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Synthesis, Anticancer And Catalytic Activities Of Novel Mono Nuclear Cu^{2+}, Co^{2+}, And Zn^{2+} Complexes Involving Benzotriazol, Ethane- 1, 2- Diamine And 4,4'- Diaminocyclohexylmethane Ligands

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Keywords:

Coordination complexes; Crystal structures; Cytotoxic effects; Catalytic activities

1. Abstract

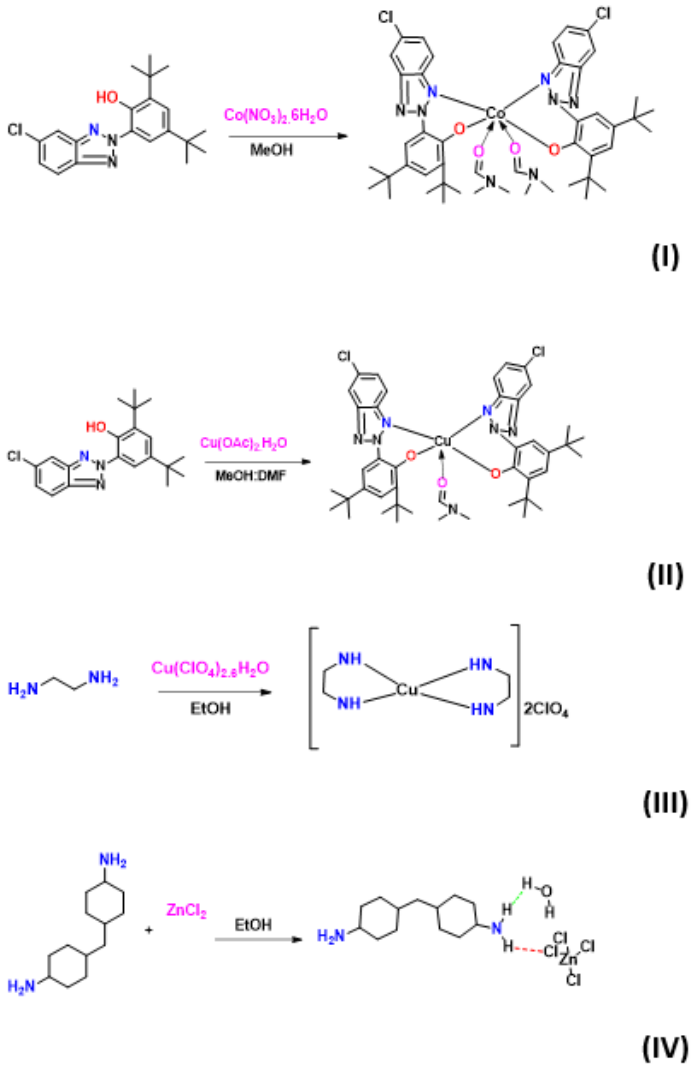
In this study, serval eco-friendly novel complexes were synthesized and characterized having the general formula of $[CoC_{46}H_{60}Cl_2N_8O_4]$ **(I)**, $[CuC_{43}H_{53}Cl_2N_7O_3]$ **(II)**, $[CuC_4H_{16}Cl_2N_4O_8]$ **(III)** and $[Cl_4Zn, C_{13}H_{28}N_2, H_2O]$ **(IV)** using benzotriazol, Ethane-1,2-Diamine, and 4,4'-Diaminocyclohexylmethane as ligands through one-pot method using anhydrous methanol or ethanol with different metal salt (2:1 eqv) metal to ligand stoichiometry. The crystal structures of these complexes were determined by X-ray diffraction and further characterized by elemental analysis, ESI-MS, IR, NMR and UV–Vis. Single-crystal XRD studies shows that the structural diversities are mainly affected and controlled by the types of central metal ions. Single-crystal XRD studies also shows that the complexes are coordinated with the ligands through N-metal and O-metal bonds, which revealed their mononuclear geometries. The anticancer activity of these complexes showed cytotoxic effects against human tumour cell Lines A549. Among them the complex **(II)** showed the best activity with IC_{50} values 19.92. The synthesized complexes were also applied for use as organic reaction catalysis and good results were obtained.

2. Introduction

Coordination complexes have many medicinal, industrial and other pharmacological applications, such as anti-cholesterol, anti-HIV, antibacterial, antifungal, analgesic, antitubercular, and anticancer activities. These references [1-10] provide their synthetic history. Soriano-García et al. (2007) synthesized 3*β*-(*p*-iodobenzoyloxy)-16*α*,17*α*-epoxypregn-4-En-6,20-dione and used it in the treatment of androgen-dependent diseases [11]. In 2020, Hasija et al. synthesized, characterized and reported on the scope of furan and naptho-furan consisting of molecules in electronic devices and their pharmacological and biological activities [12]. Salama, Ahmed, and Hassan (2017) synthesized and characterized Co^{2+} complexes of amino acid Schiff bases from salicylaldehyde and three amino acids in basic medium and studied their biological activities [13]. Iron-containing complexes are useful in agriculture and other biological applications. Arouri et al. (2021) synthesized the $FeCl_4(C_5N_2H_6)(C_5N_2H_5)$ complex and characterized it by X-ray, IR, UV methods and applied it for various uses [14]. Iyelabola, Akinkunmi, and Akinade (2020) synthesized and characterized mixed ligand complexes of Co^{+2}, Ni^{+2} and Cu^{+2} with 1,10-phenantroline and (±)-2-amino-3-(4-hydroxyphenyl)propionic acid as ligands and reported their biological activities [15]. Moriguchi, Kawata, and Jalli (2021) synthesized a new hydrogen-bonded cobalt(II) complex and used the title complex for therapeutic applications [16]. Nenwa et al. (2014) isolated an aqueous solution at room temperature and obtained a novel trinuclear heterothallic complex of Cr^{+2} [17]. Fomuta et al. 2017 synthesized and characterized a new Ag^{+2} complex [18]. Similarly, Moriguchi, Kawata, and Jalli 2021 synthesized four new europium complexes and reported photoelectronic property applications in light-emitting devices [16]. Zinc is essential to all forms of life [19]; although Cu-N complexes

are also well known for catalysing organic reactions, our research team successfully synthesized and characterized Cu^{+2}, Zn^{+2} and Co^{+2} complexes. Additionally, our synthesizing method is novel due to its fruitfulness, low toxicity compared to other synthetic methods, lack of fume production, low cost and environmental friendliness. Considering these significant factors, our product will be beneficial for anticancer activities as well as other medicinal applications and industrial applications. Although our product is air-stable, it could potentially be used for medicinal uses or other human development applications.

In this paper, we first describe the several novel complexes, $[CoC_{46}H_{60}Cl_2N_8O_4]$ **(I)**, $[CuC_{43}H_{53}Cl_2N_7O_3]$ **(II)**, $[CuC_4H_{16}Cl_2N_4O_8]$ **(III)** and $[Cl_4Zn, C_{13}H_{28}N_2, H_2O]$ **(IV)**, prepared with the one-pot method shown in **Scheme 1** and present their crystal structures obtained by single-crystal X-ray diffraction and characterization by various spectroscopic techniques. Additionally, our complexes have shown good cytotoxicity to lung cancer cells but negligible toxicity towards normal cells. The synthesized complexes were also applied for the catalysis of some important organic reactions and obtained good results.



Scheme 1: The synthetic route to complexes **(I)-(IV)**

3. Experimental

3.1. Materials and Methods

2,4-Di-tert-butyl-6-(5-chlorobenzotriazol-2-yl) phenol, ethane-1,2-diamine $Co(NO_3)_2.6H_2O$, $Cu(ClO_4)_2.6H_2O$ and $ZnCl_2$ were purchased from Acros. ^{1}HNMR spectra were obtained using a Bruker AM-300 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded using Bruker AM-500 and Bruker AM-600 spectrometers. Chemical shifts are reported in ppm (δ) with the solvent relative to tetramethylsilane (TMS), which was employed as the internal standard (residual CHCl3, δH 7.26 ppm; $CDCl_3$, *c* 77 ppm). The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet. Infrared spectra were recorded on a Mattson Galaxy Series FTIR 3000 spectrometer; the peaks are reported in cm^{-1}. Elemental analyses were performed

on an Elemental Analyser AE-3000. The crystal structures were determined by a Gemini S Ultra diffractometer.

3.2. Cytotoxicity Assay

The human tumour cell line against A549 (lung cancer) was used in the cytotoxic assay. These cell lines were obtained from ATCC (Manassas, VA, USA). Cells were cultured in RMPI-1640 or DMEM (Biological Industries, Kibbutz Beit Haemek, and Israel) supplemented with 10% foetal bovine serum (Biological Industries) at 37 °C in a humidified atmosphere with 5% CO2. The cytotoxicity assay was evaluated by using the MTS (Promega, Madison, WI, USA) assay. The cytotoxicity assay was evaluated by using the 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)- 2-(4-sulfophenyl)-2H-tetrazolium, inner salt (MTS) (Promega, Madison, WI, USA) assay. Briefly, cells were seeded into each well of a 96-well cell culture plate. After 12 h of incubation at 37 °C, a test compound (100 μM) was added. After incubation for 48 h, the cells were subjected to the MTS assay. Compounds with a growth inhibition rate of 50% were further evaluated at concentrations of 0.064, 0.32, 1.6, 8, 40 and 100 μM in triplicate with cisplatin and paclitaxel (Sigma, St. Louis, MO, USA) as positive controls.

3.3. General Experimental Details

All reactions were performed in flame-dried glassware under normal atmospheric pressure. Reagents were obtained from commercial sources. Nuclear magnetic resonance (NMR) spectra were acquired on a 500 MHz Bruker Advance III spectrometer. Infrared spectra were recorded on a Mattson Galaxy Series FTIR 3000 spectrometer; peaks are reported in cm^{-1}. Elemental analysis was performed on a VARIO ELIII elemental analyser. The crystal structures were determined by using a Gemini S Ultra diffractometer. ^{1}H and ^{13}C NMR chemical shifts are reported in ppm and referenced to CDCl3, 7.26 ppm; for DMSO-d_6, 2.50 ppm. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Melting points were measured by using a Yanaco Micro Melting Point System MP-J3 and SANSYO Melting Point Apparatus SMP-500 and are uncorrected.

3.4. General Procedure for the Synthesis of Complexes (I)-(IV)

Ligand and metal salts (molar ratio of 2:1) were heated and refluxed for 48 h, then filtration was conducted immediately after the reaction, and the filtrate was retained for slow volatilization. The metal-ligand complexes were successfully synthesized by reacting 2,4-di-tert-butyl-6-(5-chlorobenzotriazol-2-yl) phenol, ethane-1,2-diamine and 4,4'-diaminocyclohexylmethane as ligands with $Cu(ClO4)_2.6H_2O$, $Co(NO_3)_2.6H_2O$ and $ZnCl_2$, respectively, and the cultivated crystals were analysed and characterized by X-ray diffraction, IR, ^{1}HNMR, ^{12}CNMR, UV and E.A. The first key is to find the right ligands, and then the ligands and the corresponding metal salts were reacted. At the end of the reaction filtration was carried out and a suitable solvent for crystal precipitation was found. The selection between the available solvents such as anhydrous methanol, ethanol, chloroform, etc. is the most critical step.

3.4.1. Synthesis of Complex (I)

$Co(NO_3)_2.6H_2O$ (0.290 g, 0.001 mmol) dissolved in methanol (10 ml) was added dropwise to a hot solution of the ligand (0.7200 g, 0.0020 mmol) in methanol (30 ml). The mixture was refluxed with heat for 24 hr. After hot filtration, the filtrate was retained for natural evaporation at room temperature. After two days, the product was dissolved in methanol, and a small amount of DMF and the filtrate held for natural evaporation. After three days, bright red crystals appeared in the solution. These were suitable for X-ray single-crystal analysis resulting in a 85% yield, m.p. 118-120 °C, IR peaks at (KBr; ν, cm^{-1}) 3397, 2955, 1651, 1559, 1478, 1437, 1387, 1360, 1248, 1202, 1003, 1048, 937, 845, 834, 805, 752, 708, 670, 638, and 587, ^{1}H NMR results of (600 MHz, cdcl3) δ 8.02–7.99 (s, 1H), 3.54–3.51 (s, 2H), 3.49–3.46 (s, 3H), 3.44–3.41 (s, 4H), 3.36–3.33 (s, 2H), 2.99–2.96 (s, 2H), 2.94–2.91 (s, 4H), 2.90–2.87 (s, 5H), 2.85–2.82 (s, 5H), 2.82–2.79 (s, 5H), 2.75–2.72 (s, 3H), 2.63–2.60 (s, 1H), and 1.31–1.28 (s, 1H).

3.4.2 Synthesis of Complex (II)

Complex **(II)** was synthesized following the general procedure using metal salt $Cu(OAc)_2.H_2O$ (0.180 g, 0.001 mmol) dissolved in methanol (0.7200 g, 0.0020 mmol), which was added dropwise into a hot solution of ligand dissolved in methanol and DMF (3:1) mL. The solution was reflux with heat for two days, and the filtrate was retained for slow evaporation. After three days, bright blue crystals appeared in the solution. These were suitable for X-ray single-crystal analysis resulting in 80% yield, m.p. 278-280 °C and IR peaks at (KBr; ν, cm–1)2950, 2865, 1663, 1568, 1480, 1443, 1388, 1238, 1050, 916, 801, 738, 715,687, 671, 580, and 544.

3.4.3 Synthesis of Complex (III)

Similarly, complex **(III)** was also synthesized following the general procedure using ethanediamine (0.710 g, 16.10 mmol) as a ligand and $Cu(ClO_4)_2.6H_2O$ (2.964 g, 8.00 mmol) as the metal salt (2:1). The reaction mixture was refluxed with heat for two days, filtered while hot and retained for natural evaporation. After one day, blue crystals that appeared at the bottom of the beaker that were suitable for X-ray single-crystal analysis resulting in 80.2% yield, m.p. 280–285 °C. IR peaks at (KBr; ν, cm–1): 3337, 3281, 2988, 1590, 1467, 1321, 1280, 1108, 1066, 1021, 919, 884, 701, and 620. The calculated compositions in % for $[C_4H_{16}Cl_2CuN_4O_8]$ are: C, 12.56; H, 4.18; and N, 14.63 while the analysed compositions in % were: C, 12.98; H, 4.332; and N, 15.05.

3.4.4 Synthesis of Complex (IV)

For complex **(IV)**, using the general procedure, $ZnCl_2$ (1.14 g, 0.0052 mmol) metal salt was added dropwise to a hot solution of ligand (1.10 g, 0.00522 mmol) in methanol (30 ml). After hot filtration, the filtrate was retained for natural evaporation at room temperature. After two days, white crystals appeared in the solu-

tion. These were suitable for X-ray single-crystal analysis resulting in 90% yield, m.p. 320 °C. IR peaks at (KBr; ν, cm–1): 3366, 3124, 2925, 2860, 1597, 1574, 1387, 1503, 1485, 1452, 1386, 1248, 1200, 1054, 1045, 1122, 1021, 999, 971, 932, 897, 669, 657, 603, and 570. The ^{1}H NMR results were (600 MHz, cdcl$_3$) δ 12.56–12.52 (s, 23H), 9.14–9.09 (m, 3H), 7.95–7.92 (s, 1H), and 6.45–6.33 (m, 1H).

3.4.5. X-ray Structure

X-ray diffraction data for complexes **(I)-(IV)** were collected at room temperature using graphite-monochromatic Mo Kα radiation (λ= 0.71073 Å) on an Oxford Diffraction GeminiS diffractometer. Structure solutions and refinements for complexes 1-2 were carried out with the programs SHELXT [20] and SHELXL-2018/3 [21], respectively. MERCURY [22] was employed for molecular graphics and OLEX2 [23]. Nonhydrogen atoms in **(I)-(IV)** were refined anisotropically, while hydrogen atoms were treated by constrained isotropic refinement. Crystal data and refinement parameters for complexes **(I)-(IV)** are summarized in **Table 1**. The selected bond lengths and bond angles are shown in **Table S1**, and hydrogen bonds of complexes I-IV are listed in **Table 2**.

Table 1: Cell parameters and measurements of the crystallographic data of complexes (**I)-(IV)**

Complex	I	II	III	IV
Empirical formula	$C_{46}H_{60}Cl_2CoN_8O_4$	$C_{43}H_{53}Cl_2CuN_7O_3$	$C_4H_{16}Cl_2CuN_4O_8$	$Cl_4Zn,C_{13}H_{28}N_2,H_2O$
Formula mass	918.85	850.36	382.65	437.56
Temp. (K)	293(2)	98(2)	296(2)	293(2)
Wavelength (Å)	1.34139	1.34139	0.71073	1.54184
Crystal system	Monoclinic	Triclinic c	Triclinic	monoclinic
Space group	P 1 21/c 1	P-1	P -1	P 1 21/c 1
a (Å)	14.6703(6)	10.9421(16)	5.7113(18)	7.57262(12)
b Å()	18.5175(8)	13.777(2)	7.804(2)	10.62573(18)
c (Å)	18.5323(8)	14.999(2)	7.963(3)	25.0728(5)
β (°)	79.154(5)	99.918(5)°	79.154(5)	96.2309(16)
Volume (Å$^{3)}$	4846.1(4)	2129.2(6)	332.31(18)	2005.55(6)
Z	4	2	1	4
D_{calcd} (g/cm^3)	1.259	1.326	1.912	0.335
μ (mm^{-1})	2.868	3.778	2.086	1.18
F (000)	1940	894	195	912
θ ρανγε (°)	2.722-57.525.	2.707-60.698.	2.62-26.467	7.094-146.048
Total reflections	59170	47412	2393	7805
Unique reflections	9743	9750	1345	3893
R_1, wR_2 [$I > 2s$(I)]	0.0429, 0.1217	0.0488, 0.1346	0.0272, 0.0831	0.0333, 0.0884
R_1, wR_2 [all data]	0.0478, 0.1261	0.0585, 0.1397	0.0283,0.0840	0.0347, 0.0897
Residuals (e.Å^3)	0.504, -0.830	1.296, -0.554	0.295, -0.402	

Table 2. Hydrogen bond lengths (Å) and bond angles (°) for complexes **(I)-(IV)**

D–H···A (complex I)	**d(D–H)**	**d(H···A)**	**d(D···A)**	∠**D**HA
C(9)-H(9C)...O(1)	0.96	2.42	3.033(3)	121.8
C(10)-H(10A)...O(1)	0.96	2.37	2.998(3)	122.7
C(17)-H(17)...O(2)	0.93	2.46	3.102(2)	126.1
C(32)-H(32C)...O(2)	0.96	2.33	2.989(3)	125.2
C(33)-H(33A)...O(2)	0.96	2.27	2.928(3)	125.2
C(37)-H(37)...O(1)	0.93	2.38	3.117(2)	135.6
D–H···A (complex III)	**d(D–H)**	**d(H···A)**	**d(D···A)**	∠**D**HA
N1 H1C O1	0.89	2.34	3.144(4)	150.9
N2 H2C O2	0.89	2.36	3.179(3)	153.3
D–H···A (complex IV)	**d(D–H)**	**d(H···A)**	**d(D···A)**	∠**D**HA
N1 H1A Cl4	0.89	2.47	3.336(2)	165.7
N1 H1B O1	0.89	1.93	2.798(3)	163.9
N1 H1C Cl2	0.89	2.28	3.167(2)	171.2
N2 H2A Cl1	0.89	2.59	3.334(2)	141.6
N2 H2B Cl3	0.89	2.44	3.324(2)	173.3
O1 H1D Cl1	0.85	2.68	3.297(3)	130

4. Results and Discussion

4.1. Synthesis Method

Complexes **(I)-(IV)** were synthesized using the one-pot synthetic method. The synthetic route can be seen in **Scheme 1**.

(1): The syntheses of complexes **(I)-(IV)** were carried out under anhydrous methanol/ethanol using 4-di-tert-butyl-6-(5-chlorobenzotriazol-2-yl) phenol, ethane-1,2-diamine, and 2,4'-diaminocyclohexylmethane as ligands with different metal salts, i.e., $Co(NO_3)_2.6H_2O$ and $Cu(OAc)_2$. H_2O, $Cu(ClO_4)_2.6H_2O$ and $ZnCl_2$, respectively (2:1 eq). The mixtures were refluxed for 48 h. After hot filtration, crystals were obtained when the solution was evaporated slowly in the air. The crystals were confirmed and characterized by different spectroscopic techniques, such as UV, IR, and E.

A, ES-MSI as well as XRD.

4.2. Crystal Structure Analysis

(1): The crystal size of complex **(I)** is 0.15 x 0.1 x 0.1 mm^3. They have reddish colour and , belong to the monoclinic crystal system. According to the X-ray data of four round single crystals, the molecular weight of this crystal is 918.85, and the space group is P 1 21/c 1. The cell parameters are a = 14.6703(6) Å, b = 18.5175(8) Å, c = 18.5323(8) Å and α= 90°, β= 105.7200(10)°, γ= 90°, V= 4846.1(4) $Å^3$, Z= 4, D_{calc}= 1.259 Mg/m^3, and F (000) =1940. The bond lengths and angles for complex II are [(Co1)-(N1) 2.1460(13) Å], [(Co1)-(N4) 2.1816(14) Å], [(Co1)-(O1) 1.9730(12) Å], [(Co1)-(O2) 1.9642(12) Å], [(Co1)-(O3) 2.1888(14) Å], and [(Co1)-(O4) 2.1792(13) Å].

(2): Complex **(II)** was crystallized under certain experimental conditions, i.e., *P-1* shown in **Table 1**. For mono-nuclear metal complex (I), there is one metal ion and two ligands present as well as a DMF solvent molecule in the crystal structure.

The bluish crystals of complex (II) are composed of the central Cu ion and they adopt square-planar coordination by two ligands and one DMF solvent molecule. The five bond lengths are $d_{Cu1\text{-}O1}$ = 1.9055(15) Å, $d_{Cu1\text{-}O2}$ = 1.9115(15) Å, $d_{Cu1\text{-}N1}$ = 2.0446(18) Å, $d_{Cu1\text{-}N4}$ = 2.0686(18) Å and $d_{Cu1\text{-}O3}$= 2.1954(19). The angles around the Cu centre are [O(1)-Cu(1)-O(2) 178.96(6)], [O(1)-Cu(1)-N(1) 88.16(7)], [O(2)-Cu(1)-N(1) 91.05(7)], [O(1)-Cu(1)-N(4) 92.94(7)], [O(2)-Cu(1)-N(4) 88.10(7)], [N(1)-Cu(1)-N(4) 130.45(7)], [O(1)-Cu(1)-O(3) 90.64(7)], [O(2)-Cu(1)-O(3) 89.19(7)], [N(1)-Cu(1)-O(3) 122.01(8)] and [N(4)-Cu(1)-O(3) 107.51(8)].

The crystal size of the complex is 0.130 x 0.100 x 0.080 mm^3, belonging to the monoclinic crystal system. According to the X-ray data of four round single crystals, the molecular weight of this crystal is 850.36, and the space group is P-1. The cell parameters are a = 104.587(6)° Å, b = 13.777(2) Å, c = 14.999(2) Å, α= 104.587(6)°, β = 99.918(5)°, and γ= 96.032(5)°. V = 2129.2(6) Å3, D = 1.326 Mg/m3 and Z = 2. The bond lengths and angles for complex (I) are: [(Cu1)-(O1) 1.9055(15)Å], [(Cu1)-(O2) 1.9115(15) Å], [(Cu1)-(O3) 2.1954(19)Å], [(Cu1)-(N1) 2.0446(18)Å] and [(Cu)-(N4)] 2.0686(18) Å] and [O(1)-Cu(1)-O(2)] 178.96(6), [O(1)-Cu(1)-N(1)] 88.16(7), [O(2)-Cu(1)-N(1)] 91.05(7), [O(1)-Cu(1)-N(4)] 92.94(7), [O(2)-Cu(1)-N(4)] 88.10(7), [N(1)-Cu(1)-N(4)] 130.45(7), [O(1)-Cu(1)-O(3)] 90.64(7), [O(2)-Cu(1)-O(3)] 89.19(7), [N(1)-Cu(1)-O(3)] 122.01(8) and [N(4)-Cu(1)-O(3)] 107.51(8). Selected bond lengths (Å) and angles (°) are shown in **Table S2**. Hydrogen bonds for the complexes [Å and °] are shown in **(Table 2)**.

(3): The crystals of complex **(III)** have a blue colour. According to the X-ray data of four round single crystals, the molecular weight of this crystal is 382.65, the size is 0.12 x 0.1 x 0.1 mm^3, the crystal system is triclinic, and the space group is P -1. The cell parameters are: a = 5.7113(18) Å, b= 7.804(2) Å c = 7.963(3) Å and α= 75.313(4) °. β= 79.154(5)°.and γ = 77.952(4). V= 332.31(18) $Å^3$, Z= 1, D_{calc}=1.912 Mg/m^3, and F (000) =195. All bond lengths and angles for complex **(III)** are [(Cu1)-(N1) 2.018(2) Å], [(Cu1)-(N1) 2.018(2) Å], [(Cu1)-(N2) 2.015(2) Å], and [(Cu1)-(N2) 2.015(2) Å].

(4): The crystal size of complex **(IV)** is 0.22 x 0.1 x 0.1 mm3, their colour is white, and they belong to the monoclinic crystal system. According to the X-ray data of four round single crystals, the molecular weight of this crystal is 437.56, and the space group is P 1 21/c 1. The cell parameters are: a = 7.57262(12) Å, b = 10.62573(18) Å, c = 25.0728(5) Å, α= 90°, β= 96.2309(16) °, γ= 90°, V= 2005.55(6) Å3, Z= 4, Dcalc= 0.3351.259 Mg/m3, and F (000) = 912. The bond lengths and angles for complex (IV) are [(Zn1)-(Cl2) 2.2739(6) Å], [(Zn1)-(Cl4) 2.2648(6) Å], [(Zn1)-(Cl3) 2.2563(6) Å], [(Zn1)-(Cl1) 2.2889(6) Å], [(Cl2)-(Zn1)-(Cl1) 110.38(3) Å], [(Cl4)-(Zn1)-(Cl2) 106.87(2) Å], [(Cl4)-(Zn1)–(Cl1) 111.52(3) Å], [(Cl3)-(Zn1)-(Cl2) 110.25(2) Å], [(Cl3)-(Zn1)-(Cl4) 110.69(3) Å], and[(Cl3)-(Zn1)-Cl1) 107.17(2) Å].

4.3. IR spectroscopy of complexes (I)-(IV)

The IR analyses show several peaks that can be found in all IR spectra (shown in **Fig. 1**). These include all C-H stretching vibrations between 3000 and 2800 cm^{-1}, C=C stretching vibrations at approximately 11600 cm^{-1}, and C-O vibrations at 1280/1090 cm^{-1} [24]. The 3100 to 3000 cm^{-1} peak of the aromatic C-H stretching vibration combines stronger absorption at 1600 cm^{-1},, which can be referred to as aromatic C-C double bonds, and aliphatic C-H stretching vibrations in the range between 3000 and 2800 cm^{-1}. The determination of aromatic structures has been supported by the presence of the spectral region between 1500-1630 cm^{-1}; the absorbance bands at 1300 cm^{-1} to 1400 cm^{-1} can be assigned to the bending vibrations of the CH_3 group, and broad absorption in the region between 1050 and 1150 cm−1 is dominated by C-O stretching vibrations [25]. Stretching vibration peaks appeared at 600-650 cm^{-1} and 500-600 cm^{-1} for metal-nitrogen and metal-oxygen bonds, respectively, and a peak appeared at 650-700 cm^{-1} for C-Cl.

4.4. UV-visible spectroscopy for complexes I-IV

The absorption spectra of the complexes and raw materials were recorded in methanol. The broad peaks at 230 nm, 250 nm, 311-344 nm and 359 nm are due to σ-σ* and n-σ*, π-π* and n-π* transitions [21,22,23,24]. The UV spectra of the complexes are presented in **Figure 2**.

The crystal structures of complexes **(I-IV)** are shown in **Figure 1.**

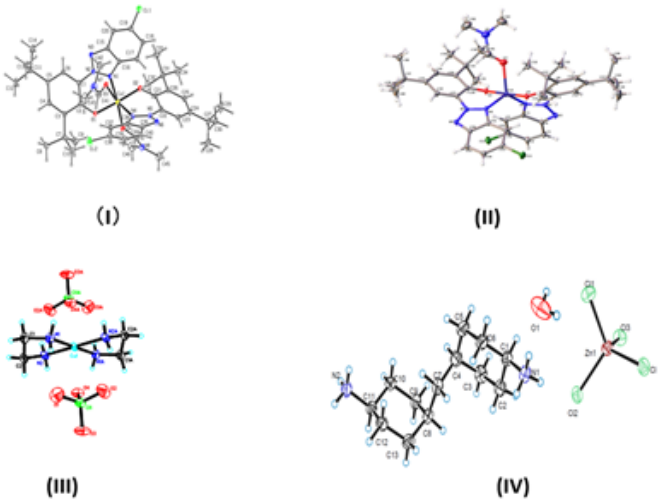
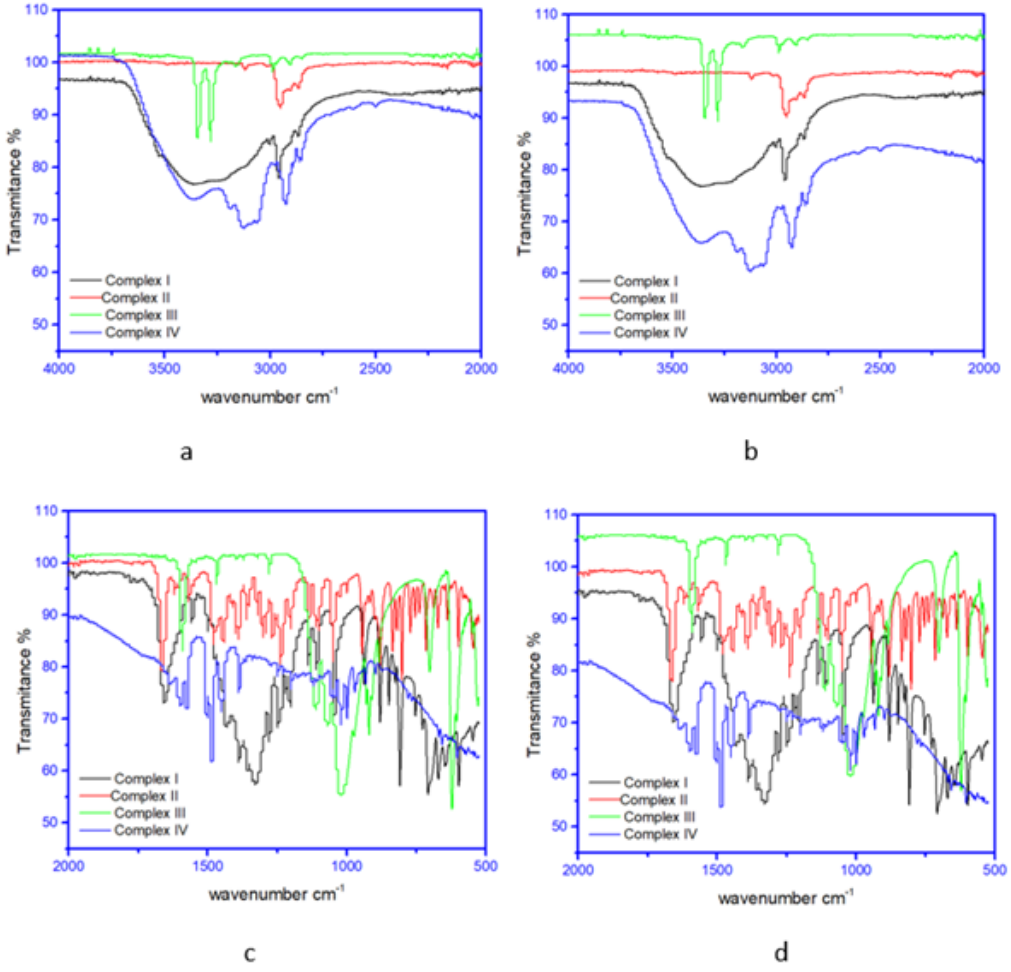


Figure 1: The ORTEP molecular structures of complexes **(I)** to **(IV)** shown as 30% thermal ellipsoid probabilities



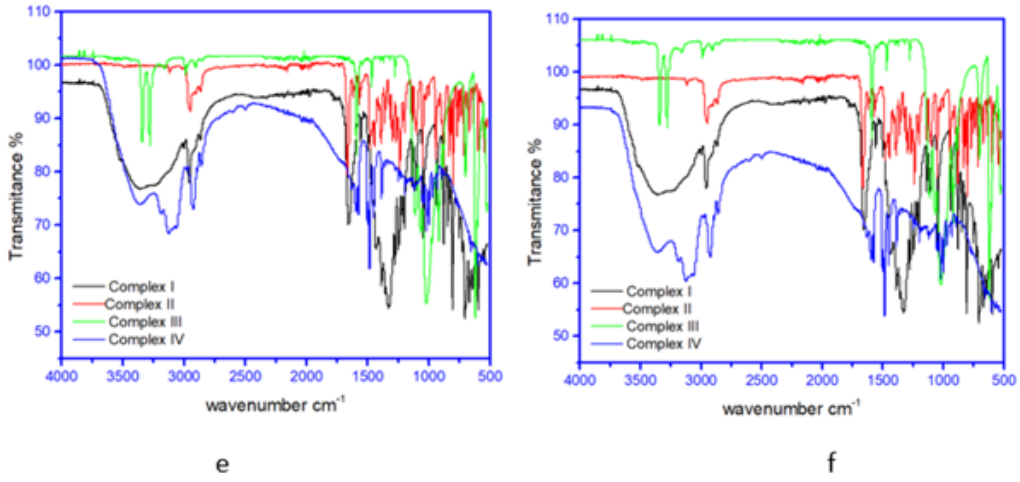


Figure 1. IR spectra of complexes **(I)-(IV)**

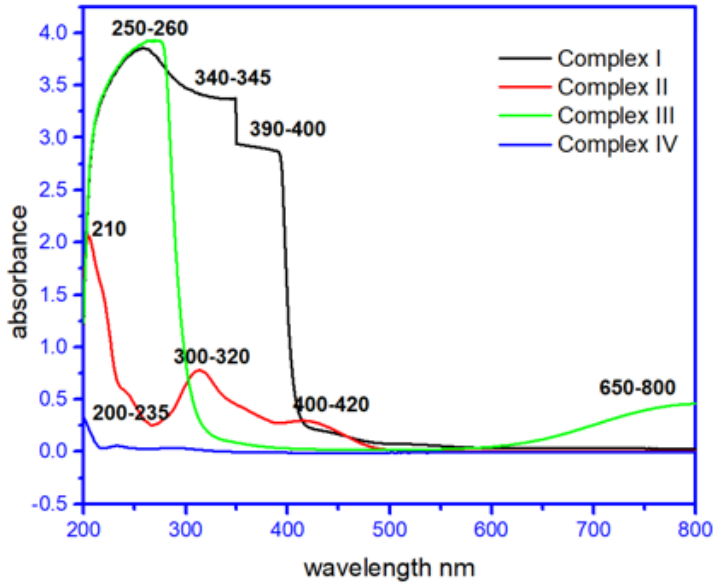


Figure 2. UV–visible spectra of complexes **(I)-(IV)**

4.5. Cytotoxicity Assay

The human tumour cell line SMMC-7721(Liver cancer) was used in the cytotoxic assays. These cell lines were obtained from ATCC (Manassas, VA, USA). Cells were cultured in RMPI-1640 or DMEM (Biological Industries, Kibbutz Beit Haemek, Israel) supplemented with 10% foetal bovine serum, (Biological Industries) at 37 °C in a humidified atmosphere with 5% CO_2. The cytotoxicity assays were evaluated by the MTS (Promega, Madison, WI, USA) assay method. The cytotoxicity assays were evaluated by the 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt (MTS) (Promega, Madison, WI, USA) assay method [12]. Briefly, cells were seeded into the wells of a 96-well cell culture plate. After 12 h of incubation at 37 °C, the 100 µM of the appropriate test compound was added to each well. After incubation for 48 h, the cells were subjected to the MTS assay. Compounds with a growth inhibition rate of 50%, or higher, were further evaluated at amounts of f 0.16, 0.8, 4.0, 20 and 100 µM in triplicate with cisplatin and paclitaxel (Sigma, St. Louis, MO, USA) as positive controls. The IC50 values of each compound were calculated with Reed and Muench's method [13]. The results are presented in Table 3.

By comparing the activity of complexes **(I)–(IV)**, complex (II) showed the best cytotoxic effects against the lung cancer cell Line A549, with an IC50 value of 19.92 µM. Cisplatin is also shown for the sake of comparison, as shown Table 3.

Table 3. Cytotoxicity of complexes **(I-IV)** against human tumour cell Lines A549, with cisplatin used as an experimental control.

	IC_{50} (mM)[a]
Complex	A549
I	>100
II	19.92
III	31.57±1.59
IV	N/A
cisplatin	24.37±0.13

[a]Cytotoxicity as IC_{50} values for each cell line, the concentration of complex that caused 50% reduction relative to untreated cells determined by the SRB assay. Cisplatin was used as the control.

4.6 Catalytic application

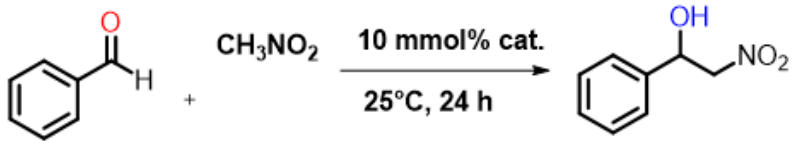
Catalysis of Henry reaction, shown in **scheme 2**, was achieved using 10 mmol% complexes **(I)** to **(IV)** without any additives. Using complexes **(I)** to **(IV)** (0.10 mmol), benzaldehyde (0.10 mL), and nitromethane (0.50 mL) were successively added together in 2 mL anhydrous methanol at room temperature for 24 h [30-38].

The catalytic activities of the novel complexes in the Henry reaction are presented in **Table 4**. This table shows that the conversion efficiency of these three of the complexes was more than 85%, and that they are good catalysts for the Henry reaction. The mechanism that can be proposed is that the complexes could greatly activate the C=O bond, and then there is a nucleophilic addition reaction of $CH_2NO_2^-$ onto the carbonyl group:

Table 4. Henry reaction of benzaldehyde catalysed by **(I)-(IV)***

Complex	Yield, %
1	>**99**
2	>**99**
3	**57**
4	>**99**

* Conv.% was determined by ^{1}HNMR; reactions were carried out with 0.1 mL PhCHO and 0.5 mL CH_3NO_2 in 2 ml anhydrous methanol using 0.10 mmol of catalyst at room temperature for 24 h.



Scheme 2. Henry reaction

5. Conclusions

In addition to describing their synthesis, and characterization this paper also presents the anticancer and catalytic activities of mononuclear Cu^{2+}, Co^{2+} and Zn^{2+} complexes involving 2,4-di-tert-butyl-6-(5-chlorobenzotriazol-2-yl) phenol and ethane-1,2-diamine ligands and 2,4'-diaminocyclohexylmethane ligands. The synthesized complexes were confirmed and characterized using techniques such as FTIR, NMR, UV–visible and E. A, as well as by single-crystal X-ray diffraction. Our synthesized complexes can be used in medicinal as well catalytic applications. Additionally, they showed cytotoxic activity against A549 cells. Among them, complex **(II)** exhibited the best bioactivity against A549 cells compared to other complexes, with an IC_{50} value of 19.92 μM. The results clearly show that the anticancer activity of these complexes depends on the type of metal ion and cell line, as well as the geometries of the corresponding compounds. These useful results provide motivation for the design and development of new therapeutic drug-like molecules. The synthesized complexes were tested in some catalytic reactions obtaining excellent results.

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