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Alkali and Alkaline Earth Complexation to Derivatives of Salicylic Acid: [Calcium(*p*-aminosalicylate)(acetate)(H_2O)](H_2O), Magnesium(salicylate)$_2$(H_2O)$_4$, Magnesium(*p*-aminosalicylate)$_2$(H_2O)$_4$, Magnesium(2,6-pyridinedicarboxylate)-(H_2O)$_3$(H_2O)$_2$ and Sodium(*p*-aminosalicylate)(H_2O)$_2$

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Abstract

[Calcium(*p*-aminosalicylate)(acetate)(H_2O)](H_2O) and sodium(*p*-aminosalicylate)(H_2O)$_2$ display extended layer formation in the crystalline state with cations bridged by multidentate ligands. The cross linking of layers results in an extended solid lattice. Magnesium(salicylate)$_2$(H_2O)$_4$, magnesium(*p*-aminosalicylate)$_2$(H_2O)$_4$ and magnesium(2,6-pyridinedicarboxylate)(H_2O)$_3$(H_2O)$_2$ show six coordinate magnesium clusters isolated from interaction with others in the unit cell. Magnesium(2,6-pyridinedicarboxylate)(H_2O)$_3$(H_2O)$_2$ crystallizes with highly unusual distorted octahedral geometry.

[Ca(*p*-aminosalicylate)(acetate)(H_2O)](H_2O) (I) $C_9H_{13}CaNO_7$; M = 287.3, monoclinic, $P2_1/n$, a = 19.530(18), b = 9.654(5), c = 6.852(4) Å, β = 110.75(6)°, V = 1197(1) Å^3, Z = 4, D_x = 1.549 g cm^{-3}, $F(000)$ = 600, λ = 0.71069 Å, μ(Mo Kα) = 5.348 cm^{-1}, 295 K, R = 9.5% for 915 observed reflections. [$I > 3\sigma(I)$].

Mg(salicylate)$_2$(H_2O)$_4$ (II) $C_{14}H_{18}MgO_{10}$; M = 370.6, monoclinic, $P2_1/n$, a = 23.088(10), b = 5.202(1), c = 6.840(1) Å, β = 90.27(3)°, V = 821.5(4) Å^3, Z = 4, D_x = 1.498 g cm^{-3}, $F(000)$ = 388, λ = 0.71069 Å, μ(Mo Kα) = 1.523 cm^{-1}, 295 K, R = 5.5% for 1308 observed reflections. [$I > 3\sigma(I)$].

[Mg(*p*-aminosalicylate)$_2$(H_2O)$_4$ (III) $C_{14}H_{20}MgN_2O_{10}$; M = 400.6, monoclinic, $P2_1/a$, a = 9.595(6), b = 13.257(4), c = 6.766(2) Å, β = 97.12(4)°, V = 854.1(7) Å^3, Z = 4, D_x = 1.558 g cm^{-3}, $F(000)$ = 420, λ = 0.71069 Å, μ(Mo Kα) = 1.554 cm^{-1}, 295 K, R = 6.7% for 1233 observed reflections [$I > 3\sigma(I)$].

Mg(2,6-pyridinedicarboxylate)(H_2O)$_3$(H_2O)$_2$ (IV) $C_7H_{13}MgNO_9$; M = 279.4, monoclinic, $P2_1/n$, a = 8.920(3), b = 9.980(5), c = 13.249(9) Å, β = 96.89(4)°, V = 1171(1) Å^3, Z = 4, D_x = 1.585 g cm^{-3}, $F(000)$ = 584, λ = 0.71069 Å, μ(Mo Kα) = 1.831 cm^{-1}, 295 K, R = 5.3% for 1449 observed reflections [$I > 3\sigma(I)$].

Na(*p*-aminosalicylate)(H_2O)$_2$ (V) $C_7H_{10}NNaO_5$; M = 211.1, monoclinic $P2_1/c$, a = 8.799(4), b = 14.620(5), c = 6.965(2) Å, β = 97.90(3)°, V = 887.5(5) Å^3, Z = 4, D_x = 1.580 g cm^{-3}, $F(000)$ = 440, λ = 0.71069 Å, μ(Mo Kα) = 1.64 cm^{-1}, 295 K, R = 5.7% for 943 observed reflections [$I > 3\sigma(I)$].

Introduction

In vitro studies have identified calcium to be a participant in chemically mediated histamine release [1–3]. Mast cells retain histamine when challenged with allergen in a calcium free environment [2]. Calcium may have to penetrate through the cell wall in its function as a cofactor. The introduction of calcium complexed to known calcium specific ionophores into the mast cell environment leads to histamine release [2]. Direct injection of calcium into the mast cell causes histamine release [4]. The conjecture that calcium may have to enter the mast cell in its mechanistic role is also supported by the observation of lipophilic cluster formation with allergens of low molecular weight. These clusters show polar groups directed towards calcium atoms lying on layers or sheets with maximum incorporation of such groups as ligands. These clusters turn nonpolar surfaces to the external environment. The single crystal X-ray studies of [calcium(nicotinate)$_2$(H_2O)$_2$](H_2O)$_3$ [5], [calcium(isonicotinamide)$_2$(H_2O)$_4$]Cl_2 [6], calcium(isonicotinate)$_2$(H_2O)$_4$ [6], calcium(phenoxymethylpenicillinate)$_2$(H_2O)$_2$ [7] and calcium$_{1.5}$(salicylate)$_2$(acetate)(H_2O)$_2$(aceticacid) [8] show this type of sheet complexation. In this series, calcium shows flexibility in coordination number and binding geometry and appears capable of movement within the layers, finding alternative groups of binding ligands with only slight movement of alkaline earth metal and bridging or binding ligands. Carboxylate groups are common, being observed as monodentate, bidentate, tri- and tetradentate ligands. Water molecules are prevalent in the

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calcium coordination sphere and are often involved in hydrogen bonding with other bound ligands.

Magnesium is unlike calcium in binding patterns [9]. Magnesium seldom displays significant deviation from octahedral geometry and is often observed as hexa-aquo magnesium with allergens only hydrogen bonded in second sphere interactions. Magnesium clusters are normally observed isolated from others of the unit cell and without close Mg...Mg contacts.

Calcium has been observed bound to histamine itself, forming a crystalline complex, $CaCl_4(H_2O)_2$-$CaCl_2(H_2O)_2(histamine)_2$ in which calcium is bound to the nitrogen atoms alpha to the side chain of two imidazole rings and to two water molecules (via oxygen) and the chloride ions [10].

Calcium has been somewhat of a forgotten element to structural chemists, having been viewed as an ionic species without the highly developed specificity exhibited by transition metals and one whose behavior has been interpreted largely on the basis of charge density, ionic radius and other ionic properties. Even while popular health related literature is suggesting avoiding the ingestion of certain drugs with milk or warning of calcium depletion with the use of other types of medication, we understand little of calcium behavior at a molecular level. However, it appears that there is something to be learned in this area. To further our knowledge of calcium binding patterns we have examined the structures of crystalline complexes of a series of alkaline and alkaline earth metals to derivatives of salicylic acid. *p*-Aminosalicylic acid has been prescribed to reduce incidence of gastrointestinal irritation. Its side effects may include skin reactions, gastrointestinal intolerance and other symptoms associated with histamine release [11].

Experimental

[Ca(p-aminosalicylate)(acetate)(H₂O)] (H₂O) (I)

0.7655 g (5 mmol) of *p*-aminosalicylic acid and 0.3954 g (2.5 mmol) of calcium acetate hydrate were dissolved in 75 ml of MeOH with stirring. Gravity filtration removed a small amount of suspended solid. Slow room temperature evaporation yielded small platelets after 1 week. Crystals proved unstable in air and were mounted in a sealed capillary in the vapor of the mother liquor.

Mg(salicylate)₂(H₂O)₄ (II)

$Mg(OAc)_2$ (0.429 g (2 mmol) and salicylic acid (0.5524 g, 4 mmol) were combined in 50 ml of water. After refluxing for 5 min, a clear solution resulted. The odor of acetic acid was noted. The solution was allowed to stand for a week yielding a white microcrystalline precipitate. This precipitate was dissolved in 10 ml of hot water, filtered to remove minor amounts of insoluble material and allowed to concentrate at room temperature. Clear, prismatic needles were observed after 48 h. These crystals were observed to be stable in air and were used for diffraction studies.

Mg(p-aminosalicylate)₂(H₂O)₄ (III)

p-Aminosalicylic acid (0.765 g, 5 mmol) was mixed with 6 ml (6 mmol) of a 1 N aqueous solution of NaOH and 5 ml of water added. Aqueous $MgCl_2$ (5 ml, 2.5 mmol of a 0.5 M solution) was added with stirring. The colorless solution was observed to darken to a light brown color. Evaporation was allowed to proceed in air at room temperature. Several days later, clear tan needles were observed to form in the dark brown solution and were used for single crystal diffraction studies without protection from air.

Magnesium(2,6-pyrdinedicarboxylate)(H₂O)₃(H₂O)₂ (IV)

Twenty ml of H_2O were added to 0.334 g (2 mmol) of 2,6-pyridinedicarboxylate and 8 ml (8 mmol) of a 1 N aqueous solution of NaOH. Gentle warming of the mixture yielded a clear solution. The addition of 8 ml (4 mmol) of a 0.5 M aqueous solution of $MgCl_2$ produced a heavy white precipitate which was not redissolved on heating. The mixture was then filtered and the resulting clean solution allowed to stand at room temperature. After 24 h, clear prisms were observed. A single crystal was mounted in a capillary in an atmosphere of the vapor of mother liquor for single crystal diffraction studies.

Na(p-aminosalicylate)(H₂O)₂ (V)

p-Aminosalicylic acid 0.3062 g (2 mmol) was added to 20 ml of H_2O along with 2.5 ml (2.5 mmol) of a 1 N solution of NaOH and stirred with warming to form a clear solution. Following the addition of 2 ml of an 0.5 M aqueous solution of $CaCl_2$ (1 mmol), the solution was observed to darken with continued heating. After filtration, the solution was allowed to stand at room temperature. Tan rhombohedra were observed to form after 48 h. No calcium containing material was isolated in solid form.

X-ray Crystallographic

Crystals of **I**, **II**, **III**, **IV** and **V** were sealed in capillaries and mounted on a Syntex P3 automated diffractometer. Unit cell dimensions (see Table 1) were determined by least-squares refinement of the best angular positions for fifteen independent reflections ($2\theta > 15°$) during normal alignment procedures using molybdenum radiation ($\lambda = 0.71069$ Å). Data [measured points, $\pm h$, $+k$, $+l$; 1580, **I**; 2261, **II**; 2164, **III**; 2768, **IV**; 2298, **V**] were collected at room temperature using a variable scan rate, a θ–2θ scan mode and a scan width of 1.2° below Kα_1 and 1.2° above Kα_2 to a maximum 2θ value of 60°. Backgrounds were measured at each side of the scan for a combined time equal to the total scan time. The intensities of three standard reflections were remeasured after every 97 reflections and as the intensities of these reflections showed less than 4% variation, corrections for decomposition were deemed unnecessary. Data were corrected for Lorentz, polarization and background effects. After removal of redundant and space group forbidden data; 915, **I**; 1308, **II**; 1233, **III**; 1449, **IV**; 943, **V**, reflections were considered observed, $I > 3.0\sigma(I)$. The structures were solved by direct methods using MULTAN [12]. Refinement of scale factor, positional and anisotropic thermal parameters for nonhydrogen atoms were continued to convergence [13]. Hydrogen atom positions for **II**, **IV** and **V** were located from a difference Fourier synthesis. Nonwater hydrogen atoms for **III** were similarly located. Hydrogen positional parameters with isotropic thermal parameters were included in the final cycles of refinement but were held invariant. The final cycles of refinement [function minimized, $\Sigma(|F_o| - |F_c|)^2$] led to a final agreement factor R = 9.5, **I**; 5.5, **II**; 6.7, **III**; 5.3, **IV**; 5.7%, **V**, [$R = (\Sigma||F_o| - |F_c||/\Sigma|F_o| \times 100]$. In the final cycles of refinement, weights equal of $1/\sigma(F)^2$ were used. Scattering factors were taken from Cromer and Mann [14]. Anomalous dispersion corrections were applied for calcium [15]. Tables 1, 3, 5, 7 and 9 list positional parameters for **I**, **II**, **III**, **IV** and **V** respectively. Tables 2, 4, 6, 8 and 10 list derived bond angles and distances.

TABLE 1. Positional parameters for (Ca(p-aminosalicylate)(acetate)(H_2O))(H_2O) (I)

Atom	$x(\sigma(x))$	$y(\sigma(y))$	$z(\sigma(z))$
Ca1	0.4805(2)	0.1058(4)	0.2309(5)
O1	0.400(1)	0.302(2)	0.149(2)
O3	0.027(2)	0.031(3)	0.146(7)
O35	0.023(2)	0.023(3)	0.416(5)
O10	0.578(1)	0.256(2)	0.169(2)
O11	0.575(1)	0.256(1)	0.481(2)
C10	0.605(1)	0.291(2)	0.350(3)
C11	0.674(1)	0.373(2)	0.423(3)
C12	0.708(1)	0.423(2)	0.284(3)
O12	0.671(1)	0.409(3)	0.064(4)
O125	0.671(1)	0.409(3)	0.774(3)
C13	0.774(1)	0.412(2)	0.343(2)
C14	0.807(1)	0.520(2)	0.559(3)
N14	0.878(1)	0.583(1)	0.626(2)
C15	0.776(1)	0.484(2)	0.703(3)
C16	0.707(1)	0.411(2)	0.634(3)
O20	0.447(1)	0.088(1)	0.540(2)
O21	0.446(1)	0.083(1)	0.851(2)
C20	0.427(1)	0.139(2)	0.677(2)
C21	0.374(1)	0.267(2)	0.625(3)

Discussion

In the solid state, [Ca(p-aminosalicylate)(acetate)(H_2O)](H_2O) (**I**), calcium shows coordination to eight atoms; the bidentate carboxylate groups of an acetate [Ca–O 2.50(1) Å av.] and a p-aminosalicylate molecule [Ca–O, 2.50(1) Å av.], oxygen atoms of two

TABLE 2. Bond distances (Å) and angles (°) for (Ca(p-aminosalicylate)(acetate)(H_2O))(H_2O) (I)

Ca1–O1	2.38(1)	O1–Ca1–O10	88.9(5)
Ca1–O10	2.52(1)	O1–Ca1–O11	88.5(4)
Ca1–O11	2.48(1)	O1–Ca1–O20	84.5(5)
Ca1–O20	2.43(1)	O1–Ca1–O21'	84.7(5)
Ca1–O21'	2.46(1)	O1–Ca1–O20''	154.9(5)
Ca1–O20''	2.52(1)	O1–Ca1–O21''	154.5(5)
Ca1–O21''	2.49(1)	O1–Ca1–N14'''	95.7(4)
Ca1–N14'''	2.61(1)	O10–Ca1–O11	51.0(4)
C10–O10	1.21(3)	O10–Ca1–O20	129.5(4)
C10–O11	1.29(2)	O10–Ca1–O21'	79.2(4)
C10–O11	1.47(2)	O10–Ca1–O20'	103.4(4)
C11–C12	1.39(3)	O10–Ca1–O21''	81.4(4)
C12–O12	1.42(3)	O10–Ca1–N14'''	158.9(5)
C12–C13	1.38(2)	O11–Ca1–O20	78.8(4)
C13–C14	1.44(2)	O11–Ca1–O21'	129.8(5)
C14–N14	1.41(2)	O11–Ca1–O20''	82.8(4)
C14–C15	1.37(3)	O11–Ca1–O21''	103.1(4)
C15–C16	1.44(3)	O11–Ca1–N14'''	154.5(5)
C16–C11	1.41(2)	O20–Ca1–O21'	149.0(4)
C16–O125	1.37(3)	O20–Ca1–O20''	70.8(4)
C20–O20	1.23(2)	O20–Ca1–O21''	119.8(4)
C20–O21	1.24(3)	O20–Ca1–N14'''	76.6(4)
C20–C21	1.55(2)	O21'–Ca1–O20''	118.7(4)
		O21'–Ca1–O20''	118.7(4)
		O21'–Ca1–O21''	70.3(4)
		O21'–Ca1–N14'''	75.7(5)
		O20''–Ca1–O21''	50.5(4)
		O20''–Ca1–N14'''	82.9(4)
		O21''–Ca1–N14'''	83.6(4)
		O10–C10–O11	119(1)
		O11–C10–C11	122(2)
		O11–C10–C11	119(1)
		C16–C11–C12	118(2)
		C10–C11–C12	120(1)
		C11–C12–O12	122(2)
		O12–C12–C13	113(2)
		C11–C12–C13	124(1)
		C12–C13–C14	117(2)
		C13–C14–N14	118(2)
		N14–C14–C15	120(1)
		C13–C14–C15	122(1)
		C14–C15–C16	119(1)
		C15–C16–C11	120(2)
		C15–C16–O125	115(2)
		O125–C16–C11	124(2)
		C16–C11–C10	121(2)
		O20–C20–O21	120(1)
		O20–C20–C21	120(1)
		O21–C20–C21	120(2)

Symmetry operation ' $x, y, -1 + z$; '', $1 - x, -y, 1 - z$; ''', $-\frac{1}{2} + x, \frac{1}{2} - y, -\frac{1}{2} + z$.

TABLE 3. Positional parameters for Mg(salicylate)$_2$(H$_2$O)$_4$ (II)

Atom	x ($\sigma(x)$)	y ($\sigma(y)$)	z ($\sigma(z)$)
Mg1	1.0000	0.0000	0.5000
O1	0.9438(1)	0.2042(5)	0.6887(3)
O2	0.9977(1)	0.2960(5)	0.3004(3)
O10	1.0695(1)	0.1479(5)	0.6416(3)
O11	1.0692(1)	−0.0032(5)	0.9442(3)
C10	1.0877(1)	0.1479(6)	0.8206(4)
C11	1.1322(1)	0.3470(6)	0.8681(4)
C12	1.1532(1)	0.5177(6)	0.7249(4)
O12	1.1350(1)	0.5011(5)	0.5357(3)
C13	1.1940(2)	0.7011(7)	0.7731(5)
C14	1.2141(2)	0.7195(8)	0.9625(5)
C15	1.1941(2)	0.5558(8)	1.1068(5)
C16	1.1536(2)	0.3700(8)	1.0595(5)

TABLE 4. Bond distances (Å) and angles (°) for Mg(salicylate)$_2$(H$_2$O)$_4$ (II)

Mg1–O1	2.120(13)	O1–Mg1–O2	90.9(5)
Mg1–O2	2.058(13)	O1–Mg1–O10	90.2(5)
Mg1–O10	2.022(14)	O2–Mg1–O10	92.9(6)
C10–O10	1.293(4)	O10–C10–O11	122.5(3)
C10–O11	1.233(4)	O10–C10–C11	115.3(3)
C10–C11	1.493(4)	O11–C10–C11	122.2(3)
C11–C12	1.410(4)	C10–C11–C12	121.6(2)
C12–O12	1.362(4)	C10–C11–C16	120.1(3)
C12–C13	1.379(5)	C12–C11–C16	118.3(3)
C13–C14	1.377(5)	C11–C12–O12	120.9(3)
C14–C15	1.384(6)	O12–C12–C13	118.6(3)
C15–C16	1.383(6)	C11–C12–C13	120.5(3)
C16–C11	1.401(4)	C12–C13–C14	119.9(3)
		C13–C14–C15	121.1(3)
		C14–C15–C16	119.4(3)
		C15–C16–C11	120.9(3)

TABLE 5. Positional parameters for Mg(*p*-aminosalicylate)$_2$-(H$_2$O)$_4$ (III)

Atom	x ($\sigma(x)$)	y ($\sigma(y)$)	z ($\sigma(z)$)
Mg1	0.5000	0.0000	1.0000
O1	0.4630(4)	0.1094(3)	1.1899(5)
O2	0.6269(4)	0.1008(3)	0.8492(5)
O10	0.3258(4)	0.0466(3)	0.8030(5)
O11	0.3456(4)	−0.0404(3)	0.5274(5)
C10	0.2866(5)	0.0249(4)	0.6197(7)
C11	0.1621(5)	0.0803(4)	0.5186(7)
C12	0.0896(6)	0.1515(4)	0.6184(7)
O12	0.1344(4)	0.1781(3)	0.8104(5)
C13	−0.0320(6)	0.1966(4)	0.5271(7)
C14	−0.0833(5)	0.1711(4)	0.3317(7)
N14	−0.2024(5)	0.2204(3)	0.2358(7)
C15	−0.0093(6)	0.1039(4)	0.2289(7)
C16	0.1094(5)	0.0582(4)	0.3209(7)

TABLE 6. Bond distances (Å) and angles (°) for Mg(*p*-aminosalicylate)$_2$(H$_2$O)$_2$ (III)

Mg1–O1	1.998(4)	O1–Mg1–O2	90.6(2)
Mg1–O2	2.149(4)	O1–Mg1–O10	90.2(1)
Mg1–O10	2.098(3)	O2–Mg1–O10	88.2(1)
C10–O10	1.284(5)	O10–C10–O11	122.9(4)
C10–O11	1.244(6)	O10–C10–C11	117.0(4)
C10–C11	1.494(7)	O11–C10–C11	120.0(4)
C11–C12	1.396(7)	C10–C11–C12	122.0(4)
C12–O12	1.363(6)	C10–C11–C16	120.5(4)
C12–C13	1.386(7)	C12–C11–C16	117.4(4)
C13–C14	1.394(7)	C11–C12–O12	121.3(4)
C14–N14	1.403(6)	O12–C12–C13	117.5(5)
C14–C15	1.380(8)	C11–C12–C13	121.2(4)
C15–C16	1.370(7)	C12–C13–C14	119.8(5)
C16–C11	1.401(7)	C13–C14–N14	119.9(5)
		N14–C14–C15	120.5(4)
		C13–C14–C15	119.4(4)
		C14–C15–C16	120.5(5)
		C15–C16–C11	121.5(5)

TABLE 7. Positional parameters for (Mg(2,6-pyridinedicarboxylate)(H$_2$O)$_3$)(H$_2$O)$_2$ (IV)

Atom	x ($\sigma(x)$)	y ($\sigma(y)$)	z ($\sigma(z)$)
Mg1	0.5526(2)	0.2760(1)	0.2714(1)
O1	0.3823(4)	0.1419(4)	0.2378(2)
O2	0.7296(4)	0.4083(3)	0.2952(2)
O3	0.5569(4)	0.3036(3)	0.1223(2)
O10	0.1362(4)	0.1201(3)	0.3510(2)
O20	0.9794(4)	0.3315(4)	0.4312(3)
N1	0.5308(4)	0.2557(3)	0.4261(2)
C2	0.4302(4)	0.3316(4)	0.4670(3)
C3	0.4101(5)	0.3201(5)	0.5678(4)
C4	0.4965(5)	0.2286(5)	0.6272(3)
C5	0.6005(6)	0.1508(5)	0.5848(3)
C6	0.6140(5)	0.1671(4)	0.4824(3)
C7	0.3468(5)	0.4244(4)	0.3904(3)
O71	0.3916(3)	0.4257(3)	0.3033(2)
O72	0.2397(4)	0.4914(3)	0.4165(2)
C8	0.7146(5)	0.0858(4)	0.4204(3)
O81	0.7058(3)	0.1155(3)	0.3274(2)
O82	0.7955(4)	−0.0034(3)	0.4638(2)

TABLE 8. Bond distances (Å) and angles (°) for (Mg(2,6-pyridinedicarboxylate)(H$_2$O)$_3$)(H$_2$O)$_2$ (IV)

Mg1–O1	2.034(4)	O1–Mg1–O2	175.0(4)
Mg1–O2	2.053(4)	O1–Mg1–O3	88.7(1)
Mg1–O3	1.999(4)	O1–Mg1–N1	89.7(1)
Mg1–N1	2.093(4)	O1–Mg1–O71	90.1(1)
Mg1–O71	2.149(4)	O1–Mg1–O81	90.7(1)
Mg1–O81	2.178(3)	O2–Mg1–O3	87.6(1)
N1–C2	1.338(5)	O2–Mg1–N1	94.1(1)
C2–C3	1.373(3)	O2–Mg1–O71	92.4(1)
C3–C4	1.379(6)	O2–Mg1–O81	88.9(1)
C4–C5	1.381(7)	O3–Mg1–N1	175.2(3)

(continued)

TABLE 8. *(continued)*

C5–C6	1.386(6)	O3–Mg1–O71	101.0(1)
C6–N1	1.325(5)	O3–Mg1–O81	110.6(1)
C7–C2	1.503(6)	N1–Mg1–O71	74.4(1)
C7–O71	1.266(6)	N1–Mg1–O81	73.9(1)
C7–O72	1.248(6)	O71–Mg1–O81	148.3(1)
C8–C6	1.522(6)	C6–N1–C2	120.5(4)
C8–O81	1.260(5)	N1–C2–C7	112.1(4)
C8–O82	1.244(5)	C7–C2–C3	126.6(4)
		N1–C2–C3	121.2(4)
		C2–C3–C4	118.8(4)
		C3–C4–C5	119.8(4)
		C4–C5–C6	118.3(4)
		C5–C6–C8	126.3(4)
		C8–C6–N1	112.2(4)
		C5–C6–N1	121.4(4)
		O71–C7–O72	125.6(4)
		O71–C7–C2	115.9(4)
		O72–C7–C2	118.4(4)
		O81–C8–O82	125.8(4)
		O81–C8–C6	115.5(4)
		O82–C8–C6	118.6(4)

TABLE 9. Positional parameters for Na(*p*-aminosalicylate)($(H_2O)_2$ (V)

Atom	x ($\sigma(x)$)	y ($\sigma(y)$)	z ($\sigma(z)$)
Na1	0.6829(3)	0.0442(2)	−0.0010(3)
O1	0.4919(6)	0.2022(4)	0.0558(8)
O2	0.5382(4)	−0.0066(3)	0.2366(5)
O10	1.2033(5)	0.0723(3)	0.1765(5)
O11	1.3730(4)	0.1173(3)	0.4214(6)
C10	1.2368(6)	0.1018(4)	0.3475(7)
C11	1.1119(6)	0.1195(4)	0.4625(7)
C12	0.9559(6)	0.1058(4)	0.3438(7)
O12	0.9196(4)	0.0764(3)	0.1975(5)
C13	0.8386(6)	0.1239(4)	0.4928(8)
C14	0.8715(6)	0.1557(4)	0.6806(8)
N14	0.7536(5)	0.1722(4)	0.7917(7)
C15	1.0251(6)	0.1693(4)	0.7602(8)
C16	1.1403(6)	0.1507(4)	0.6538(7)

symmetry related acetate molecules [Ca–O, 2.44(1) Å av.], a water molecule oxygen atom [Ca–O, 2.38(1) Å] and the nitrogen atom of a second *p*-aminosalicylate molecule [Ca–N, 2.61(1) Å] (Fig. 1). The carboxylate group of the acetate anion thus bridges three calcium atoms. Refinement of the structure revealed disorder of the phenolic hydroxyl position in the two sites *ortho* to the carboxylate group of the *p*-aminosalicylate molecule. This oxygen atom, O12(O125), was refined with 50% occupancy in each of the two positions. The disorder can be viewed as a 180° rotation about an axis passing through N14, C14, C11 and C10. The disorder of this unbound group has no effect on calcium coordination.

TABLE 10. Bond distances (Å) and angles (°) for Na(*p*-aminosalicylate)($H_2O)_2$ (V)

Na1–O1	2.915(6)	O1–Na1–O2	77.0(2)
Na1–O2	2.343(5)	O1–Na1–O2‴	81.3(2)
Na1–O2‴	2.429(4)	O1–Na1–O10″	157.3(2)
Na1–O10″	2.395(5)	O1–Na1–O12	103.8(2)
Na1–O12	2.383(4)	O1–Na1–N14′	71.2(2)
Na1–N14′	2.494(6)	O2–Na1–O2‴	86.7(1)
C10–O10	1.263(6)	O2–Na1–O10″	116.2(2)
C10–O11	1.258(6)	O2–Na1–O12	99.8(1)
C10–C11	1.469(8)	O2–Na1–N14′	148.2(2)
C11–C12	1.421(7)	O2‴–Na1–O10″	81.1(2)
C12–O12	1.360(6)	O2‴–Na1–O12	172.5(2)
C12–C13	1.390(8)	O2‴–Na1–N14′	91.1(2)
C13–C14	1.381(2)	O10″–Na1–O12	92.5(2)
C14–N14	1.400(8)	O10″–Na1–N14′	94.8(2)
C14–C15	1.403(7)	O12–Na1–N14′	85.4(2)
C15–C16	1.363(8)	O10–C10–O11	122.2(5)
C16–C11	1.400(7)	O10–C10–C11	198.6(4)
		O11–C10–C11	119.2(4)
		C10–C11–C12	121.3(4)
		C10–C11–C16	121.9(4)
		C16–C11–C12	116.9(4)
		C11–C12–O12	120.1(5)
		O12–C12–C13	119.1(4)
		C11–C12–C13	120.8(5)
		C12–C13–C14	120.6(5)
		C13–C14–N14	120.5(5)
		N14–C14–C15	120.3(5)
		C13–C14–C15	119.1(5)
		C14–C15–C16	120.4(5)
		C15–C16–C11	122.3(4)

Symmetry operation ′, $x, y, -1+z$; ″, $2-x, -y, -z$; ‴, $1-x, -y, -z$.

Calcium atoms lie close to planes, $x = 0, x = \frac{1}{2}$ and $x = 1$, and calcium atoms on each plane are bridged by tetradentate acetate groups also lying approximately on those planes [Ca...Ca separation, 4.05 Å]. Acetate groups serve as a bidentate ligand to one calcium, and each oxygen atom is simultaneously bridging to an adjacent calcium atom (Fig. 2). The water molecule coordinated to each calcium atom is also close to this plane. Planes of acetate bridged and water coordinated calcium atoms are cross-linked by *p*-aminosalicylate molecules binding to calcium atoms on adjacent planes by bidentate carboxylate and amino groups [C–N–Ca angle 111.8(9)°].

Mg(salicylate)$_2$(H$_2$O)$_4$ (**II**) (Fig. 3) shows magnesium coordinated to four water molecules and two monodentate carboxylate ions with Mg located on a center of symmetry. As in the complex of magnesium with nicotinic acid [5], magnesium avoids bidentate coordination to the carboxylate groups, the bite of the carboxylate group (O10...O11, 2.215(3) Å) being insufficiently large to permit positioning of the oxygen atoms at vertices of the octahedral coordination sphere. Oxygen atoms

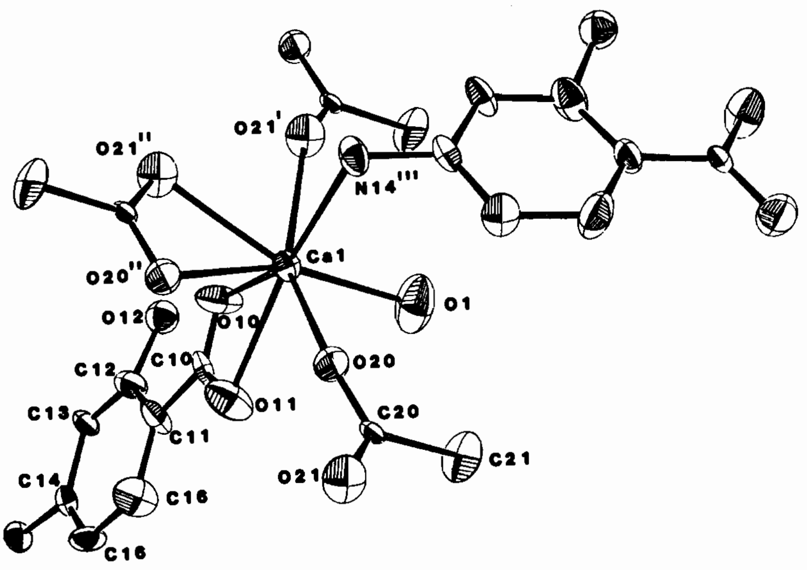

Fig. 1. Calcium coordination in [Ca(p-aminosalicylate)(acetate)(H_2O)](H_2O) (I).

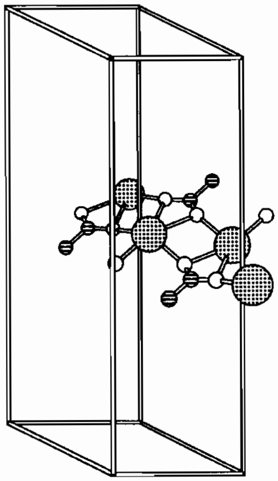

Fig. 2. Projection view of partial plane, $x = \frac{1}{2}$, showing calcium, acetate and water binding.

octahedrally coordinated to magnesium show an average 2.9 Å separation. Bidentate coordination of one carboxylic oxygen atom and the phenolic oxygen atom is thus also precluded (O10...O12 2.489(3) Å). Mg(salicylate)$_2$(H_2O)$_4$ clusters are widely separated in the unit cell.

Mg(p-aminosalicylate)$_2$(H_2O)$_4$ (**III**) (Fig. 4) is similar in structure to **II**. The magnesium atom crystallizes on an inversion center and displays octahedral coordination to the oxygen atoms of four water molecules, and to the unidentate carboxylate groups of two p-aminosalicylate molecules. Magnesium to oxygen distances display a greater range than is usually noted in magnesium complexation (Mg–O_{HOH} 1.998(4), 2.149(4) Å; Mg–$O_{carboxylate}$, 2.098(3) Å). The preferential coordination of magnesium to nitrogen rather than magnesium is unexpected [9]. Magnesium preference for octahedral geometry has been obeyed. In **II** and **III**, O–Mg–O angles fall in the range 88.2(1)–92.9(6)°.

Magnesium(2,6-pyridinedicarboxylate)(H_2O)$_3$(H_2O)$_2$ (**IV**) shows a highly unusual distorted coordination of magnesium to three water molecules [Mg–O_{HOH}, 1.999(4)–2.053(4) Å] and to the nitrogen atom [Mg–N, 2.093(4) Å] and two oxygen atoms of two monodentate carboxylate groups *ortho* to the nitrogen atom [Mg–O, 2.149(4) and 2.178(3) Å] (Fig. 5). Two additional water molecules are crystallized in the unit cell. Coordination to magnesium is severely distorted from octahedral geometry [*trans* angle, O71–Mg–O81, 148.3(1); 'right' angles, N1–Mg–O81, 73.9(1), N1–Mg–O71, 74.4-(1)°].

The structure of calcium(2,6-pyridinedicarboxylate)trihydrate [16] shows eight coordinate calcium bound to four water molecule oxygen atoms, two monodentate carboxylate oxygen atoms and the hetero ring nitrogen atom of one 2,6-pyridinedicarboxylate ligand and a monodentate carboxylate oxygen atom of an adjacent ligand. Two calcium atoms are thus linked in pairs (Ca...Ca 4.180 Å) by two 2,6-pyridinedicarboxylate molecules which are three coordinate to one calcium atom and bridging to the other. Calcium dimers are further linked in columns parallel to the c axis by bridging water molecules (Ca...Ca, 3.991 Å). Thus while calcium shows tridentate coordination to 2,6-pyridinedicarboxylate, bridging of the ligand and of water molecules serve to organize the alkaline earth cations into extended clusters unlike the isolated cluster motif observed for **IV**.

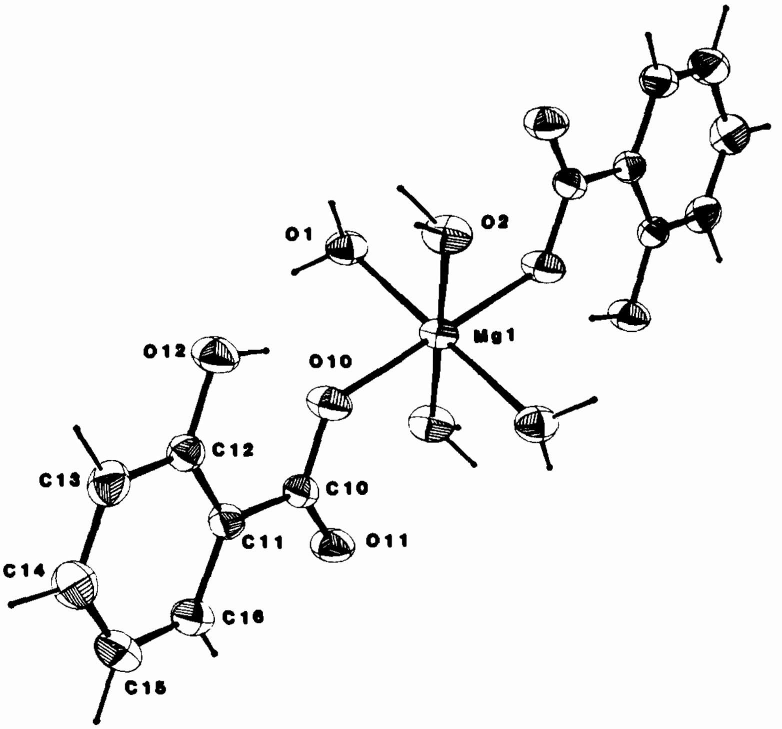

Fig. 3. Mg(salicylate)$_2$(H$_2$O)$_4$ (II).

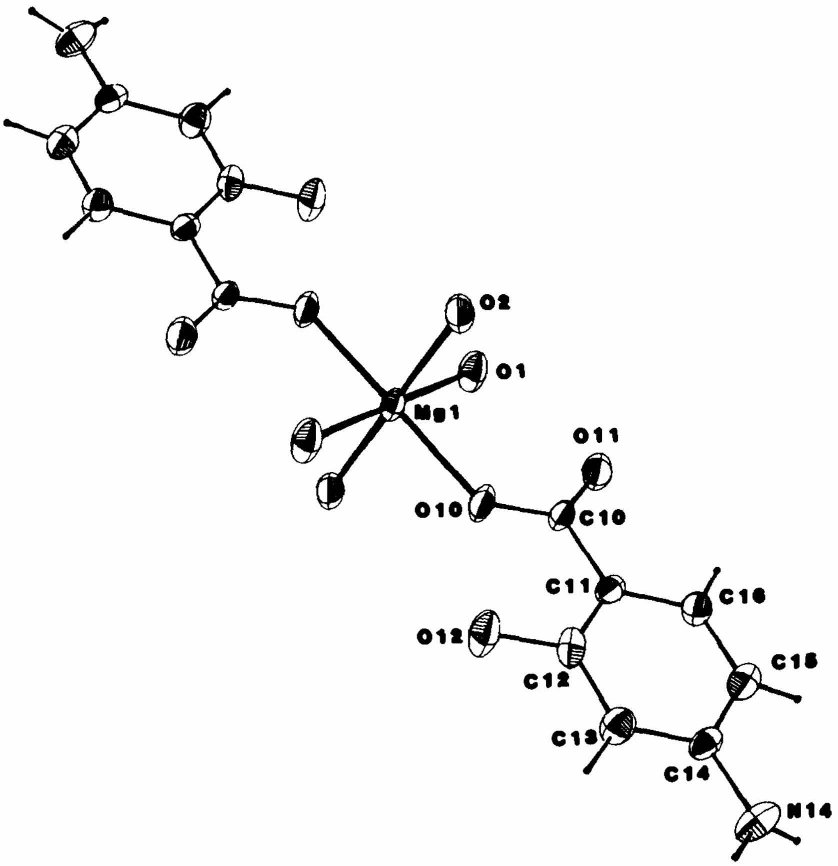

Fig. 4. Magnesium coordination in Mg(p-aminosalicylate)$_2$(H$_2$O)$_4$ (III).

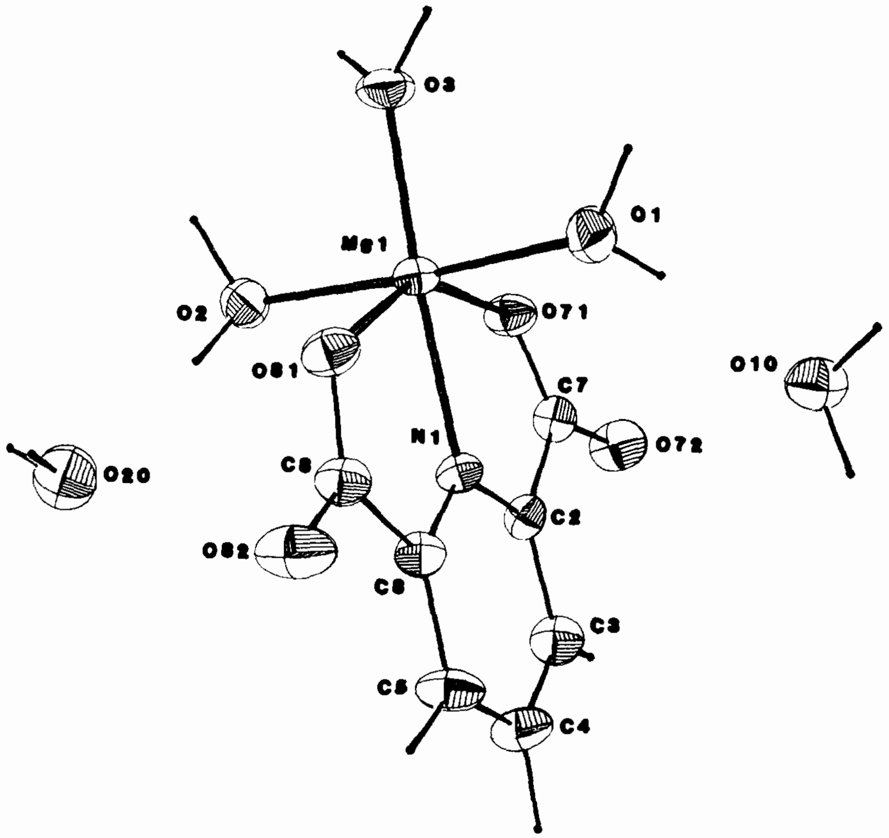

Fig. 5. Magnesium (2,6-pyrdinedicarboxylate)$(H_2O)_3(H_2O)_2$ (IV).

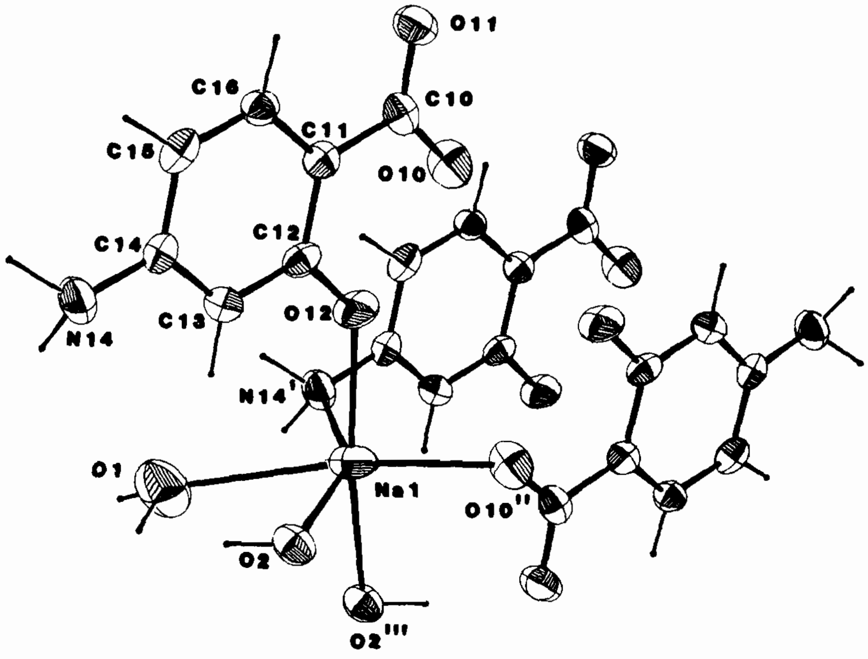

Fig. 6. Coordination sphere on sodium in Na(*p*-aminosalicylate)$(H_2O)_4$ (V).

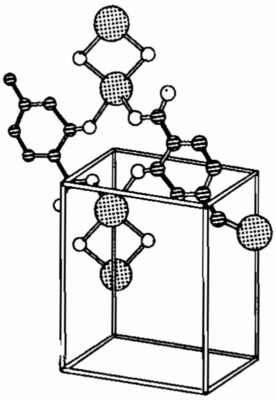

Fig. 7. Sodium layers in Na(*p*-aminosalicylate)$(H_2O)_4$ (V).

Na(*p*-aminosalicylate)$(H_2O)_4$ (V) (Fig. 6) shows octahedral sodium coordinated to the *ortho* hydroxy group of one *p*-aminosalicylate molecule, to a monodentate carboxylate group of a second *p*-aminosalicylate molecule, to the *p*-amino group of a third aromatic ligand and to three different water molecule oxygen atoms, two of which are related by symmetry. Thus the *p*-aminosalicylate molecule is a tridentate ligand in complexation to sodium **V**, bridging three different sodium atoms whereas it displays bidentate coordination to a single calcium atom in **I** and monodentate coordination to magnesium **III**. The *ortho* hydroxy group binds to the cation in **V** but not in **I** or **III**. Consideration of the packing of molecules in the unit cell (Fig. 7) shows sodium atoms bridged in pairs by two water molecules (Na...Na, 3.47 Å). Pairs of sodium atoms are linked in series by bridging *p*-aminosalicylate molecules ligated via carboxylate and *ortho* hydroxy function. Sodium atoms thus connected lie in belts which are cross linked by sodium binding to nitrogen atoms of amino groups. Thus sodium and calcium complexation in extended arrays may be contrasted with the isolated complexes observed with magnesium.

Supplementary Material

Tables of anisotropic thermal parameters, hydrogen positions and listing of F_{obs} and F_{calc} structure factors are available from the authors.

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References

1 W. Kazimierczak and B. Diamant, in P. Kallos, B. H. Waksman and A. L. de Weck (eds.), *Progress in Allergy*, Vol. 24, Karger, Basel, 1978.

2 L. M. Lichtenstein, in F. H. Bach and R. Good (eds.), *Clinical Immunology*, Academic Press, New York, 1972.

3 D. E. Cochrane and W. W. Douglas, *Proc. Natl. Acad. Sci., U.S.A., 71* (1974) 408.

4 T. Kanno, D. E. Cochrane and W. W. Douglas, *Can. J. Physiol., 51* (1973) 1001.

5 L. B. Cole and E. M. Holt, *J. Bioinorg. Chem., 108* (1985) 159.

6 L. B. Cole and E. M. Holt, *Inorg. Chim. Acta*, in press.

7 L. B. Cole and E. M. Holt, *Inorg. Chim. Acta, 137* (1987) 137.

8 R. Helems, L. B. Cole and E. M. Holt, *Inorg. Chim. Acta, 152* (1988) 9.

9 L. B. Cole and E. M. Holt, *J. Chem. Soc., Perkin Trans. II*, (1986) 1997.

10 B. B. Huff (ed.), *Physicians Desk Reference*, Charles R. Baker, New Jersey, 32nd edn., 1978.

11 R. B. Martin, Bioinorganic Chemistry of Calcium, in H. Siegel (ed.), *Metal Ions in Biological Systems*, Vol. 17, Marcel Decker, New York, 1984, Ch. 1.

12 P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. DeClercq and M. M. Wolfson, *MULTAN*, University of York, U.K., 1980.

13 J. M. Stewart (ed.), *The X-ray System, Technical Report TR446*, Computer Center, University of Maryland, College Park, MD, 1980.

14 D. T. Cromer and I. B. Mann, *Acta Crystallogr., Sect. A, 24* (1968) 321.

15 J. A. Ibers and W. C. Hamilton, *International Tables for X-Ray Crystallography*, Vol. IV, Kynoch Press, Birmingham, 1974.

16 G. Strahs and R. E. Dickerson, *Acta Crystallogr., Sect. B, 24* (1968) 571.