Synthesis, Characterizations, crystal structure, and Vitro Antifungal Activity of 4-amino-3-methyl-1H-1,2,4-triazole-5-thione and their metal complexes.

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ABSTRACT:

The compound 4-amino-3-methyl-1H-1,2,4-triazole-5-thione$C_3H_6N_4S$[LH],crystallizes in the monoclinic space group P21/C, with cell parameter a=8.872(4)A0,b=9.826(4)A0,c=6.548(3)A0,V=570.9(4)A03 and Z=4.The structure was solved by direct methods using SAELXS-97 and refined using SAELXS-97.The final residual factor is R1=0.0369 for 1004 reflections and 83 parameters. The complexes of the ligand are synthesized in their molar ratio 1:3. These complexes have been characterized by elemental analyses,molar conductance and spectroscopic stydies. The antibacterial activity of ligand and their metal complexes against various fungi has been investigated.

Keywords: **: crystal structure, triazole ,amino group, hydrogen bonding**

INTRODUCTION

Compounds of 1,2,4-triazole derivatives are found to posses diverse pharmacological activities(1) such as fungicidial,insecticidal,bactericidal,herbicidal,antitumor(2),anti-inflammatory(3),and central nervous system(CNS) stimulant properties(4).They are also used in dyes and lubricants and as analytical reagents(5) and antiviral agents(6). 1,2,4-triazole ligand complexes posses specific magnetic properties(7). The coordination chemistry of Aluminum and silicon is extensive with various geometries and coordination numbers known for both inorganic and organometallic complexes(8).Higher coordination numbers can be generated by inter/intramolecular interaction, especially in complexes where Aluminum and Lithium is bonded to electronegative atoms such as oxygen, nitrogen and sulfur. In the view of the diverse fields of applications of these complexes,we have synthesized and characterized some new ligand and their complexes with N and S doner ligands. Crystal structures of the ligand is present in this article.

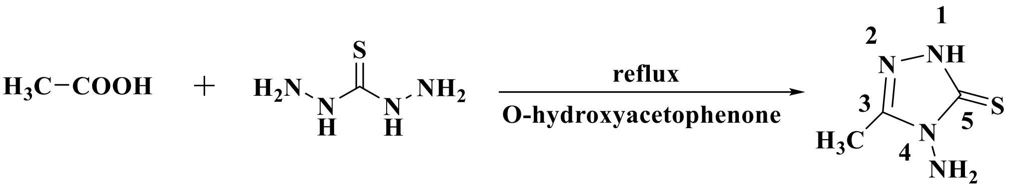
Experimental

In the synthesis of compounds chemical reagent were of abundantly pure and analytical category. By using digital capillary apparatus, the melting point of the compound were measured. With the help of Perkin -Elmer VERTEX 70 FT I.R(KBR), UV-VISIBLEspectrophotometer apparatus I.R, U.V were recorded.BY using Heidolyph NMR spectrometer in DMSO-d_6^{1}HNMR reading were recordeBy using Guoy balance magnetic susceptibility was determined.

Synthesis of triazole ligand(LH) 4-amino-3-methyl-1H-1,2,4-triazole-5-thione:

4-amino-3-methyl-1H-1,2,4-triazole-5-thione were prepared by refluxing ortho hydroxy acetophenone bythiocarbohydrazide in the presence of glacial acetic acid[9-15].

SCHIME I



4-amino-3-methyl-1H-1,2,4-triazole-5-thione

Thiocarbohydrazide was dissolved in ortho hydroxy acetophenone and it was added with glacial acetic acid. Then the mixture was refluxed for 6 hours.TLC was conducted to monitor the progress of the reaction. Then after cooling whole night sharp white crystals were obtained.

Yield: 92%, white crystal solid, M.P-(235-240)^0 C.

Analytical Calculation for $C_3H_6N_4S$:C -27.69%,H-4.61%,N-43.07%,S-24.61%

Synthesis of metal Complexes:

The two metal complexes were synthesized by the same process.

1.Synthesis of Al(III) Complex:

A ethanolic solution of $AlCl_3.6H_2O$(.307mmol,74mg) was added dropwise to a ethanolic solution of ligand(.615mmol,80mg). In this reaction mixture triethyl amine(1µmmol) was added. After this resultant mixture was continuouslystirred at room temperature 24 h. Blackish white precipitate is obtained which was filtered and washed with ethanol. The obtainedprecipitate dried under vacuum. The white crystals were obtained by the slow evaporation of blackish ethanolic solution.Yield:68mg(86%).M.P-275^{0}C.Analytical calculation for $C_9H_{15}N_{12}AlS_3$: C-26.08%,H-3.62%,N-40.57%,Al-6.44,S-7.72%

2.synthesis of Li(II) Complex:

A ethanolic solution of LiCl(.307mmol,43mg) was added to aethanolic solution of ligand (.615 mmol,80mg).In this reaction mixture triethyl amine(1µmmol) was added. After this resultant mixture was continuously stirred at room temperature 24 h. Blueish precipitate is obtained which was filtered and washed with ethanol. The obtained precipitate dried under vacuum. The blackishprecipitatewere obtained by the slow evaporation blueish ethanolic solution. Yield:70mg(88%).M.P-258^{0}C.Analytical calculation for$C_9H_{15}N_{12}LiS_3$:C-27.41%,H-3.80%,N-42’63%,Li-1.77%,S-8.12%

Single crystal X-ray structure analysis 4-amino-3-methyl-1H-1,2,4-triazole-5-thione(LH):

The single crystal X-ray of ligand was obtained by slow evaporation of liquid solution in ortho hydroxy acetophenone at room temperature. The suitable crystal for single crystal X-raywas mounted on glass fibers and it is used for data collection.The X-ray intensity data were obtained at 103 k on a Bruker smart CCD detector using Mo K αradiation(λ=0.71073 A^0).The structure solution and refinement were obtained by using the program SHELXL-97.The summary of crystal data and their crystal refinement were listed in Table 1.

Table 1

Crystal X-ray diffraction data and structure refinement parameters for LH

Bond precision: C-C = 0.0030 A Wavelength=0.71073

Cell:	a=8.872(4)	b=9.826(4)	c=6.548(3)
	alpha=90	beta=90.080(13)	gamma=90
Temperature:	296 K		

	Calculated	Reported
Volume	570.8(4)	570.9(4)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C3 H6 N4 S	?
Sum formula	C3 H6 N4 S	C3 H6 N4 S
Mr	130.18	130.18
Dx,g cm-3	1.515	1.515
Z	4	4
Mu (mm-1)	0.455	0.454
F000	272.0	272.0
F000'	272.54	
h,k,lmax	10,11,7	10,11,7
Nref	1004	1004
Tmin,Tmax		
Tmin'		

Correction method= Not given

Data completeness= 1.000 Theta(max)= 25.000

R(reflections)= 0.0286(837) wR2(reflections)= 0.0750(1004)

S = 1.018 Npar= 83

Table IA.

Hydrogen bond parameters found inCrystal Structure of ligands

D—H...A	D—H (Å)	H...A (Å)	D...A (Å)	<D-H-A (°)	Symmetry
N2—H2...S1	1.03	2.333	3.23	144.87	-x+1,+y+1/2,+z
N4—H4B...N2	1.03	2.762	3.772	166.79	-x+1,+y-1/2,-z+1/2

N4—H4B...S1	1.03	2.732	3.524	133.85	-x+1,+y-1/2,+z
C1—H1C...N3	1.08	2.813	3.591	128.95	-x,+y-1/2,-z+1/2

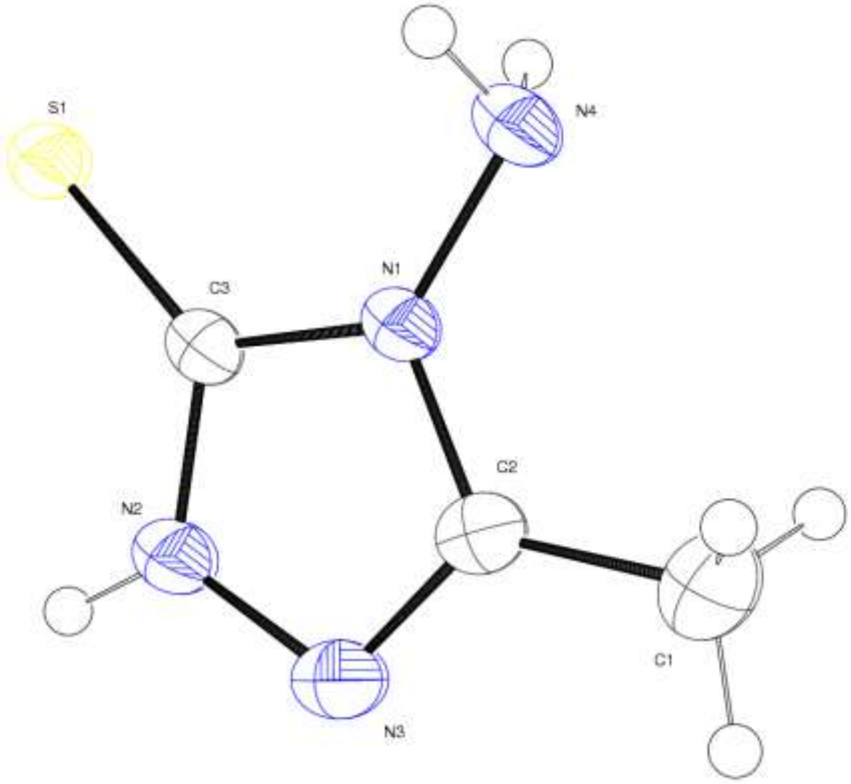


FIGURE I: ORTEP DIAGRAM

Antibacterial properties:

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

Results and discussion

Synthesis

The general synthesis of the Schiff base(HL) and its metal complexes1and2 were shown in scheme **1.**3-methyl-4-amino-1H-1,2,4-triazole-5-thiones(HL) were prepared by reacting acetic acid together with thiocarbohydrazide in molar ratio1:1in theorganic solvent ortho hydroxy acetophenone.Finally the Schiff base react with metal of Al and Li in the molar ratio 3:1 respectively to afford the complexes. The ligand and it's complexesare soluble in ethanol and highly soluble in DMSO and DMF. Theobtained complexes are microcrystalline in solid and they were stable in air with melting points above 200^{0}C.Metal ions in 1 and 2 were co-ordinated by nitrogen and sulphur doners from Schiff base ligand.The elementaland spectral analyses agree well with the proposed formula of the ligand and complexes.

IR Spectra

IR spectra of the ligands shows a band at 2700cm-1 due to presence of ν(S-H) and at 1100 cm-1 is assigned to ν(C=S)[16].In the metal complexes a band is not assigned at 2700 cm-1 due to deprotonation of thiol group and a new band appear at 750 cm-1 which is assigned to ν(C-S) indicating there by complexation through sulphur atom.Metal Sulfurr bond formation is further supported by a band at 410cm-1and 455cm-1 for ν(Al-S) and ν(Li-S)[17,18] respectively. A strong band in the region of 1623-1605 cm^{-1} for the free ligands assigned to ν(N=C-H) exhibits a shift of 10-15cm^{-1} in the spectra of the metal complexes ,indicating co-ordination through the azomethine nitrogen[19,20] atom of the Schiff base. Formation of metal nitrogen bond at 535cm^{-1} and 575cm^{-1} for ν(AL-N) and ν(Li-N)[21,22] respectively, indicating the the co-ordination of the of the ligand to the central metal atom through the azomethine nitrogen atom. The infrared spectral data of the ligands and their metal complexes are listed in Table II.

TABLE II

IR Spectroscopic Data (cm^{-1}) of the Ligands and Their Metal Complexes

	V(S-H)	V(-C=N)	v(-C=S)	V(-C-S)	V(M-S)	V(M-N)
Ligand	2750	1623	1096			
Metal Complex I	30831080			747	402	523
Metal Complex II				752	410	535

^{1}HNMR Spectra

The ^{1}HNMR spectroscopic data of the ligands and their Aluminium and Lithium complexes have been recorded in the DMSO-d$_6$.INthe NMR spectra of the metal complexes they indicate a shift of elctron density from the ligand to metal atom.The broad signal at δ10.6 ppm is due to the -SH protons in the ligands.Disapearance of the signal for the -SH protons in the spectra of the metal complexes supported to deprotation of the thiol group.The signal of the azomethine protons is shiftedto high field in the spectra of the metal complexes of Al and Li.It appears at 8.60-8.02 ppm as compared to 8.70ppm in the Schiff base ligand.This indicatescomplexation to the metal atom through the azomethine nitrogen atom.Additional signals in the spectra of the metal complexes of Al and Li were found in the range of 1.0-0.50ppm due to the methyl protons.The ^{1}HNMR spectroscopic data of the complexes are given in the Table III.

TABLE III

^{1}HNMR Chemical Shifts of the Ligands and Their Metal Complexes

	Aromatic-H	-SH	Azomethine-H	-CH3
LH	7.46-8.15	10.6	8.7	2.46
Metal Complex I	7.1-7.8		8.48	2.52,0.84
Metal Complex II	6.85-7.5		8.1	2.6,0.5

monolithium(VII) tris((3-methyl-5-sulfido-4*H*-1,2,4-triazol-4-yl)amide)

FIGURE II Proposed structure of the 1:3 metal complexes.

Antifungal Activity

The antifungal activity of the ligands and of their metals complexes with aluminium and Lithium have been screened against *Bacillus subtilis, Streptococcus pyogens, Escherichia coli, Enterococcus faecalis, Streptococcus aureus by reported method.All of the complexes tested were found to be most active against, Streptococcus aureus showing maximum inhibition, but less active against Enterococcus faecalis .The antifungal activity of the of ligand is slightly less than the* *metal complex I but more active with respect to metal complex II. The fungicidal screening data are complied in Table IV.*

Antifungal Screening Data of the Ligand and Their Metal Complexes

Stock Concentration

LH – 20 mg/ml

Metal complex I – 20 mg/ml

Metal complex II – 20 mg/ml

Solvent – DMSO

Volume loaded in well – 100 µl

So, the amount loaded in well – 2mg

Table IV: - Zone of inhibition

LH	
Organism Name	**Zone of inhibition (in mm) + S.D**
Streptococcus pyogens	17.5 ± 2.121
Bacillus subtilis	18.0 ± 2.828
Escherichia coli	17.5 ± 3.536
Enterococcus faecalis	14.5 ± 0.707
Streptococcus aureus	17.0 ± 4.243
Metal complex I	
Streptococcus pyogens	19.0 ± 9.899
Bacillus subtilis	15.5 ± 3.536
Escherichia coli	18.0 ± 2.828
Enterococcus faecalis	15.0 ± 1.414
Streptococcus aureus	22.5 ± 6.364
Metal complex II	
Streptococcus pyogens	12.5 ± 0.707
Bacillus subtilis	Nil
Escherichia coli	Nil
Enterococcus faecalis	Nil
Streptococcus aureus	16.0 ± 1.414

Zone of inhibition by DMSO – 00.00 mm

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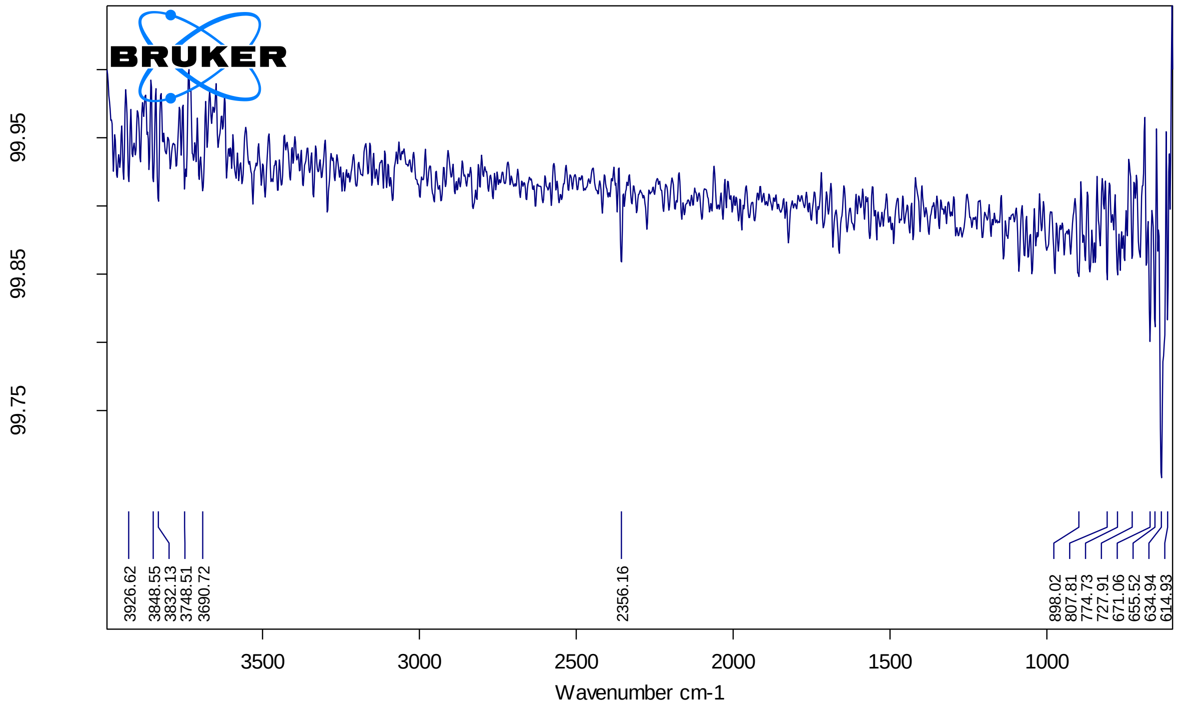

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Fig 1:IR of4-amino-3-methyl-1H-1,2,4-triazole-5-thione

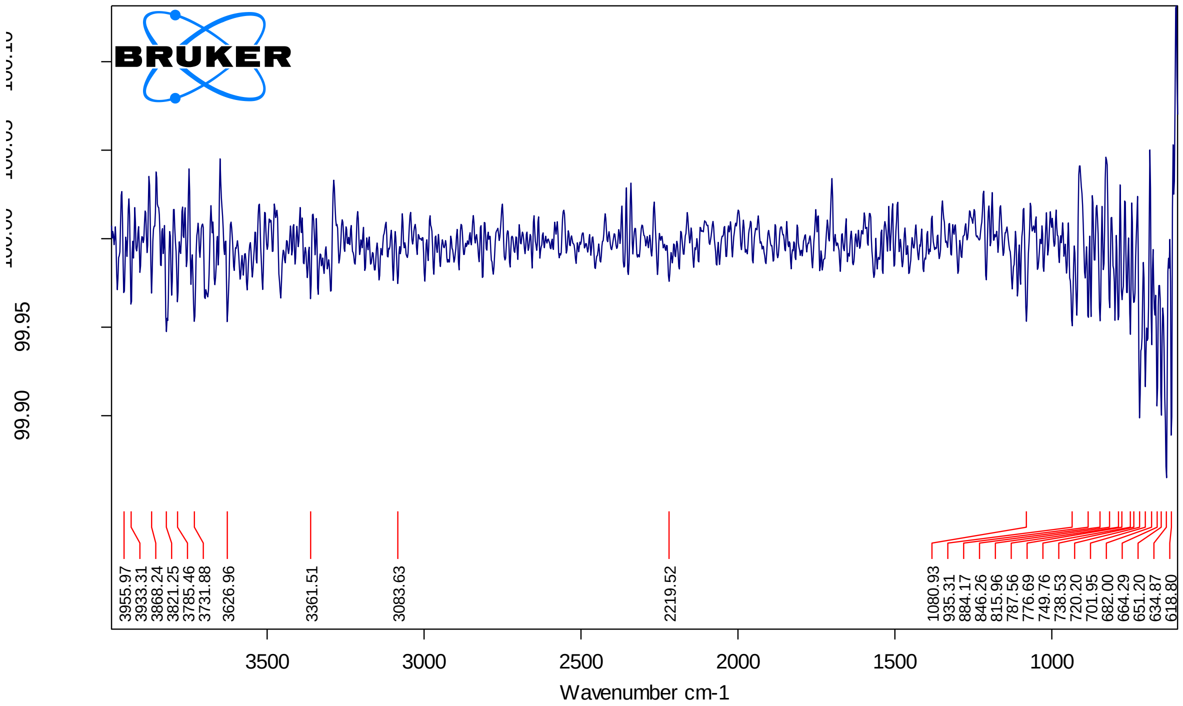

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Fig 2: IR of metal complex 1

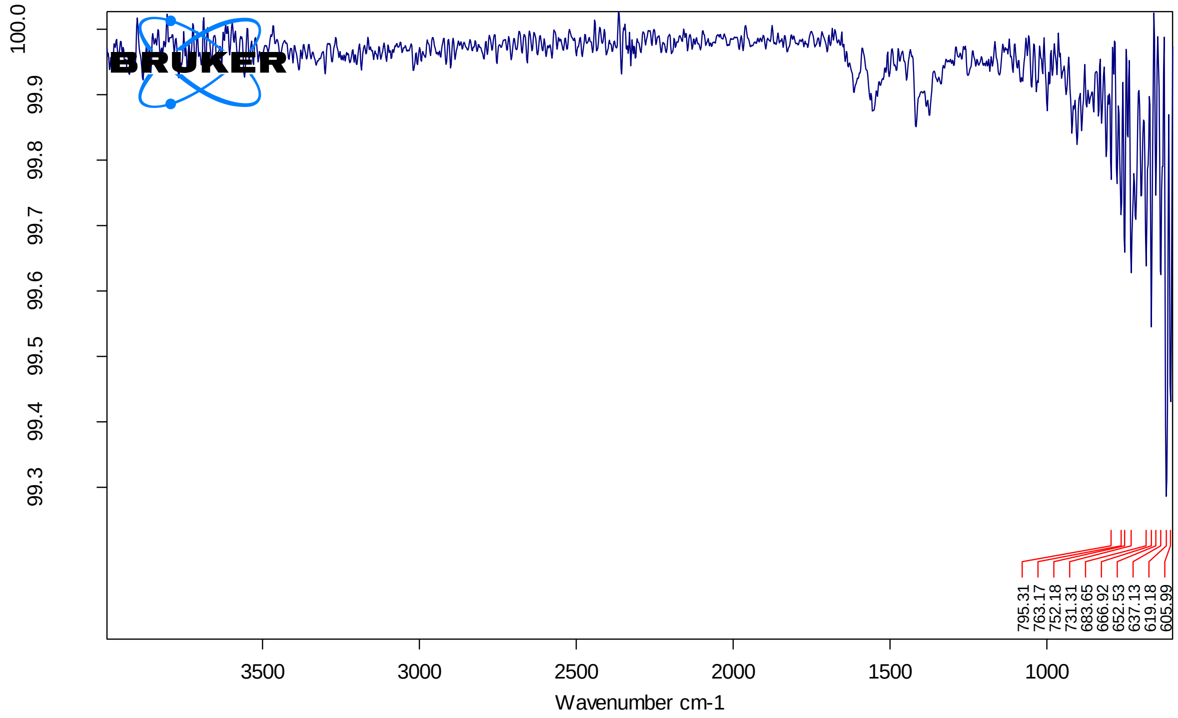

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Fig 3: IR of metal complex 2

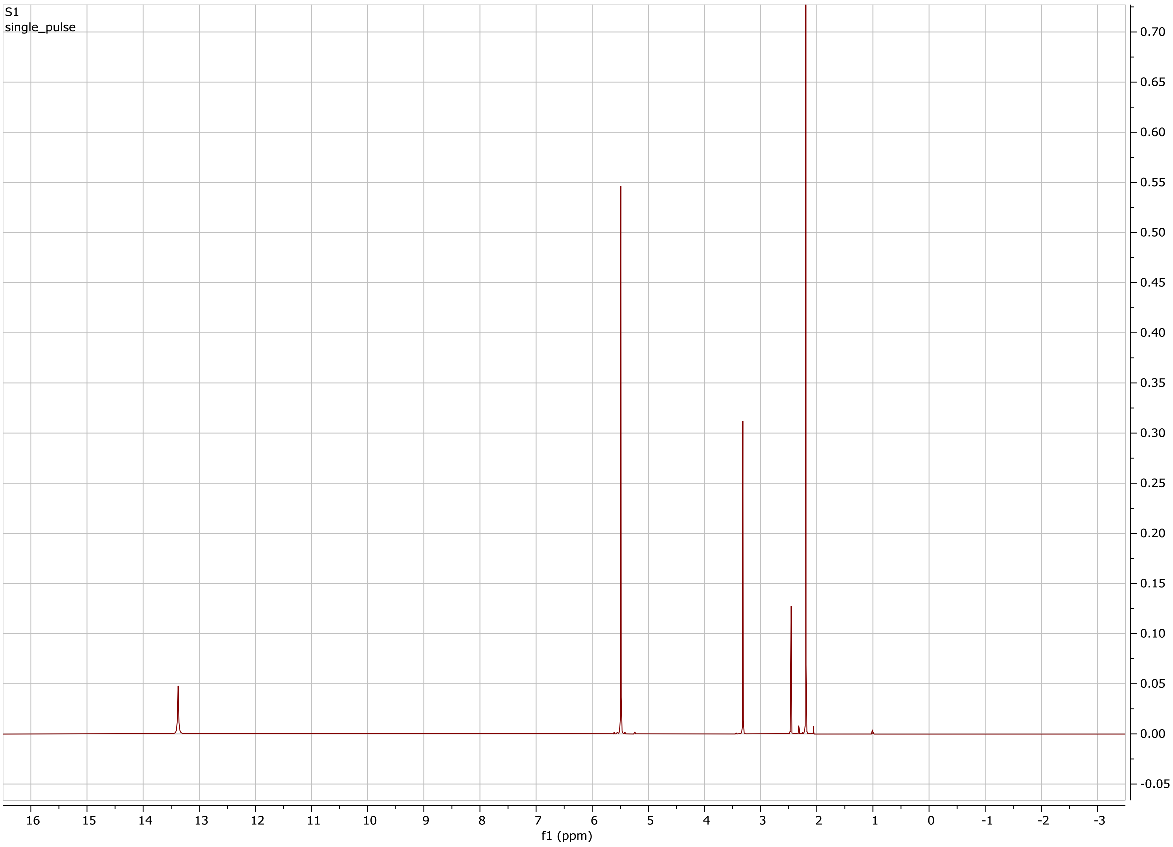

Fig4: 1HNMR of 4-amino-3-methyl-1H-1,2,4-triazole-5-thione

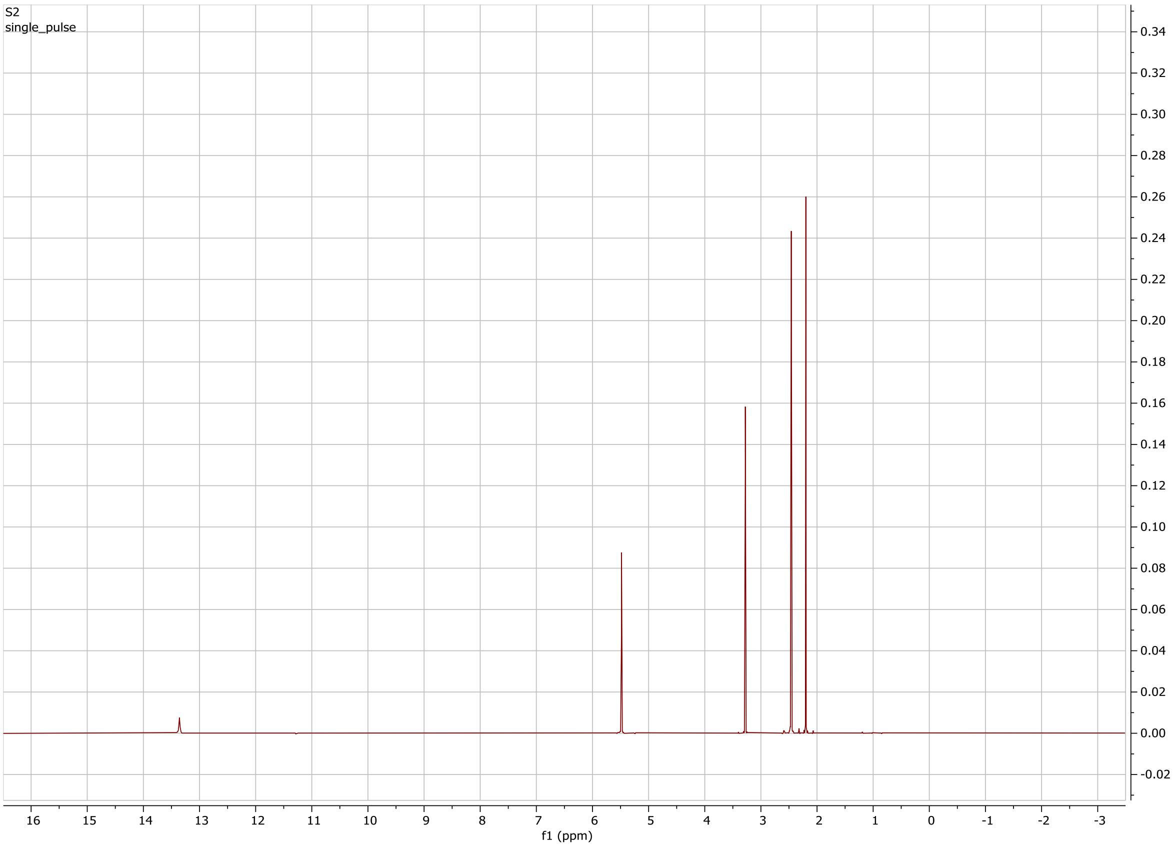

Fig5: 1HNMR of complex 1

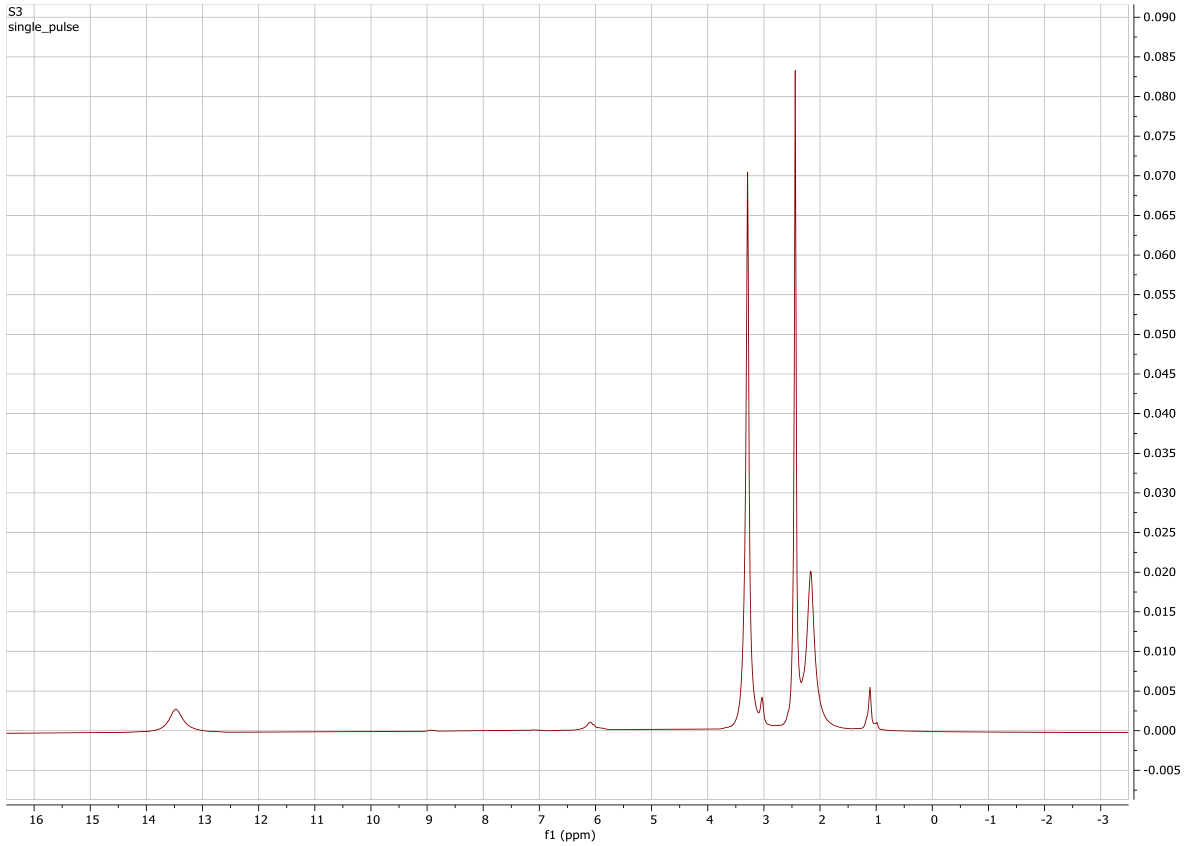

Fig6: 1HNMR of complex 2