

Magnesium Anthranilate Dihydrate

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Magnesium, Hexa(aquo) Complex of Magnesium,
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The reaction mixture of magnesium chloride with two equivalents of potassium anthranilate [$K^+ Anth^-$] in water gives on cooling to 0 °C a 60% yield of a precipitate which after drying in a vacuum has the composition $[Mg(H_2O)_6](Anth)_2$ (**1**). Recrystallization from hot water affords an octahydrate identified as $[Mg(H_2O)_6](Anth)_2(H_2O)_2$ (**2**) in a single crystal X-ray diffraction study. Contrary to findings for the related calcium, strontium and barium compounds, in the magnesium compound the anthranilate anions are not part of the coordination sphere of the metal atom. Thermal degradation of **1** or **2** at 125 °C gives the anhydrous product $[Mg(Anth)_2]$, **3**. Alternative preparative routes employed in previous studies gave only anhydrous material. The result of the present investigation confirms the outstanding stability of the hexa(aquo) complex of magnesium, as compared to the hydrates of the larger alkaline earth metals, in the presence of potential bioligands.

Introduction

Magnesium salts play a central role as cofactors for most enzymes that participate in the biochemistry of nucleic acids [1–5]. The outstanding stability of the hexahydrate dication $[Mg(H_2O)_6]^{2+}$, as compared to the hydrates of the other three metal ions most common in biological systems (sodium, potassium and calcium), is responsible for the superior template function of magnesium dications in aqueous solution under physiological conditions. However, in many cases the mode of action of Mg^{2+} on the molecular level is not perfectly understood, and few model complexes are available where structural information gives a clue as to the details of the binding sites at the substrates.

Recent structural work on magnesium complexes of amino acids [6,7] has revealed the modes

of chelate interaction for L-aspartic and L-glutamic acid which are known to be the prominent binding sites for magnesium in proteins. This information is also of key importance for an understanding of the mechanism of many biomineralization processes [8]. Complementary studies focused on complexes with β -glutamate [9], citrate [10], and orotate ligands [11].

Current interest has also been oriented towards the coordination chemistry of alkali and earth alkaline salts of salicylic [12] and anthranilic acid (**A**, **B**) which are ubiquitous constituents of biological systems and – in the case of **B** – precursors of important amino acids such as tryptophan. The two aromatic hydroxy- and amino-benzoic acids are also important models for the coordination chemistry of humic acids [13].

While the stoichiometry, structure and stability of calcium, strontium, and barium anthranilates could recently be established [14], open questions remained regarding the nature of the magnesium salts of anthranilic acid. Hill and Curran reported the precipitation of a magnesium bis-anthranilate from aqueous solution [15], but the elemental analysis and the IR and UV/Vis spectra were inconclusive. Murugavel *et al.* also obtained this product and confirmed that the material is anhydrous and insoluble in water, but could not determine its structure [14]. This result was unexpected, because magnesium ions – more than their heavier congeners – are known to trap water molecules in almost all their complexes with bio-ligands.

In this paper we present an account of our own current studies and of the successful structural characterization of magnesium anthranilates obtained *via* a slightly different preparative route.

Results

Potassium anthranilate (K^+Anth^-) is prepared by neutralization of anthranilic acid (AnthH) with potassium hydroxide in water at 20 °C. Upon addition of an aqueous solution of magnesium chloride (molar ratio K:Mg = 2:1) and cooling to 0 °C a pale-brown crystalline precipitate appears in ca. 60%, which slowly loses crystal water when stored at room temperature. The vacuum-dried product has the composition of the hexahydrate $[Mg(H_2O)_6](Anth)_2$ (**1**, by elemental analysis).

In previous attempts to prepare magnesium anthranilate, magnesium chloride and AnthH in a water/methanol mixed solvent were treated with aqueous ammonia. This procedure affords an in-

soluble anhydrous material of the composition $\text{Mg}(\text{Anth})_2$ of unknown structure [14,15].

The product obtained in the present study (1) can readily be redissolved in hot water and crystallized (at 20 °C) to give single crystals of an octahydrate (2) $\text{Mg}(\text{Anth})_2(\text{H}_2\text{O})_8$ which is to be formulated as $[\text{Mg}(\text{H}_2\text{O})_6](\text{Anth})_2(\text{H}_2\text{O})_2$ (2, by X-ray crystallography, below). Compound 2, which is probably identical with the primary product, but of higher purity, also has a high water vapour pressure and loses two of the eight water molecules when air-dried or exposed to vacuum.

On heating of the hexahydrate 1 to 125 °C the water content is reduced to the anhydrous $\text{Mg}(\text{Anth})_2$ (3, by elemental analysis). This dehydration was followed by thermogravimetric analysis, which confirmed the loss of 6 H_2O in the narrow range of 105–125 °C. According to the TGA diagram, the dehydrated residue is stable to 415 °C as already noted by earlier workers [14].

All salts (1–3) were investigated by IR-spectroscopy, but the spectra showed only small variations in the individual band characteristics. The samples of 1 and 2 exhibit the absorptions of crystal water, but these gradually disappear upon transition to 3 (125 °C). The IR spectrum of the anhydrous material has been published, as have UV/Vis and NQR data [14–16].

Crystals of $[\text{Mg}(\text{H}_2\text{O})_6](\text{Anth})_2(\text{H}_2\text{O})_2$ (2) are monoclinic, space group $P2_1/c$ with $Z = 2$ formula units in the unit cell. The structure is composed of a hexa(aquo)magnesium cation, the metal atom of which resides on a center of inversion, and two anthranilate anions and two water molecules, each pair related by symmetry (Fig. 1). The components are engaged in a network of hydrogen bonds (Table 1). A prominent intra-anionic hydrogen bond spans the amino and the carboxylate group of each anthranilate unit (N1-H1–O4). All other

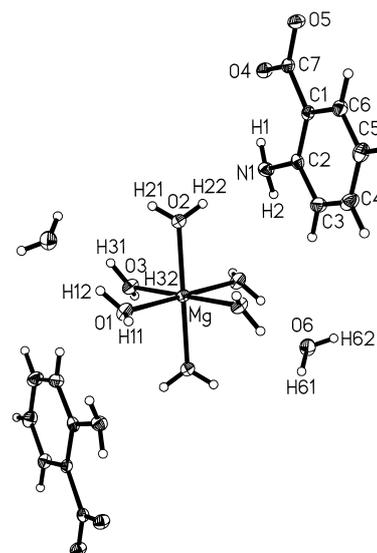


Fig. 1. Structure of $[\text{Mg}(\text{H}_2\text{O})_6](\text{Anth})_2(\text{H}_2\text{O})_2$ (2) with atomic numbering (ORTEP drawing with 50% probability ellipsoids).

hydrogen bonds of the anions involve at least one magnesium-bound water molecule, and the two interstitial water molecules are also associated with water molecules of the hexa(aquo)magnesium dication (O1-H12–O6', O3-H32–O6'').

The dications and water molecules form layers separated by layers of anthranilate anions (Fig. 2).

The structure of the magnesium anthranilate 1 is entirely different from the structures of the calcium, strontium and barium compounds, which crystallize as tri- (Ca, Sr) or monohydrates (Ba), respectively. With the heavier earth alkaline metals, the anions are part of the ligand sphere of the dications, while in the magnesium salts the integ-

Table 1. Hydrogen bonding in $[\text{Mg}(\text{H}_2\text{O})_6](\text{Anth})_2(\text{H}_2\text{O})_2$ (2).

D-H-A	d(D-H) [Å]	d(H...A) [Å]	D-H...A [°]	d(D...A) [Å]	Symmetry
O6-H61-O4	0.852	1.890	167.41	2.728	a)
O6-H61-O5	0.776	1.998	162.43	2.748	b)
O1-H11-O5	0.813	1.984	168.69	2.786	c)
O1-H12-O6	0.842	1.885	174.30	2.724	d)
O2-H21-O4	0.829	1.935	177.52	2.764	e)
O2-H22-N1	0.826	2.012	172.25	2.833	f)
O3-H31-O5	0.865	1.889	170.15	2.746	e)
O3-H32-O6	0.785	1.977	166.67	2.747	g)
N1-H1-O4	0.896	1.994	132.28	2.680	f)

a) $x+1, y, z$; b) $-x, -y+1, -z$; c) $x+1, -y+0.5, z+0.5$; d) $-x+1, -y+1, -z+1$; e) $-x, -y+1, -z+1$; f) x, y, z ; g) $x, -y+1.5, z+0.5$.

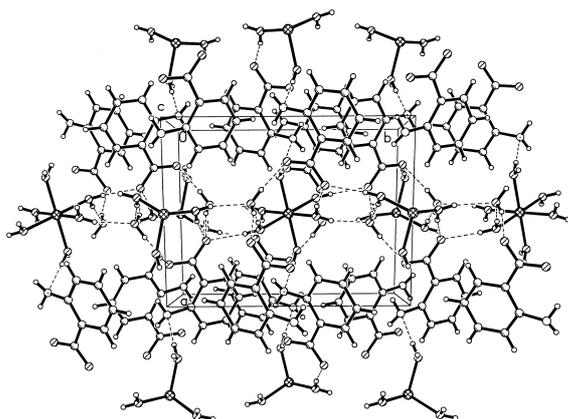


Fig. 2. Cell plot of $[\text{Mg}(\text{H}_2\text{O})_6](\text{Anth})_2(\text{H}_2\text{O})_2$ (**2**), showing the layers of anthranilate anions separated by layers of the dications and water molecules.

rity of the $[\text{Mg}(\text{H}_2\text{O})_6]^{2+}$ octahedron is strictly conserved. This result is consistent with findings for many magnesium salts with bio-relevant counterions in aqueous solution and in crystalline phases.

Experimental Section

The experiments were carried out in bidistilled water under an atmosphere of nitrogen. All reagents were commercially available. Standard glassware and equipment was used throughout.

Hexa(aquo)magnesium dianthranilate (**1**), and its dihydrate, **2**.

Anthranilic acid (2.06 g, 15 mmol) is neutralized with potassium hydroxide (0.84 g, 15 mmol) in 30 ml of bidistilled water at 20 °C. The reaction mixture is filtered, its pH adjusted to 6 with small amounts of anthranilic acid and added to a solution of magnesium chloride (1.52 g, 7.5 mmol) in 7.5 ml of water. A pale-brown precipitate is formed which dissolves on heating to reflux. Upon cooling to 20 °C a yellow solid is obtained (2.17 g, 61% yield). Heating of the product to 100 °C (but not beyond) or exposing it to a vacuum at 20 °C leaves a solid with a lower content of crystal water: Calculated for the hexahydrate $\text{C}_{14}\text{H}_{24}\text{MgN}_2\text{O}_{10}$, C 41.55, H 5.98, N 6.92, Mg 6.01; found C 41.00, H 5.90, N 6.83, Mg 6.51.

Heating of samples to temperatures above 125 °C gave *anhydrous* material as already reported in the literature. The TGA diagram shows rapid weight loss (24%) between 100 and 125 °C and decomposition (weight loss of further 35%) between 415 and 450 °C.

Careful crystal growth from a 0.01 molar solution obtained upon redissolution of **1** in hot water and slow cooling to 20 °C gave single crystals of the *octahydrate*, which must be kept in a closed vial and manipulated in a water-saturated atmosphere at 20 °C to retain its full water content.

Structure determination

The crystalline sample was placed in inert oil, mounted on a glass pin, and transferred to the cold gas stream of the diffractometer. Crystal data were collected and integrated using a Nonius DIP2020 system with monochromated Mo-K α ($\lambda = 0.71073$ Å) radiation at -130 °C. The structure was solved by direct methods using SHELXS-97 and refined by full matrix least-squares calculations on F^2 using SHELXL-97. Non-hydrogen atoms were refined with anisotropic thermal parameters. C-H atoms were placed in idealized positions and refined using a riding model with fixed isotropic contributions, whereas the N-H and O-H atoms were located and refined isotropically.

Crystal data for $\text{C}_{14}\text{H}_{28}\text{MgN}_2\text{O}_{12}$. $M = 440.69$, monoclinic, $a = 9.4416(2)$, $b = 11.7701(3)$, $c = 9.5330(2)$ Å, $\beta = 107.417(1)^\circ$, space group $P2_1/c$, $Z = 2$, $V = 1010.82(4)$ Å³, $\mu(\text{Mo-K}\alpha) = 1.53$ cm⁻¹, 37052 measured and 2318 unique reflections [$R_{\text{int}} = 0.059$], $wR2 = 0.0845$, $R = 0.0381$ for 2318 reflections [$I \geq 2\sigma(I)$] and 173 parameters. The function minimized was $wR2 = \{\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]\}^{1/2}$; $w = 1/[\sigma^2(F_o^2) + (ap)^2 + bp]$; $p = (F_o^2 + 2F_c^2)/3$; $a = 0.0277$, $b = 0.51$. Residual electron density 0.275/-0.242 Å⁻³. Thermal parameters and complete tables of interatomic distances and angles have been deposited with the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. The data are available on request on quoting CCDS-178447.

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