detailed investigation of magnetic behavior would be of interest; the correlation between bridging structure and spin coupling for this class of trimeric compounds would become evident in such a study.

Finally, the recognized difficulty in the isolation of analytically pure samples of monomeric MSALPN complexes with M-$(O_2CCH_3)_2$[8,9] may be attributed to the presence of some acetate-bridged species. We find that acetate is present in the preparations carried out with other metal ions and other related Schiff base ligands. Analytically pure monomeric FeSALPN has been prepared from $Fe(CO)_5$.[9] The Mössbauer parameters of this well-characterized species differ significantly from "FeSALPN" prepared from $Fe(O_2CCH_3)_2$,[10] possibly because of the presence of species such as **2**.

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Registry No. **1**, 136804-08-5; **2**, 136804-09-6; **3**, 136804-10-9.

Supplementary Material Available: An ORTEP drawing of molecule **2** and crystal packing diagrams and tables giving details of the X-ray structural analysis, bond lengths and bond angles, calculated hydrogen atom coordinates, and anisotropic thermal parameters for complexes **1** and **2** (12 pages); listings of observed and calculated structure factors for complexes **1** and **2** (16 pages). Ordering information is given on any current masthead page.

Contribution from the Institut für Anorganische und Analytische Chemie der Universität Freiburg, D-7800 Freiburg, Germany

A Zinc Complex of the Carbonic Anhydrase Inhibitor Acetazolamide (aaaH): Crystal Structure of $(aaa)_2Zn(NH_3)_2$

Uwe Hartmann and Heinrich Vahrenkamp*

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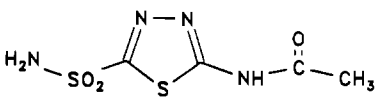
Introduction

The widely varying and well-known role of zinc in many biological processes contrasts sharply with the small number of simple zinc complexes which can serve as functional or structural models thereof. We have therefore set out to provide structural information in order to facilitate a relevant discussion at the molecular level. An attractive compound for such studies is the enzyme carbonic anhydrase (CA), whose structure and function are simple: its ligation of the zinc ion by three histidine imidazoles can be modeled by tridentate ligands,[1] and models of its CO_2 hydrating function begin to emerge.[2]

Among the many inhibitors, mostly anionic ones, of CA, acetazolamide (aaaH, **1**) is the most prominent one. The structure



1 = aaaH

of the enzyme-inhibitor complex has been determined at 3 Å resolution, and that of the enzyme-(3-(acetoxymercurio)-4-aminobenzenesulfonamide) complex at 2 Å resolution.[3] In both cases, the inhibitors act as monodentate ligands through their amidosulfonyl moieties. While the protein crystallographic data cannot differentiate between Zn-N and Zn-O binding, it has been shown by a variety of methods that the inhibitors bind to zinc through their sulfonamide N atoms.[4] Up to now, these findings have not been complemented by the structure of a simple metal complex of acetazolamide: in the nickel complex one of the ring nitrogens and in the copper complex the amide nitrogen as well as both ring nitrogens ligate the metal.[5] The simplest model compound, $(aaa)_2Zn(NH_3)_2$ (**2**), first obtained by Borrás,[6] was reported to be difficult to crystallize. We have now obtained crystalline **2**. This paper reports its structure.

Table I. Crystallographic Data for **2**

chem formula	$C_8H_{16}N_{10}O_6S_4Zn$
mol wt	542.0
space group	*Pbcn* (No. 60)
cell	a = 7.055 (1) Å, b = 10.083 (1) Å, c = 27.703 (3) Å
V	1970.8 (3) Å^3
Z	4
ρ_{obsd}, ρ_{calcd}	1.70, 1.68 g cm^{-3}
μ(Mo Kα)	16.30 cm^{-1}
T	20 °C
λ(Mo Kα)	0.710 73 Å
R(unit weights)	0.051

Table II. Atomic Coordinates and Equivalent Isotropic Temperature Factors for **2**

atom	x	y	z	U_{eq}, Å^2
Zn	0.0000	0.5802 (1)	0.2500	0.033 (1)
N1	-0.1504 (8)	0.4638 (6)	0.2046 (2)	0.047 (2)
N2	0.1804 (8)	0.6849 (5)	0.2109 (2)	0.037 (2)
S1	0.3395 (2)	0.6177 (2)	0.1814 (1)	0.033 (1)
O1	0.5093 (7)	0.6957 (5)	0.1751 (2)	0.046 (2)
O2	0.3659 (7)	0.4844 (4)	0.1997 (2)	0.046 (2)
C1	0.2652 (10)	0.5979 (6)	0.1210 (2)	0.035 (2)
S2	0.3984 (3)	0.6528 (2)	0.0729 (1)	0.039 (1)
N3	0.1133 (9)	0.5321 (6)	0.1087 (2)	0.045 (2)
N4	0.0930 (9)	0.5234 (6)	0.0599 (2)	0.048 (2)
C2	0.2312 (10)	0.5819 (7)	0.0358 (2)	0.038 (2)
N5	0.2351 (9)	0.5847 (6)	-0.0121 (2)	0.042 (2)
C3	0.3736 (12)	0.6439 (8)	-0.0377 (3)	0.051 (3)
O3	0.5145 (9)	0.6851 (7)	-0.0169 (2)	0.073 (2)
C4	0.3460 (12)	0.6536 (9)	-0.0916 (3)	0.061 (3)

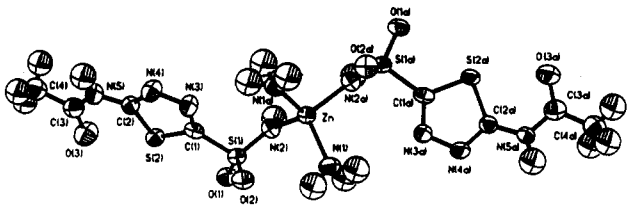


Figure 1. Thermal ellipsoid plot of the structure of **2**.

Experimental Section

Preparation. Colorless crystals of **2**[6] were obtained by dissolving **1** (500 mg, 2.24 mmol) and $Zn(ClO_4)_2$ (300 mg, 1.12 mmol) in 25% ammonia (5 and 6 mL, respectively). Both solutions were combined dropwise. Crystals were formed by slow room-temperature evaporation through a very small opening. After a period of 2 months, the yield was 516 mg (87%) of **2**.

Crystallographic Data Collection and Refinement of the Structure. Crystallographic data are summarized in Table I. The crystal used was colorless with a prismatic shape. The X-ray data were recorded with a CAD-4 Enraf-Nonius diffractometer using graphite-monochromated Mo Kα radiation. Cell dimensions were obtained by a least-squares fit from

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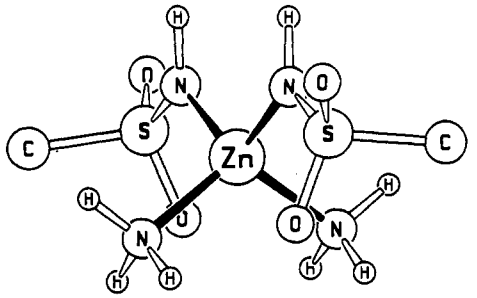

Figure 2. Coordination environment of the zinc ion in **2**.

Table III. Atomic Distances (Å) and Angles (deg) in the aaa Ligand

	free ligand aaaH	complex **2**
S1-N2	1.594 (3)	1.545 (6)
S1-O1	1.426 (2)	1.444 (5)
S1-O2	1.425 (2)	1.449 (5)
S1-C1	1.774 (3)	1.764 (7)
C1-S2	1.730 (3)	1.723 (7)
C1-N3	1.294 (3)	1.307 (9)
N3-N4	1.372 (3)	1.362 (8)
N4-C2	1.311 (3)	1.320 (9)
S2-C2	1.724 (2)	1.720 (7)
C2-N5	1.369 (3)	1.330 (8)
N5-C3	1.355 (3)	1.346 (10)
C3-O3	1.222 (2)	1.222 (10)
C3-C4	1.492 (4)	1.510 (11)
N2-S1-O1	107.8 (1)	115.3 (3)
N2-S1-O2	108.4 (1)	108.4 (3)
N2-S1-C1	106.6 (1)	109.5 (3)
O1-S1-O2	121.2 (1)	116.2 (3)
O1-S1-C1	106.6 (1)	101.1 (3)
O2-S1-C1	105.4 (1)	105.4 (3)

the setting angles of 25 well-centered reflections with $6° \leq 2\theta \leq 24°$. A total of 4517 reflections were measured with the variable-speed ω–2θ scan technique, 1199 of which were unique and nonnegative and were used in the refinement. Lorentz and polarization corrections were applied, but no absorption correction. The space group *Pbcn* was assumed throughout the structure analysis and was confirmed by the successful refinement of the structure. All calculations and drawings were done with the SHELXTL-PC program suite.[7] The positions of all atoms were determined by direct methods. All atoms with the exception of the hydrogen atoms were refined anisotropically. Hydrogen atoms were included with fixed parameters (U = 0.08 Å^2, C–H = N–H = 0.96 Å). Scattering factors were taken from Cromer and Mann.[8] The atomic parameters are listed in Table II. A thermal ellipsoid plot of the whole complex **2** is given in Figure 1. The molecules of **2** are bisected by a 2-fold crystallographic axis containing the zinc ion. Full information concerning conditions for crystallographic data collection and structure refinement, positional parameters, anisotropic thermal parameters, and observed and calculated structure factors is given in the supplementary material.

Results and Discussion

Crystals of **2** were obtained by extremely slow evaporation of an ammonia solution. The structure determination was facilitated by the fact that all atoms of the molecule including H's were located by the SHELX direct-methods routine.

The structure of the zinc complex **2** can be compared with that of the free ligand aaaH.[9] As Table III shows, the aaa units in the two compounds are virtually superimposable. All bond lengths except one are identical within 0.02 Å, as are the bond angles and practically all conformational details like the orientation of the acetamido or sulfonamido groups with respect to the thiadiazole ring. The only significant bond length change occurs for the S–N bond of the sulfonamide group, which shrinks by 0.05 Å upon coordination to the zinc. This is the major piece of information indicating that the bonding in the sulfonamide S–N unit has changed due to deprotonation converting it from an amide- to an imide-like situation. Support for this comes from the observation that bond lengths in the acetamido group remain unchanged and that one hydrogen atom each has been found experimentally on the nitrogens of the acetamido and sulfonamido groups. Thus the conclusion from spectral data[6] is confirmed that in **2** the deprotonated sulfonamide group is ligating the zinc via the nitrogen atom.

Table IV. Bonds (Å) and Angles (deg) at the Zinc Ion in **2**

Zn-N1	2.021 (6)	Zn-N2	1.977 (5)
N1-Zn-N1′	109.0 (3)	N1′-Zn-N2	108.3 (2)
N1-Zn-N2	108.3 (2)	N1′-Zn-N2′	107.9 (2)
N1-Zn-N2′	108.3 (2)	N2-Zn-N2′	115.5 (3)

The coordination about the zinc ion is tetrahedral to a very good approximation; cf. Table IV. Only the N–Zn–N angle between the two sulfonamides is 6° above the tetrahedral angle. The Zn–N(NH_3) distance of 2.03 Å compares favorably with that in $Zn(NH_3)_4^{2+}$ (average 2.01 Å).[10] Lack of precedent prevents a comparison of the Zn–N(sulfonamide) bond length of 1.98 Å. Considering the attractive force due to the charge of the ligand and the general radius reduction from an amide to an imide nitrogen, one might have expected this bond to be somewhat shorter. However, the bonds from zinc to Schiff base nitrogen atoms are also about 2.00 Å long.[11]

The structural details of **2** compare very favorably with those of the carbonic anhydrase–inhibitor complexes.[3] There are nearly identical findings for the coordination geometry, for the Zn–N distance (2.0 Å), and for the shortest Zn–O(sulfonamide) contact, which is 3.1 Å for the protein and 3.086 (7) Å for Zn–O2 in **2**. In accordance with the interpretation of the protein data, we do not consider the sulfonamide O2 atoms to be weakly ligating. The latter was suggested as the result of a molecular mechanics calculation.[12] However, an inspection of Figures 1 and 2 reveals that in order to obtain a favorable conformation for the whole complex, one sulfonamide oxygen each has to be placed between the two ammonia ligands, which results in the observed Zn–O distance and N(ammonia)–O(sulfonamide) distances of 3.07 and 3.65 Å. Actually, any rotation about the sulfonamide N–S bond would result in at least one Zn–O contact shorter than 3.4 Å. The same is the case in the enzyme–inhibitor complex,[3] which for the same reasons is not considered to contain five-coordinate zinc.

Conclusions

2 is one of the simplest aaa complexes that can be obtained. Its structure is straightforward and demonstrates unequivocally that the acetazolamide molecule has been deprotonated at the sulfonamide nitrogen for complexation, in agreement with previous conclusions based on IR data for **2**[6] and with structural and spectroscopic results on the CA–aaa enzyme–inhibitor complex.[3,4] The structural details do not conform to a proposed[12] (4 + 1) coordination mode including one of the sulfonamide oxygens. Instead, the nearly ideal tetrahedral coordination about the zinc ion closely resembles that deduced from the protein crystal work.[3]

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Registry No. 2, 109751-05-5.

Supplementary Material Available: Tables listing physical properties and main data relating to the measurement and refinement of the structure, positional and anisotropic thermal parameters, and all bond lengths and angles (5 pages); a table of observed and calculated structure factors (3 pages). Ordering information is given on any current masthead page.

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