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Synthetic aspects, crystal structures and biological activities of d- and f-metal salen-type complexes

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Salen-type Schiff bases derived from salicylaldehyde and diamines have numerous applications, such as fluorgenic agents, pesticides, herbicidal agents [1], and ion-selective electrodes for the determination of anions in analytical samples [2]. The interest in Schiff base ligands has grown recently because of their antitumor, antibacterial, antivirus, and antifungal activity improved by coordinating ligands to a metal ion [3, 4]. Transition metal complexes with salen-type ligands have applications in heterogeneous and homogenous catalysis [5–8], diagnostic pharmaceuticals and laser technology [9]. Cobalt Schiff base complexes are investigated as a models for Cobalamine (B_{12}) coenzymes classified as oxygen carriers. They have been applied as a catalyst for the preparative oxygenation of phenols and amines [10]. The interest in salen-type complexes have been also increased because of their magnetic and optical properties [11]. Requirements of metal ions determine the structure of metal complexes. Lanthanide ions show high coordination numbers as well as variable and flexible coordination environments, therefore they have great potential in the synthesis of novel crystal structures [12, 13]. One of the main factors contributing to the structural changes experienced by lanthanide ions is the well-known lanthanide contraction. The lanthanide contraction is associated with the systematic decrease in ionic radius that takes place when increasing the atomic number throughout the series of lanthanides. Its result is a decrease in the coordination number of the metal ions; the coordination number for the light lanthanides is 10 or 9, while it is 9 or 8 (sometimes 7) for the heavy ones [14–17]. Besides the metal ions' requirements, the structure of ligands is very important for the development of new coordination compounds. Flexible salen-type ligands may provide more potential for the construction of unique frameworks because of their freedom of conformation, and they can show different coordination modes with metal ions in the construction of supramolecular frameworks [18]. For example, it has been found that a flexible salen-type ligand has been used to obtain infinite one- and two-dimensional coordination polymers [19–20]. However, when a rigid salen-type ligand was used, finite monomeric complexes were obtained [21]. The self-assembly process is another factor determining the structure of the d- and f-electron compounds. This process, which leads to organisation of simple molecules in more complicated structures, involves noncovalent interactions, such as electrostatic, π–π interactions, Van der Waals, donor-acceptor, and hydrogen bonding [22]. Among the supramolecular interactions, hydrogen bonding is one the most effective instruments that organise building blocks into supramolecular structures. The number of hydrogen bonds and arrangement of the donor and acceptor groups determines the strength of hydrogen bonded complexes.

The structures of salen-type complexes are influenced by a variety of factors such as the type of metal ions, metal ionic radius, the nature of counter ions, and pH of the environment.

1 Synthesis and crystal structure of d-metal salen-type complexes

One of the methods for preparation of salen-type Schiff base complexes is a metal-promoted one-step (template) condensation reaction. The method has been used for many years for the synthesis of Schiff base macrocyclic compounds. A metal ion is used as a template to induce orientation of the reacting groups of linear substrates in the required conformation for the ring to close [23]. This method has been found very effective for obtaining salen-type complexes. The template reaction of salicylaldehyde with 4-methyl-1,3-phenylenediamine in ethanol in the presence of zinc chloride provided Zn(II) salen-type complex (**1**) containing *N*,*N*′-bis(salicylidene)-4-methyl-1, 3-phenylenediamine (Figure 1).

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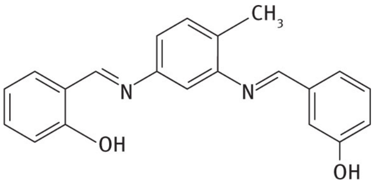

Figure 1: *N*,*N*′-bis(salicylidene)-4-methyl-1,3-phenylenediamine [24].

In the crystal structure of the complex, Zn(II) ion is four-coordinated and bonded to neutral salen ligands and two chlorides. Generally, salen-type ligands are four-coordinated, but in this case only oxygen donor atoms are involved in the coordination (Figure 2) [24].

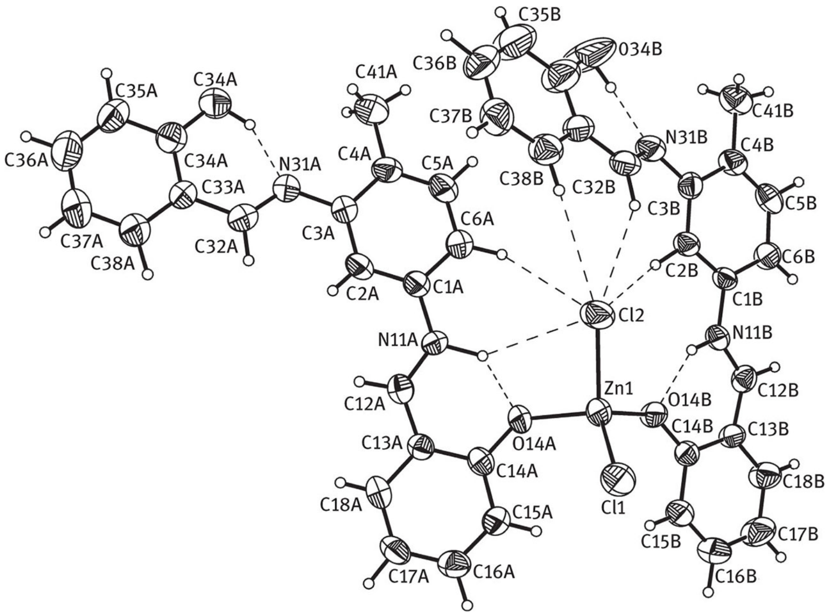

Figure 2: Crystal structure of **(1)**[24].

Another method for the preparation of salen-type Schiff base complexes is direct synthesis. The first step of direct synthesis is the preparation of an organic ligand, while the second step is the reaction of the ligand and a metal ion. This method was used to prepare of the homometalic salen-type coordination polymer of Zn(II) (**2**) or Co(II) (**3**) ions with 3-formyl-4-hydroxybenzoic acid. The crystal structure of (**2**) reveals that this compound 3D framework formed of tetranuclear [$Zn_4(\mu_4\text{-}O)$(carboxylate)$_8$] units. One Zn(II) ion is located at the center of the salen ligand and is coordinated with two nitrogen and two oxygen atoms from the ligand and the coordination resembles distorted square-planar geometry, while the other Zn(II) ion exhibits distorted tetragonal pyramid geometry. The crystal structure of (**3**) reveals that this compound adopts a 1D chain structure constructed of Co(II) ions and a ligand derived from the hydrolysis to one imine group of ligand. Co(II) ion shows octahedral geometry [25].

Other examples of salen-type complexes are compounds of Ni(II) (**4**) and Co(III) (**5**) with the pentadentate H_2L Schiff base ligand – 2,2′-{(methylimono)bis[propane-3, 1-diylnitrilomethylylidene]} diphenolate. The complexes were obtained in the reactions of nickel(II) perchlorate or cobalt(III) perchlorate with the pentadentate ligand in the presence of azide ion and acetonitrile.

In the presence of a Ni(II) ion a binuclear compound containing $m_{1,3}$-N_3 bridge was obtained, while in the presence of a Co(II) ion, a mononuclear octahedral complex was produced. In both complexes metal ions are six-coordinated and adopt a distorted octahedral geometry. In (**4**) the main structural unit can be described as a binuclear species comprising two asymmetric $[Ni(LH)]^+$ units, connected through a $\mu_{1,3}$-N_3 bridge [26].

The new one-dimensional manganese(III) complex (MnL(bix)]$ClO_4 \cdot 2H_2O$ (**6**) (H_2L = *N*,*N*′-bis(salicylidene)phenylenediamine; bix = 1,4-bis-(imidazol-1-ylmethyl) benzene) has been synthesized. Crystal structure has revealed that Mn(III) ion is coordinated by the tetradentate ligand L^{2-} in the equatorial plane, while 1,4-bis-(imidazol-1-ylmethyl)benzene ligand acts as a bridge.

The Mn(III) ion is distorted octahedral coordinated by N_2O_2 donors of one deprotonated ligand L^{2-} and two N donors from two different bix ligands. 1,4-bis-(imidazol-1-ylmethyl)benzene ligands function as a bridge linking monomeric $[Mn(L)_2]^+$ units into a 1D chain [27].

New five complexes of Cr(III) [CrL^1(en)]Br$_{03}$Cl$_{07}$ (**7**), [CrL^1(pr)]Cl (**8**), [CrL^2(en)]ClO_4 (**9**), [CrL^2(pr)]Cl (**10**) and [CrL^1(μ-OMe)]$_2$ (**11**) with ligands: *N*,*N*′-bis(2-hydroxybenzyl)-1, 2-ethanediamine (H2L^1) and *N*,*N*′-bis(2-

hydroxybenzyl)-1,3-diaminepropane (H_2L^2) have been obtained and characterized. All the complexes could be isolated as single crystals by a solvent (MeOH) evaporation process except (**8**).

The solid-state structures of the mononuclear and dinuclear complexes (**7**), (**9**), (**10**), and (**11**) were determined by X-ray crystallographic studies. (**7**), (**9**), and (**10**) crystallize as a mononuclear species with the Cr(III) ion chelated by $L^{(1)2}$ – tetradentate and 1,2-ethanediamine (en) bidentate ligands, $L^{(2)2}$ – tetradentate and 1,2-ethanediamine ligands and by $L^{(2)2}$ – tetradentate and 1,3-propanediamine (pr) bidentate ligands, respectively. (**11**) crystallizes as a dinuclear species, each chromium metal center is chelated by $L^{(1)2}$ – tetradentate ligand and connected to one another via two *cis*-methoxy bridging groups. The metals' center Cr(III) adopts a slightly distorted octahedral geometry . The hydrogenation of tetradentate Schiff bases increases ligand flexibility. The combination of polydentate ligands ($L^{(1)2}$, $L^{(2)2}$, 1,2-ethanediamine and 1,3-propanediamine) enhances the stability of Cr(III) complexes system by chelate effect. The difference of stability of these complexes is mainly due to the size of the chelate rings changing from five-membered for 1,2-ethanediamine to six-membered for 1,3-propanediamine [28].

2 Synthesis and crystal structure of metal salen-type complexes

The one-pot metal-promoted reaction between salicylaldehyde and 4-methyl-1, 3-phenylenediamine in the presence of lanthanum(III) or gadolinium(III) nitrate gave new salen-type complexes $[Ln_2(H_2L)_4(NO_3)_3]$ (La (**12**) and Gd (**13**)) containing *N*,*N*′-bis(salicylidene)-4-methyl-1,3-phenylenediamine (H_2L) (Figure 1). Crystal structure analysis has revealed that the complex exists as a centrosymmetric binuclear compound at the 2:4 metal-ligand ratio. Ln(III) ions are nine-coordinated, and the geometry around the central ions can be described as a distorted tricapped trigonal prism. Two ligands acting as bidentate chelators bridge the lanthanide ions, while the third ligand appears to be monodentate involving only one oxygen atom in coordination, the nitrogen atoms remain uncoordinated. The second oxygen atom of this ligand does not take part in any intermolecular interactions. Additionally, each metal ion is coordinated by three bidentate nitrate counterions (Figure 3) [29].

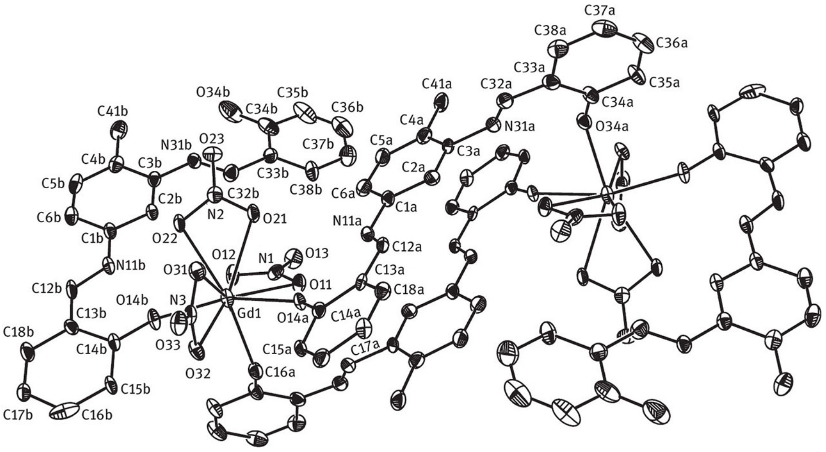

Figure 3: Crystal structure of (**13**) [29].

The result of the one pot template (metal-promoted) reaction of salicylaldehyde and putrescine (1,4-butanediamine) in the presence of lanthanum(III) ion was $[La(H_2L)_2(NO_3)_3]$ (**14**), where H_2L = *N*,*N*′-bis(salicylidene)-1,4-(butanediamine). The single-crystal X-ray analysis has revealed that complex (**14**) crystallized as an infinite $[La_2(H_2L)_4(NO_3)_6]_\infty$ polymeric structure. The La(III) ions are ten-coordinated, with the coordination polyhedron, which resembles a distorted bicapped dodecahedron, and only oxygen atoms are involved in the coordination [30].

Also new lanthanide salen-type complexes of the formula of $[Ln(H_2L)(NO_3)_3]$ (H_2L), where Ln = La(III) (**15**), Nd(III) (**16**), Eu(III) (**17**), Gd(III) (**18**), Ho(III) (**19**), Er(III) (**20**), Tb(III) (**21**), Yb(III) (**22**) and H_2L = *N*,*N*′-bis(salicylidene)-4-methyl-1,3-phenylenediamine (Figure 1) were obtained in a one pot template (metal-promoted) synthesis. All the complexes are isostructural. The Ln(III) ions are in the nine-coordinate environment with a coordination polyhedron that can be described as a tricapped trigonal prism. The three neutral ligands are coordinated with the metal ion, while the fourth molecular ligand is built into the crystal structure, but it is not bonded to the lanthanide ion (Figure 4). Interestingly, in all ligand molecules only one oxygen and none of the nitrogen atoms are involved in the coordination.

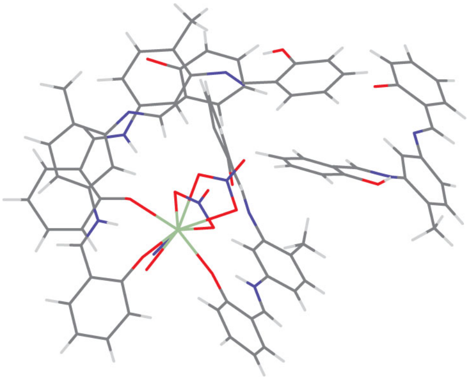

Figure 4: Crystal structure of the representative (**16**) [21].

The additional H_2L ligand molecule acts as a guest in the salicylaldimine complex host and stabilizes the overall self-assembled supramolecular network [21].

The gadolinium(III) nitrate complex $[Gd(H_2L)(NO_3)_3(EtOH)]MeOH$ (**23**), where H_2L = *N*,*N*′-bis(5-methylsalicylidene)-4-methyl-1,3-phenylenediamine (Figure 5), was obtained in one pot template (metal-promoted) synthesis, too.

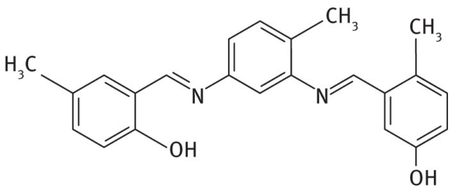

Figure 5: *N*,*N*′-bis(5-methylsalicylidene)-4-methyl-1, 3-phenylenediamine H_2L.

Single-crystal X-ray diffraction analysis has shown that the central Gd(III) ion is nine-coordinated, and as in the example above, the coordination resembles a distorted tricapped trigonal prism. Interestingly, only oxygen atoms are involved in the coordination (one oxygen from each of the ligands, six oxygen atoms from three nitrate groups, and one from the coordinated ethanol molecule). In both ligand molecules, only one oxygen and none of the nitrogen atoms are involved in coordination. The second OH group is involved in intramolecular O-H···N hydrogen bonds. In the crystal structure there is an uncoordinated solvent (methanol) molecule. It plays an important role in the crystal packing by hydrogen bonding, as it connects the complex molecules into infinite chains (Figure 6) [31].

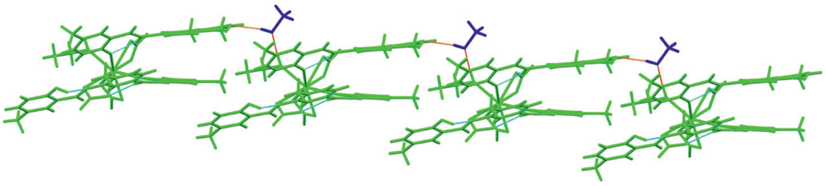

Figure 6: Fragment of the hydrogen-bonded chain of (**23**) [31].

It was found that the products of template metal-promoted reactions between 5-methylsalicylaldehyde and 4-methyl-1,3-phenylenediamine in the presence of lanthanide metal ions: La, Nd, Sm, Tb, Ho, and Yb were identified as three polymorphic forms of the ligand H_2L, with different numbers of symmetry-independent molecules: (**24**) for ligand H_2L and Sm, Tb, Ho, and Yb reactions, with one, (**25**) for La with three, and (**26**) for Nd with four molecules in the asymmetric part of the unit cell. The perspective view of one of the molecules of (**24**) is shown in Figure 7 [32].

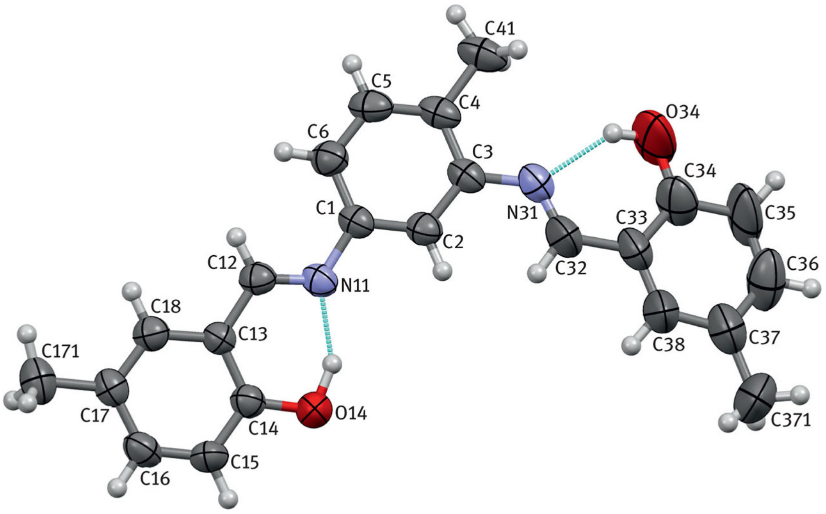

Figure 7: A perspective view of the molecule H_2L as determined in the structure of (**24**) [32].

The salen-type ligands have been proven to be particularly suitable for the synthesis of 4f SMMs (*single-molecule magnets*). In the reaction of hexadentate salen ligand *N*,*N*′-bis(3-methoxysalicylidene)cyclohexane-1,2-diamine (H_2L) with $LnCl_3·6H_2O$ (Ln = Tb(III), Dy(III), Ho(III)) the tetranuclear complexes of the formulas $[Dy_4(L)_2(HL)_2Cl_2(\mu_3\text{-}OH)_2]_2Cl_2(OH)_2·3C_2H_5OH·H_2O$ (**27**) and $[Ln_4(L)_2(HL)_2Cl_2((i_3\text{-}OH)_2]_2Cl_2·5C_2H_5OH·4CH_4Cl_2$ (Ln = Tb(III) (**28**), Ho(III) (**29**)) were obtained. X-ray crystallographic analysis reveals that all complexes are isostructural, and four Ln(III) ions with eight oxygen atoms form distorted defective dicubane $\{Ln_4O_8\}$ cores. In each of two units $Ln_4(L)_2(HL)_2$ two Ln(III) ions (Ln1(III) and Ln2(III)) are linked by two (μ_3-OH in different coordination modes. The Ln1(III) ion is eight-coordinated, adopting a distorted bicapped triangular prism, while Ln2(III) ion is nine-coordinated, forming a distorted monocapped square antiprism [33].

3 Synthesis and crystal structure of the heteronuclear salen-type complexes of d- and f-metal ion

Heterometalic polynuclear complexes (d-4f) containing d-block and lanthanide (4f) ions are currently of interest as potential new optical, electrical, and magnetic materials. The potential applications of the polynuclear Schiff base complexes are as contrast agents for medical resonance imaging, luminescent stains for fluoroimmunoassays, catalysts for the selective cleavage for RNA and DNA, and tunable photonic light-converting.

The precursor Zn-Schiff base complexes were obtained from the simple salen-type Schiff base ligands: *N*,*N*′-bis(salicylidene)ethylene-1,2-diamine or *N*,*N*′-bis(salicylidene)phenylene-1,2-diamine ($H2L^1$ or H_2L^2, respectively). Then, reaction of the respective precursors $[ZnL^1(py)]$ or $[ZnL^2(py)]$ with $Ln(NO_3)_3·6H_2O$ (Ln = Nd, Yb, Er or Gd) resulted in the formation of heterotrinuclear complexes (Zn_2Ln). The eight complexes $[ZnL^1(py)Ln(NO_3)_3]$ (Ln = Nd (**30**), Yb (**31**), Er (**32**), Gd (**33**)), and $[ZnL^2(py) Ln(NO_3)_3]$ (Ln = Nd (**34**), Yb (**35**), Er (**36**), Gd (**37**)) were obtained and characterised by analytical and spectroscopic methods.

The crystal structures of both neodymium complexes (**30** and **34**) were resolved. In both compounds, the four phenoxo oxygen atoms of two $[ZnL^1(py)]$ or $[ZnL^2(py)]$ components of (**30**) or (**34**), respectively, coordinate to one Nd(III) ion resulting in the formation of trinuclear complexes. Each Zn(II) ion has a five-coordinate environment and a distorted square pyramidal geometry. The two Nd(III) ions in (**30**) or (**34**) are nine- and ten-coordinated, respectively. Apart from phenoxo oxygen atoms, they complete their coordination environment with five or six oxygen atoms from nitrate ions, in (**30**) and (**34**), respectively [34].

Two salen-type heteronuclear Cu-Gd complexes, of the formulas $[(GdCuL^1Cl_3\ (CH_3OH)_2]$ (**38**) and $[Gd_2Cu_4L^2{}_4Cl_2(OH)](PF_6)_3$, (**39**) where ($H2L^1$ = *N*,*N* ′-bis(2-hydroxy-3-methoxybenzylidene)-1,2-diaminocyclohexane and H_2L^2 = *N*,*N* ′-bis(2-hydroxy-3-methoxybenzylidene)-1,3-diaminopropane) have been isolated. Their crystal structure analysis reveals that the molecular unit of (**38**) comprises one Gd(III) ion, one Cu(II) ion, one ligand, three chloride ions, and two methanol molecules. The Gd(III) ion is eight-coordinated to four O atoms from the ligand, two chloride ions and two O atoms from the methanol molecules. The Cu(II) ion is five-coordinated to two N, two O atoms of the ligand, and one chloride ion to give a pyramidal geometry. The Gd(III) and Cu(II) ions are bridged up by the two phenolate atoms.

The X-ray analysis reveals that (**39**) features an unusual hexanuclear Cu-Gd structure. In the asymmetric unit of the complex, the Gd(III) ion is nine-coordinated to eight oxygen atoms from two ligands and one hydroxyl O atom in a mono-capped pseudo-square anti-prismatic geometry. The Cu(II) ion is five-coordinated to two N atoms and two O atoms of the ligand and one chloride ion in a pyramidal environment. The Gd(III) and Cu(II) ions are bridged by two phenolate O atoms [35].

The heterotri- and heterodinuclear complexes of the general formulae $[Cu_2Ln(L)_2(NO_3)(H_2O)_2](NO_3)_2{\cdot}3H_2O$ (where Ln = Ce (**40**), Pr (**41**), Nd (**42**), and La (**43**)), and $[CuLn(L)(NO_3)_2(H_2O)_3MeOH]NO_3{\cdot}MeOH$ (where Ln = Dy (**44**) and Er (**45**)), involving the salen-type ligands H_2L = *N*,*N* ′-bis(5-bromo-3-methoxysalicylidene) propylene-1,3-diamine were obtained. In the crystal structure of trinuclear complexes, Cu(II) ions occupy the N_2O_2 cavity. The coordination polyhedron has distorted square pyramidal geometry with a water molecule in the apical position, while in the crystal structure of the dinuclear complexes, the coordination environment around the copper(II) ion is distorted octahedral. The Cu^{2+} ion is held within the inner N_2O_2 compartment of the Schiff base ligand. The apical vertices of the deformed octahedron are occupied by one methanol atom and one nitrate oxygen atom.

In the trinuclear complexes, Ln(III) ions are ten-coordinated into a structure of geometry resembling three face- and one edge-capped trigonal bipyramid, while in the dinuclear complexes the lanthanide(III) cations are nine-coordinated by one bidentate nitrate ion, three water oxygen atoms, and four oxygen atoms of the salen-type ligand [36].

4 Biological activities of d- and f-metal salen-type complexes

In bioinorganic chemistry, the interest in the Schiff base salen-type complexes derives from their ability to provide synthetic models for metal-containing sites in metallo-proteins and to contribute to developments in medicinal chemistry. Thus, Schiff base salen-type ligands and their complexes have a variety of applications in biological, clinical, and analytical fields [37]. Metal ions have a great influence on biological processes and have been a subject of interest in medical applications. Indeed, the mechanisms of action of these metal ions are complicated, but they are believed to involve covalent bonding to the hetero-atoms of the heterocyclic residues of biomolecules, such as proteins, enzymes, and nucleic acids. Salen-type complexes can be used as anticancer agents, therefore it is very interesting and important to study different types of coordination compounds with especially designed biologically active ligands. Mn(II), Cu(II), and Zn(II) salen-type Schiff base complexes were prepared by condensation of 2-hydroxy-1-naphthaldehyde with either 4-nitrobenzene-1,2-di-amine (Mn(II) (**46**), Cu(II) (**47**), and Zn(II) (**48**)) or 4-methylbenzene-1,2-diamine (Mn(II) (**49**), Cu(II) (**50**), and Zn(II) (**51**)). The cytotoxic activity of the compounds was evaluated on a human liver cancer cell line (HepG2) by MTT colorimetric assay. (**46**), (**49**), and (**50**) showed more potent antiproliferative activity with IC_{50} (concentration of test substance to achieve 50% inhibition) 1.24, 2.22, and 3.56 μg/ ml, respectively. The results were comparable with the effect of a standard drug 5-fluorouracil (IC_{50} 4.6 μg/ml). Interestingly, the complexes exhibited better antiproliferative effect than the ligands, as their IC_{50} values were found to be significantly low [38]. The salen-type zinc complexes have been shown to be active as anti-tumor and anti-HIV or anti-bacterial agents. The zinc(II) complexes containing *N*,*N*′-bis (salicylidene)-4-methyl-1,3-phenylenediamine (H_2L) ($[Zn(HL)Cl(H_2O)_2]{\cdot}C_2H_5OH$ (**52**) and $[Zn(H_2L)_2Cl(NO_3)(H_2O)]{\cdot}CH_3OH$) (**53**) and the ligand were tested for antimicrobial activity against *Staphylococcus aureus* in a minimum inhibitory concentration (MIC) experiment. MIC (μg/mL), which is defined as the lowest concentration of the sample that inhibits bacterial growth, was determined in sterile plates compared to the drug-free control wells. The efficiencies of the complexes and the ligand were compared with the activity of a standard antibiotic – chloramphenicol. The results revealed an MIC value of 50 μg mL^{-3} for (**52**), 500 μg mL^{-3} for (**53**), and 100 μg mL^{-3} for the free ligand. The activities of the complex and ligand could not reach the effectiveness of the conventional antibacterial agent, chloramphenicol, with an MIC value of 5 μg mL^{-3} [3].

The interactions of the complexes of Cu(II) (**54**), Ni(II) (**55**), and Zn(II) (**56**) with the ligand H_2L diethyl-2,2 (propane-1,3-diylbis((2-hydroxy-3-methoxy benzyl)azanediyl))diacetate, and calf thymus DNA were tested. The interactions were investigated by UV-Vis absorption titration, ethidium bromide displacement assay, cyclic voltammetry methods, and agarose gel electrophoresis. The compounds (**54–56**) were found to bind to calf thymus DNA through the intercalation mode. It was evidenced by a slight bathochromic shift of intraligand (π–π*) transition in the region 270–280 nm in the range of 1.6–1.7 nm. Furthermore, (**54**) was found most effective to promote cleavage of pUC19 DNA from the super coiled form to the nicked form in the presence of H_2O_2. Incubation of DNA with (**54**) leads to its conversion to forms II and III. In the absence of H_2O_2, the compounds (**54–56**) did not show any effect towards the cleavage of DNA. The antibacterial activities of (**54–56**) were tested against Gram-positive bacteria, *Streptococcus pyogenes* and *Staphylococcus aureus*, and Gram-negative bacteria, *Escherichia coli*, *Klebsiella mobilis*, *Aeromonas aquariorum*, and *Serratia marcescens*, by the diffusion method. Standard antibiotics, ampicillin and amoxicillin, were used as controls. It was found that the metal complexes were more effective than the ligand or metal salts but less active than the controls against all the bacteria tested. (**54**) showed higher antibacterial activity against *Streptococcus pyogenes* and *Escherichia Coli* than the other metal complexes, while (**55**) showed higher activity against *Klebsiella mobilis* and *Aeromonas aquariorum*, and (**56**) was found to show moderate activity towards the bacteria tested [39].

Two salen-type Schiff base complexes of cobalt(III) of the formulas $[Co(L)(L^1)(NCS)]\ ClO_4$ (**57**), where L = propane-1,2-diamine, L^1 = 2-[*N*-(2-aminopropyl)ethanimidoyl] phenolate and $[Co(L^2)(N_3)]_2{\cdot}4H_2O$ (**58**), where L^2 = 2,2′-[propane-1,2-diylbis(nitriloeth-1-yl-1-ylidene)]diphenolate ion, have been tested *in vitro* to assess their growth inhibitory activity against two Gram-positive bacteria (*Staphylococcus aureus* MTCC 2940 *Bacillus subtilis* MTCC 441) and Gram-negative bacteria (*Pseudomonas aeruginosa* MTCC 2453 and *Escherichia coli* MTCC). Antibacterial activities of the compounds were evaluated by measuring the inhibition zone diameters (IZD, the area of media in which bacteria are unable to grow). The results of the antibacterial activities indicate that both complexes exhibit broad spectrum antibacterial activity against all the four chosen reference bacteria. The IZD (cm) data show that the ligand L is active against *Streptococcus aureus* and *Escherichia Coli* but is inactive against *Bacillus subtilis* and *Pseudomonas aeruginosa*. The Schiff base H_2L^2 was found to be mildly active against *Bacillus subtilis* and *Escherichia coli* but inactive against the other two bacteria. The *Escherichia coli* bacteria were found to be the most sensitive to all the compounds. The majority of the compounds tested show mild to moderate antibacterial activities that increase with dose. However, the activities are much lower than those of the commercial antibiotic (Gattifloxacin) at similar concentrations [40].

5 Conclusions

This chapter describes methods for the syntheses of d- and f-metal salen-type complexes, characterisation of their crystal structures and biological activities. Schiff base salen-type ligands are able to coordinate many different metals and to stabilise them in various oxidation states, enabling the use of salen-type ligands to obtain compounds with numerous potential applications. The Schiff base salen-type ligands can be used to obtain mono- and polynuclear complexes and as well as supramolecular and coordination polymers.

The Schiff base salen-type complexes can be obtained in two ways. One of the methods for the synthesis of salen-type Schiff base complexes is the metal-promoted one-step (template) condensation reaction. The method has been used for many years for the synthesis of Schiff base macrocyclic compounds. A metal ion is used as a template to induce the orientation of the reacting groups of linear substrates in the required conformation for the ring to close. The template condensation reactions were successfully used for the preparation of Schiff base salen-type complexes. Another method proposed for the synthesis of salen-type Schiff base complexes is direct synthesis. The first step of direct synthesis is the preparation of the organic ligand, and the second step is the reaction of the ligand and the metal ion. The stoichiometry and structures of these complexes depend on the Schiff base ligands employed in their syntheses as well as metal ionic radius, counter ions, and reaction conditions.

Generally, Schiff-base salen-type ligands are four-coordinated, but sometimes only oxygen donor atom is involved in the coordination. Interestingly, it was confirmed that Schiff bases could act as neutral undeprotonated ligands in which only oxygen atom (and not the nitrogen atoms) are involved in the coordination. Jones and co-workers have shown four different bonding modes for salen-type complexes with ytterbium: I monodentate bonding to one Yb^{3+} ion; II tetradentate bonding to one Yb^{3+} ion; III bidentate bonding to two Yb^{3+} ions; and IV pentadentate bonding to two Yb^{3+} ions [18].

The results of antibacterial screening of the salen-type ligand and complexes have revealed their mild to moderate bactericidal activities. In addition to the synthetic and structural investigations, this study helps to evaluate the potentiality and effectiveness of new Schiff base complexes as antibacterial agents. Metal complexes and ligands have been tested against gram positive (e.g. Salmonella typhi, Streptococcus pyogenes, Staphylococcus aureus, Bacillus subtilis) and gram negative (e.g. Escherichia coli, Aeromonas aquariorum, Serratia marcescens and Pseudomonas aeruginosa) bacteria using methods: Minimum Inhibition Concentration (MIC, μg/mL), Minimal Bactericidal Concentration (MBC, mg/mL), Inhibition Zone Diameters (IZD - Kirby Bauer Method) as a qualitative assay using a standard antibiotics e.g. Kanamycine, Chloramphenicol, Ampicillin, Amoxicillin and Gattifloxacin as reference standards. The antibacterial activity tests indicate that the complexes exhibit higher antimicrobial activities against the Gram-negative and Gram-positive bacteria than the free ligand. In general, the antibacterial results show that the majority of the metal complexes were more active than their respective Schiff bases salen-type ligands [41].

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