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Study the effect of Cu(II) on the biological efficiency of py`rimidine derivatives in the presence of 1,10-phenanthroline and 2,2'-bipyridine

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***ABSTRACT*: The cupper(II) complexes $[Cu(L_1)(Bipy)(H_2O)_2]Cl_2.2.5H_2O$ (1), $[Cu(L_2)(Phen)(H_2O)_2]Cl_2.2.5H_2O$ (2) and $[Cu(L_3)(Phen)(H_2O)_2]Cl_2.0.5H_2O$ (3) (L_1=1-[4-(4-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl]ethanone, L_2=4-Oxo-6-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile, L_3=Ethyl 6-amino-4-(4-chlorophenyl)-5-cyano-2- methyl-4H-pyran-3-carboxylate, Bipy=2,2'-bipyridine, Phen=1,10-phenanthroline) were done. Elemental analysis, magnetic moment, molar conductance, thermal analysis, infrared spectra, and electronic spectrum investigations were used to describe these complexes. The molar conductance results of complexes indicated that the cupper complexes are electrolyte with 1:2. The FT-IR data showed that L_1, L_2, L_3, Phen, Bipy coordinated with metal ions as bidentate ligands. The magnetic moment of Cu(II) complexes found around (1.71 BM) which indicate the structure of complexes as octahedral geometry. The postulated stereochemistry and subsequently the predicted mechanism of heat degradation were validated by TG and DTG studies. The Horowitz-Metzger (HM) and Coats-Redfern (CR) techniques were used to compute the activation thermodynamic parameters. Thermal decomposition processes of complexes (1), (2) and (3) are non-spontaneous (negative values for ΔS*). In vitro antibacterial properties of the mixed ligand and their complexes were evaluated against several bacterial and fungi strains.**

KEYWORDS: **Phen and Bipy copper pyrimidine derivative complexes, XRD, thermal analyses, antimicrobial investigation**

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I. INTRODUCTION

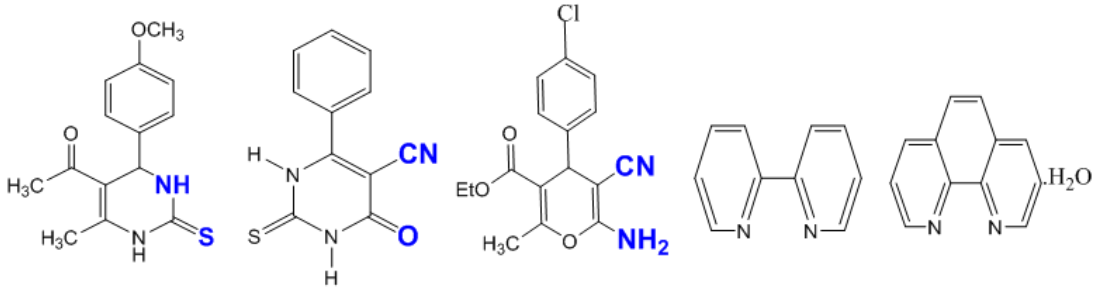
L_1 is one of the pyrimidine derivatives has an IUPAC name as 1-[4-(4-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidin-5-yl]ethanone (Scheme 1a). Bioactive aromatic compounds have lately raised a lot of interest due to their variety biological and therapeutic applications as well as their well-known chemistry of heterocyclic molecules and their derivatives **(Sadeek *et al.*, 2015; Rashad *et al.*, 2012 and Chitra *et al.*, 2009)**. Data from pyrimidine derivative investigations show that some examples of pharmacological activities include analgesic, antimitotic, antiviral, anticancer, anti-inflammatory, and antihypertensive medications **(Ghorab *et al.*, 2000; Sadeek *et al.*, 2020 and Kappe 2000)**. The formed N-heterocyclic compounds derived from pyrimidine were widely used as strong ligands for transition metals to create binding complexes, and these metal complexes were frequently used in many medical fields **(Ghorab *et al.*, 2000; Sadeek *et al.*, 2020; Kappe, 2000; Kappe *et al.*, 2000 and Stefani *et al.*, 2006)**.

L_2 is one of the pyrimidine derivatives (Scheme 1b). Due to their role as part of the components of DNA and RNA, pyrimidines enable life. Various analogues of thiopyrimidines such as 2-thio-uracil so that pyrimidines play a significant role in the production of nucleic acids and have been employed in pharmaceuticals to create drugs that are antiviral, antineoplastic, antibacterial, and antifungal **(Maga *et al.*, 2010; Callery and Gannett, 2002 and Deshmukh *et al.*, 2009)**. Similar to this, similar thiouracil compounds have antiviral, anticancer, and microbial properties and may be used as therapeutic agents **(Masoud *et al.*, 2007 and Odani *et al.*, 2007)**.

L_3 is one of the Pyrans derivatives (Scheme 1c). Alkaloids, carbohydrates, pheromones, polyether antibiotics, and iridoids are just a few examples of natural molecules that include pyrans, which are common heterocyclic components **(Boger and Weinreb, 1987 and Tietze and Kettschau 1997)**. Cardiotonic, anti-tumor, anti-bronchitic, antibacterial, antimicrobial, anti-inflammatory, antimalarial, antihistamine, antiplatelet, antigenic, and antiviral are only a few of the properties that pyranopyrimidines exhibit **(Grivsky *et al.*, 1980; Broom *et al.*,**

1976; Heber, *et al.*, 1993; Asadian *et al.*, 2018; Poola *et al.*, 2020; Aminina *et al.*, 2020; Tozkoparan *et al.*, 1999; Agarwal *et al.*, 2005 and Cerecetto *et al.*, 2000).

Bipy (Scheme 1d) and Phen (Scheme 1e) become both macromolecular and supramolecular chemistry use ligands widely **(Schubert and Eschbaumer, 2002 and Kaes *et al.*, 2000)**. The reason for that popularity is that Bipy ligands have a useful electrochemical demeanor and variable photo-optical and photo-physical properties **(Elsevier *et al.*, 2003 and Bozec and Renouard, 2000)**; in addion to they are derived easily. It is widely known that Bipy and Phen systems' derivatives react with DNA. These compounds are very convenient for supporting π stacking reactions with the DNA base pairs because of their polycyclic planar aromatic ligands. Furthermore, the two nitrogen atoms give these derivatives the capability of coordinating metal ions; therefore, working as chelating agents **(Nord, 1985)**.



Scheme1 (a) (b) (c) (d) (e)

This project's goal was focused to show the effect of Cu(II) on the efficiency of L_1 with Bipy and L_2, L_3 with Phen. A number of novel complexes purpose and the structures of the Cu(II) complexes were defined by elemental analyses, molar conductivity, magnetic susceptibility measurements, FT-IR, Uv–Vis., XRD and thermal analyses. The antibacterial and antifungal activities were also rated vs *S. aureus*, *B. subtilis* as Gram-positive bacteria and *E. coli*, *P. aeruginosa* as Gram-negative bacteria while the efficacy of antifungal properties was assessed vs *C. albicans* and *A. flavus*.

II. EXPERIMENTAL

2.1. Materials and instruments: All substances and solvents used in this inquiry were of the highest puirity and came from Aldrich or Sigma. Shimadzu UV3101PC was utilized to get the electronic spectra of the KBr discs while an FT-IR 460 Plus spectrophotometer was used to measure the Fourier transforms KBr discs infrared (FT-IR) spectra in the 4000-400 cm^{-1} region. A PerkinElmer 2400 CHN elemental analyzer was used to carry out the C, H and N% observations. The overall amount of metal was determined using atomic absorption analysis. A number of standard solutions at various concentrations were made for each element. A spectrometer with a PYE-UNICAM SP 1900 model number and an appropriate bulb was used for this **(El-Shwiniy *et al.*, 2020)**. The molar conductance of the substances in DMF (10^{-3} M) was calculated using a CONSORT K410. Using a Buchi apparatus, melting points were obtained. The thermal gravimetric analysis (TG, DTG, and DTA) data were performed on Shimadzu's TG-60H thermal analyzer utilizing a dynamic nitrogen flow of 30 ml/min. A Sherwood scientific magnetic balance and a Gouy balance were utilized to determine the magnetic susceptibilities of the powdered materials, with $Hg[Co(CSN)_4]$ serving as the calibrant. At room temperature, newly formed solutions were used for all measurements.

2.2. Synthesis of ligands: For L_1, a mix of methoxybenzaldehyde (2.5 mmol), acetyl acetone (2.5 mmol) and thiourea (3 mmol) taken with methane sulphonic acid in round bottom and stirred on magnetic stirrer at 120 °C. To gauge when the reaction was complete, TLC was utilized. The material was dissolved in ethyl acetate and cleaned with $NaHCO_3$. The final product that was produced after recrystallization with ethanol **(Krishna Rao *et al.*, 2017)**.

The yellow L_2 was synthesized by dissolving 0.76g (0.01 mol) thiourea in (30 mL) ethanol then adding 1.02 mL (0.01 mol) benzaldehyde, 1.06 mL (0.01 mol) ethyl cyanoacetate and 1.38 g (0.01 mol) potassium carbonate. The reaction mix was refluxed for 6h. The resulting clear solution was cooled at room temperature and the yellow crystalline product was separated off, sanitized with the least ethanol possible and then vacuum-dried **(Chetan *et al.*, 2019)**.

For L_3, a mixture of cinnamonitrile derivatives (0.01 mol) and ethyl acetoacetate (0.01 mol) in ethanol (20 mL), few drops of pipyridine were added. The mix was refluxed for 6h. Filtered off were the yellow crystals, which were then repeatedly washed with ethanol **(El-Sayed *et al.*, 2021)**. All ligands were dried under vacuum over anhydrous $CaCl_2$.

2.3. Synthesis of mixed ligand Cu(II) complexes: The brown solid complex $[Cu(L_1)(Bipy)(H_2O)_2]Cl_2.2.5H_2O$ (1) was produced by adding 0.5 mmol (0.115 g) of $CuCl_2$ drop-wise to a stirred mixture of 0.5 mmol (0.138 g) of L1 and 0.5 mmol (0.078 g) of Bipy in 50 mL of ethanol, in a ratio of 1:1:1 (Cu:L_1:Bipy), respectively. The reaction mix was stirred in a water bath for 16 hours at 35 ºC. The yield precipitates were filtered off and then vacuum-dried over anhydrous $CaCl_2$ after being washed in ethanol. For six hours, the mixture was refluxed. The gold residue was separated, then vacuum-dried over anhydrous $CaCl_2$. The green solid complexes $[Cu(L_2)(Phen)(H_2O)_2]Cl_2.2.5H_2O$ (2) and $[Cu(L_3)(Phen)(H_2O)_2]Cl_2.0.5H_2O$ (3) were manufactured in a similar way to how it was previously described, using ethyl alcohol as a solvent.

2.4. Antimicrobial investigation: The L_1, L_2, L_3, Phen and Bipy ligands and their Cu(II) complexes were investigated for their antimicrobial activity towards two species of gram-positive bacteria *S. aureus*, *B. subtilis* and two species of gram-negative bacteria *E. coli*, *P. aeruginosa* and two fungal species *C. albicans* and *A. flavus* using filter paper disc method **(Beecher and Wong, 1994)**. The compounds were prepared in DMSO-d6 at a concentration of 1 mg/mL. The standard-sized (5 cm) whatman filter paper discs were sanitized to sterilize them. The paper discs were submerged in the appropriate concentration of the complex solution and placed aseptically inside the petri dishes containing the nutrient agar media (agar 20 g + beef extract 3 g + peptone 5 g) seeded with *S. aureus*, *B. subtilis*, *E. coli*, *P. aeruginosa*, *C. albicans*, and *A. flavus*. Measurements were made of the inhibitory zones in the petri dishes following a 24-hour incubation period at 36 °C. Each therapy was repeated three times. The standard antifungal colitrimazole and antibiotic ampicillin's antibacterial activity was likewise assessed utilizing the same method as previously mentioned, the same concentration, and solvents. Utilizing DMSO-d_6 as a reference, the examined products were found at concentrations ranging from 0.025 to 0.100 g/mL. The % activity index for the compounds was calculated by **(Mohamed and Sadeek, 2021)**:

$$\text{Activity Index} = \frac{\text{Inhibition zone by test compound diameter}}{\text{Inhibition zone by standard diameter}} \times 100\ \% \qquad (1)$$

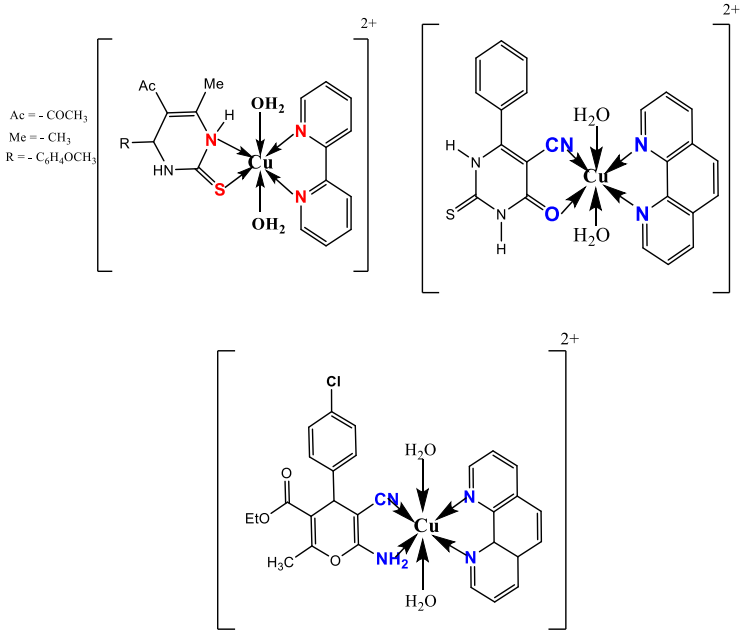
III. RESULTS AND DISCUSSION

3.1.Distribution of collected isolates: The synthesized mixed ligand Cu(II) complexes are soluble in DMSO and DMF and have a longer shelf life. The molar conductance values of complexes (1), (2) and (3) are 121.70, 106.10 and 125.94 S cm2 mol-1, respectively, the compounds' electrolyte content was determined with 1:2 (Table 1) **(Geary, 1971 and El-Hamid *et al*., 2018)**. Qualitative reactions are agreed quite well with the results of molar conductivity that indicate chloride found as counter ions. The elemental analyses and thermogravimetric analysis showed the formula of complexes. Because there are unpaired electrons available, the complexes' measured magnetic moments showed that they are paramagnetic in nature **(Drago, 1965)**.

Table (1): Elemental analysis and physico-analytical data for L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes:

Compounds M.Wt. (M.F)	Color Yield(%)	M.P. (°C)	(Calc.) Found,%					Λ S cm^2 mol^{-1}	$\mu_{eff,(B.M)}$
			C	H	N	M	Cl		
L_1 276.00 ($C_{14}H_{16}N_2O_2S$)	Black red 93.00	180	(60.87) 60.77	(5.80) 5.69	(10.14) 9.98	-	-	-	-
L_2 229 ($C_{11}H_7N_3OS$)	Yellow 75.12	315	(57.64) 57.56	(3.06) 3.00	(18.34) 18.27	-	-	-	-
L_3 318.50 ($C_{16}H_{18}N_2O_3Cl$)	Yellow 88.00	165	(60.28) 60.20	(4.71) 4.64	(8.79) 8.69	-	(11.14) 11.05	-	-
Bipy 156.20 ($C_{10}H_8N_2$)	White -	72	(76.82) 76.38	(5.21) 5.01	(17.92) 17.39	-	-	-	-
Phen 198.20 ($C_{12}H_{10}N_2O$)	White -	100	(72.72) 72.61	(5.09) 5.00	(14.13) 14.05	-	-	-	-
(1) 647.50 ($CuC_{24}H_{33}N_4O_{6.5}SCl_2$)	Brown 71.04	220	(44.48) 44.37	(5.09) 4.91	(8.65) 8.51	(9.81) 9.69	(10.96) 10.82	121.70	1.71
(2) 624.50 ($CuC_{23}H_{24}N_5O_{5.5}SCl_2$)	Green 83.26	235	(44.19) 44.10	(3.84) 3.78	(11.20) 11.12	(10.16) 10.06	(11.36) 11.28	106.10	1.83
(3) 678.00 ($CuC_{28}H_{28}N_4O_{5.5}Cl_3$)	Green 76.69	180	(49.56) 49.49	(4.13) 4.05	(8.26) 8.18	(9.37) 9.28	(15.71) 15.64	125.94	1.71

3.1. FT-IR spectra: Table 2 and Figure 1 illustrate the distinctive infrared spectrum frequencies of the ligands and Cu(II) complexes. The bands at 3357 and 1162 cm^{-1} in the L_1 data respectively, might be applied to designate the ν(N−H) and (C=S) vibration frequencies to those wavelengths **(Krishna Rao *et al.*, 2007)**.The positions of these peaks are anticipated to shift because of complexation so, L_1 bonded as a bidentate via nitrogen and Sulphur atoms as seen (Scheme 2) by the shifting of the bands related to its ν(N−H) and (C=S) groups to lower and higher values (Table 2). The characteristic bands at 2233 and 1661 cm-1, respectively, in the L_2 spectra can be utilized to explain the ν(C≡N) and ν(C=O) vibration frequencies. The ν(C≡N) was shifted to lower value 2222 cm^{-1} for complex (2) which indicated the involvement of lone pair of electrons on nitrogen atom forming coordinate bond with Cu(II) ions. Also the shift of ν(C=O) to higher values 1679 cm^{-1} assigned to the lone pair of electron on oxygen atom coordinated with metal ion. In order to evaluate the binding sites that could be associated in chelation, the spectra of the complex (3) are compared with those of L_3 and Phen. In the L_3 spectrum, the bands at 3263, 3223, and 2192 cm^{-1}, respectively, may be obtain to explain the ν(N-H) and ν(C≡N) vibration frequencies. The detected peak at 1586 cm^{-1} in Phen, which may correspond to ν(C=N), changed to lower values in the Cu(II) complex, showing that the nitrogen of the pyridine ring was a part of the development of the complex **(Li *et al.*, 2008)**. All complexes including coordinated and/or hydrated water molecules are proven to include ν(O-H) stretching vibrations by the existence of strong and wide bands at 3321-3406 cm^{-1} **(Nakamoto, 1986)**. A collection of novel bands with varying intensities that exhibit the properties of ν(M-O), ν(M-N) and ν(M-S) but are missing from the spectrum of free ligands were also visible in the spectra of the isolated solid complexes. The complexes' suggested structure and chelation mechanism for Cu(II) ions with mixed ligands are shown in (Scheme 2).



Scheme 2 The chelation mode of Cu(II) with mixed ligand

Table (2) Selected infrared spectra frequencies (cm^{-1}) of L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes:

Keys: s=strong, w=weak, m=medium, br=broad, ν=stretching, v=very.

Compounds	ν(O-H); H_2O	ν(N-H)	ν(C≡N)	ν(C=O)	ν(C=N), Bipy	ν(C=N), Phen	ν(C=S)	ν(M-O), ν(M-N) and ν(M-S)
L_1	-	3357br	-	-	-	-	1162s	-
L_2	-	3389w	2233m	1661vs	-	-	1225s	-
L_3	-	3263,3223	2192vs	-	-	-		-
Bipy	-				1578ms			-
Phen	3380mbr	-	-	-	-	1586ms	-	-
(1)	3383vw	3324vw	-	-	1566s	-	1173vs	629w, 542m,414m
(2)	3355w	-	2222w	1679m	-	1548s	-	645w, 571w
(3)	3405m	3330, 3231	2193m	-	-	1515s	-	719vs, 629m

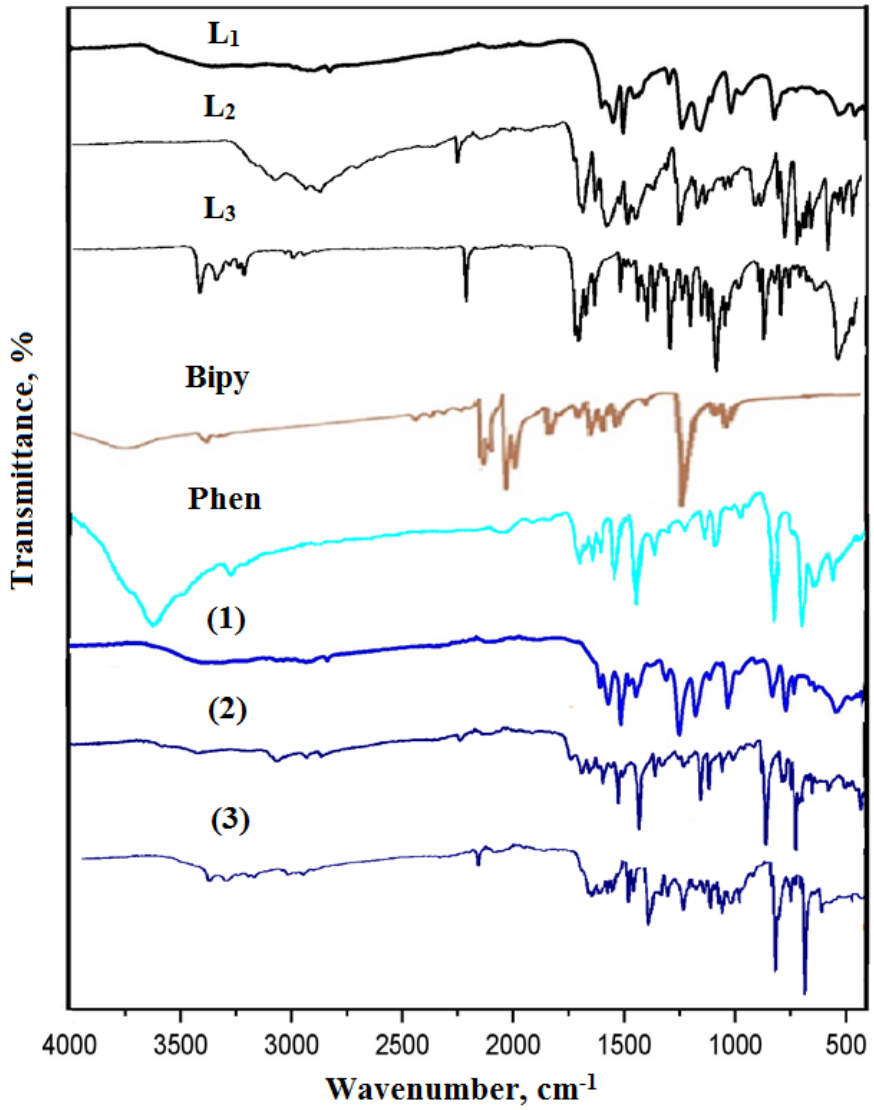


Figure 1 Infrared spectra of L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes

3.2. Uv–Visible spectra: The data of L_1, L_2, L_3, Phen, Bipy and the prepared complexes were measured from 200 to 800 nm in DMSO ($1x10^{-3}$ M) solution in Table 3 and Figure 2. Ligands exhibit an absorption bands in the ultraviolet regions at 250, 240, 245, 284 and 300 nm which refer to π-π* transition and (280, 375), (295, 330), (284, 343), 374 and 340 nm which assigned as n-π* transition for L_1, L_2, L_3, Phen and Bipy, respectively **(Krishna Rao *et al.*, 2007; Li *et al.*, 2008; Nakamoto, 1986; Sadeek *et al.*, 2006 and Sadeek *et al.*, 2009)**. Upon complexation with Cu(II) ions it's found an important change in Uv-Vis. spectra: i) An shift to higher or lower in the bands refer to π-π* and n-π* transitions in the complexes (**Sadeek *et al.*, 2006; Sadeek *et al.*, 2009; Mohamed *et al.*, 2019; Sadeek *et al.*, 2019 and Nandi, 1972)**. ii) New bands found from ligand to metal (L→M) or metal to ligand (M→L). This transition appears in visible region in the range 450-490 nm [1]. iii) The mixed ligand Cu(II) complexes has new peaks between 590 and 615 nm which refer to the d-d transition $2B_{1g}\rightarrow 2E_g$ transition and accepting distorted octahedral geometry **(Mohamed *et al.*, 2019 and Sadeek *et al.*, 2019)**.

Table (3) Uv-Vis. spectra of L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes:

Assignments (nm)	L_1	L_2	L_3	Bipy	Phen	**(1)**	**(2)**	**(3)**
Intera Ligand Transitions (π-π^* and n-π^*) λ_{max} (nm)	250,280,375	240,295,330	245,284,343	284,347	300,340	265,285,342	245,280,305	255,300,330
ν (cm^{-1})	40000,35714, 26667	41666,33898,30 303	40816,35211, 29154	35211, 28818	33333, 29412	37736,35088, 29240	40816,35714,32 787	39215,33333, 30303
Ligand-metal charge transfer	-	-	-	-	-	480	450	460,490
ν (cm^{-1})	-	-	-	-	-	20833	22222	21739,21505
d-d transition	-	-	-	-	-	610	590	615
ν (cm^{-1})	-	-	-	-	-	16393	16949	16260

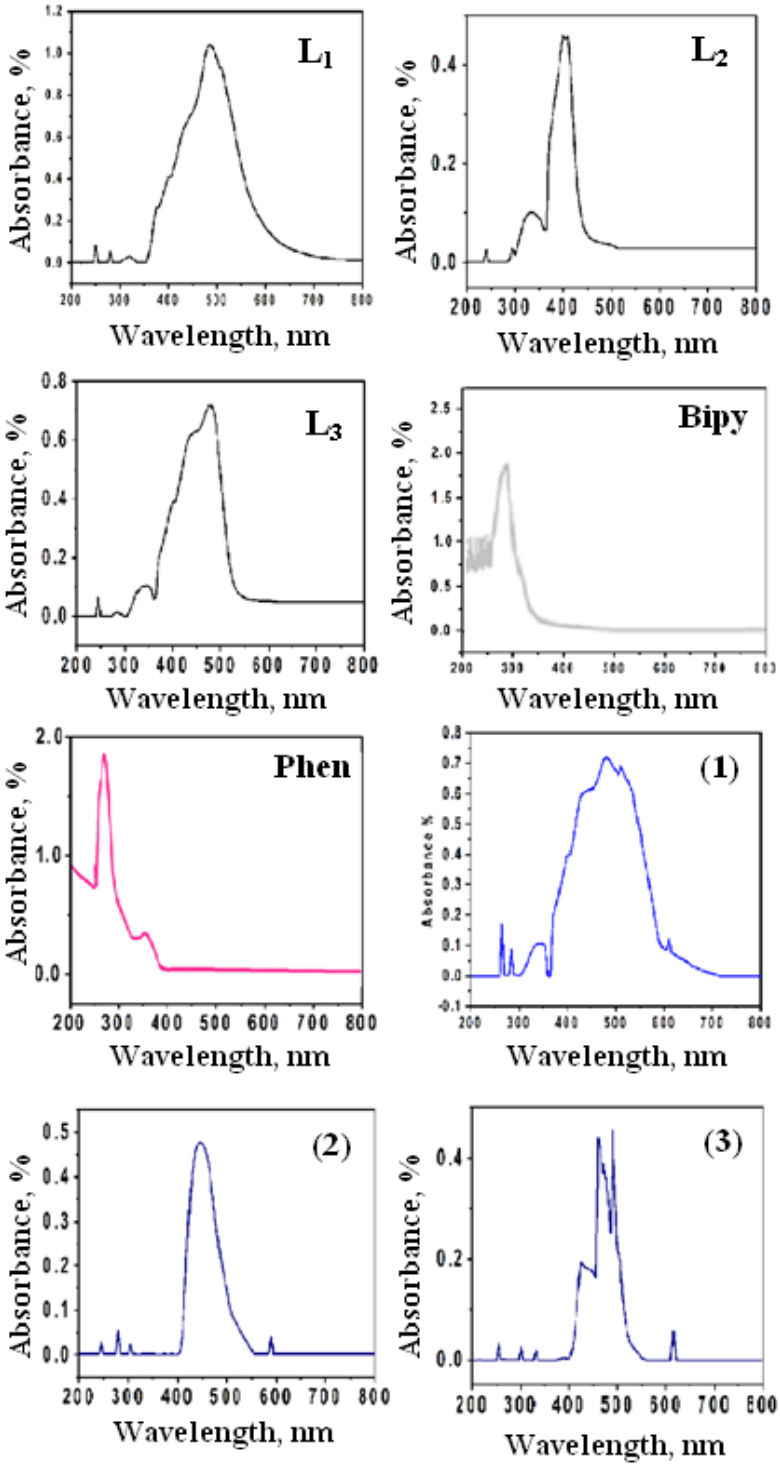


Figure 2 Electronic absorption spectra for L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes

3.3. Thermal analysis of compounds: TG may strongly confirm the formulae of the synthesized complexes and used to verify that the linked water or solvent molecules to be in the chelation sphere or in the crystalline form. The hydrated water molecules may be lost firstly with lower temperature value around 100 ºC. Table 4 and Figure 3 represent TG/DTG curves of L_1, L_2, L_3, Bipy, Phen and Cu(II) complexes. The TG curves of L_1indicated that its thermal decomposition achieved through three stages. First stage starts at 72 °C with weight loss 10.85% (calc. 10.86%), related to a loss H_2CO. Second step at 203 °C with loss 32.55% (calc. 32.60%), refers to loss of

$C_2H_4+H_2S+CO$. The third stage at 442 and 556 °C with loss 56.60% (calc. 56.52%), related to loss of $2C_4H_2+C_2H_4+N_2$ this step is confirmed by E_a of 19.76 kJmol^{-1} and the sequence of reaction is 0.981. The TG curves of L_2 and L_3 indicated that its thermal decomposition achieved through two steps. The first of L_2 one obtained at 298°C with weight loss 44.76% assigned to the loss of $C_4H_2+C_2H_2+HCN$ this stage is confirmed by E_a of 94.26 kJmol^{-1} and the sequence of reaction is 0.249. The second step of degradation obtained at 583°C maximum with loss 50.26% (calc. 49.78%), related to the loss $C_2N_2+CO+H_2S$. The first step of L_3 beginning at 137 °C and completed at 761°C, with two stages. The first stage at 239 °C with loss 58.00 % (calc. 57.93%), relating to loss of $HCl+2C_2H_2+2CO+C_3H_4$ this step is characterized with E_a of 19.76 kJmol^{-1} and the order of reaction is 0.981.The second step at 318 and 520 °C with loss 42.00% (calc. 42.07%), refers to loss of $C_5H_5N+CO+HCN$.The thermal analysis of Bipy and Phen has been found in the literature **(Hossain *et al.*, 2015 and Abd El-Hamid and Sadeek, 2016)**. Complexes (1), (2) and (3) were decomposed through three steps. In the first step found at 90, (68,111) and 58°C, respectively, with loss 6.91, 6.57 and 1.33% in connection with the discharge of all hydrated water molecules. Second step at (157, 244), (202,329) and (639,844) °C, respectively, with loss $5C_2H_2+2NO+2HCl$, $2C_2H_2+ 0.5C_4H_2+2HCL+H_2S+O_2$ and $6C_2H_2+2NO+Cl_2$, respectively.The third stepstageat maxima temperatures 303, 520 and (639,844) °C, respectively, with a weight loss $7C_2H_2+2NO+H_2S$, $C_4H_2+3.5C_2H_2+2C_2N_2+HCN$ and $7C_2H_2+CO+CO_2+N_2+HCl$, respectively. The residue for Complex (1) and (3) is Cu, while for complex (2) is CuO+C.

Table (4) The maximum temperature T_{max} (°C) and weight loss values of the decomposition stage for L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes:

Compounds	Decomposition	T_{max} (°c)	Weight loss (%) Calc.	Found	Lost species
L_1	First step	74	10.86	10.85	H_2CO
	Second step	203	32.60	32.55	$C_2H_4+H_2S+CO$
	Third step	442, 556	56.52	56.60	$2C_4H_2+C_2H_4+N_2$
	Total loss		100.00	100.00	
L_2	First step	298	44.98	44.76	$C_4H_2+ C_2H_2+HCN$
	Second step	583	49.78	50.26	$C_2N_2+CO+H_2S$
	Total loss		100.0	100.0	
	Residue		5.24	4.98	C
L_3	First step	239	57.93	58.00	$HCl+2C_2H_2+2CO+C_3H_4$
	Second step	318, 520	42.07	42.00	$C_5H_5N+CO+HCN$
	Total loss		100	100.0	
Bipy	First step	164	100.00	99.64	$4C_2H_2+C_2N_2$
	Total loss		100.00	99.64	
Phen	First step	95	9.08	8.02	H_2O
	Second step	278	90.92	91.98	$2C_4H_2+2C_2H_2+N_2$
	Total loss		100.0	100.0	
(1)	First step	90	6.95	6.91	$2.5H_2O$
	Second step	157, 244	40.62	40.89	$5C_2H_2+2NO+2HCl$
	Third step	303	42.63	42.94	$7C_2H_2+2NO+H_2S$
	Total loss		90.20	90.74	
	Residue		9.80	8.79	Cu
(2)	First step	68,111	7.2	6.57	$2.5H_2O$
	Second step	202,329	34.59	35.01	$2C_2H_2+ 0.5C_4H_2+2HCL+H_2S+O_2$
	Third step	520	43.56	44.93	$C_4H_2+3.5C_2H_2+2C_2N_2+HCN$
	Total loss		85.35	86.51	
	Residue		14.65	13.48	CuO+C
(3)	First step	58	1.33	1.33	$0.5H_2O$
	Second step	182,358	42.33	41.8	$6C_2H_2+2NO+Cl_2$
	Third step	639,844	46.97	47.16	$7C_2H_2+CO+CO_2+N_2+HCl$

	Total loss Residue		90.63 9.37	90.29 9.71	Cu

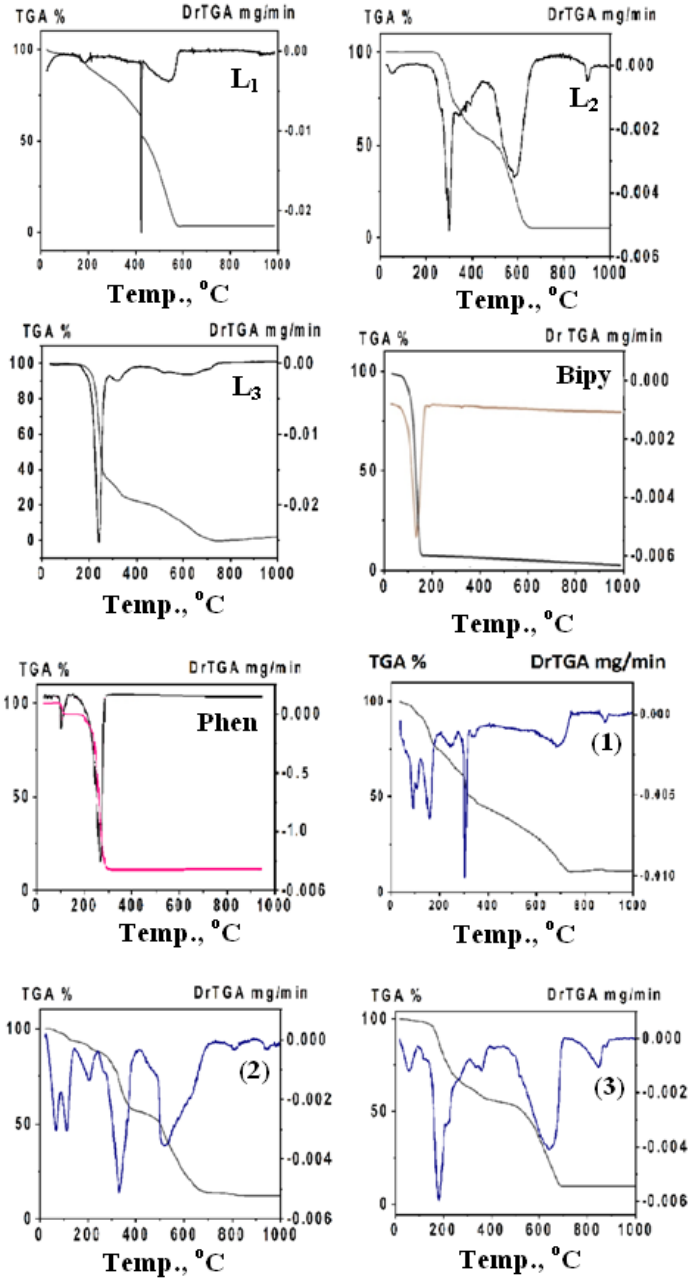


Figure 3 TG and DTG diagrams for L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes

3.4. The kinetic data: The present thermal properties of L_1, L_2, L_3, **Bipy**, **Phen** and Cu(II) complexes are shown in Table 5 and Figure 4. The kinetic parameters activation energy (E_a), enthalpy (ΔH^*), entropy (ΔS^*) and Gibbs free energy change of the breakdown (ΔG^*) were assessed by **Coats and Redfern (CR), 1964 and Horowitz and Metzger (HM), 1963** (Equations 2-8).

$$\ln X = \ln\left[\frac{-\ln(1-\propto)}{T^2}\right] = \ln\left(\frac{AR}{\varphi E_a}\right) - \frac{E_a}{RT} \qquad \text{for } n = 1 \qquad (2)$$

$$\ln X = \ln\left[\frac{1-(1-\propto)^{1-n}}{T^2(1-n)}\right] = \ln\left(\frac{AR}{\varphi E_a}\right) - \frac{E_a}{RT} \qquad \text{for } n \neq 1 \qquad (3)$$

$$\ln[-\ln(1-\propto)] = \frac{E_a\theta}{RT_s^2} \qquad \text{for } n = 1 \qquad (4)$$

$$\ln\left[\frac{1-(1-\propto)^{1-n}}{1-n}\right] = \ln\left(\frac{A}{\varphi}\frac{RT_s^2}{E_a}\right) - \frac{E_a}{RT_s} + \frac{E_a\,\theta}{RT_s^2} \qquad \text{for } n \neq 1 \qquad (5)$$

$$\Delta H^* = E_a - RT \qquad (6)$$

$$\Delta S^* = R \ln\frac{hA}{K_B T} \qquad (7)$$

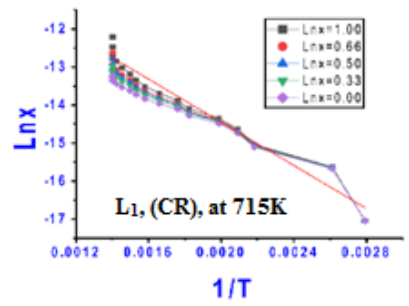
$$\Delta G^* = \Delta H^* - T\Delta S^* \qquad (8)$$

The correlation coefficients for Arrhenius Plots of thermal degradation steps were obtained between 0.861-0.998, showing an excellent match with a linear function. E_a of degradation was founded between 23.57-185.56 kJ mol^{-1} which reflect the thermal stability of the complexes **(Mahmoud *et al.*, 2013 and El-Megharbel *et al.*, 2014)**.The positive value for ΔH^* interprets the endothermic behavior for all degradation processes **(Mohamed and Sharaby, 2007 and (a) Tweedy, 1964 and (b) Sengupta *et al.*, 1998)**.

Table (5) Thermal behavior and Kinetic parameters determined using Coats–Redfern (CR) and Horowitz–Metzger (HM) operated for L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes:

Compounds	Decomposition range (K)	T_s (K)	Method	Parameters					r	SD
				E_a (kJ/mol)	A (s^{-1})	ΔS^* (kJ/mol.K)	ΔH^* (kJ/mol)	ΔG^* (kJ/mol)		
L_1	500-722	715	CR HM	23.57 43.65	4.33 4.13	-0.2740 -0.0250	17.62 37.70	213.55 55.97	0.981 0.954	0.006 0.014
L_2	501-694	571	CR HM	94.26 84.22	4.06×10^{7} 1.56×10^{7}	-0.1386 -0.1466	89.51 79.47	168.69 163.18	0.861 0.822	0.249 0.320
L_3	436-540	512	CR HM	185.56 157.18	5.08×10^{18} 7.81×10^{15}	0.0746 0.0208	181.30 152.92	143.07 142.27	0.981 0.970	0.034 0.036
Bipy	315-554	437	CR HM	75.70 95.74	6.53×10^{6} 2.79×10^{9}	-0.1176 -0.0672	72.06 92.11	123.46 121.49	0.998 0.998	0.094 0.106
Phen	394-572	551	CR HM	117.83 146.78	2.03×10^{9} 7.97×10^{11}	-0.071 -0.022	113.250 142.210	152.84 154.42	0.996 0.998	0.120 0.076
(1)	495-594	576	CR HM	30.20 45.95	1.55×10^{2} 2.44×10^{3}	-0.2424 -0.2195	25.41 41.15	165.08 167.62	0.953 0.907	0.023 0.041
(2)	299-693	602	CR HM	25.98 37.27	1.47×10^{1} 2.11×10^{2}	-0.2624 -0.2402	20.97 32.26	178.95 176.91	0.924 0.959	0.134 0.060
(3)	292-650	455	CR HM	48.70 38.55	2.33×10^{4} 5.95×10^{3}	-0.1988 -0.2101	44.91 34.77	135.39 130.40	0.842 0.758	0.265 0.407

r=correlation coefficients of the Arrhenius plots and SD=standard deviation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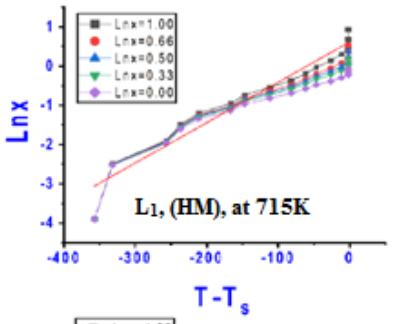
L1, (CR), at 715K
1/T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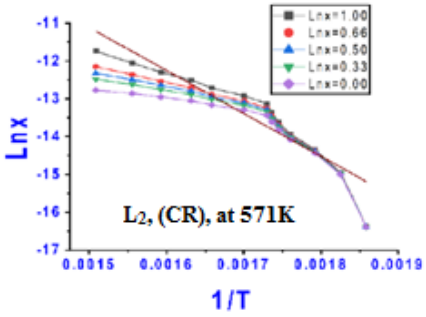
T-Ts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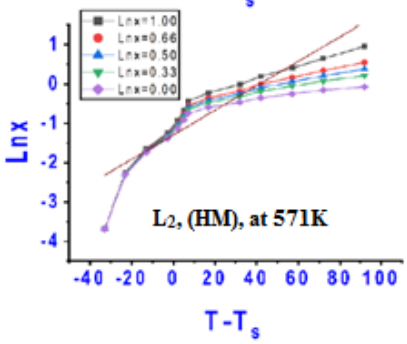
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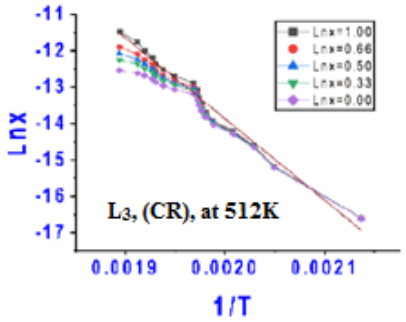
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L3, (CR), at 512K
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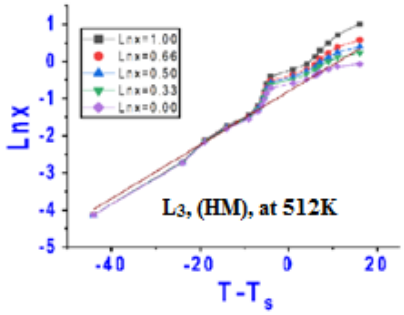
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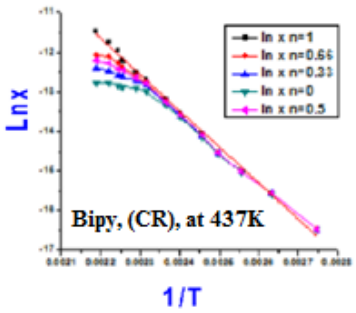
L3, (HM), at 512K
T-Ts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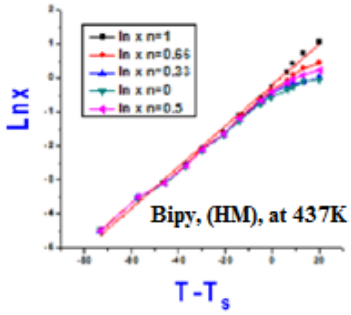
Bipy, (CR), at 437K
1/T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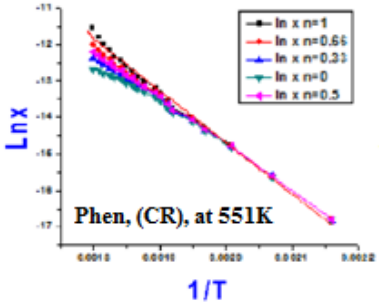
Bipy, (HM), at 437K
T-Ts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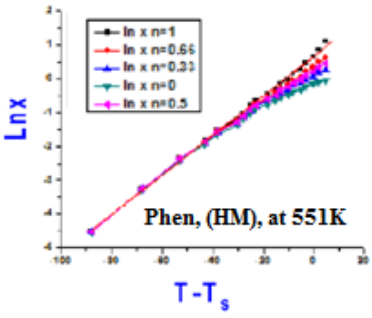
Phen, (CR), at 551K
1/T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ln x n=0
ln x n=0.5
Lnx
Phen, (HM), at 551K
T-Ts

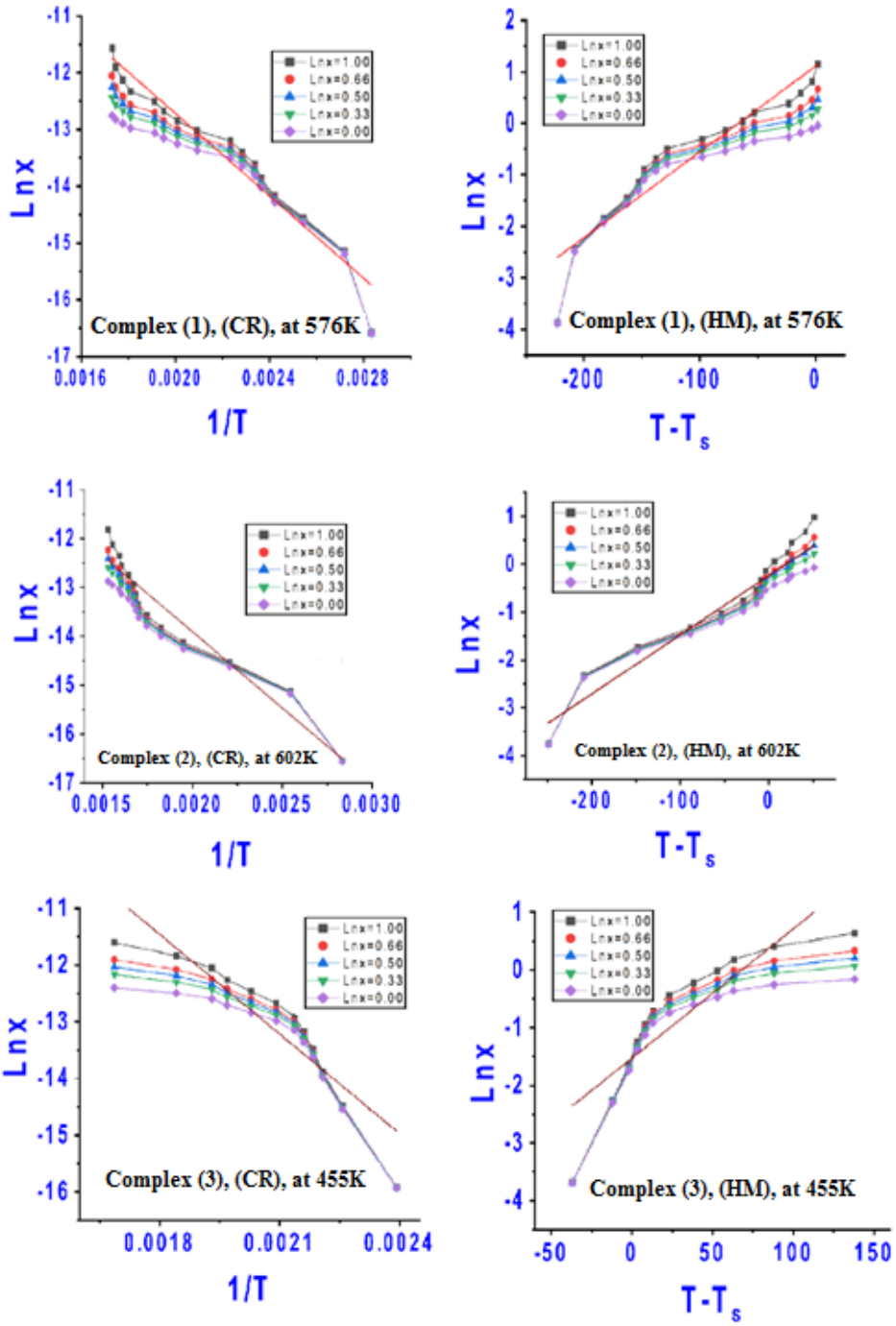

Figure 4 The diagrams of kinetic parameters of L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes using Coats-Redfern (CR) and Horowitz-Metzger (HM) equations

3.4. X-ray diffaction analysis: Consequently, despite employing a number of techniques, such as chilling and slow evaporation, we couldn't to produce appropriate nanocrystals for X-ray crystallographic investigations. Use XRD method to distinguish between crystalline and amorphous materials and to find out more about unit cell structure, lattice parameters, and Miller indices. Figure 5 shows the crystallinity and diffraction patterns of L_1, L_2, L_3, **Bipy**, **Phen**, **(1)**, **(2)** and **(3)** nanoparticle compounds through the scanning range $2\theta = 0\text{-}80^{\circ}$. Table 6 provides a summary of the diffract grams and associated statistics, including the 2θ value for each peak, the relative intensity, and the inter-planar spacing. Strong and sharp peaks indicate high crystallinity in the obtained complexes **(Geary, 1971**

and Ilhan *et al.*, 2007). In order to determine the diameters of the crystallites of the examined compounds, the Debye-Scherer equation (9) was used.

$$Cs = \frac{K\lambda}{\beta\cos\theta} \qquad (9)$$

Where, C_s is the mean particle diameter, assuming spherical particles, k is the Scherer constant (= 0.9), λ is the wavelength of the X-ray beam (0.15405 nm), β is the full width at half maximum (FWHM) of the diffracted peak in (radians), and θ is the angle of diffraction (radians) **(Al-Amiery *et al.*, 2012 and Khan *et al.*, 2013)**. The crystallite sizes of the produced compounds were discovered to range 20.43 and 80.87 nm, that is in the range of nano-size structures. The value of dislocation density (δ) was in the 2.16×10^{-3} - 7.24×10^{-4} nm^{-2} range, at which D is the number of dislocation lines per unit area of the crystal and can be obtained by equation (10) **(El-Bindary *et al.*, 2015)**.

$$D = \frac{1}{C_s^2} \qquad (10)$$

Table (6) Cs, D and FWHM of L_1, L_2, L_3, Bipy, Phen, (1), (2) and (3) compounds estimated from XRD pattern:

Compounds	2θ (º)	d (nm)	(FWHM)	C_s, (nm)	D, (nm^{-2})
L_1	18.07	0.494	0.3936	20.43	2.39×10^{-3}
L_2	6.96	1.275	0.0984	80.87	1.5×10^{-4}
L_3	17.99	4.950	0.1771	45.41	4.84×10^{-4}
Bipy	16.99	0.525	0.1181	68.01	2.16×10^{-3}
Phen	19.87	4.470	0.2170	38.93	7.24×10^{-4}
(1)	8.23	1.079	0.1968	40.46	6.11×10^{-4}
(2)	7.72	1.150	0.1771	44.95	4.9×10^{-4}
(3)	27.66	3.240	0.2168	37.78	7.00×10^{-4}

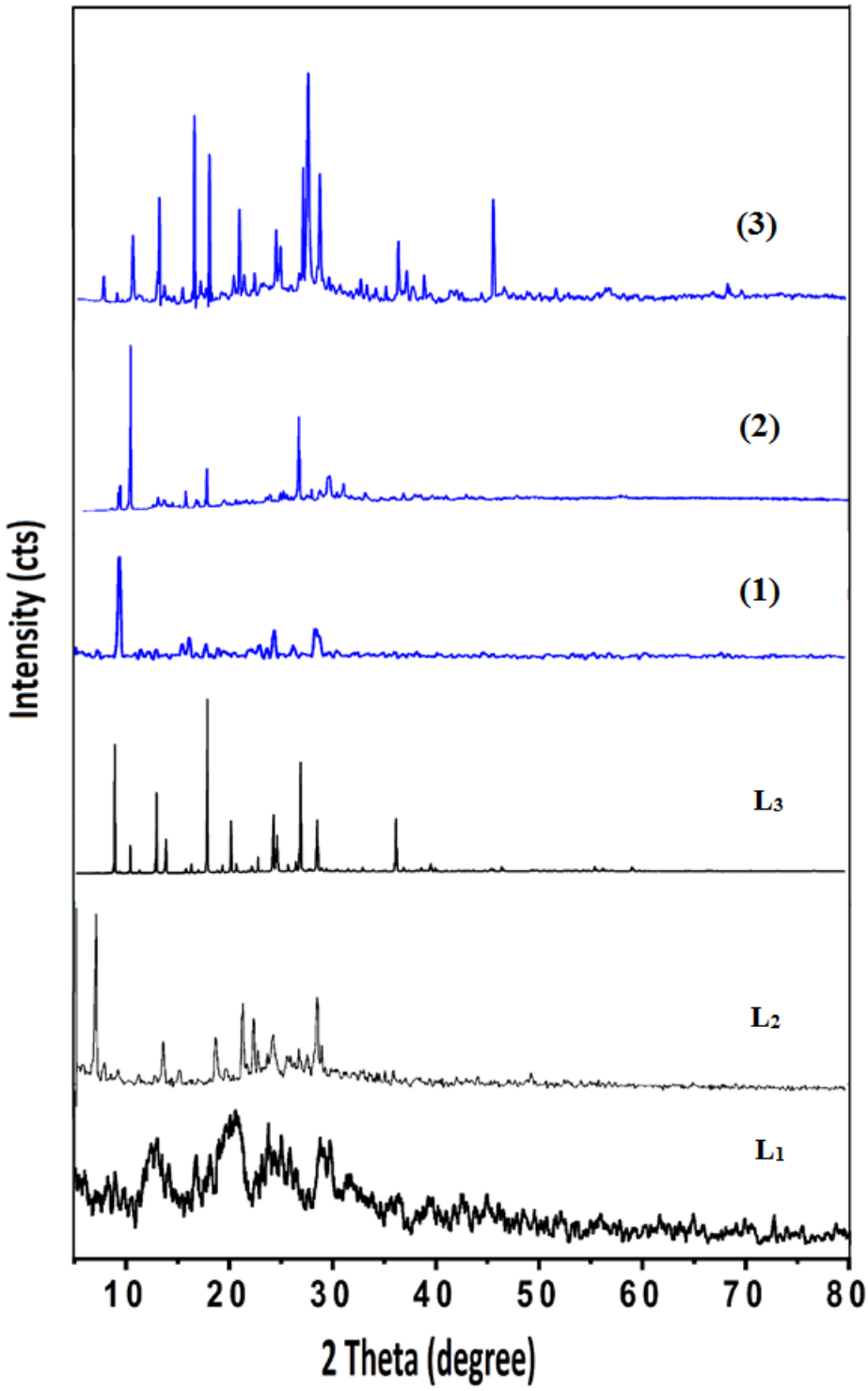

Figure 5 XRD spectra of L_1, L_2, L_3, (1), (2) and (3) compounds

3.5. Biological activity: The mixed ligand and their Complexes were examined for Gram-positive bacteria (*S. aureus*, *B. subtilisas*) and Gram-negative (*E. coli*, *P. aeruginosa*) bacteria for their antibacterial activities and two fungal species *(C. albicans* and *A. flavus)* for antifungal activities utilizing the disc diffusion sensitivity testing method **(Beecher and Wong, 1994)**. The results listed in Table 7 and found in Figure 6. The complexes were obtained to possess exceptional bactericidal abilities. A comparison of the biological activity of the Cu(II)

complexes with mixed ligand shows that complex **(1)**, **(2)** and **(3)** are not significant against all tested bacteria and fungi.

Table (7) The inhabitation diameter zone values (mm) for L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes:

Compounds		Bacteria				Fungi	
		S. aureus	*B. subtilis*	*E. coli*	*P. aeuroginosa*	*C. albicans*	*A. flavus*
L_1		9±0.44	10±0.40	5±0.35	9±0.11	10±0.14	11±0.15
L_2		9±0.66	13±0.01	7±0.11	11±0.33	6±0.11	7±0.01
L_3		9±0.22	13±0.05	8±0.01	10±0.33	12±0.14	14±0.16
Bipy		NA	4±0.90	5±0.33	7±0.02	NA	4±0.05
Phen		7^{NS}±0.04	9^{NS}±0.22	NA	4^{NS}±0.09	10^{+1}±0.33	12^{NS}±0.30
(1)		3^{NS}±0.09	4^{NS}±0.11	NA	NA	7^{NS}±0.07	6^{NS}±0.09
(2)		NA	5^{NS}±0.88	NA	4^{NS}±0.11	3^{NS}±0.11	NA
(3)		5^{NS}±0.33	8^{NS}±0.22	6^{NS}±0.22	9^{NS}±0.33	NA	7^{NS}±0.11
standard	Ampicillin	24±0.60	23±0.12	25±0.19	23±0.07	NA	NA
	Colitrimazole	NA	NA	NA	NA	27	25±0.14

ND: Non-detectable .i.e., the inhibition zones exceeds the plate diameter. Statistical significance P^{NS} P not significant, P >0.05; P^{+1} P significant, P<0.05; P^{+2} P highly significant, P<0.01; P^{+3} P very highly significant, P<0.001; student's *t*-test (Paired)

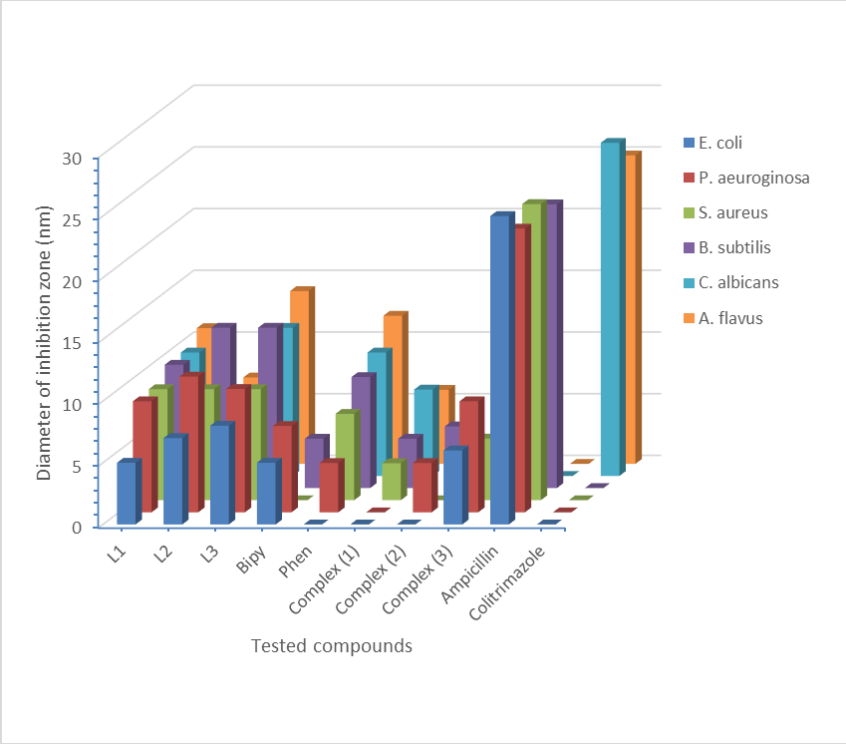

Figure 6 Statistical representation for biological activity for L_1, L_2, L_3, Phen, Bipy and their Cu(II) complexes

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