Synthesis and crystal structure of magnesium bis[2-aminoethyl-(hydrogen)phosphonate] octahydrate, $Mg(2\text{-}AEPH)_2 \cdot 8H_2O$

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(Received May 29, 1990)

Abstract

The synthesis of $Mg(2\text{-}AEPH)_2 \cdot 8H_2O$ is described and the crystal structure of this compound has been determined by X-ray diffraction methods. The compound is built from octahedral magnesium hexaaqua dications, uncoordinated 2-AEPH⁻ anions and interstitial water molecules. The latter have no metal contacts but are engaged in hydrogen bonding. The packing of the components $([Mg(H_2O)_6]^{2+}[(2\text{-}AEPH^-)_2]) \cdot 2H_2O$ in the triclinic unit cells (space group $P\bar{1}$) appears to be strongly determined by a complicated network of hydrogen bonds, involving all water molecules, the (protonated) amino functions and the O-acceptor sites of the anions.

1. Introduction

Prior to 1959, the biologically occurring organic phosphorus compounds appeared to have the organic part of the molecule attached to oxygen, or, less commonly, to nitrogen. The isolation of 2-aminoethylphosphonic acid ($2\text{-}AEPH_2$), which can be regarded as the phosphorus analogue of β-alanine, from a natural source, rumen ciliated protozoa [1], marked the discovery of the first member of a new class of naturally occurring biochemically active species containing a direct carbon phosphorus bond. Apart from 2-aminoethylphosphonic acid, several other aminophosphonic acids structurally related to $2\text{-}AEPH_2$ have been discovered in coelenterates [2, 3]. It has subsequently been shown that $2\text{-}AEPH_2$ is widely distributed in nature [4, 5] and in humans [6], and the very unique C–P bond formation has since attracted considerable interest [7–10] in a hope to understand the biosynthesis and the possible role of this compound in metabolism and biological processes. The complexation abilities of $2\text{-}AEPH_2$ towards metal ions have been investigated both in solution [11–14] and in the solid phase [15–18] employing mainly potentiometric equilibrium measurements and Raman and infrared spectroscopy, respectively, but accompanied also by susceptibility measurements and thermal analysis. The data obtained by stability constant measurements in aqueous solutions indicate that $2\text{-}AEPH_2$ forms less stable complexes than its carboxylic acid analog β-alanine, probably due to both steric and electrostatic effects, which compensate the higher basicity of the phosphonate group PO_3^{2-} as compared to that of the carboxylate function. For a series of complexes, which includes coordination compounds of 2-AEP with Mg(II), Cr(III), Mn(II), Fe(II), Co(II), Ni(II) and Zn(II), the infrared data of the solid complexes suggest that the PO_3 group is coordinated to the metal in all complexes under investigation. Crystal structure determinations of these or other metal phosphonates derived from $2\text{-}AEPH_2$ in order to study its ligating behaviour and to evaluate the bonding mode have not been carried out, however.

The results of an X-ray structure determination of the stable β form of the dimorphic free acid [19] substantiates the zwitterionic nature of the molecule in the solid state. Another interesting feature of the solid state structure of the free $^+NH_3CH_2CH_2PO_3H^-$- acid is the pronounced *trans* configuration around the central methylene linkage, which is in contrast to the *cis* form exhibited, for example, by 2-aminoethanol phosphate, $^+NH_3CH_2CH_2OPO_3H^-$ [20]. Thus, metal N,O chelation of the corresponding 2-aminoethylphosphonato anions via O,N would require a change of the ground state *trans* configuration upon complex formation.

In aqueous solutions, $2\text{-}AEPH_2$ also exists in the zwitterionic form. In the standard physiological pH range two of the protons can dissociate with p*K*

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0020-1693/90/$3.50

values of 6.21 and 10.92 for the $-PO_3H^-$ and NH_3^+ group, respectively [13]. pK values of the dissociation of $-PO_3H_2$ groups are in the order of 1.0 [11], indicating full deprotonation of this group in the physiologically most relevant pH range 5–9. In this region, the monoanion $AEPH^-$ is the dominating species in solution.

As part of a study of metal complexation by naturally occurring organophosphorus species, we now report the synthesis and crystal structure of magnesium bis[2-aminoethyl(hydrogen)phosphonate] octahydrate. Beside the octahydrate, other microcrystalline phases with different amounts of water, for example a pentahydrate [15] and a trihydrate, can be isolated from the aqueous system. Due to its closest relation to the structure of the species in solution, the structure of the most water-rich octahydrate has been given preference.

TABLE 1. Fractional atomic coordinates and equivalent isotropic thermal parameters for $Mg(2\text{-}AEPH)_2 \cdot 8H_2O$ ($U_{eq} = (U_1 \cdot U_2 \cdot U_3)^{1/3}$ where U_1, U_2, U_3 are the eigenvalues of the U_{ij} matrix; e.s.d.s in parentheses)

Atom	x/a	y/b	z/c	U_{eq}
N	0.6015(2)	−0.2604(2)	0.2592(2)	0.017
C1	0.5302(2)	−0.2418(2)	0.5558(2)	0.014
C2	0.4575(2)	−0.2716(2)	0.3475(2)	0.016
P	0.36050(4)	−0.24733(4)	0.67058(4)	0.011
O4	0.4522(1)	−0.2251(1)	0.8778(1)	0.017
O5	0.2485(1)	−0.0944(1)	0.6042(1)	0.018
O6	0.2580(1)	−0.4256(1)	0.6135(1)	0.014
MG	0.00000	0.00000	0.00000	0.014
O1	−0.2645(1)	0.0122(2)	−0.0368(2)	0.018
O2	0.0347(2)	0.0163(2)	0.2821(2)	0.027
O3	0.0343(2)	0.2668(2)	0.0086(2)	0.026
O7	−0.0229(2)	0.4862(2)	−0.2747(2)	0.017
				U_{iso}
H11	−0.336(3)	−0.072(3)	−0.057(3)	0.028(5)
H12	−0.314(3)	0.101(4)	0.023(4)	0.053(7)
H21	−0.060(3)	0.052(3)	0.316(3)	0.044(6)
H22	0.100(3)	−0.016(3)	0.366(3)	0.035(6)
H31	0.015(3)	0.323(3)	−0.083(4)	0.041(6)
H32	0.046(3)	0.345(3)	0.116(4)	0.053(7)
H41	0.599(2)	−0.126(2)	0.587(2)	0.017(4)
H42	0.615(3)	−0.326(3)	0.604(3)	0.025(5)
H51	0.384(2)	−0.183(3)	0.303(3)	0.020(5)
H52	0.405(2)	−0.389(3)	0.310(2)	0.015(4)
H61	0.662(3)	−0.158(3)	0.294(3)	0.030(5)
H62	0.673(4)	−0.345(4)	0.293(4)	0.050(7)
H63	0.560(3)	−0.268(3)	0.137(3)	0.023(5)
H71	−0.097(3)	0.462(3)	−0.367(3)	0.044(7)
H72	0.078(4)	0.519(4)	−0.311(4)	0.069(9)

Experimental

The ligand 2-aminoethylphosphonic acid was obtained from Ciba Geigy, Basel. All other chemicals were commercial grade and used without further purification. The employed water was bidistilled and carbonate free.

Magnesium bis[2-aminoethyl(hydrogen)phosphonate] octahydrate, $Mg(2\text{-}AEPH)_2 \cdot 8H_2O$

To a solution of 2-aminoethylphosphonic acid (1.00 g, 7.99 mmol) in water (20 ml) crystalline $MgCl_2 \cdot 6H_2O$ (0.81 g, 3.99 mmol) was added with stirring. The pH of the solution was adjusted to 7.0 with 0.1 m NaOH. Addition of 40 ml of 95% ethanol led to the formation of an oil, which was separated and treated with another 50 ml of ethanol. On prolonged stirring, a white precipitate separated from the oil. The mixture was filtered, the precipitate washed with small portions of methanol, dried in a vacuum, and analyzed as the octahydrate. The crude product, which was obtained in 72% yield, was dissolved in a minimum amount of water. Small colorless crystals were formed upon slow diffusion of methanol into this solution. The crystals melt at 104 °C with loss of hydrate water.

Products with different water contents can be obtained on changing the reaction conditions.

Crystal data

A single crystal of suitable size (0.25 × 0.30 × 0.35 mm) was selected, mounted in a glass capillary which was placed in a stream of cooled nitrogen on a Syntex $P2_1$ diffractometer. Intensities $0 \rightarrow h$, $-k \rightarrow k$, $-l \rightarrow l$ were measured for the triclinic cell, space group $P\bar{1}$, with $a = 8.027(1)$, $b = 7.653(1)$, $c = 7.580(1)$ Å, $\alpha = 92.72(1)$, $\beta = 106.85(1)$, $\gamma = 93.14(1)°$, $V = 444.00$ Å^3, $Z = 1$, at −50 °C (ω scans, Mo Kα radiation (λ 0.71069 Å), graphite monochromator). During data collection three intensity check reflections were measured every 2 h (300, 010, 001), and no appreciable decomposition was observed. A total of 1747 independent reflections was collected in the range of $12° < \theta < 27°$, of which 1631 reflections with $F_o \geq 4\sigma(F_o)$ were used in structure determination and refinement after absorption, geometrical and Lp corrections. The positional parameters of the magnesium atom were calculated from the Patterson map (SHELXS-86) [21]. A difference Fourier map (SHELX-76) [22] based on the metal atom phases revealed the positions of the remaining atoms, including all hydrogen atoms. The positional parameters of the atoms were refined by full matrix least-squares methods with anisotropic thermal parameters for all non-hydrogen atoms, and isotropic parameters for the hydrogen atoms to a final R (R_w) value of 0.0287 (0.0382). Atomic coordinates are listed in

Table 1, and selected interatomic distances and angles are given in Tables 2 and 3. See also 'Supplementary material'.

Results and discussion

$Mg(2\text{-}AEPH)_2\cdot 8H_2O$ was obtained by treatment of an aqueous solution of 2-aminoethylphosphonic acid ($2\text{-}AEPH_2$) with crystalline $MgCl_2\cdot 6H_2O$ in the molar ratio 2:1 at neutral pH (eqn. (1)). Addition of ethanol to the solution first led to the formation of an oil, which after separation turned into a colourless microcrystalline precipitate upon prolonged stirring and addition of ethanol.

$$2\ 2\text{-}AEPH_2 + MgCl_2\cdot 6H_2O \xrightarrow[-NaCl,\ pH=7]{+NaOH,\ H_2O} Mg(2\text{-}AEPH)_2\cdot 8H_2O \tag{1}$$

TABLE 2. Selected bond distances (Å) and angles (°) for $Mg(2\text{-}AEPH)_2\cdot 8H_2O$ (e.s.d.s in units of the last significant figure in parentheses)

Hexaaqua magnesium cation			
Mg–O(1)	2.067(1)	O(1)–MG–O(2)	87.8(1)
Mg–O(2)	2.072(1)	O(1)–Mg–O(3)	91.2(1)
Mg–O(3)	2.041(1)	O(2)–Mg–O(3)	89.3(1)
2-Aminoethyl(hydrogen)phosphonate anion			
P–O(4)	1.526(1)	C(1)–P–O(4)	106.8(1)
P–O(5)	1.530(1)	C(1)–P–O(5)	106.8(1)
P–O(6)	1.530(1)	C(1)–P–O(6)	106.6(1)
P–C(1)	1.816(1)	C(2)–C(1)–P	112.5(1)
C(1)–C(2)	1.518(2)	C(1)–C(2)–N	110.5(1)
C(2)–N	1.495(2)	O(4)–P–O(5)	111.6(1)
		O(4)–P–O(6)	112.2(1)
		O(5)–P–O(6)	112.5(1)
		P–C(1)–C(2)–N	178.3(1)

The single crystal X-ray diffraction work showed the crystals of magnesium bis[2-aminoethyl(hydrogen)phosphonate] octahydrate to consist of hexaaqua magnesium dications, two *uncoordinated* 2-aminoethyl(hydrogen)phosphonato counterions, and two interstitial water molecules, which have no direct metal contacts but are engaged in hydrogen bonding (Fig. 1). The magnesium ions occupy a crystallographic center of inversion in an octahedral environment of six oxygen atoms. Accordingly, the two anions and the two interstitial water molecules are crystallographically related by this center of symmetry at magnesium.

The $Mg\text{–}OH_2$ distances (2.041(1)–2.072(1) Å) (Table 2) are in the same range as reported previously for other hexaaqua magnesium salts, e.g. magnesium ammonium sulfate [23] and magnesium ammonium phosphate [24] hexahydrate. The structure of the 2-aminoethyl(hydrogen)phosphonate anions is closely related to that of the free acid. The most prominent feature is again the *trans* arrangement of the phosphonato and (protonated) amino functions with respect to the C–C axis, as measured by the dihedral angle P–C–C–N of 178.3(1)°. Except for the differences owing to the protonation of one oxygen atom of the PO_3 group in the free acid, the bond lengths and angles found for the $2\text{-}AEPH^-$ anion in the present structure are almost duplicates of those in the free acid $2\text{-}AEPH_2$ [19].

The packing of the ionic species in the crystal of magnesium bis[2-aminoethyl(hydrogen)phosphonate] octahydrate is clearly determined by hydrogen bonds. All water molecules, the protonated amino functions and the O-acceptor sites of the phosphonato anion participate in a complicated three dimensional network, which links not only cations and anions but also adjacent anions through hydrogen bonds between the (protonated) amino and phos-

TABLE 3. Hydrogen bond interactions (A···B–C, in Å) for $Mg(2\text{-}AEP)_2\cdot 8H_2O$

A	B	C	A···B	B–C	A···C	Angle (°)	s.o.*
O(4)	H(11)	O(1)	1.94(2)	0.82(2)	2.73(0)	165(2)	a
O(4)	H(12)	O(1)	1.80(3)	0.97(3)	2.74(0)	165(2)	b
O(4)	H(63)	N	1.96(2)	0.89(2)	2.82(0)	165(2)	c
O(5)	H(21)	O(2)	1.82(3)	0.92(3)	2.74(0)	172(2)	b
O(5)	H(22)	O(2)	2.00(2)	0.76(3)	2.75(0)	172(2)	d
O(5)	H(61)	N	2.06(2)	0.88(2)	2.92(0)	166(2)	e
O(6)	H(71)	O(7)	1.94(3)	0.78(3)	2.71(0)	171(3)	f
O(6)	H(72)	O(7)	1.74(3)	0.95(3)	2.69(0)	177(3)	g
O(6)	H(62)	N	1.97(3)	0.89(3)	2.81(0)	156(3)	h
O(7)	H(31)	O(3)	1.93(3)	0.82(3)	2.74(0)	172(2)	d
O(7)	H(32)	O(3)	1.78(3)	0.97(3)	2.72(0)	165(2)	i

*Atoms B, C are generated by the following symmetry operations: (a) $1+x, y, 1+z$; (b) $-x, -y, 1-z$; (c) $x, y, 1+z$; (d) x, y, z; (e) $1-x, -y, 1-z$; (f) $-x, -y, -z$; (g) $x, -1+y, 1+z$; (h) $1-x, -1-y, 1-z$; (i) $-x, 1-y, -z$.

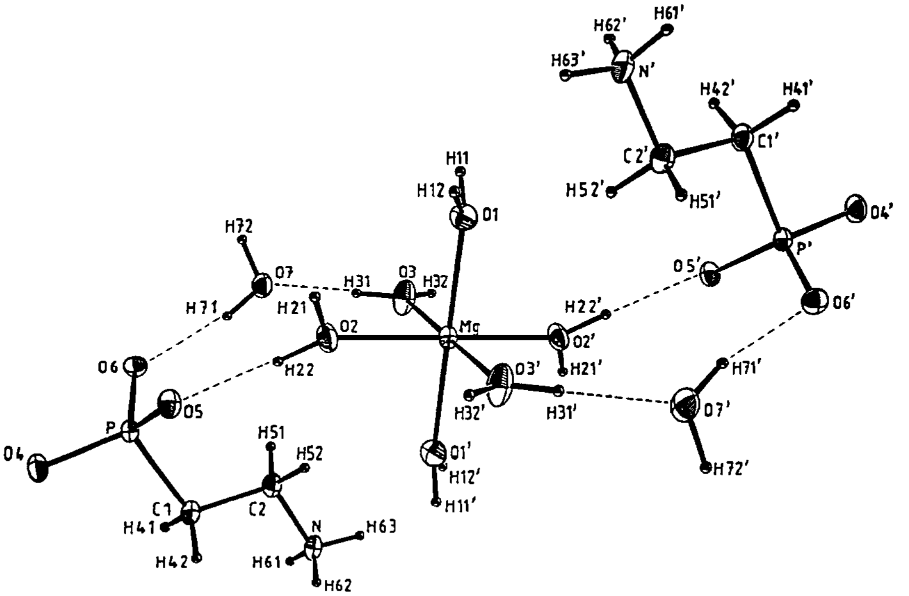

Fig. 1. Structure of $Mg(2\text{-}AEPH)_2 \cdot 8H_2O$ in the crystal and atomic numbering scheme (ORTEP [25], displacement parameters at the 50% probability level; H atoms with arbitrary radii).

phonato functions. Furthermore, the two non-coordinated water molecules play a significant role in determining the packing by connecting two adjacent hexaaqua magnesium centers. The most important hydrogen bond interactions are summarized in Table 3.

The results of the structure determination of the title compound, which is not a 'true' coordination compound, have shown that it should be formulated as $([Mg(H_2O)_6]^{2+}[2\text{-}AEPH^-]_2) \cdot 2H_2O$, and accordingly that in neutral aqueous medium 2-AEPH$^-$ is a weak ligand for magnesium and cannot compete successfully with water molecules for coordination sites in the inner coordination sphere of the metal. The delicate balance between the energies of metal coordination by aminophosphonato anions and by water molecules, both supported by a large set of different hydrogen bonds, could probably be shifted towards phosphonate coordination by employing a strongly basic medium containing the corresponding $(2\text{-}AEP)^{2-}$ dianion. The abstraction of the second proton should have a major influence on the network of hydrogen bonds on the one hand and should also enhance the chelating abilities of the ligand on the other. Studies in this direction are in progress.

Supplementary material

Calculated and observed structure factor amplitudes together with a complete list of atomic coordinates and thermal parameters have been deposited. Further details of the structure determination are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, Germany, on quoting the deposition number CSD 54687, the names of the authors, and the journal citation.

Acknowledgements

We thank Dr L. Maier, Ciba-Geigy, for support, Mr J. Riede for establishing the X-ray data set, and Professor H. Schmidbaur for helpful discussions.

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