

An-Najah National University

Faculty of Graduate Studies

**Preparation and Evaluation of the Activities of
New Mono-Cation phen- Cu(II) Complexes
Toward Cancer Cells**

By

Malak Daqqa

Supervisor

Prof. Ismail Warad

Co- Supervisor

Dr. Ashraf Sawafta

**This Thesis is Submitted in Partial Fulfillment of the Requirements for
the Degree of Master of Chemistry, Faculty of Graduate Studies, An-
Najah National University, Nablus, Palestine.**

2017

**Preparation and Evaluation of the Activities of New
Mono-Cation phen- Cu(II) Complexes Toward Cancer
Cells**

**By
Malak Daqqa**

This thesis was defended successfully on 17/12/2017 and approved by:

Defense committee Members

Signature

- | | |
|---|-------|
| – Prof. Ismail Warad / Supervisor | |
| – Dr. Ashraf Sawafta / Co-Supervisor | |
| – Dr. Lamees Majjad/External Examiner | |
| – Prof. Mohammad Al-Nuri /Internal Examiner | |

III

Dedication

I dedicate my thesis to:

My husband Mohammed Daqqa, my beloved parents Zeiad Daqqa and Hala Daqqa, and my dear uncle's wife Subheia Daqqa for their continues support during my study.

My dedication is extended to my little daughters Mela Daqqa and Selen Daqqa , my dear brothers and to my sister Manar Daqqa.

All of my friends who have studied with me, especially Malak Saif, Haneen Jumaa, Doaa Sawafta and Israa Aqel.

My teacher at the An-Najah National University –Nablus.

All people who gave me hard to complete this work.

Acknowledgments

I would like to express my deep appreciation and respect to Prof. Ismail Warad (Advisor) and Dr. Ashraf Sawafta (co-supervisor) for their direct supervision, encouragement and help throughout the course of this work. Also, I would like to thank my committee members and laboratory technicians for their help and fruitful discussions.

Special thanks go to my husband Mohammed Daqqa, my father Zeiad, my mother Hala and aunt subhia, for their continuous support and encouragement. Special thanks are extended to my sister Manar, my brothers and to my daughters Mela and Selen.

Thanks are also extended to my friends and to Mr. Nafith Dwikat for his technical support during my work in the laboratory.

الإقرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان :

Preparation and Evaluation of the Activities of New Mono-Cation phen- Cu(II) Complexes Toward Cancer Cells

أقر بأن ما اشتملت عليه هذه الرسالة إنما هو نتاج جهدي الخاص باستثناء ما تمت الإشارة إليه حيثما ورد وان هذه الرسالة ككل أو جزء منها لم يقدم من قبل لنيل أي درجة علمية أو بحث علمي أو بحثي لدى أي مؤسسة تعليمية أو بحثية.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student Name:

اسم الطالبة: ملاك دقة

Signature:

التوقيع :

Date:

التاريخ : 17/12/2017

Table of Contents

Dedication	III
Acknowledgments.....	IV
Declaration	V
Table of Contents	VI
List of Figures	VIII
List of Tables.....	XI
Abstract	XII
Chapter One.....	1
Introduction	1
1.1.The aim.....	2
1.2 Introduction.....	2
1.3 NOVELTY	4
Chapter Two.....	5
Experimental part	5
2.1 Materials.....	6
2.2 Equipment	6
2.3 Synthesis of [Cu(NO ₂ -phen) ₂ Br]Br complex	7
2.4 X-ray single-crystal data collection	8
Refinement	22
2.5 Computational method.....	28
2.6 DNA binding investigation.....	28
2.7 Viscosity measurements.....	29
Chapter Three.....	30
Results and Discussion	31
3.1 Synthesis	31
3.1.1 Crystal structure for [Cu(NO ₂ -phen) ₂ Br]Br complex.....	32
3.2 Computational studies.....	35

3.1.2 Crystal structure for [Cu(phen) ₂ Br]Br complex	44
3.3. Hirschfeld surface analysis (HSA)	45
3.4. MS, Elemental analyses and conductivity	50
3.5 Visible and ultraviolet spectra	51
3.6 Solvatochromism	53
3.7 FT- IR spectral investigation	55
3.8 TG/DTG analyses	56
Chapter Four.....	58
DNA binding studies.....	58
4.1 Absorption spectroscopy.....	59
4.2 Viscosity measurements.....	61
Chapter Five	63
Conclusions	64
Supplementary material	65
References	66
المخلص	ب

List of Figures

- Fig 3.1 The ORTEP generated diagram of (a) *cis*-[Cu(NO₂-phen)₂Br]Br and (b) *trans*-[Cu(NO₂-phen)₂Br]Br isomers. Hydrogen atoms and water molecules are omitted for clarity. 34
- Fig 3.2 The ORTEP generated diagram of (a) *cis*-[Cu(NO₂-phen)₂Br]Br and (b) *trans*-[Cu(NO₂-phen)₂Br]Br isomers. Hydrogen atoms and water molecules are omitted for clarity. 34
- Fig. 3.3 a) Perspective view of the XRD structure of *cis*-[Cu(NO₂-phen)₂Br]Br showing the atom numbering scheme. b) Side and top views of the X-ray structure. c) The optimized ground state geometry for the copper complex at B3LYP/6-31G(d) level of theory. 36
- Fig. 3.4 a) Perspective view of the XRD structure of *cis*-[Cu(NO₂-phen)₂Br]Br showing the atom numbering scheme. b) Side and top views of the X-ray structure. c) The optimized ground state geometry for the copper complex at B3LYP/6-31G(d) level of theory. 37
- Fig. 3.5 a) Perspective view of the FDT optimization of *cis*-[Cu(NO₂-phen)₂Br]Br showing the atom numbering scheme. b) Side and top views of the FDT structure. c) The optimized ground state geometry for the copper complex at B3LYP/6-31G level of theory. 37
- Fig. 3.6 Graphical correlation between experimentally determined (a) bond lengths (pm) and (b) bond angles (°) versus the calculated values determined by HF/3-21G, HF/6-31G* and B3LYP/6-31G* methods for [Cu(NO₂-phen)₂Br]Br complex. 38
- Fig. 3.7 Graphical correlation between experimentally determined (a) bond lengths (pm) and (b) bond angles (°) versus the calculated values

determined by HF/3-21G, HF/6-31G* and B3LYP/6-31G* methods for [Cu(NO ₂ -phen) ₂ Br]Br complex.	39
Fig. 3.8 The HOMO (lower) and LUMO (upper) plots of [Cu(NO ₂ -phen) ₂ Br]Br complex at the B3LYP/6-31G* level of theory.....	43
Fig 3.9 The ORTEP generated diagram of [Cu(phen) ₂ Br]Br complex.	44
Fig 3.10 Packing diagram of [Cu(phen) ₂ Br]Br complex.	45
Fig. 3.11 Hirshfeld surfaces comprising d _{norm} surface plots for [Cu(NO ₂ -phen) ₂ Br]Br complex.....	46
Fig. 3.12 Fingerprint plots of [Cu(NO ₂ -phen) ₂ Br]Br complex -0.28 au (blue) to 1.21 au (red).....	47
Fig. 3.13 Fingerprint plots of [Cu(NO ₂ -phen) ₂ Br]Br complex -0.28 au (blue) to 1.21 au (red).....	47
Fig. 3.14 Fingerprint plots of [Cu(NO ₂ -phen) ₂ Br]Br complex -0.28 au (blue) to 1.21 au (red).....	48
Fig. 3.15 Fingerprint plots of [Cu(NO ₂ -phen) ₂ Br]Br complex -0.28 au (blue) to 1.21 au (red).....	48
Fig. 3.16 Hirshfeld surfaces comprising d _{norm} surface plots for [Cu(phen) ₂ Br]Br complex.	49
Fig. 3.17 Hirshfeld surfaces comprising d _{norm} surface plots for [Cu(phen) ₂ Br]Br complex.	50
Fig. 3.18 UV spectrum of [Cu(NO ₂ -phen) ₂ Br]Br complex dissolved in water at RT (a) 1 x 10 ⁻⁴ M, Vis. spectra (b) 1 x 10 ⁻³ M, freshly prepared and (c) same solution as in (b) but after 30 days.....	52
Fig. 3.19 Absorption spectra of [Cu(NO ₂ -phen) ₂ Br]Br complex in dissolvable solvents.....	54
Fig. 3.20 Dependence of the λ _{max} of [Cu(NO ₂ -phen) ₂ Br]Br complex on DN solvent Gutmann's donor numbers.	55

- Fig. 3.21 FT-IR spectra of a) NO₂-phen free ligand and b) [Cu(NO₂-phen)₂Br]Br complex..... 56
- Fig. 3.22 TG/DTG thermal curves of [Cu(NO₂-phen)₂Br]Br complex. 57
- Fig. 4.1 .(a) Electronic spectral titration of [Cu(NO₂-phen)₂Br]Br with CT-DNA at 270 nm in Tris-HCl buffer; [Cu] = 5.0×10⁻⁵; [DNA]: *a* 0.0, *b* 5.0×10⁻⁶, *c* 1.0×10⁻⁵, *d* 1.0×10⁻⁴, *e* 1.0×10⁻³, *f* 2.0×10⁻²M. The arrow denotes the gradual decrease of [Cu(NO₂-phen)₂Br]Br concentration upon DNA addition.(b) Plot of [DNA]/(ε_a- ε_f) vs.[DNA] at λ_{max} = 270 nm to establish the K_b value..... 60
- Fig. 4.2 .(a) Electronic spectral titration of [Cu(NO₂-phen)₂Br]Br with CT-DNA at 270 nm in Tris-HCl buffer; [Cu] = 5.0×10⁻⁵; [DNA]: *a* 0.0, *b* 5.0×10⁻⁶, *c* 1.0×10⁻⁵, *d* 1.0×10⁻⁴, *e* 1.0×10⁻³, *f* 2.0×10⁻²M. The arrow denotes the gradual decrease of [Cu(NO₂-phen)₂Br]Br concentration upon DNA addition.(b) Plot of [DNA]/(ε_a- ε_f) vs.[DNA] at λ_{max} = 270 nm to establish the K_b value. 61
- Fig. 4.3 Effect of increasing amounts of [Cu] on the relative viscosities of DNA at 25.0 (±0.1) °C, [DNA] = 5.0 x 10⁻⁴ M. 62

List of Tables

Table 2.1 crystal and structure refinement data for of [Cu(NO ₂ -phen) ₂ Br]Br complex.....	9
Table 2.2 Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å ²) of [Cu(NO ₂ -phen) ₂ Br]Br complex.....	10
Table2.3 Atomic displacement parameters (Å ²) of [Cu(NO ₂ phen) ₂ Br]Br complex.....	13
Table 2.4 Experimental bond lengths (pm) and angles (°) of cis/trans-[Cu(NO ₂ -phen) ₂ Br]Br complex.	15
Table 2.5 Experimental dihedral angles (°) of cis/trans-[Cu(NO ₂ -phen) ₂ Br]Br complex.	17
Table 2.6: Crystal data	21
Table 2.7: Data collection	21
Table 2.8: Refinement.....	22
Table 2.9 Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å ²).....	22
Table 2.10 Atomic displacement parameters (Å ²) of [Cu(phen) ₂ Br]Br complex.....	24
Table 2.11 Geometric parameters (Å, °).....	26
Table 3.1 XRD selective bond lengths and anglers for [Cu(NO ₂ -phen) ₂ Br]Br complex.....	33
Table 3.2 Hydrogen bonds for [Cu(NO ₂ -phen) ₂ Br] ⁺ complex [Å and °]. ..	35
Table 3.3 Calculated electronic properties and quantum parameters for [Cu(NO ₂ -phen) ₂ Br]Br complex obtained at the B3LYP/6-31G* level of theory	41
Table 3.4 Selected experimental and calculated bond lengths (pm) and angles (°) of cis/trans-[Cu(NO ₂ -phen) ₂ Br]Br complex. Calculated values were obtained at the HF/3-21G, HF/6-31G* and B3LYP/6-31G* levels of theory.	41

**Preparation and Evaluation of the Activities of New Mono-Cation
phen- Cu(II) Complexes Toward Cancer Cells**

By

Malak Daqqa

Supervisor

Prof. Dr. Ismail Warad

Co- Supervisor

Dr. Ashraf Sawafta

Abstract

Water soluble mono-cationic copper(II) complexes of the general formula $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$, ($\text{NO}_2\text{-phen}$ = 5-nitro-1,10-phenanthroline) and $[\text{Cu}(\text{phen})_2\text{Br}]\text{Br}$ were prepared in good yield under ultrasonic irradiation. The desired complexes were isolated as bromide salts and identified by MS, EA, UV-visible, TG/DTA, FT-IR and XRD. The single-crystal X-ray diffraction and Hirshfeld analysis revealed distorted square pyramidal geometry around the Cu(II) center. The geometry of the $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]^+$ complex was fully optimized with ab-initio methods and (DFT/B3LYP) density functional theory, then structural parameters were compared to the XRD data. The Solvatochromism of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex was investigated in several polar solvents. Absorption and viscosity titration studies concluded that the $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex is a very good CT-DNA binder.

Chapter One

Introduction

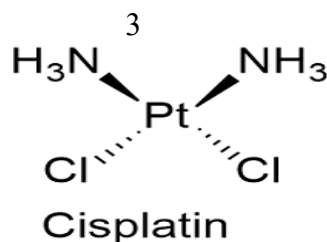
1.1. The aim

The aims of this study were:

- ❖ Two new novel copper(II) complexes will be prepared: five coordinated 1,10-phenanthroline and substituted 1,10-phenanthroline Copper(II) bromide complexes were made available.
- ❖ The desired complexes will be characterized by several available spectral analysis techniques like: IR, UV-Visible, TG/DTA, EA and, MS.
- ❖ The desired complexes will be analyzed by X-ray single crystals diffraction.
- ❖ Computational DFT and Hirschfeld surface analysis of complexes were performed; both theoretical and experimental structural parameters were compared.
- ❖ The solvatochromism behavior of the complexes in different solvents was figured out.
- ❖ The CT-DNA-binding ability of the complexes will be evaluated.

1.2 Introduction

One of large challenges in medicinal and bioinorganic chemistry is to develop new anticancer active reagents through either lab-synthesis or natural-isolation of such compounds [1-3]. Numerous coordination compounds, such as *cis*-platin complexes, have played a critical role as antib caner drugs [3-5]. Even with the satisfactory results of *cis*-platin with structure formula:



in treating several types of cancer, there are still a number of side effects such as: dose-limiting toxicity and resistance phenomena [6]. Transition metal ion complexes were engaged to solve such old standing problems [7]. Complexes of copper(I) and (II) showed promising perspectives [8–12] since the metal is an essential trace element in the body, and the complexes are water soluble so dose-limitation may be reduced [12].

1,10-Phenanthroline ligand and its derivatives find extensive applications as bidentate chelating ligands in coordination chemistry [13-16]. Many 1,10-phenanthroline and hybrid 1,10-phenanthroline ligands/metal complexes have found interesting medical applications [17].

Copper(II)/1,10-phenanthroline complexes mixed with other ligands received much attention due to their remarkable cytotoxicity which in some cases is more efficient than that of cisplatin [18-20]. Moreover, such complexes are considered one of the most active DNA binding agents, mostly through groove mode causing rapid DNA cleavage [21-25].

Solvatochromism phenomenon in complexes has gained a good awareness in organic and inorganic chemistry because of its implementation in Lewis acids and bases color-indexing [26–28]. Investigating solvatochromism in complexes has yielded a quantitative method to evaluate the role of solvents in understanding the physicochemical features of complexes [29].

Due to the strong Jahn–Teller effect in copper(II) complexes, particularly with coordination number 5, evident solvatochromic was observed [27-29]. Herein, we report the synthesis, solvatochromism, thermal, Hirshfeld surface analysis, computational study and spectroscopic properties of the mono-cation $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex. The crystal structure of the title complex was also investigated.

1.3 NOVELTY

1. Water soluble copper(II) complexes with five coordination number around the center were prepared using 5-nitro-1.10-phenanthroline and 1.10-phenanthroline ligands for the first time.
2. Novel 3D structures of each complex were solved by X-ray single analysis, compared by *Hirschfeld surface analysis (HSA)*, as well as HF and DFT theoretical calculation.
3. CT-DNA binding ability of the complexes found to be very high the K_b constants were in a 1.0×10^5 range.

Chapter Two

Experimental part

2.1 Materials

All reagents were of analytical grade and purchased from Sigma–Aldrich and used as received. Elemental analyses were recorded with an Elementar Varrio EL analyzer. The FT-IR spectra ($4000\text{--}500\text{ cm}^{-1}$) were obtained with a Perkin–Elmer 621 spectrophotometer. Thermal analyses were carried out in an open air system at a heating rate of $10\text{ }^{\circ}\text{C min}^{-1}$ and a temperature range of $0\text{--}1000\text{ }^{\circ}\text{C}$ using TA SDT-Q600 instrument. Electronic spectra were recorded in water at room temperature on Pharmacia LKB-Biochrom 4060 spectrophotometer. Mass spectrometry data were obtained by a Finnigan 711A (8 kV), modified by AMD and reported as mass/charge (m/z).

2.2 Equipment

X-Ray Diffractometer, Mysore University, India, used to determine the structure of crystalline compounds.

Perkin Elmer Spectrum 1000 FT-IR Spectrophotometer, An-Najah National University, Palestine, used to obtain the spectrum of resulting complexes, TU-1901 Double-Beam **UV–Visible Spectrophotometer**, TGA-7 Perkin Elmer **Thermogravimetric Analyzer** (Perkin Elmer Inc., Waltham, MA, USA). Mysore University, India, used to obtain **TG/DTG** for L_1 , L_2 , and their complexes **1,2**.

EI-MS: Mysore University, India, used to obtain the spectrum for complexes.

A TU-1901 double-beam UV–visible spectrophotometer was employed to record the UV-visible spectra for complexes, whereas Infrared spectra (IR) were recorded on a Perkin Elmer Spectrum 1000 FT-IR Spectrophotometer. EI-MS data were obtained with the aid of a Finnigan 711A (8 kV) (Perkin Elmer Inc., Waltham, MA, USA) instrument. Thermogravimetric analysis (TGA) and differential thermal analysis (DTA) for both complexes were accomplished by using a TGA-7 Perkin Elmer thermogravimetric analyzer (Perkin Elmer Inc., Waltham, MA, USA). Elemental analysis (C, H, and N) for complex 2 was performed out with EuroVector EA3000 (C, H, and N) instrument, and the observed results agreed with the calculated percentages to within $\pm 0.4\%$. We carried out Hirshfeld surface analysis for complexes 1,2 using the program CRYSTAL EXPLORER 3.1 [35].

2.3 Synthesis of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex

$\text{CuBr}_2 \cdot 2\text{H}_2\text{O}$ (1 mmol) was dissolved in 20 mL of ethanol under ultrasonic waves, to which an ethanolic solution (10 mL) of 2.2 mmol of $\text{NO}_2\text{-phen}$ was added drop-wise with stirring for 5 minutes until a brown precipitate was formed. The product complex was filtered, washed by dichloromethane to remove excess $\text{NO}_2\text{-phen}$ ligand and then dried under vacuum. Since the complex is highly soluble in water, crystals suitable for X-ray structural analysis were obtained by slow evaporation of an aqueous solution of the complex, The complex was isolated as a blue powder, with 81% yield, m. p. = 215.0°C , MS m/z 647.90 M^+ due to its mono-cationic

nature $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]^+$ with chemical Formula: $\text{C}_{24}\text{H}_{20}\text{Br}_2\text{CuN}_6\text{O}_7$ ($[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}\cdot 3\text{H}_2\text{O}$). Elemental Analysis: Calculated: C, 39.61; H, 2.77; N, 11.55%. Found: C, 39.22; H, 2.74; N, 11.48%. IR: 3402 ($\nu_{\text{H}_2\text{O}}$), 3050 ($\nu_{\text{C-H}}$ of phen), 1520 ($\nu_{\text{N=C}}$), 1330 (ν_{NO_2}), 518 ($\nu_{\text{Cu-N}}$). UV–Vis. in water: λ_{max} at: 270 nm ($2.8 \times 10^4 \text{ M}^{-1}\text{L}^{-1}$) and 705 nm ($1.8 \times 10^2 \text{ M}^{-1}\text{L}^{-1}$).

2.4 X-ray single-crystal data collection

Several suitable crystals were mounted and the diffraction data were collected at RT using an Oxford Xcalibur diffractometer (Mo $\text{K}\alpha$ radiation, $\lambda = 0.7107 \text{ \AA}$). Data was processed using CrysAlisPro software [30]. The structures were solved by direct methods and refined by least-squares method on F2 using the SHELXTL program package [31]. Hydrogen atoms are located on the calculated positions except those attached to water molecules. The hydrogen atoms of two water molecules are located using Fourier difference map, whereas hydrogens atoms of the water molecule (O35) could not be located. Data collection and refinement parameters are given in Table 2.2.

Table 2.1 crystal and structure refinement data for of [Cu(NO₂-phen)₂Br]Br complex

Empirical formula	C ₂₄ H ₂₀ Br ₂ CuN ₆ O ₇	
Formula weight	724.80	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 9.9902(6) Å	α = 99.274(5)°.
	b = 11.2406(6) Å	β = 105.540(5)°.
	c = 13.6643(7) Å	γ = 110.934(5)°.
Volume	1323.30(13) Å ³	
Z	2	
Density (calculated)	1.819 Mg/m ³	
Absorption coefficient	3.901 mm ⁻¹	
F(000)	716	
Crystal size	0.4 x 0.3 x 0.2 mm ³	
Theta range for data collection	3.23 to 26.30°.	
Index ranges	-9 ≤ h ≤ 12, -14 ≤ k ≤ 13, -17 ≤ l ≤ 16	
Reflections collected	9953	
Independent reflections	5353 [R(int) = 0.0243]	
Completeness to theta = 26.30°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.63506	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	5353 / 8 / 395	
Goodness-of-fit on F ²	1.053	
Final R indices [I > 2σ(I)]	R1 = 0.0507, wR2 = 0.1192	
R indices (all data)	R1 = 0.0779, wR2 = 0.1347	
Largest diff. peak and hole	0.895 and -0.723 e. Å ⁻³	

Table 2.2 Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$) of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex

$U_{\text{iso}}^*/U_{\text{eq}}$	z	y	x	
0.0418 (2)	0.27575 (5)	0.37208 (7)	0.62724 (8)	Cu1
0.0591 (2)	0.33044 (5)	0.52921 (7)	0.52929 (8)	Br1
0.0692 (2)	−0.18273 (5)	0.31886 (8)	0.84562 (8)	Br2
0.0383 (10)	0.1483 (3)	0.4305 (4)	0.6493 (5)	N1
0.0481 (13)	0.1480 (4)	0.5525 (6)	0.7330 (7)	C2
0.058*	0.2123	0.6188	0.7860	H2A
0.0487 (14)	0.0560 (5)	0.5856 (6)	0.7450 (7)	C3
0.058*	0.0594	0.6721	0.8056	H3A
0.0482 (14)	−0.0380 (5)	0.4914 (6)	0.6681 (7)	C4
0.058*	−0.1002	0.5120	0.6751	H4A
0.0424 (12)	−0.0409 (4)	0.3615 (6)	0.5772 (6)	C5
0.0499 (14)	−0.1361 (4)	0.2540 (6)	0.4893 (7)	C6
0.060*	−0.2005	0.2675	0.4952	H6A
0.0468 (13)	−0.1336 (4)	0.1352 (6)	0.3994 (7)	C7
0.0471 (13)	−0.0383 (4)	0.1029 (6)	0.3875 (7)	C8
0.0579 (16)	−0.0273 (5)	−0.0214 (6)	0.2999 (7)	C9
0.070*	−0.0869	−0.0938	0.2383	H9A
0.0659 (18)	0.0709 (6)	−0.0341 (6)	0.3064 (8)	C10
0.079*	0.0779	−0.1158	0.2489	H10A
0.0532 (15)	0.1599 (5)	0.0717 (6)	0.3963 (7)	C11
0.064*	0.2261	0.0600	0.3983	H11A

0.0434 (10)	0.1539 (3)	0.1913 (4)	0.4812 (5)	N12
0.0386 (11)	0.0565 (4)	0.2056 (5)	0.4765 (6)	C13
0.0367 (11)	0.0543 (4)	0.3347 (5)	0.5704 (6)	C14
0.0872 (16)	0.0715 (4)	0.3544 (5)	0.9653 (7)	O36
0.217 (5)	0.1058 (11)	0.2003 (12)	1.1316 (12)	O35
0.0698 (16)	−0.2380 (4)	0.0326 (6)	0.3148 (8)	N29
0.125 (3)	−0.2480 (5)	−0.0597 (7)	0.2003 (10)	O29
0.128 (3)	−0.3069 (4)	0.0415 (7)	0.3623 (9)	O30
0.0396 (10)	0.3355 (3)	0.3870 (4)	0.8518 (5)	N15
0.0513 (14)	0.3072 (4)	0.4405 (6)	0.9701 (7)	C16
0.062*	0.2565	0.4861	0.9616	H16A
0.0592 (16)	0.3506 (5)	0.4314 (7)	1.1088 (7)	C17
0.071*	0.3294	0.4711	1.1911	H17A
0.0600 (17)	0.4239 (5)	0.3638 (7)	1.1213 (8)	C18
0.072*	0.4524	0.3560	1.2123	H18A
0.0486 (14)	0.4568 (4)	0.3058 (6)	0.9985 (7)	C19
0.0635 (19)	0.5327 (5)	0.2322 (7)	0.9955 (9)	C20
0.0583 (18)	0.5644 (4)	0.1871 (6)	0.8746 (9)	C21
0.070*	0.6152	0.1413	0.8791	H21A
0.0467 (14)	0.5229 (4)	0.2071 (5)	0.7414 (7)	C22
0.0548 (16)	0.5551 (5)	0.1678 (6)	0.6146 (8)	C23
0.066*	0.6078	0.1248	0.6132	H23A
0.0615 (17)	0.5088 (5)	0.1932 (6)	0.4945 (8)	C24
0.074*	0.5309	0.1694	0.4107	H24A
0.0552 (15)	0.4283 (5)	0.2545 (6)	0.4948 (7)	C25
0.066*	0.3962	0.2689	0.4096	H25A

0.0443 (11)	0.3958 (3)	0.2932 (5)	0.6139 (5)	N26
0.0394 (12)	0.4430 (4)	0.2708 (5)	0.7361 (6)	C27
0.0391 (12)	0.4104 (4)	0.3225 (5)	0.8654 (6)	C28
0.060 (3)	0.5668 (8)	0.1729 (10)	1.0950 (11)	N32A
0.082 (3)	0.5029 (8)	0.1372 (10)	1.1474 (11)	O33A
0.082 (3)	0.6578 (8)	0.1653 (10)	1.1306 (14)	O34A
0.179 (12)*	0.1258 (16)	−0.043 (2)	0.995 (2)	O37
0.071 (4)	0.7052 (9)	0.1470 (11)	1.0440 (15)	O34B
0.071 (4)	0.6446 (10)	0.1165 (12)	0.9141 (19)	N32B
0.084 (4)	0.6439 (9)	0.0306 (10)	0.7956 (14)	O33B

Table2.3 Atomic displacement parameters ($\text{\AA}^2$) of $[\text{Cu}(\text{NO}_2\text{phen})_2\text{Br}]\text{Br}$ complex.

U^{23}	U^{13}	U^{12}	U^{33}	U^{22}	U^{11}	
0.0152 (3)	0.0148 (3)	0.0197 (3)	0.0326 (3)	0.0515 (4)	0.0431 (4)	Cu1
0.0213 (3)	0.0238 (3)	0.0484 (4)	0.0461 (3)	0.0785 (5)	0.0714 (5)	Br1
0.0142 (3)	0.0177 (3)	0.0112 (4)	0.0426 (3)	0.0856 (5)	0.0598 (5)	Br2
0.0103 (19)	0.0095 (18)	0.015 (2)	0.034 (2)	0.045 (3)	0.032 (2)	N1
0.011 (3)	0.015 (3)	0.015 (3)	0.041 (3)	0.049 (3)	0.049 (4)	C2
0.018 (3)	0.013 (3)	0.013 (3)	0.052 (3)	0.047 (3)	0.041 (3)	C3
0.023 (3)	0.018 (3)	0.022 (3)	0.046 (3)	0.061 (4)	0.043 (3)	C4
0.011 (2)	0.010 (2)	0.026 (3)	0.033 (3)	0.056 (3)	0.040 (3)	C5
0.009 (3)	0.011 (3)	0.031 (3)	0.035 (3)	0.064 (4)	0.052 (4)	C6
-0.001 (2)	0.005 (2)	0.025 (3)	0.033 (3)	0.053 (3)	0.047 (3)	C7
0.005 (3)	0.005 (3)	0.019 (3)	0.047 (3)	0.046 (3)	0.040 (3)	C8
0.002 (3)	0.010 (3)	0.018 (3)	0.059 (4)	0.048 (3)	0.053 (4)	C9
0.020 (3)	0.019 (4)	0.012 (3)	0.083 (5)	0.042 (3)	0.061 (4)	C10
0.024 (3)	0.015 (3)	0.020 (3)	0.053 (3)	0.055 (4)	0.051 (4)	C11
0.014 (2)	0.011 (2)	0.015 (2)	0.042 (2)	0.046 (3)	0.038 (3)	N12
0.008 (2)	0.010 (2)	0.020 (2)	0.036 (3)	0.046 (3)	0.034 (3)	C13
0.010 (2)	0.009 (2)	0.023 (2)	0.034 (3)	0.047 (3)	0.033 (3)	C14
0.019 (3)	0.026 (3)	0.023 (3)	0.053 (3)	0.087 (4)	0.104 (4)	O36
0.160 (12)	0.118 (10)	0.114 (9)	0.348 (16)	0.234 (12)	0.148 (9)	O35

−0.003 (3)	0.002 (3)	0.027 (4)	0.045 (3)	0.062 (4)	0.079 (5)	N29
−0.011 (3)	0.009 (4)	−0.006 (4)	0.069 (4)	0.075 (4)	0.149 (7)	O29
−0.011 (3)	0.036 (4)	0.018 (5)	0.043 (3)	0.131 (6)	0.158 (7)	O30
0.0091 (19)	0.0092 (18)	0.016 (2)	0.026 (2)	0.050 (3)	0.039 (3)	N15
0.017 (3)	0.018 (3)	0.022 (3)	0.039 (3)	0.065 (4)	0.050 (4)	C16
0.013 (3)	0.021 (3)	0.028 (4)	0.044 (3)	0.085 (5)	0.049 (4)	C17
0.005 (3)	0.009 (3)	0.040 (4)	0.045 (3)	0.083 (5)	0.052 (4)	C18
0.004 (3)	0.008 (2)	0.032 (3)	0.031 (3)	0.062 (4)	0.052 (4)	C19
0.014 (3)	0.013 (3)	0.055 (4)	0.039 (3)	0.072 (4)	0.091 (6)	C20
0.011 (3)	0.008 (3)	0.037 (4)	0.030 (3)	0.045 (3)	0.097 (6)	C21
0.005 (2)	0.013 (3)	0.017 (3)	0.031 (3)	0.037 (3)	0.064 (4)	C22
0.012 (3)	0.022 (3)	0.010 (3)	0.039 (3)	0.043 (3)	0.071 (5)	C23
0.017 (3)	0.033 (3)	0.012 (3)	0.053 (4)	0.059 (4)	0.067 (5)	C24
0.022 (3)	0.027 (3)	0.020 (3)	0.056 (3)	0.068 (4)	0.047 (4)	C25
0.015 (2)	0.017 (2)	0.023 (2)	0.035 (2)	0.055 (3)	0.047 (3)	N26
0.006 (2)	0.014 (2)	0.015 (2)	0.027 (2)	0.035 (3)	0.051 (3)	C27
−0.001 (2)	0.005 (2)	0.016 (2)	0.026 (2)	0.039 (3)	0.042 (3)	C28
0.002 (5)	0.008 (5)	0.025 (5)	0.061 (6)	0.058 (6)	0.050 (6)	N32A
0.020 (6)	0.014 (5)	0.042 (5)	0.097 (7)	0.091 (7)	0.057 (6)	O33A
0.030 (5)	0.004 (6)	0.056 (6)	0.065 (6)	0.084 (7)	0.100 (9)	O34A
0.023 (6)	−0.012 (6)	0.022 (6)	0.057 (7)	0.069 (7)	0.063 (8)	O34B
0.016 (6)	0.009 (8)	0.027 (8)	0.052 (7)	0.045 (7)	0.101 (12)	N32B
0.035 (6)	−0.003 (6)	−0.003 (6)	0.086 (8)	0.046 (6)	0.077 (8)	O33B

Table 2.4 Experimental bond lengths (pm) and angles (°) of cis/trans-[Cu(NO₂-phen)₂Br]Br complex.

121.4 (5)	C5—C14—C13	171.75 (18)	N1—Cu1—N26
121.5 (7)	O30—N29—O29	95.44 (16)	N1—Cu1—N15
120.1 (7)	O30—N29—C7	80.06 (17)	N26—Cu1—N15
118.4 (7)	O29—N29—C7	79.54 (17)	N1—Cu1—N12
118.6 (5)	C16—N15—C28	95.57 (18)	N26—Cu1—N12
130.4 (4)	C16—N15—Cu1	111.27 (17)	N15—Cu1—N12
110.9 (3)	C28—N15—Cu1	94.18 (12)	N1—Cu1—Br1
122.4 (5)	N15—C16—C17	94.04 (13)	N26—Cu1—Br1
118.8	N15—C16—H16A	128.02 (12)	N15—Cu1—Br1
118.8	C17—C16—H16A	120.70 (13)	N12—Cu1—Br1
119.0 (6)	C18—C17—C16	118.3 (4)	C2—N1—C14
120.5	C18—C17—H17A	126.1 (4)	C2—N1—Cu1
120.5	C16—C17—H17A	115.6 (3)	C14—N1—Cu1
120.5 (6)	C17—C18—C19	123.0 (5)	N1—C2—C3
119.7	C17—C18—H18A	118.5	N1—C2—H2A
119.7	C19—C18—H18A	118.5	C3—C2—H2A
116.3 (5)	C18—C19—C28	119.5 (5)	C4—C3—C2
126.5 (6)	C18—C19—C20	120.3	C4—C3—H3A
117.2 (6)	C28—C19—C20	120.3	C2—C3—H3A
109.9 (7)	C21—C20—N32A	119.1 (5)	C3—C4—C5
122.2 (6)	C21—C20—C19	120.4	C3—C4—H4A
126.5 (8)	N32A—C20—C19	120.4	C5—C4—H4A
122.1 (5)	C20—C21—C22	118.6 (5)	C14—C5—C4
119.0	C20—C21—H21A	117.5 (5)	C14—C5—C6

119.0	C22—C21—H21A	123.9 (5)	C4—C5—C6
117.6 (6)	C27—C22—C23	120.8 (5)	C7—C6—C5
117.3 (6)	C27—C22—C21	119.6	C7—C6—H6A
125.1 (6)	C23—C22—C21	119.6	C5—C6—H6A
119.1 (6)	C24—C23—C22	123.8 (5)	C6—C7—C8
120.4	C24—C23—H23A	115.3 (5)	C6—C7—N29
120.4	C22—C23—H23A	120.8 (6)	C8—C7—N29
120.5 (6)	C23—C24—C25	115.7 (5)	C13—C8—C9
119.7	C23—C24—H24A	116.4 (5)	C13—C8—C7
119.7	C25—C24—H24A	128.0 (5)	C9—C8—C7
121.8 (6)	N26—C25—C24	119.6 (6)	C10—C9—C8
119.1	N26—C25—H25A	120.2	C10—C9—H9A
119.1	C24—C25—H25A	120.2	C8—C9—H9A
118.2 (5)	C25—N26—C27	121.2 (6)	C9—C10—C11
126.7 (4)	C25—N26—Cu1	119.4	C9—C10—H10A
115.0 (4)	C27—N26—Cu1	119.4	C11—C10—H10A
122.7 (5)	N26—C27—C22	121.6 (6)	N12—C11—C10
116.1 (4)	N26—C27—C28	119.2	N12—C11—H11A
121.2 (5)	C22—C27—C28	119.2	C10—C11—H11A
123.1 (5)	N15—C28—C19	118.0 (5)	C11—N12—C13
117.0 (5)	N15—C28—C27	130.2 (4)	C11—N12—Cu1
119.9 (5)	C19—C28—C27	111.8 (3)	C13—N12—Cu1
123.5 (11)	O33A—N32A—O34A	124.0 (5)	N12—C13—C8
116.0 (10)	O33A—N32A—C20	115.9 (5)	N12—C13—C14
120.4 (10)	O34A—N32A—C20	120.1 (5)	C8—C13—C14
126.1 (13)	O34B—N32B—O33B	121.5 (5)	N1—C14—C5
		117.1 (4)	N1—C14—C13

Table 2.5 Experimental dihedral angles (°) of cis/trans-[Cu(NO₂-phen)₂Br]Br complex.

11.0 (5)	N1—Cu1—N15—C16	−127.0 (12)	N26—Cu1—N1—C2
−176.0 (5)	N26—Cu1—N15—C16	−70.5 (5)	N15—Cu1—N1—C2
91.9 (5)	N12—Cu1—N15—C16	178.8 (5)	N12—Cu1—N1—C2
−88.6 (5)	Br1—Cu1—N15—C16	58.3 (5)	Br1—Cu1—N1—C2
−164.8 (3)	N1—Cu1—N15—C28	52.9 (14)	N26—Cu1—N1—C14
8.2 (3)	N26—Cu1—N15—C28	109.4 (4)	N15—Cu1—N1—C14
−83.9 (3)	N12—Cu1—N15—C28	−1.3 (3)	N12—Cu1—N1—C14
95.6 (3)	Br1—Cu1—N15—C28	−121.8 (3)	Br1—Cu1—N1—C14
1.0 (8)	C28—N15—C16—C17	−1.0 (8)	C14—N1—C2—C3
−174.5 (4)	Cu1—N15—C16—C17	178.9 (4)	Cu1—N1—C2—C3
0.6 (9)	N15—C16—C17—C18	0.6 (9)	N1—C2—C3—C4
−0.9 (9)	C16—C17—C18—C19	0.1 (9)	C2—C3—C4—C5
−0.3 (9)	C17—C18—C19—C28	−0.3 (8)	C3—C4—C5—C14
179.9 (6)	C17—C18—C19—C20	179.3 (5)	C3—C4—C5—C6
175.7 (6)	C18—C19—C20—C21	3.1 (8)	C14—C5—C6—C7

-4.1 (9)	C28—C19—C20—C21	-176.4 (6)	C4—C5—C6—C7
-18.8 (11)	C18—C19—C20— N32A	-2.8 (9)	C5—C6—C7—C8
161.4 (7)	C28—C19—C20— N32A	-179.9 (5)	C5—C6—C7—N29
-166.2 (6)	N32A—C20—C21— C22	0.7 (9)	C6—C7—C8—C13
1.4 (9)	C19—C20—C21—C22	177.7 (5)	N29—C7—C8—C13
3.0 (8)	C20—C21—C22—C27	-177.4 (6)	C6—C7—C8—C9
-177.3 (6)	C20—C21—C22—C23	-0.5 (9)	N29—C7—C8—C9
-0.3 (8)	C27—C22—C23—C24	0.0 (9)	C13—C8—C9—C10
180.0 (6)	C21—C22—C23—C24	178.1 (6)	C7—C8—C9—C10
1.6 (9)	C22—C23—C24—C25	0.1 (10)	C8—C9—C10—C11
-1.7 (10)	C23—C24—C25—N26	-0.1 (11)	C9—C10—C11— N12
0.3 (9)	C24—C25—N26—C27	-0.1 (9)	C10—C11—N12— C13
176.0 (4)	C24—C25—N26—Cu1	179.0 (5)	C10—C11—N12— Cu1
-127.2 (12)	N1—Cu1—N26—C25	-179.2 (5)	N1—Cu1—N12— C11
175.4 (5)	N15—Cu1—N26—C25	7.5 (5)	N26—Cu1—N12— C11
-74.0 (5)	N12—Cu1—N26—C25	88.9 (5)	N15—Cu1—N12— C11
47.5 (5)	Br1—Cu1—N26—C25	-90.6	Br1—Cu1—N12—

		(5)	C11
48.5 (15)	N1—Cu1—N26—C27	−0.1 (3)	N1—Cu1—N12— C13
−8.9 (4)	N15—Cu1—N26—C27	−173.4 (4)	N26—Cu1—N12— C13
101.8 (4)	N12—Cu1—N26—C27	−91.9 (4)	N15—Cu1—N12— C13
−136.8 (4)	Br1—Cu1—N26—C27	88.6 (4)	Br1—Cu1—N12— C13
1.0 (8)	C25—N26—C27—C22	0.3 (8)	C11—N12—C13— C8
−175.1 (4)	Cu1—N26—C27—C22	−179.0 (4)	Cu1—N12—C13— C8
−175.8 (5)	C25—N26—C27—C28	−179.3 (5)	C11—N12—C13— C14
8.1 (6)	Cu1—N26—C27—C28	1.4 (6)	Cu1—N12—C13— C14
−1.1 (8)	C23—C22—C27—N26	−0.2 (8)	C9—C8—C13—N12
178.7 (5)	C21—C22—C27—N26	−178.6 (5)	C7—C8—C13—N12
175.6 (5)	C23—C22—C27—C28	179.4 (5)	C9—C8—C13—C14
−4.6 (7)	C21—C22—C27—C28	1.0 (8)	C7—C8—C13—C14
−2.4 (8)	C16—N15—C28—C19	0.8 (7)	C2—N1—C14—C5
174.0 (4)	Cu1—N15—C28—C19	−179.1 (4)	Cu1—N1—C14—C5
177.1 (5)	C16—N15—C28—C27	−177.6 (5)	C2—N1—C14—C13
−6.6 (5)	Cu1—N15—C28—C27	2.5 (6)	Cu1—N1—C14— C13

2.0 (8)	C18—C19—C28—N15	−0.2 (8)	C4—C5—C14—N1
−178.2 (5)	C20—C19—C28—N15	−179.7 (5)	C6—C5—C14—N1
−177.5 (5)	C18—C19—C28—C27	178.1 (5)	C4—C5—C14—C13
2.3 (7)	C20—C19—C28—C27	−1.4 (7)	C6—C5—C14—C13
−0.6 (7)	N26—C27—C28—N15	−2.6 (7)	N12—C13—C14— N1
−177.5 (4)	C22—C27—C28—N15	177.8 (5)	C8—C13—C14—N1
178.9 (5)	N26—C27—C28—C19	179.0 (5)	N12—C13—C14— C5
2.0 (7)	C22—C27—C28—C19	−0.6 (8)	C8—C13—C14—C5
137.9 (9)	C21—C20—N32A— O33A	24.9 (10)	C6—C7—N29—O30
−29.1 (14)	C19—C20—N32A— O33A	−152.3 (7)	C8—C7—N29—O30
−45.8 (12)	C21—C20—N32A— O34A	−157.0 (7)	C6—C7—N29—O29
147.3 (10)	C19—C20—N32A— O34A	25.8 (10)	C8—C7—N29—O29

Table 2.6: Crystal data

$F_{000} = \underline{4128}$	<u>CHBrCuNO</u>
$D_x = \underline{2.773} \text{ Mg m}^{-3}$	$M_r = \underline{186.48}$
Melting point: <u>392</u> K	$Z = \underline{48}$
Mo $K\alpha$ radiation $\lambda = \underline{0.71073} \text{ \AA}$	Hall symbol: <u>P_x</u>
Cell parameters from reflections	$a = \underline{23.368 (5)} \text{ \AA}$
$\theta = \underline{50}^\circ$	$b = \underline{30.731 (6)} \text{ \AA}$
$\mu = \underline{13.65} \text{ mm}^{-1}$	$c = \underline{7.5331 (16)} \text{ \AA}$
$T = \underline{293 (2)} \text{ K}$	$\alpha = \underline{90}^\circ$
Cell measurement pressure: <u>1</u> Pa	$\beta = \underline{97.740 (4)}^\circ$
$V = \underline{5360.3 (19)} \text{ \AA}^3$	$\gamma = \underline{90}^\circ$

Table 2.7: Data collection

<u>3658</u> reflections with $I > 2\sigma(I)$	<u>WO</u> diffractometer
$R_{\text{int}} = \underline{0.043}$	Radiation source: <u>fine-focus</u> <u>sealed tube</u>
$\theta_{\text{max}} = \underline{28.2}^\circ$	Monochromator: <u>graphite</u>
$\theta_{\text{min}} = \underline{1.3}^\circ$	$T = \underline{293(2)} \text{ K}$
$h = \underline{-29} \ \underline{30}$	$P = 1 \text{ atom}$
$k = \underline{-40} \ \underline{39}$	Absorption correction: <u>non</u>
$l = \underline{-9} \ \underline{10}$	<u>30712</u> measured reflections
Standard reflections: <u>Rigisd</u> method	<u>6369</u> independent reflections

Table 2.8: Refinement

Hydrogen site location: <u>inferred from neighboring sites</u>	Refinement on F^2
H atoms treated by a mixture of <u>independent and constrained refinement</u>	Least-squares matrix: <u>full</u>
$w = 1/[\sigma^2(F_o^2) + (0.2P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	$R[F^2 > 2\sigma(F^2)] = \underline{0.175}$
$(\Delta/\sigma)_{\max} = \underline{0.292}$	$wR(F^2) = \underline{0.514}$
$\Delta\rho_{\max} = \underline{5.46} \text{ e } \text{\AA}^{-3}$	$S = \underline{1.96}$
$\Delta\rho_{\min} = \underline{-2.52} \text{ e } \text{\AA}^{-3}$	<u>6369</u> reflections
Extinction correction: <u>none</u>	<u>276</u> parameters
Primary atom site location: <u>structure-invariant direct methods</u>	Secondary atom site location: <u>difference Fourier map</u>

Table 2.9 Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$)

$U_{\text{iso}}^*/U_{\text{eq}}$	z	y	x	
0.0710 (6)	0.55216 (19)	0.14786 (4)	0.29465 (7)	Br1
0.0535 (6)	0.8469 (2)	0.12009 (5)	0.27492 (6)	Cu1
0.059 (3)	1.0116 (14)	0.1556 (3)	0.2272 (5)	N3
0.054 (2)	0.9091 (14)	0.0594 (3)	0.3090 (5)	N2
0.052 (3)	0.8413 (15)	0.0272 (4)	0.2708 (5)	C6
0.053 (3)	0.7476 (17)	0.0410 (4)	0.2181 (5)	C5
0.055 (2)	0.7315 (15)	0.0845 (3)	0.2100 (4)	N1
0.048 (3)	1.0971 (15)	0.1866 (4)	0.2586 (5)	C17
0.058 (3)	0.8567 (17)	-0.0176 (4)	0.2819 (6)	C7

0.053 (3)	1.0812 (16)	0.1880 (4)	0.3199 (5)	C18
0.058 (2)	0.9774 (15)	0.1562 (4)	0.3372 (4)	N4
0.066 (3)	1.1628 (18)	0.2196 (5)	0.3536 (7)	C19
0.066 (4)	0.6729 (18)	0.0110 (5)	0.1746 (6)	C4
0.075 (5)	0.778 (2)	−0.0469 (5)	0.2381 (8)	C11
0.090*	0.7848	−0.0766	0.2457	H11
0.062 (3)	1.1997 (17)	0.2195 (4)	0.2355 (7)	C16
0.062 (3)	1.030 (2)	0.1536 (4)	0.1714 (6)	C13
0.074*	0.9758	0.1311	0.1488	H13
0.070 (4)	1.023 (2)	0.0018 (5)	0.3755 (7)	C9
0.084*	1.0872	−0.0056	0.4110	H9
0.069 (4)	0.6917 (18)	−0.0334 (5)	0.1857 (8)	C12
0.083*	0.6465	−0.0537	0.1580	H12
0.060 (3)	0.9938 (18)	0.0449 (5)	0.3591 (6)	C10
0.073*	1.0380	0.0658	0.3860	H10
0.096 (7)	1.2776 (19)	0.2518 (4)	0.2754 (12)	C24
0.116*	1.3432	0.2740	0.2610	H24
0.068 (4)	0.9506 (19)	−0.0308 (5)	0.3355 (6)	C8
0.082*	0.9650	−0.0602	0.3445	H8
0.075 (4)	1.262 (2)	0.2525 (5)	0.3341 (8)	C23
0.089*	1.3164	0.2740	0.3586	H23
0.071 (4)	0.633 (2)	0.0988 (5)	0.1608 (6)	C1
0.085*	0.6161	0.1287	0.1560	H1
0.089 (5)	0.557 (2)	0.0721 (8)	0.1184 (8)	C2
0.107*	0.4931	0.0835	0.0849	H2
0.085 (5)	1.130 (2)	0.2179 (5)	0.4159 (8)	C20

0.102*	1.1796	0.2389	0.4421	H20
0.073 (4)	0.576 (2)	0.0288 (6)	0.1255 (6)	C3
0.088*	0.5218	0.0103	0.0967	H3
0.077 (4)	0.950 (2)	0.1566 (6)	0.3949 (6)	C22
0.092*	0.8757	0.1362	0.4088	H22
0.075 (4)	1.217 (2)	0.2164 (5)	0.1771 (7)	C15
0.090*	1.2888	0.2362	0.1606	H15
0.087 (5)	1.133 (3)	0.1861 (6)	0.1457 (8)	C14
0.105*	1.1398	0.1853	0.1062	H14
0.083 (4)	1.037 (2)	0.1879 (6)	0.4315 (7)	C21
0.099*	1.0232	0.1864	0.4704	H21
0.289 (5)	0.7500	0.0727 (4)	0.5000	Br2

Table 2.10 Atomic displacement parameters ($\text{\AA}^2$) of $[\text{Cu}(\text{phen})_2\text{Br}]\text{Br}$ complex.

U^{23}	U^{13}	U^{12}	U^{33}	U^{22}	U^{11}	
0.0045 (5)	0.0162 (8)	0.0034 (7)	0.0599 (9)	0.0494 (8)	0.1050 (13)	Br1
−0.0052 (6)	0.0081 (7)	0.0022 (6)	0.0612 (10)	0.0460 (9)	0.0535 (9)	Cu1
0.008 (4)	0.019 (5)	0.009 (5)	0.048 (5)	0.047 (6)	0.084 (8)	N3
−0.001 (4)	0.024 (5)	0.001 (5)	0.055 (6)	0.052 (6)	0.059 (6)	N2
−0.005 (5)	0.026 (5)	0.000 (5)	0.047 (6)	0.046 (6)	0.066 (7)	C6
−0.003 (5)	0.008 (5)	−0.001 (5)	0.054 (6)	0.053 (7)	0.052 (7)	C5
−0.011 (4)	0.001 (5)	−0.001 (4)	0.068 (6)	0.044 (5)	0.050 (6)	N1
0.012 (5)	0.008 (5)	0.006 (5)	0.047 (6)	0.044 (6)	0.055 (6)	C17
0.005 (5)	0.025 (6)	0.000 (6)	0.059 (7)	0.042 (6)	0.077 (8)	C7
0.008 (5)	0.006 (5)	−0.002 (5)	0.057 (7)	0.047 (6)	0.054 (7)	C18

−0.003 (5)	0.002 (5)	0.007 (5)	0.063 (6)	0.062 (6)	0.047 (5)	N4
0.000 (6)	0.006 (6)	0.002 (7)	0.055 (7)	0.059 (8)	0.082 (10)	C19
−0.006 (6)	0.027 (6)	−0.007 (7)	0.051 (7)	0.080 (9)	0.072 (9)	C4
−0.012 (6)	0.043 (9)	−0.021 (8)	0.064 (8)	0.051 (7)	0.118 (14)	C11
0.011 (5)	0.008 (6)	0.022 (6)	0.049 (6)	0.047 (7)	0.089 (10)	C16
0.003 (6)	0.022 (6)	0.009 (6)	0.080 (9)	0.057 (7)	0.053 (7)	C13
0.022 (7)	0.027 (7)	0.023 (7)	0.066 (8)	0.064 (8)	0.084 (10)	C9
−0.013 (6)	0.024 (7)	−0.038 (8)	0.047 (7)	0.063 (8)	0.102 (11)	C12
0.005 (6)	0.014 (6)	0.016 (6)	0.061 (7)	0.069 (8)	0.053 (7)	C10
−0.003 (6)	−0.007 (10)	0.024 (10)	0.048 (8)	0.040 (7)	0.20 (2)	C24
0.019 (7)	0.020 (7)	0.018 (7)	0.068 (8)	0.064 (8)	0.076 (9)	C8
−0.003 (6)	−0.014 (8)	0.009 (7)	0.073 (9)	0.052 (8)	0.091 (11)	C23
−0.007 (7)	0.004 (7)	0.011 (6)	0.093 (10)	0.054 (7)	0.064 (8)	C1
−0.020 (10)	0.016 (8)	−0.010 (10)	0.070 (10)	0.129 (17)	0.071 (10)	C2
0.002 (8)	−0.022 (9)	−0.021 (8)	0.089 (11)	0.057 (9)	0.099 (12)	C20
−0.022 (8)	0.014 (6)	−0.009 (8)	0.065 (8)	0.103 (13)	0.053 (8)	C3
−0.016 (8)	0.017 (7)	−0.006 (7)	0.091 (11)	0.092 (11)	0.049 (7)	C22
0.003 (7)	0.023 (8)	0.031 (9)	0.066 (9)	0.069 (9)	0.095 (11)	C15
0.020 (10)	0.035 (9)	0.022 (9)	0.111 (13)	0.082 (11)	0.076 (10)	C14
0.005 (10)	0.031 (8)	−0.006 (8)	0.107 (12)	0.084 (11)	0.062 (9)	C21
0.000	0.033 (6)	0.000	0.319 (11)	0.404 (15)	0.145 (5)	Br2

Table 2.11 Geometric parameters (Å, °)

1.346 (19)	C18—C19	2.479 (2)	Br1—Cu1
1.389 (17)	N4—C22	1.974 (10)	Cu1—N1
1.37 (2)	C19—C23	1.984 (11)	Cu1—N4
1.51 (2)	C19—C20	2.057 (11)	Cu1—N2
1.39 (2)	C4—C3	2.085 (10)	Cu1—N3
1.39 (2)	C4—C12	1.317 (16)	N3—C17
1.37 (2)	C11—C12	1.330 (17)	N3—C13
1.39 (2)	C16—C15	1.333 (17)	N2—C10
1.43 (3)	C16—C24	1.384 (16)	N2—C6
1.45 (2)	C13—C14	1.401 (18)	C6—C5
1.387 (19)	C9—C10	1.401 (17)	C6—C7
1.43 (2)	C9—C8	1.352 (16)	C5—N1
1.39 (3)	C24—C23	1.430 (19)	C5—C4
1.35 (2)	C1—C2	1.357 (18)	N1—C1
1.35 (3)	C2—C3	1.422 (17)	C17—C16
1.25 (2)	C20—C21	1.454 (17)	C17—C18
1.39 (2)	C22—C21	1.41 (2)	C7—C8
1.30 (2)	C15—C14	1.43 (2)	C7—C11
125.9 (12)	N4—C18—C19	176.1 (5)	N1—Cu1—N4
113.7 (11)	N4—C18—C17	81.3 (4)	N1—Cu1—N2
120.4 (12)	C19—C18—C17	99.2 (4)	N4—Cu1—N2
116.9 (12)	C18—N4—C22	96.4 (5)	N1—Cu1—N3
115.8 (8)	C18—N4—Cu1	80.1 (5)	N4—Cu1—N3
126.4 (10)	C22—N4—Cu1	124.1 (4)	N2—Cu1—N3
124.4 (15)	C18—C19—C23	91.2 (3)	N1—Cu1—Br1

114.7 (13)	C18—C19—C20	92.2 (3)	N4—Cu1—Br1
120.8 (15)	C23—C19—C20	113.8 (3)	N2—Cu1—Br1
124.7 (15)	C3—C4—C12	122.1 (3)	N3—Cu1—Br1
116.5 (14)	C3—C4—C5	118.2 (11)	C17—N3—C13
118.6 (14)	C12—C4—C5	111.2 (9)	C17—N3—Cu1
123.4 (14)	C12—C11—C7	130.4 (10)	C13—N3—Cu1
116.9 (14)	C15—C16—C17	114.7 (11)	C10—N2—C6
126.9 (15)	C15—C16—C24	134.5 (9)	C10—N2—Cu1
116.3 (15)	C17—C16—C24	110.7 (8)	C6—N2—Cu1
120.4 (14)	N3—C13—C14	116.6 (11)	C5—C6—N2
117.1 (14)	C10—C9—C8	118.7 (11)	C5—C6—C7
119.1 (13)	C11—C12—C4	124.7 (12)	N2—C6—C7
127.0 (14)	N2—C10—C9	116.6 (11)	N1—C5—C6
124.8 (14)	C23—C24—C16	121.3 (12)	N1—C5—C4
118.8 (12)	C7—C8—C9	122.1 (12)	C6—C5—C4
115.9 (15)	C19—C23—C24	117.8 (10)	C1—N1—C5
123.5 (15)	C2—C1—N1	127.3 (9)	C1—N1—Cu1
119.0 (17)	C3—C2—C1	114.8 (8)	C5—N1—Cu1
118.6 (14)	C21—C20—C19	123.5 (12)	N3—C17—C16
121.7 (15)	C2—C3—C4	118.2 (11)	N3—C17—C18
119.0 (14)	N4—C22—C21	118.3 (12)	C16—C17—C18
120.1 (14)	C14—C15—C16	117.7 (12)	C6—C7—C8
120.6 (15)	C15—C14—C13	118.0 (13)	C6—C7—C11
124.8 (15)	C20—C21—C22	124.3 (13)	C8—C7—C11

2.5 Computational method

The molecular geometry of the title cationic complex was fully optimized without any geometric constraints in the gas phase at the DFT/B3LYP level of theory, which utilizes the three parameter Becke exchange functional, B3 [32], the nonlocal correctional functional of Lee, Yang and Parr (LYP [33]) in conjunction with the polarized 6-31G(d) main set [34]. The starting molecular geometry is extracted from the experimentally determined crystal structure. Additionally, we have employed two ab-initio methods, namely HF/3-21G [35] and HF/6-31G* [36] and reported the geometrical parameters of the optimized complex. All electronic structure calculations were performed using the Spartan 16 package.

2.6 DNA binding investigation

❖ Absorption-titration method

The experimental absorption-titration measurements were carried out in Tris–HCl buffer with 5 mM Tris–HCl, 50 mM NaCl and pH 7.2. 1.0×10^{-5} M Cu(II) concentration was used during the titration process. The CT-DNA concentrations were varied between 0 and 2.0×10^{-2} M by maintaining the volume of the total mixture constant at 10.0 mL. The resulting mixed solutions of Cu(II)/CT-DNA were left standing to equilibrate for 10 min at RT after each trial before subjecting them to absorption measurements at $\lambda_{\max} = 270$ nm. K_b binding constants were calculated using equation 1 [37].

$$[\text{DNA}]/(\epsilon_a - \epsilon_f) = [\text{DNA}]/(\epsilon_b - \epsilon_f) + 1/K_b(\epsilon_b - \epsilon_f) \quad \text{.....eq1}$$

Where [DNA] is the conc. of DNA, ϵ_a is the apparent extinction coefficient obtained by calculating $A_{obs}/[\text{complex}]$, ϵ_f corresponds to the free extinction coefficient of the complex and ϵ_b refers to the extinction coefficient of the complex in the bound form. When fitted to the above equation, a straight line with slope of $1/(\epsilon_b - \epsilon_f)$ and y-intercept of $1/K_b(\epsilon_b - \epsilon_f)$ results. Finally, K_b was determined from the ratio of the slope to intercept.

2.7 Viscosity measurements

Viscosity experiments were carried out using an Ubbelodhe viscometer at 25.0 (± 0.1) °C. The viscosities, of fixed ([DNA] = 5.0×10^{-4} M) concentration mixed with complex solutions of different concentrations (0- 6.5×10^{-5} M), were evaluated. The binding ratio [Cu]/[DNA] was plotted versus $(\eta/\eta^0)^{1/3}$ [38], where η^0 is the pure DNA viscosity and η is the viscosities of DNA in the presence of complex concentrations.

Chapter Three

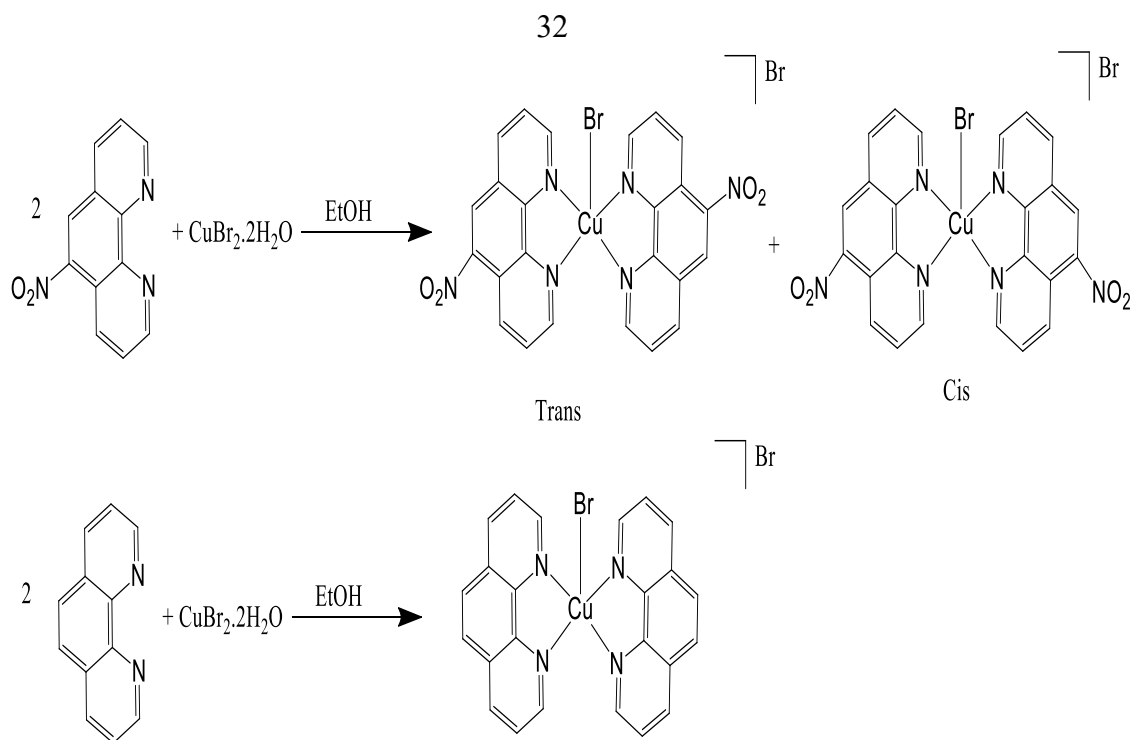
Results and Discussion

Results and Discussion

3.1 Synthesis

Water soluble mono-cationic $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complexes were prepared in good yield through the direct addition of two equivalents of $\text{NO}_2\text{-phen}$ ligand to $\text{CuBr}_2 \cdot 2\text{H}_2\text{O}$ dissolved in ethanol under an open RT ultrasonic vibration (Scheme 1). The brown color of the $\text{CuBr}_2 \cdot 2\text{H}_2\text{O}$ ethanolic solution first changed to green when $\text{NO}_2\text{-phen}$ ligand was added. By the end of the reaction, the product complexes were precipitated as a deep-brown powder. The complexes are highly soluble in DMF, DMSO and water, low solubility in ROH and insoluble in chlorinated and hydrocarbon solvents. The complex was found to be stable in solution as well as in the solid phase at ambient conditions.

The complex $[\text{Cu}(\text{R-phen})_2\text{Br}]\text{Br}$ was isolated as a racemic cis and trans mixture of mono-cationic bromide salts. Since the NO_2 group at position 5 is relatively far away from the crowded copper center, there is no strict electronic configuration preference, yielding to mixed cis/trans isomer structures confirmed only by single crystal X-ray measurements. The complex was also characterized using elemental analysis, thermal, electrochemical, spectral methods and Hirschfeld surface analysis.



Scheme 1: Synthesis of $[\text{Cu}(\text{R-phen})_2\text{Br}]\text{Br}$ complexes

3.1.1 Crystal structure for $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex

The complex crystallized in Monoclinic system with C2/c space group. All the bond lengths and angles are listed in Table 3.1.

Table 3.1 XRD selective bond lengths and angels for [Cu(NO₂-phen)₂Br]Br complex.

Value (°)	Angle type			Length (Å)	Bond type	
94.2(1)	N1	Cu1	Br1	2.416(1)	Br1	Cu1
120.7(1)	N12	Cu1	Br1	1.996(5)	N1	Cu1
128.0(1)	N15	Cu1	Br1	2.126(3)	N12	Cu1
94.0(1)	N26	Cu1	Br1	2.106(5)	N15	Cu1
79.6(2)	N12	Cu1	N1	1.999(5)	N26	Cu1
95.4(2)	N15	Cu1	N1	1.328(7)	C2	N1
171.8(2)	N26	Cu1	N1	1.355(6)	C14	N1
111.3(2)	N15	Cu1	N12	1.39(1)	C3	C2
95.6(2)	N26	Cu1	N12	1.346(8)	C4	C3
80.1(2)	N26	Cu1	N15	1.405(9)	C5	C4
126.1(4)	C2	N1	Cu1	1.431(7)	C6	C5
115.6(4)	C14	N1	Cu1	1.395(8)	C14	C5
118.3(5)	C14	N1	C2	1.329(8)	C7	C6
123.0(6)	C3	C2	N1	1.430(9)	C8	C7
119.5(6)	C4	C3	C2	1.485(7)	N29	C7
119.1(6)	C5	C4	C3	1.416(9)	C9	C8
124.0(6)	C6	C5	C4	1.403(6)	C13	C8
118.6(6)	C14	C5	C4	1.36(1)	C10	C9
117.4(5)	C14	C5	C6	1.373(8)	C11	C10
120.8(6)	C7	C6	C5	1.338(8)	N12	C11

[Cu(NO₂-phen)₂Br]Br complex crystallizes as mixture of two *cis/trans* isomers shown in the ORTEP diagram of the molecule (Fig.1). The Cu(II) is 5-coordinated center with 1 Br-atom and 4 N-donors of 2 chelating NO₂-phen in a distorted-square pyramidal geometry, three uncoordinated water molecules are present in the crystal lattice. In CuN₄Br coordination sphere, Cu1-Br1 bond length of 2.416(1) Å, Cu1-N1, Cu1-N12, Cu1-N15 and Cu-N26 bond lengths 1.996(5), 2.126(3), 2.106(5) and 1.999(5) Å, respectively. The N-Cu-N bond angles range from 79.62° to 171.82°. The XRD data is in agreement with the recent reports [1, 39, 40]. Hydrogen

bonding interactions connect water molecules and bromide anions. Hydrogen bond parameters are listed in Table 3.2.

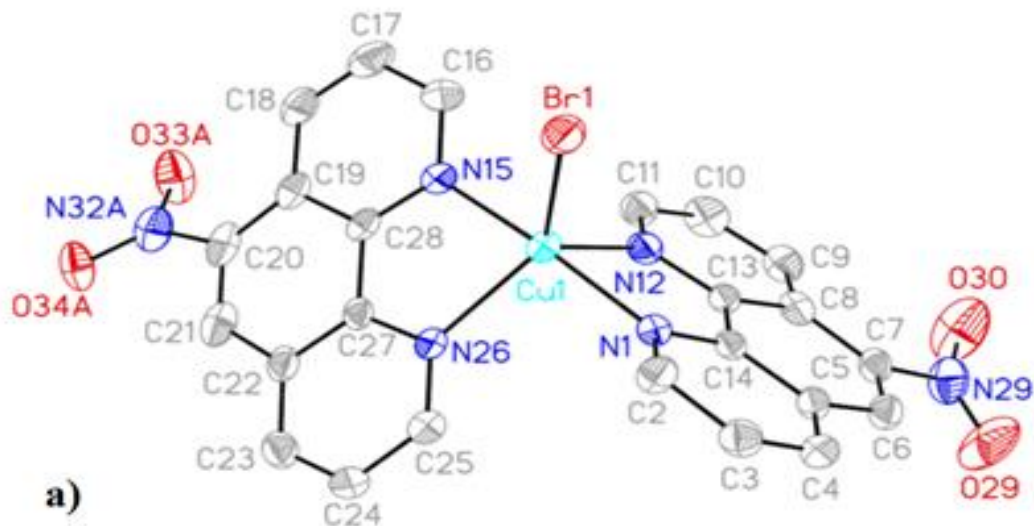


Fig 3.1 The ORTEP generated diagram of (a) *cis*-[Cu(NO₂-phen)₂Br]Br and (b) *trans*-[Cu(NO₂-phen)₂Br]Br isomers. Hydrogen atoms and water molecules are omitted for clarity.

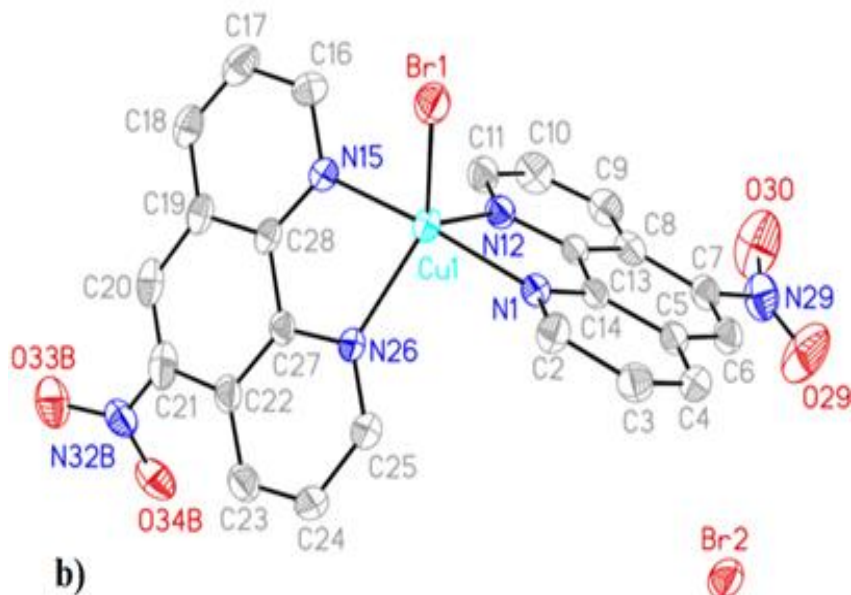


Fig 3.2 The ORTEP generated diagram of (a) *cis*-[Cu(NO₂-phen)₂Br]Br and (b) *trans*-[Cu(NO₂-phen)₂Br]Br isomers. Hydrogen atoms and water molecules are omitted for clarity.

Bromide counter ion together with the three water molecules don't directly coordinate to the copper(II) center but they stabilize the crystal structure due to many Hydrogen-bonds intermolecular forces formation (Table 3.2).

Table 3.2 Hydrogen bonds for [Cu(NO₂-phen)₂Br]⁺ complex [Å and °].

< (DHA)	d(D...A)	d(H...A)	d(D-H)	D-H...A
160.3	2.808(11)	1.85	1.00	O(36)-H(36A)...O(37)
177.0	3.274(4)	2.42	0.85	O(37)-H(37B)...Br(2)
157.4	3.339(5)	2.54	0.85	O(37)-H(37A)...Br(2) [#]

Symmetry transformations used to generate equivalent atoms: [#]1 -x+2,-y+1,-z

3.2 Computational studies.

The compound under investigation is the mono-cationic [Cu(NO₂-phen)₂Br]⁺ complex. We have examined the complex by carrying out intensive ab-initio and DFT calculations to retrieve the optimized ground state geometry and determine its electronic and quantum parameters. The optimized structure of [Cu(NO₂-phen)₂Br]⁺ at the B3LYP/6-31G* level of theory is shown in Fig 3. 2c in combination with views of the x-ray structure of the complex (Fig 3.1a and b). The performance of ab-initio methods HF/3-21G [41] and HF/6-31G* [42] along with one of the most commonly used B3LYP/6-31G* [32-36, 43, 44] model has been tested against selective experimentally determined structural parameters of the complex including bond lengths (pm) and angles (°). The correlation coefficients (CC) for bond lengths (pm) obtained at HF/3-21G, HF/6-31G* and B3LYP/6-31G* are 0.97489, 0.96605 and 0.97434 respectively.

Though all tested methods gave high correlation coefficient values for bond lengths, HF/3-21G and B3LYP/6-31G* methods produced the highest correlation coefficients. For bond angles, the calculated correlation coefficients are 0.94912, 0.94447 and 0.95839 for HF/3-21G, HF/6-31G* and B3LYP/6-31G*, respectively. It is apparent that B3LYP/6-31G* method gives the maximum correlation for angles and yields the most satisfactory results for estimating the bond angles of the title compound. Selected calculated and experimental bond lengths (pm) and angles ($^{\circ}$) are given in Table 3.3. Graphical correlations between the experimentally determined bond lengths (pm) and angles ($^{\circ}$) versus the calculated values determined by HF/3-21G, HF/6-31G* and B3LYP/6-31G* methods are shown in Fig 3.3

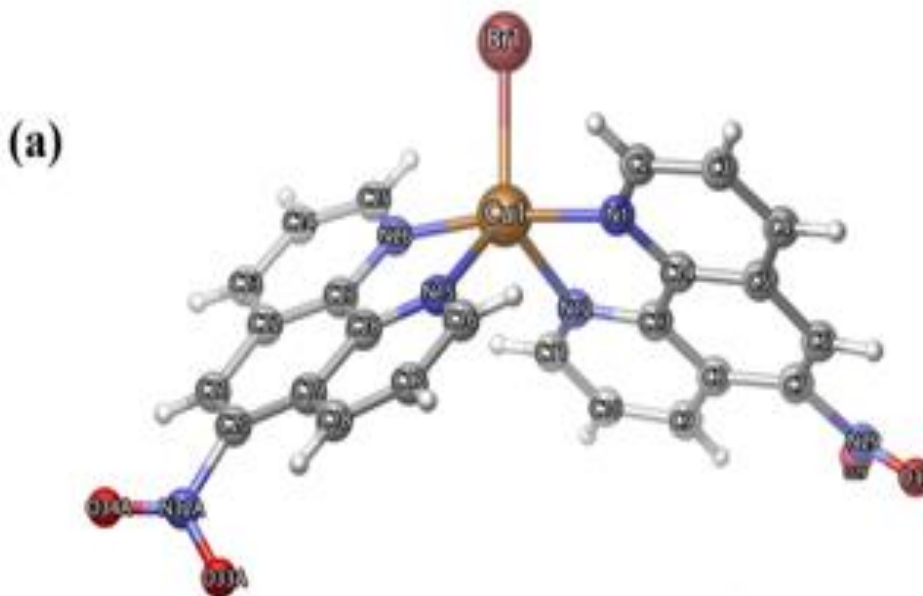


Fig. 3.3 a) Perspective view of the XRD structure of *cis*-[Cu(NO₂-phen)₂Br]Br showing the atom numbering scheme. b) Side and top views of the X-ray structure. c) The optimized ground state geometry for the copper complex at B3LYP/6-31G(d) level of theory.

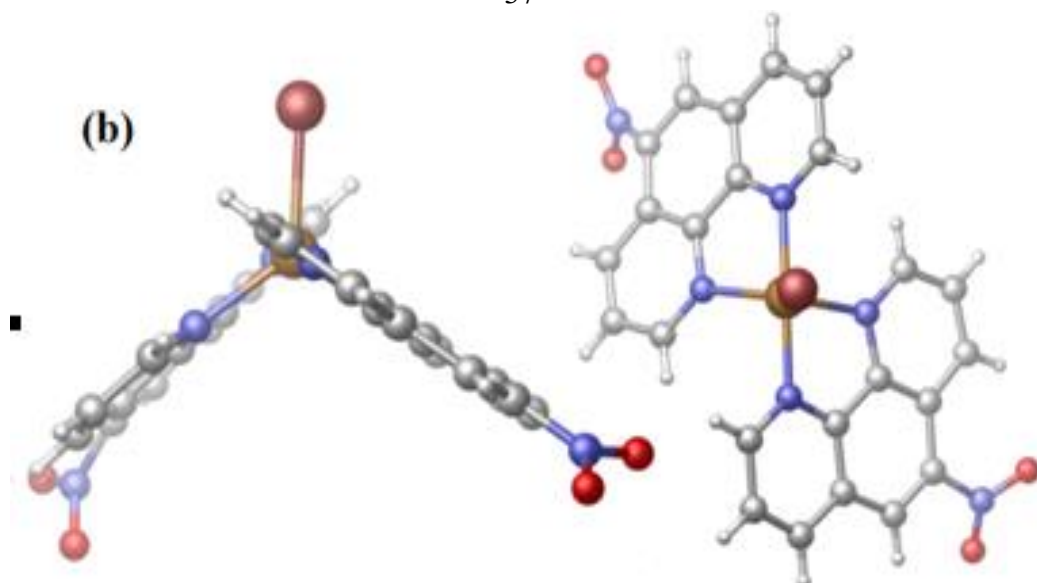


Fig. 3.4 a) Perspective view of the XRD structure of *cis*-[Cu(NO₂-phen)₂Br]Br showing the atom numbering scheme. **b)** Side and top views of the X-ray structure. **c)** The optimized ground state geometry for the copper complex at B3LYP/6-31G(d) level of theory.

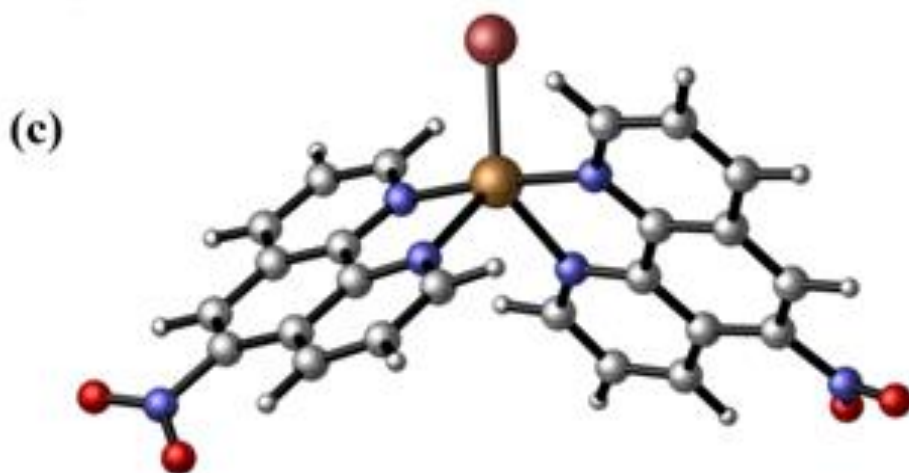
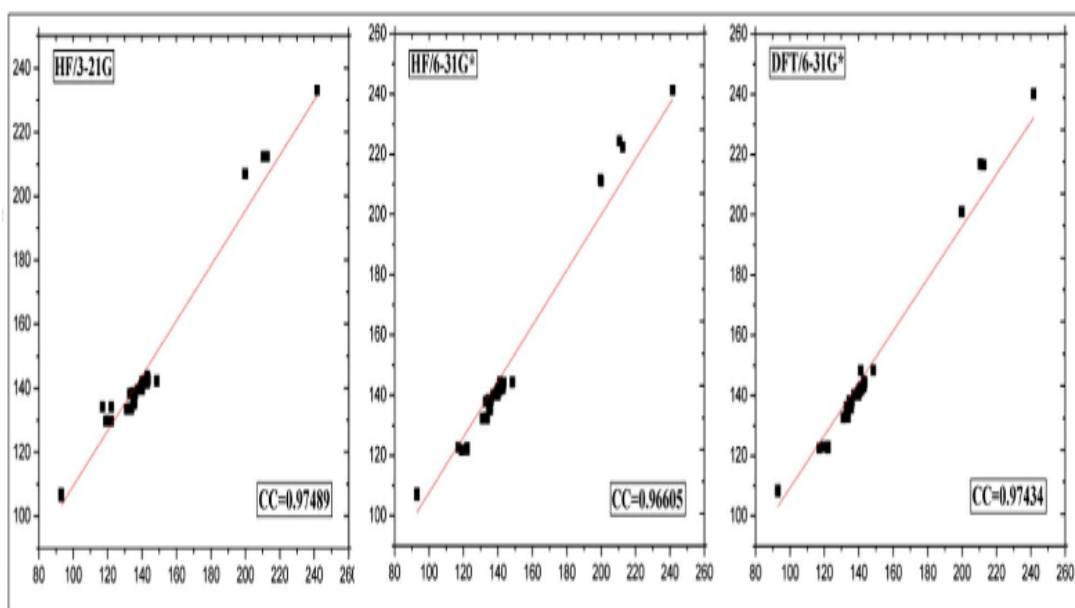


Fig. 3.5 a) Perspective view of the FDT optimization of *cis*-[Cu(NO₂-phen)₂Br]Br showing the atom numbering scheme. **b)** Side and top views of the FDT structure. **c)** The optimized ground state geometry for the copper complex at B3LYP/6-31G level of theory.

Calculated bond lengths(pm)



(a) Experimental bond lengths (pm)

Fig. 3.6 Graphical correlation between experimentally determined (a) bond lengths (pm) and (b) bond angles ($^{\circ}$) versus the calculated values determined by HF/3-21G, HF/6-31G* and B3LYP/6-31G* methods for $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex.

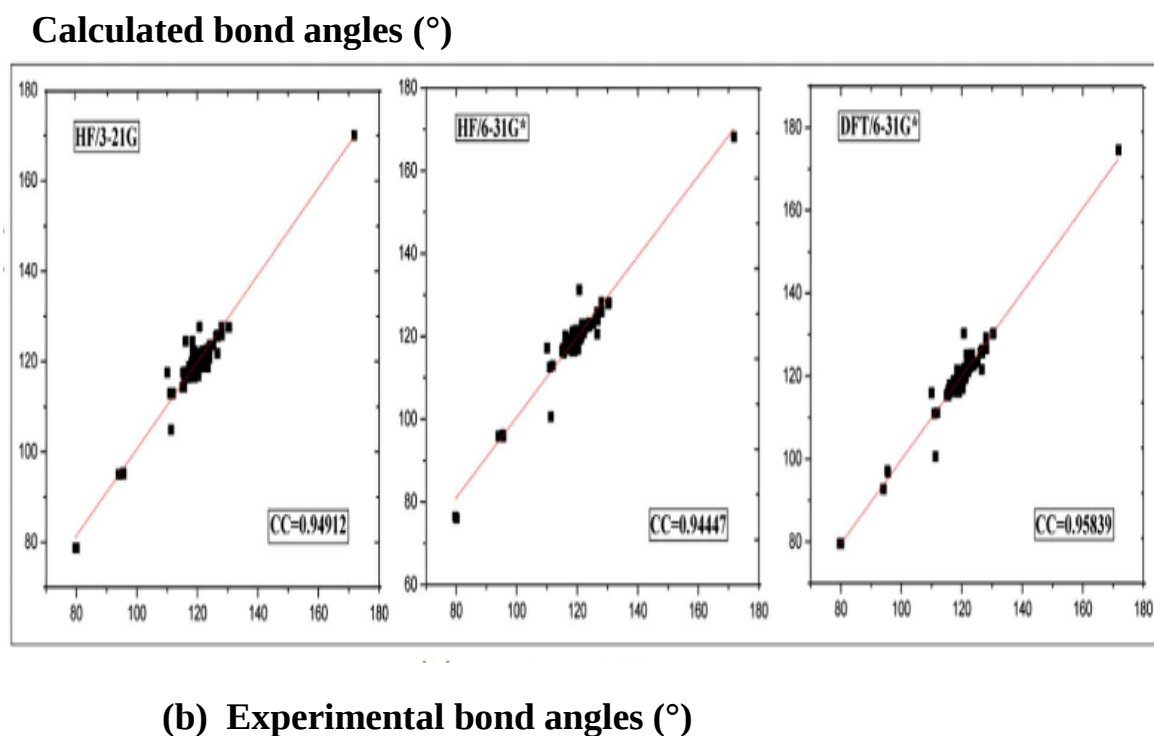


Fig. 3.7 Graphical correlation between experimentally determined (a) bond lengths (pm) and (b) bond angles (°) versus the calculated values determined by HF/3-21G, HF/6-31G* and B3LYP/6-31G* methods for $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex.

Selected electronic properties and quantum parameters of the title complex were determined and summarized in Table 3.3. Based on the frontier molecular orbital (FMO) theory, the chemical reactivity is strongly associated with the interaction between the highest occupied molecular orbital (HOMO) and the lowest unoccupied orbital (LUMO) of the reacting species. A molecule with higher value of E_{HOMO} is indicative of its ability and tendency to donate electrons to an acceptor molecule with a low E_{LUMO} value. Also, a molecule with a large band gap energy ΔE_{gap} should be less reactive than one having a smaller gap. In the present study, the total energy, the highest occupied molecular orbital (HOMO) energy, the lowest unoccupied molecular orbital (LUMO) energy (Fig. 3.4), the band gap

energy ΔE_{gap} , the ionization potential (I), the electron affinity (A), the absolute electronegativity (X), the absolute hardness (η), the softness (σ), the chemical potential (μ), the electrophilicity index (ω) and the dipole moment (D) were calculated at the B3LYP/6-31G* level of theory [40-44]. The ionization potential (I) and the electron affinity (A) can be expressed as $I = -E_{\text{HOMO}}$ and $A = -E_{\text{LUMO}}$. The absolute electronegativity (X), the absolute hardness (η), the softness (σ) and the electrophilicity index (ω) are given by [43]:

$$X = (I + A)/2, \quad \eta = (I - A)/2, \quad \sigma = 1/\eta \quad \text{and} \quad \omega = \mu^2/2\eta$$

Where μ represents the chemical potential and is given as $\mu = -X$ [44]. The electrophilicity index (ω) is a measure of the electrophilic power of a molecule [41-44]. The hardness (η) and softness (σ) are proportional of the gap between the HOMO and LUMO energies such that hard molecules have a high ΔE_{gap} and soft molecules have a small ΔE_{gap} . Therefore, the hardness is associated with the stability of molecules while the softness is a measure of the extent of chemical reactivity. Calculated reactivity indices of the title compound obtained at the B3LYP/6-31G* method are listed in Table 3.4.

Table 3.3 Calculated electronic properties and quantum parameters for $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex obtained at the B3LYP/6-31G* level of theory

E (a.u.)	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)	I (eV)	A (eV)	X (eV)	η (eV)	σ (eV)	μ (eV)	ω (eV)	D (debye)
-5766.33347	-9.06	-5.91	3.15	9.06	5.91	7.49	1.58	0.635	-7.49	17.79	2.20

Table 3.4 Selected experimental and calculated bond lengths (pm) and angles ($^\circ$) of cis/trans- $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex. Calculated values were obtained at the HF/3-21G, HF/6-31G* and B3LYP/6-31G* levels of theory.

Calculated			Exp'l	Bond (pm)
DFT/B3LYP 6-31G*	HF 6-31G*	HF 3-21G		
240.1	241.3	233.2	241.6	Cu1-Br1
201.0	211.6	207.0	199.6	Cu1-N1
216.5	222.3	212.4	212.6	Cu1-N12
216.8	224.4	212.4	210.6	Cu1-N15
201.0	211.0	207.0	199.9	Cu1-N26
133.3	132.5	133.8	132.8	N1-C2
135.8	135.2	135.1	135.5	N1-C14
108.5	107.2	106.8	93.0	C2-H2A
140.5	140.6	140.3	139.1	C2-C3
141.2	141.4	140.7	139.5	C5-C14
148.2	144.3	142.3	148.5	C7-N29
122.5	122.6	134.2	117.1	N29-O30
122.9	121.8	129.9	119.1	N29-O29
123.0	121.9	129.9	122.2	N32A-O33A
122.5	122.6	134.2	122.2	N32A-O34A
0.97434	0.96605	0.97489	-	Correlation Coefficient (CC)

				Angle (°)
92.69	95.95	94.98	94.21	Br1-Cu1-N1
130.31	131.18	127.56	120.71	Br1-Cu1-N12
129.14	128.24	127.58	128.01	Br1-Cu1-N15
92.68	95.87	95.00	94.01	Br1-Cu1-N26
79.60	76.38	78.65	79.62	N1-Cu1-N12
97.13	96.32	95.27	95.42	N1-Cu1-N15
174.62	168.18	170.02	171.82	N1-Cu1-N26
100.56	100.58	104.86	111.32	N12-Cu1-N15
96.74	95.83	95.12	95.62	N12-Cu1-N26
79.59	76.15	78.66	80.12	N15-Cu1-N26
125.56	124.33	125.53	126.14	Cu1-N1-C2
115.27	115.93	114.27	115.64	Cu1-N1-C14
119.13	119.56	119.99	118.35	C2-N1-C14
116.12	116.49	116.53	118.50	N1-C2-H2A
122.44	122.40	121.27	123.06	N1-C2-C3
0.95839	0.94447	0.94912	-	Correlation Coefficient (CC)

43

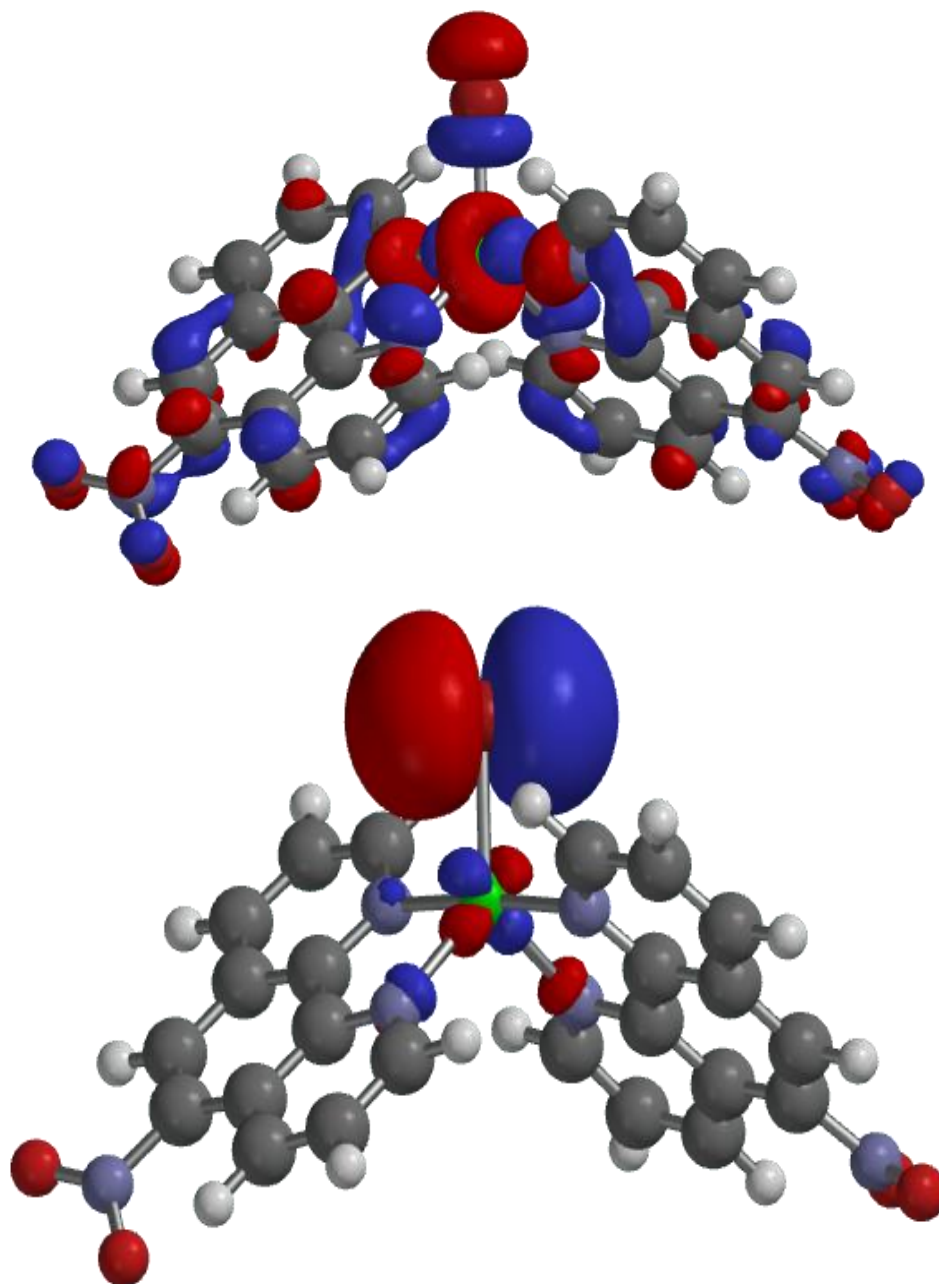


Fig. 3.8 The HOMO (lower) and LUMO (upper) plots of [Cu(NO₂-phen)₂Br]Br complex at the B3LYP/6-31G* level of theory.

3.1.2 Crystal structure for [Cu(phen)₂Br]Br complex

The structure of [Cu(phen)₂Br]Br in Figure 3.5 is similar to [Cu(NO₂-phen)₂Br]Br there is *cis/trans* isomerization possibility. The bond lengths and angles are almost the same, Cu-N bond length ranges from 1.996–1.999(10) Å. The Cu-Br bond length is 2.416(2) Å, which is comparable to the bond length found in some reported studies[9] (Cu-Br, 2.471 Å). The angles N1-Cu-Br is 94.21. The other equatorial angles N2-Cu-Br, N3-Cu-Br and N1-Cu-N3 are observed at 120.71, 128.01(3) and 94.01(5)°, respectively. The packing structures of the two complexes as viewed along b-axis are identical except for the arrangement of the free bromide in the cell axis (Figure 3.6).

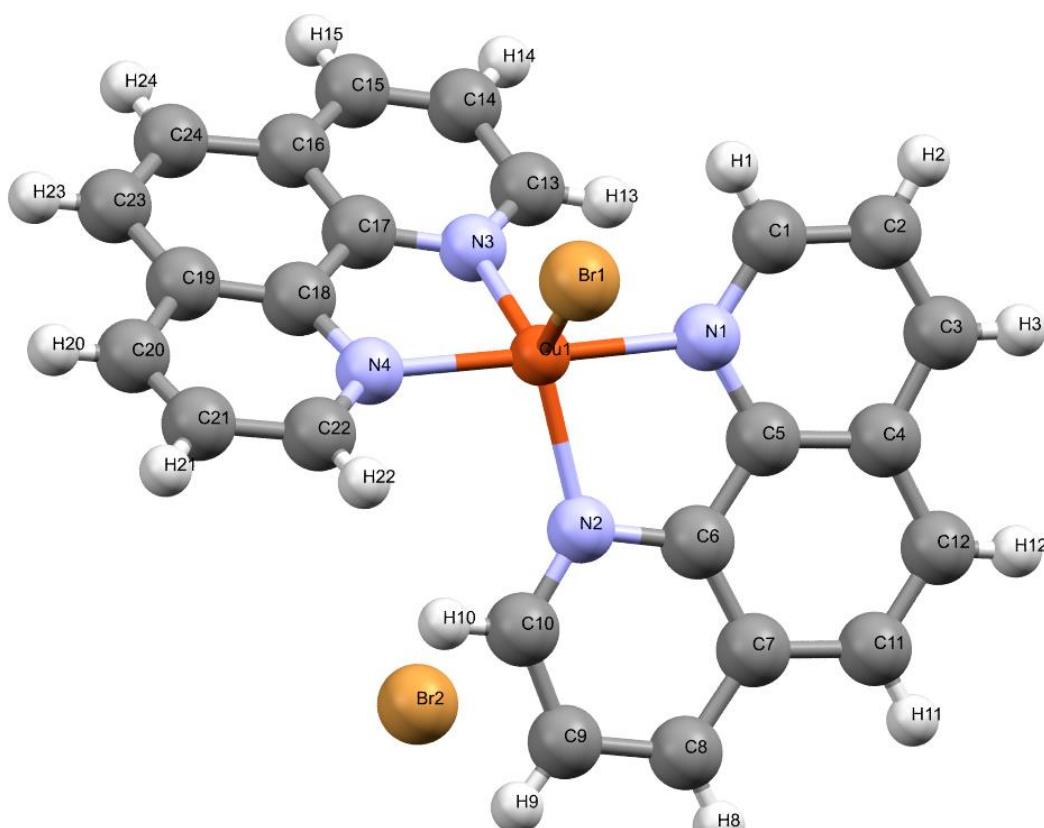


Fig 3.9 The ORTEP generated diagram of [Cu(phen)₂Br]Br complex.

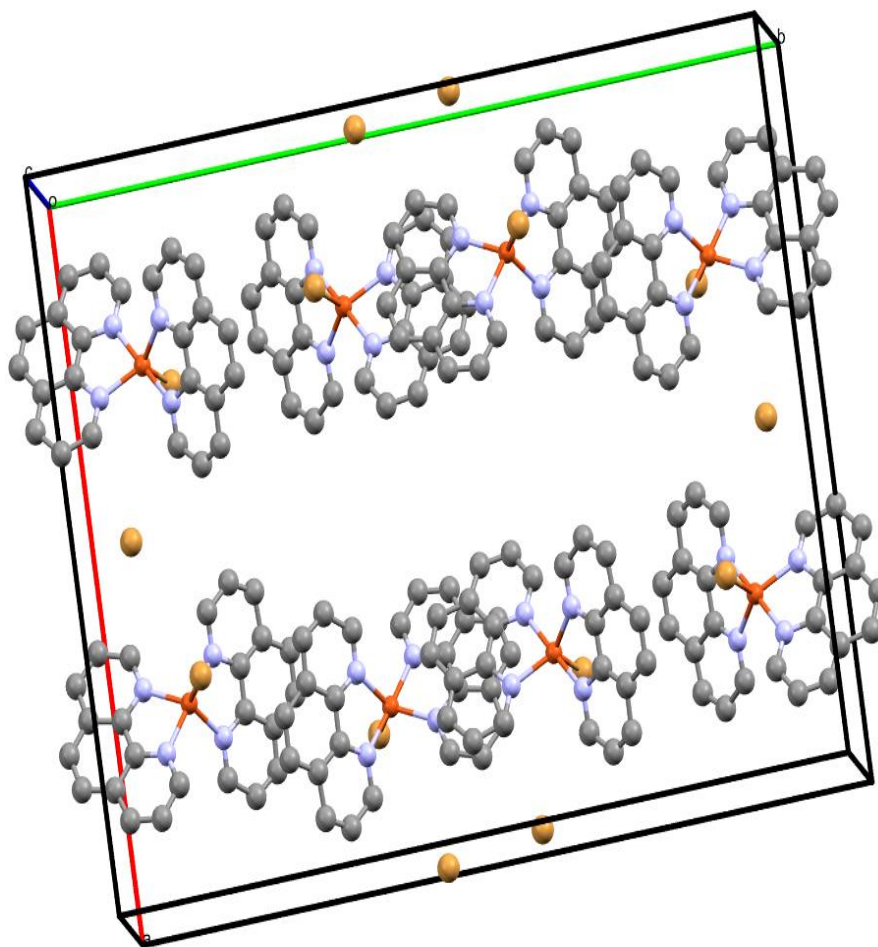


Fig 3.10 Packing diagram of $[\text{Cu}(\text{phen})_2\text{Br}]\text{Br}$ complex.

3.3. Hirschfeld surface analysis (HSA)

HSA is an excellent tool for explaining packing and intermolecular forces in the solved crystal structure [45-50]. It offers a clean picture of intermolecular interactions and molecular shape in a crystalline environment. Surface characteristic like: types of interactions (color coding reveals their strength), the distances from the surface to the nearest interior (di plots) or exterior (de plots) atom.

HSA confirmed the presence of several H-bonds in the crystal structure of the desired complex. $\text{N-H}\cdots\text{Br}$ with $2.70 \text{ \AA}$ (see Fig.3.7). HSA of the

complex revealed several red spots on the surface of the molecule as a result of the H-bond acceptors close to the bromide atoms which may have encouraged and stabilized the crystal formation.

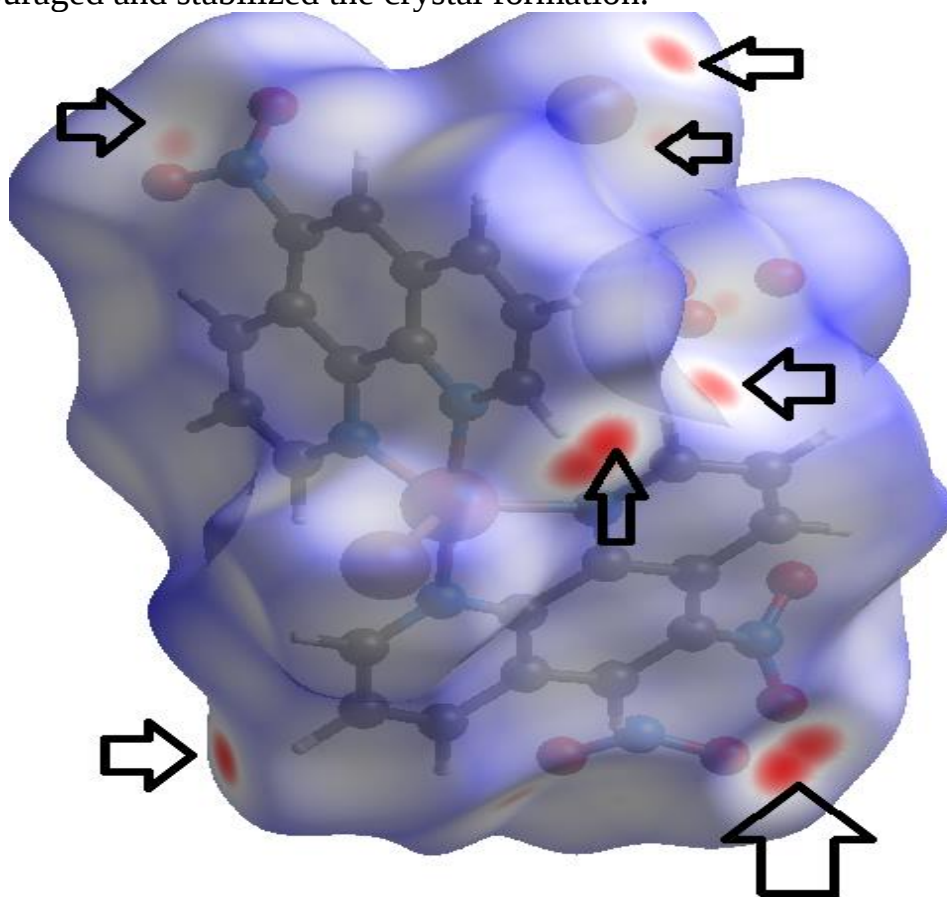


Fig. 3.11 Hirshfeld surfaces comprising d_{norm} surface plots for $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex.

Atom...atom fingerprint contacts with their percentages of HAS contact contribution are illustrated in Fig.3.8. [(a) Total, (b) H...all (33.6%), (c) H...O (13.9%), (d) H...H (7.2%), (e) H...Br (7.0%), (f) H...C (4.2%) (h) H...N (1.3%) and (1) H...Cu (0.1%)].

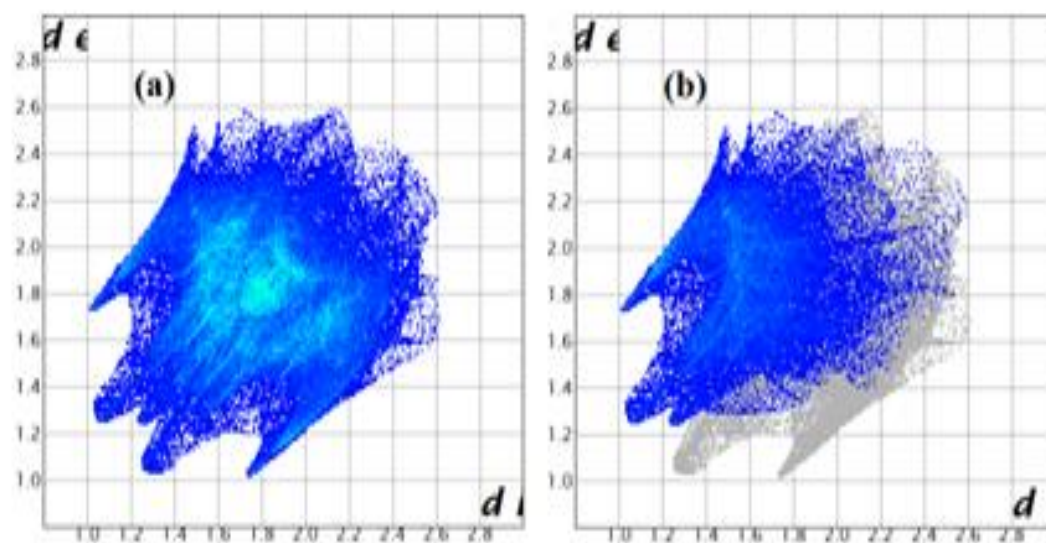


Fig. 3.12 Fingerprint plots of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex -0.28 au (blue) to 1.21 au (red).

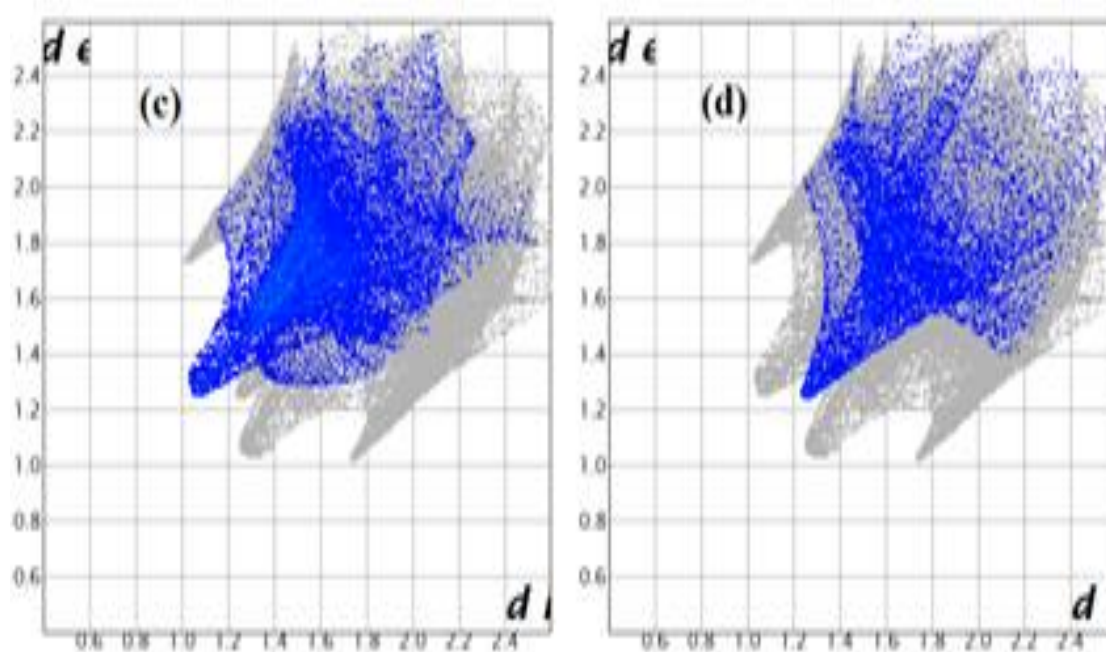


Fig. 3.13 Fingerprint plots of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex -0.28 au (blue) to 1.21 au (red).

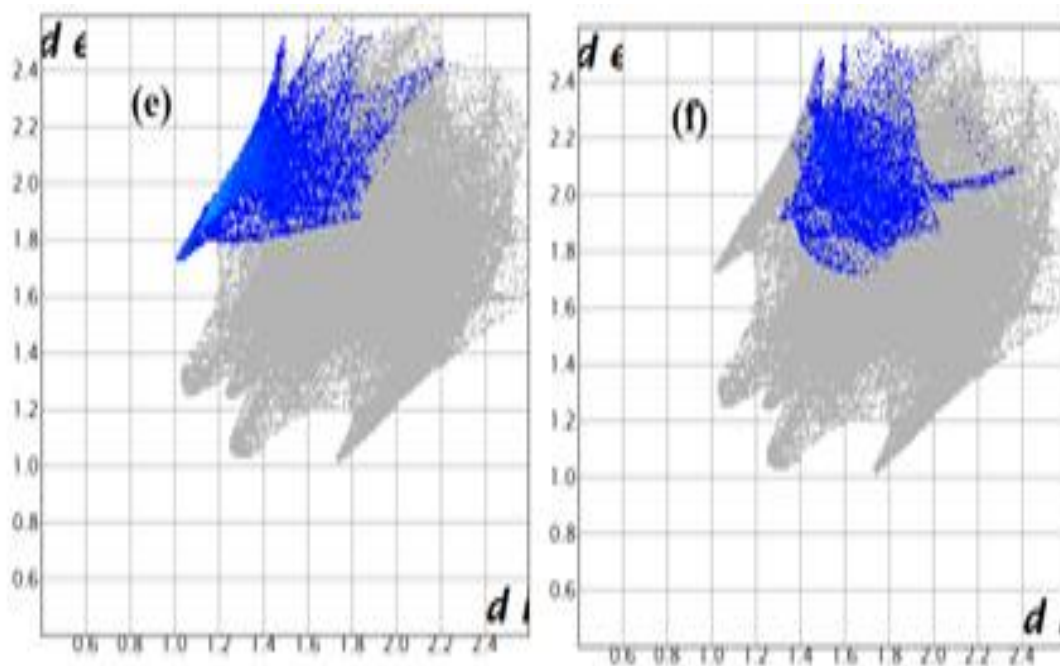


Fig. 3.14 Fingerprint plots of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex -0.28 au (blue) to 1.21 au (red).

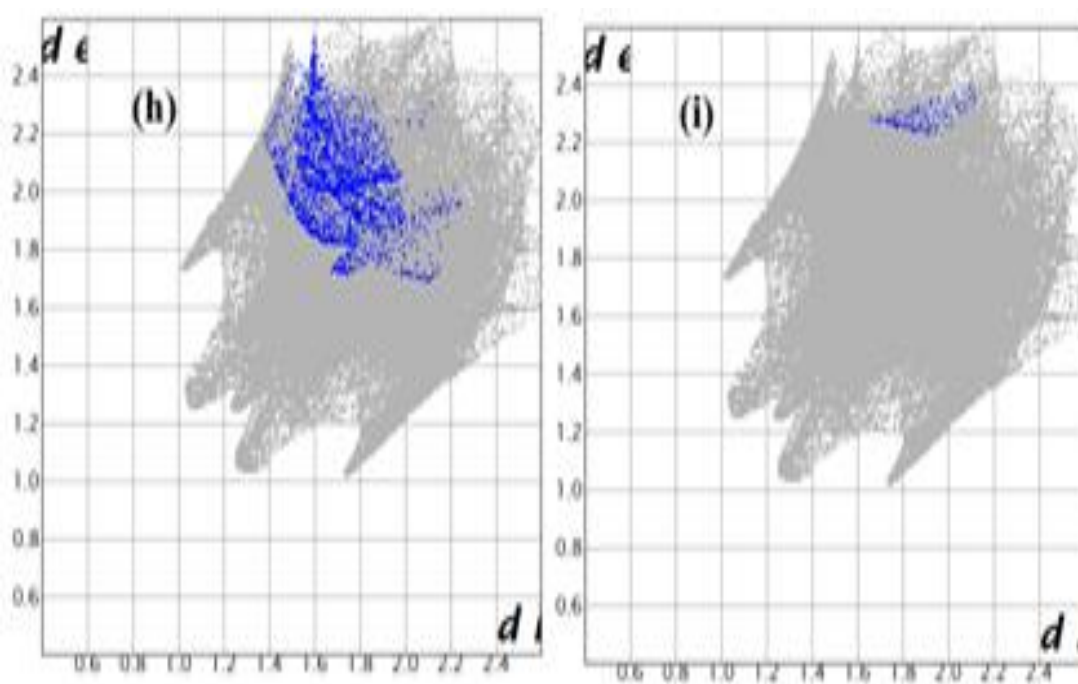


Fig. 3.15 Fingerprint plots of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex -0.28 au (blue) to 1.21 au (red).

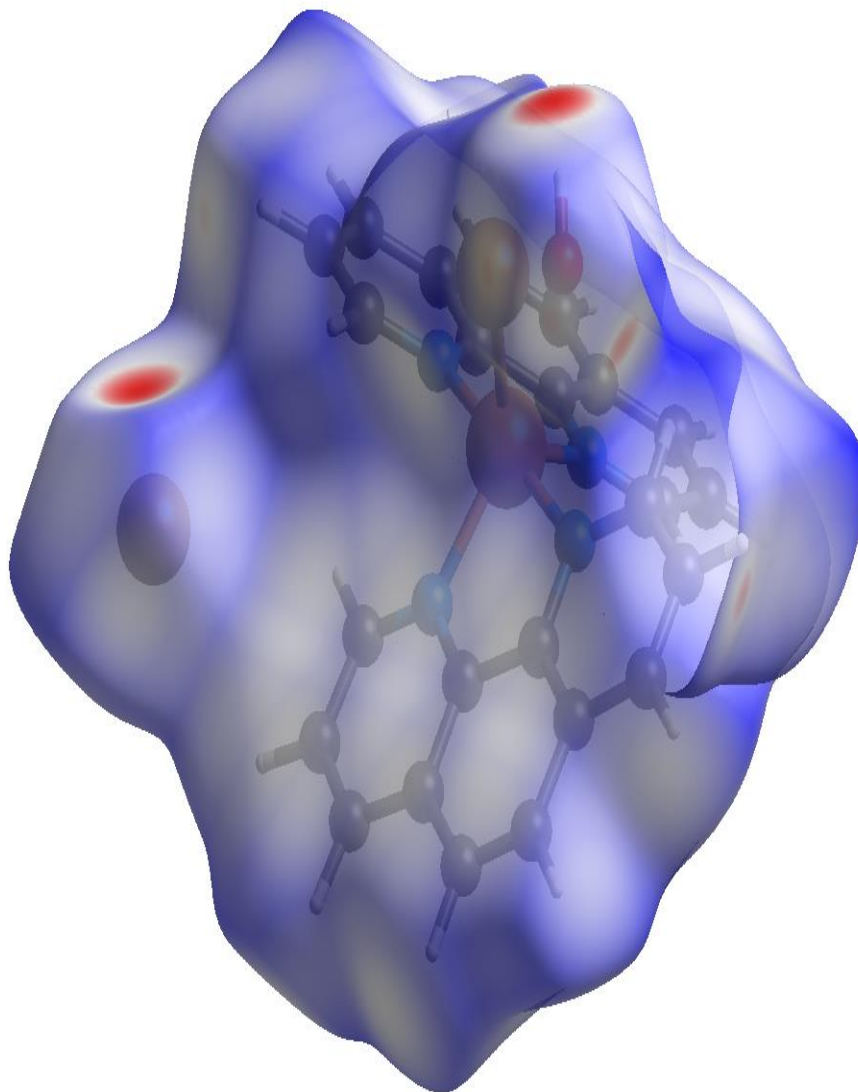


Fig. 3.16 Hirshfeld surfaces comprising d_{norm} surface plots for [Cu(phen)₂Br]Br complex.

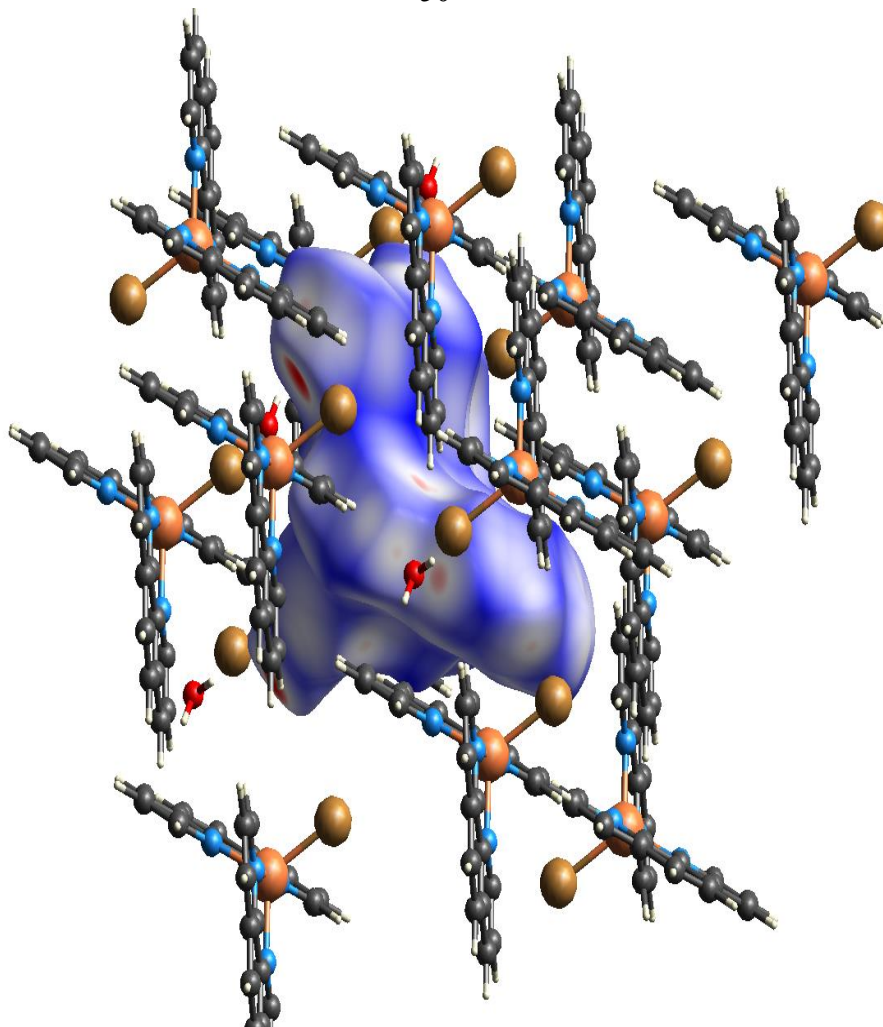


Fig. 3.17 Hirshfeld surfaces comprising d_{norm} surface plots for $[\text{Cu}(\text{phen})_2\text{Br}]\text{Br}$ complex.

3.4. MS, Elemental analyses and conductivity

The mono-cationic nature of the complex $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]^+$ was confirmed by MS $[\text{M}^+] = 647.90 \text{ m/z}$, (theoretical 647.2). The CHN elemental analysis is consistent with the proposed formula $\text{C}_{24}\text{H}_{20}\text{Br}_2\text{CuN}_6\text{O}_7$, $([\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br} \cdot 3\text{H}_2\text{O})$ of the complex and the solved XRD structure, because the two isomers in the crystal lattice have the same molecular formula. The combination of water solubility (0.05g/ml

at RT) and conductivity ($220 \Omega^{-1}\text{cm}^2 \text{mol}^{-1}$ at RT of $1 \times 10^{-3} \text{ M}$ in water) is in agreement with the mono-cationic nature of the complex. This result is also consistent with the XRD data.

3.5 Visible and ultraviolet spectra

In virtue of the visible color changes when NO_2 -phen ligand was added to the copper-bromide salt in ethanolic solution from brown to green and finally the complex precipitates as brown precipitate, the brown color of the complex changes to light blue when it is re-dissolved in water.

In the UV region, the complex showed two singles at $\sim \lambda_{\text{max}} = 270$ and 295 nm (shoulder), which were assigned to π - π electron transfer as seen in Fig. 3.11a.

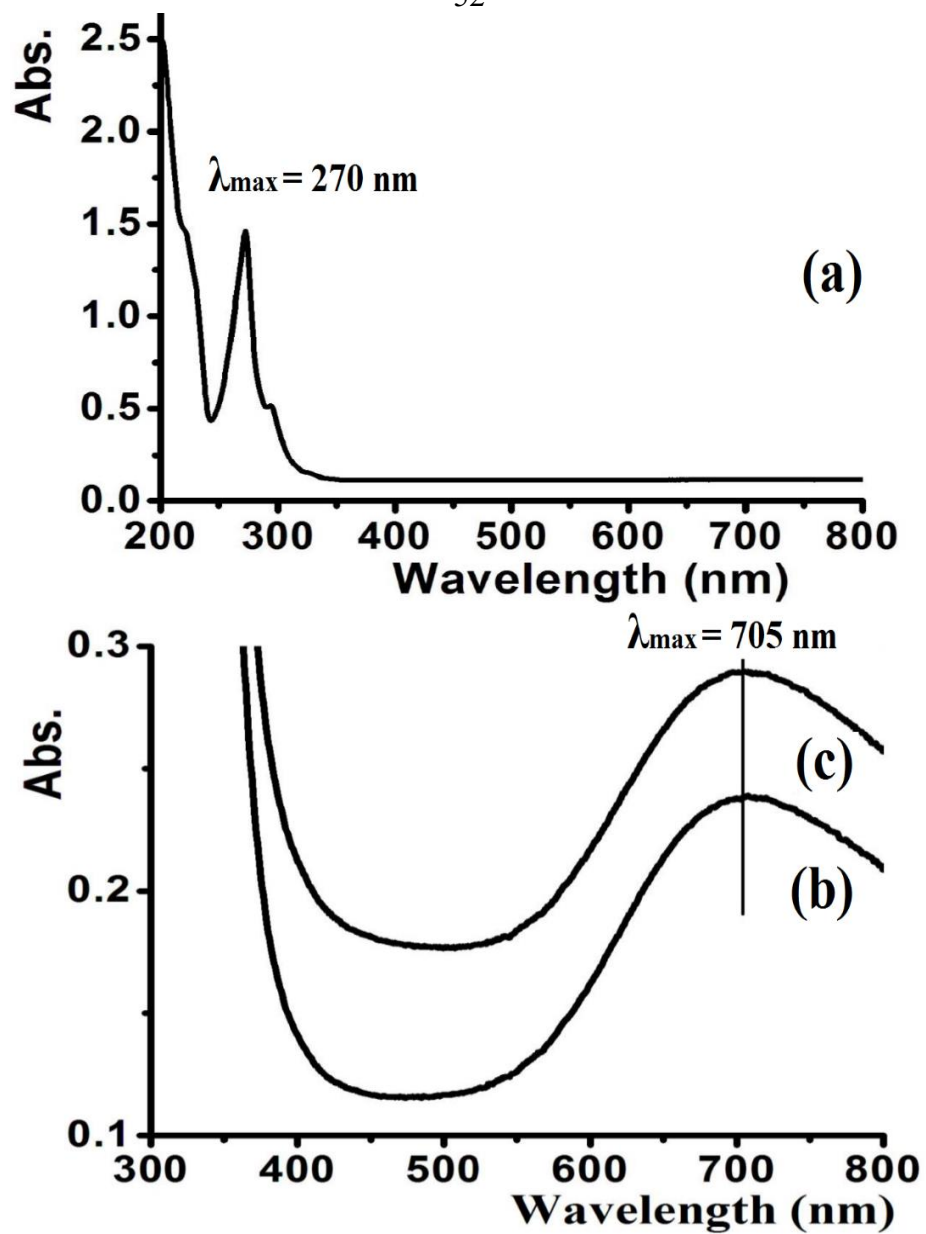


Fig. 3.18 UV spectrum of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex dissolved in water at RT (a) $1 \times 10^{-4} \text{ M}$, Vis. spectra (b) $1 \times 10^{-3} \text{ M}$, freshly prepared and (c) same solution as in (b) but after 30 days.

In the vis. region, the complex exhibited one broad absorption band at 705 nm assigned to d-d electron transition as seen in Fig 3.11b. No changes were detected on color nor on λ_{max} value when 1×10^{-3} M aqueous solution of the complex was measured after 30 days in an open atmosphere, as in Fig. 3.11c, which indicates the stability of such complexes.

3.6 Solvatochromism

The solubility of the complexes in polar solvents was limited to the number of solvents which could be investigated by the solvatochromism studies. Water, MeOH, DMF and DMSO were used. The desired mono-cationic complex is solvatochromic in such solvents due to the expected strong Jahn–Teller effect on copper(II) ions (d^9 electron configuration) [26-29, 50]. The vis. spectra of the complex in selected solvents revealed a broad band between 600-800 nm. The visible spectral changes of the λ_{max} of the complex with selected solvents are recorded in Fig. 3.12.

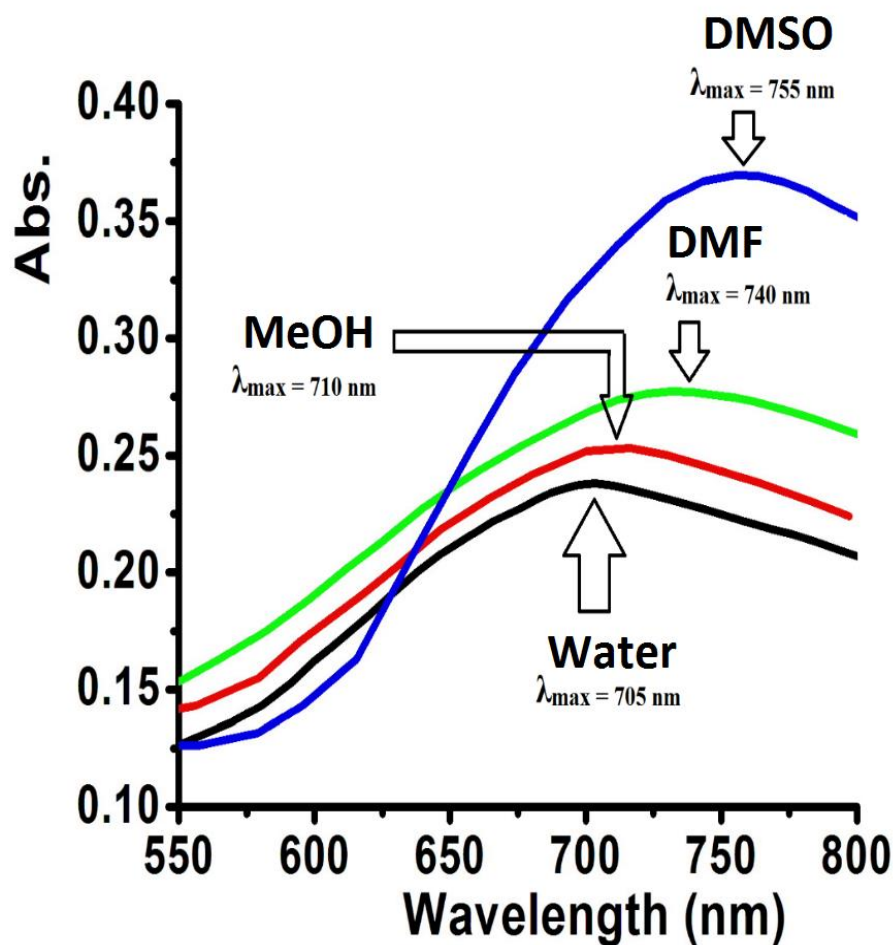


Fig. 3.19 Absorption spectra of [Cu(NO₂-phen)₂Br]Br complex in dissolvable solvents. The bathochromic spectrophotometric shifts of the complex is in agreement with the mechanism of solvatochromism behavior in such complexes [29, 50], which can be resonated to the direct coordination of the polar solvent molecules onto the vacant sites of the Cu(II) center with different strengths. Accordingly, the λ_{max} values increased linearly with the increasing of the Gutmann's donor number (DN) of the selected solvents. The linear trend of λ_{max} of the complex against DN is presented in Fig. 3.13.

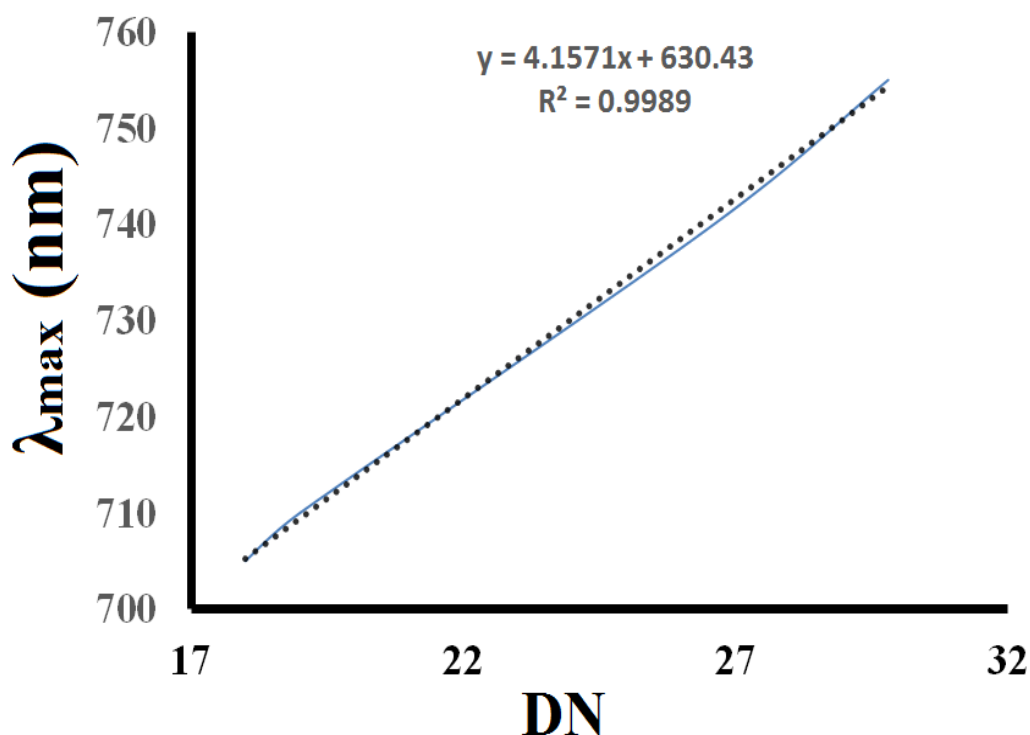


Fig. 3.20 Dependence of the λ_{max} of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex on DN solvent Gutmann's donor numbers.

3.7 FT- IR spectral investigation

The complexation reaction was monitored by mid. FT-IR as seen in Fig. 3.14. The spectra of the 5- NO_2 -phen ligand before and after coordination with CuBr_2 were recorded in solid state using KBr disk. The main bands at 3410, 3080, 1562 and 1350 cm^{-1} in the free ligand are assigned to the stretching vibrations of several functional groups like: $\nu(\text{H}_2\text{O})$, $\nu(\text{C-H})$ phen, $\nu(\text{C=N})$ and $\nu(\text{NO}_2)$, respectively. These bands are shifted to lower wavenumbers upon coordination to Cu(II) center (see experimental part and Fig. 3.14b). Appearance of a band at 518 cm^{-1} in the complex was due to the $\nu_{(\text{Cu-N})}$ stretching vibration.

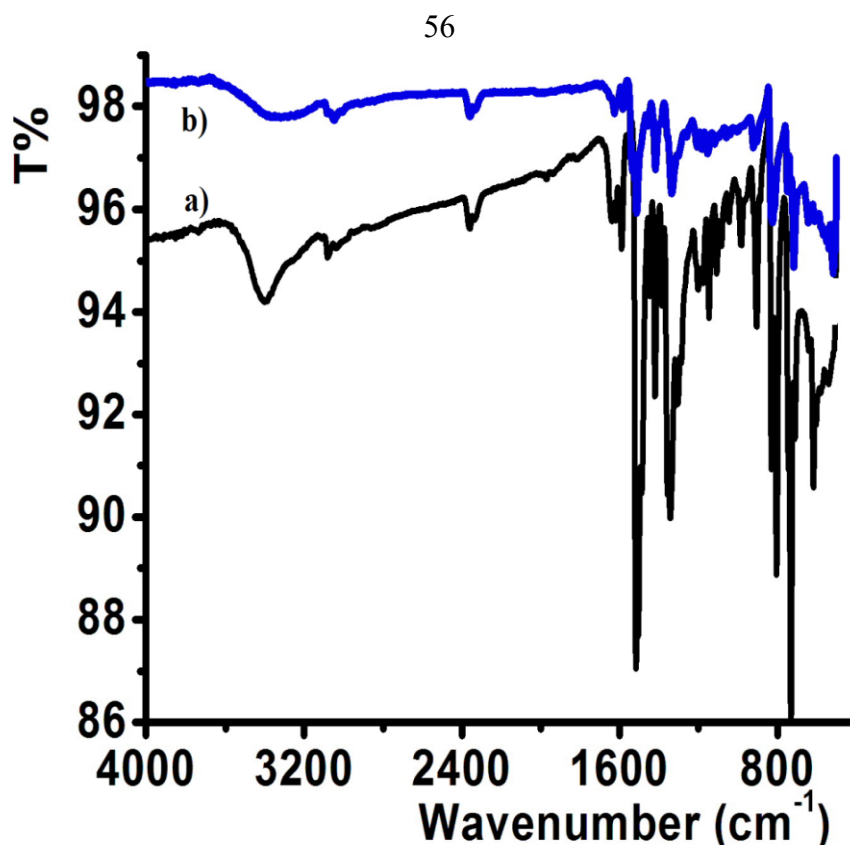


Fig. 3.21 FT-IR spectra of a) NO₂-phen free ligand and b) [Cu(NO₂-phen)₂Br]Br complex.

3.8 TG/DTG analyses

The TG/DTG thermal activities of [Cu(NO₂-phen)₂Br]Br complex were carried out in an open air system with a heating rate of 10 °C min⁻¹ and 0 to 1000 °C range of temperatures. The thermogravimetric data of [Cu(NO₂-phen)₂Br]Br complex showed two consecutive degradation steps; ligands pyrolysis and inorganic residue formation, as seen in Fig. 3.15.

TG/DTG spectra of the complex were illustrated mainly by three steps of weight loss. The first step was losing of three uncoordinated water molecules at 80-130 °C, losing ~8% of weight (7.5% calculated), which is consistent with the XRD data. The second decomposition was de-

structuring of the two NO₂-phen ligands at 200-400 °C losing ~60 % of weight (61.8% calculated) to form the CuBr₂ product. The third step which starts from 580 °C and ends at 680 °C may be due to removing of Br ions of CuBr₂ and reacting with atmospheric O₂ to form copper oxide as a final product, corresponding to 19.2 % weight lost (20% calculated). The final copper oxide product was confirmed by IR.

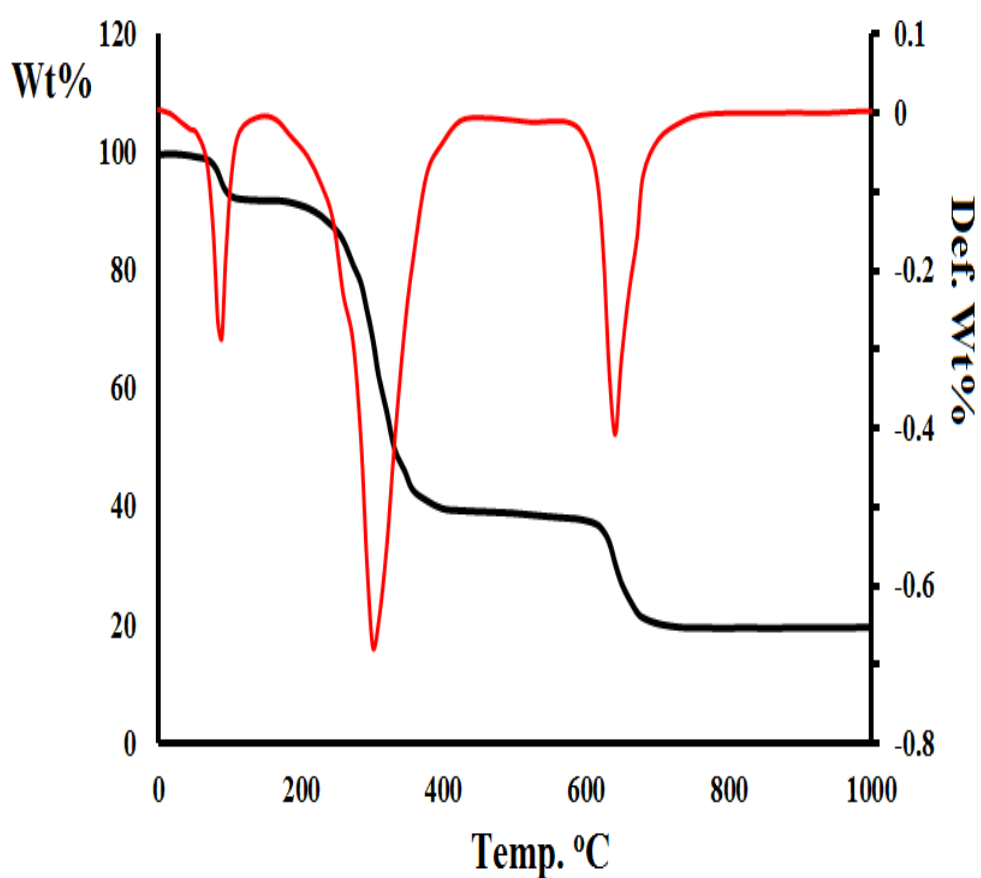


Fig. 3.22 TG/DTG thermal curves of [Cu(NO₂-phen)₂Br]Br complex.

Chapter Four

DNA binding studies

4.1 Absorption spectroscopy

Electronic absorption spectroscopy is considered to be of the most important tools to evaluate the binding strength of complexes to DNA [20-26, 51-59]. The binding of the desired complex with CT-DNA was evaluated using UV-Vis. spectroscopy to obtain the possible binding modes and to evaluate the K_b constant. DNA binding affinities of phen/Cu(II) complexes were recently reported for several complexes such as: $[\text{Cu}(\text{phen})_2\text{Cl}_2] \cdot 6\text{H}_2\text{O}$ (1.89×10^4), $[\text{Cu}(\text{phen})(\text{DMF})_2(\text{ClO}_4)_2]$ (1.47×10^5), $[\text{Cu}(\text{phen})(\text{L-tyr})(\text{H}_2\text{O})]\text{ClO}_4$ (4.0×10^3), $[\text{Cu-phen}](\text{H}_2\text{O})]\text{ClO}_4$ (2.44×10^6) and $[\text{Cu}(\text{phen})_2(\text{branched polyethyleneimine})]\text{Cl}_2 \cdot 4\text{H}_2\text{O}$ (5.95×10^5) [51-61].

Previous reports have suggested that materials that bind to DNA through intercalation usually result in bathochromism and hypochromism due to the strong π - π stacking interactions between the aromatic chromophore and DNA base pairs [20-25]. The extent of bathochromism in the UV-Vis. Band supports the strength of intercalative interaction [1].

The electronic Abs. spectra of the complex in the absence and presence of the CT-DNA are shown in Fig.3.16. There exists a band at 270 nm, by increasing the concentrations of CT-DNA the absorption band exhibited a significant decrease in absorption with a bathochromic shift of 1-2.2 nm, therefore the complex is suggested to interact with CT-DNA through intercalation mode [1].

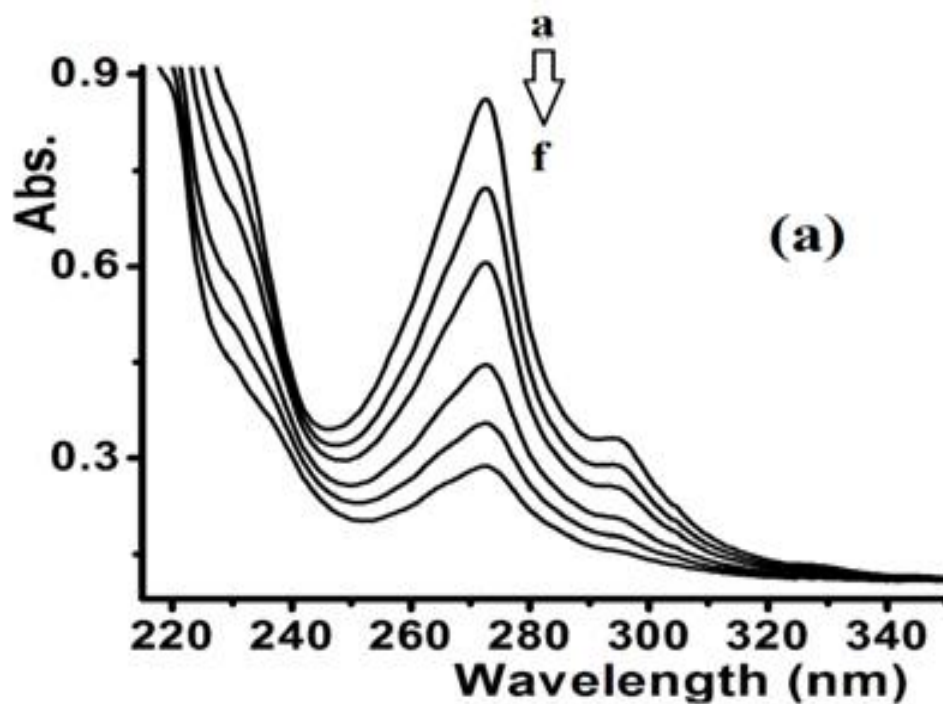


Fig. 4.1 .(a) Electronic spectral titration of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ with CT-DNA at 270 nm in Tris-HCl buffer; $[\text{Cu}] = 5.0 \times 10^{-5}$; $[\text{DNA}]$: *a* 0.0, *b* 5.0×10^{-6} , *c* 1.0×10^{-5} , *d* 1.0×10^{-4} , *e* 1.0×10^{-3} , *f* 2.0×10^{-2} M. The arrow denotes the gradual decrease of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ concentration upon DNA addition. (b) Plot of $[\text{DNA}]/(\epsilon_a - \epsilon_f)$ vs. $[\text{DNA}]$ at $\lambda_{\text{max}} = 270$ nm to establish the K_b value.

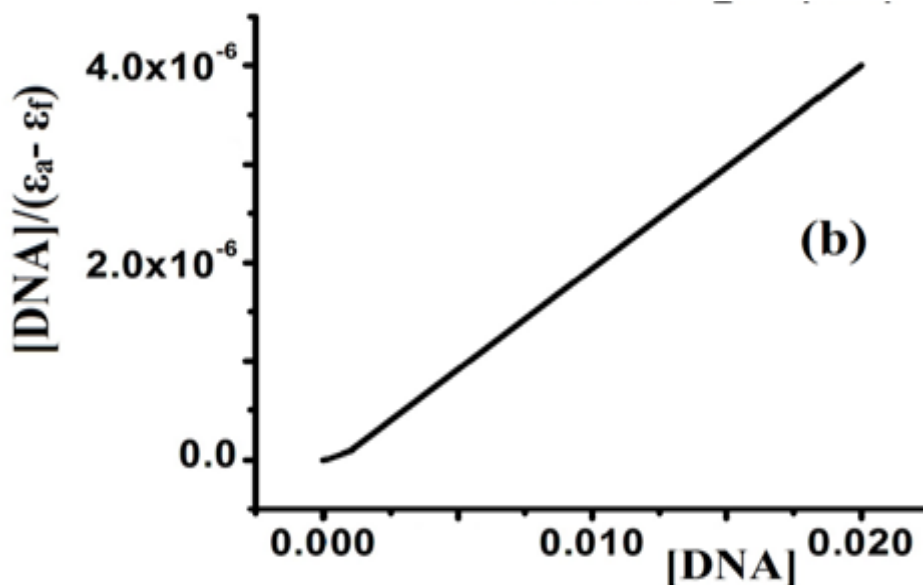


Fig. 4.2 .(a) Electronic spectral titration of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ with CT-DNA at 270 nm in Tris-HCl buffer; $[\text{Cu}] = 5.0 \times 10^{-5}$; $[\text{DNA}]$: a 0.0, b 5.0×10^{-6} , c 1.0×10^{-5} , d 1.0×10^{-4} , e 1.0×10^{-3} , f 2.0×10^{-2} M. The arrow denotes the gradual decrease of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ concentration upon DNA addition. (b) Plot of $[\text{DNA}]/(\epsilon_a - \epsilon_f)$ vs. $[\text{DNA}]$ at $\lambda_{\text{max}} = 270$ nm to establish the K_b value.

Using Eq. (1), a plot was constructed of $[\text{DNA}]/(\epsilon_a - \epsilon_f)$ vs $[\text{DNA}]$ for the titration of DNA with the complex (Fig. 3.16). K_b value was found to be $1.8 \times 10^4 \text{ M}^{-1}$.

4.2 Viscosity measurements

To further assess the Cu(II)-DNA binding mode, viscosity measurements were utilized in our investigation. A classical intercalative mode suggests that the CT-DNA helix should lengthen as base pairs are separated to accommodate the binding ligand leading to an increase in the molecular weight due to binding the complex, which increases the DNA viscosity

[39, 52-56]. The effect of $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ complex addition on the viscosity of DNA is depicted in Fig. 3.17.

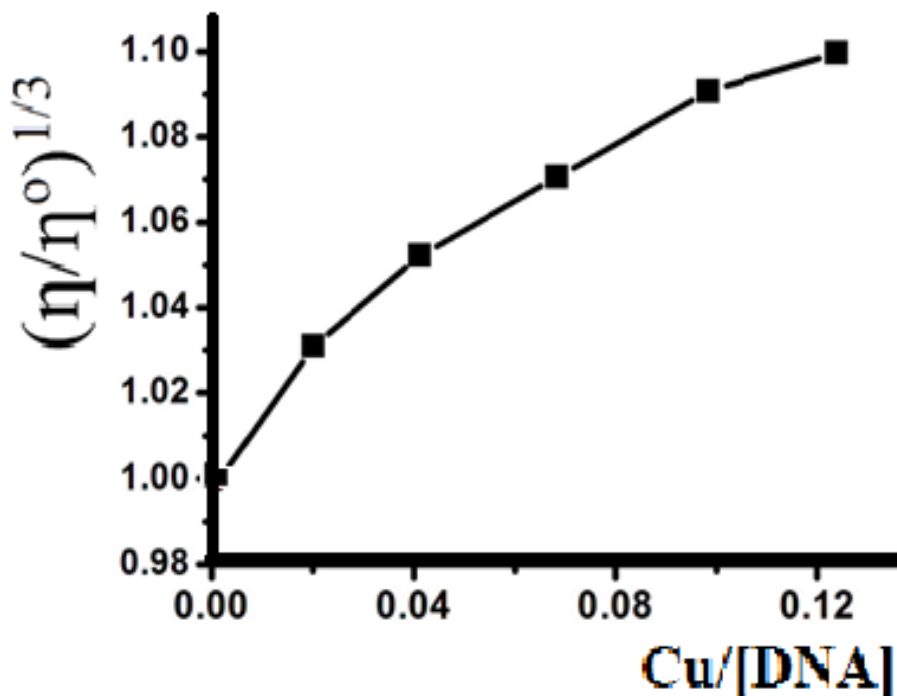


Fig. 4.3 Effect of increasing amounts of $[\text{Cu}]$ on the relative viscosities of DNA at 25.0 (± 0.1) $^\circ\text{C}$, $[\text{DNA}] = 5.0 \times 10^{-4} \text{ M}$.

Increasing of the complex concentration leads to a non-linear increase in the relative viscosity of DNA. The increased degree of viscosity reflects the degree of complex affinity to bind the DNA. The results suggest that the complex binds the DNA double helix through the intercalation mode.

Chapter Five

Conclusions

Conclusions

Water-soluble mixture of *cis/trans*-[Cu(NO₂-phen)₂Br]Br mono-cationic copper(II) complexes were prepared in 81% yield under ultrasonic mode. The mixture of two *cis/trans* isomers in the complex lattice was detected by single-crystal measurement, it is not possible to isolate *cis*-isomer and *trans*-isomer from each other. The *cis/trans* mixture complex matrix were fully characterized by elemental analyses, MS, UV-visible, FT-IR, thermal and XRD analysis. The X-ray single-crystal diffraction along with Hirshfeld surface analysis supported the formation of a distorted square pyramidal geometry around the Cu(II) center with several H-bonds. TG recorded a very stable *cis/trans*-complex that decomposed through a three-step process ended with CuO residue. The solvatochromism in several polar solvents suggested that Guttmann's DN parameter is the main contributor in increasing λ_{max} of the complex.

The structure of the complexes were theoretically studied by ab-initio and DFT methods. The geometry of the complex was fully optimized and the structural characteristics were determined by HF/3-21G and HF/6-31G* ab-initio methods and by DFT at the B3LYP/6-31G* level, and the obtained results are in good agreement with the experimental data. The viscosity and absorption measurements indicated that the desired *cis/trans*-complex is a very good CT-DNA binder. By Cu(II)-DNA absorption titration, K_b was found to be $1.8 \times 10^4 \text{ M}^{-1}$ and the binding is through the intercalation mode.

Two new mono-cation phen/Cu(II) complexes were prepared and characterized in good yields. The structures of the complexes were determined by several spectral and thermal measurements. Complex 2 demonstrated positive solvatochromism due to coordination of polar solvent molecules with different DNA to the axial site of the Cu(II) center. The single crystal X-ray diffraction data for complex 2 showed that copper ion is in a distorted square pyramidal environment. The CT-DNA binding and antitumor activities of the complexes were evaluated; results revealed high CT-DNA binding and expected antitumor activity against several types of cancer cells.

Supplementary material

Crystallographic data for $[\text{Cu}(\text{NO}_2\text{-phen})_2\text{Br}]\text{Br}$ was deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 1515203. A copies of the XRD information can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk.

References

- [1] D. Inci, R. Aydın, O. Vatan, D. Yılmaz, H. M. Genckal, Y. Zorlu, T. Cavas, *Binary and ternary new water soluble copper (II) complexes of L-tyrosine and substituted 1, 10-phenanthrolines: Effect of substitution on DNA interactions and cytotoxicities*, *Spectrochim. Acta, Part A*, 145 (2015) 313–324.
- [2] P. R. Reddy, S. Rajeshwar, B. Satyanarayana, *Synthesis, characterization of new copper (ii) Schiff base and 1,10 phenanthroline complexes and study of their bioproperties*, *J. Photochem. Photobiol. B Biol.* 160 (2016) 217–224.
- [3] F. Arnesano, G. Natile, *Mechanistic insight into the cellular uptake and processing of cisplatin 30 years after its approval by FDA*, *Coord. Chem. Rev.* 253 (2009) 2070–2081.
- [4] T.W. Hambley, *Developing new metal-based therapeutics: challenges and opportunities*, *Dalton Trans.* 43 (2007) 4929–4937.
- [5] Y.W. Jung, S.J. Lippard, *Direct cellular responses to platinum-induced DNA damage*, *Chem. Rev.* 107 (2007) 1387–1407.
- [6] P.C.A. Bruijninx, P.J. Sadler, *New trends for metal complexes with anticancer activity*, *Curr. Opin. Chem. Biol.* 12 (2) (2008) 197–206.
- [7] F. Tisato, C. Marzano, M. Porchia, M. Pellei, C. Santini, *Copper in diseases and treatments, and copper-based anticancer strategies*, *Med. Res. Rev.* 30 (4) (2010) 708–749.
- [8] P. Inamdar, R. Chauhan, J. Abraham, A. Sheela, *DNA interaction and cytotoxic activity of copper complex based on tridentate hydrazone*

- derived ligand and nitrogen donor heterocycle*, **Inorg. Chem. Comm.** 67 (2016) 67-71.
- [9] L. Jia, J. Xu, X. Zhao, S. Shen, T. Zhou, Z. Xu, T. Zhu, R. Chen, T. Ma, J. Xie, K. Dong, J. Huang, *Synthesis, characterization, and antitumor activity of three ternary dinuclear copper (II) complexes with a reduced Schiff base ligand and diimine coligands in vitro and in vivo*, **J. Inorg. Biochem.** 159 (2016) 107-119.
- [10] Z. Shokohi-pour, H. Chiniforoshan, A. Abbas, M. Borojeni, B. Notash, *A novel Schiff base derived from the gabapentin drug and copper (II) complex: Synthesis, characterization, interaction with DNA/protein and cytotoxic activity*, **J. Photochem. Photobiol. B: Biol.** 162 (2016) 34-44.
- [11] R. Pradhan, M. Banik, D. Cordes, A. Slawin, N. Sah, *Synthesis, characterization, X-ray crystallography and DNA binding activities of Co (III) and Cu (II) complexes with a pyrimidine-based Schiff base ligand*, **Inorg. Chim. Acta** 442 (2016) 70-80.
- [12] L. Abdel-Rahman, A. Abu-Dief, M. Ismael, M. Mohamed, N. Hashem, *Synthesis, structure elucidation, biological screening, molecular modeling and DNA binding of some Cu (II) chelates incorporating imines derived from amino acids*, **J. Mol. Struct.** 1103 (2016) 232-244.
- [13] I. Warad, M. Abdoh, N. Shivalingegowda, N. K. Lokanath, R. Salghi, M. Al-Nuri, S. Jodeh, S. Radi, B. Hammouti, *Synthesis, spectral, electrochemical, crystal structure studies of two novel di-m-halo-*

- bis[halo(2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline)cadmium(II)] dimer complexes and their thermolysis to nanometal oxides*, J. Mol. Struc. 1099 (2015) 323-329.**
- [14] M. Al-Noaimi, F. F. Awwadi, S. F. Haddad, W. H. Talib, S. Jodeh, S. Radi, T. B. Hadda, M. Abdoh, S. Naveen, N.K. Lokanath, I. Warad, ***Synthesis, spectral, X-ray single structure, DFT calculations and antimicrobial activities of [Co(II)X₂ (dmphen)] (X = Br and SCN)*, J. Mol. Struc. 1086 (2015) 153–160.**
- [15] A. Barakat, M. Al-Noaimi, M. Suleiman, A. S. Aldwayyan, B. Hammouti, T. B. Hadda, S. F. Haddad, A. Boshala, I. Warad, ***One Step Synthesis of NiO Nanoparticles via Solid-State Thermal Decomposition at Low-Temperature of Novel Aqua(2,9-dimethyl-1,10-phenanthroline)NiCl₂ Complex*, Int. J. Mol. Sci. 14 (2013) 23941-23954.**
- [16] I. Warad, B. Hammouti, T. B. Hadda, A. Boshala, S. F. Haddad, ***X-ray single-crystal structure of a novel di-*l*-chlorobis[chloro(2,9-dimethyl-1,10-phenanthroline)nickel(II)] complex: synthesis, and spectral and thermal studies*, Res. Chem. Intermed. 39 (2013) 4011–4020.**
- [17] D. Wesselinova, M. Neykov, N. Kaloyanov, R. Toshkova, G. Dimitrov, ***Antitumour activity of novel 1,10-phenanthroline and 5-amino-1,10-phenanthroline derivatives*, Euro. J. Med. Chem. 44 (2009) 2720–2723.**

- [18] Y. Zheng, X. Li, Y. Li, Zh. Wu, C. Yan, ***Synthesis and structure of new tetracopper(II) complexes bridged by 2-{N'-[2 (dimethylamino)-ethyl]oxamido}benzoate: DNA-binding and anticancer activity***, *J. Photochem. Photobiol. B Biol.* **114** (2012) 27–37.
- [19] Z. Tian, Y. Huang, Y. Zhang, L. Song, Y. Qiao, X. Xu, C. Wang, ***Spectroscopic and molecular modeling methods to study the interaction between naphthalimide-polyamine conjugates and DNA***, *J. Photochem. Photobiol. B Biol.* **158** (2016) 1–15.
- [20] V. Uma, M. Kanthimathi, T. Weyhermuller, B. Unnai Nair, ***Oxidative DNA cleavage mediated by a new copper (II) terpyridine complex: crystal structure and DNA binding studies***, *J. Inorg. Biochem.* **99** (2005) 2299–2307.
- [21] S. Mathur, S. Tabassum, ***Template synthesis of novel carboxamide dinuclear copper (II) complex: spectral characterization and reactivity towards calf-thymus DNA***, *Biometals* **21** (2008) 299–310.
- [22] Y.J. Liu, H. Chao, L.F. Tan, Y.X. Yuan, W. Wei, L.N. Ji, ***Interaction of polypyridyl ruthenium (II) complex containing asymmetric ligand with DNA***, *J. Inorg. Biochem.* **99** (2005) 530–537.
- [23] H. Deng, H. Xu, Y. Yang, H. Li, H. Zou, L.H. Qu, L.N. Ji, ***Synthesis, characterization, DNA-binding and cleavage studies of [Ru(bpy)₂(actatp)]²⁺ and [Ru(phen)₂(actatp)]²⁺ (actatp= acenaphthereno [1, 2-b]-1, 4, 8, 9-tetraazariphenylene)***, *J. Inorg. Biochem.* **97** (2003) 207–214.

- [24] D. Qin, Z. Yang, B. Wang, *Spectra and DNA-binding affinities of copper (II), nickel (II) complexes with a novel glycine Schiff base derived from chromone*, *Spectrochim. Acta Part A*. 68 (2007) 912–917.
- [25] P. P. Utthra, N. Pravin, N. Raman, *Scrutinizing the DNA damaging and antimicrobial abilities of triazole appended metal complexes*, *J. Photochem. Photobiol. B Biol.* 158 (2016) 136–144.
- [26] H. Golchoubian, H. Ghorbanpour, E. Rezaee, *Dinuclear copper (II) complexes with bridging oximato group: Synthesis, crystal structure and solvatochromism property*, *Inorg. Chim. Acta* 442 (2016) 30–36.
- [27] S.I. Noro, N. Yanai, S. Kitagawa, T. Akutagawa, T. Nakamura, *Binding Properties of Solvatochromic Indicators [Cu (X)(acac)(tmen)] (X= PF₆[−] and BF₄[−], acac= Acetylacetonate, tmen= N,N,N',N'-Tetramethylethylenediamine) in Solution and the Solid State*, *Inorg. Chem.* 47 (2008) 7360–7365.
- [28] R. Horikoshi, Y. Funasako, T. Yajima, T. Mochida, Y. Kobayashi, H. Kageyama, *Copper (II) solvatochromic complexes [Cu (acac)(N[^]N)(ligand)] BPh 4 with various axial ligands. Correlation between coordination geometries and d–d transition energies (acac= acetylacetonate, N[^]N= 1, 10-phenanthroline, 2,2'-bipyridyl)*, *Polyhedron* 50 (2013) 66–74.
- [29] H. Golchoubian, E. Rezaee, G. Bruno, H. A. Rudbari, *Synthesis and solvatochromism studies of new mixed-chelate dinuclear copper (II)*

- complexes with different counter ions*, **Inorg. Chim. Acta** 366 (2011) 290-297.
- [30] S.K. Wolff, D.J. Grimwood, J.J. McKinnon, D. Jayatilaka, M.A. Spackman, (2007). **Crystal Explorer 2.1** University of Western Australia, Perth, Australia.
- [31] G.M. Sheldrick, *A short history of SHELX*. **Acta. Cryst.**, A64 (2008) 112-122.
- [32] A. D. Becke, *Density - functional thermochemistry. IV. A new dynamical correlation functional and implications for exact - exchange mixing*, **J. Chem. Phys.** 104(1996) 1040-1046.
- [33] C. Lee, W. Yang, R.G. Parr, *Development of the Colic-Salvetti correlation-energy formula into a functional of the electron density*, **Phys. Rev. B.** 37(1988)785-789.
- [34] G.A. Petersson, T.G. Tensfeldt and J.A. Montgomery, *A complete basis set model chemistry. III. The complete basis set-quadratic configuration interaction family of methods*, **J. Chem. Phys.** 94 (1991) 6091-6101.
- [35] W. J. Hehre, R. F. Stewart and J. A. Pople, *Self - consistent molecular - orbital methods. i. use of gaussian expansions of Slater - type atomic orbitals*, **J. Chem. Phys.** 51 (1969) 2657-2664.
- [36] P. Pulay, G. Fogarasi, F. Pang and J. E. Boggs, *Systematic ab initio gradient calculation of molecular geometries, force constants, and dipole moment derivatives*, **J. Am. Chem. Soc.** 101 (1979) 2550-2560.

- [37] A.M. Pyle, J.P. Rehmann, R. Meshoyrer, C.V. Kumar, N.J. Turro, J.K. Barton, *Mixed-ligand complexes of ruthenium (II): factors governing binding to DNA*, J. Am. Chem. Soc. 111 (1989) 3051-3058.
- [38] M. Ganeshpandian, R. Loganathan, S. Ramakrishnan, A. Riyasdeen M. A. Akbarsha, M. Palaniandavar, *Interaction of mixed ligand copper(II) complexes with CT DNA and BSA: Effect of primary ligand hydrophobicity on DNA and protein binding and cleavage and anticancer activities*, Polyhedron 52 (2013) 924-938
- [39] A.W. Addison, T.N. Rao, J. Reedijk, J.V. Rijn, G.C. Verschoor, *Synthesis, structure, and spectroscopic properties of copper(II) compounds containing nitrogen–sulphur donor ligands; the crystal and molecular structure of aqua[1,7-bis(N-methylbenzimidazol-2'-yl)-2,6-dithiaheptane]copper(II) perchlorate*, J. Chem. Soc., Dalton Trans. 7 (1984) 1349-1356.
- [40] S. Ramakrishnan, V. Rajendiran, M. Palaniandavar, V.S. Periasamy, B.S. Srinag, H. Krishnamurthy, M. A. Akbarsha, *Induction of cell death by ternary copper (II) complexes of l-tyrosine and diimines: role of coligands on DNA binding and cleavage and anticancer activity*, Inorg. Chem. 48 (2009) 1309-1322.
- [41] K. Fukui, *The role of frontier orbitals in chemical reactions (Nobel Lecture)*, Angew. Chem. Int. Ed. Engl. 21 (1982) 801-809.

- [42] A. Lesar, I. Miosev, *Density functional study of the corrosion inhibition properties of 1,2,4-triazole and its amino derivative*, **Chem. Phys.** 483 (2009) 198-203.
- [43] R. G. Parr, L. V. Szentpaly, S. Liu, *Electrophilicity index*, **J. Am. Chem. Soc.** 121 (1999) 1922-1924.
- [44] R. G. Parr, R. A. Donnelly, M. Levy, and W. E. Palke, *Electronegativity: the density functional viewpoint*, **J. Chem. Phys.** 68 (1978) 3801-3807.
- [45] M.A. Spackman and D. Jayatilaka, *Hirshfeld surface analysis*, **Cryst. Engg. Comm.** 11 (2009) 19–32
- [46] M.A. Spackman and J.J McKinnon, *Fingerprinting intermolecular interactions in molecular crystals*, **Cryst. Engg. Comm.** 4 (2002) 378–392.
- [47] C. Tsiamis and M. Themeli, *Substituent and solvent effects in the spectra and structure of some mixed-ligand copper (II) chelates containing β -ketoenols*, **Inorg. Chim. Acta** 206 (1993) 105-115.
- [48] R. Patela, N. Singha, K. Shuklaa, J. Nicl'os-Guti'errezb, S. Astineirasb, V. Vaidyanathanc, B. Unni Nairc, *Characterization and biological activities of two copper(II) complexes with diethylenetriamine and 2,2'-bipyridine or 1,10-phenanthroline as ligands*, **Spectrochim . Acta, Part A** 62 (2005) 261–268.
- [49] I. Warad, F. Al-Rimawi, A. Barakat, S. Affouneh, N. Shivalingegowda, N. K. Lokanath, I. M. Abu-Reidah, *Synthesis, spectral, thermal, crystal structure, Hirschfeld analysis of*

- [bis(triamine)Cadmium(II)][Cadmium(IV)tetra-bromide] complexes and their thermolysis to CdO nanoparticles, Chem. Central J. 10 (2016) 1-11.***
- [50] F. Abu Saleemh, S. Musameh, A.Sawafta, P. Brandao, C. J. Tavares, S. Ferdov, A. Barakat, A. Al Ali, M. Al-Noaimi, I. Warad, ***Diethelenetriamine/diamines/copper (II) complexes [Cu(dien)(NN)]Br₂: Synthesis, solvatochromism, thermal, electrochemistry, single crystal, Hirshfeld surface analysis and their antibacterial activity, Arabian J. Chem. 2016.***
- [51] X. Liu, X. Li, Z. Zhang, Y. Dong, P. Liu, C. Zhang, ***Studies on antibacterial mechanisms of copper complexes with 1, 10-phenanthroline and amino acid on Escherichia coli, Biol. Trace Elem. Res. 154 (2013) 150–155.***
- [52] S. Dey, T. Mukherjee, S. Sarkar, H.S. Evans, P. Chattopadhyay, ***5-Nitro-1,10-phenanthroline bis (N, N-dimethylformamide-K' O)-bis (perchlorato) copper (II): synthesis, structural characterization, and DNA-binding study, Trans. Met. Chem. 36 (2011) 631–636.***
- [53] Z. Yang, Y. Wang, G. Yang, ***Copper (II) complex of 1, 10-phenanthroline and l-tyrosine with DNA oxidative cleavage activity in the gallic acid, Biometals 24 (2011) 737–745.***
- [54] P.R. Reddy, P. Manjula, ***Synthesis, Characterization, and DNA - Binding Studies of Mononuclear Copper (II)–Phenanthroline–Tyrosine Complex, Chem. Biodivers. 6 (2009) 71–78.***

- [55] M.N. Patel, D.S. Gandhi, P.A. Parmar, ***Synthesis, biological aspects and SOD mimic activity of square pyramidal copper (II) complexes with the 3rd generation quinolone drug sparfloxacin and phenanthroline derivatives***, *Inorg. Chem. Commun.* 14 (2011) 128–132.
- [56] A. Prisecaru, V. McKee, O. Howe, G. Rochford, M. McCann, J. Colleran, M. Pour, N. Barron, N. Gathergood, A. Kellett, ***Regulating bioactivity of Cu²⁺ bis-1, 10-phenanthroline artificial metallonucleases with sterically functionalized pendant carboxylates***, *J. Med. Chem.* 56 (2012) 8599–8615.
- [57] T.K. Goswami, S. Gadadhar, A.A. Karande, A.R. Chakravarty, ***Photocytotoxic ferrocene-appended (L-tyrosine) copper (II) complexes of phenanthroline bases***, *Polyhedron* 52 (2013) 1287–1298.
- [58] F. Xue, C.-Z. Xie, Y.-W. Zhang, Z. Qiao, X. Qiao, J.-Y. Xu, S.-P. Yan, ***Two new dicopper (II) complexes with oxamido-bridged ligand: Synthesis, crystal structures, DNA binding/cleavage and BSA binding activity***, *J. Inorg. Biochem.* 115 (2012) 78–86.
- [59] T. Pivetta, F. Isaia, G. Verani, C. Cannas, L. Serra, C. Castellano, F. Demartin, F. Pilla, M. Manca, A. Pani, ***Mixed-1, 10-phenanthroline–Cu (II) complexes: Synthesis, cytotoxic activity versus hematological and solid tumor cells and complex formation equilibria with glutathione***, *J. Inorg. Biochem.* 114 (2012) 28–37.

- [60] M. Al-Noaimi, M. I. Choudhar, F.F. Awwadi, W.H. Talib, T. Ben Hadda, S. Yousuf, A. Sawafta, I. Warad, ***Characterization and biological activities of two copper (II) complexes with dipropylenetriamine and diamine as ligands***, Spectrochim. Acta Part A. 127 (2014) 225–230.
- [61] M. Mohamadi, S. Y. Ebrahimipour, J. Castro, M. Torkzadeh-Mahani, ***Synthesis, characterization, crystal structure, DNA and BSA binding, molecular docking and in vitro anticancer activities of a mononuclear dioxido-uranium (VI) complex derived from a tridentate ONO aroylhydrazone***, J. Photochem. Photobiol. B Biol. 158 (2016) 219–227.

تحضير وتقييم النشاطات لمجموعة جديدة من معقدات
النحاس الثنائي-فينانثرولين باتجاه محاربة خلايا
السرطان

اعداد

ملاك زياد احمد دقة

إشراف

أ.د. إسماعيل وراذ

د. أشرف صوافطة

قدمت هذه الأطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في الكيمياء بكلية
الدراسات العليا في جامعة النجاح الوطنية في نابلس، فلسطين

2017

ب

تحضير وتقييم النشاطات لمجموعة جديدة من معقدات النحاس الثنائي-فينانثرولين باتجاه

محاربة خلايا السرطان

اعداد

ملاك زياد احمد دقة

إشراف

أ.د. إسماعيل وراد

د. أشرف صوافطة

الملخص

حضرت معقدات النحاس الثنائي/ أحادية الشحنة الذائبة بالماء ذات الصيغة العامة $[Cu(NO_2-phen)_2Br]Br$ و $[Cu(phen)_2Br]Br$, ($NO_2-phen = 5-nitro-1,10-phenanthroline$) بنسب جيدة جدا باستخدام الاشعة فوق صوتية. المعقدات المعنية تم فصلها على شكل املاح البروم وتم فحصها والتعرف عليها باستخدام اجهزة مختلفة مثل MS, EA, UV-visible, TG/DTA, FT-IR و XRD .

قياس حيود الاشعة السينية XRD وتحليل Hirschfield كشفت الشكل المربع الهرمي المشوه حول ذرة النحاس المركزية . الشكل الهندسي لمعقد $[Cu(NO_2-phen)_2Br]^+$ كان مماثل تماما مع ab-initio و (DFT/B3LYP) ، وبعدها تمت مقارنة العوامل الهيكلية مع نتائج XRD . Solvatochromism لمعقد $[Cu(NO_2-phen)_2Br]Br$ فحصت في العديد من الذيات القطبية. دراسات الامتصاص واللزوجة خلصت الى ان معقد $[Cu(NO_2-phen)_2Br]Br$ جيدة جدا في الارتباط بالحمض النووي.