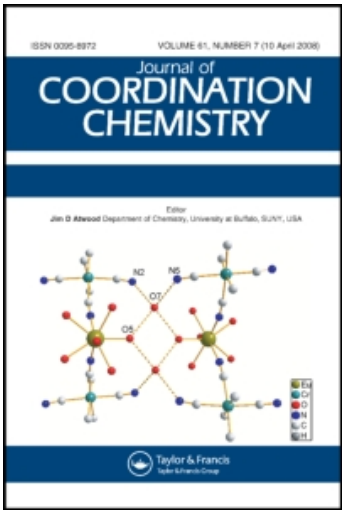

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REVIEW: NEW ADVANCES IN THE COORDINATION CHEMISTRY OF THE BERYLLIUM(II)

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REVIEW: NEW ADVANCES IN THE COORDINATION CHEMISTRY OF THE BERYLLIUM(II)

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Beryllium and its compounds are extremely toxic, but the biological mechanism of their toxicity is largely speculative. Beryllium is the second lightest metal after lithium and it is a component of materials indispensable in today's nuclear, aerospace and electronic industries. Concern about possible pollution by beryllium-containing materials is renewing interest in the chemistry of the metal. Therefore, there is much interest in the search for suitable ligands as antidotes for beryllium poisoning. The more recent studies on the coordination chemistry of beryllium(II) have concentrated attention on ligands of the following types: (a) ligands with oxo, oxocarboxylic or carboxylic groups; (b) ligands with carboxylic-phosphonic or phosphonic groups; (c) polyaminocarboxylic ligands as sequestering agents.

Keywords: Coordination chemistry; Beryllium(II); Oxo; Carboxylic; Phosphonic; Aminocarboxylic ligands

INTRODUCTION

Beryllium was first discovered by the French chemist Vauquelin in 1798 [1, 2]. Because the salts of beryllium are sweet, it has also been known as glicinium or glicinum. Beryllium metal was first prepared by a German

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metallurgist named Wöhler in 1828 [2, 3]; he suggested the name by allusion to the mineral beryl [3].

Beryllium is the second lightest metal after lithium. Its unique properties are a great asset in today's nuclear, aerospace and electronic industries [2–11]. Beryllium is used commercially in three major forms: as a pure metal, as an alloy with other metals and as a ceramic [2, 3]. A more complete discussion of the applications of beryllium was published [12].

Beryllium is the most toxic non-radioactive element in the Periodic Table [2–21]. Contact with Be(II)-containing salts yields lesions on the skin. Inhalation of beryllium-containing dusts produces chronic pulmonary granulomatosis (berylliosis) or nodules in the lung and possibly cancer [4, 6, 9, 21]. The condition develops slowly and it is often fatal. Beryllium is lethal at 1ppm of body weight. Be(II) inhibits many phosphatase enzymes; it is the strongest known inhibitor of alkaline phosphatase; it inhibits Mg(II) and K(I) activated enzymes, as well as DNA replication [13–18]. Beryllium is a dangerous substance with latent toxicity and should be handled cautiously [23, 24].

The great toxicity of beryllium is perhaps one of the most important reasons why the experimental studies of its interaction with ligands present in biological systems or in the environment are very limited indeed [2–22]. There is at present no universally accepted antidote for beryllium poisoning. Problems are encountered due to the toxic nature of the antidotes, such as aurintricarboxylic acid [5, 10, 13]. An alternative approach involves chelation therapy [4, 5, 9, 10]. Chelation therapy has proven ineffective in removing Be(II) from humans with chronic poisoning [14]. The efficacy of a few polyaminocarboxylic acids in rats with chronic beryllium exposure has been studied but with limited succes [19]. In male rats exposed to beryllium, the 2,3-dimercaptopropane-1-sulfonate (DMPS) has some beneficial effects [17]. The influence of chelating agents on the toxicity and distribution of beryllium in rats has been recently studied [25]. The search for good sequestering agents for beryllium(II) thus seems to be necessary.

Studies of the coordinating and chelating ability of beryllium(II) in aqueous solution are very limited [6, 9, 10, 26–31] because they have been conditioned not only by the afore mentioned toxicity of beryllium(II) but also by the difficulties presented by the strong tendency of this small cation to hydrolyze [32, 33]. This is due to its high charge density ($Z/r = 6.45$) [4, 6, 9], which leads to strongly polarizing characters and a great tendency to form covalent bonds with oxygen atoms. It is generally classified as strongly oxophilic, as shown in particular by the characteristic coordination chemistry in aqueous solution [5–14]. The high oxophilicity can also be held responsible for the extreme toxicity of beryllium compounds [2–21, 31] since

most biopolymers and their components offer a large variety of oxygen functions which may be the target of beryllium complexation. The small size induces a tendency to tetracoordination [33–35]. The aquo cation $[Be(H_2O)_4]^{2+}$ presents a strong tendency to hydrolyze [32, 33]. Consequently, the OH^- anion is highly competitive with regard to any other ligand for beryllium(II), and the species resulting from hydrolysis [31–33, 36–38] of Be^{2+} must be taken into consideration in the calculations in order to determine the complex species present in the solution and to obtain correct values of the stability constants.

The more recent studies of the coordination chemistry of beryllium(II) have concentrated attention on the hydrolysis of beryllium(II), including the amphoteric behavior of beryllium hydroxide, on the coordination of beryllium(II) with biochemically revelant ligand systems: aminoacids, salicylaldimines with an O–N donor set, dioxo, oxocarboxylic acid and dicarboxylic ligands, phosphate, bidentate ligands with carboxylic and phosphonate groups, bidentate ligands with phosphonate groups, and polyaminocarboxylic ligands as sequestering agents. These ligands are the subject of this review.

Other recent advances A recent review of the literature (1982–1994) of the organometallic chemistry of beryllium(II) has been carried out [39]. The crystal structure of the first beryllium periodate $Be(H_4IO_6)_2 \cdot 2.4H_2O$ has been established by single-crystal X-ray methods [40]. The use of the terphenylsubstituent $-C_6H_3$-2,6-Mes_2 has permitted the synthesis of several low-coordinate beryllium compounds (three-coordinate beryllium) [41]. Beryllium-9 quadrupole coupling constants and rotational correlation times of bis(acetylacetonate)beryllium(II) in acetonitrile at different temperatures have been determined [42]. Studies of ternary metal chelates of beryllium have also been carried out [43, 44]. The synthesis and structure of an ionic beryllium-"carbene" complex has been examined [45]. Infrared spectra of beryllium carbonyls in solid argon have been studied [46]. Solution equilibria of beryllium(II) complexes with halide and thiocianate ions have been studied in *N*,*N*-dimethyacetamide by calorimetry [47].

Different theorical studies on beryllium compounds have recently been carried out [48–57]. New analytical methods for the determination of beryllium have been studied [58–65].

HYDROLYSIS OF BERYLLIUM

The $[Be(H_2O)_4]^{2+}$ cation exists only in very acidic solutions. In less acidic media, several polynuclear hydrolytic species are formed; the model of

Bruno [36] containing the species $[Be_2(OH)]^2$, $[Be_3(OH)_3]^{3+}$, $[Be_5(OH)_6]^{4+}$, $[Be_6(OH)_8]^{4+}$ and $Be(OH)_2$ has been recently confirmed [37] using both e.m.f. methods and ^9Be NMR spectroscopy. $[Be_3(OH)_3]^{3+}$ is the cation predominant over almost all of the pH range up to precipitation of $Be(OH)_2$, which takes place at pH > 5 (Fig. 1). In solution, tetracoordination of Be^{2+} is preserved by coordinated water molecules, and tetrahedral arrangements are also to be expected for the species formed upon hydrolysis. A cyclic structure for trimeric $[Be_3(OH)_3(H_2O)_6]^{3+}$ (Fig. 2), already indicated by a ^1H-NMR study [35], has been corroborated by a recent X-ray investigation of the picrate salt $[Be_3(\mu\text{-}OH)_3(H_2O)_6]$ (picrate)$_3 \cdot 6H_2O$] [66]. The cyclic arrangement of this trimeric unit, where water molecules are replaced by bidentate ligands, such as picolinate [67], pyrazolylborate [68] and malonate [69] (Fig. 3), have been isolated and characterized as crystals.

This high hydrolytic tendency of the small cation Be^{2+}, prompted investigation of its behavior in other solvents. Fe(III) is another ion which shows a strong tendency to hydrolyze [70, 71]. Studies performed in the mixed solvent dimethyl-sulfoxide (DMSO) : WATER (80 : 20, w : w) [72, 73], indicate that the hydrolysis is strongly restricted, with less than 8% hydrolysis: at pH < 3 hydrolysis does not take place and at pH 3.5 only the hydrolytic species $[Fe(OH)]^{2+}$ exist with a percentage below 5% at

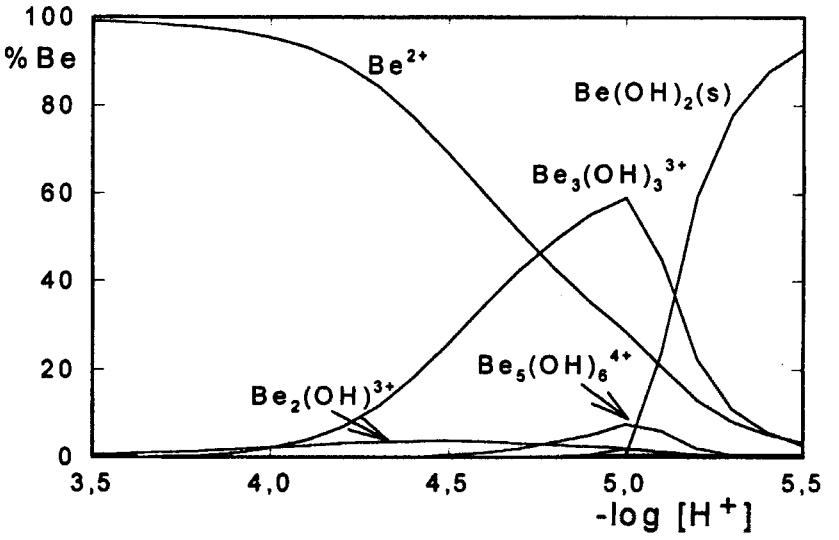


FIGURE 1 Species distribution diagram as a function of pH for beryllium(II) at $C_M = 2$ mM in aqueous solution. (Adapted from Ref. [37]).

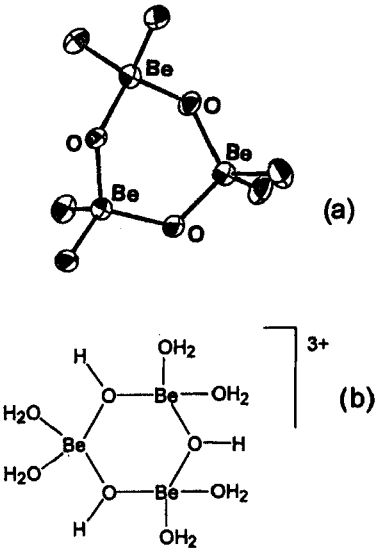


FIGURE 2 (a) ZORTEP perspective view of the trimeric species $[Be_3(\mu\text{-}OH)_3(H_2O)_6]^{3+}$. (Adapted from Ref. [66]); (b) Scheme with H-atoms.

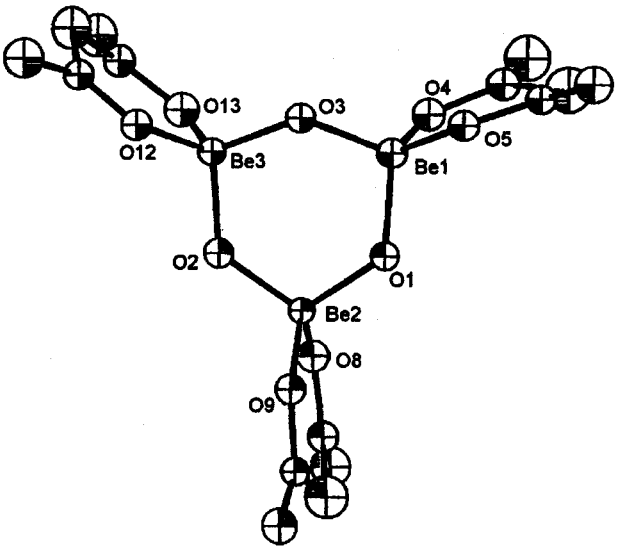


FIGURE 3 Perspective view of the trinuclear anion $[Be_3(OH)_3(malonate)_3]^{3-}$. (Adapted from Ref. [69]).

$C_M = 0.01$ M. These results prompted us to study the hydrolysis of Be(II) in this mixed solvent DMSO : WATER (80 : 20, w : w) [37]. If the hydrolysis is restricted, Be(II) complex species, which cannot be formed in water, may exist in this solvent. This is the case with iminodiacetic acids [74].

Potentiometric titrations [37] were carried out in both aqueous solution and DMSO : WATER (80 : 20, w : w) using as ionic medium 0.5 M in $NaClO_4$ at 25°C. For the equilibria:

$$pBe^{2+} + qH_2O \rightleftharpoons Be_p(OH)_q^{(2p-q)+} + qH^+ \quad \beta_{pq} \tag{1}$$

the simultaneous refinement of the formation constants of all the species using the NERNST/LETA/GRAFICA version [75] of the LETAGROP program [76, 77] has led to the results outlined in Table I.

In aqueous solution, the agreement with the values reported by Bruno [36] is satisfactory, also considering that in the latter different conditions of ionic strength (3.0 M in $NaClO_4$) was used. In the mixed solvent DMSO : WATER (80 : 20, w : w), similar results to those found in aqueous solution have been obtained for both the stoichiometry of the species and the values of the stability constants, in spite of the change of ionic activity factors due to the solvent composition. A reasonable agreement is found between the equilibrium constants obtained in the two solvents, with two exceptions: the monomeric species $[Be(OH)]^+$ appears to be well defined in the mixed solvent and the value of the formation constants for the species $Be(OH)_2$ in the mixed solvent, is two logarithmic units higher than that found in aqueous solution. $Be(OH)_2$ is more soluble in the mixed solvent. The species distribution diagrams (Figs. 1 and 4) show that in aqueous solution, the main hydrolytic species is the trimer $[Be_3(OH)_3]^{3+}$, whereas in the mixed solvent the monomeric species $[Be(OH)]^+$ and $Be(OH)_2$ are those more important, because coordination of DMSO to beryllium(II) decreases the stability of polynuclear hydroxo-complexes. ^9Be NMR spectra are in accordance with potentiometric results [37].

A calorimetric study in aqueous solution ($I = 0.5$ M in $NaClO_4$; 25°C) of beryllium(II) hydrolysis has been carried out [38]. The revelant

TABLE I Equilibrium constants for hydrolysis of Be(II) (25°C; 0.5 M $NaClO_4$)

	$-\log \beta_{pq}$					
Solvents	(1,1)	(2,1)	(3,3)	(5,6)	(6,8)	(1,2)
Water		3.20 (1)	8.68 (3)	18.31 (5)	25.77 (5)	11.68 (6)
DMSO : WATER	5.25 (3)	2.98 (2)	9.28 (3)	18.03 (3)	25.16 (4)	9.59 (3)

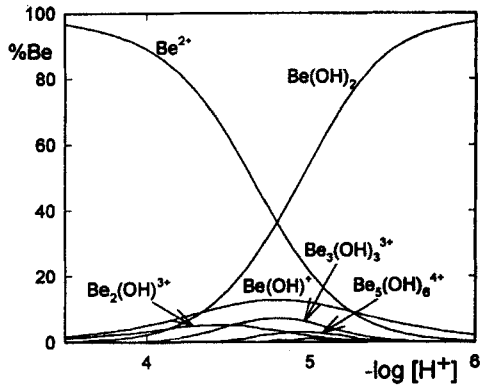


FIGURE 4 Species distribution diagram as a function of pH for beryllium(II) at $C_M = 2\,mM$ in the mixed solvent DMSO : WATER (80 : 20, w : w). (Adapted from Ref. [37]).

TABLE II Thermodynamic parameters for the formation of hydrolytic Be^{2+} species, determined in 0.50 M $NaClO_4$ at 25°C[a]

Reaction	*log K*[b]	$-\Delta G^\circ$ [$kJ\,mol^{-1}$]	$-\Delta H^\circ$ [$kJ\,mol^{-1}$]	ΔS° [$JK^{-1}\,mol^{-1}$]
$2Be^{2+} + OH^- \rightarrow [Be_2(OH)]^{3+}$	10.49 (1)	59.87 (8)	27 (2)	111 (7)
$3Be^{2+} + 3OH^- \rightarrow [Be_3(OH)_3]^{3+}$	32.39 (3)	184.9 (2)	100.8 (4)	282 (1)
$5Be^{2+} + 6OH^- \rightarrow [Be_5(OH)_6]^{4+}$	63.83 (5)	364.3 (3)	208 (3)	523 (10)
$6Be^{2+} + 8OH^- \rightarrow [Be_6(OH)_8]^{4+}$	83.75 (5)	478.0 (3)	239 (2)	802 (7)
$Be^{2+} + 2OH^- \rightarrow Be(OH)_2$	15.70 (6)	89.6 (3)	–	–

[a] Values in parentheses are standard deviations in the last significant figure.
[b] Values taken from Ref. [37].

thermodynamic data obtained are listed in Table II. In spite of various experimental modifications, it was not possible to obtain appreciable formation of the soluble species $Be(OH)_2$ in the calorimetric experiments.

Therefore, the corresponding formation enthalpy was not determined. The enthalpy changes determined in the present study for $[Be_2(OH)]^+$, $[Be_3(OH)_3]^{3+}$ and $[Be_6(OH)_8]^{4+}$ are in good agreement with those quoted in previous reports [78, 79], while no reference values could be found in the literature for $[Be_5(OH)_6]^{4+}$ [26–30]. The formation of these species is promoted by both favorable enthalphic and entropic contributions. Figure 5 shows thermodynamic functions for the formation of hydrolytic species as a function of the number of hydroxide groups bonded to Be^{2+}: an almost constant increment per OH^- group is observed in the enthalpic and entropic terms for the formation of the hydrolytic species, which is reflected by the almost steady increase of the species stability ($-\Delta G^\circ$) with the number of bonded OH^- groups.

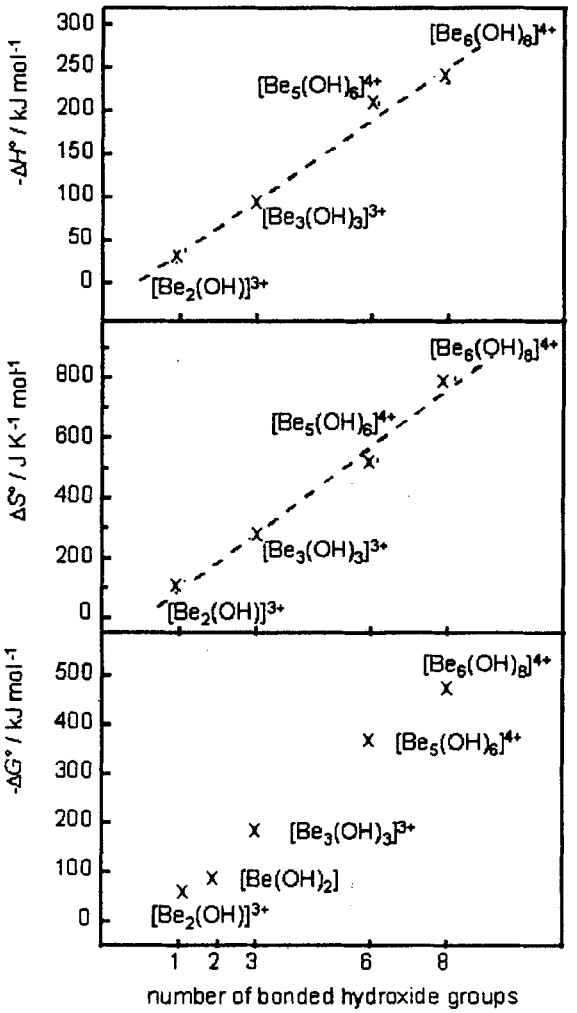


FIGURE 5 Thermodynamic functions for the formation of hydrolytic species as a function of the number of hydroxide groups bonded to Be^{2+}. (Adapted from Ref. [38]).

AMPHOTERIC BEHAVIOR OF BERYLLIUM HYDROXIDE

Beryllium hydroxide has amphoteric behavior; like aluminium hydroxide, beryllium hydroxide dissolves in both strong aqueous acid and base [3, 7, 80, 81]. The nature of the species that appear in acid solution was indicated in the last paragraph (HYDROLYSIS), however knowledge about

the equilibria established with base is very limited. A large number of polynuclear aquo/hydroxo/oxo beryllate anions have been proposed [82, 83], but none of these has been identified unequivocally or structrally characterized. In the older literature, the simple $[Be(OH)_4]^{2-}$ has been postulated as the dominant species in strongly alkaline solution (pH 12–14) [3, 7, 10, 79, 84, 85]. The calcium salt, $Ca[Be(OH)_4]$ was crystallized in the form of various hydrates [82, 83], but the structures could not be determined. Recently, Schmidbaur, *et al.*, isolated single crystals of $Na_2[Be_4(OH)_{10}](H_2O)_5$ (**1**) [86] and $Ca_2[Be_2(OH)_7][H_3O_2](H_2O)_2$ (**2**) [87]. A single-crystal X-ray diffraction analysis of (**1**), the new disodium decahydroxytetraberyllate revealed that the beryllate component of the lattice is a tetranuclear unit with an adamantane-type structure, which had never been considered for aqueous beryllium chemistry (Fig. 6). This dianionic unit has the net formula $[(BeOH)_4(OH)_6]^{2-}$ with the beryllium atoms at the vertices of a regular tetrahedron, six hydroxyl groups bridging the six edges of the tetrahedron, and one terminal hydroxy group attached to each of the four beryllium atoms. Each beryllium atom is thus surrounded by four OH groups which again form a tetrahedron. A structural investigation of single crystals of (**2**), has shown that it contains the anions $[Be_2(OH)_7]^{3-}$ (Fig. 7) associated with hydrated calcium cations and, even more surprising, hydroxide hydrate anions $[HO-H-OH]^-$. In the dinuclear beryllate trianion (Fig. 7) the two beryllium atoms are bridged by a hydroxide anion. The results of both papers [86, 87] show the condensation of $[Be(OH)_4]^{2-}$ dianions with extrusion of OH^- anions (Eq. (2)):

$$4[Be(OH)_4]^{2-} \underset{+2OH^-}{\overset{-2OH^-}{\rightleftharpoons}} 2[Be_4(OH)_7]^{3-} \underset{+4OH^-}{\overset{-4OH^-}{\rightleftharpoons}} [Be_4(OH)_{10}]^{2-} \qquad (2)$$

Is an energetically balanced process even for cases where the OH^- anion liberated is taken on only by a water molecule to give the hydrogen-bonded

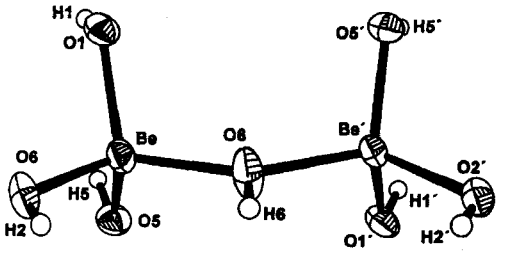


FIGURE 6 Molecular structure of the hydroxyberyllate dianion $[(BeOH)_4(OH)_6]^{2-}$. (Adapted from Ref. [86]).

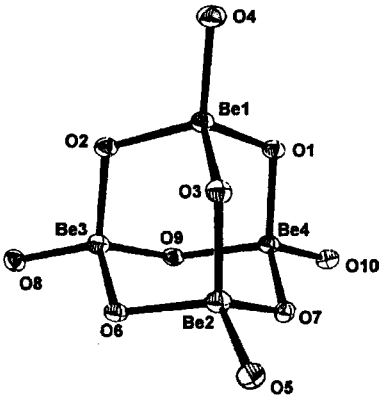


FIGURE 7 Molecular structure of the hydroxyberyllate trianion $[Be_2(OH)_7]^{3-}$. (Adapted from Ref. [87]).

species $[O_2H_3]^-$. Extrusion of four additional hydroxide anions between two of the $[Be_2(OH)_7]^{3-}$ anions will then lead to the $[Be_4(OH)_{10}]^{2-}$ dianion.

AMINO ACIDS

Perkins [88] calculated the overall formation constants β_2 from potentiometric measurements for a whole range of α-amino acid derivatives. However, these values have been rejected by Sóvago *et al.* [28], because Perkins did not take into consideration the hydrolysis of beryllium(II) in his calculations.

Chinea [31, 74] studied the coordinating ability of beryllium(II) in aqueous solution with the aminoacids glycine (gli), α-alanine (α-al), β-alanine (β-al), phenylalanine (ph-al) and glutamic (glu) acid and in the mixed solvent DMSO : WATER 80 : 20 w : w with the aminoacids gli, α-al, β-al, ph-al, methionine (met), glu and aspartic acid (asp) (25°C and $I = 0.5$ M in $NaClO_4$). The potentiometric data were analyzed by means of the LETAGROP program [75, 76], taking into account the hydrolytic species of beryllium(II) in both solvents. The values for the stability constants of the complex species formed are presented in Table III. Species with excess of ligand are not present.

The α-aminoacids, gli, α-al, ph-al and met form five-membered ring chelates with a N–O donor set in the complex $[BeL]^+$, whereas β-al forms a six-membered ring chelate. For both solvents (Tab. III) the order of complexation (complex $[BeL]^+$) β-al > α-al > gli > ph-al is found, as

TABLE III Formation constants for Be(II)-aminoacid systems (25°C, $I = 0.5$ M in $NaClO_4$)

	log K						
Species	*gli*	*α-al*	*β-al*	*ph-al*	*met*	*glu*	*asp*
In aqueous solution							
$[BeL]^+$	6.25	6.39	7.36	6.26			
$[Be_3(OH)_3L]^{2+}$	38.92	38.74	39.45	38.82			
$[BeHL]^+$						1.55	
[BeL]						6.89	
In DMSO:WATER 80:20 w:w							
$[BeHL]^{2+}$	3.16	3.52	3.99	3.07	3.36		
$[BeL]^+$	8.18	8.55	8.84	7.23	8.16		
[Be(OH)L]	18.86	19.49	19.19	18.43	19.31		
$[Be(OH)_2L]^-$	28.65	29.07	29.06	28.23	28.25		
$[BeH_2L]^{2+}$						2.83	2.95
$[BeHL]^+$						4.96	4.81
BeL						10.48	9.78
$[Be(OH)L]^-$						19.64	19.80
$[Be(OH)_2L]^{2-}$						30.46	29.67

expected. It has been found that six-membered ring chelates are the most stable for Be(II) [20, 38, 89, 90], in a similar manner to other elements of the first short period, such as boron and carbon, while Cu(II), Ni(II), lanthanides, and other heavier elements prefer five-membered ring chelates. The stability constants of the complexes $[BeL]^+$ are greater in the mixed solvent DMSO:WATER 80:20 (w/w), since the aminoacids are acids weaker in the mixed solvent (pKi values) [74].

However, the species distribution diagrams as a function of pH (Figs. 8 and 9 for the Be(II)-α-al system) show that the hydrolytic species

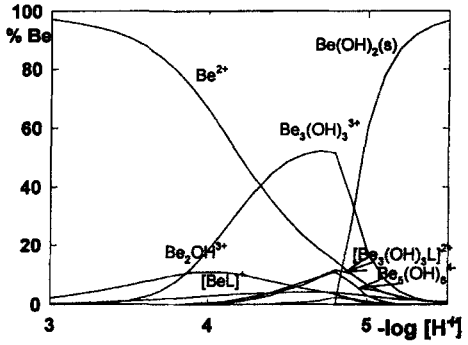


FIGURE 8 Species distribution diagram as a function of pH for beryllium(II)-α-alanine at metal:ligand 1:1, $C_M = 2$ mM in aqueous solution. (Adapted from Ref. [31]).

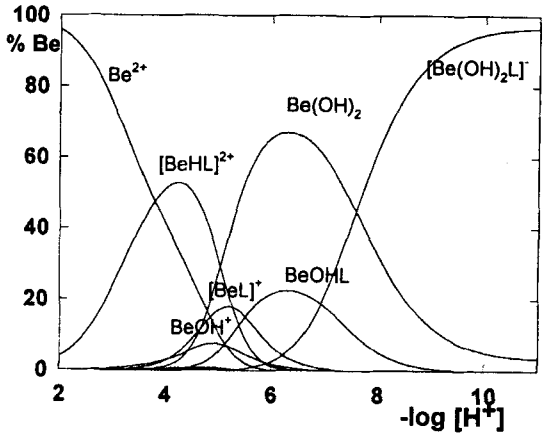


FIGURE 9 Species distribution diagram as a function of pH for beryllium(II)-α-alanine at metal : ligand 1 : 1, $C_M = 2$ mM. in the mixed solvent DMSO : WATER (80 : 20, w : w). (Adapted from Ref. [31]).

$[Be_3(OH)_3]^{3+}$ and complex species $[Be_3(OH)_3L]^{2+}$ derived in aqueous solution, and $[Be(OH)]^+$, [Be(OH)L], $Be(OH)_2$ and $[Be(OH)_2L]^-$ in the mixed solvent are the predominant species. The diagrams indicate that (ligand : metal ratio 1 : 1) the complex $[BeL]^+$ begins to form at pH > 3.5 (maximum percentage only 10% at pH 4) in aqueous solution, and pH > 4 (maximum percentage only 20% at pH 5) in mixed solvent. The strength of the Be—OH bond hinders the formation of the complex with excess of ligand, BeL_2.

The formation of binary and ternary complexes of beryllium(II) with nitrilotriacetic and coordinated aminoacids has been studied [91].

SALICYLALDIMINES WITH AN O–N DONOR SET

The reported complexes with Schiff bases have been poorly characterized and no crystal structure determination of beryllium Schiff bases complexes have been reported [10, 92].

In a recent paper, Midollini *et al.* [93] report the X-ray structure of [Be(sal)(OH)]∞ (sal = salicylaldehide), $[Be(sal)_2]$, $[Be(sal\text{-}NH)_2]$, $[Be(sal\text{-}N\text{-}R)_2]$ (R = *i*–Pr(**1**), Ph(**2**)). The complexes **1** (Fig. 10) and **2** were prepared as previously reported [94–96]. In both structures the beryllium center displays a slightly distorted tetrahedral environment, being linked to the oxygen and nitrogen atoms from two salicylaldiminato ligands.

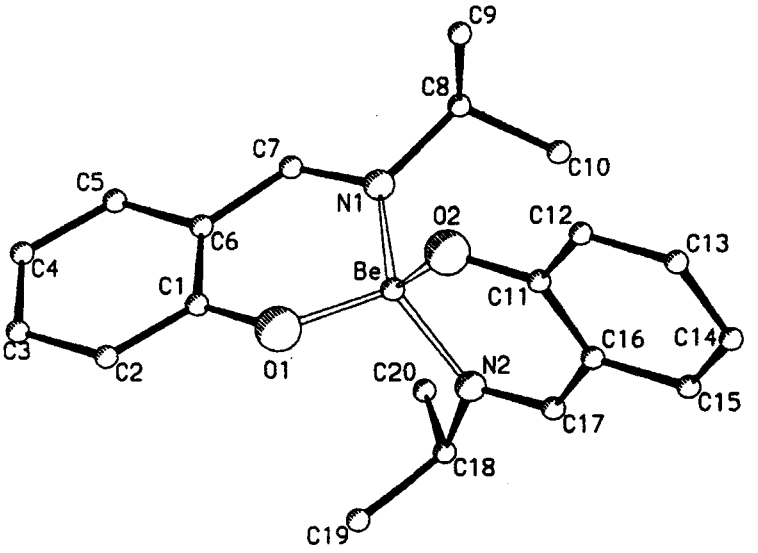


FIGURE 10 PLUTO view of the complex unit [Be(Sal-N-*i*-Pr)$_2$]. (Drawn using data from Ref. [93]).

DIOXO, OXO-CARBOXYLIC AND DICARBOXYLIC LIGANDS

(a) *Dioxo ligands* Klüfers *et al.* [97] crystallize the complex $Na_2[Be(C_6H_4O_3)_2] \cdot 5H_2O$ from concentrated alkaline aqueous solutions. The polyol anhydroerythritol is deprotonated twice in the mononuclear, homoleptic complex anions. The preference of beryllium(II) for the binding of *cis*-furanoid diols is shown. The beryllium(II) cation occupies the center of a slightly distorted tetrahedron formed by the deprotonated oxo atoms of the two diol ligands. Similarly, Schmidbaur *et al.* [98] prepare the crystalline $Na_2[Be(o\text{-}C_6H_4O_2)_2] \cdot 5H_2O$ from beryllium hydroxide and a strongly alkaline aqueous solution of catechol. In an X-ray structure determination the complex shows dianions $[Be(o\text{-}C_6H_4O_2)_2]^{2-}$ with two chelating catechol ligands. The beryllium(II) also occupies the center of a slightly distorted tetrahedron formed by the deprotonated oxygen atoms of the two catechol ligands. The ^{9}Be-NMR spectrum of an aqueous solution of the compound shows a singlet at $\delta = 7.5$; this signal is shifted considerably from the $Be^{2+}(aq)$ reference and indicates persistence of the complexation of the metal ion by the catecholate ligands in alkaline aqueous solution. This result is important in light of the ubiquitous availability of phenolic groups in many biomolecules, such as *e.g.*, catechol-amines.

The complexation of beryllium(II) with hydroxamic acids has recently been studied [99]. The stability constants of the mono and bis complexes were determined by the combined pH-spectral titration method at $25 \pm 0.1°C$ in aqueous medium of 0.1 M ionic strength.

(b) *Oxocarboxylic ligands* The chemistry of natural waters can be studied by investigating the properties of the simple hydroxycarboxylic acids. Plant roots produce and release citric and tartaric acids, which they use to take up trace metals from the soil. The metal speciation in the presence of these acids is important, for instance, in understanding how the soil pH affects the chemical form of metals and thus their availability to plants. Complex formation equilibria of beryllium(II) with five aliphatic α-hydroxycarboxylic acids, *viz.* glycolic (HL), lactic (HL), 2-hydroxyisobutiric (HL), L(+)-tartaric (H_2L) and citric (H_3L) acids, were studied by means of potentiometric (glass electrode) titrations at 25°C in ionic medium of 0.5 M in $NaClO_4$ [100]. Glycolic and 2-hydroxyisobutyric acid complexation with beryllium forms three rather weak complexes, $[BeL]^+$, $[BeL_2]$ and $[Be_3(OH)_3L]^{2+}$ (Fig. 11). Lactic acid was not found to form $[BeL_2]$ species. Tartaric acid forms the three complexes mentioned above together with two deprotonated complexes $[Be(H_{-1}L)_2]^{4-}$ and $[Be_3(OH)_3(H_{-1}L)]$. Citric acid also forms protonated and binuclear species prior to the formation of hydrolyzed complexes. The experimetal potentiometric data were analyzed by means of the LETAGROP program [77, 101] and the stability constants of the complexes formed were determined. The species distribution diagrams were made using the program SOLGAS WATER [102].

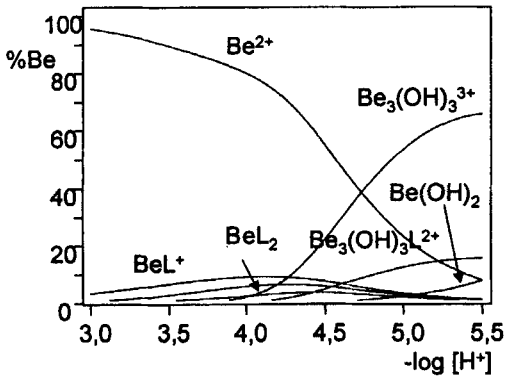


FIGURE 11 Species distribution diagram as a function of pH for beryllium(II)-glycolate at metal : ligand 1 : 5 and $C_M = 3$ mM. (Drawn using data from Ref. [100]).

With glycolic acid, Schmidbaur *et al.* [102b] have isolated an analytically well-defined beryllium complex of glycolic acid from aqueous solutions under near-physiological conditions, crystallized it and determined its structure by X-ray diffraction. The hexanuclear complex features beryllium in two differents environments, mono- and bis-chelated by glycolate ligands with deprotonated hydroxyl groups. In ^{9}Be-NMR studies of aqueous solutions of the complex (pH 6) the persistence of complexation in two different environments of Be(II) could also be confirmed. The new structure may serve as a model for beryllium complexation with large bioligands. The Be(II) is indeed effectively chelated by hydroxy-carboxylic acids in almost neutral aqueous solutions. Beryllium is thus unique in its affinity for alcoholic hydroxy groups in biomolecules.

The aromatic α-hydroxycarboxylic, salicylic acid (H_2L), has been regarded as one of the simplest model ligands for humic substances occurring in natural waters. The salicylic acid derivatives are the most widely studied group of ligands for the quelation of beryllium poisoning [4, 9, 10]. A potentiometric study of the complex formation of beryllium(II) with salicylate $[L]^{2-}$ using a glass electrode (25°C; I = 1 M $NaClO_4$) shows the formation of the three major species $[Be(HL)L]^{-}$, $[BeL]$ and $[BeL_2]^{2-}$ and at least one or even all of the four minor species $[Be(HL)]^{+}$, $[Be(HL)_2]$, $[Be(OH)L]^{-}$ and $[Be_3(OH)_3L_3]^{3-}$ (Fig. 12). The stability constants were determined [103]. The major species in solution [BeL] and $[BeL_2]^{2-}$ (Fig. 12), were prepared as well-defined crystalline complexes by Schmidbaur *et al.*: $Be(C_6H_4OCO_2)(H_2O)_2$ (ratio beryllium(II) : salicylate(2-)), 1 : 1 (Fig. 13) [104], and $(NH_4)_2[Be(C_6H_4OCO_2)_2] \cdot 2.25H_2O$ (ratio beryllium(II) : salicylate(2-)), 1 : 2 (Fig. 14) [105]. $Na_3[Be_2(OH)(CO_3)(C_7H_6OCO_2)_2] \cdot 8H_2O$

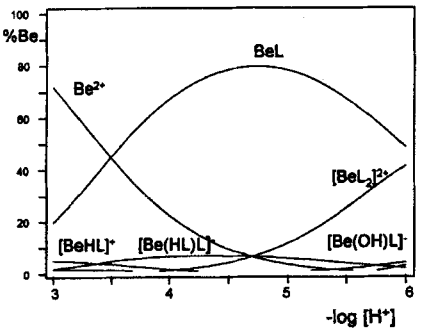


FIGURE 12 Species distribution diagram as a function of pH for beryllium(II)-salicylate at metal : ligand 1 : 2 and $C_M = 2$ mM. (Drawn using data from Ref. [103]).

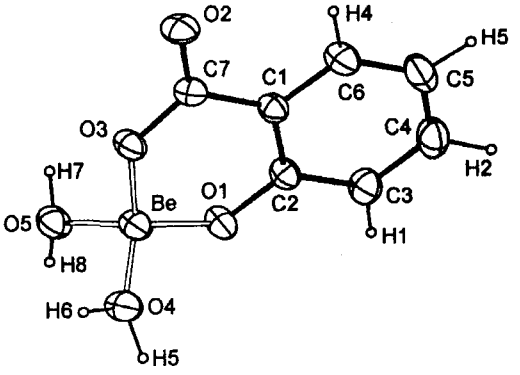


FIGURE 13 Crystal structure of $Be(C_6H_4OCO_2)(OH_2)_2$. (Adapted from Ref. [104]).

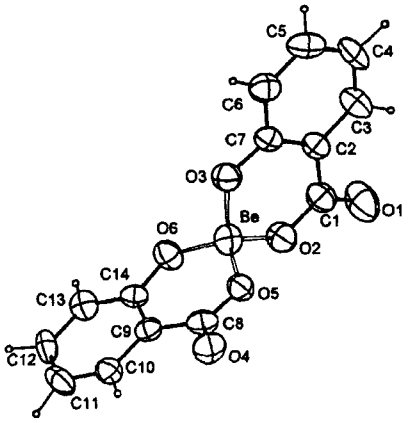


FIGURE 14 Crystal structure of the $[Be(C_6H_4OCO_2)_2]^{2-}$ dianion. (Adapted from Ref. [105]).

with *o*-cresotic acid [105] was also prepared. The structures have been determined by X-ray structure analysis. ^{9}Be NMR studies in aqueous solutions containing $BeSO_4 \cdot 4H_2O$ and sodium salicylate (1-) or sodium *o*-cresolate (1-) in the molar ratios 1:1 and 1:2 show that a variety of beryllium/salicylate (2-) and beryllium/*o*-cresolate (2-) species are present in solution, the most prominent being $[Be(C_6H_4OCO_2)(H_2O)_2]$ and $[Be(C_6H_4OCO_2)_2]^{2-}$ (and their *o*-cresolate analogs). In light of the ubiquitous availability of phenolic and carboxylic groups in many biomolecules, the finding of strong bonding of Be(II) to these functions in aqueous solution is very important.

Formation constants of 1:1 binary Be(II)-L and 1:1:1 ternary Be(II):L:L′ complexes, where L = salicylic acid, or monosodium salt of

5-sulfosalicylic acid, or 2,5-dinitrosalicylic acid, and L′ = 2-hydroxyacetophenone, or 2,5-dihydroxyacetophenone, or 5-chloro-2-hydroxyacetophenone, were determined potentiometrically in 20% (vol./vol.) ethanolic aqueous medium at 20°C and at three different ionic strengths of 0.15, 0.10 and 0.05 $NaNO_3$ [106].

(c) *Dicarboxylic ligands* In view of the importance of carboxylate ligands in biological systems we have undertaken re-examination of the interactions of oxalate, malonate and succinate with beryllium(II) in aqueous solution [38, 69] (25°C; $I = 0.5$ M in $NaClO_4$) by means of potentiometric, microcalorimetric and multinuclear (^1H, ^{13}C and ^9Be) NMR-spectroscopic measurements. The potentiometric data were analyzed by means of the HYPERQUAD program [107, 108]. The enthalpies of reaction were determined from the calorimetric data by means of the AAAL program [109]. The complex species and thermodynamic parameters ($\log K$, $-\Delta G°$, $-\Delta H°$ and $\Delta S°$) are presented in Table IV.

Complex formation of beryllium(II) with a dicarboxylate is invariably promoted by favorable entropic contributions ($\Delta S° > 0$), while the enthalpic terms are always unfavorable ($\Delta H° > 0$). Malonate forms by far the most stable complexes owing to a more favorable (less endothermic)

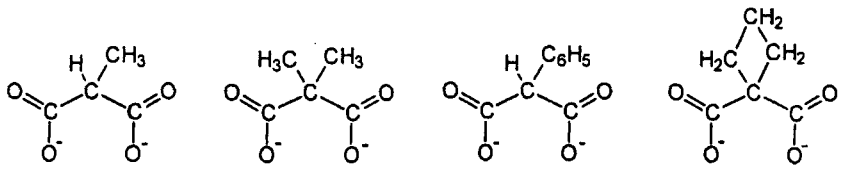
TABLE IV Thermodynamic parameters for the complexation of Be^{2+} by oxalate, malonate, and succinate anions, determined in 0.50 M $NaClO_4$ at 25°C[a]

Reaction	*log K*	$-\Delta G°$ [$kJ\,mol^{-1}$]	$-\Delta H°$ [$kJ\,mol^{-1}$]	$\Delta S°$ [$JK^{-1}\,mol^{-1}$]
L = oxalate				
$Be^{2+} + L^{2-} \rightarrow [BeL]$	3.47(2)[b]	19.8(1)[b]	−19.5(3)	132(1)
$[BeL] + L^{2-} \rightarrow [BeL_2]^{2-}$	1.77(7)[b]	10.1(4)[b]	−31(1)	138(3)
$Be^{2+} + 2L^{2-} \rightarrow [BeL_2]^{2-}$	5.24(7)[b]	29.9(4)[b]	−49(2)	263(6)
$[Be_3(OH)_3]^{3+} + L^{2-} \rightarrow [Be_3(OH)_3L]^{+}$	3.78(7)[b]	21.7(4)[b]	−10.9(8)	109(3)
$[Be_3(OH)_3]^{3+} + 3L^{2-} \rightarrow [Be_3(OH)_3L_3]^{3-}$	8.3(1)[b]	47.7(8)[b]	−28(1)	254(6)
L = malonate				
$Be^{2+} + L^{2-} \rightarrow [BeL]$	5.36(2)[b]	30.6(1)[b]	−10.53(6)	138.0(5)
$[BeL] + L^{2-} \rightarrow [BeL_2]^{2-}$	3.85(1)[b]	21.91(5)[b]	−5.19(8)	91.2(4)
$Be^{2+} + 2L^{2-} \rightarrow [BeL_2]^{2-}$	9.21(2)[b]	52.50(8)[b]	−15.82(8)	229.2(5)
$[Be_3(OH)_3]^{3+} + L^{2-} \rightarrow [Be_3(OH)_3L]^{+}$	5.26(7)[b]	30.1(4)[b]	−8.4(8)	129(3)
$[Be_3(OH)_3]^{3+} + 3L^{2-} \rightarrow [Be_3(OH)_3L_3]^{3-}$	12.84(6)[b]	73.3(3)[b]	−18.8(8)	309(3)
L = succinate				
$Be^{2+} + L^{2-} \rightarrow [BeL]$	3.04(1)	17.34(4)	−21.1(1)	129(5)
$[BeL]^{+} L^{2-} \rightarrow [BeL_2]^{2-}$	1.0(2)	6(1)	−15(1)	69(5)
$Be^{2+} + 2L^{2-} \rightarrow [BeL_2]^{2-}$	4.1(2)	23.1(1)	−36(1)	198(5)
$[Be_3(OH)_3]^{3+} + L^{2-} \rightarrow [Be_3(OH)_3L]^{+}$	2.03(6)	11.6(3)	−42(1)	181(3)

[a] Values in parentheses are standard deviations in the last significant figure.
[b] Values taken from Ref. [69].

enthalpic contribution. Malonate forms a six-membered chelate ring; oxalate, a five-membered chelate ring; succinate, a seven-membered chelate ring. There is a distinct selectivity for the binding of Be(II) species by those ligands capable of forming a six-membered chelate ring. Also, knowing the concentrations of the various species in solution (speciation diagrams as a function of the pH and of the concentrations) we were able to develop a rational approach to the isolation of solid beryllium complexes which resulted is the preparation of two new complexes, $K_3[Be_3(OH)_3(oxalato)_3]\cdot 3H_2O$ and $K_3[Be_3(OH)_3(malonato)_3]\cdot 6H_2O$ [69]. The crystal structure of the last complex has been determined by X-ray diffraction (Fig. 3). The structures of the un-hydrolyzed complexes $K_2[Be(oxalato)_2]$ [110] and $K_2[Be(malonato)_2]\cdot 0.5H_2O$ [111] have been previously determined. Recently, sodium, potassium and ammonium bis(succinato)-beryllates $M_2[Be(C_4H_4O_4)_2]$ and beryllium succinate dihydrate $[Be(C_4H_4O_4)]\cdot 2H_2O$ have been prepared and characterized [112].

More recently, Alderighi *et al.* [113] studied the interaction of aqueous beryllium(II) with a set of related ligands: methylmalonate (memal), phenylmalonate (phmal), dimethylmalonate (dimemal) and 1,1-cyclobutanedicarboxylate (cbdc) as shown in Scheme 1. The aim was to investigate the effects of small changes in the steric requirements of ligands on the properties of the complexes. Recently, Schmidbaur *et al.* [114], isolated a beryllium complex with phthalate. The aromatic dicarboxylic phthalic acid reacts with $Be(OH)_2$ in aqueous solution at pH 4.4, (25°C), to give solutions containing the complex $(H_2O)_2Be[(OOC)_2C_6H_4]$. Adjusting to pH 5.9 with ammonia, $(NH_4)_2\{Be[(OOC)_2C_6H_4]_2\}$ is obtained. An aqueous solution of this compound with acetone leads to precipitation of single crystals suitable for an X-ray structure determination. This salt was found to contain the bis-chelated dianion $\{Be[(OOC)_2C_6H_4]_2\}^{2-}$, with the beryllium atom in the spiro center of two seven-membered rings and an overall geometry approaching C_2 symmetry (Fig. 15) [114]. For comparison, we have therefore also included the phthalate ligand in this study [113]. The complexes formed



memal dimemal phmal cbdc

SCHEME 1

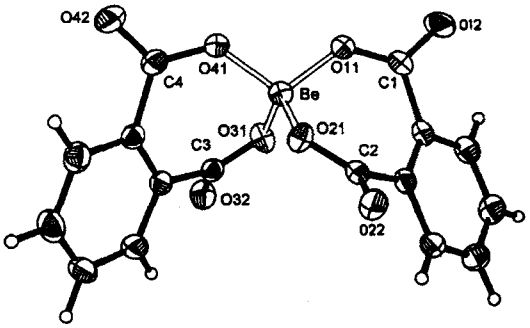


FIGURE 15 Structure of the $[Be(phthalato)_2]^{2-}$ dianion. (Adapted from Ref. [114]).

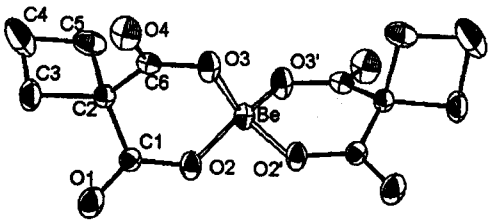


FIGURE 16 Ortep view of the anionic complex $[Be(cbdc)_2]^{2-}$ (cbdc = cyclobutane 1,1-dicarboxylate). (Adapted from Ref. [113]).

by beryllium(II) with the dicarboxylate ligands memal, ph-mal, dimemal, cbdc and phthalate have been investigated in aqueous solution (25°C; I = 0.5 M in $NaClO_4$) through potentiometric and ^9Be NMR spectroscopic measurements. The interaction of beryllium(II) in aqueous solution with substituted malonates and phthalate leads to the formation of the same complex species as were found with malonate itself [38, 69], namely, the complexes [BeL], $[BeL_2]^{2-}$, $[Be_3(OH)_3L]^+$ and $[Be_3(OH)_3L_3]^{3-}$. With cbdc the species $[Be_3(OH)_3L]^+$ was not characterized nor was the species $[Be_3(OH)_3L_3]^{3-}$ characterized with L = phthalate, probably because the concentration of these species were too low. The phthalate complexes are significantly less stable than the malonate complexes but of approximately the same stability as succinate complexes [38]. This correlates with the fact that the chelates rings formed by phthalate and succinate have seven members, and that seven-membered rings are less stable than six-membered rings in the chemistry of beryllium [38, 69, 89, 90]. The structure of $K_2[Be(cbdc)_2] \cdot 2H_2O$ has been determined by an X-ray structure analysis (Fig. 16) [113].

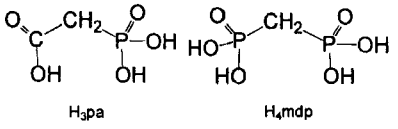
With maleic acid, a potassium bis(maleato)beryllate $K_2\{Be[(OOC—CH)_2]_2\} \cdot H_2O$ is obtained as a crystalline monohydrate, the structure of which has been determined by X-ray methods [112]. The lattice contains spiro-bicyclic dianions, with the beryllium atom chelated by two dicarboxylate ligands. The maleate forms seven-membered chelate rings. The compounds undergo slow hydrolysis in water forming various complexes as shown by time and pH-dependent ^{9}Be NMR spectroscopy [112].

PHOSPHATE COMPLEXES

The phosphate group is of biological interest since beryllium inhibits the DNA replication and phosphatase enzymes [13–18]. The complexation equilibria between Be^{2+} and phosphate ions were studied at 25°C and $I = 3.0$ M in $NaClO_4$ by potentiometric titration with a glass electrode [115]. The concentration of beryllium(II) was varied between 5×10^{-4} and 0.03 M, whereas $0.5\ [Be(II)] \leq [P(V)] \leq 3[Be(II)]$. The experimental data were explained with the formation of species $[BeH_2PO_4]^+$, $[Be(H_2PO_4)_2]_{(aq)}$, $[Be_2H_{-2}(H_3PO_4)]^{2+}$, $[Be_3H_{-6}(H_3PO_4)_3]_{(aq)}$, $[Be_3H_{-8}(H_3PO_4)_6]^{2-}$ and $[Be_3H_{-5}(H_3PO_4)]^+$ or $[Be_3H_{-6}(H_3PO_4)]_{(aq)}$. The equilibrium constants with standards deviations are given [30, 115].

BIDENTATE LIGANDS WITH PHOSPHONATE GROUPS

Thirty years ago, Dyatlova *et al.* [116, 117], on the basis of potentiometric measurements, reported that both methylenediphosphonic acid and hexamethylenediphosphonic acid form beryllium complexes of stoichiometry BeHL and BeL_2. In the latter case the diphosphonate anion should bridge two metal ions [116, 117]. Recently, the interaction of beryllium(II) in aqueous solution (25°C; ionic strength 0.5 M made up with $NaClO_4$ and $(CH_3)_4NCl$) with the ligands phosphonoacetic acid (H_3pa) and methylenediphosphonic acid (H_4mdp) (Scheme 2) were investigated using both potentiometric and multinuclear magnetic resonance measurements



H_3pa H_4mdp

SCHEME 2

(^{31}P {^1H}, ^{13}C {^1H} and ^9Be) [118]. These ligands are potentially capable of forming six-membered chelate rings. For comparison, the interaction of beryllium(II) with methylphosphonic acid (H_2mp) was also considered. It is known that ligands which contain phosphonate groups show a propensity to form complexes with the sodium ion [119]. In order to investigate these complexes potentiometric measurements were made on solutions containing the two salts NaCl and $(CH_3)_4Cl$ in varying proportions adjusted so that the total ionic strength was constant at 0.50 M. Near-optimal experimental conditions for both emf and NMR measurements were identified with the aid of HYSS [120], a new program developed from the HYPHEN program in HYPERQUAD [108].

In Table V, the complex species formed and formation constants ($\log K$) are presented for H_3pa, H_4mdp, H_2mp, and for comparison purposes malonic acid. The data given in Table V, show that the stability of the simple complexes [BeL] and [BeL_2] increases along the series malonate < methylphosphonate < phosphonoacetate < methylenediphosphonate. This indicates that the rule that phosphonates form more stable complexes than carboxylates applies also in the case of these beryllium complexes. Phosphonate is able to displace water from $[Be(H_2O)_4]^{2+}$ without the assistance of a chelate effect, even at very low pH values. The complexes $[BeL_2]^{n-}$ (L = pa, $n = 4$; L = mpd, $n = 6$) are predominant species at physiological pH values (Fig. 17). With methylenediphosphonate, the complexes [BeL] and [BeL_2] are so stable that the beryllium ions are sequestered in these complexes where the pH might favor the formation of hydrolyzed complexes, so much so that there is not even appreciable precipitation of beryllium hydroxide (Fig. 17). The complex

TABLE V Decimal logarithms of the Be^{2+} complex formation constants, determined in 0.50 M $NaClO_4$ at 25°C (Ref. [118])

	$\log K$ [a]			
Reaction	*Malonic acid*	*mp*	*H_3pa*	*H_4mdp*
$Be + L \rightarrow BeL$	5.36 (2)	6.17 (3)	9.24 (1)	13.7 (1)
$BeL + L \rightarrow BeL_2$	3.85 (1)	5.36 (8)	5.74 (2)	7.66 (7)
$BeL + H \rightarrow BeHL$		3.3 (1)	3.36 (1)	5.04 (5)
$BHL + H \rightarrow BeH_2L$				2.6 (1)
$BeL_2 + H \rightarrow BeHL_2$			5.05 (6)	6.3 (1)
$BeHL_2 + H \rightarrow BeH_2L_2$			≈ 3	6.5 (2)
$Be + HL \rightarrow BeHL$			4.53 (1)	8.3 (1)
$Be + H_2L \rightarrow BeH_2L$		2.0 (1)		4.0 (2)
$Be + 2H_2L \rightarrow Be(H_2L)_2$				7.6 (2)
$Be_3(OH)_3 + L \rightarrow Be_3(OH)_3L$	5.26 (7)		7.2 (3)	
$Be_3(OH)_3 + 3L \rightarrow Be_3(OH)_3L_3$	12.84 (6)		20.86 (3)	

[a] Values in parentheses are standard deviations. The charges of the species have been omitted for simplicity.

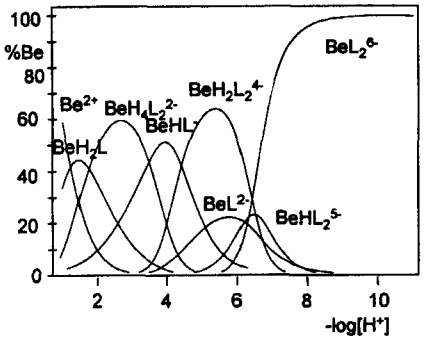


FIGURE 17 Species distribution diagram as a function of pH for beryllium(II)–methylenediphosphonate at metal : ligand 1 : 2 and $C_M = 3$ mM. (Drawn using data from Ref. [118]).

$K_2[Be(H_2mdp)_2] \cdot 2H_2O$ was isolated in the solid state from reaction of $Be(OH)_2$ with H_4mdp and KOH, in aqueous solution, at pH 2.6 and its composition has been confirmed through ESMS spectra.

In conclusion, the ligand mdp^{4-}, which is currently used as a $^{99}T_c$ carrier in diagnostical nuclear medicine [121], could be tested as a potential Be^{2+} sequestering agent. Moreover, preliminary studies have shown that the system $BeSO_4$–diphosphonic acid (molar ratio 1 : 2) behaves as the system $BeSO_4$–H_4mpd, the complex $[Be(P_2O_7)_2]^{6-}$ being practically the only species present in aqueous solution at pH values higher than 7 [122]. Therefore, the investigation of the interactions of beryllium(II) with biological molecules containing phosphate groups appears to deserve particular attention. Indeed, as far we know, only a short report about the interaction of beryllium(II) with ATP has been published [123].

The coordinating ability of the beryllium(II) with phosphonopropionic acid (H_3L) has been studied in aqueous solution (25°C; $I = 0.5$ M made up with $NaClO_4$ and $(CH_3)_4NCl$) using both potentiometric and multinuclear resonance measurements [124]. For beryllium(II), the phosphonoacetate complexes [118] (six-membered chelate rings) are more stable than the phosphonopropionate complexes [124] (seven-membered chelate rings), as expected.

POLYAMINOCARBOXYLIC ACIDS AS SEQUESTERING AGENTS: SELECTIVE UPTAKE OF BERYLLIUM(II) IONS

The small size of the beryllium(II) ion tends to tetracoordination. Bidentate ligands such as aminoacids [31, 74, 125], oxocarboxylate or biscarboxylate

ligands (*vide supra*), or tridentate ligands such as iminodiacetic acids [126] do not satisfy the coordination of the beryllium(II), and do not hinder formation of hydrolytic species of beryllium(II). Even bischelate complexes with oxo-carboxylic or dicarboxylic ligands (*vide supra*) do not hinder the formation of the hydrolytic species of beryllium(II) in aqueous solution. (Figs. 11 and 12; Tab. IV). Only bischelate complexes with methylene-diphosphonic acid (Fig. 17) (ligands with phosphonate groups, see last paragraph) hinder the formation of hydrolytic species in aqueous solution and practically sequester the beryllium(II) at physiological pH. For these reasons, good beryllium sequestering agents could be polyaminocarboxylic acids, tetra- penta- or hexacoordinated. Moreover, beryllium(II) prefers six-membered chelate rings [20, 31, 38, 89, 90].

We present an analysis of the characteristics of a series of polyamino-carboxylic ligands with a view to their possible use as sequestering agents for beryllium(II) [20, 31].

(a) potentially tetradentate ligands: nitrilotriacetic, NTA; nitrilodiacetic-propionic, NDAP; nitriloaceticdipropionic, NADP; and nitrilotripropionic, NTP, acids. (b) potentially hexadentate ligands derived from aliphatic 1,2-diamines: ethylenediaminetetraacetic, EDTA; ethylene-diamine-*N*,*N'*-diacetic-*N*,*N'*-dipropionic, EDADP; ethylenediamine-*N*,*N*,*N'*,*N'*-tetrapropionic, EDTP; 1,2-propylene-diamine-*N*,*N*,*N'*,*N'*-tetraacetic, 1,2-PDTA; and *trans*-1,2-cyclohexane-diamine-*N*,*N*,*N'*,*N'*-tetraacetic, CDTA, acids. (c) potentially hexadentate ligands derived from aromatic 1,2-diamines: *o*-phenylenediamine-*N*,*N*,*N'*,*N'*-tetraacetic, *o*-PhDTA; 3,4-toluene-diamine-*N*,*N*,*N'*,*N'*-tetraacetic, 3,4-TDTA; and 4-chloro-*o*-phenylenediamine-*N*,*N*,*N'*,*N'*-tetraacetic, 4-Cl-*o*-PhDTA acids. All the ligands fulfill the coordination requirements of Be(II). These allow comparison of: (a) hexadentate ligands from aliphatic diamines with hexadentate ligands from aromatic diamines in order to study the competition of Be^{2+} and the H^+ for the bond to atoms of N of different basicity; (b) ligands that form five-membered ring chelates (acetic groups) with ligands that form six-membered ring chelates (propionic groups).

The selective uptake of beryllium(II) was analyzed by means of chemical speciation diagrams [127, 128] as well as the so-called conditional effective formation constants [13, 20, 129, 130] $K^{\text{eff}}_{\text{ML}}$. The species distribution diagrams as a function of pH show the selective uptake of Be^{2+} ions [13, 20, 129] in the presence of H^+ ions or in the presence of H^+ and Mg^{2+} ions. The diagrams and the effective formation constants in the presence of Mg^{2+} were also be determined, because, as indicated earlier, the Be^{2+} ion inhibits numerous enzymes competitive to magnesium [5, 8, 13].

The values of the effective stability constants ($\log K^{eff}_{BeL}$) of beryllium(II) with different polyamino carboxylic acids, both with respect to H^+ and with respect to Mg(II) and H^+ are presented in Ref. [20]. The species distribution diagrams as a function of pH show that for EDTA (Fig. 18) and its analogs 1,2-PDTA and CDTA at pH > 4.5 the diprotonated species of the ligand H_2L^{2-} competes favorably with the complex $[BeL]^{2-}$: the competition between the H^+ and the Be^{2+} cation for the coordination to the donor atoms of the ligands and specially to the N atoms retards to higher pH the formation of the complex species, thus facilitating the continued presence of the hydrolytic species of Be(II), such that the hydroxo complex $[Be_3(OH)_3(HL)]$ is the most important species. These results are reflected in the low values of K^{eff}_{BeL} for EDTA [20]. Similar behavior for EDDADP and EDTP is found [20]. The unfavorable effect of the high basicity of nitrogen atoms supersedes the favorable effect of the formation of six-membered chelate rings. In a similar study [131] with polyaminocarboxylic acids derived from the aliphatic diamines 1,3-propylenediamine and 1,4-buthylenediamine, 1,3-PDTA, 1,3-PDTP, 1,4-BDTA and 1,4-BDTP acids, the high basicity of the nitrogen atoms retarded formation of the complex species of Be(II) and did not hinder formation of the trimeric hydrolytic species. Consequently, these ligands are not good sequestering agents for beryllium(II).

On the contrary, the lower basicity of the nitrogen atoms of the aromatic diamines allows the complex $[BeL]^{2-}$ to compete favorably with the species H_2L^{2-} and HL^{3-} in *o*-PhDTA, 3,4-TDTA (Fig. 19) and 4-Cl-*o*-PhDTA acids, its formation beginning at pH < 4, hindering the formation of the trimeric species $[Be_3(OH)_3]^{3+}$ and its corresponding hydroxocomplex $[Be_3(OH)_3(HL)]$. This favorable situation is also manifested in the higher values of the effective stability constants [20], allowing *o*-PhDTA acid to be

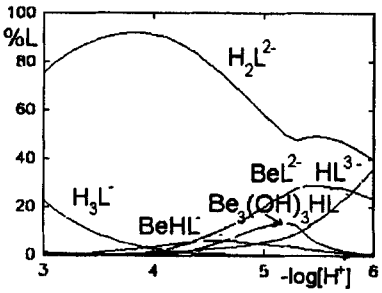


FIGURE 18 Species distribution diagram as a function of pH for beryllium(II)–EDTA system at metal:ligand 1:1 and C_M = 2 mM. (Adapted from Ref. [31]).

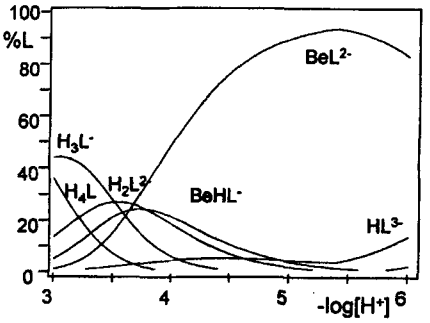


FIGURE 19 Species distribution diagram as a function of pH for beryllium(II)–3,4-TDTA system at metal : ligand 1 : 1 and $C_M = 2\,\text{mM}$. (Drawn using data from Ref. [20]).

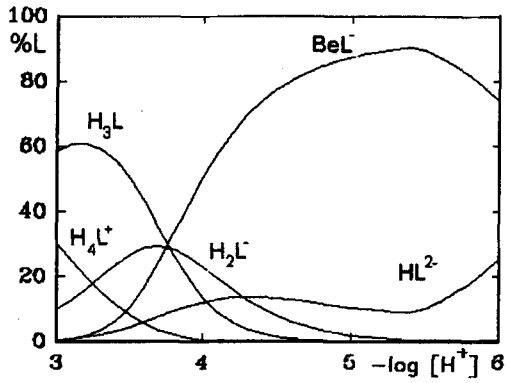


FIGURE 20 Species distribution diagram as a function of pH for beryllium(II)–NTP system at metal : ligand 1 : 1 and $C_M = 2\,\text{mM}$. (Adapted from Ref. [31]).

used for the titrimetric determination of Be(II) [132]. The favorable effect of the lower basicity of the nitrogen atoms supersedes the less favorable effect of the formation of five-membered chelate rings. *o*-PhDTA and 3,4-TDTA acids are better sequestering agents for Be(II) than EDTA, EDDADP and EDTP acids.

NTP (Fig. 20) and NADP also begin to form the nonprotonated complex $[BeL]^-$ at pH < 4, hindering formation of the trimeric species $[Be_3(OH)_3]^{3+}$ and its corresponding hydroxo complexes. The high basicity of the species HL^{2-} of the ligands NTP and NADP [20] is compensated by the chelate effect that results from satisfiying the coordination index of four of the small Be^{2+} cations and by the formation of the more stable six-membered chelate rings, as observed in the structure of complex $[Be(NTP)]^-$ (Fig. 23) and

crystalline data [20]. The shape of the diagrams is seen in the high values of K^{eff}_{BeL} for NTP and NADP acids [20]. Contrarily, NTA and NDAP do not hinder the formation of the trimeric hydrolytic species (Tab. VI).

The species distribution diagrams as a function of pH and the order found for K^{eff}_{BeL} of 3,4-TDTA $\geq$ *o*-PhDTA > 4-Cl-*o*-PhDTA $\geq$ ADP $\geq$ NTP $\gg$ NDAP > EDTA > EDTP > EDDADP indicate that, in competition with the H^+, *o*-PhDTA, 3,4-TDTA, 4-Cl-*o*-PhDTA, NADP and NTP are good sequestering agents at pH 4.5–6 (or above 6 with an excess of ligand) for Be(II), since these ligands sequester Be(II) at a sufficiently low pH to impede hydrolysis of this small cation.

It has already been pointed out that one of the causes of the toxicity of Be^{2+} is inhibition of numerous enzymes competitive to magnesium [5, 8, 13]. We therefore analyzed the selective uptake of Be^{2+} in the presence of Mg^{2+}. Table VI shows the values obtained for the stability constants of the nonprotonated complexes of Mg(II) and Be(II) with the better sequestering agents of Be(II), 3,4-TDTA, *o*-PhDTA, 4-Cl-*o*-PhDTA, NTP and NADP. Comparing the values of $\log K$, it was found (Tab. VI) that for the potentially hexadentate ligands derived from aromatic diamines 3,4-TDTA, *o*-PhDTA and 4-Cl-*o*-PhDTA, $\log K_{BeL} \approx \log K_{MgL}$. This result is accounted for by the fact that Be(II) tends to tetrahedral coordination [34, 133] with less strain of the six-membered chelate rings, while Mg(II) tends to octahedral coordination [34, 133] and the five-membered chelate rings undergo less strain. 3,4-TDTA, *o*-PhDTA and 4-Cl-*o*-PhDTA form five-membered chelate rings. In contrast (Tab. VI), for the potentially

TABLE VI Stability constant ($\log K$) of complexes of Be(II) and Mg(II) with polyamino carboxylic acids (25°C, $I = 0.5\,M$ in $NaClO_4$) [20] (protonated complexes are not included)

	Ligands, H_4L, derived from aliphatic 1,2-*diamines*				
Species	EDTA	EDDADP	EDTP	1,2-PDTA	CDTA
$[BeL]^{2-}$	7.90	8.50	8.45	7.83	7.84
$[Be_3(OH)_3(HL)]$	36.70	36.86	36.71	36.60	36.07
	Ligands, H_4L, derived from aromatic 1,2-*diamines*				
Species	*o*-PhDTA	3,4-TDTA	4-Cl-*o*-PhDTA		
$[BeL]^{2-}$	6.51	6.88	5.80		
	Ligands, H_3L				
Species	NTA	NDAP	NADP	NTP	
$[BeL]^{-}$	6.68	8.12	9.25	9.24	
$[Be_3(OH)_3(HL)]^{+}$	34.92	35.80			
	Mg(II) complexes				
Species	*o*-PhDTA	3,4-TDTA	4-Cl-*o*-PhDTA	NADP	NTP
$[MgL]^{2-}$	6.40	6.80	6.10		
$[MgL]^{-}$				2.95	2.97

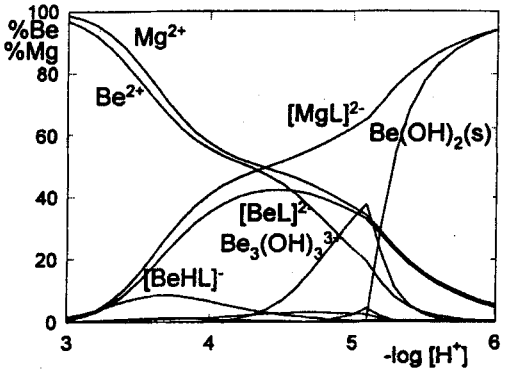


FIGURE 21 Species distribution diagram as a function of pH for Be(II)–Mg(II)–*o*-PhDTA system, ratio 1 : 1 : 1 and $C_M = 2$ mM. (Adapted from Ref. [31]).

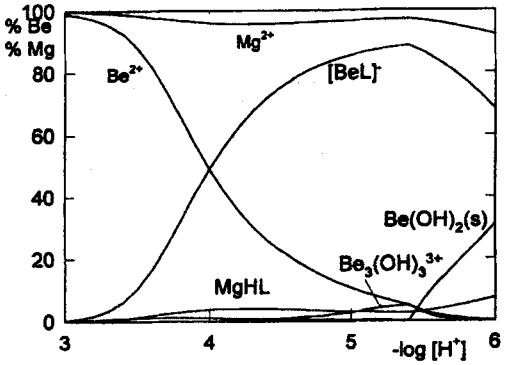


FIGURE 22 Species distribution diagram as a function of pH for Be(II)–Mg(II)–NTP system, ratio 1 : 1 : 1 and $C_M = 2$ mM. (Adapted from Ref. [31]).

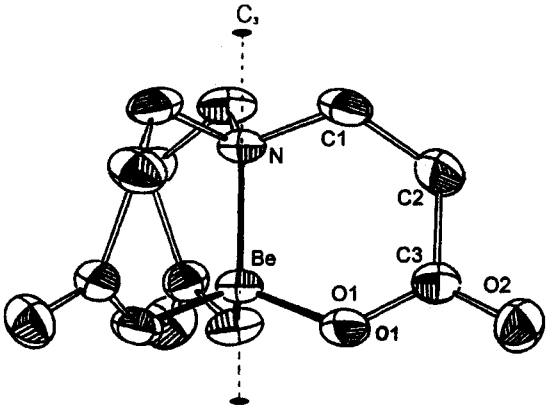


FIGURE 23 Structure of $[Be(NTP)]^-$ anionic monochelate complex. (Adapted from Ref. [20]).

tetradentate ligands NADP and NTP, $\log K_{BeL} \gg \log K_{MgL}$, since these ligands form six-membered chelate rings (prefered by Be(II) but not by Mg(II)) and they fulfill the tetracoordination for Be(II) (Fig. 23) but not the hexacoordination for Mg(II). The calculation [20] of the K^{eff}_{BeL} in presence of Mg^{2+} and H^+ indicates NTP $\approx$ NADP $\gg$ *o*-PhDTA $\approx$ 3,4-TDTA > 4-Cl-*o*-PhDTA.

The preference of the ligands NTP and NADP for selective uptake of Be(II) in the presence of Mg(II) is manifested in the chemical speciation diagrams as a function of pH (ligand : Be(II) : Mg(II), 1 : 1 : 1). Figure 21 shows that *o*-PhDTA and, analogously 3,4-TDTA and 4-Cl-*o*-PhDTA, between pH 4–6 simultaneously sequester Be(II) and Mg(II), while Figure 22 indicates that NTP and NADP practically only sequester Be(II). The advantages of NTP and NADP acids to specifically sequester Be(II) are evident. The beryllium(II) cation in the $[Be(NTP)]^-$ complex (Fig. 23) lies at the center of a slightly distorted tetrahedron toward C_{3v} symmetry with a longer Be—N bond and three equal Be—O bonds and this tetrahedron is more regular than other tetrahedra described in the literature with bidentate ligands [20, 69, 93, 97, 98, 104, 105, 110, 111, 113, 114].

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