The spectra also showed strong band at 445-400 nm characteristic to S-M(II) LMCT transition.

Copper (II) complex $[L_2Cu]$ gives a room temperature magnetic moment 1.78 B.M. indicating magnetically diluted Cu(II) ion. Its electronic spectrum showed an intense band at 380 nm due to intraligand and LMCT transition which support the tetragonally distorted copper (II) complex.

Nickel (II) complex showed bands at ; 590, 500, 413 nm assignable to $^1A_{1g}\rightarrow^1A_{2g}$, $^1A_{1g}\rightarrow^1B_{1g}$ for d-d transitions and $^1A_{1g}\rightarrow^1E_g$ for strong CT transition, respectively, characteristic to square planar nickel(II) complexes.

The zero magnetic moment of $[L_2Ni]$ assure the square planar geometry.

Table 3: Electronic spectral data (nm):

Compound	Intraligand and CT	d-d transition
$[L_2Cu]$ $C_{42}H_{30}N_8S_2O_2$ Cu	380	-
$[L_2Ni]$ $C_{42}H_{30}N_8S_2O_2$ Ni	337,350, 408	413, 500, 590

Thermal analysis : The thermogravimetric (TG) and the derivative thermogravimetric (DTG) plots of the complexes in the 25-1200°C range under nitrogen. $[L_2Cu]$ exhibit two significant steps ; the first decomposition step in the temperature range (158-315)°C with net weight loss of 52.0%, (%calc.=52.14%) which correspond to 2 BTA+2 C_6H_6N, and The second step (445-549)°C, with net weight loss of 36.1 (% calc.=36.22), corresponds to the loss of SO_2 and 2 C_9H_5.

$[L_2Ni]$ exhibit two significant steps. The first decomposition step in the temperature range (220-330)°C with net weight loss of 52.3%, (%calc.=52.45%) which correspond to **2 BTA+2 C_6H_6N.** The second step (410-610)°C with net weight loss of 36.1 (% calc.=36.0), corresponds to the loss of SO_2 and 2 C_9H_5.

Table 4: Thermogravimetric characteristics of Cu(II) and Ni(II) complexes

Compound	Molar mass	TG range (°C)	Weight loss		Assignment	Metallic residue
			Calcd	Found		
$[L_2Cu]$ $C_{42}H_{30}N_8S_2O_2$ Cu	806.42	158-315	52.14	52.0	2BTA+ $2C_6H_6N$	CuS
		445-549	36.0	36.1	SO_2+ 2 C_9H_5	
$[L_2Ni]$ $C_{42}H_{30}N_8S_2O_2$ Ni	801.56	220-330	52.45	52.3	2BTA+ $2C_6H_6N$	NiS
		410-610	36.22	36.1	SO_2+ 2 C_9H_5	

Biological activity, The antibacterial activity of HL and metal (II) complexes were studied, and the results show that $[L_2Cu]$ complex is active towards *staphylococcus aurous and salmonella sp[1],* while $[L_2Ni]$ complex is not, on the other hand both complexes were found to be inactive towards *Salmonlla sp[2]*. Both complexes are active towards *Bacillus.*

The biological activity of metal complexes is governed by the following factors [35] :a) the chelate effect of the ligands. b) the nature of donor atoms, c) the nature of the metal ion, d) the total charge on the complex ion, e) the nature of the counter ions that the neutralize the complex-if ionic- and f) the geometrical structure of the complex [36]. Comparing $[L_2Cu]$ and $[L_2Ni]$, both have the same donating atoms(S/O) with the same (C.N=4), same chelate effect (6 membered chelating rings), they are neutral and no counter ion and have same metal oxidation state, therefore the effective factor is the geometrical shape and nature of central atom. The higher antimicrobial activity of Cu(II) complex may also attributed to the stronger Cu-Ligand bond.

Conclusion

- The interaction of HL with Cu^{2+} and Ni^{2+}leads to the formation of neutral comlpexes $[L_2M]$.
- Their structures are determined by elemental analysis, spectral properties, magnetism and thermal analysis.
- The $[L_2Cu]$ has a distorted tetragonal structure whereas $[L_2Ni]$ is square planar
- The $[L_2Cu]$ is more antibacterial effective than $[L_2Ni]$.

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References

1. Curtis A.D.M., N. Jennings *1,2,4-Triazoles, Comprehensive Heterocyclic Chemistr*y III, 2008, Chapter 5.02, Pages 159-209
2. Chai X., J. Zhang, H. Hu, S. Yu, Q. Sun, Z. Dan, Y. Jiang, Q. Wu, Design, synthesis, and biological evaluation of novel triazole derivatives as inhibitors of cytochrome P450 14α-demethylase, Eur. J. Med. Chem., 2009, 441913-1920.
3. Padmavathi V., G. Sudhakar Reddy, A. Padmaja, P. Kondaiah, A. Shazia, Synthesis, antimicrobial and cytotoxic activities of 1,3,4-oxadiazoles, 1,3,4-thiadiazoles and 1,2,4-triazoles, Eur. J. Med. Chem., 2009, 44, 2106-2112.
4. Padmavathi V., A.V. Nagendra Mohan, P. Thriveni, A. Shazia, Synthesis and bioassay of a new class of heterocycles pyrrolyl oxadiazoles/thiadiazoles/triazoles, Eur. J. Med. Chem., 2009, 44, 2313-2321.
5. Li W., J. Zha, P. A. Spear, Z. Li, L.Yang, Z. Wang, Changes of thyroid hormone levels and related gene expression in Chinese rare minnow

(Gobiocypris rarus) during amino-1,2,4-triazole exposure and recovery, Aq.Tox., 2009 92, 50-57.
6. Liu J., L. Li, H. Dai, Z. Liu and J. Fang, Synthesis and biological activities of new 1H-1,2,4-triazole derivatives containing ferrocenyl moiety, J. Organometall. Chem, 2006, 69, 2686-2690
7. Tian L., Y. Sun, H. Li, X. Zheng, Y. Cheng, X. Liu and B. Qian, Synthesis, characterization and biological activity of triorganotin 2-phenyl-1,2,3-triazole-4- carboxylates, J. Inorg. Biochem., 2005, 9,1646-1652
8. Jamkhandi C.M., J.I. Disouza,.Synthesis and antimicrobial evaluation of 2-(1H-1,2,3-Benzotriazol-1-yl)-N-phenylacetamide derivatives Research Journal of Pharmacy and Technology, 2012, 5 (8), pp. 1072-1075
9. Modzelewska-Banachiewicz B., J. Banachiewicz, A. Chodkowska, E. Jagiełło-Wójtowicz and L. Mazur, Synthesis and biological activity of new derivatives of 3- (3,4-diaryl-1,2,4-triazole-5-yl)propenoic acid, Eur. J. Med. Chem., 2004,39 873- 877.
10. Kim D.-K., J. Kim and H.-J. Park, Synthesis and biological evaluation of novel 2- pyridinyl-[1,2,3]triazoles as inhibitors of transforming growth factor β1 type 1 receptor Bioorg. & Med. Chem.Lett., 2004, 14, 2401-2405
11. Asami Y T. Y. Ki Min, N. Nagata, K.Yamagishi, S. T. S.ujioka, N. Murofushi, I amaguchi, and S.Yoshida, Characterization of brassinazole, a triazole-type brassinosteroid biosynthesis inhibitor, Plant Physiol, 2000, 123 93-100.
12. HaasnooJ. G. t. Mononuclear, oligonuclear and polynuclear metal coordination compounds with 1,2,4-triazole derivatives as ligands, Coord. Chem. Rev.,2000, 200- 202,131-185.
13. Xiong R.G., X. Xue, H. Zhao, X.Z. You, B.F. Abrahams, Z. Xue, Novel, Acentric Metal-Organic Coordination Polymers from Hydrothermal Reactions Involving In Situ Ligand Synthesis Angew. Chem., Int. Ed. Engl, 2002, 41, 3800-3803
14. Brammer L., Developments in inorganic crystal engineering, Chem. Soc. Rev., 2004,8, 476-490.
15. Lopez N., T.E. Vos, A.M. Arif, W.W. Shum, J.C. Noveron, J.S. Miler, Structure and magnetic properties of a hydroxo-bridged copper(II) distorted cubane stabilized via supramolecular hydrogen bonding with an ionic hexafluoroacetylacetonate. Inorg. Chem., 2006, 45, 4325-4327.
16. Shu M.H., C.L. Tu, W.D. Xu, H.B. Jin, J. Sun, Reversible Anion Exchanges of Porous Metal−Organic Frameworks: Syntheses and Structures of SilverComplexes with Novel Rigid Tripodal Nitrogen Ligands Cryst. Growth Des, 2006, 6, 1890-1896.
17. Maspoch D., D. Ruiz-Molina, J. Veciana, Old materials with new tricks: multifunctional open-framework materials" Chem. occ. Rev., (2007) 36, 770-818.
18. Alvaro M., E. Carbonell, B. Ferrer, F.X.L. Xamena, H. Garcia, Semiconductor Behavior of a Metal-Organic Framework (MOF) Chem. Eur. J. 13 (2007) 5106-5112.
19. Wang Y., T.-A. Okamura, W.-Y. Sun, N. Ueyama, Large (H2O)56(OH)6 and (H2O)20 Clusters inside a Nanometer-Sized M6L8 Cage Constructed by Five- Coordinated Copper(II) and Flexible Carboxamide-Containing Tripodal Ligand, Cryst. Growth Des., 8 (2008) 802-804.
20. Hoogenboom R., D. Fournier, U.S. Schubert, Asymmetrical supramolecular interactions as basis for complex responsive macromolecular architectures, Chem. Commun., 2008, 155-162.
21. Meng X., S. Jin, H. Hou, C. Du, S.W. Ng, Self-assembly of four supramolecular archtectures: From)-D to 2-D frameworks based on unsymmetrical N-heterocycliuc ligands, Inorg. Chim. Acta, 2009, 362, 1519 – 1527.
22. Zhou X.-Y., Y.-Q Huang and W.-Y. Sun, Synthesis, structures and photoluminscent property of coordination complexes with 2-(1H-1,2,4-triazol-1-yl)acetic acid, Inorg. Chim. Acta, 2009, 362, 1399 – 1404.
23. El-Dissouky A., N. M. Shuaib and N. A. Al-Awadi, Alaa Abbas and Ahmad El- Sherif, Synthesis, characterization, potentiometric and thermodynamic studies of some transition metal complexes with 1-benzotriazol-1-yl-1-[(p-ethoxyphenyl)hydrazono]- propan-2-one. J. Coord. Chem., 2008, 61, 579-594
24. Garoufis A., S.K. Hadjikakou, N. Hadjiliadis, Palladium coordination compounds as anti-viral, anti-fungal, anti-microbial and anti-tumor agents, Coord.Chem.Rev. 2009, 253,1384-1397.
25. Sawant V.A., S.N. Gotpagar, B.A. Yamgar, S.K. Sawant, R.D. Kankariya, S.S. Chavan Characterization and electrochemical studies of Mn(II), Co(II), Ni(II) and Cu(II) complexes with 2-mercapto-3-substituted-quinazolin-4-one and 1,10-phenanthroline or ethylenediamine as ligands, Spectrochim. Acta Part A: 2009, 72, 663-669.
26. Ana I. Matesanz, Pilar Souza Palladium and platinum3,5-diacetyl-1,2,4-triazol bis(thiosemicarbazones): Chemistry, cytotoxic activity and structure–activity relationships, J.of Inorg. Biochem., 2007,101, 245-253.
27. Kovala-Demertzi D., A. Papageorgiou, L. Papathanasis, A. Alexandratos, P. Dalezis, J. R.

Miller, M. A. Demertzis In vitro and in vivo antitumor activity of platinum(II) complexes with thiosemicarbazones derived from 2-formyl and 2-acetyl pyridine and containing ring incorporated at N(4)-position: Synthesis, spectroscopic study and crystal structure of platinum(II) complexes with thiosemicarbazones, potential anticancer agents, Eur. J. Med. Chem., 2009, 441, 296-1302

28. Lippard S. J., Ion sulphur coordination compounds and proteins, Acc.Chem. Res., 1973, 6, 282-288.
29. Al-Saleh B., M.A. El-Apasery and M.H.Elnagdi,"Synthesis of new azoyl azoles and azinyl azoles" *J. Heterocyclic Chem.,2005, 42(4),483*
30. Ezeifeka G.I., M.U.Orji, T.I.Mbata and A.O.Patrick. "Antimicrobial activities of *Cajanus cajan*, *Garcinia Kola* and *Xylopia aethiopica* on pathogenic microorganisms", Biotechnology, 2004,3(1), 41.
31. Kandil S.S., N. El-Brollosy and A. El-disouky."Synthesis and characterization of Mn^{2+}, Ni^{2+}, and Cu^{2+}complexes of 4- arylideneamino-3-mercapto-6-methyl-1,2,4-triazin-5-one".Synthesis And Reactivity In Inorganic And Metal-Organic Chemistry, 2000, 30(6), 979.
32. Fabretti A.C.,G.C.Franchini and G.Peyronel, "Tin(IV) tetrahalide complexes of 2,5-disubstituted 1,3-dithiazoles". Spectrochimica Acta, 1980,36A, 517.
33. Rao C.N.R., R. Venkataraghavan and T.Kastyri, " Contribution to the infrared spectra of organosulphur compounds". Canadian Journal of chemistry, 1964, 42(1), 36.
34. Singh B.,M.M.P. Rukhaiyar and R.J. Sinha, "thioamide bands and nature of bonding-IV:chelating behavior of 2- mercaptoquinazole-4-one".Journal Of Inorganic and Nuclear Chemistry, 1977, 39(1), 29.
35. Chohan Z.H., "Antibacterialand antifungal ferrocene incorporated dithiothione and dithioketone compounds". Applied organometallic chemistry, 2005, 20(2), 112
36. Russell A.D., " Densification, Sterilization and Preservation", Lee and Gebinger, Philadelphia, Pa, USA, 4th edition, 1991

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