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Article

Complexes of 4-amino-3-methyl-1H-1,2,4-triazole-5-thione with Lithium(I), Aluminum (III), Cadmium(II), and Mercury(II)

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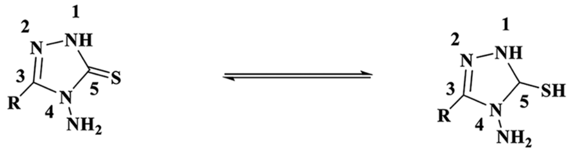
ABSTRACT

This aim report the synthesis of a new class of triazole Schiff base derivatives from the condensation reaction of thiocarbazide and glacial acetic acid and their Cd(II), Hg(II), AL(III) and Li(I) metal complexes. The obtained metal complexes were characterized for elemental analysis, conductivity, functional group identification with IR. Also, these metal complexes are screened for antimicrobial activity against *Streptococcus pyogenes, Bacillus subtilis, Escherichia coli, Enterococcus faecalis* and *Streptococcus aureus* bacteria.

Key words: Triazole, Schiff base, Thiocarbazide, Metal complexes, Antimicrobial activity.

1. INTRODUCTION

Triazoles and their derivatives occupy a central position in modern heterocyclic chemistry due to their biologically active nature. These compounds constitute heterocyclic groups that are commonly incorporated into compounds of pharmaceutical interest [1]. Triazole compounds such as fluconazole are a broad spectrum antifungal [2], trazodone is used as an antidepressant [3] vorozole, anastrozole, and letrozole are potentially used to inhibit breast cancer [4]. It is evident that the azomethine linkage (C=N) is an essential structural requirement for biological activity [5]. Several azomethine group-containing compounds have been reported to possess remarkable antibacterial [6], antifungal [7] and anticancer activities [8]. In view of above mentioned biological behavior of triazole and azomethine linkage (C=N) many triazole-based Schiff bases have also been reported to possess antibacterial [9], antifungal [10], antitumor [11], plant growth regulating [12] and cytotoxic [13] activities. It is also known that N and S atoms play a key role in the coordination of metals at the active sites of numerous biomolecules. Metallo-organic chemistry is becoming an emerging area of research due to the demand for new metal-based antibacterial and antifungal compounds [13-15]. Various investigations have proved that binding of a drug to a metallo-organic enhances its activity and in some cases, the complex possesses even more healing properties than the parent drug [16]. In the present studies, metalloelement such as cadmium, mercury, and zinc have been focused due to their smaller size and comparatively higher nuclear charge and thus have a great affinity to form coordination compounds. A bulk of literature [17-23] reveals that upon coordination with these metalloelements biologically inactive compounds become active and less biologically active compounds become more active. In view of the significant structural and biological applications of triazole compounds, I was motivated to report the synthesis of a new class of triazole Schiff base derivatives from the condensation reaction of thiocarbazide and glacial acetic acid and their Cd(II), Hg(II), AL(III), and Li(I) metal complexes.



Thione Thiol

(Where R=CH_3, ClC_6H_5)

4-amino-3-methyl-1H-1,2,4-triazole-5-thione (AMTTH) possesses several donor site.

2. EXPERIMENTAL

2.1. Preparation of Complexes

1. Preparation of Al(III) and Li(I) Complexes

Procedure – The complexes of Al(III) and Li(I) were prepared in dry ethanol. Anhydrous Al(III) Chloride (5 millimole) was taken in (30-35) ml anhydrous ethanol and treated with solid AMTTH(15 millimole). The ligand (AMTTH) went into solution on heating. The P^H of mixed solution was raised by adding a few drops of triethylamine. The resulting solution on heating and concentrating, white precipitate of tris ligand aluminum (III) complexes separated. The product was collected, washed with ether and dried in a vacuum desiccator over anhydrous $CaCl_2$. The lithium (I) complexes were prepared following the above procedure and dried in a desiccator over anhydrous $CaCl_2$. The results of elemental analysis are recorded in Table 1.

2. Preparation of Zn(II),Cd(II), and Zn(II) Complexes

Procedure – About 2 millimoles of metal chloride were taken in (20–25) ml aqueous methanol and treated with 5 millimoles of 4-amino-3-methyl-4-H 1,2,4-triazole(AMTTH) dissolved in 25 ml hot methanol. The resulting solution was refluxed on a steam bath for half an hour by raising the P^H of the mixed solution by dropwise addition of aqueous ammonia. On raising P^H to (7–8) granular precipitate of

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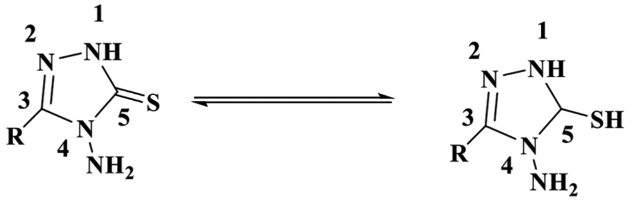
Table 1: Analytical results and color of the complex

S. No.	Complex	% Element: Calc./(Found)						μ_{eff} at (30–31)°C in B.M
		Color	M	MM C	NN H	N	S	
1	$C_3H_6N_4S$ (LH)	Creamy White		26.21 (26.11)	4.11 (4.01)	40.23 (40.18)	22.3 (22.1)	6.41
2	$(C_3H_3N_4S)_3AL$	White	6.6 (6.2)	26.40 (26.29)	2.20 (2.16)	41.17 (40.79)	23.52 (23.11)	6.34
3	$(C_3H_5N_4S)$ Li	White	(5.14)	26.40 (25.89)	3.67 (2.02)	41.17 (39.09)	23.52 (21.4)	5.83
4	$(C_3H_4N_4S)_2Cd$	Brown	30.43 (30.43)	19.56 (19.21)	2.17 (2.02)	30.43 (30.12)	17.39 (16.89)	6.39
5	$(C_3H_4N_4S)_2Hg$	Redish Brown	43.85 (42.12)	15.70 (14.97)	1.75 (2.02)	24.56 (23.89)	14.03 (13.78)	6.51

metal complexes started separating. The product was digested on the steam bath for (15–20) min, cooled at room temperature and filtered on buchner funnel. The product was washed with aqueous methanol and dried over anhydrous $CaCl_2$. The complexes were analyzed and results of elemental analysis are recorded in Table 1.

3. RESULTS AND DISCUSSION

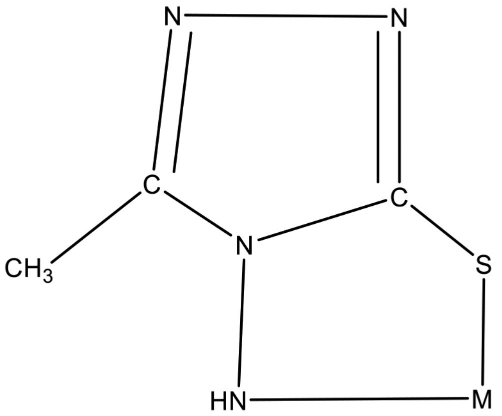
4-amino-5-mercapto-3-methyl-1-H-1,2,4-triazole(AMMTH) is a potential nitrogen and sulfur donor ligand. It has 4-amino nitrogen and 5-mercapto sulfur is suitably located for the formation of five-membered chelate ring.

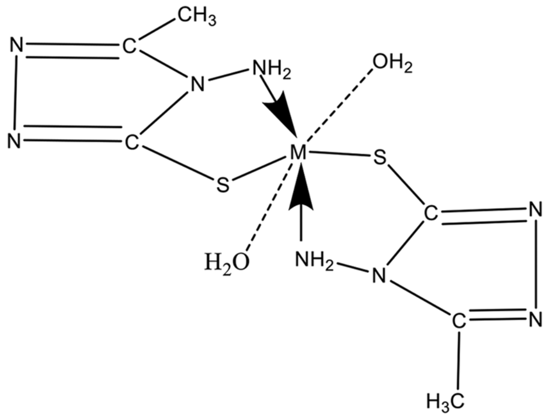


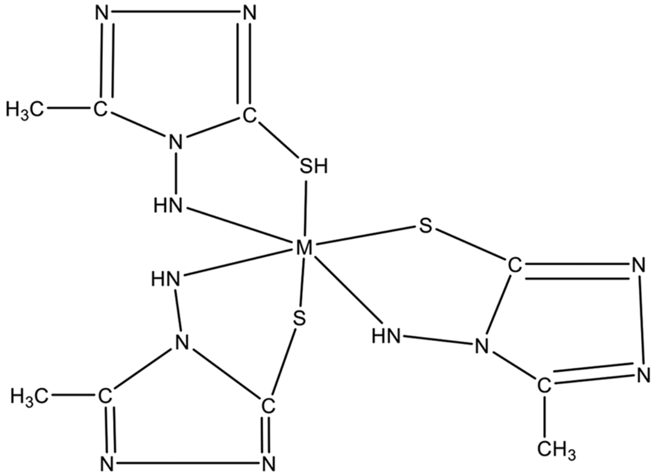
Thione (A) Thiol (B)

(AMMTH) (AMMTH)

The ligand can exist in both thione(A) and thiol(B) tautomer. The thiol tautomer can redealy be deprotonated in presence of metal ion to form neutral chelate complexes with mono, dianionic, and triligated species (C,D, and E).







The complexes formed with Zn(II), Cd(II), and Hg(II) are cream-colored compound where as stable to room temperature. The complexes of monovalent Li^+ and trivalent Aluminum Al^{3+} are almost white and stable in air and have elemental composition [Li(AMMT)] and $Al(AMMT)_3$]. The complexes in general are insoluble in water and methanol but have fair solubility in dimethyl sulphoxide and dimethylformamide(DMF). The solution of freshly distilled A.R.DMF does not show appreciable electrical and electrical conductance value occur in the range of (8-14) $mole^{-1}ohm^{-1}cm^2$ supporting non-ionic in nature of complexes (Table 2). The magnetic susceptibility of compound at room temperature was determined by Gouy method as used and expected Li^+, Al^{3+}, Zn^{2+}, Cd^{2+}, and Hg^{2+} complexes was diamagnetic. The complexes of Zn(II), Cd(II), and

Table 2: Solubility and electrical conductance data (31°C)

Complex	Qualitative value in solvents				Molar conductance value Ohm^{-1}mol^{-1} cm^{2}{DMF}
	Water	Methanol	Benzene	DMF	
$C_3H_6N_4S$ (LH)	INS	SLS	SLS	FS	12
$(C_3H_3N_4S)_3Al$	INS	SLS	SLS	FS	6
$(C_3H_3N_4S)$ Li	INS	SLS	INS	FS	8
$(C_3H_4N_4S)_2Cd$	INS	SLS	INS	FS	10
$(C_3H_4N_4S)_2Hg$	INS	SLS	INS	FS	30

SLS: Slightly; S: Soluble; FS: Fairly soluble; INS: Insoluble

Table 3: I.R. Spectral bands of ligand (AMMTH)

S. No.	Band Positions in cm^{-1}	Assignments
1	3271.02	√(NH$_2$) phenolic
2	3111.64	√(NH)
3	2895	√(C-H) phenyl
4	1628.71	√(C=N)
5	1575.18	δ(NH)
6	1508.91	δ(NH$_2$)
7	1477.97	Phenyl ring (C=C)
8	1457.16	δ(CH$_3$)
9	1374.82	δ(C-C) phenyl group skeletal bands
10	1319.15	δ(C-C) phenyl group skeletal bands
11	1268.10	δ(C-N) +√(N-N)
12	1220.69	δ(C-N) +√(N-N)
13	1101.99	δ(C-N) +√(N-N)
14	1040.59	δ(C-N) +√(N-N)
15	984.41	δ(C-C)+out of plane phenyl ring
16	919.08	δ(C-C) + out of plane phenyl ring
17	741.61	δ(C-C) + out of plane phenyl ring
18	696.76	δ(C-C)
19	662.34	δ(C-N)
20	639.02	δ(N-N) + ring deformation vibration
21	538.25	δ(N-N) + ring deformation vibration
22	437.68	δ(N-N) + ring deformation vibration
23	415.52	δ(N-N) + ring deformation vibration

Table 4: I.R. Spectral bands of Aluminium complex

S. No.	Band Positions in cm^{-1}	Assignments
1	2208	√(NH$_2$)
2	1971	√(NH)
3	1867	√(C-H) phenyl
4	1789	√(C=N)
5	1621	δ(NH)
6	1557	δ(NH$_2$)
7	1485	Phenyl ring (C=C)
8	1460	δ(CH$_3$)
9	1300	δ(C-C) phenyl group skeletal band
10	1245	δ(C-C) phenyl group skeletal band
11	1152	√(C-N)+ √(N-N)
12	1019	√(C-N)+ √(N-N)
13	809	√(C-H) vibration
14	801	δ(N-N) + ring deformation vibration
15	732	δ(N-N) + ring deformation vibration
16	615	δ(N-N) + ring deformation vibration

Table 5: I.R. Spectral bands of lithium complex

S.No	Band Positions in cm^{-1}	Assignments
1	3302	√(NH$_2$)
2	2900	√(NH)
3	2216	√(C-H) phenyl
4	1650	√(C=N)
5	1610	δ(NH)
6	1557	δ(NH$_2$)
7	1485	Phenyl ring (C=C)
8	1460	δ(CH$_3$)
9	1320	δ(CH$_3$)
10	1245	δ(C-C) phenyl group skeletal bands
11	1152	δ(C-C) phenyl group skeletal bands
12	1029	√(C-N) +√(N-N)
13	942	√(C-N) +√(N-N)
14	801	√(C-H) Vibration
15	732	δ(N-N) ring deformation
16	622	δ(N-N) ring deformation vibration

Hg(II) are also colored and show strong charge transfer electronic band below 420nm.

The i.r spectrum of ligand shows (Tables 3-5) √(NH) and √(NH$_2$) vibration at 3271 and 3111cm^{-1}. A weak band located at 2895 cm-^{1} is attributed to (C-H) stretch of methyl group of ligand molecule. The prominent I.R. band located at 1628.75 cm^{-1}(I.R -1) is attributed to stretch of triazole ring. I.R band of ligand located at 1575 cm^{-1} are due to δ(NH$_2$) and δ(NH) vibration. The i.r. band found at 1977 and 1457cm^{-1} are due to δ(CH$_3$) of methyl group situated at 3rd position. The number of i.r. band in fingerprint region

Table 6: Zone of inhibition

Organism Name	Zone of inhibition (in mm) + S.D
LH (AMMTH)	
Streptococcus pyogenes	15.5±2.121
Bacillus subtilis	17.0±2.828
Escherichia coli	16.5±3.536
Enterococcus faecalis	13.5±0.707
Streptococcus aureus	16.0±4.243
Metal complex- I [(Al (AMMT)$_3$]	
Streptococcus pyogenes	18.0±9.899
Bacillus subtilis	15.5±3.536
Escherichia coli	17.0±2.828
Enterococcus faecalis	15.0±1.414
Streptococcus aureus	21.5±6.364
Metal complex- II [(Cd (AMMT)$_2$]	
Streptococcus pyogenes	13.5±0.707
Bacillus subtilis	Nil
Escherichia coli	Nil
Enterococcus faecalis	Nil
Streptococcus aureus	15.0±1.514

Zone of inhibition by DMSO – 00.00 mm

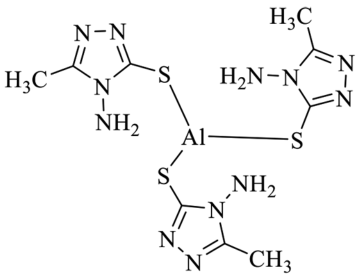
observation at 1374,13119,1289,1266,1220,1101, and 1040 cm^{-1}are due to √(N-N),√(C-C),√(C-N), and normal √(N-N) vibrations of 4-aminotriazole ring. A prominent i.r. band at 984 cm^{-1} present in ligand which disappears in complexes is assigned to (C=S) thione group present in ligand. Thione (C=S) gets tautomerized to (–N=C-SH) and deprotonated to form a neutral chelate ring with metal ions. The i.r. bands of ligands present at 741,656,633,532 473, and 475 cm^{-1} are out-of-plane bending bands and deformation vibrations. The i.r. band located at (732-721) cm^{-1} in complexes is assigned to √(C-S) vibrations of deprotonated and coordinated thiol sulfur of mercapto groups. Thus from i.r. spectral bands studies, it is cleared that the ligand 4-amino-5-mercapto-3-methyl-1,2,4- triazole is coordinated to metal atoms in complexes with deprotonated thiol sulfur and terminal –NH$_2$ nitrogen attached to 4th position of triazole ring nitrogen.

The ^{1}HNMR spectrum of ligand in CDCl$_3$ shows CH$_3$ group signal as singlet located at δ=2.18ppm and NH$_2$ signal at 2.41ppm. The ring (N-H) signal can be assigned to ^{1}HNMR band at 554 ppm. A small ^{1}HNMR signal located at δ 3.35 ppm is attributed to partially thiol (S-H) tautomer present in the ligand molecule. The (S-H) signal present in ligand is absent in complexes supported the deprotonation of (N-H) and (S-H) protons signal in complexes.

5. CONCLUSIONS

Thus from the physicochemical studies, the probable structure of complexes is shown below

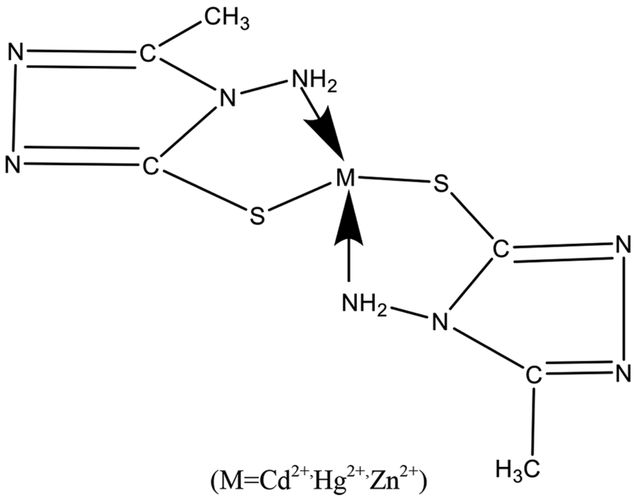
structure of aluminum complexes [Al(AMMT)$_3$]



tris((4-amino-5-methyl-4*H*-1,2,4-triazol-3-yl)thio)aluminum

(A)

Structure of Zn(II),Cd(II) and Hg(II) Complexes[M(AMTT)$_2$]



(B)

5.1. Antibacterial Properties

Antibacterial properties were analyzed for ligand and all the synthesized metal complexes using different bacterial stains (Table 6). The mixture was boiled for 40 minutes by stirring it continuously. About 0.002 g of the sample was taken on the strips of filter paper positioning on the petri dish with the help of a micropipette.

Antibacterial Screening Data of the Ligand and Their Metal Complexes.

5.2. Stock Concentration

LH(AMMTH) – 25 mg/ml

Metal complex – I [(Al(AMMT)$_3$] – 25 mg/ml

Metal complex – II [Cd(AMMT)$_2$] – 25 mg/ml

Solvent – DMSO

Volume loaded in well – 105µl

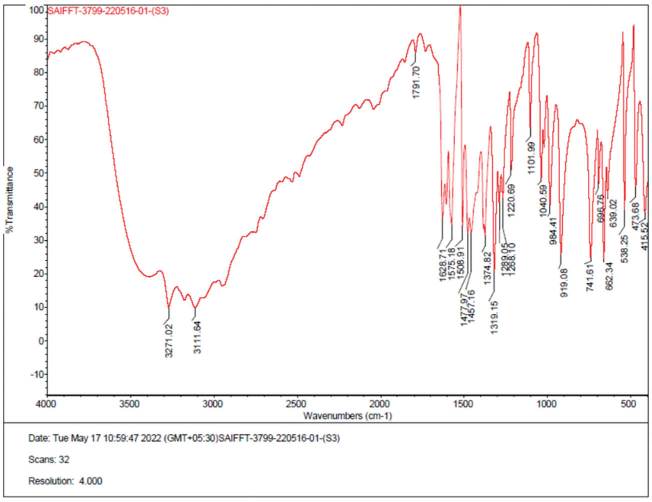
Hence, the amount loaded in well – 2mg

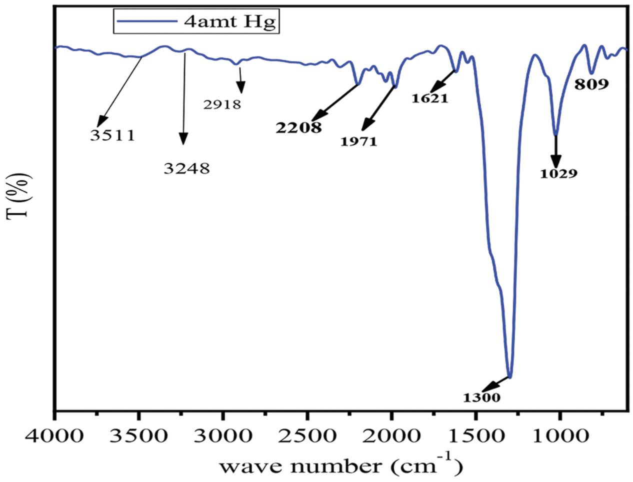
REFERENCES

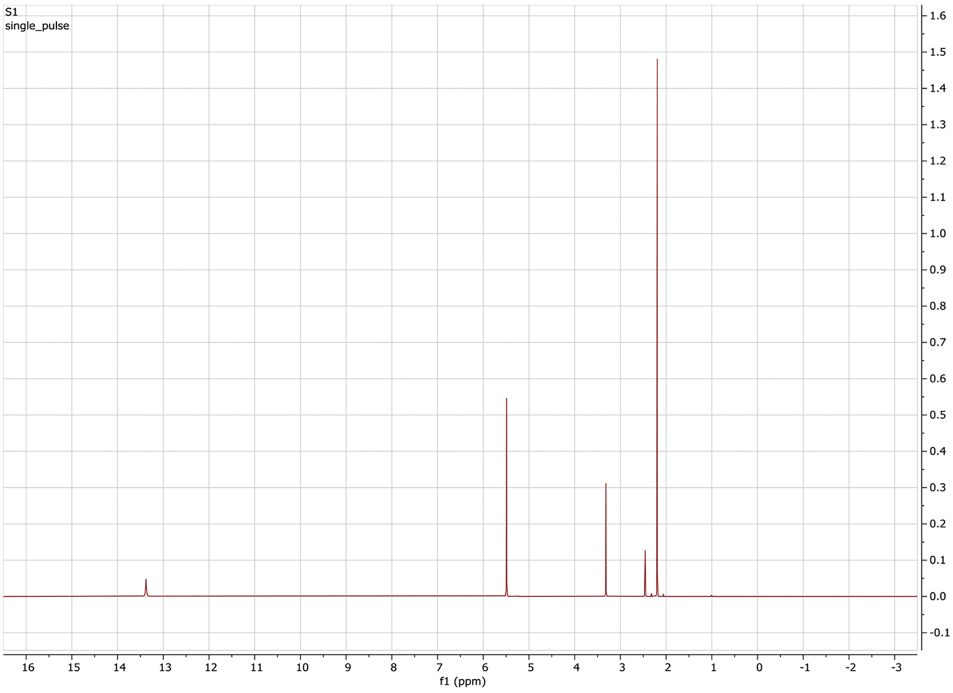
1. A. I. Al-Masoudi, Y. A. Al-Soud, N. J. Al-Salihi, N. A. Al-Masoudi. (2006) 1,2,4-Triazoles: Synthetic approaches and pharmacological importance. (Review), ***Chemistry of Heterocyclic Compounds***, **42:** 1377.
2. T. Propst, W. Vogel, A. Propst, O. Dietze, H. Braunsteiner, (1992) Synthesis, characterization, antibacterial studies of Co(II), Ni(II),

Cu(II) and Zn(II) complexes of some schiff base ligands, ***Journal of Molecular Medicine***, **70:** 55-58.

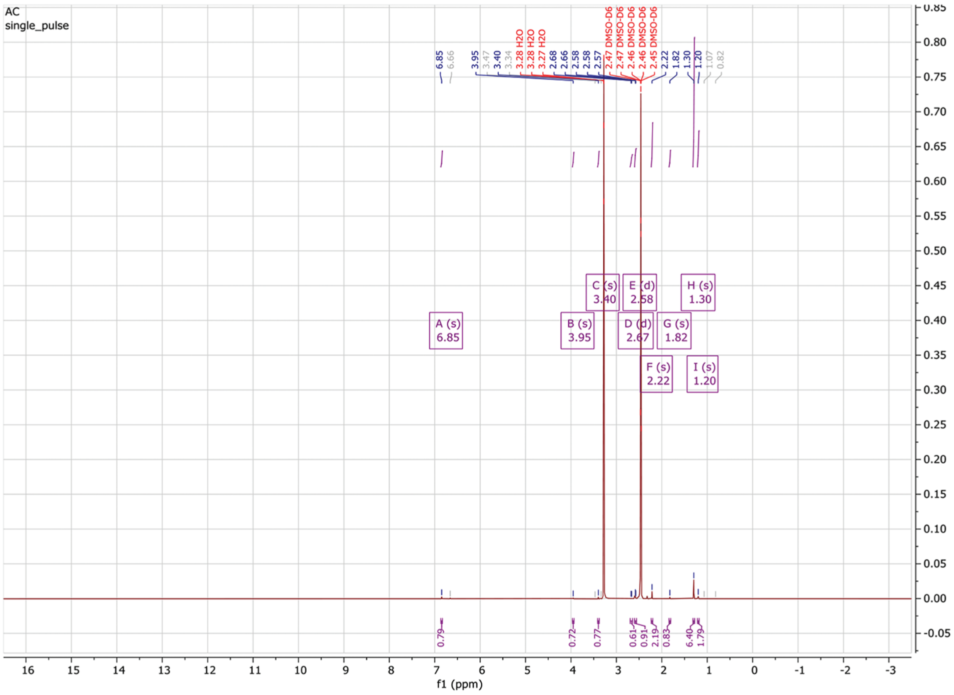
3. S. M. Stahl, (2008) Selective histamine H1 antagonism: Novel hypnotic and pharmacologic actions challenge classical notions of antihistamines, ***CNS Spectrums***, **13:** 1027-1038.
4. G. Capranico, G. Zagotto, M. Palumbo, (2004) Development of DNA topoisomerase-related therapeutics: A short perspective of new challenges, ***Current Medicinal Chemistry***, **4:** 335-345.
5. A. Iqbal, H.L. Siddiqui, C.M. Ashraf, M. Ahmad, G.W. Weaver, (2007) Synthesis, characterization and antibacterialactivity of azomethine derivatives derived from 2-formylphenoxyacetic acid, ***Molecules***, **12**:245-254
6. K. Vashi, H. B. Naik, (2004) Synthesis of novel schiff base and azetidinone derivatives and their antibacterial activity, ***E-Journal of Chemistry***, **1:** 272-276.
7. M. E. Hossain, M. N. Allam, J. Begum, M. A. Akbar, M. N. Uddin, F. E. Smith, R. C. Hynes, (1996) The preparation, characterization, crystal structure and biological activities of some Cu(II) complexes of the 2-benzoyl pyridine Schiff bases of S-methyl-and S-benzyldithiocarbazate, ***Inorganica Chimica Acta***, **249:** 207-213.
8. K. P. Sharma, V. S. Jolly, P. Phatak, (1998) Schiff base and their derivatives as potential anticancer agents, ***Journal of Ultra Scientist of Physical Sciences***, **10:** 263-266.
9. A. K. Sadana, Y. Mirza, K. R. Aneja, O. Prakash, (2003) Hypervalent iodine mediated synthesis of 1-aryl/hetryl-1,2,4-triazolo[4,3-a] pyridines and 1-aryl/hetryl 5-methyl-1,2,4-triazolo[4,3-a]quinolines as antibacterial agents, ***European Journal of Medicinal Chemistry***, **38:** 533-536.
10. Z. Rezaei, S. Khabnadideh, K. Pakshir, Z. Hossaini, F. Amiri, E. Assadpour, (2009) Design, synthesis, and antifungal activity of triazole and benzotriazole derivatives, ***European Journal of Medicinal Chemistry***, **44:** 3064-3067.
11. H. Guo-Qiang, H. Li-Li, X. Song-Qiang, H. Wen-Long, (2008) Design, Synthesis and Antitumor Activity of Asymmetric Bis(s-triazole Schiff-base)s Bearing Functionalized Side-Chain, ***Chinese Journal of Chemistry***, **26:** 1145-1149.
12. J. Jin, L. Zhang, A. Zhang, X. X. Lei, J. H. Zhu, (2007) Synthesis and biological activity of some novel derivatives of 4-amino-3-(D-galactopentitol-1-yl)-5-mercapto-1,2,4-triazole, ***Molecules***, **12:** 1596-1605.
13. G. B. Bagihalli, P. G. Avaji, S. A. Patil, P. S. Badami, (2008) Synthesis, spectral characterization, *in vitro* antibacterial, antifungal and cytotoxic activities of Co(II), Ni(II) and Cu(II) complexes with 1,2,4-triazole schiff bases, ***European Journal of Medicinal Chemistry***, **43:** 2639-2649.
14. Z. H. Chohan, M. Hanif, (2011) Synthesis and characterization of biologically active new Schiff bases containing 3-functionalized 1,2,4-triazoles and their zinc(II) complexes: crystal structure of 4-bromo-2-[(E)-(1H-1,2,4-triazol-3-ylimino)- methyl]phenol, ***Applied Organometallic Chemistry***, **25:** 753-760.
15. N. D. Jayanna, T. Manjuraj, M. Imadadulla (2024) Synthesis, Characterization, Density Functional Theory, Molecular Docking Studies, and Biological Activities of 6,8-dichloro-3-phenyl[1,2,4] triazolo[3,4-b] [1,3]benzoxazole Derivatives, ***Indian Journal of Advances in Chemical Science***, **12**: 204-211.
16. S. J. Lippard, J. M. Berg, (1999) ***Principles of Bioinorganic Chemistry***, Mill Valley, CA: University Science Books.
17. Z. H. Chohan, S. H. Sumrra, M. H. Youssoufi, T. B. Hadda, (2010) Synthesis, antiviral activity and cytotoxicity evaluation of Schiff bases of some 2-phenyl quinazoline-4(3)H-ones, ***European Journal of Medicinal Chemistry***, **63:** 3981-3998.
18. D. M. Taylor, D. R. William, (1995) ***Trace Element Medicine and Chelation Therapy***, United Kingdom: The Royal Society of Chemistry.
19. R. J. P. Williams, (2008) Metal ions in biological systems, ***Biological Reviews***, **28**: 381-4212.
20. Y. Lu, N. Yeung, N. Sieracki, N. M. Marshall, (2009) Design of functional metalloproteins, ***Nature***, **460:** 855-862.
21. S. Vidyasagar Babu, K. Hussain Reddy, (2013) Second derivative spectrophotometric determination of copper(II) using 2-acetylpyridine semicarbazone in biological, leafy vegetable and synthetic alloysamples, ***Indian Journal of Advances in Chemical Science***, **1:** 105-111.
22. G. Matela, R. Aman, C. Sharma, S. Chaudhary, (2013) Synthesis, characterization and antimicrobial evaluation of diorganotin(IV) complexes of schiff base, ***Indian Journal of Advances in Chemical Science***, **3:** 157-163.
23. S. Vidyasagar Babu, K. Hussain Reddy, (2012) Direct spectrophotometric determination of mercury (II) using 2-acetylpyridine thiosemicarbazone in environmental samples, ***Indian Journal of Advances in Chemical Science***, 1: 65-72.







^{1}HNMR OF LIGAND (AMMTH)



^{1}HNMR OF COMPLEX (Cd)