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X-ray structural analysis of biologically relevant aluminium(III) complexes

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Abstract

The X-ray crystal structures of selected aluminium compounds which may be of relevance to understanding aluminium binding in biological contexts are described. These fall into four main categories: (a) those complexes where the metal is in a mononuclear environment, as would be found in siderophore and similar chelating agent complexes, exemplified by the structures observed with oxygen donors and with N/O donors; (b) polynuclear aluminium complexes which are possibly important species in hydrolysing environments and relevant to aluminium uptake and bioavailability; (c) aluminium in environments found in metalloproteins; and (d) aluminium minerals relevant to bioavailability and to aluminium biomineralization and storage.

Keywords: Aluminium complexes; X-ray crystal structure; Bioavailability

List of abbreviations

ox	oxalic acid
malo	malonic acid
nta	nitrilotriacetic acid
edta	ethylenediaminetetraacetic acid
cit	citric acid
Hhbo	2-(2′-hydroxyphenyl)-2-oxazoline
heidi	*N*-(2-hydroxyethyl)iminodiacetic acid
TEA	triethanolamine
THF	tetrahydrofuran
OEP	octaethylporphyrin

1. Introduction

In this article we describe X-ray crystal structures of aluminium compounds which may be of relevance to understanding aluminium binding in biological contexts. Our aim has been to highlight compounds which illustrate the chemically important species that aluminium can form which are of biological relevance.

1.1. General aspects of aluminium(III) chemistry

Aluminium is found in an environment of six oxygen atoms in most aluminium minerals [1], and this underlines the highly oxophilic character of the trivalent metal ion. Thus, in biological situations where oxygen ligands are found there is likely to be good binding of aluminium(III), possibly at the expense of iron(III) binding, particularly in situations where kinetic effects are important, as iron(III) is far more labile than aluminium(III). Since iron is mostly taken up as a trivalent ion as mononuclear complexes with oxygen or mixed oxygen and nitrogen binding, it is relevant to compare the structures observed for aluminium(III) in similar ligand environments. In terms of biological environments, the hydrolytic chemistry of the two metal ions will be an important influence on the solubility and bioavailability of metal species. These in turn are governed by factors such as pH, binding by ligands, relative concentrations of ligand and metal, dilution and ionic strength.

1.2. Comparison with high-spin iron(III)

Aluminium(III) has an ionic radius of 54 pm, whereas high-spin iron(III) has a radius of 65 pm, larger than the aluminium radius but comparable to that of gallium(III) at 62 pm. Thus it is likely that these three metals will form analogous compounds favouring similar types of ligands, although the higher polarizing power of aluminium(III) makes it even more oxophilic than the other two.

1.3. The use of X-ray crystallography

Single-crystal X-ray structure determinations on aluminium complexes can provide metrical information and give insights into preferred binding modes. However, it must be borne in mind that complexes which crystallize out of solution may not necessarily be important species in solution. The technique requires single crystals of reasonable dimensions, preferably stable under ambient conditions. It is interesting that whereas gallium and indium analogues of iron(III) high-spin complexes crystallize relatively easily, there are few reports of the corresponding aluminium crystal structures. The paucity of published structures of aluminium coordination compounds is probably a reflection of the difficulties in obtaining suitable single crystal samples. With the advent of more powerful diffractometers it should be possible to measure data on smaller crystals.

2. Biological relevance, uptake, transport and storage: the role of hydrolysis

Owing to the extensive hydrolysis of iron(III) in aqueous media, which results in the formation of insoluble oxyhydroxide mineral phases, it has been necessary for nature to devise ways of controlling this hydrolysis. For iron uptake this means that the iron must be in a soluble and easily transported form, whereas for iron storage the opposite is necessary. We discuss here structures of aluminium compounds which can be thought of as relevant to the coordination environments in which aluminium will be found in biological situations. It appears that the aluminium(III) ion can be assimilated and transported using the iron pathways, but not stored in the same way, and it is at this point that the toxic effects of aluminium manifest themselves by disrupting the biochemistries of other metal ions such as calcium(II) and magnesium(II) and possibly also phosphate biochemistry [2]. Therefore, we consider first compounds which might be relevant to aluminium uptake and transport, then species relevant to its storage, *i.e.* mineralization, and lastly species which might be toxic, making reference to any complexes of iron(III), *etc.*, which shed light on the behaviour of aluminium(III).

If aluminium utilizes iron uptake and transport pathways, it is necessary to compare the structures for the aluminium analogues of iron complexes which are known or thought to be important for iron uptake. These can be divided into small molecule complexes such as siderophores and complexes with ligands such as citrate which will be found in the gastrointestinal (GI) tract and aluminium complexes with transferrin and models for this. A problem for bacterial iron uptake is the insoluble nature of iron oxyhydroxide minerals. This has led to the development of special chelating agents, siderophores, by these systems. These are capable of abstracting iron in a mononuclear form from such minerals but not aluminium, which is largely present in the form of very insoluble aluminosilicates. Thus it has not been necessary for bacteria to develop a means of discriminating against aluminium(III) since it is not bioavailable under normal conditions. However, at present there are new sources of more bioavailable aluminium arising from the activities of mankind, allowing aluminium to be assimilated and accumulated by organisms. It seems likely that siderophore pathways could be utilized for aluminium uptake since it is well known that aluminium can be removed from humans using the siderophore desferrioxamine [3].

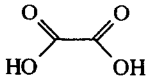
3. Description of structures relevant to aluminium biochemistry

3.1. Structures with oxygen donors

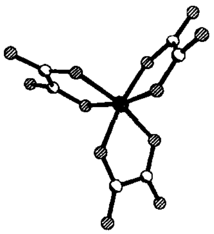
We consider first the structures found for aluminium complexes in which the metal is in an environment of six oxygen donors.

3.1.1. Interactions of aluminium with malonic and oxalic acid

Aluminium forms a trischelate complex with oxalic acid (**1**), $[Al(ox)_3]^{3-}$ (**2**) [4,5], analogous to the iron(III) and chromium(III) structures [4,6].

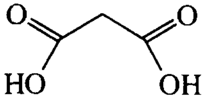


(1)

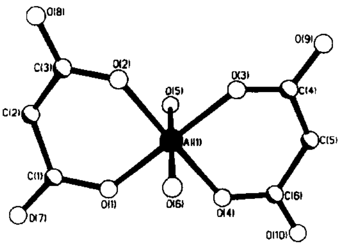


(2)

With malonic acid (**3**), aluminium is also thought to form a trischelate, $[Al(malo)_3]^{3-}$, [7] on the basis of a unit cell determination and spectroscopic evidence, which is likely to be analogous to the iron(III) trischelate [8]. A recent investigation revealed that the bischelate $[Al(malo)_2(H_2O)_2]^-$ complex (**4**) is an important species in solution and can be readily crystallized from aqueous media [9]. Interestingly, the malonate ligands adopt an equatorial configuration, leaving the two coordinated water molecules *trans* to each other. In solution, this is in equilibrium with the trischelate form as revealed by the ^{13}C NMR spectra [9]. This implies that conversion to the trischelate complex would involve a reorganization of the ligand coordination if this *trans* configuration is the dominant form in solution, which might have implications when considering the relatively sluggish kinetics of aluminium(III) compared with iron(III) high-spin complexes.



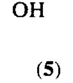
(**3**)



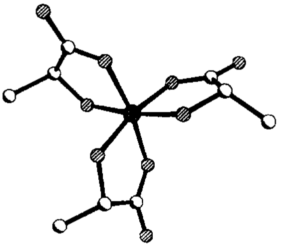
(**4**)

3.1.2. Interactions of aluminium with lactic acid

The molecular structure of the mononuclear aluminium(III) trischelate formed with lactate (**5**) reveals the metal to be in a distorted octahedral environment of six oxygen atoms provided by the deprotonated carboxylate groups and the protonated hydroxy groups of the ligands (**6**) [10]. The fact that the hydroxy groups remain protonated is probably a result of crystallizing the compound at low pH. This compound is used to administer aluminium(III) to experimental animals and cell cultures largely because aluminium hydroxide precipitation does not occur at physiological pH.



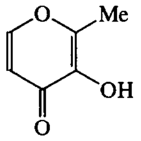
(**5**)



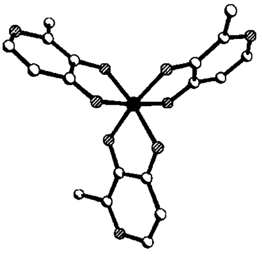
(**6**)

3.1.3. Interactions of aluminium with maltol and isomaltol

Maltol (**7**) is a natural product obtained by the alkaline hydrolysis of streptomycin and is used as a flavouring agent in baked goods. The trischelate forms easily with aluminium(III) [11] and has the structure shown in **8**.

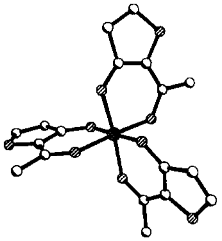


(7)

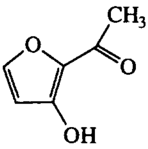


(**8**)

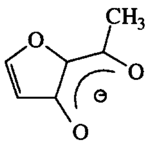
An AlO_6 neutral trischelate complex (**9**) [12] forms with isomaltol (**10**), which can act as an analogue of the acetylacetonate ion (**11**). Isomaltol is a starch by-product, and as such is likely to be found in the GI tract. Thus the complex formed with aluminium(III) could be relevant to aluminium uptake from the gut.



(**9**)



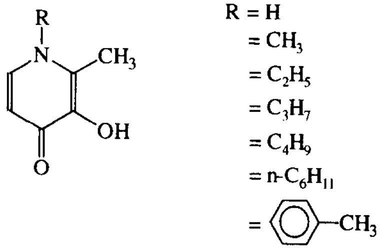
(**10**)



(**11**)

3.1.4. Complexes which model siderophore coordination

The pyridinone ligands of general formula shown in **12** chelate to metals in a bidentate fashion through the deprotonated hydroxyl group and the keto oxygen, providing neutral trischelate complexes with trivalent metal ions. Many derivatives have been produced in the quest to find suitable iron chelators to use in the clinical treatment of iron overload. The most effective drug for this disease is still Desferal, which is the commercial name for the natural siderophore, desferrioxamine, which can be isolated from bacteria. The production of synthetic alternatives is attractive for a number of reasons, the major one being to find a treatment which can be taken orally rather than by injection. Thus these clinical chelators tend to have properties similar to those of naturally occurring siderophores. Trischelate iron(III) complexes with such ligands have been extensively studied. Trischelate aluminium complexes with analogous coordination have been structurally characterized for $R = C_2H_5$ (**13**) [13,14], CH_3 [13,15], C_3H_7, C_4H_9 [16] and tolyl [17]. A feature of the crystal structures is that the trischelates form rigidly facial geometries with extensive hydrogen bonding interactions to channels of water molecules involving every available oxygen atom in the unit cell. Such circular hydrogen bonding arrays have been described for the crystal structures of ice and clathrate hydrates [18,19]. These solid-state structures are thought to have an influence on the solution properties in water [15]. A large number of gallium and indium analogues have also been reported in these papers.



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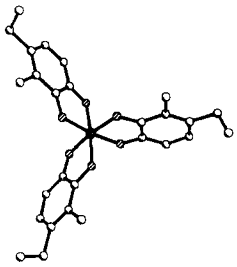


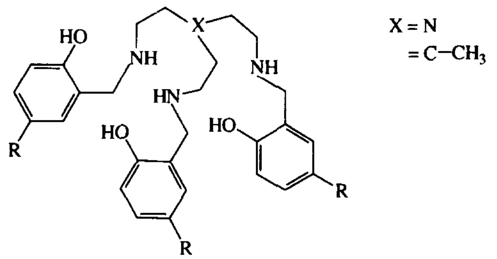
(13)

3.2. *Complexes of aluminium with N/O donors*

Although aluminium(III) is highly oxophilic, it will coordinate to N-donor ligands, particularly if they are part of a mixed N/O-donating ligand. Hexadentate N/O chelates model siderophores such as pyochelin. In addition, there are large numbers of N/O donating ligands to be found in natural aqueous environments deriving from amino acids, chelators such as nta and edta. This type of binding is often also provided within organisms at metal binding sites in metalloproteins such as transferrin and in DNA [2].

3.2.1. *Interactions of aluminium with amine phenol ligands*

The interaction of the amine phenol ligands **14** for $X = CCH_3$ and N provide mixed N/O donation. When $X = CCH_3$, the ligand **14** is potentially hexadentate with an N_3O_3 donor set. This bonding mode is observed in the complex formed for R = Br with aluminium shown in **15** [20]. The paper cited also reports gallium and indium complexes with analogous ligands.



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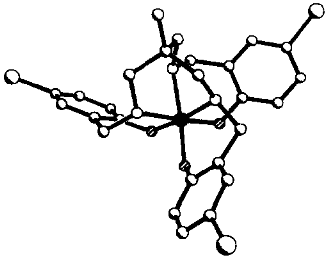
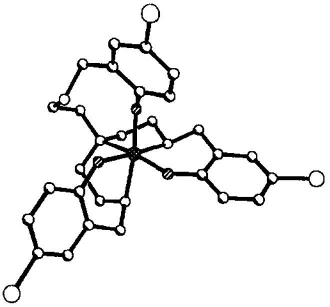


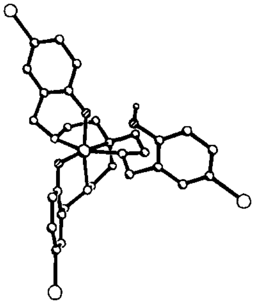
(15)

Reactions between aluminium perchlorate and the potentially heptadentate tripodal amine phenol ligand where X = N and R = Cl (**14**) resulted in the isolation of the complex shown in **16** [21]. In this complex the aluminium is octahedrally coordinated by an N_3O_3 donor set from the ligand. The donor set consists of three nitrogen atoms of the secondary amines and three oxygen atoms from the deprotonated hydroxy groups of the ligand. The fourth secondary amine is protonated and uncoordinated. This is surprising as the chelate effect is lost. However, hydrogen bonding from the amine to two phenolates gives the complex added stability. If the aluminium is constrained to be six-coordinate, then this bonding arrangement allows for the greatest number of oxygen ligands.



(16)

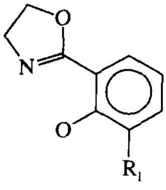
In the case of the gallium complex where X = N and R = Br (**14**), the metal is octahedrally coordinated by an N_4O_2 donor set and in this case a phenol is protonated and not coordinated, see **17** [21]. This bonding arrangement leads to the greatest number of five- and six-membered chelate rings for six-coordination. The indium analogue is seven-coordinate.



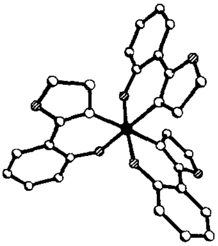
(17)

3.2.2. *Interactions of aluminium with hydroxyphenyl-2-oxazoline*

The hydroxyphenyl-2-oxazoline ligands shown in **18** were found to coordinate through the deprotonated hydroxy group and the nitrogen of the oxazoline as neutral aluminium trischelates for R = H and CH_3 [22]. Both structures have the ligands coordinating in what can be described as a *mer* geometry, as shown for R = H in **19**. Gallium and indium analogues were also reported.



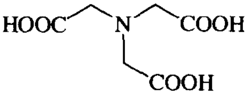
(18)



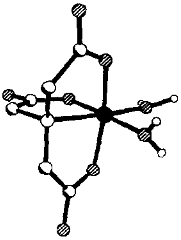
(19)

3.2.3. *Interactions of aluminium with nitrilotriacetic acid*

The interaction of aluminium hydroxide with nitrilotriacetic acid shown in **20** results in the formation of a number of aluminium species [23], amongst which is the mononuclear complex [Al(nta)$(H_2O)_2$] (**21**), whose structure was determined. The aluminium is coordinated by the fully deprotonated nta ligand and two water molecules. The complex crystallizes along with an acetone and water of crystallization which interact with the coordinated water molecules in the hydrogen bonding network of the crystal structure. The two coordinated water molecules are constrained to be *cis* to each other because of the tetradentate nature of the ligand.



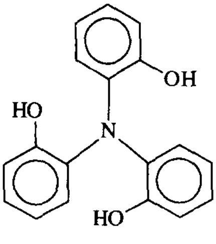
(20)



(21)

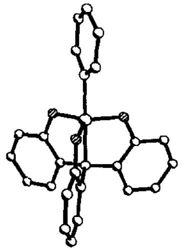
3.2.4. *Interactions of aluminium with nitrilotriphenol*

The reaction of the ligand shown in **22** with aluminium under various conditions led to the isolation of two mononuclear complexes [24].



(22)

A mononuclear pyridine adduct (**23**) formed in a reaction where pyridine was present. Here the ligand is fully deprotonated and coordinates through the central nitrogen and three phenolate oxygens to the aluminium with the fifth coordination site taken by the pyridyl nitrogen. A quinuclidinium adduct can be formed and the crystal structure for the compound, which includes an incorporated water molecule, reveals once again five-coordination of the aluminium with the fifth site taken by what can be regarded as a coordinated hydroxide group linked to a protonated quinuclidinine moiety, as shown in **24**.



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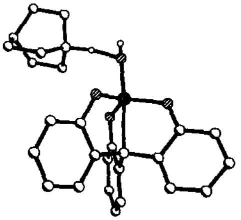


(24)

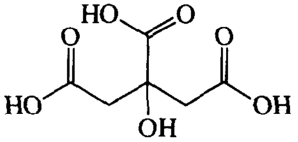
3.3. *Polynuclear aluminium complexes*

Polynuclear aluminium complexes are often formed through the activation of coordinated OH groups becoming deprotonated and bridging between metal centres. For aluminium in aqueous environments this usually occurs through the activation of coordinated water molecules, leading to hydroxide bridges, *i.e.* hydrolysis. Such behaviour is also observed in non-aqueous media when OH groups belonging to a ligand are activated, as seen in the case of triethanolamine below.

3.3.1. *Interactions of aluminium with citric acid*

The interaction of aluminium(III) with citrate has long been of interest to solution-state chemists, largely because much of the aluminium derived from the human diet is thought to be taken up from the gut in the form of an aluminium–citrate complex [25]. Unfortunately, some controversy surrounds the interpretation of the solution state data in terms of the speciation profiles, and a closer examination of the measurements reveals that most have been performed under a variety of experimental conditions. Thus, factors likely to be important influences on solution-state speciation, such as dilution, ionic strength and source of aluminium, have not yet been explored thoroughly. The neutralization of an equimolar solution of $Al(NO_3)_3 \cdot 9H_2O$ and citric acid (**25**) in water with ammonia (to pH 7.5) results in the formation of a trinuclear 1 : 1 aluminium–citrate complex $[Al_3(H_{-1}cit)_3(OH)(H_2O)]^{4-}$ (**26**) in which each aluminium centre is octahedrally coordinated to six oxygen donors [26]. As shown in **27**, one citrate binds to all three aluminium centres via three monodentate carboxylate oxygens (O3, O6 and O8) and bridges Al1 and Al2 via the deprotonated hydroxy group O5. A second citrate bridges the same aluminiums with the deprotonated hydroxy group O12 and provides two carboxylate oxygens to Al2 (O10 and

O15) and one carboxylate oxygen to Al1 (O13). The final citrate bridges Al1 and Al3 via the deprotonated hydroxy group O19 and provides two carboxylate oxygens (O17 and O20) to Al3 and one O22 to Al1. Al3 and Al2 are linked by a hydroxy group, O2, and the remaining sixth coordination site on Al3 is taken by a coordinated water, O1.



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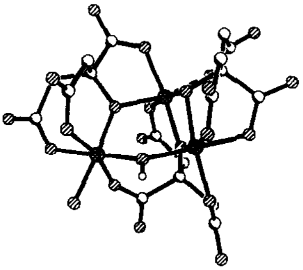

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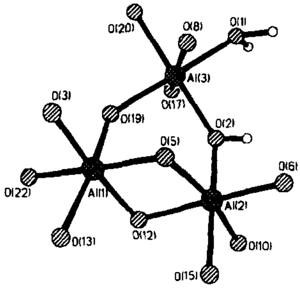
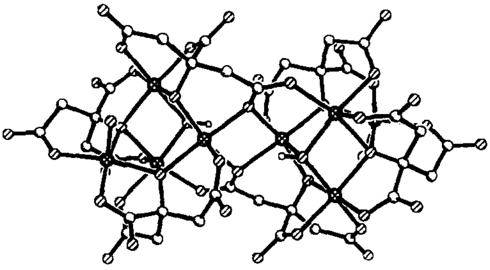


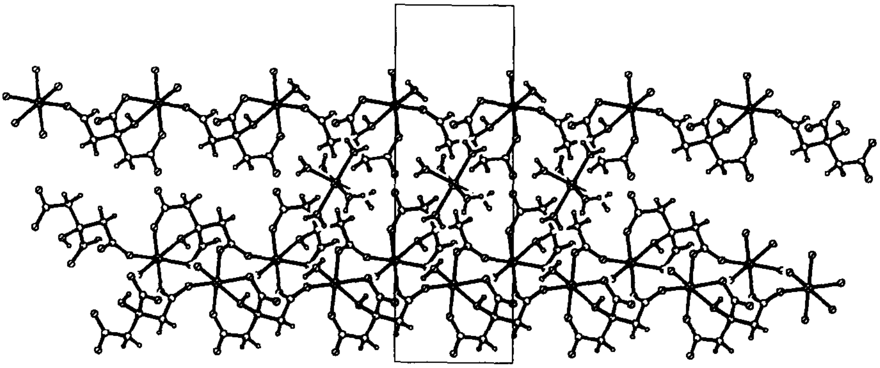
(27)

Such binding modes of fully deprotonated citrate have been observed previously in the octanuclear $[Ni_4(H_{-1}cit)_3(OH)(H_2O)]_2$; see **28** [27]. All the nickel atoms are in an octahedral environment of oxygen donors with bridging between metal centres effected by deprotonated hydroxy groups displaying both μ_2 and μ_3 modes.



(28)

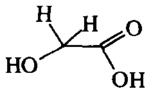
In the structure of magnesium citrate, the ligand is trinegative with only the carboxylate groups deprotonated. The ligand still acts as a tetradentate chelate and the crystal structure contains chains of magnesium citrate entities where the metal centres are linked by bidentate carboxylate groups (**29**). These chains have magnesium hexaaquo counterions sandwiched between them. This general structural type is observed for a number of divalent metals, including iron(II) [27,28].



(29)

3.3.2. *Interactions of aluminium with glycolic acid*

Aqueous solutions of aluminium and glycolic acid (**30**) are known to contain a variety of species [29]. One of these has been crystallographically characterized, $Na_3H_3[Al(C_2H_2O_3)_3]_2$, and reveals two octahedrally coordinated aluminium centres held together by strong hydrogen bonding. The structure can be viewed as two aluminium trischelate entities where the glycolic acid is deprotonated at both the carboxylate and hydroxy groups, as shown for one entity in **31**.



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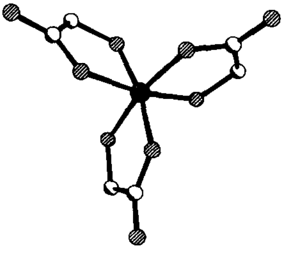
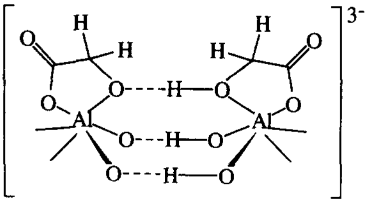


(31)

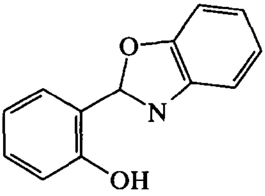
These are joined by three symmetrical hydrogen bonds formed by the presence of three protons between the deprotonated hydroxy groups, as indicated in **32**.



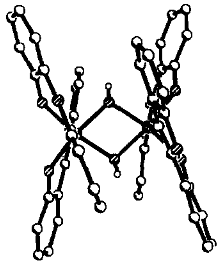
(32)

3.3.3. *Interactions of aluminium with 2-(2′-hydroxyphenyl)-2-oxazoline*

The ligand Hhbo (**33**) is related to the oxazoline ligands described in Section 3.2.2 and is known to form trischelates when the ligand is in excess, although no crystal structures have been reported. When less ligand is available, the dinuclear hydroxo-bridged compound shown in **34** can be isolated [30]. The Hhbo ligand binds in a fashion analogous to the oxazoline binding, *i.e. via* the deprotonated OH of the phenol group and the N of the oxazoline moiety. There are two such ligands per metal plus the two μ_2-hydroxides, resulting in a neutral compound. Although recent potentiometric investigations suggest that the dimeric species $[Al_2(\mu OH)_2]^{4+}$ does not occur to a significant extent [31], the growing number of crystallographically characterized molecules suggests that this species is indeed important in aqueous solution.



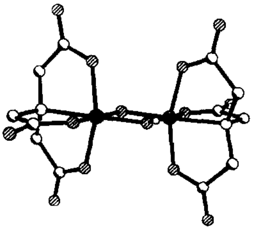
(33)



(34)

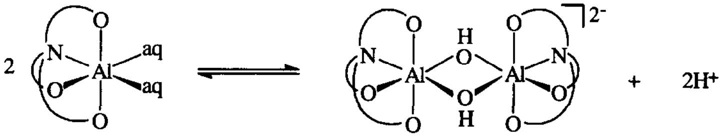
3.3.4. *Interactions of aluminium with nitrilotriacetic acid*

The reaction of aluminium hydroxide with nta described previously can also produce a compound of formula $[Al(H_2O)_2][Al_2(nta)_2(\mu\text{-}OH)_2]OH{\cdot}3H_2O$ [23]. The structure consists of binuclear aluminium units where each aluminium is octahedrally coordinated by one tetradentate fully deprotonated nta ligand and two μ_2-hydroxide bridges which link the metals together, as shown in **35**.



(35)

The whole crystal structure is held together by aluminium counterions coordinated to two *trans* water molecules and carboxylate groups from four dinuclear units. This dinuclear unit is related to the previously described monomer (Section 3.2.3) according to the reaction scheme shown in **36**, corresponding to the early stages of aluminium(III) hydrolysis and a change in the speciation.

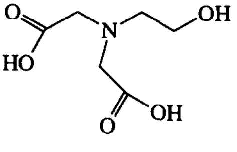


(36)

It is interesting to compare this with the structure of an iron nta analogue formed under analogous conditions [32], which has the same bonding arrangement of the nta ligands but now the iron centres are linked by a single μ_2-oxide bridge and the coordination sphere of each iron is completed by a coordinated water molecule. This appears to be a common difference in the details of the hydrolysis of the two metals, since diol bridges are rarely observed for iron(III) whilst single oxide bridges appear to be highly unfavourable for aluminium(III).

3.3.5. *Interactions of aluminium with N-(2-hydroxyethyl)iminodiacetic acid*

In the interaction of aluminium with the ligand heidi (**37**), a dinuclear compound [Al(heidi)(H_2O)]$_2$ (**38**) forms easily from aqueous solution [33]. The alcohol function of the ligand is deprotonated to form a bridge between the two aluminium centres in a way directly analogous to the previously reported iron(III) analogue [34]. Further hydrolysis of such solutions produces larger clusters, one of which has been crystallographically characterized and is described in Section 3.3.5.



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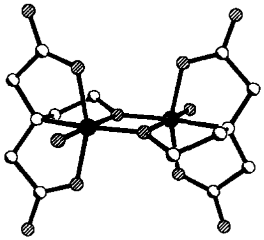
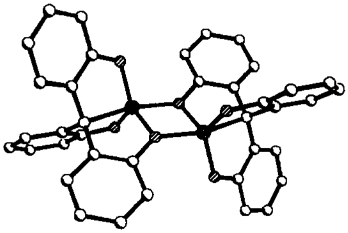


(38)

3.3.6. *Interactions of aluminium with nitrilotriphenol*

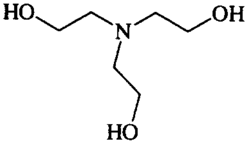
Heating of the mononuclear pyridine adduct of nitrotriphenol described in Section 3.2.4 leads to the formation of the dinuclear complex **39** in which the aluminiums are again five-coordinate, with the fifth site now occupied by a bridging phenolate from the ligand attached to the neighbouring aluminium.



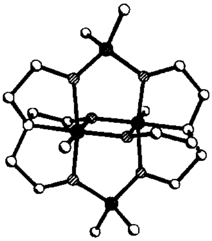
(39)

3.3.7. Interactions of aluminium with triethanolamine

The reaction between TEA (**40**) and $AlMe_3$ results in the formation of the tetranuclear alkoxide bridged complex shown in **41** [35]. The molecule is centrosymmetric with two of the four aluminiums being octahedrally coordinated by one nitrogen and three deprotonated hydroxides from the ligand bridging to the three further aluminium centres. The fifth coordination site is taken by an alkoxide from the other TEA ligand, with the sixth site being occupied by a coordinated methyl group. The remaining two aluminiums have tetrahedral geometries fulfilled by two bridging alkoxides from the octahedrally coordinated aluminiums and two coordinated methyl groups. The complex contains two TEA ligands which have fully deprotonated alcohol groups. These form alkoxide bridges amongst the aluminium centres.



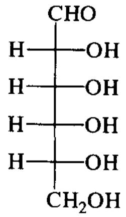
(40)



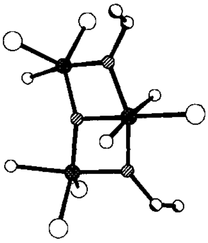
(41)

3.3.8. Interactions of aluminium with glucose

The reduction of glucose (**42**) by ethyl aluminium dichloride in 10% pyridine–toluene results in the formation of a trinuclear aluminium species [36]. Two of the aluminium atoms adopt a distorted trigonal bipyramidal geometry, with the third being a distorted octahedron (**43**). The two five-coordinate aluminiums are bridged to the six-coordinate aluminium by a μ_3-oxide bridge and by a bidentate bridging ethanolate. The remaining three sites are taken by two coordinated chlorides and a nitrogen from a coordinated pyridine. The octahedral aluminium is coordinated by the μ_3 bridging oxide, two pyridyl nitrogens, one chloride and the oxygens of the ethanolate bridge to the other two aluminium centres.



(42)



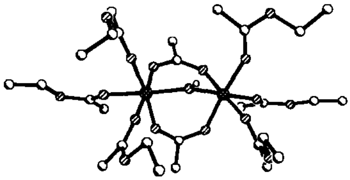
(43)

3.4. *Aluminium and proteins*

If, as described earlier (Section 2), it is true that aluminium enters the body by being mistaken for iron(III), then it is also valid to assume that aluminium is capable of disrupting iron binding sites within proteins and therefore any aluminium structures which model protein sites must be relevant to aluminium toxicity. Since many such iron centres rely on redox processes to function, it is clear that if aluminium(III) were able to bind at these sites it would result in the protein losing activity.

3.4.1. *Interactions of aluminium with ethyl acetate*

The reaction between aluminium chloride and ethyl acetate results in the formation of a dinuclear aluminium compound shown in **44**. In this complex the two aluminium centres have an octahedral geometry with each aluminium atom being coordinated by three ethyl acetates and linked to each other by two bridging carboxylates and a hydroxide group [37]. This compound could be proposed as a possible analogue for a binuclear iron centre in proteins such as haemerythrin [38].

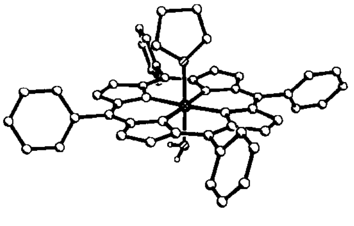


(44)

3.4.2. *Interactions of aluminium with porphyrins and phthalocyanines*

Cytochrome *c* oxidase catalyses the reduction of dioxygen to water. Four redox active centres (two irons and two coppers) are employed in this reduction. A model for this enzyme had been synthesized where an aluminium porphyrin complex (**45**) is the cation [39]. The aluminium adopts an octahedral geometry and sits in the centre of the porphyrin plane. Its bonding requirements are satisfied by the four pyrrole nitrogens of the porphyrin, a coordinated water molecule and a coordinated

THF molecule. This aluminium(III) porphyrin is the first such cation to be characterized by single-crystal X-ray diffraction, although the neutral [Al(OEP)(CH_3)] complex shown in **46** has also been structurally characterized [40]. Here the aluminium adopts a square pyramidal geometry with its bonding requirements being satisfied by the four central nitrogen atoms of the porphyrin (which form the base of the square pyramid), with the fifth site being occupied by a methyl group (which forms the apex). The possibility of the replacement of iron by aluminium, as demonstrated here, has catastrophic implications for the enzyme in that the presence of aluminium will inhibit the redox reactions.



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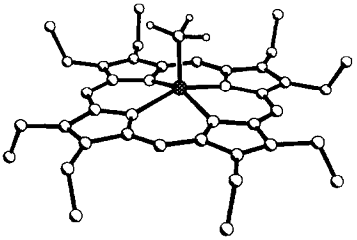
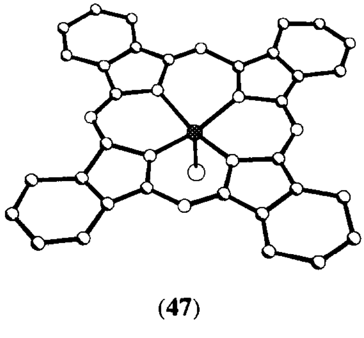


(46)

Phthalocyanine molecules model porphyrins in that they provide a plane of four nitrogen donors for coordination to a central metal iron. The structures of two aluminium phthalocyanine complexes have also been reported [41,42]. The first is a monomeric compound in which the aluminium adopts a square pyramidal geometry as was observed for **46**, and again its bonding requirements are satisfied by the four central nitrogen atoms of the phthalocyanine. However, here the fifth site is occupied by a chloride atom (**47**) [41]. The second complex takes the form of an oxo-bridged dimer (**48**) [42]. Again, each aluminium is pentacoordinate and adopts a square pyramidal geometry. Four nitrogens of the phthalocyanine provide the base of the pyramid with the oxygen atom being the apex. The oxygen atom sits on an inversion centre, resulting in the phthalocyanine rings adopting an eclipsed geometry.



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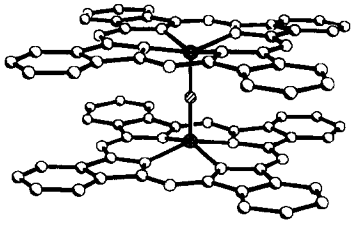


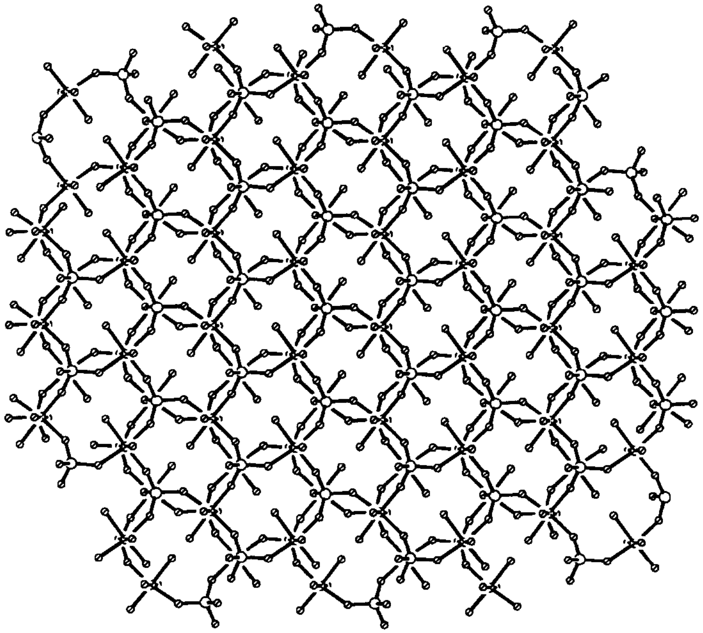
(48)

3.5. *Aluminium minerals*

The mineralization of aluminium affords a means for organisms to expel or store the metal. This is desirable in order to prevent the Al^{3+} ion from interfering with biochemical processes. Common aluminium minerals include phosphates, silicates, hydroxides, oxides and oxyhydroxides. It is thought that phosphate minerals may be a means for bacteria to expel aluminium in the form of aluminophosphate granules [43]. These minerals may also have a bearing on the bone disorders produced in situations of excess aluminium where the metal is thought to occupy Ca^{2+} sites [44]. Silicate minerals have been implicated in the neurofibrillary tangles found in the brains of people suffering from Alzheimer's disease [45]. It has also been suggested that such minerals play a vital role in controlling the bioavailability of aluminium [46].

3.5.1. *Silicate and phosphate minerals*

The interaction of aluminium chloride with phosphoric acid in ethanol at 0 °C leads to the crystallization of the species $\{Al(PO_4)(EtOH)_3\}_4$ [47], which has a structure consisting of a cube of octahedral aluminium and tetrahedral phosphate ions somewhat akin to the arrangement seen in the mineral metavariscite (**49**) [48].



(49)

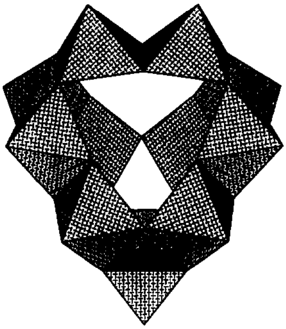
In contrast, the compound isolated from the interaction of an aluminophosphate gel with isopropylamine under high-temperature conditions (423 K for 4 days) contains both four- and six-coordinate aluminium of empirical formula

$7AlPO_4 \cdot 2(C_3H_7NH_2) \cdot 2H_2O$. This consists of a framework of linked PO_4 and AlO_4 tetrahedra and $AlO_5(OH)$ octahedra encapsulating an isopropylamine species, which is probably electrostatically coupled with a water cross-linking two aluminium atoms in the framework [49].

A doubly anionic aluminosilsesquioxane [50] in which two aluminosilicate cubes are joined by an oxide bridge is cited as an example of a compound which violates Loewenstein's rule, which states that whenever two MO_4, for $M = Al$ or Si, tetrahedra are linked by one oxygen bridge, only one of these can be occupied by aluminium and the other must be occupied by silicon. This structure has an important bearing on predicting and rationalizing the structures of aluminium distributions in aluminosilicates. A phosphine oxide precursor of this has also been reported [51].

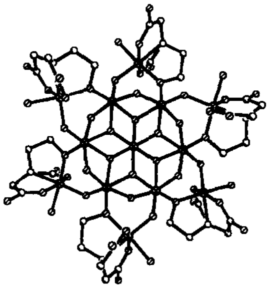
3.5.2. *The role of hydrolysis in mineralization*

A species which has been identified as forming in hydrolysed solutions of aluminium(III) salts has the formula $[Al_{13}O_4(OH)_{24}(H_2O)_{12}]^{7+}$ (**50**) [52,53]. This species appears to be important only under a narrow range of conditions and in the absence of chelating ligands. Its structure consists of a central AlO_4^{5-} tetrahedron linked to twelve octahedrally coordinated aluminium centres *via* μ_2-hydroxy bridges. This structure is the same as that observed for the Keggin ion structure of heteropolymolybdates.



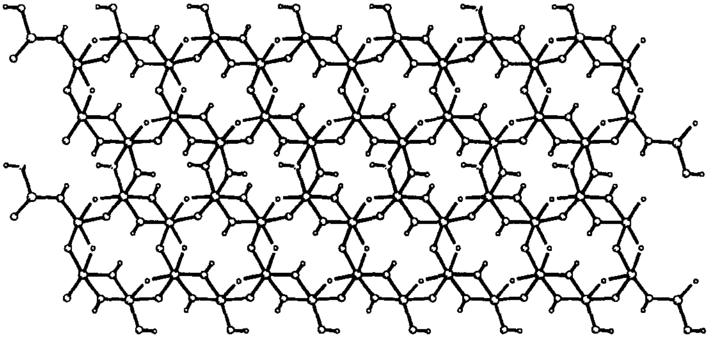
(**50**)

The natural hydrolysis of aluminium leads to the formation of minerals such as gibbsite. In the presence of ligands which can modify this hydrolysis, different types of mineral structures can be observed. There are parallels here with the effect of organic templates on the mineralization processes operating within organisms (biomineralization). For aluminium such species are important in terms of both its bioavailability and storage as an inert material. In this review, we have pointed out the often similar chemistries of iron(III) and aluminium. The modification of hydrolysis of these metals by the presence of the ligand heidi (**37**) leads to the isolation of two types of compound directly analogous to one another. The dinuclear system has already been described (Section 3.3.5). The further hydrolysis results in the trapping of a portion of $M(OH)_2^{\infty+}$ with a structure corresponding to the mineral brucite for both metals [33]. In both cases this is not the expected mineral type for a trivalent metal and it is the charge compensation afforded by the metal–ligand shell encapsulating the mineral fragment which stabilizes the system. For aluminium the cluster $[Al_{13}(\mu_3\text{-}OH)_6(\mu_2\text{-}OH)_{12}(\text{heidi})_6(H_2O)_6]^{3+}$ (**51**) crystallizes with the structure shown [33].



(51)

The relationship of the mineral trapped to a naturally occurring hydroxide of aluminium can clearly be seen in gibbsite (**52**). Here aluminium centres are linked by μ_2-hydroxy bridges to form intersecting $\{Al_6(\mu_2\text{-}OH)_{12}\}^{6+}$ rings. In **51** the aluminiums are linked by μ_3-hydroxy bridges. Removal of the central aluminium of **51** would result in an $\{Al_6(\mu_2\text{-}OH)_{12}\}^{6+}$ ring, as observed in gibbsite.



(52)

Whereas the hydrolysis of iron(III) leads to the formation of highly insoluble minerals, that of aluminium can produce soluble species. In the case of the modified hydrolysis of these metals in the presence of heidi, the aluminium compound **51** is found to be freely soluble whereas the iron analogue is not. This has important implications for the bioavailability of these metals in aqueous environments where similar ligands are present.

4. Concluding remarks

In this review, we have tried to highlight key aspects of the chemistry of aluminium(III) as revealed in single-crystal X-ray diffraction studies which have a bearing on the biological role that aluminium has been observed to fulfil in recent years. Since all of biology functions without the presence of the Al^{3+} ion, its major function is to disrupt the biochemistries of other inorganic species. This is most dramatically revealed in studies which concentrate on the toxic effect of this ion. The toxicity is directly linked to the bioavailability of a species. This in turn will depend on factors such as solubility, charge, shape and size of a given compound. We have shown the types of structures that aluminium can readily adopt and these can help us to understand the structural parameters important in aluminium complexes but not predict the bioavailibility of the metal. This can only be done by testing the toxicity of the compounds.

Acknowledgements

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