Metal Ion Binding by Amino Acids

Preparation and Crystal Structures of two Calcium L-Aspartate Hydrates

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Crystalline calcium(II) L-aspartate dihydrate, Ca(L-Asp) · $2H_2O$ (**2**), has been obtained in a three-step procedure from $CaCO_3$ and L-aspartic acid L-$AspH_2$ via calcium bis(L-hydrogenaspartate) Ca(L-$AspH)_2$ and calcium hydrogen L-aspartate chloride dihydrate Ca(L-AspH)Cl · $2H_2O$. The crystals of **2** are orthorhombic, space group $P2_12_12_1$. The structure is a coordination polymer with the metal atoms arranged in double chains interconnected by aspartate dianions. Each Asp^{2-} ligand is coordinated to the metal ion as a N,O_α,O_β tripod. In addition, two water molecules and three β-carboxylate oxygen atoms from neighbouring units are also coordinated to each metal atom, giving a coordination number of eight for each calcium. The β-carboxylate oxygen atoms form also a bridge between metals of a parallel chain of metal atoms. – A crystalline tetrahydrate (monoclinic, space group $C2$) Ca(L-Asp) · $4H_2O$ (**1**) has been prepared from L-$AspH_2$ and $Ca(OH)_2$. The structure contains two molecules in the asymmetric unit. Each calcium atom is seven-coordinate and surrounded by an N,O_α-chelating L-Asp^{2-} ligand, four water molecules, and one oxygen atom of the β-carboxylate group of a neighbouring molecule. Due to this interaction, the monomeric units are linked to give a one-dimensional coordination polymer chain. – In both structures the double strands and chains, respectively, are cross-linked by a network of hydrogen bonds.

Bindung von Metall-Ionen durch Aminosäuren. – Darstellung und Kristallstrukturen zweier Calcium-L-aspartat-Hydrate

Aus L-Asparaginsäure L-$AspH_2$ und $CaCO_3$ wurde in einer dreistufigen Synthese über Calcium-bis(L-hydrogenaspartat) Ca(L-$AspH)_2$ und Calcium-(L-hydrogenaspartat)-chlorid-Dihydrat Ca(L-AspH)Cl · $2H_2O$ ein kristallines Calcium-L-aspartat-Dihydrat Ca(L-Asp) · $2H_2O$ (**2**) erhalten. In den orthorhombischen Kristallen, Raumgruppe $P2_12_12_1$, liegen Doppelstränge von Calciumatomen vor, die über die Liganden L-Asp^{2-} verknüpft sind. Jedes Dianion L-Asp^{2-} fungiert als N,O_α,O_β-Tripod für ein Calcium-Ion, welches seinerseits an drei weitere Sauerstoffatome von β-Carboxylatgruppen benachbarter Einheiten koordiniert ist. Zusammen mit zwei Wassermolekülen ergibt sich für die Metallzentren die Koordinationszahl acht. Die β-Carboxylatgruppen wirken dabei in den Nachbarsträngen nicht nur chelatisierend, sondern auch metallverbrückend. – Aus L-$AspH_2$ und $Ca(OH)_2$ konnte ein kristallines Tetrahydrat (monoklin, Raumgruppe $C2$) Ca(L-Asp) · $4H_2O$ (**1**) gewonnen werden. Die Struktur enthält zwei Moleküle in der asymmetrischen Einheit. Jedes der beiden Calciumatome ist hier in vergleichbarer Weise siebenfach koordiniert durch einen zweizähnig (N,O_α) wirkenden Liganden Asp^{2-}, vier Wassermoleküle und ein Sauerstoffatom der β-Carboxylatgruppe einer benachbarten Einheit. Durch diese zusätzliche Komplexbildung werden die Monomeren zu einem eindimensionalen Koordinationspolymeren verknüpft. Die Ketten sind – ebenso wie die Doppelstränge des Dihydrats – über Wasserstoffbrücken weiter vernetzt.

Among the naturally occuring α-amino acids the two acidic dicarboxylic species – aspartic and glutamic acid – play a special role in metal binding by complexation$^{1-3)}$. Although the stability constants of the coordination compounds of these acids with important metal ions such as Mg^{2+} or Ca^{2+} are relatively low$^{4)}$, the corresponding complexes are extremely important for metal transport, temporary metal fixation, and template functions$^{5)}$.

Metal complexation by aspartic and glutamic acid from aqueous solution is strongly dependent on temperature, concentration and pH. In order to obtain further insight into the structure and stability of these complexes under different conditions, we have initiated structural investigations of the alkaline earth metal complexes of the two acids as a function of the parameters outlined above. In the present study we describe the preparation and crystal structure analysis of Ca(L-Asp) · $2H_2O$ (**2**) and Ca(L-Asp) · $4H_2O$ (**1**). These two hydrates of calcium L-aspartate appear to be the predominant species in contact with basic solutions containing calcium and L-aspartate ions. The structure of a complex Ca(L-Glu) · $3H_2O$ has already been reported$^{6)}$, while we have presented results on magnesium, strontium, and barium L-glutamate, which crystallise as tetra- (Mg) and hexahydrates (Sr, Ba)$^{7)}$. Furthermore, we have elucidated the structure of the corresponding magnesium L-aspartate, which crystallises as a trihydrate$^{8)}$.

Results and Discussion

Surprisingly the attempts to obtain a "basic" calcium L-aspartate, Ca(L-Asp), described in this paper, yielded two different crystalline hydrates, a dihydrate and a tetrahydrate. The *dihydrate*, Ca(L-Asp) · $2H_2O$ (**2**), was obtained from the "acidic" L-aspartate Ca(L-$AspH)_2$ via L-aspartate chloride

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Ca(L-AspH)Cl which on treatment with one equivalent of KOH gave this product (eq. 1 – 3). This dihydrate crystallised very slowly from the resulting aqueous solution, which contained the corresponding quantity of KCl and had been adjusted to pH 10. Once precipitated, the material was only sparingly soluble in water.

$$\mathrm{CaCO_3 + 2\,L\text{-}AspH_2 \rightarrow [Ca(L\text{-}AspH)_2]_{aq} + CO_2 + H_2O} \qquad (1)$$

$$\mathrm{Ca(L\text{-}AspH)_2 + CaCl_2 \rightarrow 2\,[Ca(L\text{-}AspH)Cl]_{aq}} \qquad (2)$$

$$\mathrm{Ca(L\text{-}AspH)Cl + KOH \rightarrow [Ca(L\text{-}Asp)]_{aq} + KCl + H_2O} \qquad (3)$$

The intermediates of the reaction sequence (1 – 3) are known only in the patent literature[9], although Ca(L-AspH)Cl has now been isolated and characterized as a dihydrate. This compound was precipitated from aqueous methanol.

The *tetrahydrate*, Ca(L-Asp) · $4\,H_2O$ (**1**), was obtained on treating solutions of $Ca(OH)_2$ with one equivalent of L-aspartic acid. Crystallisation from these solutions was readily initiated on cooling.

Ca(L-Asp) · $4\,H_2O$ **1** Ca(L-Asp) · $2\,H_2O$ **2**

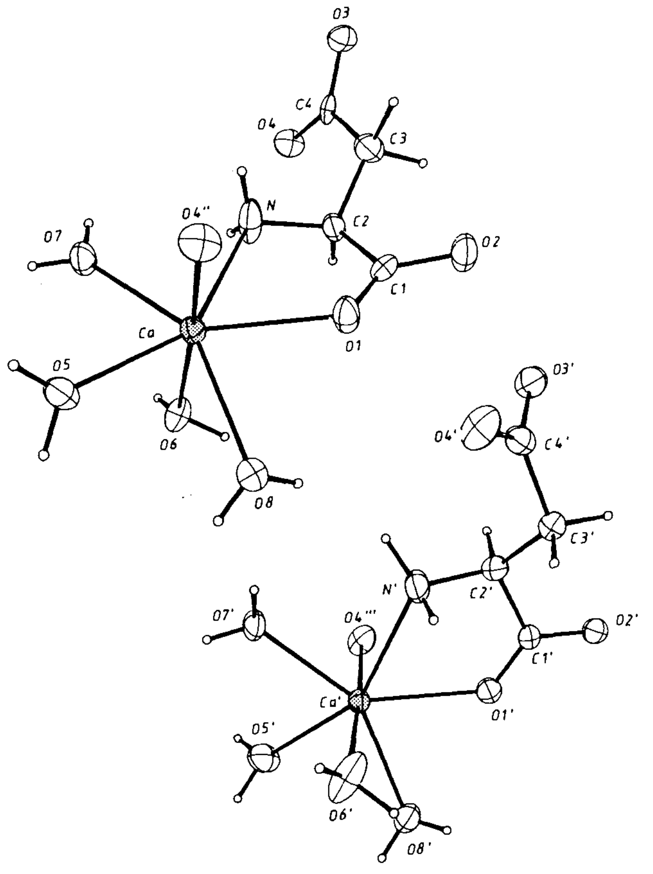

Figure 1. Molecular structures of the two independent calcium centers of Ca(L-Asp) · $4\,H_2O$ (**1**) in the crystal (ORTEP, ellipsoids at the 50% probability level, H atoms with arbitrary radii). The torsion angles O3/O4 – C4 – C3 – C2 are 157.8/ – 22.8 and – 80.7/ 99.6° for both molecules, respectively

The material, once precipitated, dissolves more readily in water than the dihydrate, and in solution has a slightly higher pH (10.5 instead of 10.0).

$$\mathrm{Ca(OH)_2 + L\text{-}AspH_2 \rightarrow [Ca(L\text{-}Asp)]_{aq} + 2\,H_2O} \qquad (4)$$

The reasons for the crystallisation of two different hydrates under the conditions described is not yet clear. The only obvious differences between the two systems are a small variation in pH and the presence or absence of other salts.

Crystal Structure of Ca(L-Asp) · $4\,H_2O$ (1)

The solid state structure of this hydrate consists of complex units of the given stoichiometry (Figure 1). Two molecules per asymmetric unit were found (see Experimental Section). Each calcium atom is seven-coordinate and surrounded by one *N,O*-chelating L-aspartate anion, four water molecules, and an oxygen atom of the β-carboxylate group

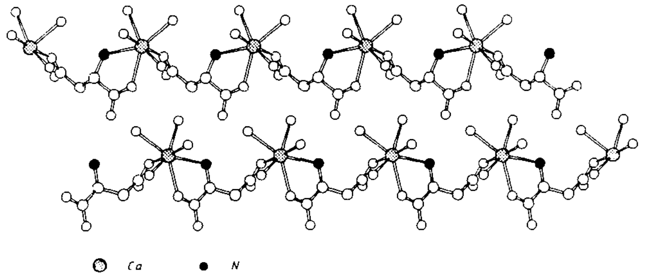

Figure 2. Structure of the two independent polymer chains of Ca(L-Asp) · $4\,H_2O$ (**1**) in the crystal

Table 1. Hydrogen bonds (A --- B ··· C) [Å] of Ca(L-Asp) · $4\,H_2O$ (**1**) and Ca(L-Asp) · $2\,H_2O$ (**2**)

A---B•••C	A--B	B••C	A••C	SYM.OP.
Structure 1				
O5 -H51•••O2'	0.936	1.856	2.777	a
O5 -H52•••O3'	0.868	1.930	2.776	b
O6 -H61•••O2'	0.919	1.877	2.785	c
O6 -H62•••O2	0.947	1.738	2.684	d
O7 -H71•••O3'	0.855	1.939	2.762	c
O7 -H72•••O3'	0.843	2.054	2.881	e
O8 -H81•••O6'	0.866	2.301	3.159	d
O8 -H82•••O1	0.888	1.952	2.833	d
O5'-H5'1••O2	0.918	1.966	2.854	f
O5'-H5'2••O3	0.792	2.053	2.828	g
O6'-H6'1••O2	0.858	1.899	2.738	h
O6'-H6'2••O2'	0.972	1.788	2.754	i
O7'-H7'1••O3	0.879	1.982	2.859	h
O7'-H7'2••O3	0.927	1.787	2.711	j
O8'-H8'1••O6	0.885	2.191	3.075	d
O8'-H8'2••O1'	0.836	2.018	2.847	i
N1'-H1'2••O4	0.982	2.296	3.275	j
Structure 2				
O5 -H51•••O1	0.93	2.25	3.14	k
O5 -H52•••O6	0.87	2.01	2.84	l
O6 -H61•••O2	0.86	1.94	2.75	m
O6 -H62•••O2	0.87	1.93	2.79	n
N -H12•••O1	0.84	2.38	3.21	m

Symmetry operations:
a: X,Y,Z-1
b: 1.5-X,0.5+Y,1-Z
c: X,Y+1,Z-1
d: 2-X,Y,1-Z
e: 1.5-X,1.5+Y,1-Z
f: X,Y,Z
g: 1.5-X,Y-0.5,1-Z
h: X,Y-1,Z
i: 2-X,Y,2-Z
j: 1.5-X,Y-1.5,1-Z
k: 2-X,0.5+Y,1.5-Z
l: X-0.5,0.5-Y,2-Z
m: 2-X,Y-0.5,1.5-Z
n: 1.5-X,-Y,0.5+Z

from a neighbouring molecule. Due to this intermolecular coordination interaction, the monomeric units are linked to give a one-dimensional coordination polymer (Figure 2).

The coordination environment of the calcium is pseudopentagonal bipyramidal, with the chelate ring attached to two equatorial sites and the β-carboxylate oxygen atom of the neighbouring molecule occupying one of the apical positions. The remaining vertices are occupied by water molecules.

Since all four water molecules are already engaged in metal coordination, there is no interstitial water in the crystal. The two coordination polymer chains derived from the two molecules per asymmetric unit are crosslinked by hydrogen bonds between the noncoordinated carboxylate oxygen atoms of the L-aspartate ligand and the water molecules of neighbouring chains (Table 1). This network is very complicated and beyond the scope of the present paper.

Table 2. Distances [Å] and angles [°] for Ca(L-Asp) · $4H_2O$ (1) (esd's in units of the last significant figure in parentheses)

Distances			
Ca -O1	2.409(2)	Ca -O4"	2.314(2)
Ca -O5	2.393(3)	Ca -O6	2.435(3)
Ca -O7	2.398(2)	Ca -O8	2.461(3)
Ca -N1	2.532(4)	O1 -C1	1.238(5)
O2 -C1	1.271(4)	C1 -C2	1.539(5)
C2 -N1	1.478(4)	C2 -C3	1.523(4)
C3 -C4	1.517(5)	C4 -O3	1.266(4)
C4 -O4	1.237(4)	Ca'-O1'	2.434(2)
Ca'-O4*	2.296(2)	Ca'-O5'	2.411(3)
Ca'-O6'	2.396(3)	Ca'-O7'	2.401(2)
Ca'-O8'	2.428(2)	Ca'-N1'	2.548(4)
O1'-C1'	1.253(4)	O2'-C1'	1.263(4)
C1'-C2'	1.526(4)	C2'-N1'	1.468(5)
C2'-C3'	1.531(4)	C3'-C4'	1.518(5)
C4'-O3'	1.252(4)	C4'-O4'	1.262(4)
Angles			
O1 -Ca -N1	65.4(1)	O1 -Ca -O4"	81.3(1)
O1 -Ca -O5	143.5(1)	O1 -Ca -O6	102.7(1)
O1 -Ca -O7	137.4(1)	O1 -Ca -O8	72.5(1)
N1 -Ca -O4"	94.6(1)	N1 -Ca -O5	147.9(1)
N1 -Ca -O6	92.9(1)	N1 -Ca -O7	72.4(1)
N1 -Ca -O8	131.5(1)	O4"-Ca -O5	81.1(1)
O4"-Ca -O6	172.4(1)	O4"-Ca -O7	97.3(1)
O4"-Ca -O8	102.1(1)	O5 -Ca -O6	92.0(1)
O5 -Ca -O7	76.6(1)	O5 -Ca -O8	80.2(1)
O6 -Ca -O7	84.1(1)	O6 -Ca -O8	73.4(1)
O7 -Ca -O8	146.9(1)	Ca -O1 -C1	126.2(2)
Ca -O4"-C4"	151.1(2)	Ca -N1 -C2	115.7(2)
O1 -C1 -O2	123.3(4)	O1 -C1 -C2	118.1(3)
O2 -C1 -C2	118.5(3)	N1 -C2 -C1	109.4(3)
N1 -C2 -C3	112.4(3)	C1 -C2 -C3	111.2(3)
C2 -C3 -C4	117.4(3)	O3 -C4 -O4	124.4(3)
O3 -C4 -C3	114.3(3)	O4 -C4 -C3	121.3(3)
O1'-Ca'-N1'	65.4(1)	O1'-Ca'-O4*	83.0(1)
O1'-Ca'-O5'	140.6(1)	O1'-Ca'-O6'	100.4(1)
O1'-Ca'-O7'	138.7(1)	O1'-Ca'-O8'	71.6(1)
N1'-Ca'-O4*	89.8(1)	N1'-Ca'-O5'	151.1(1)
N1'-Ca'-O6'	90.8(1)	N1'-Ca'-O7'	74.9(1)
N1'-Ca'-O8'	130.6(1)	O4*-Ca'-O5'	83.5(1)
O4*-Ca'-O6'	176.4(1)	O4*-Ca'-O7'	85.7(1)
O4*-Ca'-O8'	108.2(1)	O5'-Ca'-O6'	94.3(1)
O5'-Ca'-O7'	76.5(1)	O5'-Ca'-O8'	77.9(1)
O6'-Ca'-O7'	91.1(1)	O6'-Ca'-O8'	74.0(1)
O7'-Ca'-O8'	149.2(1)	Ca'-O1'-C1'	125.1(2)
Ca'-O4*-C4*	136.3(2)	Ca'-N1'-C2'	116.1(2)
O1'-C1'-O2'	123.3(3)	O1'-C1'-C2'	118.9(3)
O2'-C1'-C2'	117.5(3)	C1'-C2'-N1'	111.3(3)
C1'-C2'-C3'	111.8(3)	N1'-C2'-C3'	112.5(3)
C2'-C3'-C4'	111.1(3)	C3'-C4'-O3'	118.2(3)
C3'-C4'-O4'	118.5(3)	O3'-C4'-O4'	123.4(3)

Symmetry operations:
O4" and O4* were derived from O4 by the operations X, Y-1, Z and X, Y+1, Z respectively.

Bond distances and angles for the structure of the tetrahydrate are listed in Table 2, atomic coordinates and thermal parameters in Table 3.

Table 3. Fractional atomic coordinates and equivalent isotropic thermal parameters for Ca(L-Asp) · $4H_2O$ (1) [$U_{eq} = (U_1 \cdot U_2 \cdot U_3)^{1/3}$, where U_1, U_2, U_3 are the eigenvalues of the U_{ij} matrix; esd's in parentheses]

ATOM	X/A	Y/B	Z/C	U(eq.)
CA	0.87876(3)	0.54876	0.28790(5)	0.017
O1	0.9273(1)	0.6381(5)	0.4693(2)	0.041
O2	0.9384(1)	0.8286(5)	0.6018(2)	0.042
O3	0.7556(1)	1.3269(4)	0.4175(2)	0.026
O4	0.8136(1)	1.3524(5)	0.3337(2)	0.025
O5	0.8581(1)	0.2693(5)	0.1704(2)	0.029
O6	0.9509(1)	0.7134(4)	0.2321(2)	0.019
O7	0.7940(1)	0.6765(4)	0.1268(2)	0.035
O8	0.9839(1)	0.3695(5)	0.3769(2)	0.028
N1	0.8409(2)	0.8874(6)	0.3251(2)	0.044
C1	0.9199(2)	0.8013(7)	0.5056(3)	0.027
C2	0.8823(1)	0.9747(5)	0.4293(2)	0.024
C3	0.8435(2)	1.1008(6)	0.4688(3)	0.039
C4	0.8018(1)	1.2732(6)	0.4000(2)	0.017
CA′	0.87694(3)	0.31470(9)	0.78511(5)	0.016
O1′	0.9261(1)	0.2249(4)	0.9685(2)	0.016
O2′	0.9318(1)	0.0461(5)	1.1015(2)	0.017
O3′	0.7627(1)	−0.4206(4)	0.9243(2)	0.020
O4′	0.8044(1)	−0.5130(5)	0.8220(2)	0.029
O5′	0.8624(1)	0.6045(5)	0.6740(2)	0.038
O6′	0.9479(1)	0.1368(5)	0.7354(2)	0.053
O7′	0.7838(1)	0.2218(4)	0.6248(2)	0.021
O8′	0.9816(1)	0.4850(5)	0.8750(2)	0.024
N1′	0.8378(2)	−0.0236(7)	0.8229(3)	0.021
C1′	0.9087(1)	0.0784(5)	1.0052(3)	0.018
C2′	0.8530(1)	−0.0588(5)	0.9314(2)	0.017
C3′	0.8663(2)	−0.2845(5)	0.9624(3)	0.018
C4′	0.8068(2)	−0.4150(6)	0.8983(3)	0.019

Crystal Structure of Ca(L-Asp) · $2H_2O$ (2)

The structure of the dihydrate is also a coordination polymer, however the metal atoms are arranged in double chains, and three of the carboxylate oxygen atoms (O3′, O4′, O4″) bridge the calcium ions in a complicated pattern. The coordination sphere of Ca is composed of an L-aspartate anion bound to the calcium as an N,O_α,O_β tripod ligand, two water molecules, and three carboxylate oxygen atoms from neighbouring complex units. The coordination number of calcium is eight (Figure 3).

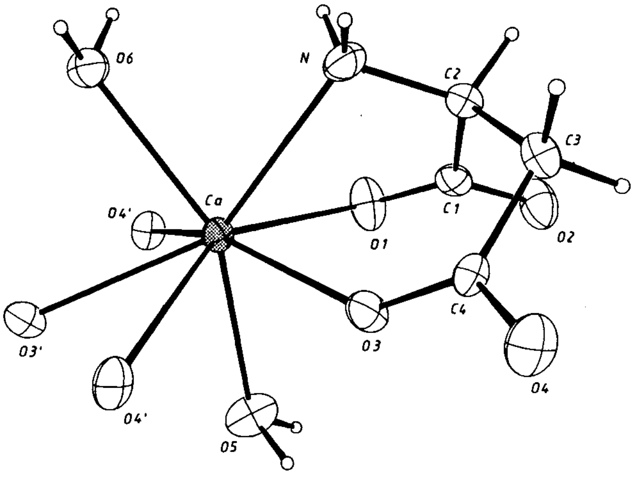

Figure 3. Molecular structure of the calcium centers of Ca(L-Asp) · $2H_2O$ (2)

The O1 oxygen atom of the α-carboxylate group is associated with only one calcium atom, while the oxygen atoms of the β-carboxylate group (O3, O4) are each associated with two calcium atoms (Figure 4). In reference to the double strings of calcium atoms shown in Figure 4, the β-carboxylates are seen to chelate a metal atom of one chain while being simultaneously attached to two metal atoms of the parallel chain. This mode of coordination is similar to the basic structural form detected for the strontium and barium L-glutamate hexahydrates, although the coordination numbers and geometries are different.

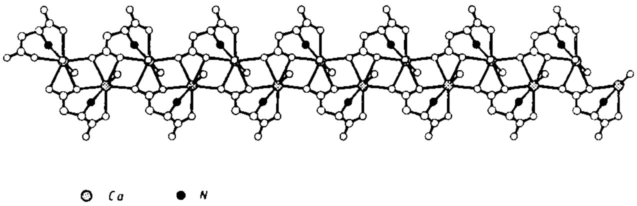

Figure 4. Polymer chains of Ca(L-Asp) · 2 H_2O (**2**)

The polymeric strands in the structure of Ca(L-Asp) · 2 H_2O are crosslinked to neighbouring strands by hydrogen bonds (Table 1). These hydrogen bonds are mainly derived from the water molecules and the α-carboxylate groups, which have the appropriate orientation. The amino and β-carboxylate groups, by contrast, do not participate in additional hydrogen-bonding since they are already fully occupied in metal coordination. A description of details of the hydrogen-bridging network is beyond the scope of this paper.

Table 4. Distances [Å] and angles [°] for Ca(L-Asp) · 2 H_2O (**2**) (esd's in units of the last significant figure in parentheses)

Distances			
Ca-O1	2.429(1)	Ca-O3	2.396(1)
Ca-O5	2.458(1)	Ca-O6	2.536(1)
Ca-N1	2.563(2)	Ca-O3'	2.557(1)
Ca-O4'	2.608(1)	Ca-O4"	2.337(1)
O1-C1	1.248(2)	O2-C1	1.258(2)
O3-C4	1.260(2)	O4-C4	1.250(2)
N1-C2	1.474(2)	C1-C2	1.537(3)
C2-C3	1.528(3)	C3-C4	1.513(2)
Angles			
O1 -Ca-N1	64.8(1)	O1 -Ca-O6	116.5(1)
O1 -Ca-O4"	83.0(1)	O1 -Ca-O3'	148.0(1)
O1 -Ca-O4'	144.2(1)	O1 -Ca-O5	82.4(1)
O1 -Ca-O3	81.4(1)	N1 -Ca-O6	73.0(1)
N1 -Ca-O4"	121.0(1)	N1 -Ca-O3'	144.0(1)
N1 -Ca-O4'	117.3(1)	N1 -Ca-O5	134.9(1)
N1 -Ca-O3	70.8(1)	O6 -Ca-O4"	80.4(1)
O6 -Ca-O3'	75.5(1)	O6 -Ca-O4'	96.7(1)
O6 -Ca-O5	152.0(1)	O6 -Ca-O3	126.2(1)
O4"-Ca-O3'	69.3(1)	O4"-Ca-O4'	117.3(1)
O4"-Ca-O5	81.9(1)	O4"-Ca-O3	153.2(1)
O3'-Ca-O4'	50.1(1)	O3'-Ca-O5	78.1(1)
O3'-Ca-O3	116.8(1)	O4'-Ca-O5	72.7(1)
O4'-Ca-O3	67.6(1)	O5 -Ca-O3	74.5(1)
Ca -O1-C1	114.6(1)	O1 -C1-O2	124.6(2)
O1 -C1-C2	119.0(2)	O2 -C1-C2	116.3(2)
C1 -C2-N1	110.7(2)	N1 -C2-C3	110.7(1)
C1 -C2-C3	112.6(2)	C2 -C3-C4	115.0(2)
C3 -C4-O3	120.1(2)	O4 -C4-C3	118.8(2)
O3 -C4-O4	121.1(1)	Ca -O3-C4	140.0(1)
Ca -N1-C2	106.6(1)		

Symmetry operations:
O3' and O4' were derived from O3 and O4 respectively by the operations 0.5+X, 0.5-Y, 2-Z
O4" was derived from O4 by the operations X+1, Y, Z.

Relevant distances and angles for the structure of the dihydrate are summarized in Table 4, and the atomic coordinates and thermal parameters are listed in Table 5.

Table 5. Fractional atomic coordinates and equivalent isotropic thermal parameters for Ca(L-Asp) · 2 H_2O (**2**) [$U_{eq} = (U_1 \cdot U_2 \cdot U_3)^{1/3}$, where U_1, U_2, U_3 are the eigenvalues of the U_{ij} matrix; esd's in parentheses]

ATOM	X/A	Y/B	Z/C	U(eq.)
CA	0.93080(6)	0.18091(4)	0.92511(3)	0.032
O1	0.9275(2)	0.2087(2)	0.7394(1)	0.046
O2	0.7015(3)	0.2339(2)	0.6172(1)	0.049
O3	0.5900(2)	0.2469(2)	0.90344(9)	0.044
O4	0.2688(2)	0.2244(2)	0.9045(1)	0.046
O5	0.9220(2)	0.4633(2)	0.9189(1)	0.075
O6	1.0634(2)	-0.0710(1)	0.99507(9)	0.047
N	0.7557(3)	-0.0355(2)	0.8273(1)	0.053
C1	0.7683(3)	0.1726(2)	0.6975(1)	0.036
C2	0.6488(3)	0.0377(2)	0.7416(1)	0.036
C3	0.4413(3)	0.0852(2)	0.7750(1)	0.037
C4	0.4332(3)	0.1917(2)	0.8668(1)	0.030

Crystal and Solution Structures

Due to the application of calcium L-aspartate in calcium therapy the structures of the material both in the solid and in solution are of importance. It is obvious from the two crystal structures that calcium ions can accommodate L-aspartate dianions both as bidentate and as tridentate (tripod) chelating ligands. The amino acid is therefore particularly flexible as a ligand for this kind of metal. Clearly, in aqueous solution there is a competition between the amino acid and water molecules for metal coordination and for hydrogen bonding. The existence of two crystalline hydrates suggests that energy differences between L-aspartic complexation and hydration are very small. Slight alterations in the reaction system can induce a change in complex stoichiometry and structure. A second feature evident from the two structures is the variation in the coordination number of the metal: For the tetrahydrate the calcium atom is seven-coordinate, and for the dihydrate the calcium atom is eight-coordinate. In comparison to the magnesium analogues this is a significant difference. In these complexes the magnesium atom is strictly six-coordinate throughout the series of known structures. Hence, L-aspartate is more selective for magnesium than for calcium, which is in agreement with a higher complex formation constant.

Furthermore, the L-aspartate system seems to be more flexible than the L-glutamate system, where hitherto only bidentate chelation has been observed.

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Experimental

The experiments were carried out in pure, fully desalinated water. Reagents were of p. a. quality. – pH measurements: Knick apparatus and Ingold electrodes. — Elemental analyses: Standard procedures, Microanalytical Laboratory of this Institute.

Calcium(II) Hydrogen L-Aspartate Chloride Dihydrate, Ca(L-AspH)Cl · $2H_2O$: L-Aspartic acid (26.6 g, 0.20 mol) was added to calcium carbonate (10.0 g, 0.10 mol) in 100 ml of water to give a solution of calcium(II) bis(hydrogen L-aspartate) Ca(L-AspH)$_2$. A solution of an equimolar quantity of calcium(II) chloride (11.1 g, 0.10 mol) was then added, and the reaction mixture was stirred at room temperature for 1 d. The solution was then concentrated to a volume of 25 ml, the product precipitated by addition of methanol and recrystallized from hot water/methanol over a 7-d period. Yield 16.6 g (68%). Solubility in water at 22°C is 0.3 g/l. The saturated solution has pH 5.85.

$C_4H_{10}CaClNO_4$ (243.7) Calcd. C 19.72 H 4.19 N 5.75
Found C 20.55 H 4.70 N 5.77

Calcium(II) L-Aspartate Dihydrate, Ca(L-Asp) · $2H_2O$: A sample of Ca(L-AspH)Cl · $2H_2O$ (2.40 g, 10 mmol) was dissolved in 20 ml of water and treated with KOH (0.60 g, 10 mmol). The solution, which had pH 10.0, was heated to reflux temp. for a short time, filtered while hot and allowed to cool to room temperature. Crystallisation occured very slowly, sometimes requiring several months. Yield 1.4 g (70%). The compound is sparingly soluble in water: 0.003 mol/l at 22°C. The saturated solutions have pH 10.0.

$C_4H_9CaNO_6$ (207.2) Calcd. C 23.19 H 4.38 N 6.76 O 46.33
Found C 22.65 H 4.36 N 6.51 O 46.23

Calcium(II) L-Aspartate Tetrahydrate, Ca(L-Asp) · $4H_2O$: A suspension of L-aspartic acid (1.33 g, 10.0 mmol) in 15 ml of water was warmed to 60°C and treated with calcium hydroxide (0.76 g, 10.0 mmol) in small portions. The resulting mixture was heated to reflux for 3 h, filtered while hot, and allowed to cool slowly to room temperature. Crystallisation was observed in the course of about 12 h. After several days a yield of 1.4 g (75%) could be achieved. Solubility in water is 0.028 g/l at 22°C. The pH of the saturated solution is 10.50.

$C_4H_{13}CaNO_8$ (243.2) Calcd. C 19.75 H 5.39 N 5.76 O 52.62
Found C 19.65 H 5.28 N 5.67 O 53.10

Crystal Structure Determinations: Crystal data and data collection parameters for Ca(L-Asp) · $4H_2O$ (**1**) and Ca(L-Asp) · $2H_2O$ (**2**) are listed in Table 6. Throughout the data collection of both structures three standard reflections were periodically measured (**1**: 0 0 2, 0 4 0, 4 0 0; **2**: 0 5 2, 3 0 −4, −2 1 −6) and no appreciable decomposition was observed. Intensity data were corrected for absorption effects. Structure **2** was solved by automated Patterson methods while structure **1** was solved using direct methods (SHELXS-86).

For structure **1** considerable effort was spent to resolve an apparent relationship between the atomic coordinates of the two independent molecules in the asymmetric unit which suggested the possibility of the centrosymmetric space group $C2/c$ (No. 15). Most striking are similar x coordinates, a shift in z by $+0.5$ and (after an appropriate shift of the origin) an inversion in y. Closer inspection reveals, however, that the latter is only partially fulfilled for the aspartate atoms (particularly for atoms C2, C3, and O3; see Table 3). Actually, as Figures 1 and 2 show, the absolute configuration of the two independent amino acids is the same and correct. It should also be noted that the torsion angles O3/O4−C4−C3−C2 are noticeably different for both amino acids (Figure 1). Thus, while the disposition of the calcium atoms and the complexing O atoms in the cell is according to the centrosymmetric space group $C2/c$, that of the amino acids only adheres to C2. In other words, the chiral amino acids are embedded in a "matrix" of achirally disposed calcium atoms. Further proof for the correctness of this description comes from the following observations: (a) the additional systematic absences required for $C2/c$ ($h0l$: l = odd) are violated; (b) the calcium coordination centers (including the complexed O atoms) may be refined in $C2/c$ to $R = 0.17$, but further refinement including the amino acid atoms fails.

Table 6. Crystallographic data for **1** and **2**

	Ca(L-Asp) · $4H_2O$	Ca(L-Asp) · $2H_2O$
Emp. formula	$C_4H_{13}CaNO_8$	$C_4H_9CaNO_6$
M_r	243.23	207.20
Crystal system	monoclinic	orthorhombic
Space group	$C2$ (No. 5)	$P2_12_12_1$ (No. 19)
a [Å]	23.298(1)	6.776(1)
b [Å]	6.532(1)	8.695(1)
c [Å]	14.587(2)	13.013(1)
β [°]	118.09(1)	90.0
V [Å^3]	1958.4	766.7
$d_{\text{calcd.}}$ [gcm^{-3}]	1.650	1.795
Z	2 × 4	4
$F(000)$ [e]	1024	432
μ(Mo-K_α) [cm^{-1}]	6.44	7.90
T [°C]	23	23
Diffractometer	Syntex $P2_1$	Enraf-Nonius CAD-4
Scan	ω	$\Theta - 2\Theta$
Scan width [° in ω]	0.80	$0.80 + 0.35 \tan\Theta$
Scan speed [°/min]	0.9−29.3	1−10
hkl range	$\pm 27, \pm 7, +17$	$+8, +11, \pm 16$
$[(\sin\Theta)/\lambda]_{\max}$ [Å^{-1}]	0.594	0.637
Measured reflections	4465	1920
Unique reflections	3432	1659
R_{int}	0.02	0.02
Observed reflections	3242 [$I_o \geqslant 2\sigma(I)$]	1603 [$I_o \geqslant 2\sigma(I)$]
Refined parameters	252	109
R [a]	0.032	0.022
R_w [b]	0.039	0.027
(Shift/error)$_{\max}$	0.002 .	0.002
$\Delta\varrho_{\text{fin}}$ (max/min) [e/Å^3]	$+0.80/-0.37$	$+0.45/-0.38$

[a] $R = \Sigma(||F_o| - |F_c||/\Sigma|F_o|$. — [b] $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w F_o^2]^{1/2}$, $w = 1/\sigma^2(F_o)$.

Both structures were refined by full matrix methods (SHELX-76), and all hydrogen atoms were located but not refined. Hydrogen atoms were all assigned a fixed thermal parameter ($U_{\text{iso}} = 0.05$ Å^2). Atomic coordinates for structures **1** and **2** are listed in Tables 3 and 5, respectively. Calculated and observed structure factor amplitudes together with a complete list of atomic coordinates and thermal parameters have been deposited. This data may be obtained from Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, FRG, on quoting the depository number CSD-53766, the names of the authors, and the journal citation.

CAS Registry Numbers

1 (cc entry): 120927-42-6 / **1** (salt entry): 120927-43-7 / **2** (cc entry): 120927-41-5 / **2** (salt entry): 120927-44-8 / Ca(L-AspH)Cl: 92533-40-9

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