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Different Complexation Properties of Some Hydroxy Keto Heterocycles toward Beryllium(II) in Aqueous Solutions: Experimental and Theoretical Studies

**Franco Cecconi,[†] Carlo A. Ghilardi,[†] Andrea Ienco,[†] Palma Mariani,[‡] Carlo Mealli,[†] Stefano Midollini,[†,*]
Annabella Orlandini,[†] and Alberto Vacca[‡]**

*Istituto della Chimica dei Composti Organometallici, CNR, Via Jacopo Nardi 39,
50132 Firenze, Italy, and Dipartimento di Chimica, Università di Firenze,
50019 Sesto Fiorentino, Italy*

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Four heterocycles containing hydroxy and keto functionalities have been tested as chelating agents of beryllium(II). These are in the order (i) 3-hydroxy-2-methyl-4*H*-pyran-4-one (maltol, H*ma*), (ii) 5-hydroxy-2-(hydroxymethyl)-4*H*-pyran-4-one (kojic acid, H*ka*), (iii) 3-hydroxy-1,2-dimethyl-4-pyridinone (H*dpp*), (iv) 1-(3-hydroxy-2-furanyl)ethanone (isomaltol, H*ima*). Although the skeletons of the first three species, with one nitrogen or oxygen heteroatom at the six-membered ring, are almost superimposable, straightforward synthesis and crystallization is achieved only for the 1:2 adduct Be(*dpp*)$_2$, **1**. Also the complex Be(*ima*)$_2$, **2**, precipitates in high yield but the *ima*$^-$ ligand has a different skeletal structure. X-ray determinations of **1** and **2** showed that the Be^{2+} ion is pseudotetrahedrally coordinated by two chelating ligands with slightly asymmetric Be–O$_{\text{alkoxo}}$ and Be–O$_{\text{keto}}$ bonds. The complex Be(*ma*)$_2$ precipitates in low yields together with large amounts of unreacted H*ma* while, under the same conditions, no trace of the analogous species Be(*ka*)$_2$ has been observed. This paper presents the results of potentiometric and NMR studies in the aqueous solutions as well as of DFT structural optimizations for all of the free acids, their associated bases, and the adducts of the type [BeL(H$_2$O)$_2$]$^+$ and BeL$_2$ in the gas phase. It is consistently found that the basicity of the ligands and the stability of their complexes decrease in the order *dpp*$^-$ > *ma*$^-$ > *ka*$^-$ > *ima*$^-$. In solution, all of the anionic ligands form adducts of the type [BeL(H$_2$O)$_2$]$^+$ at low pH values, whereas higher concentrations of the free anion are required to form 1:2 adducts. The pH, the basicity, and the stability constants of the complexes as well as the formation of competing beryllium hydroxide species are strictly correlated factors for the obtainment of the latter type of adduct. The DFT calculations account nicely for the different donor powers of the various chelates in terms of electronic redistribution and associated energetics.

Introduction

Toxicity of beryllium is a chronic problem.[1] Once confined largely to military applications, beryllium is now used in the manufacture of countless industrial and consumer products, from satellites to toasters. Although the exposure to beryllium compounds is toxicologically most dangerous in the work place, there is some concern for the spreading of beryllium-containing substances into the environment. Thus, reliable monitoring of beryllium contents in food and drinking waters[2] has been recently recommended by the International Programme on Chemical Safety (ICPS).[3] Notwithstanding such a framework, little is known about the biochemistry of Be(II), and the molecular mechanism of beryllium toxicity remains only speculative.[4] Moreover, no efficient antidote has been devised as yet. In this context, remarkable attention has been recently devoted to biorelevant ligands able to capture the beryllium(II) ion in aqueous solution and to the determination of the relative equilibria.[5−7]

In the course of our investigations of beryllium(II) coordination chemistry,[8−13] we now focus on a series of comparable dioxygen chelates that may have good extraction

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[*] Author to whom correspondence should be addressed. E-mail: midolla@fi.cnr.it.

[†] Istituto della Chimica dei Composti Organometallici.

[‡] Dipartimento di Chimica, Università di Firenze.

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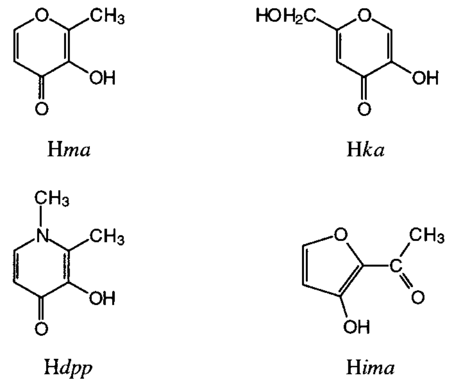
Chart 1



capabilities toward the toxic metal. The ligands in question are the associated bases of the pyrone derivatives 3-hydroxy-2-methyl-4*H*-pyran-4-one (maltol, H*ma*) and 5-hydroxy-2-(hydroxymethyl)-4*H*-pyran-4-one (kojic acid, H*ka*), the closely related pyridinone molecule 3-hydroxy-1,2-dimethyl-4-pyridinone (H*dpp*), and, by extension, the isomer of maltol 1-(3-hydroxy-2-furanyl)ethanone (isomaltol, H*ima*). All of the latter are conveniently depicted in Chart 1.

These molecules have been proved to be suitable ligands for hard ions (Fe^{3+}, Al^{3+})[14−16] and have been occasionally used in chelation therapy.[17] Extensive investigations have been carried out on the protonation equilibria of several 3-hydroxy-4-keto heterocyclics and, besides the chelating capabilities of the latter toward the metals of the main groups 3 and 4, also the reactivity toward transition metals and lanthanides has been the subject of many studies.[18]

The affinity of pyrones toward beryllium(II) is mentioned only in an old report of 1960.[19] The formation of stable mono- and dikojiate complexes, announced in the latter, has ever since been taken for granted in subsequent review articles.[20] With pyridinones, comparable beryllium(II)−*dpp* adducts have been supported by ^{9}Be NMR spectroscopy.[21] By assuming that all of the associated bases of the HL acids in Chart 1 can easily form complexes of the type $[BeL(H_2O)_2]^+$ and BeL_2, the lack of precise details about their stereochemistry initially inspired this study. In this context, the complexes Be(*dpp*)$_2$, **1**, and Be(*ima*)$_2$, **2**, have been prepared in high yields from aqueous solutions at physiological pH values and their structures have been fully characterized by means of X-ray analysis. In contrast, Be(*ma*)$_2$, **3**, precipitates in low yields together with large amounts of solid H*ma* whereas the expectedly stable complex Be(*ka*)$_2$, **4**, could not be prepared at all. For this reason, we considered opportune detailed aqueous solution studies of the different complexation models via potentiometric measurements and NMR spectroscopy. In this manner, the relative formation of the mono- and bis-chelate complexes, as well as that of other species present in the solution, can be monitored in the pH range where no precipitation occurs. The study is then completed by a theoretical analysis, based on DFT calculations for the various sets of HL, L^-, $[BeL(H_2O)_2]^+$, and BeL_2 gas-phase molecules. Obviously, the latter approach totally neglects the evaluation of the relevant solvation energies and entropic factors. However, it allows a systematic comparison between the structural, electronic, and energetic properties of the various species. Eventually, the combined experimental and theoretical study provides a reasonable explanation for the initially unclear different behaviors of the comparable ligands toward beryllium in water.

Experimental Section

Safety Note. *CAUTION! In view of the extreme toxicity of beryllium compounds, established procedures for handling dangerous materials were followed rigorously in all phases of the syntheses and measurements. All experimental synthetic work was carried out in a well-ventilated fume cupboard used exclusively for this purpose. Any spillage of the beryllium solutions was washed out immediately.*

Materials. All reagents and solvents were commercial products of analytical grade and were used without any further purification. Carbon dioxide free water was produced from deionized water that was twice distilled in a quartz apparatus and stored under purified nitrogen. Isomaltol was prepared according to the literature procedure.[22]

Stock solutions, about 0.2 mol dm^{-3}, of the hydroxy keto heterocycles were prepared by dissolving the solids in water, and the concentrations of the ligands were determined potentiometrically using the Gran procedure.[23] $NaClO_4$ was obtained by double recrystallization of the commercial product (Merck, analytical grade) from an ethanol−water mixture. Stock solutions of $HClO_4$ (0.2 mol dm^{-3}), NaOH (0.1 mol dm^{-3}), and $Be(ClO_4)_2{\cdot}4H_2O$ (0.02 mol dm^{-3}) solutions were prepared as previously described.[9]

Preparation of Be(*dpp*)$_2$·MeOH, 1. 3-Hydroxy-1,2-dimethyl-4-pyridinone (H*dpp*) (3.0 g, 21.5 mmol) was added to $BeSO_4{\cdot}4H_2O$ (1.91 g, 10.8 mmol) in 60 mL of water. After complete dissolution, at room temperature, the pH was adjusted to 8.5 with concentrated

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NH_3. Evaporation of the solvent at 323−333 K and cooling at room temperature allowed the precipitation of off-white crystals. These were filtered off, washed with cold water, and dried in air. Recrystallization from methanol/diethyl ether gave 2.77 g of **1** (yield: 81%). Anal. Found: C, 57.48; H, 6.33; N, 8.98. Calcd for $C_{15}H_{20}Be_1N_2O_5$: C, 56.77; H, 6.35; N, 8.83. ^{9}Be NMR (D_2O): δ 7.75 ppm ($w_{1/2} = 30$ Hz). ^{1}H NMR (D_2O): δ 7.54 (d, H(6), $^3J_{H-H} = 7$ Hz), 6.52 (d, H(5)), 3.72 (s, N−CH_3), 2.27 (s, C−CH_3) ppm.

Preparation of Be(*ima*)$_2$, 2. Isomaltol (H*ima*) (1.0 g, 7.9 mmol) was added to $BeSO_4{\cdot}4H_2O$ (0.7 g, 3.95 mmol) in 50 mL of H_2O at room temperature. After dissolution the pH was adjusted at 6.5 with 2 N NaOH. An oil separated, which crystallized on standing at 275 K. The solid was filtered, washed with cold water, and dried in air (0.798 g, yield: 78%). Anal. Found: C, 55.66; H, 3.90. Calcd for $C_{12}H_{10}Be_1O_6$: C, 55.60; H, 3.89. Recrystallization from methanol/water gave large, off-white crystals, suitable for X-ray analysis. ^{9}Be NMR (CD_2Cl_2): δ 3.29 ppm ($w_{1/2} = 3$ Hz). ^{1}H NMR (CD_2Cl_2): δ 7.64 (d, H(5)), $^3J_{H-H} = 2$ Hz, 6.14 (d, H(6)), 2.36 (s, CH_3) ppm. ^{9}Be NMR (D_2O): δ 3.42 ($w_{1/2} = 14$ Hz), 1.86 ($w_{1/2} =$ 19 Hz) ppm.

Reaction of $BeSO_4$ and H*ma*. Maltol (2.0 g, 15.87 mmol) was added to $BeSO_4{\cdot}4H_2O$ (1.4 g, 7.9 mmol) in 40 mL of H_2O at 323 K. The pH was adjusted to ca. 7.5 by addition of 2 N NaOH, and a pale brown solution was obtained. Water was evaporated till a volume of ca. 30 mL. Cooling at room temperature afforded an off-white material, which was filtered and dried in air. This was dissolved in 30 mL of dichloromethane, the insoluble products were filtered off, and evaporation of the solvent afforded 1.7 g of an off-white microcrystalline powder. ^{9}Be NMR (CD_2Cl_2): δ 7.8 (s, $w_{1/2} = 9$ Hz) ppm. ^{1}H NMR (CD_2Cl_2): δ 8.0 (d, $^3J_{H-H} = 2.5$ Hz, H(6)), 7.72 (d, $^3J_{H-H} = 2.8$ Hz, H(6) uncoordinated maltol), 6.69 (d, H(5)), 6.36 (d, H(5) uncoordinated maltol), 2.45 (s, CH_3), 2.33 (s, CH_3, uncoordinated maltol)) ppm. The integral ratio between corresponding signals of uncoordinated and coordinated maltol was 1.28. ^{9}Be NMR (D_2O): δ 7.10 ($w_{1/2} = 34$ Hz), 4.37 ($w_{1/2} = 47$ Hz) ppm, integral ratio = ca. 1/2. Recrystallization of the mixture from ethanol, benzene/ethanol, and dichloromethane/ethanol did not allow any remarkable separation.

Reaction of $BeSO_4$ and H*ka*. Kojic acid (3.21 g, 22.6 mmol) was added to $BeSO_4{\cdot}4H_2O$ (2.8 g, 11.3 mmol) in 40 mL of H_2O, at room temperature. The pH was adjusted to ca. 6.8 by addition of 2 N NaOH, and an orange solution was obtained. Water was evaporated under a current of nitrogen to afford a syrup-like material. Successive workup allowed the isolation of kojic acid as the only identifiable compound.

X-ray Data Collection and Structure Solution. Diffraction data for complexes **1** and **2** were collected at room temperature on an Enraf Nonius CAD4 automatic diffractometer. Unit cell parameters were determined by least-squares refinement of the setting angles of 25 carefully centered reflections. Crystal data and data collection details for both structures are given in Table 1. The intensities I were assigned the standard deviations $\sigma(I)$ calculated by using a value of 0.03 for the instability factor k.[24] They were corrected for Lorentz−polarization effects, and an empirical absorption correction was applied.[25] Atomic scattering factors for neutral atoms were taken from ref 26. Both $\Delta f'$ and $\Delta f''$ components of anomalous dispersion were included for all non-hydrogen atoms.[27] Both structures were solved by direct methods and refined by full-matrix F^2 refinement, with anisotropic thermal parameters assigned to all non-hydrogen atoms. The hydrogen atoms, which were detected from Δ Fourier maps in both structures, were refined in **2**, but not in **1** due to the poor data/variables ratio. The function minimized during the refinement was $\sum w(F_o^2 - F_c^2)^2$, with $w = 1/[\sigma^2(F_o^2) + (0.0730P)^2 + 0.63P]$ and $1/[\sigma^2(F_o^2) + (0.0928P)^2 + 1.14P]$ for **1** and **2**, respectively ($P = (\max(F_o^2, 0) + 2F_c^2)/3$). The absolute structure of **1** was established through the Flack parameter.[28] All of the calculations were performed on a Pentium processor, using the package WINGX[29] (SIR97,[30] SHELX97,[31] ORTEP-III[32]).

Table 1. Crystal Data and Structure Refinement for **1** and **2**

	1	**2**
empirical formula	$C_{15}H_{20}BeN_2O_5$	$C_{12}H_{10}BeO_6$
fw	317.34	259.21
temp (K)	293(2)	293(2)
wavelength, Å	0.71073	0.71073
cryst syst; space group	orthorhombic; *C*2*cb*	orthorhombic; *Pbca*
unit cell dimens		
a, Å	10.165(9)	8.146(5)
b, Å	12.365(9)	13.175(9)
c, Å	12.697(6)	22.995(7)
α, deg	90	90
β, deg	90	90
γ, deg	90	90
vol, Å^3	1596(2)	2468(2)
Z; calcd density, Mg/m^3	4; 1.321	8; 1.395
abs coeff, mm^{-1}	0.098	0.111
F(000)	672	1072
cryst size, mm	0.45 × 0.35 × 0.25	0.30 × 0.27 × 0.25
θ range, deg	3.05−22.02	3.06−22.44
limiting indices	$0 \le h \le 10$, $0 \le k \le 12$, $0 \le l \le 13$	$0 \le h \le 8$, $0 \le k \le 14$, $0 \le l \le 24$
reflns collected/unique	530/530 [*R*(int) = 0.0000]	1601/1601 [*R*(int) = 0.0000]
refinement meth	full-matrix least-squares on F^2	
data/restraints/params	530/1/114	1601/0/212
GOF on F^2	1.059	1.020
final *R* indices [$I > 2\sigma(I)$]	R1 = 0.0358, wR2 = 0.0924	R1 = 0.0536, wR2 = 0.1397
R indices (all data)	R1 = 0.0386, wR2 = 0.0947	R1 = 0.0850, wR2 = 0.1594
largest diff peak and hole, e Å^{-3}	0.116 and −0.148	0.303 and −0.189

Potentiometric Measurements. The equilibrium constants were determined at 298 K through potentiometric titrations. The ionic strength of the solutions in the cell was kept constant to 0.50 mol dm^{-3} with $NaClO_4$. This electrolyte was chosen due to the poor aptitude of the perchlorate ion to coordinate the beryllium ion.[5] The adopted instrumental and experimental methodologies have been previously described.[9] The potentiometric titrations were carried out by adding a solution of 0.1 mol dm^{-3} NaOH to solutions, acidified with $HClO_4$, that contained the ligand (in the deprotonation experiments) or $Be(ClO_4)_2$ and the ligand (in the experiments for the complex formation). The glass electrode was calibrated in concentration of hydrogen ions, [H_3O^+], by using the Gran procedure;[23] so the value of the logarithm of the ionic product of water resulted as −13.69, in very good agreement with the values

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previously determined.[33] The basicity constants of the ligands were determined in separate experiments using different total ligand concentrations (T_L). At least three titration curves were drawn for each ligand, with T_L ranging from 0.002 to 0.020 mol dm^{-3} and pH ($= -\log [H_3O]^+$) values from 3 to 10. In the complex formation experiments, the total concentration of the beryllium ion (T_M) and that of the ligand (T_L) were varied, in each titration, within the limits $0.001 \leq T_M \leq 0.01$ and $0.002 \leq T_L \leq 0.02$. A minimum of five titrations were carried out with values of the molar ratio T_L/T_M in the range 1−10. The emf data were collected in the pH range from 3 to about 6, where precipitation occurred. Equilibria corresponding to the formation of beryllium(II) hydroxo species were considered in the analysis of the data leading to the formation constants of the complexes. The chemical model for the hydrolysis of Be^{2+} in 0.50 mol dm^{-3} $NaClO_4$ has been illustrated previously.[34]

The HYPERQUAD2000 computer program[35] was used for the least-squares refinement of the equilibrium constants. The sum of the weighted squared residuals on the observed emf values was minimized; the weights were derived from the estimated errors in emf (0.2 mV) and titrant volume (0.002 cm^3). In the complex formation systems several chemical models were tried, and the most probable model was selected by following a strategy described elsewhere.[36,37]

The species distribution diagrams were obtained using the HySS computer program.[38] In order to reveal the possible precipitation of $Be(OH)_2(s)$, the solubility product of this compound was introduced into the HySS calculation. The value used, $K_{sp} = [Be^{2+}][H^+]^{-2} = 10^{6.87}$ mol^{-1} dm^3, was reported by Bruno.[39]

NMR Spectroscopy Measurements. NMR spectra were recorded in 5 mm tubes, at 295 K, in D_2O solutions, on a Bruker AC-200 spectrometer operating at 200.13 (^{1}H) and 28.12 (^{9}Be) MHz. ^{1}H chemical shifts are relative to external TMS; ^{9}Be chemical shifts are relative to external 0.1 M $BeSO_4$ in D_2O. Downfield values of the chemical shifts are reported as positive. The value of pD was adjusted using a minimum volume of either concentrated D_2SO_4 or NaOD; the pD values were measured using a Radiometer PHM210 pH meter, equipped with a combined glass Ag/AgCl microelectrode (INGOLD); the values were corrected according to the relationship pD = pH′ + 0.40,[40] where pH′ is the pH meter reading, calibrated using standard aqueous buffer solutions.

Computational Details. Structural optimizations were carried out, with the Gaussian98 program,[41] at the hybrid density functional theory level. The Becke's three-parameter hybrid exchange-correlation functional[42] was used that contains the nonlocal gradient correction of Lee, Yang, and Parr (B3LYP).[43] All optimized structures were confirmed as minima by calculation of the vibrational frequencies. A collection of Cartesian coordinates and total energies for all of the optimized molecules is available from the authors upon request. The basis set used in the calculations for all atoms was the 6−31G(d,p).

Results and Discussion

Synthesis and Characterization of the BeL_2 Complexes. The complexes Be(*dpp*)$_2$, **1**, and Be(*ima*)$_2$, **2**, were prepared in high yield, from aqueous solution, by reacting $BeSO_4$ with the appropriate HL acid in the molar ratio 1:2. The pH was adjusted in the range 6.5−8.5 by addition of NaOH. The *dpp* complex is somewhat soluble in water (>0.1 mM) whereas the *ima* complex is only sparingly soluble (<0.1 mM). Also, while **2** is quite soluble in most polar organic solvents (e.g., dichloromethane, THF, methanol), **1** is fairly soluble in methanol but practically insoluble in dichloromethane. The ^{9}Be NMR spectrum of **1** in D_2O shows a broad singlet at 7.75 ppm, in agreement with the results of a previous spectroscopic study on the system $BeSO_4$/H*dpp*, 1:3.[21] The ^{1}H NMR spectrum is consistent with the coordination of the ligand to beryllium. In fact, the peaks of the coordinated ligand are slightly displaced with respect to the chemical shifts of H*dpp* (the ring doublets move from δ 7.46 and 6.33 to 7.54 and 6.62 ppm, respectively; the peak of the *N*-methyl group moves from 3.61 to 3.72 ppm, and that of the *C*-methyl one from 2.24 to 2.27 ppm). Concerning the complex **2**, the NMR spectra in CD_2Cl_2 confirm the Be(*ima*)$_2$ formulation. The ^{9}Be spectrum consists of a fairly sharp singlet at δ 3.29 ($w_{1/2} = 3$ Hz) ppm. The remarkable high-field shift with respect to the complex Be(*dpp*)$_2$ is consistent with the presence of six-membered, rather than five-membered, metallacycles.[11] The ^{1}H spectrum shows the ring doublets at δ 7.64 and 6.13 ppm and the methyl singlet at 2.36 ppm. These chemical shifts are somewhat displaced with respect to those of H*ima* (7.31, 6.30, and 2.38 ppm, respectively). Conversely the ^{9}Be NMR spectrum of **2** in D_2O (pD = 6.2) supports the hydrolytic process of eq 1. As a matter of fact the spectrum shows two broad peaks centered respectively at 3.42 and 1.86 ppm. The first resonance is likely due to the Be(*ima*)$_2$ species, whereas the upfield signal is attributable to the [Be(*ima*)$(H_2O)_2$]$^+$ cation. This spectrum is consistent with that of solutions of beryllium sulfate and H*ima*, 1:2, at comparable pD values.

$$BeL_2 + 3H_2O \rightarrow [BeL(H_2O)_2]^+ + HL + OH^- \qquad (1)$$

Analogous reactions were carried out in order to prepare the corresponding derivatives Be(*ma*)$_2$ and Be(*ka*)$_2$, **3** and **4**, respectively. Concerning **3**, we obtained a crystalline off-white material that, in the NMR spectrum, appeared to be

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actually a mixture of H*ma* and Be(*ma*)$_2$. In fact, the ^{9}Be NMR spectrum of this material, in CD_2Cl_2 solution, showed a singlet at 7.8 ppm ($w_{1/2}$ = 9 Hz), as expected for a tetrahedrally coordinated beryllium(II) ion, with two five-membered chelate rings.[11] On the other hand the ^{1}H NMR spectrum consists of the peaks of the uncoordinated maltol with the additional resonances at δ 8.00 (d, H(6), $^3J_{H-H}$ = 2.5 Hz), 6.69 (d, H(5)), and 2.45 (s,CH_3) ppm. These can be assigned to the coordinated maltolate in Be(*ma*)$_2$. The integral ratio of the corresponding maltol and maltolate resonances was 1.28, indicating that the mixture contained 28% of **3**. The ^{9}Be NMR spectrum of the mixture, in D_2O, pD = 6.7, with two broad resonances at δ 7.10 and 4.37 ppm (attributable to Be(*ma*)$_2$ and [Be(*ma*)(H_2O)$_2$]$^+$, respectively), supports the hydrolytic process of eq 1. The remarkable broadness of the signals ($w_{1/2}$ = 34 and 47 Hz) is indicative of an exchange equilibrium. Maltol and Be(*ma*)$_2$ show quite similar solubilities in common organic solvents such as dichloromethane, THF, methanol, ethanol, acetone, and benzene. Since the separation of the two products is not straightforward, no further attempt to isolate pure Be(*ma*)$_2$ was made on account of the hazardous workup of beryllium derivatives.

In the case of the system beryllium−kojic acid, a similar reaction afforded a brown solution (pH = 6.8). The ^{9}Be NMR spectrum, with a broad band at ca. 4.0 ppm, indicated only the presence of the [Be(*ka*)(H_2O)$_2$]$^+$ species. Successive workup allowed the isolation of kojic acid as the only identifiable compound. Another attempt performed by reacting $Be(OH)_2$ (prepared in situ from $Ba(OH)_2$ and $Be(SO_4)$) with kojic acid did not allow better results.

The different behaviors of the systems Be^{2+}/2HL (L = *dpp*$^-$, *ma*$^-$, *ka*$^-$, and *ima*$^-$) in aqueous solution, at pH values of ca. 7, are noteworthy. When L is *dpp*$^-$, the species BeL_2 is formed almost quantitatively, the hydrolytic process of eq 1 being practically negligible. When L is *ma* or *ima*, both the species BeL_2 and [BeL(H_2O)$_2$]$^+$ are present in comparable amounts. However, in the case of isomaltol, the fair solubility of HL, combined with the low solubility of BeL_2, allows the separation of this latter compound in an almost quantitative yield. In contrast, the solubilities of the species H*ma* and Be(*ma*)$_2$ are comparable and allow precipitation of the product mixture. Finally when L= *ka*, there is evidence only for the monocharged derivative [BeL(H_2O)$_2$]$^+$ that is formed before the precipitation of beryllium hydroxide.

Description of the Structures. The molecular structures of **1** and **2** consist of discrete complex molecules of Be(*dpp*)$_2$ and Be(*ima*)$_2$, respectively. In **1**, disordered solvent molecules of methanol are interspersed in the lattice. Perspective views of the complex molecules **1** and **2** are reported in Figures 1 and 2, respectively. The corresponding bond distances and angles are also given in Tables 2 and 3.

In both structures the beryllium center displays a tetrahedral environment, being linked to four oxygen atoms of two *dpp*$^-$ ligands in **1** and to those of two *ima*$^-$ ligands in **2**. While in **2** only a slight distortion from the ideal tetrahedral geometry is envisaged, with the O−Be−O angles ranging from 105.0(3)° to 111.9(3)°, in **1** the same angles range from 98.8(1)° to 120.9(5)°. Actually, the conformation and the bite size of the two ligands (the five-chelate ring *dpp*$^-$ and the six-chelate ring *ima*$^-$) are responsible of the differences. The Be−O bond distances are consistent with the sum of the covalent radii (1.63 Å) and in good agreement with the values reported for analogous linkages in the literature.[8−12] Interestingly, in both structures two larger and two shorter Be−O bonds are observed [in **1**, 1.646(4), 1.646(4) and 1.617(4), 1.617(4) Å; in **2**, 1.646(5), 1.637(5) and 1.596(6), 1.601(6) Å]. Even if the above differences are small, they appear chemically meaningful and indicative of the residue localizations of the keto and enolic functionalities at the oxygen donors. The same trends are clearly confirmed by the DFT calculations (vide infra).

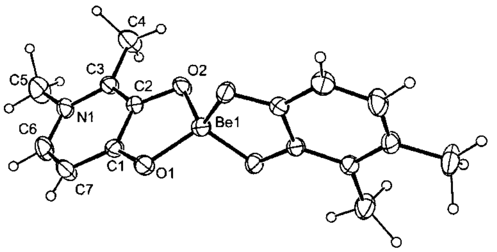

Figure 1. Perspective view of the complex molecule Be(*dpp*)$_2$, **1**. ORTEP drawing with 30% probability ellipsoids.

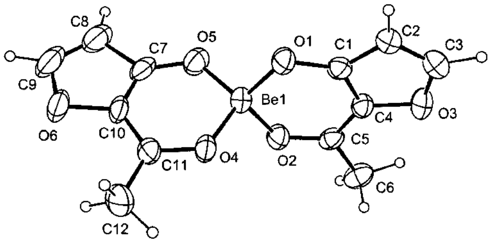

Figure 2. Perspective view of the complex molecule Be(*ima*)$_2$, **2**. ORTEP drawing with 30% probability ellipsoids.

Table 2. Bond Lengths (Å) and Angles (deg) for **1**

Be(1)−O(2)	1.617(4)	N(1)−C(5)	1.470(5)
Be(1)−O(2)#1[a]	1.617(4)	C(1)−C(2)	1.395(5)
Be(1)−O(1)#1	1.646(4)	C(1)−C(7)	1.404(5)
Be(1)−O(1)	1.646(4)	C(2)−C(3)	1.355(5)
O(1)−C(1)	1.292(4)	C(3)−C(4)	1.490(6)
O(2)−C(2)	1.337(4)	C(6)−C(7)	1.342(5)
N(1)−C(6)	1.344(5)	O(3)−C(8)	1.416(19)
N(1)−C(3)	1.364(5)		
C(1)−O(1)−Be(1)	105.9(2)	O(2)−C(2)−C(3)	124.7(3)
C(2)−O(2)−Be(1)	106.3(2)	O(2)−C(2)−C(1)	113.0(3)
C(6)−N(1)−C(3)	120.8(3)	C(3)−C(2)−C(1)	122.3(3)
C(6)−N(1)−C(5)	118.1(3)	C(2)−C(3)−N(1)	118.2(3)
C(3)−N(1)−C(5)	121.1(3)	C(2)−C(3)−C(4)	122.3(3)
O(1)−C(1)−C(2)	115.6(3)	N(1)−C(3)−C(4)	119.6(3)
O(1)−C(1)−C(7)	127.1(3)	C(7)−C(6)−N(1)	122.5(4)
C(2)−C(1)−C(7)	117.3(3)	C(6)−C(7)−C(1)	118.9(4)
O(2)−Be(1)−O(2)#1	115.3(5)	O(2)−Be(1)−O(1)	98.8(1)
O(2)−Be(1)−O(1)#1	112.0(1)	O(1)#1−Be(1)−O(1)	120.9(5)

[a] Symmetry transformations used to generate equivalent atoms: #1 x, $-y$, $-z + 1$.

It is remarkable that crystal structures of metal complexes containing any of the present hydroxo keto heterocyclic ligands (*dpp*$^-$, *ma*$^-$, *ka*$^-$ and *ima*$^-$) are limited.[44−57] In spite of being considered good complexing agents, the ligand *ima*$^-$ has been structurally characterized only in an octahedral

Table 3. Bond Lengths (Å) and Angles (deg) for **2**

Be(1)−O(5)	1.596(6)	O(6)−C(10)	1.389(4)
Be(1)−O(1)	1.601(6)	C(1)−C(4)	1.386(5)
Be(1)−O(2)	1.637(5)	C(1)−C(2)	1.403(5)
Be(1)−O(4)	1.646(5)	C(2)−C(3)	1.326(6)
O(1)−C(1)	1.291(4)	C(4)−C(5)	1.373(5)
O(2)−C(5)	1.267(4)	C(5)−C(6)	1.491(5)
O(3)−C(3)	1.362(5)	C(7)−C(10)	1.363(6)
O(3)−C(4)	1.388(4)	C(7)−C(8)	1.426(6)
O(4)−C(11)	1.272(4)	C(8)−C(9)	1.348(9)
O(5)−C(7)	1.282(5)	C(10)−C(11)	1.380(6)
O(6)−C(9)	1.348(8)	C(11)−C(12)	1.491(7)
C(7)−O(5)−Be(1)	117.7(3)	C(4)−C(5)−C(6)	122.2(4)
C(9)−O(6)−C(10)	103.4(5)	O(5)−C(7)−C(10)	125.3(3)
O(1)−C(1)−C(4)	123.2(3)	O(5)−C(7)−C(8)	127.5(5)
O(1)−C(1)−C(2)	129.7(3)	C(10)−C(7)−C(8)	107.2(5)
C(4)−C(1)−C(2)	107.1(3)	C(9)−C(8)−C(7)	103.7(6)
C(3)−C(2)−C(1)	106.4(4)	C(8)−C(9)−O(6)	115.1(5)
C(2)−C(3)−O(3)	112.8(4)	C(7)−C(10)−C(11)	126.4(3)
C(5)−C(4)−O(3)	125.1(3)	C(7)−C(10)−O(6)	110.7(4)
C(5)−C(4)−C(1)	126.4(3)	C(11)−C(10)−O(6)	122.9(4)
O(3)−C(4)−C(1)	108.5(3)	O(4)−C(11)−C(10)	116.9(4)
O(2)−C(5)−C(4)	118.8(3)	O(4)−C(11)−C(12)	118.5(5)
O(2)−C(5)−C(6)	118.9(4)	C(10)−C(11)−C(12)	124.6(4)
O(5)−Be(1)−O(1)	110.4(3)	O(2)−Be(1)−O(4)	105.0(3)
O(5)−Be(1)−O(2)	111.9(3)	C(1)−O(1)−Be(1)	118.4(3)
O(1)−Be(1)−O(2)	110.0(3)	C(5)−O(2)−Be(1)	122.8(3)
O(5)−Be(1)−O(4)	109.1(3)	C(3)−O(3)−C(4)	105.2(3)
O(1)−Be(1)−O(4)	110.3(3)	C(11)−O(4)−Be(1)	124.4(3)

aluminum complex[54] and the ligand *dpp*$^-$ is reported in a few structures of trivalent metal ions (Fe,[44,45] Co,[49] Ga,[46] Al,[46,47] and In[48]). For the latter, the average bond distances between the metal ions and the donor oxygen atoms have been correlated with the stabilities of the corresponding metal complexes.

Equilibria in Solution. The logarithms of the protonation constants for the ligands employed in this study are given in Table 4. The basicity increases in the order *ima*$^-$ < *ka*$^-$ < *ma*$^-$ < *dpp*$^-$, isomaltol and 3-hydroxy-1,2-dimethyl-4-pyridinone being the strongest and the weakest acid, respectively. For the latter H*dpp* compound, an additional protonation step (to give H_2*dpp*$^+$) has been detected and the corresponding basicity constant has been determined. Such a behavior is not observed for the other compounds, for which the addition of a second proton occurs in very acidic regions, outside of the pH range of the potentiometric experiments. The agreement between our values and those reported in the literature[18,58] is quite good, also by considering the different experimental conditions of temperature and/or ionic strength adopted in the previous determinations.

Table 4. Ligand Basicity Constants and Beryllium Complex Formation Constants Determined at 298.15 K in Aqueous 0.5 mol dm^{-3} $NaClO_4$

	log *K*			
reaction	*dpp*	*ma*	*ka*	*ima*
$L^- + H^+ \rightarrow HL$	9.58(1)	8.32(1)	7.66(1)	5.63(1)
$HL + H^+ \rightarrow H_2L^+$	3.58(3)			
$Be^{2+} + L^- \rightarrow [BeL]^+$	8.47(1)	5.73(6)	5.01(8)	4.11(5)
$[BeL]^+ + L^- \rightarrow BeL_2$	7.16(3)			3.1(1)
$[Be_3(OH)_3]^{3+} + L^- \rightarrow [Be_3(OH)_3L]^{2+}$	8.24(6)			
$[Be_3(OH)_3]^{3+} + 2L^- \rightarrow [Be_3(OH)_3L_2]^+$	14.9(3)			
$[Be_3(OH)_3]^{3+} + 3L^- \rightarrow Be_3(OH)_3L_3$	21.4(1)	13.8(1)	11.4(1)	
$Be(OH)_2 + 2L^- \rightarrow [Be(OH)_2L_2]^{2-}$	6.38(3)			

Concerning the complex formation experiments, the results of the selection process performed with the program HYPERQUAD2000[35] are presented in Table 4. All of the ligands considered above form 1:1 adducts of the type $[BeL(H_2O)_2]^+$. The order of the stability constants for these species coincides with that of the basicity constants, namely, *dpp*$^-$ > *ma*$^-$ > *ka*$^-$ > *ima*$^-$. Such a trend was already established for the complexes of the same ligands with Al^{3+}.[16,54] Moreover, an analogous correlation was found between the basicity constants of related ligands, such as substituted 3-hydroxy-4*H*-pyran-4-one, and the stability constants of their complexes with Al^{3+}.[59] The formation constant of the complex $[Be(dpp)(H_2O)_2]^+$ determined by us (log $\beta = 8.47$) is in good agreement with that measured via NMR techniques and reported in the literature (log β = 8.7).[21] Not at all satisfactory is the comparison for the complex $[Be(ka)(H_2O)_2]^+$, with the literature value[19] being too high (log $\beta = 10.7$) and, most likely, unreliable. No other similar comparison is possible for the remaining ligands.

It is evident from the data reported in Table 4 that complexes of type BeL_2 are detected only for the ligands *dpp*$^-$ and *ima*$^-$, whereas *ka*$^-$ and *ma*$^-$ form at most 1:1 adducts.

Two different species are needed to find a satisfactory agreement between the calculated and experimental data of the systems involving H*ma*, H*ka*, and H*ima*, respectively. For L = *ma* or *ka*, the relevant species are $[BeL(H_2O)_2]^+$ and $Be_3(OH)_3L_3$ and no BeL_2 species is involved. In contrast, for L = *ima*, both the species $[BeL(H_2O)_2]^+$ and BeL_2 are detectable. Finally, the system H*dpp* requires the involvement of up to six species, including both $[Be(dpp)(H_2O)_2]^+$ and $Be(dpp)_2$ (see Table 4). The overall complex formation modeling is similar to that previously found for the system formed by Be^{2+} and some dicarboxylate ligands such as

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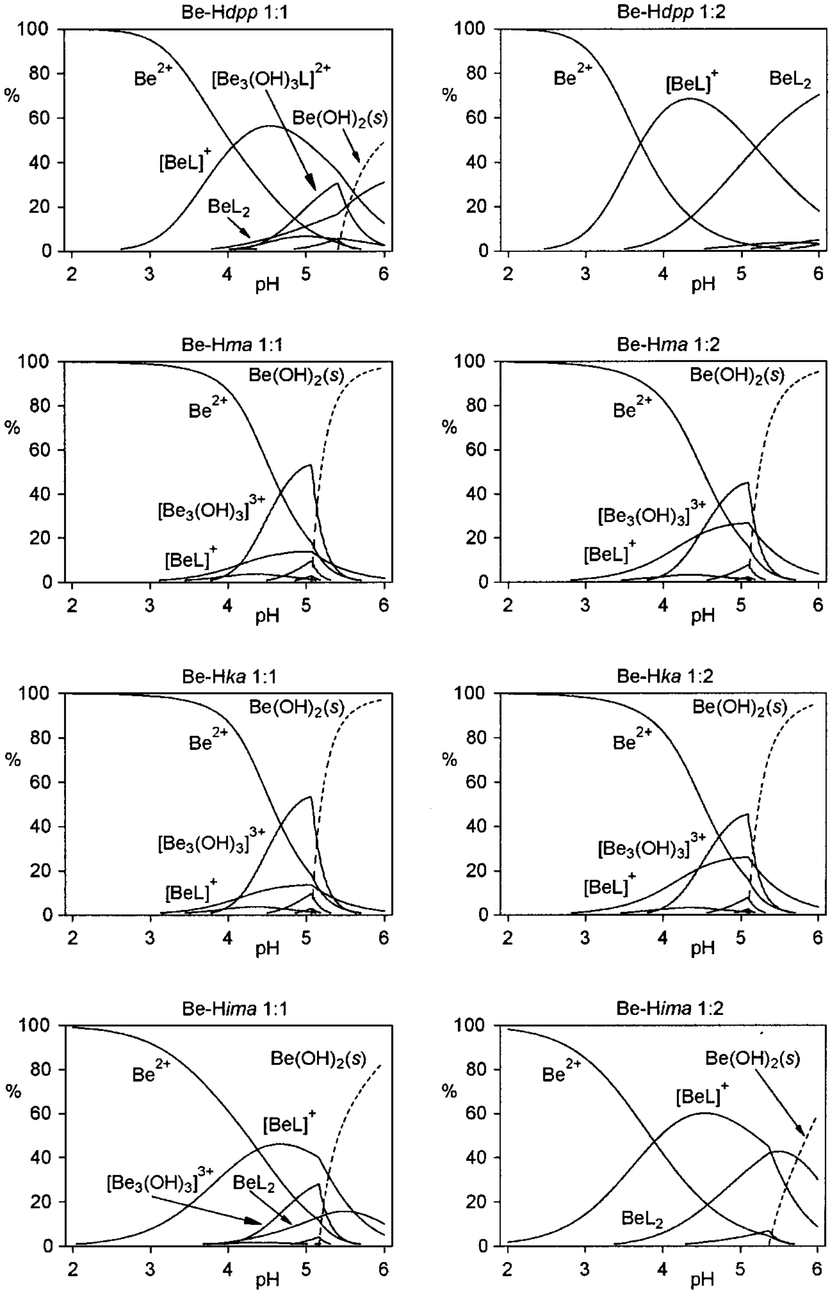

Figure 3. Calculated distribution diagrams for the systems Be^{2+}/HL (L = *dpp*$^-$, *ma*$^-$, *ka*$^-$, and *ima*$^-$) 1:1 and 1:2 (C_{Be} = 0.003 mol dm^{-3}). The percentages are calculated relative to total beryllium concentration. For simplicity, only the curves relative to the major species are labeled and the formulas do not contain the water molecules that complete the coordination sphere of beryllium(II).

oxalate, malonate, and succinate.[9,33] The distribution diagrams for the four studied systems, in stoichiometric ratios 1:1 and 1:2, are presented in Figure 3.

These results are consistent with the ^{9}Be NMR spectra in the pH range 2−6. Figure 4 shows the ^{9}Be NMR spectra for the systems BeSO$_4$−H*ima* (1/2) and Be(SO$_4$)−H*ma* (1/2) together with the distribution diagrams calculated for the same Be^{2+} concentration of 3 × 10^{-2} M. Notice that the ca. 30 times higher concentration modifies significantly the percentage profiles with respect to those of the potentiometric measurements. Variable pH ^{9}Be NMR spectra had already been reported for the H*dpp* system.[21] The interpretation of the spectra in the upper part of Figure 4 is straightforward, as the distribution diagram shows that the species [Be(*ima*)(H$_2$O)$_2$]$^+$ and Be(*ima*)$_2$ have maximum concentration in distinct pH zones. In the case of the H*ma* system (Figure 4), we may assign the broad resonance at δ ca. 4.0 ppm to the overlapped signals of the species [Be(*ma*)(H$_2$O)$_2$]$^+$ and [Be$_3$(OH)$_3$(*ma*)$_3$]. These species should have comparable chemical shifts, as found for the related BeSO$_4$−oxalic acid system.[9] The upfield broad signal must be attributed to the overlapped resonances of uncomplexed hydroxo species.[9] The ^{9}Be NMR spectrum of the system BeSO$_4$−H*ka* shows trends very similar to those of the corresponding H*ma* system, and it is not reported. Conversely, the previously reported spectra of the system BeSO$_4$−H*dpp*[21] did not show, at high pH values, the presence of any hydroxo species, likely because of a BeSO$_4$:H*dpp* molar ratio of 1/3.

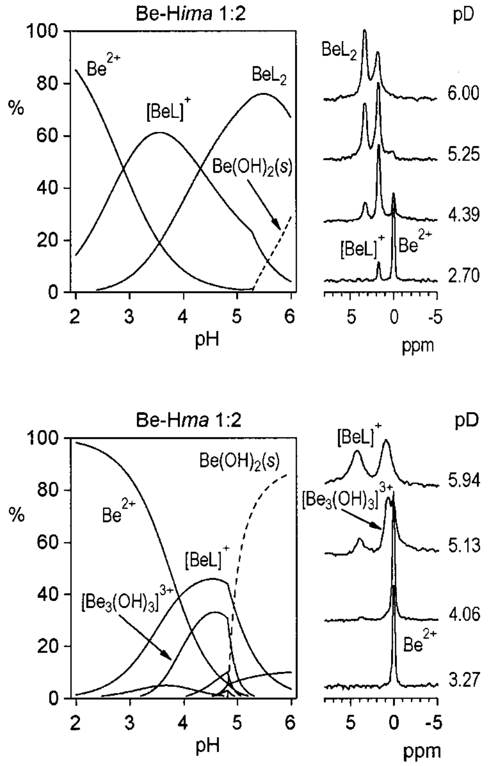

Figure 4. Distribution diagram and ^{9}Be NMR spectra for the system $BeSO_4$−H*ima* 1:2 and $BeSO_4$−H*ma* 1:2 (C_{Be} = 0.03 mol dm^{-3}). The percentages are calculated relative to total beryllium concentration. For the sake of clarity, only the curves relative to the major species are labeled and the water molecules that complete the coordination sphere of the beryllium ion have been omitted in the formulas.

An apparent incongruity relative to the formation of the beryllium bismaltolate complex needs to be pointed out. In fact, the preparative results are consistent with the formation of Be(*ma*)$_2$ from aqueous solution at pH > 6 whereas such a species is not detectable from the potentiometric analysis. However, the latter can identify only the species that are present in a significant amount under the given measurement conditions, e.g., low reagent concentrations, high ionic strength, and limited pH range. Beyond these limits, a species such as Be(*ma*)$_2$ may be formed and it can be even isolated in view of its low solubility.

Also, the fact that Be(*ima*)$_2$ is detected in solution at pH < 6, in spite of its low stability constant, may appear inconsistent. The affinity of the various chelates toward the Be^{2+} ion in the aqueous solution, cannot be simply ordered in terms of their relative stability constants. Consider, in fact, that the ligand exerts its basicity not only toward the positive metal but toward the proton as well. Thus, very high pHs are needed in order to have a very basic ligand in the free anionic form and in a concentration sufficient to coordinate the metal. Consequently, the hydroxide ions in high concentration compete effectively in capturing the metal ion and forming hydroxo compounds of a different nature. In turn, the reduced presence of Be^{2+} ions in solution limits the extent of complex formation with the ligand. In conclusion, the complexation of the various $[BeL(H_2O)_2]^+$ and BeL_2 complexes is regulated, not only by the stability constant but also by the ligand protonation constant as well as by the pH of the solution.

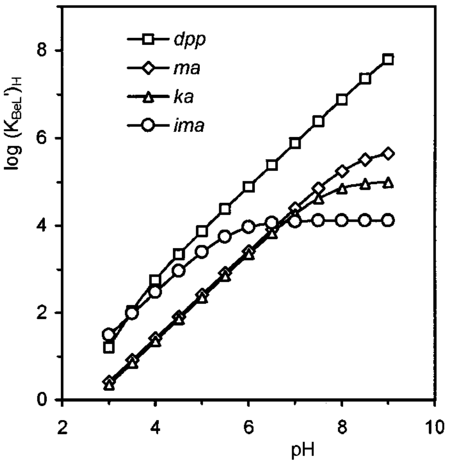

Figure 5. Plot of the pH dependence of the "effective" formation constant of $[BeL(H_2O)_2]^+$ (L = *dpp*$^-$, *ma*$^-$, *ka*$^-$, and *ima*$^-$).

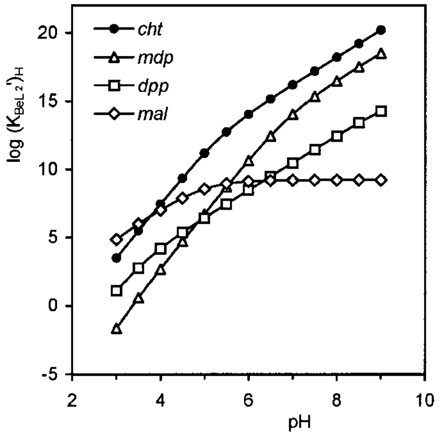

Figure 6. Plot of the pH dependence of the "effective" formation constant of $[BeL_2]^{n-}$ (L = *cht*$^{4-}$, *mdp*$^{4-}$, *dpp*$^-$, and *mal*$^{2-}$).

In order to account for the relation between the coordinating capabilities of a ligand and the pH of the solution, the "effective" or "apparent" formation constant of the corresponding metal complex can be used, in the form defined by Schwarzenbach.[60]

$$(K_{ML}')_H = \frac{[ML]}{[M][L^*]} = \frac{K_{ML}}{1+\sum_{i=1}^{m}[H^+]^i\beta_{H_iL}} \qquad (2)$$

In eq 2, [L*] is the total concentration of ligand not combined with the metal, K_{ML} is the stability constant of the complex ML, *m* is the total number of protons which can be attached to the L base (proticity), and β_{H_iL} is the *i*th cumulative basicity constant. The quantity $(K_{ML}')_H$ allows one to estimate the capability of the ligand L to form a 1:1 metal complex in a given acidic environment. Figure 5 compares the situation of the four ligands investigated. It is evident that, at low pH values, *ima*$^-$ and *dpp*$^-$ are definitely

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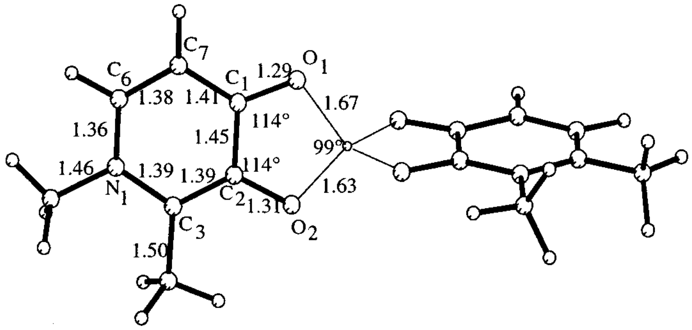
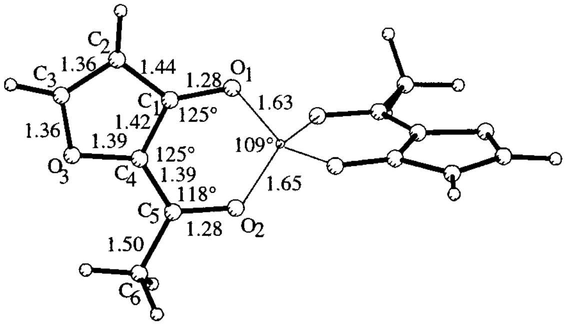
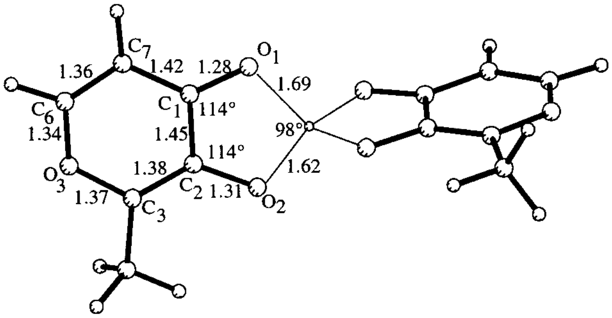


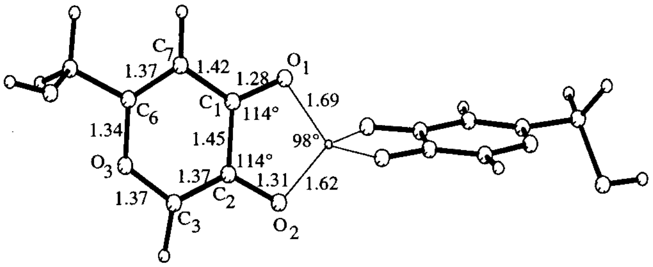
Be(dpp)$_2$ **1a**



Be(ima)$_2$ **2a**



Be(ma)$_2$ **3a**



Be(ka)$_2$ **4a**

Figure 7. Calculated optimized structures of the various BeL_2 complexes and their structural parameters.

stronger ligands than ma^- and ka^-. Only at pH > 6, the latter become appreciably stronger than ima^-.

On the basis of the previous findings, the dpp^- anion appears to be an efficient sequestering agent for the Be(II) ion in aqueous solution also in view of the high stability of the 1:2 adduct Be(dpp)$_2$. In order to make a comparison with other known strong chelates, we present in Figure 6 the pH dependences of the "effective" formation constants for the 1:2 complexes formed by dpp^-, malonate (mal^{2-}), methylene−diphosphonate (mdp^{4-}), and the anion (cht^{4-}) of the chromotropic acid. Also in view of its high negative charge, the latter ligand (1,8-dihydroxynaphthalene-3,6-disulfonic acid) is known to be the strongest chelate for beryllium.[5,20]

The "effective" formation constant of 1:2 complexes is given by a somewhat modified formula with respect to that of eq 2 (for the 1:1 complex), i.e.,

$$(K_{\mathrm{ML}_2}')_{\mathrm{H}} = \frac{[\mathrm{ML}_2]}{[\mathrm{M}][\mathrm{L}^*]^2} = \frac{K_{\mathrm{ML}_2}}{\{1 + \sum_{i=1}^{m} [\mathrm{H}^+]^i \beta_{\mathrm{H}_i\mathrm{L}}\}^2} \qquad (3)$$

The calculations have been carried out using the equilibrium constant for dpp^- listed in Table 4, while the constants used for the other three ligands are those available from the most recent literature.[9,21,61,62] The plots in Figure 6 confirm that all of the highly negatively charged ligands form very stable complexes for increasing pHs. Also, the monoanion dpp^- is comparably strong as, for instance, it shows a sequestering capability toward Be(II) that is already larger than that of mal^{2-} at the neutral pH.

Theoretical Calculations

Structural Optimizations. DFT calculations were initially carried out to optimize the known structures of the beryllium complexes **1** and **2**. From a comparison of the models **1a** and **2a** with the corresponding X-ray structures, it appears that the computational method works sufficiently well with this type of beryllium compound. The drawings and structural parameters of **1a** and **2a**, both having quasi C_2 symmetry, are shown in Figure 7. The angle O−Be−O, subtended by the dpp^- chelating ligand (five-membered cycle), is as small as 99° in **1a** (98.8(1)° in **1**). In contrast, the larger size of the Be−ima metallacycle (six membered) forces the same angle to open up, almost to the ideal tetrahedral value, in **2a** (ca. 109° as in **2**). In both cases, the two endocyclic Be−O bonds are somewhat asymmetric with the longer distance involving the less basic keto oxygen atom. The difference between the two Be−O bonds is smaller in **2a** than in **1a** (0.02 vs 0.04 Å). The same trend is also observed experimentally, but the corresponding Δ is too small to be of much significance (0.01 Å). Computationally, however, the strict similarity of the compared objects and the unique model chemistry adopted allow one to take the differences as useful indicators of the electronic trends.

Encouraged by the acceptable reproducibility of the experimental trends, we have also optimized the unknown structures of the complexes Be(ma)$_2$ and Be(ka)$_2$. The corresponding structures **3a** and **4a** are also presented in Figure 7. In the latter, the substitution of one methyl group for a methoxy one, at a different position of the six-membered heterocycle, has no evident structural effect. Also, the differences with respect to the ddp complex **1a** are small and provide no hint for the different stabilities of **3a** and **4a**. In all cases, the beryllium ion has the same pseudotetrahedral conformation with

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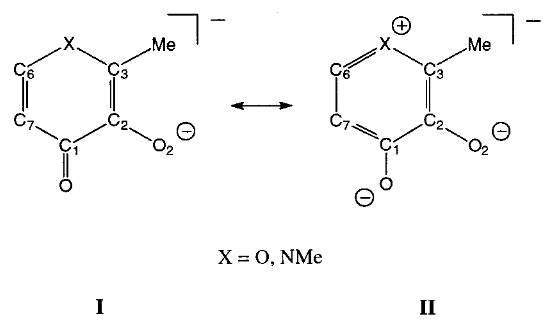
(61) Letkeman, P.; Martell, A. E.; Motekaitis, R. J. *J. Inorg. Nucl. Chem.* **1980**, *29*, 1947.

(62) Alderighi, L.; Vacca, A.; Cecconi, F.; Midollini, S.; Chinea, E.; Dominguez, S.; Valle, A.; Dakternieks, D.; Duthie, A. *Inorg. Chim. Acta* **1999**, *285*, 39.

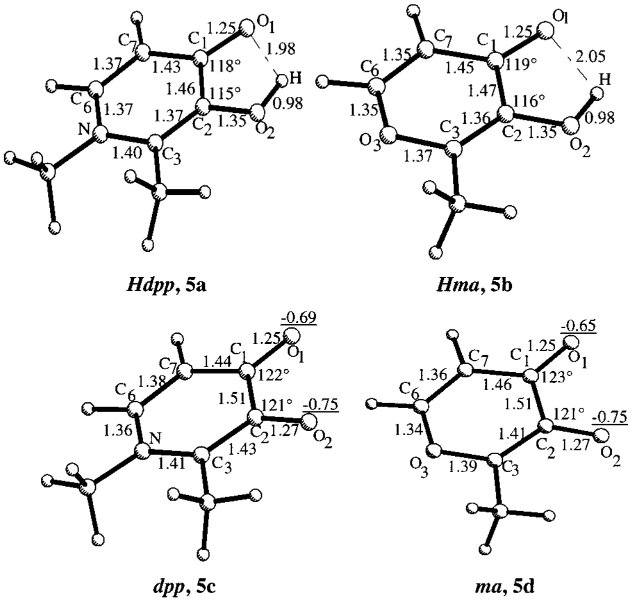
Scheme 1



equal endocyclic O−Be−O angles (ca. 98−99°). Only, the larger asymmetry of the metallacyclic Be−O distances in **3a** and **4a** (Δ = 0.07 vs 0.04 Å in **1a**) suggests a reduced basicity at the keto oxygen atom of the ligand *ma*$^-$ and *ka*$^-$. Also, a less isotropic environment about the metal atom may be an indication of higher instability. For the most comparable *dpp*$^-$ and *ma*$^-$ ligands, it is chemically intuitive that the larger is the weight of the resonance structure **II** (Scheme 1), the more similar is the donor power of the two exocyclic oxygen atoms. With the hope of verifying the latter point through the structural parameters, we have also optimized the structures of the acids H*dpp* and H*ma* as well as of their associated bases *dpp*$^-$ and *ma*$^-$ (see Figure 8).

The C_2−C_3 and C_6−C_7 distances are ca. 0.01−0.02 Å shorter in the *ma* complex **3a** than in *dpp* analogue **1a**. This holds also for the acids H*ma*, **5b**, and H*dpp*, **5a**, as well as for their associated bases *ma*$^-$, **5d**, and *dpp*$^-$, **5c**. Altough the Δ values are quite small, they do not dismiss the idea that an oxygen in place of a nitrogen heteroatom favors the concentration of C═C double bonding at the opposite sides of the six-membered ring (resonance structure **I**). Along the same line, the computed net charges of the O_{keto} atom in the free bases *dpp*$^-$ and *ma*$^-$ (0.69 and 0.65, respectively) is suggestive of a somewhat larger basicity of *dpp*$^-$ in agreement with the general findings of this study. Interestingly, the charge of the O_{alkoxy} atom is exactly the same (0.75) for *dpp*$^-$ and *ma*$^-$.

The engagement of the O_{alkoxy} atom in binding a strong acid, either H^+ or Be^{2+}, causes the elongation of the corresponding C−O_{alkoxy} bond. For instance, in both H*ma* and H*dpp* the C_2−O_2 bond is stretched by as much as 0.08 Å with respect to *ma*$^-$ and *dpp*$^-$. In complexes **1a** and **3a**, the effect is halved for this bond while also the C═O_{keto} bond stretches by ca. 0.03−0.04 Å. Another relevant feature for understanding the acid−base properties of the gas phase models is the closing of both the C−C−O angles in the presence of a cation (either H^+ or Be^{2+}). When *dpp*$^-$ or *ma*$^-$ acts as a chelate toward the Be^{2+} center, the closing can be as large as 7−8° with respect to the free ligands (**5c** and **5d**). However, when a single proton is bound to the O_{alkoxy} atom (compounds **5a** and **5b**), closing of both C−C−O angles favors the formation of a H···O_{keto} hydrogen bond. The effect is evidently larger in H*dpp* than in H*ma* distance (compare the H−O_{keto} distances of 1.98 and 2.05 Å, respectively). It may be deduced that the proton is more effectively inserted in the OCCO cavity of *dpp*$^-$ than in that of *ma*$^-$. This will be also substantiated by the greater energy cost necessary to extract the proton from *dpp*$^-$ (see the following section). Finally, it must be remarked that analogous calculations on H*ka* and its associated base *ka*$^-$ (not reported) do not show significant geometric variations with respect to the pair H*ma* and *ma*$^-$. However, smaller values of the charges at the atoms O_1 and O_2 (−0.70 and −0.59, respectively) are consistent with the reduced basicity of both oxygen atoms.



Hdpp, **5a**

Hma, **5b**

dpp, **5c**

ma, **5d**

Figure 8. Calculated optimized structures of the H*dpp*, *dpp*$^-$, H*ma*, and *ma*$^-$ species and their structural parameters.

Energetic Considerations.[63] The total energy differences $E_{HL} - E_L$ may be taken as the deprotonation energies for the corresponding gas phase reactions. The values calculated for the series *dpp*$^-$ (ΔE = 364.5 kcal mol^{-1}), *ma*$^-$ (ΔE = 356.8 kcal mol^{-1}), *ka*$^-$ (ΔE = 354.3 kcal mol^{-1}), and *ima*$^-$ (ΔE = 351.0 kcal mol^{-1}) are all large and certainly favored by the strong electrostatic interaction between cation and anion. Much reduced endothermicities may be expected for the deprotonations in the presence of a polar solvent such as water. However, no attempt to calculate the solvatation energies has been made (CPCM approach) as the correlations between the ΔE values and the acidities are already consistent with the available pK_a values. In fact, the proton affinities decrease in the order *dpp*$^-$ > *ma*$^-$ > *ka*$^-$ > *ima*$^-$ in full agreement with the potentiometric measurements.

Also, the potentiometric measurements have shown that H*dpp* can add a second proton with relative ease, while all of the other monoprotic acids require extreme acidic conditions. Computationally, we observe that protonation of H*dpp* at the O_{keto} atom is exothermic by 234.9 kcal mol^{-1} while the analogous protonation of H*ma* releases ca. 15 kcal mol^{-1} less.[64]

At this point, we consider systematically the relative energetics for the formation of various 1:1 and 1:2 Be^{2+} complexes starting from the tetrahydrate precursor. An optimization of the species $[Be(H_2O)_4]^{2+}$ compares well with the results of previous computational studies.[65−67] Moreover, we have optimized the complexes of the type $[BeL(H_2O)_2]^+$ for all of the considered ligands. In this manner, the *isodesmic* reactions for the various replacements of the ligands may be considered (see Table 5). Substitution of four water molecules for two chelating ligands is in any case a very exothermic reaction in the gas phase with a release of heat generally close to 400 kcal mol^{-1}.[68]

The direct comparison of the ΔE values for the relative formation of the complexes **1a**−**4a** shows that the largest reaction energy

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(63) Non SI unit employed: cal = 4.184 J.

(64) Since it cannot be excluded that the endocyclic N atom of H*dpp* has enough basicity to compete for the second protonation site, we have optimized a H_2dpp^+ isomer with a tetracoordinated N atom. The latter is more destabilized by ca. 45 kcal mol^{-1}, and it is likely unattainable.

(65) Bock, C. W.; Glusker, J. P. *Inorg. Chem.* **1993**, *32*, 1242.

(66) Markham, G. D.; Glusker, J. P.; Bock, C. L.; Trachtman, M.; Bock, C. W. *J. Phys. Chem.* **1996**, *100*, 3488.

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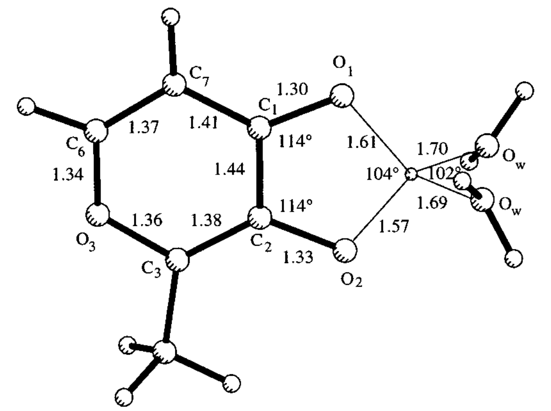

Figure 9. Calculated optimized structure of the $[Be(\mathit{ma})(H_2O)_2]^+$ complex and its structural parameters.

Table 5. Calculated Energetics of Different Substitution Reactions at Be^{2+} Involving the Ligands dpp^-, ma^-, ka^-, and ima^-

reaction	E (kcal mol^{-1})	ΔE (kcal mol^{-1})
$[Be(H_2O)_4]^{2+} + 2\mathit{dpp}^- \rightarrow Be(\mathit{dpp})_2 + 4H_2O$	−395.73	0.00
$[Be(H_2O)_4]^{2+} + 2\mathit{ma}^- \rightarrow Be(\mathit{ma})_2 + 4H_2O$	−375.94	19.80
$[Be(H_2O)_4]^{2+} + 2\mathit{ka}^- \rightarrow Be(\mathit{ka})_2 + 4H_2O$	−370.68	25.06
$[Be(H_2O)_4]^{2+} + 2\mathit{ima}^- \rightarrow Be(\mathit{ima})_2 + 4H_2O$	−369.63	26.10
$[Be(H_2O)_4]^{2+} + \mathit{dpp}^- \rightarrow [Be(\mathit{dpp})(H_2O)_2]^+ + 2H_2O$	−271.78	0.00
$[Be(H_2O)_4]^{2+} + \mathit{ma}^- \rightarrow [Be(\mathit{ma})(H_2O)_2]^+ + 2H_2O$	−253.91	17.87
$[Be(H_2O)_4]^{2+} + \mathit{ka}^- \rightarrow [Be(\mathit{ka})(H_2O)_2]^+ + 2H_2O$	−251.02	20.76
$[Be(H_2O)_4]^{2+} + \mathit{ima}^- \rightarrow [Be(\mathit{ima})(H_2O)_2]^+ + 2H_2O$	−250.06	21.71
$[Be(\mathit{dpp})(H_2O)_2]^+ + \mathit{dpp}^- \rightarrow Be(\mathit{dpp})_2 + 2H_2O$	−123.95	0.00
$[Be(\mathit{ma})(H_2O)_2]^+ + \mathit{ma}^- \rightarrow Be(\mathit{ma})_2 + 2H_2O$	−122.02	1.93
$[Be(\mathit{ka})(H_2O)_2]^+ + \mathit{ka}^- \rightarrow Be(\mathit{ka})_2 + 2H_2O$	−119.66	4.30
$[Be(\mathit{ima})(H_2O)_2]^+ + \mathit{ima}^- \rightarrow Be(\mathit{ima})_2 + 2H_2O$	−119.57	4.38

occurs with the dpp^- ligands, the exothermicity of the ma^-, ka^- and ima^- ligands being smaller by 19.8, 25.1, and 26.1 kcal mol^{-1}, respectively. It is also interesting to point out that, in general, about two-thirds of the overall exothermicity is produced with the entering of the first ligand (e.g., for *dpp*, −271.8 over −395.7 kcal mol^{-1}). Also, the greater affinity of dpp^- toward Be^{2+} is already produced at this step. For example, substitution of the first dpp^- ion produces a net energy gain of 17.87 kcal mol^{-1} with respect to the ma^- one, while the difference reduces to only 1.93 kcal mol^{-1} for the second substitution step.

The generally greater metal−ligand binding energy of the 1:1 adducts is also consistent with the experimental observation that the complexes $[Be(\mathit{ma})(H_2O)_2]^+$ and $[Be(\mathit{ka})(H_2O)_2]^+$ are observed in solution at low pH values, while the corresponding 1:2 adducts are not. A reasonable explanation comes from the comparison of the optimized structures. As shown in Figure 9, the complex $[Be(\mathit{ma})(H_2O)_2]^+$ presents significantly shorter Be−O bonds than the bischelate analogue **3a** (1.57 and 1.61 Å vs the corresponding values of 1.62 and 1.69 Å). This can be easily accounted for by the more effective positive charge of the Be^{2+} ion in $[Be(\mathit{ma})(H_2O)_2]^+$, which is not yet quenched by the presence of a preexisting chelating anion.

In order to find out whether the larger stabilization energies of the dpp^- ligand may have causes other than the greater basicity of the oxygen donors, we have performed a comparative analysis of the various energy components in the 1:2 complexes, including the interligand repulsion and the ligand deformation energy upon coordination. As shown in Table 6, the latter term is almost constant for the four ligands considered, whereas the greatest repulsive effect occurs between two dpp^- ligands. For example, the $E_{(L-L)rep}$ repulsion term disfavors the complex $Be(\mathit{dpp})_2$, with respect to the $Be(\mathit{ma})_2$ one, by ca. 6 kcal mol^{-1}. Evidently, the latter term is compensated by a binding energy to the metal (25.5 kcal mol^{-1}) that is greater than the relative stabilization energy of the two complexes (i.e., 19.8 kcal mol^{-1} as derived from the *isodesmic* reaction).

Table 6. Calculated Energy Contributions (kcal mol^{-1}) in the Formation of BeL_2 Complexes

L	$E_{binding}$[a]	E_{Ldef}[b]	$E_{(L-L)rep}$[c]
dpp^-	−915.3	9.9	108.3
ma^-	−889.8	10.2	101.9
ka^-	−883.4	10.6	100.0
ima^-	−887.0	10.1	105.6

[a] Net energy gain for assembling the complex from the separated components, corrected for the positive terms. [b] Deformation energy (the energy spent by the ligand to adapt to metal coordination). [c] Repulsion between two ligands ready to coordinate but in the absence of the Be^{2+} ion.

In conclusion, the DFT calculations have provided an insight of the geometric and energetic parameters which may affect the coordination capabilities of the various chelating ligands toward Be^{2+}. In particular, they nicely confirm the trend for the "effective" stability constants of the complexes (see Figure 5), namely, $\mathit{dpp}^- > \mathit{ma}^- > \mathit{ka}^- > \mathit{ima}^-$. Obviously, the used gas phase model neglects some important aspects occurring under the synthetic conditions from aqueous solution as well as under those specific to the potentiometric measurements. In particular, we have not explored the competition of other fundamental reaction pathways, especially those leading to beryllium hydroxo compounds of different nuclearities. The formation of hydroxides from hydrated species is a study of a certain complexity whose computational ab initio aspects have been tackled only very recently and limited to the simplest beryllium monohydroxide.[69]

Conclusions

Two molecules of pyridinone and isomaltol ligands chelate a Be^{2+} ion to precipitate uncharged tetrahedral BeL_2 complexes from aqueous acid solutions. Conversely, pyran-4-one acids (maltol and kojic acid) show different behavior under the same reaction conditions. The complex $Be(\mathit{ma})_2$ is obtained in the solid state as the minor product together with H*ma*. No evidence for the corresponding $Be(\mathit{ka})_2$ complex has been found. The potentiometric measurements in the exploitable range of pH 2−6 show for all of the ligands the formation of the 1:1 adducts, with the stability constants in the order $\mathit{dpp}^- > \mathit{ma}^- > \mathit{ka}^- > \mathit{ima}^-$. The complexes BeL_2 are detected only for the ligands dpp^- and ima^-, the complex $Be(\mathit{dpp})_2$ having a significantly larger stability constant. The theoretical analysis agrees with the above trend and proposes a rationale for it as the largest stability of the *dpp* species can be ascribed to a greater basicity of the *dpp* oxygen atoms, especially the O_{keto} one. On the other hand, also the complexes $Be(\mathit{ma})_2$ and $Be(\mathit{ka})_2$, not detected by

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(68) It is worth mentioning the conclusions of previous thermodynamic studies for the complexation of comparable dioxygen chelates in aqueous solution.[33] Namely, a favorable entropic contribution overwhelms the unfavorable enthalpy of the process. This is consistent with the large amount of energy that the entering chelate must spend to penetrate the Be^{2+} hydration sphere. Obviously, this cannot be evidentiated by our gas phase calculations which focus only on one part of the enthalpic contribution, i.e., the binding energy.

(69) Trachtman, M.; Markham, G. D.; Glusker, J. P.; George, P.; Bock, C. W. *Inorg. Chem.* **2001**, *40*, 4230.

the potentiometry, are computed to have large stabilization energies which are comparable with that of the least stable product Be(*ima*)$_2$.

A reasonable explanation may be found by considering the peculiar effect in the aqueous solutions. Being a weak acid, H*dpp* barely dissociates at relatively low pHs, but the large stability of its adducts with Be^{2+} shifts the equilibrium toward the formation of both 1:1 and 1:2 complexes. In contrast, the structurally comparable acid H*ma* (as well as H*ka*), even if more dissociated at the same pH value, presents smaller complex stability constants. Nonetheless, at pH < 6 the 1:1 adduct [Be(*ma*)(H_2O)$_2$]$^+$ (as well as [Be(*ka*)(H_2O)$_2$]$^+$) can be obtained, on account of the strong Be−O bond. On the other hand, the calculations have shown that the entering of the second chelating ligand in the coordination sphere is not energetically so advantageous. Low basicity anions, such as *ma*$^-$ or *ka*$^-$, can compensate such a difficulty in forming the 1:2 adducts if their concentration is sufficiently high, as it may occur at higher pH. However, under these circumstances, other hydroxo beryllium species are formed and prevent the formation of the 1:2 adducts. As concerns the *ima* ligand, the complex Be(*ima*)$_2$ should be the most difficult to obtain due to its relatively smaller stability. On the contrary, the complex is observed at low pH and it is easily crystallized. In agreement with the above arguments, even at low pH, the concentration of the anion *ima*$^-$ can be already quite high to favor the formation of both the 1:1 and 1:2 adducts, in spite of the relatively low stability constant.

Ligands that are similarly structured and have comparable chelating capabilities toward a toxic metal such as beryllium must be first carefully selected on the basis of subtly different factors. The intrinsic electronic structure of the various ligands affects the donor capabilities of the oxygen donors and certainly plays an important role. However, there may be several other species in the aqueous solution (e.g., hydroxo complexes) toward which the equilibria may be shifted. The final outcome will be strongly dependent on the pH and on the relative solubilities of the involved species. As an additional comment on the latter result, the formation of six-membered metallacycles formed by the *ima* chelate can provide an extra stability especially with a very small ion such as Be^{2+}.[70] Eventually, such an energetic term counterbalances but it does not overwhelm the very weak basicity of the anion as assessed both experimentally and computationally.

A final warning can be addressed to researchers in the biological or medicinal fields who make in vivo experiments with solutions of Be^{2+} and then use chelating ligands such as those studied here as potential mobilizing antidotes. They must consider with suspicion the formation constants reported in the old literature. In fact, many of these data are affected by errors, sometimes severe, because the effects due to the hydrolysis associated with the Be^{2+} ion have been overlooked in their determination.

Acknowledgment. The computing time provided by CINECA under the agreement with CNR is kindly acknowledged.

Supporting Information Available: Tables of crystallographic data for structures **1** and **2** and a CIF containing crystallographic information. This material is available free of charges via the Internet at http://pubs.acs.org.

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