

Metal Ion Binding by Amino Acids

Preparation and Crystal Structures of Magnesium, Strontium, and Barium L-Glutamate Hydrates

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Crystalline magnesium, strontium, and barium L-glutamate complexes containing the dianion $L\text{-Glu}^{2-}$ have been prepared as the tetrahydrate (Mg) and hexahydrates (Sr, Ba), respectively. Their aqueous solutions have pH values of 10.45, 11.05, and 10.93, respectively. The solid state structures of the Mg and Sr complexes have been determined by single crystal X-ray methods, and the structure of the Ba analogue inferred through its isomorphism with the Sr analogue. The crystals are orthorhombic, space group $P2_12_12_1$. The magnesium atoms were found to be hexacoordinated with the L-glutamate functioning as a chelating N,O_α -donor. Four water molecules complete the first coordination sphere. The γ -carboxylate group is only engaged in hydrogen bonding. Strontium and barium are nine-coordinated. The α -carboxylate group of the $L\text{-Glu}^{2-}$ ligand is O,O -chelating to one metal and forming oxygen bridges to two further metal atoms. The γ -carboxylate group is also chelating a neighbouring strontium atom, but the nitrogen function is not engaged in metal coordination. By $M-O-M$ bridging double strings of metal-oxygen chains are formed, which are interlinked by the amino acids to give a layered structure. Three water molecules are also part of the first coordination sphere of each metal, while three others are interlayer hydrogen-bonded components. The amino groups are also involved in this hydrogen bonding.

Bindung von Metall-Ionen durch Aminosäuren. — Darstellung und Struktur von Magnesium-, Strontium- und Barium-L-glutamat-Hydraten

Magnesium-, Strontium- und Barium-L-glutamate mit dem Dianion-Liganden $L\text{-Glu}^{2-}$ wurden als Tetrahydrate (Mg) bzw. Hexahydrate (Sr, Ba) kristallisiert. Ihre wäßrigen Lösungen zeigen pH-Werte von 10.45, 11.05 bzw. 10.93. Die Kristallstrukturen der Magnesium- und der Strontiumverbindungen wurden durch Einkristall-Röntgenbeugungsanalysen bestimmt, die Struktur der Bariumverbindung kann wegen der Isomorphiebeziehung zum Strontiumanalogen als weitgehend analog betrachtet werden. Alle Kristalle sind orthorhombisch, Raumgruppe $P2_12_12_1$. Die Magnesiumatome sind sechsfach koordiniert und besitzen in der ersten Koordinationssphäre das als N,O_α -Chelatligand fungierende $L\text{-Glu}^{2-}$ -Anion sowie vier Wassermoleküle. Die γ -Carboxylatgruppe wird nur zu Wasserstoffbrücken beansprucht. Strontium und Barium sind neunfach koordiniert. Die α -Carboxylatgruppe des $L\text{-Glu}^{2-}$ -Liganden wirkt einerseits O,O -chelatisierend für ein Sr(Ba)-Atom, ist andererseits aber auch in Brückenfunktionen zu benachbarten Sr(Ba)-Atomen engagiert. Auch die γ -Carboxylatgruppe wirkt auf ein weiteres Sr(Ba)-Atom O,O -chelatisierend, während die Aminogruppe an der Sr(Ba)-Koordination nicht beteiligt ist. Durch die $M-O-M$ -Verbrückung über die α -Carboxylat-Sauerstoffatome werden gewellte Metall-Sauerstoff-Doppelstränge gebildet, die über die γ -Carboxylatgruppen zu Schichten verbunden sind. Drei Wassermoleküle sind den Sr(Ba)-Atomen zugeordnet, die übrigen drei beteiligen sich an einem Netzwerk von Wasserstoffbrücken, das auch die Amino-Gruppe umfaßt.

Complexation by amino acids and proteins of several of the alkaline earth metals, mainly magnesium and calcium, plays an important role in many biological processes¹⁻³. Evidence suggests that glutamate and aspartate units are among the principal mediators in most calcium- and magnesium-protein interactions⁴⁻⁶. These amino acids have been found, e.g., at the metal binding sites of several crystalline proteins⁷⁻¹⁰. In solution the amino acid complexes with magnesium and calcium have only limited stability¹¹. This characteristic is very important, however, for metal transport and release in biological systems. Magnesium and calcium therapy with aspartates and glutamates are examples for the application of these well-documented observations¹².

Complex formation constants with the alkaline earth metals in aqueous solution are higher for amino acids than for hydroxy carboxylic acids and the related nonsubstituted carboxylic acids, which suggests a participation of the amino group in the coordination. The differences in association constants for the various ligands become smaller, however, as the radius of the metal increases, and hence for strontium and barium complex stability is also strongly reduced¹¹. It appears that with the heavy group-II metals the amino function in both aspartic and glutamic acid is much less significant for metal complexation, probably due to the unfavourable chelation of large metals in five- or six-membered rings.

As part of a current study on the bioinorganic chemistry of magnesium and its homologues oriented towards, for ex-

ample, the development of an improved magnesium therapy, we have recently investigated the structure of magnesium *aspartate* trihydrate $\text{Mg}(\text{L-Asp}) \cdot 3 \text{H}_2\text{O}$, both in solution and in the crystal¹³. In this complex the aspartate dianion L-Asp^{2-} acts as a tridentate ligand to an octahedrally coordinated magnesium atom. This arrangement is very similar to arrangements encountered with other small divalent metals like manganese(II)¹⁴, zinc(II)¹⁵ etc.¹⁶. However, as discovered in a later study¹⁷, these structural features differ significantly from those observed with the two hydrates of calcium *aspartate*, $\text{Ca}(\text{L-Asp}) \cdot 2 \text{H}_2\text{O}$ and $\text{Ca}(\text{L-Asp}) \cdot 4 \text{H}_2\text{O}$, where the dianion offers only two coordination sites to octa-coordinated calcium ions¹⁷.

The structure of the corresponding magnesium *glutamate* has not yet been determined, but its calcium analogue $\text{Ca}(\text{L-Glu}) \cdot 3 \text{H}_2\text{O}$ has been investigated by single crystal X-ray diffraction¹⁸. The latter is a three-dimensional network structure, where the metals are again octa-coordinate, and the Glu^{2-} ligand functions as an *N,O*- and (twice) an *O,O*-bidentate to three different Ca centers (Figure 1).

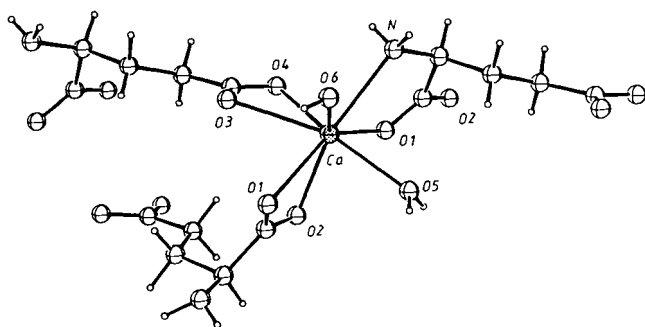
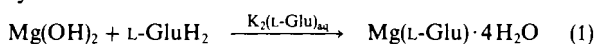


Figure 1. Coordination geometry of the Ca^{2+} ions in $\text{Ca}(\text{L-Glu}) \cdot 3 \text{H}_2\text{O}$ as drawn from the coordinates reported in ref.¹⁸. Each Ca^{2+} ion is coordinated to three symmetry-related amino acids and two water molecules. The third water molecule is not metal-coordinated and is omitted from the drawing as is the second disordered H atom at O6

In an attempt to generalize these findings we have now also prepared and structurally characterized the compounds $\text{Mg}(\text{L-Glu}) \cdot 4 \text{H}_2\text{O}$ (1), $\text{Sr}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ (2), and $\text{Ba}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ (3). The results are presented in this report, while work on the calcium aspartate hydrates is included in the following paper¹⁷.

Results and Discussion

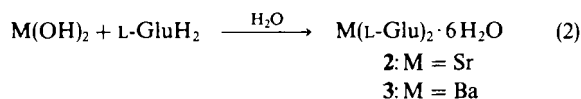
The preparation of a crystalline magnesium L-glutamate could not be accomplished by direct neutralisation of L-glutamic acid with the weakly basic magnesium hydroxide. Even upon extensive concentration of the resulting solution no well-defined product could be isolated. It was only upon treatment of the reaction mixture with basic potassium L-glutamate that a material of the expected composition was obtained. The crystalline product was shown to represent a tetrahydrate.



1

Compound 1 is soluble in water (0.017 mol/l) and the saturated solutions are basic (pH 10.45). Preparation and properties are thus similar to those reported for the corresponding L-aspartate¹⁴, where the auxiliary base $\text{K}_2(\text{L-Glu})$ was also necessary. The basic L-aspartate, however, crystallizes as a trihydrate.

The basicity of both strontium and barium hydroxide are sufficient for complete neutralisation of L-glutamic acid according to equation (2). Crystalline hexahydrates are obtained for $\text{M} = \text{Sr}$ and Ba .



It appears, therefore, that magnesium L-glutamate forms a *tetrahydrate*, while calcium L-glutamate forms a *trihydrate*, and the strontium and barium analogues form *hexahydrates*. The latter result may be considered as indicative of analogous structures, and indeed $\text{Sr}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ (2) and $\text{Ba}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ (3) have been found to be isostructural (see below). In contrast, $\text{Mg}(\text{L-Glu}) \cdot 4 \text{H}_2\text{O}$ and $\text{Ca}(\text{L-Glu}) \cdot 3 \text{H}_2\text{O}$ have entirely different structures.

Crystal Structure of $\text{Mg}(\text{L-Glu}) \cdot 4 \text{H}_2\text{O}$ (1)

The crystals of the magnesium compound contain monomeric complex units, in which the metal is hexacoordinate with an *N,O*-chelating glutamate dianion and four water molecules as ligands in the inner coordination sphere (Figure 2). An oxygen atom of the carboxylate group next to the amino group is attached to magnesium with formation of a five-membered ring. The γ -carboxylate function is uncoordinated, however, and only engaged in hydrogen bonding with neighbouring molecules (Table 1).

These features are surprising, since in the aspartate analogue the amino acid acts as a *N,O,O*-tripod ligand with both carboxylate groups and the amino group coordinated

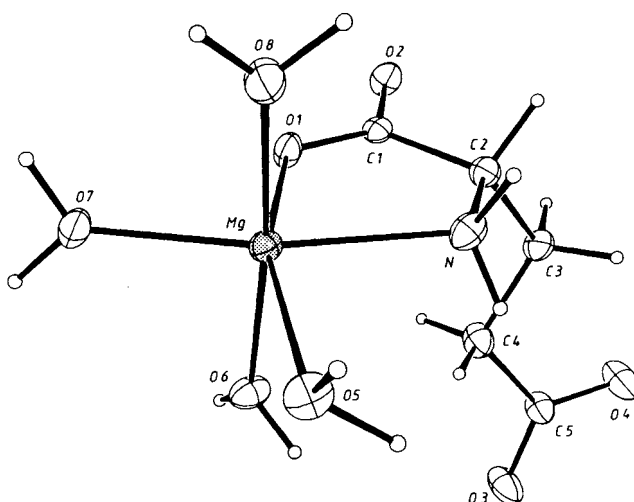


Figure 2. Molecular structure of the complex $\text{Mg}(\text{L-Glu}) \cdot 4 \text{H}_2\text{O}$ (1) in the crystal (ORTEP, ellipsoids at the 50% probability level, H atoms with arbitrary radii)

to give a bicyclic structure comprising a five- and a six-membered ring. It appears that the seven-membered ring which would result from a coordination of the γ -carboxylate group to magnesium in **1** is much less favourable. The uncoordinated γ -carboxylate group is equally unexpected. In related complexes this function is accommodated at the metal of a neighbouring molecule by replacement of water molecules. In **1** the four water molecules, which are probably also present at the four vertices of an octahedron in aqueous solution, are not substituted upon packing of the molecules **1** into a three-dimensional crystal lattice. Rather, the packing is accompanied by the formation of a number of intermolecular hydrogen bonds (Table 1). Therefore the solid state structure of this compound probably resembles closely the structure in solution, while in other cases the coordination polymers present in the crystal have to be degraded by hydration in the dissolution process to give the solvated monomers.

Table 1. Hydrogen bonds (A—B...C) [\AA] of **1** and **2**

Structure 1 : Mg(L-Glu) · 4 H ₂ O					
A—B...C	A—B	B...C	A...C	SYM.	OP.
O5—H51...O2	0.90	1.94	2.81	a	
O5—H52...O3	0.99	1.85	2.83	b	
O6—H61...O4	0.87	1.79	2.65	b	
O6—H62...O2	0.91	1.85	2.73	c	
O7—H71...O2	0.89	1.99	2.88	d	
O7—H72...O3	0.91	1.82	2.72	e	
O8—H81...O1	0.81	1.91	2.71	d	
O8—H82...O4	0.92	1.78	2.68	f	
N—HN1...O3	0.90	2.28	3.11	b	
N—HN2...O6	0.94	2.58	3.31	g	
N—HN2...O4	0.94	2.48	3.34	f	

Structure 2 : Sr(L-Glu) · 6 H ₂ O					
O5—HO51...O3	0.83	1.91	2.73	h	
O5—HO52...O9	0.86	1.93	2.75	i	
O6—HO61...O9	0.89	1.94	2.75	i	
O6—HO62...O3	0.88	1.94	2.81	d	
O7—HO71...O8	1.05	1.78	2.78	c	
O7—HO72...O10	0.84	2.14	2.95	j	
O8—HO81...O5	0.88	1.97	2.79	k	
O8—HO82...N	1.08	1.69	2.75	l	
O9—HO91...O4	0.87	1.88	2.72	m	
O9—HO92...O10	1.01	1.73	2.75	j	
O10—H101...O8	1.03	1.79	2.80	j	
O10—H102...O6	0.84	2.27	2.83	g	
N—HN11...O7	0.89	2.50	3.14	l	
N—HN12...O4	1.09	2.40	3.34	h	

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

Details of bond distances and angles are summarized in Table 2. Deviations from standard octahedral, tetrahedral, or trigonal geometries are minimal. Atomic coordinates are presented in Table 3.

In the published^[8] structure of calcium L-glutamate trihydrate the calcium ion is found to be eight-coordinate (Figure 1). The environment of the metal is composed of one N,O-chelating and two O,O-coordinated glutamate ligands, along with two water molecules. (The third water molecule is not attached to calcium and functions as an interstitial hydrogen-bonding species.) The N,O-chelate in the calcium analogue, which is similar to Mg(L-Glu) · 4 H₂O (**1**), is formed with an oxygen atom from the α -carboxylate group

Table 2. Distances [\AA] and angles [$^\circ$] for Mg(L-Glu) · 4 H₂O (**1**) (esd's in units of the last significant figure in parentheses)

Distances			
Mg1—N	2.211(2)	Mg1—O1	2.090(1)
Mg1—O5	2.125(1)	Mg1—O6	2.054(1)
Mg1—O7	2.054(1)	Mg1—O8	2.028(1)
C1—C2	1.530(2)	C1—O1	1.254(2)
C1—O2	1.266(2)	C2—C3	1.533(2)
C2—N	1.477(2)	C3—C4	1.527(2)
C4—C5	1.527(2)	C5—O3	1.250(2)
C5—O4	1.257(2)		

Angles			
N—Mg1—O1	76.3(1)	N—Mg1—O7	169.0(1)
N—Mg1—O5	85.5(1)	N—Mg1—O6	95.7(1)
N—Mg1—O8	90.5(1)	O1—Mg1—O7	93.8(1)
O1—Mg1—O5	160.6(1)	O1—Mg1—O6	91.9(1)
O1—Mg1—O8	96.6(1)	O6—Mg1—O7	89.4(1)
O5—Mg1—O7	104.8(1)	O7—Mg1—O8	85.8(1)
O5—Mg1—O8	83.0(1)	O6—Mg1—O8	170.4(1)
O5—Mg1—O8	90.2(1)	Mg1—N—C2	113.4(1)
Mg1—O1—C1	121.0(1)	C2—C1—O1	119.0(1)
C2—C1—O2	117.3(1)	O1—C1—O2	123.6(2)
C1—C2—C3	113.5(1)	C1—C2—N	109.8(1)
C3—C2—N	112.0(1)	C2—C3—C4	115.1(1)
C3—C4—C5	113.5(1)	C4—C5—O3	118.5(2)
C4—C5—O4	118.5(2)	O3—C5—O4	122.9(2)

Table 3. Fractional atomic coordinates and equivalent isotropic thermal parameters for Mg(L-Glu) · 4 H₂O (**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.)
Mg1	0.8716(1)	0.7883(1)	0.1525(1)	0.013
C1	0.5432(2)	0.6526(2)	0.1806(1)	0.013
C2	0.6505(2)	0.5699(2)	0.2541(1)	0.014
C3	0.5826(2)	0.5706(2)	0.3635(1)	0.016
C4	0.5856(2)	0.7051(2)	0.4161(1)	0.020
C5	0.5602(2)	0.6969(2)	0.5310(1)	0.017
N	0.8307(2)	0.6120(2)	0.2489(1)	0.016
O1	0.6115(1)	0.7482(1)	0.1356(1)	0.017
O2	0.3900(1)	0.6172(1)	0.1665(1)	0.018
O3	0.5848(2)	0.7985(1)	0.5831(1)	0.024
O4	0.5155(2)	0.5882(1)	0.5690(1)	0.023
O5	1.1218(1)	0.7905(1)	0.2145(1)	0.019
O6	0.8252(1)	0.9240(1)	0.2652(1)	0.018
O7	0.8700(2)	0.9387(1)	0.0476(1)	0.019
O8	0.9532(2)	0.6720(1)	0.0367(1)	0.020

and gives rise to a five-membered ring. One of the two O,O-chelates arises from double-coordination of a γ -carboxylate group of another glutamate ligand, whereas the second O,O-chelate results from a similar interaction with an α -carboxylate group. One of the α -carboxylate oxygens is, therefore, bridging two calcium cations, bringing these metal atoms relatively close to each other. This feature is absent in the magnesium compound (above), but recurs in the strontium and barium compounds (below). It is noteworthy that there are few parallels between the structures of the magnesium and the calcium complexes; the only clear analogy is the N,O-chelation of the glutamate ligand. Major discrepancies arise in the coordination number and geometry of the metal, the coordination of the γ -carboxylate group, and the relative importance of water coordination. Furthermore, these differences will probably be of relevance for the solution state.

Crystal Structures of Strontium and Barium L-Glutamate Hexahydrate

The crystals of Sr(L-Glu) · 6 H₂O (**2**) and Ba(L-Glu) · 6 H₂O (**3**) are *isomorphous*, and the X-ray diffraction patterns suggest that the compounds are isostructural. Therefore,

only the structure of the strontium glutamate has been determined. The lattice is composed of a complicated network built through strontium-glutamate as well as hydrogen-bond type interactions (Table 1). Each strontium ion is nine-coordinate. Only three of the six water molecules are actually part of the first coordination sphere of the metal, while the other three are again interstitial hydrogen-bonded species. Contrary to the results with the magnesium and calcium analogues, the nitrogen atoms have no interaction with the strontium atoms, but are only involved in hydrogen bonding. Each strontium is chelated by one γ - and one α -carboxylate (of different amino acids). In addition, the strontium is coordinated by two oxygen atoms of two further α -carboxylates which are in bridging positions to neighbouring strontium ions (Figure 3). This feature of metal bridging by α -carboxylate oxygen atoms has been observed already in the structure of the calcium analogue $\text{Ca}(\text{L-Glu}) \cdot 3 \text{H}_2\text{O}$. By these contacts double chains of strontium ions bridged by the α -carboxylate groups are formed, with wedge-type OCOSr rings and rhombohedral OSrOSr rings in an alternating sequence (Figure 4). The double-strings of metal ions are interlinked by the glutamate ligands.

Bond distances and angles of $\text{Sr}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ are listed in Table 4, atomic coordinates in Table 5. For details of

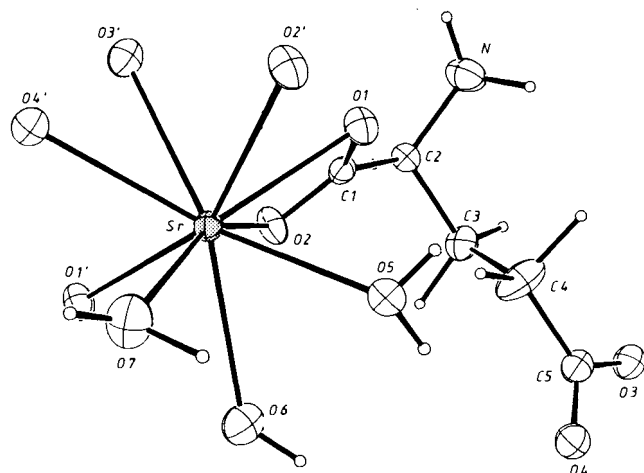


Figure 3. Molecular structure of $\text{Sr}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ (2) in the crystal (ORTEP). Complexation of Sr^{2+} by three additional (symmetry-related) amino acids is indicated only by the coordinating carboxy O atoms O1, O2, and O3/O4

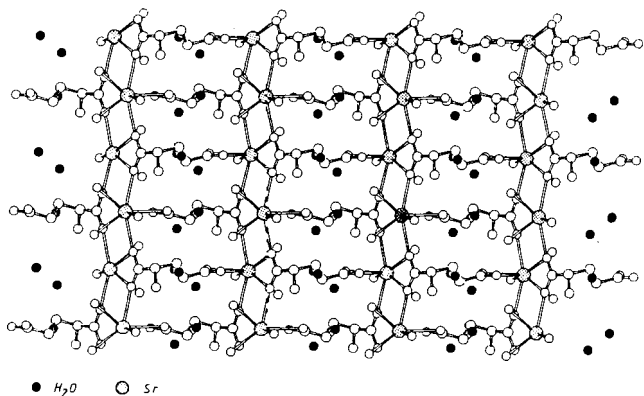


Figure 4. Extended layer structure of $\text{Sr}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ (2) (Sr: dotted; interstitial water molecules: black)

structure solution and crystallographic data see the Experimental Section and Table 7, which also contains data for $\text{Ba}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$.

Table 4. Distances [Å] and angles [°] for $\text{Sr}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ (2) (esd's in units of the last significant figure in parentheses)

Distances			
Sr-O1	2.724(2)	Sr-O2	2.665(2)
Sr-O1'	2.642(2)	Sr-O2'	2.651(2)
Sr-O3'	2.677(2)	Sr-O4'	2.658(2)
Sr-O5	2.658(2)	Sr-O6	2.708(2)
Sr-O7	2.640(2)	O1-C1	1.268(3)
O2-C1	1.258(3)	C1-C2	1.521(3)
C2-N	1.469(3)	C2-C3	1.526(3)
C3-C4	1.524(4)	C4-C5	1.513(4)
C5-O3	1.264(3)	C5-O4	1.264(3)
Angles			
O1-Sr-O1'	115.4(1)	O1-Sr-O2	48.4(1)
O1-Sr-O2'	67.8(1)	O1-Sr-O3'	75.4(1)
O1-Sr-O4'	120.8(1)	O1-Sr-O5	74.8(1)
O1-Sr-O6	105.7(1)	O1-Sr-O7	146.5(1)
O2-Sr-O1'	68.8(1)	O2-Sr-O2'	115.3(1)
O2-Sr-O3'	79.3(1)	O2-Sr-O4'	122.1(1)
O2-Sr-O5	98.4(1)	O2-Sr-O6	76.8(1)
O2-Sr-O7	154.8(1)	O2'-Sr-O1'	153.8(1)
O2'-Sr-O3'	75.4(1)	O2'-Sr-O4'	78.9(1)
O2'-Sr-O5	70.9(1)	O2'-Sr-O6	138.1(1)
O2'-Sr-O7	86.7(1)	O3'-Sr-O1'	80.4(1)
O3'-Sr-O4'	48.8(1)	O3'-Sr-O5	141.3(1)
O3'-Sr-O6	145.3(1)	O3'-Sr-O7	120.2(1)
O4'-Sr-O1'	77.7(1)	O4'-Sr-O5	137.2(1)
O4'-Sr-O6	130.7(1)	O4'-Sr-O7	72.0(1)
O1'-Sr-O5	135.2(1)	O1'-Sr-O6	67.7(1)
O1'-Sr-O7	97.1(1)	O7-Sr-O5	76.5(1)
O7-Sr-O6	78.5(1)	O6-Sr-O5	67.6(1)
O1-C1-O2	122.1(2)	O1-C1-C2	119.7(3)
O2-C1-C2	118.2(3)	C1-C2-N	114.5(2)
N-C2-C3	111.1(2)	C1-C2-C3	109.9(2)
C2-C3-C4	114.5(2)	C3-C4-C5	114.1(3)
C4-C5-O3	119.7(2)	C4-C5-O4	118.7(2)
O3-C5-O4	121.5(2)		

Symmetry operations:

O1' was derived from O1 by the operation $0.5+X, 0.5-Y, -Z$,
 O2' from O2 by the operation $X-0.5, 0.5-Y, -Z$,
 O3' and O4' from O3 and O4 respectively by the operation $X, Y-1, Z$.

Table 5. Fractional atomic coordinates and equivalent isotropic thermal parameters for $\text{Sr}(\text{L-Glu}) \cdot 6 \text{H}_2\text{O}$ (2) [$U_{\text{eq}} = (U_1 \cdot U_2 \cdot U_3)^{1/3}$, 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.)
Sr	0.9078(1)	0.1999(1)	0.0562(1)	0.016
O1	0.7595(2)	0.3566(2)	-0.0465(1)	0.023
O2	1.0591(2)	0.3655(2)	-0.0393(1)	0.022
C1	0.9123(4)	0.4069(2)	-0.0655(1)	0.017
C2	0.9206(4)	0.5254(3)	-0.1202(1)	0.019
N	0.7562(3)	0.5338(3)	-0.1612(1)	0.031
C3	0.9679(4)	0.6810(3)	-0.0913(1)	0.024
C4	0.8471(4)	0.7306(3)	-0.0342(1)	0.033
C5	0.8953(4)	0.8849(3)	-0.0059(1)	0.021
O3	0.9030(3)	0.9998(2)	-0.0434(1)	0.024
O4	0.9172(3)	0.8970(2)	0.0557(1)	0.026
O5	0.7C71(3)	0.4172(2)	0.1114(1)	0.029
O6	1.1116(3)	0.4051(2)	0.1232(1)	0.030
O7	0.8664(3)	0.1049(2)	0.1788(1)	0.034
O8	0.3894(3)	-0.1997(3)	0.2655(1)	0.042
O9	0.9133(3)	-0.3339(2)	0.1451(1)	0.033
O10	0.7665(3)	-0.1770(3)	0.2495(1)	0.047

Crystal and Solution Structures

As mentioned in the discussion of the X-ray results above, in the series of alkaline earth metal glutamates the structure of $\text{Mg}(\text{L-Glu}) \cdot 4 \text{H}_2\text{O}$ (1) is the only case, where the crystal and solution structure are likely to be similar. It is this

compound alone, where the crystals contain individual molecules interlinked only by hydrogen bonds but without metal bridging complexation. The calcium, strontium, and barium analogues form coordination polymers, which must be degraded by solvation when dissolved in water. Changes in the conformation and coordination are most likely to occur with this degradation due to a change from inter- to intramolecular coordination.

When speculating on the mode of coordination in the case of the Ca, Sr, and Ba complex in solution, the most probable feature is the complexation solely by carboxylate oxygen atoms. This assumption appears to be justified as the growing size of the metals makes chelation in small rings increasingly unlikely. The high coordination numbers (eight for Ca, nine for Sr and Ba) allow for a large variety of coordination interactions, and therefore detailed predictions are impossible.

Hitherto spectroscopic data are also not very conclusive. The differences in chemical shifts and coupling constants of the *NMR spectra* of aqueous solutions are very small (Table 6). However, for any interpretation it should be noted that these systems are characterized by rapid ligand and site exchange, since the formation constants for these complexes are small, the kinetics are rapid, and the competition of the water molecules for coordination sites and hydrogen bonds is of great importance.

Table 6. ^1H - and $\{^1\text{H}\}^{13}\text{C}$ -NMR data of the metal(II) L-glutamates (D_2O solvent; δ in ppm rel. to internal sodium 3-(trimethylsilyl)-1-propanesulfonate (^1H) and dioxane (^{13}C), respectively; J in Hz; $T = 25^\circ\text{C}$)

	Mg(L-Glu)	Sr(L-Glu)	Ba(L-Glu)
δCH	3.37, dd	3.25, t	3.24, t
$^3J(\text{CH}-\text{CH}_2)$	5.4/7.3	6.4	6.4
δCH_2 (β)	1.96, m	1.87, m	1.87, m
	1.84, m	1.77, m	1.77, m
δCH_2 (γ)	2.24, t	2.21, t	2.20, t
$^3J(\text{CH}_2-\text{CH}_2)$	7.80	8.10	8.31
δCH	55.75	56.53	56.59
δCH_2 (β)	29.89	32.29	32.29
δCH_2 (γ)	34.57	34.76	34.83
δCO_2	182.77	183.61	183.55
	179.59	183.61	183.61

In order to obtain more reliable information and an indication of the trends, it will be necessary to undertake both temperature- and pH-dependent NMR studies. These investigations should also be coupled with IR measurements and determination of optical rotation, since these methods are also sensitive to conformational and coordination changes. These studies are currently being pursued.

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Experimental

General: All experiments were carried out using bidistilled water. Reagents were of p.a. quality. pH values: Knick apparatus, reference electrodes (AgCl/KCl) Ingold. — NMR spectra: Jeol FX 60 and CX 270 spectrometers. — Elemental analyses: Microanalytical laboratory of this Institute following standard procedures.

Magnesium(II) L-Glutamate Tetrahydrate (1): To a solution of L-glutamic acid (14.7 g, 0.10 mol) in 50 ml of water magnesium hydroxide (5.83 g, 0.10 mol) was added with stirring. The reaction mixture was then heated for 2 h to reflux, filtered while hot, and cooled to room temperature. No crystallisation occurred even after reduction of the volume to one half in vacuo and standing for several days. The solution was then treated with 25 ml of an aqueous solution of L-glutamic acid (14.7 g, 0.10 mol) and KOH (11.4 g, 0.2 mol), heated to reflux for a short time, and allowed to cool to room temperature. Crystallisation of a tetrahydrate ensued after 3 d; yield 10.0 g (41%). Solubility in water is 0.017 mol/l, the pH of this solution is 10.45.

$\text{C}_5\text{H}_{15}\text{MgNO}_8$ (241.5) Calcd. C 24.87 H 6.26 N 5.80 O 53.0
Found C 24.82 H 6.31 N 5.71 O 54.3

Strontium(II) L-Glutamate Hexahydrate (2): To a suspension of L-glutamic acid (14.7 g, 0.10 mol) in 50 ml of water strontium hydroxide hexahydrate (22.2 g, 0.10 mol) was added in portions with stirring. The mixture was heated under reflux for 3 h and then filtered while hot and allowed to cool slowly for ca. 12 h. After 5 d slow crystallisation was observed, and after 2 weeks a crop of 7.65 g (22%) of a hexahydrate could be collected. The compound has a solubility of 0.023 g/l at 20°C , and the saturated solution shows pH 11.05.

$\text{C}_5\text{H}_{19}\text{NO}_{10}\text{Sr}$ (340.8) Calcd. C 17.62 H 5.62 N 4.71 O 46.94
Found C 17.42 H 5.60 N 4.02 O 46.99

Barium(II) L-Glutamate Hexahydrate (3): As described for the strontium analogue, 14.7 g of L-glutamic acid (0.10 mol) and 27.9 g barium hydroxide hexahydrate (0.10 mol) gave 10.5 g (27%) of the hexahydrate, which has a solubility in water at 20°C of 0.028 mol/l. The saturated aqueous solution shows pH 10.93.

$\text{C}_5\text{H}_{19}\text{BaNO}_{10}$ (390.5) Calcd. C 15.38 H 4.90 N 3.59 O 40.97
Found C 15.01 H 4.56 N 3.50 O 40.46

Crystal Structure Determinations: Crystal data and data collection parameters for **1** and **2** are listed in Table 7. Unit cell data for **3** were obtained from precession photographs and are also listed in Table 7. During data collection for **1** and **2** three standard reflections were periodically measured (**1**: 4 0 0, 0 6 0, 0 0 2; **2**: 6 0 0, 0 0 12, 0 -5 2). For structure **1** no decomposition was observed whereas a slight linear decomposition (1%) for **2** was subsequently corrected. Only the intensity data for **2** were corrected for absorption effects. Both structures were solved by automated Patterson methods (SHELXS-86) and then refined by full matrix methods (SHELX-76). All hydrogen atoms for both structures were located but not refined; they were all assigned a fixed thermal parameter ($U_{\text{iso}} = 0.05 \text{ \AA}^2$). Atomic coordinates for the structures of **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 the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, FRG, on quoting the depository number CSD-53767, the names of the authors, and the journal citation.

Table 7. Crystallographic data of the compounds 1–3 (all orthorhombic, space group $P2_12_12_1$, Nr. 19)

	1	2	3
Crystal size [mm]	0.20 × 0.40 × 0.55	0.20 × 0.25 × 0.45	
Emp. formula	C ₃ H ₁₅ MgNO ₈	C ₅ H ₁₉ NO ₁₀ Sr	C ₅ H ₁₉ BaNO ₁₀
M_r	241.48	340.83	390.55
a [Å]	7.838(1)	7.355(1)	7.54
b [Å]	10.113(1)	8.772(1)	8.96
c [Å]	13.156(1)	20.283(1)	20.25
V [Å ³]	1042.8	1308.6	1368.1
d_{calc} [g cm ⁻³]	1.538	1.730	
Z	4	4	
$F(000)$ [e]	512	696	
$\mu(\text{Mo-K}\alpha)$ [cm ⁻¹]	1.9	40.3	
T [°C]	-40	22	
Diffractometer	Syntex P2 ₁	Enraf-Nonius CAD4	
Scan	ω	Θ -2 Θ	
Scan width [° in ω]	0.80	0.85 + 0.35 tan Θ	
Scan speed [°/min]	0.7–29.3	1–10	
hkl range	+9, +12, ± 15	± 9 , +11, ± 25	
$[\sin \Theta/\lambda]_{\text{max}}$ [Å ⁻¹]	0.595	0.637	
Measured reflections	2110	6141	
Unique reflections	1839	2840	
R_{int}	0.02	0.02	
Observed reflections [$I \geq 2\sigma(I)$]	1786	2637	
Relat. transmiss.	—	0.81–1.00	
Refined parameters	136	154	
R^a	0.025	0.020	
R_w^b	0.030	0.018	
(Shift/error) _{max} ΔQ_{fit} (max/min) [e/Å ³]	0.001 +0.38/–0.27	0.002 +0.44/–0.64	

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

CAS Registry Numbers

1: 120312-22-3 / 2 (coordination structure): 120312-23-4 / 2 (salt):
120312-20-1 / 3 (coordination structure): 120312-24-5 / 3 (salt):
120312-21-2

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