Nitrilotripropionic Acid (NTP) and Other Polyamino Carboxylic Acids as Sequestering Agents for Beryllium(II). X-ray Crystal Structure of Sodium (Nitrilotripropionato)beryllate(II) Trihydrate, Na[Be(NTP)]·3H₂O

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Potentiometric studies in aqueous solution at 25 °C and ionic strength 0.5 mol dm⁻³ in NaClO₄ show that beryllium(II) with different polyamino carboxylic acids forms the following complexes: EDTA (ethylenedi-aminetetraacetic), 1,2-PDTA (1,2-propylenediamine-N,N,N',N'-tetraacetic), and CDTA (*trans*-1,2-cyclohexanedi-amine-N,N,N',N'-tetraacetic) (ligands, H₄L), [BeHL]⁻, [BeL]²⁻, and [Be₃(OH)₃(HL)]; EDDADP (ethylenediamine-N,N'-diacetic-N,N'-dipropionic) and EDTP (ethylenediamine-N,N,N',N'-tetrapropionic) (ligands, H₄L), [BeH₂L], [BeHL]⁻, [BeL]²⁻, and [Be₃(OH)₃(HL)]; *o*-PhDTA (*o*-phenylenediamine-N,N,N',N'-tetraacetic), 3,4-TDTA (3,4-toluenediamine-N,N,N',N'-tetraacetic) and 4-Cl-*o*-PhDTA (4-chloro-*o*-phenylenediamine-N,N,N',N'-tetraacetic) (ligands, H₄L), [BeHL]⁻ and [BeL]²⁻; NTA (nitrilotriacetic) (ligand H₃L), [BeL]⁻ and [Be₃(OH)₃(HL)]⁺; NDAP (nitrilodiaceticpropionic) (ligand H₃L), [BeH₂L]⁺, [BeHL], [BeL]⁻, [Be₃(OH)₃(HL)]⁺, and [Be₃(OH)₃L]; NADP (nitriloaceticdipropionic) (ligand, H₃L), [BeHL] and [BeL]⁻; NTP (nitrilotripropionic) (ligand, H₃L), [BeL]⁻. The following complexes are formed analogously for magnesium(II): *o*-PhDTA, 3,4-TDTA, and 4-Cl-*o*-PhDTA, [MgHL]⁻ and [MgL]²⁻; NADP and NTP, [MgHL] and [MgL]⁻. The stability constants were determined. From an aqueous solution of Be(OH)₂ and NTP (ratio 1:1), boiled until the Be(OH)₂ was completely dissolved, crystals of the complex sodium (nitrilotripropionato)beryllate(II) trihydrate, Na[Be(NC₉H₁₂O₆)]·3H₂O were obtained. X-ray diffraction structural analysis revealed that, in the chelate complex [Be(NTP)]⁻ (hexagonal), $P6_3$, $a = 11.4768(7)$ Å, $b = 11.4768(7)$ Å, $c = 6.2807(3)$ Å, $V = 716.44(7)$ Å³, $Z = 2$, $R1 = 0.0433$, w$R2 = 0.1110$), the tetrahedron BeNO₃ is almost regular with a very slight distortion toward the symmetry C_{3v}. ¹H, ¹³C, and ⁹Be NMR, IR spectra, and thermal analyses are studied. The selective uptake of beryllium(II), a very toxic cation, was analyzed by means of the chemical speciation diagrams as well as the so-called conditional or effective formation constants $K_{BeL}{}^{eff}$. With respect to H⁺, the order 3,4-TDTA ≥ *o*-PhDTA > 4-Cl-*o*-PhDTA ≥ NADP ≥ NTP ≫ NDAP > EDTA > EDTP > EDDADP is found for $K_{BeL}{}^{eff}$. This result indicates that, in competition with H⁺, *o*-PhDTA, 3,4-TDTA, 4-Cl-*o*-PhDTA, NADP, and NTP are good sequestering agents at pH 4.5−6 for beryllium(II), and analogously to *o*-PhDTA, these ligands can potentially be used for the analytical determination of beryllium(II). In the presence of Mg²⁺ and H⁺ (Be²⁺ inhibits numerous enzymes that compete with Mg²⁺), the order NTP ≈ NADP ≫ *o*-PhDTA ≈ 3,4-TDTA > 4-Cl-*o*-PhDTA is found. In the presence of Mg²⁺, at pH 4−6, NTP and NADP practically only sequester Be²⁺! The advantages of NTP and NADP acids to sequester specifically beryllium(II) are evident. ¹H, ¹³C, and ⁹Be NMR studies confirm the potentiometric studies.

Introduction

Beryllium is the second lightest metal after lithium, and its unique properties are a great asset in today's nuclear, aeroespace, and electronic industries.[2−6,11] However, beryllium is the most toxic nonradioactive element in the Periodic Table.[2−10] Beryllium and its compounds are toxic to mammalian cells, can interfere with normal immune functions, and, after inhalation, can give rise to an incapacitating lung disease and possibly cancer.[2,3,8] Our understanding of the molecular basis of

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beryllium toxicity is still rather speculative.[2-4] Elements such as Na^+, K^+, Mg^{2+}, and Ca^{2+} are homeostatically controlled such that biological systems are well potected against excesses of these elements, e.g. marine organisms.[7] Beryllium is a different case; biological systems have had no opportunity to develop protection against this *rare* element, and problems of beryllium binding are numerous.[7] At neutral pH the Be^{2+} readily precipitates as colloidal $Be(OH)_2$.[11] Thus, in the buffered physiological environment of the tissues (ca. pH 7.0), precipitated beryllium salts are either adsorbed onto tissue or taken up by cells.[12] Little is known about the tissue sites that react with Be^{2+} except that only proteins appear to be involved, there being no known interactions with carbohydrates and lipids.[2,3] In vitro the Be^{2+} itself inhibits numerous enzymes competitive to magnesium or potassium and noncompetitive in the form of beryllium binding to the enzymes. The strongest inhibition was found in alkaline phosphatase and other phosphatases, but beryllium also inhibits a number of other quite different metabolically critical enzymes.[3,5] This metal and its compounds should therefore be handled with great care.[2-9]

This great toxicity of the 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.[3,8,13-16]

The present treatment for beryllium poisoning involves the formation of nontoxic *lakes* by chelation with organic substrates such as aurintricarboxylic acid[4,5,7] {5-[(3-carboxy-4-hydroxy-phenyl)(3-carboxy-4-oxocyclohexa-2,5-dien-1-ylidene)methyl]-2-hydroxybenzoic acid}. The inherent toxicity of this acid, however, means that there is at present no universally accepted antidote to beryllium poisoning. An alternative approach to the development of beryllium ion inactivation involves the "chelation therapy"[2-5] or "metal encapsulation".[15] The search for good sequestering agents for beryllium(II) thus seems to be a necessary task.

However, studies of the coordinating and chelating ability of beryllium(II) in aqueous solution are very limited,[3,4,18-20] because they have been conditioned not only by the aforementioned toxicity of beryllium(II) but also by the difficulties presented by the strong tendency of this small cation to hydrolyze.[21] This is due to its high density of charge ($z/r = 6.45$),[2,3] which leads to a strongly polarizing character and a great tendency to form covalent bonds with the oxygen atom. The small size induces a tendency to tetracoordination.[22,23] Consequently, the OH^- anion is highly competitive with regard to any other ligand for beryllium(II), and the species resulting
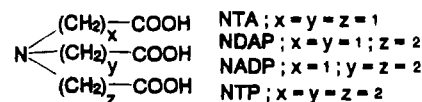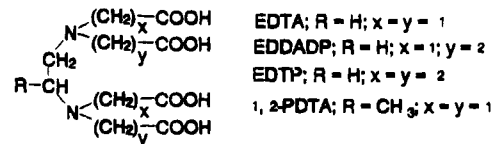
Chart 1

NTA ; x = y = z = 1
NDAP ; x = y = 1 ; z = 2
NADP ; x = 1 ; y = z = 2
NTP ; x = y = z = 2

Chart 2

EDTA; R = H; x = y = 1
EDDADP; R = H; x = 1; y = 2
EDTP; R = H; x = y = 2
1, 2-PDTA; R = CH₃; x = y = 1

Chart 3

Chart 4
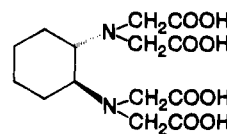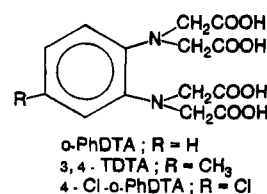

o-PhDTA ; R = H
3, 4 - TDTA ; R = CH₃
4 - Cl -o-PhDTA ; R = Cl

from the hydrolysis[24] 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.

In this work an analysis is presented of the characteristics of a series of polyamino carboxylic ligands with a view to their possible use as sequestering agents for beryllium(II). These ligands have been selected on the basis of the following considerations: (a) To compare potentially tetradentate ligands (nitrilotriacetic, NTA; nitrilodiaceticpropionic, NDAP; nitrilo-aceticdipropionic, NADP; and nitrilotripropionic, NTP, acids; Chart 1), with potentially hexadentate ligands (ethylenediamine-tetraacetic, EDTA; ethylenediamine-N,N'-diacetic-N,N'-dipro-pionic, EDDADP; ethylenediamine-N,N,N',N'-tetrapropionic, EDTP; and 1,2-propylene-diamine-N,N,N',N'-tetraacetic, 1,2-PDTA, acids; Chart 2) (*trans*-1,2-cyclohexanediamine-N,N,N',N'-tetraacetic, CDTA, acid; Chart 3) (*o*-phenylenediamine-N,N,N',N'-tetraacetic, *o*-PhDTA; 3,4-toluenediamine-N,N,N',N'-tetraacetic, 3,4-TDTA; and 4-chloro-*o*-phenylenediamine-N,N,N',N'-tet-raacetic, 4-Cl-*o*-PhDTA, acids; Chart 4), since both groups fulfill the coordination requirements of Be(II); (b) to compare hexa-dentate 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; (c) to compare ligands that form five-membered ring chelates (acetic groups) with ligands that form six-membered ring chelates (propionic groups). It has been found that six-membered ring chelates are the most stable for Be(II),[25,26] 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.

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Once the conventional stability constants are known, the chemical speciation diagrams[27] as a function of pH will show the selective uptake of Be^{2+} ions[7,28] in the presence of H^+ ions. In accord with da Silva and Williams,[7,28] the uptake is based upon equilibrium considerations, varying according to the effective stability constants K_{ML}^{eff} that depend on the conventional stability constants K_{ML}, of the concentration of free ion and of that of H^+ or other competing metallic cations or ligands. From the biological point of view, the preferred pH is 6, close to precipitation of $Be(OH)_2$,[24] which is retarded by the good chelating agents, above the physiological buffer. The preferred ligands are not only of biological interest but also of analytical interest for the titrimetric determination of beryllium(II).[29] The effective stability constants in the presence of Mg(II) will also be determined, because, as indicated earlier, the Be^{2+} ion inhibits numerous enzymes competitive to magnesium.[5-7]

Experimental Section

Materials. NTP,[25,30] EDDADP,[31] EDTP,[31] and o-PhDTA[32] were synthesized as previously reported, while analytical grade EDTA, 1,2-PDTA, and CDTA were purchased from Fluka. The solution of Be-$(ClO_4)_2$ was prepared by reacting metallic Be (Aldrich) with an excess of $HClO_4$ (Merck, analytical grade), its free acidity[33] being determined, as well as the concentration of Be(II) in aqueous solution which was evaluated gravimetrically.[34,35] The solution of $Mg(ClO_4)_2$ was prepared from an Aldrich product and was evaluated complexometrically. A carbonate-free sodium hydroxide solution was prepared from an ampule of 9959Titrisol (Merck) and standardized against potassium hydrogen phthalate. $NaClO_4$ was prepared by recrystallization of $NaClO_4$ (Merck ag).

Potentiometry Measurements. The potentiometric titrations were carried out in aqueous solution at ionic strength 0.5 mol dm^{-3} in $NaClO_4$. The sealed 100 mL thermostated double-walled glass reaction vessel was fitted with a Radiometer G202B glass electrode, a Radiometer K711 calomel reference electrode, inert argon atmosphere inlet and outlet tubes, a magnetic stirrer, and a titrant inlet. Readings of potentials were obtained with a Radiometer type PHM-85 potentiometer. The titrant was delivered through an immersed capillary tip from a Crison Microbur 2031 piston buret, and the temperature was maintained at 25.00 ± 0.01 °C by the circulating of water from a refrigerated constant-temperature bath. A Basic program[36] (APT program from microcomputer ITS80286) was used to monitor, for each titration point, the emf values and the volume of titrant added. When the observed emf was constant, within user-defined limits, the next volume of titrant was added automatically and the cycle repeated until the predefined total volume of titrant had been added. The cell constants $E°$ and the liquid junction potentials J were determined according to the method of Biedermann and Sillén,[37-39] by means of a least-squares program. It was found that $pK_w = 13.71$, in accord with the literature.[40]

Measurements were taken of ligands alone at the concentrations $C_L = 1.00 \times 10^{-3}$ and 2.00×10^{-3} mol dm^{-3} (titrations with NaOH and

$HClO_4$) and of the ligands in the presence of Be(II) at the ligand:metal ratios 2:1, 1:1, and 1:2 and concentrations $C_M = 1.00 \times 10^{-3}$ and 2.00×10^{-3} mol dm^{-3}, respectively. For Mg(II), measurements were made of the ligands in the presence of metallic cation at the ligand:metal ratios 2:1 and 1:1 and concentrations $C_M = 3.00 \times 10^{-3}$ and 5.00×10^{-3} mol dm^{-3}, respectively. The experimental potentiometric data were analyzed by means of the NERNST/LETA/GRAFICA version[41] of the LETAGROP program.[42-44] Hydrolysis of Be(II) was previously studied under the same experimental conditions.[24,45]

NMR Spectroscopy. The 200.0-MHz ^1H NMR and 50.32-MHz ^{13}C spectra were recorded on a Bruker AC-200 spectrometer, in D_2O solutions for ^1H to provide a lock signal and with DMSO as standard reference for ^{13}C. A stock solution with ratio 1:1 ligand:Be(II) was obtained by dissolving ligand and $BeSO_4 \cdot 4H_2O$ with $C_L = 0.03$ mol dm^{-3}. All measurements were made in D_2O (25 °C), and pH was adjusted with a Radiometer GK 2401C mixed electrode using minimum volumes of either concentrated D_2SO_4 or NaOH, the value being amended according to $pD = pH + 0.4$.[46]

^9Be NMR spectra were recorded on a Bruker AMX-500 spectrometer at 70.28 MHz. The magnetic field homogeneity was adjusted by shimming on the D_2 resonance of D_2O. All the experiments were run in the unlocked mode using 10 mm o.d. sample tubes without spinning. The probe temperature was 300 K. The acquired free induction decay (FID), obtained with 80 scans using a zg30 PULPROG, was multiplied by the same line broadening window function (LB = 3 Hz) before transformation. Some other parameters used are as follows: digital resolution 0.3 Hz per point; spectral window 2825 Hz; pulse width (P1 = 90) 22.5 μs; acquisition time 1.45 s; pulse delay (D1) 5.0 s. Chemical shifts are quoted relative to an external 3.0 mol dm^{-3} $BeSO_4$ solution in D_2O. The integral accuracy was considered to be acceptable since all the lines were not very broad ($W_{1/2} = 10-20$ Hz) and was carried out using the standard Bruker software. The pH measurements were made with a combination electrode connected to a micro pH 2002 Crison apparatus. Solutions were prepared using regular water purified by the inverse osmosis method. The samples were prepared in each case by adding to a 0.030 mol dm^{-3} ligand solution sufficient $BeSO_4$ to form a ca. 20% ligand excess. The pH was adjusted by the addition of a minimum volume of a very concentrated solution of NaOH or H_2SO_4 in the same solvent.

Other Physical Measurements. Infrared spectra were measured as KBr disks using a Nicolet 710 FT-IR spectrometer. Thermogravimetric and calorimetric analyses were performed on a Netzsch STA 409 EP simultaneous thermobalance (TG) and a differential scanning calorimeter (DSC) at a heating rate of 5 °C min^{-1} (20-950 °C) in oxygen atmosphere.

Preparation of the Complex Na[Be(NTP)]·3H₂O. In 0.04 dm^{-3} of water are dissolved 0.25 g (5.8×10^{-3} mol) of $Be(OH)_2$ with 2.7 g of NTP (1.2×10^{-2} mol). The solution is taken to boiling until the $Be(OH)_2$ is completely dissolved. After cooling, the pH is adjusted to 6.5 by adding NaOH (this being the most suitable pH for the formation of the complex $[Be(NTP)]^-$; see distribution diagrams of species in Figure S7b). Crystals suitable for X-ray crystallography are obtained by slow evaporation at room temperature after a few days.

Crystal anal. Found: C, 34.15; H, 5.87; N, 4.44; Na, 7.30; Be, 2.94. Calcd for $NaBeNC_9H_{18}O_9$: C, 34.17; H, 5.70; N, 4.43; Na, 7.28; Be, 2.85. Elemental analyses were performed on a Carlo Erba 1106 automatic analyzer. Be and Na were determined by atomic absorption. ^1H NMR spectrum (Chart 1, Figure 2): $\delta = 2.43$ ppm, triplet (α-CH_2), $\delta = 2.78$ ppm, triplet (β-CH_2). ^{13}C NMR spectrum: $\delta = 37.25$ ppm (α-C), $\delta = 56.76$ ppm (β-C), $\delta = 185.55$ ppm (C, carboxylic). ^9Be NMR spectrum: $\delta = 2.36$ ppm, $[Be(NTP)]^-$. IR spectrum: 3369.7 cm^{-1} ($\nu(H_2O)$), 1615.4 cm^{-1} (ν_a(COOBe)), 1409.1 cm^{-1} (ν_s(COOBe)). In thermal analysis, one water molecule is removed at 111.2 °C and two water molecules are removed at 127.2 °C, thermal decomposition beginning at 312.8 °C.

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Table 1. Crystal Data and Structure Refinement for Na[Be(NTP)]·3H₂O

chem formula	C₉H₁₈NO₉NaBe	D_{obsd}, g·cm⁻³	1.43
fw	316.24	radiation (λ, Å)	Mo Kα, graph monochrom (0.7107)
space group	hexagonal, $P6_3$	μ, cm⁻¹	1.53
a, Å	11.4768(7)	temp, K	293(2)
b, Å	11.4768(7)	θ range, deg	2.05–50.17
c, Å	6.2807(3)	data colld	3024
V, Å³	716.44(7)	no. of unique data ($I > 2\sigma(I)$)	1246
Z	2	$R1^a$	0.0433
D_{calcd}, g·cm⁻³	1.466	$wR2^b$	0.1110

$^a R1 = (1/r)\Sigma|F_o - F_c|/(1/r)\Sigma F_o. \ ^b wR2 = (1/r)[\Sigma[w(F_o^2 - F_c^2)^2]/(1/r)\Sigma[w(F_o^2)^2]]^{1/2}.$

Table 2. Atomic Coordinates (×10⁴) and Equivalent Isotropic Displacement Parameters (Å² × 10³)

|	x	y	z	$U_{eq}{}^a$
Na	10000	10000	7785(2)	42(1)
O(1W)	8151(1)	9180(1)	5269(2)	48(1)
Be	3333	6667	9066(5)	32(1)
N	3333	6667	11900(3)	33(1)
C(1)	2281(2)	6952(2)	12700(2)	48(1)
C(2)	1012(2)	6316(2)	11401(2)	48(1)
C(3)	1220(2)	6882(2)	9174(2)	38(1)
O(1)	2314(1)	7133(1)	8243(1)	41(1)
O(2)	6698(1)	9643(1)	8331(2)	50(1)

$^a U_{eq}$ is defined as one-third of the trace of the orthogonalized $\mathbf{U}_{ij}$ tensor.

X-ray Structure Analysis. Many of the details of the structure analysis carried out on the beryllium compound are listed in Table 1. X-ray diffraction measurements were made using a Nonius CAD-4 diffractometer. Graphite-monochromated molybdenum Kα radiation ($\lambda = 0.710\ 69$ Å) was used as the X-ray source. Cell dimensions were determined from 19 centered reflections ($12.711 \leq \theta \leq 34.376$). Corrections were applied for Lorentz and polarization but not for absorption. The structure was solved by direct methods (MULTAN-88)[47] and refined with (SHELX-93).[48] Refinement was made on F^2 for all reflections except for zero with very negative F^2 or flagged by the user for potential systematic errors. Weighted R-factors wR and all goodnesses of fit S values are based on F^2; conventional R-factors R are based on F, with F set to zero for negative F^2. The observed criterion of $F^2 > 2\sigma(F^2)$ is used only for calculating the R factor observed, etc., and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R factors based on all data will be even larger. Reflections were weighted according to the formula $w = 1/[2(F_o^2) + (0.0666P)^2 + 0.0845P]$, where $P = (F_o^2 + 2F_c^2)/3$. The hydrogen atoms of the water molecule were located and refined, and the rest of the hydrogen atoms were constrained to ideal geometries. All the hydrogen atoms were refined with a common isotropic displacement parameter. Since the compound crystallizes in a polar space group, polar axis restraints were applied by the method of Flack and Schwarzenbach,[49] and the absolute structure of the crystal used for the investigation was established as described by Flack.[50] Final difference syntheses showed no chemically significant features, the largest maxima being close to the metal or sodium atoms. Refinement converged (mean shift/esd < 0.009) smoothly to the residuals given in Table 1. Tables 2 and 3 report the positional parameters, etc. Other crystallographic data are summarized in Tables S1–S6. Scattering factors, dispersion corrections, and absorption coefficients were taken from ref 51. Figures 1 and S1 were made with PLUTO,[52] and Figure 2 is an ORTEP[53] view.

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Table 3. Selected Bond Lengths (Å) and Angles (deg) for Na[Be(NTP)]·3H₂O^a

(a) Coordination Sphere of Beryllium

Be–O(1)	1.596(1)	Be–N	1.780(3)
O(1)–Be–N	108.9(1)	O(1)ⁱ–Be–O(1)	110.0(1)
O(1)ⁱⁱ–Be–O(1)	110.0(1)		

(b) In the NTP Ligand

N–C(1)	1.488(2)	C(1)–C(2)	1.502(2)
C(2)–C(3)	1.510(2)	C(3)–O(1)	1.279(2)
C(3)–O(2)	1.226(2)		
C(1)–N–C(1)ⁱ	109.2(1)	C(1)–N–Be	109.7(1)
C(1)–C(2)–C(3)	112.7(1)	O(1)–C(3)–C(2)	116.6(1)
O(2)–C(3)–C(2)	120.1(2)		

(c) Coordination Sphere of the Sodium

Na–O(1W)	2.427(2)	Na–O(1W)ⁱⁱⁱ	2.427(2)
Na–O(1W)ⁱᵛ	2.427(2)	Na–O(1W)ᵛ	2.414(1)
Na–O(1W)ᵛⁱ	2.414(1)	Na–O(1W)ᵛⁱⁱ	2.414(1)

^{a} Symmetry transformation used to generate equivalent atoms: (i) $-y + 1, x - y + 1, z$; (ii) $-x + y, -x + 1, z$; (iii) $-y + 2, x - y + 1, z$; (iv) $-x + y + 1, -x + 2, z$; (v) $x - y + 1, x, z + \frac{1}{2}$; (vi) $y, -x + y + 1, z + \frac{1}{2}$; (vii) $-x + 2, -y + 2, z + \frac{1}{2}$.
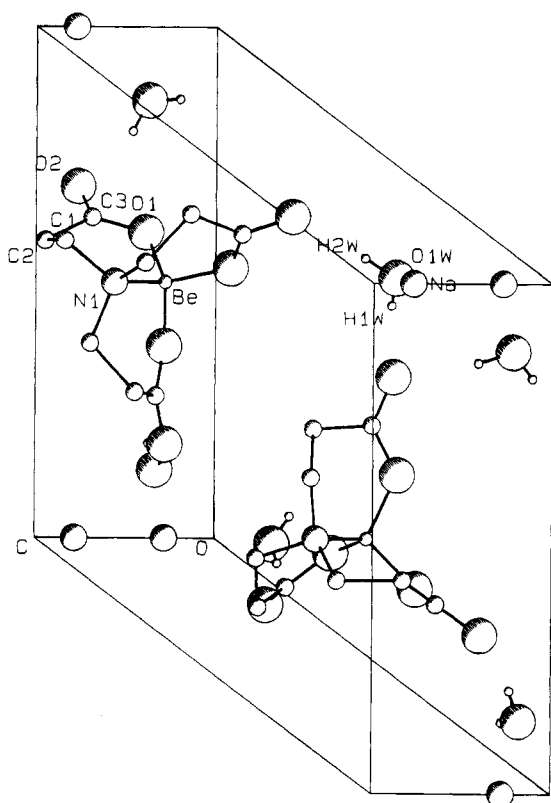

Figure 1. Molecular packing for the compound Na[Be(NTP)]·3H₂O.

Results and Discussion

Description of the Structure. In the crystal packing (Figure 1) there are [Be(NTP)]⁻ complex anions and hexahydrated sodium cations. Each sodium cation (Figure S1) is surrounded by 6 molecules of water with a slightly distorted O_h geometry. These water molecules are bridge molecules between two atoms

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(53) Johnson, C. K. ORTEP. Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN, 1971.
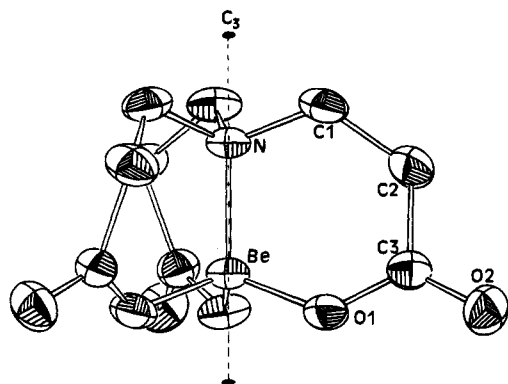
Figure 2. ORTEP view of the [Be(NTP)]⁻ anionic chelate complex (50% probability ellipsoids; H atoms excluded).

of sodium, [Na(μ-OH₂)₃]ₙⁿ⁺, forming unidimensional columns.

The beryllium(II) cation in the [Be(NTP)]⁻ complex (Figure 2) 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 (Table 3). The Be—N bond length (1.78 Å) is similar to the Be—N bond in the tetrahedral coordination in [Be₃(OH)₃-(pic)₃] [pic = picolinate][54] (1.79 Å) and in bis(dimethyl-amino)beryllium[55] (1.78 Å). The three Be—O bonds (1.596 Å) are somewhat shorter than the Be—O bond with carboxylate oxygens in six-membered chelate rings in more distorted tetrahedra [(in Å) salicylate[13] (1.612), bis(salicylate)[56] (1.62 and 1.63), and malonate[57] (1.609 and 1.623)] and in other six-membered chelate rings [bis(acetylacetonate)[58] (1.70) and bis-(9-oxido-phenalenone)[59] (1.610 and 1.621)] but somewhat longer than in Be—OH or BeO bonds in the six-membered chelate ring from [Be₃(OH)₃(pic)₃][54] (1.577 Å) and salicylate[13] (1.572 Å), respectively. The three bond angles O—Be—O (110.03°) and the three bond angles O—Be—N (108.91°) are also equal (Table 3) and indicate that the tetrahedron BeNO₃ is almost regular with a very slight distortion toward the symmetry C_{3v}. This tetrahedron found in the chelate complex [Be(NTP)]⁻ with the tetradentate ligand NTP is more regular than other tetrahedra described in the literature with bidentate ligands: BeN₄ in bis-(dimethylamino)[55] (shortest angle N—Be—N, 91.2°); BeNO₃ in [Be₃(OH)₃(pic)₃][54] (92.5—114.9°); BeO₄ in salicylate dihydrate[13] (106.9—112.5°), in bis(salicylate)[56] (107.0—112.5), in bis-(malonate)[57] (107.1—111.4), in bis(acetylacetonate) (106.9—112.6),[58] in bis(9-oxidophenalenone)[59] (107.0—112.0), in bis-(catecholate)[14] (99.4—116.8), and in bis(oxalate)[60] (99.6—115.4). The tetrahedron is more distorted in bis(catecholate) and in bis-(oxalate) with a five-membered chelate ring than in bis-(malonate)[57] with a six-membered chelate ring. The data in Table 3, Figure 2, indicate that the NTP ligand is an excellent encapsulating agent for Be(II). In accord with our data, the chelate complex [Be(NTP)]⁻ is the first crystalline structure to

be determined of a chelate of Be(II) with a potentially tetra- or hexadentate polyamino carboxylic chelating agent.

Ionization Constants of the Acids. The ionization constants of the acids K_i (LETAGROP program;[41-44] ligands, H₄L, EDTA, EDDADP, EDTP, 1,2-PDTA, and CDTA) are given in Table 4. The values found for pK_i are in good agreement with those previously found in the literature,[18,19] taking into account the differences in ionic strength and temperature. The most basic protonations (equilibria (5) and (6), Table 4), analogously to EDTA,[62] correspond to protons situated fundamentally over nitrogen atoms, while the remaining protonations (equilibria (1)—(4)) mainly correspond to carboxylic protons. The values of pK_i for o-PhDTA and analogous ligands and for NTA and analogues, Table 4, have been previously determined at the same ionic strength and temperature (refs 61 and 26, respectively).

Stability Constants of the Complexes Formed. The analysis of the experimental potentiometric data for each of the metal—ligand systems was performed by means of the NERNST/LETA/GRAFICA version[41] of the LETAGROP program,[42-44] and the model that best fits the experimental results is that which corresponds to the complex species and log K values reported in Table 5.

The following order of stability CDTA ≈ 1,2-PDTA ≈ EDTA < EDDADP ≈ EDTP is found for the complexes [BeHL]⁻ and [BeL]²⁻. This order confirms that six-membered ring chelates are the most stable for Be(II).[26,63] This greater stability of the six-membered ring chelates is manifested in the EDDADP and EDTP acids by propionic groups that stabilize the acid complex [BeH₂L].

Table 4. Ionization Constants of EDTA, EDDADP, EDTP, 1,2-PDTA, and CDTA (25 °C; I = 0.5 mol dm⁻³ in NaClO₄) Ligands, H₄L

	pK_i(H₄L)				
equilibria	EDTA	EDDADP	EDTP	1,2-PDTA	CDTA
(1) H₆L²⁺/H₅L⁺			2.24(2)ᵃ		
(2) H₅L⁺/H₄L		2.03(1)	3.03(1)	1.42(4)	1.91(3)
(3) H₄L/H₃L⁻	1.68(1)	3.13(1)	3.45(1)	2.39(3)	2.45(2)
(4) H₃L⁻/H₂L²⁻	2.48(2)	3.82(2)	4.28(3)	2.71(3)	3.35(1)
(5) H₂L²⁻/HL³⁻	6.05(1)	6.02(2)	6.24(3)	6.05(3)	5.80(2)
(6) HL³⁻/L⁴⁻	8.90(1)	9.73(2)	9.56(2)	8.76(4)	9.31(3)
[σ(z)]	0.008	0.014	0.014	0.015	0.014
no. of points	94	204	268	85	85
−log [H⁺] range	2.70–	2.07–	2.06–	2.00–	2.50–
	10.10	10.40	10.50	9.60	10.40

	pK_i^b(H₄L)		
equilibria	o-PhDTA	3,4-TDTA	4-Cl-o-PhDTA
H₄L/H₃L⁻	2.92(1)	2.92(6)	3.21(9)
H₃L⁻/H₂L²⁻	3.50(1)	3.51(3)	3.69(8)
H₂L²⁻/HL³⁻	4.58(2)	4.62(2)	4.69(7)
HL³⁻/L⁴⁻	6.42(3)	6.78(2)	5.82(9)

	pK_i^c(H₃L)		
equilibria	NTA	NDAP	NADP	NTP
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H₄L⁺/H₃L		1.07(3)	1.95(3)	2.71(5)
H₃L/H₂L⁻	1.82(5)	2.22(1)	3.12(2)	3.77(5)
H₂L⁻/HL²⁻	2.38(2)	3.65(2)	4.00(2)	4.28(4)
HL²⁻/L³⁻	9.05(1)	9.29(2)	9.55(3)	9.59(5)

ᵃ Values in parentheses are standard deviations. ᵇ From ref 61. ᶜ From ref 26.

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Table 5. Stability Constants of the Complexes of Be(II) with Polyamino Carboxylic Acids (25 °C; $I = 0.5$ mol dm^{-3} in NaClO$_4$)

species	log K (ligands, H$_4$L)				
	EDTA	EDDADP	EDTP	1,2-PDTA	CDTA
BeH$_2$L		2.31(7)^a	2.34(8)		
[BeHL]$^-$	3.38(6)	4.09(6)	4.20(6)	3.26(4)	3.09(9)
[BeL]$^{2-}$	7.90(3)	8.50(3)	8.45(4)	7.83(5)	7.83(7)
[Be$_3$(OH)$_3$(HL)]	36.69(9)	36.86(3)	36.70(8)	36.59(8)	36.07(5)
[σ(z)]	0.016	0.026	0.017	0.025	0.025
no. of points	133	220	192	154	234
range	2.8–5.5	3.1–5.5	3.1–5.7	2.6–5.6	2.8–5.8

species^b	log K (H$_4$L)		
	o-PhDTA	3,4-TDTA	4-Cl-o-PhDTA
[BeHL]$^-$	3.37(6)	3.74(5)	3.59(9)
[BeL]$^{2-}$	6.51(4), 6.48^c	6.88(4)	5.79(9)

species^d	log K (ligands, H$_3$L)			
	NTA	NDAP	NADP	NTP
[BeH$_2$L]$^+$		1.33(3)		
[BeHL]		2.08(4)	2.37(9)	
[BeL]$^-$	6.68(3)	8.12(3)	9.25(4)	9.23(9)
[Be$_3$(OH)$_3$HL]$^+$	34.92(3)	35.79(9)		
[Be$_3$(OH)$_3$L]		40.00(9)		
[σ(z)]	0.009	0.005	0.026	0.068
no. of points	99	364	311	28
−log [H$^+$] range	2.3–5.9	1.9–5.8	2.5–6.5	3.2–5.1

^{a} Values in parentheses are standard deviations. ^{b} From ref 61. ^{c} 25 °C; $I = 1.0$ mol dm^{-3} in NaClO$_4$; ref 29. ^{d} Experimental potentiometric data from ref 26, recalculated.

The presence of the complex species [Be$_3$(OH)$_3$(HL)] derived from the trimeric hydrolytic species [Be$_3$(OH)$_3$]$^{3+}$ has been confirmed in the solid state by determination by X-ray diffraction of the crystalline structure of the complex [Be$_3$(OH)$_3$-(pic)$_3$].[54] The species [Be$_3$(OH)$_3$(HL)] has also been found for 1,3-PDTA, 1,4-BDTA, 1,3-PDTP, and 1,4-BDTP acids.[63] 1,3-PDTP and 1,4-BDTA acids also form the complex [Be$_3$(OH)$_3$-(H$_2$L)]$^+$. In Table 5 are also included the values of log K for the complex species that form Be(II) with o-PhDTA, 3,4-TDTA, and 4-Cl-o-PhDTA acids (from ref 61) and those that form Be(II) with NTA, NDAP, NADP, and NTP acids: experimental potentiometric data from an other work[26] were also analyzed by means of the LETAGROP program.[41]

Selective Uptake of Beryllium(II) Ions: Species Distribution Diagrams and Effective Stability Constants. The selective uptake of beryllium(II) was analyzed by means of the chemical speciation diagrams[27] as well as the so-called conditional or effective formation constants[7,28,66] K_{ML}^{eff}. The species distribution diagrams as a function of pH show the selective uptake of Be^{2+} ions[7,28] in the presence of H$^+$ ions and were calculated from the values of ionization constants of the ligands (Table 4), stability constants of the complexes (Table 5), and formation constants of the hydrolytic species of Be(II),[24,45] for EDTA 1,2-PDTA, CDTA, EDDADP, and EDTP (Figures S5 and S6). For o-PhDTA, 3,4-TDTA, and 4-Cl-o-PhDTA acids data were taken from ref 61, and for NTA, NDAP, NADP, and NTP acids data were taken from ref 26 and Table 5 (Figures S7 and S8). The species distribution diagrams as a function of pH of o-PhDTA and NTP acids in the presence of Be^{2+} and Mg^{2+} (ligand:Be(II):Mg(II) 1:1:1 ratio, $C_M = 2 \times 10^{-3}$ mol dm^{-3}; calculated from the data of Tables 4−6 and the hydrolysis of Be(II)[24,25]) show the selective uptake of Be^{2+} ions in the presence of Mg^{2+} and H$^+$ ions (Figure S9).

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The stability constants that should be used to describe the binding of metal ions to the ligands are not the usual stoichiometric stability constants K_{ML} determined in aqueous solutions for simple metal−ligand equilibria but the so-called conditional or effective binding constants,[7,28,66] which take into account the competition of the proton and the other metal ions (in our case, Be^{2+} and Mg^{2+}) for the sites of M and also the competition of other ligands present for M (in our case, the OH$^-$ ligand for Be^{2+}). This competition has very important effects on selectivity.[7,28]

The effective stability constants are related to the conventional stability constants by the expressions (considering competitive complex formation for only two metal ions, Be^{2+} and Mg^{2+}, and two ligands, polyamino carboxylic L and OH$^-$)

$$\log K_{BeL}^{eff} = \log K_{BeL} - \log \alpha_L - \log \alpha_{Be(OH)}$$

where $\alpha_{Be(OH)} = 1 + 3[Be^{2+}]^2[H^+]^{-3}\beta_{-33}$ (taking into account that the trimer hydroxo complex [Be$_3$(OH)$_3$]$^{3+}$ is the only important one[24,45]) and

$$\alpha_L = 1 + \sum_{i=1}^{i=N}\beta_i^H[H^+]^i +$$

$$[Mg^{2+}]\left(K_{MgL} + \frac{K_{MgHL}[Mg^{2+}][H^+]}{\beta_1^H}\right)$$

The β_i^H values are the overall formation constants of the species H$_i$L. K_{MgL} and K_{MgHL} are the stability constants of the complexes formed between Mg^{2+} and L.

In effect, α_L is the reduction in L available to Be^{2+} due to the presence of H$^+$ and Mg^{2+}, while $\alpha_{Be(OH)}$ is the reduction of Be^{2+} available to L due to the removal of Be^{2+} by the formation of the hydroxo complex [Be$_3$(OH)$_3$]$^{3+}$. The values of K_{BeL}^{eff} may be much smaller than K_{BeL} (Table 6a,b). In Table 6c are presented the stability constants (log K) for the complexes of Mg(II).

Figure S5a shows that for EDTA and its analogs 1,2-PDTA and CDTA at pH > 4.5 the diprotonated species of the ligand H$_2$L^{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 especially to the N atoms retards to a 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 complex species. These results are reflected in the low values of K_{BeL}^{eff} for EDTA (Table 6a).

The presence of propionic groups allows a greater stability of the protonated complex species [BeH$_2$L] and [BeHL]$^-$ in EDDADP and EDTP acids (Table 5, Figure S5b). But Figure S5b also shows that the high basicity of the nitrogen atoms retards to a higher pH the formation of the complex [BeL]$^{2-}$, allowing the species [Be$_3$(OH)$_3$]$^{3+}$ and its hydroxo complex [Be$_3$(OH)$_3$(HL)] to persist. These results are also reflected in the low values of K_{Bel}^{eff} (Table 6a), for EDDADP and EDTP. The unfavorable effect of the high basicity of nitrogen atoms supersedes the favorable effect of the formation of six-membered chelate rings.

Contrarily, the lesser basicity of the nitrogen atoms of the aromatic diamines allows the complex [BeL]$^{2-}$ to compete favorably with the species H$_2$L^{2-} and HL^{3-} in o-PhDTA, 3,4-TDTA, and 4-Cl-o-PhDTA acids (Figure S7a), its formation beginning at pH < 4, hindering the formation of the trimeric species [Be$_3$(OH)$_3$]$^{3+}$ and its corresponding hydroxo complex

Table 6. Effective Stability Constants (log K_{BeL}^{eff}) of Beryllium(II) with Different Polyamino Carboxylic Acids (25 °C; I = 0.5 mol dm⁻³ in NaClO₄)

(a) With Respect to H⁺

pH	o-PhDTA	3,4-TDTA	4-Cl-o-PhDTA	NTP	NADP	NDAP	EDTA	EDDADP	EDTP
5.00	4.94	4.94	4.75	4.56	4.66	3.79	2.77	2.22	2.57
5.20	5.18	5.19	4.98	4.79	4.87	4.00	3.11	2.57	2.98
5.40	5.39	5.42	5.17	5.01	5.08	4.20	3.53	2.96	3.38
5.60	5.59	5.63	5.33	5.22	5.29	4.41	3.93	3.37	3.76
5.80	5.78	5.83	5.46	5.43	5.49	4.61	4.30	3.73	4.12
6.00	5.94	6.02	5.56	5.63	5.70	4.81	4.63	4.07	4.44

(b) With Respect to Magnesium(II) and H⁺

pH	o-PhDTA	3,4-TDTA	4-Cl-o-PhDTA	NTP	NADP
5.00	3.07	2.79	2.36	4.56	4.66
5.20	3.15	2.92	2.36	4.79	4.87
5.40	3.23	3.10	2.36	5.01	5.08
5.60	3.32	3.29	2.36	5.22	5.29
5.80	3.42	3.48	2.36	5.43	5.49
6.00	3.53	3.67	2.36	5.63	5.70

(c) Stability Constants (log K) of the Magnesium(II) Complexes
(25 °C; I = 0.5 mol dm⁻³ in NaClO₄)

complex	o-PhDTA	3,4-TDTA	4-Cl-o-PhDTA	NTP	NADP
[MgHL]⁻	3.60(4)ᶜ	3.85(2)	3.20(8), 3.33ᵇ		
[MgL]²⁻	6.40(5), 6.48ᵃ	6.80(4)	6.09(9), 6.13		
[MgHL]				2.24(6)	1.33(4)
[MgL]⁻				2.96(7)	2.94(6)

ᵃ 25 °C; I = 1.0 mol dm⁻³ in NaClO₄.[64] ᵇ 25 °C; I = 0.1 mol dm⁻³ in KCl.[65] ᶜ Values in parentheses are standard deviations.

[Be₃(OH)₃(HL)]. This favorable situation is also manifested in the higher values of K_{BeL}^{eff} (Table 6a), allowing o-PhDTA acid to be used for the titrimetric determination of Be(II).[29] 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!

NTP and NADP (Figure S7b) also begin to form the nonprotonated complex [BeL]⁻ at pH < 4, hindering the formation of the trimeric species [Be₃(OH)₃]³⁺ and its corresponding hydroxo complexes. The high basicity of the species HL²⁻ (Table 4) of the ligands NTP and NADP is compensated by the chelate effect that results from satisfying the coordination index of four of the small Be²⁺ cations and by the formation of the more stable six-membered chelate rings, as observed in the structure (Figure 2) and crystalline data of the complex (Table 3). The shape of the diagrams is seen in the high values of K_{BeL}^{eff} (Table 6a) for NTP and NADP acids.

The species distribution diagrams as a function of pH and the order found for K_{BeL}^{eff} (Table 6a) of 3,4-TDTA ≥ o-PhDTA > 4-Cl-o-PhDTA ≥ NADP ≥ NTP ≫ NDAP > EDTA > EDTP > EDDADP indicate therefore 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 the hydrolysis of this small cation. Analogously to o-PhDTA,[29] these ligands can potentially be used for the analytical determination of Be(II).

It has already been pointed out that one of the causes of the toxicity of Be²⁺ is to inhibit numerous enzymes competitive to magnesium.[5−7] We therefore considered it worthwhile to analyze the selective uptake of Be²⁺ in the presence of Mg²⁺. In Table 6c are shown the values obtained for the stability constants of Mg(II) with the better sequestering agents of Be(II), 3,4-TDTA, o-PhDTA, 4-Cl-o-PhDTA, NTP, and NADP. Upon comparison with the values of log K for Be(II), Table 5, it was found that for the potentially hexadentate ligands derived from aromatic diamines 3,4-TDTA, o-PhDTA, and 4-Cl-o-PhDTA

log K_{BeL} ≈ log K_{MgL}. This result is accounted for by the fact that Be(II) tends to tetrahedral coordination[22,67] with the lesser degree of strain of the six-membered chelate rings, while Mg-(II) tends to octahedral coordination[22,67] and the five-membered chelate rings undergo a lesser degree of strain. 3,4-TDTA, o-PhDTA, and 4-Cl-o-PhDTA form five-membered chelate rings. Contrarily, for the potentially tetradentate ligands NADP and NTP log K_{BeL} ≫ log K_{MgL}, since these ligands form six-membered chelate rings (preferred by Be(II) but not by Mg(II)) and they fulfill the necessities of tetracoordination for Be(II) (Figure 2) but not the necessities of hexacoordination for Mg-(II). The calculation of the K_{BeL}^{eff} in presence of Mg²⁺ and H⁺ (Table 6b) also indicates NTP ≈ NADP ≫ o-PhDTA ≈ 3,4-TDTA > 4-Cl-o-PhDTA. The preference of the ligands NTP and NADP for the selective uptake of Be(II) is manifested in the chemical speciation diagrams as a function of pH (ligand: Be(II):Mg(II), 1:1:1): Figure S9a 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 S9b indicates that NTP and analogously NADP practically only sequester Be(II)! The advantages of NTP and NADP acids to sequester specifically Be(II) are evident. In any case, o-PhDTA and 3,4-TDTA could be administered as a complex of magnesium, analogously to EDTA that is administered as a complex of zinc to remove lead(II) ions from blood plasma and tissue, since two essential metals, zinc and manganese, will be coexcreted with the lead complex.[27,68]

NMR Studies. To complement the potentiometric studies, ¹H, ¹³C, and ⁹B NMR studies of the most significative Be(II)− ligand systems have been carried out (ligand:metal ratio 1:1, C_M = 20 × 10⁻³ mol dm⁻³; δ in ppm).

NTP−Be(II) System. ¹H NMR spectra as a function of the pD have been performed. The spectrum at pD = 2.7 indicates the presence of two triplets of the same intensity corresponding

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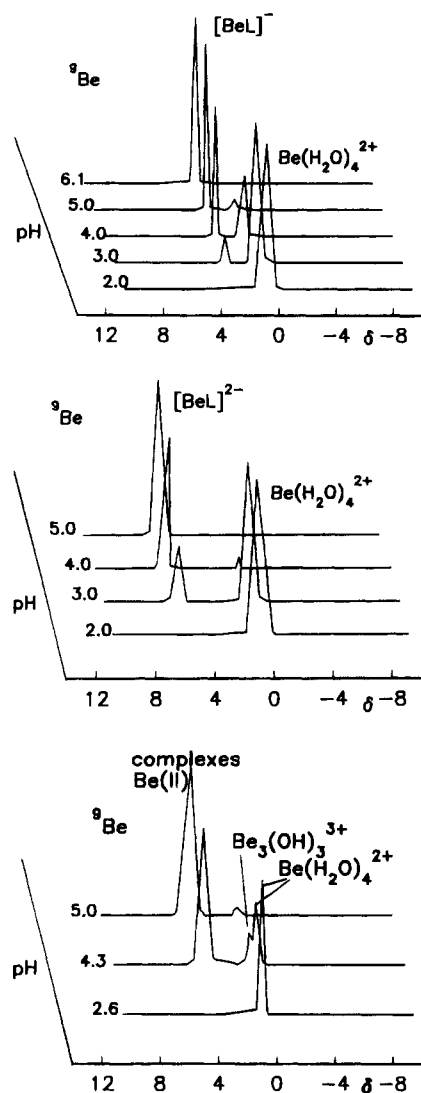
Figure 3. ^{9}Be NMR spectra as a function of the pH: (a, top) for the NTP—Be(II) system; (b, middle) for the *o*-PhDTA—Be(II) system; (c, bottom) for the EDDADP—Be(II) system.

to two types of protons, α and β (δ = 2.69 and 3.26, respectively), corresponding to the propionic groups of the free ligand, and when the pD increases, two new triplets appear (pD 3.3) at higher field (δ = 2.41 and 2.79, respectively). These two new triplets increase in intensity and are analogous to those corresponding to the aqueous solution of the complex [BeL]$^-$ (see Experimental Section), Figure 2. The triplet corresponding to the β protons, which are closer to atom N, undergoes a greater shift (Δδ = 0.47) to higher field than the triplet corresponding to the α protons (Δδ = 0.28), confirming coordination of the atom of N to the Be(II) (Figure 2). The net difference in position between the triplets corresponding to the free ligand and the complexed ligand and the constancy in δ of the latter show slow equilibria between L^{3-} and [BeL]$^-$, and with slow breaking of both M—N and M—O bonds, contrarily to what occurs with alkali and other alkaline earth ions and EDTA.[69] The ^{9}Be NMR (Figure 3a) shows an analogous situation: at pH 2 the resonance peak appears corresponding to [Be(H$_2$O)$_4$]$^{2+}$ (δ = 0).[45] As the pH increases, a new peak occurs at lower field (δ = 2.36), corresponding to the complex [BeL]$^-$ (see Experimental Section), the intensity of which increases as the intensity of the peak corresponding to [Be(H$_2$O)$_4$]$^{2+}$ decreases.

The simple form taken by both peaks indicates a highly regular environment[70] in the two species [Be(H$_2$O)$_4$]$^{2+}$ and [BeL]$^-$ (Figure 2). The constancy of δ also indicates slow equilibria between L^{3-} and [BeL]$^-$. Consequently, the ^{1}H and ^{9}Be NMR studies confirm the species distribution diagram of the NTP—Be(II) system and that the NTP is an excellent sequestering agent for Be(II) (Figure 2).

o-**PhDTA**—**Be(II) System.** ^{1}H NMR spectra as a function of the pD have been performed: at pD 2.3, δ = 4.13, a single peak corresponding to protons CH$_2$ acetate groups, is observed. At higher pD, a new resonance peak appears at δ = 3.75, higher field, corresponding to acetate groups in the complex [BeL]$^{2-}$, the intensity of which increases as the peak corresponding to the noncomplexed ligand decreases. Upon formation of the complex [BeL]$^{2-}$, a new multiplet appears at lower field corresponding to the aromatic protons, which confirms coordination of the N atoms. Since Be(II) tends to tetracoordination, the existence of a single peak for the protons of the complexed and noncomplexed acetate groups in the complex [BeL]$^{2-}$ indicates rapid exchange between these groups. It has been observed that this situation is maintained at −10 °C. This situation for the complex [BeL]$^{2-}$ is different from that found by Yamamoto et *al.*[71] for diamagnetic lanthanoid(III) ion complexes with *o*-PhDTA where the appearance of several sets of AB patterns for the acetate methylene protons is expected for a planar five-membered chelate ring. The constancy of δ for the CH$_2$ protons in the complex [BeL]$^{2-}$ also shows slow equilibria between L^{4-} and [BeL]$^{2-}$. Analogously Figure 3b, corresponding to ^{9}Be NMR, confirms at pH 2.0 the presence of the species [Be(H$_2$O)$_4$]$^{2+}$ and at greater pHs the appearance of a new peak corresponding to the formation of the complex [BeL]$^{2-}$, the intensity of which increases as the intensity of the peak corresponding to the species [Be(H$_2$O)$_4$]$^{2+}$ decreases. The ^{13}C NMR spectra as a function of the pD both for the ligand alone and for the *o*-PhDTA—Be(II) system show the peaks corresponding to the five types of carbon atoms[72,73] (Chart 4). A shift of the peaks is observed at lower field by the formation of the complex [BeL]$^{2-}$ at pD > 3. The simultaneous variation of the peaks corresponding to the five types of C atoms (Chart 4) confirms the coordination of the N atoms and those of the atoms of O of the carboxylate groups to the Be(II). Consequently, the ^{1}H, ^{9}Be, and ^{13}C NMR spectra confirm the species distribution diagram as a function of the pH for the *o*-PhDTA—Be(II) system and that the ligand *o*-PhDTA is a good sequestering agent for the Be(II).

EDTA—**Be(II) System.** The species distribution diagrams as a function of the pH for the EDTA—Be(II) system are more complex due to the persistence at pH > 4 of the hydrolytic trimer species [Be$_3$(OH)$_3$]$^{3+}$ and its derived complex [Be$_3$(OH)$_3$-(HL)], contrarily to what occurs with the *o*-PhDTA—Be(II) and NTP—Be(II) systems. This difference is also observed in the ^{1}H NMR spectra for the EDTA—Be(II) system: at pD 5.3, peaks at δ = 3.69 (acetate groups in the noncomplexed EDTA anion[62,69]), δ = 3.49 (acetate groups in [Be$_3$(OH)$_3$HL] complex, Chart 5, with a small shift for δ due to the OH$^-$ complexed to the metal ion[74] and a similarity between the proton and the Be^{2+} cation for the nitrogen atoms in this complex[16]), δ = 2.92 (acetate groups in the [BeL]$^{2-}$ complex), δ = 3.47 (ethylenic

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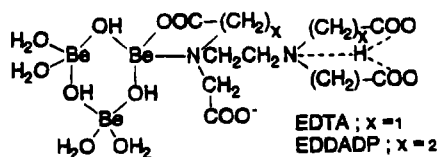(73) Wehrli, F. W.; Marchand, A. P.; Wehrli, S. *Interpretation of Carbon-13 NMR spectra*, 2nd ed.; John Wiley: New York, 1988.
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Chart 5

protons in noncomplexed EDTA[62,69]), and $\delta = 3.36$ (ethylenic protons in the both complexes [Be₃(OH)₃HL] and [BeL]²⁻) are observed. In any case, the spectrum is more complicated than for the remaining alkaline earth ions that have spectra with two singlets consistent with rapid bond-breaking of both M—N and B—O bonds,[69] while, for the Be²⁺, the ¹H NMR spectra for the EDTA—Be(II) system indicate that the lifetime of the Be—O bond is short, while that of the Be—N bond is long.[75]

EDDADP—Be(II) System. The species distribution diagram as a function of pH for the EDDADP—Be(II) system indicates that at pH 5 the complexes [BeHL]⁻, [Be₃(OH)₃HL], and [BeL]²⁻ are present, in addition to the H₂L²⁻ species corresponding to the noncomplexed ligand. This complexity is reflected in the ¹H NMR spectrum at pD 5: $\delta = 3.69$ (singlet, acetate groups), $\delta = 3.54$ (singlet, N—CH₂—CH₂—N protons), $\delta = 3.33$ (triplet, β-CH₂, propionate groups), and $\delta = 2.51$ (triplet, α-CH₂, propionate groups) corresponding to noncomplexed EDDADP.[62,69] The peaks corresponding to the respective resonances of the complexes appear at higher fields. The methylene protons of the acetate groups present a typical AB splitting pattern[75] with a coupling constant $J_{AB} = 14.5$ Hz, indicating the coordination of the N atoms and the propionate groups in the [BeL]²⁻ complex. The shift to high field of the triplet at $\delta = 2.51$ from the free ligand corresponding to the α protons in the propionate groups, giving place to the three new triplets at $\delta = 2.49$, 2.40, and 2.31, indicates three different magnetic environments for the α protons in the propionate groups, which we attribute to these protons in the three complexes, [BeHL]⁻, [Be₃(OH)₃HL], and [BeL]²⁻, indicating in turn the coordination of the propionate groups to the Be²⁺ cation. The triplet at $\delta = 3.33$, corresponding to the β protons in the propionate groups in the free ligand, is shifted to $\delta = 2.79$ in the complexes.

Figure 3c shows the ⁹Be NMR spectra as a function of the pH for the EDDADP—Be(II) system. The spectra corresponding to the NTP—Be(II) and o-PhDTA—Be(II) systems (Figure 3a,b, respectively) only show the peak corresponding to [Be(H₂O)₄]²⁺ and to the complexes [BeL]⁻ (NTP) and [BeL]²⁻ (o-PhDTA), respectively, such that when the intensity of the peak corresponding to [Be(H₂O)₄]²⁺ decreases, the intensity of the peak corresponding to the Be(II) complex increases. This situation is also observed for the EDDADP—Be(II) system (Figure 3c), but moreover at pH > 4 a new peak appears at $\delta = 0.76$,

corresponding to the hydrolytic trimer species[45] [Be₃(OH)₃]³⁺. Consequently, the ⁹Be NMR spectra are in accord with the species distribution diagram as a function of the pH that shows the persistence of the [Be₃(OH)₃]³⁺ species at pH > 4 and indicates that EDDADP is not a good sequestering agent for Be(II).

The sharp ⁹Be NMR signals of the [Be(H₂O)₄]²⁺ and Be(II) complexes reflect the slow relaxation resulting from tetrahedral symmetry leading to vanishing field gradients. ⁹Be relaxation responds very sensitively to some distortion of the symmetry.[76] The relationship between the size of the chelate ring and δ has been previously reported for Al(III),[77] Si(IV),[78] and Be(II).[16] In all cases, six-membered chelate rings were shifted to higher field compared to the five-membered chelate ring analogues: [BeL]²⁻, o-PhDTA, five-membered chelate rings, $\delta = 4.95$; [BeL]²⁻, EDDADP, both five- and six-membered chelate rings, $\delta = 3.86$; [BeL]⁻, NTP, six-membered chelate rings, $\delta = 2.36$. The higher δ values indicate progressive deshielding and distortion caused by chelation to the beryllium nuclei. Schmidbaur et al. find $\delta = 7.5$ for bis(catecholate) complex (two five-membered chelate rings)[14] and $\delta = 4.0$ for the bis(salicylate) complex (two six-membered chelate rings).[56] The value of δ for the [BeL]⁻ complex in NTP acid is smaller than that of other complexes of Be(II),[14,16,56] in accord with the high symmetry of the complex (Figure 2).

Supplementary Material Available: Listings of crystal data and structure refinement, atomic coordinates and equivalent isotropic displacement parameters, complete bond lengths and angles, anisotropic displacement parameters, hydrogen coordinates and isotropic displacement parameters (Tables S1-S5), protonation equilibria constants of the ligands, β_{pr} (Table S6), formation constants of the complexes, β_{pqr} (Table S7), and effective stability constants, pH 3—6 (Table S8), and figures showing coordination geometry of the sodium cations (Figure S1), Z(pH) curves for ligand—Be(II) systems (Figures S3 and S4), species distribution diagrams for ligands (Figure S2) and other ligand—Be(II) systems (Figures S5—S9), ¹H NMR spectra (Figures S10 and S11), and ¹³C NMR spectra (Figure S12), with figure captions included (29 pages). Ordering information is given on any current masthead page.

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