Supporting Information

Variable coordination and C-S bond cleavage activity of N-substituted imidazolidine-2-thiones towards copper: synthesis, spectroscopy, structures, ESI-mass and antimicrobial studies†

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1S.Molecular Structures of 5-11

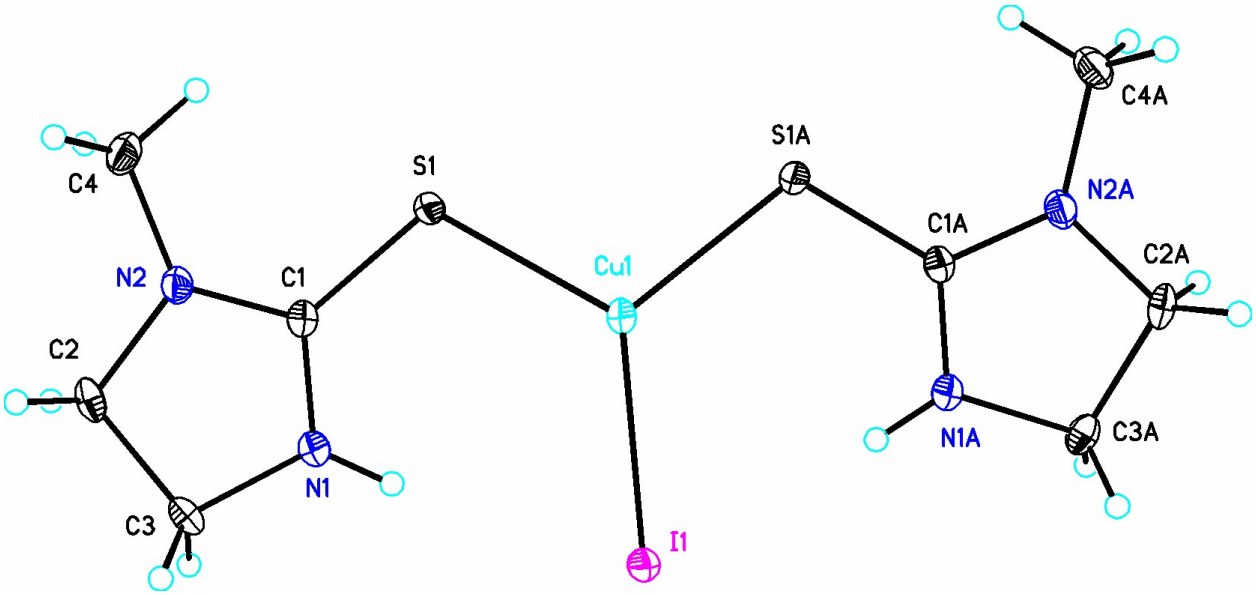


Figure S1. Ortep drawing of [CuI(κ^1-S-L-Me)$_2$] **5** with 30% probability ellipsoids.Selected bond lengths/Å and angles/°: Cu1–S1, 2.2397(11); Cu1–S1*, 2.2397(11); Cu1–I1, 2.5608(19); S1–C1, 1.710(3); S1–Cu1–S1*, 112.16(6); S1–Cu1– I1, 123.92(3); S1*–Cu1– I1, 123.92(3); Cu1– S1–C1, 109.82(12).

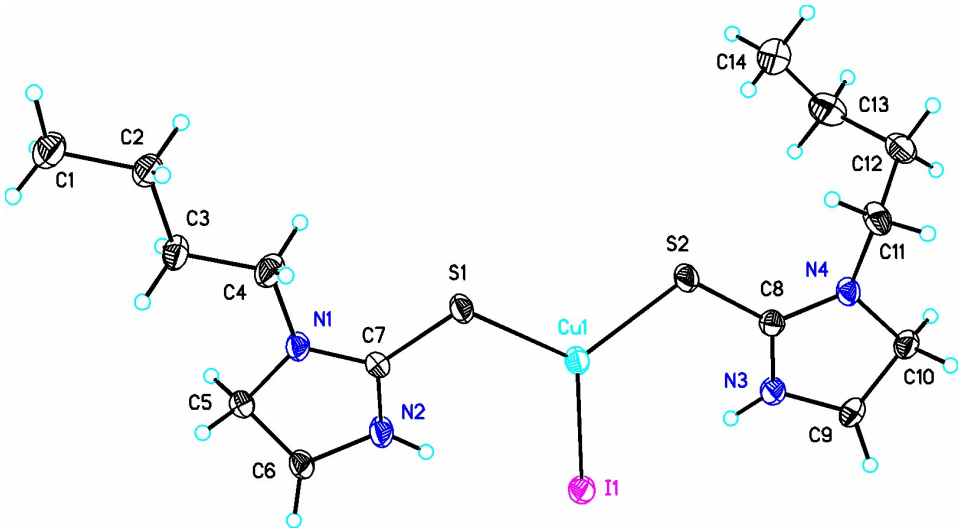


Figure S2. Ortep drawing of [CuI(κ^1-S-L-Bu^n)$_2$] **6** with 30% probability ellipsoids. Selected bond lengths/Å and angles/°: Cu1–S1, 2.2386(9); Cu1–S2, 2.2338(9); Cu1–I1, 2.5397(4); S1–C7, 1.705(3); S2–C8, 1.700(3); S1–Cu1–S2, 111.19(3); S1–Cu1– I1, 124.63(3); S2–Cu1– I1, 124.18(3); Cu1– S1–C7, 110.55(11); Cu1– S2–C8, 110.46(16).

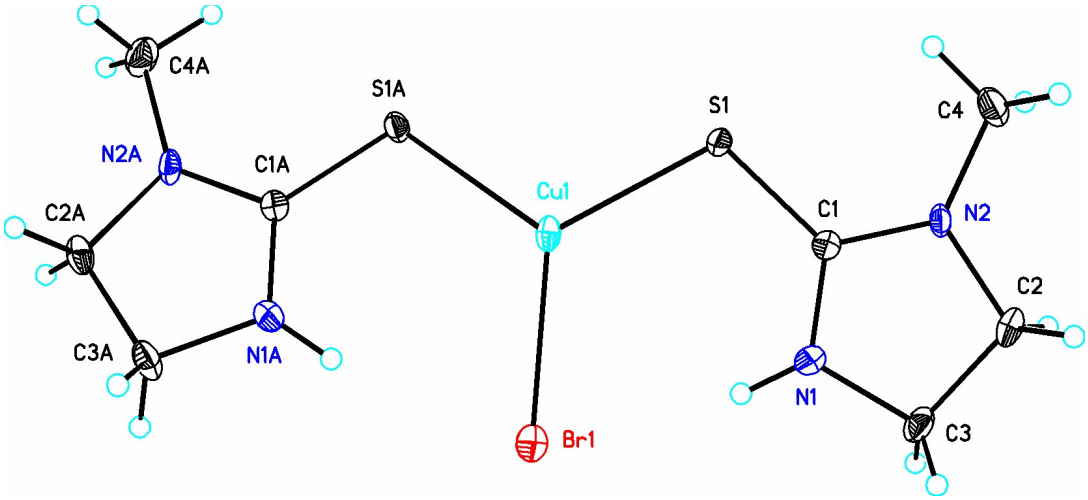


Figure S3. Ortep drawing of [CuBr(κ^1-S-L-Me)$_2$] **7**. with 30% probability ellipsoids. Selected bond lengths/Å and angles/°: Cu1–S1, 2.2282(13); Cu1–S1*, 2.2282(13); Cu1–Br1, 2.4124(13); S1–C1, 1.707(5); S1–Cu1–S1*, 116.80(7); S1–Cu1– Br1*, 121.60(4); S1–Cu1– Br1, 121.60(4); Cu1– S1–C1, 108.12(17).

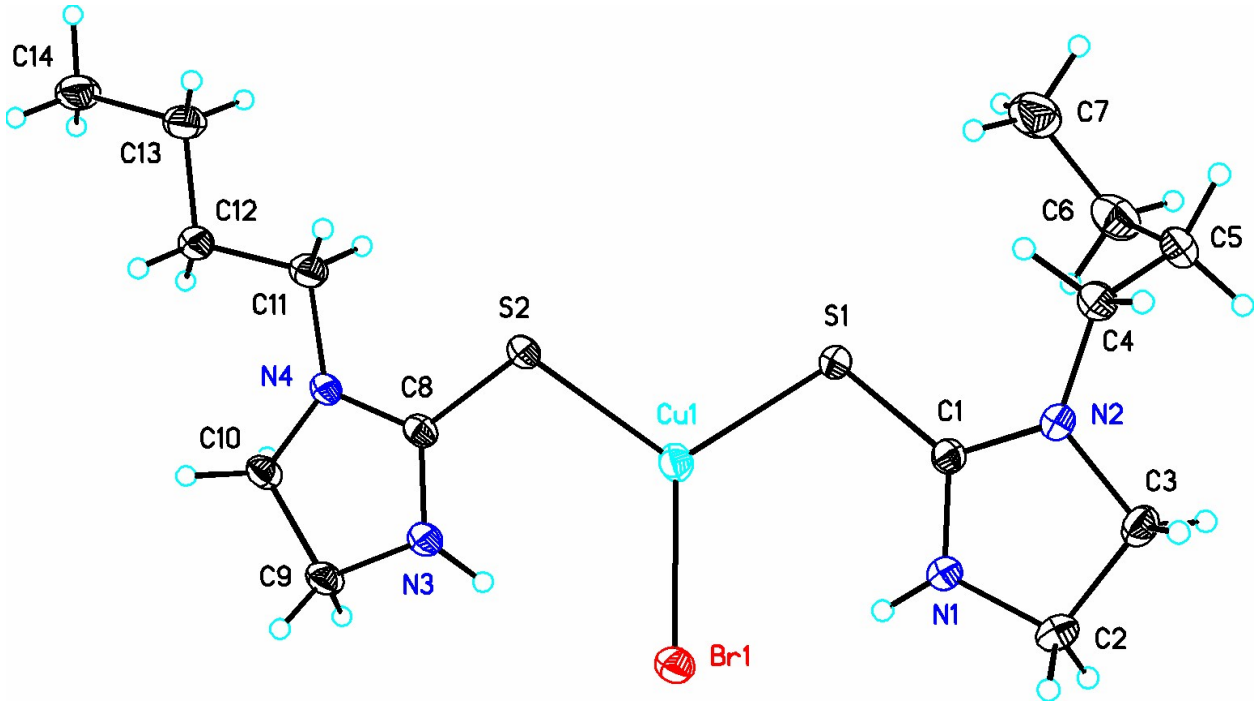


Figure S4. Ortep drawing of [CuBr(κ^1-S-L-Bu^n)$_2$] **8** with 30% probability ellipsoids. Selected bond lengths/Å and angles/°: Cu1–S1, 2.2231(8); Cu1–S2, 2.2256(8); Cu1–Br1, 2.3798(5); S1–C1, 1.710(3) 1.705(3); S2–C8, 1.704(3); S1–Cu1–S2, 112.81(3); S1–Cu1– Br1, 122.93(3); S2–Cu1– Br1, 124.26(3); Cu1– S1–C1, 109.71(10); Cu1– S2–C8, 109.21(10).

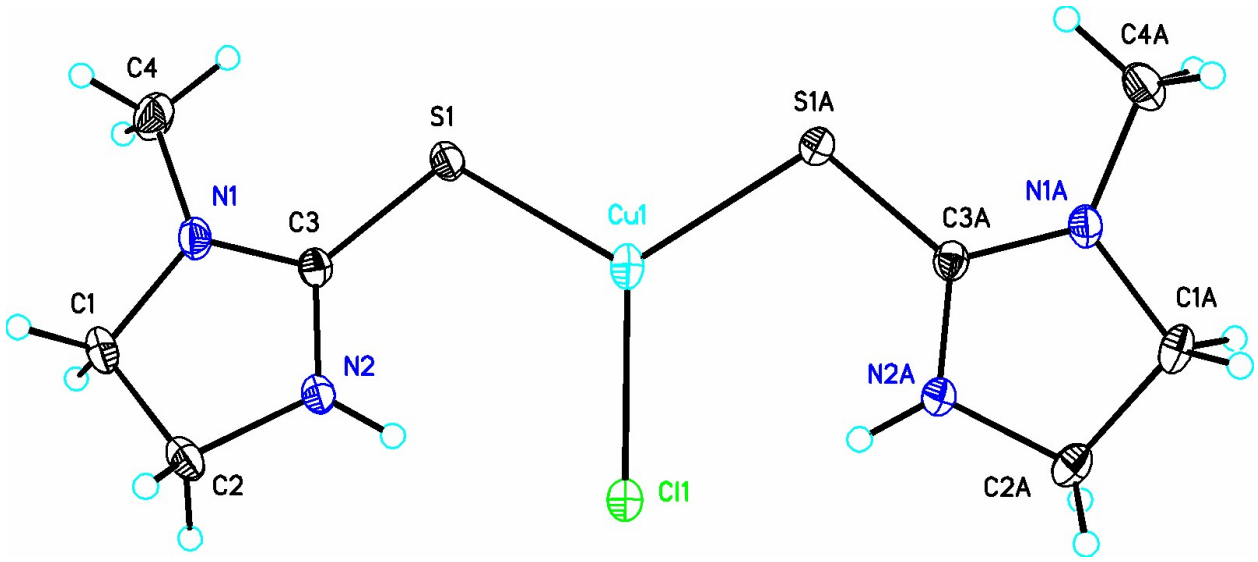


Figure S5. Ortep drawing complex [CuCl(κ^1-S-L-Me)$_2$] **9** of with 30% probability ellipsoids. Selected bond lengths/Å and angles/°: Cu1–S1, 2.2297(7); Cu1–S1*, 2.2297(7); Cu1–Cl1, 2.2969(11); S1–C3, 1.711(2) ; S1–Cu1–S1*, 119.47(4); S1–Cu1– Cl1, 120.26(2); S1–Cu1–Cl1*, 120.26(2); Cu1– S1–C3, 107.22(9).

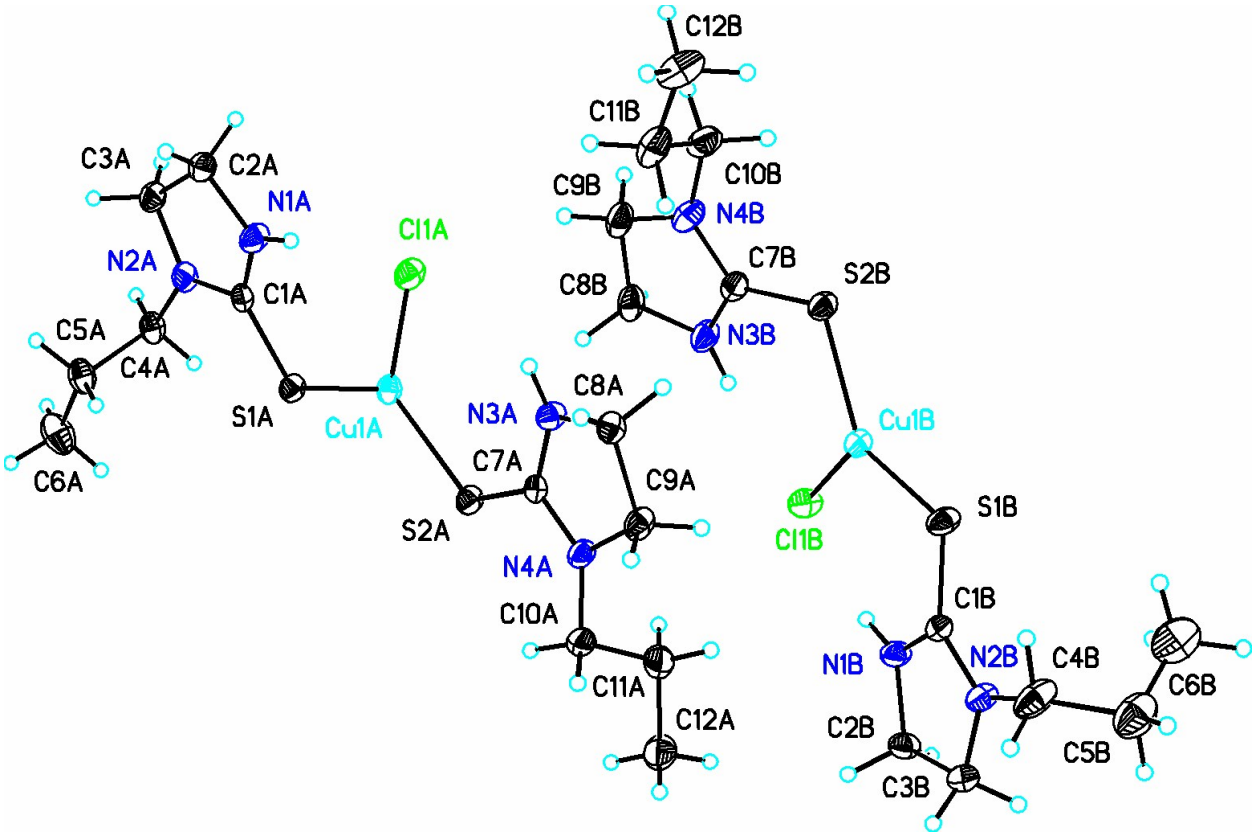


Figure S6. Ortep drawing complex $[CuCl(\kappa^1\text{-S-L-Pr}^n)_2]$ **10** of with 30% probability ellipsoids.. Selected bond lengths/Å and angles/°: Molecule 1: Cu1A–S1A, 2.2270(6); Cu1A–S2A, 2.2146(7); Cu1A–Cl1A, 2.2660(7), ; S1A–C1A, 1.709(2) ; S2A–C7A, 1.711(2); S1A–Cu1A–S2A, 119.75(3); S1A–Cu1A– Cl1A, 120.15(2); S2A–Cu1A– Cl1A, 120.09(2); Cu1A– S1A–C1A, 107.66(8), Cu1A–S2A–C7A, 108.21(8). Molecule 2. : Cu1B – S1B, 2.2145(7), Cu1B–S2B, 2.2254(7); Cu1B –Cl1B, 2.2718(7); S1B–C1B, 1.711(2) ; S2B–C7B, 1.712(3); S1B–Cu1B–S2B, 122.85(3) ; S1B–Cu1B–Cl1B, 120.17(3); S2B–Cu1B– Cl1B, 116.96(3); Cu1B–S1B–C1B, 108.18(8), Cu1B–S2B–C7B, 107.99(9).

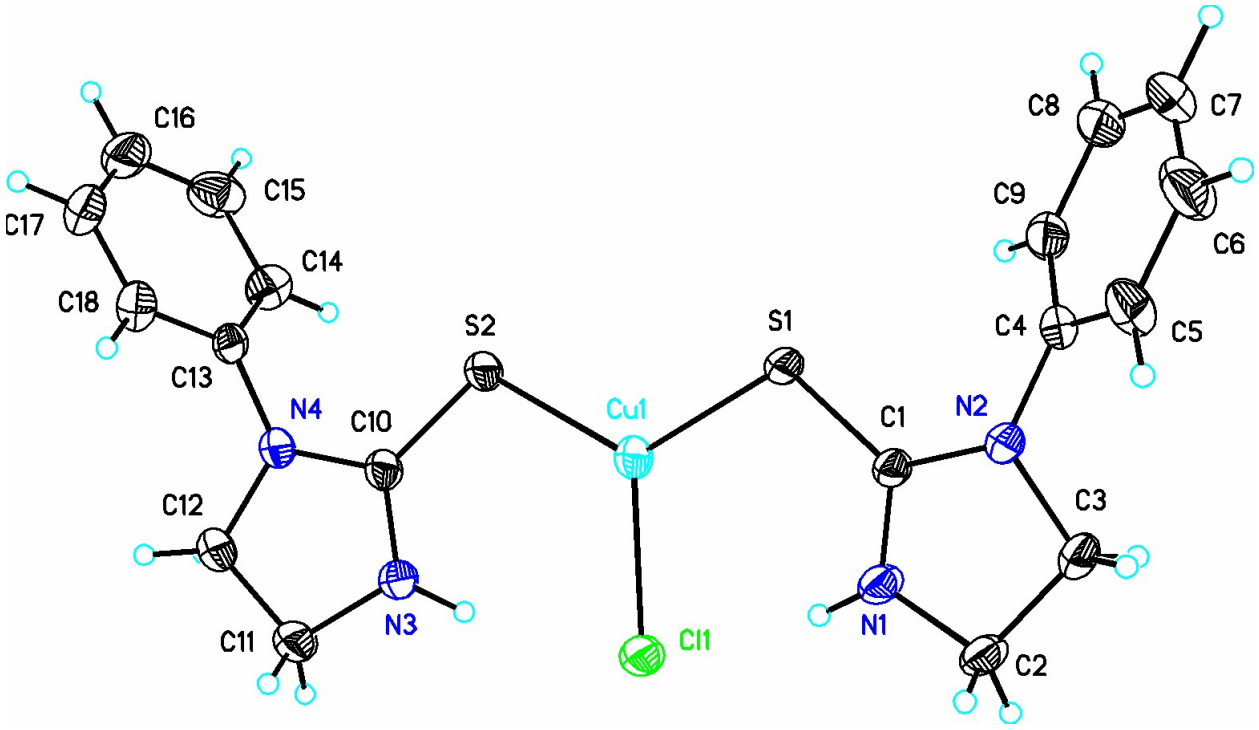


Figure S7. Ortep drawing complex [CuCl(κ^1:S-L-Ph)$_2$] **11** with 30% probability ellipsoids Molecular structure of trigonal planar, Selected bond lengths/Å and angles/°: Cu1–S1, 2.2263(6); Cu1–S2, 2.2287(6); Cu1–Cl1, 2.3074(7); S1–C1, 1.707(2); S2–C10, 1.702(2); S1–Cu1–S2, 124.44(2); S1–Cu1– Cl1, 117.32(2) ; S2–Cu1– Cl1, 118.24(2); Cu1– S1–C1, 109.09(8);. Cu1–S2–C10,, 107.34(8).

2S. ESI-mass data.

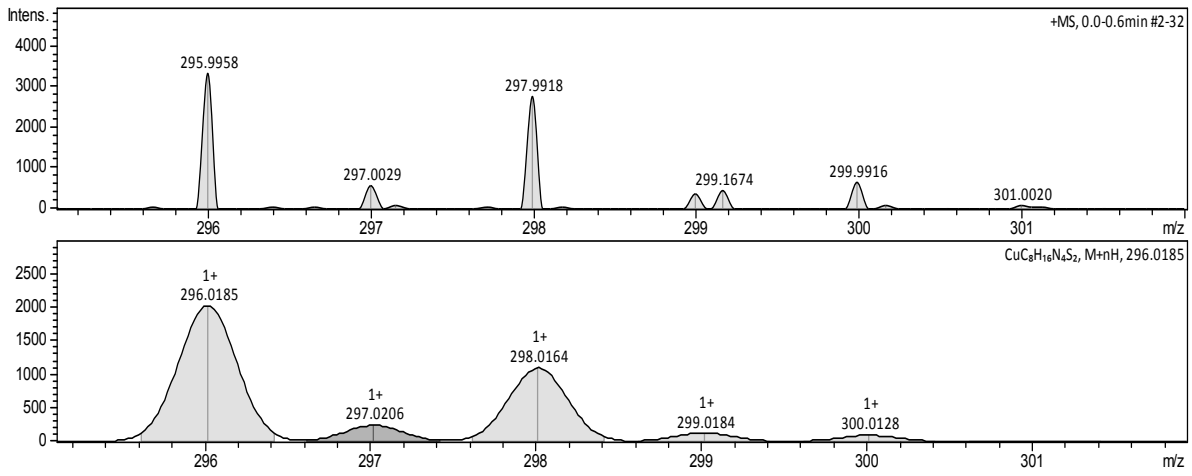


Figure S8. ESI-mass spectrum due to $[Cu(\kappa^1\text{-S-L-Me})_2 + H]^+$ (m/z = calcd, 296.01, obsd 295.99) with isotopic pattern (complex **5**).

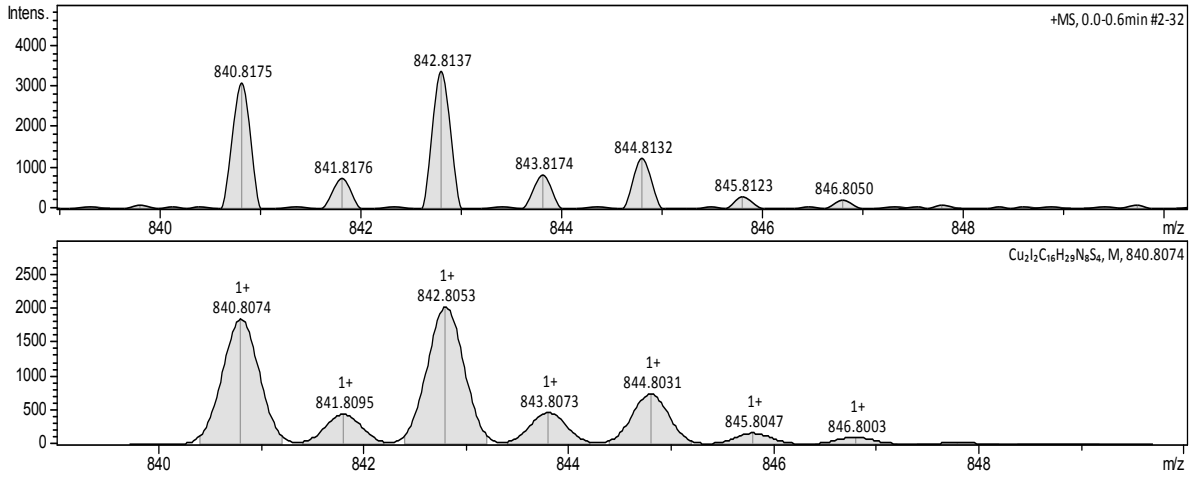


Figure S9. ESI-mass spectrum due to $[Cu_2I_2(\kappa^1\text{-S-L-Me})_4 - 3H]^+$ (m/z = calcd, 840.80, obsd 840.81) with isotopic pattern (complex **5**).

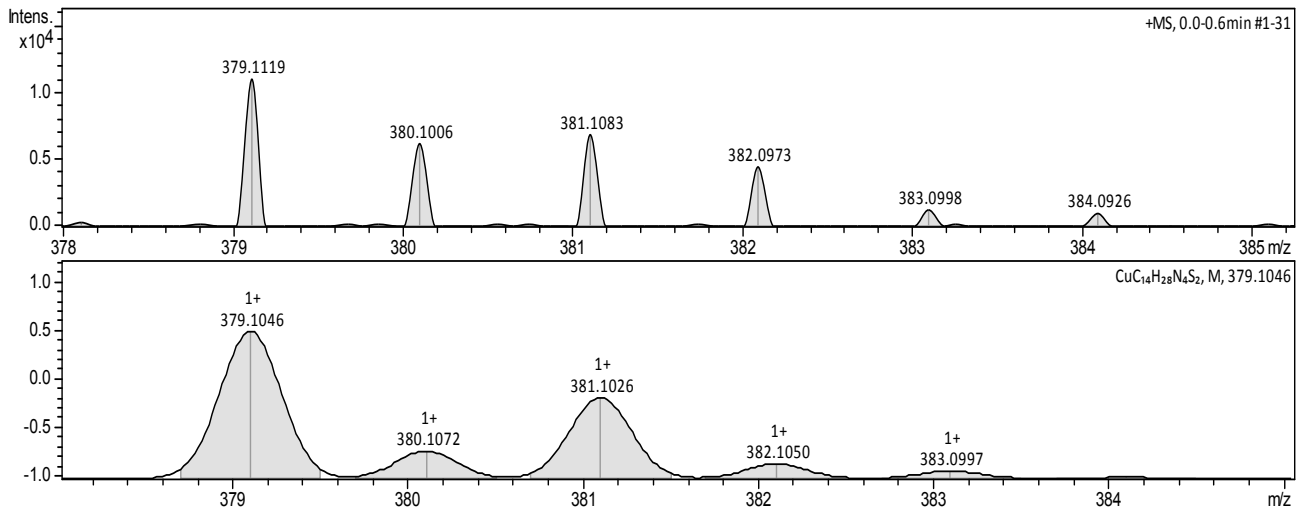


Figure S10. ESI-mass spectrum due to $[Cu(\kappa^1\text{-S-L-Bu})_2]^+$ (m/z = calcd, 379.10, obsd 379.11) with isotopic pattern (complex **6**).

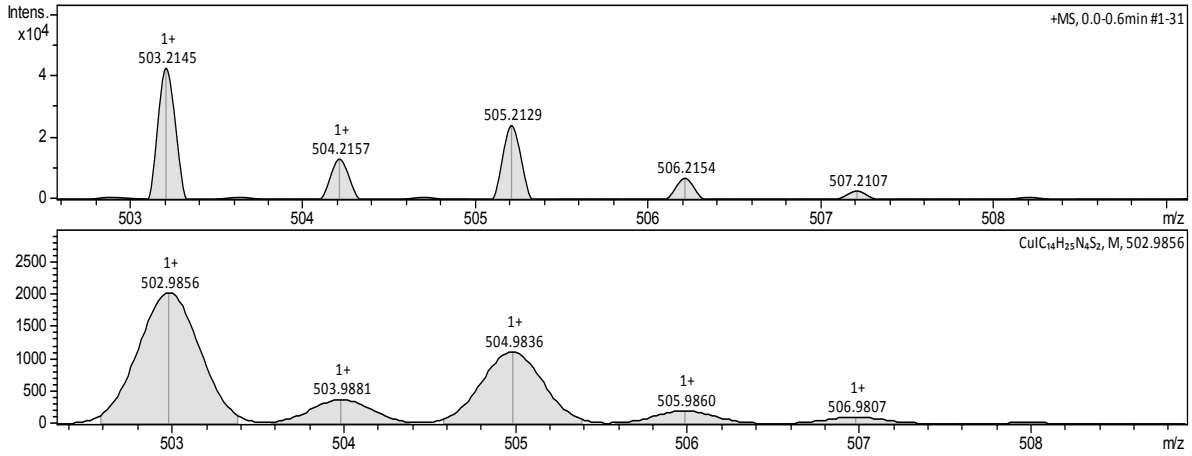


Figure S11. ESI-mass spectrum due to $[CuI(\kappa^1\text{-S-L-Bu})_2 - 3H]^+$ (m/z = calcd, 502.98, obsd 503.21) with isotopic pattern (complex **6**).

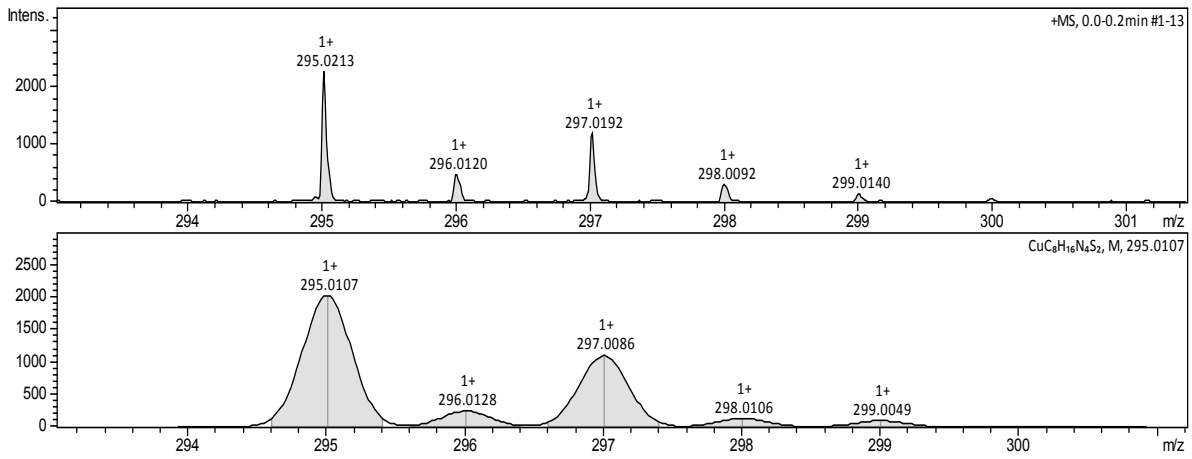


Figure S 12. ESI-mass spectrum due to $[Cu(\kappa^1\text{-S-L-Me})_2]^+$ (m/z = calcd, 295.01, obsd 295.02) with isotopic pattern (complex **7**).

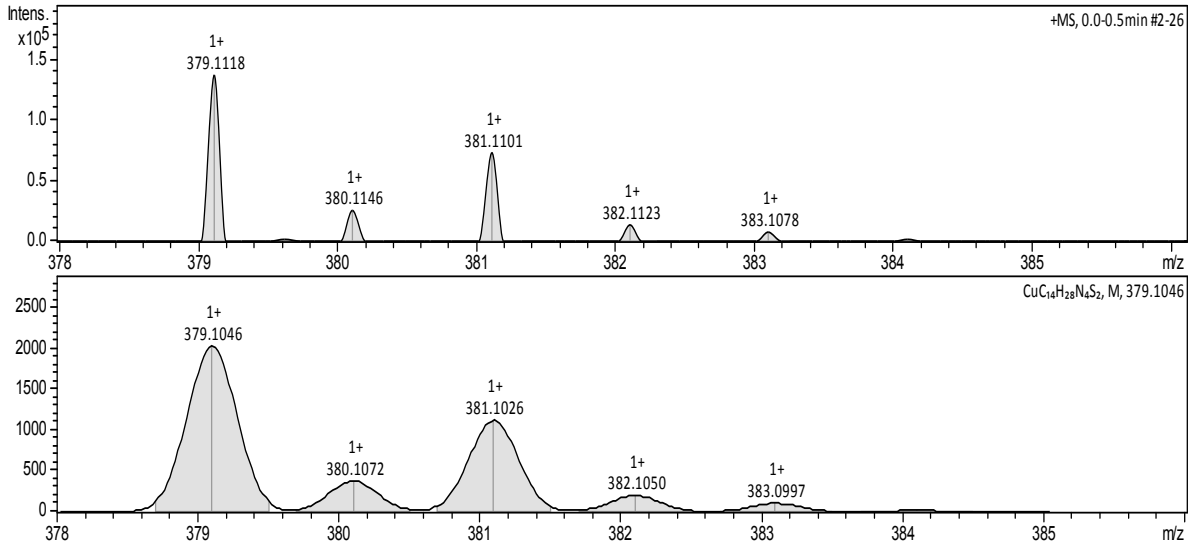


Figure S13. ESI-mass spectrum due to $[Cu(\kappa^1\text{-S-L-Bu})_2]^+$ (m/z = calcd, 379.10, obsd 379.11) with isotopic pattern (complex **8**).

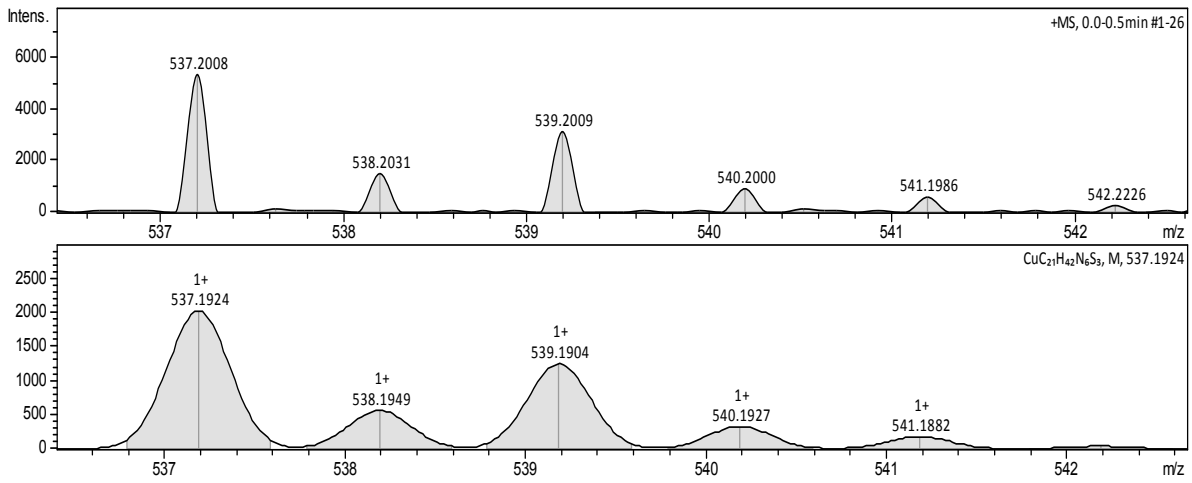


Figure S14.. ESI-mass spectrum due to $[Cu(\kappa^1\text{-S-L-Bu})_3]^+$ (m/z = calcd, 537.19, obsd 537.20) with isotopic pattern (complex **8**).

3S. X-ray data

Table 1S. Crystal data of complexes 5-11

	5(trigonal planar)	6(trigonal planar)	**7**(trigonal planar)	**8**(trigonal planar)
Empirical formula	$C_8H_{16}CuIN_4S_2$	$C_{14}H_{28}CuIN_4S_2$	$C_8H_{16}CuBrN_4S_2$	$C_{14}H_{28}BrCuN_4S_2$
M	422.84	506.96	375.82	459.97
T /K	100(2)	293(2)	173(2)	173(2
Crystal system	Monoclinic	Triclinic	Monoclinic	Triclinic
Space group	C2/c	P -1	C 2/c	P -1
a(Å)	13.710(5)	7.4901(4)	13.2573(9)	7.3515(4)
b(Å)	7.422(5)	10.3906(4)	7.4836(5)	10.0895(5)
c(Å)	14.723(5)	14.1896(8)	14.3879(10)	14.3386(6)
α (º)	-	102.429(4)	-	102.109(4)
β (º)	109.448(5)	100.467(5)	107.330(7)	101.930(4)
γ (º)	-	100.840(4)	-	100.673(4)
V(Å^3)	1412.7(12)	1030.40(9)	1362.66(17)	987.95(8
Z	4	2	4	2
D_{calcd} (g.cm^{-3})	1.988	1.634	1.832	1.546
μ (mm^{-1})	4.008	2.762	8.405	5.907
F(000)	824	508	752	472
Reflections collected	12376	12340	2188	6681
Unique reflections 11	1621 (R_{int} = 0.0376)	6759 (R_{int} = 0.0382)	1292 (R_{int} = 0.0362)	3752 (R_{int} =0.0299)
Data/restraints/	1621/1/77	6759 / 0 /201	1292 / 0 / 76	3752 / 0 / 201

Parameters				
Reflections with [I > 2r(I)]	1469	4756	1211	3269
Final R Indices [I > 2r(I)]	R_1 = 0.0269 wR_2 = 0.0689	R_1 = 0.0421 wR_2 = 0.0845	R_1 = 0.0562 wR_2 = 0.1554	R_1 = 0.0355 wR_2 = 0.0926
Final R indices (all data)	R_1 = 0.0311 wR_2 =0.0721	R_1 = 0.0698 wR_2 = 0.0983	R_1 = 0.0585 wR_2 = 0.1583	R_1 = 0.0417 wR_2 = 0.0980
Largest diff. Peak and hole / e.Å^{-3}	0.746 and -0.690	1.012, and -0.782	1.921 and -1.024	0.681 and -0.375
	9(trigonal planar)	**10**(trigonal planar)	**11**(trigonal planar)	
Empirical formula	$C_8H_{16}ClCuN_4S_2$	$C_{12}H_{24}ClCuN_4S_2$	$C_{18}H_{20}ClCuN_4S_2$	
M	331.36	387.46	455.49	
T /K	173(2)	173(2)	173(2)	
Crystal system	Monoclinic	Monoclinic	Monoclinic	
Space group	C2/c	P 2_1/c	I2/c	
a(Å)	12.9744(16)	14.0097(4)	13.5161(5)	
b(Å)	7.6298(10)	14.0814(3)	10.4367(5)	
c(Å)	14.1661(16)	18.9263(6)	28.1083(14)	
α (º)	-	-	-	
β (º)	105.936(13)	108.984(3)	92.378(5)	
γ (º)	-	-	-	
V(Å^3)	1348.4(3)	3530.66(18)	3961.6(3)	
Z	4	8	8	

D_{calcd} (g.cm^{-3})	1.632	1.458	1.527
μ (mm^{-1})	2.107	1.621	1.458
F(000)	680	1616	1872
Reflections collected	4253	29554	15929
Unique reflections	2223 (R_{int} = 0.0525)	11848 (R_{int} = 0.0341)	6586 (R_{int} = 0.0371)
Data/restraints/ Parameters	2223 / 0 / 75	11848 / 0 /365	6586 / 0 / 235
Reflections with [I > 2r(I)]	1824	8285	4400
Final R Indices [I > 2r(I)]	R_1 = 0.0489 wR_2 = 0.1182	R_1 = 0.0425 wR_2 = 0.0927	R_1 = 0.0429 wR_2 = 0.0977
Final R indices (all data)	R_1 = 0.0608 wR_2 = 0.1303	R_1 = 0.0747 wR_2 = 0.1090	R_1 = 0.0759 wR_2 = 0.1181
Largest diff. Peak and hole / e.Å^{-3}	0.561 and -0.900	1.185 and -0.524	0.359 and --0.404

4S. Antimicrobial Experimental Details. of Complexes.

Test organisms and inoculum preparation.

The reference strains of bacteria and yeasts were obtained from Microbial Type Culture Collection (MTCC), Institute of Microbial Technology (IMTECH), Chandigarh, India and the clinical isolate Methicillin resistant *Staphylococcus aureus* (MRSA) was obtained from Post graduate Institute of Medical Education and Research, (PGIMER), Chandigarh, India. Reference strains included Gram positive bacteria: *Staphylococcus aureus* (MTCC- 740), Gram negative bacteria: *Klebsiella pneumoniae* (MTCC- 109), *Salmonella typhimurium* (MTCC-1251), and one yeast strain: *Candida albicans* (MTCC- 227).

A loopful of isolated bacterial and yeast colonies were inoculated into 5 mL of their respective medium and incubated at 37ºC and 25ºC, respectively for 4 h. This was used as inoculums after adjusting the turbidity as per Mc Farland turbidity standard. This turbidity is equivalent to approximately 1 to 2 x 10^8 colony forming units per mL (CFU/mL). The inoculum thus prepared were used for further testing.

Antimicrobial screening

A 100 µL of activated test organism (prepared as above) was inoculated onto suitable medium plates by spread plate method. Wells measuring 8 mm in diameter were cut out in the medium using sterilized stainless steel borer. Each well was filled with 0.1 mL of test complex dissolved in DMSO and kept for incubation in an upright position for 18 – 24 h. Sensitivity was measured in terms of diameter of the resultant zone of inhibition. Any organism with a clear zone of inhibition ≤ 12mm was considered to be resistant to the compound.

Minimum inhibitory concentration (MIC)

Minimum inhibitory concentration of the selected complex compounds dissolved in DMSO was worked out by the agar dilution method for their antimicrobial activity against the sensitive microorganisms. A stock solution of a complex under investigation of concentration (50 mg/mL) was prepared and incorporated into Muller Hinton agar medium for bacteria and yeast malt extract medium for yeast. The final concentration of the compound in the medium containing plates ranged from (0.005–2 mg/ mL). These plates were then inoculated with 0.1 mL of the activated bacterial and yeast strains by streaking with a sterile swab. The plates were incubated at 37ºC for bacteria and 25 ºC for yeast for 24 h each. The minimum concentration of the extract causing complete inhibition of the microbial growth was taken as MIC. The results were compared with that of control (i.e. DMSO).

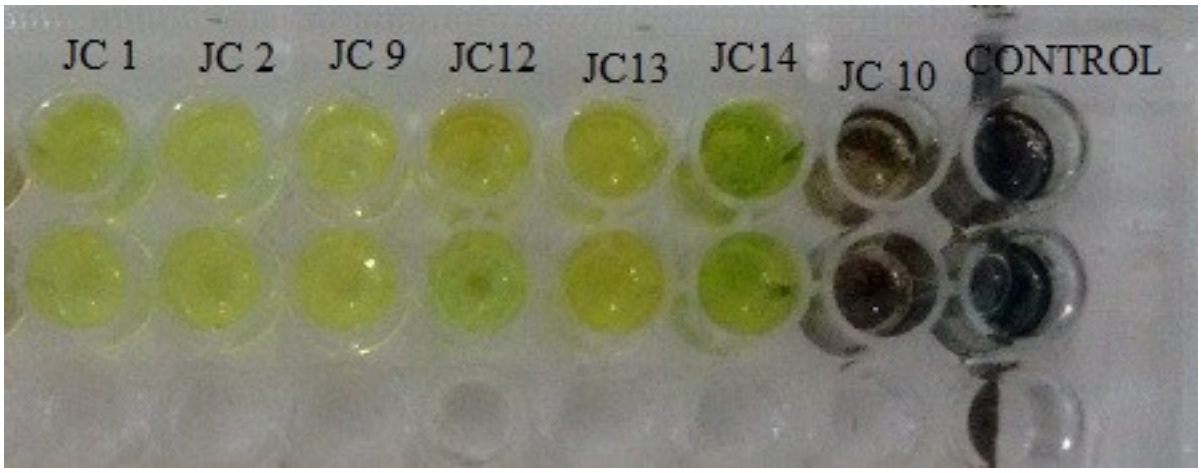
MTT toxicity assay

In order to check the level of cellular toxicity of the test compounds dissolved in DMSO, MTT [3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide] assay was performed (Ref. J. G. Onsare and D.S. Arora, J. Applied Microbiology 2014, 118, 313-325) as follows. Ten milliliter of sheep blood was taken into injection syringe containing 3 mL of Alsever's solution (anticoagulant) and transferred to sterile centrifuge tubes. The blood was centrifuged at 16,000 rpm at room temperature (25°C) for 20 min so as to separate the plasma from the cells. The supernatant was discarded and 6 mL phosphate buffer saline (PBS) added which was again centrifuged. The blood cells were washed thrice with PBS by centrifugation and the pellet was re-suspended in 6 mL of PBS. Various dilutions of these cells were prepared using PBS and counted with the help of a hemocytometer under a light microscope so as to obtain cells

equivalent to 1×10^5 cells/mL. One hundred microlitre (100 µL) of this diluted suspension was added in each well and incubated at 37 °C for overnight. The supernatant was removed carefully and 200 µL of the sample solution (contains 10 mg/mL) was added and incubated further for 24 h. Supernatant was removed again and added 20 µL MTT solution (5 mg/mL) to each well and incubated further for 3.5 h at 37 °C on orbital shaker at 60 rpm. After incubation, the supernatant was removed without disturbing the cells and 50 µL of DMSO was added to each well to dissolve the formazan crystals. The absorbance was measured at 590 nm using an automated microplate reader (Biorad 680-XR, Japan). The wells with untreated cells served as control. Reduction of MTT can only occur in metabolically active cells, as MTT is converted into formazan crystals and hence the absorbance directly represents the viability of the cells.

% viability- OD of Treated / OD of Control X 100. If the percent viability of the blood cells is quite high, then the compounds are non-cytotoxic in nature.

Microtitre plate showing Cytotoxicity of Complexes by MTT assay



JC-1 Complex **5**; JC-2, complex **4**; JC-9, complex **8**; JC-12, complex **14**; JC-13, complex **10;**JC-14, Complex **13;** JC-10, complex **12**. Control – DMSO. Complex **12** showed purple coloration which is comparable to that of control and is treated as non-cytotoxic. Other complexes showed no purple coloration and are thus cytotoxic.

TIME KILL ASSAY

The time kill assay for each of the selected complex compound under study was performed by the viable cell count method (VCC). A stock solution (50 mg mL^{-1}) was prepared. Five milli liter of inoculums as prepared above was serially diluted to 10^3 times with the respective double strength broth medium. An equal volume of each diluted inoculums and the compound to be tested were mixed at their respective predetermined MIC values and incubated at the respective temperature of 25°C for yeast and 37°C for bacteria. A 0.1 mL of the mixed suspension was spread on suitable agar plates in duplicate at different time intervals viz. 0, 2, 4,6, 8· ·····24 h, and incubated for 24 h at suitable temperature. The mean number of colonies was determined and compared with that of control that is DMSO.

JC-1 Complex **5**; JC-2, complex **4**; JC-9, complex **8**; JC-12, complex **14**; JC-13, complex **10;**JC-14, Complex **13;** JC-10, complex **12**. Control – DMSO. Complex **12** showed purple coloration which is comparable to that of control and is treated as non-cytotoxic. Other complexes showed no purple coloration and are thus cytotoxic.

Analytical data for reported complexes **14-16** is given to confirm their stoichiometry .

[CuCl(κ^1-S-Et)$_2$] (**14**). Anal. calcd for $C_{10}H_{20}CuClN_4S_2$: C, 33.42; H, 5.57; N, 15.59; S, 17.82 ; found: C, 33.87; H, 6.26; N, 16.21; S, 17.00 [Ref. 42]-see main paper

[CuBr(κ^1-S-Et)$_2$] (**15**). Anal. calcd for $C_{10}H_{20}CuBrN_4S_2$: C, 29.73; H, 4.95; N, 13.87; S, 15.86 ; found: C, 28.83; H, 5.21; N, 13.58; S, 14.85. [Ref. 44]- see main paper

[CuI(κ^1-S-Pr^n)$_2$] (**16**). Anal. calcd for $C_{12}H_{24}CuIN_4S_2$: C, 30.90; H, 5.01; N, 11.70; S, 13.37 ; found: C, 30.89; H, 5.45; N, 12.06; S, 13.70. [Ref. 44]- see main paper