Faculty of Graduated Studies
Master Program in Applied Chemistry

Synthesis, Characterization, and Biological Activity of Novel Mixed Ligand Complexes of Zn(II) Naproxen with Nitrogen Based Ligands

تحضير وتشخيص ودراسة الفعالية الحيوية لمركبات تحتوي ايون الزنك الثنائي والنبروكسين وقواعد نيتروجينية

This Thesis was submitted in partial fulfillment of the requirements for the Degree of Master in Applied Chemistry at Faculty of Graduate Studies at Birzeit University, Ramallah, Palestine

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Ramallah, June, 2012

Hadeel Fares

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ABBREVIATIONS

Nap	naproxen
Na(nap)	sodium naproxen
M.P	melting point
1,10-phenan	1,10-phenanthroline
2,9-dmphen	2,9-dimethyl-1,10-phenanthroline
2,2-bipy	2,2-bipyridine
4,4-bipy	4,4-bipyridine
2-ampy	2-amino pyridine
4-pic	4-picoline
imid	imidazole
1,2-dmimid	1,2-dimethyl imidazole
quin	quinoline
$CDCl_3$	chloroform (d)
MeOH	methanol
DMSO	dimethyl sulfoxide
Me_4Si	tetramethyl silane
aliph	aliphatic
ar	aromatic
IR	Infrared
UV-Vis	Ultraviolet-Visible
NMR	Nuclear Magnetic Resonance
s	singlet
d	doublet
t	triplet
q	quartet
dd	doublet of doublet

bs	broad singlet
m	multiplet
MIC	minimum inhibition concentration
(G^+) bacteria	gram positive bacteria
(G^-) bacteria	gram negative bacteria
rt	room temperature

ABSTRACT

In this present work eleven novel Zn(II) complexes $[Zn_2(nap)_4]$ **(1)**, $[Zn(nap)_2$1,10-phen] **(2)** $[Zn(nap)_2$2,9-dmphen] **(3)**, $[Zn(nap)_2$2,2-bipy] **(4)**, $[Zn(nap)_2(2\text{-ampy})_2]$ **(5)**, $[Zn_2(nap)_4(4\text{-pic})_2]$ **(6)**, $[Zn(nap)_2$4,4-bipy$]_n$ **(7)**, $[Zn_2(nap)_4(quin)_2]$ **(8)**, $[Zn(nap)_2(imid)_2]$ **(9)**, $[Zn(nap)_2(1,2\text{-dmimid})_2]$ **(10)**, $[Zn(nap)_2(pyrazole)_2]$ **(11)** were synthesized and characterized by IR, UV-Vis, ^{1}H NMR, ^{13}C{^{1}H} NMR spectroscopy. X-ray crystallography for complex **3** was also determined. In order to assess the effect of the metal ions on the anti-bacterial activity, the ligands and their complexes **1-11** have been screened *in-vitro*, against Gram positive, (G^+) bacteria (*Staphylococcus aureus* and *Micrococcus luteus)* and Gram negative, (G^-) bacteria *(Klebsiella pneumoniae, Pseudomonas aeruginosa, Proteus mirabilis and Escherichia coli)* using the agar well diffusion method. All complexes exhibit anti-bacterial activity against the tested bacterial species except complex **8**. Due to the higher anti-bacterial activity of complexes **2, 3**, **5** they were chosen and tested with their parent nitrogen donor ligands to determine the effect of the complexation on the anti-bacterial activity. Complex **2** showed lower anti-bacterial activity against the tested bacterial species than the 1,10-phenanthroline ligand, so in this complex the anti-bacterial activity decreased due to complexation. Complex **3** showed higher anti-bacterial activity against G^- bacteria than its parent ligand, 2,9-dimethyl-1,10-phenanthroline, but this ligand showed higher anti-bacterial activity against G^+ than complex **3**. Complex **5** showed anti-bacterial activity only against G^+, and 2-amino pyridine ligand did not show anti-bacterial activity against the tested bacterial species.

ملخص

في هذا البحث، تم تحضير احد عشر مركبا مهما لايون الزينك ثنائي الشحنة:

$[Zn_2(nap)_4]$ **(1)**, $[Zn(nap)_2$1,10-phen] **(2)** $[Zn(nap)_2$2,9-dmphen] **(3)**, $[Zn(nap)_2$2,2-bipy] **(4)**, $[Zn(nap)_2(2\text{-ampy})_2]$ **(5)**, $[Zn_2(nap)_4(4\text{-pic})_2]$ **(6)**,$[Zn(nap)_2$4,4-bipy$]_n$ **(7)**, $[Zn_2(nap)_4(quin)_2]$ **(8)**, $[Zn(nap)_2(imid)_2]$ **(9)**, $[Zn(nap)_2(1,2\text{-dmimid})_2]$ **(10)**, $[Zn(nap)_2(pyrazole)_2]$ **(11)**.

وايضا تم تشخيص هذه المركبات من خلال استخدام الاجهزه التالية: جهاز مطياف الاشعة تحت الحمراء، جهاز طيف الرنين المغناطيسي، جهاز مطياف الاشعة الفوق البنفسجية و جهاز تحديد اشكال المركبات باستخدام الاشعة السينية لمعرفة الشكل البلوري للمركب المعقد **(3)**.

ومن اجل تقييم تاثير الايونات الفلزية على النشاط المضاد للبكتيريا، تم فحص القواعد النيتروجينية والمركبات المعقدة المرتبطه بها **1-11**، في المختبر ضد البكتيريا موجبة غرام (*Staphylococcus aureus* and *Micrococcus luteus*) وسالبة غرام *(Klebsiella Pneumonia,* *Proteus mirabilis, Escherichia coli* and *Pseudomonas aeruginosa*) باستخدام اسلوب الانتشار في الاجار. جميع المركبات المعقدة كان لها نشاط مضاد لبعض انواع البكتيريا ماعدا المركب **(8)**. ونتيجة لزيادة النشاط المضاد للبكتيريا للمركبات المعقدة **(2, 3, 5)** تم اختيارها مع القواعد النيتروجينية المرتبطة بها لتحديد التغير في تاثير هذه المركبات عند ارتباطها في مركبات معقدة على نشاط البكتيريا .

اظهر المركب المعقد **(2)** انخفاض الفعالية ضد جميع انواع البكتيريا بالمقارنة مع القاعدة النيتروجينية المرتبطة به (1,10-phenanthroline) وذلك نتيجة ارتباطه في مركب معقد. والمركب المعقد **(3)** اظهر ارتفاع الفعالية ضد البكتيريا سالبة غرام بالمقارنة مع القاعدة النيتروجينية المرتبطة به (2,9-dimethyl-1,10-phenanthroline) ، ولكن هذه القاعدة

النيتروجينية اظهرت ارتفاع الفعالية ضد البكتيريا موجبة غرام بالمقارنة مع المركب المعقد **(3)**.

اظهر المركب المعقد **(5)** نشاطا ضد البكتيريا موجبة غرام فقط، ولكن القاعدة النيتروجينية (2-amino pyridine) لم تظهر أي نشاط مضاد لجميع انواع البكتيريا.

1. INTRODUCTION

1.1 General Introduction

Metallic elements are essential components for many of the processes that are necessary for healthy human and animal life. A number of metallic elements, namely, sodium, potassium, calcium and magnesium, are required in bulk and are sometimes referred to as minerals. Other essential metallic elements, referred to as trace elements, are present in amounts that are less than 0.01% of the average human body mass. Examples of trace elements are: lithium, chromium, manganese, molybdenum, nickel, selenium, iodine, tin and zinc. Besides trace and mineral elements, the healthy human body normally contains small amounts of other elements, such as silicon, arsenic and boron which do not appear to be essential for maintaining health. Figure 1.1, the Periodic Table, shows how well biological systems utilize the lighter (more abundant) and available elements in almost all groups.[1]

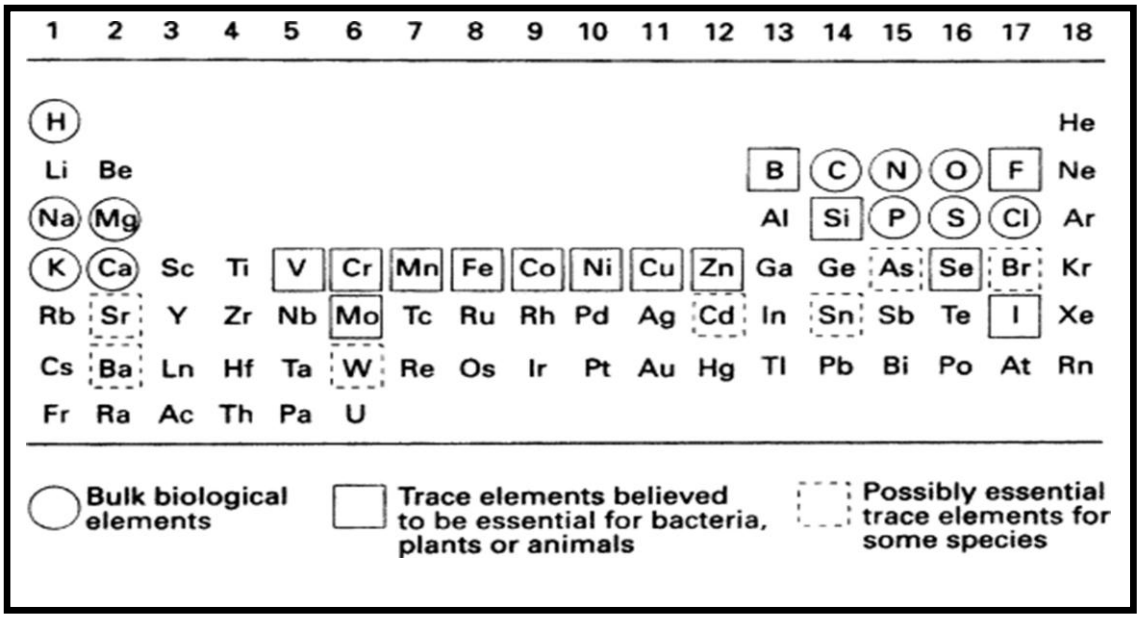


Figure 1.1. The Periodic Table indicating how well biological systems utilize the lighter (more abundant) and available elements in almost all groups.[2]

An element is considered an essential element when a deficient intake produces an impairment of function and when restoration of physiological levels of that element relieves the impaired function or prevents impairement.[3]

1.2 Metal in biology and medicine

Metal ions play important roles in many biological systems. Metal that are present in bulk have various biological roles. A part from its structural function in bone, calcium together with sodium and potassium, is involved in signal transduction through the nervous systems. Calcium is also important in triggering actions e.g; in muscle while magnesium is found in some phosphohydrolase and phosphotransferase enzymes. Sodium and calcium are important extracellular bulk metals while potassium and magnesium are major cellular metals.

Trace metals are involved in a wide variety of biochemical processes, including the transport and storage of dioxygen, the dissolution of carbon dioxide in blood, in oxidation–reduction reactions, in energy metabolism, the breakdown of proteins, the removal of harmful species such as superoxide, as catalyst in enzyme systems and many other chemical transformations. They can also have structural functions such as controlling the folding of proteins.[4,5]

In particular, metal ions are required for the activity of a large number of enzymes and proteins. Metal ions are well suited for these functions because of the following properties: (i) metal ions are positively charged and, hence, act as electrophiles. They can act as Lewis acids for binding and activating substrates. (ii) Many metals can exist in a number of different oxidation states differing by one or by several units. This allows these metals to participate in various types of oxidation–reduction processes. (iii) metal ions generally bind four or more ligands. By binding several

protein side chains, metals can act as multidentate cross linking agents.[6]

1.3 The chemistry of zinc

Zinc is element number 30 in the Periodic Table, it is a diamagnetic metal and mostly colorless. Its atomic weight of 65.37 is a consequence of its five stable isotopes mixture: Zn^{64}, Zn^{66}, Zn^{67}, Zn^{68} and Zn^{70}. It also has two radioisotopes, Zn^{65} and Zn^{69}.[7] Zinc has an outer shell of $4s^2 3d^{10}$ electron configuration and behaves as a very electropositive metal, losing its two *4s* electrons readily to form Zn(II) cations with filled d-orbital. Consequently, only the zinc(II) oxidation state is important, and redox reaction don't occur readily.[8] This allows for the formation of four covalent bonds by accepting four electron pairs and thus obeying the octet rule. Upon complexation the stereochemistry is mainly tetrahedral and the bonds may be described as being formed from sp^3 hybrid orbitals on the zinc ion.[9]

Why does zinc have a unique role in life processes rather than other transition metals?

Zinc has highly distinctive properties that make it more suitable than other elements for this purpose. These properties include the small size of the zinc ion that gives it a highly concentrated charge and strong electrostatic binding capacity. Its high affinity for electrons makes zinc a stronger Lewis acid. These properties are not unique to zinc only, as copper and nickel, also have strong electrostatic binding. However, unlike them, zinc does not show different valences and oxidation states, and consequently does not introduce the risk of free radical oxidative damage when used in biological compartment.[7]

1.3.1 Zinc in biology and medicine

Zinc is considered essential for many processes in living organisms. It is one of the most important trace elements in the body for its biological functions.[10] It is found throughout the human body in a variety of tissues, such as skin, bone, liver, muscles and brain. In fact, this element is the most abundant transition metal in the brain after iron.[11]

The average adult human contains 3 g of zinc and requires a daily intake of 15 to 20 mg, only half of which is absorbed, to maintain this level.[12] Low concentrations cause deficiency diseases[1] like growth retardation, testicular atrophy, skin lesions, poor appetite, loss of body hair,[12] and disorders of the central nervous system.[13] Too high concentrations are toxic[1] and also can lead to apoptosis and neuronal death.[14]

Zinc plays an important role in various biological systems; it is critical for numerous cell processes and is a major regulatory ion in the metabolism of cells.[13] Zinc is also required for the biological activity of such proteins as metallothioneins, which protect cells from oxidative damage and therefore prevent cell death.[15] In addition to physiological functions, zinc and its compounds have important roles in clinical medicine. Anti-bacterial, anti-viral activity[16] and the wound-healing effect of zinc containing ointments have been known for several centuries.[17] Zinc may also act as an anti-sickling agent and play an important role in the prevention of pain crisis used in sickle-cell disease.[18] Zinc also used in the treatment of Alzheimer disease, acrodermatitis, enteropathica, Wilsons disease, gastrointestinal disorders and other diseases.[17]

Zinc compounds like zinc sulfate, zinc oxide, zinc complexes with organic ligands such as zinc salicylate, zinc propionate and zinc acetate are also used in medicine as anti-bacterial, anti-viral, anti-inflammatory and anti-fungal agents.[13,16-19]

Zinc(II) pyrithione complex is used in shampoos as an anti-dandruff agent,[16] zinc acetate with erythromycin is used for acne therapy.[20] Finally, zinc picolinate and zinc aspartate are effective for the treatment of diseases caused by Herpes Simplex Virus.[21]

1.3.2 Zinc enzymes

Zinc is an essential component that is necessary for the occurrence of reactions that are required in the metabolic processes of living organisms.[22] It has been found to be an integral component of nearly 300 enzymes in different species of all phyla.[23] It is transported by proteins (macroglobulin, transferrin and albumin), it is stored in the protein thionein, and is also bound to histidines, carboxylate containing residues and cysteines.[22]

Zinc enzymes may be classified into: (i) DNA and RNA polymerases, (ii) alkaline phosphatases (AP), (iii) peptidases, (iv) carbonic anhydrases (CA), (v) alcohol dehydrogenases (ADH), (vi) beta-lactamase, (vii) phospholipase C and (viii) P1-nuclease (Figure 1.2).[24,25]

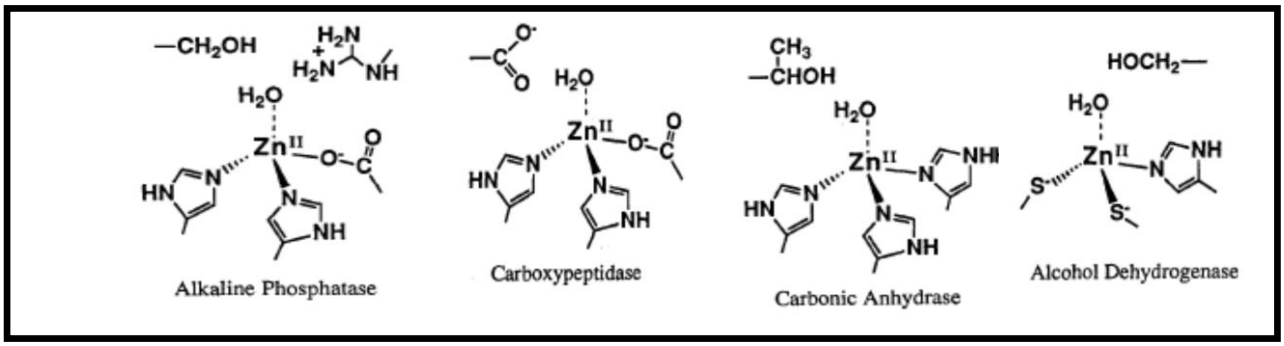


Figure 1.2. The structure of zinc enzymes.[24]

Zinc ions exist primarily in the form of complexes with proteins and nucleic acids and participate in all aspects of intermediary metabolism, transmission and regulation of the expression of genetic information, storage, synthesis and action of peptide hormones and structural maintenance of chromatin, biomembranes and extracellular matrices.[26]

The zinc ion can have three different roles in enzymes: catalytic, co-catalytic and structural. Catalytic role: the ion is located at the active center of an enzyme and

participates directly in the bond making or breaking step in the catalytic mechanism,[7] the removal of this ion from the enzyme active site can be carried out by chelating agents.[27] For example: in carbonic anhydrase the water coordinates to zinc, that binds to three neutral histidine nitrogens, and is used as catalyst with different types of hydration and hydrolysis reactions (Figure 1.3a).[22] In multi-metal enzymes, two or more zinc or other metal atoms operate in concert in a co-catalytic role. For example: alkaline phosphatase. In structural sites: the function of the zinc ion is to stabilize the tertiary structure and the quaternary structure of the metalloenzyme.[7] Also in this site the zinc ion is coordinated by four amino acids in a tetrahedral geometry, for example: aspartate transcarbamylase (Figure1.3b).[22]

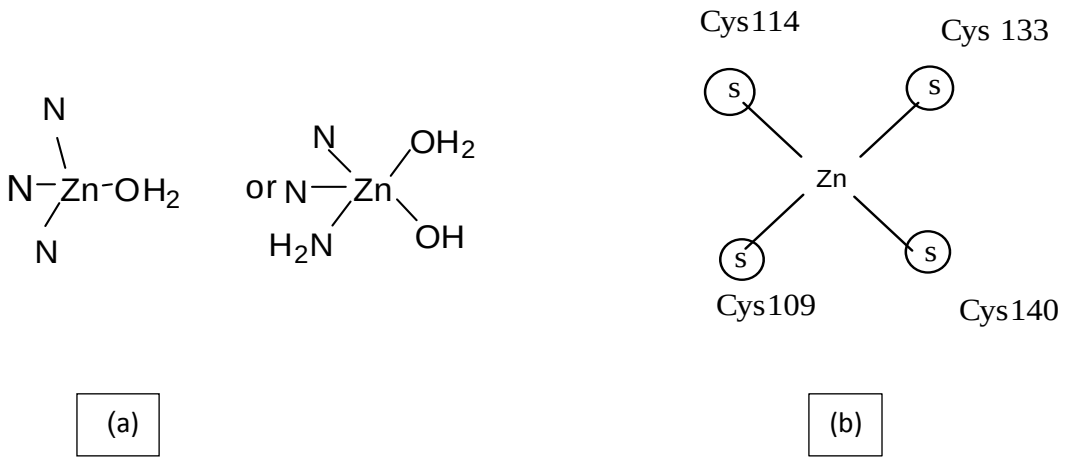


Figure 1.3. (a) Carbonic anhydrase as a catalytic zinc site, (b) Aspartate transcarbamylase as a structural zinc site.[22]

1.3.3 Anti-bacterial activity of zinc compounds

There are many developed anti-bacterial agents containing inorganic metal atoms or ions such as zinc, copper and silver. Compared to organic anti-bacterial agents, inorganic anti-bacterial agents possess many outstanding properties, such as long-lasting effects, broad spectrum anti-biosis and better heat resistance, that can be used in the manufacture of anti-bacterial materials and products.[28] Zinc ions possess some anti-bacterial effects, good thermal and color stability with low cost and little toxicity.[28] The growth of *Escherichia coli* is inhibited at high concentrations of zinc(II), however low concentrations of zinc(II) have a promoting action on the growth of *E-coli*.[29] Zinc also can inhibits the growth of *Escherichea coli, Streptococcus faecalis, Klebsiella preumoniae, Staphylococcus aureus* and some soil bacteria.[21] A large number of metal complexes exhibit anti-microbial activity. The activity of these complexes may be due to either the presence of a toxic metal ion or a biologically active ligand.[1] Many anti-bacterial drugs when chelated to the metal, show altered bioability and sometimes the chelated drug is more effective than the free ligand.[30] This is due to the chelation of a bulky ligand to a metal cation which reduces the polarity of the ion and increases the lipophilicity of the metal complex, which can result in increased damage to bacterial cell walls and the transfer of zinc into the cell.[31]

1.4 The chemistry of metal carboxylates

Metal carboxylates have been the subject of extensive research for a few decades. They are used as model compounds of metalloenzymes[32] or as anti-bacterial agents.[33] Metal carboxylate complexes have different structural and physical features and show

versatile practical applications such as in dyes, extractants, drugs, pesticides, catalysts, magnetism and host-guest chemistry.[34]

Within the carboxylate ion there is one delocalized negative charge, and each oxygen atom has two lone pairs disposed at 120° to its C-O bond in the plane of the carboxyl group. It is evident from a variety of crystal structures that a given carboxylate group may bind to several cations and, in some cases, the carboxyl group may share the metal cation between both its oxygen atoms. The two locations for a cation when attracted to a carboxylate group in the directions of lone pair electrons are designated *syn* and *anti*. In the *syn* conformation (Z-form) Zn and the non-coordinated carboxylate oxygen are on the same side of the C-O bond. On the other hand, in the *anti*-conformation (E-form) Zn and the non-coordinated carboxylate oxygen are on the opposite side of the C-O bond, which normally gives weaker bonds (Figure 1.4). Also some studies have shown that the *syn* conformation is more stable than the *anti*-conformation by 4.5 Kcal/mole, implying that the *syn* lone pairs are more basic than the *anti*-lone pairs, so carboxylates in the active sites of the enzymes generally employ the more basic *syn* lone pairs for metal chelation, rather than the less basic *anti* lone pairs.[35,36]

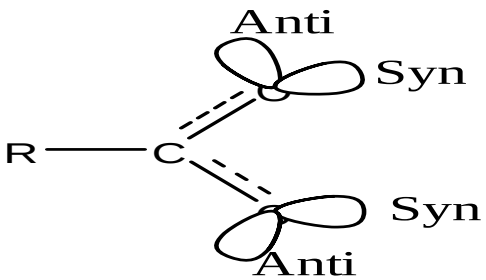


Figure 1.4. Syn and anti lone pairs in carboxyl and carboxylate groups.[35]

The binding mode of carboxyl group with metal atom is also represented by different types (purely ionic and different degree of covalent bonding as monodentate, bidentate bridging and chelating)[32,37] (Figure 1.5).

One technique to determine the binding mode of the carboxylate group is the infrared spectroscopy (IR).[31,35]

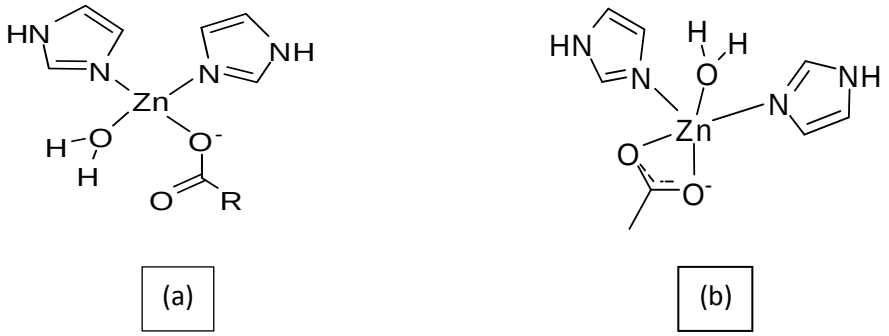


Figure 1.5. (a) Monodentate structure, (b) Bidentate structure.[36]

A metal ion interacts equally with the two oxygen atoms of the COO^- group in the bidentate form, whereas it interacts with only one of those oxygen atoms in the monodentate form. In the bridging mode, the carboxylate group bridges between two metal atoms.[38]

Deacon and Phillips[39] have examined the structures and vibrational frequencies observed for a number of acetate salts in the solid state and have found an empirical rule for the correlation between $\Delta\upsilon_{as\text{-}s}$ (frequency separation between the COO^- anti-symmetric and symmetric stretches): $\Delta = \upsilon_{as}(COO^-) - \upsilon_s(COO^-)$. This empirical rule is applied to assign the type of the carboxylate coordination in inorganic complexes and biomolecules.[38] Generally, the following order is proposed for divalent metal carboxylates.[33]

$$\Delta \text{ (chelating)} < \Delta \text{ (bridging)} < \Delta \text{ (ionic)} < \Delta \text{ (monodentate)}$$

Monodentate coordination mode removes the equivalences of the two oxygen atoms. If the carbon-oxygen bond orders are appreciably affected, this should increase υ_{as} (COO^-) and increase the separation (Δ) between the $\upsilon(COO^-)$ frequencies, since Δ_{as-s} value of the ionic carboxylate is around 164 cm^{-1}. A (ΔCOO^-) value less than ionic values indicates chelating or bridging modes, Both symmetrical chelating and bridging carboxylates maintain the equivalence of the two carbon-oxygen bonds found in the free ion, although in chelating systems the COO angle is usually smaller than that found in bridging systems.[39,40]

1.4.1 Zinc Carboxylates

The carboxylate group can bind to zinc with different coordination modes such as: bridging and chelating, as well as bi- and mono-dentacity. Zelenak et al.[17] studied the complexes of zinc with $RCOO^-$ (R = H-, CH_{3-}, $CH_3CH_2CH_2$-, $(CH_3)_2CH$-, XCH_2-, X=Cl, Br, I) and the interaction of these complexes with caffeine and nicotinamide. They showed that in the $Zn(CH_3COO)_2.2H_2O$ and $Zn(ICH_2COO)_2$ the carboxylate group is bidentately coordinated, but in $Zn(ICH_2COO)_2$ the splitting of both carboxylate stretches indicated the presence of *syn–anti* addition bridging. On the contrary, in the substituted analogues $Zn(ClCH_2COO)_2.2H_2O$ and Zn $(BrCH_2COO)_2.2H_2O$ the carboxylate groups are monodentately coordinated. Moreover, [Zn(salicylate)$_2$.$2H_2O$],[41] [Zn(salicylate)$_2$(urea)$_2$.$2H_2O$],

[Zn(5-chlorosalicylate)$_2$.$2H_2O$],[29] [Zn(formate)$_2$(phenazone)$_2$], [Zn(acetate)$_2$ (phenazone)$_2$], [Zn(butyrate)$_2$(phenazone)$_2$], [Zn(propionate)$_2$(phenazone)$_2$],[42] [Zn(propionate)$_2$.$2H_2O$], [Zn(acetate)$_2$theophylline],[19] [Zn(propionate)$_2$ (nicotinamide)$_2$],[10] and [Zn(benzoate)$_2$(caffeine)$_2$].[43] exhibit similar monodentate coordination mode. Zheng et al.[44] determined the structure of [Zn(4-hydroxy

benzoate)$_2$(benzimidazole)$_2$.0.25H_2O] in which the zinc(II) atom is coordinated by two 4-hydroxy benzoate anions and two benzimidazole molecules, resulting in a distorted ZnO_2N_2 tetrahedral geometry, (Figure 1.6.a).

Lemoine et al.[45] determined The structure of [Zn(salicylate)$_2$(2,2-bipyridyl)] In which the Zn atom is shown to be coordinated to one 2,2-bipyridyl ligand and to two salicylate anions in a bidentate chelating manner involving the carboxylate O-atom, (Figure 1.6.b). There are many examples of bidentate carboxylate coordination mode such as [Zn(aspirinate)$_2$.2H_2O],[41] [Zn(acetate)(adenine).H_2O],[46] [Zn(salicylate)$_2$.(theophylline)$_2$.2H_2O][29] and [Zn_2(OH)(acetate)(theophylline)$_2$] in which the coordination mode is a bidentate bridging.[47]

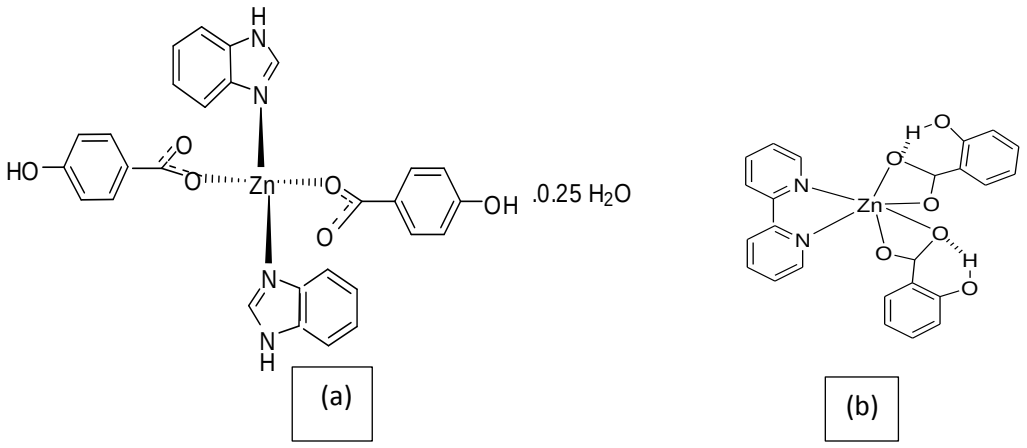


Figure 1.6. The structure of (a) [Zn(4-hydroxybenzoate)$_2$ (benzimidazole)$_2$0.25H_2O],[44] (b) [Zn(salicylate)$_2$(2,2-bipyridyl)].[45]

Angelo et al.[48] determined the structure of [Zn(3-nitro-4-hydroxybenzoate)$_2$.4H_2O] complex in which the geometry around the zinc is a distorted octahedron and the carboxylate groups are coordinated in monodentate fashion (Figure 1.7).

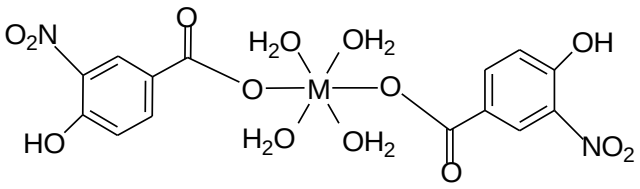


Figure 1.7. Distorted octahedron structure of [Zn(3-nitro-4-hydroxybenzoate)$_2$.4H_2O] complex.[48]

On the other hand, dinuclear and trinuclear zinc carboxylate complexes have been synthesized, for example, Clegg et al.[49] determined the crystal structure of [Zn_3(MeCH=CHCO_2)$_6$-(C_6H_7N)$_2$], this complex is linear trinuclear and contains four bidentate and two monodentate bridging crotonate ligands in the solid state, (Figure 1.8).

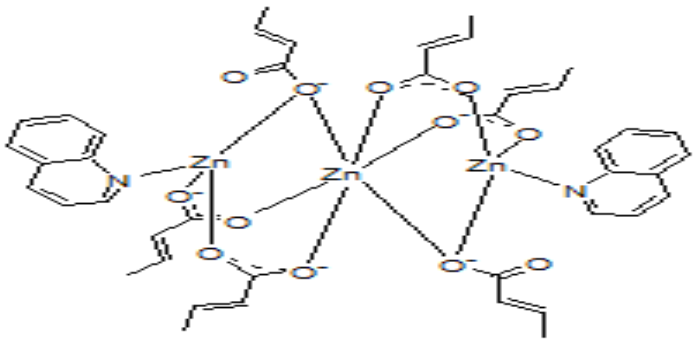


Figure 1.8. The trinuclear structure of [Zn_3(MeCH=CHCO_2)$_6$-(C_6H_7N)$_2$].[49]

Clegg et al.[50] also determined the structure of the dinuclear complex [Zn_2($C_5H_4O_2$)$_4$($C_6H_4N_2$)$_2$], with four crotonate ligands bridging a pair of Zn atoms, each of which carries an axial 4-cyanopyridine ligands in square pyramidal geometry with no metal-metal bond (Figure 1.9).

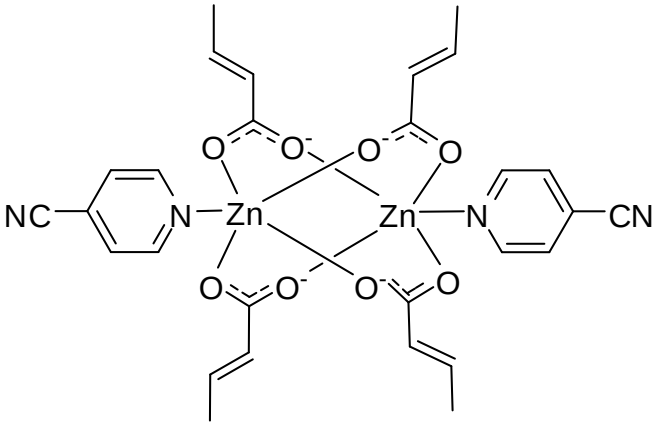


Figure 1.9. The dinuclear structure of $[Zn_2(C_5H_4O_2)_4(C_6H_4N_2)_2]$.[50]

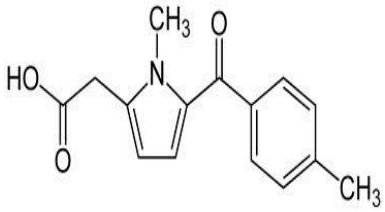
Many crystal structures of the zinc carboxylate complexes have been determined by Zelenak et al.[33] for example: the crystal structures of $[Zn(cinnamate)_2(H_2O)_2]$ with chelating bidentate carboxylate group, $[Zn_2(benzoate)_4(papaverine)_2]$ showed *syn–anti* bridging carboxylate and $[Zn(nicotinato)_2(H_2O)_4]$ with ionic carboxylate coordination mode also showed that Δ_{exp} is higher than Δ_{calc} due to the conjugation effect between the carboxylate anion and the hydrogen bonding between the carboxylate oxygens and water ligands of the neighbouring $[Zn(nicotinato)_2(H_2O)_4]$ units.

1.4.2 Non-steroidal anti-Inflammatory drugs

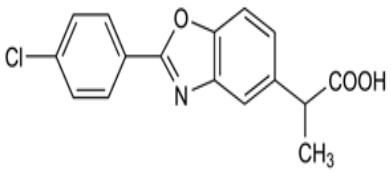
Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most frequently used medicinal drugs as analgesic, anti-pyretic and in higher doses, with anti-inflammatory effects. Additionally, NSAIDs have exhibited chemopreventive and anti-tumorigenic activity by reducing the number and size of carcinogen-induced colon tumors and exhibiting a synergistic role on the activity of certain anti-tumor drugs.[51,52]

There are many simpler aryl and heteroaryl-acetic acid and propionic acids which have been introduced as non-steroidal anti-inflammatory agents. They include Benoxaprofen, Tolmetin, Zomepirac, Ibuprofen and Naproxen. They are used

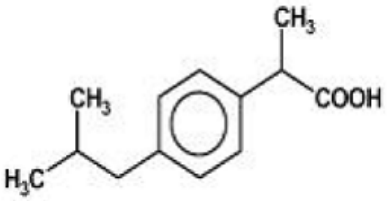
primarily to reduce hormones that cause pain, swelling, tenderness and stifness in conditions such as osteoarthritis and rheumatoid arthritis.[51]



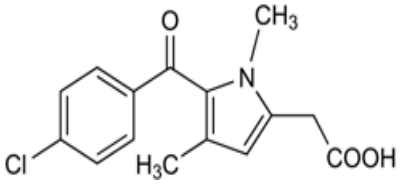
Tolmetin



Benoxaprofen



Ibuprofen



Zomepirac

Figure 1.10. Structural formula of anti-inflammatory drugs.[53]

1.4.3 Naproxen

Naproxen [(+)-6-methoxy-α-methyl-2-naphthalene acetic acid], (Figure 1.11) is a non-steroidal drug with antipyretic, anti-inflammatory and analgesic properties, with brand names Aleve, Naprosyn, Anaprox and Naprelan.[54]

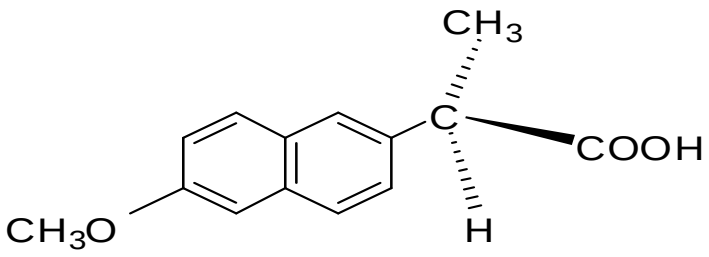


Figure 1.11. Structural formula of D-naproxen.[55]

In addition, naproxen is used to relieve fever, pain and symptoms of arthritis, gout, bursitis and menstrual cramping.[56] It acts as cyclooxygenase inhibitor that interferes with the COX-1 and COX-2 forms of that enzyme. Its effect on COX-2 gives it fever reducing (anti-pyretic), analgesic (pain relief) and anti-inflammatory function. Moreover, its effect on COX-1 gives it several undesirable effects, it is an anti-coagulant and it irritates the stomach lining.[56]

Naproxen has a relatively long plasma half-life, and 13 h to 14 h or longer duration of analgesia has been confirmed in a study in which 300-600 mg of naproxen statistically decreased pain for 7 h to 8 h. Since alkali metal salts of weak organic acids dissolve rapidly in a specific solvent as compared to their parent acid itself, the sodium salt of naproxen was developed to improve its bioavailability. Earlier studies of sodium naproxen demonstrated that significantly higher plasma levels were obtained with sodium salt as compared to naproxen.[57]

1.4.4 Metal naproxen complexes

Some anti-inflammatory drugs are sodium salts of carboxylic acids; the Na metal can be replaced by transition metals to improve some of these drugs characteristics. Metal ion complexation with naproxen increases the transport of naproxen into the cells as supported by the fact that the transport of organic ligands into cells can be facilitated by the formation of metal complexes.[54,57]

$Zn(naproxen)_2$ complexes have been synthesized and characterized by IR, NMR and it is anti-inflammatory studies were performed, also zinc naproxen was found to be more effective as anti-inflammatory agent than naproxen.[54] The interactions of this drug have been studied widely for copper with biologically active N-donor ligands such as 2,2-bipyridine, 1,10-phenanthroline and pyridine. The crystal structures of

(2,2-bipyridine)bis-(naproxenato)copper(II) (Figure 1.12: a) and (1,10-phenanthroline) bis -(naproxenato)copper(II), (Figure 1.12: b) have been determined by X-ray crystallography; the copper atom is six coordinated and is surrounded by two naproxenato ligands and a bidentate 1,10-phenanthroline ligand showing a distorted octahedral geometry with the six corners occupied by two nitrogen and four oxygen atoms, giving CuN_2O_4 chromophore. The same complex with 2,2-bipyridine instead of 1,10-phenanthroline has similar structure. In addition, the DNA and albumin- binding of the $[Cu(naproxen)_2(pyridine)_2(H_2O)]$, [(1,10-phenanthroline) bis(naproxenato) copper(II)] and $[Cu_2(naproxen)_4(H_2O)_2]$ have been evaluated.[52]

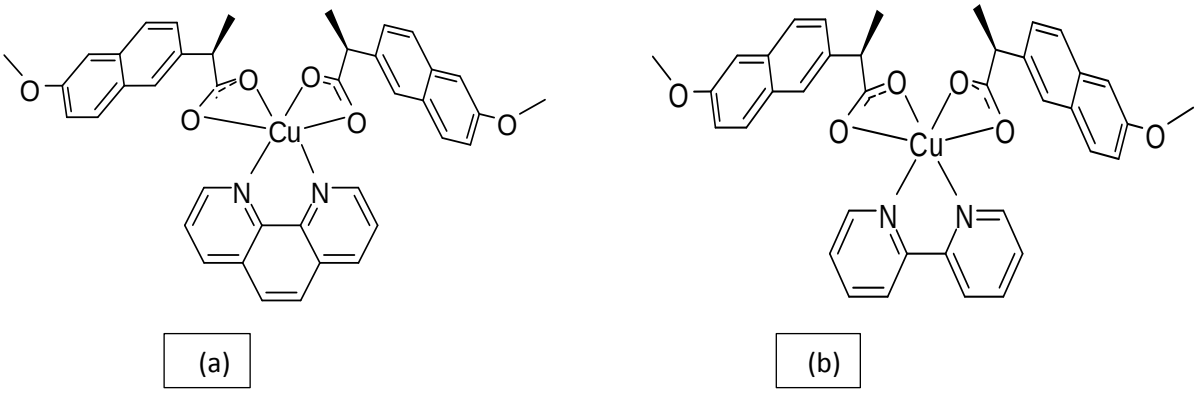


Figure 1.12. The structure of (a) $[Cu(nap)_2(phen)_2H_2O]$ and (b) $[Cu(nap)_2(bipy)_2.H_2O]$.[52]

Moreover, the synthesis and spectral characterization of binary copper(II) complex with naproxen of the formula, $[Cu_2(nap)_4]_n$ and its ternary complex with 3-pyridylmethanol of the formula, $[Cu(nap)_2(3\text{-}pym)_2]_n$ were investigated. The X-ray structure of $[Cu(nap)_2(3\text{-}pym)_2]_n$ was also determined; the copper(II) atom adopted tetragonal bipyramidal geometry and coordinated to two oxygen atoms of a pair of monodentate naproxenate anions, and two nitrogen atoms from a pair of neutral 3-pyridylmethanol molecules, (Figure 1.13). The hydrogen atoms of the methanolic

hydroxyl groups form hydrogen bonds with the non-coordinated oxygen atoms of the carboxylate ions; these hydrogen bonds create a six member metallocyclic ring which stabilizes the molecular structure.[58]

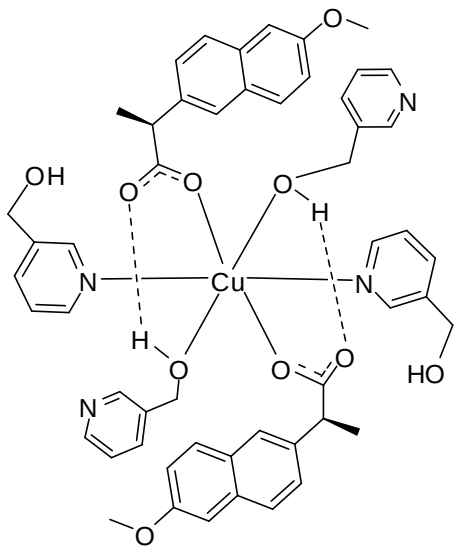


Figure 1.13. The structure of $[Cu(nap)_2(3\text{-}pym)_2]_n$.[58]

Other metal complexes of naproxen such as; the cobalt(II) complexes with naproxen in the presence of nitrogen–donar heterocyclic ligands (1,10-phenanthroline, 2,2-bipyridine and pyridine) have been synthesized and characterized with physiochemical and spectroscopic techniques. The crystal structure of $[Co(nap)_2(py)_2(H_2O)_2]$ (Figure 1.14) has been determined by X-ray crystallography. Also the cobalt atom is six coordinated and is surrounded by two naproxenato ligands and two pyridine molecules in monodentate mode and two aqua ligands to form a distorted octahedral geometry. The anti-oxidant of the compounds has been evaluated indicating their high scavenging activity against hydroxyl free radicals and superoxide radicals.[59]

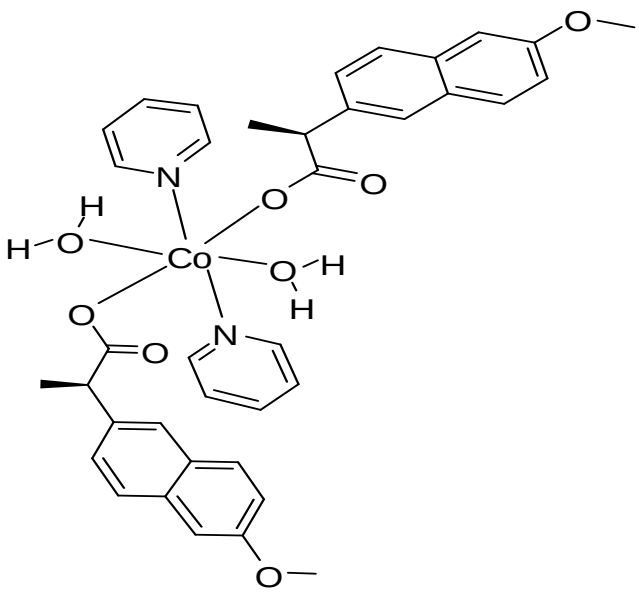


Figure 1.14. The structure of $[Co(nap)_2(py)_2(H_2O)_2]$.[59]

The vanadyl(IV) $[VO(nap)_3.5CH_3OH]$ complex was synthesized, characterized and its biological activity on the proliferation of two osteoblast-like cells in culture was tested and compared with that of the vanadyl(IV) cation. The complex exhibited different effects depending on the concentration and the cellular type, while no effect was observed for its parent drug.[53]

1.5 Heterocyclic Nitrogen Compounds

Heterocycles containing nitrogens form the largest classical part of organic chemistry and are of immense importance in biological and industrial applications. The majority of pharmaceuticals and biologically active agrochemicals are heterocyclic compounds, while countless additives and modifiers used in industrial applications ranging from cosmetics, reprography, information storage and plastics are heterocyclic in nature.[60] Most of the organic compounds containing nitrogen atoms show better biological activity than non-nitrogen compounds. Compounds containing pyridine ring, such as vitamin B, nicotinamide and nicotinic acid, play

important roles in metabolism.[61] Heterocyclic compounds have many important properties, one of these properties is the basicity of the heterocyclic compounds due to the presence of the lone pair of electrons on each nitrogen atom.

The ligands 1,10-phenanthroline and 2,2-bipyridine bind with many first row transition metals as a bidentate and possess a variety of uses such as: anti-bacterial, [62,63] anti-viral,[64,65] and anti-malarial.[66,67] The 2-amino pyridine ligand is primarily used as an intermediate in the manufacture of pharmaceuticals, particularly: anti-histamines and anti-bacterial agents.[68] Imidazole was incorporated into many important biological molecules such as in histidine which has imidazole side chain, vitamin B_{12} and Biotin as well as many chemotherapeutic agents. Imidazole is also present in anti-cancer medications like mercaptopurine and in anti-bacterial activity against four pathogenic bacteria (*E-coli, Pseudomonas areuginosa, Klebsiella pneumoniae*, and *Staphylococcus aureus*).[68-70] Benzimidazole is a very important pharmacophore in drug discovery and its derivatives are an important class of bioactive molecules in the field of drugs and pharmaceuticals. It possesses a variety of uses such as: anti-bacterial, anti-viral, anti-fungal, anti-inflammatory and anti-tumor agents.[68,71-73] Quinolines, 8-hydroxy quinolone and their derivatives are receiving increasing importance due to their wide range of biological and pharmacological activities. There are many biological activities which have been associated with quinoline containing compounds like: anti-inflammatory, anti-allergic, anti-malarial, anti-bacterial, anti-proliferative, anti-cancer and anti-parasitic activities.[74] Pyrazole ligand refers to the class of simple aromatic organic compounds of the heterocyclic series characterized by a 5-membered ring structure composed of three carbon atoms and two nitrogen atoms in adjacent positions. Pyrazole derivatives have a long history of application in agrochemicals and pharmaceutical industry. Also it possesses diverse

pharmacological activities; anti-tumor, anti-microbial, anti-fungal, anti-inflammatory, anti-convulsant, anti-pyretic and anti-depressant.[75-77] Ten nitrogen donor ligands were used in the present work: 1,10-phenanthroline, 2,9-dimethyl-1,10-phenanthroline, 2,2-bipyridine, 2-amino pyridine, 4-picoline, imidazole, 1,2-dimethyl imidazole, 4,4-bipyridine, quinoline and pyrazole, (Figure 1.15).

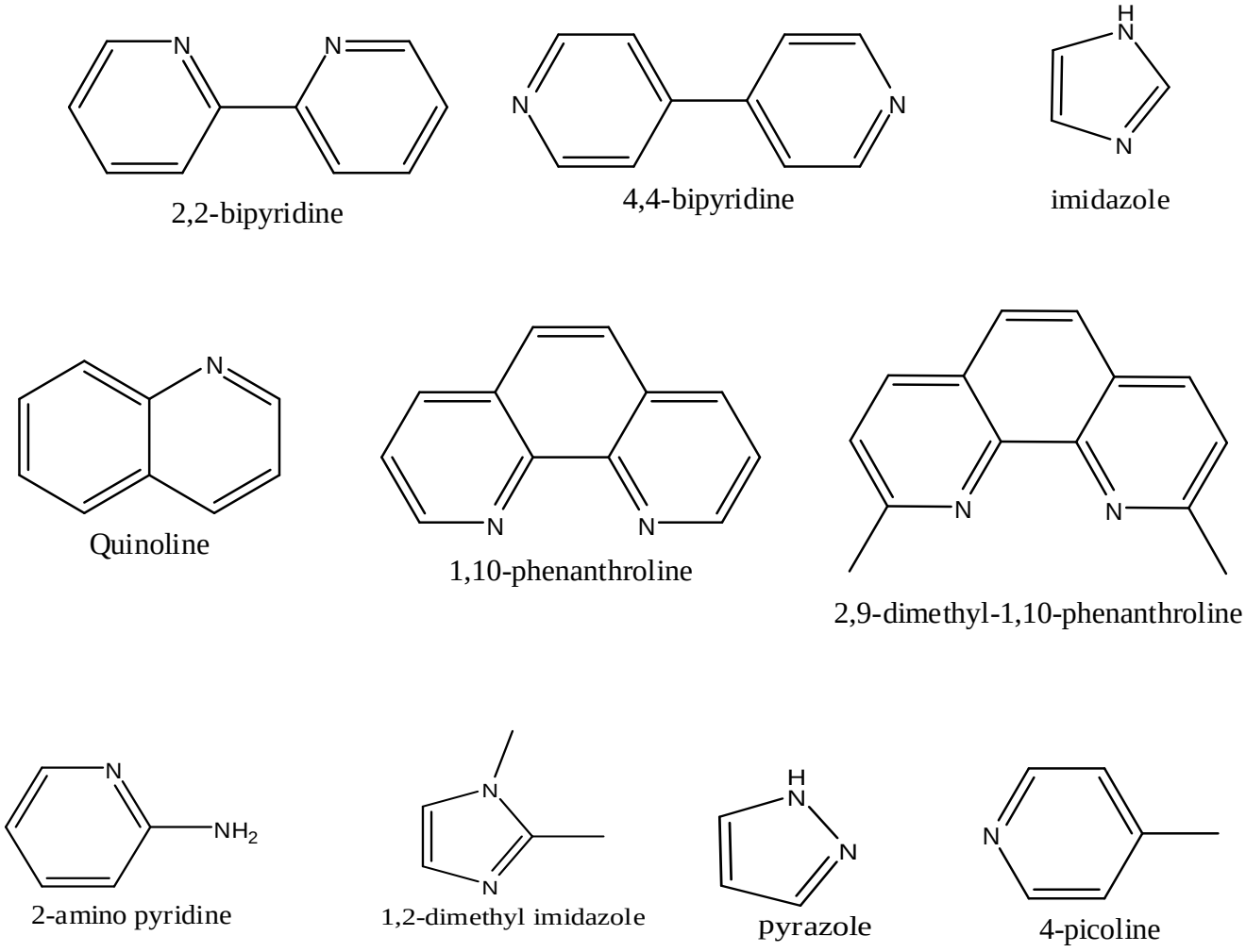


Figure 1.15. Heterocyclic nitrogen donor ligands used in this work.

1.6 Zinc carboxylate complexes with N-donor ligands

Zinc carboxylate complexes are part of coordination compounds which were studied from both chemical and biological point of view, especially, when interacting with biologically active N-donar ligands. Gyoryova et al. studied the complexes of zinc formate, bromobutyrate, isobutyrate and propionate with N-donor ligands such as: thiourea, caffeine, theophylline, nicotinamide, papaverine and phenazone. These complexes showed both anti-bacterial activity and fungistatic effect.[10,29,78-80]

Zinc(II) complexes with 5-chlorosalicylate, 4-chlorosalicylate and salicylate with heterocyclic ligands such as urea, theophylline, theourea, nicotinamide, caffeine and theobromine were synthesized and their thermal, spectral and biological properties were studied.[29,81-83] Moreover, the anti-bacterial and anti-fungal activity of zinc(II) carboxylates such as $Zn(RCOO)_2.nH_2O$ [R = H-, CH_3-, $CH_3CH_2CH_2$-, $(CH_3)CH$-, XCH_2-, X = Cl, Br, I, (n = 0 or 2), $[Zn(XCH_2COO)_2(Caf)_2.2H_2O]$ (Caf = Caffeine, X = Cl, Br) were studied against bacterial strains *Staphylococcus aureus* and *Escherichia coli*.[17]

The complexes of zinc acetate, benzoate and 2-bromobenzoate compounds were studied with N-donor ligands such as theophylline, nicotinamide, urea, phenazone, caffeine and adenine. Also the IR-spectroscopy and the anti-bacterial activity against G^+ and G^- bacteria of these complexes were tested.[20,43,46,47,84,85]

2. Aim of the research

The main objective of the present work is to synthesize new complexes of zinc naproxen with heterocyclic N-donor ligands, and then characterize them by IR-spectroscopy, NMR, UV-visible spectroscopy and, when possible, X-ray structural analysis of the new compounds will be determined.

Moreover, the anti-bacterial activity of these complexes will be tested and evaluated against Gram positive and Gram negative bacteria for the first time.

3. EXPERIMENTAL

3.1 Instruments

Infrared (IR) absorption spectra were recorded using a Varian 600 FT-IR spectrometer in the region of 400-4000 cm^{-1} using KBr pellet technique. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded in $CDCl_3$ and DMSO (d^6) as solvents with a Varian Unity spectrometer (300 and 75 Hz) for ^{1}H and $^{13}C\{^{1}H\}$ nucleus, respectively. Tetramethylsilane Me_4Si (TMS) was used as an internal standard.

UV-Vis measurements were recorded on a Hewlett Packard 8453 photo diode-array spectrometer in the 200–800 nm region using DMSO, $CHCl_3$, and CH_3OH as solvents. Melting points were determined in capillary tube with EZ-melt apparatus and are uncorrected.

3.2 Materials

The starting materials used in the present work were purchased from Aldrich chemicals with high purity and were used without further purification. Solvents were also purchased from commercial sources. Pure cultures of *Micrococcus luteus*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis* were obtained from the Biology and Biochemistry Department at Birzeit University.

3.3 Experimental and synthesis

3.3.1 Synthesis of $[Zn_2(nap)_4]$ (1)

Zinc naproxen complex was prepared by reacting 1 eq of zinc chloride with 2 eq of sodium naproxen in H_2O solvent. The complex thus formed was filtered, washed with water and air dried. Zinc naproxen was also previously prepared as shown in the literature.[54,57] The complex is soluble in acetone, dichloromethane and acetonitrile. **$[Zn_2(nap)_4]$ (1)**: (86%) yield**,** M.p. (228-233) ^oC; ^1H NMR ($CDCl_3$): δ = 1.39 (d, 3H, CH_3), 3.70 (bs, 1H, CH), 3.90 (s, 3H, OCH_3), 7.00 (bs, 1H, CH), 7.08 (d, 1H, CH, ^3J = 8.4 Hz), 7.42 (bs, 1H, CH), 7.54 (s, 1H, CH), 7.58 (d, 1H, CH), 7.61 (d, 1H, CH); $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ = 19.59 (CH_3), 48.37 (**C**H-CH_3), 55.44 (O-CH_3), 105.70 (CH), 118.82 (CH), 125.88 (CH), 126.87 (CH), 127.17 (CH), 129.26 (CH), 133.51 (CH), 157.44 (**C**-OCH_3), 181 (C=O); IR (cm^{-1}, KBr): 3080, 2955, 1696, 1630, 1600, 1485, 1455, 1390, 1370, 1260, 1210, 1160, 1027, 974, 927, 811, 744, 615, 591; UV-Vis, ($CHCl_3$), λ (nm): 264, 274, 333.

3.3.2 Synthesis of $[Zn(nap)_2$1,10-phen] (2)

1,10-Phenanthroline (0.45 g, 2.3 mmol) was dissolved in acetone and added drop-wise to a stirred acetone solution of $[Zn(naproxen)_2]$ **(1)** (0.6 g, 1.1 mmol). The solution was stirred for 2 h and a white solid was formed which was then filtered and air dried. The compound is soluble in dichloromethane and methanol.

$[Zn(nap)_2$1,10-phen] (2): (80%) yield, M.p. (220-230) ^oC; ^1H NMR ($CDCl_3$): δ = 1.52 (d, 3H, CH_3, $^3J_{H-H}$ = 6.9 Hz), 3.87 (bs, 4H, CH, OCH_3), 7.02 (d, 1H, CH, $^3J_{H-H}$ = 3 Hz), 7.06 (d, 1H, CH, $^3J_{H-H}$ = 1.5 Hz), 7.40 (d, 2H, CH, $^3J_{H-H}$ = 8.1 Hz), 7.49 (d, 1H,

CH, $^{3}J_{H-H}$ = 8.7 Hz), 7.52 (d, 2H, 2CH), 7.60 (bs, 2H, CH_{Phen}), 7.68 (t, 2H, CH_{Phen}, $^{3}J_{H-H}$ = 7.8 Hz), 7.81 (bs, 2H, CH_{Phen}), 8.53 (d, 2H, CH_{Phen}); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ = 19.58 (CH_3), 46.67 (**C**H-CH_3), 55.49 (O-CH_3), 105.69 (CH), 118.59 (CH), 120.96 ($2CH_{Phen}$), 125.86 (CH), 126.74 (CH), 127.34 (CH), 129.12 (CH), 129.44 ($2CH_{Phen}$), 133.48 (CH), 138.68 ($2CH_{Phen}$), 139.91 ($2CH_{Phen}$), 149.64 ($2CH_{Phen}$), 157.38 (**C**-OCH_3), (C=O) was undetectable; IR (cm^{-1}, KBr): 3058, 2969, 2931, 2837, 1603, 1522, 1483, 1458, 1430, 1388, 1262, 1159, 1121, 1061, 1029, 960, 927, 852, 824, 777, 726, 697, 543, 475, 429; UV-Vis, (MeOH), λ (nm): 233, 271, 292, 319, 333.

3.3.3 Synthesis of [Zn(nap)$_2$2,9-dmphen] (3)

2,9-Dimethyl-1,10-phenanthroline (0.49 g, 2.3 mmol) was dissolved in acetone and added to a stirred acetone solution of [Zn(naproxen)$_2$] **(1)** (0.67 g, 1.15 mmol). The solution was stirred for 2 h and a white solid was formed which was then filtered and air dried. The compound was dissolved in 1:1 mixture of hot acetonitrile and chloroform to give suitable crystals used for X-ray structural analysis. The compound is soluble in chloroform, acetonitrile and acetone.

[Zn(nap)$_2$2,9-dmphen]: (72%) yield, M.p. (209-213) ^{o}C; ^{1}H NMR ($CDCl_3$): δ = 1.49 (d, 3H, CH_3, $^{3}J_{H-H}$ = 7.2 Hz), 2.74 (s, 6H, CH_{3Phen}), 3.86 (q, 1H, CH), 3.89 (s, 3H, OCH_3), 7.03 (bs, 1H, CH), 7.06 (d, 1H, CH, $^{3}J_{H-H}$ = 2.7 Hz), 7.40 (d, 2H, CH_{Phen}, $^{3}J_{H-H}$ = 2.7 Hz), 7.43 (d, 1H, CH), 7.51 (d, 2H, CH_{nap}, $^{3}J_{H-H}$ = 8.7 Hz), 7.59 (bs, 1H, CH), 7.69 (d, 2H, CH_{Phen}, $^{3}J_{H-H}$ = 3.9 Hz), 8.17 (d, 2H, CH_{Phen}, $^{3}J_{H-H}$ = 8.4 Hz); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ = 19.75 (CH_3), 24.81 ($2CH_{3Phen}$), 47.06 (**C**H-CH_3), 55.48 (O-CH_3), 105.70 (CH), 118.49 (CH), 125.70 ($2CH_{Phen}$), 125.81 (CH), 126.36 ($2CH_{Phen}$), 126.61 (CH), 127.12 (CH), 127.39 ($2C_{phen}$), 129.29 (CH), 132.12 ($2CH_{Phen}$), 133.40 (CH), 139.11 ($2CH_{Phen}$), 157.29 (**C**-OCH_3), 160.76 ($2CH_{Phen}$), 181.87 (C=O); IR (cm^{-1},

KBr): 3056, 2964, 2930, 1605, 1505, 1453, 1375, 1270, 1212, 1156, 1121, 1033, 927, 852, 813, 782, 750, 683, 661, 549, 475, 416; UV-Vis, (DMSO), λ (nm): 274, 298, 319, 333.

3.3.4 Synthesis of [Zn(nap)$_2$2,2-bipy] (4)

2.2-Bipyridine (0.42 g, 2.66 mmol) was dissolved in acetone and added drop-wise to a stirred acetone solution of [Zn(naproxen)$_2$] **(1)** (0.70 g, 1.33 mmol). The solution was stirred for 2 h to give a white solid which was then filtered and air dried. The compound is soluble in chloroform, acetonitrile, dichloromethane.

[Zn(nap)$_2$2,2-bipy]: (81%) yield, M.p. (195-198) ^{o}C; ^{1}H NMR ($CDCl_3$): δ = 1.54 (d, 3H, CH_3), 3.90 (bs, 4H, CH, OCH_3), 7.04 (bs, 1H, CH), 7.06 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 5.4 Hz), 7.42 (d, 2H, CH, $^{3}J_{H\text{-}H}$ = 4.5 Hz), 7.51 (t, 2H, $CH_{bip,}$ $^{3}J_{H\text{-}H}$ = 5.1 Hz), 7.54 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 5.1 Hz), 7.61 (bs, 2H, CH), 7.74 (bs, 2H, CH_{bip}), 7.90 (bs, 1H, CH_{bip}), 8.59 (bs, 2H, CH_{bip}); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ = 19.37 (CH_3), 46.46 (**C**H-CH_3), 55.27 (O-CH_3), 105.41 (CH), 118.80 (CH), 120.63 (2CH_{bip}), 125.69 (CH), 126.45 (CH), 127.22 (CH), 128.86 (2CH_{bip}) 129.07 (CH), 129.30 (C) 133.20 (CH), 138.45 (CH_{bip}), 149.40 (2CH_{bip}), 157.10 (**C**-OCH_3), 183.73 (C=O); IR (cm^{-1}, KBr): 3045, 3030, 2975, 2932, 1603, 1484, 1446, 1388, 1314, 1264, 1212, 1161, 1121, 1060, 1029, 961, 926, 854, 822,766, 544, 475, 416; UV-Vis, (DMSO), λ (nm): 275, 319, 334.

3.3.5 Synthesis of [Zn(nap)$_2$(2-ampy)$_2$] (5)

2-Amino pyridine (0.18 g, 1.9 mmol) was dissolved in acetone and added drop-wise to a stirred acetone solution of [Zn(naproxen)$_2$] **(1)** (0.50 g, 0.96 mmol). The solution was stirred for 2 h and then was evaporated under vacuum, washed with ether to

afford an oily product which was dried under vacuum. The compound is soluble in chloroform, dichloromethane, acetonitrile, ethanol and acetone.

[Zn(nap)$_2$(2-ampy)$_2$]: (80%) yield, M.p. (74-80) ^{o}C; ^{1}H NMR ($CDCl_3$): δ = 1.52 (d, 3H, CH_3, $^{3}J_{H-H}$ = 6.9 Hz), 3.86 (q, 1H, CH), 3.88 (s, 3H, OCH_3), 5.71 (bs, 2H, NH_2), 6.23 (t, 1H, CH_{pyr}, $^{3}J_{H-H}$ = 6.3 Hz), 7.04 (bs, 1H, CH), 7.07 (d, 1H, CH, $^{3}J_{H-H}$ = 2.1 Hz), 7.18 (t, 1H, CH_{pyr}, $^{3}J_{H-H}$ = 6.9 Hz), 7.42(d, 1H, CH), 7.45 (d, 1H, CH_{Pyr}), 7.55 (d, 1H, CH, $^{3}J_{H-H}$ = 7.8 Hz), 7.58 (d, 1H, CH, $^{3}J_{H-H}$ = 3.9 Hz), 7.59 (d, 1H, CH_{pyr}, $^{3}J_{H-H}$ = 5.1 Hz), 7.64 (s, 1H, CH); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ = 19.60 (CH_3), 47.53 (**C**H-CH_3), 55.50 (O-CH_3), 105.75 (CH), 111.36 (CH_{pyr}), 113.00 (CH_{pyr}), 118.66 (CH), 125.96 (CH), 126.80 (CH), 127.36 (CH), 129.34 (CH), 139.23 (CH_{pyr}), 146.17 (CH_{pyr}), 157. 40 (**C**-OCH_3), 159.19 (C-$NH_{2\ pyr}$), 181.52 (C=O); IR (cm^{-1}, KBr): 3335, 3211, 3056, 2970, 2933, 1605, 1501, 1452, 1389, 1358, 1267, 1212, 1160, 1120, 1063, 1031, 960, 927, 853, 812, 771, 691, 522, 475, 417; UV-Vis, ($CHCl_3$), λ (nm): 265, 275, 320, 333.

3.3.6 Synthesis of [Zn$_2$(nap)$_4$(4-pic)$_2$] (6)

4-Picoline (0.2 ml, 2.28 mmol) was added drop-wise to a stirred acetone solution of [Zn(naproxen)$_2$] **(1)** (0.60 g, 1.14 mmol). The solution was stirred for 2 h and then was evaporated under vacuum, ether was added to form a white solid which was then filtered and air dried. The compound is soluble in methanol, acetone and chloroform.

[Zn$_2$(nap)$_4$(4-pic)$_2$]: (67%) yield, M.p. (110-116) ^{o}C; ^{1}H NMR ($CDCl_3$): δ = 1.50 (d, 3H, CH_3, $^{3}J_{H-H}$ = 6.9 Hz), 2.21 (s, 3H, $CH_{3\ Pic}$), 3.89 (m, 4H, OCH_3, CH), 6.81 (d, 2H, CH_{pic}), 7.02 (bs, 1H, CH), 7.07 (d, 1H, CH), 7.42 (d, 1H, CH, $^{3}J_{H-H}$ = 8.4 Hz), 7.51 (d, 1H, CH, $^{3}J_{H-H}$ = 10.8 Hz), 7.54 (d, 1H, CH, $^{3}J_{H-H}$ = 9.3 Hz), 7.61 (s, 1H, CH), 8.23 (d, 2H, $2CH_{pic}$, $^{3}J_{H-H}$ = 4.2 Hz); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$) δ = 19.52 (CH), 21.38 (CH_{3pic}), 47.32 (**C**H-CH_3), 55.50 (O-CH), 105.68 (CH), 118.55 (CH), 125.55 (CH),

125.95 (CH_{Pic}), 126.74 (CH), 127.33 (CH), 129.14 (CH), 129.51 (C), 133.48 (CH), 148.97 (C_{Pic}), 150.65 (CH_{Pic}), 157.84 (**C**-OCH_3), 182.216 (C=O); IR (cm^{-1}, KBr): 3056, 2966, 2933, 1604, 1504, 1436, 1390, 1267, 1210, 1066, 1031, 960, 925, 858, 811, 749, 690, 672, 554, 491; UV-Vis, (DMSO), λ (nm): 264, 274, 320, 334.

3.3.7 Synthesis of $[Zn(nap)_2 4,4\text{-bipy}]_n$ (7)

4,4-Bipyridine (0.30 g, 1.9 mmol) was dissolved in acetone and added drop-wise to a stirred acetone solution of $[Zn(naproxen)_2]$ **(1)** (0.50 g, 0.96 mmol). The solution was stirred for 2 h and the obtained solid was then filtered and air dried. The compound is soluble in chloroform and DMSO.

$[Zn(nap)_2(4,4\text{-bipy})]_n$: (78%) yield, M.p. (234-241) ^oC; ^1H NMR (DMSO-d^6): δ = 1.40 (d, 3H, CH_3, $^3J_{H\text{-}H}$ = 6.9 Hz), 3.69 (q, 1H, CH, $^3J_{H\text{-}H}$ = 7.2 Hz), 3.82 (s, 3H, OCH_3), 7.06 (d, 1H, CH, $^3J_{H\text{-}H}$ = 2.4 Hz), 7.09 (d,1H, CH, $^3J_{H\text{-}H}$ = 2.1 Hz), 7.43 (d, 1H, CH, $^3J_{H\text{-}H}$ = 8.7 Hz), 7.66 (d, 1H, CH, $^3J_{H\text{-}H}$ = 8.4 Hz), 7.69 (d, 1H, CH, $^3J_{H\text{-}H}$ = 9.9 Hz), 7.68 (s, 1H,CH), 7.79 (dd, 2H, CH_{bipy}, $^3J_{H\text{-}H}$ = 4.8 Hz, $^4J_{H\text{-}H}$ = 1.5Hz), 8.69 (d, 2H, CH_{bipy}, $^3J_{H\text{-}H}$ = 5.7 Hz); $^{13}C\{^1H\}$ NMR (DMSO-d^6): δ = 20.51 (CH_3), 46.92 (**C**H-CH_3), 55.76 (O-CH_3), 106.27 (CH), 119.00 (CH), 122.26 (CH_{bipy}), 125.98 (CH), 126.97 (CH), 127.73 (CH), 129.10 (CH), 129.68 (C)133.556 (CH), 145.36 ($2C_{bipy}$), 151.04 ($4CH_{bipy}$), 157.44 (**C**-OCH_3), 180.24 (C=O); IR (cm^{-1}, KBr): 3059, 2981, 1604, 1583, 1502, 1451, 1389, 1270, 1212, 1161, 1065, 1030, 925, 857, 807, 749, 649, 627, 545, 474; UV-Vis, ($CHCl_3$), λ (nm): 265, 321, 334.

3.3.8 Synthesis of $[Zn_2(nap)_4(quin)_2]$ (8)

Quinoline (0.37 ml, 1.9 mmol) was added drop-wise to a stirred acetone solution of $[Zn(naproxen)_2]$ **(1)** (0.50 g, 0.96 mmol). The solution was stirred for 2 h and was then evaporated under vacuum to afford an oily product which was washed with petroleum ether to give a solid product. The product was filtered and air dried. The compound is soluble in chloroform, dichloromethane and acetonitrile.

$[Zn_2(nap)_4(quin)_2]$: (75%) yield, M.p. (105-115) ^oC; ^1H NMR (DMSO-d^6): δ = 1.38 (d, 3H, CH_3, $^3J_{H-H}$ = 7.2 Hz), 3.66 (q, 1H, CH, $^3J_{H-H}$ = 6.9 Hz), 3.83 (s, 3H, OCH_3), 7.07 (d, 1H, CH, $^3J_{H-H}$ = 2.7 Hz), 7.10 (d, 1H, CH, $^3J_{H-H}$ = 2.4 Hz), 7.42 (d, 1H, CH, $^3J_{H-H}$ = 8.4 Hz), 7.52 (t, 1H, CH_{quin}, $^3J_{H-H}$ = 4.2 Hz), 7.54 (s, 1H, CH), 7.62 (d, 1H, CH, $^3J_{H-H}$ = 7.5 Hz), 7.68 (s, 1H, CH), 7.72 (t, 1H, CH_{quin}, $^3J_{H-H}$ = 9.6 Hz), 7.76 (d, 1H, CH_{quin}), 7.99 (t, 1H, CH_{quin}, $^3J_{H-H}$ = 8.1 Hz), 8.03 (d, 1H, CH_{quin}, $^3J_{H-H}$ = 8.4 Hz), 8.37 (d, 1H, CH_{quin} $^3J_{H-H}$ = 8.1 Hz), 8.90 (d, 1H, CH_{quin}); $^{13}C\{^1H\}$ NMR (DMSO-d^6): δ = 20.56 (CH_3), 46.92 (**C**H-CH_3), 55.77 (O-CH_3), 106.29 (CH), 119.00 (CH), 122.18 (CH_{quin}), 125.30 (CH), 126.95 (CH), 127.30 (CH), 127.76 (CH_{quin}), 128.81 (CH_{quin}), 129.11 (CH), 129.68 (C), 130.27 ($2CH_{quin}$), 133.54 (CH), 136.92 (CH_{quin}), 151.30 (CH_{quin}), 157.44 (**C**-OCH_3), 180.06 (C=O); IR (cm^{-1}, KBr): 3057, 2970, 1605, 1554, 1510, 1459, 1378, 1266, 1234, 1213, 1161, 1081, 1025, 960, 927, 858, 810, 786, 715, 637, 537, 474; UV-Vis, (DMSO), λ (nm): 264, 274, 314, 334.

3.3.9 Synthesis of $[Zn(nap)_2(imid)_2]$ (9)

Imidazole (0.26 g, 3.8 mmol) was dissolved in acetone and added drop-wise to a stirred acetone solution of $[Zn(naproxen)_2]$ **(1)** (1.0 g, 1.9 mmol). The solution was stirred for 2 h and the formed solid was then filtered and air dried. The compound is soluble in chloroform and DMSO.

$[Zn(nap)_2(imid)_2]$: (78%) yield, M.p. (152-155) ^oC; ^1H NMR (DMSO-d^6): δ = 1.44 (d, 3H, CH_3, $^3J_{H-H}$ = 6.9 Hz), 3.74 (q, 1H, CH, $^3J_{H-H}$ = 6.9 Hz), 3.83 (s, 3H, OCH_3), 7.10 (d, 1H, CH, $^3J_{H-H}$ = 8.4 Hz and 2H, CH_{Imid}), 7.23 (s, 1H, CH), 7.46 (d, 1H, CH, $^3J_{H-H}$ = 8.7 Hz), 7.69 (bs, 2H, 2CH and CH_{Imid}), 7.71 (d, 1H, CH, $^3J_{H-H}$ = 12 Hz), 8.02 (bs, 1H, NH_{Imid}); $^{13}C\{^1H\}$ NMR (DMSO-d^6): δ = 20.36 (CH_3), 47.04 (**C**H-CH_3), 55.76 (O-CH_3), 106.32 (CH), 119.08 (CH), 125.97 (CH), 127.13 (CH), 127.54 (CH), 129.15 (CH), 129.69 (CH_{Imid}), 133.63 (CH), 139.32 (CH_{Imid}), 157.51 (**C**-OCH_3), 178.93 (C=O); IR (cm^{-1}, KBr): 3127, 3055, 2935, 2865, 1608, 1586, 1503, 1452, 1390, 1342, 1265, 1208, 1160, 1072, 1027, 956, 927, 857, 814, 760, 692, 624, 534, 473, 413; UV-Vis, ($CHCl_3$), λ (nm): 264, 274, 320, 334.

3.3.10 Synthesis of $[Zn(nap)_2(1,2\text{-}dmimid)_2]$ (10)

1,2-Dimethyl imidazole (0.2 ml, 2.3 mmol) was added drop-wise to a stirred acetone solution of $[Zn(naproxen)_2]$ **(1)** (0.6 g, 1.15 mmol). The solution was stirred for 2 h and the obtained solid was then filtered and air dried. The compound is soluble in chloroform, dichloromethane, ethanol and acetonitrile.

$[Zn(nap)_2(1,2\text{-}dmimid)_2]$: (83%) yield, M.p. (132-136) ^oC; ^1H NMR ($CDCl_3$): δ = 1.50 (d, 3H, CH_3, $^3J_{H-H}$ = 7.2 Hz), 2.01 (s,3H, $CH_{3\ Imid}$), 3.23 (s, 3H, CH_{3Imid}), 3.83 (q, 1H, CH), 3.87 (s, 3H, OCH_3), 6.53 (bs, 1H, CH_{Imid}), 6.83 (bs, 1H, CH_{Imid}), 7.03 (s,

1H, CH), 7.05 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 2.4 Hz), 7.49 (d, 1H, CH), 7.51 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 6 Hz), 7.56 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 9.3 Hz), 7.65 (s, 1H, CH); $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ = 11.70 (CH_{3Imid}), 19.83 (CH_3), 33.21 (N-CH_{3Imid}), 47.83 (**C**H-CH_3), 55.49 (O-CH_3), 105.66 (CH), 118.33 (CH), 120.37 (CH_{Imid}), 125.84 (CH), 126.35 (CH), 127.74 (CH), 129.17 (CH), 129.45 (CH_{Imid}), 133.28 (CH), 146.67 (C_{Imid}), 157.20 (**C**-OCH_3), 180.54 (C=O); IR (cm^{-1}, KBr): 3118, 3056, 2966, 2932, 1605, 1505, 1461, 1418, 1376, 1341, 1265, 1212, 1157, 1119, 1093, 1062, 1029, 958, 926, 854, 824, 776, 747, 674, 652, 553, 479, 445; UV-Vis, ($CHCl_3$), λ (nm): 264, 274, 320, 335.

3.3.11 Synthesis of $[Zn(nap)_2(pyrazole)_2]$ (11)

Pyrazole (0.13 g, 1.9 mmol) was dissolved in acetone and added drop-wise to a stirred aceton solution of $[Zn(naproxen)_2]$ **(1)** (0.50 g , 0.95 mmol). The solution was stirred for 2 h then was evaporated under vacuum to afford a solid product. The compound is soluble in acetonitrile and chloroform.

$[Zn(nap)_2(Pyrazole)_2]$: (74%) yield, M.p. (147-149) ^{o}C; ^{1}H NMR (DMSO-d^6): δ = 1.43 (d, 3H, CH_3, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 3.77 (q, 1H, CH, $^{3}J_{H\text{-}H}$ = 6.9 Hz), 3.84 (s, 3H, OCH_3), 6.26 (bs, 1H, $CH_{Pyrazole}$), 7.10 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 2.4 Hz), 7.13 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 2.7 Hz), 7.43 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 8.4 Hz), 7.62 (s, 1H, CH), 7.70 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 3.6 Hz), 7.71 (d, 1H, CH, $^{3}J_{H\text{-}H}$ = 6.3 Hz), 7.73 (d, 2H, $2CH_{pyrazole}$, $^{3}J_{H\text{-}H}$ = 1.8 Hz), 7.75 (s, 1H, CH); $^{13}C\{^{1}H\}$ NMR (DMSO-d^6): δ = 19.99 (CH_3), 46.37 (**C**H-CH_3), 55.80 (O-CH_3), 105.04 ($CH_{Pyrazole}$), 106.33 (CH), 119.22 (CH), 126.09 (CH), 127.29 (CH), 127.38 (CH), 129.11 (CH), 129.74 ($2CH_{Pyrazole}$), 133.75 (CH), 157.62 (**C**-OCH_3), (C=O) was undetectable; IR (cm^{-1}, KBr): 3125, 3040, 2970, 2933, 1602, 1504, 1481, 1390, 1354, 1264, 1212, 1165, 1131, 1065, 1026, 961, 925, 891, 854,810, 772, 718, 689, 563, 522, 478, 412; UV-Vis, ($CHCl_3$), λ (nm): 265, 274, 320, 334..

3.4 X-ray Crystallography

Single crystals suitable for X-ray determination of complex **3** was attached to a glass fiber, with epoxy glue, and transferred to a Bruker SMART APEX CCD X-ray diffractometer system controlled by a Pentium-based PC running the SMART software package,[86] The crystal was mounted on the three-circle goniometer with χ fixed at +54.76°. The diffracted graphite-monochromated Mo Kα radiation (λ = 0.71073 A) was detected on a phosphor screen held at a distance of 6.0 cm from the crystal operating at -43 °C. A detector array of 512 X 512 pixels, with a pixel size of approximately 120 μm, was employed for data collection. The detector centroid and crystal-to-detector distance were calibrated from a least-squares analysis of the unit cell parameters of a carefully centered YLID reference crystal. After the crystal of the complex had been carefully optically centered within the X-ray beam, a series of 30 data frames measured at 0.3° increments of ω were collected with three different 2θ and φ values to assess the overall crystal quality and to calculate a preliminary unit cell. For the collection of the intensity data, the detector was positioned at a 2θ value of -28° and the intensity images were measured at 0.3° intervals of ω with a duration of 20 sec. each. The data frames were collected in four distinct shells which, when combined, measured more than 1.3 hemispheres of intensity data with a maximum 2θ of 46.5°. Immediately after collection, the raw data frames were transferred to a second PC computer for integration by the SAINT program package.[87] The background frame information was updated according to the equation B' = (7B+C)/8, where B' is the update pixel value, B is the background pixel value before updating, and C is the pixel value in the current frame. The integration was also corrected for spatial distortion induced by the detector. In addition, pixels that reside outside the detector active area or behind the beam stop were masked during frame integration.

The integrated intensities for the four shells of data were merged to one reflection file. The data file was filtered to reject outlier reflections. The rejection of a reflection was based on the disagreement between the intensity of the reflection and the average intensity of the symmetry equivalents to which the reflection belongs. In the case of strong reflections ($I>99\sigma(I)$) which contains only two equivalents, the larger of the two equivalents was retained. The structure was solved and refined by the SHELXTL software package.[88]

Table 3.1. Crystal data and structure refinement for [Zn(nap)$_2$2,9-dimethyl-1,10-phenanthroline] **(3)**

Empirical formula	C44 H41N3 O6 Zn
Formula weight	773.17
Temperature	173(1) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 15.0063(9) Å α = 90°. b = 14.1711(8) Å β = 91.705(1)°. c = 17.796(1) Å γ = 90°.
Volume	3782.7(4) Å^3
Z	4
Density (calculated)	1.358 Mg/m^3
Absorption coefficient	0.703 mm^{-1}
F(000)	1616
Crystal size	0.28 x 0.24 x 0.17 mm^3
Theta range for data collection	2.26 to 27.00°.
Index ranges	-18<=h<=19, -18<=k<=18, -22<=l<=22
Reflections collected	31490
Independent reflections	16184 [R(int) = 0.0398]
Completeness to theta = 27.00°	99.8 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	16184 / 1 / 963
Goodness-of-fit on F^2	0.993
Final R indices [I>2sigma(I)]	R1 = 0.0698, wR2 = 0.1714
R indices (all data)	R1 = 0.0978, wR2 = 0.1878
Absolute structure parameter	0.043(13)
Largest diff. peak and hole	1.132 and -0.647 e.Å^{-3}

a $R1=\sum ||Fo|-|Fc|| / \sum Fo$ and $wR2 = \{\sum[w(F02 - Fc2)2] / \sum[w(Fo2)2]\}1/2$

3.5 Anti-bacterial activity

Zn(II) complexes **2**, **3** and **5** were screened for their anti-bacterial activity against G^+ bacteria (*Staphylococcus aureus* and *Micrococcus luteus)* and G^- bacteria *(Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa* and *Escherichia coli).* These complexes were tested *in-vitro* using the agar well diffusion method. First, single bacteria colonies were dissolved in sterile saline to obtain suspended cells with turbidity equivalent to a MC Farland 0.5 standard, then the plates were inoculated with one species of bacteria using a sterile cotton swab, then 6 mm diameters wells were dug in agar medium using sterile glassy borer.

The Zinc(II) complexes were prepared in DMSO (8.5 mmol/L) and were introduced into the respective wells using 50 μl pipette, one of the wells was supplemented with DMSO as control. These plates were placed in a 37 ^oC incubator for 24 h to allow bacterial growth. After 24 hours, the diameter of the inhibition zone (in mm) was measured.

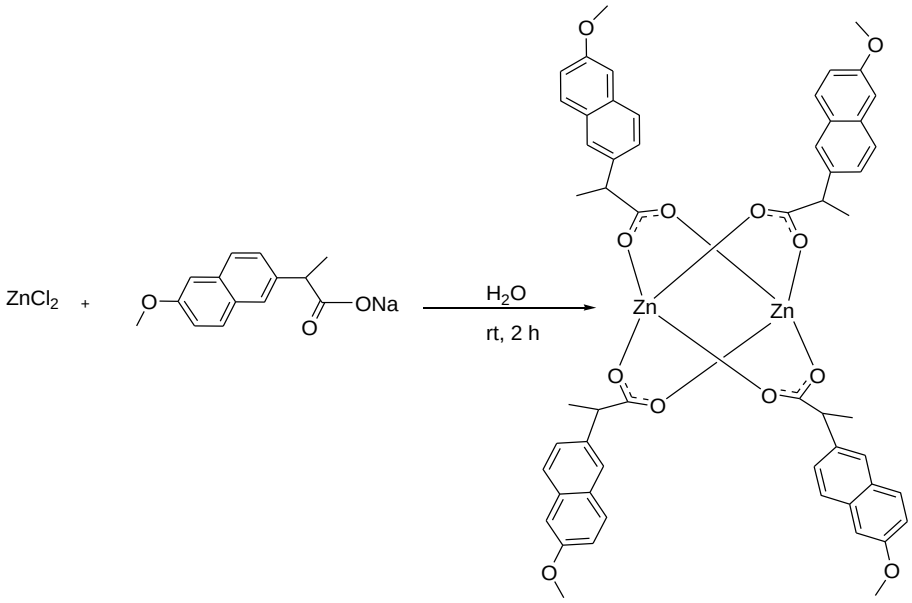
The minimum inhibitory concentration (MIC) was determined for each complex as the lowest concentration which was capable of stopping bacterial growth. Sequential dilutions of these complexes and their parent ligands in DMSO in the range 8.5 mmol/L to 0.265 mmol/L, were prepared to determine the MIC using the same procedure. When inhibition was present, the clear zone around the well for each complex was compared with its parent ligands in the same plate and the diameter of the inhibition zone was measured.

4. RESULTS AND DISCUSSION

4.1 Synthesis of zinc complexes

Dinuclear complex $[Zn_2(nap)_4]$ **(1)** was prepared by reacting 1 eq of zinc chloride with 2 eq of sodium naproxen in H_2O (Scheme 4.1). The desired product was obtained as a white solid. The melting point (228-233) ^oC was also determined. The complex is soluble in acetone, dichloromethane and acetonitrile.

Scheme 4.1. Synthesis of complex **1**.



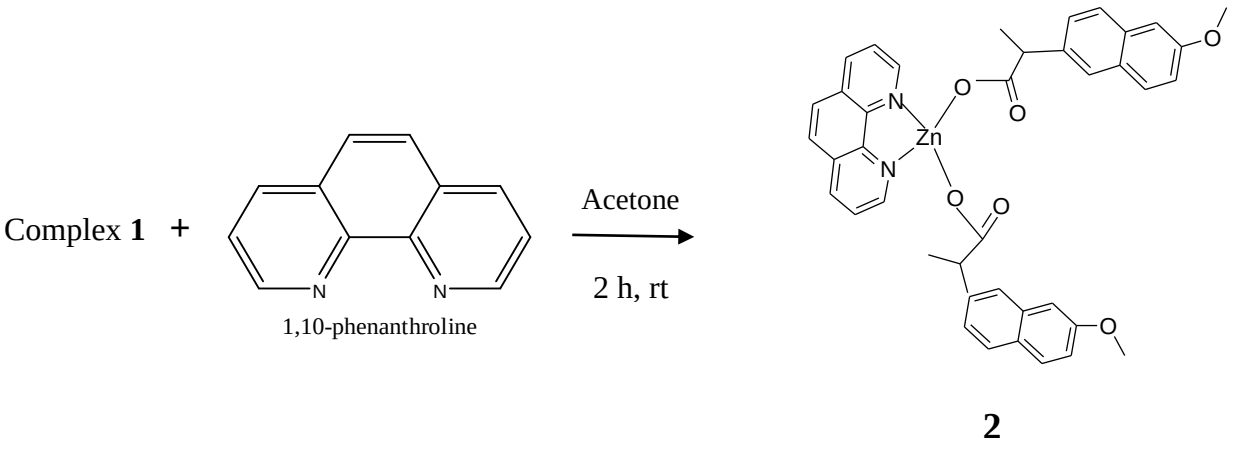
1

Many zinc naproxen compounds have been prepared by adding nitrogen donor ligands to the $[Zn_2(nap)_4]$ **(1)** complex. (See Scheme 4.2). These zinc naproxen complexes were obtained from the reaction of 1:2 molar ratio of $[Zn_2(nap)_4]$ **(1)** with nitrogen donor ligands in acetone and stirred for two hours. (See Table 4.1). The physical properties of zinc naproxen complexes **1-11** were also determined.

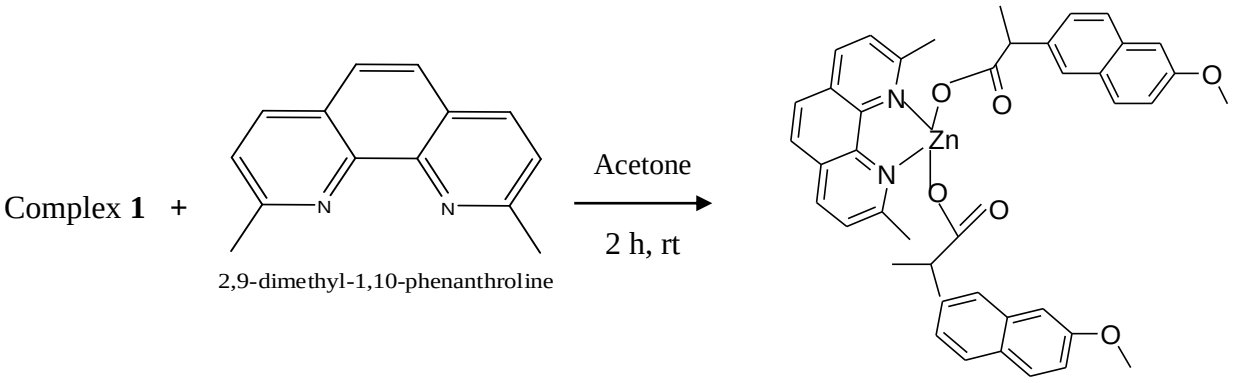
Table 4.1. Physical properties of zinc naproxen complexes **1-11**.

Complex	Yeild %	M.p. (˚C)	Solubility
$[Zn_2(nap)_4]$ **(1)**	86	228-233	Acetone, acetonitrile, dichloromethane.
$[Zn(nap)_2$1,10-Phen] **(2)**	80	220-230	Dichloromethane, methanol.
$[Zn(nap)_2$2,9-dmphen] **(3)**	72	209-213	Chloroform, acetonitrile, acetone.
$[Zn(nap)_2$2,2-bipy] **(4)**	81	195-198	Chloroform, acetonitrile, dichloromethane.
$[Zn(nap)_2(2\text{-ampy})_2]$ **(5)**	80	74-80	Ethanol, acetone, acetonitrile, dichloromethane, chloroform.
$[Zn_2(nap)_4(4\text{-pic})_2]$ **(6)**	67	110-116	Methanol , chloroform, acetone.
$[Zn(nap)_2$4,4-bipy$]_n$ **(7)**	78	234-241	Chloroform , DMSO.
$[(Zn_2(nap)_4\ (quin)_2]$ **(8)**	75	105-115	Chloroform, acetonitrile, dichloroform.
$[Zn(nap)_2(imid)_2]$ **(9)**	78	152-155	Chloroform , DMSO.
$[Zn(nap)_2(1,2\text{-dmimid})_2]$ **(10)**	83	132-136	Ethanol, chloroform, acetonitrile ,dichloromethane.
$[Zn(nap)_2(pyrazole)_2]$ **(11)**	74	147-149	Acetonitrile, chloroform.

Scheme 4.2. Synthesis of complexes **2-11.**



2



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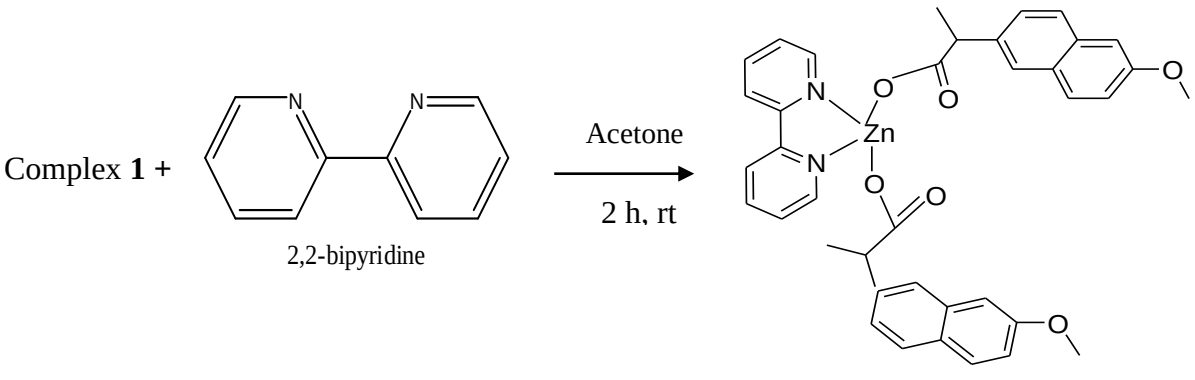
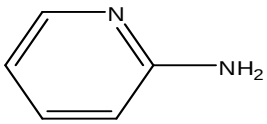


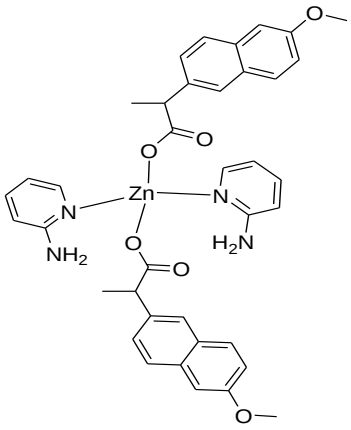
4

Scheme 4.2. Cont.

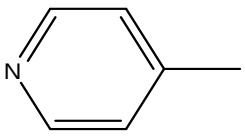
Complex **1** + 

2-amino pyridine

Acetone
2 h, rt

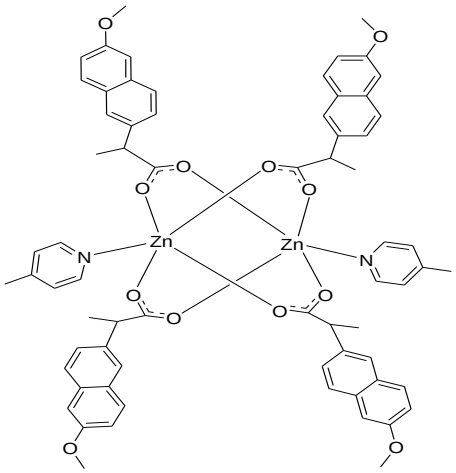


5

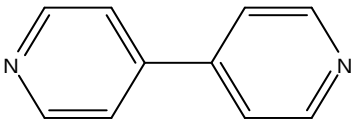
Complex **1** + 

4-picoline

Acetone
2 h, rt

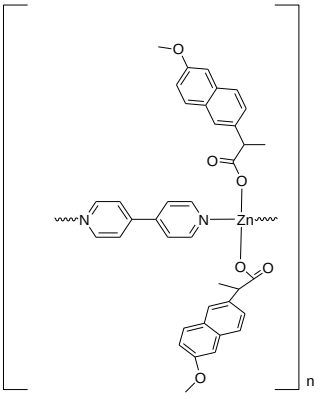


6

Complex **1** + 

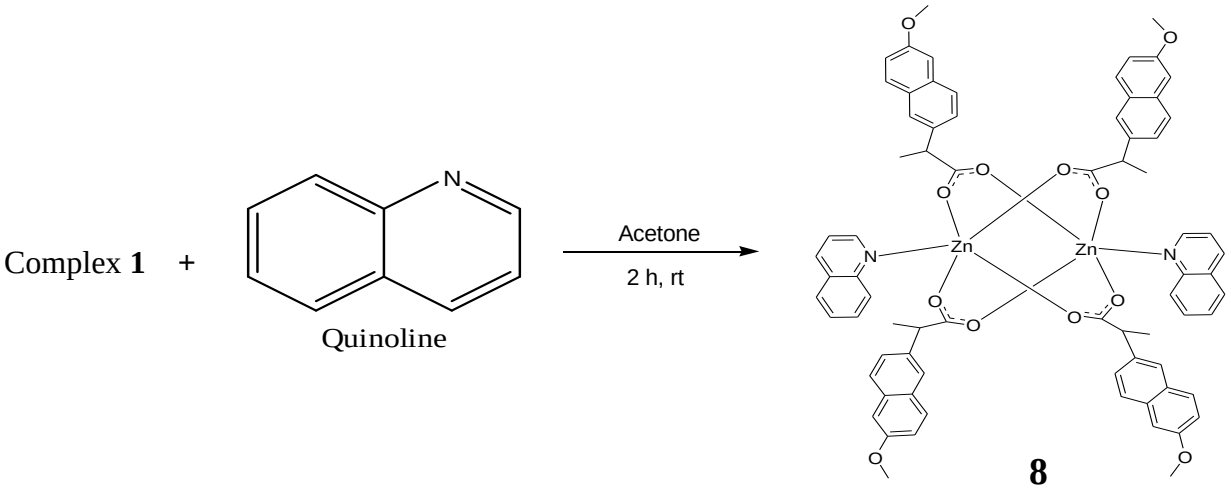
4,4-bipyridine

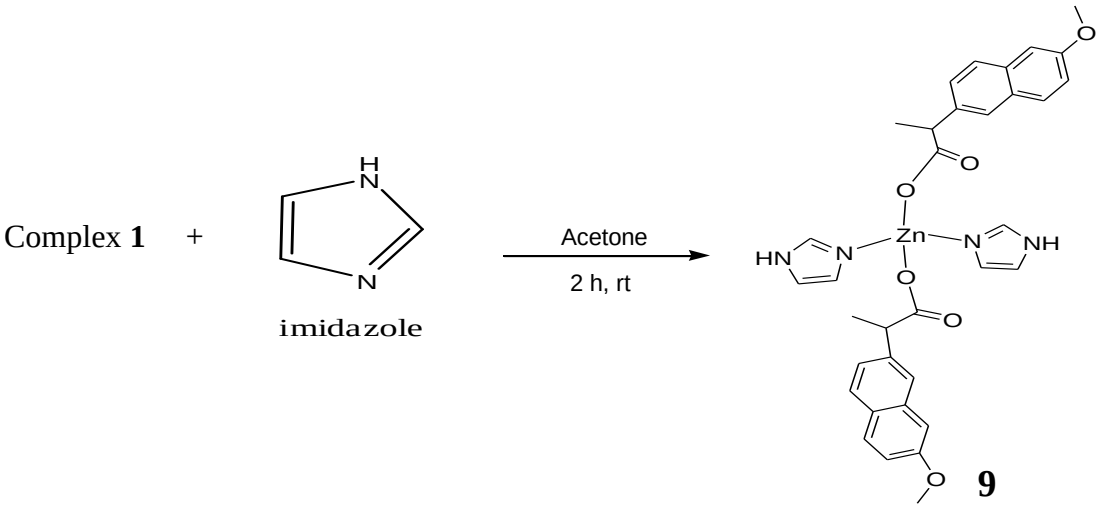
Acetone
2 h, rt

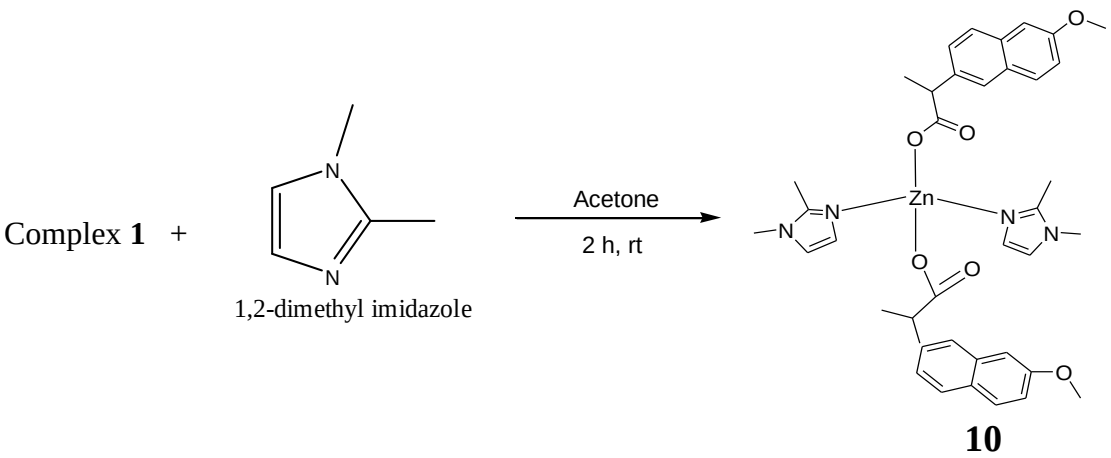


7

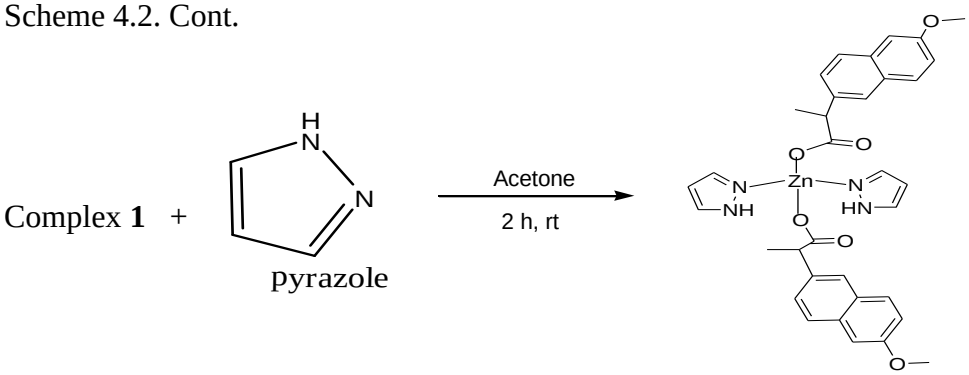
Scheme 4.2. Cont.







Scheme 4.2. Cont.



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4.2 X-ray crystallographic study of complex 3

The X-ray crystallographic analysis for complex **3** was also determined and suitable crystals were obtained from slow evaporation of a 1:1 mixture of hot acetonitrile and chloroform at room temperature. The crystal structure of complex **3** with the atomic labeling is illustrated in Figure 4.1 and a summary of selected bond lengths and bond angles are given in Table 4.2.

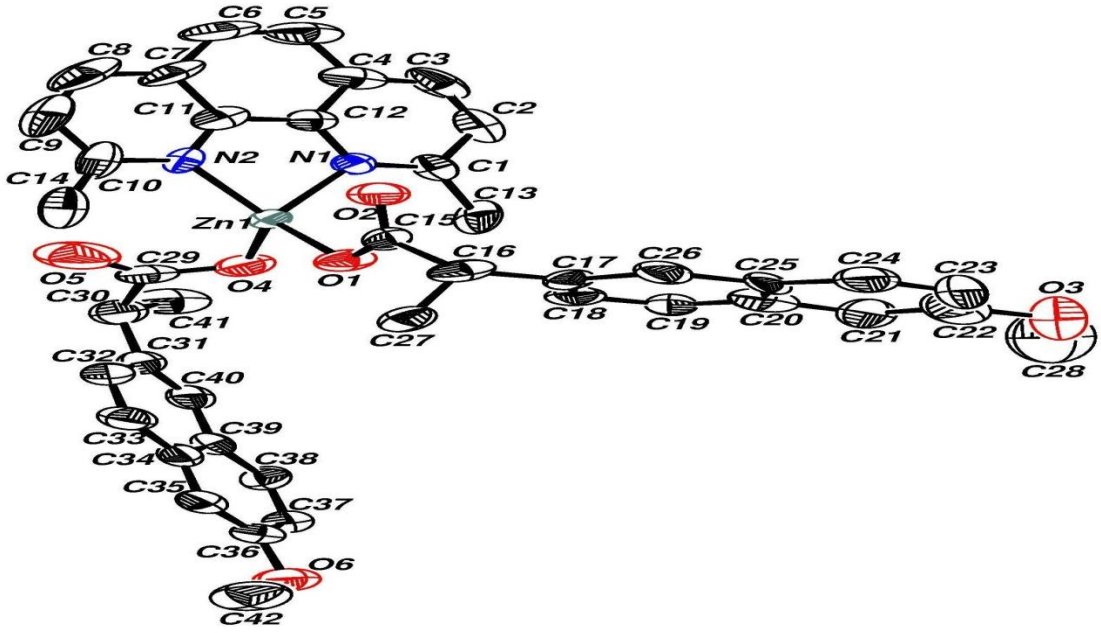

Figure 4.1. View of the molecular structure of **3** showing the atom labeling scheme.

Complex **3** crystallizes in the monoclinic space group $P_2(1)$ with four molecules in the unit cell. Zinc(II) is tetrahedrally coordinated to form ZnO_2N_2 chromophore; the Zn atom is coordinated to two monodentate oxygen atoms from naproxen ligands with $Zn\text{-}O_1$ and $Zn\text{-}O_4$ distances of 1.960(4) and 1.978(4), respectively. In the monodentate zinc benzoate complexes, zinc nitro benzoate complexes and 4-hydroxy benzoate complexes the Zn-O distances are in the range of 1.96-2.20 Å.[16,18,44]

The observed Zn-O distances of the naproxen in complex **3** were found in this range. Moreover, the Zn-O average distance is in agreement with the value of Cu-O distance of $[Cu(nap)_2(3\text{-}pym)_2]$, 1.95 Å,[58] and is lower than the value of Co-O distance, 2.096 Å of $[Co(nap)_2(py)_2(H_2O)]$.[59]

Table 4.2. Crystal data of complex **3**

Bond distance (Å)			
Zn(1)-N(1)	2.100(5)	C(1)-N(1)	1.323(8)
Zn(1)-N(2)	2.044(4)	C(15)-O(1)	1.233(7)
Zn(1)-O(1)	1.960(4)	C(15)-O(2)	1.250(7)
Zn(1)-O(4)	1.978(4)	C(29)-O(5)	1.192(9)
C(11)-N(2)	1.348(9)	C(29)-O(4)	1.258(8)
C(10)-N(2	1.345(8)	C(15)-C(16)	1.562(8)
C(12)-N(1)	1.334(7)	C(29)-C(30)	1.549(9)
Bond angle (^{o})			
O(1)-Zn(1)-N(1)	119.32(19)	O(4)-Zn(1)-N(2)	131.55(17)
O(1)-Zn(1)-N(2)	119.81(19)	C(15)-O(1)-Zn(1)	115.6(4)
N(2)-Zn(1)-N(1)	80.8(2)	C(29)-O(4)-Zn(1)	109.0(4)
O(1)-Zn(1)-O(4)	101.12(18)	O(1)-C(15)-O(2)	126.5(6)
O(4)-Zn(1)-N(1)	101.9(2)	O(5)-C(29)-O(4)	127.7(7)

The zinc atom coordinated with two nitrogen atoms from one bidentate 2,9-dmphen ligand with $Zn\text{-}N_1$ and $Zn\text{-}N_2$ distances of 2.100(5) Å and 2.044(4) Å, respectively, these bond distances are similar to the [Zn(3,5-diisopropylsalicylate)$_2$2,9-dmphen]

ligand, 2.106(2) Å and 2.059(2) Å.[41] The Zn-N_2 bond is shorter than Zn-N_1 by 0.056 Å, so the Zn-N_1 is weakly coordinated to Zn(II) than Zn-N_2.

The C_{15}-O_1 and C_{15}-O_2 bond distances are 1.233(7) Å and 1.250(7) Å, respectively, also C_{29}-O_5 and C_{29}-O_4 bond distances are 1.192(9) Å and 1.258(8) Å, respectively. The C_{15}-O_1 and C_{29}-O_5 bond distances are shorter than the C_{15}-O_2 and C_{29}-O_4, respectively, indicating that the monodentate linkage make the carboxylate group to be less delocalized.

The observed bond angle O_1-Zn_1-N_1 119.32(19), O_1-Zn_1-O_4 101.12 and O_4-Zn_1-N_2 131.55(17) is in agreement with the distorted tetrahedral angle, but the N_2-Zn_1-N_1 80.8(2) angle is lower than the tetrahedral angle which may be due to the steric effect of the methyl groups of 2,9-dmphen ligand that forms a five-membered ring when coordinated to the zinc atom.

4.3 Infrared Spectral results

Infrared spectral data of zinc naproxen complexes **1-11** in the 400-4000 cm^{-1} range as KBr disk are shown in Table 4.3, Table 4.4 and Table 4.5.

The medium-weak bands at 2865-2980 and 3030-3080 cm^{-1} are assigned to the aliphatic and aromatic C-H stretching frequencies, respectively.

The IR frequencies for the sodium salts of naproxen and complex **1** are given in Table 4.3 and are compared with previous literature data,[53,54,57,89,90] the asymmetric and symmetric $\upsilon(COO^-)$ stretching vibrations for sodium naproxen have been observed at 1540 and 1385 cm^{-1}, respectively, and the separation between them $\Delta\upsilon(COO^-)$ = 155 cm^{-1}. In complex **1**, $\upsilon_{as}(COO^-)$ occurs at 1600 cm^{-1} and $\upsilon_s(COO^-)$ at 1390 cm^{-1} and the

separation between them, $\Delta\upsilon(COO^-)$ = 210 cm^{-1} which is higher than the $\Delta\upsilon(COO^-)$ of sodium naproxen, also in this work and compared with copper naproxen $[Cu_2(nap)_4]$ that act as bridging bidentate ligands with $\Delta\upsilon(COO^-)$ is equal to 185 cm^{-1},[58] so complex **1**, $[Zn_2(nap)_4]$ coordinated as *syn-syn* bridging bidentate ligand.

Table 4.3. IR data of complex **1** and Na(nap) in (cm^{-1}).

Assignments	Na(nap)	$[Zn_2(nap)_4]$ (1)
$\upsilon(C\text{-}H)_{ar}$	3070	3080
$\upsilon(C\text{-}H)_{aliph}$	2959	2955
$\upsilon_{as}(COO^-)$	1540	1600
$\upsilon_s(COO^-)$	1385	1390
υ(ring) + δ(C-H)	1625,1480,1440,1360,1207,1160,1028	1630,1485,1455,1370,1210,1160,1027
υ(C-O)	1260	1260
$\Delta\upsilon(COO^-)$	155	210

In accordance with literature data $\upsilon_{Zn\text{-}O}$ stretching vibrations for complexes **1-11** were found in the 412-578 cm^{-1} range.[44,57]

The IR frequencies of complexes **2-8** are given in Table 4.4. $\upsilon_{as}(COO^-)$ for complexes **2, 3**, **4, 5** and **7** were observed at 1603, 1605, 1603, 1605 and 1604 cm^{-1}, respectively, and $\upsilon_s(COO^-)$ at 1388, 1375, 1388, 1389 and 1389 cm^{-1}, respectively. Moreover the separation between them $\Delta\upsilon(COO^-)$ = 215, 230, 215, 216 and 215 cm^{-1}, respectively, which suggest monodentately coordinated carboxylate groups to the zinc atom (Scheme 4.2), also $\Delta\upsilon(COO^-)$ of **2, 3, 4, 5** and **7** is higher than $\Delta\upsilon(COO^-)_{Na(nap)}$ (155 cm^{-1}). This result is in agreement with the crystal structure of complex **3** (Figure 4.1).

Table 4.4. IR data of complexes **2-8** in (cm^{-1}).

Assignments	2	3	4	5	6	7	8
υ_{as}(N-H)	-	-	-	3335	-	-	-
υ_{s} (N-H)	-	-	-	3211	-	-	-
υ(C-H)$_{ar}$	3056	3056	3045,3030	3057	3056	3059	3057
υ (C-H)$_{aliph}$	2969,2931	2964,2930	2975,2932	2970,2933	2966,2933	2981	2970
υ_{as}(COO^-)	1603	1605	1603	1605	1604	1604	1605
υ(ring) + δ(C-H)	1522,1483 1458	1505,1453	1484,1446 1314	1501,1452	1504,1436	1583,1504 1451	1554,1510 1459
υ_{s}(COO^-)	1388	1375	1388	1389	1390	1389	1378
υ(C-NH_2)	-	-	-	1358	-	-	-
υ(C-O)	1262	1267	1264	1267	1267	1271	1266
υ(ring)	1211,1159 1121,1061 1029	1212,1156 1121,1033	1212,1161 1121,1060	1212,1160 1120,1063 1031	1210,1161 1120,1066 1031	1212,1161 1065,1030	1234,1213 1161,1025
γ(C-H)	853,824	852,813	854,822,767	853,771	858,811	856,807	858,810,786
$\Delta\upsilon$(COO^-)	215	230	215	216	214	215	227

In the spectrum of complex **5** two bands were noticed at 3335 and 3211 cm^{-1} which are attributed to the primary NH_2 group, υ_{as}(N-H) and υ_{s}(N-H), respectively. Compared to the NH_2 stretching frequencies of 2-ampy ligand [ν_{as}(N-H) = 3447 and ν_{s}(N-H) = 3171 cm^{-1})], some shift caused by coordination to zinc was noticed.

υ_{as}(COO^-) for complexes **6** and **8** were observed at 1604 and 1605 cm^{-1} and υ_{s}(COO^-) at 1390 and 1378 cm^{-1}, respectively, and their $\Delta\upsilon$(COO^-) is 214 and 227 cm^{-1}, respectively, which is indicative of a *syn-syn* bridging coordination mode. This coordination mode is in agreement with similar unpublished zinc carboxylate complexes that act a *syn-syn* bridging coordination mode.[91]

The IR frequencies of complexes **9, 10** and **11** are given in Table 4.5 υ_{as}(COO^-) for complexes **9, 10** and **11** were observed at 1608, 1605 and 1602 cm^{-1}, respectively, and υ_{s}(COO^-) at 1390, 1376 and 1390 cm^{-1}, respectively, also $\Delta\upsilon$(COO^-) is 196, 229 and 212 cm^{-1}, respectively, which is indicative of a monodentately coordination mode.

This coordination mode is in agreement with similar zinc carboxylate complexes that act as monodentate coordination mode.[92]

In the IR spectrum of complexes **9** and **11** one broad band at 3127 and 3125 cm^{-1}, respectively, was observed which is attributed to the secondary NH bond stretching in the pyrimidine ring. Compared to the NH stretching frequencies of imidazole and pyrazole ligands (3125 and 3155 cm^{-1}), respectively, a shift caused by coordination to zinc was also noticed.

Table 4.5. Selected IR results of complexes **9-11** in (cm^{-1}).

Assignments	9	10	11
υ(N-H)	3127	-	3125
$\upsilon(C\text{-}H)_{ar}$	3055	3056	3040
$\upsilon\ (C\text{-}H)_{aliph}$	2935,2865	2966,2932	2970,2933
$\upsilon_{as}(COO^-)$	1608	1605	1602
υ(ring) + δ(C-H)	1608,1503,1586 1452	1605,1505,1461 1418	1602,1504,1481
$\upsilon_s(COO^-)$	1390	1376	1390
υ(C-N)	1342	1341	1354
υ(C-O)	1265	1264	1264
υ(ring)	1208,1160 1072,1027	1212,1157 1119,1062 1029	1212,1165 1131,1064 1026
γ(C-H)	857,814,760	853,824,747	854,809,772
$\Delta\upsilon(COO^-)$	196	229	212

The IR frequencies of all zinc complexes, **2-11** were compared with their parent ligands and other zinc complexes.[13,93-96]

4.4 UV-Vis absorption spectral results

UV-Visible absorption of all zinc complexes, **1-11** in the 200-700 nm range were performed and compared with their parent ligands but only small shift caused by coordination to zinc was observed, (Table 4.6).

The absorption bands of these metal complexes (in the 200-350 nm range) may be attributed to π-π* and n-π* transitions, however, metal to ligand charge transfer transition may occur in this range although it was difficult to assign any of them due to overlap with ligand transition. Moreover, the *d* orbital in the zinc(II) atom is completely filled; so no *d-d* transition bands have been detected in all zinc complexes.

Table 4.6. UV-Vis data of complexes **1-11.**

Complex	λ_{max}(nm)	ε_{max}(L.mol^{-1}.cm^{-1})
1	264, 274, 333	962, 923, 270
2	233,271, 292,318,333	17903, 4902, 1349, 419, 455
3	274, 298, 319,333	3400, 1531, 571, 560
4	275, 319, 334	29590, 5947, 6683
5	265,275, 320, 333	1418, 1626, 520, 500
6	264, 274,320, 333	1264, 1100, 425, 500
7	265, 321, 334	2086, 418, 503
8	264,274, 314, 334	840, 878, 358, 325
9	264, 274,320, 334	1064, 1148, 470, 491
10	264, 274,320, 335	632, 705, 350, 400
11	264, 274,320, 334	793, 775, 150, 209

4.5 ^{1}H-NMR and ^{13}C{^{1}H} NMR results

^{1}H and ^{13}C{^{1}H} NMR spectral data of complex **1** and naproxen are given in Table 4.7. Comparison of the ^{1}H NMR spectra of complex **1** and naproxen showed the absence of the O-H resonance in the spectra of **1** and slight upfield shift for the (**C**H-CH_3) resonance from 3.86 ppm to 3.70 ppm in **1** and for the (CH_3) resonance from 1.57 ppm 1.39 ppm in **1**. Again, slight upfield shift in the naproxen aromatic protons of

complex **1** have been observed. Moreover, in the $^{13}C\{^{1}H\}$ NMR spectra of complex **1** the C=O resonance was shifted downfield from 180.0 to 181.41 ppm indicating that donation of electrons from the carboxylate anion to zinc causes deshielding of the C=O group. Downfield shift for the resonance of the carbon atom adjacent to carbonyl group was also observed, i.e. **C**H-CH_3 from 45.91 to 48.37 ppm and CH_3 from 19.07 to 19.59 ppm which is also indicative of interaction of the carboxyl group with zinc, but with a small chemical shift difference.

Table 4.7. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **1** and naproxen.

^{1}H NMR for $[Zn_2(nap)_4]$(1)		**^{1}H NMR for (nap)**	**$^{13}C\{^{1}H\}$ NMR for $[Zn_2(nap)_4]$ (1)**		**$^{13}C\{^{1}H\}$ for NMR(nap)**
(d, 3H, CH_3)	1.39	1.57	(CH_3)	19.59	19.07
(bs, 1H, **CH**-CH_3)	3.70	3.86	(**C**H-CH_3)	48.37	45.91
(s, 3H, OCH_3)	3.90	3.87	(O-CH_3)	55.44	55.26
(bs, 1H, CH)	7.00	7.08	(CH)	105.70	105.4
(d, 1H, CH, ^{3}J= 8.4Hz)	7.08	7.12	(CH)	118.82	118.60
(bs, 1H, CH)	7.42	7.40	(CH)	125.88	126.0
(s, 1H, CH)	7.54	7.66	(CH)	126.87	126.18
(d, 1H, CH)	7.58	7.67	(CH)	127.17	127.1
(d, 1H, CH)	7.61	7.67	(CH)	129.26	128.86
		(COOH) 12.34	(CH)	133.51	133.0
			(**C**-OCH_3)	157.44	156.1
			(C=O)	181.41	180.0

The ^{1}H and $^{13}C\{^{1}H\}$ NMR data of zinc complexes **2-11** and their parent nitrogen donor ligands are given in Tables 4.8-4.17.

Table 4.8. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **2** and 1,10-phen.

^{1}H NMR for (2)		**^{1} H NMR for 1,10-phenanthroline[95]**	**$^{13}C\{^{1}H\}$ NMR for (2)**		**$^{13}C\{^{1}H\}$ NMR for 1,10- Phenanthroline[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 6.9Hz)	1.52		(CH_3)	19.58	
(bs, 4H, CH, OCH_3)	3.87		(**C**H-CH_3)	46.67	
(d, 1H, CH, $^{3}J_{H-H}$ = 3Hz)	7.02		(O-CH_3)	55.49	
(d, 1H, CH, $^{3}J_{H-H}$ = 1.5 Hz)	7.06		(CH)	105.69	
(d, 2H, CH, $^{3}J_{H-H}$ = 8.1 Hz)	7.40		(CH)	118.59	
(d, 1H, CH, $^{3}J_{H-H}$ = 8.7 Hz)	7.49		($2CH_{Phen}$)	120.96	122.90
(d, 2H, 2CH)	7.52		(CH)	125.86	
(bs, 2H, CH_{Phen})	7.60	8.20	(CH)	126.74	
(t,2H,CH_{Phen}, $^{3}J_{H-H}$ = 7.8 Hz)	7.68	7.58	(CH)	127.34	
(bs, 2H, CH_{Phen})	7.81	8.22	(CH)	129.12	
(d, 2H, CH_{Phen})	8.53	9.18	($2CH_{Phen}$)	129.44	128.46
			(CH)	133.48	
			($2CH_{Phen}$)	138.68	135.81
			($2CH_{Phen}$)	139.91	146.10
			($2CH_{Phen}$)	149.64	150.12
			(**C**-OCH_3)	157.38	

Table 4.9. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **3** and 2,9-dmphen.

^{1}H NMR for (3)		**^{1} H NMR for 2,9-dimethyl-1,10-phenanthroline[95]**	**$^{13}C\{^{1}H\}$ NMR for (3)**		**^{13} C{^{1}H} NMR for 2,9-dimethyl-1,10 phenanthroline[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 7.2 Hz)	1.49		(CH_3)	19.75	
(s, 6H, CH_{3Phen})	2.74	2.92	($2CH_{3Phen}$)	24.81	25.79
(q, 1H, CH)	3.86		(**C**H-CH_3)	47.06	
(s, 3H, OCH_3)	3.89		(O-CH_3)	55.48	
(bs, 1H, CH)	7.03		(CH)	105.70	
(d, 1H, CH, $^{3}J_{H-H}$ = 2.7 Hz)	7.06		(CH)	118.49	
(d, 2H, CH_{Phen}, $^{3}J_{H-H}$ = 2.7 Hz)	7.40	7.46	($2CH_{Phen}$)	125.70	123.44
(d, 1H, CH)	7.43		(CH)	125.81	
(d, 2H, CH_{nap}, $^{3}J_{H-H}$ = 8.7 Hz)	7.51		($2CH_{Phen}$)	126.36	125.40
(bs, 1H, CH)	7.59		(CH)	126.61	
(d, 2H, CH_{Phen}, $^{3}J_{H-H}$ = 3.9 Hz)	7.69	7.69	(CH)	127.12	
(d, 2H, CH_{Phen}, $^{3}J_{H-H}$ = 8.4 Hz)	8.17	8.10	($2C_{phen}$)	127.39	126.78
			(CH)	129.29	
			($2CH_{Phen}$)	132.12	136.23
			(CH)	133.40	
			($2CH_{Phen}$)	139.11	145.27
			(**C**-OCH_3)	157.29	
			($2CH_{Phen}$)	160.76	159.23
			(C=O)	181.87	

Table 4.10. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **4** and 2,2-bipy.

^{1}H NMR for (4)		**^{1} H NMR for 2,2-bipyridine[95]**	**$^{13}C\{^{1}H\}$ NMR for (4)**		**$^{13}C\{^{1}H\}$ NMR for 2,2-bipyridine[95]**
(d, 3H, CH_3)	1.54		(CH_3)	19.37	
(bs, 4H, CH, OCH_3)	3.90		(**C**H-CH_3)	46.46	
(bs, 1H, CH)	7.04		(O-CH_3)	55.27	
(d, 1H, CH, $^{3}J_{H-H}$ = 5.4 Hz)	7.06		(CH)	105.41	
(d, 2H, CH, $^{3}J_{H-H}$ = 4.5 Hz)	7.42		(CH)	118.31	
(t, 2H, CH_{bip} $^{3}J_{H-H}$ = 5.1 Hz)	7.51	7.12	($2CH_{bip}$)	120.63	121.00
(d, 1H, CH, $^{3}J_{H-H}$ = 5.1 Hz)	7.54		(CH)	125.69	
(bs, 2H, CH)	7.61		(CH)	126.45	
(bs, 2H, CH_{bip})	7.74	7.66	(CH)	127.22	
(bs, 1H, CH_{bip})	7.90	8.50	($2CH_{bip}$)	128.86	123.63
(bs, 2H, CH_{bip})	8.59	8.59	(CH)	129.07	
			(C)	129.30	
			(CH)	133.20	
			(CH_{bip})	138.45	136.75
			($2CH_{bip}$)	149.40	149.12
			(**C**-OCH_3)	157.10	
			(C=O)	183.73	

Table 4.11. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **5** and 2-ampy.

^{1}H NMR for (5)		**^{1} H NMR for 2-amino pyridine[95]**	**$^{13}C\{^{1}H\}$ NMR for (5)**		**$^{13}C\{^{1}H\}$ NMR for 2-amino pyridine[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 6.9 Hz)	1.52		(CH_3)	19.60	
(q, 1H, CH)	3.86		(**C**H-CH_3)	47.53	
(s, 3H, OCH_3)	3.88		(O-CH_3)	55.50	
(bs, 2H, NH_2)	5.71	4.63	(CH)	105.75	
(t, 1H, CH_{pyr}, $^{3}J_{H-H}$ = 6.3 Hz)	6.23	6.47	(CH_{pyr})	111.36	108.66
(bs, 1H, CH)	7.04		(CH_{pyr})	113.00	113.67
(d, 1H, CH, $^{3}J_{H-H}$ = 2.1 Hz)	7.07		(CH)	118.66	
(t, 1H, CH_{pyr}, $^{3}J_{H-H}$ = 6.9 Hz)	7.18	6.60	(CH)	125.96	
(d, 1H, CH)	7.42		(CH)	126.80	
(d, 1H, CH_{Pyr})	7.45	7.38	(CH)	127.36	
(d, 1H, CH, $^{3}J_{H-H}$ = 7.8 Hz)	7.55		(CH)	129.34	
(d, 1H, CH, $^{3}J_{H-H}$ = 3.9 Hz)	7.58		(CH_{pyr})	139.23	137.66
(d, 1H, CH_{pyr}, $^{3}J_{H-H}$ = 5.1 H)	7.59	8.05	(CH_{pyr})	146.17	147.98
(s, 1H, CH)	7.64		(**C**-OCH_3)	157.40	
			(C-$NH_{2\ pyr}$)	159.19	158.85
			(C=O)	181.52	

Table 4.12. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **6** and 4-pic.

^{1}H NMR for (6)		**^{1} H NMR for 4-picoline[95]**	**$^{13}C\{^{1}H\}$ NMR for (6)**		**$^{13}C\{^{1}H\}$ NMR for 4-picoline[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 6.9 Hz)	1.50		(CH)	19.52	
(s, 3H, $CH_{3\ pic}$)	2.21	2.35	(CH_{3pic})	21.38	20.89
(m,4H, OCH_3, CH)	3.89		(**C**H-CH_3)	47.32	
(d, 2H, CH_{pic})	6.81	7.10	(O-CH)	55.50	
(bs, 1H, CH)	7.02		(CH)	105.68	
(d, 1H, CH)	7.07		(CH)	118.55	
(d, 1H, CH, $^{3}J_{H-H}$ = 8.4 Hz)	7.42		(CH)	125.55	
(d, 1H, CH, $^{3}J_{H-H}$ = 10.8 Hz)	7.51		(CH_{Pic})	125.95	124.63
(d, 1H, CH, $^{3}J_{H-H}$ = 9.3 Hz)	7.54		(CH)	126.74	
(s, 1H, CH)	7.61		(CH)	127.33	
(d, 2H, $2CH_{pic}$, $^{3}J_{H-H}$ = 4.2 Hz)	8.23	8.46	(CH)	129.14	
			(C)	129.51	
			(CH)	133.48	
			(C_{Pic})	148.97	146.93
			(CH_{Pic})	150.65	149.60
			(**C**-OCH_3)	157.84	
			(C=O)	182.22	

Table 4.13. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **7** and 4,4-bipy.

^{1}H NMR for (7)		**^{1} H NMR for 4,4-bipyridine[95]**	**$^{13}C\{^{1}H\}$ NMR for (7)**		**$^{13}C\{^{1}H\}$ NMR for 4,4-bipyridine[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 6.9 Hz)	1.40		(CH_3)	20.51	
(q, 1H, CH, $^{3}J_{H-H}$ = 7.2 Hz)	3.69		(**C**H-CH_3)	46.92	
(s, 3H, OCH_3)	3.82		(O-CH_3)	55.76	
(d, 1H, CH, $^{3}J_{H-H}$ = 2.4 Hz)	7.06		(CH)	106.27	
(d,1H, CH, $^{3}J_{H-H}$ = 2.1 Hz	7.09		(CH)	119.00	
(d, 1H, CH, $^{3}J_{H-H}$ = 8.7 Hz)	7.43		($4CH_{bipy}$)	122.26	121.37
(d, 1H,CH, $^{3}J_{H-H}$ = 8.4 Hz)	7.66		(CH)	125.98	
(d, 1H, CH, $^{3}J_{H-H}$ = 9.9 Hz)	7.69		(CH)	126.97	
(s, 1H,CH)	7.68		(CH)	127.73	
(dd, 2H, CH_{bipy}, $^{3}J_{H-H}$ = 4.8 Hz, $^{4}J_{H-H}$ = 1.5Hz)	7.79	7.53	(CH)	129.10	
(d,2H, CH_{bipy}, $^{3}J_{H-H}$ = 5.7 Hz)	8.69	8.74	(C)	129.68	
			(CH)	133.56	
			($2C_{bipy}$)	145.36	145.42
			($4CH_{bipy}$)	151.04	150.66
			(**C**-OCH_3)	157.44	
			(C=O)	180.24	

Table 4.14. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **8** and quin.

^{1}H NMR for (8)		**^{1}H NMR for quinoline[95]**	**$^{13}C\{^{1}H\}$ NMR for (8)**		**$^{13}C\{^{1}H\}$ NMR for quinoline[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 7.2 Hz)	1.38		(CH_3)	20.56	
(q, 1H, CH, $^{3}J_{H-H}$ = 6.9 Hz)	3.66		(**C**H-CH_3)	46.92	
(s, 3H, OCH_3)	3.83		(O-CH_3)	55.77	
(d, 1H, CH, $^{3}J_{H-H}$ = 2.7 Hz)	7.07		(CH)	106.29	
(d, 1H, CH, $^{3}J_{H-H}$ = 2.4 Hz)	7.10		(CH)	119.00	
(d, 1H, CH, $^{3}J_{H-H}$ = 8.4 Hz)	7.42		(CH_{Chin})	122.18	120.95
(t, 1H, CH_{Chin}, $^{3}J_{H-H}$ = 4.2 Hz)	7.52	7.39	(CH)	125.30	
(s, 1H, CH)	7.54		(CH)	126.95	
(d, 1H, CH, $^{3}J_{H-H}$ = 7.5 Hz)	7.62		(CH)	127.30	
(s, 1H, CH)	7.68		(CH_{Chin})	127.76	126.43
(t, 1H, CH_{Chin}, $^{3}J_{H-H}$ = 9.6 Hz)	7.72	7.55	(CH_{Chin})	128.81	127.72
(d, 1H, CH_{Chin})	7.76	7.72	(CH)	129.11	
(t, 1H, CH_{Chin}, $^{3}J_{H-H}$ = 8.1 Hz)	7.99	7.82	(C)	129.68	
(d, 1H, CH_{Chin}, $^{3}J_{H-H}$ = 8.4 Hz)	8.03	8.12	($2CH_{Chin}$)	130.27	129.35
(d, 1H, CH_{Chin}, $^{3}J_{H-H}$ = 8.1 Hz)	8.37	8.15	(CH)	133.54	
(d, 1H, CH_{Chin})	8.90	8.92	(CH_{Chin})	136.92	135.90
			(CH_{Chin})	151.30	150.26
			(**C**-OCH_3)	157.44	
			(C=O)	180.06	

Table 4.15. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **9** and imid.

^{1}H NMR for (9)		**^{1}H NMR for imidazole[95]**	**$^{13}C\{^{1}H\}$ NMR for (9)**		**$^{13}C\{^{1}H\}$ NMR for imidazole[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 6.9Hz)	1.44		(CH_3)	20.36	
(q, 1H, CH, $^{3}J_{H-H}$ = 6.9 Hz)	3.74		(**C**H-CH_3)	47.04	
(s, 3H, OCH_3)	3.83		(O-CH_3)	55.76	
(d, 1H, CH, $^{3}J_{H-H}$ = 8.4 Hz and 2H, CH_{Imid})	7.10	7.13	(CH)	106.32	
(s, 1H, CH)	7.23		(CH)	119.08	
(d, 1H, CH, $^{3}J_{H-H}$ = 8.7 Hz)	7.46		(CH)	125.97	
(bs, 2H, 2CH and CH_{Imid})	7.69		(CH)	127.13	
(d, 1H, CH, $^{3}J_{H-H}$ = 12 Hz)	7.71		(CH)	127.54	
(bs, 1H, NH_{Imid})	8.02	7.73	(CH)	129.15	
			(CH_{Imid})	129.69	121.88
			(CH)	133.63	
			(CH_{Imid})	139.32	135.35
			(**C**-OCH_3)	157.51	
			(C=O)	178.93	

Table 4.16. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **10** and 1,2-dmimid.

^{1}H NMR for (10)		**^{1}H NMR for 1,2-dimethyl imidazole[95]**	**$^{13}C\{^{1}H\}$ NMR for (10)**		**$^{13}C\{^{1}H\}$ NMR for 1,2-dimethyl imidazole[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 7.2 Hz)	1.50		(CH_{3Imid})	11.70	12.77
(s, 3H, $CH_{3\ Imid}$)	2.01	2.35	(CH_3)	19.83	
(s, 3H, CH_{3Imid})	3.23	3.54	(N-CH_{3Imid})	33.21	32.67
(q, 1H, CH	3.83		(**C**H-CH_3)	47.83	
(s, 3H, OCH_3)	3.87		(O-CH_3)	55.49	
(bs, 1H, CH_{Imid})	6.53	6.77	(CH)	105.66	
(bs, 1H, CH_{Imid})	6.83	6.86	(CH)	118.33	
(s, 1H, CH)	7.03		(CH_{Imid})	120.37	120.36
(d, 1H, CH, $^{3}J_{H-H}$ = 2.4 Hz)	7.05		(CH)	125.84	
(d, 1H, CH)	7.49		(CH)	126.35	
(d, 1H, CH, $^{3}J_{H-H}$ = 6 Hz)	7.51		(CH)	127.74	
(d, 1H, CH, $^{3}J_{H-H}$ = 9.3 Hz)	7.56		(CH)	129.17	
(s, 1H, CH)	7.65		(CH_{Imid})	129.45	126.79
			(CH)	133.28	
			(C_{Imid})	146.67	144.80
			(**C**-OCH_3)	157.20	
			(C=O)	180.54	

Table 4.17. ^{1}H and $^{13}C\{^{1}H\}$ NMR data for complex **11** and pyrazole.

^{1}H NMR for (11)		**^{1} H NMR for pyrazole[95]**	**$^{13}C\{^{1}H\}$ NMR for (11)**		**$^{13}C\{^{1}H\}$ NMR for pyrazole[95]**
(d, 3H, CH_3, $^{3}J_{H-H}$ = 6.9 Hz)	1.43		(CH_3)	19.99	
(q, 1H, CH, $^{3}J_{H-H}$ = 6.9 Hz)	3.77		(**C**H-CH_3)	46.37	
(s, 3H, OCH_3)	3.84		(O-CH_3)	55.80	
(bs, 1H, $CH_{Pyrazole}$)	6.26	6.10	($CH_{Pyrazole}$)	105.04	104.81
(d, 1H, CH, $^{3}J_{H-H}$= 2.4 Hz)	7.10		(CH)	106.33	
(d, 1H, CH, $^{3}J_{H-H}$ =2.7 Hz)	7.13		(CH)	119.22	
(d, 1H, CH, $^{3}J_{H-H}$ = 8.4 Hz)	7.43		(CH)	126.09	
(s, 1H, CH)	7.62		(CH)	127.28	
(d, 1H, CH, $^{3}J_{H-H}$ = 3.6 Hz)	7.70		(CH)	127.38	
(d, 1H, CH, $^{3}J_{H-H}$ = 6.3 Hz)	7.71		(CH)	129.11	
(d, 2H, $2CH_{pyrazole}$, $^{3}J_{H-H}$ = 1.8 Hz)	7.73	7.74	($2CH_{Pyrazole}$)	129.74	133.59
(s, 1H, CH)	7.75		(CH)	133.75	
			(**C**-OCH_3)	157.62	

As shown from the previous NMR data presented in Tables 4.8- 4.17 slight shifts in the ^{1}H and ^{13}C resonances were noticed upon complexation.

The structure of complexes **2, 3, 4, 6, 7** and **8** might be suggested from the integration of the ^{1}H NMR signals, of the proton adjacent to carbonyl group, i.e. C**H**-CH_3 in naproxen and the proton adjacent to nitrogen atom in pyridine and pyrimidine rings, since the ratio between naproxen and nitrogen based ligands is 2:1. However in complexes **5, 9, 10** and **11** the ratio between naproxen and nitrogen based ligands is 2:2. Also the proposed structures were determined by comparison with similar published and unpublished various spectroscopic data.[52, 91]

In all complexes and their parent ligands the ortho and para hydrogen atoms and carbon atoms of the pyridine or pyrimidine rings in ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR are downfield shifted due to the higher electronegativity of the nitrogen atom.[97]

4.6 *In-vitro* anti-bacterial activity results

Zinc naproxen complexes **1-11** were tested for their anti-bacterial activity against G^{+} bacteria *(S. aureus* and *M. luteus)* and G^{-} bacteria *(K. pneumoniae, P. mirabilis, P. aeruginosa* and *E. coli).* These complexes were tested *in-vitro* using the agar well diffusion method, using a concentration of (8.5 mmol/L) in DMSO. The values of anti-bacterial activity are the average of three trials and are stated as average ± standard deviation. The anti-bacterial screening data were summarized in Table 4.18 using a DMSO as a negative control.

Table 4.18. Anti-bacterial activity data of complexes **1-11** in (mm).

Complex	*M. luteus* (G^+)	*S. aureus* (G^+)	*P. aeruginosa* (G^-)	*E. coli* (G^-)	*K. pneumoniae* (G^-)	*P. mirabilis* (G^-)
(1)	----------	----------	----------	10.0 ± 1.0	10.0 ± 1.0	8.0 ± 0.6
(2)	16.0 ± 2.1	16.0 ± 1.1	19.0 ± 1.1	20.0 ± 2.1	20.0 ± 2.5	21.0 ± 1.0
(3)	20.0 ± 1.5	20.0 ± 1.0	----------	7.7 ± 1.2	11.0 ± 1.2	----------
(4)	----------	----------	----------	10.3 ± 0.6	7.7 ± 0.6	----------
(5)	12.3 ± 1.2	12.3 ± 0.6	----------	----------	----------	----------
(6)	12.7 ± 1.5	9.7 ± 2.1	----------	----------	----------	----------
(7)	----------	----------	----------	10.3 ± 0.6	9.7 ± 0.6	----------
(8)	----------	----------	----------	----------	----------	----------
(9)	----------	----------	----------	9.7 ± 0.6	9.7 ± 0.6	----------
(10)	8.7 ± 0.6	8.3 ± 1.2	----------	----------	----------	----------
(11)	----------	7.3 ± 0.6	----------	10.3 ± 0.6	9.7 ± 0.6	----------

Complex **1** showed low anti-bacterial activity with inhibition zone 8-10 mm for *P. mirabilis, E. coli* and *K. pneumoniae*. Complex **2** showed higher anti-bacterial activity against all tested bacterial species with inhibition zone 16-21 mm. Complex **3** showed higher anti-bacterial activity against G^+ bacterial (*M. luteus* and *S. aereus*) with inhibition zone 20 mm, but showed lower anti-bacterial activity against G^- bacteria (*E. coli* and *K. pneumonia)* with inhibition zone 8-11 mm. The complexes **4, 7** and **9** showed low anti-bacterial activity against G^- bacteria (*E. coli* and *K. pneumonia)* with inhibition zone 8-10 mm, however, the anti-bacterial activity against G^+ and *P. areuginosa* was negative. Complexes **5, 6** and **10** showed intermediate anti-bacterial activity against G^+ bacteria (*M. luteus* and *S. aureus)* with inhibition zone of 8-12 mm, whereas complexes **5, 6** and **10** where not active against G^- bacteria. Complex **11** demonstrated lower anti-bacterial activity against G^- bacteria with inhibition zone of 10 mm and inhibition zone of 7 mm against *S. aureus*. Complex **8** was not active

against all tested bacteria. Moreover, *P.aeruginosa* is a G^- bacteria but it does not show sensitivity to the compounds as seen in other G^- bacteria. This might be due to its ability to metabolize several inorganic and organic compounds. It has been shown that *Pseudomonas* species can also metabolize xenobiotics. The relative resistance of *P.aeruginosa* to the compounds that show anti-bacterial activity against other G^- cells (like compound **1, 3, 4, 7, 9** and **11**) could be explained in these terms, rather than on the basis of the cell wall structure.[98]

Due to the higher anti-bacterial activity for complexes **2, 3** and **5** they were chosen and tested with their parent nitrogen donor ligands against all tested bacterial species to determine the effect of the complexation on anti-bacterial activity. Different dilutions of these complexes and their parent ligands in DMSO in the 8.50-2.12 mmol/L range were prepared using the same procedure, but in this part the complexes and their parent ligands were tested in the same plate and in the same conditions. The anti-bacterial data were summarized in Tables 4.19-4.21.

Table 4.19. Anti-bacterial activity data of complex (**2**) and 1,10-phenan ligand.

Concentration	***M. luteus*** **(G^+)**	***S. aureus*** **(G^+)**	***P. aeruginosa*** **(G^-)**	***E. coli*** **(G^-)**	***K. pneumoniae*** **(G^-)**	***P. mirabilis*** **(G^-)**
Diameter of inhibition zone of Complex **(2)** (mm)						
8.50 mmol/L	16.0	16.0	19.0	20.0	20.0	21.0
4.25 mmol/L	13.0	14.0	14.0	16.0	17.0	16.0
2.12 mmol/L	9.0	10.0	12.0	14.0	14.0	14.0
Diameter of inhibition zone of 1,10-phenanthroline ligand (mm)						
8.50 mmol/L	29.0	30.0	8.0	27.0	25.0	30.0
4.25 mmol/L	25.0	24.0	7.0	23.0	20.0	24.0
2.12 mmol/L	17.0	17.0	----------	18.0	15.0	17.0

Table 4.20. Anti-bacterial activity data of complex (**3**) and 2,9-dmphen ligand.

Concentration	*M. luteus* (G^+)	*S. aureus* (G^+)	*P. aeruginosa* (G^-)	*E. coli* (G^-)	*K. pneumoniae* (G^-)	*P. mirabilis* (G^-)
Diameter of inhibition zone of Complex **(3)** (mm)						
8.50 mmol/L	20.0	20.0	-------	7.7	11.0	--------
4.25 mmol/L	18.0	18.0	-------	7.7	11.0	--------
2.12 mmol/L	17.0	16.0	-------	7.0	10.0	-------
Diameter of inhibition zone of 2,9-dimethyl-1,10-phenanthroline ligand (mm)						
8.50 mmol/L	21.0	24.0	--------	--------	8.0	-------
4.25 mmol/L	19.0	21.0	--------	--------	7.0	-------
2.12 mmol/L	12.0	19.0	--------	--------	------	-------

Table 4.21. Anti-bacterial activity data of complex (**5**) and 2-ampy ligand.

Concentration	*M. luteus* (G^+)	*S. aureus* (G^+)	*P. aeruginosa* (G^-)	*E. coli* (G^-)	*K. pneumoniae* (G^-)	*P. mirabilis* (G^-)
Diameter of inhibition zone of Complex **(5)** (mm)						
8.50 mmol/L	12.0	12.0	----------	---------	----------	----------
4.25 mmol/L	10.0	10.0	----------	----------	---------	----------
2.12 mmol/L	9.0	8.0	----------	----------	----------	----------
Diameter of inhibition zone of 2-amino pyridine ligand (mm)						
8.50 mmol/L	------	-------	---------	----------	----------	----------
4.25 mmol/L	------	-------	--------	--------	----------	--------
2.12 mmol/L	------	--------	----------	---------	----------	---------

As shown in Table 4.19 the anti-bacterial activity of 1,10-phenanthroline ligand showed higher anti-bacterial activity than complex **2** against all tested bacterial species, indicating that the complexation of the ligand 1,10-phenanthroline with zinc naproxen decreased the anti-bacterial activity.

The results presented in Table 4.20 for complex **3** showed higher anti-bacterial activity against G^+ bacteria (*S. aureus* and *M. luteus),* but showed lower anti-bacterial activity against G^- bacteria (*K. pneumoniae* and *E. coli).* The 2,9-dimethyl-1,10-phenanthroline ligand showed higher anti-bacterial activity than complex **3** against G^+

bacteria and did not show anti-bacterial activity against *P. aeruginosa.* On the other hand, it showed lower anti-bacterial activity than complex **3** against G^- bacteria (*K. pneumoniae)* and did not show anti-bacterial activity against *E. coli* and *P. mirabilis.*

The results in Table 4.21 for complex **5** showed higher anti-bacterial activities against G^+ bacteria *(M. luteus* and *S. aureus)* and did not show anti-bacterial activity against *P. mirabilis* and all G^- bacteria, this is may be due to the difference in the wall structure of G^+ and G^-. 2-Amino pyridine ligand did not show anti-bacterial activity against all tested bacterial species. So we concluded that the complexation of the ligand 2-amino pyridine with zinc naproxen increased the anti-bacterial activity.

The minimum inhibition concentration (MIC), the lowest concentration which was capable of stopping the bacterial growth was determined for complexes **2, 3, 5** and their parent ligands. Sequential dilutions of these complexes were prepared in DMSO with 5-fold decreasing concentration, and were tested against all tested bacterial species. The results are summarized in Table 4.22.

Table 4.22. Minimum inhibition concentration (MIC) of complex **2, 3, 5** and their parent ligands against G^+ and G^- bacteria.

Minimum inhibition concentration (MIC) (mmol/L)						
Compound	***M. luteus*** **(G^+)**	***S. aureus*** **(G^+)**	***P. aeruginosa*** **(G^-)**	***E. coli*** **(G^-)**	***K. pneumoniae*** **(G^-)**	***P. mirabilis*** **(G^-)**
(2)	2.12	1.06	2.12	0.265	1.06	1.06
(3)	0.531	0.265	> 8.50	1.06	0.265	> 8.50
(5)	0.531	1.06	> 8.50	> 8.50	> 8.50	> 8.50
1,10-phenan	0.531	1.06	4.25	0.531	0.531	0.531
2,9-dmphen	2.12	0.265	> 8.50	> 8.50	4.25	> 8.50
2-amino pyridine	> 8.50	> 8.50	> 8.50	> 8.50	> 8.50	> 8.50

From the results presented in Table 4.22, it can be seen that complex **2** was active against G^+ and G^- bacteria and the MIC values for complex **2** against G^+ bacteria (*M. luteus)* was 2.12 mmol/L, but against *S. aureus* was 1.06 mmol/L also the MIC values for 1,10-phenanthroline ligand against G^+ bacteria (*M. luteus* and *S. aureus*) were 0.531 and 1.06 mmol/L, respectively. On the other hand, the MIC values for complex **2** against G^- bacteria (*E. coli, P. mirabilis, P. aeruginosa* and *K. pneumoniae)* were 0.265, 1.06, 2.12 and 1.06 mmol/L, respectively. The MIC values for 1,10-phenanthroline against G^- bacteria (*E. coli, P. mirabilis* and *K. pneumoniae)* were 0.531 mmol/L, but against *P. aeruginosa* was 4.25 mmol/L. From the MIC results, 1,10-phenanthroline ligand has lower MIC values than complex **2** against G^+ and G^- bacteria for all bacterial species except *E. coli* and *P. aeruginosa* . So we can conclude that the complexation with zinc naproxen decreased the anti-bacterial activity.

Complex **3** was active against G^+ and G^- bacteria and the MIC values against G^+ bacteria (*M. luteus* and *S. aureus)* were 0.531 and 0.265 mmol/L, respectively. The MIC values for 2,9-dimethyl-1,10-phenanthroline ligand against G^+ bacteria (*M. luteus* and *S. aureus)* were 2.12 and 0.265 mmol/L. On the other hand, the MIC values for complex **3** against G^- (*E. coli* and *K. pneumoniae)* were 1.06 and 0.265 mmol/L, respectively. The MIC values for 2,9-dimethyl-1,10-phenanthroline ligand against G^- bacteria (*K. pneumonia*e) was 4.25 mmol/L. Moreover, the complexation of zinc naproxen with 2,9-dimethyl-1,10-phenanthroline increases the anti-bacterial activity against G^- bacteria, but the MIC against G^+ are the same.

Complex **5** was active against G^+ bacteria and the MIC values against G^+ bacteria (*M. luteus* and *S. aureus)* were 0.531 and 1.06 mmol/L, respectively, and the MIC values against G^- were larger than 8.50 mmol/L.

From the above mentioned results and in some cases, the anti-bacterial potency increases upon complexation as compared to uncomplexed compounds against the tested bacterial species. It is suggested that the positive charge of the metal ion is partially shared with the donor atoms and there is electron delocalization over the whole chelate ring system having counter anions, also that chelation tends to make the ligands act as a more powerful and potent bactericidal agents, thus killing more of the bacteria than the parent ligands. It is suspected that factors, such as solubility and cell permeability mechanisms (influenced by the presence of metal ions) may be the possible reasons for the increased biological activity.[70]

The anti-bacterial activity of 1,10-phenanthroline, 2,9-dimethyl-1,10-phenanthroline and 2-amino pyridine, and their metal complexes have been studied in literature.[62,63,99-101]

5. CONCLUSION

The synthesis of eleven novel Zn(II) complexes with the non-steroidal anti-inflammatory drug naproxen in the presence of nitrogen donor ligands, $[Zn_2(nap)_4]$ **(1)**, $[Zn(nap)_2$1,10-Phen] **(2)** $[Zn(nap)_2$2,9-dmphen] **(3)**, $[Zn(nap)_2$2,2-bipy] **(4)**, $[Zn(nap)_2(2\text{-ampy})_2]$ **(5)**, $[Zn_2(nap)_4(4\text{-pic})_2]$ **(6)**, $[Zn(nap)_2$4,4-bipy$]_n$ **(7)**, $[Zn_2(nap)_4(quin)_2]$ **(8)**, $[Zn(nap)_2(imid)_2]$ **(9)**, $[Zn(nap)_2(1,2\text{-dmimid})_2]$ **(10)**, $[Zn(nap)_2(pyrazole)_2]$ **(11)** have been achieved and were fully characterized by IR, UV-Vis, ^{1}H NMR, ^{13}C{^{1}H} NMR spectroscopy. X-ray chrystallography for complex **3** was also determined, which showed a distorted tetrahedral structure with two monodentate naproxen groups and one bidentate 2,9-dmphen ligand.

The structure of other complexes could be determined by using IR, ^{1}H NMR and ^{13}C {^{1}H} NMR spectroscopic techniques. Complex **1** showed four *syn-syn* bridging bidentate naproxenate groups with two zinc atoms, complexes **2** and **4** showed two monodentate naproxenate groups and one bidentate 1,10-phenan and 2,2-bipy ligands, respectively, complexes **5, 9, 10** and **11** showed two monodentate naproxenate groups and two monodentate 2-ampy, imid, 1,2-dmimid and pyrazole ligands, respectively, complex **6** showed four *syn-syn* bridging bidentate naproxenate groups and two monodentate 4-pic ligand with two zinc atoms, complex **7** showed polynuclear structure with four monodentate naproxenate groups and two monodentate 4,4-bipy ligand with two zinc atoms, complex **8** showed four *syn-syn* bridging bidentate naproxenate groups and two monodentate quin ligand with two zinc atoms.

All complexes exhibit anti-bacterial activity against all tested bacterial species except for complex **8**. Due to their higher anti-bacterial activity, complexes **2, 3** and **5** were chosen and tested with their parent nitrogen donor ligands against all tested bacterial

species. Complex **2** showed lower anti-bacterial activity against all available bacterial species when compared to 1,10-phenanthroline ligand, so in this complex the anti-bacterial activity decreased upon complexation. Complex **3** showed higher anti-bacterial activity against G^- bacteria compared to 2,9-dimethyl-1,10-phenanthroline ligand, but this ligand showed higher anti-bacterial activity against G^+ than complex **3**. Complex **5** showed anti-bacterial activity only against G^+, and 2-amino pyridine ligand did not show anti-bacterial activity against all tested bacterial species so in this complex the anti-bacterial activity increased with complexation.

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APPENDIX

X-ray crystal data for [Zn(nap)$_2$2,9-dmphen] (**3**)

Table 1. Crystal data and structure refinement for [Zn(nap)$_2$2,9-dmphen] (3).

Empirical formula	C44 H41 N3 O6 Zn	
Formula weight	773.17	
Temperature	173(1) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 15.0063(9) Å	α= 90°.
	b = 14.1711(8) Å	β= 91.705(1)°.
	c = 17.796(1) Å	γ = 90°.
Volume	3782.7(4) Å^3	
Z	4	
Density (calculated)	1.358 Mg/m^3	
Absorption coefficient	0.703 mm^{-1}	
F(000)	1616	
Crystal size	0.28 x 0.24 x 0.17 mm^3	
Theta range for data collection	2.26 to 27.00°.	
Index ranges	-18<=h<=19, -18<=k<=18, -22<=l<=22	
Reflections collected	31490	
Independent reflections	16184 [R(int) = 0.0398]	
Completeness to theta = 27.00°	99.8 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	16184 / 1 / 963	
Goodness-of-fit on F^2	0.993	
Final R indices [I>2sigma(I)]	R1 = 0.0698, wR2 = 0.1714	
R indices (all data)	R1 = 0.0978, wR2 = 0.1878	
Absolute structure parameter	0.043(13)	
Largest diff. peak and hole	1.132 and -0.647 e.Å^{-3}	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for [Zn$(nap)_2$2,9-dmphen] (3).
U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	3870(4)	6879(5)	6498(4)	50(2)
C(2)	4167(4)	7792(5)	6705(5)	68(2)
C(3)	4153(4)	8066(5)	7412(6)	77(3)
C(4)	3870(4)	7487(6)	7953(4)	63(2)
C(5)	3822(6)	7722(8)	8724(6)	88(3)
C(6)	3534(6)	7125(9)	9217(5)	100(4)
C(7)	3258(4)	6153(7)	9041(3)	72(3)
C(8)	2957(6)	5460(11)	9522(4)	105(4)
C(9)	2709(5)	4605(9)	9286(4)	92(4)
C(10)	2757(4)	4378(6)	8519(4)	64(2)
C(11)	3294(4)	5890(5)	8282(3)	50(2)
C(12)	3602(3)	6561(4)	7737(3)	42(1)
C(13)	3855(5)	6545(6)	5693(3)	72(2)
C(14)	2507(5)	3440(6)	8221(5)	83(3)
C(15)	4634(4)	3798(5)	6843(4)	52(2)
C(16)	5319(4)	3135(5)	6462(3)	57(2)
C(17)	5777(4)	3651(5)	5833(3)	50(2)
C(18)	5288(4)	4167(5)	5271(3)	59(2)
C(19)	5690(5)	4637(5)	4690(4)	66(2)
C(20)	6554(5)	4601(5)	4601(4)	67(2)
C(21)	6984(5)	5042(6)	3937(5)	80(2)
C(22)	7846(6)	4982(7)	3893(6)	97(3)
C(23)	8389(5)	4495(7)	4409(5)	92(3)
C(24)	8022(5)	4051(7)	5038(5)	88(3)
C(25)	7089(4)	4140(6)	5125(5)	79(3)
C(26)	6684(4)	3610(6)	5791(5)	71(2)
C(27)	4880(4)	2231(5)	6180(4)	58(2)
C(28)	7818(9)	5756(12)	2787(9)	177(6)
C(29)	1517(5)	4707(5)	6264(4)	59(2)
C(30)	773(4)	4719(6)	5642(4)	68(2)
C(31)	919(4)	3872(6)	5117(4)	56(2)
C(32)	1110(4)	2977(5)	5434(4)	60(2)

C(33)	1257(5)	2201(5)	4997(3)	65(2)
C(34)	1184(4)	2283(5)	4186(3)	52(2)
C(35)	1344(5)	1480(5)	3722(4)	62(2)
C(36)	1331(5)	1607(5)	2967(4)	63(2)
C(37)	1118(4)	2497(5)	2652(3)	54(2)
C(38)	954(4)	3252(5)	3094(3)	56(2)
C(39)	1009(4)	3148(5)	3878(3)	48(2)
C(40)	858(3)	3933(5)	4360(3)	50(2)
C(41)	715(5)	5658(6)	5263(5)	86(3)
C(42)	1622(7)	-3(6)	2714(5)	99(3)
C(43)	3799(4)	2366(4)	1343(3)	40(1)
C(44)	4049(4)	1417(4)	1452(3)	48(1)
C(45)	4038(4)	1011(5)	2146(4)	56(2)
C(46)	3813(4)	1573(4)	2770(3)	47(1)
C(47)	3815(4)	1211(5)	3526(4)	55(2)
C(48)	3624(4)	1790(5)	4111(4)	55(2)
C(49)	3390(3)	2766(5)	3979(3)	44(1)
C(50)	3196(4)	3400(5)	4571(3)	50(2)
C(51)	3008(3)	4310(5)	4394(3)	44(1)
C(52)	2974(3)	4616(4)	3635(3)	39(1)
C(53)	3360(3)	3116(4)	3244(3)	35(1)
C(54)	3582(3)	2506(4)	2634(3)	38(1)
C(55)	3797(5)	2780(5)	583(3)	56(2)
C(56)	2768(4)	5623(5)	3432(4)	53(2)
C(57)	1511(4)	4449(6)	1363(4)	58(2)
C(58)	577(4)	4497(6)	989(4)	66(2)
C(59)	645(4)	5000(6)	235(4)	57(2)
C(60)	863(4)	5909(6)	202(4)	59(2)
C(61)	964(4)	6387(5)	-497(4)	60(2)
C(62)	1218(5)	7307(6)	-522(4)	71(2)
C(63)	1364(5)	7753(6)	-1191(5)	80(2)
C(64)	1236(5)	7285(5)	-1861(4)	64(2)
C(65)	971(4)	6390(6)	-1875(5)	69(2)
C(66)	820(4)	5899(5)	-1167(4)	57(2)
C(67)	560(4)	4939(6)	-1147(4)	68(2)
C(68)	482(4)	4498(6)	-462(5)	74(2)
C(69)	-105(4)	4946(7)	1496(4)	87(2)
C(70)	1307(6)	7339(7)	-3169(4)	86(2)

C(71)	4519(4)	5448(5)	1686(3)	45(1)
C(72)	5038(3)	6085(4)	1171(3)	47(1)
C(73)	6487(3)	5307(3)	538(2)	118(4)
C(74)	5569(3)	5407(3)	589(2)	84(3)
C(75)	4999(2)	4914(4)	101(3)	98(3)
C(76)	5346(2)	4320(3)	-439(3)	155(7)
C(77)	6263(2)	4220(2)	-491(2)	97(3)
C(78)	6834(2)	4713(2)	-2(2)	54(2)
C(79)	7751(2)	4613(4)	-54(3)	170(7)
C(80)	8098(3)	4019(4)	-594(3)	163(7)
C(81)	7528(3)	3526(3)	-1082(2)	78(2)
C(82)	6610(3)	3626(3)	-1030(2)	107(4)
C(83)	5572(6)	6810(7)	1642(5)	101(3)
C(84)	7564(5)	2282(6)	-1921(4)	75(2)
C(85)	8692(5)	6898(6)	10158(5)	74(2)
C(86)	8573(6)	6769(7)	9378(5)	91(3)
C(87)	9445(9)	2501(11)	6896(7)	133(5)
C(88)	10085(7)	2636(10)	7537(8)	157(6)
N(1)	3615(3)	6282(3)	7021(2)	37(1)
N(2)	3037(3)	5032(4)	8032(2)	40(1)
N(3)	3567(3)	2889(3)	1927(2)	35(1)
N(4)	3149(3)	4015(3)	3081(2)	36(1)
N(5)	8774(7)	6987(6)	10783(5)	122(3)
N(6)	8904(8)	2532(10)	6468(6)	152(4)
O(1)	3927(3)	3928(3)	6487(2)	57(1)
O(2)	4861(3)	4167(4)	7457(2)	68(1)
O(3)	8358(4)	5344(6)	3314(5)	120(2)
O(4)	2250(3)	5034(4)	6060(2)	65(1)
O(5)	1331(6)	4440(6)	6874(3)	124(3)
O(6)	1479(4)	917(4)	2441(3)	75(1)
O(7)	1720(3)	4957(4)	1910(3)	73(1)
O(8)	2047(3)	3897(4)	1112(3)	75(2)
O(9)	1409(4)	7801(4)	-2501(3)	86(2)
O(10)	3736(2)	5195(3)	1415(2)	47(1)
O(11)	4833(3)	5157(3)	2286(3)	63(1)
O(12)	7993(3)	2974(4)	-1476(3)	73(1)
Zn(1)	3142(1)	4895(1)	6894(1)	36(1)
Zn(2)	3061(1)	4260(1)	1933(1)	36(1)

Table 3. Bond lengths [Å] and angles [°] for [Zn(nap)$_2$ 2,9-dmphen] (3).

C(1)-N(1)	1.323(8)
C(1)-C(2)	1.413(10)
C(1)-C(13)	1.509(9)
C(2)-C(3)	1.317(11)
C(2)-H(2)	0.9500
C(3)-C(4)	1.344(11)
C(3)-H(3)	0.9500
C(4)-C(5)	1.415(12)
C(4)-C(12)	1.423(10)
C(5)-C(6)	1.301(14)
C(5)-H(5)	0.9500
C(6)-C(7)	1.470(15)
C(6)-H(6)	0.9500
C(7)-C(8)	1.387(15)
C(7)-C(11)	1.404(8)
C(8)-C(9)	1.332(15)
C(8)-H(8)	0.9500
C(9)-C(10)	1.406(11)
C(9)-H(9)	0.9500
C(10)-N(2)	1.345(8)
C(10)-C(14)	1.476(12)
C(11)-N(2)	1.348(9)
C(11)-C(12)	1.443(9)
C(12)-N(1)	1.334(7)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-O(1)	1.233(7)
C(15)-O(2)	1.250(7)
C(15)-C(16)	1.562(8)
C(16)-C(27)	1.518(9)
C(16)-C(17)	1.520(10)
C(16)-H(16)	1.0000

C(17)-C(26)	1.366(8)
C(17)-C(18)	1.424(9)
C(18)-C(19)	1.383(9)
C(18)-H(18)	0.9500
C(19)-C(20)	1.313(9)
C(19)-H(19)	0.9500
C(20)-C(25)	1.377(11)
C(20)-C(21)	1.499(11)
C(21)-C(22)	1.301(11)
C(21)-H(21)	0.9500
C(22)-C(23)	1.393(13)
C(22)-O(3)	1.402(11)
C(23)-C(24)	1.409(12)
C(23)-H(23)	0.9500
C(24)-C(25)	1.420(9)
C(24)-H(24)	0.9500
C(25)-C(26)	1.544(12)
C(26)-H(26)	0.9500
C(27)-H(27A)	0.9800
C(27)-H(27B)	0.9800
C(27)-H(27C)	0.9800
C(28)-O(3)	1.353(14)
C(28)-H(28A)	0.9800
C(28)-H(28B)	0.9800
C(28)-H(28C)	0.9800
C(29)-O(5)	1.192(9)
C(29)-O(4)	1.258(8)
C(29)-C(30)	1.549(9)
C(30)-C(41)	1.494(12)
C(30)-C(31)	1.542(10)
C(30)-H(30)	1.0000
C(31)-C(40)	1.350(9)
C(31)-C(32)	1.414(10)
C(32)-C(33)	1.367(10)
C(32)-H(32)	0.9500
C(33)-C(34)	1.448(8)
C(33)-H(33)	0.9500
C(34)-C(39)	1.365(9)

C(34)-C(35)	1.431(10)
C(35)-C(36)	1.355(9)
C(35)-H(35)	0.9500
C(36)-O(6)	1.377(8)
C(36)-C(37)	1.412(10)
C(37)-C(38)	1.354(9)
C(37)-H(37)	0.9500
C(38)-C(39)	1.403(8)
C(38)-H(38)	0.9500
C(39)-C(40)	1.425(9)
C(40)-H(40)	0.9500
C(41)-H(41A)	0.9800
C(41)-H(41B)	0.9800
C(41)-H(41C)	0.9800
C(42)-O(6)	1.405(10)
C(42)-H(42A)	0.9800
C(42)-H(42B)	0.9800
C(42)-H(42C)	0.9800
C(43)-N(3)	1.330(6)
C(43)-C(44)	1.409(8)
C(43)-C(55)	1.474(8)
C(44)-C(45)	1.363(9)
C(44)-H(44)	0.9500
C(45)-C(46)	1.417(9)
C(45)-H(45)	0.9500
C(46)-C(54)	1.386(8)
C(46)-C(47)	1.440(9)
C(47)-C(48)	1.363(9)
C(47)-H(47)	0.9500
C(48)-C(49)	1.444(9)
C(48)-H(48)	0.9500
C(49)-C(53)	1.399(7)
C(49)-C(50)	1.421(9)
C(50)-C(51)	1.354(9)
C(50)-H(50)	0.9500
C(51)-C(52)	1.419(8)
C(51)-H(51)	0.9500
C(52)-N(4)	1.335(7)

C(52)-C(56)	1.501(9)
C(53)-N(4)	1.342(7)
C(53)-C(54)	1.435(8)
C(54)-N(3)	1.371(7)
C(55)-H(55A)	0.9800
C(55)-H(55B)	0.9800
C(55)-H(55C)	0.9800
C(56)-H(56A)	0.9800
C(56)-H(56B)	0.9800
C(56)-H(56C)	0.9800
C(57)-O(8)	1.216(9)
C(57)-O(7)	1.244(9)
C(57)-C(58)	1.534(8)
C(58)-C(69)	1.524(10)
C(58)-C(59)	1.524(9)
C(58)-H(58)	1.0000
C(59)-C(60)	1.331(10)
C(59)-C(68)	1.444(10)
C(60)-C(61)	1.429(10)
C(60)-H(60)	0.9500
C(61)-C(62)	1.359(10)
C(61)-C(66)	1.389(10)
C(62)-C(63)	1.371(11)
C(62)-H(62)	0.9500
C(63)-C(64)	1.373(11)
C(63)-H(63)	0.9500
C(64)-C(65)	1.330(11)
C(64)-O(9)	1.384(9)
C(65)-C(66)	1.463(10)
C(65)-H(65)	0.9500
C(66)-C(67)	1.415(11)
C(67)-C(68)	1.379(10)
C(67)-H(67)	0.9500
C(68)-H(68)	0.9500
C(69)-H(69A)	0.9800
C(69)-H(69B)	0.9800
C(69)-H(69C)	0.9800
C(70)-O(9)	1.362(9)

C(70)-H(70A)	0.9800
C(70)-H(70B)	0.9800
C(70)-H(70C)	0.9800
C(71)-O(11)	1.225(7)
C(71)-O(10)	1.307(7)
C(71)-C(72)	1.518(8)
C(72)-C(83)	1.537(9)
C(72)-C(74)	1.636(7)
C(72)-H(72)	1.0000
C(73)-C(74)	1.3900
C(73)-C(78)	1.3900
C(73)-H(73)	0.9500
C(74)-C(75)	1.3900
C(75)-C(76)	1.3900
C(75)-H(75)	0.9500
C(76)-C(77)	1.3900
C(76)-H(76)	0.9500
C(77)-C(78)	1.3900
C(77)-C(82)	1.3900
C(78)-C(79)	1.3900
C(79)-C(80)	1.3900
C(79)-H(79)	0.9500
C(80)-C(81)	1.3900
C(80)-H(80)	0.9500
C(81)-O(12)	1.272(6)
C(81)-C(82)	1.3900
C(82)-H(82)	0.9500
C(83)-H(83A)	0.9800
C(83)-H(83B)	0.9800
C(83)-H(83C)	0.9800
C(84)-O(12)	1.404(8)
C(84)-H(84A)	0.9800
C(84)-H(84B)	0.9800
C(84)-H(84C)	0.9800
C(85)-N(5)	1.123(10)
C(85)-C(86)	1.407(11)
C(86)-H(86A)	0.9800
C(86)-H(86B)	0.9800

C(86)-H(86C)	0.9800
C(87)-N(6)	1.097(14)
C(87)-C(88)	1.482(16)
C(88)-H(88A)	0.9800
C(88)-H(88B)	0.9800
C(88)-H(88C)	0.9800
N(1)-Zn(1)	2.100(5)
N(2)-Zn(1)	2.044(4)
N(3)-Zn(2)	2.086(4)
N(4)-Zn(2)	2.073(4)
O(1)-Zn(1)	1.960(4)
O(4)-Zn(1)	1.978(4)
O(7)-Zn(2)	2.241(5)
O(8)-Zn(2)	2.141(5)
O(10)-Zn(2)	1.920(4)

N(1)-C(1)-C(2)	119.8(6)
N(1)-C(1)-C(13)	118.1(6)
C(2)-C(1)-C(13)	122.0(7)
C(3)-C(2)-C(1)	120.3(7)
C(3)-C(2)-H(2)	119.8
C(1)-C(2)-H(2)	119.8
C(2)-C(3)-C(4)	121.3(7)
C(2)-C(3)-H(3)	119.4
C(4)-C(3)-H(3)	119.4
C(3)-C(4)-C(5)	125.3(8)
C(3)-C(4)-C(12)	117.5(7)
C(5)-C(4)-C(12)	117.2(9)
C(6)-C(5)-C(4)	121.9(9)
C(6)-C(5)-H(5)	119.0
C(4)-C(5)-H(5)	119.0
C(5)-C(6)-C(7)	124.2(8)
C(5)-C(6)-H(6)	117.9
C(7)-C(6)-H(6)	117.9
C(8)-C(7)-C(11)	115.4(9)
C(8)-C(7)-C(6)	128.8(8)
C(11)-C(7)-C(6)	115.8(8)
C(9)-C(8)-C(7)	122.8(7)

C(9)-C(8)-H(8)	118.6
C(7)-C(8)-H(8)	118.6
C(8)-C(9)-C(10)	119.5(8)
C(8)-C(9)-H(9)	120.2
C(10)-C(9)-H(9)	120.2
N(2)-C(10)-C(9)	119.6(9)
N(2)-C(10)-C(14)	118.0(6)
C(9)-C(10)-C(14)	122.4(8)
N(2)-C(11)-C(7)	122.5(7)
N(2)-C(11)-C(12)	117.8(5)
C(7)-C(11)-C(12)	119.6(7)
N(1)-C(12)-C(4)	121.3(6)
N(1)-C(12)-C(11)	117.4(6)
C(4)-C(12)-C(11)	121.3(6)
C(1)-C(13)-H(13A)	109.5
C(1)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(1)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(10)-C(14)-H(14A)	109.5
C(10)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(10)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
O(1)-C(15)-O(2)	126.5(6)
O(1)-C(15)-C(16)	115.8(5)
O(2)-C(15)-C(16)	117.7(6)
C(27)-C(16)-C(17)	111.3(5)
C(27)-C(16)-C(15)	111.5(5)
C(17)-C(16)-C(15)	110.3(5)
C(27)-C(16)-H(16)	107.8
C(17)-C(16)-H(16)	107.8
C(15)-C(16)-H(16)	107.8
C(26)-C(17)-C(18)	118.5(7)
C(26)-C(17)-C(16)	119.5(6)
C(18)-C(17)-C(16)	122.0(5)

C(19)-C(18)-C(17)	123.0(6)
C(19)-C(18)-H(18)	118.5
C(17)-C(18)-H(18)	118.5
C(20)-C(19)-C(18)	121.7(8)
C(20)-C(19)-H(19)	119.1
C(18)-C(19)-H(19)	119.1
C(19)-C(20)-C(25)	119.7(8)
C(19)-C(20)-C(21)	121.9(7)
C(25)-C(20)-C(21)	118.4(7)
C(22)-C(21)-C(20)	118.1(8)
C(22)-C(21)-H(21)	120.9
C(20)-C(21)-H(21)	120.9
C(21)-C(22)-C(23)	123.8(10)
C(21)-C(22)-O(3)	126.0(10)
C(23)-C(22)-O(3)	110.1(8)
C(22)-C(23)-C(24)	120.6(8)
C(22)-C(23)-H(23)	119.7
C(24)-C(23)-H(23)	119.7
C(23)-C(24)-C(25)	117.2(9)
C(23)-C(24)-H(24)	121.4
C(25)-C(24)-H(24)	121.4
C(20)-C(25)-C(24)	121.6(8)
C(20)-C(25)-C(26)	121.1(6)
C(24)-C(25)-C(26)	117.0(8)
C(17)-C(26)-C(25)	115.8(7)
C(17)-C(26)-H(26)	122.1
C(25)-C(26)-H(26)	122.1
C(16)-C(27)-H(27A)	109.5
C(16)-C(27)-H(27B)	109.5
H(27A)-C(27)-H(27B)	109.5
C(16)-C(27)-H(27C)	109.5
H(27A)-C(27)-H(27C)	109.5
H(27B)-C(27)-H(27C)	109.5
O(3)-C(28)-H(28A)	109.5
O(3)-C(28)-H(28B)	109.5
H(28A)-C(28)-H(28B)	109.5
O(3)-C(28)-H(28C)	109.5
H(28A)-C(28)-H(28C)	109.5

H(28B)-C(28)-H(28C)	109.5
O(5)-C(29)-O(4)	127.7(7)
O(5)-C(29)-C(30)	118.1(7)
O(4)-C(29)-C(30)	114.1(6)
C(41)-C(30)-C(31)	115.3(6)
C(41)-C(30)-C(29)	111.3(6)
C(31)-C(30)-C(29)	108.2(6)
C(41)-C(30)-H(30)	107.2
C(31)-C(30)-H(30)	107.2
C(29)-C(30)-H(30)	107.2
C(40)-C(31)-C(32)	117.5(6)
C(40)-C(31)-C(30)	123.3(7)
C(32)-C(31)-C(30)	119.2(6)
C(33)-C(32)-C(31)	121.9(6)
C(33)-C(32)-H(32)	119.1
C(31)-C(32)-H(32)	119.1
C(32)-C(33)-C(34)	119.6(7)
C(32)-C(33)-H(33)	120.2
C(34)-C(33)-H(33)	120.2
C(39)-C(34)-C(35)	121.1(6)
C(39)-C(34)-C(33)	118.7(6)
C(35)-C(34)-C(33)	120.2(6)
C(36)-C(35)-C(34)	117.9(7)
C(36)-C(35)-H(35)	121.0
C(34)-C(35)-H(35)	121.0
C(35)-C(36)-O(6)	125.5(7)
C(35)-C(36)-C(37)	120.6(7)
O(6)-C(36)-C(37)	113.8(6)
C(38)-C(37)-C(36)	121.1(6)
C(38)-C(37)-H(37)	119.4
C(36)-C(37)-H(37)	119.4
C(37)-C(38)-C(39)	119.3(7)
C(37)-C(38)-H(38)	120.4
C(39)-C(38)-H(38)	120.4
C(34)-C(39)-C(38)	119.9(6)
C(34)-C(39)-C(40)	119.4(6)
C(38)-C(39)-C(40)	120.7(6)
C(31)-C(40)-C(39)	122.8(6)

C(31)-C(40)-H(40)	118.6
C(39)-C(40)-H(40)	118.6
C(30)-C(41)-H(41A)	109.5
C(30)-C(41)-H(41B)	109.5
H(41A)-C(41)-H(41B)	109.5
C(30)-C(41)-H(41C)	109.5
H(41A)-C(41)-H(41C)	109.5
H(41B)-C(41)-H(41C)	109.5
O(6)-C(42)-H(42A)	109.5
O(6)-C(42)-H(42B)	109.5
H(42A)-C(42)-H(42B)	109.5
O(6)-C(42)-H(42C)	109.5
H(42A)-C(42)-H(42C)	109.5
H(42B)-C(42)-H(42C)	109.5
N(3)-C(43)-C(44)	120.0(5)
N(3)-C(43)-C(55)	120.1(5)
C(44)-C(43)-C(55)	120.0(5)
C(45)-C(44)-C(43)	121.2(6)
C(45)-C(44)-H(44)	119.4
C(43)-C(44)-H(44)	119.4
C(44)-C(45)-C(46)	118.9(6)
C(44)-C(45)-H(45)	120.6
C(46)-C(45)-H(45)	120.6
C(54)-C(46)-C(45)	117.6(6)
C(54)-C(46)-C(47)	119.8(6)
C(45)-C(46)-C(47)	122.6(6)
C(48)-C(47)-C(46)	120.3(6)
C(48)-C(47)-H(47)	119.8
C(46)-C(47)-H(47)	119.8
C(47)-C(48)-C(49)	120.5(6)
C(47)-C(48)-H(48)	119.7
C(49)-C(48)-H(48)	119.7
C(53)-C(49)-C(50)	117.8(6)
C(53)-C(49)-C(48)	119.6(6)
C(50)-C(49)-C(48)	122.6(6)
C(51)-C(50)-C(49)	118.4(5)
C(51)-C(50)-H(50)	120.8
C(49)-C(50)-H(50)	120.8

C(50)-C(51)-C(52)	120.9(5)
C(50)-C(51)-H(51)	119.5
C(52)-C(51)-H(51)	119.5
N(4)-C(52)-C(51)	120.4(5)
N(4)-C(52)-C(56)	118.2(5)
C(51)-C(52)-C(56)	121.5(5)
N(4)-C(53)-C(49)	122.7(5)
N(4)-C(53)-C(54)	117.9(5)
C(49)-C(53)-C(54)	119.5(5)
N(3)-C(54)-C(46)	122.4(5)
N(3)-C(54)-C(53)	117.3(5)
C(46)-C(54)-C(53)	120.3(5)
C(43)-C(55)-H(55A)	109.5
C(43)-C(55)-H(55B)	109.5
H(55A)-C(55)-H(55B)	109.5
C(43)-C(55)-H(55C)	109.5
H(55A)-C(55)-H(55C)	109.5
H(55B)-C(55)-H(55C)	109.5
C(52)-C(56)-H(56A)	109.5
C(52)-C(56)-H(56B)	109.5
H(56A)-C(56)-H(56B)	109.5
C(52)-C(56)-H(56C)	109.5
H(56A)-C(56)-H(56C)	109.5
H(56B)-C(56)-H(56C)	109.5
O(8)-C(57)-O(7)	120.3(6)
O(8)-C(57)-C(58)	118.4(7)
O(7)-C(57)-C(58)	121.3(7)
C(69)-C(58)-C(59)	112.9(6)
C(69)-C(58)-C(57)	112.5(6)
C(59)-C(58)-C(57)	108.6(5)
C(69)-C(58)-H(58)	107.5
C(59)-C(58)-H(58)	107.5
C(57)-C(58)-H(58)	107.5
C(60)-C(59)-C(68)	118.2(7)
C(60)-C(59)-C(58)	121.0(7)
C(68)-C(59)-C(58)	120.8(7)
C(59)-C(60)-C(61)	122.1(7)
C(59)-C(60)-H(60)	119.0

C(61)-C(60)-H(60)	119.0
C(62)-C(61)-C(66)	119.1(7)
C(62)-C(61)-C(60)	121.4(7)
C(66)-C(61)-C(60)	119.5(7)
C(61)-C(62)-C(63)	121.5(8)
C(61)-C(62)-H(62)	119.2
C(63)-C(62)-H(62)	119.2
C(62)-C(63)-C(64)	120.6(8)
C(62)-C(63)-H(63)	119.7
C(64)-C(63)-H(63)	119.7
C(65)-C(64)-C(63)	120.7(8)
C(65)-C(64)-O(9)	123.5(8)
C(63)-C(64)-O(9)	115.8(7)
C(64)-C(65)-C(66)	119.4(8)
C(64)-C(65)-H(65)	120.3
C(66)-C(65)-H(65)	120.3
C(61)-C(66)-C(67)	119.6(7)
C(61)-C(66)-C(65)	118.5(7)
C(67)-C(66)-C(65)	121.8(7)
C(68)-C(67)-C(66)	119.2(7)
C(68)-C(67)-H(67)	120.4
C(66)-C(67)-H(67)	120.4
C(67)-C(68)-C(59)	121.4(7)
C(67)-C(68)-H(68)	119.3
C(59)-C(68)-H(68)	119.3
C(58)-C(69)-H(69A)	109.5
C(58)-C(69)-H(69B)	109.5
H(69A)-C(69)-H(69B)	109.5
C(58)-C(69)-H(69C)	109.5
H(69A)-C(69)-H(69C)	109.5
H(69B)-C(69)-H(69C)	109.5
O(9)-C(70)-H(70A)	109.5
O(9)-C(70)-H(70B)	109.5
H(70A)-C(70)-H(70B)	109.5
O(9)-C(70)-H(70C)	109.5
H(70A)-C(70)-H(70C)	109.5
H(70B)-C(70)-H(70C)	109.5
O(11)-C(71)-O(10)	123.2(6)

O(11)-C(71)-C(72)	122.3(5)
O(10)-C(71)-C(72)	114.3(5)
C(71)-C(72)-C(83)	109.7(5)
C(71)-C(72)-C(74)	107.6(4)
C(83)-C(72)-C(74)	118.8(6)
C(71)-C(72)-H(72)	106.7
C(83)-C(72)-H(72)	106.7
C(74)-C(72)-H(72)	106.7
C(74)-C(73)-C(78)	120.0
C(74)-C(73)-H(73)	120.0
C(78)-C(73)-H(73)	120.0
C(73)-C(74)-C(75)	120.0
C(73)-C(74)-C(72)	127.2(3)
C(75)-C(74)-C(72)	112.8(3)
C(76)-C(75)-C(74)	120.0
C(76)-C(75)-H(75)	120.0
C(74)-C(75)-H(75)	120.0
C(75)-C(76)-C(77)	120.0
C(75)-C(76)-H(76)	120.0
C(77)-C(76)-H(76)	120.0
C(78)-C(77)-C(76)	120.0
C(78)-C(77)-C(82)	120.0
C(76)-C(77)-C(82)	120.0
C(79)-C(78)-C(77)	120.0
C(79)-C(78)-C(73)	120.0
C(77)-C(78)-C(73)	120.0
C(80)-C(79)-C(78)	120.0
C(80)-C(79)-H(79)	120.0
C(78)-C(79)-H(79)	120.0
C(81)-C(80)-C(79)	120.0
C(81)-C(80)-H(80)	120.0
C(79)-C(80)-H(80)	120.0
O(12)-C(81)-C(80)	108.4(4)
O(12)-C(81)-C(82)	131.3(4)
C(80)-C(81)-C(82)	120.0
C(81)-C(82)-C(77)	120.0
C(81)-C(82)-H(82)	120.0
C(77)-C(82)-H(82)	120.0

C(72)-C(83)-H(83A)	109.5
C(72)-C(83)-H(83B)	109.5
H(83A)-C(83)-H(83B)	109.5
C(72)-C(83)-H(83C)	109.5
H(83A)-C(83)-H(83C)	109.5
H(83B)-C(83)-H(83C)	109.5
O(12)-C(84)-H(84A)	109.5
O(12)-C(84)-H(84B)	109.5
H(84A)-C(84)-H(84B)	109.5
O(12)-C(84)-H(84C)	109.5
H(84A)-C(84)-H(84C)	109.5
H(84B)-C(84)-H(84C)	109.5
N(5)-C(85)-C(86)	178.6(11)
C(85)-C(86)-H(86A)	109.5
C(85)-C(86)-H(86B)	109.5
H(86A)-C(86)-H(86B)	109.5
C(85)-C(86)-H(86C)	109.5
H(86A)-C(86)-H(86C)	109.5
H(86B)-C(86)-H(86C)	109.5
N(6)-C(87)-C(88)	168.1(19)
C(87)-C(88)-H(88A)	109.5
C(87)-C(88)-H(88B)	109.5
H(88A)-C(88)-H(88B)	109.5
C(87)-C(88)-H(88C)	109.5
H(88A)-C(88)-H(88C)	109.5
H(88B)-C(88)-H(88C)	109.5
C(1)-N(1)-C(12)	119.7(5)
C(1)-N(1)-Zn(1)	128.8(4)
C(12)-N(1)-Zn(1)	111.4(4)
C(10)-N(2)-C(11)	120.1(6)
C(10)-N(2)-Zn(1)	127.4(5)
C(11)-N(2)-Zn(1)	112.5(4)
C(43)-N(3)-C(54)	119.9(5)
C(43)-N(3)-Zn(2)	128.8(4)
C(54)-N(3)-Zn(2)	111.1(3)
C(52)-N(4)-C(53)	119.8(5)
C(52)-N(4)-Zn(2)	127.8(4)
C(53)-N(4)-Zn(2)	112.3(3)

C(15)-O(1)-Zn(1)	115.6(4)
C(28)-O(3)-C(22)	109.8(9)
C(29)-O(4)-Zn(1)	109.0(4)
C(36)-O(6)-C(42)	116.8(6)
C(57)-O(7)-Zn(2)	88.0(5)
C(57)-O(8)-Zn(2)	93.5(5)
C(70)-O(9)-C(64)	116.4(7)
C(71)-O(10)-Zn(2)	119.6(4)
C(81)-O(12)-C(84)	119.4(5)
O(1)-Zn(1)-O(4)	101.12(18)
O(1)-Zn(1)-N(2)	119.81(19)
O(4)-Zn(1)-N(2)	131.55(17)
O(1)-Zn(1)-N(1)	119.32(19)
O(4)-Zn(1)-N(1)	101.9(2)
N(2)-Zn(1)-N(1)	80.8(2)
O(10)-Zn(2)-N(4)	124.71(17)
O(10)-Zn(2)-N(3)	116.28(17)
N(4)-Zn(2)-N(3)	80.65(17)
O(10)-Zn(2)-O(8)	102.26(18)
N(4)-Zn(2)-O(8)	131.00(19)
N(3)-Zn(2)-O(8)	91.38(19)
O(10)-Zn(2)-O(7)	99.99(18)
N(4)-Zn(2)-O(7)	97.04(17)
N(3)-Zn(2)-O(7)	137.47(19)
O(8)-Zn(2)-O(7)	58.2(2)

Symmetry transformations used to generate equivalent atoms: