$[\alpha]_D = -112.8$ (88% *ee*, $c = 0.5$, EtOH). SPH-1339 (**15**),[15] a slightly more potent inhibitor of Ache than (−)-galanthamine **1**, was prepared in 56% yield by this one-pot process, by using propylamine instead of methylamine.

This new synthesis of galanthamine (8 steps, 96% *ee*, 14.8% overall yield from **7** and **8**) is a significant improvement over and successfully addresses many of the shortcomings of the previous synthesis (14 steps, 88% *ee*, 1.5% overall yield). Furthermore, by exchanging methylamine for other alkyl amines in the last step various galanthamine derivatives are easily accessible, as demonstrated by the synthesis of **15**. This is the shortest and most efficient nonbiomimetic total synthesis of (−)-galanthamine to date. The sequential palladium-catalyzed AAA and intramolecular Heck reaction followed by a diastereoselective allylic oxidation provided the key intermediate **5** with all the functionality installed, except the hydrobenzazepine ring. The one-pot reductive cyclization represents a simple and efficient strategy to form the latter and to access many galanthamine analogues. All the stereochemistry emanates from the palladium-catalyzed AAA. This strategy should allow for entry into a variety of *Amaryllidaceae* alkaloids related to galanthamine.

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[1] For reviews see: O. Hoshino in *The Alkaloids*, *Vol. 51* (Ed.: G. A. Cordell), Academic Press, New York, **1998**, pp. 323–424; S. F. Martin in *The Alkaloids*, *Vol. 30* (Ed.: A. Brossi), Academic Press, New York, **1987**, pp. 251–376.

[2] M. Weinstock, *CNS Drugs* **1999**, *12*, 307–323; U. Thatte, *Curr. Opin. Cent. Peripher. Nerv. Syst. Invest. Drugs* **1999**, *1*, 357–372; K. Unni, *CNS Drugs* **1998**, *10*, 447–460; A. Nordberg, A.-L. Svensson, *Drug Saf.* **1998**, *19*, 465–480; M. Rainer, *Drugs Today* **1997**, *33*, 273–279; H. A. M. Mucke, *Drugs Today* **1997**, *33*, 251–257.

[3] W.-C. Shieh, J. A. Carlson, *J. Org. Chem.* **1994**, *59*, 5463–5465.

[4] B. Küenburg, L. Czollner, J. Fröhlich, U. Jordis, *Org. Process Res. Dev.* **1999**, *3*, 425–431.

[5] D. H. R. Barton, G. W. Kirby, *J. Chem. Soc.* **1962**, 806; T. Kametani, K. Yamaki, H. Yagi, K. Fukumoto, *J. Chem. Soc. D* **1969**, 425–426; T. Kametani, K. Yamaki, H. Yagi, K. Fukumoto, *J. Chem. Soc. C* **1969**, 2602–2605; T. Kametani, K. Yamaki, T. Terui, *J. Heterocycl. Chem.* **1973**, *10*, 35; K. Shimizu, K. Tomioka, S. Yamada, K. Koga, *Heterocycles* **1977**, *8*, 277–282; K. Shimizu, K. Tomioka, S. Yamada, K. Koga, *Chem. Pharm. Bull.* **1978**, *26*, 3765–3771; D. Krikorian, R. Vlahov, S. Parushev, M. Chinova, I. Vlahov, H. J. Schaefer, H. Duddeck, G. Snatzke, *Tetrahedron Lett.* **1984**, *25*, 2969–2972; R. Vlahov, D. Krikorian, G. Spassov, M. Chinova, I. Vlahov, S. Parushev, G. Snatzke, L. Ernst, K. Kieslich, W.-R. Abraham, W. S. Sheldrick, *Tetrahedron* **1989**, *45*, 3329–3345; J. Szewczyk, J. W. Wilson, A. H. Lewin, F. I. Carroll, *J. Heterocycl. Chem.* **1995**, *32*, 195–199; D. A. Chaplin, N. Fraser, P. D. Tiffin, *Tetrahedron Lett.* **1997**, 7931; L. Czollner, W. Frantsits, B. Küenburg, U. Hedenig, J. Fröhlich, U. Jordis, *Tetrahedron Lett.* **1998**, *39*, 2087–2088; Y. Kita, M. Arisawa, M. Gyoten, M. Nakajima, R. Hamada, H. Tohma, T. Takada, *J. Org. Chem.* **1998**, *63*, 6625–6633; D. Krikorian, V. Tarpanov, S. Parushev, P. Mechkarova, *Synth. Commun.* **2000**, *30*, 2833–2846; M. Node, S. Kodama, Y. Hamashima, T. Baba, N. Hamamichi, K. Nishide, *Angew. Chem.* **2001**, *113*, 3150–3152; *Angew. Chem. Int. Ed.* **2001**, *40*, 3060–3062.

[6] B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **2000**, *122*, 11262–11263.

[7] B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **1998**, *120*, 815–816; B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **1998**, *120*, 9074–9075; B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **1999**, *121*, 3543–3544; B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **1999**, *121*, 4545–4554; B. M. Trost, H. C. Tsui, F. D. Toste, *J. Am. Chem. Soc.* **2000**, *122*, 3534–3535.

[8] C. Pilger, B. Westermann, U. Flörke, G. Fels, *Synlett* **2000**, 1163–1165.

[9] P. J. Parsons, M. D. Charles, D. M. Harvey, L. R. Sumoreeah, A. Shell, G. Spoors, A. L. Gill, S. Smith, *Tetrahedron Lett.* **2001**, *42*, 2209–2211.

[10] C. Guillou, J.-L. Beunard, E. Gras, C. Thal, *Angew. Chem.* **2001**, *113*, 4881–4882; *Angew. Chem. Int. Ed.* **2001**, *40*, 4745–4746.

[11] S. Y. Han, J. E. Sweeney, E. S. Bachman, E. J. Schweiger, G. Forloni, J. T. Coyle, B. M. Davis, M. M. Joullie, *Eur. J. Med. Chem.* **1992**, *27*, 673–687.

[12] G. M. Bores, R. W. Kosley, Jr., *Drugs Future* **1996**, *21*, 621–635.

[13] S. Y. Han, S. C. Mayer, E. J. Schweiger, B. M. Davis, M. M. Joullie, *Bioorg. Med. Chem. Lett.* **1991**, *1*, 579–580, and references therein.

[14] A. Mary, D. Z. Renko, C. Guillou, C. Thal, *Bioorg. Med. Chem.* **1998**, *6*, 1835–1850; C. Guillou, A. Mary, D. Z. Renko, E. Gras, C. Thal, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 637–639.

[15] U. Jordis, J. Fröhlich, M. Treu, M. Hirnschall, L. Czollner, B. Kälz, S. Welzig, PCT Int. Appl., WO 0174820, **2001**.

[16] A. Mary, D. Z. Renko, C. Guillou, C. Thal, *Tetrahedron Lett.* **1997**, *38*, 5151–5152.

[17] J. E. Toth, P. R. Hamann, P. L. Fuchs, *J. Org. Chem.* **1988**, *53*, 4694–4708.

[18] H. Amri, M. Rambaud, J. Villieras, *Tetrahedron* **1990**, *46*, 3535–3546.

[19] R. C. Larock, D. E. Stinn, *Tetrahedron Lett.* **1988**, *29*, 4687–4690.

[20] B. K. Wilk, *Synth. Commun.* **1993**, *23*, 2481–2484; M. C. Aesa, G. Baán, L. Novák, C. Szántay, *Synth. Commun.* **1995**, *25*, 1545–1550.

[21] K. C. Nicolaou, N. A. Petasis, *Selenium in Natural Products Synthesis*, CIS, Philadelphia, **1984**.

[22] B. M. Trost, D. L. Van Vranken, *J. Am. Chem. Soc.* **1993**, *115*, 444–458.

[23] K. Shibuya, *Synth. Commun.* **1994**, *24*, 2923–2941.

Monomeric Compounds Containing the *cis*-$[V(=O)(OH)]^+$ Core

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Monomeric metal compounds with terminal hydroxy ligands are important functional units in metalloproteins.[1] Metal–OH (M–OH) units are proposed as the active species

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in a wide variety of proteins and enzymes. The *cis*-$[M(=O)(OH)]^{n+}$ center was identified in structurally characterized vanadium haloperoxidases[2, 3] and it has also been postulated as a key intermediate species in molybdoenzymes.[4] At present, only a few examples of structurally characterized model mononuclear metal compounds with terminal hydroxy ligands are known.[5] Furthermore, only the isolation of one model monomeric compound containing the *cis*-$[M(=O)(OH)]^{n+}$ unit (but without structural characterization),[6] has been reported. In almost all cases tripodal ligands with bulky substituents were used to isolate monomeric metal species containing terminal hydroxy ligands or the *cis*-$[M(=O)(OH)]^{n+}$ fragment. Herein, we report the isolation, structural, and physicochemical[7] characterization of the compounds **1** and **2**$\cdot H_2O$ which contain the *cis*-$[V^{IV}O(OH)]^+$ structural unit supported by the bidentate ligands 2,2′-bipyridine (bipy) and 1,10-phenanthroline (phen). The electronic and magnetic properties of the complexes **1** and **2**$\cdot H_2O$ have been studied by continuous-wave electron paramagnetic resonance (c.w. EPR), electron spin echo envelope modulation (ESEEM) spectroscopy, and ab initio theoretical studies.

cis-$[V^{IV}O(OH)(bipy)_2][BF_4]$ **1**

cis-$[V^{IV}O(OH)(phen)_2][BF_4]$ **2**

The mononuclear yellow-brown compound **1** was prepared by addition of $AgBF_4$ (5.6 mmol) to a stirred aqueous solution (~10 mL, pH ≈ 1) of $[VOCl_2(thf)_2]$ (2.8 mmol). After removal of the AgCl, the filtrate was treated with bipy (5.6 mmol). Upon addition of bipy the blue color of the solution immediately changed to red, a yellow-brown precipitate was formed and the pH value of the solution changed to ≈4. Compound **2**$\cdot H_2O$, the phen analogue of **1**, was synthesized in a similar fashion to **1**.

X-ray structural analysis of **1** (compound **2**$\cdot H_2O$ has a similar overall structure)[8] revealed the presence of a discrete cation *cis*-$[V^{IV}O(OH)(bipy)_2]^+$ (Figure 1) and a BF_4^- anion per molecule. The geometry of the complex cation is best described as a severely distorted octahedron with the vanadium center being displaced above the mean equatorial plane defined by three bipy nitrogen atoms and the hydroxy oxygen atom by 0.25 Å towards the oxo ligand. The notable structural feature of **1** is the presence of a hydroxy group in a position *cis* to the oxo ligand. The hydroxy group competes with the O^{2-} center for the same vacant d_{xz} vanadium orbital (see below) and this results in the substantial lengthening of the V=O bond (1.687(2) Å). The V=O bond in **1** lies well outside the range observed for oxovanadium(IV) complexes (≈1.56–1.63 Å).[9] The two bipy ligands are unsymetrically ligated to vanadium, with two long bonds (V–N4 2.247(3) Å and V–N2 2.175(3) Å) *trans* to the oxo and hydroxy ligands and two short bonds (V–N1 and N3, ≈2.114(3) Å) *trans* to each other. Bond valence sum calculation for O2 gives a value of 1.02, which is clearly indicative of monoprotonation for this oxygen atom.[10] The O1-V-O2 angle, 106.8(2)°, of the *cis*-$[V^{IV}O(OH)]^+$ core is almost identical to that observed for the closely related *cis*-$[V^VO_2(bipy)_2]^+$ ion (106.5(2)°) and very close to other hexacoordinate mononuclear vanadium(V) compounds (hmvc) containing the *cis*-$[V^VO_2]^+$ unit (~105°),[9e] in which the two V=O bonds of the *cis*-$[V^VO_2]$ center do not differ by more than ~0.02 Å unless there are different donor atoms in positions *trans* to the oxo ligands. In hmvc containing the *cis*-$[V^VO(OR)]^{2+}$ core the (O)-V-(OR) angles are ≈103° and the V^V=O and V^V–OR bonds are ≈1.60 and 1.74 Å, respectively.[9e,f, 11, 12]

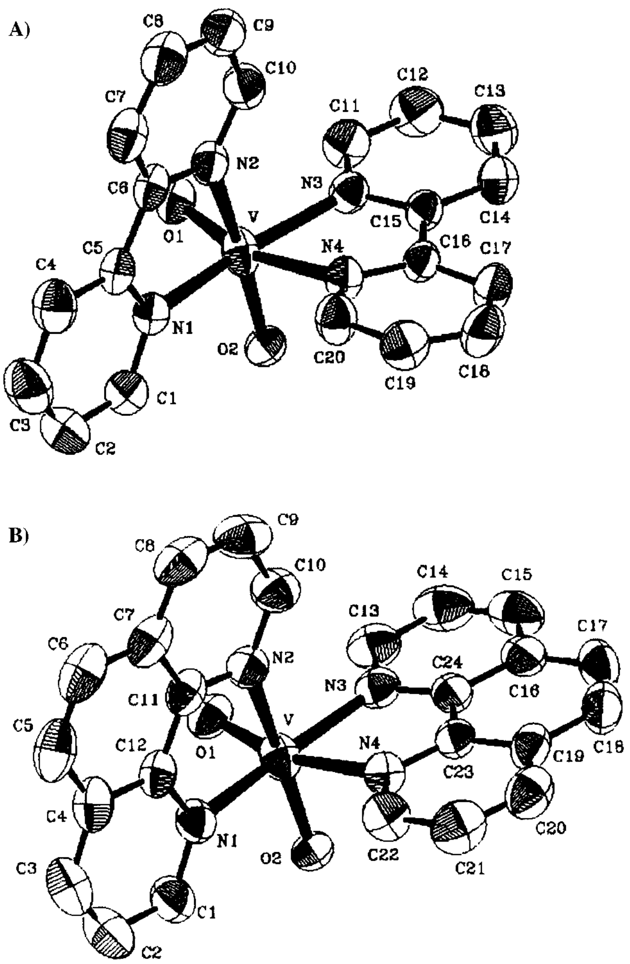

Figure 1. Molecular structures of the cations of **1** (A) and **2**$\cdot H_2O$ (B). Selected bond lengths [Å] and angles [°] for **1** [and **2**$\cdot H_2O$ in square brackets]: V-O1 1.687(2)[1.677(3)], V-O2 1.761(2) [1.778(2)], V-N1 2.115(3) [2.113(3)], V-N2 2.175(3) [2.173(3)], V-N3 2.111(3) [2.111(3)], V-N4 2.247(3) [2.246(3)]; O1-V-O2 106.8(12) [106.35(12)], O1-V-N3 93.10(12) [92.73(14)], O2-V-N3 92.20(10) [94.34(11)], O1-V-N1 100.05(11) [97.42(13)], O2-V-N1 90.13(11) [90.20(12)], N3-V-N1 165.44(11) [167.25(12)], O1-V-N2 89.56(11) [90.28(11)], O2-V-N2 160.27(11) [160.29(12)], N3-V-N2 98.88(10) [95.36(12)], N1-V-N2 75.17(11) [76.96(12)], O1-V-N4 161.75 (11) [163.74(12)], O2-V-N4 87.57(11) [86.11(12)], N3-V-N4 74.07(11) [75.61(12)], N1-V-N4 91.68(10) [92.85(12)], N2-V-N4 79.92(10) [79.76(11)].

The frozen-solution EPR spectra for **1** and **2**$\cdot H_2O$, recorded at 77 K, were characteristic of mononuclear $V^{IV}O^{2+}$ complexes.[13, 14] The ^{51}V spin-Hamiltonian parameters, were derived from simulations of the EPR spectra and are the following: $g_x = 1.981$, $g_y = 1.978$, $g_z = 1.944$; $A_x = 53$, $A_y = 64$, $A_z = 163 \times 10^{-4}\,cm^{-1}$ for **1** and **2**$\cdot H_2O$ as well. The g and A tensors for **1** and **2**$\cdot H_2O$ are identical and this can be interpreted as an indication of similar equatorial donor atoms in both complexes.[14] Information concerning the hyperfine coupling of the hydroxy proton was obtained by two-dimensional ESEEM[15] spectroscopy (HYSCORE)[16].

The HYSCORE spectra for **1** contain two characteristic sets of cross-peaks arising from the presence of $^{14}N(I=1)$ nuclei.[17] One set consists of cross-peaks at frequencies $[\nu_\alpha, -\nu_\beta] = [3.4\,MHz, -7.1\,MHz]$ and $[\nu_\beta, -\nu_\alpha] = [7.1\,MHz, -3.4\,MHz]$ which can be assigned to an interacting $^{14}N(I=1)$ with $A_{iso} = [\nu_\beta - \nu_\alpha]/8\nu_I = 4.6\,MHz$. The second pair of cross-peaks occur at frequencies $[\nu_\alpha, -\nu_\beta] = [4.7\,MHz, -8.8\,MHz]$ and $[\nu_\beta, -\nu_\alpha] = [8.8\,MHz, -4.7\,MHz]$ which corresponds to an interacting $^{14}N(I=1)$ with $A_{iso} = [\nu_\beta - \nu_\alpha]/8\nu_I = 6.6\,MHz$. The two A_{iso} values, that is, 4.6 MHz and 6.6 MHz, correspond to two types of equatorially coordinated nitrogen atoms. Based on the crystal structure (Figure 1) we assign the $A_{iso}(^{14}N) = 4.6\,MHz$ to the two equivalent nitrogen atoms N1 and N3 oriented *trans* to each other. In the same context we assign the $A_{iso}(^{14}N) = 6.6\,MHz$ to the atom N2, *trans* to OH^- group.

More interestingly the 2D HYSCORE spectrum of **1** (Figure 2) contains arc-shaped features centered at the proton Larmor frequency, that is, near 14.4 MHz, which correspond to a $^1H(I=1/2)$ coupled to the $V^{IV}O^{2+}$ electron spin. From the HYSCORE spectrum is deduced[18] that the hyperfine coupling of this proton is characterized by $A_{iso} = 2.2\,MHz$ and strong anisotropy, that is, $T = 3.5\,MHz$. The size of this specific proton coupling falls between the hyperfine couplings reported for the two water protons in $[V^{IV}O(H_2O)_5]^{2+}$ species.[19] The anisotropic coupling of 3.5 MHz, when interpreted in the point-dipole model,[17] implies a distance of 2.8 Å between the coupled proton and the metal spin. Overall the information from the HYSCORE data is consistent with a single ^1H nucleus located two bonds away from the metal, with the bond-pathway being mediated by an oxygen atom. Based on this, we assign this coupling to a hydroxy proton from the equatorial OH^- moiety (*trans* to N2). Overall, the c.w. EPR and HYSCORE data provide conclusive evidence that the complex **1** in solution has a planar donor set comprised of three nitrogen atoms plus one OH^- group.

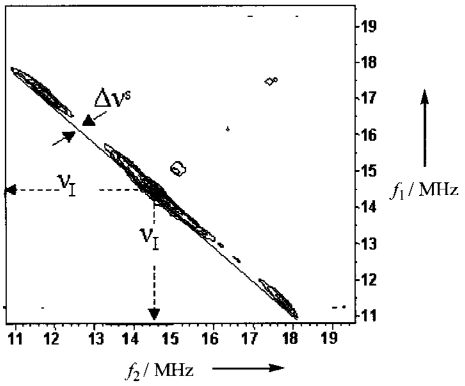

Figure 2. Contour plot of experimental frequency-domain main HYSCORE spectrum for the complex **1** in EtOH:H_2O (3:7) solution. $\Delta\nu^s$ is the maximum vertical shift from the antidiagonal at $(\nu_I, -\nu_I)$. Experimental conditions: $H = 3460$ Gauss, $\tau = 120$ ns, sample temperature 4 K. Time between successive pulse sets, 2 ms; microwave frequency, 9.64 GHz. The contour plots of HYSCORE frequency-domain spectrum were obtained after Fourier Transform in the magnitude mode, of 2D time-domain patterns containing 256×256 points with a step of 16 ns.

A DFT computational study of $[V^{IV}O(OH)(bipy)_2]^+$ has been carried out at the Becke3LYP computational level,[20] using the effective core potential approximation of Hay and Wadt[21] with a valence double-ζ basis set,[22] and the calculations were performed using the Gaussian98 package.[23] Full geometry optimizations starting from appropriate geometries were carried out without symmetry constraint and gave two minima, namely *cis*-$[V^{IV}O(OH)(bipy)_2]^+$ and *trans*-$[V^{IV}O(OH)(bipy)_2]^+$, both being real minima in the potential-energy surface of the molecule according to frequency calculations.

The *cis* isomer was calculated to be 10.9 $kcal\,mol^{-1}$ more stable than the *trans* and its geometry agrees well with the experimental data. The two vanadium–oxygen bonds were calculated to be 1.690 and 1.780 Å for the oxo and hydroxy oxygen atoms, respectively. The V–N bond lengths are 2.195 and 2.254 Å for the nitrogen atoms N2 and N4 *trans* to OH^- and O^{2-}, respectively, and 2.121 Å and 2.126 Å for N1 and N3. The optimization of the *trans* isomer gave a distorted structure, with the vanadium–oxygen bonds of 1.625 Å and 1.907 Å for the oxo and hydroxy oxygen atoms, respectively, and with a mean V–N bond lengths of 2.202 Å. A full discussion of the structural aspects of the calculated complexes will be published elsewhere.

Both the experimental and calculated bond lengths within the vanadium coordination sphere deserve some comments. Thus, whereas the elongation of the V–N2 bond by about 0.06 Å is nicely attributed to the *trans* influence of OH^- group, the substantial elongation of the V=O bond by approximately 0.1 Å, compared to normal $V^{IV}{=}O$ bond lengths (mean $d(V^{IV}{=}O)$ 1.60 Å), needs some attention. Possible intramolecular $V{=}O\cdots H{-}O{=}V$ hydrogen bond or intermolecular $V{=}O\cdots H{-}O{-}V$, $V{=}O\cdots H_2O$ or $V{=}O\cdots O{=}V$ interactions resulting in this elongation are excluded, because of the long calculated $V{=}O\cdots H$ distance (3.297 Å) and the absence of relevant short contacts in the crystal lattice of **1**. Such an elongation of the V=O bond has not been found in $[V^VO_2(bipy)_2]^+$ (**3**;[11] mean $d(V{=}O) \approx 1.626$ Å) or in the closely related alkoxo compounds $[V^VO(OC_2H_5)Cl_2(Hpheca)]$ (**4**)[12] (Hpheca = *N*-(phenyl)pyridine-2-carboxamide), V=O 1.585 Å, V–OR 1.746 Å), both adopt the *cis* orientation of the O-V-O moiety. Both **3** and **4** are compounds of vanadium(v) whereas **1** is vanadium(iv). Thus, it seems that the excess positive charge on vanadium(v) in **3** and **4** lowers the d-block, makes the metal a better π acceptor, enforces the π interactions within the O-V-O moiety, and reduces the extent of V=O elongation. The V=O elongation in **1** has not been found in other $V^{IV}O^{2+}$ complexes. Thus, it can not be attributed only to the oxidation state of vanadium and still needs some explanation on the basis of electronic factors present in this particular case. According to our calculations this elongation could be explained as follows: The π-type donor orbitals of both the hydroxy (p_{OH}) and oxo oxygen atoms ($p_{=O}$) interact with the same vacant vanadium (d_{xz}) orbital. The d_{xz}/p_{OH} interaction destabilizes d_{xz} and increases the $d_{xz}/p_{=O}$ energy difference, which results in a decrease of the extent of the $d_{xz}/p_{=O}$ interaction and decrease of the doublebond character of the $V^{IV}O^{2+}$ group. The shape of the occupied bonding molecular orbital resulting from this three-orbital/four-electron interaction, calculated at the DFT level, is shown in Figure 3. Finally, the weaker V=O bond results in a weaker *trans* influence of O^{2-} to the *trans* V–N bond, which is around 2.25 Å long, instead of its normal value of ~2.34 Å.

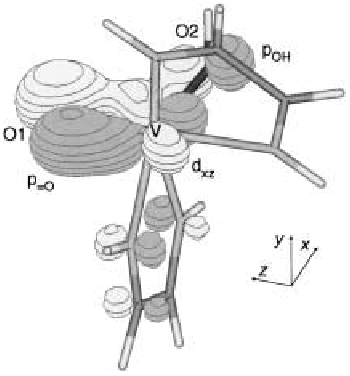

Figure 3. Shape of the occupied bonding molecular orbital resulting from the $p_{OH}/d_{xz}/p_{=O}$ interaction, calculated at the DFT level. Only atoms the atomic orbitals of which participate in the molecular orbital are shown.

In conclusion, two monomeric oxovanadium(IV) compounds **1** and **2** · H_2O were isolated by treating $V^{IV}O^{2+}$ species with the bidentate ligands bipy or phen. These two compounds are the first examples of species containing the *cis*-$[V^{IV}O(OH)]^+$ center to be structurally characterized. The presence of the hydroxy group *cis* to the O^{2-} center causes substantial changes in the bond lengths of these two compounds. The orbital interaction responsible for these changes can be explained by density functional computational studies. The continuous wave EPR and ESEEM parameters, obtained for **1** and **2** · H_2O provide spectroscopic signatures that enable the assignment of the *cis*-$[V^{IV}O(OH)]^+$ center in vanadoproteins and $V^{IV}O^{2+}$-substituted proteins.

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[1] a) W. N. Lipscomb, N. Sträter, *Chem. Rev.* **1996**, *96*, 2375; b) B. A. Brennan, G. Alms, M. J. Nelson, L. T. Durney, R. C. Scarrow, *J. Am. Chem. Soc.* **1996**, *118*, 9194; c) C. W. Hoganson, G. T. Babcock, *Science* **1997**, *277*, 1953.

[2] a) A. Messerschmidt, R. Wever, *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 392; b) M. Weyand, H.-J. Hecht, M. Keiß, M.-F. Liaud, H. Vilter, D. Schomburg, *J. Mol. Biol.* **1999**, *293*, 595.

[3] The existence of the *cis*-$[V^{IV}O(OH)]^+$ center has been claimed in the reduced vanadium haloperoxidases and in solution after acidification of dioxovanadium(V) species as well as in a $V^{IV}O^{2+}$ dimeric compound. See for example: a) T. S. Smith, C. A. Root, J. W. Kampf, P. G. Rasmussen, V. L. Pecoraro, *J. Am. Chem. Soc.* **2000**, *122*, 767; b) T. S. Smith II, R. Lobrutto, V. L. Pecoraro, *Coord. Chem. Rev.* **2002**, in press, and references therein; c) X. Li, M. S. Lah, V. L. Pecoraro, *Inorg. Chem.* **1988**, *27*, 4657; d) G. J. Colpas, B. J. Hamstra, J. W. Kampf, V. L. Pecoraro, *Inorg. Chem.* **1994**, *33*, 4669; e) M. Kosugi, S. Hikishi, M. Akita, Y. Moro-oka, *Inorg. Chem.* **1999**, *38*, 2567.

[4] a) H. J. Cohen, I. Fridovish, K. V. Rajagopalan, *J. Biol. Chem.* **1971**, *246*, 374; b) M. W. W. Adams, L. E. Mortenson in *Molybdemum Enzymes* (Ed.: T. G. Spiro), Wiley, New York, **1985**, p. 519; c) A. V. Astashkin, M. L. Mader, A. Pacheco, J. H. Enemark, A. M. Raitsimirg, *J. Am. Chem. Soc.* **2000**, *122*, 9194.

[5] C. E. MacBeth, B. S. Hammes, V. G. Young, Jr., A. S. Borovik, *Inorg. Chem.* **2001**, *40*, 4733.

[6] Z. Xiao, R. W. Gable, A. G. Wedd, C. G. Young, *J. Am. Chem. Soc.* **1996**, *118*, 2912.

[7] Elemental analysis (%) calcd for **1** ($C_{20}H_{17}BF_4O_2N_4V$): C 49.72, H 3.55, N 11.60, V 10.54; found: C 49.63, H 3.54, N 11.42, V 10.62; Elemental analysis (%) calcd for **2** · H_2O ($C_{24}H_{19}BF_4O_3N_4V$): C 52.49, H 3.49, N 10.21, V 9.28; found: C 52.39, H 3.58, N 10.03, V 9.50. Some characteristic IR bands for **1**: $\tilde{\nu} = 3582$ [ν(O-H)], 1602 [ν(C=C,C=N)], 1053 [ν(B-F)], 970, 961 cm^{-1} [ν(V=O)]. Some characteristic IR bands for **2** · H_2O: $\tilde{\nu} = 3600$ [ν(O-H)], 3452 [ν(O-H)) from H_2O], 1629 [ν(C=C,C=N)], 1062 [ν(B-F)], 968 cm^{-1} [ν(V=O)]. UV/Vis for **1** [CH_3CN, absorption, λ/nm(ε/$dm^3 mol^{-1} cm^{-1}$)]: 744.0(23), 518(sh)(35), 304.2(21553), 245.4(14840), 194.4(43240). UV/Vis for **2** · H_2O [CH_3CN, absorption, λ/nm(ε/$dm^3 mol^{-1} cm^{-1}$)]: 742.5(23), 437(350), 292.5(sh)(14750), 273.6(43472), 226.8(47083), 204.6(50528). μ_{eff}(25 °C) for **1**: 1.75 μ_B. μ_{eff}(25 °C) for **2** · H_2O: 1.77μ_B. Conductivity value for **1** (CH_3CN, $C = 10^{-3}$ M, $\Lambda/\Omega^{-1} mole^{-1} cm^2$): 166. Conductivity value for **2** · H_2O (CH_3CN, $C = 10^{-3}$ M, $\Lambda/\Omega^{-1} mole^{-1} cm^2$): 168.

[8] Crystals of **1** and **2** · H_2O, suitable for X-ray analysis, were obtained by slow evaporation of a concentrated solution of **1** or **2** in CH_3CN:EtOH (1:1 v/v). Crystal data for **1**: $[V^{IV}O(OH)(bipy)_2](BF_4)$:$C_{20}H_{17}BF_4O_2N_4V$, $M_r = 483.13$, space group $P\bar{1}$, $a = 8.116(4)$, $b = 9.490(5)$, $c = 13.652(7)$ Å, $V = 1023.0(9)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.568$ $g cm^{-3}$, $T = 298$ K. $R1$(final) = 0.0598, $wR2 = 0.1687$; crystal data for **2** · H_2O: $[V^{IV}O(OH)(phen)_2](BF_4) \cdot H_2O$: $C_{20}H_{17}BF_4O_2N_4V$, $M_r = 549.18$, triclinic, space group $P\bar{1}$, $a = 9.585(4)$, $b = 15.911(8)$, $c = 7.833(3)$ Å, $V = 1166.2(9)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.564$ $g cm^{-3}$, $T = 293(2)$ K. $R1$(final) = 0.0657, $wR2 = 0.1940$. CCDC 177661 (**1**) and CCDC 177662 (**2** · H_2O) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

[9] a) D. Wang, M. Ebel, C. Schulzke, C. Grüning, S. K. S. Hazari, D. Rehder, *Eur. J. Inorg. Chem.* **2001**, 935; b) W. Priebsch, D. Rehder, *Inorg. Chem.* **1990**, *29*, 3013; c) A. D. Keramidas, A. B. Papaioannou, A. Vlahos, T. A. Kabanos, G. Bonas, A. Makrigiannis, C. P. Raptopoulou, A. Terzis, *Inorg. Chem.* **1996**, *35*, 357; d) E. J. Tolis, V. I. Teberekidis, C. P. Raptopoulou, A. Terzis, M. P. Sigalas, Y. Deligiannakis, T. A. Kabanos, *Chem. Eur. J.* **2001**, *7*, 601; e) W. A. Nugent, J. M. Mayer, *Metal-Ligand Multiple Bonds*, Wiley, New York, **1988**; f) C. J. Carrano, M. Mohan, S. M. Holmes, R. Rosa, A. Butler, J. M. Charnock, C. D. Garner, *Inorg. Chem.* **1994**, *33*, 646.

[10] I. D. Brown in *Structure and Bonding in Crystals, Vol. II* (Eds.: M. O'Keefe, A. Navrotdsky), Academic Press, New York, **1981**, p. 1.

[11] S. G. Brand, N. Edelstein, C. J. Hawkins, G. Shalimoff, M. R. Snow, E. R. T. Tiekink, *Inorg. Chem.* **1990**, *29*, 434.

[12] K. D. Soulti, A. Troganis, A. Papaioannou, T. A. Kabanos, A. D. Keramidas, Y. G. Deligiannakis, C. R. Raptopoulou, A. Terzis, *Inorg. Chem.* **1998**, *37*, 6785.

[13] N. D. Chasteen in *Biological Magnetic Resonance*, *Vol. 3* (Eds.: L. Berliner, J. Reuben), Plenum, New York, **1981**, p. 53.

[14] A. J. Tasiopoulos, A. N. Troganis, A. Evangelou, C. P. Raptopoulou, A. Terzis, Y. Deligiannakis, T. A. Kabanos, *Chem. Eur. J.* **1999**, *5*, 910.

[15] A. Schweiger, J. Jesche, *Principles of Pulsed Electron Paramagnetic Resonance*, Oxford University Press, Oxford, **2001**.

[16] ESEEM is a pulsed EPR technique eminently suited for measuring weak magnetic interactions between the electron spin, that is, the $V^{IV}O^{2+}$ ion ($S = 1/2$) in the present case, and nearby nuclei, that is, the ligand atoms. The principles of ESEEM are thoroughly analyzed in the book of Schweiger and Jesche, ref. [15]. In the present case we rely on the application of HYSCORE (Hyperfine Sublevel Correlation Spectroscopy ref. [17, 18] which is a 2D ESEEM technique based on the four-pulse [$\pi/2 - \tau - \pi - t1 - \pi/2 - t2 - \pi/2 - \tau -$echo] sequence. The applications of HYSCORE to study the coordination environment of metal centers, including VO^{2+} complexes, have been reviewed by Deligiannakis et al. ref. [17].

[17] The methodology of peak assignment in a HYSCORE spectrum can be found in the following review article: Y. Deligiannakis, M. Louloudi, N. Hadjiliadis, *Coord. Chem. Rev.* **2000**, *104*, 1.

[18] The proton hyperfine couplings have been estimated from Figure 2, based on the observed maximum shift $\Delta\nu^s$, according to the method of Pöppl and Kevan (A. Pöppl, L. Kevan, *J. Phys. Chem. B* **1996**, *100*, 3387). In Figure 2, $\Delta\nu^s$ is 0.3 MHz which based on the relationship $T = (\frac{2}{3})[8\Delta\nu^s\nu_I/(2)^{1/2}]^{1/2}$ gives a hyperfine anisotropy for this proton $T = 3.27$ MHz. Using this as starting value, we have calculated the proton isotropic hyperfine coupling based on numerical simulations. The final values are $A_{iso} = 2.2$ MHz, $T = 3.5$ MHz.

[19] A. M. Tyryshkin, S. A. Dikanov, R. G. Evelo, A. J. Hoff, *J. Chem. Phys.* **1992**, *97*, 42.

[20] a) D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648; b) C. T. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785.

[21] a) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 270; b) W. R. Wadt, P. J. Hay, *J. Chem. Phys.* **1985**, *82*, 284; c) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299.

[22] T. H. Dunning Jr., P. J. Hay *in Modern Theoretical Chemistry, Vol. 3* (Ed.: H. F. Schaefer III), Plenum, New York, **1976**, p. 1.

[23] Gaussian 98 (Revision A.7), M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. G. Johnson, W. Chen, M. W. Wong, J. L. Andres, M. Head-Gordon, E. S. Replogle, J. A. Pople, Gaussian, Inc., Pittsburgh, PA, **1998**.

Polyoxomolybdenum(v) Sulfite Complexes: Synthesis, Structural, and Physical Studies[**]

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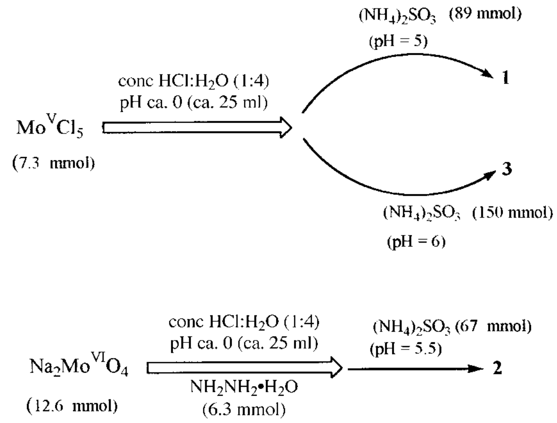
The contemporary interest in polyoxometalates reflects the ubiquitous nature of this family of inorganic networks, which exhibit a diverse compositional range and considerable structural versatility,[1] as well as important magnetic,[2] optical,[1] and catalytic properties.[1] A great deal of attention has been paid to heteropolyanions containing inorganic anionic ligands,[3] mainly tetrahedral phosphate groups, because of the fascinating electronic and structural properties of polyoxomolybdenum and vanadium phosphates.[4] Among these derivatized polyoxoanions, examples incorporating the pyramidal sulfite anion as the inorganic ligand are largely unknown, except for the molybdenum(vi) derivative $[Mo_5^{VI}O_{15}(SO_3)_2]^{4-}$.[5] The lack of such complexes is surprising for two main reasons: first, metal–sulfite chemistry is very attractive in view of its potential for restricting the serious environmental problem of acid rain,[6] and second, exploring the possibility of incorporating the pyramidal sulfite anion into frameworks, rather than the more frequently used tetrahedral phosphate groups, could result in unprecedented structural features and novel properties for these frameworks.[7] Furthermore, molybdenum–sulfite chemistry is of great biological interest, since the enzyme sulfite oxidase, which is associated with the in vivo oxidation of SO_3^{2-} to SO_4^{2-}, contains a molybdenum atom at its active center.[8] Herein, we describe the synthesis, structural, and physicochemical characterization of the first polyoxomolybdenum(v) sulfite complexes **1**–**3**.

$(NH_4)_{20}[(Mo_2^VO_4)_6(\mu_2\text{-}SO_3)_{12}(\mu_3\text{-}SO_3)_4]\cdot 4H_2O$ **1**

$(NH_4)_{15}\{Na[(Mo_2^VO_4)_6(\mu_2\text{-}SO_3)_3(\mu_6\text{-}SO_3)]_2\}\cdot 5H_2O$ **2**

$(NH_4)_8[(Mo_2^VO_4)(SO_3)_4(\mu_2\text{-}SO_3)]\cdot 2H_2O$ **3**

Complex **1** was prepared by treating Mo^VCl_5 (7.3 mmol) in concentrated (37 %) HCl:H_2O (1:4 v/v, pH approximately 0) with solid $(NH_4)_2SO_3$ (Scheme 1). Upon addition of $(NH_4)_2SO_3$ (89 mmol) the pH of the solution changed to approximately 5, and thus it is apparent that the SO_3^{2-} ion performs the dual role of raising the pH of the solution, as well as acting as a ligand. However, if the same reaction was performed with a larger quantity of $(NH_4)_2SO_3$ (150 mmol, final pH of the solution was approximately 6), complex **3** was isolated (Scheme 1). Reduction of $Na_2Mo^{VI}O_4$ dissolved in concentrated (37 %) HCl:H_2O (pH approximately 0) with an excess of hydrazine, followed by addition of $(NH_4)_2SO_3$ (final pH of the solution was approximately 5.5) resulted in the formation of **2** (Scheme 1).



Scheme 1. The synthetic routes leading to the isolation of **1**–**3**.

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