

## Bis-(*N*-hydroxy-iminodiacetate)vanadate(IV), a Synthetic Model of 'Amavadin'

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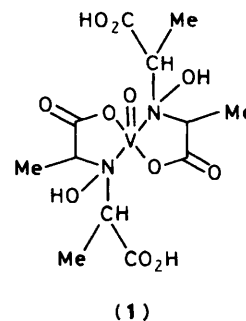
The vanadium(IV) octaco-ordinated complex  $(\text{NH}_4^+)[\text{N}(\text{CH}_3)_4^+][\text{V}(\text{HIDA})_2]$  (HIDA = *N*-hydroxy-iminodiacetate), whose anion is a likely model for the natural compound 'amavadin,' has been prepared and its crystal and molecular structures have been determined by X-ray crystallography; this is the first example of an octaco-ordinated vanadium(IV) complex with just N and O donor atoms.

It has been known for over fifty years that some toadstools of the *Amanita* species concentrate unusually large amounts of vanadium,<sup>1,2</sup> but it was not until 1972 that Bayer and Kneifel isolated a vanadium-containing compound from a German variety of *Amanita muscaria* which they named 'Amavadin';<sup>3</sup> analysis, e.p.r., and i.r. spectra and chemical reactions led these authors to suggest the structure (1) for this compound, a five-co-ordinated 1:2 oxovanadium(IV) complex of a rather simple but unknown ligand: *N*-hydroxy-imino- $\alpha,\alpha'$ -dipropionic acid (HIDPA).<sup>4</sup>

In 1983 one of us and collaborators reported the synthesis and the results of a study of the complexation reactions of this ligand as well as of the related compounds *N*-hydroxy-iminodiacetic acid (HIDA) and imino- $\alpha,\alpha'$ -dipropionic acid (IDPA).<sup>5-7</sup> The analogy of natural amavadin in frozen segments of Portuguese *Amanita muscaria* to the 1:2 complex of oxovanadium(IV) with HIDPA was confirmed by the e.p.r. spectra which were identical but quite different from those of the vanadyl complexes of many other amino-acid and amino-

polycarboxylate ligands,<sup>5</sup> as also found by Gillard and Lancashire for samples of British *Amanita*.<sup>8</sup>

More recently, Bayer and collaborators reported the synthesis of the above-mentioned ligands and achieved the separation of the isomers of HIDPA.<sup>9</sup> A study of their complexation properties afforded essentially the same results



as ours, but much higher values for the stability constants of the 1 : 2 oxovanadium(IV) complexes of HIDPA and HIDA were determined.<sup>10</sup>

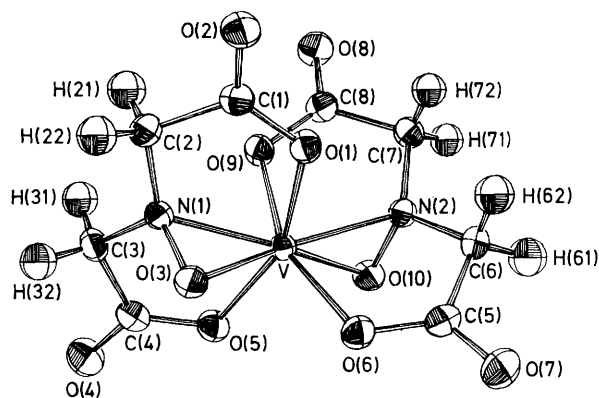
The values reported by Bayer and collaborators ( $\log \beta_2$  ca. 22–23) seem improbably high for a 1 : 2 pentaco-ordinated vanadyl complex (cf. the value for VO-EDTA:  $\log K_{(VO)L} = 18.77$ ), so these authors admitted the possibility that the hydroxyl group of the ligands HIDPA and HIDA might co-ordinate to the metal.<sup>10</sup> Subsequently, even the presence of the oxovanadium(IV) ion became doubtful when large angle X-ray scattering experiments indicated that the shortest vanadium–ligand distances were probably larger than 1.9 Å,<sup>11</sup> but more direct evidence seems necessary to confirm this idea. Recently, we have been able to crystallize a mixed ammonium tetramethylammonium salt of the vanadium complex of HIDA, a compound which is sufficiently similar to the natural ligand to afford an adequate model for ‘amavadin,’ obtained by slow evaporation of a mixture of VOCl<sub>2</sub>, HIDA, and ammonium and tetramethylammonium hydroxides. This compound proved to be ammonium tetramethylammonium bis-(*N*-hydroxy-iminodiacetate)vanadate(IV), i.e. it contains not a vanadyl but a vanadium(IV) complex anion in which the hydroxy-imino groups are ionised.

The e.p.r. spectra confirms the oxidation state (IV) but the i.r. spectrum does not show the band at 985 cm<sup>-1</sup> reported for the natural product isolated from *Amanita muscaria*;<sup>4,9</sup> this now needs to be confirmed.

The structure of ammonium tetramethylammonium bis-(*N*-hydroxy-imino diacetate)vanadate(IV) was determined by X-ray analysis.<sup>†</sup> One crystallographically independent [V(HIDA)<sub>2</sub>]<sup>2-</sup> anion per two cations, N(CH<sub>3</sub>)<sub>4</sub><sup>+</sup> and NH<sub>4</sub><sup>+</sup>, were found in the structure.

The complex anion, which is the first example of a vanadium(IV) eightfold co-ordinated to nitrogen and oxygen atoms, has an approximate C<sub>2</sub> point symmetry. Each ligand residue is chelated to the metal via two carboxylate oxygens and the nitrogen and oxygen of the hydroxy-imino group. Due to the geometry and the tetradentate chelating character of the ligand, the co-ordination around the vanadium exhibits a distorted dodecahedral configuration.<sup>12–14</sup> According to the notation of Hoard and Silverton, the chelation is along one *a* and two *g* edges, the *a* edge being a bonding distance (N–O). Bond lengths are in close agreement with those found in other vanadium(IV) compounds (Figure 1).<sup>15</sup>

It seems probable that ‘amavadin’ has a form that corresponds to the 1 : 2 vanadium(IV) complex of *N*-hydroxy-imino- $\alpha,\alpha'$ -dipropionate, similar to that we have just described. The structure of such a complex anion justifies a much higher stability constant and the consequent disruption of the very stable vanadium–oxygen bond of the vanadyl ion. Since the oxo group may be removed together with the two protons of the hydroxy-imino groups to form water, the effect does not show in the titration curves, and the ionisation of those groups



**Figure 1.** Molecular structure of the complex anion bis-(*N*-hydroxy-iminodiacetate)vanadate(IV), a model for the probable structure of ‘amavadin.’ Selected bond lengths (Å): V–O(1) 2.071(3); V–N(1) 2.003(4); V–O(3) 1.973(3); V–O(5) 2.065(3); V–O(6) 2.063(3); V–N(2) 2.002(3); V–O(9) 2.070(3); V–O(10) 1.976(3). Selected bond angles (°): N(1)–V–O(1) 78.5(2); O(3)–V–O(1) 81.8(2); O(3)–V–N(1) 40.6(1); O(5)–V–O(1) 157.3(1); O(5)–V–N(1) 79.0(2); O(5)–V–O(3) 82.5(2); O(6)–V–O(1) 89.4(2); O(6)–V–N(1) 120.3(2); O(6)–V–O(3) 80.0(2); O(6)–V–O(5) 103.9(2); N(2)–V–O(1) 80.0(2); N(2)–V–N(1) 150.7(1); N(2)–V–O(3) 152.2(1); N(2)–V–O(5) 120.2(2); N(2)–V–O(6) 78.9(2); O(9)–V–O(1) 84.7(2); O(9)–V–N(1) 79.9(2); O(9)–V–O(3) 120.5(2); O(9)–V–O(5) 89.3(2); O(9)–V–O(6) 157.3(1); O(9)–V–N(2) 78.5(2); O(10)–V–O(1) 120.6(2); O(10)–V–N(1) 152.2(1); O(10)–V–O(3) 151.3(1); O(10)–V–O(5) 79.9(2); O(10)–V–O(6) 82.4(2); O(10)–V–N(2) 40.6(1), O(10)–V–O(9) 81.9(2).

can be overlooked, leading to erroneous assumptions. The reversible vanadium(IV)–vanadium(V) redox behaviour of 1 : 2 VO<sup>2+</sup>–HIDPA mixtures<sup>16</sup> may now be understood and the biological function of ‘amavadin’ can be examined on a new basis.

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<sup>†</sup> *Crystal data:* The intensities of 3528 reflections ( $1.5^\circ \leq \theta \leq 25.0^\circ$ ) were measured using graphite monochromatized Mo- $K_\alpha$  radiation by the  $\omega/2\theta$  scan mode in an Enraf-Nonius CAD4 diffractometer. Cell dimensions were determined by least-squares refinement of setting angles for 25 automatically centred reflections with  $15.0^\circ \leq \theta \leq 17.0^\circ$ .

The crystal is monoclinic, space group C2/c with  $a = 15.820(9)$ ,  $b = 16.450(6)$ ,  $c = 16.311(4)$  Å,  $\beta = 118.92(3)^\circ$ ,  $U = 3715.42$  Å<sup>3</sup>,  $Z = 8$ ,  $D_x = 1.56$  g cm<sup>-3</sup>,  $F(000) = 2028$ ,  $\mu(\text{Mo-}K_\alpha) = 5.59$  cm<sup>-1</sup>,  $M = 434.9$  for C<sub>12</sub>H<sub>24</sub>N<sub>4</sub>O<sub>10</sub>V.

2782 Reflections with  $|F_o| \geq 3\sigma|F_o|$  were used for structure determination and refinement. The vanadium position was located from a Patterson synthesis and the positions of all the other atoms, including hydrogens, were successively located by difference Fourier syntheses. Full-matrix least-squares refinement was carried out to a final  $R = 0.029$  and  $R_w = 0.04$ .