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Review

From mono to polydentate azole and benzazole derivatives, versatile ligands for main group and transition metal atoms

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Dedicated to Stanley Kirschner, friend and colleague, in recognition of his contribution to coordination chemistry.

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ABSTRACT

Herein we discuss contributions in the coordination chemistry of azoles and benzazoles, from our and some other research groups. Reactions of polydentate ligands with a diverse combination of donor atoms, as N, O, S, P, with main group and transition metals are commented, as well as their structural analysis. There is a versatile chemistry involved in these compounds, based on a great structural diversity. The ligands promote hypervalent atoms, a wide spectrum of molecular geometries and interactions. The central atoms vary from tri- to octacoordinated. Metallacycles are formed with the participation of the metal ion into the electronic delocalization of the organic π-systems. The high electron density of the ligands, their planar delocalized and rigid framework favor many weak interactions, giving place to macromolecular assemblies based on hydrogen bonds, π-stacking and Lewis acid–base coordination. The compounds offer the possibility of their use as antiparasites drugs, biocides or anticancer substances and in materials science.

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1. Introduction

The biological relevance of azoles and their potential in the search of new drugs, as well as the broad spectra of their applications in materials science, have stimulated the research on this field and a large number of contributions have appeared over the time, therefore, an exhaustive review is beyond the scope of this paper. Herein we mainly discuss our contribution together with examples of other authors.

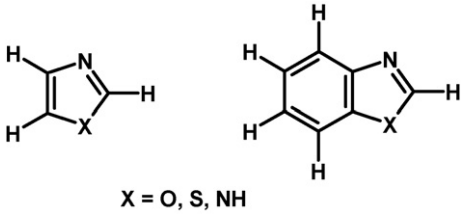
Azole and benzazole heterocycles (Scheme 1) are involved in several important functions in biological systems, many of them by interacting with biological occurring metal atoms. The imidazole has been related with the synthesis of nitrogenated biomolecules in prebiotic conditions [1,2]. It plays a relevant role in biological systems as part of the histidine aminoacid present in most of the metal binding sites of a great variety of metalloenzymes [3,4].

On the other hand, benzazoles are involved in biological systems performing other functions. For example, benzimidazole is coordinated to a cobalt(II) atom in vitamin B12 [5]. A recent review of the X-ray structural analyses of cobalamins has been reported [6]. Some benzoxazole derivatives have been found in some marine organisms and have probed to posses antimycobacterial properties [7]. The luciferase enzyme, used in nature for bioluminescence, is constituted by benzothiazole and thiazole fragments [8]. Modified azoles and benzazoles are broadly used as biocides, fungicides and antiparasitaries [9–18]. The use of benzazoles in the treatment of neurocysticercosis is known [19–21]. The effect of benzimidazolic coordination compounds on electron transfer reactions in photosynthesis, has been studied by their interactions with plastocyanin [22].

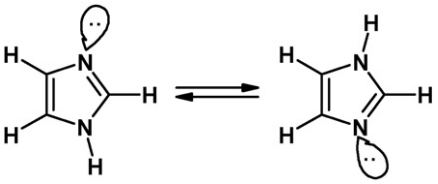
Derivatives of imidazole [23], benzimidazole [24,25], benzoxazole [26–28], and benzothiazole have shown antineoplasic properties [29]. The biological activity of some benzimidazole compounds may be attributed to their intercalation in DNA, due to its planar structure, which is stabilized by weak interactions [30]. Benzimidazole L-ribosides have shown antiviral activity [31,32].

The emergence of resistance to the major classes of antibacterial agents is a problem of increasing significance. Based on the fact that the presence of the metal ions modifies the biological activity of the ligands, the biocide and antineoplasic activities were investigated for a series of coordination compounds of benzimidazole derivatives [33,34].

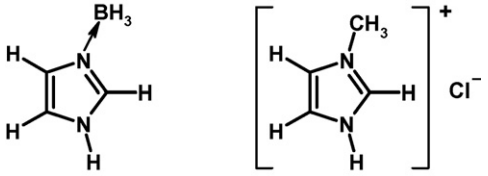
In order to evaluate the use of azoles and benzazoles as ligands, we have analyzed their structure, reactivity and delocalized electronic systems, as well as their conformational equilibria and tautomerism. With the aim to transform azoles into multidentate molecules, coordinating groups have been added affording a great diversity of new coordination compounds. We have studied their coordination sites by protonation and deprotonation, by formation of boron adducts or by the substitution of the labile hydrogen atoms with boron, phosphorus, tin or transition metal atoms. Our research has been focused in the knowledge of the coordination compounds of azoles with biological related transition and main group metal ions, including alkaline and alkaline earth. In order to contribute to the understanding of the noxious biological effects of toxic metals, cadmium, lead, mercury and tin have been also investigated.



Scheme 1. Azole and benzazole heterocycles.



Scheme 2. Tautomeric equilibrium in imidazole.



Scheme 3. Isolobal heterocycles bearing N → BH_3 and N–CH_3^+ groups [35].

2. Imidazole

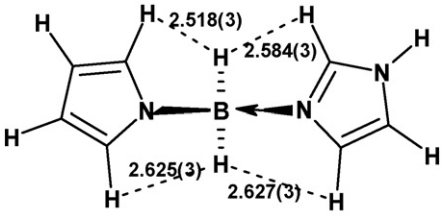
2.1. Imidazole bearing alkyl groups

Imidazole is a very simple heterocycle, it has a coordinating sp^2 nitrogen bearing a lone pair and a NH group with a labile proton. NH proton tautomeric equilibrium occurs in the molecule (Scheme 2). The sp^2 nitrogen atom is easily coordinated to Lewis acids or metallic ions, whereas the substitution of C–H or N–H protons allows the synthesis of complex derivatives.

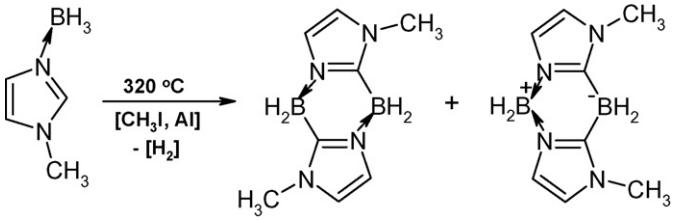
NMR studies of imidazole N-coordinated to BH_3, BF_3, or N-quaternized by protonation or methylation, allowed one to investigate the tautomeric equilibria as well as the ring substitution effects on the ^{13}C chemical shifts and coupling constants. ^{13}C NMR data were useful in establishing the structure of new substituted compounds in solution [35]. The NMR spectral similarity between isolobal heterocycles, for example those bearing [N–BH_3] and [N–CH_3]$^+$ groups, was evaluated (Scheme 3).

NOE NMR experiments were employed in order to assign proton–hydride (C–$H^{\delta+}\cdots^{\delta-}$H–B) and proton–fluoride (C–$H^{\delta+}\cdots^{\delta-}$F–B) stabilizing interactions in solution. X-ray analyses confirmed the presence of short distances between protons and hydrides, or fluorides [shorter than the sum of the van der Waals radii (Σr_{vdw}) for hydride–proton ($H^{\delta+}$ 1.20 Å; $H^{\delta-}$ 1.37–1.54 Å) [36]. The short contacts were interpreted as weak interactions [37]. Distances between protons and hydrides, found in the X-ray structure of pyrrol-BH_2 N-coordinated to imidazole, are in Scheme 4.

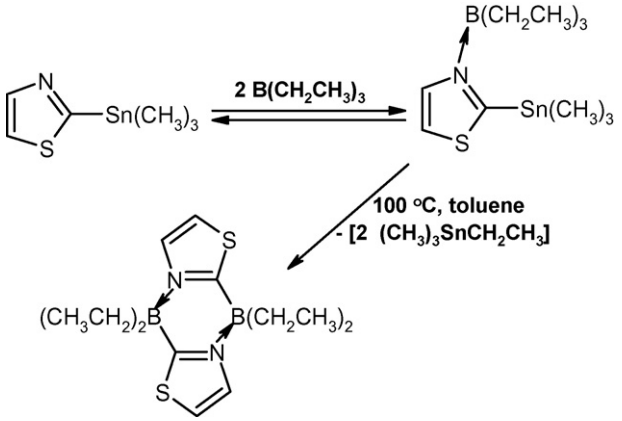
The N–BH_3 adducts of imidazoles and benzazoles are stable molecules which can be used as hydroborating agents. NMR data of a series of these adducts were used for the characterization of new N-substituted heterocycles [35,38].



Scheme 4. Proton–hydride (C–$H^{\delta+}\cdots^{\delta-}$H–B) interactions, distances (Å) between hydrides and protons are shorter than the Σr_{vdw} (2.57–2.74 Å) [37].



Scheme 5. Synthesis of *cis* and *trans* imidazabole by heating N–BH_3 adducts in the presence of aluminum and CH_3I [39].



Scheme 6. Synthesis of tetraalkylimidazabole, from 2-trimethyltin-1,3-thiazole and triethylborane [39].

N–BH_3 adducts are good starting materials for the synthesis of boron heterocycles, for example, the N–BH_3 imidazole is transformed in two isomeric azaboles by heating in the presence of a catalyst [39] (Scheme 5).

When 2-trimethylstannyl azoles react with BEt_3, adduct formation takes place, followed by elimination of tetraalkyltin and formation of the corresponding azaboles [39] (Scheme 6).

The solid state structure of the *trans* isomer of *N*-methylazabole was found by X-ray diffraction [40] (Fig. 1). The molecule is formed by three planar fused heterocycles. The determination of the nature of the bonding in the delocalized structure was a puzzle. The problem was to find, if the molecule was formed by dimerization of two carbene borane adducts or by two N-borane adducts (Scheme 7).

The actual carbenic nature of the carbon bound to the boron atom was established for several azaboles, based on their X-ray diffraction analyses [40]. The C–B bonds are longer than N–B bonds (Fig. 1).

The tripodal nitrogen-anchored *tris*(carbene) ligands form Cu(I)/(II), Ni(0)/(I), and Co(I)/(II)/(III) complexes bearing a cavity which protects the reactivity of the coordinated metal center. The nature of the metal–carbene bond in these complexes was determined by X-ray and DFT computational [41] (Scheme 8).

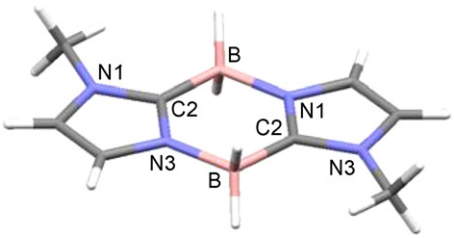
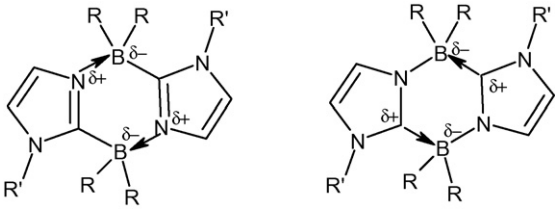
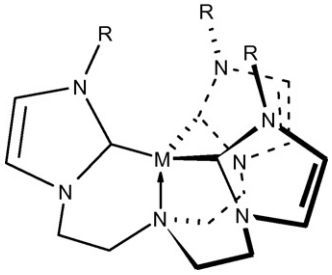


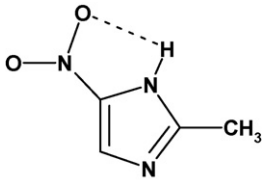
Fig. 1. X-ray diffraction structure of *N,N′*-dimethyl-imidazabole. C–B bonds [1.590(4) Å] are longer than N–B bonds [1.554(4) Å], N1–C2 [1.355(3) Å], C2–N3 [1.346(3) Å] [40].



Scheme 7. Two possible different types of dimers for imidazaboles: an amine borane adduct (right) or a carbene aminoborane (left).



Scheme 8. Tripodal nitrogen-anchored *tris*(carbene) transition metal complexes.



Scheme 9. 2-Methyl-5-nitro-imidazole (nitroimidazole).

2.2. Nitroimidazole derivatives

Substitution of some imidazole protons by rich in lone pairs functional groups, affords interesting polydentate ligands. An example of these derivatives is the nitroimidazole, which has been used as chemotherapeutic agent, particularly in protozoa and anaerobic microbial infections [42] (Scheme 9). The nitro group may act as a coordinating site, as can be deduced from its more stable tautomer, which has an N–H···O hydrogen bond forming a five-membered ring.

The reaction of nitroimidazole with CuX_2 (X–) affords hexacoordinated copper(II) complexes where the nitro group participates in the coordination to the metal atom, forming an oxygen and nitrogen chelate in a tetracyclic planar system [43]. The two ligands and the halides are *trans*-coordinated (Fig. 2). Intermolecular interactions as π-stacking and X···HN hydrogen bonds are shown for the bromo analogue [43] (Fig. 3).

A similar planar coordination mode was found for the copper(II) nitrate compound, where two nitrate anions are *trans*-coordinated

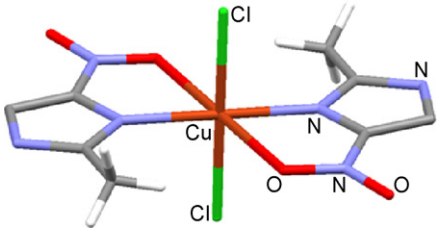


Fig. 2. Hexacoordinated copper(II) chloride compound derived from nitroimidazole [43].

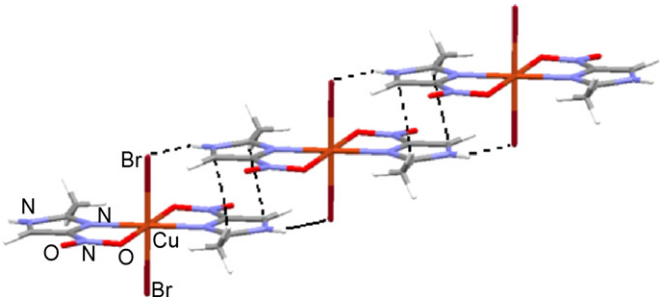


Fig. 3. Intermolecular association of the nitroimidazole copper(II) bromide compound [43].

to the metal ion [43]. Fig. 4 shows intermolecular strong π-stacking between two nitrates.

A series of ruthenium(II) compounds $[RuCl_2(DMSO)_2L_n]$; $n = 1$ or 2; L = 4-nitroimidazole derivative] were characterized by ^1H NMR and X-ray photoelectron spectroscopy. The complexes showed radiosensitizer properties toward hypoxic tumor cells [44].

Complexes involving 4-nitroimidazole as pentacyano(4-nitroimidazolato)ferrate(II) are of interest because of its facile reduction to a radical anion, allowing to study metal-complexed radicals and coordinated metals in unusual low oxidation states compounds [45].

Silver(I) complexes derived from imidazole and nitroimidazole with high antibacterial and antifungal activity were studied. [Ag_2(imidazole)(salicylic acid)$_2$] and [Ag(MeNO$_2$imidazole)$_2$]$ClO_4 \cdot H_2O$ were analyzed [46].

2.3. Metronidazole

Metronidazole [1-(β-hydroxy-ethyl)-2-methyl-5-nitroimidazole] is used in the treatment of anaerobic protozoan and bacterial infection [47] (Fig. 5). Its activity is based in DNA interaction [48].

In metronidazole, the imidazole N–H proton is substituted by 2-ethanol. The presence of two functionalized substituents in the molecule offers different sites for metal coordination and supramolecular arrangements. The free ligand shows intermolecular π-stacking interactions and strong OH → N hydrogen bonds [49] (Fig. 6).

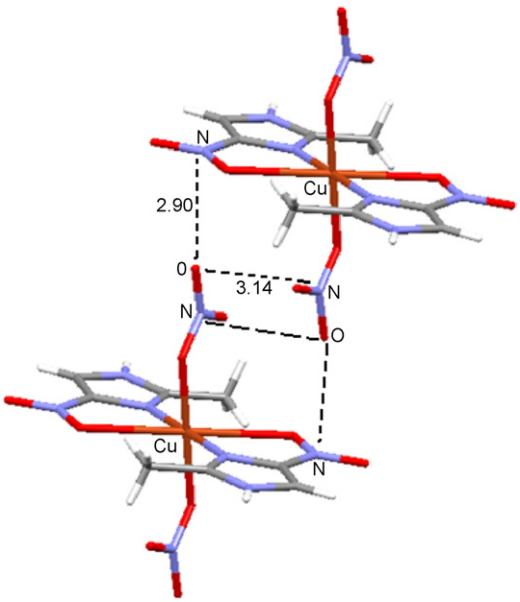


Fig. 4. Nitroimidazole copper(II) coordination compound. Intermolecular interactions (Å) are shown [43].

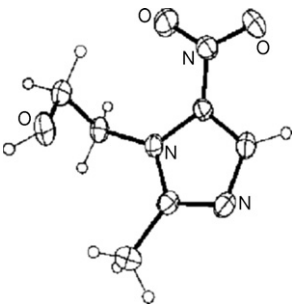


Fig. 5. X-ray diffraction structure of metronidazole [49].

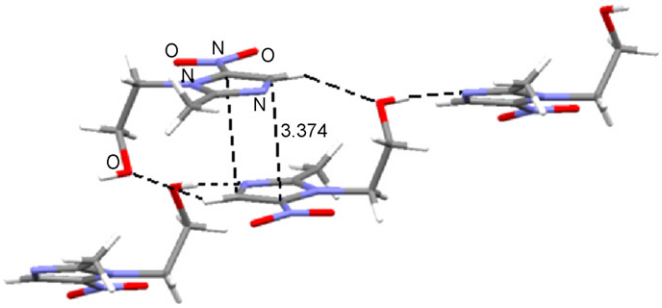


Fig. 6. Intermolecular interactions (Å) in the crystal structure of metronidazole [49].

Coordination of two metronidazole molecules, to cobalt(II) and zinc(II) halides, gives place to tetrahedral compounds (Fig. 7). The functional groups of the ligand stabilized zig-zag chains, which, by interchain hydrogen bonding interactions, form a 2D pleated sheet supramolecular arrangement [49].

In the dinuclear copper(II) chloride compound of metronidazole, the metal atoms are bridged by two chlorides. Four ligands are in axial position perpendicular to the four-membered ring plane. The two copper(II) atoms distance is 3.4519(5) Å (Σr_{vdw} Cu···Cu 4.0 Å). This short distance favors antiferromagnetic coupling (Fig. 8).

Reaction of copper(II) acetate and metronidazole produces a dinuclear compound, with four bridging acetates. The Cu···Cu distance [2.648(2) Å] gives place to an antiferromagnetic coupling between the metal atoms (Fig. 9). The dimers are associated via intermolecular hydrogen bonding forming a zig-zag chain. Divers supramolecular arrangements were found in metronidazole coordination compounds, *via* intermolecular hydrogen bonding [49].

Platinum(II) complexes [$PtCl_2(NH_3)$(L); L = metronidazole, misonidazole and etanidazole] were characterized by ^{195}Pt NMR. Their electrochemical behavior was studied. These compounds present

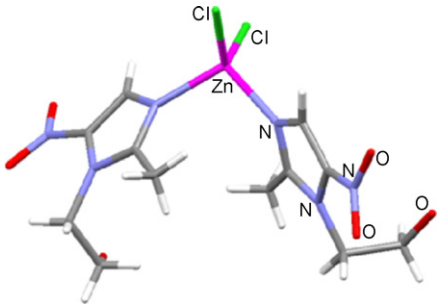


Fig. 7. X-ray crystal structure of the $ZnCl_2$ compound coordinated to metronidazole [49].

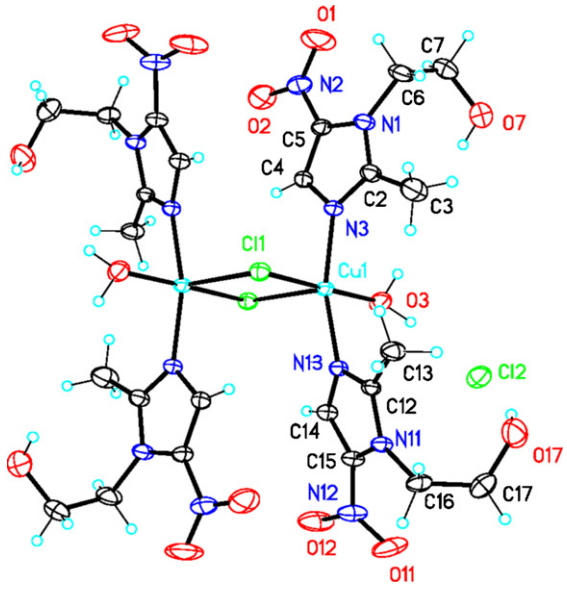


Fig. 8. Dinuclear copper(II) compound of metronidazole [49].

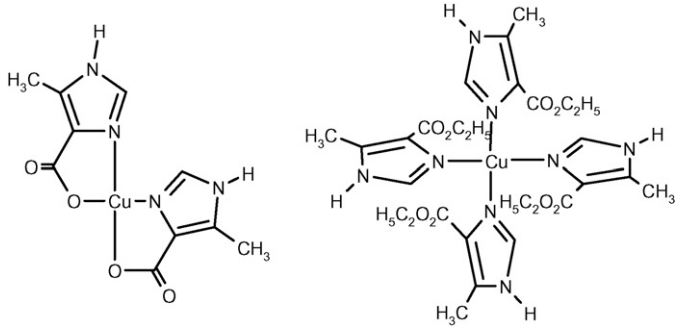
biological properties as radiosensitizers and hypoxic cytotoxins [50].

2.4. Ethyl 4-methyl-5-imidazole carboxylate

In order to investigate the difference between a nitro and an ethylcarboxylate group, as coordination sites, complexes of ethyl 4-methyl-5-imidazole carboxylate were synthesized (Fig. 10). The presence of a C=O group gives place to five-membered chelates [51], similar to those of nitroimidazole.

With copper(II) salts, ethyl 4-methyl-5-imidazole carboxylate affords different types of compounds, depending on the metal:ligand ratio. A copper(II) compound, bearing four ligands, was formed by using four equivalents of the imidazole, while in an excess of copper(II), the ethyl group is hydrolyzed and a spiro compound is formed (Scheme 10).

Equimolar reaction afforded a compound where the ligand acts as a chelate. Its X-ray diffraction analysis shows a copper(II) compound bearing one ligand and two chlorides (Fig. 11). It is a planar molecule forming a polymer by two intermolecular interactions. One of them is a Cl → Cu interaction [2.9135(7) Å], the second one is a π-interaction O1 → Cu (3.21 Å), giving an hexacoordinated octahedral copper(II) atom. Both distances are shorter than the Σr_{vdw} for Cu–Cl (3.8 Å) and for Cu–O (3.55 Å) [52].



Scheme 10. Ethyl 4-methyl-5-imidazole carboxylate copper(II) derivatives. Spiro (left), tetra-imidazole copper (right) [51].

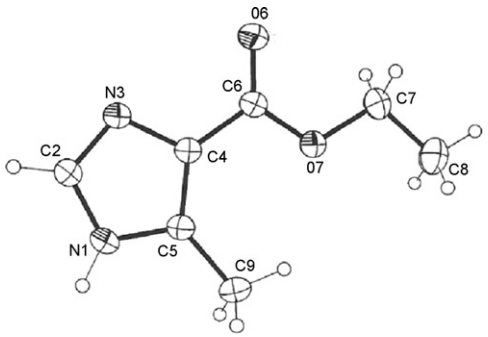


Fig. 10. Structure of ethyl 4-methyl-5-imidazole carboxylate [51].

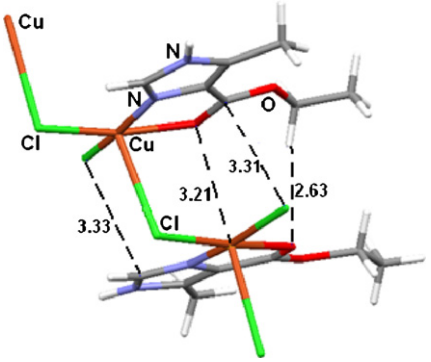


Fig. 11. Polymeric copper(II) compound derived from $CuCl_2$ and ethyl-4-methyl-5-imidazole carboxylate. Intermolecular interactions (Å) are shown [51].

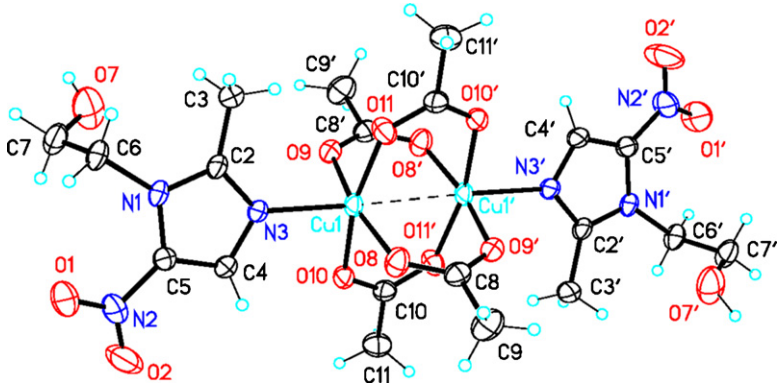


Fig. 9. Dinuclear compound derived from copper(II) acetate and metronidazole. The Cu···Cu distance is 2.648(2) Å [49].

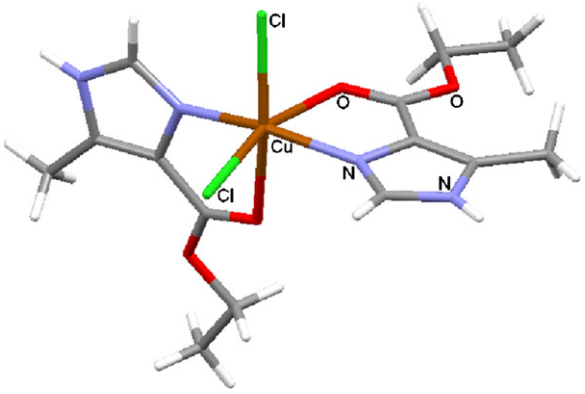


Fig. 12. *Cis* isomer of the copper(II) chloride compound derived from ethyl 4-methyl-5-imidazole carboxylate [51].

Addition of two ligands to the Cu(II) halides gives the octahedral *cis* isomer depicted in Fig. 12. The molecules belong to a C2 point group. The all-*trans* isomer was obtained from the corresponding nitrate, where the axial positions are occupied by two water molecules (Fig. 13).

The stability on aqueous solution of the analogous *cis* and *trans* octahedral cobalt(II), nickel(II) and copper(II) (halide and nitrate) compounds was investigated. Conversion in solution of the halide *cis* isomers compounds into the *trans* isomers, by replacing the halides by two axial water molecules. The effect of these compounds on photosynthetic activities has been studied. The compounds proved to be inhibitors of the photosynthesis electron flow, whereas the ligand and the metal salts, by themselves, had no significant activity [53,54].

A recent review of the coordination properties of some heterocyclic alcohols and aldehydes derived from imidazole, pyrazole or pyridine has been reported [55].

2.5. Tris(2-imidazolyl) derivatives

Mono and polynuclear copper(II) complexes containing tripodal imidazole ligand [4-[*bis*(1-methylimidazole-2-yl-methyl)aminoalkyl]imidazole] were structurally characterized by X-ray diffraction. In these compounds the solid state geometry of pentacoordinated copper(II) ion is maintained in solution. Temperature dependent magnetic susceptibility measurements showed an antiferromagnetic coupling for some of the compounds [56].

An imidazole tripodal ligand [*bis*(1-methylimidazol-2-yl)methyl)(2-(pyridyl-2-yl)ethyl)amine] afforded copper(II)–nitrite complexes where the metal atom is in a distorted square pyramidal geometry, with one coordinated nitrite ion. The geometrical arrangement of the tripodal ligand and the coordinated nitrite ion may be a biomimetic structural model for nitrite reductases [57].

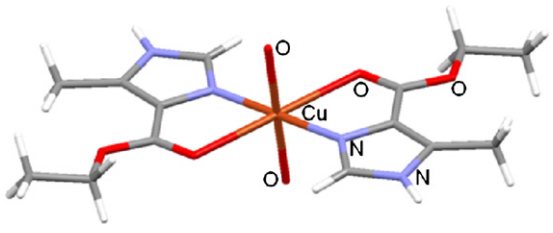


Fig. 13. All-*trans* isomer obtained from ethyl 4-methyl-5-imidazole carboxylate and copper(II)nitrate, two water molecules are occupying the axial positions [51].

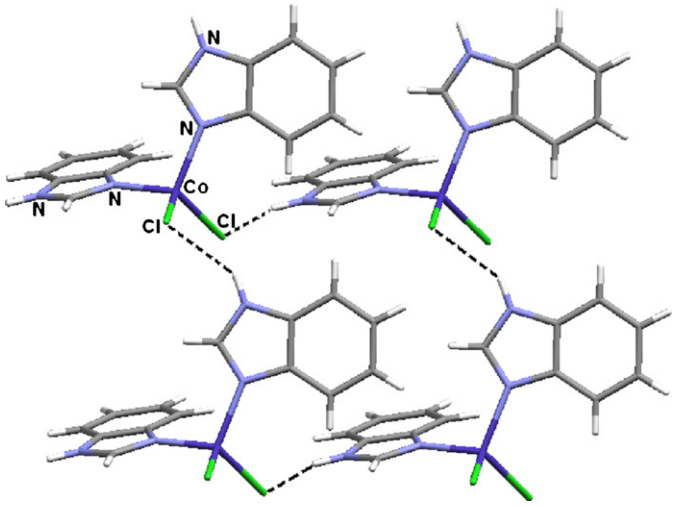


Fig. 14. Supramolecular arrangement of the tetrahedral dichloro*bis*(1H-benzimidazole)cobalt(II) [59].

3. Benzazoles

3.1. Benzazoles derivatives

Benzimidazole by itself gives place to a variety of coordination compounds, where one to four ligands are coordinated to the metal atom and the geometries may vary from tetrahedral, square planar, trigonal bipyramidal, square pyramidal to octahedral.

Two coupled benzimidazole ligands were complexed with copper(II) ions. These bidentate diimine metal compounds displayed superoxide dismutasa-mimicking and antitumor activity [58].

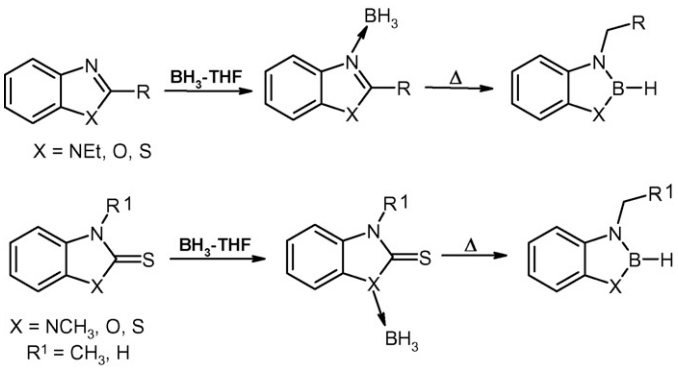
A classical example of benzimidazole coordination compounds is the tetrahedral structure of dichloro*bis*(1H-benzimidazole)cobalt(II) [59] (Fig. 14).

Benzazoles react with borane to yield N → BH_3 adducts, which are very reactive compounds, transforming themselves into the corresponding benzazolborole N-substituted, by a reductive transposition [38] (Schemes 11 and 12).

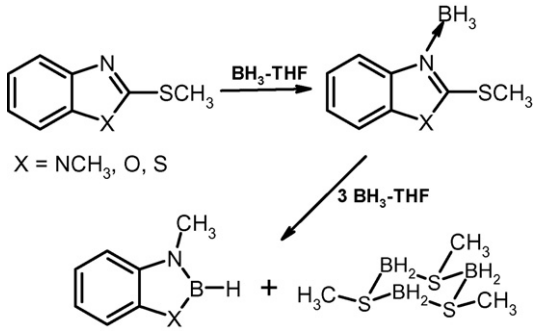
3.2. Benzazoles bearing organyl groups at C2

3.2.1. Tris(2-benzimidazolylmethyl)amine

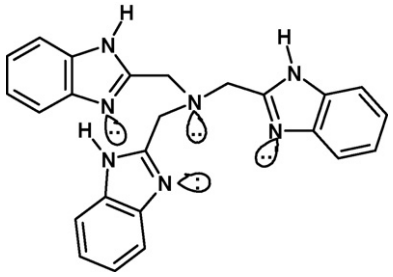
The tripodal *tris*(2-benzimidazolylmethyl)amine (ntb) (Scheme 13) gives coordination compounds with a diversity of coordination numbers and geometries. X-ray diffraction studies of the complexes showed that the ligand is strongly coordinated to the metal ion by three imidazolic nitrogen atoms, and weakly by the tertiary amine.



Scheme 11. Transposition reduction of N → BH_3 benzazoles [38].



Scheme 12. Ring opening reaction of 2-thiomethyl benzazoles by BH_3·THF [38].



Scheme 13. Structure of *tris*(2-benzimidazolylmethyl)amine.

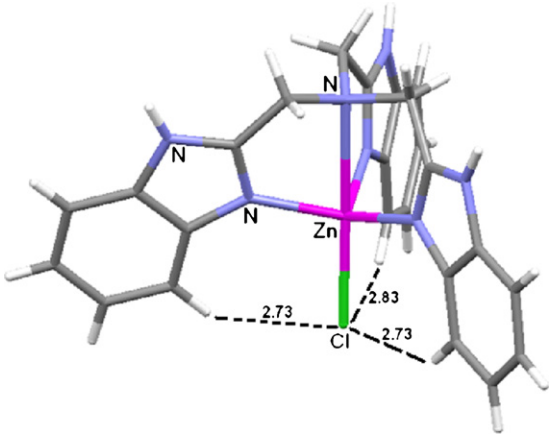


Fig. 15. Pentacoordinated zinc(II) compound derived from *tris*(2-benzimidazolylmethyl)amine (Å) [60].

The diamagnetic nature of zinc(II), cadmium(II) and mercury(II) compounds allowed study by NMR in solution [60]. In solid state and in solution, the compounds maintained the same coordination modes stabilized by three cooperative intramolecular hydrogen bonding from the benzyl C–H protons (Fig. 15).

Five-, six-, and seven-coordinate manganese(II) complexes have been reported [61,62] as well as iron derivatives [63] and mono-, bi-, tri-, and tetranuclear Ag(I) complexes [64]. The reaction of the

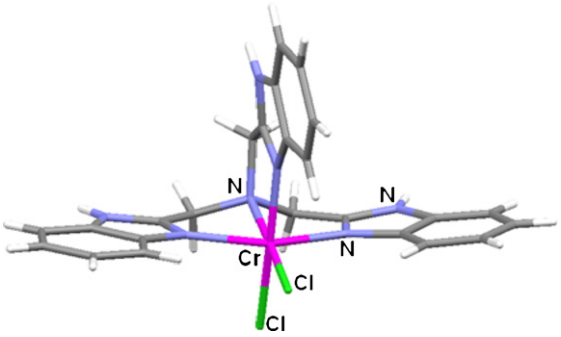


Fig. 16. Octahedral chromium(III) complex formed by *tris*(2-benzimidazolylmethyl)amine [66].

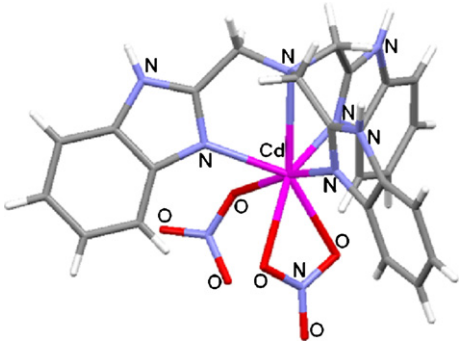


Fig. 17. Heptacoordinated cadmium(II) derivative of *tris*(2-benzimidazolylmethyl)amine [60].

ligand with copper chloride dihydrate and ferric chloride hexahydrate under mild conditions gave $[Cu(ntb)Cl]_2[CuCl_4]\cdot 2H_2O$ and $[Fe(ntb)Cl_2]Cl\cdot 3H_2O$ [63].

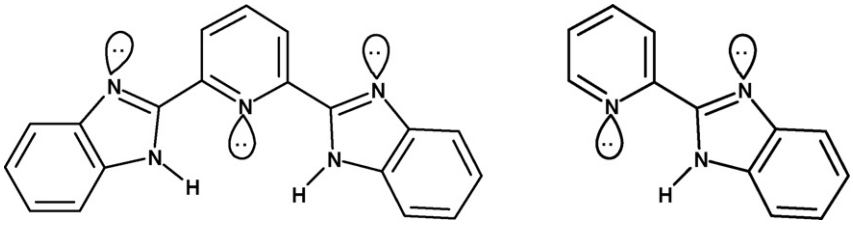
Reaction with $Ln(ClO_4)_3$ Ln = La, Sm, Pr, in the presence of the spacer *N*1,*N*4-*bis*(pyridin-4-ylmethylene)-benzene-1,4-diamine (BDA4BPy), afforded polymers of the formula $\{[Ln\text{-}(ntb)_2](ClO_4)_3(BDA_4BPy)_3 2MeCN\}\infty$. The structures have helical cylindrical arrays containing polycompartmental cavities for guest inclusion [65].

The pentacoordinated zinc(II) and cobalt(II) analogous compounds were submitted to *in vitro* antimicrobial activity analyses and also were evaluated against human cancer cell lines, HeLa, HCT-15 and SKLU-1, some of them showed promising activity [33].

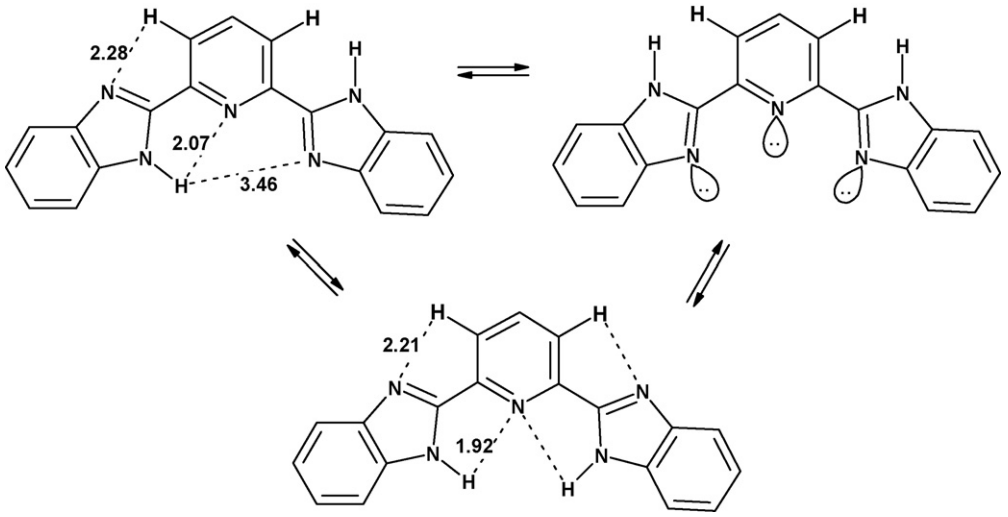
In the chromium(III) compound, the metal ion is hexacoordinated and adopts an octahedral geometry. Two chlorine atoms are *cis* and two benzimidazole moieties of the ligand are forced to be coplanar, while the third is perpendicular to this plane [66] (Fig. 16).

In the heptacoordinated cadmium(II) compound two nitrate groups are bound in two different modes to the metal atom [60] (Fig. 17).

Chiral monomers and polymers propeller-like derived from cadmium and *tris*(5-methyl-2-benzimidazolylmethyl)amine have been recently reported [67].



Scheme 14. 2,6-*Bis*(benzimidazol-2′-yl)pyridine and 2-(benzimidazol-2′-yl)pyridine.



Scheme 15. Hydrogen bonding in three tautomers or conformers of 2,6-*bis*(benzimidazol-2′-yl)pyridine. Distances (Å) were calculated [68].

3.2.2. 2,6-Bis(benzimidazol-2′-yl)pyridine and 2-(benzimidazol-2′-yl)pyridine

Association of the benzimidazole to pyridine gives bi- and tridentate planar ligands (Scheme 14). Protonation by trichloroacetic acid or fuming sulfuric acid or deprotonation by sodium and LiH in the pyridine benzimidazole derivatives, allowed the study of the intramolecular hydrogen bonds and tautomeric equilibria [68].

Conformers and tautomers of this ligand, as well as some calculated distances (Å) between atoms, are indicated in Scheme 15.

Two tridentate 2,6-*bis*(benzimidazol-2′-yl)pyridine molecules are coordinated to cobalt(III) as shown in Fig. 18. This diamagnetic compound was studied in solution by NMR.

Three ligands are coordinated to the metal ion in the bidentate 2-(2′-pyridyl)benzimidazole cobalt(III) compound [69], The geometry adopted by the metal ion is a distorted octahedron, with a *mer* configuration, C_1 (Fig. 19).

Mononuclear and mixed-valence binuclear oxovanadium complexes with 2,6-*bis*[benzimidazol-2′-yl]pyridine), 2,6-*bis*[*N*-methylbenzimidazol-2′-yl]pyridine, (*tris*[benzimidazol-2′-yl-methyl]amine) and *tris*[*N*′-methylbenzimidazol-2′-yl-methyl]amine) have been synthesized [70].

Complexes with tripodal ligands have diverse applications, for example, the supramolecular conjugated polymers prepared from metal ions, such as Zn^{2+} and 2,6-*bis*(19-methylbenzimidazolyl)pyridine have interesting optical properties [71], whereas the luminescent alkynylplatinum(II) complexes of 2,6-*bis*(*N*-alkylbenzimidazol-2'-yl)pyridine-type showed ready tunability of the nature of the emissive states by solvent and electronic property modulation [72].

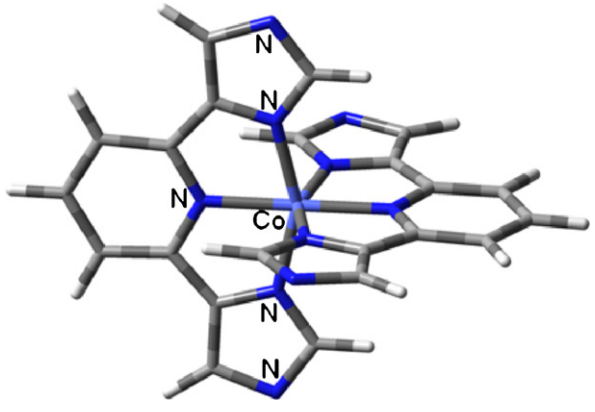


Fig. 18. Modeled structure of the Co(III) compound derived from 2,6-*bis*(benzimidazol-2′-yl)pyridine [68].

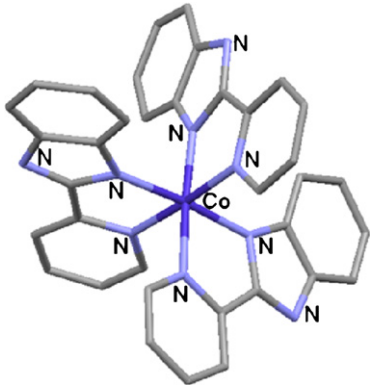


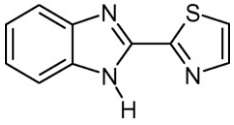
Fig. 19. X-ray diffraction structure of the cobalt(III) compound derived from 2-(2′-pyridyl)-benzimidazole [69].

3.2.3. Thiabendazole

Thiabendazole is widely used as fungicide and in the treatment of parasitic diseases [73] (Scheme 16) A variety of *bis*- and *tris*-chelate coordination compounds were obtained [74]. The *tris*-chelates gave different isomers. Some examples are shown below. The nickel(II) all-*trans tris*-chelate isomer is a dissymmetric C_3 molecule, while the cobalt(II) afforded the C_1 isomer (Fig. 20).

The cadmium(II) compound of Fig. 21, shows a distorted geometry for the metal ion, in between octahedral and regular trigonal prism. The non-planarity of the ligand was attributed to the large metal size.

In the *bis*-chelates, the anions are included in the coordination sphere of the metal ion, giving interesting supramolecular associations. A distorted octacoordinated Cd compound was formed with two thiabendazole molecules and two nitrates groups. The butter-



Scheme 16. Thiabendazole.

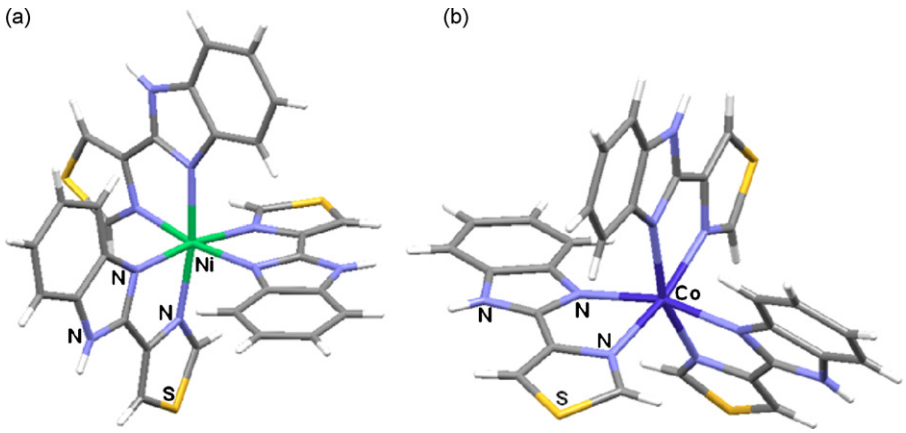


Fig. 20. (a) All-*trans tris*-chelate nickel(II) and (b) *cis tris*-chelate cobalt(II) compounds derived from thiabendazole [74].

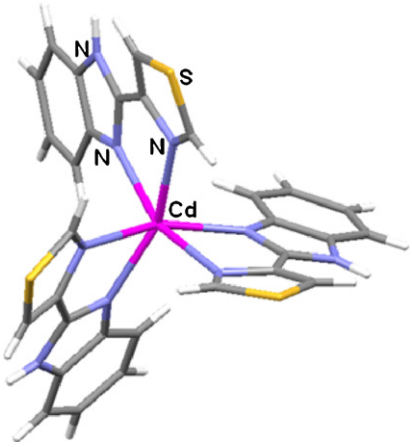


Fig. 21. Distorted octahedral cadmium(II) *tris*-chelate derived from thiabendazole [74].

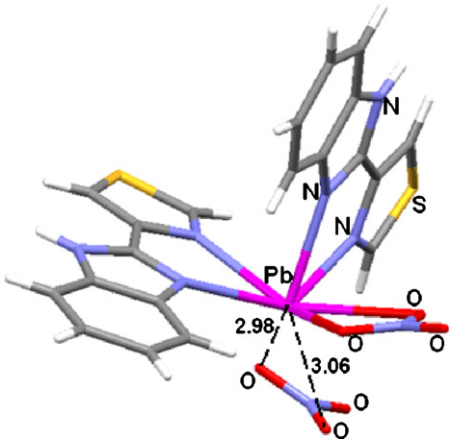


Fig. 23. Solid state structure of the octacoordinated lead(IV) compound derived from thiabendazole [74].

fly shape molecule belongs to the C_2 point group. The ligands are oriented head to tail (Fig. 22).

Another octacoordinated compound was obtained with lead(IV), which crystallized with two thiabendazole molecules and two nitrates. Two orthogonal ligands oriented head to head are coordinated to the metal atom, in contrast to the cadmium(II) compound. One nitrate is bound through two oxygen atoms, a second nitrate has a π-interaction with the lead atom (Fig. 23).

Two hexacoordinated cobalt(II) and nickel(II) thiabendazole with two ligands present a *cis* octahedral *bis*-chelate (C_1) geometry (Fig. 24).

The copper(II) derivative, presents an interesting distorted structure [74]. This compound has two thiabendazole molecules and a nitrate group bound to the metal atom (Fig. 25). The planes of the ligands have a closed dihedral angle (41°) whereas the plane of the nitrate group coincides with the equatorial plane of the molecule. The distortion could be explained by the ring tension produced by the ligands.

Coordination compounds of thiabendazole with alkaline metal ions were obtained. The most interesting fact in the X-ray diffraction structure of the sodium compound (Fig. 26), is that the ligand

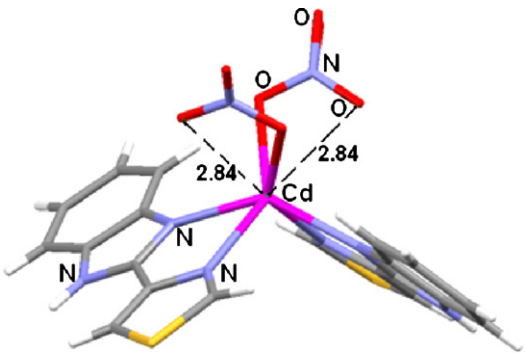


Fig. 22. Cadmium compound derived from thiabendazole, the O → Cd coordination bond length is 2.84 Å whereas the covalent Cd–O bond length is 2.336 Å [74].

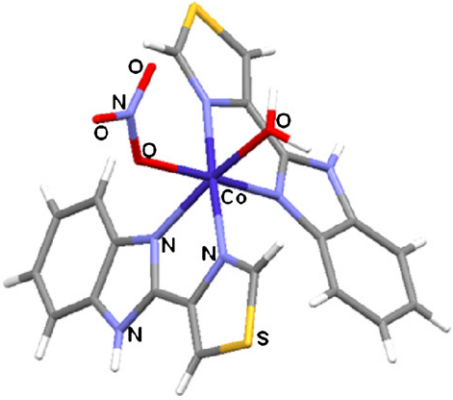


Fig. 24. *Cis*-octahedral cobalt(II) compound derived from thiabendazole bearing a nitrate and a water molecule [74].

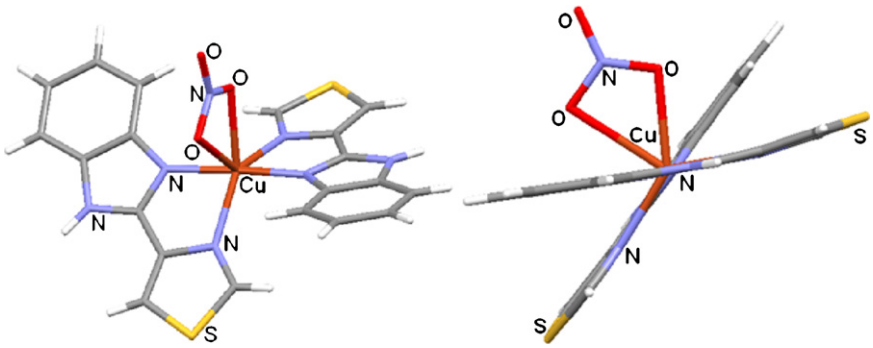


Fig. 25. Two views of the distorted geometry of the copper(II) compound, showing the planes of the thiabendazole molecules and the coordinated nitrate group [74].

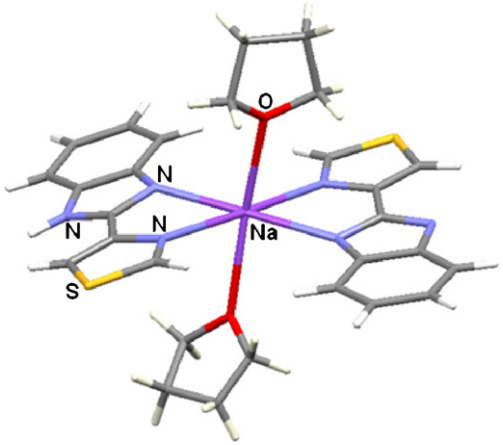


Fig. 26. Sodium *bis*-chelate coordination compound with thiabendazole [74].

is chelating the sodium atom by the two nitrogen atoms, in a similar mode to that of the transition metal coordination compounds. However its *trans* arrangement differs from the *cis* configuration of the transition metal compounds. A neutral sodium compound was afforded due to the fact that one of the ligands is deprotonated. The two THF molecules are coordinated orthogonally to the plane depicted by the ligands [74].

3.2.4. 2-(2-Hydroxyphenyl)-1H-benzimidazole

This is a very interesting molecule which stabilized fused planar heterotetracycles (Fig. 27). The heterocycle has a strong O–H···N intramolecular hydrogen bond [69].

When reacting this ligand with PCl_3, tri, tetra, penta and hexacoordinated phosphorus compounds were stabilized, by substitution of the OH and NH protons. The phosphorus atom is part of the six-membered heterocycle [75] (Scheme 17).

The X-ray diffraction analysis of the phosphorus heterotetracycle bearing a P = Se bond shows the ring conformation (Fig. 28). In solid state, formation of dimers is observed, by two C–H···N cooperative hydrogen bonds together with π-stacking of two molecules (Fig. 29).

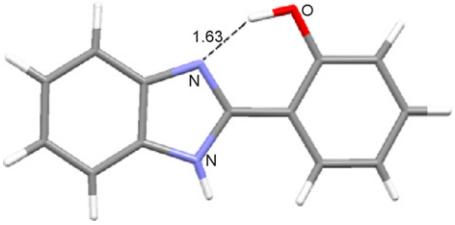
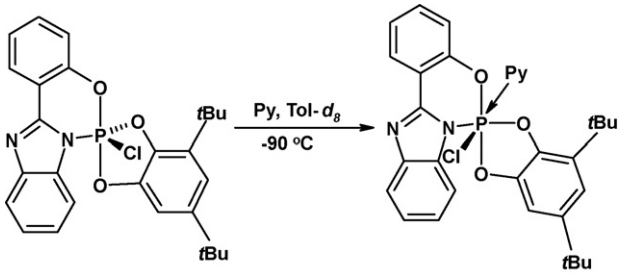


Fig. 27. X-ray diffraction structure of 2-(2-hydroxyphenyl)-1H-benzimidazole [69].



Scheme 17. Pentacoordinated phosphorus compound derived from 2-(2-hydroxyphenyl)-1H benzimidazole, which behaves as a Lewis acid coordinating a pyridine molecule [75].

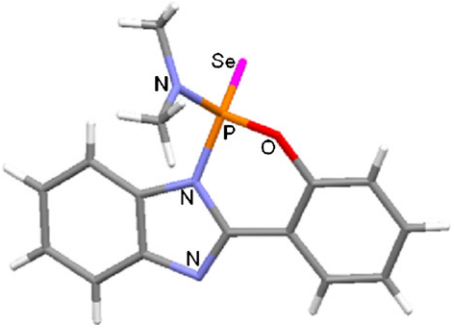


Fig. 28. 2-Seleno oxazaphosphorinane obtained from 2-2-(2-hydroxyphenyl)-1H-benzimidazole [75].

The formation of fused planar boron heterotetracycles can be done by heating the N–BH_3 adduct of 2-(2-methoxyphenyl)-1H-benzimidazole or 2-(2-methoxyphenyl)-1H-benzothiazole provoking an intramolecular rearrangement and the benzazole ring opening [38] (Scheme 18).

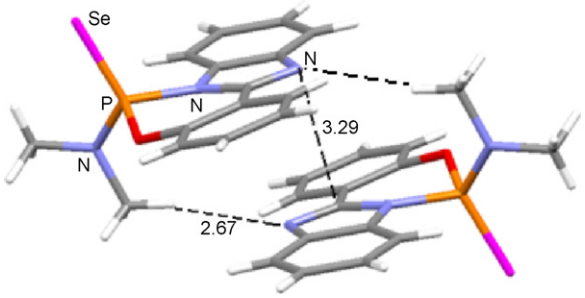
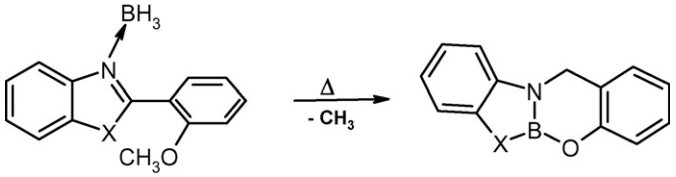


Fig. 29. Dimeric association of 2-seleno oxazaphosphorinane obtained from 2-(2-hydroxyphenyl)-1H-benzimidazole ligand (Å) [75].



Scheme 18. Rearrangement of N–BH_3 adducts of 2-(2-methoxyphenyl)-1H-benzazoles, X = N–Et or S [38].

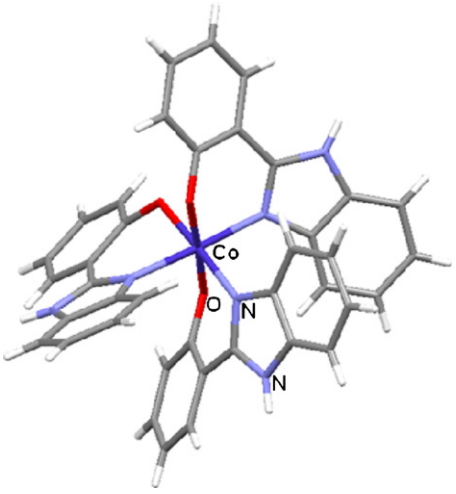


Fig. 30. X-ray diffraction structure of the distorted *mer*-octahedral Co(III) compound derived from 2-(2-hydroxyphenyl)-1H-benzimidazole [69].

A very distorted hexacoordinated Co(III) compound was obtained, by the coordination of three anionic ligands, through oxygen and nitrogen (Fig. 30). The compound has a distorted *mer*-octahedral structure (C1 point group). The distortion originates from the tension of the six-membered chelate rings [69]. The diamagnetic nature of the molecule allowed the NMR study.

Rhenium $[Re_2(CO)_6$-{2-(2-hydroxyphenyl)benzimidazole)}$_2]$ [76] and beryllium(II) complexes with substituted 2-(2-hydroxyphenyl)benzimidazoles have been reported [77]. Its iron complexes undergo, upon drying, a core conversion toward an oxo-bridged di-ferric species reversible through recrystallization from wet EtOH [78], while the six-coordinate monomeric Mn(III) compound presented superoxide dismutase-like activity [79]. Photoluminescence is reported for two zinc(II) compounds [80].

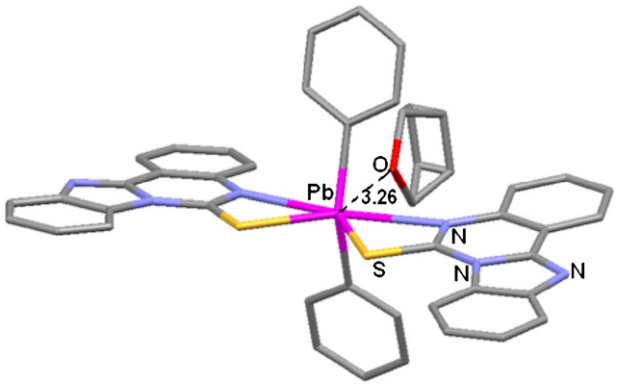


Fig. 31. Heptacoordinated Pb compound derived from 5H-benzimidazo[1,2-*c*]quinazoline-6 thione [83].

3.2.5. 2-(2-Aminophenyl)-1H-benzimidazole

2-(2-Aminophenyl)-1H-benzimidazole gives tri-, tetra- and pentacoordinated phosphorus heterocycles [81] (Scheme 19).

Selective sensors for zinc(II) based on 2-substituted 2-phenyl benzimidazole, use the inhibition of intramolecular proton transfer excited state and have useful biological applications [82].

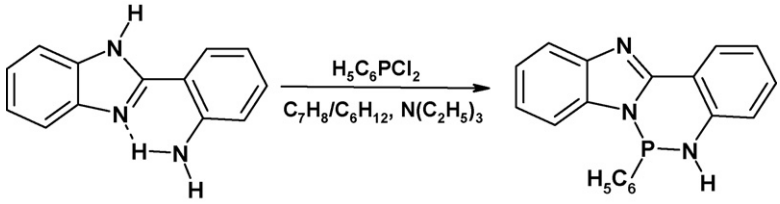
The reaction of 2-(2-aminophenyl)-1H-benzimidazole with CS_2 gave the tetracyclic compound 5H-benzimidazo[1,2-*c*]quinazoline-6-thione, which may present three tautomers (Scheme 20).

The resulting fused tetracyclic compound is a planar ligand in compounds with tin and lead, giving place to penta, hexa and heptacoordinated derivatives. The metal atom is bound to the sulfur atom and weakly coordinated by the nitrogen atom. The ^{119}Sn and ^{207}Pb NMR were useful for the characterization of these compounds in solution. The X-ray diffraction structure showed that the lead atom is heptacoordinated, with a pentagonal bipyramidal geometry, being a *cis–mer* isomer [83] (Fig. 31). The sulfur atoms lie very close to each other, due to a stabilizing S···S interaction. The angle S–Pb–S is 79.94° whereas N–Pb–N is 165.47°.

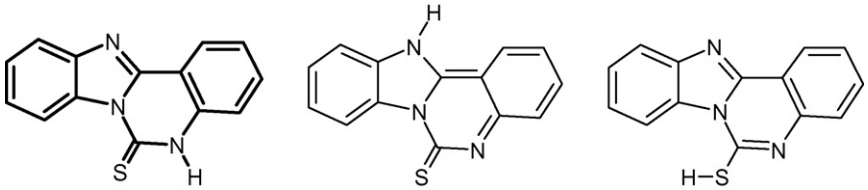
3.3. Benzazoles bearing N-substitutens at C2

2-Aminobenzimidazole derivatives show relevant biocidal activities [84]. The compound has been used as a synthon in a broad variety of new substances of scientific, pharmaceutical and industrial applications [85].

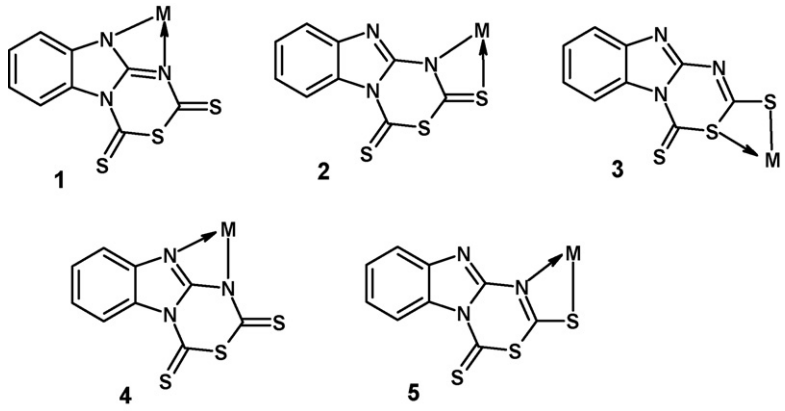
Reaction of 2-aminobenzimidazole with CS_2, in the presence of KOH, affords the potassium salt of a tricyclic compound, 9H-



Scheme 19. Synthesis of a tricoordinated phosphorus fused tetracycle [81].



Scheme 20. Tautomers for 5H-benzimidazo[1,2-c]quinazoline-6-thione [83].



Scheme 21. Metal coordination modes for 9H-3-thia-1,4a,9-triaza-fluorene-2,4-dithione [86].

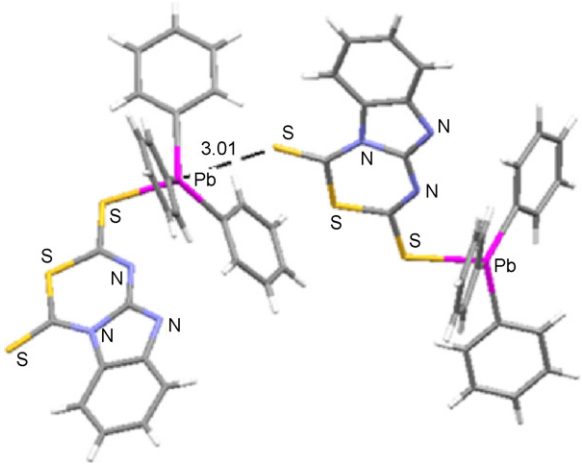


Fig. 32. X-ray crystal structure of the triphenyllead compound derived from 9H-3-thia-1,4a,9-triaza-fluorene-2,4-dithione [86].

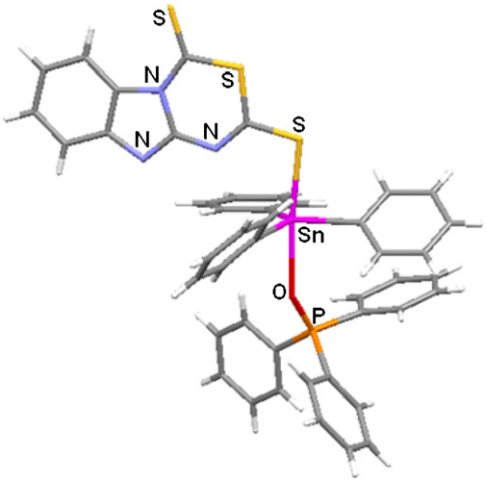
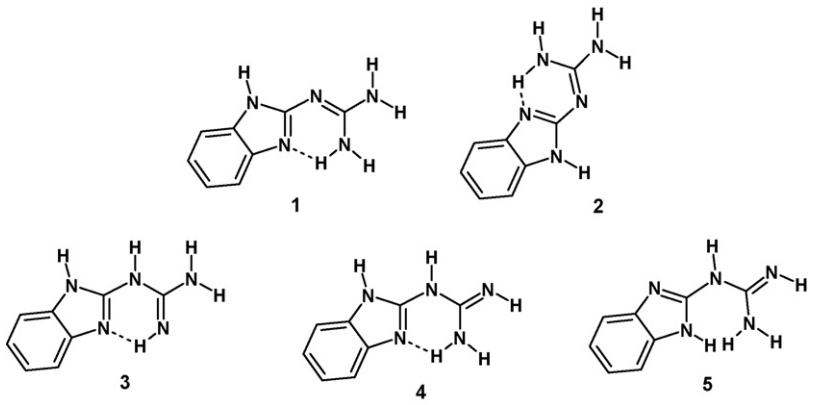


Fig. 33. Hexacoordinated tin compound obtained from 9H-3-thia-1,4a,9-triaza-fluorene-2,4-dithione and Ph_3PO [86].

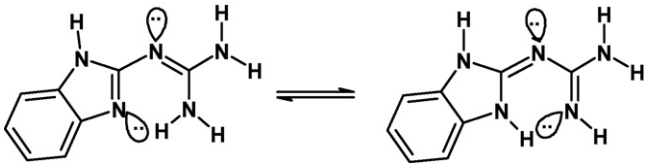
3-thia-1,4a,9-triaza-fluorene-2,4-dithione. The investigation of the coordination compounds of this ligand is relevant, due to its several coordination sites [86] (Scheme 21).

Triphenyl lead, tin and germanium coordination compounds were obtained from 9H-3-thia-1,4a,9-triaza-fluorene-2,4-dithione, by metathesis reactions of its potassium salt with Ph_3MCl [M = Ge, Sn and Pb]. The corresponding metal pentacoordinated compounds were obtained and studied in solution by ^{119}Sn and ^{207}Pb NMR. The metal atoms are bound to the sulfur atom and weakly coordinated by N10, (structure 5 of Scheme 21). The N → Pb coordination forms a four-membered metallacycle. The X-ray structure of the lead compound shows an intermolecular S → Pb bond (3.01 Å) which allows a polymeric arrangement of hexacoordinated lead atoms (Fig. 32).

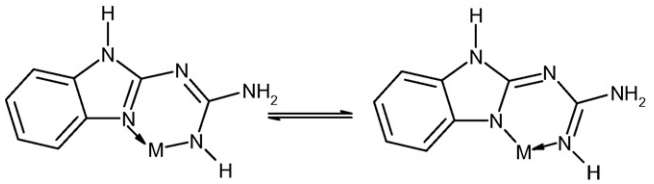
The metal atoms, in the compounds derived from 9H-3-thia-1,4a,9-triaza-fluorene-2,4-dithione, behave as strong Lewis acids. This fact, and the spatial arrangement of the three phenyl groups, allowed an additional coordination of the solvent. Hexacoordinated compounds were obtained by addition of pyridine, DMSO, $Ph_3P=O$, water or THF. X-ray diffraction analysis for all of them



Scheme 22. Five possible conformers and tautomers of 2-guanidinobenzimidazole.



Scheme 23. Resonance contributors to the more stable tautomer in 2-guanidinobenzimidazole. The hydrogen bond and the resonance stabilize the structure by 22.6 kcal/mol [87].



Scheme 24. Two resonance contributors are involved in the coordination compounds of 2-guanidinobenzimidazole, as deduced from N3 and N12 bond lengths [88,89].

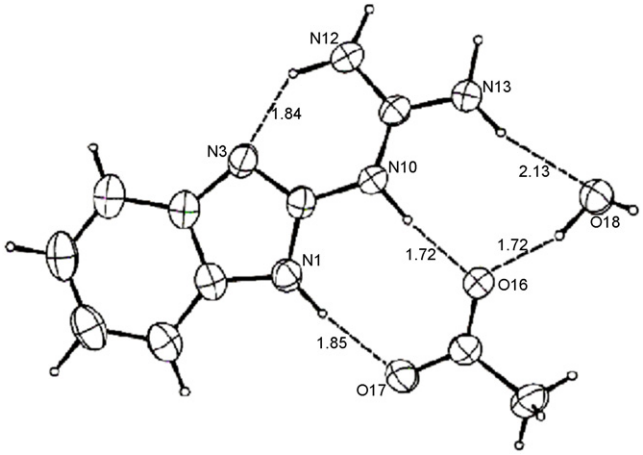


Fig. 34. X-ray diffraction analysis of protonated 2-guanidinobenzimidazole (Å) [88].

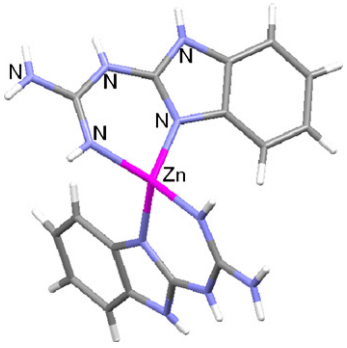


Fig. 35. Tetrahedral zinc coordination compound derived from 2-guanidinobenzimidazole [88].

was performed. As an example, the $Ph_3P{=}O$ compound is shown in Fig. 33.

3.3.1. 2-Guanidinobenzimidazole

The polyfunctional 2-guanidinobenzimidazole is an important planar ligand, rich in nitrogen atoms, lone pairs and N–H labile protons. The molecule has complex equilibria between several conformers and tautomers (Scheme 22).

A theoretical study of the ligand was performed (RHF/6-321, NBO), indicating that the more stable structure of the ligand has a NH proton forming a hydrogen bond through a six-membered ring (the stabilization energy was calculated as being 22.6 kcal/mol). This structure is in resonance between two contributors [87] (Scheme 23).

This ligand coordinates protons, methyl cations, Lewis acids and metal ions. The X-ray diffraction analysis of the protonated ligand, confirms that the molecule has an internal strong hydrogen bond N12–H···N3 and that protonation occurs at N10 instead of N3 [88] (Fig. 34).

Cobalt(II), nickel(II), copper(II) and zinc(II) coordination compounds derived from 2-guanidinobenzimidazole, were reported together with a theoretical analyses. Two different coordination modes were found, mono and bidentate, the first by N3 in cobalt(II) compounds, the latter one, by N3 and N12 [89].

In the transition metal coordination compounds, formally the N12 proton is substituted by the metal atom, and coordinated by the imidazolic N3. However, the resulting structure is the average of two resonance contributors. The existence of a delocalization in these coordination compounds is deduced from the C–N and N–M bond lengths, which are in between single and double bonds [88,89] (Scheme 24).

The reaction of $Zn(NO_3)_2{\cdot}H_2O$ with 2-guanidinebenzimidazole afforded the protonated tetracoordinated zinc compound, with two nitrates outside the coordination sphere [88] (Fig. 35).

From the reaction performed with the ligand, $NiCO_3$ and $2Ni(OH)_2{\cdot}4H_2O$, a neutral nickel(II) compound was obtained. The metal atom is in a square planar geometry, where the two bidentate ligands are in different planes (Fig. 36) [88]. Whereas, the reaction with $Ni(NO_3)_2{\cdot}6H_2O$ afforded the protonated ionic complex.

The bond lengths obtained from the X-ray diffraction analyses of both nickel(II) compounds are shown in Scheme 25. From

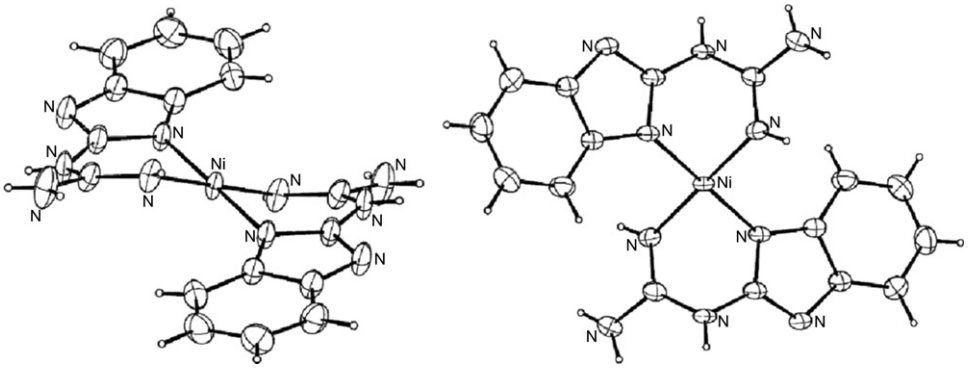
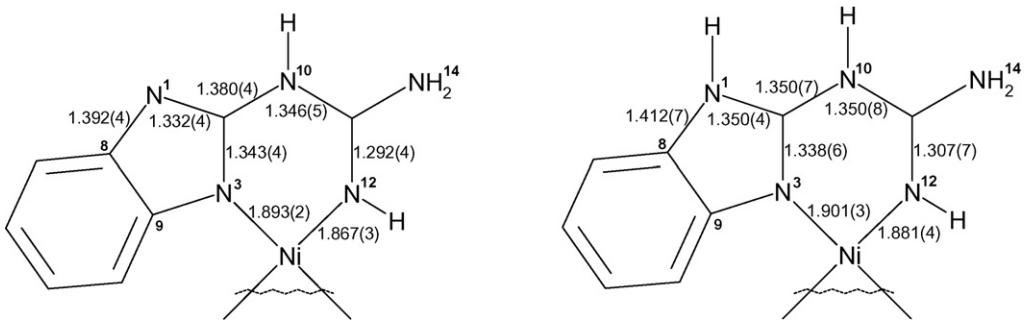


Fig. 36. Two views of the solid state structure of the neutral nickel compounds derived from 2-guanidinobenzimidazole [88].



Scheme 25. Bond lengths in the metallocycles with 2-guanidinobenzimidazole; (left) neutral nickel(II) compound [64]; (right) ionic (protonated) nickel(II) compound [88].

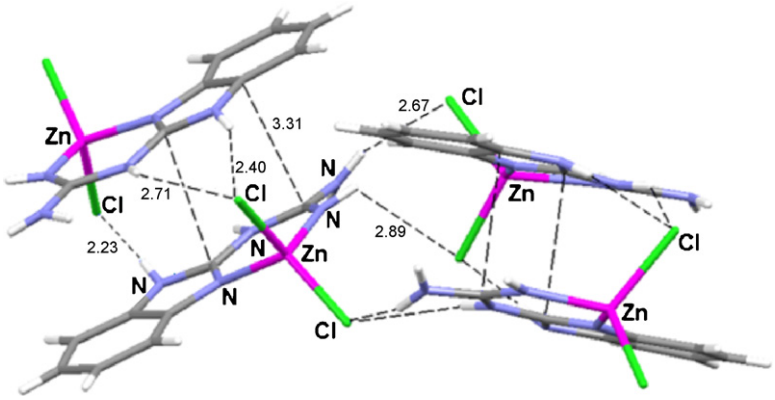


Fig. 37. Dichlorozinc coordination compounds bearing a 2-guanidinebenzimidazole ligand. Intermolecular interactions (Å) are shown.

these data, the electronic delocalization of these metallocycles is observed.

Recently, a dichloro zinc(II) 2-guanidinobenzimidazole compound was obtained [34]. The molecule presents intermolecular interactions by π-stacking and cooperative N–H···Cl hydrogen bonds (Fig. 37).

A dinuclear chromium compound derived from 2-guanidine was synthesized, which has two bidentate ligands bound to each chromium(III) and two O–H bridges. The two chromium(III) ions and two oxygen atoms form a four-membered ring. The distance Cr–O is 1.960 Å and Cr···Cr is 3.085 Å, (Σr_{vdw} = 4.1 Å [52]). The ligands are coordinated to each metal atom in equatorial-axial positions. Interestingly, the ligand is not planar, the guanidine heterocycle is out of the plane. The distortion is provoked by strong intermolecular hydrogen bonds with water molecules and ClO_4^- (not shown) (Fig. 38). The short distances between the metal atoms are favored by π-stacking of the benzimidazole rings (3.46 Å) [60].

The X-ray diffraction analyses of two [Cu(guanidinobenzimidazole)$_2$(CF$_3$SO$_3$)$_2$] show that the Cu(II) atoms adopt a distorted tetrahedral geometry in both compounds [90]. Supramolecular structures based on doublet (DA) or triplet (DAD) hydrogen bonding motifs were found in crystals of copper(II) complexes of bidentate guanidino derivatives [91].

The studied cytotoxicity of 2-guanidinobenzimidazole coordination compounds, among several 2-substituted benzimidazoles, presents promising antineoplasic activity [34].

2-Guanidinobenzimidazole heterocycles are formed by boron substitution of the N12 proton and N3 coordination [92]. NMR and X-ray diffraction analyses of several boron heterocycles were performed. The boron forms a six-membered ring, with the two N–B bond distances in between a covalent and a coordination bond. The boron acquires a negative charge, whereas the positive charge is delocalized among the nitrogen atoms (Fig. 39).

A pentacoordinated tin compound was obtained from 2-guanidinobenzimidazole and SnR$_3$Cl in the presence of a base [93]. The tin heterocycle was identified by NMR (Scheme 26).

3.3.2. 2-Uroylbenzimidazole

The presence of a urea group bound to C2 in 2-uroylbenzimidazole, allows several tautomers (Scheme 27). This behavior could give place to different types of coordination modes which will depend on the more stable tautomer.

The X-ray diffraction analysis of 2-uroylbenzimidazole (Fig. 40) showed that its tautomers in the solid state corresponded to the first

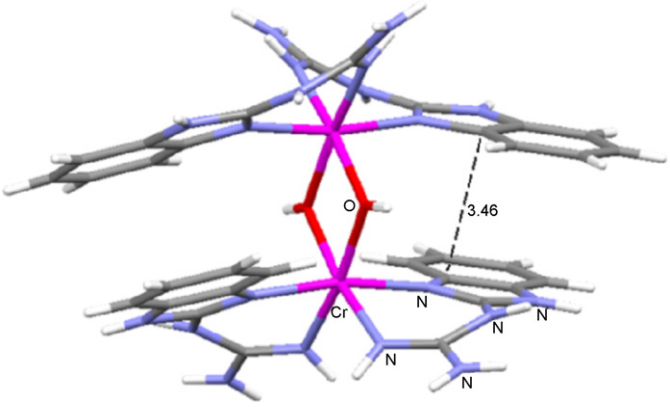


Fig. 38. Chromium(III) dinuclear compound derived from 2-guanidinobenzimidazole (Å).

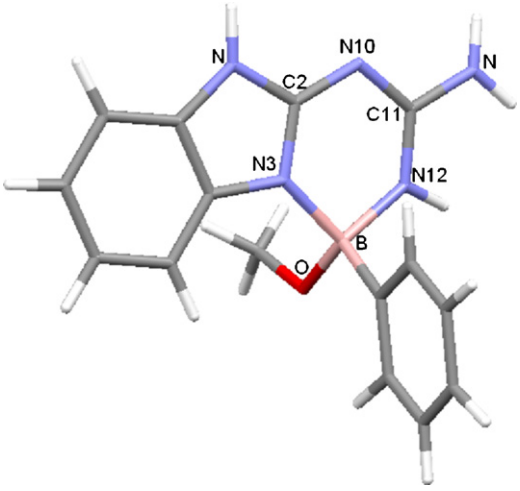
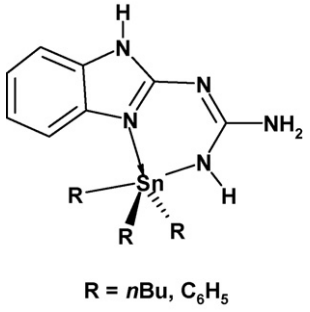


Fig. 39. X-ray diffraction structure of a phenylboron heterocycle derived from 2-guanidinobenzimidazole. The bond lengths (Å) B–N3 1.568(5), B–N12 1.550(5), N3–C2 1.345(5), N12–C11 1.314(5), N10–C2 1.342(5), N10–C11 1.347(5) indicate the ring electronic delocalization [92].

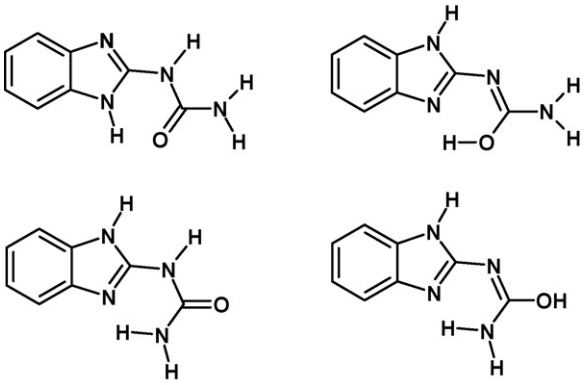


Scheme 26. 2-Guanidinobenzimidazole with a pentacoordinated tin atom [93].

structure in Scheme 27. The molecule has a strong intramolecular N–H···O hydrogen bond (2.20 Å) and two cooperative intermolecular N–H···O (2.15 Å) [94].

In the cadmium(II) and zinc(II) coordination compounds derived from 2-uroylbenzimidazole, the ligand is monodentate. The preferred conformation has an N–H hydrogen bound to the carbonyl group forming a six-membered ring (Scheme 28) [94]. The copper(II), nickel(II) and cobalt(II) complexes contain bidentate ligands, through the oxygen and nitrogen atoms (Scheme 29).

Recently, an octahedral copper(II) nitrate compound with uroylbenzimidazole was isolated and its X-ray crystal structure was



Scheme 27. Four possible tautomers for 2-uroylbenzimidazole.

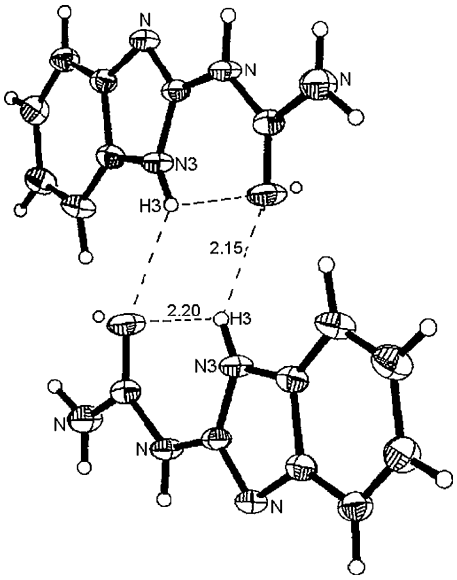
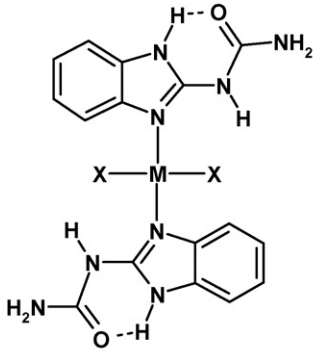
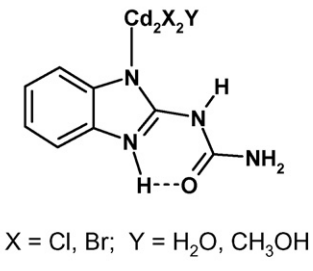


Fig. 40. X-ray diffraction analysis of 2-uroylbenzimidazole [94].

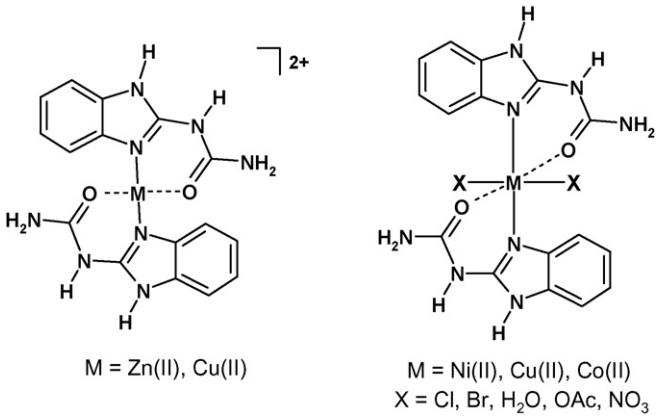
determined. The metal ion is in an octahedral geometry with two coplanar bidentate ligands, and coordinated to two ethanol molecules in axial positions [95] (Fig. 41).

The reaction of the 2-uroylbenzimidazole with diphenylboronic acid gives two different heterocycles, in one, the boron is linked by two nitrogen atoms, in the other by oxygen and nitrogen [94] (Scheme 30). The reaction of the ligand with diphenylchloroborane





Scheme 28. Monodentate uroylbenzimidazole derivatives [94].



Scheme 29. Bidentate, tetra and hexacoordinated, uroylbenzimidazole derivatives [94].

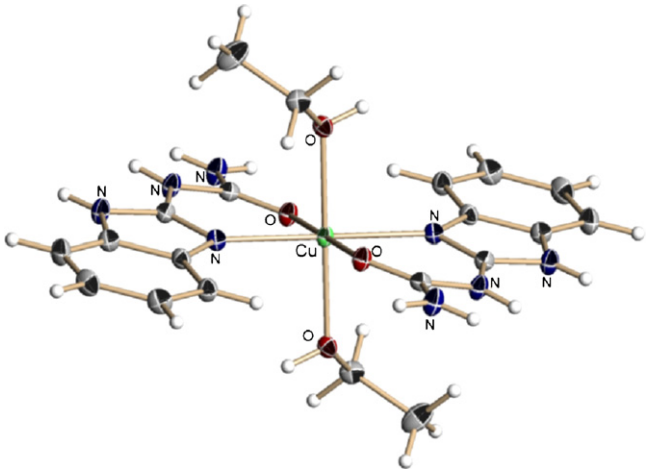


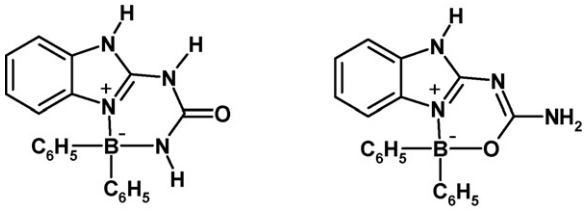
Fig. 41. Copper(II) coordination compound of 2-uroylbenzimidazole [96].

affords only the compound where boron is bound to two nitrogen atoms.

3.3.3. 2-Aminobenzothiazole

Recently, this azole has been used for the synthesis of coordination compounds. Niobium derivatives were obtained from $[[\eta\text{-}5\text{-}C_5H_4SiMe_3]_2Nb(H)_3]$ with 2-substituted benzothiazole heterocycles, yielding niobiocene complexes [97]. With transition metal ions, the tetrahedral complexes of Co(II) acetate and Zn(II) chloride with 2-aminobenzothiazole, $Co(CH_3COO)_2$(2-aminobenzothiazole)$_2$ and $ZnCl_2$(2-aminobenzothiazole)$_2$ [98] and *bis*(2-aminobenzothiazole-*N*)dichlorocobalt(II) have been synthesized [99].

3.3.3.1. 2-Aminobenzothiazole phosphoramides. 2-Aminobenzothiazole phosphoramides are polyfunctional and very effective



Scheme 30. Two different boron heterocycles obtained from diphenylborinic acid and 2-uroylbenzimidazole [94].

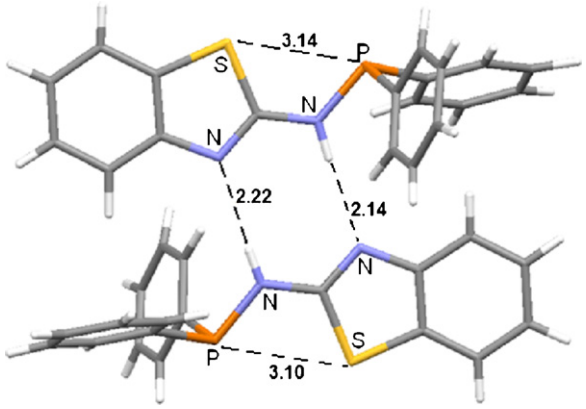


Fig. 42. X-ray diffraction structure of 2-aminobenzothiazole diphenylphosphane, distances P–S are 3.10 and 3.14 Å [96].

ligands. In the 2-aminobenzothiazole-diphenylphosphane a P → S weak interaction has been found [96] (Fig. 42). The phosphorus lone pair is pointing to the sulfur atom, with a distance P → S of 3.14 Å shorter than the Σr_{vdw} (3.75 Å [52]). In the crystal, the molecule forms dimers *via* two cooperative N–H···N hydrogen bonds.

Oxidation of 2-aminobenzothiazolediphenylphosphane by oxygen, sulfur and selenium gives molecules, where the chalcogen atoms are in *cis* position, that could be explored as ligands. From the X-ray of the P=S molecule, short contacts S···S of 3.13 Å (Σr_{vdw} = 3.6 Å [52]) were observed, with the formation of a dimer by four cooperative hydrogen bonds [96] (Fig. 43).

The reaction of 2-aminobenzothiazole-diphenylphosphane, with *n*BuLi in THF, in the presence of 1,4,7,10,13,16-hexaoxacyclooctadecane, afforded a dilithium compound derived from the oxidation of the ligand and isolated after slow crystallization (Fig. 44). A THF molecule was coordinated to the lithium. The preference of the endocyclic nitrogen coordination to lithium, instead of to sulfur is noteworthy. The molecule has a fused heptacyclic compound bearing, six-, five- and four-membered rings.

The equimolar reaction of 2-aminobenzothiazole-diphenylphosphane with $Pb(NO_3)_2$, in THF and NEt_3HCl, gave the diphenyltetrachloro plumbate, with the protonated ligand. Phenyl and chloro migration from phosphorus to lead atom was the origin of the reaction product [96] (Fig. 45).

3.3.3.2. Thio derivatives of 2-aminobenzothiazole. We have prepared a series of 2-aminobenzothiazole derivatives, having as coordinating sites nitrogen and sulfur atoms. These polyfunctional molecules

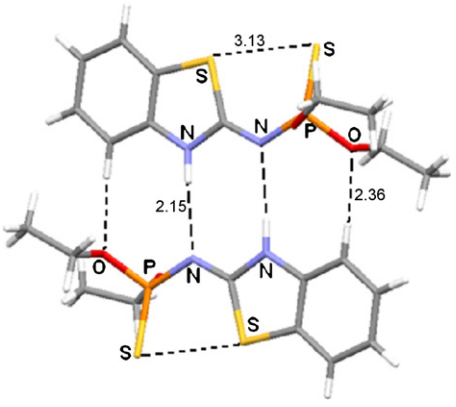


Fig. 43. X-ray diffraction showing the dimeric association of 2-aminobenzothiazole-diethylphosphane sulfide and intra- and intermolecular interactions (Å) [96].

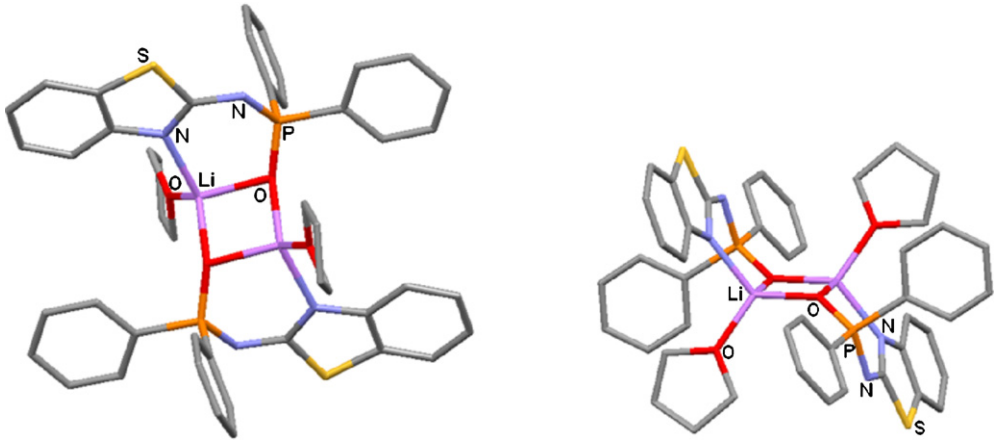


Fig. 44. Two views of the fused heptacyclic lithium compound derived from 2-aminobenzothiazole-diphenylphosphane oxide [96].

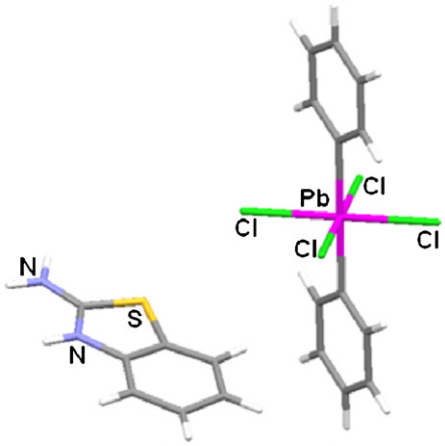


Fig. 45. X-ray diffraction analysis of the 2-aminobenzothiazolium diphenyltetrachloro plumbate [96].

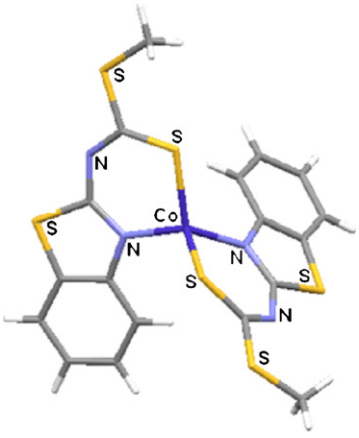


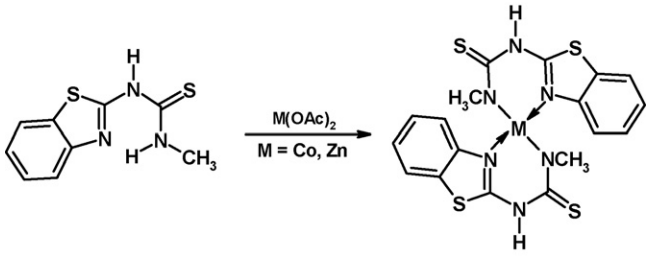
Fig. 46. Solid state structure of the cobalt(II) compound derived of methyl *N*-(benzothiazol-2-yl)-dithiocarbamic ester [100].

proved to be versatile ligands giving interesting coordination compounds with transition metal ions [100].

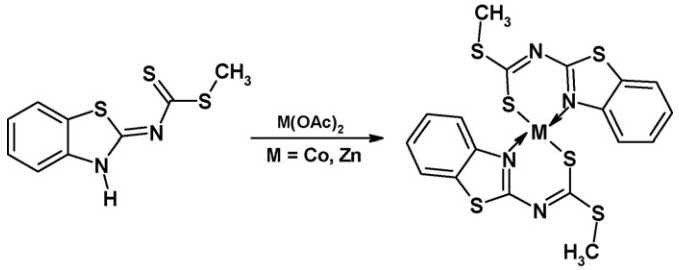
Cobalt(II) and zinc(II) ions are tetracoordinated in the *N*-(benzothiazol-2-yl)-dithiocarbamic acid methyl ester compounds. Two ligands are bound through the endocyclic nitrogen and a sulfur atom [100] (Scheme 31). The X-ray diffraction structure of the tetrahedral cobalt compound is in Fig. 46.

On the other hand with 1-benzothiazole-2-ylid-3-methyl-thiourea a different coordination mode was found, two nitrogen atoms were coordinated to the metal ion, as was deduced from NMR analyses [100] (Scheme 32).

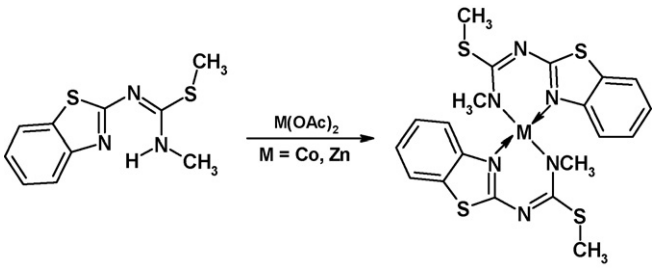
Bis-chelate compounds were obtained with 1-benzothiazole-2-yl-2,3-dimethyl-*iso*-thiourea and the cobalt(II) and zinc(II) acetates (Scheme 33). Crystal structure analyses showed that the metal ion



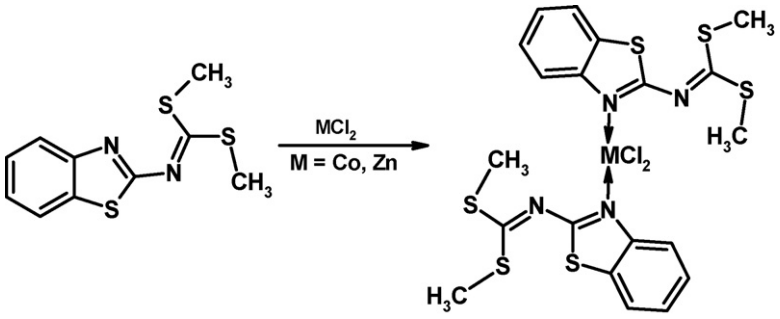
Scheme 32. Cobalt(II) and zinc(II) coordination compounds of 1-benzothiazole-2-ylid-3-methyl-thiourea [100].



Scheme 31. *N*-(benzothiazol-2-yl)-dithiocarbamic acid methyl ester gives cobalt(II) and zinc(II) spiranic compounds [100].



Scheme 33. 1-Benzothiazole-2-yl-2,3-dimethyl-*iso*-thiourea reacted with cobalt(II) and zinc(II) acetates to give tetrahedral compounds [100].



Scheme 34. Synthesis of cobalt(II) and zinc(II) coordination compounds derived from *N*-(benzothiazol-2-yl)-*S*,*S*′-dimethyl-dithio-carboimine [100].

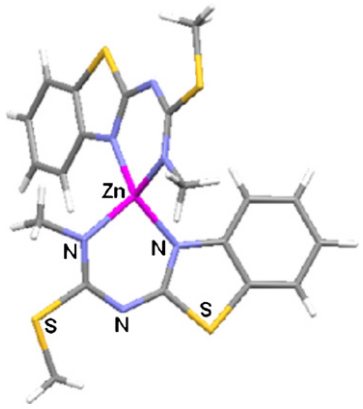
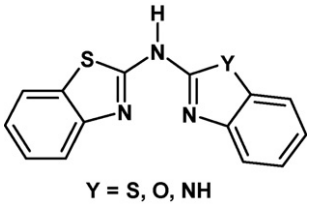


Fig. 47. Zinc compound derived from 1-benzothiazole-2-yl-2,3-dimethyl-*iso*-thiourea [100].

is bound to the two nitrogen atoms [100]. The solid state structure for the zinc(II) compound is in Fig. 47.

A different behavior was found for *N*-(benzothiazol-2-yl)-*S*,*S*′-dimethyl-dithio-carboimine, which acts as a monodentate ligand, through N3 [100]. The metal atom is in a tetrahedral geometry (C_2 point group) (Scheme 34, Fig. 48).

3.3.3.3. Bis(benzazole-2-yl)amine. The *bis*(benzazole-2-yl)amine derivatives, obtained from 2-aminobenzothiazole, proved to be excellent ligands [101] (Scheme 35). The non-symmetrical ligand, when Y = O, NH, could give 12 tautomers and conformers, indicating several possible coordination modes for these planar molecules (Scheme 36). Compounds offer a couple of atoms (nitrogen, sulfur or oxygen) conveniently arranged for a bidentate coordination to a metal atom.



Scheme 35. *Bis*(benzazole-2-yl)amines [101].

Coordination compounds with cobalt(II), nickel(II), zinc(II) and mercury(II) acetates with *bis*(benzazole-2-yl)amine gave different structures [101]. When a ratio 2:1 [ligand:metal] was used, *bis*-chelate tetrahedral compounds were obtained. The crystal structures of cobalt(II), zinc(II) and mercury(II) are similar, the latter is in Fig. 49. This compound has two orthogonal planar ligands forming each one a planar five fused ring system, the metal atom being in a six-membered ring. It is interesting that the ligand is bound through both nitrogen atoms. The distance of the vicinal C–H protons to the coordinated nitrogen atoms are quite close to the metal ions. In the different compounds (≈3.0 Å) is shorter than the sum of the van der Walls radii [Σr_{vdw} 3.25 Å [52]).

The fused planar tetracycles form dimers by π-contacts (distance between nitrogen atoms is 3.53 Å) and by two cooperative C–H···N hydrogen bonds (2.64 Å) (Fig. 50).

The fused ring systems in these compounds merit some comments. The four N → M bonds are similar and relatively short. The C–N bond lengths for the six-membered metallacycles are in between double and single bonds, indicating that the metal atom is participating in the electronic delocalization of the π-system (Scheme 37). This delocalization is observed in the electronic spectrum of the tetrahedral cobalt(II) compound (orange crystals), which shows a broad electronic transition in the UV–vis region [101].

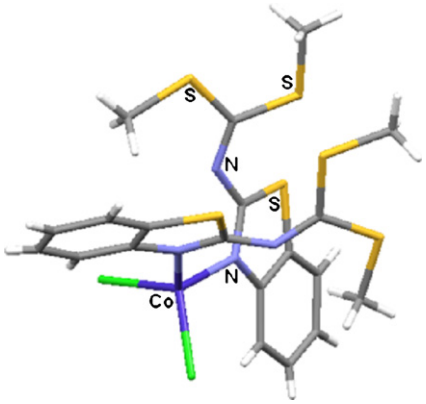


Fig. 48. Cobalt(II) compound derived from *N*-(benzothiazol-2-yl)-*S*,*S*′-dimethyl-dithio-carboimine [100].

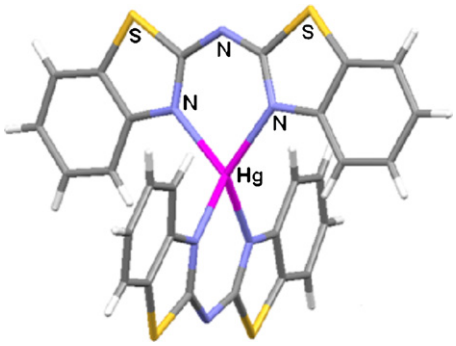
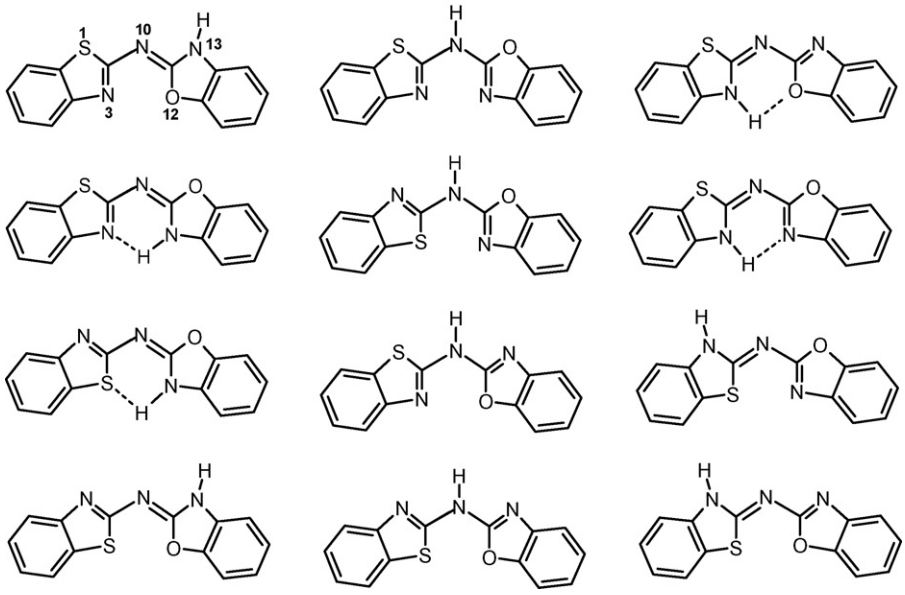


Fig. 49. X-ray diffraction structure of the mercury compound derived from 2-(2-benzothiazolylamino)benzothiazole [101].



Scheme 36. Twelve possible tautomers and conformers for 2-(2-aminobenzothiazolylamino)benzoxazole.

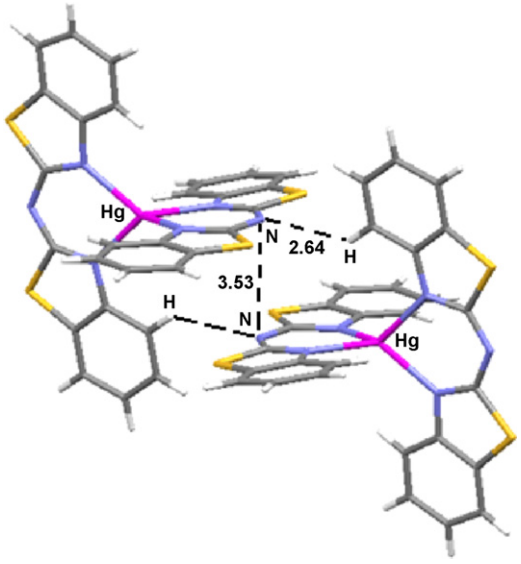


Fig. 50. Dimeric association by π-contacts and two cooperative C–H···N hydrogen bonds in the mercury compound, derived from 2-(2-benzothiazolylamino)benzothiazole [101].

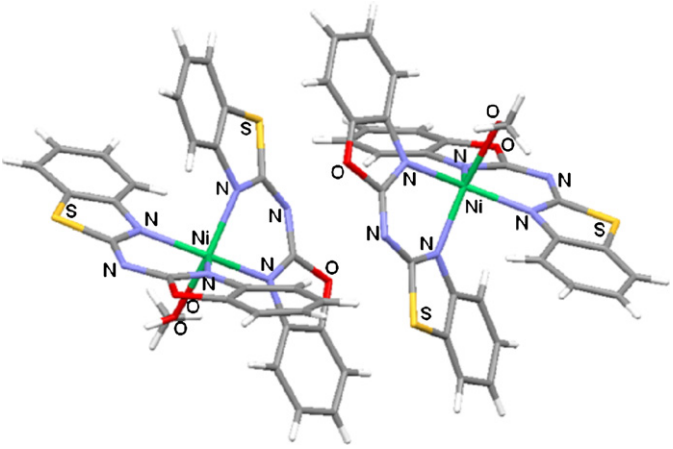


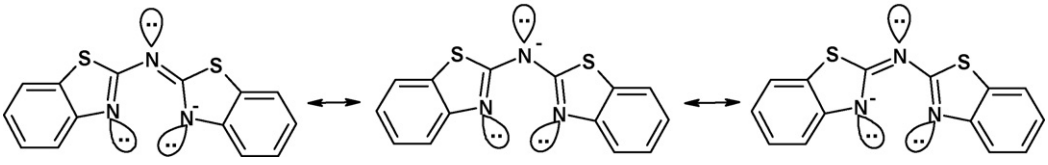
Fig. 51. Enantiomeric structures of a pentacoordinated square pyramidal nickel(II) compound derived from 2-(2-aminobenzothiazolylamino)benzoxazole [101].

With the non-symmetrical ligand 2-(2-aminobenzothiazolylamino)benzoxazole several nickel(II) coordination compounds were obtained, where the metal ion acquires different geometries. In the spiranic pentacoordinated nickel(II) complex, the metal ion is in a square pyramidal geometry, with the fifth position occupied by an ethanol molecule. The molecule belongs to the C1 point group, both enantiomers are shown in Fig. 51.

Another nickel compound, bearing one bidentate ligand and one bidentate acetate, both lying in the same plane, and two ethanol molecules *trans* coordinated, was synthesized (Fig. 52).

Examination of the equatorial plane of the molecule shows that the C4-protons of the benzyl rings form strong hydrogen bond with the oxygen atoms of the acetate, depicting a fused and planar heterocyclic system of nine rings (Fig. 53), of C_1 symmetry.

The planar rings give interesting strong intermolecular π-interactions (≈3.3 Å), together with two strong cooperative OH···N hydrogen bonds (2.10 Å), giving a dimeric association. The oxygen atoms are tricoordinated (Fig. 54).



Scheme 37. Delocalization of the negative charge at the deprotonated 2-(2-benzothiazolylamino)benzothiazole.

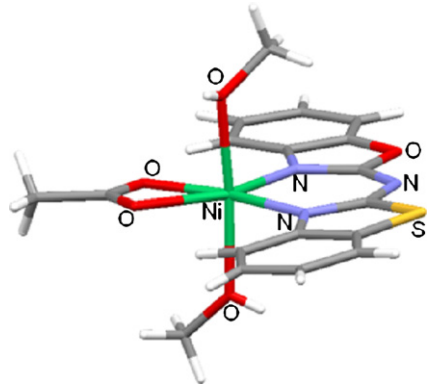


Fig. 52. X-ray diffraction analyses of the nickel(II) acetate compound derived from 2-(2-aminobenzo-thiazolylamino)benzoxazole [101].

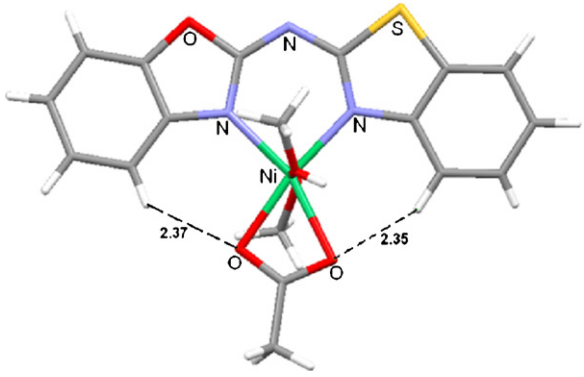


Fig. 53. View of the equatorial plane of the nickel(II) acetate derived from 2-(2-aminobenzo-thiazolylamino)benzoxazole [101].

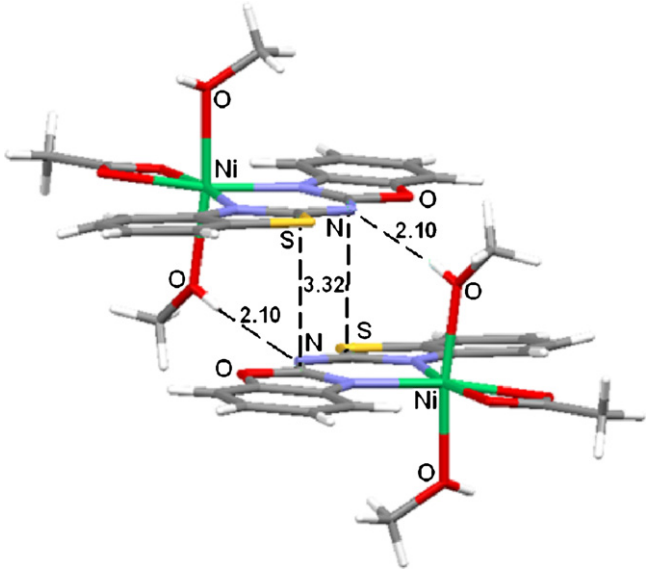


Fig. 54. The octahedral nickel(II) acetate compound derived from 2-(2-aminobenzothiazolylamino)benzoxazole forms dimers by cooperative OH···N hydrogen bonds and π-stacking [101].

4. Concluding remarks

This review summarizes contributions from our and some other research groups in the coordination chemistry of azoles and benzazoles. These brief comments show that there is a versatile chemistry involved in these compounds, based on a great structural diversity, reactivity and applications. From the structural point of view, the ligands offer a diverse combination of donor atoms, promoting hypervalent atoms and a wide spectrum of molecular geometries and interactions. The formation of metallacycles allows one to study the participation of the metal ion into the electronic delocalization of the organic π-systems. The high electron density of the ligands, the planar delocalized and rigid framework favor many weak interactions, giving place to an enormous possibility of macromolecular assemblies based on hydrogen bonds, π-stacking and Lewis acid–base coordination.

The preliminary biological screening of many of these compounds opens the possibility for their use as future antiparasitics, biocides or anticancer drugs. The compounds could also be used in materials science as synthons for the construction of nano or microdevices.

The research done up to now in this subject is only a glimmer of the potential of this field, and a small sample of the enormous possibilities of future research in this area.

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