entire library of 66 catalysts involved five sequential runs. As shown in Table 1 the preparation and screening of the Pt/Pd/In ternary catalyst library took about 2.5 days to complete. Although this represents a significant advance over conventional methods, which may take months to achieve the same objectives, further acceleration of the overall process is clearly possible. For example, increasing the number of microreactors in each array, that is increasing the level of parallel processing, and decreasing the times for impregnation, drying, calcination, and reduction can significantly speed up the process. However, the latter issues must be carefully implemented as even minor modifications in catalyst preparation methods can dramatically alter the performance of the catalysts. On the other hand, the minimization of catalyst preparation times can be the objective of a combinatorial study such as that described here.

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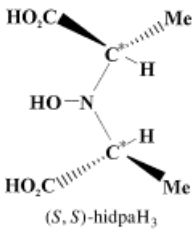
The Structural Characterization of Amavadin**

Robert E. Berry, Elaine M. Armstrong, Roy L. Beddoes, David Collison, S. Nigar Ertok, Madeleine Helliwell, and C. David Garner*

One fascinating aspect of bioinorganic chemistry is that of metal accumulation by living organisms, for example, to provide an appropriate concentration for the use of the metal in one or more specific biochemical functions and/or as a means of protection against toxicity that arises from an excess of metal. A striking example of metal accumulation is provided by three species of *Amanita* mushrooms: *A. muscaria*, the "fly agaric"; *A. regalis*; and *A. velatipes*. Each species concentrates vanadium to levels of up to 400 times those typically found in plants. Studies by Ter Meulen,[1] Bertrand,[2, 3] and Meisch et al.[4] have shown that the accumulation of vanadium by these species of *Amanita* is independent of the age of the mushrooms, unrelated to the vanadium content of the soil, and essentially equally distributed between the stem, skin, and cap.

In 1972 Bayer and Kneifel[5] isolated a blue, vanadium-containing compound from *A. muscaria* collected in the Black Forest. They named this compound "amavadin" and showed that it is constituted as a 1:2 complex of vanadium and the pro-ligand (*S*,*S*)-2,2′-(hydroxyimino)dipropionic acid ((*S*,*S*)-hidpaH$_3$).[6] Further studies[7–10] led to the proposal that the vanadium center of amavadin exists as an eight-coordinate, non-oxo complex with a novel structure. Herein, we report confirmation of this postulate by X-ray crystallographic determinations on a sample of amavadin crystallized as a phosphoric acid derivative;[11] and as the salt **1** with Ca^{2+} countercations.[12]



(*S*, *S*)-hidpaH$_3$

$[Ca(H_2O)_5][\Delta\text{-V}((S,S)\text{-hidpa})_2]\cdot 2H_2O$ **1**

The use of Ca^{2+} counterions to crystallize amavadin proved valuable in obtaining good quality crystals for X-ray diffraction analysis, as demonstrated previously for related chemical systems.[13] The lattice of **1** is comprised of $[Ca(H_2O)_5]^{2+}$ and $[\Delta\text{-V}((S,S)\text{-hidpa})_2]^{2-}$ ions that are linked in the form of infinite chains; a portion of a chain is shown in Figure 1. Each anion is bound by two Ca^{2+} ions through a carboxylate group

[*] Prof. C. D. Garner, R. E. Berry, Dr. E. M. Armstrong, R. L. Beddoes, Dr. D. Collison, Dr. M. Helliwell
Department of Chemistry, University of Manchester
Manchester, M13 9PL (UK)
Fax: (+44) 161-275-4616
E-mail: dave.garner@man.ac.uk
Dr. S. N. Ertok
Ege Üniversitesi, Fen Facültesi Dekanligi
Kimya Bölümü (Turkey)

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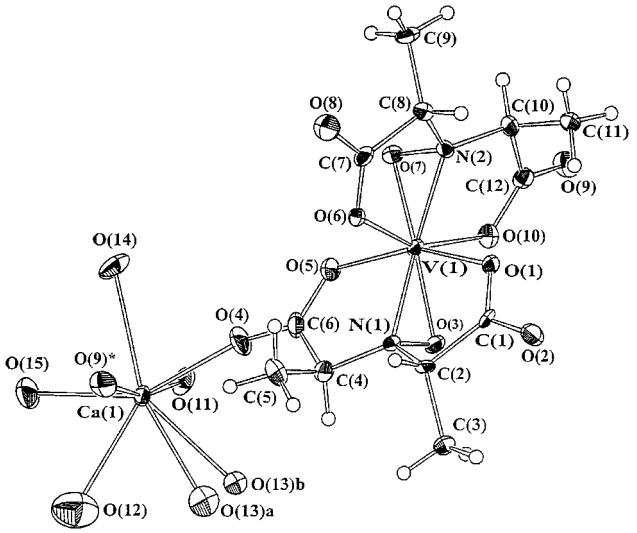

Figure 1. ORTEP view of a portion of the lattice of **1**. (Ellipsoids are shown at the 30% probability level). Selected bond lengths [Å] and angles [°]: V(1)–O(1) 2.028(7), V(1)–O(3) 1.940(7), V(1)–O(5) 2.028(9), V(1)–O(6) 2.042(8), V(1)–O(7) 1.956(7), V(1)–O(10) 2.070(8), V(1)–N(1) 1.999(8), V(1)–N(2) 1.982(8), Ca(1)–O(4) 2.300(9), Ca(1)–O(9) 2.312(9), Ca(1)–O(11) 2.326(9), Ca(1)–O(12) 2.582(17), Ca(1)–O(13a) 2.36(2), Ca(1)–O(13b) 2.48(2), Ca(1)–O(14) 2.571(9), Ca(1)–O(15) 2.389(12), O(1)–C(1) 1.237(12), O(2)–C(1) 1.274(14), O(3)–N(1) 1.395(11), O(4)–C(6) 1.241(15), O(5)–C(6) 1.291(14), O(6)–C(7) 1.242(13), O(7)–N(2) 1.385(12), O(8)–C(7) 1.259(15), O(9)–C(12) 1.243(14), O(10)–C(12) 1.290(13); O(1)-V(1)-O(6) 86.4(3), O(1)-V(1)-O(10) 91.2(3), O(3)-V(1)-N(1) 41.4(3), O(5)-V(1)-O(6) 89.2(3), O(5)-V(1)-O(10) 101.8(3), O(7)-V(1)-N(2) 41.2(3).

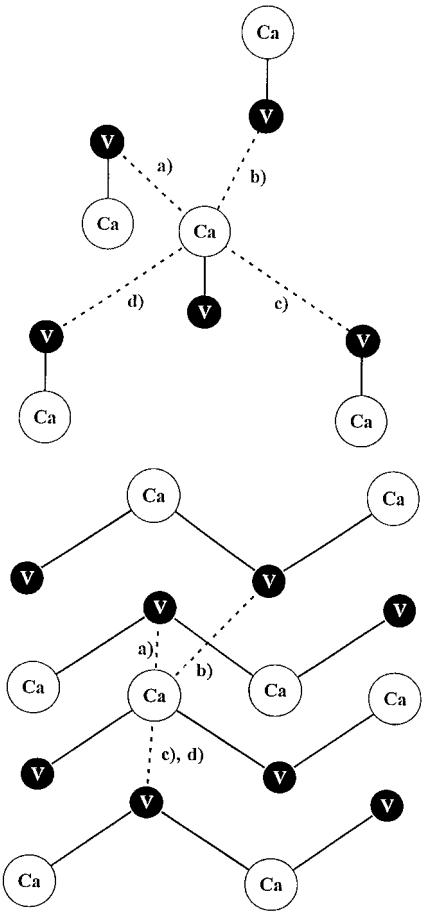

Figure 2. View down the ends (top) and along (bottom) neighboring chains of **1**: only V and Ca atoms are shown (solid lines denote Ca-O-C-O-V linkages, dashed lines denote hydrogen bonding/close contacts between chains (<2.90 Å)): a) water O(11)···O(7) oxyimino oxygen [2.723(12) Å] and water O(15)···O(5) carboxylate oxygen [2.825(14) Å]; b) water O(11)···O(2) carboxylate [2.867(12) Å]; c) water O(13a) and O(13b)···O(8) carboxylate [2.84(2) and 2.70(2) Å, respectively]; d) water O(14)···O(2) carboxylate [2.743(13) Å].

on each (*S*,*S*)-hidpa^{3-} ligand. Each Ca^{2+} ion is coordinated by an approximately pentagonal bipyramidal arrangement of oxygen atoms comprising five H_2O molecules (O(11), O(12), O(13a,b) O(14), and O(15)) and two unidentate carboxylato groups bound through the O(4) and O(9)* oxygen atoms. The Ca(1)–O(9)* and Ca–O(11) bonds are approximately mutually *trans* (167.3(3)°) and each is orientated approximately perpendicular to an "equatorial plane" formed by the oxygen atoms of two of the Ca^{2+}-bound H_2O molecules and the carboxylate O(4) atom.[14] The Ca^{2+}-bound H_2O molecules have close contacts to carboxylate and oxyimino oxygen atoms on four neighboring chains, as illustrated in Figure 2. Thus, the seven water molecules play a significant role in the structure of **1**.[14]

The structure of the amavadin anion approximates to C_2 symmetry with the twofold axis bisecting the normals to the V(η^2-NO) planes from each ligand projected onto the least-squares plane of the vanadium atom and four O donor atoms of the unidentate carboxylato groups (the VO_4 plane). The planes of the two V(η^2-NO) groups are close to being mutually perpendicular (93.6°) and each is essentially perpendicular (89.4° and 91.8° for the V(η^2-NO) planes involving N(1) and N(2), respectively) to the VO_4 least-squares plane. The unidentate carboxylate oxygen atoms in the same ligand are bonded to the V^{IV} center in a mutually *trans* manner and each of these atoms is significantly displaced from the VO_4 least-squares plane towards the η^2-NO$^-$ group of that ligand: the atoms O(1) and O(5) sit below (−0.42 and −0.36 Å, respectively) and O(6) and O(10) sit above (0.43 and 0.36 Å, respectively). The results of EPR studies accomplished for *A. muscaria*[15] and freshly dissolved crystals of **1** are consistent with the V^{IV} center in the former occupying an environment essentially identical to that observed in the latter. This type of coordination geometry was first identified in $[NMe_4][NH_4][V(hida)_2]$ (hidaH$_3$ = (hydroxyimino)diacetic acid).[9]

Although the structure of the phosphoric acid derivative **2** of amavadin has been solved to a lower resolution[11] than that obtained for **1**, it is clear that this system possesses the same type of vanadium center as in **1**. However, the chirality at the metal is of the opposite hand to that in **1**, namely *Λ* as opposed to *Δ*. Thus, the geometry of the inner coordination sphere of

$[\Lambda\text{-V}((S,S)\text{-hidpaH})_2]\cdot H_3PO_4\cdot H_2O$ **2**

the vanadium center in amavadin and related complexes leads to a special chirality at the metal center. The handedness of this chirality is determined by the relative positions of the two η^2-NO$^-$ groups, as viewed perpendicular to the VO_4 plane (Figure 3).

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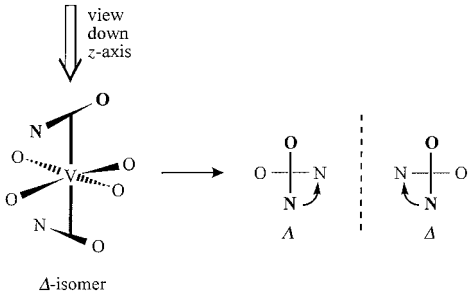

Figure 3. A representation of the chirality at the vanadium center in amavadin.

Thus, amavadin possesses five chiral centers. In the isolated natural product, consistent with earlier conclusions,[6] the four chiral carbon atoms all have the *S* stereochemistry. We have observed both isomers at the vanadium center in our crystallographic studies: only the *Δ* form was observed in the crystal selected for X-ray crystallographic analysis of **1**,[12] whereas the crystal of the H_3PO_4 derivative investigated[11] contained only the *Λ* form. Spectroscopic studies of solutions of amavadin[16] and its V^V counterpart[10] have shown that, as isolated, amavadin exists as an approximate 1:1 mixture of *Δ*- and *Λ*-helical forms.

The ability of the carboxylato groups of amavadin-like anions to bind cations, for example, Ca^{2+}, and/or become involved in hydrogen bonding may be relevant to the means whereby amavadin is stored within the *Amanita* mushrooms and possibly to the biological role(s) of this species.

Experimental Section

Isolation of natural amavadin: *Amanita muscaria* was collected from Dunham Forest golf course near Altrincham, Cheshire (UK). An aqueous solution of amavadin was isolated by using the procedure published by Bayer and Kneifel[5] and crystallized by very slow evaporation. An X-ray crystallographic study[11] showed these crystals to be constituted as **2**.

Crystallization of natural amavadin with Ca^{2+} counterions: The crystallized amavadin from the procedure detailed above (20 mg, 0.05 mmol) was dissolved in H_2O (0.5 cm^3). $CaCl_2$ (5 mg, 0.05 mmol) was added and allowed to dissolve before the solution was filtered. A triple layer diffusion with an equal volume of MeOH on top of the amavadin-containing solution, and a top layer of isopropyl alcohol was set up in a sealed Pasteur pipette. After the mixture had stood at room temperature for nine days blue, needle-shaped crystals were collected by filtration.

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[12] Crystal data for **1**: The structure was solved by direct methods[17] and expanded with Fourier techniques.[18] The oxygen atoms O(13) and O(17) were disordered over two sites A and B, which were constrained to sum to 1. These atoms were refined isotropically whilst all other non-hydrogen atoms were refined anisotropically. Hydrogen atoms bonded to carbon atoms were placed in calculated positions and refined isotropically; other hydrogen atoms were not included. Data were corrected for Lorentz and polarization effects and an empirical absorption correction, based on azimuthal scans of several reflections, was applied (transmission factors 0.620 – 1.000). The absolute configuration was determined by refinement of the Flack parameter to give a final value of 0.01(10).[19] The selection of overall chirality led to the assignment of *S* stereochemistry at all chiral carbon atoms for both **1** and **2**. This stereochemistry had been deduced spectroscopcially in the previous independent study.[6] A refinement was carried out with SHELX97[20] and other calculations were performed with the TEXSAN[21] crystallographic software package. Data: $C_{12}H_{22}CaN_2O_{15}V$, $M_r = 525.33$, orthorhombic, space group $P2_12_12_1$, $a = 13.447(7)$, $b = 16.913(7)$, $c = 10.224(4)$ Å, $V = 2325.1(18)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.501$ Mg m^{-3}, $T = 293(2)$ K, $\theta_{max} = 25.06°$. Blue needle crystals ($0.50 \times 0.07 \times 0.05$mm), 2345 reflections measured, 1856 observed with [$I > 2.0\sigma(I)$], Rigaku AFC-5R diffractometer, $Mo_{K\alpha}$ radiation $\lambda = 0.7107$ Å, *R* values ($R(F)$, $wR(F^2)$) 0.0767, 0.2062. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-102680 and -102668. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).
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