

Study of the 4,6-diamino-3-cyano pyridine-2(1H)-thione complexes

M. A. El Nawawy

¹. Department of Chemistry, Faculty of science, Al-Azhar Univ., Nasr- City, Cairo, Egypt.
nawawym60@yahoo.com

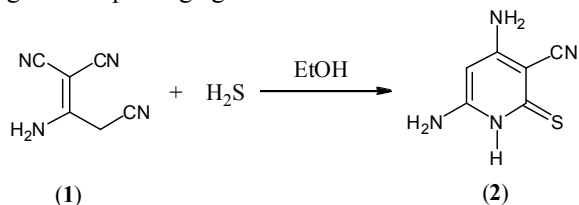
Abstract: Complexes of 4,6-diamino-3-cyano pyridine-2(1H)-thione with Cu(II), Co (II), Mn(II), Ni(II) and Zn(II) ions have been prepared. The formation of 2: 1 (metal:ligand) complexes was identified by elemental analyses, spectrophotometric and electrical conductance measurements. The nature of bonding in the isolated complexes has been investigated by infrared (FTIR), proton nuclear magnetic resonance (¹H N.M.R) spectra as well as thermogravimetry (TGA), magnetic properties and mass spectrometric data. The biological activities of the ligand and metal complexes have also been studied.

[M. A. El Nawawy. Study of the 4,6-diamino-3-cyano pyridine-2(1H)-thione complexes. New York Science Journal 2011;4(10):26-29]. (ISSN: 1554-0200). <http://www.sciencepub.net/newyork>.

Keywords: Species richness; beta-diversity; taxonomic diversity; forest

1. Introduction

Interest in development of efficient synthetic approaches for the preparation of functionalized 3-cyano-2(1H)-pyridinethiones is related to their use as versatile precursors in the preparation of dyes, herbicides, bactericides and other biologically active compounds²⁻⁴. The considerable activity of polyfunctionally substituted pyridines⁵⁻⁷ as calcium channel blockers and as antiviral agent has stimulated considerable interest in the synthesis of pyridin derivatives⁸⁻¹⁰. It was reported¹ that 4,6-diamino-3-cyanopyridin-2(1H)-thione (**2**) was obtained in a very good yield by the reaction of 3-amino-2-cyanopent-2-enedinitrile (**1**) with H₂S. In this paper we use 4,6-diamino-3-cyanopyridin-2(1H)-thione (**2**) as a complexing agent where the basic structure contains four substituents in order to be capable to make a good complexing agent.



2. Experimental

2.1. Preparation of complexes

The complexes were prepared by the addition of stoichiometric amounts (0.02 mol) of Cu(CH₃COO)₂·2H₂O, Co(CH₃COO)₂·4H₂O, Ni(CH₃COO)₂·4H₂O, Mn(CH₃COO)₂·4H₂O, Zn(CH₃COO)₂·2H₂O in absolute ethanol to a solution of the ligand (**2**) (0.01mol). The reaction mixture was heated under reflux for 3h. The resulting slurry was filtered to obtain a solid, washed with ethanol and dried in air and yields were estimated to be 65 – 75 %. Elemental analyses data, given in Table 1 for all

the complexes (2a-2e), indicate 2:1 (metal:ligand) ratio. The complexes are insoluble in chloroform, carbon tetrachloride, methanol and ethanol but soluble in DMF and DMSO. The molar conductivity data obtained in DMSO suggest that all the complexes are non-electrolyte in nature.

Table 1

Cpd. No.	Yield %	MP °C	Molecular formula	Elemental Analysis Calculated/ found		
				N%	%S	MP%
2a	65	350	Cu ₂ C ₁₄ H ₂₂ N ₄ O ₁₀ S	99/9.5	5.6/5.1	22.5/22.9
2b	67	350	Co ₂ C ₁₄ H ₂₀ N ₄ O ₁₄ S	8.9/8.4	5.1/4.8	18.7/18.3
2c	70	350	Mn ₂ C ₁₄ H ₂₀ N ₄ O ₁₂ S	9.6/8.1	5.5/5.2	18.8/18.4
2d	73	350	Ni ₂ C ₁₄ H ₂₀ N ₄ O ₁₂ S	9.4/9.6	5.4/4.9	19.8/19.3
2e	75	350	Zn ₂ C ₁₄ H ₂₀ N ₄ O ₁₂ S	9.3/9.2	5.3/5.1	21.6/21.4

2.2. Samples characterization

2.2.1. Melting Point

The apparatus used to determine the electrothermal melting point was Goffine and Gerge made in U.K.

2.2.2. Infrared Spectra

A Perkin Elmer spectrophotometer 57928 RXIFT-IR system, using KBr technique was used in performing the infrared spectra, Chemistry Department, Faculty of Science, Al-Azhar University.

2.2.3. Nuclear Magnetic Resonance

The ¹H NMR spectra were recorded by a Varian, Gemini 200 MHz at Cairo University.

2.2.4. Spectrophotometric Measurements

The absorption in the UV-Vis region was recorded by a Perkin Elmer Lambda 35 Spectrophotometer at Chemistry Department, Faculty of Science, Al-Azhar University.

2.2.5. Mass Spectra

The mass spectra were performed by Hewlett Packard mass spectrometer model MS 5988 at Chemistry Department, Faculty of Science, Al-Azhar University.

2.2.6. Conductometric Titration and Molar Conductance

The measurements were carried out on YSI Model conductivity bridge.

2.2.7. TGA Measurements:

TGA data were measured from room temperature up to 800°C at a heating rate of 20°C/min. The data were performed with a Shimadzu TGA- 50H.

2.2.8. Magnetic Measurements:

Magnetic susceptibility measurements were carried out by the Faraday method at room temperature, at Faculty of Science, Cairo University.

3. Results and discussion

3.1. Infrared spectra

The main absorption frequencies due to stretching modes of (C≡N) and two (NH₂) groups in the infrared spectra of the ligand and metal chelates are listed in table (2). The ligand shows a characteristic spectral feature at 2540 cm⁻¹ attributed to ν S-H group. This observation suggest that the ligand is characterized by the thiol group which unaffected on complexation, implying non-involvement of this group in the coordination. The implications of four coordination binding sites on the ligand are more likely to maintain relative stability to metal complexes. Comparing the spectra of the ligand with those of its metal chelates showed that the ν (C≡N) of the ligand observed at 2200 cm⁻¹ is shifted to the higher frequency side in the spectra of corresponding complexes. It was reported that the CN group acts as σ- donor by donating electrons to the metal and also as a π-acceptor by accepting electron from the metal σ- donation. This tends to shift the ν (CN) frequency to the higher energy side⁽¹¹⁻¹⁵⁾ due to strong electron-withdrawing effect of the CN group. Consequently, it is most likely that CN participating in the complexation. On the

contrary, both ν (NH₂) vibrational frequencies of the different complexes which are superimposed on each other are shifted to lower wave numbers, suggesting the participation of the two NH₂ groups in the coordination. Peaks observed in the spectra of complexes around ~ 1625 cm⁻¹ are attributed to ν (C=O) of the acetate group indicating the involvement of acetate group in bonding to metal ion⁽¹⁶⁾. This observation is further supported by the appearance of a band corresponding to the metal–nitrogen stretching vibration⁽¹⁷⁾ at 554–579 cm⁻¹. All complexes exhibit a broad band at 3500–3300 cm⁻¹ simultaneously appeared with a band at 723–790 cm⁻¹, attributed to lattice held and/or coordinated water molecules.⁽¹⁸⁾

Table 2 Infrared spectra of the ligand and complexes

Cpd NO.	vibrational frequencies (cm ⁻¹)			
	νC≡N		ν 2(NH ₂)	
2	2200	2208	3464-3370	3448-3352
2a		2204		3416-3344
2b		2208		3320-3252
2c		2204		3324-3222
2d		2204		3434-3352
2e		2206		3438-3350

Molecular ratios of complexes

Stoichiometry application using molar ratios⁽¹⁹⁾, continuous variation⁽²⁰⁾ and slope ratio methods⁽²¹⁾ of λ_{max} for complexes confirm that the most stable complex structures are (1:1) and (2:1) metal-ligand molar ratios.

Conductometric titration

Compleximetric titrations of a 10⁻³ M solution of the ligand with 10⁻² M solutions of the metal ions yield curves characterized by two fairly well defined breaks corresponding to the formation of (1:1) and (2:1) metal to ligand molar ratios.

Mass Spectra

The mass spectra of Cu and Co complexes were recorded to confirm the binuclear nature of these complexes. The spectra at high temperature showed that the attached water molecules are lost and the ligand behaves as a tetradentate towards two metal ions suggesting that the formed Cu and Co complexes have (2:1) metal to ligand molar ratio.

¹H-NMR

Structural Analyses of the ligand-binding properties by ¹H-NMR of Zn₂L(CH₃COO)₄·4(H₂O) showed that a signal due to –NH is no longer present in favour of a new peak observed at 4.3 ppm due to –

SH group This suggests the existence of the ligand in the thiol form in these complexes and, thus the non-involvement of the –SH group in coordination. The CH proton of the pyridine ring resonates at 6.39 ppm, while OCH₃ of the acetate group resonates at 3.5 ppm. These data indicate the involvement of acetate group in complexation and there are two NH₂ group appear as multiplied signal at 5.2-6.3 ppm.

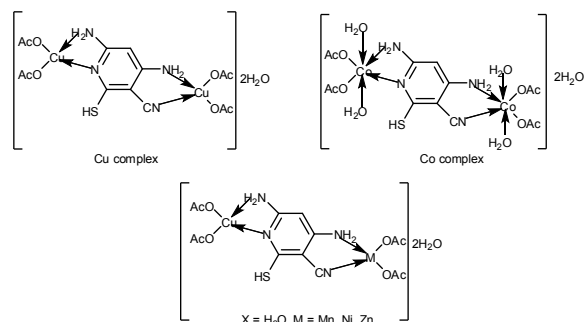
Magnetic properties of metal complexes

The calculated μ_{eff} at 1.8 BM of the Cu complex is quite close to the spin only value of d^1 . The value of μ_{eff} for the Co complex was 5.9 which is higher than that predicted using spin only formula due to orbital contribution with ${}^5T_{2g}$ and E_g^2 arrangements in octahedral structure. The Ni complex gave a μ_{eff} value close to the spin only value at 2.79 BM. The calculated μ_{eff} of Mn complex was 5.5 BM which is close to that the spin only formula (d^5) of the high spin Mn(II) configuration supporting an octahedral arrangement. The Zn complex shows the expected diamagnetic behavior, and hence there are no unpaired electrons.

TGA of the complexes indicate that the Co and Cu complexes have two water molecules of crystallization which could be removed within the temperature range 70–130°C. On the other hand, the Co, Ni, Mn and Zn complexes contain four coordinated water molecules which are removed in the temperature range 160–280°C. The next step corresponds to the loss of acetate groups within (290-400°C), and the sample burns starting from 460 up to 700°C.

Conclusions:

Based on the above results one may therefore suggest the following structural formulas of complexes which are closely related to data analysis:



Antimicrobial activity

The standardized disc– agar diffusion method (**Bauer – Kirby 1966**) was determined to monitor the activity of the synthesized compounds against microorganisms.

Test Organisms

Cultures of the following microorganism were used in the test:

Gram- positive bacteria: *Staphylococcus aureus* (ATCC 25923) and *Streptococcus pyogenes* (ATCC 19615), Gram – negative bacteria: *Pseudomonas fluorescens* (S 97) and *Salmonella typhimurium* (ATCC 14028), Yeast: *Candida albicans* and Fungus: *Aspergillus fumigatus*.

Screening for the antimicrobial potential

Preparation of tested compound

The tested compounds were dissolved in dimethyl formamide [(DMF) which have no inhibition activity] to get concentrations of 2 mg/ml and 1 mg/ ml. In the case of insoluble compounds, the compounds were suspended in DMF and vortexed then processed.

Testing for anti-bacterial activity:

Bacterial cultures were grown in nutrient broth medium at 30°C. After 16 h of growth, each microorganism, at a concentration of 10⁸ cells/mL, was inoculated on the surface of Mueller-Hinton agar plates using sterile cotton swab. Subsequently, uniform size filter paper disks (6 mm in diameter) were impregnated by equal volume (10 μ l) from the specific concentration of dissolved compounds and carefully placed on surface of each inoculated plate.

The plates were then incubated in the upright position at 30°C for 48 hours. Four replicates were carried out for each extract against each of the test organism. Simultaneous addition of the respective solvent instead of extracts was carried out as negative controls. After incubation, the diameters of the growth inhibition zones formed around the disc were measured with transparent ruler in millimeter, averaged and the mean values were tabulated.

Testing for anti-fungal activity:

Active inoculum for experiments were prepared by transferring many loopfuls of spores from the stock cultures to test tubes of sterile distilled water (SDW) that were agitated and diluted with sterile distilled water to achieve optical density corresponding to 2.0x10⁵ spore/ml. Inoculum of 0.1 % suspension was swabbed uniformly and the inoculum was allowed to dry for 5 minutes then the same procedure was followed as described above.

Standard references: The antibiotic chloramphenicol was used as standard reference in the case of Gram – negative bacteria, Cephalothin was used as standard reference in the case of Gram – positive bacteria and

cycloheximide was used as antifungal standard reference.

Activity index:

The activity of tested compounds was categorized as follows:

- Low activity = Mean of zone diameter \leq 1/3 of mean zone diameter of control.
- Intermediate activity = Mean of zone diameter \leq 2/3 of mean zone diameter of control.
- High activity = Mean of zone diameter $>$ 2/3 of mean zone diameter of control.⁽²²⁾
- Agar plates using sterile cotton swab. Subsequently, uniform size filter paper disks (6 mm in diameter) were impregnated by equal volume (10 μ l) from the specific concentration of dissolved compounds and carefully placed on surface of each inoculated plate.

		Mean* of zone diameter nearest whole mm											
		Gram - positive bacteria				Gram - negative bacteria				Yeasts and Fungi**			
Organism		Staphylococcus aureus (ATCC 25923)		Streptococcus pyogenes (ATCC 19615)		Salmonella typhimurium (ATCC 14028)		Pseudomonas fluorescens (S 97)		Candida albicans		Aspergillus fumigatus	
Conc.		2 mg /ml	1mg /ml	2 mg /ml	1mg /ml	2 mg /ml	1mg /ml	2 mg /ml	1mg /ml	2 mg /ml	1mg /ml	2 mg /ml	1mg /ml
Sample													
2		2L	-	-	-	2L	-	6L	4L	2L	-	-	-
2 a		7L	4L	-	-	14I	7L	3L	2L	-	-	-	-
2 b		2L	-	-	-	3L	4L	-	-	-	-	3L	-
2 c		-	-	-	-	-	-	-	-	3L	-	-	-
2 d		3L	-	3L	2L	4L	3L	8L	4L	14I	8L	-	-
2 e		2L	-	5L	3L	3L	2L	-	-	-	-	-	-
Control #		42	28	38	30	36	25	38	30	40	28	40	31

* = Calculate from 3 values.

** = identified on the basis of routine cultural, morphological and microscopical characteristics.

- = No effect.

L: Low activity = Mean of zone diameter \leq 1/3 of mean zone diameter of control.

I: Intermediate activity = Mean of zone diameter \leq 2/3 of mean zone diameter of control.

H: High activity = Mean of zone diameter $>$ 2/3 of mean zone diameter of control.

#: Chloramphenicol in the case of Gram-positive bacteria, Cephalothin in the case of Gram-negative bacteria and cycloheximide in the case of fungi.

References

1. F. A. Abu-Shanab, *J. Chem. Res. (S)*, 430 (1999).
2. V. P.Litvino, L. A.Rodinovskaya, Yu. A.Sharanin, A. M.Shestopalov, A. Senning, *Sulfur Rep.*, 13 155 (1992).
3. A.M.Shestopalov, V. K. Promomenkov, Yu. A. Sharanin, L. A. Rodinovskaya, Sharanin, S. Yu., *Zh. Org. Khim.*, 20, 1517 (1984).

4. A.M.Shestopalov, V. K. Promomenkov, Yu. A. Sharanin, *Enaminocarbonyl Compounds in synthesis of 3-cyano-2(1H)- pyridinethione, in Itogi Nauki I Techniki, Ser. Organicheskaya Khimiya* ed. Kabachnie, VINITI Moscow, vol. 17, pp. 72-156 (1989) and references therein.
5. M.Pallas, A.Timenez, P.Victory, J. I.Borrell, A.Vidal-Ferran, E.Escubedo, J.Camarasa, *Pharm.armacol. Lell.* 3, 36 (1993).
6. V.Yuii, T.Shigeru, I. Satochi, Y.Teruki, *J. Pharm.armacol.* 45, 1077 (1993)
7. K. Vera, *Collect. Gzech. Chem. Commun.*, 58, 1195, (1993).
8. T.Kenichi, S.Takehiko, S.Junko, Takeo, H., *Heterocycles*, 35, 915 (1993).
9. F. A. Abu-Shanab, M. H. Elnagdi, F. A. Ali, B. J.Wakefield, *J. Chem. Soc., Perkin Trans. 1*, 1449 (1994).
10. F. A. Abu-Shanab, A. D. Redhouse, J. R. Thompson, B. J. Wakefield, *Synthesis*, 557 (1995).
11. A.G. Sharp *The Chemistry of the cyano complexes of the transition metals*, Academic press New York 1976
12. W.P. Griffith, *Coord. Chem. Rev.* 17, 177, (1975)
13. P.Rigo and A.Turco, *Coord. Chem. Rev* 13, 133(1974)
14. L.H. Jones and B.I.Swanson, *Accounts Chem. Res.* 9, 128(1976)
15. B.M.Chadwick and S.G.Frankiss *J. Mol. Struct.* 31 1 (1976)
16. K.Nakamoto, *Infrared and Raman Spectra of Inorganic and Coordination compounds* Wiley 1986
17. 12. M. Tümer, H. Köksal, S.Serine, *Synth. React. Inorg. Met-Org. Chem.* 27 (1997) 775
18. J.R.Durig, W.A.McAllistel and E.E.Mercev *J.Inog.Nucl. Chem.*, 29 1441 (1967)
19. Joe, J.H. and Jones, A.L., *Ind. Chem.* 16, 111(1964)
20. Vasburgh, W.C. and Cooper, GR.,*J. Am. Chem. Soc.* 63. 437(1941)
21. Harvey, A.E. and Manning, DL, *J. Am. Chem. Soc.* 72. 4488(1950) susceptibility testing by a standardized single disc method., *American Journal of Clinical Pathology* 1966, 45:493-496.

9/5/2011