Calcium Complexes of Mixed Ligands: $Ca_2(acetate)_4(HOH)_2$ and $Ca_{1.5}(salicylate)_2(acetate)(HOH)_2(acetic\ acid)$

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Abstract

The single crystal X-ray structures of $Ca_2(acetate)_4(HOH)_2$ **(I)** $Ca_2C_8H_{16}O_{10}$, $a = 6.737(4)$, $b = 10.237(8)$, $c = 12.288(10)$ Å, $\alpha = 81.75(1)$, $\beta = 86.21(1)$, $\gamma = 112.71(1)^\circ$, $V = 766.5(1)$ Å^3, $D_{calc} = 1.526$ g cm^{-3}, $Z = 2$, triclinic space group $P\bar{1}$ and $Ca_{1.5}(salicylate)_2(acetate)(HOH)_2(acetic\ acid)$ **(II)** $Ca_{1.5}C_{18}H_{21}O_{12}$, $a = 14.778(7)$, $b = 8.183(3)$, $c = 19.556(7)$ Å, $\beta = 115.15(3)^\circ$, $V = 2142.2(15)$ Å^3, $D_{calc} = 1.517$ g cm^{-3}, $Z = 4$, monoclinic space group $P2_1/n$ have been determined. Each structure has two calcium sites of differing coordination number per asymmetric unit. Seven and eight coordinate calcium are found in **I**, six and seven coordinate calcium in **II**. The structures display a variety of modes of carboxylate binding which link calcium atoms together in layers.

Introduction

Calcium has been demonstrated to be a necessary participant in chemically mediated histamine release [1–3]. Studies have shown that whereas mast cells challenged with allergen do not release histamine in the absence of calcium, exodus is observed on restoration of calcium concentration [2]. Other work suggests that the role calcium plays in allergic manifestations requires calcium transport into the cell. Direct injection of calcium into the mast cell triggers histamine release [4]. Mast cells challenged with calcium in the presence of known calcium ionophores release histamine in the absence of allergen [2].

Calcium has been shown to bind to histamine itself [5] in a 1:2 complex, $CaCl_4(H_2O)_2CaCl_2(H_2O)_2(histamine)_2$, in which one calcium atom binds to two water molecules, two chloride atoms and to the nitrogen atoms alpha to the side chains of two histamine imidazole rings (and not to the protonated nitrogen atoms of the aminoethyl side chains). A second complex in which the unprotonated side chain amine group displaces a bound chloride from calcium seems likely. An increase in calcium concentration has not been reported in mast cells which have released histamine and thus a calcium-histamine complex may be operative in calcium and histamine egress from the mast cell.

Comparison of calcium and magnesium complexation to allergens; nicotinic acid [6] and para-aminosalicylate [7] has demonstrated that these low molecular weight allergens crystallize with calcium atoms lying in layers and bridged by carboxylate ions or water molecules. Varying geometries and coordination numbers are displayed for calcium. Calcium appears capable of movement within these layers from one set of ligands to another with little disruption of the bonding ligands. Thus these structures are perhaps representative of calcium behavior in an environment similar to that of the channels in a cell wall. Calcium tends to maximize use of ligation sites, organizing ligands such that all unshared pairs of electrons are pulled inward and the bound ligands turn a nonpolar facade to the surrounding environment. This view of calcium complexation is also supported by solid state observation [8] of the calcium/penicillin V complex, calcium(phenoxymethylpenicillinate)$_2(H_2O)_2$, in which calcium binds to carboxyl and amide carbonyl oxygen atoms. Magnesium, on the other hand, forms discrete and isolated complexes with nicotinic acid and para-aminosalicylate, coordination at magnesium deviating little from idealized octahedral geometry. Thus the inability of magnesium to replace calcium in the mechanistic sequence of histamine release may be due to its rigid geometrical requirements or to its formation of isolated complexes. Both alkaline earth metals tend to include water molecules in their coordination spheres irrespective of the identities of other available ligands.

These simple ideas represent the extent of knowledge of calcium participation at a molecular level in the allergy sequence. It is of importance to evaluate calcium binding to molecules which offer ligation sites appropriate to biological systems in order to develop more specific expectations of calcium behavior in such systems.

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Calcium binding to carboxylate groups has been well documented with monodentate, bidentate and alpha (involving a single carboxylate oxygen and an alpha substituent as a bidentate ligand) modes predominating in carboxylate–calcium interactions in the solid state [9, 10]. Most of the crystalline calcium–carboxylate systems that have been subjected to single crystal X-ray characterization, involve simultaneous ligation to water as well as to carboxylate groups. Thus structures such as calcium tartrate·$4H_2O$ [11], calcium glutamate·$3H_2O$ [12], calcium(glutamate)$_2$·$4H_2O$ [13] and calcium(cycloheptanecarboxylate)·$5H_2O$ [14] are common. Mixed ligand complexes in which calcium is complexed to more than one type of ligand other than H_2O (and ignoring halide complexes) are relatively rare. The few that come to light are Ca(acetate)(thioacetate)·$3H_2O$ [15], and calcium(benzo-15-crown-5)$_2$(3,5-dinitrobenzoate)$_2$(HOH)$_3$ [16]. The structural chemistry of calcium in these mixed ligand systems may not be relevant to the structural chemistry of calcium in many biological systems because the ligands are not typical of those found *in vitro*. Calcium shows a broad range of coordination numbers (6–10) and it is reasonable to speculate that its binding in such a situation may be to a combination of available ligands. We have prepared a series of complexes from mixed ligand syntheses to examine the structural patterns of these complexes and report here the solid state structures of Ca_2(acetate)$_4$-$(H_2O)_2$ **(I)** and the mixed ligand complex $Ca_{1.5}$-(salicylate)$_2$(acetate)$(H_2O)_2$(acetic acid) **(II)**.

Experimental

Crystals of Ca_2(acetate)$_4$(HOH)$_2$ **(I)** were grown over a long period of time from a solution of acetic acid in water to which $CaCl_2$ and histamine hydrochloride were added in 1:1 stoichiometry. The clear colorless needles were air stable.

$Ca_{1.5}$(salicylate)$_2$(acetate)(HOH)$_2$(acetic acid) **(II)** was prepared by dissolving 0.7909 g (5 mmol) of Ca(acetate)$_2$ and 1.8015 g (10 mmol) of acetylsalicylic acid in 40 ml of 75% aqueous methanol solution with stirring. The solution was allowed to stand at room temperature for several weeks, yielding clear, colorless plates.

Crystals of **I** and **II** were mounted on a Syntex P3 automated diffractometer. Unit cell dimensions (Table I) were determined by least squares refinement of the best angular positions for fifteen independent reflections ($2\theta > 15°$) during normal allignment procedures using molybdenum radiation (λ = 0.71069 Å). Data, (3915 points **(I)**; 5391 points **(II)**) were collected at room temperature using a variable scan rate, a θ–2θ scan mode and a scan width of 1.2° below $K\alpha_1$ and 1.2° above $K\alpha_2$ to a maximum 2θ value of 50.0°. 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 that 6% variation, corrections for decomposition were deemed unnecessary. Data were corrected for Lorentz, polarization and background effects. After removal of redundant data, (and space group forbidden data for **II** only) observed data, (2297 points **(I)**, 2576 points **(II)**) ($I > 3.0\sigma(I)$) was used for solution and refinement. The structures were solved for heavy atom positions using direct methods [17]. Successive cycles of least squares refinement and difference Fourier syntheses allowed location of the remainder of the nonhydrogen atoms. Least squares refinement [18] converged with anisotropic thermal parameters. Hydrogen positions were not located for **I**. For **II**, the hydrogens of the aromatic ring and those attached to water oxygen atom O21 were located from a difference Fourier synthesis. These ten hydrogen positions were included in the final refinement with isotropic thermal parameters but held invariant. A difference Fourier revealed no electron density of interpretable level. Scattering factors were taken from Cromer and Mann [19]. The final cycle of refinement–function minimized $\Sigma(|F_o| - |F_c|)^2$, led to final agreement factor, R = 6.4% **(I)**; 7.8% **(II)**, $R = (\Sigma \| F_o| - |F_c \| / \Sigma |F_o|) \times 100$. Unit weights were used throughout. Tables II and III list positional parameters. Tables IV and V show bond angles and distances.

TABLE I. Crystal Data for Ca_2(acetate)$_4$(HOH)$_2$ **(I)** and $Ca_{1.5}$(salicylate)$_2$(acetate)(HOH)$_2$(acetic acid) **(II)**

	I	II
Formula	$Ca_2C_8H_{16}O_{10}$	$Ca_{1.5}C_{18}H_{21}O_{12}$
MWT	352.4	489.5
a (Å)	6.735(4)	14.778(7)
b (Å)	10.237(8)	8.183(3)
c (Å)	12.288(10)	19.556(7)
α (°)	81.75(1)	90.0
β (°)	86.21(1)	115.15(3)
γ (°)	112.71(1)	90.0
V (Å^3)	766.5(1)	2142.2(15)
F(000)	368	1020
μ(Mo Kα) (cm^{-1})	7.64	4.61
λ(Mo Kα) (Å)	0.71069	0.71069
D_{calc} (g cm^{-3})	1.526	1.517
Z	2	4
Obs. refl.	2297	2576
R (%)	6.4	7.8
Space group	$P\bar{1}$	$P2_1/n$

TABLE II. Positional Parameters for $Ca_2C_8H_{16}O_{10}$ (I)

Atom	$x(\sigma(x))$	$y(\sigma(y))$	$z(\sigma(z))$
Ca1	0.2241(2)	0.4426(1)	0.5963(1)
Ca2	−0.3761(2)	0.1658(1)	0.5849(1)
C10	0.1068(10)	0.1345(7)	0.6129(6)
C11	0.9902(13)	0.0259(9)	0.3449(8)
C20	0.6119(10)	0.2145(7)	0.3475(6)
C21	0.6043(15)	0.2455(10)	0.2239(7)
C30	0.7369(10)	0.4850(7)	0.6497(6)
C31	0.2364(15)	0.4894(12)	0.2337(8)
C40	0.1088(12)	0.2992(9)	0.8746(7)
C41	0.1980(24)	0.3507(16)	0.9800(9)
O1	0.7767(12)	−0.0011(9)	0.0884(7)
O8	0.6125(9)	0.1288(7)	0.7779(5)
O10	−0.0158(7)	0.1964(5)	0.5823(4)
O11	0.3075(7)	0.2063(5)	0.6102(5)
O20	0.5218(8)	0.0867(5)	0.4007(4)
O21	0.7100(8)	0.3162(5)	0.3973(4)
O30	0.8423(7)	0.4256(5)	0.6031(4)
O31	0.3857(7)	0.4682(6)	0.4032(4)
O40	0.1820(9)	0.3864(6)	0.7860(5)
O41	0.9702(9)	0.1744(7)	0.8845(5)

TABLE III. Positional Parameters for $Ca_{1.5}$(salicylate)$_2$-(acetate)$(HOH)_2$(acetic acid) (II)

	x	y	z
Ca1	1.0000	0.0000	1.0000
Ca2	0.7923(1)	−0.0215(2)	0.7748(1)
C1	0.8533(6)	0.2288(12)	0.6737(4)
C2	0.9031(6)	0.2300(11)	0.6208(4)
C3	0.8752(6)	0.3442(12)	0.5618(4)
C4	0.4273(8)	0.1534(15)	0.0161(5)
C5	0.5015(8)	0.2605(17)	0.0278(6)
C6	0.0277(8)	0.1232(16)	0.5846(6)
C7	0.9778(7)	0.1193(13)	0.6317(5)
O1	0.8888(4)	0.1390(8)	0.7309(3)
O2	0.7783(5)	0.3211(9)	0.6590(3)
O3	0.3003(5)	0.0482(9)	0.0466(4)
C11	0.9681(6)	0.1299(11)	0.1409(4)
C12	0.9196(6)	0.1918(11)	0.1884(4)
C13	0.8188(7)	0.1625(13)	0.1695(5)
C14	0.7759(8)	0.2246(15)	0.2169(6)
C15	0.8340(9)	0.3130(15)	0.2803(6)
C16	0.9338(9)	0.3432(15)	0.2999(6)
C17	0.9760(7)	0.2790(13)	0.2542(5)
O10	0.9173(4)	0.0513(9)	0.0820(3)
O11	0.0597(4)	0.1605(8)	0.1603(3)
O13	0.7591(5)	0.0793(10)	0.1074(4)
O22	0.8564(4)	0.1104(8)	0.9014(3)
O23	0.7406(4)	0.2478(8)	0.8105(3)
C20	0.2954(6)	0.2722(11)	0.3806(4)
C21	0.2835(8)	0.1633(13)	0.4382(5)
O32	0.5487(5)	0.1257(12)	0.3827(4)
O33	0.5856(5)	0.2598(11)	0.2993(4)
C30	0.6096(8)	0.1630(15)	0.3594(6)
C31	0.7170(8)	0.1007(18)	0.3915(6)
O21	0.6316(4)	0.0313(8)	0.6768(3)
O31	0.0669(6)	0.2665(10)	0.0188(3)

TABLE IV. Bond Angles (°) and Distances (Å) for $Ca_2C_8H_{16}O_{10}$ (I) [a]

Ca1–O10	2.451(5)	C11′–C10–O10	119.4(6)
Ca1–O11	2.672(7)	C11′–C10–O11	120.1(7)
Ca1–O30′	2.773(6)	O10–C10–O11	120.5(6)
Ca1–O31	2.479(6)	C21–C20–O20	120.0(7)
Ca1–O21′	2.348(6)	C21–C20–O21	120.1(6)
Ca1–O31′	2.427(5)	O20–C20–O21	120.0(7)
Ca2–O11″	2.332(6)	C31–C30–O30	120.8(8)
Ca2–O30	2.547(2)	C31–C30–O31′	118.6(8)
Ca2–O20	2.559(2)	O30–C30–O31′	120.5(7)
Ca2–O8″	2.339(6)	C41–C40–O40	117.0(7)
Ca2–O10	2.322(5)	C41–C40–O41′	117.9(8)
Ca2–O20″	2.359(6)	O40–C40–O41′	125.1(8)
Ca2–O21″	2.477(5)		
C10–O10	1.265(10)		
C10–O11	1.260(7)		
C10–C11′	1.508(10)		
C20–O20	1.263(8)		
C20–O21	1.265(9)		
C20–C21	1.515(12)		
C30–O30	1.258(10)		
C30–O31′	1.273(10)		
C30–C31	1.503(12)		
C40–O40	1.239(9)		
C40–O41′	1.240(9)		
C40–C41	1.539(15)		

[a]Symmetry transformations: ′ = $1-x$, $1-y$, $1-z$; ″ = $-1+x, y, z$.

TABLE V. Bond Angles and Distances for $Ca_{1.5}$(salicylate)$_2$-(acetate)$(H_2O)_2$(acetic acid) (II) [a]

Ca1–O10	2.431(7)	O10–Ca1–O22	93.3(2)
Ca1–O22	2.359(5)	O10–Ca1–O31	88.1(5)
Ca1–O31	2.359(8)	O22–Ca1–O31	86.9(2)
Ca2–O1	2.354(8)	O1–Ca2–O2′	169.2(2)
Ca2–O2′	2.361(8)	O1–Ca2–O11″	84.0(2)
Ca2–O11″	2.310(6)	O1–Ca2–O22	94.9(2)
Ca2–O22	2.490(6)	O1–Ca2–O23	85.1(2)
Ca2–O23	2.526(7)	O1–Ca2–O23′	99.2(2)
Ca2–O23′	2.426(6)	O1–Ca2–O21	99.1(2)
Ca2–O21	2.373(5)	O2′–Ca2–O11″	88.0(2)
C1–O1	1.25(1)	O2′–Ca2–O22	76.2(2)
C1–O2	1.27(1)	O2′–Ca2–O23	93.9(3)
C1–C2	1.50(1)	O2′–Ca2–O23′	86.9(2)
C2–C3	1.40(1)	O2′–Ca2–O21	91.1(2)
C3–O3	1.34(1)	O11″–Ca2–O22	78.1(2)
C3–C4	1.41(2)	O11″–Ca2–O23	127.2(2)
C4–C5	1.35(2)	O11″–Ca2–O23′	82.0(2)
C5–C6	1.39(2)	O11″–Ca2–O21	157.4(2)
C6–C7	1.40(2)	O22–Ca2–O23	51.6(2)
C7–C2	1.37(2)	O22–Ca2–O23′	154.3(2)
C11–O10	1.25(1)	O22–Ca2–O21	123.5(2)
C11–O11	1.27(1)	O23–Ca2–O23′	150.8(2)
C11–C12	1.48(1)	O23–Ca2–O21	75.4(2)
C12–C13	1.40(1)	O23′–Ca2–O21	75.4(2)
C13–O13	1.34(1)	O1–C1–O2	123.2(10)

(continued)

Table V. (*continued*)

C13–C14	1.42(2)	O1–C1–C2	118.4(8)
C14–C15	1.38(1)	O2–C1–C2	118.4(8)
C15–C16	1.38(2)	C1–C2–C3	120.7(8)
C16–C17	1.39(2)	C1–C2–C7	119.1(8)
C17–C12	1.39(1)	C3–C2–C7	120.2(10)
C20–O22	1.26(1)	C2–C3–C4	118.8(9)
C20–O23	1.27(1)	C2–C3–O3	123.0(10)
C20–C21	1.50(2)	C4–C3–O3	118.1(9)
C30–O32	1.21(2)	C3–C4–C5	120.7(10)
C30–O33	1.33(1)	C4–C5–C6	120.8(12)
C30–C31	1.52(2)	C5–C6–C7	119.6(11)
		C6–C7–C2	119.7(10)
		C10–C11–O11	121.6(9)
		O10–C11–C12	119.4(7)
		O11–C11–C12	119.1(7)

[a]Symmetry transformations: ' = 1.5 − *x*, −0.5 + *y*, 1.5 − *z*; " = 1 − *x*, −*y*, 1 − *z*.

Discussion

In $Ca_2(acetate)_4(HOH)_2$ (I), (Fig. 1) two calcium atoms with approximately the same *z* coordinate (Ca1, *z* = 0.5963, Ca2, *z* = 0.5849) and their symmetry related atoms at *z* aver. 0.409 form a network of calcium atoms (minimum separation 3.93 Å) lying on two close layers perpendicular to the *c* axis and separated from calcium atoms on similar bilayers in adjacent cells by more than 5.5 Å. Calcium atoms are linked by a network of bridging acetate groups. Three different modes of acetate binding are seen, involving acetate binding to one or three or four different calcium atoms (Fig. 2). Acetate 10 links calcium atoms in series parallel to the *x* axis

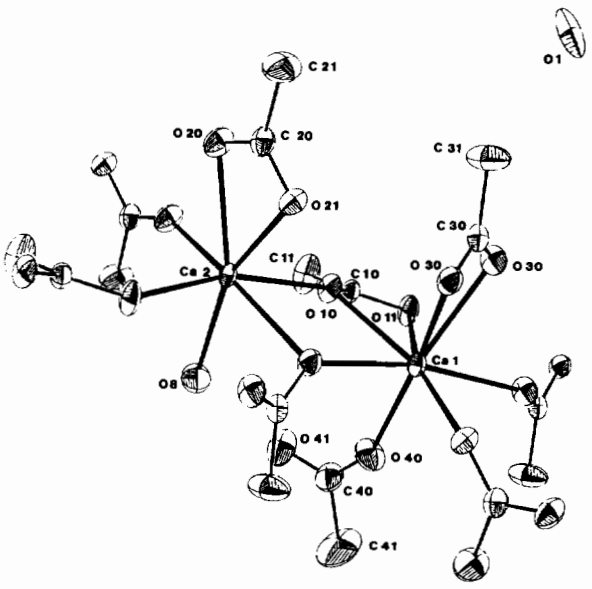

Fig. 1. Coordination spheres of Ca1 and Ca2 of I.

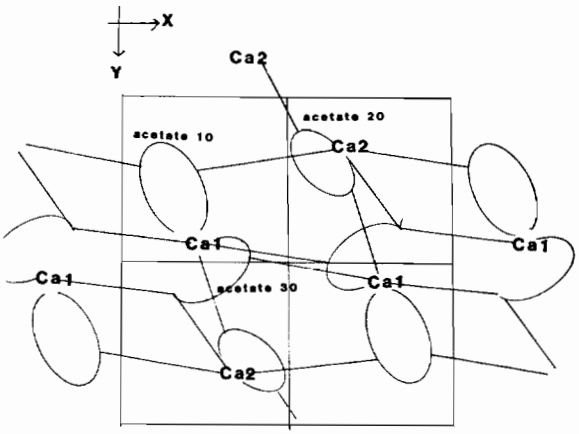

Fig. 2. Schematic unscaled view of packing of I showing cross linking of calcium atoms into continuous sheet. Monodentate acetate 40 and water molecules have been omitted. Carboxylate groups are represented by ovals discontinuous at the calcium atom to which they are bound. Additional binding to adjacent calcium atoms is represented by straight lines.

of the cell, being bidentate in ligation to Ca1. Each carboxylate oxygen atom binds as well to one of two different Ca2 atoms (related by *x*, *y*, *z*; 1 + *x*, *y*, *z*). Acetate 30 is found linking four different calcium atoms which lie on two lines parallel to the *a* axis. O30 is bound to a Ca1 atom (−*x*, 1 − *y*, 1 − *z*, 2.504(2) Å) and a Ca2 atom (1 − *x*, 1 − *y*, 1 − *z*, 2.547(2) Å). O31 links a Ca1 atom (1 − *x*, 1 − *y*, 1 − *z*, 2.428(2) Å) to a second Ca1 atom, (*x*, *y*, *z* 2.479(2) Å). Acetate 30 shows incipient bidentate bridging to Ca1, Ca1–O30, 2.772(2) Å. Acetate 20 is bidentate to Ca2 but bridges a Ca1 atom and a symmetry related Ca2 atom on a diagonal of the *xy* plane. A second diagonal linkage is provided by the 40 acetate which is bound to Ca1 via carboxylate oxygen, O41, but hydrogen bonded to the water molecule oxygen atom, O8, which is bound to Ca2. Thus two of the acetate molecules act as tetradentate ligands, linking a total of 3 calcium atoms. A third tetradentate acetate molecule binds four different calcium atoms. The 40 series acetate molecule serves as a monodentate ligand to calcium. Ca1 is eight coordinate and Ca2 is eight coordinate. A second water molecule in the unit cell is not coordinated to calcium but hydrogen bonded to the oxygen atom of the coordinated water molecule. The line between calcium atoms is uncrowded with ligands and lined with oxygen atoms. It seems likely that calcium atoms might move from one ligand set (Ca1 set) to another (Ca2 set) with only slight twisting of acetate groups necessary to provide a suitable ligand environment at positions intermediate between the Ca1 and Ca2 sites.

In (II), $Ca_{1.5}$(salicylate)$_2$(acetate)$(H_2O)_2$ acetic acid, Ca1 lies on an inversion center and is six coordinate, binding to two water oxygen atoms, two oxygen atoms of the single oxygen donor carboxylate groups of two different salicylate anions and two oxygen atoms from two different acetate carboxylate groups. Ca2 coordinates to the oxygen atom of a water molecule, to a bidentate acetate group and to three different single oxygen donor carboxylate (salicylate) groups. Ca2 is seven coordinate (Fig. 3). The pattern of binding is better understood in a schematic view (Fig. 4). Calcium atoms are grouped in trimeric linear arrays (Ca2, x, y, z; Ca1 1.0, 0.0, 1.0; Ca2 $2.0 - x, -y, 2.0 - z$) with each Ca1–Ca2 pair bridged by a O10, O11, O13, C11–C17 salicylate carboxylate group. Ca1–Ca2, 4.15 Å. These calcium trimeric units are then cross linked into sheets with the central Ca1 atom of each trimer lying on a single 101 plane. Cross linking is accomplished by the acetate molecules which bind a single Ca2 in bidentate fashion, directing a pair of electrons towards the adjacent Ca1 and also binding to a Ca2 atom related by $1.5 - x, -0.5 + y, 1.5 - z$, (Ca2–Ca2′ separation, 4.26 Å). Thus each acetate molecule links three different calcium atoms. The same two Ca2 atoms are also cross linked by salicylate O1, O2, O3, C1–C7

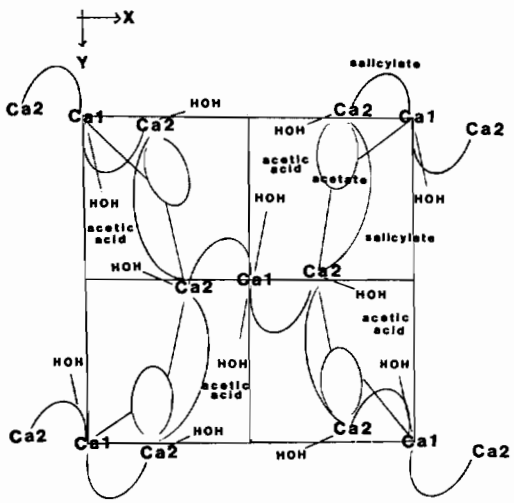

Fig. 4. Schematic unscaled view of a single 101 plane showing cross linking of acetate and salicylate groups and the projection of bound water molecules towards acetic acid molecules in the crystal lattice.

which is involved only with the two calcium atoms. Each calcium trimer is thus linked to 4 other triplets by these bridging acetate and salicylate interactions. The calcium motif thus resembles a chain linked

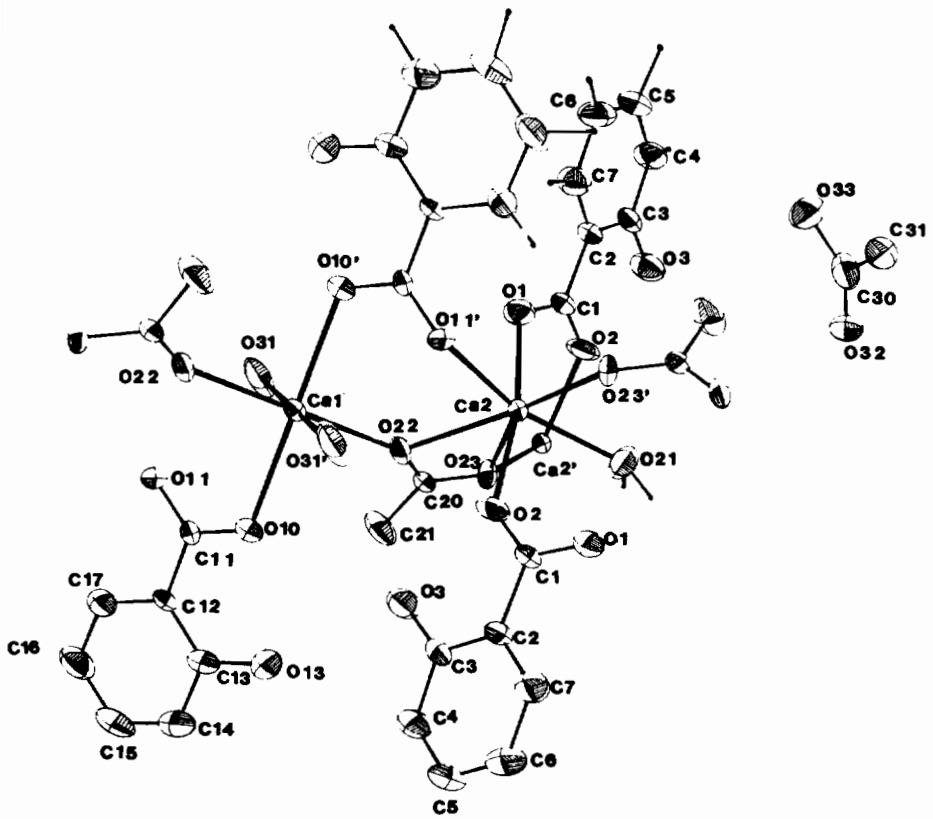

Fig. 3. Coordination spheres of calcium atoms of II.

fence with acetic acid molecules lying above and below the open spaces in the array and held in place by hydrogen bonding to calcium bound water molecules. The hydroxyl oxygen atoms are not involved in binding to calcium.

Both **I** and **II** are layer structures in which calcium atoms lie in close proximity, bridged in twos, threes and fours by carboxylate groups. Hydrogen bonding occurs between molecules in the calcium coordination sphere and does not link layers of calcium bound ligands. Analysis of the acetate *vs.* acetate/salicylate binding is complicated by the introduction of a molecule of acetic acid in the cell of **II**.

The details of **I** and **II** may be compared with those of Ca(salicylate)$_2$·2H$_2$O in which Ca lies on a two-fold axis and is eight coordinate. Further details of binding are unreported [20] by this group but a more complete solution in the same unit cell and space group [21] reports atom coordinates from which the binding pattern can be seen (Fig. 5). Calcium atoms are linked in series parallel to the *z* direction (Ca separation 3.99 Å) with two salicylate groups showing bidentate coordination to each calcium atom and one carboxylic oxygen atom of each carboxylate group showing a bonding distance to an adjacent but different calcium atom. In this manner the two salicylate ligands link a single calcium atom to two calcium neighbors $x, -y, \frac{1}{2}+z$ and $x, -y, -\frac{1}{2}+z$. The ortho hydroxyl group shows a hydrogen bonding interaction with the remaining carboxylic oxygen presumably inhibiting its lone pair from a binding interaction with a second calcium atom. Thus each salicylate molecule shows binding interaction with three different calcium atoms and not to four. Two water molecules complete the eight fold coordination of calcium. The overall binding is that of strands of calcium atoms bridged by ligand.

The simple linear strands of Ca and salicylic acid as seen in Fig. 5 have given way to a more complicated pattern in **II**, in which the variety of available ligands has permitted calcium binding of a more varied and complicated nature. Similarly the smaller acetate ligand of **I** compared to the bulky salicylic acid has permitted a higher density of ligand to calcium atoms in **I**.

The ligand binding seen in **I** and **II** and in Ca(salicylate)$_2$(H$_2$O)$_2$ is different from that seen with glutamate and aspartate residues which are common sites of calcium binding in proteins. In these structures [12, 22, 23], Ca(glutamate)·3H$_2$O, Ca(glutamate)$_2$·4H$_2$O, and Ca(glutamate)chloride monohydrate, there are no tetradentate carboxylate bridges between calcium atoms. Monodentate carboxylate binding is common. Two carboxylate groups of a single dicarboxylic acid or a carboxylate group and an amine group of a single glutamate may each

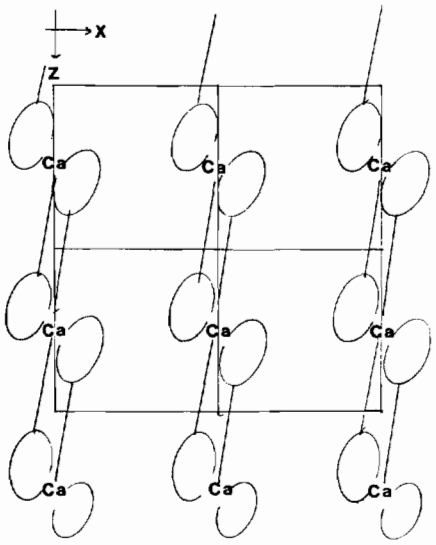

Fig. 5. Schematic unscaled view of the cross linking of calcium atoms into chains in Ca(salicylate)$_2$(H$_2$O)$_2$ using the coordinates of ref. 21.

serve as monodentate ligands to one or perhaps two calcium atoms. Thus a single amino acid links three calcium atoms at a maximum. The only instance of tridentate carboxylate binding in the three structures occurs in glutamate trihydrate. Hydrogen bonds occupy the remaining unshared pairs of the carboxylate oxygen atoms. In these structures calcium atoms are widely separated (4.792, 7.562 and 3.840 Å, respectively) and surrounded with noninteractive atoms of the ligand. The organization of calcium atoms in layers is not observed. Hydrogen bonding interactions are prevalent. These differences may be indicative of a fundamental difference between Ca behavior in protein environments and in situations where smaller molecules offering only carboxylate ligation are present.

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Supplementary Material

Anisotropic thermal parameters, hydrogen positional parameters for **II**, and structure factor tables are available from the authors on request.

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