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A new two dimensional copper (II) coordination complex with sulphonamide: Synthesis, crystal structure and DNA binding study

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ABSTRACT

A novel copper (II) complex, $[Cu(HL)_2]$ (where, HL = 3-(4-(sulphonamine)phenylimino)-1-phenylbut-1-en-1-ol) has been synthesized and characterized by IR, UV–vis, magnetic susceptibility measurement and single crystal X-ray crystallographic studies. The crystal data confirm the square planarity of the prepared complex having an orthorhombic space group Pca2 (1). Molecular packing of the complex is stabilized by N—H…O hydrogen bonding and weak N—H…O, C—H…Cg π-ring intermolecular interactions, hence forming a two dimensional supramolecular network structure. CT-DNA binding studies have been carried out by monitoring electronic absorption titrations, luminescence titrations, a DNA melting, cyclic voltametry and viscosity measurement studies. An intercalative mode of DNA binding is suggested for the prepared copper (II) complex.

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Sulphonamide imines are Schiff base compounds which contain a carbon–nitrogen double bond (C N) and a sulphonamide (—SO_2—NH—) functional group in the parent structural unit. Systems containing both azomethine (C N) and a sulphonamide (—SO_2—NH—) groups are related to potential biological and pharmaceutical compounds that display anti-cancer [1], anti-tubercular [2], anti-inflammatory and anti-microbial [3] activities. However, their biological activity can be altered depending upon the substituent present on the parent structural unit or by complexation with a metal ion. The coordination chemistry of sulphonamide imine complexes has undergone noticeable development in recent years due to the interesting properties of these substances, such as the presence of artificial chemical nucleases in a DNA binding study which plays a major role as a molecular tool in biochemistry [4]. The importance of metal–DNA interactions in living systems, and their potential applications, especially in the treatment and diagnosis of diseases, has stimulated considerable recent interest in this area. Understanding how metal complexes interact with DNA has become an active area of research at the interface between chemistry, molecular biology and medicine. In this paper we report a synthesis, crystallographic, spectroscopic and DNA binding study of a new sulphonamide imine Schiff base copper (II) complex, $C_{32}H_{30}CuN_4O_6S_2$.

Preparation of the ligand (Fig. S1) and complex along with elemental analyses, magnetic measurements and crystal data are described [5].

The electronic spectrum of the copper (II) complex in DMF shows a broad absorption band *ca.* 640 nm which may be assigned to the $^2A_{1g} \rightarrow {}^2B_{1g}$ transition and a square planar geometry (Fig. S2), similar to that suggested around the copper (II) ion [6] with the sulphonamide imine ligand as an N, O-donor. In the IR spectrum of the complex the ν(C N) band was observed *ca.* 1586 cm^{-1} (Fig. S3), which shows a marked shift ($\Delta\nu = 34\ cm^{-1}$) as compared to the free ligand (1620 cm^{-1}) (Fig. S4), suggesting coordination of the azomethine N-atom to the Cu(II) ion [7]. It has been observed that the lowering of the frequency of the enolic ν(O—H) band of the ligand (*ca.* 3346–3062 cm^{-1}) is a result of intra-molecular (—OH....N—) hydrogen bonding within the respective ligand molecules [8]. The presence of observed bands in the region, *ca.* 1321–1332 and 1163–1162 cm^{-1}, may be assigned to the $\nu_a(SO_2)$ and $\nu_s(SO_2)$, respectively, for the ligand and the complex [9]. In the title complex, the ν(Cu—N) and ν(Cu—O) vibration modes are assigned to bands in the region at 516 cm^{-1} and 463 cm^{-1}, respectively. In the thermal analysis data of the complex, a loss of two ligand molecules started at *ca.* 220 °C and was completed *ca.* 620 °C which was accompanied by an exotherm *ca.* 500 °C (Fig. S5).

The square planarity of the title copper (II) complex has been confirmed by single crystal X-ray crystallography. The copper (II) ion is coordinated by a N_2O_2-donor set of the two sulphonamide imine ligand molecules (Fig.1). It crystallizes in an orthorhombic, Pca2(1) space group with one monomeric $C_{32}H_{30}CuN_4O_6S_2$ group in the asymmetric unit and maintains a slightly distorted square planar geometry. The six-membered chelate rings are nearly planar, while the N2—C19 (1.34(1) Å) and N1—C3 (1.33(1) Å) bonds retain their double bond

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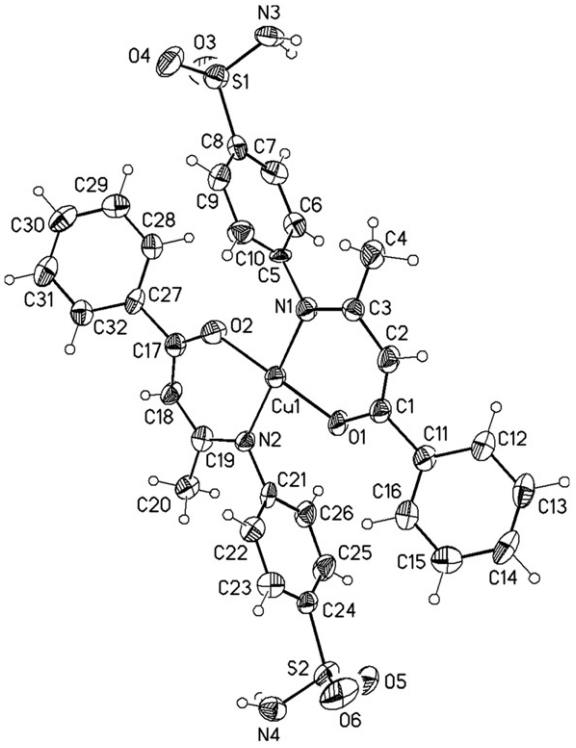

Fig. 1. An ortep view of the copper (II) complex with 50% ellipsoidal probability, showing the atom numbering scheme. Some selected bond lengths (Å) and angles (°): Cu—O1, 1.906(4); Cu—O2, 1.894(4); Cu—N1, 1.991(5); Cu—N2, 1.973(5); O1—Cu1—O2, 179.4(3); O1—Cu1—N1, 92.63(19); O1—Cu1—N2, 87.81(19); O1—Cu1—O2, 87.35(19); N1—Cu1—N2, 179.5(2).

character. The bond lengths of Cu1—N (1.973 (4) Å; 1.991 (5) Å) and Cu1—O (1.894 (4) Å; 1.906 (4) Å) are similar to each other. The dihedral angle between the mean planes of the 11-membered chelate group surrounding the Cu1-atom (Cu1/O1/C1/C2/C3/N1/O2/C17/C18/C19/N2) and the substituted benzene rings (C11—C16 (32.8(0)°); C27—C32 (31.6(6)°)), and the sulphonamide (—SO_2—NH—) substituted benzene rings (C5—C10 (86.0 (8)°); C21—C25 (85.9 (2)°)) shows a significant twisting of these rings relative to the 11-membered, square planar ring system. Intra-molecular hydrogen bonds (N3—H3B....O4 (2.38 (4) Å) and N4—H4B....O5(2.24 (17) Å)) are observed. Crystal packing is stabilized by N—H....O hydrogen bonds and weak N—H....O, C—H…Cg π-ring intermolecular interactions forming a 2D supramolecular network which displays one molecule of the complex surrounded by six additional molecules (Fig. 2).

A DNA binding study with the free ligand and complex has been carried out by monitoring electronic absorption titrations, luminescence titrations, a thermal behavior study, cyclic voltammetry and viscosity measurement studies. Electronic absorption titrations were carried out on a Perkin Elmer UV–vis Lambda 35 spectrophotometer. By maintaining a constant concentration of the free ligand and complex (7.2×10^{-5} M) and varying the concentration of a CT-DNA solution (approximately 2.9 to 8.9×10^{-6} M) which was added, the absorbance for each addition of the DNA concentration was subsequently recorded. The intrinsic binding constant was determined from the absorption spectral data by application of the equation [10],

$$[\mathrm{DNA}]/(\varepsilon_a-\varepsilon_f) = [\mathrm{DNA}]/(\varepsilon_b-\varepsilon_f) + 1/K_b(\varepsilon_b-\varepsilon_f) \quad (1)$$

where, ε_a, ε_f, and ε_b correspond to extinction coefficients of the apparent, free and bound ligand or metal complex, respectively. [DNA] is the molar concentration of DNA and was measured by electronic absorption spectroscopy using the molar absorption coefficient ($6600\ M^{-1}\ cm^{-1}$) at 258 nm. The solution of CT-DNA was prepared by using a 5 mM, Tris–HCl buffer (pH = 7.1). The ratio of UV-absorbance at 260 nm and 280 nm, A_{260}/A_{280}, was found to be *ca.*1.88, indicating that the DNA was satisfactorily free of protein [11]. A graph of $[\mathrm{DNA}]/(\varepsilon_b-\varepsilon_f)$ *vs.* [DNA] was plotted with K_b calculated by a ratio of the slope to the *y*-intercept. The absorption spectrum of the complex and free ligand in presence of increasing concentration of the CT-DNA (approximately

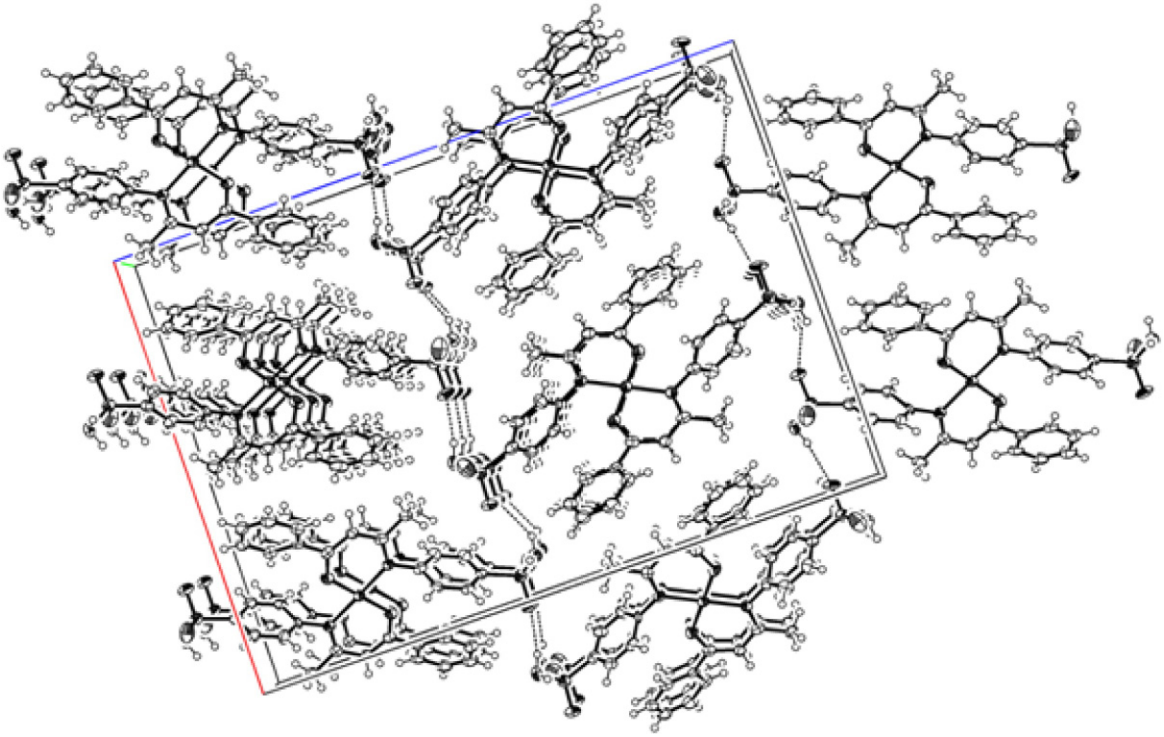

Fig. 2. Molecular packing structure of the copper (II) complex viewed along the b axis. Dashed lines indicate N—H....O hydrogen bonds forming a 2D supramolecular network where one molecule of the complex is surrounded by six molecules of the complex.

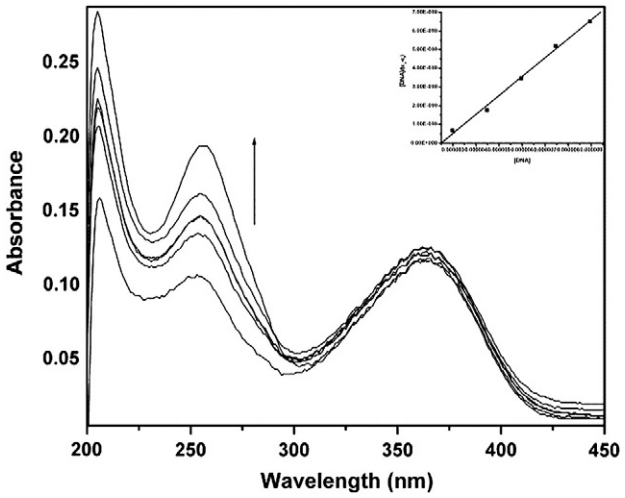

Fig. 3. Absorption spectrum of the copper (II) complex in the presence of different concentrations of CT-DNA. The arrow indicates the increase in absorbance of the complex with increasing CT-DNA concentration. Inset: plot of [DNA]/($\varepsilon_a - \varepsilon_f$) *vs.* [DNA] and a linear fit of the titration curve.

2.9, 4.5, 5.9, 7.5, 8.9×10^{-6} M) showed a considerable amount of hyperchromism with a slight red shift (Fig. 3 and S6). Hyperchromism in the spectrum might be the result of damage of the double stranded DNA helix through an intercalative mode of binding of the complex with DNA molecules [12]. The intrinsic binding constant (K_b) of the complex and free ligand was found to be 5.55×10^5 and 2.57×10^5 M^{-1} respectively. A thermal behavior study of DNA was performed by measuring the absorption intensity of CT-DNA at 258 nm at a temperature range 25–100 °C, both in the absence and presence of the complex and free ligand. The thermal denaturation behavior in the presence of the copper (II) complex provides insight into conformational changes when the temperature is raised. The strength of interaction between the ligand/complex and the DNA can also be monitored. As the temperature of the solution increases, the double stranded DNA tends to dissociate into a single strand thereby displaying a hyperchromic effect on the absorption spectra of DNA, which was observed. The DNA melting temperature, T_m, where half of the total base pairs becomes non-bonded, was determined experimentally and found to be 75 °C which increases to 81°, 82°, 86 °C and 80, 81, 82 °C with increasing ratio of DNA to complex and ligand concentrations (0, 0.1, 0.2 and 0.4), respectively (Fig. 4 and S7). These results both suggest and provide support for the presence of an intercalative effect with DNA. The observed mode of DNA stabilization is similar to that seen in chlorobenzylidine [13]. As the prepared ligand

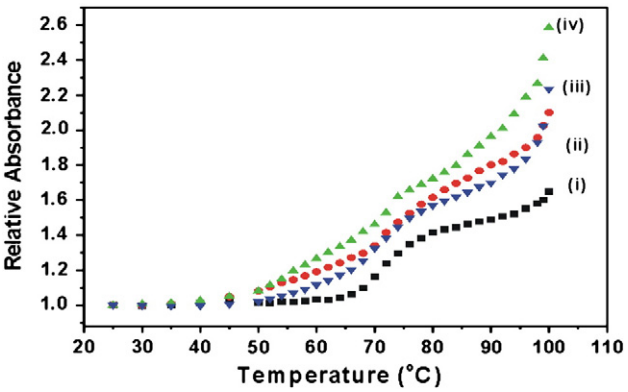

Fig. 4. Thermal denaturation profiles of CT-DNA (i) in the absence and presence of different concentrations of the complex (ii) 0.1, (iii) 0.2 and (iv) 0.4, respectively.

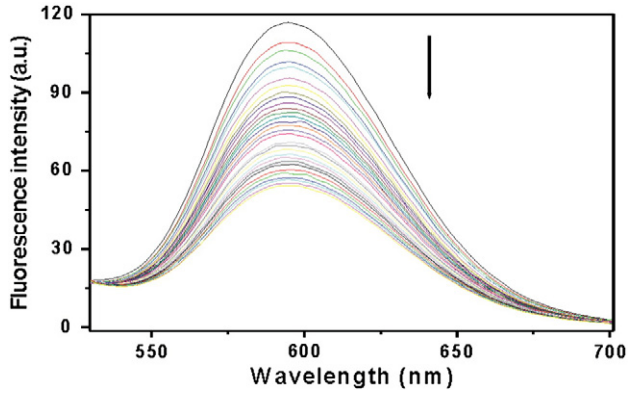

Fig. 5. Emission spectrum of ethidium bromide bound CT-DNA in the absence (topmost curve) and in the presence (subsequent curves) of increasing concentration of the copper (II) complex. The arrow shows the reduction in emission intensity with increasing concentration of the complex.

and complex were found non-emissive, ethidium bromide (EB) bound DNA adduct was used to study the luminescence titrations method. Fluorescence emission intensities of EB at 595 nm with an excitation slit 274 nm were measured with different concentrations of the complex and free ligand. The fluorescence quenching of EB bound to DNA by the complex and free ligand is in good agreement with the classical linear Stern–Volmer equation [14].

$$I_o/I = 1 + K_{sv}[Q] \tag{2}$$

where I_o and I are the emission intensity in the absence and presence of the complex/free ligand, respectively. K_{sv} is the linear Stern–Volmer quenching constant and Q is the ratio of the total concentration of the complex/free ligand to that of DNA. The K_{sv} value for the complex and free ligand were found to be 3.31 and 2.33 respectively which is given by the slope to y-intercept value from the plot of I_o/I versus [Q] (Fig. S8).

The apparent binding constant (K_{app}) was also calculated by the equation,

$$K_{EB}[EB] = K_{app}[Complex] \tag{3}$$

where the concentration of the complex and ligand was determined by the value at a 50% reduction of the fluorescence intensity of ethidium bromide (EB) and $K_{EB} = 1\times10^7$ M^{-1} ([EB] = 1.3×10^{-6} M). Ethidium bromide (EB) emits an intense fluorescent light when intercalated between two DNA base pairs. In presence of an additional DNA binding

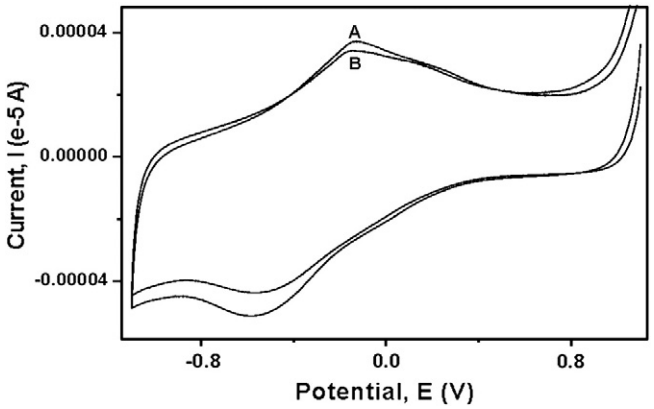

Fig. 6. Cyclic voltammogram of the copper (II) complex (A) in absence and (B) presence of CT-DNA.

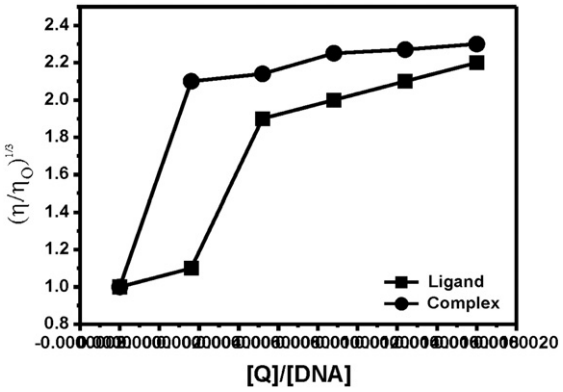

Fig. 7. Effect of increasing amount of the ligand (filled square) and the complex (filled circle) on the relative viscosity of CT-DNA in a Tris–HCl buffer. [DNA] = 77 μM, [Ligand] or [Complex] = 0–100 μM at 20 ± 0.1 °C.

molecule, the emission of the DNA-EB adduct is quenched, either by replacing the EB and or by accepting the excited state electron of the EB through a photoelectron transfer mechanism [15]. The emission spectrum of the EB-bound to DNA in the absence and presence of variable concentrations of the complex and free ligand is shown (Fig. 5 and S9). A reduction in emission intensity was observed, indicating that the complex binds to the DNA helix. The apparent association constant (K_{app}) value was measured to be 1.44×10^6 and 1.01×10^6 M^{-1} respectively for the complex and ligand.

The cyclic voltammogram (CV) of the title copper (II) complex in absence and presence of the CT-DNA concentrations was recorded in the range −1.1 to 1.1 V. The complex exhibits a one electron oxidation and reduction wave, *ca.* −0.584 and −0.129 V, respectively. In presence of CT-DNA, the cyclic voltammogram of the complex shows a minor but significant anodic and cathodic shift, *ca.* −0.571 and −0.149 V, with a decrease in the current peaks from -5.087×10^{-5} A to -4.348×10^{-5} A (for anodic current) and 3.775×10^{-5} A to 3.443×10^{-5} A (for the cathodic peak current), respectively (Fig. 6). The decrease in the peak currents of the complex in presence of CT-DNA may be the result of slow diffusion of the complex into the DNA molecules, forming an equilibrium mixture of the free and DNA-bound copper (II) complex to the electrode surface [16]. As a complement to the absorption spectral titrations, luminescence titrations and DNA melting temperature experiments, the CV data suggest that the sulphonamide imine copper (II) complex binds the DNA helix.

In order to further clarify the DNA interaction mode of the newly prepared ligand and complex, viscosity measurements have been carried out on CT-DNA (77 μM) by varying the complex concentration (0–100 μM). Viscosity measurements provide the most critical test for the DNA binding mode [17]. In classical intercalation, the DNA helix lengthens as base pairs are separated to accommodate the bound adduct leading to increased DNA viscosity whereas a partial, non-classical intercalation causes a bend in the DNA helix reducing its effective length and thereby its viscosity. The effects of the free ligand and complex on the viscosity of CT-DNA are shown in Fig. 7. Upon increasing the amount of the free ligand and complex, the relative viscosity of CT-DNA increases steadily, which suggests that the free ligand and complex are bound to the DNA helix by intercalation. An increased degree of relative viscosity, depending on their affinity to the DNA, follows the order in which the complex > free ligand. These results were consistent with our spectroscopic measurements.

In conclusion, a new Sulphonamide imine copper (II) complex has been synthesized and characterized by analytical and single crystal X-ray diffraction. Spectroscopic, cyclic voltametry and viscosity measurement studies suggest that the free ligand and complex can bind CT-DNA in an intercalative mode, where the prepared complex has greater CT-DNA binding affinity than the free ligand itself.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.inoche.2012.05.006.

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[5] All the reagents were of analytical reagent grade. (A) The Sulphonamide imine Schiff base ligand was prepared by refluxing sulphanilamide (2 mmol, 0.328 g) and Benzoylacetone (2 mmol, 0.326 g) in about 15 ml of methanol for 3 hours at *ca.* 70 C in presence of 1–2 drops of conc. H_2SO_4. The precipitated light yellow coloured ligand was filtered and air dried. The purity of the ligand was checked by TLC and melting point determination method. Yield: 2.74 g (~90%). M.P.: 154 C. Anal. Calc. for $C_{16}H_{16}N_2O_3S$ (M.W.: 316.04 g/mol): C, 60.50; H, 4.73; N, 4.42. Found: C, 60.49; H, 4.68; N, 4.33. (B) The title copper(II) complex was synthesized by reaction of the above prepared ligand (2 mmol, 0.638 g) with copper acetate monohydrate (1mmol, 0.198 g) in about 20 ml of methanol solution at 70 C. Block, black coloured single crystals suitable for X-ray analysis was obtained on slow evaporation of the reaction mixture solution. Yield: 0.55 g (~80%). Anal. Calc. for $C_{32}H_{30}CuN_4O_6S_2$ (M.W.: 694.26 g/mol): C, 55.31; H, 4.32; N, 8.07. Found: C, 55.21; H, 4.36; N, 8.17. μ_{eff} = 1.78 B.M. The diffraction data of a block, black crystal (size 0.22x 0.15x 0.12 mm) was collected on an Oxford Diffraction Gemini-E CCD system with graphite monochromated MoKα (λ = 0.71073) at 170 K. Data reduction and an absorption correction were performed with the CrysAlis program [18]. The structure of the complex was solved by direct methods using the SHELX97 software [19]. The non-H-atoms were anisotropically refined using the full-matrix least square method on F^2. Hydrogen atoms H3A, H3B, H4A, and H4B were allowed to refine at N--H distance restraints of 0.87(1) Å and H--N—H angle restraints of 1.35(2) Å. All remaining hydrogen atoms were placed at calculated positions and refined riding on the parent atoms with atom-hydrogen lengths and isotropc displacement parameters (CH) 0.95 Å and ~1.2 times Ueq of the parent atoms, (CH_3) 0.98 Å and ~1.5 times Ueq of the parent atoms. Refinement of the C5 thermal amplitude was adjusted with an ISOR constraint. Crystal data: C_{32} H_{30} Cu N_4 O_6 S_2, Mr. 694.26 g mol^{-1}, Orthorhombic space group Pca2 (1), a = 19.9292(11) Å, b = 5.4243(4) Å, c = 28.6159(18) Å, V = 3093.4 93) $Å^{-3}$, Z = 4, Dc = 1.491 Mg m^{-3}, $F(000)$ = 1436, R_1 = 0.0757, wR_2 = 0.1333
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