

Supporting Information

Design, synthesis and structure of a trinuclear copper(II) complex having Cu₃OH core with regard to aspects of antiproliferative activity and magnetic properties

Naba Kr Mandal^a, Sudeshna Nandi^{b,c}, Samia Benmansour,^d Carlos J. Gómez-García^d,
Krishnendu Acharya^b, Jnan Prakash Naskar^{*a}

^a*Department of Chemistry, Jadavpur University, Kolkata 700 032, India*

^b*Department of Botany, Molecular and Applied Mycology and Plant Pathology Laboratory, University of Calcutta, 35 Ballygunge Circular Rd., Kolkata 700 019, India*

^c*Department of Botany, Vedanta College, Kadapara, Phoolbagan, Kolkata 700 054, India*

^d*Departamento de Química Inorgánica, Universidad de Valencia, Dr. Moliner, 50, 46100 Burjasot (Valencia), Spain*

**Corresponding author: Jnan Prakash Naskar*

Fax: +91 33 2414 6223; E-mail: jpnaskar@rediffmail.com

Experimental

Materials

Analytical reagent grade 5-bromothiophene carboxaldehyde (97%) and 2,3-butanedionemonoxime ($\geq 99.0\%$); reagent grade hydrazine hydrate (50-60%) were purchased from Sigma-Aldrich (St. Louis, Missouri, United States). High purity (99.9%) spectroscopic grade methanol, procured from Spectrochem (Mumbai, India), was used for electronic spectroscopic work. Dulbecco's Modified Eagles Medium (DMEM), 4',6-diamidino-2-phenylindole (DAPI), Acridine orange (AO), Ethidium bromide (EtBr) were purchased from Himedia (Mumbai, India). Water soluble tetrazolium (WST) was purchased from Takara Bio Inc, Japan. Trypan blue dye and crystal violet were purchased from Sigma-Aldrich (St. Louis, Missouri, United States). Antibiotic-PenStrep, Amphotericin B and Foetal bovine serum (FBS) were procured from MP Biomedicals, United States and Trypsin EDTA from Gibco, Waltham (MA, USA). All other chemicals were of analytical grade and were used as received.

Compound **1** was dissolved in dimethyl sulfoxide (DMSO) (Merck, Kenilworth, NJ, USA) to have a mother stock of 40 mM, which had been further diluted for various experimental

assays. Care had been taken so that the concentration of DMSO did not exceed 0.5-0.8% at any point of our experimental procedure.

Physical measurements

Melting point of the ligand (**HL**) was determined with an electro-thermal digital melting point instrument (SUNSIM, India). It is uncorrected. NMR (^1H and ^{13}C) spectra of **HL** were acquisitioned on a Bruker DPX (300 MHz) spectrometer. Tetramethylsilane (TMS) was used as an internal standard reference. A UV-1900i spectrophotometer (SHIMADZU) (JAPAN) was employed to record the electronic spectra of **HL** and **1** in spectroscopic grade methanol at room temperature. FT-IR spectra ($4000\text{-}400\text{ cm}^{-1}$) of **HL** and **1** were accrued, using KBr pellets, on a SHIMADZU FTIR-8400S spectrophotometer (JAPAN). Electron ionisation mass spectrum of **HL** was recorded on a MStation-JMS-700, JEOL (JAPAN). Ionic conductivity measurement of **1** were performed in methanolic solution at room temperature with a Systronics India direct conductivity meter (Model 304). The conductometer was calibrated using a standard 0.1M KCl solution. EPR measurements on **1** were carried out on a Magnettech GmbH MiniScope MS400 spectrometer. The spectrum was recorded at low temperature (143 K) in frozen N,N-dimethylformamide (DMF) solution. The spectrometer was equipped with a temperature controller, TC H03. The spin resonance spectrometer was equipped with an FC400 frequency detector. EPR spectrum of **1** was simulated using the EasySpin software package.¹

Variable-temperature magnetic susceptibility measurements were carried out in the temperature range 2-300 K with an applied magnetic field of 100 mT on a polycrystalline sample with a mass of 71.872 mg using a Quantum Design MPMS-XL-5 SQUID susceptometer. The susceptibility data were corrected for the sample holder previously measured using the same conditions and for the diamagnetic contribution of the sample as deduced by using Pascal's constant tables.²

Crystallographic data collection and refinement

Single dark green needle-shaped crystals of **1** were used. A suitable crystal with dimensions $0.12 \times 0.21 \times 0.24\text{ mm}^3$ was selected and mounted on a tiny fiber glass. The crystal data was collected on a Bruker D8 Venture Microfocus APEX-II diffractometer with a Mo-K α (graphite-monochromated) radiation source ($\lambda = 0.71073\text{ \AA}$) (equipped with a CCD area detector). The diffraction data was collected with a ω scan width of 1.00 degree and exposure time 10s. The data collection for **1** was managed by the APEX3(v2017.3-0) software

package. The crystal was kept at low temperature, $T = 145(2)$ K during data collection. Data were measured using ω/ϕ scans with Mo $K\alpha$ radiation. The diffraction pattern was indexed and the total number of runs and images was based on the strategy calculation from the program Bruker APEX2.³ The maximum resolution that was achieved was $\Theta = 21.00^\circ$ (0.99Å). The structure was solved and the space group $P-1$ (# 2) was determined by the ShelXT 2014/5 solution program package using iterative methods.⁴ Olex2 1.5-dev was used as the graphical interface.⁵ Data reduction, scaling and absorption corrections were performed using Bruker SAINT. Data reduction, scaling and absorption corrections were performed using Bruker SAINT. The final completeness is 99.85 % out to 21.00° in Θ . SADABS.⁶ The absorption coefficient of **1** is 4.435 mm^{-1} at wavelength(λ) 0.71073 Å. The minimum and maximum transmissions are respectively of 0.495 and 0.746. The model was refined with olex2.refine1.5-dev using full matrix least squares minimisation on F^2 .⁷ All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were calculated geometrically and refined using the riding model. Hydrogen atom positions were calculated geometrically and refined using the riding model. The crystallographic refinement data of **1** are tabulated in Table S1. The structure quality indicators are presented in Table S2. Some selected bond lengths in Å and bond angles in $^\circ$ are tabulated in Tables S3 and S4 respectively.

Table S1 Crystal data and structure refinement for **1**

CCDC	2270365
Formula	$\text{C}_{28}\text{H}_{33}\text{Br}_3\text{Cl}_2\text{Cu}_3\text{N}_9\text{O}_{14}$
	S_3
$D_{\text{calc.}}/\text{g cm}^{-3}$	1.961
μ/mm^{-1}	4.435
Formula Weight	1317.077
Colour	dark green
Shape	needle-shaped
Size/ mm^3	$0.12 \times 0.21 \times 0.24$
T/K	145(2)
Crystal System	triclinic
Space Group	$P-1$
$a/\text{Å}$	8.140(5)
$b/\text{Å}$	14.632(10)
$c/\text{Å}$	19.569(11)
$\alpha/^\circ$	85.11(4)
$\beta/^\circ$	85.25(2)
$\gamma/^\circ$	74.26(2)
$V/\text{Å}^3$	2231(2)
Z	2
Z'	1
Wavelength/Å	0.71073
Radiation type	Mo $K\alpha$
$\Theta_{\text{min}}/^\circ$	2.47
$\Theta_{\text{max}}/^\circ$	21.00
Measured Refl's.	24437
Indep't Refl's	4784

Ref'l's $I \geq 2 \sigma(I)$	3404
R_{int}	0.1042
Parameters	547
Restraints	0
Largest Peak	1.5671
Deepest Hole	-0.7822
GooF	1.0791
$wR2(\text{all data})$	0.1372
$wR2$	0.1176
$RI(\text{all data})$	0.0771
RI	0.0494

Table S2 Structure quality indicators

Reflections	d min (MoK α)	$I/\sigma(I)$	R_{int}	Full 42.0°
	2 Θ = 42.0° 0.99	11.8	10.42%	100
Refinement	Shift	Max Peak	Min Peak	GooF
	-0.001	1.6	-0.8	1.079

Table S3 Selected bond lengths in Å for **1**

Atoms	Length/Å	Atoms	Length/Å
Cu1-O2	1.941(6)	Cu3-N7	176.9(3)
Cu1-O1	1.964(7)	Cu3-N8	91.3(3)
Cu1-O5	1.968(6)	Cu2-O1	87.0(3)
Cu1-N2	2.042(7)	Cu2-O3	100.3(3)
Cu1-N1	2.344(7)	Cu2-O6	80.6(3)
Cu3-O4	1.936(6)	Cu2-N4	159.2(3)
Cu3-O1	1.951(7)	Cu2-N5	90.5(3)

Table S4 Selected Bond Angles in ° for **1**.

Atoms	Angle/°	Atoms	Angle/°
O1-Cu1-O2	91.4(3)	N8-Cu3-O4	101.5(3)
O5-Cu1-O2	90.5(2)	N8-Cu3-O1	166.9(3)
O5-Cu1-O1	97.4(2)	N8-Cu3-N7	80.8(3)
N2-Cu1-O2	100.2(3)	O3-Cu2-O1	91.4(2)
N2-Cu1-O1	159.2(3)	O6-Cu2-O1	92.3(2)
N2-Cu1-O5	99.7(3)	O6-Cu2-O3	96.7(3)
N1-Cu1-O2	176.8(3)	N4-Cu2-O1	88.2(3)
N1-Cu1-O1	87.0(3)	N4-Cu2-O3	175.4(3)
N1-Cu1-O5	92.4(3)	N4-Cu2-O6	88.0(3)
N1-Cu1-N2	80.6(3)	N5-Cu2-O1	166.1(3)
O1-Cu3-O4	90.6(2)	N5-Cu2-O3	100.3(3)
N7-Cu3-O4	176.6(3)	N5-Cu2-O6	93.7(3)
N7-Cu3-O1	87.3(3)	N5-Cu2-N4	79.5(3)

The crystals were poorly diffracting and of low quality at higher bragg angles. Therefore, no reflections at higher theta angle were detected. On repeated recrystallisation and fresh preparation over several times, we could not generate single crystal of satisfactory diffraction quality. We have attached below two images $I/\sigma(I)$ vs. Resolution and Rmerge vs. resolution.

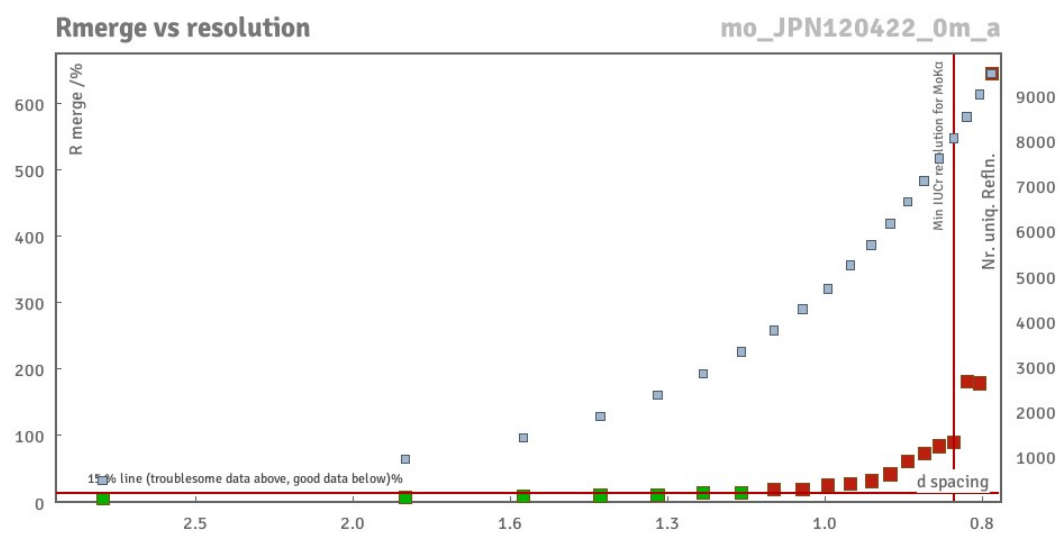
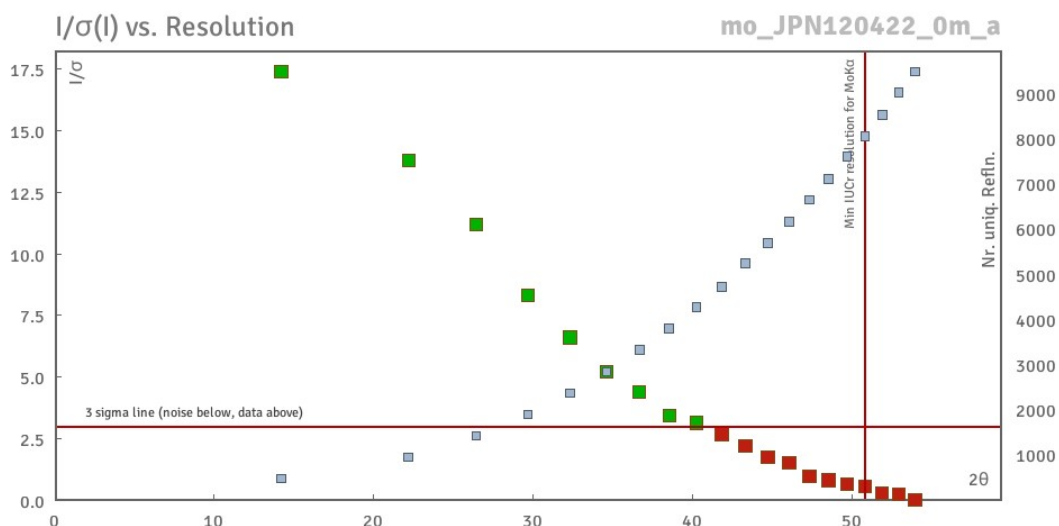


Table S5 Shorter intra- and inter-trimer interactions in compound **1**.

Atoms	D-H (Å)	H···A (Å)	D-H···A (°)	D···A (Å)
*C5-H5···O2	0.950	2.121	149.4	2.978
*C14-H14···O3	0.950	2.200	138.9	2.982
*C23-H23···O4	0.950	2.088	157.2	2.987
C2-H2A···S2	0.980	2.916	171.4	3.887
O8···Br3				3.134
O8···Br2				3.295
O1···O13				2.695
O12···O13				3.015
O9···O13				2.739
O6···O13				2.891

* Intra-trimer H-bonds.

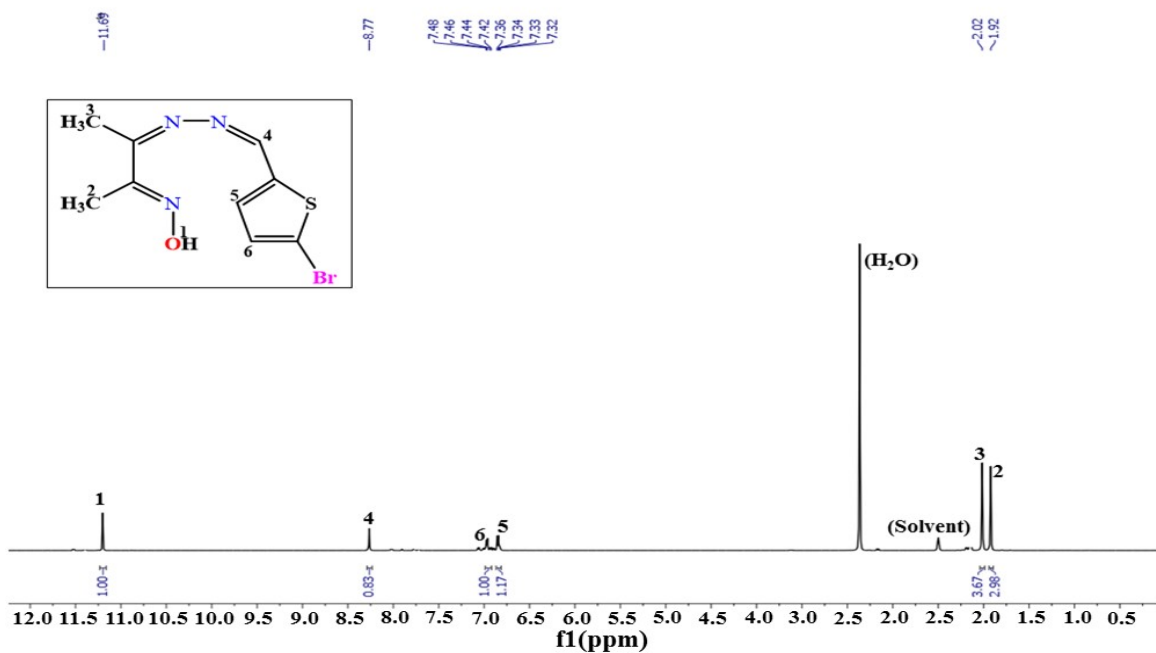


Fig. S1: ^1H NMR spectrum of ligand (HL) in DMSO-d_6

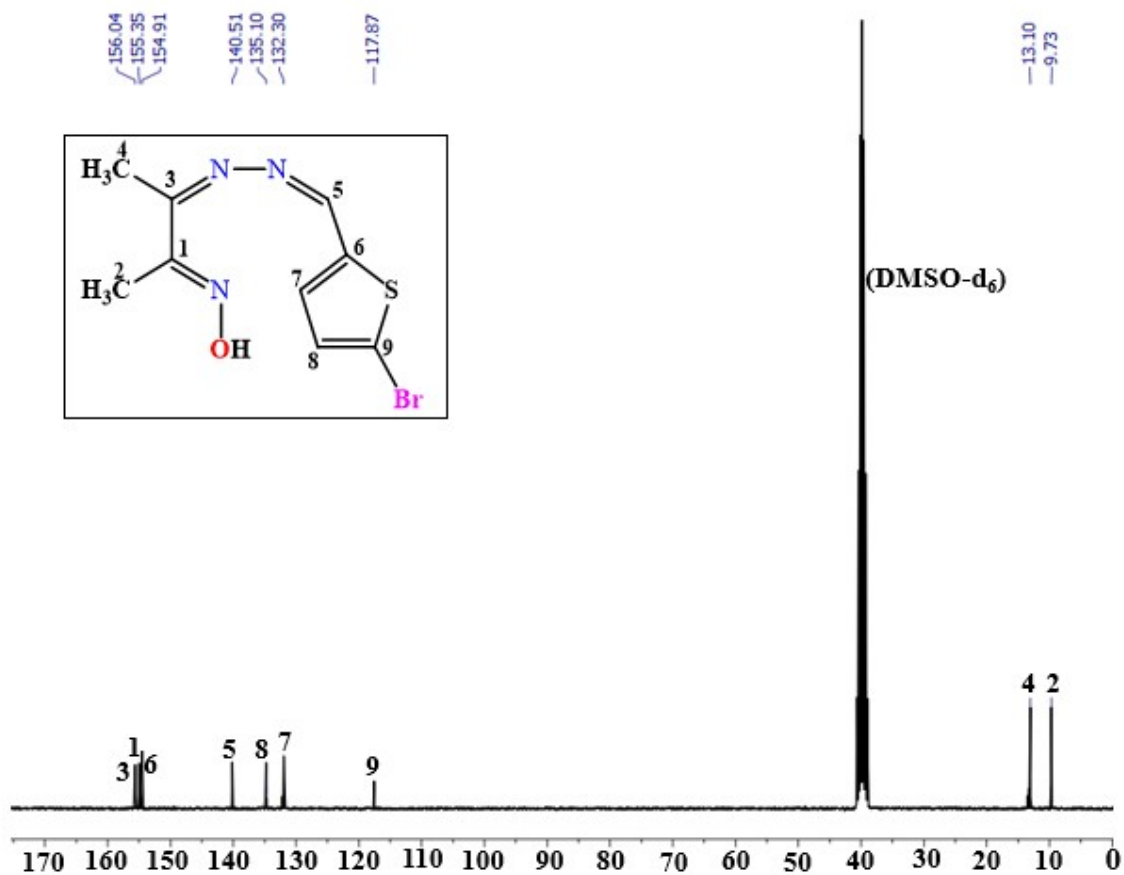


Fig. S2. ^{13}C NMR spectrum of HL in DMSO-d_6

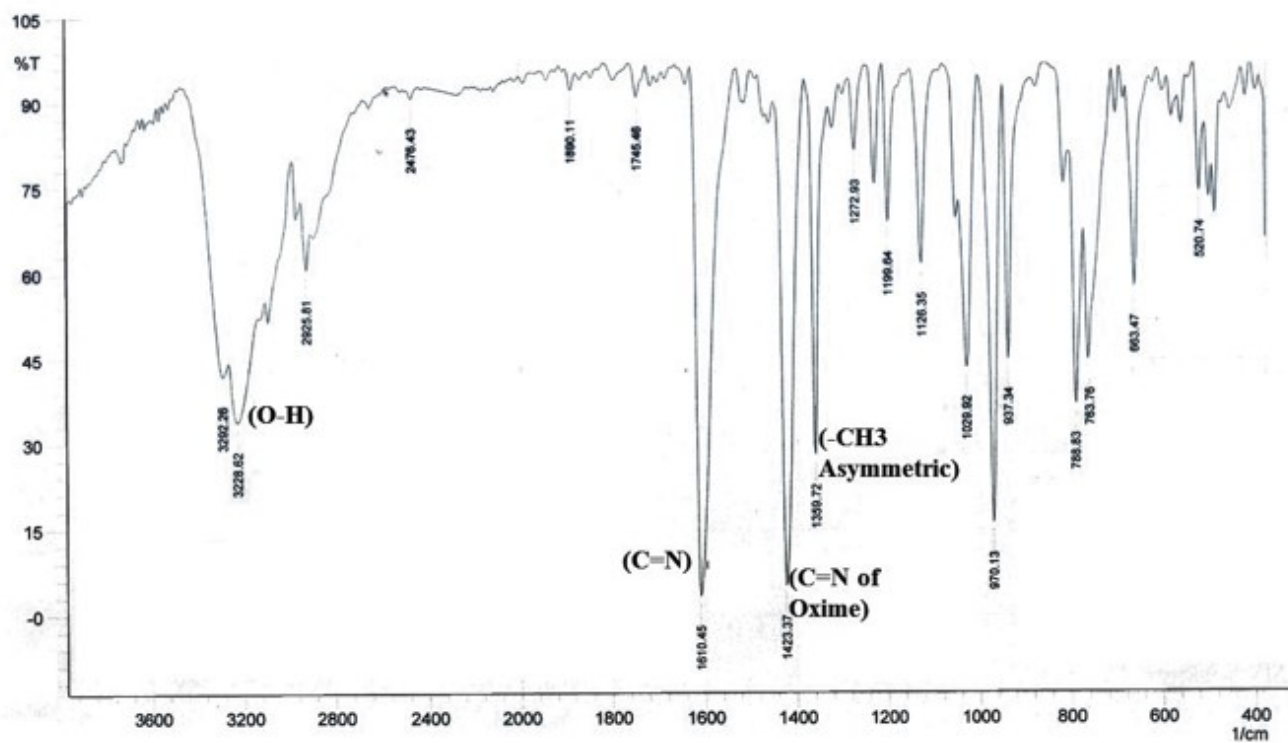


Fig. S3. FT-IR spectrum of HL

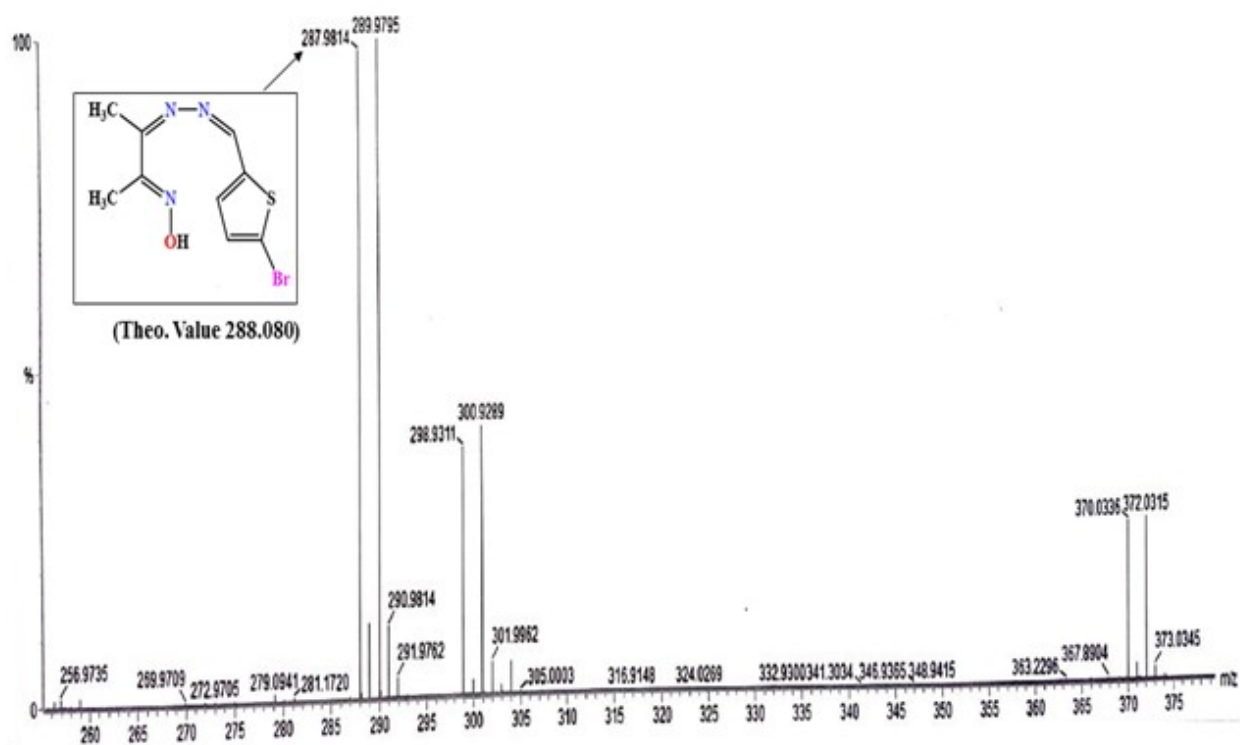


Fig. S4. ESI-MS of ligand (HL)

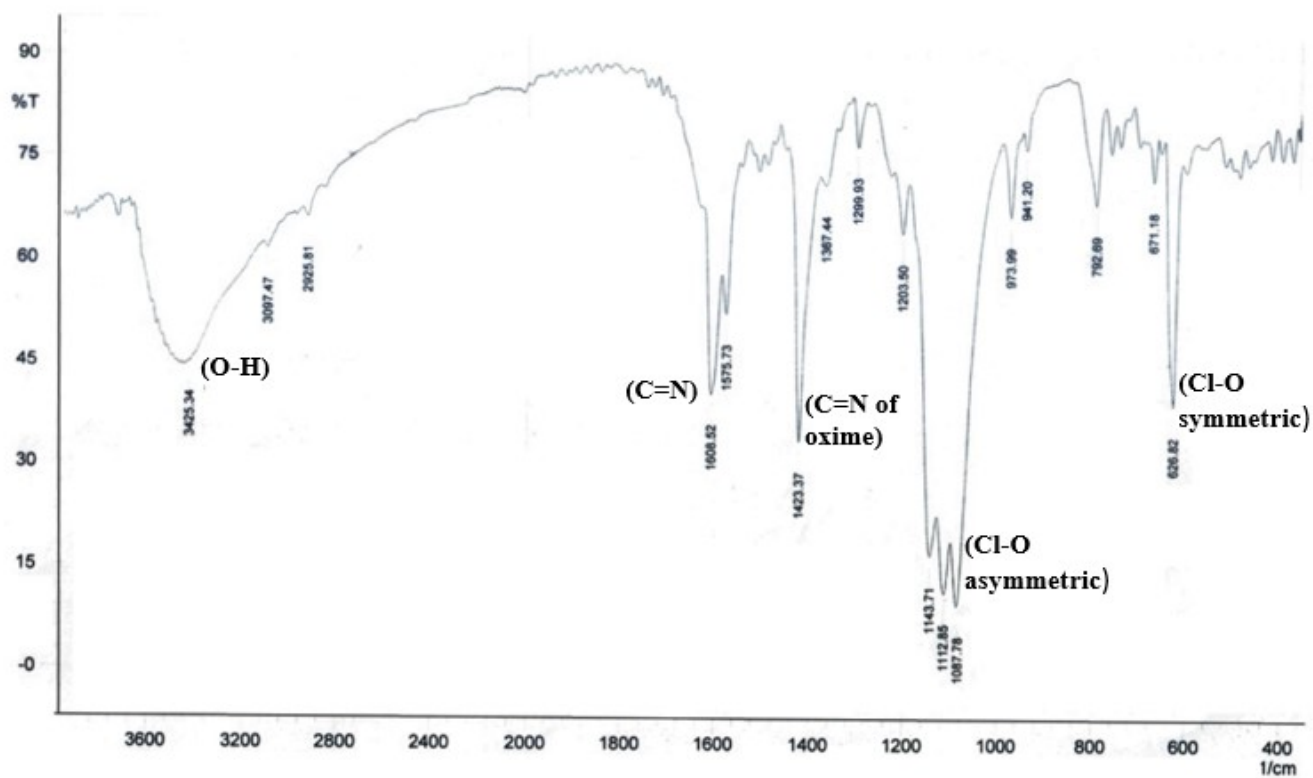


Fig. S5. FT-IR spectrum of complex 1

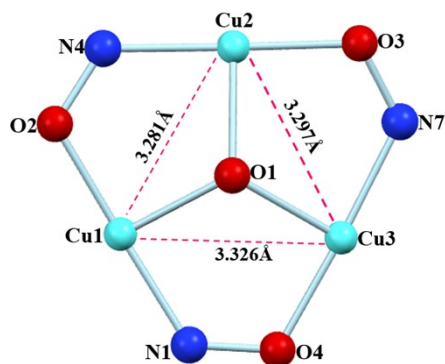


Fig. S6 The *inverse*-metallacrown core as present in 1.

References

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