Metal Ion Binding by Amino Acids

Preparation and Crystal Structures of Lithium Hydrogen L-Aspartate Hydrate and Potassium Hydrogen L-Aspartate Dihydrate

Hubert Schmidbaur*, **Ina Bach**, **Dallas L. Wilkinson**, and **Gerhard Müller**

Anorganisch-chemisches Institut der Technischen Universität München,
Lichtenbergstraße 4, D-8046 Garching

Received February 20, 1989

Key Words: L-Aspartate complexes / Lithium hydrogen L-aspartate hydrate / Potassium hydrogen L-aspartate dihydrate / Amino acid complexes

Lithium hydrogen L-aspartate, prepared by neutralisation of lithium carbonate with aqueous L-aspartic acid L-AspH$_2$, crystallizes as the monohydrate Li(L-AspH) · H_2O. Saturated solutions show pH 7.30. Potassium hydrogen L-aspartate, synthesized similarly from L-AspH$_2$ and KOH, crystallizes from aqueous solutions (pH 7.52) as the dihydrate K(L-AspH) · 2 H_2O. The NMR spectra of the two complexes exhibit no major differences. – Crystalline *Li(L-AspH) · H$_2$O* has a *layer* structure, in which each lithium atom is in a tetrahedral environment of four oxygen atoms belonging to four different amino acids. The hydrate water molecule and the nitrogen function (protonated to give an ammonium center) have no metal contacts, but are components of a network of hydrogen bonds interconnecting the layers. One of the carboxylate oxygen atoms is in a bridging position between the metal atoms, which are arranged in pairs and participate in edge-sharing six-membered rings. In each of the layers large empty channels are formed. – Crystals of *K(L-AspH) · 2 H$_2$O* show a *chain* structure with the potassium atoms exhibiting coordination number 7. The metal atoms are again arranged in double strings with the β-carboxylate oxygen atoms of the L-AspH$^-$ counter anions in chelating and bridging positions. The α-carboxylate and protonated amino functions show no metal contacts, but are part of the hydrogen-bonding system interconnecting the chains of the coordination polymer. Both hydrate water molecules are K-coordinated, one in a metal-bridging position.

Bindung von Metall-Ionen durch Aminosäuren. – Darstellung und Struktur von Lithium-L-hydrogenaspartat-Hydrat und Kalium-L-hydrogenaspartat-Dihydrat.

Lithium-L-hydrogenaspartat wurde dargestellt durch Neutralisation von Lithiumcarbonat mit L-Asparaginsäure L-AspH$_2$ und aus wäßriger Lösung als Monohydrat Li(L-AspH) · H_2O kristallisiert. Gesättigte Lösungen haben pH 7.30. Kalium-L-hydrogenaspartat wurde entsprechend aus Kaliumhydroxid und L-AspH$_2$ gewonnen. Es kristallisiert aus wäßriger Lösung (pH 7.52) als Dihydrat, K(L-AspH) · 2 H_2O. Die NMR-Spektren der beiden Komplexe unterscheiden sich nur unwesentlich. – *Li(L-AspH) · H$_2$O* hat im Kristall eine *Schicht*struktur, in der jedes Li-Atom tetraedrisch von vier Sauerstoffatomen umgeben ist. Das Kristallwasser und die Aminofunktion (die durch Protonierung als Ammoniumgruppe auftritt) sind nicht an das Metall koordiniert, sondern nur an einem Netz von Wasserstoffbrücken beteiligt, das die Schichten untereinander weiter verknüpft. Von den Li-koordinierten Carboxylat-Sauerstoffatomen hat eines eine Brückenfunktion zwischen den Metallatomen, die in Doppelsträngen angeordnet und an kantenverknüpften Sechsringen beteiligt sind. Innerhalb jeder Schicht sind Kanäle ausgebildet. – *K(L-AspH) · 2 H$_2$O* bildet im Kristall unendliche *Ketten*, in denen die K-Atome die Koordinationszahl 7 aufweisen. An den wieder in Doppelsträngen angeordneten Kationen treten die L-AspH$^-$-Gegenionen mit ihrer β-Carboxylat-Gruppierung als chelatisierende und verbrückende Strukturelemente auf. Die α-Carboxylat-Einheiten und die protonierte Amino-Gruppe haben keine Metall-Kontakte, sondern sind nur Bestandteil des H-Brücken-Netzwerks. Beide Hydratwassermoleküle sind K-koordiniert, eines davon metallverbrückend.

Complexes of lithium and potassium have a long history in chemotherapy[1-3]. The metal ions are administered in a variety of compositions. Apart from simple inorganic salts a large number of complexes with organic ligands have also been succesfully used. However, it should be noted that the role of the anionic component is not always well understood[4-6].

As part of a current study of the coordination chemistry of the alkali and alkaline earth metals with amino acids[7-12] we have also investigated the syntheses and the crystal structures of the two title compounds. *Lithium* aspartates and glutamates have been mentioned in the literature occasionally[13,14], however the exact stoichiometry, structural details, or spectroscopic data have not been considered. By contrast, the *potassium* salts of these two amino acids are more common and have appeared on the list of prescribed drugs for several decades.

It was to be anticipated that lithium should be strongly complexed by the multifunctional aspartate or glutamate anions, with the very small metal ion in a low coordination number. By contrast, the larger potassium ion was expected to exhibit a much higher coordination number with metal-acid contacts largely ionic in character. Thus, the investigations should provide information on two almost extreme

0009 – 2940/89/0808 – 1427 $ 02.50/0

cases of alkali metal ion binding by amino acids. Structural data on sodium, rubidium, and caesium salts are not yet available[15].

Results and Discussion

Aqueous solutions of lithium hydrogen L-aspartate Li(L-AspH) are obtained by treatment of an aqueous solution of L-aspartic acid (L-AspH$_2$) with equivalent portions of lithium carbonate. Carbon dioxide is evolved. Concentration of the reaction mixture by evaporation of the solvent at 60°C in vacuo followed by cooling to 20°C gives monoclinic crystals of the monohydrate. This hydrate can be dissolved in water to give a solution of pH 7.30.

$$2\,\text{L-AspH}_2 + \text{Li}_2\text{CO}_3 \xrightarrow{\text{H}_2\text{O}} \text{CO}_2 + 2\,\text{Li(L-AspH)}\cdot\text{H}_2\text{O}$$

Potassium hydrogen L-aspartate can be prepared by neutralization of aqueous L-aspartic acid with a potassium hydroxide solution. The product crystallizes as the dihydrate on concentration of the solution in vacuo and storage of the viscous residue at room temperature for several months. The product is very soluble in water, giving a solution of pH 7.52.

$$\text{L-AspH}_2 + \text{KOH} \xrightarrow{\text{H}_2\text{O}} \text{K(L-AspH)}\cdot 2\,\text{H}_2\text{O}$$

The NMR spectra of the solutions of both compounds show the resonances of the L-AspH$^-$ anion. There is little influence of the cation on the chemical shifts and coupling constants observed, indicating at least partial electrolytical dissociation of the compounds.

Li(L-AspH) · H$_2$O crystallizes in a layer structure, in which each lithium ion is coordinated to four L-aspartate anions – by one oxygen atom each – to give a tetrahedral coordination environment for each metal center (Figure 1). The amino groups and the water molecules are not coordinated to the lithium ions. By protonation the amino group is converted into an ammonium function which is only engaged in hydrogen bonding, in particular hydrogen bonding with the interstitial water molecule (Table 3).

Within each layer double strings of lithium ions are bridged by the L-aspartate anions forming a two-dimensional coordination polymer. Both α-carboxylate oxygen atoms (O1, O2) and one β-carboxylate oxygen atom (O3) are coordinated to the (different) lithium centers. Oxygen atoms O1 are located in bridging positions between two lithium ions giving Li ··· Li separations of only 3.155(5) Å. The noncoordinated oxygen atom (O4) only participates in hydrogen-bonding with the interstitial water molecule and the ammonium function (Table 3).

The polymer network contains six-membered rings, which are illustrated in a projection along the sheets in Figure 2. A second projection along the sheets, perpendicular to the first one, shows the existence of large channels within the layers (Figure 3).

Bond distances, bond angles, and crystal data are summarized in Tables 1 and 4.

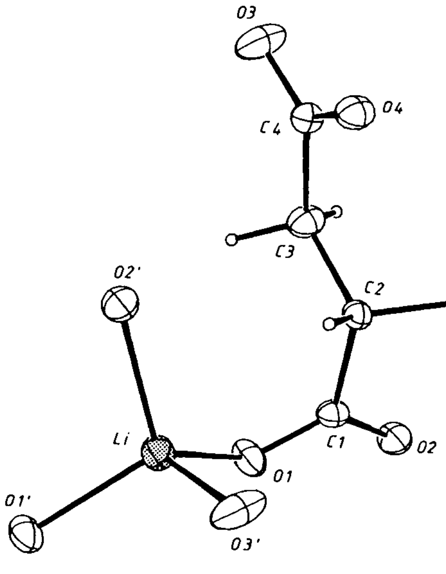

Figure 1. Lithium coordination in Li(L-AspH) · H$_2$O in the crystal (ORTEP, ellipsoids at the 50% probability level, H atoms with arbitrary radii)

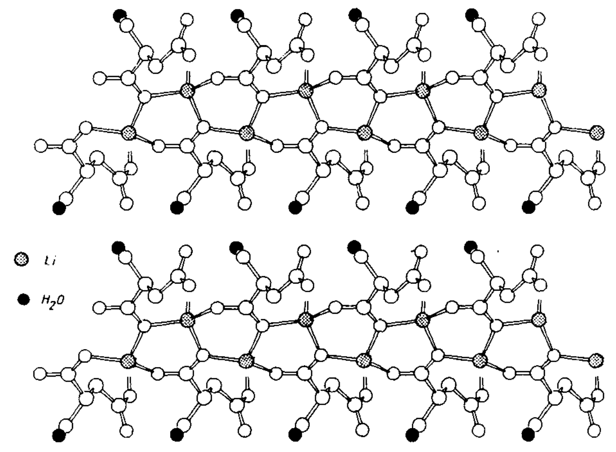

Figure 2. Structure of the coordination polymer layers of Li(L-AspH) · H$_2$O in the crystal (projected down the layers)

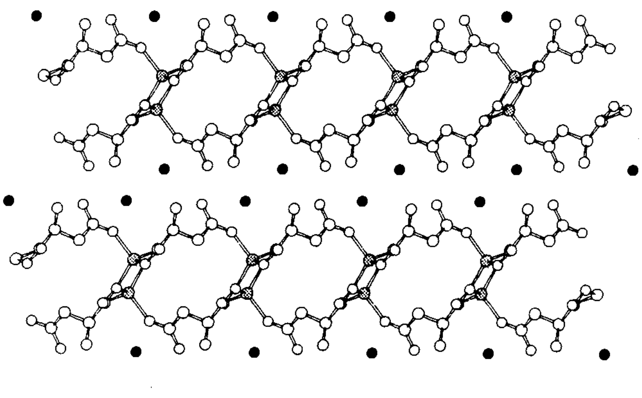

Figure 3. The layers of Li(L-AspH) · H$_2$O in a different projection (compare Figure 2) showing the noncoordinated water molecules and the large channels in the structure

Table 1. Bond distances [Å] and angles [°] for Li(L-AspH) · H_2O (esd's in units of the last significant figure in parentheses)

Distances			
Li-O1	1.990(3)	Li-O1'	1.943(3)
Li-O2'	1.961(3)	Li-O3'	1.938(3)
O1-C1	1.258(2)	O2-C1	1.247(2)
O3-C4	1.250(2)	O4-C4	1.266(2)
N1-C2	1.488(2)	C1-C2	1.535(2)
C2-C3	1.524(2)	C3-C4	1.521(2)
Angles			
O1 -Li-O1'	112.5(2)	O1 -Li-O2'	115.8(1)
O1 -Li-O3'	109.6(1)	O2'-Li-O1'	108.6(2)
O2'-Li-O3'	99.3(1)	O1'-Li-O3'	110.2(2)
Li -O1-C1	128.1(1)	O1 -C1-O2	126.7(1)
O1 -C1-C2	115.6(1)	O2 -C1-C2	117.7(1)
N1 -C2-C1	108.7(1)	N1 -C2-C3	111.4(1)
C1 -C2-C3	110.8(1)	C2 -C3-C4	113.6(1)
O3 -C4-O4	123.4(1)	O3 -C4-C3	118.1(1)
O4 -C4-C3	118.5(1)		

Symmetry operations:
O1' was derived from O1 by the operation -X, Y-0.5, 1-Z,
O2' from O2 by the operation X, Y-1, Z, and
O3' from O3 by the operation X-1, Y, Z.

K(L-AspH) · 2 H_2O forms a chain structure, where the metal atoms are arranged in double strings connected by the L-AspH$^-$ anions. Each potassium atom is heptacoordinate (Figure 4). As illustrated in Figure 5, the β-carboxylate groups of the monoanions function as bridges between three cations. One of the metal centers is chelated by both oxygen atoms (O3' and O4'), and these oxygen atoms have one further contact each to another neighbouring metal ion. Neither the amino group nor the α-carboxylate group are coordinated to a potassium ion.

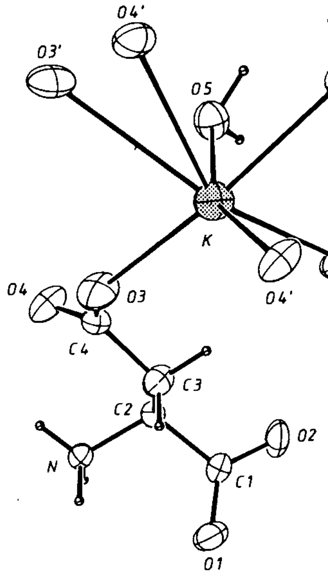

Figure 4. Potassium coordination in K(L-AspH) · 2 H_2O in the crystal

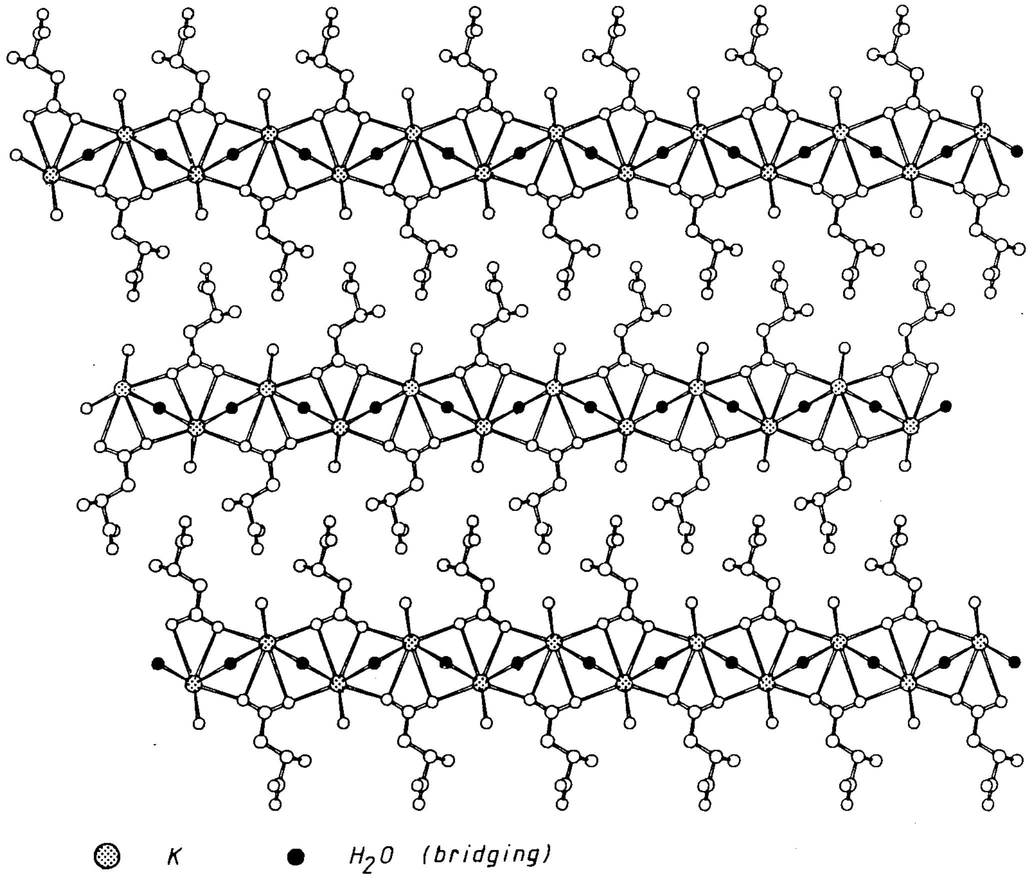

Figure 5. "Stacking" of the polymer chains of K(L-AspH) · 2 H_2O in the crystal to give hydrogen-bonded layers. The bridging H_2O molecules (black) are situated on special positions (twofold axes)

The two water molecules are all present in the first coordination sphere of the metal ion. One of the water molecules is in a bridging position between two metal centers which is a most unique feature amongst all the structures of metal aspartate and glutamate hydrates known to date. The other water molecule is associated with only one metal ion.

The stacking of the individual chains indicating the hydrogen bonding network is also illustrated in Figure 5. Bond distances, bond angles, and hydrogen bond dimensions are summarized in Tables 2 and 3, crystal data are included in Table 4.

Table 2. Bond distances [Å] and angles [°] for K(L-AspH) · 2 H_2O (esd's in units of the last significant figure in parentheses)

Distances			
K -O3	2.771(2)	K -O3"	3.193(2)
K -O4'	2.698(2)	K -O4"	3.185(2)
K -O5	2.689(2)	K -O6	2.807(2)
K -O7	2.855(2)	C1-O1	1.226(2)
C1-O2	1.252(2)	C1-C2	1.534(2)
C2-N	1.488(2)	C2-C3	1.526(2)
C3-C4	1.517(3)	C4-O3	1.259(3)
C4-O4	1.250(3)		
Angles			
O3 -K -O3"	76.5(1)	O3 -K -O4"	113.9(1)
O3 -K -O5	80.1(1)	O3 -K -O6	158.1(1)
O3 -K -O7	92.9(1)	O3 -K -O4"	120.3(1)
O3"-K -O4"	21.5(1)	O3"-K -O5	113.9(1)
O3"-K -O6	101.1(1)	O3"-K -O7	144.6(1)
O3"-K -O4'	118.2(1)	O4"-K -O5	94.9(1)
O4"-K -O6	72.4(1)	O4"-K -O7	148.2(1)
O4"-K -O4'	85.0(1)	O5 -K -O6	78.4(1)
O5 -K -O7	72.1(1)	O5 -K -O4'	157.8(1)
O6 -K -O7	76.4(1)	O6 -K -O4'	80.4(1)
O7 -K -O4'	96.5(1)	K -O3-C4	136.8(1)
O3 -C4-O4	124.6(2)	O3 -C4-C3	115.9(2)
O4 -C4-C3	119.5(2)	C4 -C3-C2	116.0(2)
C3 -C2-N	110.3(2)	C3 -C2-C1	108.5(1)
N -C2-C1	109.2(1)	C2 -C1-O1	117.4(2)
C2 -C1-O2	116.2(2)	O1 -C1-O2	126.3(2)

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

Table 3. Hydrogen bonds (A–B···C) [Å] for K(L-AspH) · 2 H_2O

A-B•••C	A-B	B••C	A••C	SYM. OP.
Li(L-AspH)•H_2O				
O5-H51•••O3	0.90	1.86	2.75	a
O5-H52•••O4	0.96	1.86	2.82	b
N1-H11•••O4	C.91	2.04	2.89	b
N1-H12•••O5	C.90	1.87	2.72	c
N1-H13•••O4	0.82	2.10	2.88	a
K(L-AspH)•2H_2O				
N -H11•••O7	0.91	2.36	3.15	d
N -H12•••O2	0.88	1.90	2.77	e
N -H13•••O2	0.98	1.82	2.78	f
O5-H51•••O3	0.99	1.80	2.74	g
O6-H61•••O4	0.98	2.02	2.87	g
O7-H71•••O1	1.06	1.58	2.64	h
O7-H72•••O3	1.00	1.96	2.94	i

Symmetry Operations:
a: X, 1+Y, Z
b: 1-X, 0.5+Y, -Z
c: X-1, Y, Z
d: X+1, Y, Z+1
e: X+0.5, 1.5-Y, -Z
f: X, Y, Z+1
g: 1-X, 1-Y, Z-1
h: X-0.5, 1.5-Y, -Z
i: X, Y, Z-1

The results obtained for *potassium hydrogen L-aspartate dihydrate* are similar to those reported for strontium L-glutamate hexahydrate[8]. Both structures have the metal centers arranged in double strings with a similar mode of coordination for the carboxylate ligands to the metals. However, the strontium glutamate structure forms layers, whereas the potassium aspartate structure is only a chain structure. The high metal coordination numbers and the noncoordination of the amino groups are further common features of these amino acid complexes.

For *lithium hydrogen L-aspartate hydrate* no structural parallel is available at present, because the coordination number four has previously only been found for zinc hydrogen L-aspartate *chloride*. For this structure the chloride is also present in the coordination sphere of the zinc ion. For Li(L-AspH) · H_2O it is most surprising that the lithium ion has a preference for oxygen over nitrogen coordination, since for other small metal ions, like magnesium, nitrogen coordination has always been observed. Taking into account the literature data on *sodium* salts of aspartic and glutamic acid[15] it appears that for alkali metals nitrogen coordination is generally not an important feature of complexation with aminodicarboxylic acids in the solid state, and probably also in aqueous solutions.

We thank *Deutsche Forschungsgemeinschaft* (Leibniz-Programm) and *Fonds der Chemischen Industrie* for financial support. D. L. W. wishes to thank the *Alexander von Humboldt-Stiftung* for a fellowship. We thank Dr. *J. Helbig* of Verla-Pharm GmbH for helpful discussions and *J. Riede* for careful work with the X-ray data collection.

Experimental

All experiments were carried out with bidistilled water. Reagents were of p.a. quality. pH values were measured using a Knick apparatus and Ingold reference cells. – Elemental analyses: Microanalytical laboratory of this Institute. – NMR spectra: Jeol FX 60 (^{13}C), Jeol CX 270 (^1H), with dioxane (δ = 67.3) and sodium 3-(trimethylsilyl)propanesulfonate (δ = 0.0) as internal standards, respectively.

Lithium Hydrogen L-Aspartate Monohydrate: A suspension of 13.3 g (100 mmol) of L-aspartic acid in 100 ml of water was treated at room temp. with 3.70 g (50 mmol) of lithium carbonate, which was added in small portions. When the strong effervescence had ceased, the reaction mixture was heated to 60°C for 3 h. After cooling to 20°C the solution was filtered and the clear filtrate concentrated in vacuo to 1/3 of the original volume. On standing crystals appeared after ca. 3 weeks. The initial yield was 5.5 g (32%), but additional product separated on prolonged standing. The colourless, transparent crystals are soluble in water to give a pH of 7.30. – ^1H NMR (D_2O, 20°C): δ = 3.88 (CH, X), 2.80 (CH_2, A), 2.66 (CH_2, B), ABX system, J(AX) = 3.1, J(BX) = 9.1, J(AB) = 17.6 Hz. – $^{13}C\{^1H\}$ NMR: δ = 178.2 and 174.9 (CO_2); 52.9 (CH); 37.2 (CH_2). – $^7Li\{^1H\}$ NMR: δ = −0.014 (rel. ext. aqueous LiCl; half width 16 Hz).

$C_4H_8LiNO_5$ (157.0)
Calcd. C 30.59 H 5.13 N 8.92 O 50.94 Li 4.45
Found C 30.33 H 5.07 N 8.94 O 51.03 Li 4.20

Potassium Hydrogen L-Aspartate Dihydrate: An aqueous solution of the compound was prepared from 13.3 g (100 mmol) of L-aspartic acid and 5.6 g (100 mmol) of potassium hydroxide in 40 ml of water at room temperature. Slow evaporation of the solution in vacuo (to a quarter of the original volume) lead to crystallisation of the viscous residue after about 4 months. After 5 months total crystalli-

Table 4. Crystallographic data for Li(L-AspH) · H_2O and K(L-AspH) · 2 H_2O

	Li(L-AspH) · H_2O	K(L-AspH) · 2 H_2O
Emp. formula	$C_4H_8LiNO_5$	$C_4H_{10}KNO_6$
M_r	157.05	207.23
Crystal system	Monoclinic	Orthorhombic
Space group	$P2_1$ (No. 4)	$P2_12_12$ (No. 18)
a [Å]	6.417(1)	6.934(1)
b [Å]	5.123(1)	24.626(2)
c [Å]	10.133(1)	5.008(1)
β [°]	98.19(1)	90
V [Å^3]	329.72	855.15
$d_{calcd.}$ [gcm^{-3}]	1.582	1.609
Z	2	4
$F(000)$ [e]	164	432
μ(Mo-K_α) [cm^{-1}]	1.3	6.1
T [°C]	23	23
Diffractometer	Enraf-Nonius CAD4	Enraf-Nonius CAD4
Scan	$\Theta-2\Theta$	$\Theta-2\Theta$
Scan width [° in ω]	0.9 + 0.35 tanΘ	0.8 + 0.35 tanΘ
Scan speed [°/min]	1–10	1–10
hkl range	$+7, \pm 6, \pm 12$	$\pm 8, \pm 31, +7$
$[(\sin\Theta)/\lambda]_{max}$ [Å^{-1}]	0.615	0.637
Measured reflections	1405	3746
Unique reflections	1282	1861
R_{int}	0.01	0.03
Observed reflections	1257 [$F_o \geq 4\sigma(F_o)$]	1814 [$F_o \geq 4\sigma(F_o)$]
Refined parameters	99	110
R [a]	0.024	0.032
R_w [b]	0.027 [c]	0.035
(Shift/error)$_{max}$	0.001	0.002
$\Delta\varrho_{fin}$ (max/min) [e/Å^3]	+0.32/−0.33	+0.34/−0.72

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

Table 5. Fractional atomic coordinates and equivalent isotropic thermal parameters for Li(L-AspH) · H_2O [$U_{eq} = (U_1 \cdot U_2 \cdot U_3)^{1/3}$, 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.)
LI	0.0010(4)	0.2852(7)	0.4092(3)	0.031
O1	0.1053(2)	0.6501(3)	0.4341(1)	0.034
O2	0.2006(2)	1.0322(4)	0.3535(1)	0.037
O3	0.7839(2)	0.2677(4)	0.2555(1)	0.058
O4	0.4995(2)	0.29670	0.1043(1)	0.032
O5	0.8614(2)	0.8695(4)	0.0868(1)	0.068
N1	0.2863(2)	0.8090(4)	0.1280(1)	0.029
C1	0.1885(2)	0.7892(4)	0.3535(2)	0.026
C2	0.2895(3)	0.6399(4)	0.2476(2)	0.025
C3	0.5130(3)	0.5560(4)	0.3025(2)	0.034
C4	0.6067(2)	0.3610(4)	0.2141(2)	0.030

Table 6. Fractional atomic coordinates and equivalent isotropic thermal parameters for K(L-AspH) · 2 H_2O (U_{eq} see Table 5)

ATOM	X/A	Y/B	Z/C	U(eq.)
K	0.24584(7)	0.53956(2)	0.1724(1)	0.031
C1	0.8363(3)	0.73865(8)	0.0430(4)	0.021
O1	0.8164(3)	0.77621(6)	0.2013(3)	0.050
O2	0.8047(2)	0.74028(6)	-0.2029(3)	0.054
C2	0.8938(3)	0.68315(7)	0.1573(4)	0.019
N	1.0192(2)	0.69136(6)	0.3950(3)	0.019
C3	0.7107(3)	0.65272(8)	0.2356(4)	0.022
C4	0.7390(3)	0.59573(7)	0.3438(4)	0.021
O3	0.5880(2)	0.57104(6)	0.4126(4)	0.026
O4	0.9055(2)	0.57648(6)	0.3594(4)	0.037
O5	0.50000	0.50000	-0.1834(5)	0.037
O6	0.00000	0.50000	-0.2279(5)	0.033
O7	0.2851(3)	0.61730(6)	-0.2469(4)	0.041

sation had occured (100% yield). The compound is very soluble in water. Its solutions show a pH of 7.52. According to the X-ray structure analysis (see below) the compound crystallizes with *two* K-coordinated water molecules. Elemental analyses indicate a higher water content, however, which approaches the composition of a *tri*hydrate. It appears that part of the crystal water is lost during the drying of the material. – ^{1}H NMR (D_2O, 20°C): δ = 3.71 (CH, X), 2.62 (CH_2, A), 2.48 (CH_2, B), ABX system, J(AX) = 3.7, J(BX) = 9.3, J(AB) = 17.4 Hz. – ^{13}C{^{1}H} NMR: δ = 178.3 and 175.0 (CO_2), 52.9 (CH), 37.3 (CH_2).

$C_4H_{12}KNO_7$ (trihydate, 225.2); $C_4H_{10}KNO_6$ (dihydrate, 207.2)

	C	H	N	O
Calcd.	C 21.33	H 5.37	N 6.22	O 49.72 (3 H_2O)
Calcd.	C 23.18	H 4.86	N 6.76	O 46.32 (2 H_2O)
Found	C 22.00	H 5.16	N 6.47	O 48.37

X-ray Structure Determinations: Crystal data and data collection parameters for Li(L-AspH) · H_2O (a) and K(L-AspH) · 2 H_2O (b) are listed in Table 4. During data collection three standard reflections were periodically measured (a: 3 −2 1, 0 1 5, −2 −2 2; b: 1 −4 3, 3 −7 −1, 4 14 0; Mo-K_α radiation, λ = 0.71069 Å, graphite monochromator), and no appreciable decomposition was observed for both structures. Intensity data were not corrected for absorption effects. Both structures were solved by direct methods (SHELXS-86) and then refined by full matrix methods (SHELX-76). All hydrogen atoms for both structures were located but not refined and all were assigned a fixed thermal parameter (U_{iso} = 0.05 Å^2). Atomic coordinates for both structures are listed in Tables 5 and 6, 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-53765, the names of the authors, and the journal citation.

CAS Registry Numbers

lithium hydrogen L-aspartate monohydrate: 120579-30-8 / potassium hydrogen L-aspartate dihydrate: 36221-97-3

---

[1] N. J. Birch in *Metal Ions in Biological Systems* (H. Sigel, Ed.), vol. 14, p. 257ff., Marcel Dekker Inc., New York 1984.

[2] N. J. Birch, M. S. Heighes, G. M. H. Thomas, S. Partridge, *Magnesium Bull.* **8** (1986) 145.

[3] A. Fournell in *Biochemische Eigenschaften und Möglichkeiten der klinischen Anwendung von Kalium-Magnesium-Aspartat* (R. Beer, U. Finsterer, Eds.), Editio Cantor, Aulendorf 1971.

[4] C. A. Evans, R. Guerremont, D. L. Rabenstein in *Metal Ions in Biological Systems* (H. Sigel, Ed.), vol. 9, p. 41ff., Marcel Dekker Inc., New York 1973.

[5] H. C. Freeman in *Inorganic Biochemistry* (J. Eichhorn, Ed.), vol. 1, p. 129ff., Elsevier, Amsterdam 1973.

[6] T. Doyle, *Adv. Protein Chem.* **22** (1966) 600.

[7] H. Schmidbaur, G. Müller, J. Riede, J. Helbig, M. Manninger, *Angew. Chem.* **98** (1986) 1014; *Angew. Chem. Int. Ed. Engl.* **25** (1986) 1013.

[8] H. Schmidbaur, I. Bach, D. L. Wilkinson, G. Müller, *Chem. Ber.* **122** (1989) 1433, following paper.

[9] H. Schmidbaur, I. Bach, D. L. Wilkinson, G. Müller, *Chem. Ber.* **122** (1989) 1439.

[10] H. Einspahr, C. E. Bugg, *Acta Cryst., Sect. B*, **35** (1979) 316.

[11] H. Einspahr, C. E. Bugg, *Acta Cryst., Sect. B*, **33** (1977) 3385.

[12] H. Einspahr, C. E. Bugg, *Acta Cryst., Sect. B*, **30** (1974) 1034.

[13] B. Müller-Oerlinghausen, M. Imiela, *Pharmacopsychiatry* **19** (1986) 284.

[14] W. Greil, K. Schnelle, S. Seibold, *Arzneim.-Forsch.* **24** (1974) 1079.

[15] S. T. Rao, M. Mallikarjunan, *Acta Cryst., Sect. A*, **31** (1975) 48.

[57/89]