Intensive Hydrogen Bonding in a Monomeric Magnesium Salicylate Tetrahydrate

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Introduction

We[1] and others[2-4] are exploring the chemistry of the alkaline earth metals (Mg, Ca, Sr, and Ba), which have until recently been a largely underdeveloped area of the periodic table. We have initiated a program to investigate the coordination chemistry of these metals in both aqueous and nonaqueous media.

Magnesium is important biologically, and it has been suggested that this element was in fact involved with some of the earliest forms of life due to its important role in DNA and protein synthesis.[6] It plays an essential role in the activation of enzymes, complexed with nucleic acids, inside cells necessary for nerve impulse transmissions, muscle contractions, and the metabolism of carbohydrates.[7]

The roles of the two metals magnesium and calcium are quite different in the body, and this may possibly be due to magnesium having a higher charge to radius ratio. This results in the stable octahedral strongly hydrated $[Mg(H_2O)_6]^{2+}$ dication existing in a wide range of magnesium complexes. This also results in calcium having a coordination number of greater than 6 (often with a distorted stereochemistry) in its complexes.

In view of their widespread occurrence in the body and in nature (e.g. magnesium in chlorophyll and calcium hydroxyapatite in bone).[5] A range of model magnesium complexes have previously been prepared as probes to elucidate the mode of binding of this metal in vivo and in vitro.[8] Such studies are of fundamental importance in aiding our understanding of the problems of magnesium deficiency in the body[9] and have focused on the use of aspartate, glutamate, orontate, or pyroglutamate.[10] These materials have been extensively studied in the solid state by X-ray crystallography,[8] but to date little research on their solution behavior or their stability over a wide pH range has been reported.

Salicylates have found widespread application both as antiseptics and as medicinal agents, and studies of hydrated salicylates have been previously initiated to improve our understanding of the modes of coordination of this ligand to a wide range of metal ions. Salicylic acid has been noted to be one of the simplest models for humic substances in natural waters.[11] Studies on the group IIA metal salicylates have revealed that beryllium forms a monomeric four-coordinate salicylate complex, $Be(sal)(H_2O)_2$,[12] whereas the heavier metals calcium and strontium form isostructural oligomeric hydrogen-bonded networks of $M(sal)_2(H_2O)_2$.[13] Surprisingly, to date there have been no reports of the corresponding magnesium or barium complexes, and we now wish to report the solid-state structure of the magnesium compound and the spectroscopic properties of the magnesium and related calcium and barium hydrate compounds.

Experimental Section

General Procedures. All alcohol solvents were rigorously dried and then distilled from sodium metal by standard methods. Elemental analysis were performed by the microanalytical department of Butterworth Laboratories. The melting points were measured under argon in sealed capillaries and are uncorrected values.

Instrumentation. NMR data were recorded on a JEOL GS 270 NMR spectrometer, using the protio impurities of the deuterated solvent as reference for ^1H spectra and the ^{13}C resonance of the solvent as a reference for ^{13}C spectra. Chemical shifts were also independently referenced to tetramethylsilane (<1%) added by volume. The NMR samples were prepared in Wilmad 5-mm NMR tubes, equipped with J. Youngs valves to ensure reproducibility of NMR spectra and ensure sample stability. All chemical shifts are positive to high frequency of the standard.

Infrared spectra were recorded on a Perkin-Elmer FTIR 1720 spectrometer as Nujol mulls between 25 × 4 mm KBr plates. The Nujol was predried with 4A molecular sieves prior to use, and the Nujol samples were protected from the atmosphere by an O-ring-sealed Presslok holder.

Mass spectroscopic measurements were performed on a Kratos MS30 in electron impact mode at the Royal School of Pharmacy, London.

Starting Materials. Magnesium chloride, magnesium acetate, calcium chloride, barium acetate, and salicylic acid were purchased from Aldrich Chemicals and used as received. The materials described here are all air and moisture stable but were all routinely prepared under dry nitrogen using thoroughly degassed fully desalinated water and dry solvents.

Preparation of $[Mg(C_6H_4(OH)CO_2)_2(OH_2)_4]$ (1). Magnesium chloride hexahydrate (7.04 g, 34.63 mmol) and salicylic acid (9.57 g, 69.29 mmol) were dissolved with vigorous stirring in 100 mL of MeOH. The reaction mixture was then stirred for 30 min at ambient temperature, producing a clear solution. Addition of concentrated (880) ammonia solution (25 mL) resulted in a white precipitate, which was filtered off under suction and dried in air for 3 h. The solid was dissolved in warm water (100 mL). Concentration of the reaction mixture to 15 mL at 60 °C resulted in a pale yellow oil, and transfer of the reaction flask to a water bath at the same temperature, followed by cooling overnight, resulted in a large crop of colorless crystals: yield 8.52 g (66.4%) of $[Mg(C_6H_4(OH)CO_2)_2(H_2O)_4]$ (mp >320 °C dec). Anal. Calcd for $MgC_{14}H_{18}O_{10}$: C, 45.41; H, 4.87. Found: C, 45.70; H, 4.56. IR (Nujol; ν, cm^{-1}): 3258 (s, br), 2925 (s), 2854 (s), 2574 (w, br), 1556 (s), 1524 (s), 1462 (s), 1388 (s), 1322 (m), 1257 (s), 1156 (s), 1138 (m), 1037 (w), 955 (w), 892 (w), 862 (w), 768 (m), 757 (s), 711 (s). ^1H NMR (D_2O, 270 MHz, 20 °C, internal standard TMS): δ 1.73 (s, 1H), 4.65 (s, 4H), 6.68 (m, 2H), 7.20 (m, 1H), 7.63 (m, 1H). ^1H NMR (d_6-DMSO, 270 MHz, 20 °C, internal standard TMS): δ 1.77 (s, 1H), 4.94 (s, 4H), 6.73 (m, 2H), 7.22 (m, 1H), 7.71 (m, 1H). ^{13}C NMR (D_2O, 67.94 MHz, 20 °C): δ 115.67 (s, C4), 117.84 (s, C5), 118.84 (s, C3), 131.14 (s, C6), 132.36 (s, C2), 161.99 (s, C1), 175.53 (CO). ^{13}C NMR (d_6-DMSO, 67.94 MHz, 20 °C): δ 116.88 (s, C4), 118.05 (s, C5), 119.78 (s, C3), 131.24 (s, C6), 133.33 (s, C2), 162.29 (s, C1), 173.39 (CO). Molecular mass: M/z 335 $[M^+ - 2H_2O]$, 300 $[M^+ - 4H_2O]$, 196 $(M^+ - L - 4H_2O]$. UV/visible in DMSO (nm (ϵ)) of 3.17 × 10^{-3} M solution of **1**: 230 (1.071 × 10^3), 296 (0.573 × 10^3). UV/visible in DMSO (nm (ϵ)) of 1.06 × 10^{-3} M solution of **1**: 210 (2.185 × 10^3), 230 (1.98 × 10^3), 296 (1.061 × 10^3). UV/visible in DMSO (nm (ϵ)) of 3.17 × 10^{-3} M solution of ligand: 234 (17.301 × 10^3), 296 (9.064 × 10^3).

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(1) Drake, S. R.; Otway, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 517; Drake, S. R.; Otway, D. J. *Polyhedron* **1992**, *11*, 753. Drake, S. R.; Hursthouse, M. B.; Otway, D. J.; Malik, K. M. *Polyhedron* **1992**, *11*, 1995.
(2) McCormick, M. J.; Moon, K. B.; Jones, S. R.; Hanusa, T. P. *J. Chem. Soc., Chem. Commun.* **1990**, 778.
(3) Hitchcock, P. B.; Lappert, M. F.; Lawless, G. A.; Royo, B. *J. Chem. Soc., Chem. Commun.* **1990**, 1141 and references therein.
(4) Westerhausen, H. *Inorg. Chem.* **1991**, *30*, 90.
(5) Drake, S. R.; Arunasalam, V. C. *Polyhedron*, in press. Timkovich, R.; Tulinsky, A. *J. Am. Chem. Soc.* **1969**, *91*, 4430.
(6) Abdulla, M.; Behbehani, A.; Dashli, H. *Magnesium Health Disease* **1989**, 111.
(7) Classen, H. G.; Nowitski, S.; Schimatschek, H. F. *Magnesium Bull.* **1991**, *132*, 39.
(8) Schmidbaur, H.; Classen, H. G.; Riede, J.; Helbig, J. *Angew. Chem., Int. Ed. Engl.* **1991**, *29*, 1090 and references therein.
(9) Kreiger, G.; Classen, H. G. *Magnesium Bull.* **1979**, *3*, 191.
(10) For leading references see: Schmidbaur, H.; Muller, G.; Riede, J.; Helbig, J. *Angew. Chem., Int. Ed. Engl.* **1986**, *24*, 11. Schmidbaur, H.; Bach, I.; Wilkinson, D. L.; Muller, G. *Chem. Ber.* **1989**, *122*, 1433. Schmidbaur, H.; Bach, I.; Wilkinson, D. L.; Muller, G. *Chem. Ber.* **1989**, *122*, 1445.
(11) Maeda, M.; Murata, Y.; Ito, K. *J. Chem. Soc., Dalton Trans.* **1987**, 1853.
(12) Schmidbaur, H.; Kumberger, O.; Riede, J. *Inorg. Chem.* **1991**, *30*, 3101.
(13) Debuyst, R.; Dejehet, F.; Dekandelaer, M.-C.; Declercq, J.-P.; Germain, G.; Meerssche, M. V. *J. Chim. Phys.* **1979**, *76*, 1117.

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Table I. Crystallographic Data for $[Mg(C_7H_5O_{10})_2(H_2O)_4]$

chem formula: $C_{14}H_{18}O_{10}Mg$	space group: $P2_1/n$ (No. 14)
fw = 370.569	$Z = 2$
$a = 23.116(5)$ Å	$\rho = 1.496$ g cm^{-3}
$b = 5.2066(4)$ Å	$F(000) = 388$
$c = 6.8372(6)$ Å	μ(Mo Kα) = 1.52 cm^{-1}
$\beta = 90.32(1)°$	abs cor factors: min, max = 0.887, 1.065
$V = 822.90$ Å^3	
$T = 295$ K	
$\rho_{min}, \rho_{max} = 0.22, 0.20$ e Å^{-2}	$(\Delta/\sigma)_{max} = 0.009$
$R^a = 0.0374$	$R_w{}^b = 0.0410$

^{a} $R = \sum[(F_o) - (F_c)]/\sum(F_o)$. ^{b} $R_w = [\sum w((F_o) - (F_c))^2/\sum w(F_o)^2]^{1/2}$, with $w = 1$.

Table II. Fractional Atomic Coordinates (×10^3) and Equivalent Isotropic Temperature Factors (Å^2 × 10^3) for $[Mg(C_7H_5O_3)_2(H_2O)_4]$

	x	y	z	U_{eq}
Mg	0[a]	0[a]	0[a]	25(1)
O(1)	698(1)	1472(4)	1416(2)	33(1)
O(2)	694(1)	-27(4)	4444(2)	36(1)
O(3)	1351(1)	5030(4)	353(2)	36(1)
O(4)	-562(1)	2032(4)	1891(3)	33(1)
O(5)	16(1)	-2971(4)	1988(3)	36(1)
C(1)	878(1)	1485(5)	3199(3)	26(1)
C(2)	1321(1)	3462(5)	3676(3)	25(1)
C(3)	1539(1)	3701(6)	5586(4)	34(1)
C(4)	1942(1)	5558(6)	6060(4)	42(1)
C(5)	2143(1)	7188(6)	4623(4)	40(1)
C(6)	1940(1)	6999(6)	2722(4)	35(1)
C(7)	1533(1)	5166(5)	2255(3)	26(1)
H(3)	1398(11)	2530(41)	6538(29)	39(8)[b]
H(4)	2092(11)	5941(58)	7324(18)	45(8)[b]
H(5)	2439(10)	8413(46)	4867(44)	55(9)[b]
H(6)	2051(11)	8146(43)	1711(29)	42(8)[b]
H(31)	1117(14)	3732(66)	340(44)	51(10)[b]
H(41)	-869(16)	2512(78)	1290(78)	75(12)[b]
H(42)	-630(14)	1194(70)	2897(50)	59(11)[b]
H(51)	-99(16)	-4416(78)	2088(51)	68(12)[b]
H(52)	189(16)	-2402(80)	3013(57)	84(13)[b]

^{a} Invariant parameters. ^{b} U_{iso}.

Preparation of $[Ca(C_6H_4(OH)CO_2)_2(OH_2)_2]_\infty$ (2). Calcium chloride (2.898 g, 19.71 mmol) and salicylic acid (5.49 g, 39.75 mmol) were dissolved with vigorous stirring in 50 mL of MeOH. The reaction mixture was then stirred for 30 min at ambient temperature, producing a clear solution. Addition of concentrated (880) ammonia solution (12 mL) did not produce a precipitate, but after a 10-min reflux, a white precipitate resulted. This was filtered off under suction and dried in air for 30 min. The solid was recrystallized from warm water 100 (mL), and concentration of the reaction mixture to 15 mL at 60 °C resulted in a pale yellow oil. Transfer of the flask to a water bath at the same temperature, followed by gradual cooling overnight, resulted in a large crop of colorless crystals: yield 7.26 g (45.1%) of $[Ca(C_6H_4(OH)CO_2)_2(H_2O)_2]$ (mp >270 °C dec). Anal. Calcd for $CaC_{14}H_{18}O_8$: C, 47.29; H, 4.43. Found: C, 44.70; H, 3.89. IR (Nujol; ν, cm^{-1}): 3250 (s, br), 2922 (s), 2851 (s), 2570 (w, br), 1554 (s), 1524 (s), 1459 (s), 1383 (s), 1316 (m), 1249 (s), 1152 (w), 1133 (m), 1035 (w), 950 (w), 888 (w), 856 (w), 762 (m), 753 (s), 710 (s). ^{1}H NMR (d_6-DMSO, 270 MHz, 20 °C): δ 3.53 (s, br, 4H), 6.68 (m, 2H), 7.20 (m, 1H), 7 29 (m, 1H). ^{13}C NMR (D_2O, 67.94 MHz, 20 °C): δ 116.13 (s, C4), 117.01 (s, C5), 119.59 (s, C3), 130.69 (s, C6), 132.43 (s, C2), 162.49 (s, C1), 173.09 (CO). Molecular mass: M/z 341 [M$^+$], 305 [M$^+$ - 2H$_2$O], 178 [M$^+$ - L - 2H$_2$O]. UV/visible in DMSO (nm (ϵ)) of 4.00 × 10^{-5} M solution of **2**: 298.8 (8.0 × 10^3), 235.6 (15 × 10^3), 222.7 (15.0 × 10^3). UV/visible in DMSO (nm (ϵ)) of 1.06 × 10^{-3} M solution of **2**: 300.8 (9.875 × 10^3), 235.6 (22.25 × 10^3), 223.7 (17.625 × 10^3).

Preparation of $[Ba(C_6H_4(OH)CO_2)_2(OH_2)_2]_\infty$ (3). Barium acetate (10.061 g, 39.11 mmol) was dissolved with stirring in 50 mL of distilled water over a period of 5 min. A solution of salicyclic acid (10.88 g, 78.28 mmol) in methanol (40 mL) was added, yielding a slightly cloudly solution. To this reaction mixture was added concentrated (880) ammonia solution (18 mL), but no precipitate was obtained. After a 10-min reflux and reduction to near dryness on a rotary evaporator at 60 °C, a white solid was obtained. The solid was recrystallized from hot water (20 mL), which resulted in a moderate crop of colorless crystals: yield of 5.66 g (31.49%) of $[Ba(C_6H_4(OH)CO_2)_2(H_2O)_2]$ (mp 320 °C dec). Anal. Calcd for $BaC_{14}H_{18}O_8$: C, 37.23; H, 3.98. Found: C, 37.51; H, 4.06. IR (Nujol; ν, cm^{-1}): 3249 (s, br), 2923 (s), 2851 (s), 2572 (w, br), 1551 (s), 1522 (s), 1458 (s), 1380 (s), 1319 (m), 1248 (s), 1151 (w), 1136 (m), 1035 (w), 951 (w), 894 (w), 860 (w), 767 (m), 757 (s), 710 (s). ^{1}H NMR

Table III. Selected Bond Lengths (Å) and Angles (deg) for $[Mg(C_7H_5O_3)_2(H_2O)_4]$

O(1)-Mg	2.026(4)	O(4)-Mg	2.120(4)
O(5)-Mg	2.059(4)	C(1)-O(1)	1.287(4)
C(1)-O(2)	1.237(4)	C(7)-O(3)	1.367(4)
C(2)-C(1)	1.486(4)	C(3)-C(2)	1.403(4)
C(7)-C(2)	1.406(4)	C(4)-C(3)	1.381(5)
C(5)-C(4)	1.381(5)	C(6)-C(5)	1.382(5)
C(7)-C(6)	1.376(4)		
O(4)-Mg-O(1)	90.5(2)	O(5)-Mg-O(1)	87.6(2)
O(5)-Mg-O(4)	88.9(2)	C(1)-O(1)-Mg	135.1(2)
O(2)-C(1)-O(1)	122.5(3)	C(2)-C(1)-O(1)	115.6(3)
C(2)-C(1)-O(2)	122.0(3)	C(3)-C(2)-C(1)	120.6(3)
C(7)-C(2)-C(1)	121.9(3)	C(7)-C(2)-C(3)	117.5(3)
C(4)-C(3)-C(2)	121.3(3)	C(5)-C(4)-C(3)	119.5(3)
C(6)-C(5)-C(4)	120.8(4)	C(7)-C(6)-C(5)	119.7(3)
C(2)-C(7)-O(3)	121.2(3)	C(6)-C(7)-O(3)	117.6(3)
C(6)-C(7)-C(2)	121.2(3)		

Table IV. Dimensions of the Unique Hydrogen Bonds (Distances, Å; Angles, deg) in $[Mg(C_7H_5O_3)_2(H_2O)_4]$

A-B···C[a]	A-B	B···C	A···C	∠ABC
O(3)-H(31)···O(1)[a]	0.86(4)	1.70(3)	2.501(3)	154(3)
O(5)-H(52)···O(2)[a]	0.86(4)	1.96(4)	2.756(3)	154(4)
O(4)-H(42)···O(2)[b]	0.83(4)	1.92(4)	2.733(2)	165(3)
O(4)-H(41)···O(3)[c]	0.86(4)	2.03(4)	2.827(3)	154(4)
O(5)-H(51)···O(4)[d]	0.80(4)	2.14(4)	2.925(3)	164(4)

^{a} Key to symmetry: (a) x, y, z; (b) $-x, -y, 1 - z$; (c) $-x, 1 - y, -z$; (d) $x, -1 + y, z$.

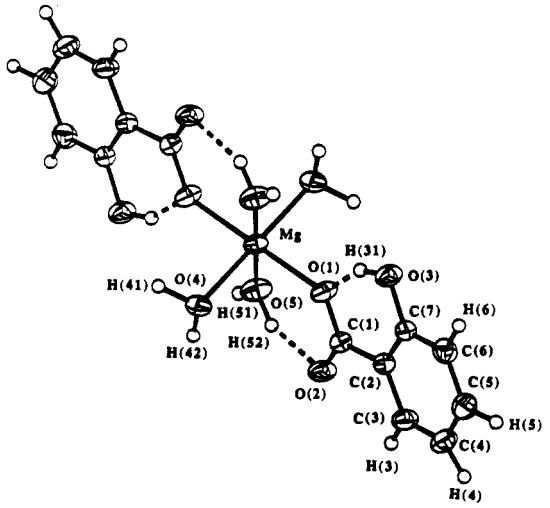

Figure 1. General view of the centrosymmetric molecule $[Mg(C_7H_5O_3)_2(H_2O)_4]$ (**1**). Only the unique atoms are numbered.

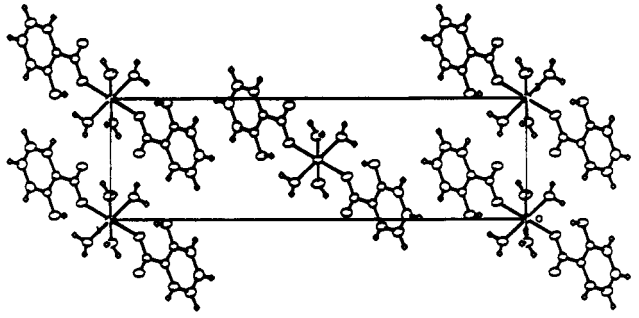

Figure 2. Packing of $[Mg(C_7H_5O_3)_2(H_2O)_4]$ (**1**) molecules viewed along the b axis.

(d_6-DMSO, 270 MHz, 20 °C): δ 3.50 (s, br 4H), 6.64 (m, 2H), 7.16 (m, 1H), 7.22 (m, 1H). ^{13}C NMR (D_2O, 67.94 MHz, 20 °C): δ 116.15 (s, C4), 117.10 (s, C5), 119.64 (s, C3), 130.62 (s, C6), 132.47 (s, C2), 162.56 (s, C1), 173.21 (CO).

X-ray Structure Determination of [Mg(salicylate)$_2$(H$_2$O)$_4$] (1). A summary of the crystallographic data is given in Table I. The X-ray measurements were made on a colorless plate of approximate dimensions 0.50 × 0.40 × 0.15 mm^3, which was mounted using Araldite and transferred to a goniostat. The unit cell parameters and intensity data were obtained at 295 K using a Delft-Instruments FAST TV area detector diffractometer and graphite-monochromated Mo Kα radiation (λ 0.710 69 Å) following previously described procedures.[14]

The total of 3357 intensities measured within θ range 2.6–29.9°, corresponding to slightly more than one hemisphere, yielded 1920 unique and 1193 observed [$F_o > 3\sigma(F)$] reflections (merging R = 0.0413). The data were corrected for Lorentz and polarization effects, and also for absorption using the program DIFABS,[15] adapted for FAST geometry.[16] The structure was solved via the Patterson and Fourier methods and refined (on F) by full-matrix least-squares techniques (SHELX-76)[17] to a final R value of 0.0374 for 1193 observed data and 151 parameters. All non-hydrogen atoms were treated anisotropically; the hydrogen atoms were all located from difference maps and refined with isotropic temperature factors. All calculations were performed on a T800 transputer hosted by an IBM/AT personal computer.

Final atomic paramers are given in Table II, selected bond lengths and angles in Table III, and the hydrogen-bond dimensions in Table IV. The structure of a single molecule (drawn with SNOOPI)[18] and the atom numbering are shown in Figure 1, and a packing diagram is presented in Figure 2.

Results

(a) Synthesis. The synthesis of the group IIA metal salicylate complexes could not be achieved by the direct reaction of either the metal chlorides or acetates with 2 molar equiv of salicylic acid in methanol. On concentration of this reaction mixture, only unreacted salicyclic acid was obtained, but upon addition of aqueous ammonia, the reaction was found to proceed in high yield, according to the following equation:

$$M(OAc)_2 + 2(1,2\text{-}C_6H_4(OH)COOH) \xrightarrow{NH_3} [M(C_6H_4(OH)COO)_2(H_2O)_n]$$
$$\mathbf{1\text{–}3}$$

M = Mg (**1**), n = 4; M = Ca (**2**) or Ba (**3**), n = 2

After filtration of the crude reaction mixture (obtained on addition of aqueous ammonia), the complexes were recrystallized in excellent yield. The saturated solutions were acidic with pH values of 5.22 (**1**), 5.20 (**2**), and 5.19 (**3**), respectively. The basicity of the magnesium, calcium, and barium starting materials [e.g. metal chlorides or acetates (or even the magnesium and calcium hydroxides)] was not sufficient for complete neutralization of the salicylic acid according to the above equation. This may be contrasted with recent observations on the more basic hydroxides of the heavier metals strontium and barium.[10]

Complexes **1–3** were characterized in solution by IR, multinuclear NMR, and UV/visible spectroscopy, in the gas phase by mass spectrometry, and in the solid state by microanalysis. A single-crystal X-ray structure was obtained for **1**.

(b) X-ray Structure of [Mg(salicylate)$_2$(H$_2$O)$_4$] (1). Structural analysis of the magnesium salicylate (**1**) shows it to be a centrosymetric tetrahydrated complex [Mg(C$_6$H$_4$(OH)-CO$_2$)$_2$(H$_2$O)$_4$], on the basis of a nearly regular octahedral geometry with O(1)–Mg–O(4) of 90.5(2)°, O(5)–Mg–O(1) of 87.6(2)°, and O(5)–Mg–O(4) of 88.9(2)°.

There are several features that are interesting in this structure. For example, in contrast to those in the recently characterized beryllium–salicylate complex,[12] the salicylate ligands in the present complex act as monodentate O-donors, involving one O atom of the deprotonated carboxylate group. The complex is an example of a "neutral" monomeric species in which the Mg–O bond lengths vary from 2.026(4) (Mg–O$_{carboxylate}$) to 2.120(4) Å (Mg–O$_{water}$) and are comparable with those in other magnesium complexes supported by six O-donor atoms.[16]

The molecule is also characterized by the presence of several strong intra- and intermolecular hydrogen bonds (Table IV). The phenolic oxygen [O(3)] is a donor, and the carboxylato oxygens [O(1) and O(2)] are both acceptors. In contrast to this scenario, one water molecule [O(5)] is an acceptor whereas the other [O(4)] is both donor and acceptor. It is also interesting to note that the geometry around O(5) is virtually planar [sum of three interbond angles is 360(3)°], while O(4) shows a tetrahedral geometry [three angles at O(4) are 111(3), 111(3), and 113(3)°]. Of the two unique water molecules, only O(4) participates in intermolecular hydrogen bonding, which may explain the lengthening of the Mg–O(4) bond compared with the Mg–O(5) bond [2.120(4) vs 2.059(4) Å]. The extensive internal hydrogen-bonding system probably results in the primary "monomeric" nature of the magnesium salicylate and its excellent stability in the presence of both air and moisture.

complex	donor capacity of Sal	M–O- (carboxylato), Å	M–O- (water), Å	coordn. no.	ref
[Be(Sal)(H$_2$O)$_2$]	2	1.572	1.658	4	12
[Mg(Sal)$_2$(H$_2$O)$_4$]	1	2.026	2.120	6	this work
[Ca(Sal)$_2$(H$_2$O)$_2$]$_\infty$	2/3	2.444/2.632	2.379	8	13
[Sr(Sal)$_2$(H$_2$O)$_2$]$_\infty$	2/3	2.573/2.753	2.538	8	13

The molecular structure of **1** may also be contrasted with other structurally characterized salicylates as shown in the preceding table; for example, a recently characterized beryllium complex [Be(Sal)(H$_2$O)$_2$] exhibits a tetrahedral geometry, with the salicylate acting as a chelating ligand and the water molecules being involved in intensive hydrogen bonding.[12] This structure is not unexpected, given the known tendency of beryllium to form four-coordinate complexes. The heavier alkaline earth complexes [M(Sal)$_2$(H$_2$O)$_2$]$_\infty$ (M = Ca, Sr) exhibit 8-fold coordination with oxygen atoms in a distorted square antiprismatic environment.[13] The salicylate acts as a bidendate ligand binding through the carboxylate, with intensive hydrogen bonding within individual molecules. A striking difference between these heavier metal complexes and their lighter congeners is their ability to form a one-dimensional array with η^2-salicylates further bonding to neighboring metal atoms through the carboxylato oxygens. In contrast, [Zn(Sal)$_2$(H$_2$O)$_2$]$_\infty$ consists of Zn–O tetrahedra held together by hydrogen bonding between the individual tetrahedra of oxygen bonds.[19]

One may note a "periodic trend" in this range of alkaline earth salicylate complexes, from the discrete molecular complexes of beryllium and magnesium (with coordination numbers of 4 and 6 being observed) to those of the heavier metals, where coordinative saturation of the metals calcium and strontium is achieved through the agency of salicylates acting as bridging ligands between metal centers. To date, we have been unable to obtain single crystals of the barium salicylate (**3**) due to persistent twinning problems.

A further parallel to our work may be found with the recently structurally characterized magnesium L-glutamate hydrate complex [Mg(L-Glu)(H$_2$O)$_4$].[10] The metal ion in this complex is also hexacoordinate, with an N,O-chelating dianionic ligand and

(14) Danopoulos, A. A.; Wilkinson, G.; Hussain-Bates, B.; Hursthouse, M. B. *J. Chem. Soc., Dalton Trans.* **1991**, 1855.
(15) Walker, N. P. C.; Stuart, D. *Acta Crystallogr., Sect. A* **1983**, *39*, 1980.
(16) Karaulov, A. Thesis, University of Wales, College of Cardiff, 1991.
(17) G. M. Sheldrick, University of Cambridge, 1976: scattering factor data as included in the SHELX S86 program (G. M. Sheldrick, University of Gottingen, 1986).
(18) Davies, K. Thesis, University of Oxford, 1983.
(19) Klug, H. P.; Alexander, L. E.; Sumner, G. G. *Acta Crystallogr.* **1958**, *11*, 41.

four water molecules completing the coordination sphere. The γ-carboxylate functionality was found not to be coordinated to the metal and is "engaged" in intermolecular hydrogen bonding with neighboring molecules. This is not surprising, since if the second carboxylate were to coordinate, a seven-membered ring would result, implying that the pK_a's of the two different OH groups are quite different.

(c) Spectral Characterization of the Complexes. We have found that these complexes are soluble in water, dimethyl sulfoxide, ether, alcohol, and, to a limited extent, benzene. They are readily recrystallized from hot water. The IR (Nujol) spectra of these complexes show bands characteristic of coordinated water molecules (3258 br) and also coordinated salicylic metal–oxygen vibrations.

The ^1H and ^{13}C NMR spectra of **1–3** in either D_2O or d_6-DMSO reveal the presence of phenolic alcohol groups on the starting salicylic acid, and the coordinated ligand shows only small chemical shifts. The observation of only one salicylate environment indicates that the monodendate ligands either are equivalent in solution or are undergoing a rapid exchange process at ambient temperature in both aqueous and nonaqueous media. This observation though does not preclude the possible existence in solution of other complexes; e.g., for magnesium, aquo-solvated compounds $\{[Mg(H_2O)_6]^{2+},2(\text{salicylate})-\}$ or other oligomeric or hydrogen-bonded species may occur. This situation may occur in either aqueous or nonaqueous solution (see UV/visible spectroscopy discussion), where the solvent may form secondary or tertiary solvation shells and thus increase the effective hydrogen bonding between individual molecules.

Mass spectroscopic results for **1** obtained by using electron impact reveal the presence of a series of ions. The highest molecular mass species present is found to be monomeric, $[Mg(Sal)_2(H_2O)_2]^+$ (mass of 336 amu), with further fragmentation yielding the ion $[Mg(Sal)_2]^+$ with a mass of 300 amu and a further species $[Mg(Sal)]^+$ with a mass of 196 amu. Besides the fragmentation observed for the magnesium complex, an intense signal is seen at 138 amu, associated with salicylic acid, and an equally intense signal is observed at 94 amu, due to a phenolic fragment. Related behavior is observed for the corresponding calcium complex (**2**), with a molecular ion observed at 341 amu and fragment ions observed at 305 amu $[M^+ - 2H_2O]$ and 178 amu $[M^+ - 2H_2O - L]$. The conditions of the mass spectroscopic experiments support the presence of a monomeric species in the gas phase. No satisfactory molecular ion could be observed for **3**; instead, the only peak observed was at 138 amu, associated with the ligand.

The UV/visible spectra of these three complexes show absorbance bands due to coordinated salicylic acid. Spectra obtained for the complexes in water show appreciable dissociation to free ligand and solvated metal ion (see Experimental Section). However, when complexes **1** and **2** are studied in nonaqueous solvents, small shifts in λ_{max} (ca. 10 nm) are observed. These UV/visible spectra may be interpreted in terms of contact ion pair/solvent separated ion pair equilibria, because the bulk solvent (dimethyl sulfoxide) may itself coordinate to these hard metal centers, e.g.

$$[Mg(L)_2(H_2O)_4] + S \rightleftharpoons [Mg(L)(S)(H_2O)_{4-n}]^+\|L^-$$

$$[Mg(L)(S)(H_2O)_{4-n}]^+ + S \rightleftharpoons [Mg(S)_n(H_2O)_{4-n}]^{2+}\|2L^-$$

The formation of solvent separated ion pairs is well precedented for complexes containing ligands coordinated in a monodenate mode.[1] In such cases, the solvent may penetrate the first coordination sphere and produce SSIP's, provided of course that the solvent is sufficiently polarizing or is a sufficiently strong Lewis base; dimethyl sulfoxide fulfills these criteria.

Discussion

Our studies have demonstrated that magnesium salicylate is a monomeric octahedral complex of formulation $[Mg(Sal)_2(H_2O)_4]$. This material is prepared in excellent yield via the use of either chloride or acetate hydrate salts of magnesium in methanol, followed by the addition of aqueous ammonia to ensure that the reaction is driven to completion. This behavior with respect to the product that is formed, is similar to that of other known divalent metal salicylate complexes. It differs because of the known ability of magnesium to form octahedral six-coordinate complexes; in this respect, complexation occurs via internal inter- and intramolecular hydrogen bonding.

The spectroscopic data for complexes **1–3** are alone rather inconclusive. The small differences in chemical shifts and coupling constants in the NMR spectra recorded in both aqueous and nonaqueous solvents make any meaningful interpretation very difficult. This is most likely to be caused by either fast ligand and or site exchange, which is further complicated by extensive competition from the attached water molecules in nonaqueous solvents, or alternatively the bulk solvent if in aqueous media.

These complexes appear to be remarkably stable (cf. recent comments on a related beryllium salicylate compound)[12] in both aqueous and nonaqueous media. Surprisingly, pH studies have shown that both the magnesium and calcium materials have a remarkable stability over a wide range, and as such, the use of multidentate ligands with functional groups which may be switched on or off by varying the pH warrants further exploration. Preliminary studies have shown that 2,3-dihydroxy-5-nitrobenzoic acid is an ideal candidate. This ligand has a choice of possible binding sites; at low pH the salicylate functional group coordinates, while at higher pH the catecholate will coordinate. This flexibility may yield a stronger complexant over a wide pH range and is an essential property if the complex is to have any biosuitability for in vivio or in vitro studies, with either O- or O,N-donors.[20]

Finally, to obtain more detailed information, we are currently employing both pH-dependent NMR (also to obtain a measure of the stability of these three complexes via formation constants and to optimize chelate effects) and UV/visible spectroscopy, since these techniques are sensitive to both coordination and conformation changes in solution which are more than likely to occur.

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Supplementary Material Available: Tables giving anisotropic thermal parameters, bond lengths and angles involving the H atoms, and selected nonbonded distances (2 pages). Ordering information is given on any current masthead page.

(20) Seeling, D. *Magnesium Deficiency in the Pathogenisis of Disease*, 1st ed.; Plenum Medical: New York, 1968; p 29. Ludi, H.; Schatzmann, H. J. *J. Physiol.* **1987**, *390*, 367. Flatman, P. W. *Magnesium Res.* **1988**, *1*, 1.